Nanotechnology for Dentistry Applications

Online at: https://doi.org/10.1088/978-0-7503-3671-0

About the Series

The Series in Physics and Engineering in Medicine and Biology will allow IPEM to enhance its mission to 'advance physics and engineering applied to medicine and biology for the public good'.

Focusing on key areas including, but not limited to:

- clinical engineering
- diagnostic radiology
- informatics and computing
- magnetic resonance imaging
- nuclear medicine
- physiological measurement
- radiation protection
- radiotherapy
- rehabilitation engineering
- ultrasound and non-ionising radiation.

A number of IPEM–IOP titles are published as part of the EUTEMPE Network Series for Medical Physics Experts.

Nanotechnology for Dentistry Applications

Edited by
Ashutosh Kumar Shukla
Ewing Christian College, Prayagraj, India

IOP Publishing, Bristol, UK

ISBN 978-0-7503-3671-0 (ebook)
ISBN 978-0-7503-3669-7 (print)
ISBN 978-0-7503-3672-7 (myPrint)
ISBN 978-0-7503-3670-3 (mobi)

DOI 10.1088/978-0-7503-3671-0

Version: 20211201

IOP ebooks

British Library Cataloguing-in-Publication Data: A catalogue record for this book is available from the British Library.

Published by IOP Publishing, wholly owned by The Institute of Physics, London

IOP Publishing, Temple Circus, Temple Way, Bristol, BS1 6HG, UK

US Office: IOP Publishing, Inc., 190 North Independence Mall West, Suite 601, Philadelphia, PA 19106, USA

To my parents

Contents

Preface

This collection highlights the applications of Nanotechnology for dentistry applications. There are 13 chapters contributed by the experts from different laboratories/regions. Nanotechnology applications in different fields of wide interest including dental caries and erosion and dental implants have been covered in detail. Chapters covering the nanotechnology applications for dental therapeutics and periodontal disease management are undoubtedly meant to connect the reader to the promising trends and alternative therapies. In addition, individual chapters with focus on nanotechnology applications in specialties like orthodontics, endodontics and prosthodontics have been included that are of interest to novice researchers in addition to professionals. A chapter on neurotoxicity of different nanomaterials used in dentistry needs a special mention as this emphasizes the need to proceed cautiously while exploring the new dimensions of 'Nano'. Contributors have mostly adopted a bottom-up approach. I have tried my best to avoid intrusion in the plan of contributing experts and this is probably the reason that individual chapters have come up with a sense of completeness in them.

I sincerely thank Michael Slaughter, Senior Commissioning Editor—Bioengineering, Medical Physics, Biophysics, IOP Publishing for giving me an opportunity to present this volume. I wish to thank Phoebe Hooper, ebooks Editorial Assistant, IOP Publishing for extending all the support during the different publication stages of this project. I sincerely thank the expert contributors for contributing to this volume in a timely fashion and helping me to meet the schedule.

Ashutosh Kumar Shukla, Prayagraj, India
June 2021

Editor biography

Ashutosh Kumar Shukla

With two decades of physics teaching and research experience, publications in peer reviewed journals, review articles, books and many edited volumes prepared in collaboration with experts from different countries, I intend to continue in academics.

List of contributors

Ra'ed Al-Dboush
The University of Alberta, Edmonton, AB, Canada
Jordanian Royal Medical Service, Amman, Jordan

B Alekhya
Postgraduate Student, Department of Oral Pathology and Microbiology, GITAM Dental College and Hospital, Visakhapatnam, India

Nafiu Aminu
Department of Pharmaceutics and Pharmaceutical Microbiology, Faculty of Pharmaceutical Sciences, UsmanuDanfodiyo University, Sokoto, Nigeria

Meena Ajay Aras
Department of Prosthodontics, Goa Dental College and Hospital, Bambolim, Goa, India

Heitor Ceolin Araujo
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

Laís Salomão Arias
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

Papia Basuthakur
Department of Applied Biology, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Uppal Road, Tarnaka, Hyderabad, Telangana, India

Shatarupa Biswas
Department of Microbiology, School of Life Science and Biotechnology, Adamas University, Kolkata, India

Anupama Bonam
Graduate Student, GITAM Dental College and Hospital, Visakhapatnam, India

Wilmer Ramírez Carmona
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

Saptarshi Chatterjee
Department of Microbiology, School of Life Science and Biotechnology, Adamas University, Kolkata, India

Anne Caroline Morais Caldeirão
Graduate Program in Dentistry (GPD—Master's Degree), University of Western São Paulo (UNOESTE), Presidente Prudente/São Paulo, Brazil

Cora Abigail Coutinho
Prosthodontics, Dental Concepts Dental Clinic, Margao, Goa, India

Ivy Fernandes Coutinho
Department of Prosthodontics, Goa Dental College and Hospital, Bambolim, Goa, India

Alberto Carlos Botazzo Delbem
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

Dongmei Deng
Academic Center for Dentistry Amsterdam (ACTA), Department of Preventive Dentistry, Amsterdam, The Netherlands

Kathleen Manuela D'Souza
Department of Prosthodontics, Goa Dental College and Hospital, Bambolim, Goa, India

Tarek El-Bialy
The University of Alberta, Edmonton, AB, Canada

Rob Exterkate
Academic Center for Dentistry Amsterdam (ACTA), Department of Preventive Dentistry, 1081 LA, Amsterdam, The Netherlands

Beatriz Díaz Fabregat
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

Amir I O Ibrahim
Faculty of Dentistry, Department of Restorative Dentistry, Nile University, Khartoum, Sudan

Arundeep Kaur
Department of Periodontics, Maulana Azad Institute of Dental Sciences, B.S. ZafarMarg, New Delhi, India

Monalisa Mishra
Neural Developmental Biology Lab, Department of Life Science, NIT Rourkela, Rourkela, Odisha, India

Douglas Roberto Monteiro
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil
Graduate Program in Dentistry (GPD—Master's Degree), University of Western São Paulo (UNOESTE), Presidente Prudente/São Paulo, Brazil

Desigar Moodley
Smile Center, Wolfurt, Austria

Neeharika Mortha
GITAM Dental College and Hospital, Oral Pathology and Microbiology, Visakhapatnam, India

Eman Osman
Chemical Metrology Division, National Institute of Standards, Egypt

Chitta Ranjan Patra
Department of Applied Biology, CSIR-Indian Institute of Chemical Technology (CSIR-IICT), Uppal Road, Tarnaka, Hyderabad, Telangana, India

Juliano Pelim Pessan
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

Anju Rana
Senior Resident, Maulana Azad Institute of Dental Sciences, B.S. Zafar Marg, New Delhi, India

Banashree Roy
Department of Microbiology, School of Life Science and Biotechnology, Adamas University, Kolkata, India

Caio Sampaio
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

Divya Uppala
Department of Oral Pathology and Microbiology, GITAM Dental College and Hospital, Visakhapatnam, India

Muhammad Sohail Zafar
Department of Restorative Dentistry, College of Dentistry, Taibah University, Al-Madina Al-Munawara, Saudi Arabia

Igor Renan Zen
São Paulo State University (Unesp), School of Dentistry, Araçatuba, Department of Preventive and Restorative Dentistry, Araçatuba/São Paulo, Brazil

IOP Publishing

Nanotechnology for Dentistry Applications

Ashutosh Kumar Shukla

Chapter 1

Use of phosphate-based nanoparticles to enhance the effects of fluoride against dental caries and erosion

Juliano Pelim Pessan, Caio Sampaio, Igor Zen, Dongmei Deng, Rob Exterkate, Alberto Carlos Botazzo Delbem and Douglas Roberto Monteiro

Fluoride therapy is considered one of the main strategies for dental caries control and is responsible for the substantial decrease in the prevalence of this disease worldwide. Nonetheless, despite the large body of evidence on the effects of fluoride on caries dynamics, concerns on its potential side-effects, the limited action against dental erosion, and the polarization of dental caries, have stimulated the study of alternative strategies to enhance the effects of conventional fluoridated products on dental caries and erosion. In this sense, the association of fluoride and polyphosphate salts has shown to be effective in enhancing enamel remineralization and reducing enamel demineralization and erosive wear, both in professionally-applied and self-application products; such effects have been recently reported to be enhanced by the use of nanoparticles. In addition to polyphosphates, nanoparticles of hydroxyapatite, silver, calcium fluoride, calcium sodium phosphosilicate, and bioactive glass, have demonstrated promising effects on variables related to dental caries and dental erosion. This chapter will present the main data on the association of fluoride and different nano-sized compounds, from studies with different levels of evidence, assessing the effects on enamel de- and re-mineralization, erosive tooth wear, and on dental biofilm. Insights on the mechanisms of action and future steps for research will also be addressed.

1.1 Introduction

The use of fluoride (F), in several vehicles and different modes of application, is regarded as one of the main strategies for dental caries control worldwide. Its main mechanism of action is related to its presence in the oral environment (e.g., biofilm, saliva, mucosa, tooth surfaces), even at low concentrations, where it is able reduce

doi:10.1088/978-0-7503-3671-0ch1

demineralization (by protecting and/or incorporating into the apatite crystallites) and to catalyze remineralization [1, 2]. Furthermore, the application of high fluoride concentrations promotes the formation of calcium fluoride (CaF_2) globules on tooth surfaces, which are dissolved under acidic conditions, allowing the release of calcium (Ca) and F in the oral environment [2–4].

Robust evidence attests that F varnishes, gels, mouthwashes and toothpastes promote significant effects on the caries dynamic [5–8]. Nonetheless, the marked decrease in caries incidence and prevalence in most industrialized countries owing to the widespread availability of F, has been accompanied by increasing concerns on its side effects, such as acute or chronic (i.e., enamel fluorosis) toxicity [9, 10]. Furthermore, the polarization of this disease in low-income countries [11], as well as the lack of substantial action on dental erosion [12], has encouraged the search for novel strategies aiming to enhance the preventive effect of F-products, aiming to maximize the therapeutic effects, while minimizing unwanted side-effects.

Among the most studied compounds, cyclophosphates salts have been extensively assessed over recent years. It has been extensively documented that the addition of sodium trimetaphosphate (TMP) or sodium hexametaphosphate (HMP) in F-containing products substantially improves their protective effects on dental caries dynamics, under *in vitro*, *in situ*, and *in vivo* conditions [13–21]. Also, significant effects have been reported against dental erosion [22–29]. Taking into account the promising results described above, recent studies have further assessed the performance of these compounds when applied in the nano-size form, with more pronounced effects of nanoparticles over micrometric ones.

Special attention has also been given to silver nanoparticles, which have been shown to act synergistically with fluoride on microorganisms related to dental caries [30–33], besides demonstrating promising protective effects on enamel de- and re-mineralization processes [33]. Another agent comprehensively studied is nano-hydroxyapatite (nano-HAp). In spite of being often assessed alone, the incorporation of nano-HAp to F-vehicles has demonstrated promising beneficial effects on parameters related to dental caries, dental erosion and dentin hypersensitivity, due to its similar composition to the hard dental tissues, and to the increased surface area of nanoparticles, which may facilitate the availability of calcium phosphate ions to enamel [34, 35].

In addition, nano-sized CaF_2 has presented promising effects regarding parameters related to biofilms, mechanical behavior, and F release of restorative materials such as nanocomposites [36, 37] and resin-modified glass ionomer (RMGI) [38], resulting in the improvement of the preventive properties without compromising the mechanical capacity of the materials. Bioactive glass (nBAG) is another nanoparticle that has gained interest in recent years. It is often used on glass ionomer cement (GIC) and RMGI [39], as it is able to maintain a high alkaline pH that leads to a supersaturated ion environment, resulting in antibacterial effects [40]. Also, nBAG acts directly on the enamel and dentine remineralization, acting by dentine tubules occlusion and promoting rapid apatite formation [39–41].

Considering the context above, this chapter addresses the main findings on the association of F and nano-sized cyclophosphates (TMP and HMP), nano-HAp,

silver nanoparticles, nano-CaF_2, and nano bioglass, from studies with *in vitro*, *in situ* and *in vivo* protocols assessing the effects on enamel de-/re-mineralization, erosive wear, and on dental biofilms. Insights on the mechanism of action, future steps for research and the current level of evidence for each strategy will also be addressed. It is noteworthy that some of the technologies above have been also studied alone (i.e., without fluoride), but will not be addressed in the present chapter due to its scope.

1.2 Nano-sized sodium trimetaphosphate

Sodium trimetaphosphate (TMP) is an inorganic phosphate widely employed in the food and cosmetic industry for several decades. This polyphosphate has been shown to increase the effects of fluoridated products on de- and re-mineralizaion, tooth erosion, dentine tubule obliteration, and biofilm formation [20, 22, 23, 42]. When co-administered with fluoride in dentifrices, gels, varnishes or mouthwashes, the resulting therapeutic/protective effects are similar to or greater than those attained by using twice as much fluoride [22–24, 26, 27], which is highly desirable from a clinical standpoint. Regarding biofilm formation, TMP alone is known to promote a reduction in the metabolism and components of the cellular matrix, in addition to forming a less compact biofilm, the latter favoring acid neutralization by saliva through the biofilm's layers, thus preventing tooth demineralization and/or enhancing remineralization [20]. The synergism between fluoride and TMP observed in laboratory studies was confirmed in a randomized clinical trial, given that children who brushed with a toothpaste containing 500 ppm F containing TMP developed significantly fewer caries lesions than those who used a conventional (1100 ppm F) toothpaste [31].

In light of the promising results of conventional TMP (microparticulate) and considering the advantages of nanoparticles over micrometric ones, intensive research has focused on studies with nano-sized TMP (nTMP) over recent years. An *in vitro* study assessed the effects of fluoridated toothpastes (1100 ppm F) containing micrometric TMP or nTMP on enamel remineralization, showing that the enamel treated with nTMP-containing toothpaste became 62% harder compared with 1100 ppm F, and 32% harder than its counterpart containing micrometric TMP [42]. This study also showed that the nTMP-containing toothpaste was more effective in increasing enamel uptake by ~100% and ~150% compared with 1100 ppm F and TMP toothpastes, respectively. Similar effects have been reported on the protection of enamel against demineralization and erosive tooth wear. The use of a nTMP-containing toothpaste was 44% more effective in reducing demineralization and promoted enamel F uptake 73% higher than its counterpart with micrometric TMP [43]. In addition, the toothpaste supplemented with nTMP was 30% more effective against erosive tooth wear compared with micrometric TMP, in an *in vitro*/*ex vivo* protocol. Interestingly, the effects of the nTMP toothpaste were similar to those attained by the use of a 5000 ppm F toothpaste, reinforcing its potential use in erosion-prone patients, including children and adolescents. The main studies assessing the effects of nano-sized sodium trimetaphosphate on variables related to dental caries, erosion and biofilms are summarized in table 1.1.

Table 1.1. Summary of the main studies assessing the effects of nano-sized sodium trimetaphosphate related to different variables assessed

Author (year)	Technology	Protocol	Vehicle	Main findings
Silva *et al* (2019) [101]	nTMP	*In vitro*	GIC	1.25% CHX and 14% nTMP added to a GIC increased its antimicrobial/antibiofilm action and its ability to reduce enamel demineralization, with minimal effects on the mechanical properties of RMGIC.
Emerenciano *et al* (2018) [102]	nTMP	*In situ*	Toothpaste	1100 ppm NaF/nTMP promoted a greater protective effect against enamel demineralization and significantly affected the composition of biofilm formed *in situ* when compared to 1100 ppm NaF toothpaste.
Danelon *et al* (2018) [28]	nTMP	*In vitro*	Toothpaste	The addition of 3% nTMP to 1100 ppm NaF toothpastes significantly increased the protective effect against enamel erosion compared with its counterparts with mTMP or without TMP. This effect was not influenced by the presence of acquired enamel pellicle and saliva.
Danelon *et al* (2017) [43]	nTMP	*In vitro*	Toothpaste	Fluoride toothpaste containing nTMP at 3% significantly decreased enamel demineralization compared to its counterparts without TMP or supplemented with mTMP.
Souza *et al* (2016) [103]	nTMP	*In situ*	Toothpaste	The protective effect of 250 ppm NaF-nTMP dentifrice was similar to a conventional dentifrice (1100 ppm F) for most of the variables studied, having a more pronounced effect on the subsurface lesion.
Danelon *et al* (2015) [42]	nTMP	*In situ*	Toothpaste	Addition of 3% nTMP to a conventional toothpaste (1100 ppm F) promoted an additional remineralizing effect of artificial caries lesions compared with counterparts with mTMP or without TMP.

TMP: sodium trimetaphosphate; **nTMP:** nano-sized sodium trimetaphosphate; **mTMP:** micro-sized sodium trimetaphosphate; **NaF:** sodium fluoride; **RMGIC:** resin-modified glass ionomer cement; **CHX:** chlorhexidine.

These results taken together support the hypothesis that the effects of nTMP are similar to those reported for micrometric particles, but potentiated by the properties of nano-sized materials, such as their high ratio of surface area to volume, as well as a high percentage of atoms on the surface compared to larger particles, which makes them more reactive compared to micrometric particles [43]. In brief, TMP has been

suggested to retain charged ions of CaF^+ and Ca^{++} by replacing Na^+ from a cyclic structure [23]. At acidic pH, these linkages are broken, releasing Ca^{++} and CaF^+, which can further take part in a series of events that ultimately would lead to the formation of neutrally charged species ($CaHPO_4^\circ$ and HF_0) that have a higher diffusion coefficient into the enamel than charged species [44]. Furthermore, the association of F and TMP has been shown to enhance the formation of CaF_2 deposits on the exposed tooth surfaces [22, 28, 42–45], which are known to be key players on the dynamics of both caries and erosion [4, 46–48].

1.3 Nano-sized sodium hexametaphosphate

HMP is an inorganic cyclophosphate that has demonstrated extensive effects on enamel de- and re-mineralization processes, on dental erosion, as well as on oral biofilms. Due to its great affinity to metallic ions (Mg^{2+}, Ca^{2+}, K^+, Al^+, Fe^{3+}), HMP interacts with the dental surface, which substantially reduces mineral solubility [14, 15, 18]. Due to these features, when co-administered with F, this phosphate enhances the effects of dentifrices or gels on enamel de- and re-mineralization processes, in comparison to conventional products not supplemented with HMP [13–15, 17]. A synergistic effect between F and HMP administered in the form of a gel was also observed on dental erosion in an *in situ*/*ex vivo* model. It was shown that a low-F gel (4500 ppm F) promoted significantly lower enamel wear and mineral loss compared with a conventional formulation containing twice as much F (9000 ppm F) [49]. In addition to HMP's effects on the dental hard tissues, promising results have been demonstrated on biofilms *in vitro*. HMP, associated or not with other actives such as silver or F, was shown to have antimicrobial potential, besides interfering with the composition of the biofilm's extracellular matrix [50–52]. Although the mechanism by which HMP acts on biofilms is still not completely clear, it is possible that the great affinity that this phosphate presents to metallic ions (forming ionic complexes) helps HMP to bind to Ca^{2+} and $Mg^{2+}$from the bacterial cell walls, thus increasing cell permeability [53, 54].

Similarly to TMP, the great effect of HMP on the above-mentioned caries and erosion parameters has also encouraged the evaluation of this phosphate as nanoparticles (nHMP), given that reducing the size of the particles could enhance its effects in comparison to the commercial version of the product (i.e., microparticles) [55]. In that sense, although no evidence is available on the effects of nHMP over conventional HMP on dental erosion, *in vitro* and *in situ* studies attest to the additional benefits of nHMP over microparticles on enamel de- and re-mineralization processes, and on biofilms. The most studied vehicle for coadministration of F and nHMP is dentifrice, which has been shown to promote superior protective effects against enamel demineralization [55, 56], besides promoting an additional remineralizing effect of artificial caries lesions [57] compared with a F-toothpaste containing micrometric HMP. In addition to the effects on tooth enamel, the association between F and nHMP was shown to significantly reduce the cariogenicity of the dental biofilm formed *in situ*, as it significantly increased F and Ca concentrations and significantly reduced the amount of insoluble extracellular

Table 1.2. Summary of the main studies assessing the effects of nano-sized sodium hexametaphosphate related to different variables assessed

Author (year)	Technology	Protocol	Vehicle	Main findings
Danelon *et al* (2019) [57]	nHMP	*In situ*	Toothpaste	The addition of nHMP to a F-toothpaste was able to promote an additional remineralizing effect of artificial caries lesions compared with its counterparts with mHMP or without HMP.
Garcia *et al* (2018) [56]	nHMP	*In situ*	Toothpaste	F-dentifrice supplemented with nHMP demonstrated a greater protective effect against enamel demineralization and on the composition of biofilm when compared with a conventional F-toothpaste or a F-toothpaste containing mHMP.
Hosida *et al* (2018) [104]	nHMP	*In vitro*	GIC	HMP incorporation, especially in the nano-sized form, in restorative GIC increased antimicrobial activity and F release, and decreased enamel demineralization, despite reduced its physico-mechanical properties, in comparison to a conventional GIC without nHM.
Dalpasquale *et al* (2017) [55]	nHMP	*In vitro*	Toothpaste	The addition of nHMP to a F-toothpaste enhanced its protective effects against enamel demineralization when compared to its counterpart containing mHMP or a conventional F-toothpaste.

HMP: sodium hexametaphosphate; **nHMP:** nano-sized sodium hexametaphosphate; **mHMP:** micro-sized sodium hexametaphosphate; **GIC:** glass ionomer cement.

polysaccharides in comparison to its counterparts containing micrometric HMP or containing F alone [57]. Furthermore, the addition of nHMP to a GIC was shown to improve F release and its antimicrobial activity, in spite of reducing the physico-mechanical properties of the product [58]. Table 1.2 summarizes the main studies assessing the effects of nano-sized sodium hexametaphosphate on tooth structures and on biofilms.

1.4 Nano-hydroxyapatite

Hydroxyapatite (HAp) is one of the most studied compounds for the control of dental caries, erosion and/or hypersensitivity, since it is a mineral essentially composed by calcium and phosphate [$Ca_{10}(PO_4)_6(OH)_2$] found in dental enamel, dentine and bone [59]. Knowledge on the composition of the hard dental structures can help to better understand how nano-HAp might be an interesting alternative for the enhancement of F-vehicles.

Briefly, permanent dental enamel is an acellular and avascular structure composed mainly of inorganic material, essentially hydroxyapatite (accounting for ~85% of the composition), arranged as apatite crystals, which then form the enamel prisms. The remaining volume—disposed among the crystals—is composed of water (~12%) and organic material (~3%, mainly collagen) [2, 60, 61]. As for dentine, although its structure is also composed of mineral content in the form of hydroxyapatite, the volume is lower. Dentine tissue is constituted of ~47% of minerals, ~33% organic material and ~20% water, which makes dentine more prone to acid dissolution in comparison to enamel. Unlike dental enamel, dentine is a vascular and cellular tissue, which means that it is susceptible to response to outer stimuli [2, 62].

In turn, nano-HAp consists of a bioactive and biocompatible material, which acts by facilitating the availability of calcium phosphate ions to enamel, due to its similar composition to the hard dental tissues and to the increased surface area of the nanoparticles compared with micrometric ones [34, 35]. Although most of the studies have proposed the incorporation of nano-HAp in oral care products (e.g., toothpastes, gels and varnishes) as an alternative to F, this compound has also been studied in association with F, in products for the control of dental caries, erosion and dentine hypersensitivity. In brief, the effects of nano-HAp on variables related to dental caries have been assessed in a larger number of studies compared to those for dental erosion or dentin hypersensitivity. The data, however, is somehow conflicting. Although some studies reported that nano-HAp enhanced the protective and therapeutic effects of F-toothpastes on enamel de- and re-mineralization processes [63], most of them either did not include a suitable positive control group (i.e., a conventional F-dentifrice) or adopted a protocol insufficient to attest such promising trends, as detailed below.

The main studies assessing the effects of nano-HAp on several variables are described in table 1.3. A toothpaste containing nano-HAp combined with F led to a lower demineralization depth in comparison to a placebo toothpaste [35]; however, this study did not include a positive control group containing the active compounds alone, which hinders any conclusion on the actual effects of this association. Another work also observed that a toothpaste containing 7% nano-HAp and 1000 ppm NaF promoted a higher remineralizing effect compared with a F-only toothpaste. Nonetheless, the only parameter analyzed was surface hardness, and the experimental groups had to be adjusted prior to statistical analysis due to protocol limitations [64]. Besides F-toothpastes, the addition of nano-HAp to a fluoridated varnish was also shown to promote a higher remineralizing effect of enamel surface in comparison to a conventional F-varnish or to a paste containing casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) [64]. Despite the interesting effects reported above, some methodological issues were identified, which suggest that further *in vitro* studies are still demanded prior their study under clinical conditions.

In addition to the above-mentioned findings, other studies have reported less promising trends on the effects of nano-HAp combined with F on caries-related variables. An experimental toothpaste containing nano-HAp, regardless of the

Table 1.3. Summary of the main studies assessing the effects of nano-hydroxyapatite related to different variables assessed

Author (year)	Technology	Protocol	Vehicle	Main findings
Ionescu *et al* (2020) [105]	Nano-HAp	*In vitro*	Toothpaste	F, Mg, Sr-carbonate substituted n-HAp toothpaste reduced the microbial colonization on resin-based composite.
Leal *et al* (2020) [66]	Nano-HAp	*In vitro*	Toothpaste	Nano-HAp did not improve the effect of dentifrices containing 5000 μg F/g on root dentin demineralization.
Demito *et al* (2019) [35]	Nano-HAp	*In situ*	Undefined product	Groups treated with nano-HAp combined with 9000 ppm NaF presented lower demineralization depth in relation to the negative control group.
Kooshki *et al* (2019) [64]	Nano-HAp	*In vitro*	Varnish	F-varnish containing nano-HAp promoted a higher remineralizing effect of enamel surface in comparison to a conventional F-varnish (not supplemented with nano-HAp) or to a paste containing casein phosphopeptide-amorphous calcium phosphate (CPP-ACP).
Soares *et al* (2018) [71]	Nano-HAp	*In vitro*	Gel	1.23% F gel containing nano-HAp modified the composition and morphology of the enamel surface.
Yu *et al* (2017) [78]	Nano-FHAp and nano-HAp	*In vitro*	Powder	nano-FHAp formulation showed higher plugging rate and penetrating depth into the tubules in comparison to F or nano-HAp.
Ebadifar *et al* (2017) [63]	Nano-HAp	*In vitro*	Toothpaste	The F-toothpaste containing nano-HAp was more effective than the F-toothpaste without nano-HAp for the purpose of remineralization.
Souza *et al* (2015) [68]	Nano-HAp	*In situ*	Toothpaste	Nano-HAp/F toothpaste was the only product able to significantly reduce dentine demineralization in comparison to toothpastes containing CPP-ACP + NaF, NaF alone or a placebo formulation. The test toothpaste also enhanced enamel remineralization compared to the placebo.

Taha *et al* (2015) [77]	Nano-FHAp	*In vitro*	Paste	Nano-FHAp pastes may offer immediate short-term relief of dentin hypersensitivity because of their ability to occlude tubules and to adhere to wet dentin surfaces; its long-term effect is due to ion release.
Comar *et al* (2013) [65]	Nano-HAp	*In vitro*	Paste	The experimental nano-HAp pastes, regardless of the addition of F, were unable to reduce dental demineralization.
Wang *et al* (2012) [70]	Nano-HAp	*In vitro*	Paste	nano-FAp paste with neutral pH value (7.5) for enamel erosion repair significantly enhanced the enamel surface hardness, reduced enamel mass loss and increased surface roughness.
Lin *et al* (2011) [69]	Nano-FHAp and nano-FAp	*In vitro*	GIC	The F release properties of the GIC was improved by incorporating nano-FAp or nano-FHAp, simultaneously maintaining a clinically sufficient bond strength when nano-FAp was added.
Jeong *et al* (2007) [67]	Nano-Carbonated apatite	*In vitro*	Toothpaste	The dentifrice containing 5% nano carbonated apatites and 25% silica was the most effective in remineralizing early caries lesion.

Nano-HAp: Nano-hydroxyapatite; **F:** fluoride; **Mg:** magnesium; **Sr:** strontium; **Nano-FHAp:** nano-fluorhydroxyapatite; **Nano-FAp:** nano-fluorapatite; **CPP-ACP:** amorphous casein-phosphate stabilized by casein phosphopeptides; **GIC:** glass ionomer cement.

addition of F, was unable to reduce dental demineralization compared with a placebo toothpaste [65]. Moreover, despite a toothpaste containing nano-HAp promoted protective effects against dentin demineralization similar to those observed for a 1100 ppm F toothpaste, no additional benefit was observed when nano-HAp was coadministered with F in formulations containing 1100 or 5000 μg F g^{-1} [66]. Furthermore, a F-dentifrice containing 30% nano-HAp decreased the enamel surface hardness, while the incorporation of 5 or 15% nano-HAp into a F-dentifrice did not significantlly promote an additional effect on the enamel surface hardness when compared to their counterpart without nano-HAp [67].

On the other hand, a well-designed *in situ* study compared the effects of a toothpaste containing 10% HAp, 0.2% NaF, nano-HAp/F with toothpastes containing amorphous casein-phosphate and NaF or NaF only and observed discrete differences among the treatments on dental de- and re-mineralization processes, although the nano-HAp containing toothpaste was the only one able to reduce

dentine demineralization (ΔZ) and to improve enamel remineralization (ΔΔZ) compared to the negative control group (placebo) [68]. Furthermore, nano-HAp or nano-fluorhydroxyapatite (nano-FHAp), incorporated to a GIC led to a higher F release, without compromising its mechanical properties, in comparison to a conventional GIC not supplemented with nano-HAp or nano-FHAp [69].

Unlike for dental caries, little is available in the literature regarding the effect of nano-HAp associated with F on dental erosion. It was verified *in vitro* that a neutral pH (7.5) paste containing nano-HAp and F significantly enhanced the enamel surface hardness, avoided the enamel mass loss and increased surface roughness [70], which could be interesting for erosion repair. In addition, an acidulated phosphate F-gel (1.23% F) containing nano-HAp modified the composition and morphology of the enamel surface, in comparison to its counterpart without nano-HAp [71]. Due to the scarce data available on the effects of nano-HAp combined with F on dental erosion, this field still needs to be further explored in order to verify the actual effects of this combination for the control and/or treatment of dental erosion in humans.

Despite the robust body of evidence on the effect of nano-HAp alone on dentin hypersensitivity [72–77], the literature is scarce on the effect of nano-HAp associated with F for that purpose. It has been demonstrated *in vitro* that pastes containing nano-fluorhydroxyapatite (n-FHAp) may offer immediate short-term relief of dentin hypersensitivity because of their ability to occlude the tubules and to adhere to wet dentin surfaces [80]. Another study found that a new toothpaste containing nano-FHAp showed higher plugging rate and penetrating depth into the tubules in comparison to another product containing only F or nano-HAp [78].

Given the context above, it is safe to consider that the combination of nano-HAp and F is still an open topic for all the variables described in this section (i.e., dental caries, erosion and dentin hypersensitivity) due to the lack of more robust evidence on the action of these two compounds when co-administered. Thus, further studies should be performed to clarify the above-mentioned trends, preferably associating *in vitro* with *in situ* protocols, which are useful in providing different insights into mechanisms of action.

1.5 Silver nanoparticles

Fluoridated silver nanoparticles (or silver nanoparticles fluoride—SNF) have been proposed as an alternative to silver diamine fluoride (SDF), and are reported to have antimicrobial activity, along with the advantage of not staining dental and mucosa tissues [30, 79]. *In vitro* studies attest such effects against *Streptococcus mutans* [83, 84], and *Lactobacillus* [80], showing significant reductions on acidogenicity and adherence of these microorganisms [32]. The antimicrobial mechanism of SNF is related to their ability to penetrate the bacteria cell wall and cause denaturation of the plasma membrane, in addition to interruption on DNA replication, leading to damage to the bacterial membrane [81, 82]. SNF can also release Ag ions to the cell's interior and produce reactive oxygen species, disturbing protein synthesis and leading to cell lysis [83]. Due to their smaller particle size, this compound acts against both planktonic and colonized bacteria [84].

SNF also has the ability to prevent demineralization of sound enamel and to reduce the incidence of enamel caries lesions, with effects on both mineral loss and lesion depth, assessed by transverse microradiography [85]. The effects of solutions containing fluoride and SNF particles were shown to be dose-dependent, which were also able to promote increases in surface mineral density owing to mineral deposition [85]. Also, an *in vitro* study demonstrated that treatment of dentin subsurface lesions with a solution containing 5% NaF and 4000 ppm Ag nanoparticles promoted a similar remineralizing effect compared with 5% NaF alone, without promoting significant color changes compared with the respective controls (placebo or 5% NaF) [86]. Similar findings were observed in another *in vitro* study assessing enamel remineralization using optical coherence tomography, demonstrating that silver nanoparticles do not interfere with fluoride owing to the ionic stability of the latter, which do not react when associated with other biomaterials [87].

Another effect is related to the ability to not stain tooth and mucosa tissues [33, 86]. This is a clear advantage over SDF, as tooth staining has been widely documented as a side effect when applied to carious lesions, leading to a tooth black stain and minor injuries to the oral mucosa tissue [88]. An *in vivo* study showed the use of SNF had a success rate of 66.7% when compared to the control group (water) in arresting tooth decay and staining dental tissue [89]; this success rate is similar to that attained by SDF use (66.9%), as reported in a previous study [90]. Interestingly, a randomized clinical trial evaluated once a year the application of 5% SNF and 38% SDF in primary carious molar teeth, showing that both groups inhibited dentine caries progression and presented equivalent effects; SNF had a success rate of 77% and SDF 71%, the latter not leading to tooth staining [89]. As aforementioned about the staining, this black stain in carious tissue occurs due to the oxidation process of the ionic silver chloride contained in SDF formulation [86, 91], and with nanoparticle size reduction, leads to the non-teeth-staining due to the contact surface increase [92]. The main studies assessing the effects of SNF are summarized in table 1.4.

1.6 Nano-CaF_2

Unlike the above-mentioned agents, which have been added mostly to F-containing toothpastes or solutions, nano-CaF_2 has been extensively studied combined with restorative materials or with products for orthodontic cementation, such as composites and RMGIC, leading to promising effects on parameters related to biofilms and mechanical properties, besides enhancing their F release. The main results from studies assessing the effects of nano-CaF_2 are displayed in table 1.5.

It was shown *in vitro* that experimental composites containing nano-CaF_2 produced high F release at low filler levels. Furthermore, these composites presented higher flexural strength and elastic modulus in comparison to a control composite without nano-CaF_2 or a RMGIC [93]. Another study verified that a novel CaF_2 nanocomposite combined with chlorhexidine (CHX) reduced *S. mutans* biofilm formation, acid production, CFU-counting and metabolic activity, in comparison to commercial composites (containing or not F) or to an RMGIC. Although such

Table 1.4. Summary of the main studies assessing the effects of fluoride and silver nanoparticles related to different variables assessed

Author (year)	Technology	Protocol	Vehicle	Main findings
Aldhaian *et al* (2021) [85]	SNF	*In vitro*	Solution	Fluoride and silver nanoparticles reduced mineral loss and lesion depth in a dose-response manner.
Yin *et al* (2020) [86]	SNF	*In vitro*	Solution	NaF solution with AgNPs remineralized artificial dentine caries without significant tooth stain compared to its counterparts.
Yin *et al* (2020) [33]	SNF	*In vitro*	Solution	NaF solution with AgNPs showed antibacterial activity against SM and also no tooth staining effect .
Zhao *et al* (2020) [91]	SNF	*In vitro*	Solution	NaF + PEG-AgNPs and SDF had a similar remineralizing effect in artificial dentine caries. Moreover, NaF with PEG-AgNPs does not stain dentine caries.
Tirupathi *et al* (2019) [79]	SNF	RCT	Varnish and solution	Annual application of SNF has the same clinical efficacy as SDF in preventing the progression of dentinal caries and does not stain tooth.
Costa e Silva *et al* (2019) [87]	SNF	*In vitro*	Solution	SNF has an efficient effect in remineralizing dental enamel.
Teixeira *et al* (2018) [32]	SNF	*In vitro*	Toothpaste	SNF formulation had a better antibacterial effect compared to NaF dentifrices and similar action on the demineralization of enamel indicating their potential effectiveness to prevent caries.
Freire *et al* (2017) [31]	SNF	RCT	Solution	SNF decreased number of CFUs of SM, proving to be an effective dental biofilm inhibitor.
Santos Jr *et al* (2014) [89]	SNF	RCT	Solution	The use of SNF decreased risk of caries at seven days (81%) and five (72.2) and 12 months (66.7) when compared to control group (H_2O).
Targino *et al* (2014) [30]	SNF	*In vitro*	Solution	SNF proved to be antimicrobial agent, with low toxicity to living cells, and potential advantage of not staining teeth black.

RCT: Randomized clinical trial; **PEG-AgNPs:** Polyethylene glycol-coated silver nanoparticles; **SDF:** Sodium diamine fluoride; **SNF:** silver nanoparticles fluoride; **NaF:** Sodium Fluoride; **CFU:** colony-forming units; **SM:** *Streptococcus mutans*.

reductions were more evident for the CHX-containing CaF_2 composite, a substantial trend of decrease in metabolism and acid production was also observed for a nano-CaF_2 composite without CHX, in comparison to a F-free composite [36]. It was also verified from another nanocomposite containing CaF_2 that F release values

Table 1.5. Summary of the main studies assessing the effects of nano-sized calcium fluoride related to different variables assessed

Author (year)	Technology	Protocol	Vehicle	Main findings
Fei *et al* (2020) [95]	Nano-CaF_2	*In vitro*	Pit and fissure sealant	Experimental sealant containing nano-CaF_2 and dimethylaminohexadecyl methacrylate had increased hardness and increased F ion release compared with the commercial control. The pH in biofilm medium in contact with the experimental sealant was higher (pH 6.8) than that of commercial sealant (pH 4.7). No changes in paste flow and enamel bond strength were observed for the experimental sealant compared with the control.
Shin *et al* (2019) [96]	Nano-CaF_2	*In vitro* and *in vivo* (animal)	Nano composite hydrogel	F released from nano-CaF_2 in the composite hydrogel not only functioned as a stimulating agent for cell proliferation and migration, but also inhibited the growth of bacteria *in vitro*.
Yi *et al* (2019) [38]	Nano-CaF_2	*In vitro*	Orthodontic cement	The novel F ion-rechargeable orthodontic cement containing nano-CaF_2 presented acceptable enamel shear bond strength, good biocompatibility, and sustained F ion recharge and re-release (1.8-fold higher than a commercial formulation without nano-CaF_2).
Yi *et al* (2019) [94]	Nano-CaF_2	*In vitro*	Resin-modified glass ionomer cement (RMGIC)	The addition of Nano-CaF_2 and dimethylaminohexadecyl methacrylate to a RMGIC led to stronger antibacterial and remineralization capabilities, and greater enamel hardness than the commercial control (GC Ortho LC), without compromising the orthodontic bracket-enamel shear bond strength and biocompatibility.
Cheng *et al* (2012) [36]	Nano-CaF_2	*In vitro*	Nanocomposite	The novel CaF_2 nanocomposite with chlorhexidine was shown to reduce biofilm formation, acid production, CFU and metabolic activity of biofilms.
Xu *et al* (2010) [37]	Nano-CaF_2	*In vitro*	Nanocomposite	CaF_2 nanoparticles produced high F release at low filler levels, thereby making room in resin for reinforcement glass.

Nano-CaF_2: nano-sized calcium fluoride; **F:** fluoride; **RMGIC:** resin-modified glass ionomer cement; **CFU:** colony-forming units.

exceeded releases of traditional and RMGIC materials. In addition, the experimental CaF_2-nanocomposite presented relatively high strength and sustained release of F ions in comparison to traditional composites or RMGIC [93].

Promising data have also been reported for the incorporation of nano-CaF_2 to RMGIC. The addition of nano-CaF_2 to a conventional RMGIC (GC Ortho LC, Fuji, Aichi-ken, Japan) reduced several parameters related to biofilms (i.e., metabolic activity, production of extracellular polysaccharides and lactic acid, total microbial counts, and the counts of total streptococci and *S. mutans*), in comparison to a conventional RMGIC or to an adhesive system for orthodontic cementation, especially when combined with dimethylaminohexadecyl methacrylate (DMAHDM). Furthermore, the RMGIC containing nano-CaF_2 promoted an increase in enamel hardness and a decrease in lesion depth of artificial enamel lesions [94]. In addition, another nano-CaF_2-containing orthodontic cement presented higher F release in comparison to a conventional RMGIC (GC Ortho LC, Fuji, Aichi-ken, Japan) [38].

The incorporation of nano-CaF_2 in a pit and fissure sealant was also shown to increase F release and hardness compared with a counterpart without nano-CaF_2 (Helioseal F, Ivoclar, Mississauga, ON, Canada) [95]. Moreover, a novel alginate nanocomposite hydrogel containing nano-CaF_2 showed that F released from the nano-CaF_2 in the composite hydrogel functioned as a stimulating agent for cell proliferation and migration, in addition to inhibiting bacteria growth *in vitro*. This combination has also been shown to promote a decrease in the bacterial load, in comparison to its counterpart without nano-CaF_2 [96].

1.7 Bioactive glass

In addition to the above-mentioned compounds, which have been studied more extensively in vehicles and modes of administration, other lesser studied compounds deserve attention, whose results are summarized in table 1.6.

Bioactive glass or bioglass (BAG) is another material with marked remineralizing effects on dental structures, and has been used as an strategy to enhance the effects of GICs [39, 40]. *In vitro* studies have shown that nanosized BAG particles create a supersaturate ionic environment on dentine tubules (leading to dentine tubule occlusion), and a fast apatite formation, which prevents dentine hypersensitivity compared to micrometric particles [40, 41]. Moreover, a study assessing enamel demineralization and antibacterial effects of orthodontic bonding resins showed that the addition of fluoride to BAG resulted in higher antibacterial activity in a concentration-dependent trend, enhanced protective effects against demineralization, and the ability to prevent white spot lesions in comparison with a commercially orthodontic bonding adhesive [41].

Furthermore, it has been shown that teeth sonochemically coated with magnesium fluoride (MgF_2) nanoparticles significantly inhibited *S. mutans* biofilm formation *in vitro* in comparison to uncoated teeth [97]. In addition, the incorporation of nano-chitosan (nano-CH) in a conventional GIC led to higher compressive strength, wear resistance, as well as F release for 7 days *in vitro*, in comparison to its counterpart without nano-CH [98].

Table 1.6. Summary of the main studies assessing the effects of nanoparticles of bioactive glass, magnesium fluoride, amorphous calcium phosphate and β-tricalcium phosphate, related to different variables assessed

Author (year)	Technology	Protocol	Vehicle	Main findings
Nam *et al* (2019) [41]	BAG	*In vitro*	BAG and OBA	BAG presented a higher antibacterial activity in a concentration-dependent, better anti-demineralization effect, and ability to prevent white spot lesion when compared to its counterpart.
Yli-Urpo *et al* (2004) [39]	BAG	*In vitro*	GIC and RMGIC	RMGIC with BAG had the ability to remineralize dentine *in vitro.*
Eshed *et al* (2013) [97]	Nano-MgF_2	*In vitro*	Artificial teeth coated with MgF_2 nanoparticles	The artificial tooth surface covered with an nano-MgF_2 layer successfully inhibited *S. mutans* biofilm formation by over 60%.
Karimi *et al* (2019) [100]	Nano-ACP	*In vitro*	GIC	The working time of the formulated resin-modified glass ionomer decreased significantly upon increase of nano-ACP content from 5 to 20%. Nano-ACP-incorporated RMGICs showed improved photopolymerization and setting. The addition of nano-ACP to of RMGICs did not affect compressive strength or F release. The biocompatibility of the test RMGICs improved at ~20%. Alkaline phosphatase activity and osteogenic differentiation of mesenchymal stem cells noticeably increased after exposure to ACP-incorporated RMGIC.
Seyedlar *et al* (2019) [106]	Nano-TCP	*In vitro*	Solution	Nano-TCP solution was not more effective than the NaF 0.05 wt% in preventing demineralization.
Iafisco *et al* (2018) [99]	Nano-ACP	*In vitro*	Biomimetic amorphous calcium phosphate doped with F ions	The experimental material showed good ability to partially occlude the tubules of acid-etched dentin and to restore demineralized enamel into its native structure.

(*Continued*)

Table 1.6. (*Continued*)

Author (year)	Technology	Protocol	Vehicle	Main findings
Kumar *et al* (2017) [98]	Nano-CH	*In vitro*	GIC	Nano-CH GIC had significantly higher compressive strength values, flexural strength, wear resistance and higher F release for 7 days, compared with a conventional GIC.

Nano-ACP: nano-sized amorphous casein-phosphate; **Nano-TCP:** nano-sized β-tricalcium phosphate; **Nano-CH:** nano-chitosan; **Nano-MgF_2**: nano-sized magnesium fluoride; **NaF:** sodium fluoride; **GIC:** glass ionomer cement; **F:** fluoride; wt%: weight percent; **BAG:** bioactive glass; **RMGIC:** resin modified glass ionomer cement; **OBA:** orthodontic bonding adhesive.

Furthermore, the effects of a nano-biomimetic amorphous calcium phosphate doped with F ions were assessed on dental remineralization and dentin tubules occlusion. This compound was shown to promote partial occlusion of the tubules of acid-etched dentin and to restore demineralized enamel into the original structure, with no significant influence on the chemical-physical features of ACP, apart from the quicker conversion in the crystalline phase when immersed in aqueous solution [99]. Nano-ACP was also evaluated when incorporated to an RMGIC, resulting in enhanced alkaline phosphatase activity, without compromising the material's compressive strength or F release [100]. Such effects noticeably increased osteogenic differentiation of mesenchymal stem cells after exposure to ACP-incorporated RMGIC [100].

1.8 Conclusions

Considering the above-mentioned context on the nanoparticles presented, most of these compounds can be considered as promising alternatives for the enhancement of the F-vehicles on dental caries (effects on dental hard tissues and biofilms), on dental erosion and on dentine hypersensitivity. Despite relevant data on the mechanisms of action of these technologies achieved by *in vitro* protocols, it is important to emphasize that the literature is still scarce on data from *in vivo* studies. Thus, future research should focus on *in situ* and/or *in vivo* methodologies, as they are paramount in the determination of the actual effects of these nanoparticles.

References

[1] Featherstone J D 1999 Prevention and reversal of dental caries: role of low level fluoride *Community Dent. Oral Epidemiol.* **27** 31–40

[2] Buzalaf M A R, Pessan J P, Honorio H M and ten Cate J M 2011 Mechanisms of action of fluoride for caries control *Monogr. Oral Sci.* **22** 97–114

[3] RØlla G 1988 On the role of calcium fluoride in the cariostatic mechanism of fluoride *Acta Odontol. Scand.* **46** 341–5

[4] Ten Cate J M and Buzalaf M A R 2019 Fluoride mode of action: once there was an observant dentist *J. Dent. Res.* **98** 725–30
[5] Marinho V C, Chong L Y, Worthington H V and Walsh T 2016 Fluoride mouthrinses for preventing dental caries in children and adolescents *Cochrane Database Syst. Rev.* **29** CD002284
[6] Marinho V C, Worthington H V, Walsh T and Chong L Y 2015 Fluoride gels for preventing dental caries in children and adolescents *Cochrane Database Syst. Rev.* **15** CD002280
[7] Marinho V C, Worthington H V, Walsh T and Clarkson J E 2013 Fluoride varnishes for preventing dental caries in children and adolescents *Cochrane Database Syst. Rev.* CD002279
[8] Walsh T, Worthington H V, Glenny A M, Marinho V C and Jeroncic A 2019 Fluoride toothpastes of different concentrations for preventing dental caries *Cochrane Database Syst. Rev.* **3** CD007868
[9] Sampaio C, Delbem A C B, Paiva M F, Zen I, Danelon M, Cunha R F and Pessan J P 2020 Amount of dentifrice and fluoride concentration influence salivary fluoride concentrations and fluoride intake by toddlers *Caries Res.* **54** 234–41
[10] Whitford G M 2011 Acute toxicity of ingested fluoride *Monogr. Oral Sci.* **22** 66–80
[11] Frencken J E, Sharma P, Stenhouse L, Green D, Laverty D and Dietrich T 2017 Global epidemiology of dental caries and severe periodontitis—a comprehensive review *J. Clin. Periodontol.* **44** S94–105
[12] Huysmans M C, Young A and Ganss C 2014 The role of fluoride in erosion therapy *Monogr. Oral Sci.* **25** 230–43
[13] Wefel J S, Stanford C M, Ament D K, Hogan M M, Harless J D, Pfarrer A M, Ramsey L L, Leusch M S and Biesbrock A R 2002 *In situ* evaluation of sodium hexametaphosphate-containing dentifrices *Caries Res.* **36** 122–8
[14] da Camara D M, Pessan J P, Francati T M, Santos Souza J A, Danelon M and Delbem A C 2015 Synergistic effect of fluoride and sodium hexametaphosphate in toothpaste on enamel demineralization *in situ J Dent.* **43** 1249–54
[15] da Camara D M, Pessan J P, Francati T M, Souza J A, Danelon M and Delbem A C 2016 Fluoride toothpaste supplemented with sodium hexametaphosphate reduces enamel demineralization *in vitro Clin. Oral Investig.* **20** 1981–5
[16] Wierichs R J, Zelck H, Doerfer C E, Appel P, Paris S, Esteves-Oliveira M and Meyer-Lueckel H 2017 Effects of dentifrices differing in fluoride compounds on artificial enamel caries lesions *in vitro Odontology* **105** 36–45
[17] Gonçalves F M C, Delbem A C B, Pessan J P, Nunes G P, Emerenciano N G, Garcia L S G, Báez Quintero L C, Neves J G and Danelon M 2018 Remineralizing effect of a fluoridated gel containing sodium hexametaphosphate: an *in vitro* study *Arch. Oral Biol.* **90** 40–4
[18] Neves J G, Danelon M, Pessan J P, Figueiredo L R, Camargo E R and Delbem A C B 2018 Surface free energy of enamel treated with sodium hexametaphosphate, calcium and phosphate *Arch. Oral Biol.* **90** 108–112
[19] Freire I R, Pessan J P, Amaral J G, Martinhon C C R, Cunha R F and Delbem A C B 2016 Anticaries effect of low-fluoride dentifrices with phosphates in children: a randomized, controlled trial *J. Dent.* **50** 37–42
[20] Cavazana T P, Hosida T Y, Pessan J P, Sampaio C, Monteiro D R and Delbem A C B 2019 Activity of sodium trimetaphosphate, associated or not with fluoride, on dual-species biofilms *Biofouling* **35** 710–18

[21] Cavazana T P, Pessan J P, Hosida T Y, Sampaio C, Amarante V O Z, Monteiro D R and Delbem A C B 2020 Effects of sodium trimetaphosphate, associated or not with fluoride, on the composition and pH of mixed biofilms, before and after exposure to sucrose *Caries Res.* **54** 358–68

[22] Manarelli M M, Delbem A C, Lima T M, Castilho F C and Pessan J P 2014 *In vitro* remineralizing effect of fluoride varnishes containing sodium trimetaphosphate *Caries Res.* **48** 299–305

[23] Manarelli M M, Vieira A E, Matheus A A, Sassaki K T and Delbem A C 2011 Effect of mouth rinses with fluoride and trimetaphosphate on enamel erosion: an *in vitro* study *Caries Res.* **45** 506–9

[24] Moretto M J, Delbem A C, Manarelli M M, Pessan J P and Martinhon C C 2013 Effect of fluoride varnish supplemented with sodium trimetaphosphate on enamel erosion and abrasion: an *in situ/ex vivo* study *J. Dent.* **41** 1302–6

[25] Moretto M J, Magalhães A C, Sassaki K T, Delbem A C and Martinhon C C 2010 Effect of different fluoride concentrations of experimental dentifrices on enamel erosion and abrasion *Caries Res.* **44** 135–40

[26] Pancote L P, Manarelli M M, Danelon M and Delbem A C 2014 Effect of fluoride gels supplemented with sodium trimetaphosphate on enamel erosion and abrasion: *in vitro* study *Arch. Oral Biol.* **59** 336–40

[27] Cruz N V, Pessan J P, Manarelli M M, Souza M D and Delbem A C 2015 *In vitro* effect of low-fluoride toothpastes containing sodium trimetaphosphate on enamel erosion *Arch Oral Biol.* **60** 1231–6

[28] Danelon M, Pessan J P, Prado K M, Ramos J P, Emerenciano N G, Moretto M J, Martinhon C C R and Delbem A C B 2020 Protective effect of fluoride varnish containing trimetaphosphate against dentin erosion and erosion/abrasion: an *in vitro* study *Caries Res.* **22** 1–4

[29] Danelon M, Pessan J P, Santos V R D, Chiba E K, Garcia L S G, de Camargo E R and Delbem A C B 2018 Fluoride toothpastes containing micrometricor nano-sizedsodium trimetaphosphate reduceenamelerosion *in vitro Acta Odontol. Scand.* **76** 119–24

[30] Targino A G, Flores M A, dos Santos Junior V E, de Godoy Bené Bezerra F, de Luna Freire H, Galembeck A and Rosenblatt A 2014 Aninnovative approach totreating dental decay in children. A new anti-caries agent *J. Mater. Sci. Mater. Med.* **25** 2041–7

[31] Freire P L L, Albuquerque A J R, Sampaio F C, Galembeck A, Flores M A P, Stamford T C M and Rosenblatt A 2017 AgNPs: the new allies against *S. mutans* biofilm a pilot clinical trial and microbiological assay *Braz. Dent. J.* **28** 417–22

[32] Teixeira J A *et al* 2018 Effects of a new nano-silver fluoride-containing dentifrice on demineralization of enamel and *Streptococcus mutans* adhesion and acidogenicity *Int. J. Dent.* **8** 2018 1351925

[33] Yin I X, Zhao I S, Mei M L, Lo E C M, Tang J and Li Q 2020 Synthesis and characterization of fluoridated silver nanoparticles and their potential as a non-staining anti-caries agent *Int. J. Nanomed.* **15** 3207–15 A

[34] Tschoppe P, Zandim D L, Martus P and Kielbassa A M 2011 Enamel and dentine remineralization by nano-hydroxyapatite toothpastes *J. Dent.* **39** 430–7

[35] Demito C F, Costa J V D, Fracasso M L C and Ramos A L 2019 Efficacy of fluoride associated with nano-hydroxyapatite in reducing enamel demineralization adjacent to orthodontic brackets: *in situ* study *Dental Press. J. Orthod.* **24** 48–55

[36] Cheng L, Weir M D, Xu H H, Kraigsley A M, Lin N J, Lin-Gibson S and Zhou X 2012 Antibacterial and physical properties of calcium-phosphate and calcium-fluoride nanocomposites with chlorhexidine *Dent. Mater.* **28** 573–83

[37] Xu H H, Moreau J L, Sun L and Chow L C 2010 Novel CaF_2 nanocomposite with high strength and fluoride ion release *J. Dent. Res.* **89** 739–45

[38] Yi J, Weir M D, Melo M A S, Li T, Lynch C D, Oates T W, Dai Q, Zhao Z and Xu H H K 2019 Novel rechargeable nano-CaF_2 orthodontic cement with high levels of long-term fluoride release *J. Dent.* **90** 103214

[39] Yli-Urpo H, Vallittu P K, Narhi T O, Forsback A-P and Variparta M 2004 Release of silica,calcium, phosphorous and fluoride from glass ionomer cement containingbioactive glass *J. Biomater. Appl.* **19** 5–20

[40] Erol-Taygun M, Zheng K and Boccaccini A R 2013 Nanoscale bioactive glasses in medical applications *Int. J.App.l Glass Sci.* **4** 136–48

[41] Nam H J, Kim Y M and Kwon Y H *et al* 2019 Fluorinated bioactive glass nanoparticles: enamel demineralization prevention and antibacterial effect of orthodontic bonding resin *Materials (Basel)*. **12** 1813

[42] Danelon M, Pessan J P, Neto F N, Camargo E R and Delbem A C B 2015 Effect of toothpaste with nano-sized trimetaphosphate on dental caries: *in situ* study *J. Dent.* **2459** 1–8

[43] Danelon M, Pessan J P, Souza-Neto F N, de Camargo E R and Delbem A C B 2017 Effect of fluoride toothpaste with nano-sized trimetaphosphate on enamel demineralization: an *in vitro* study *Arch. Oral Biol.* **78** 82–7

[44] Cochrane N J, Saranathan S, Cai F, Cross K J and Reynolds E C 2008 Enamel subsurface lesion remineralisation with casein phosphopeptidestabilised solutions of calcium, phosphate and fluoride *Caries Res.* **42** 88–97

[45] Delbem A C, Souza J A, Zaze A C, Takeshita E M, Sassaki K T and Moraes J C S 2014 Effect of trimetaphosphate and fluoride association on hydroxyapatite dissolution and precipitation *in vitro Braz. Dent. J.* **25** 479–48

[46] Rios D, Honório H M, Magalhães A C, Delbem A C B, Machado M A A M, Silva S M B and Buzalaf M A R 2007 Effect of salivary stimulation on erosion of human and bovine enamel subjected or not to subsequent abrasion: an *in situ/ex vivo* study *Caries Res.* **40** 218–23

[47] Magalhães A C, Rios D, Delbem A C, Buzalaf M A and Machado M A 2007 Influence of fluoride dentifrice on brushing abrasion of eroded human enamel: an *in situ/ex vivo* study *Caries Res.* **41** 77–9

[48] Ganss C, Lussi A, Grunau O, Klimek J and Schlueter N 2011 Conventional and anti-erosion fluoride toothpastes: effect on enamel erosion and erosion-abrasion *Caries Res.* **45** 581–9

[49] Conceição J M, Delbem A C, Danelon M, da Camara D M, Wiegand A and Pessan J P 2015 Fluoride gel supplemented with sodium hexametaphosphate reduces enamel erosive wear *in situ J. Dent.* **43** 1255–60

[50] Humphreys G, Lee G L, Percival S L and McBain A J 2011 Combinatorial activities of ionic silver and sodium hexametaphosphate against microorganisms associated with chronic wounds *J. Antimicrob. Chemother.* **66** 2556–61

[51] Mendes-Gouvêa C C, do Amaral J G, Fernandes R A, Fernandes G L, Gorup L F, Camargo E R, Delbem A C B and Barbosa D B 2018 Sodium trimetaphosphate and hexametaphosphate impregnated with silver nanoparticles: characteristics and antimicrobial efficacy *Biofouling* **34** 299–308

[52] Hosida T Y, Pessan J P, Cavazana T P, Sampaio C, Monteiro D R and Delbem A C B 2021 Effect of sodium hexametaphosphate and fluoride on dual-species biofilms of *Candida albicans* and *Streptococcus mutans Biofouling* (Accepted)

[53] Shibata H and Marioka T 1982 Antibacterial action of condensed phosphates on the bacterium *Streptococcus mutans* and experimental caries in the hamster *Arch. Oral Biol.* **27** 809–16

[54] Choi I K, Wen W W and Smith R W 1993 The effect of a long chain phosphate on the adsorption of collectors on kaolinite *Miner. Eng.* **6** 1191–7

[55] Dalpasquale G, Delbem A C B, Pessan J P, Nunes G P, Gorup L F, Neto F N S, de Camargo E R and Danelon M 2017 Effect of the addition of nano-sized sodium hexametaphosphate to fluoride toothpastes on tooth demineralization: an *in vitro* study *Clin. Oral Investig.* **21** 1821–7

[56] Garcia L S G, Delbem A C B, Pessan J P, Dos Passos Silva M, Neto F N S, Gorup L F, de Camargo E R and Danelon M 2018 Anticaries effec to F toothpaste with nano-sized sodium hexametaphosphate *Clin.Oral Investig.* **23** 3535–42

[57] Danelon M, Garcia L G, Pessan J P, Passarinho A, Camargo E R and Delbem A C B 2019 Effect of fluoride toothpaste containing nano-sized sodium hexametaphosphate on enamel remineralization: an *in situ* study *Caries Res.* **53** 260–7

[58] Hosida T Y, Delbem A C B, Morais L A, Moraes J C S, Duque C, Souza J A S and Pedrini D 2019 Ion release, antimicrobial and physio-mechanical properties of glass ionomer cement containing micro or nano-sized hexametaphosphate, and their effect on enamel demineralization *Clin. Oral Investig.* **23** 2345–54

[59] Pepla E, Besharat L K, Palaia G, Tenore G and Migliau G 2014 Nano-hydroxyapatite and its applications in preventive, restorative and regenerative dentistry: a review of literature *Ann. Stomatol. (Roma).* **5** 108–14

[60] Featherstone J D B and Adrian L 2006 Understanding the chemistry of dental erosion *Dental Erosion.*vol 20 (Basel: Karger Publishers) 66–76

[61] ten Cate J M 2008 Remineralization of deep enamel dentine caries lesions *Aust. Dent. J.* **53** 281–5

[62] Frank R M and Voegel J C 1980 Ultrastructure of the human odontoblast process and its mineralisation during dental caries *Caries Res.* **14** 367–80

[63] Ebadifar A, Nomani M and Fatemi S A 2017 Effect of nano-hydroxyapatite toothpaste on microhardnessofartificial carious lesions created on extracted teeth *J. Dent. Res. Dent. Clin. Dent. Prospects. Winter* **11** 1–14

[64] Kooshki F, Pajoohan S and Kamareh S 2019 Effects of treatment with three types of varnish remineralizing agents on the microhardness of demineralized enamel surface *J Clin. Exp. Dent.* **11** e630–5

[65] Comar L P, Souza B M, Gracindo L F, Buzalaf M A R and Magalhães A C 2013 The impact of experimental pastes containing hydroxyapatite nanoparticles, with or without fluoride, on the dental demineralization *in vitro Braz. Dent. J.* **24** 273–8

[66] Leal A M C, Beserra dos Santos M V, da Silva Filho E C, Menezes de Carvalho A L, Tabchoury C P M and Vale G C 2020 Development of an experimental dentifrice with hydroxyapatite nanoparticles and high fluoride concentration to manage root dentin demineralization *Int. J. Nanomedicine.* **15** 7469–79

[67] Jeong S H, Hong S J, Choi C H and Kim B I 2007 Effect of new dentifrice containing nano-sized carbonated apatite on enamel remineralization *Key Eng. Mater.* **330–332** 291–4

[68] Souza B M, Comar L P, Vertuan M, FernandesNeto C, Buzalaf M A and Magalhães A C 2015 Effect of an experimental paste with hydroxyapatite nanoparticles and fluoride on dental demineralisation and remineralisation *in situ Caries Res.* **49** 499–507
[69] Lin J, Zhu J, Gu X, Wen W, Li Q, Fischer-Brandies H, Wang H and Mehl C 2011 Effects of incorporation of nano-fluorapatite or nano-fluorohydroxyapatite on a resin-modified glass ionomer cement *Acta Biomater.* **7** 1346–53
[70] Wang C, Zhang Y, Wei J and Wei S 2012 Effects of different pH conditions on enamel erosion repair by nano fluorapatite pastes *J. Nanosci. Nanotechnol.* **12** 7346–53
[71] Soares L E S, da Silva Magalhães J, Marciano F R and Lobo A O 2018 Surface characteristics of a modified acidulated phosphate fluoride gel with nano-hydroxyapatite coating applied on bovine enamel subjected to an erosive environment *Microsc. Res. Tech.* **81** 1456–66
[72] Browning W D, Cho S D and Deschepper E J 2012 Effect of a nano-hydroxyapatite paste on bleaching-related tooth sensitivity *J Esthet. Restor. Dent.* **24** 268–76
[73] Vano M, Derchi G, Barone A and Covani U 2014 Effectiveness of nano-hydroxyapatite toothpaste in reducing dentin hypersensitivity: a double-blind randomized controlled trial *Quintessence Int.* **45** 703–11
[74] Amaechi B T, Mathews S M, Ramalingam K and Mensinkai P K 2015 Evaluation of nanohydroxyapatite-containing toothpaste for occluding dentin tubules *Am. J. Dent.* **28** 33–9
[75] Wang L, Magalhães A C, Francisconi-Dos-Rios L F, Calabria M P, Araújo D, Buzalaf M, Lauris J and Pereira J C 2016 Treatment of dentin hypersensitivity using nano-hydroxyapatite pastes: a randomized three-month clinical trial *Oper. Dent.* **41** E93–101
[76] Vano M, Derchi G, Barone A, Pinna R, Usai P and Covani U 2018 Reducing dentine hypersensitivity with nano-hydroxyapatite toothpaste: a double-blind randomized controlled trial *Clin. Oral Investig.* **22** 313–20
[77] Taha S T, Han H, Chang S R, Sovadinova I, Kuroda K, Langford R M and Clarkson B H 2015 Nano/micro fluorhydroxyapatite crystal pastes in the treatment of dentin hypersensitivity: an *in vitro* study *Clin. Oral Investig.* **19** 1921–30
[78] Yu Q, Liu H, Liu Z, Peng Y, Cheng X, Ma K and Ji Y 2017 Comparison of nanofluoridated hydroxyapatite of varying fluoride content for dentin tubule occlusion *Am. J. Dent.* **30** 109–15
[79] Tirupathi S, Nirmala S V S G, Rajasekhar S and Nuvvula S 2019 Comparative cariostatic efficacy of a novel Nano-silver fluoride varnish with 38% silver diamine fluoride varnish a double-blind randomized clinical trial *J. Clin. Exp. Dent.* **11** e105–12
[80] Kasraei S, Sami L, Hendi S, Alikhani M Y, Rezaei-Soufi L and Khamverdi Z 2014 Antibacterial properties of composite resins incorporating silver and zinc oxide nanoparticles on *Streptococcus mutans* and *Lactobacillus Restor. Dent. Endod.* **39** 109
[81] Morones J R, Elechiguerra J L, Camacho A, Holt K, Kouri J B, Ramirez J T and Yacaman M J 2005 The bactericidal effect of silver nanoparticles *Nanotechnology* **16** 2346–53
[82] Peng J J-Y, Botelho M G and Matinlinna J P 2012 Silver compounds used in dentistry for caries management: a review *J. Dent.* **40** 531–41
[83] Jacob S J, Finub J S and Narayanan A 2012 Synthesis of silver nanoparticles using *Piper longum* leaf extracts and its cytotoxic activity against Hep-2 cell line *Colloids Surf. B. Biointerfaces* **1** 212–4
[84] Pérez-Díaz M A, Boegli L, James G, Velasquillo C, Sánchez-Sánchez R, Martínez-Martínez R E, Martínez-Castañón G A and Martinez-Gutierrez F 2015 Silver nanoparticles

with antimicrobial activities against Streptococcus mutans and their cytotoxic effect *Mater. Sci. Eng.* C **55** 360–6

[85] Aldhaian B A, Balhaddad A A, Alfaifi A A, Levon J A, Eckert G J, Hara A T and Lippert F 2021 *In vitro* demineralization prevention by fluoride and silver nanoparticles when applied to sound enamel and enamel caries-like lesions of varying severities *J. Dent.* **104** 103536

[86] Yin I X, Yu O Y, Zhao I S, Mei M L, Li Q L, Tang J and Chu C H 2020 Inhibition of dentine caries using fluoride solution with silver nanoparticles: an *in vitro* study *J. Dent.* **103** 103512 B

[87] Costa e Silva A V, Teixeira J A and Melo Júnior P C *et al* 2019 Remineralizing potential of nano-silver-fluoride for tooth enamel: an optical coherence tomography analysis *Pesqui. Bras. Odontopediatria Clín. Integr.* **19** e4002

[88] Rosenblatt A, Stamford T C M and Niederman R 2009 Silver diamine fluoride: a caries 'silver-fluoride bullet' *J. Dent. Res.* **88** 116–25

[89] dos Santos V E Jr, Vasconcelos Filho A, Targino A G R, Flores M A P, Galembeck A, Caldas A F Jr and Rosenblatt A 2014 A new 'Silver-Bullet' to treat caries in children–nano silver fluoride: a randomised clinical trial *J. Dent.* **42** 945–51

[90] dos Santos V E Jr, Vasconcelos F M, Ribeiro A G and Rosenblatt A 2012 Paradigm shift in the effective treatment of caries in schoolchildren at risk *Int. J. Dent.* **62** 47–51

[91] Zhao I S, Yin I X, Mei M L, Lo E C M, Tang J, Li Q and Chu C H 2020 Remineralising dentine caries using sodium fluoride with silver nanoparticles: an *in vitro* study *Int. J. Nanomed.* **15** 2829–39

[92] Hernández-Sierra J F, Ruiz F, Cruz Pena D C, Martínez-Gutiérrez F, Martínez A E, de Jesús Pozos Guillén A, Tapia-Pérez H and Martínez C 2008 The antimicrobial sensitivity of Streptococcus mutans to nanoparticles of silver, zinc oxide, and gold *Nanomedicine* **4** 237–40

[93] Xu H H, Moreau J L, Sun L and Chow L C 2008 Strength and fluoride release characteristics of a calcium fluoride based dental nanocomposite *Biomaterials* **29** 4261–7

[94] Yi J, Dai Q, Weir M D, Melo M A S, Lynch C D, Oates T W, Zhang K, Zhao Z and Xu H H K A 2019 Nano-CaF_2-containing orthodontic cement with antibacterial and remineralization capabilities to combat enamel white spot lesions *J. Dent.* **89** 103172

[95] Fei X, Li Y, Weir M D, Baras B H, Wang H, Wang S, Sun J, Melo M A S, Ruan J and Xu H H K 2020 Novel pit and fissure sealant containing nano-CaF_2 and dimethylaminohexadecyl methacrylate with double benefits of fluoride release and antibacterial function *Dent. Mater.* **36** 1241–53

[96] Shin D Y, Cheon K H, Song E H, Seong Y J, Park J U, Kim H E and Jeong S H 2019 Fluorine-ion-releasing injectable alginate nanocomposite hydrogel for enhanced bioactivity and antibacterial property *Int. J. Biol. Macromol.* **123** 866–77

[97] Eshed M, Lellouche J, Banin E and Gedanken A 2013 MgF_2 nanoparticle-coated teeth inhibit *Streptococcus mutans* biofilm formation on a tooth model *J. Mater. Chem.* B **1** 3985–91

[98] Kumar R S, Ravikumar N, Kavitha S, Mahalaxmi S, Jayasree R, Sampath Kumar T S and Haneesh M 2017 Nanochitosan modified glass ionomer cement with enhanced mechanical properties and fluoride release *Int. J. Biol. Macromol.* **104** 1860–5

[99] Iafisco M, DegliEsposti L, Ramírez-Rodríguez G B, Carella F, Gómez-Morales J, Ionescu A C, Brambilla E, Tampieri A and Delgado-López J M 2018 Fluoride-dopedamorphous

calcium phosphate nanoparticles as a promising biomimetic material for dental remineralization *Sci. Rep. Nov.* 19 **8** 17016

[100] Karimi M, Hesaraki S, Alizadeh M and Kazemzadeh A 2019 Effect of synthetic amorphous calcium phosphate nanoparticles on the physicochemical and biological properties of resin-modified glass ionomer cements *Mater.Sci. Eng. C. Mater. Biol. Appl.* **98** 227–40

[101] Silva M E R, Danelon M, Santos Souza J A, Silva D F, Pereira J A, Pedrini D, de Camargo E R, Botazzo Delbem A C and Duque C 2019 Incorporation of chlorhexidine and nano-sized sodium trimetaphosphate into a glass-ionomer cement: Effect on mechanical and microbiological properties and inhibition of enamel demineralization *J. Dent.* **84** 81–8

[102] Emerenciano N G, Botazzo Delbem A C, Pessan J P, Nunes G P, Souza Neto F N, de Camargo E R and Danelon M 2018 *In situ* effect of fluoride toothpaste supplemented with nano-sized sodium trimetaphosphate on enamel demineralization prevention and biofilm composition *Arch. Oral Biol.* **96** 223–9

[103] Souza M D B, Pessan J P, Lodi C S, Souza J A S, Camargo E R, Souza Neto F N and Delbem A C B 2017 Toothpaste with nanosized trimetaphosphate reduces enamel demineralization *JDR Clin. Trans. Res.* **2** 233–40

[104] Hosida T Y, Delbem A C B, Morais L A, Moraes J C S, Duque C, Souza J A S and Pedrini D 2019 Ion release, antimicrobial and physio-mechanical properties of glass ionomer cement containing micro or nanosized hexametaphosphate, and their effect on enamel demineralization. *Clin. Oral Investig.* **23** 2345–54

[105] Ionescu A C, Cazzaniga G, Ottobelli M, Garcia-Godoy F and Brambilla E 2020 Substituted nano-hydroxyapatite toothpastes reduce biofilm formation on enamel and resin-based composite surfaces *J. Funct. Biomater.* **11** 36

[106] Seyedlar R M, Rezvani M, Barari S, Imani M, Nodehi A and Atai M 2019 Synthesis of plate-like β-tricalcium phosphate nanoparticles and their efficiency in remineralization of incipient enamel caries *Prog. Biomater.* **8** 261–76

Full list of references

Chapter 1

[1] Featherstone J D 1999 Prevention and reversal of dental caries: role of low level fluoride *Community Dent. Oral Epidemiol.* **27** 31–40

[2] Buzalaf M A R, Pessan J P, Honorio H M and ten Cate J M 2011 Mechanisms of action of fluoride for caries control *Monogr. Oral Sci.* **22** 97–114

[3] RØlla G 1988 On the role of calcium fluoride in the cariostatic mechanism of fluoride *Acta Odontol. Scand.* **46** 341–5

[4] Ten Cate J M and Buzalaf M A R 2019 Fluoride mode of action: once there was an observant dentist *J. Dent. Res.* **98** 725–30

[5] Marinho V C, Chong L Y, Worthington H V and Walsh T 2016 Fluoride mouthrinses for preventing dental caries in children and adolescents *Cochrane Database Syst. Rev.* **29** CD002284

[6] Marinho V C, Worthington H V, Walsh T and Chong L Y 2015 Fluoride gels for preventing dental caries in children and adolescents *Cochrane Database Syst. Rev.* **15** CD002280

[7] Marinho V C, Worthington H V, Walsh T and Clarkson J E 2013 Fluoride varnishes for preventing dental caries in children and adolescents *Cochrane Database Syst. Rev.* CD002279

[8] Walsh T, Worthington H V, Glenny A M, Marinho V C and Jeroncic A 2019 Fluoride toothpastes of different concentrations for preventing dental caries *Cochrane Database Syst. Rev.* **3** CD007868

[9] Sampaio C, Delbem A C B, Paiva M F, Zen I, Danelon M, Cunha R F and Pessan J P 2020 Amount of dentifrice and fluoride concentration influence salivary fluoride concentrations and fluoride intake by toddlers *Caries Res.* **54** 234–41

[10] Whitford G M 2011 Acute toxicity of ingested fluoride *Monogr. Oral Sci.* **22** 66–80

[11] Frencken J E, Sharma P, Stenhouse L, Green D, Laverty D and Dietrich T 2017 Global epidemiology of dental caries and severe periodontitis—a comprehensive review *J. Clin. Periodontol.* **44** S94–105

[12] Huysmans M C, Young A and Ganss C 2014 The role of fluoride in erosion therapy *Monogr. Oral Sci.* **25** 230–43

[13] Wefel J S, Stanford C M, Ament D K, Hogan M M, Harless J D, Pfarrer A M, Ramsey L L, Leusch M S and Biesbrock A R 2002 *In situ* evaluation of sodium hexametaphosphate-containing dentifrices *Caries Res.* **36** 122–8

[14] da Camara D M, Pessan J P, Francati T M, Santos Souza J A, Danelon M and Delbem A C 2015 Synergistic effect of fluoride and sodium hexametaphosphate in toothpaste on enamel demineralization *in situ J Dent.* **43** 1249–54

[15] da Camara D M, Pessan J P, Francati T M, Souza J A, Danelon M and Delbem A C 2016 Fluoride toothpaste supplemented with sodium hexametaphosphate reduces enamel demineralization *in vitro Clin. Oral Investig.* **20** 1981–5

[16] Wierichs R J, Zelck H, Doerfer C E, Appel P, Paris S, Esteves-Oliveira M and Meyer-Lueckel H 2017 Effects of dentifrices differing in fluoride compounds on artificial enamel caries lesions *in vitro Odontology* **105** 36–45

[17] Gonçalves F M C, Delbem A C B, Pessan J P, Nunes G P, Emerenciano N G, Garcia L S G, Báez Quintero L C, Neves J G and Danelon M 2018 Remineralizing effect of a fluoridated gel containing sodium hexametaphosphate: an *in vitro* study *Arch. Oral Biol.* **90** 40–4

[18] Neves J G, Danelon M, Pessan J P, Figueiredo L R, Camargo E R and Delbem A C B 2018 Surface free energy of enamel treated with sodium hexametaphosphate, calcium and phosphate *Arch. Oral Biol.* **90** 108–112

[19] Freire I R, Pessan J P, Amaral J G, Martinhon C C R, Cunha R F and Delbem A C B 2016 Anticaries effect of low-fluoride dentifrices with phosphates in children: a randomized, controlled trial *J. Dent.* **50** 37–42

[20] Cavazana T P, Hosida T Y, Pessan J P, Sampaio C, Monteiro D R and Delbem A C B 2019 Activity of sodium trimetaphosphate, associated or not with fluoride, on dual-species biofilms *Biofouling* **35** 710–18

[21] Cavazana T P, Pessan J P, Hosida T Y, Sampaio C, Amarante V O Z, Monteiro D R and Delbem A C B 2020 Effects of sodium trimetaphosphate, associated or not with fluoride, on the composition and pH of mixed biofilms, before and after exposure to sucrose *Caries Res.* **54** 358–68

[22] Manarelli M M, Delbem A C, Lima T M, Castilho F C and Pessan J P 2014 *In vitro* remineralizing effect of fluoride varnishes containing sodium trimetaphosphate *Caries Res.* **48** 299–305

[23] Manarelli M M, Vieira A E, Matheus A A, Sassaki K T and Delbem A C 2011 Effect of mouth rinses with fluoride and trimetaphosphate on enamel erosion: an *in vitro* study *Caries Res.* **45** 506–9

[24] Moretto M J, Delbem A C, Manarelli M M, Pessan J P and Martinhon C C 2013 Effect of fluoride varnish supplemented with sodium trimetaphosphate on enamel erosion and abrasion: an *in situ*/*ex vivo* study *J. Dent.* **41** 1302–6

[25] Moretto M J, Magalhães A C, Sassaki K T, Delbem A C and Martinhon C C 2010 Effect of different fluoride concentrations of experimental dentifrices on enamel erosion and abrasion *Caries Res.* **44** 135–40

[26] Pancote L P, Manarelli M M, Danelon M and Delbem A C 2014 Effect of fluoride gels supplemented with sodium trimetaphosphate on enamel erosion and abrasion: *in vitro* study *Arch. Oral Biol.* **59** 336–40

[27] Cruz N V, Pessan J P, Manarelli M M, Souza M D and Delbem A C 2015 *In vitro* effect of low-fluoride toothpastes containing sodium trimetaphosphate on enamel erosion *Arch Oral Biol.* **60** 1231–6

[28] Danelon M, Pessan J P, Prado K M, Ramos J P, Emerenciano N G, Moretto M J, Martinhon C C R and Delbem A C B 2020 Protective effect of fluoride varnish containing trimetaphosphate against dentin erosion and erosion/abrasion: an *in vitro* study *Caries Res.* **22** 1–4

[29] Danelon M, Pessan J P, Santos V R D, Chiba E K, Garcia L S G, de Camargo E R and Delbem A C B 2018 Fluoride toothpastes containing micrometricor nano-sizedsodium trimetaphosphate reduceenamelerosion *in vitro Acta Odontol. Scand.* **76** 119–24

[30] Targino A G, Flores M A, dos Santos Junior V E, de Godoy Bené Bezerra F, de Luna Freire H, Galembeck A and Rosenblatt A 2014 Aninnovative approach totreating dental decay in children. A new anti-caries agent *J. Mater. Sci. Mater. Med.* **25** 2041–7

[31] Freire P L L, Albuquerque A J R, Sampaio F C, Galembeck A, Flores M A P, Stamford T C M and Rosenblatt A 2017 AgNPs: the new allies against *S. mutans* biofilm a pilot clinical trial and microbiological assay *Braz. Dent. J.* **28** 417–22

[32] Teixeira J A *et al* 2018 Effects of a new nano-silver fluoride-containing dentifrice on demineralization of enamel and *Streptococcus mutans* adhesion and acidogenicity *Int. J. Dent.* **8** 2018 1351925

[33] Yin I X, Zhao I S, Mei M L, Lo E C M, Tang J and Li Q 2020 Synthesis and characterization of fluoridated silver nanoparticles and their potential as a non-staining anti-caries agent *Int. J. Nanomed.* **15** 3207–15 A
[34] Tschoppe P, Zandim D L, Martus P and Kielbassa A M 2011 Enamel and dentine remineralization by nano-hydroxyapatite toothpastes *J. Dent.* **39** 430–7
[35] Demito C F, Costa J V D, Fracasso M L C and Ramos A L 2019 Efficacy of fluoride associated with nano-hydroxyapatite in reducing enamel demineralization adjacent to orthodontic brackets: *in situ* study *Dental Press. J. Orthod.* **24** 48–55
[36] Cheng L, Weir M D, Xu H H, Kraigsley A M, Lin N J, Lin-Gibson S and Zhou X 2012 Antibacterial and physical properties of calcium-phosphate and calcium-fluoride nano-composites with chlorhexidine *Dent. Mater.* **28** 573–83
[37] Xu H H, Moreau J L, Sun L and Chow L C 2010 Novel CaF_2 nanocomposite with high strength and fluoride ion release *J. Dent. Res.* **89** 739–45
[38] Yi J, Weir M D, Melo M A S, Li T, Lynch C D, Oates T W, Dai Q, Zhao Z and Xu H H K 2019 Novel rechargeable nano-CaF_2 orthodontic cement with high levels of long-term fluoride release *J. Dent.* **90** 103214
[39] Yli-Urpo H, Vallittu P K, Narhi T O, Forsback A-P and Variparta M 2004 Release of silica,calcium, phosphorous and fluoride from glass ionomer cement containingbioactive glass *J. Biomater. Appl.* **19** 5–20
[40] Erol-Taygun M, Zheng K and Boccaccini A R 2013 Nanoscale bioactive glasses in medical applications *Int. J.App.l Glass Sci.* **4** 136–48
[41] Nam H J, Kim Y M and Kwon Y H *et al* 2019 Fluorinated bioactive glass nanoparticles: enamel demineralization prevention and antibacterial effect of orthodontic bonding resin *Materials (Basel)*. **12** 1813
[42] Danelon M, Pessan J P, Neto F N, Camargo E R and Delbem A C B 2015 Effect of toothpaste with nano-sized trimetaphosphate on dental caries: *in situ* study *J. Dent.* **2459** 1–8
[43] Danelon M, Pessan J P, Souza-Neto F N, de Camargo E R and Delbem A C B 2017 Effect of fluoride toothpaste with nano-sized trimetaphosphate on enamel demineralization: an *in vitro* study *Arch. Oral Biol.* **78** 82–7
[44] Cochrane N J, Saranathan S, Cai F, Cross K J and Reynolds E C 2008 Enamel subsurface lesion remineralisation with casein phosphopeptidestabilised solutions of calcium, phosphate and fluoride *Caries Res.* **42** 88–97
[45] Delbem A C, Souza J A, Zaze A C, Takeshita E M, Sassaki K T and Moraes J C S 2014 Effect of trimetaphosphate and fluoride association on hydroxyapatite dissolution and precipitation *in vitro Braz. Dent. J.* **25** 479–48
[46] Rios D, Honório H M, Magalhães A C, Delbem A C B, Machado M A A M, Silva S M B and Buzalaf M A R 2007 Effect of salivary stimulation on erosion of human and bovine enamel subjected or not to subsequent abrasion: an *in situ/ex vivo* study *Caries Res.* **40** 218–23
[47] Magalhães A C, Rios D, Delbem A C, Buzalaf M A and Machado M A 2007 Influence of fluoride dentifrice on brushing abrasion of eroded human enamel: an *in situ/ex vivo* study *Caries Res.* **41** 77–9
[48] Ganss C, Lussi A, Grunau O, Klimek J and Schlueter N 2011 Conventional and anti-erosion fluoride toothpastes: effect on enamel erosion and erosion-abrasion *Caries Res.* **45** 581–9

[49] Conceição J M, Delbem A C, Danelon M, da Camara D M, Wiegand A and Pessan J P 2015 Fluoride gel supplemented with sodium hexametaphosphate reduces enamel erosive wear *in situ J. Dent.* **43** 1255–60

[50] Humphreys G, Lee G L, Percival S L and McBain A J 2011 Combinatorial activities of ionic silver and sodium hexametaphosphate against microorganisms associated with chronic wounds *J. Antimicrob. Chemother.* **66** 2556–61

[51] Mendes-Gouvêa C C, do Amaral J G, Fernandes R A, Fernandes G L, Gorup L F, Camargo E R, Delbem A C B and Barbosa D B 2018 Sodium trimetaphosphate and hexametaphosphate impregnated with silver nanoparticles: characteristics and antimicrobial efficacy *Biofouling* **34** 299–308

[52] Hosida T Y, Pessan J P, Cavazana T P, Sampaio C, Monteiro D R and Delbem A C B 2021 Effect of sodium hexametaphosphate and fluoride on dual-species biofilms of *Candida albicans* and *Streptococcus mutans Biofouling* (Accepted)

[53] Shibata H and Marioka T 1982 Antibacterial action of condensed phosphates on the bacterium *Streptococcus mutans* and experimental caries in the hamster *Arch. Oral Biol.* **27** 809–16

[54] Choi I K, Wen W W and Smith R W 1993 The effect of a long chain phosphate on the adsorption of collectors on kaolinite *Miner. Eng.* **6** 1191–7

[55] Dalpasquale G, Delbem A C B, Pessan J P, Nunes G P, Gorup L F, Neto F N S, de Camargo E R and Danelon M 2017 Effect of the addition of nano-sized sodium hexametaphosphate to fluoride toothpastes on tooth demineralization: an *in vitro* study *Clin. Oral Investig.* **21** 1821–7

[56] Garcia L S G, Delbem A C B, Pessan J P, Dos Passos Silva M, Neto F N S, Gorup L F, de Camargo E R and Danelon M 2018 Anticaries effec to F toothpaste with nano-sized sodium hexametaphosphate *Clin.Oral Investig.* **23** 3535–42

[57] Danelon M, Garcia L G, Pessan J P, Passarinho A, Camargo E R and Delbem A C B 2019 Effect of fluoride toothpaste containing nano-sized sodium hexametaphosphate on enamel remineralization: an *in situ* study *Caries Res.* **53** 260–7

[58] Hosida T Y, Delbem A C B, Morais L A, Moraes J C S, Duque C, Souza J A S and Pedrini D 2019 Ion release, antimicrobial and physio-mechanical properties of glass ionomer cement containing micro or nano-sized hexametaphosphate, and their effect on enamel demineralization *Clin. Oral Investig.* **23** 2345–54

[59] Pepla E, Besharat L K, Palaia G, Tenore G and Migliau G 2014 Nano-hydroxyapatite and its applications in preventive, restorative and regenerative dentistry: a review of literature *Ann. Stomatol. (Roma).* **5** 108–14

[60] Featherstone J D B and Adrian L 2006 Understanding the chemistry of dental erosion *Dental Erosion.*vol 20 (Basel: Karger Publishers), 66–76

[61] ten Cate J M 2008 Remineralization of deep enamel dentine caries lesions *Aust. Dent. J.* **53** 281–5

[62] Frank R M and Voegel J C 1980 Ultrastructure of the human odontoblast process and its mineralisation during dental caries *Caries Res.* **14** 367–80

[63] Ebadifar A, Nomani M and Fatemi S A 2017 Effect of nano-hydroxyapatite toothpaste on microhardnessofartificial carious lesions created on extracted teeth *J. Dent. Res. Dent. Clin. Dent. Prospects. Winter* **11** 1–14

[64] Kooshki F, Pajoohan S and Kamareh S 2019 Effects of treatment with three types of varnish remineralizing agents on the microhardness of demineralized enamel surface *J Clin. Exp. Dent.* **11** e630–5

[65] Comar L P, Souza B M, Gracindo L F, Buzalaf M A R and Magalhães A C 2013 The impact of experimental pastes containing hydroxyapatite nanoparticles, with or without fluoride, on the dental demineralization *in vitro Braz. Dent. J.* **24** 273–8

[66] Leal A M C, Beserra dos Santos M V, da Silva Filho E C, Menezes de Carvalho A L, Tabchoury C P M and Vale G C 2020 Development of an experimental dentifrice with hydroxyapatite nanoparticles and high fluoride concentration to manage root dentin demineralization *Int. J. Nanomedicine.* **15** 7469–79

[67] Jeong S H, Hong S J, Choi C H and Kim B I 2007 Effect of new dentifrice containing nano-sized carbonated apatite on enamel remineralization *Key Eng. Mater.* **330–332** 291–4

[68] Souza B M, Comar L P, Vertuan M, FernandesNeto C, Buzalaf M A and Magalhães A C 2015 Effect of an experimental paste with hydroxyapatite nanoparticles and fluoride on dental demineralisation and remineralisation *in situ Caries Res.* **49** 499–507

[69] Lin J, Zhu J, Gu X, Wen W, Li Q, Fischer-Brandies H, Wang H and Mehl C 2011 Effects of incorporation of nano-fluorapatite or nano-fluorohydroxyapatite on a resin-modified glass ionomer cement *Acta Biomater.* **7** 1346–53

[70] Wang C, Zhang Y, Wei J and Wei S 2012 Effects of different pH conditions on enamel erosion repair by nano fluorapatite pastes *J. Nanosci. Nanotechnol.* **12** 7346–53

[71] Soares L E S, da Silva Magalhães J, Marciano F R and Lobo A O 2018 Surface characteristics of a modified acidulated phosphate fluoride gel with nano-hydroxyapatite coating applied on bovine enamel subjected to an erosive environment *Microsc. Res. Tech.* **81** 1456–66

[72] Browning W D, Cho S D and Deschepper E J 2012 Effect of a nano-hydroxyapatite paste on bleaching-related tooth sensitivity *J Esthet. Restor. Dent.* **24** 268–76

[73] Vano M, Derchi G, Barone A and Covani U 2014 Effectiveness of nano-hydroxyapatite toothpaste in reducing dentin hypersensitivity: a double-blind randomized controlled trial *Quintessence Int.* **45** 703–11

[74] Amaechi B T, Mathews S M, Ramalingam K and Mensinkai P K 2015 Evaluation of nanohydroxyapatite-containing toothpaste for occluding dentin tubules *Am. J. Dent.* **28** 33–9

[75] Wang L, Magalhães A C, Francisconi-Dos-Rios L F, Calabria M P, Araújo D, Buzalaf M, Lauris J and Pereira J C 2016 Treatment of dentin hypersensitivity using nano-hydroxyapatite pastes: a randomized three-month clinical trial *Oper. Dent.* **41** E93–101

[76] Vano M, Derchi G, Barone A, Pinna R, Usai P and Covani U 2018 Reducing dentine hypersensitivity with nano-hydroxyapatite toothpaste: a double-blind randomized controlled trial *Clin. Oral Investig.* **22** 313–20

[77] Taha S T, Han H, Chang S R, Sovadinova I, Kuroda K, Langford R M and Clarkson B H 2015 Nano/micro fluorhydroxyapatite crystal pastes in the treatment of dentin hypersensitivity: an *in vitro* study *Clin. Oral Investig.* **19** 1921–30

[78] Yu Q, Liu H, Liu Z, Peng Y, Cheng X, Ma K and Ji Y 2017 Comparison of nanofluoridated hydroxyapatite of varying fluoride content for dentin tubule occlusion *Am. J. Dent.* **30** 109–15

[79] Tirupathi S, Nirmala S V S G, Rajasekhar S and Nuvvula S 2019 Comparative cariostatic efficacy of a novel Nano-silver fluoride varnish with 38% silver diamine fluoride varnish a double-blind randomized clinical trial *J. Clin. Exp. Dent.* **11** e105–12

[80] Kasraei S, Sami L, Hendi S, Alikhani M Y, Rezaei-Soufi L and Khamverdi Z 2014 Antibacterial properties of composite resins incorporating silver and zinc oxide nanoparticles on *Streptococcus mutans* and *Lactobacillus Restor. Dent. Endod.* **39** 109

[81] Morones J R, Elechiguerra J L, Camacho A, Holt K, Kouri J B, Ramirez J T and Yacaman M J 2005 The bactericidal effect of silver nanoparticles *Nanotechnology* **16** 2346–53
[82] Peng J J-Y, Botelho M G and Matinlinna J P 2012 Silver compounds used in dentistry for caries management: a review *J. Dent.* **40** 531–41
[83] Jacob S J, Finub J S and Narayanan A 2012 Synthesis of silver nanoparticles using *Piper longum* leaf extracts and its cytotoxic activity against Hep-2 cell line *Colloids Surf. B. Biointerfaces* **1** 212–4
[84] Pérez-Díaz M A, Boegli L, James G, Velasquillo C, Sánchez-Sánchez R, Martínez-Martínez R E, Martínez-Castañón G A and Martinez-Gutierrez F 2015 Silver nanoparticles with antimicrobial activities against Streptococcus mutans and their cytotoxic effect *Mater. Sci. Eng.* C **55** 360–6
[85] Aldhaian B A, Balhaddad A A, Alfaifi A A, Levon J A, Eckert G J, Hara A T and Lippert F 2021 *In vitro* demineralization prevention by fluoride and silver nanoparticles when applied to sound enamel and enamel caries-like lesions of varying severities *J. Dent.* **104** 103536
[86] Yin I X, Yu O Y, Zhao I S, Mei M L, Li Q L, Tang J and Chu C H 2020 Inhibition of dentine caries using fluoride solution with silver nanoparticles: an *in vitro* study *J. Dent.* **103** 103512 B
[87] Costa e Silva A V, Teixeira J A and Melo Júnior P C *et al* 2019 Remineralizing potential of nano-silver-fluoride for tooth enamel: an optical coherence tomography analysis *Pesqui. Bras. Odontopediatria Clín. Integr.* **19** e4002
[88] Rosenblatt A, Stamford T C M and Niederman R 2009 Silver diamine fluoride: a caries 'silver-fluoride bullet' *J. Dent. Res.* **88** 116–25
[89] dos Santos V E Jr, Vasconcelos Filho A, Targino A G R, Flores M A P, Galembeck A, Caldas A F Jr and Rosenblatt A 2014 A new 'Silver-Bullet' to treat caries in children–nano silver fluoride: a randomised clinical trial *J. Dent.* **42** 945–51
[90] dos Santos V E Jr, Vasconcelos F M, Ribeiro A G and Rosenblatt A 2012 Paradigm shift in the effective treatment of caries in schoolchildren at risk *Int. J. Dent.* **62** 47–51
[91] Zhao I S, Yin I X, Mei M L, Lo E C M, Tang J, Li Q and Chu C H 2020 Remineralising dentine caries using sodium fluoride with silver nanoparticles: an *in vitro* study *Int. J. Nanomed.* **15** 2829–39
[92] Hernández-Sierra J F, Ruiz F, Cruz Pena D C, Martínez-Gutiérrez F, Martínez A E, de Jesús Pozos Guillén A, Tapia-Pérez H and Martínez C 2008 The antimicrobial sensitivity of Streptococcus mutans to nanoparticles of silver, zinc oxide, and gold *Nanomedicine* **4** 237–40
[93] Xu H H, Moreau J L, Sun L and Chow L C 2008 Strength and fluoride release characteristics of a calcium fluoride based dental nanocomposite *Biomaterials* **29** 4261–7
[94] Yi J, Dai Q, Weir M D, Melo M A S, Lynch C D, Oates T W, Zhang K, Zhao Z and Xu H H K A 2019 Nano-CaF_2-containing orthodontic cement with antibacterial and remineralization capabilities to combat enamel white spot lesions *J. Dent.* **89** 103172
[95] Fei X, Li Y, Weir M D, Baras B H, Wang H, Wang S, Sun J, Melo M A S, Ruan J and Xu H H K 2020 Novel pit and fissure sealant containing nano-CaF_2 and dimethylaminohexadecyl methacrylate with double benefits of fluoride release and antibacterial function *Dent. Mater.* **36** 1241–53
[96] Shin D Y, Cheon K H, Song E H, Seong Y J, Park J U, Kim H E and Jeong S H 2019 Fluorine-ion-releasing injectable alginate nanocomposite hydrogel for enhanced bioactivity and antibacterial property *Int. J. Biol. Macromol.* **123** 866–77

[97] Eshed M, Lellouche J, Banin E and Gedanken A 2013 MgF_2 nanoparticle-coated teeth inhibit *Streptococcus mutans* biofilm formation on a tooth model *J. Mater. Chem.* B **1** 3985–91
[98] Kumar R S, Ravikumar N, Kavitha S, Mahalaxmi S, Jayasree R, Sampath Kumar T S and Haneesh M 2017 Nanochitosan modified glass ionomer cement with enhanced mechanical properties and fluoride release *Int. J. Biol. Macromol.* **104** 1860–5
[99] Iafisco M, DegliEsposti L, Ramírez-Rodríguez G B, Carella F, Gómez-Morales J, Ionescu A C, Brambilla E, Tampieri A and Delgado-López J M 2018 Fluoride-dopedamorphous calcium phosphate nanoparticles as a promising biomimetic material for dental remineralization *Sci. Rep. Nov.* 19 **8** 17016
[100] Karimi M, Hesaraki S, Alizadeh M and Kazemzadeh A 2019 Effect of synthetic amorphous calcium phosphate nanoparticles on the physicochemical and biological properties of resin-modified glass ionomer cements *Mater.Sci. Eng. C. Mater. Biol. Appl.* **98** 227–40
[101] Silva M E R, Danelon M, Santos Souza J A, Silva D F, Pereira J A, Pedrini D, de Camargo E R, Botazzo Delbem A C and Duque C 2019 Incorporation of chlorhexidine and nano-sized sodium trimetaphosphate into a glass-ionomer cement: Effect on mechanical and microbiological properties and inhibition of enamel demineralization *J. Dent.* **84** 81–8
[102] Emerenciano N G, Botazzo Delbem A C, Pessan J P, Nunes G P, Souza Neto F N, de Camargo E R and Danelon M 2018 *In situ* effect of fluoride toothpaste supplemented with nano-sized sodium trimetaphosphate on enamel demineralization prevention and biofilm composition *Arch. Oral Biol.* **96** 223–9
[103] Souza M D B, Pessan J P, Lodi C S, Souza J A S, Camargo E R, Souza Neto F N and Delbem A C B 2017 Toothpaste with nanosized trimetaphosphate reduces enamel demineralization *JDR Clin. Trans. Res.* **2** 233–40
[104] Hosida T Y, Delbem A C B, Morais L A, Moraes J C S, Duque C, Souza J A S and Pedrini D 2019 Ion release, antimicrobial and physio-mechanical properties of glass ionomer cement containing micro or nanosized hexametaphosphate, and their effect on enamel demineralization. *Clin. Oral Investig.* **23** 2345–54
[105] Ionescu A C, Cazzaniga G, Ottobelli M, Garcia-Godoy F and Brambilla E 2020 Substituted nano-hydroxyapatite toothpastes reduce biofilm formation on enamel and resin-based composite surfaces *J. Funct. Biomater.* **11** 36
[106] Seyedlar R M, Rezvani M, Barari S, Imani M, Nodehi A and Atai M 2019 Synthesis of plate-like β-tricalcium phosphate nanoparticles and their efficiency in remineralization of incipient enamel caries *Prog. Biomater.* **8** 261–76

Chapter 2

[1] Thesleff I and Tummers M 2009 Tooth organogenesis and regeneration *StemBook* (Cambridge, MA: Harvard Stem Cell Institute)
[2] Goldberg M, Kulkarni A B, Young M and Boskey A 2011 Dentin: structure, composition and mineralization: the role of dentin ECM in dentin formation and mineralization *Front. Biosci.* **3** 711
[3] Balic A 2018 Biology explaining tooth repair and regeneration: a mini-review *Gerontology* **64** 382–8
[4] Lynnerup N and Klaus H D 2019 Fundamentals of human bone and dental biology: structure, function, and development *Ortner's Identification of Pathological Conditions in Human Skeletal Remains* (Amsterdam: Elsevier), pp 35–58

[5] Yen A-H and Yelick P 2011 Dental tissue regeneration–a mini-review *Gerontology* **57** 85–94
[6] Giacaman R, Perez V and Carrera C 2016 Mineralization processes in hard tissues: teeth. *Biomineralization and Biomaterials* (Amsterdam: Elsevier), pp 147–85
[7] Chen H and Liu Y T 2014 *Advanced Ceramics for Dentistry* (Amsterdam: Elsevier), pp 5–21
[8] Zhou T, Pan J and Wu P *et al* 2019 Dental follicle cells: roles in development and beyond *Stem Cells Int.* **2019** 9159605
[9] Kim T-H, Bae C-H and Lee J-Y *et al* 2015 Temporo-spatial requirement of Smad4 in dentin formation *Biochem. Biophys. Res. Commun.* **459** 706–12
[10] Olley R, Xavier G M and Seppala M *et al* 2014 Expression analysis of candidate genes regulating successional tooth formation in the human embryo *Front. Physiol.* **5** 445
[11] Tompkins K 2006 Molecular mechanisms of cytodifferentiation in mammalian tooth development *Connect. Tissue Res.* **47** 111–8
[12] Xavier J R, Desai P, Varanasi V G, Al-Hashimi I and Gaharwar A K 2015 Advanced nanomaterials: promises for improved dental tissue regeneration *Nanotechnology in Endodontics* (Berlin: Springer), pp 5–22
[13] Adair T H and Montani J-P A 2010 *Colloquium Series on Integrated Systems Physiology: from Molecule to Function* 2010 (Williston, VT: Morgan & Claypool Life Sciences), pp 1–84
[14] Zhao M, Wang J, Xi X, Tan N and Zhang L 2018 SNHG12 promotes angiogenesis following ischemic stroke via regulating miR-150/VEGF pathway *Neuroscience* **390** 231–40
[15] Barui A K, Jhelum P and Nethi S K *et al* 2020 Potential therapeutic application of zinc oxide nanoflowers in the cerebral ischemia rat model through neuritogenic and neuroprotective properties *Bioconjugate Chem.* **31** 895–906
[16] Thurston G and Kitajewski J 2008 VEGF and Delta-Notch: interacting signalling pathways in tumour angiogenesis *Br. J. Cancer* **99** 1204–9
[17] Das S, Roy A and Barui A K *et al* 2020 Anti-angiogenic vanadium pentoxide nanoparticles for the treatment of melanoma and their *in vivo* toxicity study *Nanoscale* **12** 7604–21
[18] Jeong I-H, Bae W-Y, Choi J-S and Jeong J-W 2020 Ischemia induces autophagy of endothelial cells and stimulates angiogenic effects in a hindlimb ischemia mouse model *Cell Death Dis.* **11** 1–11
[19] Johnson T, Zhao L, Manuel G, Taylor H and Liu D 2019 Approaches to therapeutic angiogenesis for ischemic heart disease *J. Mol. Med.* **97** 141–51
[20] Ucuzian A A, Gassman A A, East A T and Greisler H P 2010 Molecular mediators of angiogenesis *J. Burn Care Res.* **31** 158–75
[21] Neve A, Cantatore F P, Maruotti N, Corrado A and Ribatti D 2014 Extracellular matrix modulates angiogenesis in physiological and pathological conditions *BioMed Res. Int.* **2014** 756078
[22] Krock B L, Skuli N and Simon M C 2011 Hypoxia-induced angiogenesis: good and evil *Genes Cancer* **2** 1117–33
[23] Mao J 2011 Tooth regeneration: current status *Preprosthetic and Maxillofacial Surgery* (Amsterdam: Elsevier), pp 363–73
[24] Tatullo M, Marrelli M, Shakesheff K M and White L J 2015 Dental pulp stem cells: function, isolation and applications in regenerative medicine *J. Tissue Eng. Regen. Med.* **9** 1205–16
[25] Aranha A M, Zhang Z, Neiva K G, Costa C A, Hebling J and Nör J E 2010 Hypoxia enhances the angiogenic potential of human dental pulp cells *J. Endodontics* **36** 1633–7

[26] Hilkens P, Fanton Y and Martens W *et al* 2014 Pro-angiogenic impact of dental stem cells *in vitro* and *in vivo Stem Cell Res.* **12** 778–90
[27] Roberts-Clark D and Smith A 2000 Angiogenic growth factors in human dentine matrix *Arch. Oral Biol.* **45** 1013–6
[28] Saghiri M A, Asatourian A, Sorenson C M and Sheibani N 2015 Role of angiogenesis in endodontics: contributions of stem cells and proangiogenic and antiangiogenic factors to dental pulp regeneration *J. Endodontics* **41** 797–803
[29] Caviedes-Bucheli J, Gomez-Sosa J, Azuero-Holguin M, Ormeño-Gomez M, Pinto-Pascual V and Munoz H 2017 Angiogenic mechanisms of human dental pulp and their relationship with substance P expression in response to occlusal trauma *Int. Endod. J.* **50** 339–51
[30] Kim Y-S, Min K-S, Jeong D-H, Jang J-H, Kim H-W and Kim E-C 2010 Effects of fibroblast growth factor-2 on the expression and regulation of chemokines in human dental pulp cells *J. Endodontics* **36** 1824–30
[31] Vaseenon S, Chattipakorn N and Chattipakorn S C 2020 The possible role of basic fibroblast growth factor in dental pulp *Arch. Oral Biol.* **109** 104574
[32] Takeuchi N, Hayashi Y and Murakami M *et al* 2015 Similar *in vitro* effects and pulp regeneration in ectopic tooth transplantation by basic fibroblast growth factor and granulocyte-colony stimulating factor *Oral Dis.* **21** 112–32
[33] Ishimatsu H, Kitamura C and Morotomi T *et al* 2009 Formation of dentinal bridge on surface of regenerated dental pulp in dentin defects by controlled release of fibroblast growth factor–2 from gelatin hydrogels *J. Endodontics* **35** 858–65
[34] Kim J, Park J C and Kim S H *et al* 2014 Treatment of FGF-2 on stem cells from inflamed dental pulp tissue from human deciduous teeth *Oral Dis.* **20** 191–204
[35] Baranova J, Büchner D, Götz W, Schulze M and Tobiasch E 2020 Tooth formation: are the hardest tissues of human body hard to regenerate? *Int. J. Mol. Sci.* **21** 4031
[36] Aparicio C, Gil F and Planell J 2002 Human-osteoblast proliferation and differentiation on grit-blasted and bioactive titanium for dental applications *J. Mater. Sci., Mater. Med.* **13** 1105–11
[37] Bengtsson U G and Hylander L D 2017 Increased mercury emissions from modern dental amalgams *Biometals* **30** 277–83
[38] Peng J-Y, Botelho M and Matinlinna J 2012 Silver compounds used in dentistry for caries management: a review *J. Dent.* **40** 531–41
[39] Swift E Jr 1989 *In vitro* caries-inhibitory properties of a silver cermet *J. Dent. Res.* **68** 1088–93
[40] Pissiotis E and Spngberg L 2000 Reaction of bony tissue to implanted silver glass ionomer and a reinforced zinc oxide-eugenol cement *Oral Surg. Oral Med. Oral Pathol. Oral Radiol. Endodontol.* **89** 623–9
[41] Sheikh F A, Barakat N A and Kanjwal M A *et al* 2010 Electrospun titanium dioxide nanofibers containing hydroxyapatite and silver nanoparticles as future implant materials *J. Mater. Sci., Mater. Med.* **21** 2551–9
[42] Denry I and Kelly J R 2008 State of the art of zirconia for dental applications *Dent. Mater.* **24** 299–307
[43] Malkondu Ö, Tinastepe N, Akan E and Kazazoğlu E 2016 An overview of monolithic zirconia in dentistry *Biotechnol. Biotechnol. Equip.* **30** 644–52
[44] Huang C-C, Narayanan R, Alapati S and Ravindran S 2016 Exosomes as biomimetic tools for stem cell differentiation: applications in dental pulp tissue regeneration *Biomaterials* **111** 103–15

[45] Rodríguez-Lozano F-J, Insausti C-L and Iniesta F *et al* 2012 Mesenchymal dental stem cells in regenerative dentistry *Med. Oral Patol. Oral Cir. Bucal* **17** e1062
[46] Nevins M, Camelo M, Nevins M L, Schenk R K and Lynch S E 2003 Periodontal regeneration in humans using recombinant human platelet-derived growth factor-BB (rhPDGF-BB) and allogenic bone *J. Periodontol.* **74** 1282–92
[47] Sigurdsson T J, Lee M B, Kubota K, Turek T J, Wozney J M and Wikesjö U M 1995 Periodontal repair in dogs: recombinant human bone morphogenetic protein-2 significantly enhances periodontal regeneration *J. Periodontol.* **66** 131–8
[48] Murakami S, Takayama S and Kitamura M *et al* 2003 Recombinant human basic fibroblast growth factor (bFGF) stimulates periodontal regeneration in class II furcation defects created in beagle dogs *J. Periodontal Res.* **38** 97–103
[49] Khan A, Hussain A and Sidra L *et al* 2017 Fabrication and *in vivo* evaluation of hydroxyapatite/carbon nanotube electrospun fibers for biomedical/dental application *Mater. Sci. Eng.* C **80** 387–96
[50] Khan W, Muntimadugu E, Jaffe M and Domb A J 2014 Implantable medical devices *Focal Controlled Drug Delivery* (Berlin: Springer), pp 33–59
[51] Ratner B D 2001 Replacing and renewing: synthetic materials, biomimetics, and tissue engineering in implant dentistry *J. Dent. Educ.* **65** 1340–7
[52] LaVenus S, Louarn G and Layrolle P 2010 Nanotechnology and dental implants *Int. J. Biomater.* **2010** 915327
[53] Inoue T and Matsuzaka K 2015 Surface modification of dental implant improves implant–tissue interface *Interface Oral Health Science 2014* (Berlin: Springer), pp 33–44
[54] Ananth H, Kundapur V, Mohammed H, Anand M, Amarnath G and Mankar S 2015 A review on biomaterials in dental implantology *Int. J. Biomed. Sci.: IJBS* **11** 113
[55] Love R and Jenkinson H 2002 Invasion of dentinal tubules by oral bacteria *Crit. Rev. Oral Biol. Med.* **13** 171–83
[56] Chiang Y-C, Lin H-P and Chang H-H *et al* 2014 A mesoporous silica biomaterial for dental biomimetic crystallization *ACS Nano* **8** 12502–13
[57] Zhang J, Wu R and Fan Y *et al* 2014 Antibacterial dental composites with chlorhexidine and mesoporous silica *J. Dent. Res.* **93** 1283–9
[58] Cheung H-Y, Lau K-T, Lu T-P and Hui D 2007 A critical review on polymer-based bio-engineered materials for scaffold development *Compos. Part B: Eng.* **38** 291–300
[59] Muzzarelli R A 2011 Chitosan composites with inorganics, morphogenetic proteins and stem cells, for bone regeneration *Carbohydr. Polym.* **83** 1433–45
[60] Muzzarelli R A 2009 Chitins and chitosans for the repair of wounded skin, nerve, cartilage and bone *Carbohydr. Polym.* **76** 167–82
[61] Dash M, Chiellini F, Ottenbrite R M and Chiellini E 2011 Chitosan—a versatile semi-synthetic polymer in biomedical applications *Prog. Polym. Sci.* **36** 981–1014
[62] Pallela R, Venkatesan J, Janapala V R and Kim S K 2012 Biophysicochemical evaluation of chitosan-hydroxyapatite-marine sponge collagen composite for bone tissue engineering *J. Biomed. Mater. Res.* A **100** 486–95
[63] Eniwumide J, Yuan H, Cartmell S, Meijer G and de Bruijn J D 2007 Ectopic bone formation in bone marrow stem cell seeded calcium phosphate scaffolds as compared to autograft and (cell seeded) allograft *Eur. Cells. Mater.* **14** 30–8

[64] Tanase C, Sartoris A, Popa M, Verestiuc L, Unger R and Kirkpatrick C 2013 *In vitro* evaluation of biomimetic chitosan–calcium phosphate scaffolds with potential application in bone tissue engineering *Biomed. Mater.* **8** 025002
[65] Cao X, Cai X, Chen R, Zhang H, Jiang T and Wang Y 2019 A thermosensitive chitosan-based hydrogel for sealing and lubricating purposes in dental implant system *Clin. Implant Dent. Relat. Res.* **21** 324–35
[66] Prasad S, Ehrensberger M, Gibson M P, Kim H and Monaco E A Jr 2015 Biomaterial properties of titanium in dentistry *J. Oral Biosci.* **57** 192–9
[67] Gaffney-Stomberg E 2019 The impact of trace minerals on bone metabolism *Biol. Trace Elem. Res.* **188** 26–34
[68] Yamaguchi M 1998 Role of zinc in bone formation and bone resorption *J. Trace Elem. Exp. Med.* **11** 119–35
[69] Zreiqat H, Howlett C and Zannettino A *et al* 2002 Mechanisms of magnesium-stimulated adhesion of osteoblastic cells to commonly used orthopaedic implants *J. Biomed. Mater. Res.* **62** 175–84
[70] Hu H, Zhang W, Qiao Y, Jiang X, Liu X and Ding C 2012 Antibacterial activity and increased bone marrow stem cell functions of Zn-incorporated TiO_2 coatings on titanium *Acta Biomater.* **8** 904–15
[71] Jin G, Cao H, Qiao Y, Meng F, Zhu H and Liu X 2014 Osteogenic activity and antibacterial effect of zinc ion implanted titanium *Colloids Surf.* B **117** 158–65
[72] Yu Y, Jin G, Xue Y, Wang D, Liu X and Sun J 2017 Multifunctions of dual Zn/Mg ion co-implanted titanium on osteogenesis, angiogenesis and bacteria inhibition for dental implants *Acta Biomater.* **49** 590–603
[73] Huang H-L, Chang Y-Y, Lai M-C, Lin C-R, Lai C-H and Shieh T-M 2010 Antibacterial TaN-Ag coatings on titanium dental implants *Surf. Coat. Technol.* **205** 1636–41
[74] Grech J and Antunes E 2019 Zirconia in dental prosthetics: a literature review *J. Mater. Res. Technol.* **8** 4956–64
[75] Nistor L, Grădinaru M and Rîcă R *et al* 2019 Zirconia use in dentistry-manufacturing and properties *Curr. Health Sci. J.* **45** 28
[76] Abd El-Ghany O S and Sherief A H 2016 Zirconia based ceramics, some clinical and biological aspects *Future Dent. J.* **2** 55–64
[77] Oliva J, Oliva X and Oliva J D 2008 Zirconia implants and all-ceramic restorations for the esthetic replacement of the maxillary central incisors *Eur. J. Esthetic Dent.* **3** 174–85
[78] Gautam C, Joyner J, Gautam A, Rao J and Vajtai R 2016 Zirconia based dental ceramics: structure, mechanical properties, biocompatibility and applications *Dalton Trans.* **45** 19194–215
[79] Scarano A, Di Carlo F, Quaranta M and Piattelli A 2003 Bone response to zirconia ceramic implants: an experimental study in rabbits *J. Oral Implantol.* **29** 8–12
[80] Priyadarsini S, Mukherjee S and Mishra M 2018 Nanoparticles used in dentistry: a review *J. Oral Biol. Craniofac. Res.* **8** 58–67
[81] Hamouda I M 2012 Current perspectives of nanoparticles in medical and dental biomaterials *J. Biomed. Res.* **26** 143–51
[82] Song W and Ge S 2019 Application of antimicrobial nanoparticles in dentistry *Molecules* **24** 1033
[83] Bennadi D 2014 Antimicrobial stewardship—an alarming call in dentistry *Int. J. Pharm. Sci.* **6** 46–9

[84] Heta S and Robo I 2018 The side effects of the most commonly used group of antibiotics in periodontal treatments *Med. Sci.* **6** 6
[85] Sánchez-López E, Gomes D and Esteruelas G *et al* 2020 Metal-based nanoparticles as antimicrobial agents: an overview *Nanomaterials* **10** 292
[86] Cao W, Zhang Y and Wang X *et al* 2018 Novel resin-based dental material with anti-biofilm activity and improved mechanical property by incorporating hydrophilic cationic copolymer functionalized nanodiamond *J. Mater. Sci., Mater. Med.* **29** 162
[87] Jiao Y, Tay F R, Niu L-n and Chen J-h 2019 Advancing antimicrobial strategies for managing oral biofilm infections *Int. J. Oral Sci.* **11** 1–11
[88] Rodrigues C T, De Andrade F and De Vasconcelos L *et al* 2018 Antibacterial properties of silver nanoparticles as a root canal irrigant against Enterococcus faecalis biofilm and infected dentinal tubules *Int. Endodontic J.* **51** 901–11
[89] Jadhav R D, Bhide S V, Prasad B and Shimpi J 2016 Applications of silver nanoparticles in prosthodontics: an overview *Eur. J. Prosthodont.* **4** 45
[90] Cheng L, Weir M D and Xu H H *et al* 2012 Antibacterial amorphous calcium phosphate nanocomposites with a quaternary ammonium dimethacrylate and silver nanoparticles *Dent. Mater.* **28** 561–72
[91] Rodrigues M C, Rolim W R and Viana M M *et al* 2020 Biogenic synthesis and antimicrobial activity of silica- coated silver nanoparticles for esthetic dental applications *J. Dent.* **96** 103327
[92] Heo D N, Ko W-K and Lee H R *et al* 2016 Titanium dental implants surface-immobilized with gold nanoparticles as osteoinductive agents for rapid osseointegration *J. Colloid Interface Sci.* **469** 129–37
[93] Salem D, Natto Z, Elangovan S and Karimbux N 2016 Usage of bone replacement grafts in periodontics and oral implantology and their current levels of clinical evidence—A systematic assessment *J. Periodontol.* **87** 872–9
[94] Misch C 2001 The importance of dental implants *Gen. Dent.* **49** 38–45
[95] Crisan L, Crisan B and Soritau O *et al* 2015 *In vitro* study of biocompatibility of a graphene composite with gold nanoparticles and hydroxyapatite on human osteoblasts *J. Appl. Toxicol.* **35** 1200–10
[96] Jadhav K, Rajeshwari H and Deshpande S *et al* 2018 Phytosynthesis of gold nanoparticles: characterization, biocompatibility, and evaluation of its osteoinductive potential for application in implant dentistry *Mater. Sci. Eng.* C **93** 664–70
[97] Rokaya D, Srimaneepong V, Sapkota J, Qin J, Siraleartmukul K and Siriwongrungson V 2018 Polymeric materials and films in dentistry: an overview *J. Adv. Res.* **14** 25–34
[98] Beyer M, Reichert J, Heurich E, Jandt K D and Sigusch B W 2010 Pectin, alginate and gum arabic polymers reduce citric acid erosion effects on human enamel *Dent. Mater.* **26** 831–9
[99] Beyer M, Reichert J, Sigusch B W, Watts D C and Jandt K D 2012 Morphology and structure of polymer layers protecting dental enamel against erosion *Dent. Mater.* **28** 1089–97
[100] Carvalho T and Lussi A 2014 Combined effect of a fluoride-, stannous-and chitosan-containing toothpaste and stannous-containing rinse on the prevention of initial enamel erosion–abrasion *J. Dent.* **42** 450–9
[101] Covarrubias C, Trepiana D and Corral C 2018 Synthesis of hybrid copper-chitosan nanoparticles with antibacterial activity against cariogenic Streptococcus mutans *Dental Mater. J.* **37** 379–84

[102] Liu Y J and Chen X 2003 Evaluations of the effective material properties of carbon nanotube-based composites using a nanoscale representative volume element *Mech. Mater.* **35** 69–81
[103] Guldi D M and Martín N 2010 *Carbon Nanotubes and Related Structures: Synthesis, Characterization, Functionalization, and Applications* (New York: Wiley)
[104] Zhang Y, Lim C T, Ramakrishna S and Huang Z-M 2005 Recent development of polymer nanofibers for biomedical and biotechnological applications *J. Mater. Sci., Mater. Med.* **16** 933–46
[105] Kai D, Tan M J and Prabhakaran M P *et al* 2016 Biocompatible electrically conductive nanofibers from inorganic-organic shape memory polymers *Colloids Surf.* B **148** 557–65
[106] Tetteh G, Khan A, Delaine-Smith R, Reilly G and Rehman I 2014 Electrospun polyurethane/hydroxyapatite bioactive Scaffolds for bone tissue engineering: the role of solvent and hydroxyapatite particles *J. Mech. Behav. Biomed. Mater.* **39** 95–110
[107] Tian M, Gao Y and Liu Y *et al* 2007 Bis-GMA/TEGDMA dental composites reinforced with electrospun nylon 6 nanocomposite nanofibers containing highly aligned fibrillar silicate single crystals *Polymer* **48** 2720–8
[108] Qasim S B and Rehman I U 2018 Application of nanomaterials in dentistry *Micro and Nanomanufacturing* vol. II (Berlin: Springer), pp 319–36
[109] Subramani K and Ahmed W 2012 *Nanobiomaterials in Clinical Dentistry* (Norwich, NY: William Andrew)
[110] Padovani G C, Feitosa V P and Sauro S *et al* 2015 Advances in dental materials through nanotechnology: facts, perspectives and toxicological aspects *Trends Biotechnol.* **33** 621–36
[111] Bhattarai G, Lee Y-H, Lee M-H, Park I-S and Yi H-K 2015 Insulin-like growth factor binding protein-3 affects osteogenic efficacy on dental implants in rat mandible *Mater. Sci. Eng.* C **55** 490–6
[112] Miyakoshi N, Richman C, Qin X, Baylink D J and Mohan S 1999 Effects of recombinant insulin-like growth factor-binding protein-4 on bone formation parameters in mice *Endocrinology* **140** 5719–28
[113] Kawai M and Rosen C J 2012 The insulin-like growth factor system in bone: basic and clinical implications *Endocrinol. Metab. Clin.* **41** 323–33
[114] Chard T 1994 Insulin-like growth factors and their binding proteins in normal and abnormal human fetal growth *Growth Regul.* **4** 91
[115] Raschke M, Wildemann B and Inden P *et al* 2002 Insulin-like growth factor-1 and transforming growth factor-β1 accelerates osteotomy healing using polylactide-coated implants as a delivery system: a biomechanical and histological study in minipigs *Bone* **30** 144–51
[116] Yilgor P, Hasirci N and Hasirci V 2010 Sequential BMP-2/BMP-7 delivery from polyester nanocapsules *J. Biomed. Mater. Res. Part* A **93** 528–36
[117] Saghiri M A, Asatourian A, Garcia-Godoy F and Sheibani N 2016 A new era considering inorganic trace elements and biological activity of dental biomaterials (angiogenic activity) *Acta Biomater. Odontol. Scand.* **2** 93–4
[118] Kargozar S, Ramakrishna S and Mozafari M 2019 Chemistry of biomaterials: future prospects *Curr. Opin. Biomed. Eng.* **10** 181–90
[119] Yun H-M, Kang S-K and Singh R K *et al* 2016 Magnetic nanofiber scaffold-induced stimulation of odontogenesis and pro-angiogenesis of human dental pulp cells through Wnt/MAPK/NF-κB pathways *Dent. Mater.* **32** 1301–11

[120] Shabestari Khiabani S, Farshbaf M, Akbarzadeh A and Davaran S 2017 Magnetic nanoparticles: preparation methods, applications in cancer diagnosis and cancer therapy *Artif. Cells Nanomed. Biotechnol.* **45** 6–17
[121] Xia Y, Chen H and Zhang F *et al* 2018 Injectable calcium phosphate scaffold with iron oxide nanoparticles to enhance osteogenesis via dental pulp stem cells *Artif. Cells Nanomed. Biotechnol.* **46** 423–33
[122] Liu W, Zhang G and Wu J *et al* 2020 Insights into the angiogenic effects of nanomaterials: mechanisms involved and potential applications *J. Nanobiotechnol.* **18** 1–22
[123] Alsuraifi A 2020 Metallic nanoparticles in dental biomaterials: a review *Int. J. Mol. Sci.* **3** 27–37
[124] Augustine R, Nethi S K, Kalarikkal N, Thomas S and Patra C R 2017 Electrospun polycaprolactone (PCL) scaffolds embedded with europium hydroxide nanorods (EHNs) with enhanced vascularization and cell proliferation for tissue engineering applications *J. Mater. Chem.* B **5** 4660–72
[125] Nethi S K, Veeriah V and Barui A K *et al* 2015 Investigation of molecular mechanisms and regulatory pathways of pro-angiogenic nanorods *Nanoscale* **7** 9760–70
[126] Barui A K, Veeriah V and Mukherjee S *et al* 2012 Zinc oxide nanoflowers make new blood vessels *Nanoscale* **4** 7861–9
[127] Patra C R and Barui A K 2013 Nanoflowers: a future therapy for cardiac and ischemic disease? *Nanomedicine* **8** 1735–8
[128] Barui A K, Nethi S K and Patra C R 2017 Investigation of the role of nitric oxide driven angiogenesis by zinc oxide nanoflowers *J. Mater. Chem.* B **5** 3391–403
[129] Nethi S K, Barui A K, Bollu V S, Rao B R and Patra C R 2017 Pro-angiogenic properties of terbium hydroxide nanorods: molecular mechanisms and therapeutic applications in wound healing *ACS Biomater. Sci. Eng.* **3** 3635–45
[130] Fan C, Joshi J and Li F *et al* 2020 Nanoparticle-mediated drug delivery for treatment of ischemic heart disease *Front. Bioeng. Biotechnol.* **8** 687
[131] Zhang J, Park Y-D and Bae W-J *et al* 2015 Effects of bioactive cements incorporating zinc-bioglass nanoparticles on odontogenic and angiogenic potential of human dental pulp cells *J. Biomater. Appl.* **29** 954–64
[132] Vemuri S K, Nethi S K, Banala R R, Goli P V S, Annapareddy V G R and Patra C R 2019 Europium hydroxide nanorods (EHNs) ameliorate isoproterenol-induced myocardial infarction: an *in vitro* and *in vivo* investigation *ACS Appl. Bio Mater.* **2** 1078–87
[133] Roy A, Nethi S K, Suganya N, Raval M, Chatterjee S and Patra C R 2020 Attenuation of cadmium-induced vascular toxicity by pro-angiogenic nanorods *Mater. Sci. Eng.* C **115** 111108
[134] Mukherjee S, Sriram P and Barui A K *et al* 2015 Graphene oxides show angiogenic properties *Adv. Healthcare Mater.* **4** 1722–32
[135] Ahtzaz S, Nasir M and Shahzadi L *et al* 2017 A study on the effect of zinc oxide and zinc peroxide nanoparticles to enhance angiogenesis-pro-angiogenic grafts for tissue regeneration applications *Mater. Des.* **132** 409–18
[136] Bose R J, Kim B J and Arai Y *et al* 2018 Bioengineered stem cell membrane functionalized nanocarriers for therapeutic targeting of severe hindlimb ischemia *Biomaterials* **185** 360–70
[137] Das S, Singh S and Dowding J M *et al* 2012 The induction of angiogenesis by cerium oxide nanoparticles through the modulation of oxygen in intracellular environments *Biomaterials* **33** 7746–55

[138] Kargozar S, Baino F, Hamzehlou S, Hamblin M R and Mozafari M 2020 Nanotechnology for angiogenesis: opportunities and challenges *Chem. Soc. Rev.* **49** 5008–57
[139] Kargozar S and Mozafari M 2018 Nanotechnology and nanomedicine: start small, think big *Mater. Today Proc.* **5** 15492–500
[140] Posada O M, Tate R and Grant M 2015 Toxicity of cobalt–chromium nanoparticles released from a resurfacing hip implant and cobalt ions on primary human lymphocytes *in vitro J. Appl. Toxicol.* **35** 614–22
[141] Lee Y J, Kim J and Oh J *et al* 2012 Ion-release kinetics and ecotoxicity effects of silver nanoparticles *Environ. Toxicol. Chem.* **31** 155–9
[142] Rathore M, Singh A and Pant V A 2012 The dental amalgam toxicity fear: a myth or actuality *Toxicol. Int.* **19** 81
[143] Bartold P M, Xiao Y, Lyngstaadas S P, Paine M L and Snead M L 2006 Principles and applications of cell delivery systems for periodontal regeneration *Periodontology 2000* **41** 123–35

Chapter 3

[1] Ring M E 1995 A thousand years of dental implants: a definitive history—part 1 *Compend. Contin. Educ. Dent.* **16** 1060–9
[2] Sullivan R M 2001 Implant dentistry and the concept of osseointegration: a historical perspective *J. Calif. Dent. Assoc.* **29** 737–45 PMID: 11806052
[3] Linkow L I and Cherchève R 1970 *Theories and Techniques of Oral Implantology* ed M Jones vol 1 (St. Louis: CV Mosby)
[4] Brånemark P I, Hansson B O, Adell R, Breine U, Lindström J, Hallén O and Ohman A 1977 Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period *Scand. J. Plast. Reconstr. Surg. Suppl.* **16** 1–132
[5] Bencharit S, Byrd W C, Altarawneh S, Hosseini B, Leong A, Reside G, Morelli T and Offenbacher S 2014 Development and applications of porous tantalum trabecular metal-enhanced titanium dental implants *Clin. Implant Dent. Relat. Res.* **16** 817–26
[6] Lee J W, Wen H B, Gubbi P and Romanos G E 2018 New bone formation and trabecular bone microarchitecture of highly porous tantalum compared to titanium implant threads: a pilot canine study *Clin. Oral Implant Res.* **29** 164–74
[7] Mendonça G, Mendonça D B, Aragão F J and Cooper L F 2008 Advancing dental implant surface technology–from micron- to nanotopography *Biomaterials* **29** 3822–35
[8] Prodanov L, Lamers E, Domanski M, Luttge R, Jansen J A and Walboomers X F 2013 The effect of nanometric surface texture on bone contact to titanium implants in rabbit tibia *Biomaterials* **34** 2920–7
[9] Liaw K, Delfini R H and Abrahams J J 2015 Dental implant complications *Semin. Ultrasound, CT, MR* **36** 427–33
[10] Mohamed Hamouda I 2012 Current perspectives of nanoparticles in medical and dental biomaterials *J. Biomed. Res.* **26** 143–51
[11] Bapat R A, Chaubal T V, Joshi C P, Bapat P R, Choudhury H, Pandey M, Gorain B and Kesharwani P 2018 An overview of application of silver nanoparticles for biomaterials in dentistry *Mater. Sci. Eng.* C **91** 881–98
[12] Wood N J, Jenkinson H F, Davis S A, Mann S, O'Sullivan D J and Barbour M E 2015 Chlorhexidine hexametaphosphate nanoparticles as a novel antimicrobial coating for dental implants *J. Mater. Sci. - Mater. Med.* **26** 201

[13] de Castro D T, do Nascimento C, Alves O L, de Souza Santos E, Agnelli J and Dos Reis A C 2018 Analysis of the oral microbiome on the surface of modified dental polymers *Arch. Oral Biol.* **93** 107–14

[14] Li Z, Sun J, Lan J and Qi Q 2016 Effect of a denture base acrylic resin containing silver nanoparticles on Candida albicans adhesion and biofilm formation *Gerodontology* **33** 209–16

[15] Bacali C *et al* 2020 Flexural strength, biocompatibility, and antimicrobial activity of a polymethyl methacrylate denture resin enhanced with graphene and silver nanoparticles *Clin. Oral Investig.* **24** 2713–25

[16] Mishra P and Tyagi S 2018 Surface analysis of gutta percha after disinfecting with sodium hypochlorite and silver nanoparticles by atomic force microscopy: an *in vitro* study *Dent. Res. J.* **15** 242–7

[17] Ioannidis K, Niazi S, Mylonas P, Mannocci F and Deb S 2019 The synthesis of nano silver-graphene oxide system and its efficacy against endodontic biofilms using a novel tooth model *Dent. Mater.* **35** 1614–29

[18] Suzuki T, Gallego J, Assunção W G, Briso A and Dos Santos P H 2019 Influence of silver nanoparticle solution on the mechanical properties of resin cements and intrarradicular dentin *PLoS One* **14** e0217750

[19] Vazquez-Garcia F, Tanomaru-Filho M, Chávez-Andrade G M, Bosso-Martelo R, Basso-Bernardi M I and Guerreiro-Tanomaru J M 2016 Effect of silver nanoparticles on physicochemical and antibacterial properties of calcium silicate cements *Braz. Dent. J.* **27** 508–14

[20] Samiei M, Ghasemi N, Asl-Aminabadi N, Divband B, Golparvar-Dashti Y and Shirazi S 2017 Zeolite-silver-zinc nanoparticles: biocompatibility and their effect on the compressive strength of mineral trioxide aggregate *J. Clin. Exp. Dent.* **9** e356–60

[21] Li P, Tong Z, Huo L, Yang F and Su W 2016 Antibacterial and biological properties of biofunctionalized nanocomposites on titanium for implant application *J. Biomater. Appl.* **31** 205–14

[22] Pokrowiecki R, Zaręba T, Szaraniec B, Pałka K, Mielczarek A, Menaszek E and Tyski S 2017 *In vitro* studies of nanosilver-doped titanium implants for oral and maxillofacial surgery *Int. J. Nanomed.* **12** 4285–97

[23] Lampé I *et al* 2019 Investigation of silver nanoparticles on titanium surface created by ion implantation technology *Int. J. Nanomed.* **14** 4709–21

[24] Salaie R N, Besinis A, Le H, Tredwin C and Handy R D 2020 The biocompatibility of silver and nanohydroxyapatite coatings on titanium dental implants with human primary osteoblast cells *Mater. Sci. Eng.* C **107** 110210

[25] Zhou W, Jia Z, Xiong P, Yan J, Li Y, Li M, Cheng Y and Zheng Y 2017 Bioinspired and biomimetic AgNPs/gentamicin-embedded silk fibroin coatings for robust antibacterial and osteogenetic applications *ACS Appl. Mater. Interfaces* **9** 25830–46

[26] Hernández-Gómora A E, Lara-Carrillo E, Robles-Navarro J B, Scougall-Vilchis R J, Hernández-López S, Medina-Solís C E and Morales-Luckie R A 2017 Biosynthesis of silver nanoparticles on orthodontic elastomeric modules: evaluation of mechanical and antibacterial properties *Molecules* 22 1407

[27] Espinosa-Cristóbal L F, López-Ruiz N and Cabada-Tarín D *et al* 2018 Antiadherence and antimicrobial properties of silver nanoparticles against streptococcus mutants on brackets and wires used for orthodontic treatments *J. Nanomater.* **2018** 9248527

[28] Halkai K R, Mudda J A, Shivanna V, Rathod V and Halkai R S 2017 Biosynthesis, characterization and antibacterial efficacy of silver nanoparticles derived from endophytic fungi against *P. gingivalis J. Clin. Diag. Res.: JCDR* **11** ZC92–6

[29] Panáček A *et al* 2016 Silver nanoparticles strongly enhance and restore bactericidal activity of inactive antibiotics against multiresistant *Enterobacteriaceae Colloids Surf.* B **142** 392–9

[30] Singh P *et al* 2018 *In vitro* anti-inflammatory activity of spherical silver nanoparticles and monodisperse hexagonal gold nanoparticles by fruit extract of *Prunus serrulata*: a green synthetic approach *Artif. Cells Nanomed. Biotechnol.* **46** 2022–32

[31] Sugiharti R, Widyasar E, Rusminah N and Mustika I 2019 Evaluation of silver nanoparticles addition in periodontal dressing for wound tissue healing by 99mTc-ciprofloxacin *J. Young Pharm.* **11** 17–20

[32] Dizaj S M, Barzegar-Jalali M, Zarrintan M H, Adibkia K and Lotfipour F 2015 Calcium carbonate nanoparticles as cancer drug delivery system *Expert Opin. Drug Deliv.* **12** 1649–60

[33] Mehdipour M, TaghaviZenouz A, Bahramian A, Yazdani J, Pouralibaba F and Sadr K 2010 Comparison of the effect of mouthwashes with and without zinc and fluocinolone on the healing process of erosive oral *Lichen planus J. Dent. Res. Dent. Clin. Dent. Prosp.* **4** 25–8

[34] Memarzadeh K, Sharili A S, Huang J, Rawlinson S C and Allaker R P 2015 Nanoparticulate zinc oxide as a coating material for orthopedic and dental implants *J. Biomed. Mater. Res.* A **103** 981–9

[35] Anu K, Maleeka Begum S, Rajesh G and Renuka Devi K 2016 Wet biochemical synthesis of copper oxide nanoparticles coated on titanium dental implants *Int. J. Adv. Res. Sci. Eng. Technol.* **3** 1191–94

[36] Varoni E, Tarce M, Lodi G and Carrassi A 2012 Chlorhexidine (CHX) in dentistry: state of the art *Minerva Stomatol.* **61** 399–419

[37] Safarabadi M, Khansari N and Rezaei A 2014 An experimental investigation of HA/AL_2O_3 nanoparticles on mechanical properties of restoration materials *Eng. Solid Mech.* **2** 173–82

[38] Samiei M, Aghazadeh M, Lotfi M, Shakoei S, Aghazadeh Z and Vahid Pakdel S M 2013 Antimicrobial efficacy of mineral trioxide aggregate with and without silver nanoparticles *Iran. Endod. J.* **8** 166–70

[39] Lotfi M, Vosoughhosseini S, Ranjkesh B, Khani S, Saghiri M and Zand V 2011 Antimicrobial efficacy of nanosilver, sodium hypochlorite and chlorhexidine gluconate against *Enterococcus faecalis Afr. J. Biotechnol.* **10** 6799–803

[40] Flores C Y, Diaz C, Rubert A, Benítez G A, Moreno M S, Fernández Lorenzo de Mele M A, Salvarezza R C, Schilardi P L and Vericat C 2010 Spontaneous adsorption of silver nanoparticles on Ti/TiO_2 surfaces. Antibacterial effect on *Pseudomonas aeruginosa J. Colloid Interface Sci.* **350** 402–8

[41] Zhao L, Wang H, Huo K, Cui L, Zhang W, Ni H, Zhang Y, Wu Z and Chu P K 2011 Antibacterial nano-structured titania coating incorporated with silver nanoparticles *Biomaterials* **32** 5706–16

[42] Yamamoto K, Ohashi S, Aono M, Kokubo T, Yamada I and Yamauchi J 1996 Antibacterial activity of silver ions implanted in SiO_2 filler on oral streptococci *Dent. Mater.* **12** 227–9

[43] Meachim G and Williams D F 1973 Changes in nonosseous tissue adjacent to titanium implants *J. Biomed. Mater. Res.* **7** 555–72

[44] Galante J O, Lemons J, Spector M, Wilson P D Jr and Wright T M 1991 The biologic effects of implant materials *J. Orthop. Res.* **9** 760–75

[45] Martini D *et al* 2003 Detachment of titanium and fluorohydroxyapatite particles in unloaded endosseous implants *Biomaterials* **24** 1309–16
[46] Franchi M, Bacchelli B, Martini D, Pasquale V D, Orsini E, Ottani V, Fini M, Giavaresi G, Giardino R and Ruggeri A 2004 Early detachment of titanium particles from various different surfaces of endosseous dental implants *Biomaterials* **25** 2239–46
[47] Ducheyne P, Willems G, Martens M and Helsen J 1984 *In vivo* metal-ion release from porous titanium-fiber material *J. Biomed. Mater. Res.* **18** 293–308
[48] Ferguson A B J, Akahoshi Y, Laing P G and Hodge E S 1962 Characteristics of trace ions released from embedded metal implants in the rabbit *JBJS* **44** 323–36
[49] Noronha V T, Paula A J, Durán G, Galembeck A, Cogo-Müller K, Franz-Montan M and Durán N 2017 Silver nanoparticles in dentistry *Dent. Mater.* **33** 1110–26
[50] Beer C, Foldbjerg R, Hayashi Y, Sutherland D S and Autrup H 2011 Toxicity of silver nanoparticles—nanoparticle or silver ion? *Toxicol. Lett.* **208** 286–92
[51] Liao C, Jin Y, Li Y and Tjong S C 2020 Interactions of zinc oxide nanostructures with mammalian cells: cytotoxicity and photocatalytic toxicity *Int. J. Mol. Sci.* **21** 6305
[52] Biola-Clier M, Beal D, Caillat S, Libert S, Armand L, Herlin-Boime N, Sauvaigo S, Douki T and Carriere M 2017 Comparison of the DNA damage response in BEAS-2B and A549 cells exposed to titanium dioxide nanoparticles *Mutagenesis* **32** 161–72
[53] Li L, Pan H, Tao J, Xu X, Mao C, Gu X and Tang R 2008 Repair of enamel by using hydroxyapatite nanoparticles as the building blocks *J. Mater. Chem.* **18** 4079–84
[54] Tang N, Li Y P, Kurosu S, Matsumoto H, Koizumi Y and Chiba A 2011 Interfacial reactions between molten Al and a Co–Cr–Mo alloy with and without oxidation treatment *Corros. Sci.* **53** 4324–26
[55] Dorkhan M, Hall J, Uvdal P, Sandell A, Svensäter G and Davies J R 2014 Crystalline anatase-rich titanium can reduce adherence of oral streptococci *Biofouling* **30** 751–9
[56] Rutkowski J L, Camm D P and El Chaar E 2020 AAID white paper: management of the dental implant patient during the COVID-19 pandemic and beyond *J. Oral Implantol.* **46** 454–66

Chapter 4

[1] Aminu N, Bello I, Umar N M, Tanko N, Aminu A and Audu M M 2020 The influence of nanoparticulate drug delivery systems in drug therapy *J. Drug Deliv. Sci. Technol.* **60** 101961
[2] Florence A T 2009 Pharmaceutical aspects of nanotechnology *Modern Pharmaceutics* ed A T Florence and J Siepmann 5th edn (New York: Informa Healthcare USA, Inc.), pp 453–92
[3] Zafar M S, Khurshid Z, Najeeb S, Zohaib S and Rehman I U 2017 Therapeutic applications of nanotechnology in dentistry *Nanostructures for Oral Medicine* (Amsterdam: Elsevier), pp 833–62
[4] Williams R O III and Vaughn J M 2007 Nanoparticle engineering *Encyclopedia of Pharmaceutical Technology* ed J Swarbrick 3rd edn (New York: Informa Healthcare USA, Inc.), pp 2384–98
[5] Perrie Y 2013 Pharmaceutical nanotechnology and nanomedicines *Aulton's Pharmaceutics the Design and Manufacture of Medicines* ed M E Aulton and K M G Taylor 4th edn (London: Elsevier), pp 777–96
[6] AlKahtani R N 2018 The implications and applications of nanotechnology in dentistry: a review *Saudi Dent. J.* **30** 107–16

[7] 2021 United States Budget https://nano.gov/2021budgetsupplement)
[8] Narang R S and Narang J K 2015 Nanomedicines for dental applications-scope and future perspective *Int. J. Pharm. Investig.* **5** 121–3
[9] Abiodun-Solanke I, Ajayi D and Arigbede A 2014 Nanotechnology and its application in dentistry *Ann. Med. Health Sci. Res.* **4** 171–7
[10] Hua S, de Matos M B C, Metselaar J M and Storm G 2018 Current trends and challenges in the clinical translation of nanoparticulate nanomedicines: pathways for translational development and commercialization *Front. Pharmacol.* **9** 1–14
[11] Kankala R K 2018 Nanomedicine: the next-generation therapeutics *J. Nanomed.* **2** 1–5
[12] Kirtane A R, Wong H L, Guru B R, Lis L G, Georg G I and Gurvich V J *et al* 2015 Reformulating tylocrebrine in epidermal growth factor receptor targeted polymeric nanoparticles improves its therapeutic index *Mol. Pharm.* **12** 2912–23
[13] Aminu N and Toh S M 2017 Applicability of nanoparticles-hydrogel composite in treating periodontal diseases and beyond. *Asian J. Pharm. Clin. Res.* **10** 65–70
[14] Khurshid Z, Zafar M, Qasim S, Shahab S, Naseem M and AbuReqaiba A 2015 Advances in nanotechnology for restorative dentistry *Materials* **8** 717–31
[15] Adeola H A, Sabiu S, Adekiya T A, Aruleba R T, Aruwa C E and Oyinloye B E 2020 Prospects of nanodentistry for the diagnosis and treatment of maxillofacial pathologies and cancers *Heliyon* **6** e04890
[16] Aminu N, Chan S Y and Toh S M 2018 Formulation design and optimization of triclosan loaded nanoparticles for enhanced drug delivery across gingival sulcus by Resolution IV modeling of Design-Expert® *J. Biomed. Clin. Sci.* **3** 83–90
[17] Aminu N, Chan S Y, Khan N H and Toh S M 2018 Concurrent determination of triclosan and flurbiprofen by high-performance liquid chromatography in simulated saliva and its application in dental nanogel formulation *Acta Chromatogr.* **30** 219–24
[18] Pramod K, Aminu N and Ali J 2014 Targeted drug delivery systems for the treatment of periodontal infections *Biotechnology Volume 8: Novel Drug Delivery* ed B Singh, O P Katare and J N Govil (Houston, TX: Studium Press LLC), pp 97–128
[19] Foong L K, Foroughi M M, Mirhosseini A F, Safaei M, Jahani S and Mostafavi M *et al* 2020 Applications of nano-materials in diverse dentistry regimes *RSC Adv.* **10** 15430–60
[20] Aminu N, Yam M-F, Chan S-Y, Bello I, Umar N M and Nuhu T *et al* 2020 The evaluation of healing effect of triclosan and flurbiprofen-loaded nanogels in experimental periodontitis in rats by morphometric analysis *Saudi Dent. J.* in press
[21] Amini H, Shenkin J D and Chi D L 2019 Dental public health issues in pediatric dentistry *Pediatric Dentistry* (Amsterdam: Elsevier), pp 159–68
[22] Gokulgandhi M R, Patel A, Cholkar K, Barot M and Mitra A K 2014 Nanoscale drug delivery systems *Advanced Drug Delivery* ed A K Mitra, C H Lee and K Cheng (Hoboken, NJ: Wiley), pp 140–55
[23] Pelaz B, Alexiou C, Alvarez-Puebla R A, Alves F, Andrews A M and Ashraf S *et al* 2017 Diverse applications of nanomedicine *ACS Nano.* **11** 2313–81
[24] Elkassas D and Arafa A 2017 The innovative applications of therapeutic nanostructures in dentistry *Nanomed. Nanotechnol. Biol. Med.* **13** 1543–62
[25] Hubbs A F, Sargent L M, Porter D W, Sager T M, Chen B T and Frazer D G *et al* 2013 Nanotechnology: toxicologic pathology *Toxicol. Pathol.* **41** 395–409
[26] Ledet G and Mandal T K 2012 Nanomedicine: emerging therapeutics for the 21st century https://uspharmacist.com/article/nanomedicine-emerging-therapeutics-for-the-21st-century)

[27] Caruthers S D, Wickline S A and Lanza G M 2007 Nanotechnological applications in medicine *Curr. Opin. Biotechnol.* **18** 26–30
[28] Odiba A, Ottah V, Ottah C, Anunobi O, Ukegbu C and Edeke A *et al* 2017 Therapeutic nanomedicine surmounts the limitations of pharmacotherapy *Open Med.* **12** 271–87
[29] Chandra Hembram K, Prabha S, Chandra R, Ahmed B and Nimesh S 2016 Advances in preparation and characterization of chitosan nanoparticles for therapeutics. *Artif. Cells Nanomed. Biotechnol.* **44** 305–14
[30] Raura N, Garg A, Arora A and Roma M 2020 Nanoparticle technology and its implications in endodontics: a review *Biomater. Res.* **24** 21
[31] Najeeb S, Khurshid Z, Agwan A, Zafar M, Alrahabi M and Bin Qasim S *et al* 2016 Dental applications of nanodiamonds *Sci. Adv. Mater.* **8** 2064–70
[32] Fernandez C C, Sokolonski A R, Fonseca M S, Stanisic D, Araújo D B and Azevedo V *et al* 2021 Applications of silver nanoparticles in dentistry: advances and technological innovation *Int. J. Mol. Sci.* **22** 1–21
[33] Adam R Z and Khan S B 2021 Antimicrobial efficacy of silver nanoparticles against *Candida albicans*: a systematic review protocol *PLoS One* **16** 1–13
[34] Fattah Z, Jowkar Z and Rezaeian S 2021 Microshear bond strength of nanoparticle-incorporated conventional and resin-modified glass ionomer to caries-affected dentin. *Int. J. Dent.* 2021 1–8
[35] Bouropoulos N and Moradian–Oldak J 2003 Analysis of hydroxyapatite surface coverage by amelogenin nanospheres following the langmuir model for protein adsorption *Calcif. Tissue Int.* **72** 599–603
[36] Vasiliu S, Racovita S, Gugoasa I A, Lungan M-A, Popa M and Desbrieres J 2021 The benefits of smart nanoparticles in dental applications *Int. J. Mol. Sci.* **22** 1–23
[37] Aminu N, Baboota S, Pramod K, Singh M, Dang S and Ansari S H *et al* 2013 Development and evaluation of triclosan loaded poly-ε-caprolactone nanoparticulate system for the treatment of periodontal infections *J. Nanoparticle Res.* **15** 2075
[38] Aminu N, Chan S Y and Toh S M 2018 Development and validation of a stability-indicating HPLC-UV method for the simultaneous determination of flurbiprofen and triclosan in dental nanogel formulations *J. Phys. Sci.* **29** 1–7
[39] Toledano M, Osorio R, Osorio E, Medina-Castillo A L, Toledano-Osorio M and Aguilera F S 2017 Ions-modified nanoparticles affect functional remineralization and energy dissipation through the resin-dentin interface *J. Mech. Behav. Biomed. Mater.* **68** 62–79
[40] Moradpoor H, Safaei M, Mozaffari H R, Sharifi R, Imani M M and Golshah A *et al* 2021 An overview of recent progress in dental applications of zinc oxide nanoparticles *RSC Adv.* **11** 21189–206
[41] Akram Z, Aati S, Ngo H and Fawzy A 2021 pH-dependent delivery of chlorhexidine from PGA grafted mesoporous silica nanoparticles at resin-dentin interface *J. Nanobiotechnol.* **19** 1–16
[42] Enan E T, Ashour A A, Basha S, Felemban N H and Gad El-Rab S M F 2021 Antimicrobial activity of biosynthesized silver nanoparticles, amoxicillin, and glass-ionomer cement against *Streptococcus mutans* and *Staphylococcus aureus Nanotechnology* **32** 215101
[43] Kim T-H, Eltohamy M, Kim M, Perez R A, Kim J-H and Yun Y-R *et al* 2014 Therapeutic foam scaffolds incorporating biopolymer-shelled mesoporous nanospheres with growth factors *Acta Biomater.* **10** 2612–21

[44] Nakashima S, Yoshie M, Sano H and Bahar A 2009 Effect of a test dentifrice containing nano-sized calcium carbonate on remineralization of enamel lesions *in vitro J. Oral Sci.* **51** 69–77

[45] Priyadarsini S, Mukherjee S and Mishra M 2018 Nanoparticles used in dentistry: a review *J. Oral Biol. Craniofac. Res.* **8** 58–67

[46] Aminu N, Chan S Y, Yam M F and Toh S M 2019 A dual-action chitosan-based nanogel system of triclosan and flurbiprofen for localised treatment of periodontitis *Int. J. Pharm.* **570** 118659

[47] Bottino M C, Yassen G H, Platt J A, Labban N, Windsor L J and Spolnik K J *et al* 2015 A novel three-dimensional scaffold for regenerative endodontics: materials and biological characterizations *J. Tissue Eng. Regen. Med.* **9** E116–23

[48] Zafar M, Najeeb S, Khurshid Z, Vazirzadeh M, Zohaib S and Najeeb B *et al* 2016 Potential of electrospun nanofibers for biomedical and dental applications *Materials* **9** 1–21

[49] Mohandesnezhad S, Pilehvar-Soltanahmadi Y, Alizadeh E, Goodarzi A, Davaran S and Khatamian M *et al* 2020 *In vitro* evaluation of Zeolite-nHA blended PCL/PLA nanofibers for dental tissue engineering *Mater. Chem. Phys.* **252** 123152

[50] Sanaei-rad P, Jamshidi D, Adel M and Seyedjafari E 2021 Electrospun poly(L-lactide) nanofibers coated with mineraltrioxide aggregate enhance odontogenic differentiation ofdental pulp stem cells *Polym. Adv. Technol.* **32** 402–10

[51] Ainola M, Tomaszewski W, Ostrowska B, Wesolowska E, Wagner H D and Swieszkowski W *et al* 2016 A bioactive hybrid three-dimensional tissue-engineering construct for cartilage repair *J. Biomater. Appl.* **30** 873–85

[52] Tang J, Han Y, Zhang F, Ge Z, Liu X and Lu Q 2015 Buccal mucosa repair with electrospun silk fibroin matrix in a rat model *Int. J. Artif. Organs* **38** 105–12

[53] Joshi D, Garg T, Goyal A and Rath G 2015 Development and characterization of novel medicated nanofibers against periodontitis *Curr. Drug Deliv.* **12** 564–77

[54] Ranjbar-Mohammadi M, Zamani M, Prabhakaran M P, Bahrami S H and Ramakrishna S 2016 Electrospinning of PLGA/gum tragacanth nanofibers containing tetracycline hydrochloride for periodontal regeneration *Mater. Sci. Eng.* C **58** 521–31

[55] Qasim S B, Najeeb S, Delaine-Smith R M, Rawlinson A and Ur Rehman I 2017 Potential of electrospun chitosan fibers as a surface layer in functionally graded GTR membrane for periodontal regeneration *Dent. Mater.* **33** 71–83

[56] Samprasit W, Kaomongkolgit R, Sukma M, Rojanarata T, Ngawhirunpat T and Opanasopit P 2015 Mucoadhesive electrospun chitosan-based nanofibre mats for dental caries prevention *Carbohydr. Polym.* **117** 933–40

[57] Aadil K R, Nathani A, Sharma C S, Lenka N and Gupta P 2019 Investigation of poly (vinyl) alcohol-gellan gum based nanofiber as scaffolds for tissue engineering applications *J. Drug Deliv. Sci. Technol.* **54** 101276

[58] Zinger A, Adir O, Alper M, Simon A, Poley M and Tzror C *et al* 2018 Proteolytic nanoparticles replace a surgical blade by controllably remodeling the oral connective tissue *ACS Nano.* **12** 1482–90

[59] Ghazal M, Albashaireh Z S and Kern M 2008 Wear resistance of nanofilled composite resin and feldspathic ceramic artificial teeth *J. Prosthet. Dent.* **100** 441–8

[60] Nagar N and Vaz A C 2013 Comparison of shear bond strengths of conventional orthodontic composite and nano-ceramic restorative composite: an *in vitro* study *Indian J. Dent. Res.* **24** 713–8

[61] Yang Y, Xu Z, Guo Y, Zhang H, Qiu Y and Li J *et al* 2021 Novel core–shell CHX/ACP nanoparticles effectively improve the mechanical, antibacterial and remineralized properties of the dental resin composite *Dent. Mater.* **37** 636–47

[62] Mutar M A and Mahdi M S 2019 Synthesis and characterization of novel nanocomposites with nanofillers particles and their applications as dental materials *Period. Eng. Nat. Sci.* **7** 1512–38

[63] Zaki D Y, Safwat E M, Nagi S M, Salem H N, Hamdy T M and Moharam L M *et al* 2021 A novel dental re-mineralizing blend of hydroxyethyl-cellulose and cellulose nanofibers oral film loaded with nepheline apatite glass: preparation, characterization and *in vitro* evaluation of re-mineralizing effect *Carbohydr. Polym. Technol. Appl.* **2** 100035

[64] Yushau U S, Almofeez L and Bozkurt A 2020 Novel polymer nanocomposites comprising triazole functional silica for dental application *Silicon* **12** 109–16

[65] Yushau U S, Almofeez L and Bozkurt A 2019 Aminotriazole functional silica incorporated BisGMA/TEGDMA resins as dental nanocomposites *Polym. Polym. Compos.* **27** 488–95

[66] Jaymand M, Lotfi M, Barar J, Eskandani M and Maleki H 2018 Novel dental nanocomposites: fabrication and investigation of their physicochemical, mechanical and biological properties *Bull. Mater. Sci.* **41** 84

[67] Elshereksi N, Muchtar A and Azhari C 2021 Effects of nanobarium titanate on physical and mechanical properties of poly(methyl methacrylate) denture base nanocomposites *Polym. Polym. Compos.* **29** 484–96

[68] Kanaparthy R and Kanaparthy A 2011 The changing face of dentistry: nanotechnology *Int. J. Nanomed.* **6** 2799–804

[69] Kasaj A, Willershausen B, Reichert C, Röhrig B, Smeets R and Schmidt M 2008 Ability of nanocrystalline hydroxyapatite paste to promote human periodontal ligament cell proliferation *J. Oral Sci.* **50** 279–85

[70] Gupta K C, Haider A, Choi Y and Kang I 2014 Nanofibrous scaffolds in biomedical applications *Biomater. Res.* **18** 5

[71] Wehlage D, Blattner H, Mamun A, Kutzli I, Diestelhorst E and Rattenholl A *et al* 2020 Cell growth on electrospun nanofiber mats from polyacrylonitrile (PAN) blends *AIMS Bioeng.* **7** 43–54

[72] Kamsani N H, Haris M S, Pandey M, Taher M and Rullah K 2021 Biomedical application of responsive 'smart' electrospun nanofibers in drug delivery system: A minireview *Arab. J. Chem.* **14** 103199

[73] Liang D, Hsiao B S and Chu B 2007 Functional electrospun nanofibrous scaffolds for biomedical applications *Adv. Drug. Deliv. Rev.* **59** 1392–412

[74] Perán M, García M A, López-Ruiz E, Bustamante M, Jiménez G and Madeddu R *et al* 2012 Functionalized nanostructures with application in regenerative medicine *Int. J. Mol. Sci.* **13** 3847–886

[75] Baghaban-Eslaminejad M, Oryan A, Kamali A and Moshiri A 2017 The role of nanomedicine, nanotechnology, and nanostructures on oral bone healing, modeling, and remodeling *Nanostructures for Oral Medicine* (Amsterdam: Elsevier), pp 777–832

[76] He X, Cheng L, Zhang X, Xiao Q, Zhang W and Lu C 2015 Tissue engineering scaffolds electrospun from cotton cellulose *Carbohydr. Polym.* **115** 485–93

[77] Ardeshirzadeh B, Anaraki N A, Irani M, Rad L R and Shamshiri S 2015 Controlled release of doxorubicin from electrospun PEO/chitosan/graphene oxide nanocomposite nanofibrous scaffolds *Mater. Sci. Eng.* C **48** 384–90

[78] Qasim S B, Zafar M S, Najeeb S, Khurshid Z, Shah A H and Husain S *et al* 2018 Electrospinning of chitosan-based solutions for tissue engineering and regenerative medicine *Int. J. Mol. Sci.* **19** 1–26
[79] Cavalcanti B N, Zeitlin B D and Nör J E 2013 A hydrogel scaffold that maintains viability and supports differentiation of dental pulp stem cells *Dent. Mater.* **29** 97–102
[80] Park C H, Rios H F, Jin Q, Bland M E, Flanagan C L and Hollister S J *et al* 2010 Biomimetic hybrid scaffolds for engineering human tooth-ligament interfaces *Biomaterials* **31** 5945–52
[81] Zafar M S, Alnazzawi A A, Alrahabi M, Fareed M A, Najeeb S and Khurshid Z 2019 Nanotechnology and nanomaterials in dentistry *Advanced Dental Biomaterials* (Amsterdam: Elsevier), pp 477–505
[82] Saunders S A 2009 Current practicality of nanotechnology in dentistry. Part 1: Focus on nanocomposite restoratives and biomimetics *Clin. Cosmet. Investig. Dent.* **1** 47–61
[83] Kukulka E C, Sato T P, Archangelo K C, Santos J D, De Souza J R and Borges A L S 2021 Development of electrospun-based polyetherimide fibers and diameter analysis for potential use in dental materials *Brazil. Dent. Sci.* **24** 1–5
[84] Feng L, Li S, Li H, Zhai J, Song Y and Jiang L *et al* 2002 Super-hydrophobic surface of aligned polyacrylonitrile nanofibers *Angew Chem. Int. Ed.* **41** 1221–3
[85] Bhattarai R, Bachu R, Boddu S and Bhaduri S 2018 Biomedical applications of electrospun nanofibers: drug and nanoparticle delivery *Pharmaceutics.* **11** 5
[86] Nugroho D A, Nuryono W, Asmara W, Rahmasari A and Dyota E 2021 Tensile strength and microscopic adhesion observation of dental composite restorative material manufactured from Sisal nanofiber as filler *Adv. Heal. Sci. Res.* **33** 268–72
[87] Antonova O Y, Kochetkova O Y and Shlyapnikov Y M 2021 ECM-mimetic nylon nanofiber scaffolds for neurite growth guidance *Nanomaterials* **11** 516
[88] Chaughule R, Raorane D, Pednekar S and Dashaputra R 2018 Nanocomposites and their use in dentistry *Dental Applications of Nanotechnology* (Cham: Springer), pp 59–79
[89] Sen M 2020 Nanocomposite materials *Nanotechnology and the Environment* (London: IntechOpen), pp 1–12
[90] Nikolaidis A K, Koulaouzidou E A, Gogos C and Achilias D S 2021 Synthesis of novel dental nanocomposite resins by incorporating polymerizable, quaternary ammonium silane-modified silica nanoparticles *Polymers* **13** 1682
[91] Alamgir M, Mallick A and Nayak G C 2021 Mechanical and thermal behavior of pHEMA and pHEMA nanocomposites targeting for dental materials *Appl. Nanosci.* **11** 1257–65
[92] Wang W, Sun X, Huang L, Gao Y, Ban J and Shen L *et al* 2014 Structure–property relationships in hybrid dental nanocomposite resins containing monofunctional and multifunctional polyhedral oligomeric silsesquioxanes *Int. J. Nanomed.* **9** 841–52
[93] Nikolaidis A K, Koulaouzidou E A, Gogos C and Achilias D S 2019 Synthesis and characterization of dental nanocomposite resins filled with different clay nanoparticles *Polymers* **11** 730
[94] Gawdzinska K, Paszkiewicz S, Piesowicz E, Bryll K, Irska I and Lapis A *et al* 2019 Preparation and characterization of hybrid nanocomposites for dental applications *Appl. Sci.* **9** 1381
[95] Calisir M 2019 Nanotechnology in dentistry: past, present, and future *Nanomaterials for Regenerative Medicine Stem Cell Biology and Regenerative Medicine* (Cham: Springer), pp 197–216

[96] Wilson D J 2018 https://news-medical.net/health/What-is-Nanodentistry.aspx
[97] Pokrowiecki R, Pałka K and Mielczarek A 2018 Nanomaterials in dentistry: a cornerstone or a black box? *Nanomedicine* **13** 639–67
[98] Dogra S, Gupta A, Goyal V, Chib A S and Kataria V 2020 Recent trends, therapeutic applications, and future trends of nanomaterials in dentistry *Nanomaterials in Diagnostic Tools and Devices* (Amsterdam: Elsevier), pp 257–92
[99] Moezizadeh M 2013 Future of dentistry, nanodentistry, ozone therapy and tissue engineering *J. Dev. Biol. Tissue Eng.* **5** 1–6
[100] Freitas R A 2005 Nanotechnology, nanomedicine and nanosurgery *Int. J. Surg.* **3** 243–6
[101] Sousa M G C, Maximiano M R, Costa R A, Rezende T M B and Franco O L 2020 Nanofibers as drug-delivery systems for infection control in dentistry *Expert Opin. Drug. Deliv.* **17** 919–30
[102] Barot T, Rawtani D and Kulkarni P 2021 Nanotechnology-based materials as emerging trends for dental applications *Rev. Adv. Mater. Sci.* **60** 173–89
[103] Makvandi P, Josic U, Delfi M, Pinelli F, Jahed V and Kaya E *et al* 2021 Drug delivery (nano)platforms for oral and dental applications: tissue regeneration, infection control, and cancer management *Adv. Sci.* **8** 1–28
[104] Abou Neel E A, Bozec L, Perez R A, Kim H-W and Knowles J C 2015 Nanotechnology in dentistry: prevention, diagnosis, and therapy *Int. J. Nanomed.* **10** 6371–94
[105] Neves P B A, das, Agnelli J A M, Kurachi C and Souza CWO de 2014 Addition of silver nanoparticles to composite resin: effect on physical and bactericidal properties *in vitro Braz. Dent. J.* **25** 141–5
[106] Li F, Weir M D, Fouad A F and Xu H H K 2014 Effect of salivary pellicle on antibacterial activity of novel antibacterial dental adhesives using a dental plaque microcosm biofilm model *Dent. Mater.* **30** 182–91
[107] Allaker R P and Ian Douglas C 2015 Non-conventional therapeutics for oral infections *Virulence.* **6** 196–207
[108] Besinis A, De Peralta T and Handy R D 2014 Inhibition of biofilm formation and antibacterial properties of a silver nano-coating on human dentine *Nanotoxicology* **8** 745–54
[109] Mielczarek A, Gedrange T and Michalik J 2015 An *in vitro* evaluation of the effect of fluoride products on white spot lesion remineralization *Am. J. Dent.* **28** 51–6
[110] Tschoppe P, Zandim D L, Martus P and Kielbassa A M 2011 Enamel and dentine remineralization by nano-hydroxyapatite toothpastes *J. Dent.* **39** 430–7
[111] Hernández-Sierra J F, Ruiz F, Cruz Pena D C, Martínez-Gutiérrez F, Martínez A E and de Jesús Pozos Guillén A *et al* 2008 The antimicrobial sensitivity of *Streptococcus mutans* to nanoparticles of silver, zinc oxide, and gold. *Nanomed. Nanotechnol. Biol. Med.* **4** 237–40
[112] Kasimoglu Y, Tabakcilar D, Guclu Z A, Yamamoto-Nemoto S, Tuna E. B. and Ozen B *et al* 2020 Nanomaterials and nanorobotics in dentistry: a review *J. Dent. Indones.* **27** 77–84
[113] Parvanian S, Mostafavi S M and Aghashiri M 2017 Multifunctional nanoparticle developments in cancer diagnosis and treatment *Sens. Bio.-Sensing Res.* **13** 81–7
[114] Aeran H, Kumar V, Uniyal S and Tanwer P 2015 Nanodentistry: is just a fiction or future *J. Oral. Biol. Craniofac. Res.* **5** 207–11
[115] Punyadeera C and Slowey P D 2019 Saliva as an emerging biofluid for clinical diagnosis and applications of MEMS/NEMS in salivary diagnostics *Nanobiomaterials in Clinical Dentistry*. (Amsterdam: Elsevier), pp 543–65

[116] Li K C P, Pandit S D, Guccione S and Bednarski M D 2004 Molecular imaging applications in nanomedicine *Biomed. Microdevices* **6** 113–6
[117] Jain K 2003 Nanodiagnostics: application of nanotechnology in molecular diagnostics *Expert Rev. Mol. Diagn.* **3** 153–61
[118] Jain K K 2005 Nanotechnology in clinical laboratory diagnostics *Clin. Chim. Acta* **358** 37–54
[119] Mupparapu M 2006 New nanophosphor scintillators for solid-state digital dental imagers *Dentomaxillofac. Radiol.* **35** 475–6
[120] Chandki R, Kala M, Kiran Kumar N, Brigit B, Banthia P and Banthia R 2012 'Nanodentistry': exploring the beauty of miniature *J. Clin. Exp. Dent.* **4** 119–24
[121] Schleyer T L 2000 Nanodentistry *J. Am. Dent. Assoc.* **131** 1567–8
[122] Chandak P G, Ghanshyamdasj M, Chandak C, Relan K N, Chandak M and Rathi C *et al* 2021 Nanoparticles in endodontics—a review *J. Evol. Med. Dent. Sci.* **10** 976–82
[123] Wong J, Zou T, Lee A H C and Zhang C 2021 The potential translational applications of nanoparticles in endodontics *Int. J. Nanomed.* **16** 2087–106
[124] Yamauchi N, Yamauchi S, Nagaoka H, Duggan D, Zhong S and Lee S M *et al* 2011 Tissue engineering strategies for immature teeth with apical periodontitis *J. Endod.* **37** 390–7
[125] Albuquerque M T P, Valera M C, Nakashima M, Nör J E and Bottino M C 2014 Tissue-engineering-based strategies for regenerative endodontics *J. Dent. Res.* **93** 1222–31
[126] Utneja S, Nawal R R, Talwar S and Verma M 2015 Current perspectives of bio-ceramic technology in endodontics: calcium enriched mixture cement—review of its composition, properties and applications *Restor. Dent. Endod.* **40** 1
[127] Fioretti F, Mendoza-Palomares C, Avoaka-Boni M C, Ramaroson J, Bahi S and Richert L *et al* 2011 Nano-odontology: nanostructured assemblies for endodontic regeneration *J. Biomed. Nanotechnol.* **7** 471–5
[128] Aminu N, Chan S Y and Toh S M 2017 Roles of nanotechnological approaches in periodontal disease therapy *J. Appl. Pharm. Sci.* **7** 234–42
[129] Pragati S, Ashok S and Kuldeep S 2009 Recent advances in periodontal drug delivery systems *Int. J. Drug Deliv.* **1** 1–14
[130] Ripamonti U, Crooks J, Petit J-C and Rueger D C 2001 Periodontal tissue regeneration by combined applications of recombinant human osteogenic protein-1 and bone morphogenetic protein-2. A pilot study in Chacma baboons (Papio ursinus) *Eur. J. Oral Sci.* **109** 241–8
[131] Wikesjo U M E, Sorensen R G, Kinoshita A, Jian Li X and Wozney J M 2004 Periodontal repair in dogs: effect of recombinant human bone morphogenetic protein-12 (rhBMP-12) on regeneration of alveolar bone and periodontal attachment. A pilot study *J. Clin. Periodontol.* **31** 662–70
[132] Ozak S T and Ozkan P 2013 Nanotechnology and dentistry *Eur. J. Dent.* **7** 145–51
[133] Lacerda-Pinheiro S, Marchadier A, Donãs P, Septier D, Benhamou L and Kellermann O *et al* 2008 An *in vivo* model for short-term evaluation of the implantation effects of biomolecules or stem cells in the dental pulp *Open Dent. J.* **2** 67–72
[134] Ghavimi M A, Negahdari R, Shahabadi A B, Sharifi S, Kazeminejad E and Shahi S *et al* 2020 Preparation and study of starch/collagen/polycaprolactone nanofiber scaffolds for bone tissue engineering using electrospinning technique *Eur. Chem. Commun.* **2** 122–7

Chapter 5

[1] Papapanou P N, Sanz M, Buduneli N, Dietrich T, Feres M and Fine D H *et al* 2018 Periodontitis: consensus report of Workgroup 2 of the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions *J. Periodontol.* **89** S173–S82 Suppl 1

[2] Shah N, Pandey R M, Duggal R, Mathur V P and Rajan K 2007 Oral health in India: a report of the multi centric study, Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India and World Health Organisation Collaborative Program

[3] Manjunath R G and Rana A 2015 Nanotechnology in periodontal management *J. Adv. Oral Res.* **6** 1–8

[4] Su E P, Justin D F, Pratt C R, Sarin V K, Nguyen V S, Oh S and Jin S 2018 Effects of titanium nanotubes on the osseointegration, cell differentiation, mineralisation and antibacterial properties of orthopaedic implant surfaces *Bone Joint J.* **100-B** 9–16 (1 Suppl. A)

[5] Liang J, Peng X, Zhou X, Zou J and Cheng L 2020 Emerging applications of drug delivery systems in oral infectious diseases prevention and treatment *Molecules* **25** 516

[6] Seneviratne C J, Leung K C, Wong C H, Lee S F, Li X and Leung P C *et al* 2014 Nanoparticle-encapsulated chlorhexidine against oral bacterial biofilms *PLoS One* **9** e103234

[7] Chen F, Rice K C, Liu X M, Reinhardt R A, Bayles K W and Wang D 2010 Triclosan-loaded tooth-binding micelles for prevention and treatment of dental biofilm *Pharm. Res.* **27** 2356–64

[8] Moura L A, Ribeiro F V, Aiello T B, Duek E A, Sallum E A and Nociti Junior F H *et al* 2015 Characterization of the release profile of doxycycline by PLGA microspheres adjunct to non-surgical periodontal therapy *J. Biomater. Sci. Polym. Ed.* **26** 573–84

[9] Phaechamud T, Chanyaboonsub N and Setthajindalert O 2016 Doxycycline hyclate-loaded bleached shellac *in situ* forming microparticle for intraperiodontal pocket local delivery *Eur. J. Pharm. Sci.* **93** 360–70

[10] Marziyeh R M, Zamani M, Prabhakaran M P, Bahrami S H and Ramakrishna S 2016 Electrospinning of PLGA/gum tragacanth nanofibers containing tetracycline hydrochloride for periodontal regeneration *Mater. Sci. Eng. C: Mater. Biol. Appl.* **58** 521–31

[11] Kimura S, Toda H, Shimabukuro Y, Kitamura M, Fujimoto N and Miki Y *et al* 2010 Topical chemotherapy in human periodontitis using a new controlled-release insert containing ofloxacin. I. Microbiological observation *J. Periodontal. Res.* **26** 33–41

[12] Tian Y, Shen Y and Jv M 2016 Synthesis, characterization and evaluation of tinidazole-loaded mPEG–PDLLA (10/90) *in situ* gel forming system for periodontitis treatment *Drug Deliv.* **23** 2726–35

[13] de Avila E, van Oirschot B and van den Beucken J 2020 Biomaterial-based possibilities for managing peri-implantitis *J. Periodont. Res.* **55** 165–73

[14] Chauhan S, Bansal M, Khan G, Yadav S K, Singh A K and Prakash P *et al* 2018 Development, optimization and evaluation of curcumin loaded biodegradable crosslinked gelatin film for the effective treatment of periodontitis *Drug Dev. Ind. Pharm.* **44** 1212–21

[15] Nasra M M, Khiri H M, Hazzah H A and Abdallah O Y 2017 Formulation, in-vitro characterization and clinical evaluation of curcumin *in situ* gel for treatment of periodontitis *Drug Deliv.* **24** 133–42

[16] Srivastava M, Kohli K and Ali M 2016 Formulation development of novel *in situ* nanoemulgel (NEG) of ketoprofen for the treatment of periodontitis *Drug Deliv.* **23** 154–66

[17] Sundararaj S C, Thomas M V, Peyyala R, Dziubla T D and Puleo D A 2013 Design of a multiple drug delivery system directed at periodontitis *Biomaterials* **34** 8835–42

[18] De Santana R B and de Santana C M 2015 Human intrabony defect regeneration with rhFGF-2 and hyaluronic acid—a randomized controlled clinical trial *J. Clin. Periodontol.* **42** 658–65

[19] Oortgiesen D A, Walboomers X F, Bronckers A L, Meijer G J and Jansen J A 2014 Periodontal regeneration using an injectable bone cement combined with BMP-2 or FGF-2 *J. Tissue Eng. Regen. Med.* **8** 202–9

[20] Oortgiesen D A, Meijer G J, Bronckers A L, Walboomers X F and Jansen J A 2013 Regeneration of the periodontium using enamel matrix derivative in combination with an injectable bone cement *Clin. Oral Investig.* **17** 411–21

[21] Pradeep A R, Karvekar S, Nagpal K, Patnaik K, Guruprasad C N and Kumaraswamy K M 2015 Efficacy of locally delivered 1.2% rosuvastatin gel to non-surgical treatment of patients with chronic periodontitis: a randomized, placebo-controlled clinical trial *J. Periodontol.* **86** 738–45

[22] Gunjiganur Vemanaradhya G, Emani S, Mehta D S and Bhandari S 2017 Effect of 1.2% of simvastatin gel as a local drug delivery system on Gingival Crevicular Fluid interleukin-6 & interleukin-8 levels in non surgical treatment of chronic periodontitis patients *Arch. Oral Biol.* **82** 55–61

[23] Rao N S, Pradeep A R, Bajaj P, Kumari M and Naik S B 2013 Simvastatin local drug delivery in smokers with chronic periodontitis: a randomized controlled clinical trial *Aust. Dent. J.* **58** 156–62

[24] Pradeep A R, Anuj S, Rao N S, Pavan B, Naik S B and Minal K 2012 Local drug delivery of alendronate gel for the treatment of patients with chronic periodontitis with diabetes mellitus: a double-masked controlled clinical trial *J. Periodontol.* **83** 1322–8

[25] Li H, Wang Q, Xiao Y, Bao C and Li W 2013 25-Hydroxyvitamin D 3-loaded PLA microspheres: *in vitro* characterization and application in diabetic periodontitis models *Aaps Pharmscitech* **14** 880–9

[26] Pei B, Wang W, Dunne N and Li X 2019 Applications of carbon nanotubes in bone tissue regeneration and engineering: superiority, concerns, current advancements, and prospects *Nanomaterials (Basel)* **9** 1501

[27] Diniz I M, Chen C, Ansari S, Zadeh H H, Moshaverinia M and Chee D *et al* 2016 Gingival Mesenchymal Stem Cell (GMSC) delivery system based on RGD-coupled alginate hydrogel with antimicrobial properties: a novel treatment modality for peri-implantitis *J. Prosthodont.* **25** 105–15

[28] Fisher P D, Clemens J, Zach Hilt J and Puleo D A 2016 Multifunctional poly(beta-amino ester) hydrogel microparticles in periodontal *in situ* forming drug delivery systems *Biomed. Mater.* **11** 025002

[29] Besinis A, Hadi S D, Le H R, Tredwin C and Handy R D 2017 Antibacterial activity and biofilm inhibition by surface modified titanium alloy medical implants following application of silver, titanium dioxide and hydroxyapatite nanocoatings *Nanotoxicology* **11** 327–38

[30] Bottino M C, Munchow E A, Albuquerque M T P, Kamocki K, Shahi R and Gregory R L *et al* 2017 Tetracycline-incorporated polymer nanofibers as a potential dental implant surface modifier *J. Biomed. Mater Res. B Appl. Biomater.* **105** 2085–92

[31] Yang Y, Ren S, Zhang X, Yu Y, Liu C and Yang J *et al* 2018 Safety and efficacy of PLGA (Ag-Fe_3O_4)-coated dental implants in inhibiting bacteria adherence and osteogenic inducement under a magnetic field *Int. J. Nanomed.* **13** 3751–62

Chapter 6

[1] Foster J S and Kolenbrander P E 2004 Development of a multispecies oral bacterial community in a saliva-conditioned flow cell *Appl. Environ. Microbiol.* **70** 4340–8

[2] Verma D, Garg P K and Dubey A K 2018 Insights into the human oral microbiome *Arch. Microbiol.* **200** 525–40

[3] Van Acker H, Van Dijck P and Coenye T 2014 Molecular mechanisms of antimicrobial tolerance and resistance in bacterial and fungal biofilms *Trends Microbiol.* **22** 326–33

[4] Ardekani S M, Dehghani A, Ye P, Nguyen K A and Gomes V G 2019 Conjugated carbon quantum dots: potent nano-antibiotic for intracellular pathogens *J. Colloid Interface Sci.* **552** 378–87

[5] Liu Y, Shi L, Su L, van der Mei H C, Jutte P C, Ren Y and Busscher H J 2019 Nanotechnology-based antimicrobials and delivery systems for biofilm-infection control *Chem. Soc. Rev.* **48** 428–46

[6] Gupta A, Mumtaz S, Li C H, Hussain I and Rotello V M 2019 Combatting antibiotic-resistant bacteria using nanomaterials *Chem. Soc. Rev.* **48** 415–27

[7] Patil S, Rao R S, Majumdar B and Anil S 2015 Clinical appearance of oral *Candida* infection and therapeutic strategies *Front. Microbiol.* **6** 1391

[8] Pires de Carvalho Bianchi C M, Bianchi H A, Tadano T, Paula C R, Hoffmann-Santos H D, Leite D P Jr and Hahn R C 2006 Factors related to oral candidiasis in elderly users and non-users of removable dental prostheses *Rev. Inst. Med. Trop. Sao Paulo.* **58** 17

[9] Davies A N, Brailsford S R and Beighton D 2006 Oral candidosis in patients with advanced cancer *Oral Oncol.* **42** 698–702

[10] Stecksen-Blicks C, Granstrom E, Silfverdal S A and West C E 2015 Prevalence of oral *Candida* in the first year of life *Mycoses* **58** 550–56

[11] Lima S L, Colombo A L and de Almeida Junior J N 2019 Fungal cell wall: emerging antifungals and drug resistance *Front. Microbiol.* **10** 2573

[12] Song J, Zhou J, Zhang L and Li R 2020 Mitochondria-mediated azole drug resistance and fungal pathogenicity: opportunities for therapeutic development *Microorganisms* **8** 1574

[13] Arias L S, Pessan J P, Vieira A P M, Lima T M T, Delbem A C B and Monteiro D R 2018 Iron oxide nanoparticles for biomedical applications: a perspective on synthesis, drugs, antimicrobial activity, and toxicity *Antibiotics (Basel)* **7** 46

[14] Waghule T, Sankar S, Rapalli V K, Gorantla S, Dubey S K, Chellappan D K, Dua K and Singhvi G 2020 Emerging role of nanocarriers based topical delivery of anti-fungal agents in combating growing fungal infections *Dermatol. Ther.* **33** e13905

[15] Garg A, Sharma G S, Goyal A K, Ghosh G, Si S C and Rath G 2020 Recent advances in topical carriers of anti-fungal agents *Heliyon* **6** e04663

[16] Verma S and Utreja P 2019 Vesicular nanocarrier based treatment of skin fungal infections: potential and emerging trends in nanoscale pharmacotherapy *Asian J. Pharm. Sci.* **14** 117–29

[17] Senna J P, Barradas T N, Cardoso S, Castiglione T C, Serpe M J, Silva K and Mansur C R E 2018 Dual alginate-lipid nanocarriers as oral delivery systems for amphotericin B *Colloids Surf.* B **166** 187–94

[18] de Bastiani F, Spadari c c, de Matos J K R, Salata G C, Lopes L B and Ishida K 2019 Nanocarriers provide sustained antifungal activity for amphotericin B and miltefosine in the topical treatment of murine vaginal candidiasis *Front. Microbiol.* **10** 2976

[19] Araujo H C, Arias L S, Caldeirao A C M, Assumpção L C F, Morceli M G, de Souza Neto F N, de Camargo E R, Oliveira S H P, Pessan J P and Monteiro D R 2020 Novel colloidal

nanocarrier of cetylpyridinium chloride: antifungal activities on *Candida* species and cytotoxic potential on murine fibroblasts *J. Fungi (Basel)* **6** 218.

[20] AriasL S, Pessan J P, de Souza Neto F N, Lima B H R, de Camargo E R, Ramage G, Delbem A C B and Monteiro D R 2020 Novel nanocarrier of miconazole based on chitosan-coated iron oxide nanoparticles as a nanotherapy to fight *Candida* biofilms *Colloids Surf.* B **192** 111080

[21] VieiraA P M, Arias L S, de Souza Neto F N, Kubo A M, Lima B H R, de Camargo E R, Pessan J P, Delbem A C B and Monteiro D R 2019 Antibiofilm effect of chlorhexidine-carrier nanosystem based on iron oxide magnetic nanoparticles and chitosan *Colloids Surf.* B **174** 224–31

[22] de Lima T M, Arias L S, Afanaci L F, Ferraresse R F, Neto F N S, de Lima B H, Straioto F G, de Camargo E R, Pessan J P and Monteiro D R 2020 Assembly and antifungal effect of a new fluconazole-carrier nanosystem *Future Microbiol.* **15** 273–85

[23] Hussein-Al-Ali S H, El Zowalaty M E, Kura A U, Geilich B, Fakurazi S, Webster T J and Hussein M Z 2014 Antimicrobial and controlled release studies of a novel nystatin conjugated iron oxide nanocomposite *BioMed Res. Int.* **2014** 651831

[24] Sakima V T, Barbugli P A, Cerri P S, Chorilli M, Carmello J C, Pavarina A C and Mima E G O 2018 Antimicrobial photodynamic therapy mediated by curcumin-loaded polymeric nanoparticles in a murine model of oral candidiasis *Molecules* **23** 2075

[25] Trigo Gutierrez J K, Zanatta G C, Ortega A L M, Balastegui M I C, Sanita P V, Pavarina A C, Barbugli P A and Mima E G O 2017 Encapsulation of curcumin in polymeric nanoparticles for antimicrobial photodynamic therapy *PLoS One* **12** e0187418

[26] Li L P *et al* 2018 Antifungal activity of osthol *in vitro* and enhancement in vivo through Eudragit S100 nanocarriers *Virulence* **9** 555–62

[27] Pupe C G, Villardi M, Rodrigues C R, Rocha H V, Maia L C, de Sousa V P and Cabral L M 2011 Preparation and evaluation of antimicrobial activity of nanosystems for the control of oral pathogens *Streptococcus mutans* and *Candida albicans Int. J. Nanomed.* **6** 2581–90

[28] Araujo H C, da Silva A C G, Paiao L I, Magario M K W, Frasnelli S C T, Oliveira S H P, Pessan J P and Monteiro D R 2020 Antimicrobial, antibiofilm and cytotoxic effects of a colloidal nanocarrier composed by chitosan-coated iron oxide nanoparticles loaded with chlorhexidine *J. Dent.* **101** 103453

[29] Arias L S, Brown J L, Butcher M C, Delaney C, Monteiro D R and Ramage G 2020 A nanocarrier system that potentiates the effect of miconazole within different interkingdom biofilms *J. Oral Microbiol.* **12** 1771071

[30] Lin J H, Feng F, Yu M C, Wang C H and Chang P C 2017 Modulation of periodontitis progression using pH-responsive nanosphere encapsulating metronidazole or N-phenacylthialzolium bromide *J. Periodontal Res.* **53** 2–8

[31] Guru S R, Reddy K A, Rao R J, Padmanabhan S, Guru R and Srinivasa T S 2020 Comparative evaluation of 2% turmeric extract with nanocarrier and 1% chlorhexidine gel as an adjunct to scaling and root planing in patients with chronic periodontitis: a pilot randomized controlled clinical trial *J. Indian Soc. Periodontol.* **24** 244–52

[32] Shaheen M A, Elmeadawy S H, Bazeed F B, Anees M and Saleh N M 2020 Innovative coenzyme Q10-loaded nanoformulation as an adjunct approach for the management of moderate periodontitis: preparation, evaluation, and clinical study *Drug Deliv. Transl. Res.* **10** 548–64

[33] Kim T H, Singh R K, Kang M S, Kim J H and Kim H W 2015 Inhibition of osteoclastogenesis through siRNA delivery with tunable mesoporous bioactive nanocarriers *Acta Biomater.* **29** 352–64

[34] Lee J H, Mandakhbayar N, El-Fiqi A and Kim H W 2017 Intracellular co-delivery of Sr ion and phenamil drug through mesoporous bioglass nanocarriers synergizes BMP signaling and tissue mineralization *Acta Biomater.* **15** 93–108

[35] Kang M S, Kim J H, Singh R K, Jang J H and Kim H W 2015 Therapeutic-designed electrospun bone scaffolds: mesoporous bioactive nanocarriers in hollow fiber composites to sequentially deliver dual growth factors *Acta Biomater.* **16** 103–16

[36] Mahapatra C, Singh R K, Kim J J, Patel K D, Perez R A, Jang J H and Kim H W 2016 Osteopromoting reservoir of stem cells: bioactive mesoporous nanocarrier/collagen gel through slow-releasing FGF18 and the activated BMP signaling *ACS Appl. Mater. Interfaces* **8** 27573–84

[37] Lian M, Sun B, Qiao Z, Zhao K, Zhou X, Zhang Q, Zou D, He C and Zhang X 2019 Bi-layered electrospun nanofibrous membrane with osteogenic and antibacterial properties for guided bone regeneration *Colloids Surf.* B **176** 219–29

[38] Bukhari S, Kim D, Liu Y, Karabucak B and Koo H 2018 Novel endodontic disinfection approach using catalytic nanoparticles *J. Endod.* **44** 806–12

[39] Li X, Li X, Wang S, Leung K C F, Zhang C and Jin L 2018 Infiltration and profiles of mesoporous silica nanoparticles in dentinal tubules *ACS Biomater. Sci. Eng.* **4** 1428–36

[40] Ertem E, Gutt B, Zuber F, Allegri S, Ouya B L, Mefti S, Formentin K, Stellacci F and Ren Q 2017 Core–shell silver nanoparticles in endodontic disinfection solutions enable long-term antimicrobial effect on oral biofilms *ACS Appl. Mater. Interfaces* **9** 34762–72

[41] Arafa M G, Mousa H A and Afifi N N 2020 Preparation of PLGA-chitosan based nanocarriers for enhancing antibacterial effect of ciprofloxacin in root canal infection *Drug Deliv.* **27** 26–39

[42] Farhadian N, Godiny M, Moradi S, Azandaryani A H and Shahlaei M 2018 Chitosan/gelatin as a new nano-carrier system for calcium hydroxide delivery in endodontic applications: Development, characterization and process optimization *Mater. Sci. Eng. C: Mater. Biol. Appl.* **92** 540–46

[43] Javidi M, Afkhami F, Zarei M, Ghazvini K and Rajabi O 2014 Efficacy of a combined nanoparticulate/calcium hydroxide root canal medication on elimination of *Enterococcus faecalis Aust. Endod. J.* **40** 61–5

[44] Fan W, Li Y, Sun Q, Ma T and Fan B 2016 Calcium-silicate mesoporous nanoparticles loaded with chlorhexidine for both anti-*Enterococcus faecalis* and mineralization properties *J. Nanobiotechnol.* **14** 72

[45] Lee D K *et al* 2015 Nanodiamond-guttapercha composite biomaterials for root canal therapy *ACS Nano.* **9** 11490–501

[46] Nam H J, Kim Y M, Kwon Y H, Yoo K H, Yoon S Y, Kim I R, Park B S, Son W S, Lee S M and Kim Y I 2019 Fluorinated bioactive glass nanoparticles: enamel demineralization prevention and antibacterial effect of orthodontic bonding resin *Materials (Basel)* **12** 1813

[47] Lee J H, El-Fiqi A, Jo J K, Kim D A, Jun S K, Kim H W and Lee H H 2016 Development of long-term antimicrobial poly (methyl methacrylate) by incorporating mesoporous silica nanocarriers *Dent. Mater.* **32** 1564–74

[48] Jo J K, Fiqi A E, Lee J H, Kim D A, Kim H W and Lee H H 2017 Rechargeable microbial anti-adhesive polymethylmethacrylate incorporating silver sulfadiazine-loaded mesoporous silica nanocarriers *Dent. Mater.* **33** e361–72

[49] Helling A L, Tsekoura E K, Biggs M, Bayon Y, Pandit A and Zeugolis D I 2017 *In vitro* enzymatic degradation of tissue grafs and collagen biomaterials by matrix metalloproteinases: improving the collagenase assay *ACS Biomater. Sci. Eng.* **3** 1922–32

[50] Aguda A H, Panwar P, Du X, Nguyen N T, Brayer G D and Brömme D 2014 Structural basis of collagen fiber degradation by cathepsin K *Proc. Natl Acad. Sci. USA* **111** 17474–9

[51] Osorio R, Osorio E, Medina-Castillo A L and Toledano M 2014 Polymer nanocarriers for dentin adhesion *J. Dent. Res.* **93** 1258–63

[52] Jun S, Yang S A, Kim Y, El-Figi A and Mandkhbayer N 2018 Functional nano-adhesive releasing therapeutic ions for MMP-deactivation and remineralization *Sci. Rep.* **8** 5663

[53] Hoppe A, Güldal N S and Boccaccini A R 2011 A review of the biological response to ionic dissolution products from bioactive glasses and glass-ceramics *Biomaterials* **32** 2757–74

[54] Mathur V P and Dhillon J K 2018 Dental caries: a disease which needs attention *Indian J. Pediatr.* **85** 202–6

[55] Tafere Y, Chanie S, Dessie T and Gedamu H 2018 Assessment of prevalence of dental caries and the associated factors among patients attending dental clinic in Debre Tabor general hospital: a hospital-based cross-sectional study *BMC Oral Health* **18** 119

[56] Petersen P E and Ogawa H 2016 Prevention of dental caries through the use of fluoride—the WHO approach *Community Dent. Health* **33** 66–8

[57] Salunke S, Shah V, Ostbye T, Gandhi A, Phalgune D, Ogundare M O and Sable V 2019 Prevalence of dental caries, oral health awareness and treatment—seeking behavior of elderly population in rural Maharashtra *Indian J. Dent. Res.* **30** 332–6

[58] Carvalho J C and Schiffner U 2019 Dental caries in european adults and senior citizens 1996–2016: ORCA Saturday Afternoon Symp. in Greifswald, Germany—Part II *Caries Res.* **53** 242–52

[59] Meng Y, Wu T, Billings R, Kopycka-Kedzierawski D T and Xiao J 2019 Human genes influence the interaction between *Streptococcus mutans* and host caries susceptibility: a genome-wide association study in children with primary dentition *Int. J. Oral Sci.* **11** 19

[60] Cavalcante L L R, Tedesco A C, Takahashi L A U, Curylofo-Zotti F A, Souza-Gabriel A E and Corona S A M 2020 Conjugate of chitosan nanoparticles with chloroaluminiumphthalocyanine: Synthesis, characterization and photoinactivation of *Streptococcus mutans* biofilm *Photodiagnosis Photodyn. Ther.* **30** 101709

[61] Lu M M *et al* 2018 Redox/pH dual-controlled release of chlorhexidine and silver ions from biodegradable mesoporous silica nanoparticles against oral biofilms *Int. J. Nanomed.* **13** 7697–709

[62] de Melo N F S, Campos E V R, Gonçalves C M, de Paula E, Pasquoto T, de Lima R, Rosa A H and Fraceto L F 2014 Development of hydrophilic nanocarriers for the charged form of the local anestheticarticaine *Colloids Surf.* B **121** 66–73

[63] Ribeiro L N, Franz-Montan M, Breitkreitz M C, Alcântara A C, Castro S R, Guilherme V A, Barbosa R M and de Paula E 2016 Nanostructured lipid carriers as robust systems for topical lidocaine-prilocaine release in dentistry *Eur. J. Pharm. Sci.* **93** 192–202

[64] You P, Yuan R and Chen C 2017 Design and evaluation of lidocaine- and prilocaine-coloadednanoparticulate drug delivery systems for topical anesthetic analgesic therapy: a

comparison between solid lipid nanoparticles and nanostructured lipid carriers *Drug Des. Devel. Ther.* **11** 2743–52

[65] Gong P, Zhao Q, Dai D, Zhang S, Tian Z, Sun L, Ren J and Liu Z 2017 Functionalized ultrasmall fluorinated graphene with high NIR absorbance for controlled delivery of mixed anticancer drugs *Chemistry* **23** 17531–41

[66] Nam H Y, Min K H, Kim D E, Choi J R, Lee H J and Lee S C 2017 Mussel-inspired poly (L-DOPA)-templated mineralization for calcium phosphate-assembled intracellular nanocarriers *Colloids Surf.* B **157** 215–22

[67] Li L *et al* 2018 Synergistic anticancer effects of nanocarrier loaded with berberine and *miR-122 Biosci. Rep.* **38** BSR20180311

Chapter 7

[1] Kovvuru S, Mahita V, Manjunatha B S and Buma S 2012 Nanotechnology: the emerging science in dentistry *J Orofacial Res.* **2** 33–6

[2] Feynman R P 1960 There's plenty of room at the bottom *Calif. Inst. Technol. J. Eng. Sci.* **4** 23–6

[3] Taniguchi N 1974 On the basic concept of 'nano-technology' *Proc. Intl. Conf. Prod. Eng. Tokyo, Part II* (Japan Society of Precision Engineering)

[4] Shashirekha G, Jena A and Mohapatra S 2017 Nanotechnology in dentistry: clinical applications, benefits, and hazards *Compend. Contin. Educ. Dent.* **38** e1–4

[5] Zarbin M A, Montemagno C, Leary J F and Ritch R 2010 Nanotechnology in ophthalmology *Can. J. Ophthalmol.* **45** 457–76

[6] El-Bialy T 2019 Nanotechnology in orthodontics—2: facts and possible future applications *Nanobiomaterials in Clinical Dentistry* ed K Subramani and W Ahmed 2nd edn (Amsterdam: Elsevier), pp 299–308

[7] Freitas R A 2000 Nanodentistry *J. Am. Dent. Assoc.* **131** 1559–65

[8] Govind S, Jena A and Mohapatra S 2017 Nanotechnology in dentistry: clinical applications, benefits, and hazards *Compend. Contin. Educ. Dent.* **38** e1–4

[9] Lavenus S, Louarn G and Layrolle P 2010 Nanotechnology and dental implants *Int. J. Biomater.* **2010** 915327

[10] Rossouw P E 2003 Friction: an overview *Semin. Orthod.* **9** 218–22

[11] Drescher D, Bourauel C and Schumacher H A 1989 Frictional forces between bracket and arch wire *Am. J. Orthod. Dentofacial. Orthop.* **96** 397–404

[12] Pizzoni L, Ravnholt G and Melsen B 1998 Frictional forces related to self-ligating brackets *Eur. J. Orthod.* **20** 283–91

[13] Tenne R, Margulis L, Genut M and Hodes G 1992 Polyhedral and cylindrical structures of tungsten disulphide *Nature* **360** 444–6

[14] Katz A, Redlich M, Rapoport L, Wagner H D and Tenne R 2006 Self-lubricating coatings containing fullerene-like WS_2 nanoparticles for orthodontic wires and other possible medical applications *Tribol. Lett.* **21** 135–9

[15] Rapoport L, Fleischer N and Tenne R 2005 Applications of WS_2 (MoS_2) inorganic nanotubes and fullerene-like nanoparticles for solid lubrication and for structural nanocomposites *J. Mater. Chem.* **15** 1782–8

[16] Rapoport L, Bilik Y, Feldman Y, Homyonfer M, Cohen S R and Tenne R 1997 Hollow nanoparticles of WS_2 as potential solid-state lubricants *Nature* **387** 791–3

[17] Redlich M, Katz A, Rapoport L, Wagner H D, Feldman Y and Tenne R 2008 Improved orthodontic stainless steel wires coated with inorganic fullerene-like nanoparticles of WS_2 impregnated in electroless nickel-phosphorous film *Dent. Mater.* **24** 1640–6
[18] Batra P 2018 Applications of nanoparticles in orthodontics *Dental Applications of Nanotechnology*. ed R Chaughule (Cham: Springer)
[19] Samorodnitzky-Naveh G R, Redlich M, Rapoport L, Feldman Y and Tenne R 2009 Inorganic fullerene-like tungsten disulfide nanocoating for friction reduction of nickel–titanium alloys *Nanomedicine* **4** 943–50
[20] Gavrilovic I 2014 White spot lesions in orthodontic patients: formation, prevention and treatment *Oral Hyg. Health* **2** 154
[21] Al-Anezi S A and Harradine N W T 2012 Quantifying plaque during orthodontic treatment: *Angle Orthod.* **82** 748–53
[22] Zachrisson S and Zachrisson B U 1972 Gingival condition associated with orthodontic treatment *Angle Orthod.* **42** 26–34
[23] Freitas A O A, Marquezan M, Nojima M da C G, Alviano D S and Maia L C 2014 The influence of orthodontic fixed appliances on the oral microbiota: a systematic review *Dental Press J. Orthod.* **19** 46–55
[24] Rosenbloom R G and Tinanoff N 1991 Salivary *Streptococcus mutans* levels in patients before, during, and after orthodontic treatment *Am. J. Orthod. Dentofacial Orthop.* **100** 35–7
[25] Campbell C H C T 2003 Alteração da microflora bucalempacientesportadores de aparelhoortodônticofixo *Ortodon.gaúch.* 98–109
[26] Borzabadi-Farahani A, Borzabadi E and Lynch E 2014 Nanoparticles in orthodontics, a review of antimicrobial and anti-caries applications *Acta Odontol. Scand.* **72** 413–17
[27] Govindankutty D 2015 Applications of nanotechnology in orthodontics and its future implications: a review *Int. J. Appl. Dental Sci.* **1** 166–71
[28] Allaker R P 2010 The use of nanoparticles to control oral biofilm formation *J. Dent. Res.* **89** 1175–86
[29] Cao B 2013 Preparation of an orthodontic bracket coated with an nitrogen-doped $TiO_{2-x}N_y$ thin film and examination of its antimicrobial performance *Dental Mater. J.* **32** 311–16
[30] Ahn S, Lee S, Kook J and Lim B 2009 Experimental antimicrobial orthodontic adhesives using nanofillers and silver nanoparticles *Dent. Mater.* **25** 206–13
[31] Poosti M, Ramazanzadeh B, Zebarjad M, Javadzadeh P, Naderinasab M and Shakeri M T 2013 Shear bond strength and antibacterial effects of orthodontic composite containing TiO_2 nanoparticles *Eur. J. Orthod.* **35** 676–79
[32] Elsaka S E, Hamouda I M and Swain M V 2011 Titanium dioxide nanoparticles addition to a conventional glass-ionomer restorative: influence on physical and antibacterial properties *J. Dent.* **39** 589–98
[33] Lin J, Zhu J and Gu X *et al* 2011 Effects of incorporation of nano-fluorapatite or nano-fluorohydroxyapatite on a resin-modified glass ionomer cement *Acta Biomater.* **7** 1346–53
[34] Enan E T and Hammad S M 2013 Microleakage under orthodontic bands cemented with nano-hydroxyapatite-modified glass ionomer *Angle Orthod.* **83** 981–6
[35] Cheng L, Zhang K, Weir M D, Melo M A S, Zhou X and Xu H H K 2015 Nanotechnology strategies for antibacterial and remineralizing composites and adhesives to tackle dental caries *Nanomedicine* **10** 627–41

[36] Cavalcanti A, Rosen L, Kretly L C, Rosenfeld M and Einav S December 2004 Nanorobotic challenges in biomedical applications, design and control *Proc. of the 2004 11th IEEE Int. Conf. on Electronics, Circuits and Systems, 2004. ICECS 2004* 447–50
[37] Arosarena O A 2007 Cleft lip and palate *Otolaryngol. Clin. North Am.* **40** 27–60
[38] Subtelny J D and Brodie A G 1954 An analysis of orthodontic expansion in unilateral cleft lip and cleft palate patients *Am. J. Orthod.* **40** 686–97
[39] Hong C, Song D and Lee D *et al* 2017 Reducing posttreatment relapse in cleft lip palatal expansion using an injectable estrogen-nanodiamond hydrogel *Proc. Natl. Acad. Sci. USA* **114** E7218–25
[40] Gurel H G, Memili B, Erkan M and Sukurica Y 2010 Long-term effects of rapid maxillary expansion followed by fixed appliances *Angle Orthodon.* **80** 5–9
[41] Raza H, Major P, Dederich D and El-Bialy T 2016 Effect of low-intensity pulsed ultrasound on orthodontically induced root resorption caused by torque: a prospective, double-blind, controlled clinical trial *Angle Orthod.* **86** 550–7
[42] El-Bialy T, Farouk K and Carlyle T D *et al* 2020 Effect of low intensity pulsed ultrasound (LIPUS) on tooth movement and root resorption: a prospective multi-center randomized controlled trial *J. Clin. Med.* **9** 804
[43] Lapatki B G and Paul O 2007 Smart brackets for 3D-force-moment measurements in orthodontic research and therapy—developmental status and prospects *J. Orofac. Orthop.* **68** 377–96
[44] Lapatki B G, Bartholomeyczik J, Ruther P, Jonas I E and Paul O 2007 Smart bracket for multi-dimensional force and moment measurement *J. Dent. Res.* **86** 73–8

Chapter 8

Afkhami F, Akbari S and Chiniforush N 2017 Entrococcus faecalis elimination in root canals using silver nanoparticles, photodynamic therapy, diode laser, or laser-activated nanoparticles: an *in vitro* study *J. Endod.* **43** 279–82
Albuquerque M T, Nagata J and Bottino M C 2017 Antimicrobial efficacy of triple antibiotic–eluting polymer nanofibers against multispecies biofilm *J. Endod.* **43** S51–6
Alhomrany R, Zhang C and Chou L 2019 Cytotoxic effect of chitosan nanoparticles on normal human dental pulp cells *Nanosci. Nanotechnol.* **3** 1
Arias-Moliz M, Baca P, Solana C, Toledano M, Medina-Castillo A, Toledano-Osorio M and Osorio R 2021 Doxycycline-functionalized polymeric nanoparticles inhibit Enterococcus faecalis biofilm formation on dentine *Int. Endod. J.* **54** 413–26
Baras B H, Melo M A S, Sun J, Oates T W, Weir M D, Xie X, Bai Y and Xu H H 2019 Novel endodontic sealer with dual strategies of dimethylaminohexadecyl methacrylate and nanoparticles of silver to inhibit root canal biofilms *Dent. Mater.* **358** 1117–29
Barreras U S, Méndez F T, Martínez R E M, Valencia C S, Rodríguez P R M and Rodríguez J P L 2016 Chitosan nanoparticles enhance the antibacterial activity of chlorhexidine in collagen membranes used for periapical guided tissue regeneration *Mater. Sci. Eng.* C **58** 1182–7
Barros J, Silva M, Rodrigues M, Alves F, Lopes M, Pina-Vaz I and Siqueira J Jr 2014 Antibacterial, physicochemical and mechanical properties of endodontic sealers containing quaternary ammonium polyethylenimine nanoparticles *Int. Endod. J.* **47** 725–34
Beloin C, Valle J, Latour-Lambert P, Faure P, Kzreminski M, Balestrino D, Haagensen J A, Molin S, Prensier G and Arbeille B 2004 Global impact of mature biofilm lifestyle on *Escherichia coli* K-12 gene expression *Mol. Microbiol.* **51** 659–74

Bhushan M, Tyagi S, Nigam M, Choudhary A, Khurana N and Dwivedi V 2015 Bioactive materials: a short review *J. Orofac. Res.* **5** 138–41

Bottino M, Kamocki K, Yassen G, Platt J, Vail M, Ehrlich Y, Spolnik K and Gregory R 2013 Bioactive nanofibrous scaffolds for regenerative endodontics *J. Dent. Res.* **92** 963–9

Bottino M C, Yassen G H, Platt J A, Labban N, Windsor L J, Spolnik K J and Bressiani A H 2015 A novel three-dimensional scaffold for regenerative endodontics: materials and biological characterizations *J. Tissue Eng. Regen. Med.* **9** E116–123

Brown M R, Allison D G and Gilbert P 1988 Resistance of bacterial biofilms to antibiotics a growth-rate related effect? *J. Antimicrob. Chemother.* **22** 777–80

Bukhari S, Kim D, Liu Y, Karabucak B and Koo H 2018 Novel endodontic disinfection approach using catalytic nanoparticles *J. Endod.* **44** 806–12

Carrotte P 2004 Endodontics: Part 1 the modern concept of root canal treatment *Br. Dent. J.* **197** 181–3

Chan D C, Chung A K and Paranjpe A 2018 Antibacterial and bioactive dental restorative materials: do they really work? *Am. J. Dent.* **31**(Sp Is B) 3B–5B

Chuang Y-C, Chang C-C, Yang F, Simon M and Rafailovich M 2021 TiO_2 nanoparticles synergize with substrate mechanics to improve dental pulp stem cells proliferation and differentiation *Mater. Sci. Eng.* C **118** 111366

Costerton J W, Stewart P S and Greenberg E P 1999 Bacterial biofilms: a common cause of persistent infections *Science* **284** 1318–22

del Carpio-Perochena A, Bramante C M, Duarte M A H, de Moura M R, Aouada F A and Kishen A 2015a Chelating and antibacterial properties of chitosan nanoparticles on dentin *Restor. Dent. Endod.* **40** 195–201

del Carpio-Perochena A, Kishen A, Shrestha A and Bramante C M 2015b Antibacterial properties associated with chitosan nanoparticle treatment on root dentin and 2 types of endodontic sealers *J. Endod.* **41** 1353–8

Del Fabbro M, Afrashtehfar K I, Corbella S, El-Kabbaney A, Perondi I and Taschieri S 2018 *In vivo* and *in vitro* effectiveness of rotary nickel-titanium vs manual stainless steel instruments for root canal therapy: systematic review and meta-analysis *J. Evid. Based Dent. Pract.* **18** 59–69

Divya K and Jisha M S 2018 Chitosan nanoparticles preparation and applications *Environ. Chem. Lett.* **16** 101–12

Dua K, Singh G, Goel M and Sachdeva G 2012 Endodontic biofilm and its relevance in endodontic infection *Indian J. Dent. Sci.* **4** 110–14

Dutta P K, Dutta J and Tripathi V 2004 Chitin and chitosan: Chemistry, properties and applications *J. Sci. Indus. Res.* **63** 20–31

Evans M, Davies J K, Sundqvist G and Figdor D 2002 Mechanisms involved in the resistance of *Enterococcus faecalis* to calcium hydroxide *Int. Endod. J.* **35** 221–8

Farber P A and Seltzer S 1988 Endodontic microbiology. I. Etiology *J. Endod.* **14** 363–71

Feynman R P 1960 There's plenty of room at the bottom *Eng. Sci.* **23** 22–36

Flemming H C and Wingender J 2010 The biofilm matrix *Nat. Rev. Microbiol.* **8** 623–33

Giannousi K, Lafazanis K, Arvanitidis J, Pantazaki A and Dendrinou-Samara C 2014 Hydrothermal synthesis of copper based nanoparticles: antimicrobial screening and interaction with DNA *J. Inorg. Biochem.* **133** 24–32

Gomes-Filho J E, Silva F O, Watanabe S, Cintra L T A, Tendoro K V, Dalto L G, Pacanaro S V, Lodi C S and de Melo F F F 2010 Tissue reaction to silver nanoparticles dispersion as an alternative irrigating solution *J. Endod.* **36** 1698–702

Gomes B P F A, Pinheiro E T, Gadê-Neto C R, Sousa E L R, Ferraz C C R, Zaia A A, Teixeira F B and Souza-Filho F J 2004 Microbiological examination of infected dental root canals *Oral Microbiol. Immunol.* **19** 71–6

Gupte M and Ma P 2012 Nanofibrous scaffolds for dental and craniofacial applications *J. Dent. Res.* **91** 227–34

Haapasalo H K, Sirén E K, Waltimo T M T, Òrstavik D and Haapasalo M P P 2000 Inactivation of local root canal medicaments by dentine: an *in vitro* study *Int. Endod. J.* **33** 126–31

Haapasalo M, Qian W, Portenier I and Waltimo T 2007 Effects of dentin on the antimicrobial properties of endodontic medicaments *J. Endod.* **33** 917–25

Haapasalo M, Udnæs T and Endal U 2003 Persistent, recurrent, and acquired infection of the root canal system post-treatment *Endod. Topics* **6** 29–56

He L, Kim S G, Gong Q, Zhong J, Wang S, Zhou X, Ye L, Ling J and Mao J J 2017 Regenerative endodontics for adult patients *J. Endod.* **43** S57–64

Hemmanur S and Nasim I 2020 Antibacterial efficacy of nanoparticle-incorporated root canal sealer against common endodontic pathogens-an *in vitro* Study *J. Pharm. Res. Int.* 68–74

Hülsmann M, Peters O A and Dummer P M 2005 Mechanical preparation of root canals: shaping goals, techniques and means *Endod. Topics* **10** 30–76

Ibrahim A, Moodley D, Petrik L and Patel N 2017 Use of antibacterial nanoparticles in endodontics *S. Afr. Dent. J.* **72** 105–12

Jhajharia K, Parolia A, Vikram Shetty K and Mehta L K 2015 Biofilm in endodontics: a review *J. Int. Soc. Prev. Community Dent.* **5** 1–12

Jung Y, Yoon J-Y, Dev Patel K, Ma L, Lee H-H, Kim J, Lee J-H and Shin J 2020 Biological effects of tricalcium silicate nanoparticle-containing cement on stem cells from human exfoliated deciduous teeth *Nanomaterials* **10** 1373

Kakehashi S, Stanley H R and Fitzgerald R J 1965 The effects of surgical exposures of dental pulps in germ-free and conventional laboratory rats *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* **20** 340–9

Kim S G, Zhou J, Solomon C, Zheng Y, Suzuki T, Chen M, Song S, Jiang N, Cho S and Mao J J 2012 Effects of growth factors on dental stem/progenitor cells *Dent. Clin.* **56** 563–75

Kishen A 2010 Advanced therapeutic options for endodontic biofilms *Endod. Topics* **22** 99–123

Kishen A, Shi Z, Shrestha A and Neoh K G 2008 An investigation on the antibacterial and antibiofilm efficacy of cationic nanoparticulates for root canal disinfection *J. Endod.* **34** 1515–20

Kokare C, Chakraborty S, Khopade A and Mahadik K 2009 Biofilm: Importance and applications *Indian J. Biotechnol.* **8** 159–68

Kolenbrander P E, Palmer R J, Periasamy S and Jakubovics N S 2010 Oral multispecies biofilm development and the key role of cell–cell distance *Nat. Rev. Microbiol.* **8** 471–80

Lee J-H, Kang M-S, Mahapatra C and Kim H-W 2016 Effect of aminated mesoporous bioactive glass nanoparticles on the differentiation of dental pulp stem cells *PLoS One* **11** e0150727

Leite M L, Soares D G, Anovazzi G, Mendes Soares I P, Hebling J and de Souza Costa C A 2020 Development of fibronectin-loaded nanofiber scaffolds for guided pulp tissue regeneration *J. Biomed. Mater. Res.* B **109** 1244–58

Lim C T 2017 Nanofiber technology: current status and emerging developments *Prog. Polym. Sci.* **70** 1–17

Longo J P F, Leal S C, Simioni A R, Almeida-Santos M d F M, Tedesco A C and Azevedo R B 2012 Photodynamic therapy disinfection of carious tissue mediated by aluminum-chloride-phthalocyanine entrapped in cationic liposomes: an *in vitro* and clinical study *Lasers Med. Sci.* **27** 575–84

Love R M 2004 Invasion of dentinal tubules by root canal bacteria *Endod. Topics* **9** 52–65

Loyola-Rodríguez J P, Torres-Méndez F, Espinosa-Cristobal L F, García-Cortes J O, Loyola-Leyva A, González F J, Soto-Barreras U, Nieto-Aguilar R and Contreras-Palma G 2019 Antimicrobial activity of endodontic sealers and medications containing chitosan and silver nanoparticles against *Enterococcus faecalis J. Appl. Biomater. Funct. Mater.* **17** 2280800019851771

Lynch I and Dawson K A 2008 Protein-nanoparticle interactions *Nano Today* **3** 40–7

Moazami F, Sahebi S and Ahzan S 2018 Tooth discoloration induced by imidazolium based silver nanoparticles as an intracanal irrigant *J. Dent.* **19** 280

Mohammadi Z and Dummer P M H 2011 Properties and applications of calcium hydroxide in endodontics and dental traumatology *Int. Endod. J.* **44** 697–730

Mohammadi Z, Palazzi F, Giardino L and Shalavi S 2013 Microbial biofilms in endodontic infections: an update review *Biomed. J.* **36** 59–70

Mohan A, Dipallini S, Lata S, Mohanty S, Pradhan P, Patel P, Makkar H and Verma S 2020 Oxidative stress induced antimicrobial efficacy of chitosan and silver nanoparticles coated Gutta-percha for endodontic applications *Mater. Today Chem.* **17** 100299

Mohn D, Bruhin C, Luechinger N, Stark W J, Imfeld T and Zehnder M 2010 Composites made of flame-sprayed bioactive glass 45S5 and polymers: bioactivity and immediate sealing properties *Int. Endod. J.* **43** 1037–46

Monzavi A, Eshraghi S, Hashemian R and Momen-Heravi F 2015 *In vitro* and *ex vivo* antimicrobial efficacy of nano-MgO in the elimination of endodontic pathogens *Clin. Oral Investig.* **19** 349–56

Mozayeni M A, Dianat O, Tahvildari S, Mozayani M and Paymanpour P 2017 Subcutaneous reaction of rat tissues to nanosilver coated gutta-percha *Iran. Endod. J.* **12** 157

Murray P E, Garcia-Godoy F and Hargreaves K M 2007 Regenerative endodontics: a review of current status and a call for action *J. Endod.* **33** 377–90

Nair P 2004 Pathogenesis of apical periodontitis and the causes of endodontic failures *Crit. Rev. Oral Biol. Med.* **15** 348–81

Nair R P N 1987 Light and electron microscopic studies of root canal flora and periapical lesions *J. Endod.* **13** 29–39

Narayanan L L and Vaishnavi C 2010 Endodontic microbiology *J. Conserv. Dent.* **13** 233–9

Ørstavik D and Haapasalo M 1990 Disinfection by endodontic irrigants and dressings of experimentally infected dentinal tubules *Endod. Dent. Traumatol.* **6** 142–9

Östby B N 1961 The role of the blood clot in endodontic therapy an experimental histologic study *Acta Odontol. Scand.* **19** 323–53

Pagonis T C, Chen J, Fontana C R, Devalapally H, Ruggiero K, Song X, Foschi F, Dunham J, Skobe Z and Yamazaki H 2010 Nanoparticle-based endodontic antimicrobial photodynamic therapy *J. Endod.* **36** 322–8

Peciuliene V, Maneliene R, Balcikonyte E, Drukteinis S and Rutkunas V 2008 Microorganisms in root canal infections: a review *Stomatologija* **10** 4–9

Pelgrift R Y and Friedman A J 2013 Nanotechnology as a therapeutic tool to combat microbial resistance *Adv. Drug Delivery Rev.* **65** 1803–15

Portenier I, Haapasalo H, Rye A, Waltimo T, Ørstavik D and Haapasalo M 2001 Inactivation of root canal medicaments by dentine, hydroxylapatite and bovine serum albumin *Int. Endod. J.* **34** 184–88

Raura N, Garg A, Arora A and Roma M 2020 Nanoparticle technology and its implications in endodontics: a review *Biomater. Res.* **24** 1–8

Ravi Kumar M N V 2000 A review of chitin and chitosan applications *React. Funct. Polymers* **46** 1–27

Ravindran A, Chandran P and Khan S S 2013 Biofunctionalized silver nanoparticles: advances and prospects *Colloids Surf.* B **105** 342–52

Rinaudo M 2006 Chitin and chitosan: properties and applications *Prog. Polym. Sci.* **31** 603–32

Rodrigues C T, De Andrade F, De Vasconcelos L, Midena R, Pereira T, Kuga M, Duarte M and Bernardineli N 2018 Antibacterial properties of silver nanoparticles as a root canal irrigant against *Enterococcus faecalis* biofilm and infected dentinal tubules *Int. Endod. J.* **51** 901–11

Salas-Orozco M, Niño-Martínez N, Martínez-Castañón G-A, Méndez F T, Jasso M E C and Ruiz F 2019 Mechanisms of resistance to silver nanoparticles in endodontic bacteria: a literature review *J. Nanomater.* **2019** 7630316

Saleh T A 2020 Nanomaterials: Classification, properties, and environmental toxicities *Environ. Technol. Innov.* **20** 101067

Samiei M, Farjami A, Dizaj S M and Lotfipour F 2016 Nanoparticles for antimicrobial purposes in Endodontics: A systematic review of *in vitro* studies *Mater. Sci. Eng.* C **58** 1269–78

Sanchez F and Sobolev K 2010 Nanotechnology in concrete–a review *Constr. Build. Mater.* **24** 2060–71

Sanvicens N and Marco M P 2008 Multifunctional nanoparticles–properties and prospects for their use in human medicine *Trends Biotechnol.* **26** 425–33

Sauer K, Camper A K, Ehrlich G D, Costerton J W and Davies D G 2002 Pseudomonas aeruginosa displays multiple phenotypes during development as a biofilm *J. Bacteriol.* **184** 1140–54

Seil J T and Webster T J 2012 Antimicrobial applications of nanotechnology: methods and literature *Int. J. Nanomed.* **7** 2767–81

Shrestha A, Hamblin M R and Kishen A 2014 Photoactivated rose bengal functionalized chitosan nanoparticles produce antibacterial/biofilm activity and stabilize dentin-collagen *Nanomed. Nanotechnol. Biol. Med.* **10** 491–501

Shrestha A and Kishen A 2012 The effect of tissue inhibitors on the antibacterial activity of chitosan nanoparticles and photodynamic therapy *J. Endod.* **38** 1275–8

Shrestha A and Kishen A 2014 Antibiofilm efficacy of photosensitizer-functionalized bioactive nanoparticles on multispecies biofilm *J. Endod.* **40** 1604–10

Shrestha A and Kishen A 2016 Antibacterial nanoparticles in endodontics: a review *J. Endod.* **42** 1417–26

Shrestha A, Zhilong S, Gee N K and Kishen A 2010 Nanoparticulates for antibiofilm treatment and effect of aging on its antibacterial activity *J. Endod.* **36** 1030–35

Siqueira J, Perez A, Marceliano-Alves M, Provenzano J, Silva S, Pires F, Vieira G, Rocas I and Alves F 2017 What happens to unprepared root canal walls: a correlative analysis using micro-computed tomography and histology/scanning electron microscopy *Int. Endod. J,* **51** 501–8

Siqueira J F 2001 Strategies to treat infected root canals *J. Calif. Dental Assoc.* **29** 825–38

Siqueira J F 2002 Endodontic infections: Concepts, paradigms, and perspectives *Oral. Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **94** 281–93

Siqueira J F and Rôças I N 2014 Present status and future directions in endodontic microbiology *Endod. Topics* **30** 3–22

Siqueira J F, Rôças I N and Ricucci D 2010 Biofilms in endodontic infection *Endod. Topics* **22** 33–49

Siqueira J F and Sen B H 2004 Fungi in endodontic infections *Oral. Surg. Oral Med. Oral Pathol. Oral Radiol. Endod.* **97** 632–41

Stojicic S, Shen Y and Haapasalo M 2013 Effect of the source of biofilm bacteria, level of biofilm maturation, and type of disinfecting agent on the susceptibility of biofilm bacteria to antibacterial agents *J. Endod.* **39** 473–7

Stuart C H, Schwartz S A, Beeson T J and Owatz C B 2006 *Enterococcus faecalis*: its role in root canal treatment failure and current concepts in retreatment *J. Endod.* **32** 93–8

Sundqvist G and Figdor D 2003 Life as an endodontic pathogen *Endod. Topics* **6** 3–28

Svensäter G and Bergenholtz G 2004 Biofilms in endodontic infections *Endod. Topics* **9** 27–36

Tiwari J N, Tiwari R N and Kim K S 2012 Zero-dimensional, one-dimensional, two-dimensional and three-dimensional nanostructured materials for advanced electrochemical energy devices *Prog. Mater Sci.* **57** 724–803

Tomson R M, Polycarpou N and Tomson P 2014 Contemporary obturation of the root canal system *Br. Dent. J.* **216** 315–22

Torabinejad M, Shabahang S, Aprecio R M and Kettering J D 2003 The antimicrobial effect of MTAD: an *in vitro* investigation *J. Endod.* **29** 400–3

Tronstad L and Sunde P T 2003 The evolving new understanding of endodontic infections *Endod. Topics* **6** 57–77

Ulusoy A T, Turedi I, Cimen M and Cehreli Z C 2019 Evaluation of blood clot, platelet-rich plasma, platelet-rich fibrin, and platelet pellet as scaffolds in regenerative endodontic treatment: a prospective randomized trial *J. Endod.* **45** 560–66

Usha H 2010 Biofilm in endodontics: new understanding to an old problem *Int. J. Contemp. Dent.* **1** 44–51

Valko M, Leibfritz D, Moncol J, Cronin M T, Mazur M and Telser J 2007 Free radicals and antioxidants in normal physiological functions and human disease *Int. J. Biochem. Cell Biol.* **39** 44–84

Vaudt J, Bitter K and Kielbassa A M 2007 Evaluation of rotary root canal instruments *in vitro*: a review *Endod. Pract. Today* **1** 189–203

Vazquez-Garcia F, Tanomaru-Filho M, Chávez-Andrade G M, Bosso-Martelo R, Basso-Bernardi M I and Guerreiro-Tanomaru J M 2016 Effect of silver nanoparticles on physicochemical and antibacterial properties of calcium silicate cements *Br. Dent. J.* **27** 508–14

Waltimo T M T, Sirén E K, Torkko H L K, Olsen I and Haapasalo M P P 1997 Fungi in therapy-resistant apical periodontitis *Int. Endod. J.* **30** 96–101

Wang D, Lin Z, Wang T, Yao Z, Qin M, Zheng S and Lu W 2016 Where does the toxicity of metal oxide nanoparticles come from: the nanoparticles, the ions, or a combination of both? *J. Hazard. Mater.* **308** 328–34

Wang Z, Shen Y and Haapasalo M 2012 Effectiveness of endodontic disinfecting solutions against young and old Enterococcus faecalis biofilms in dentin canals *J. Endod.* **38** 1376–9

Xia Y, Chen H, Zhang F, Wang L, Chen B, Reynolds M A, Ma J, Schneider A, Gu N and Xu H H 2018 Injectable calcium phosphate scaffold with iron oxide nanoparticles to enhance osteogenesis via dental pulp stem cells *Artif. Cells Nanomed. Biotechnol.* **46**(sup 1) 423–33

Zein N, Harmouch E, Lutz J-C, Fernandez De Grado G, Kuchler-Bopp S, Clauss F, Offner D, Hua G, Benkirane-Jessel N and Fioretti F 2019 Polymer-based instructive scaffolds for endodontic regeneration *Materials* **12** 2347

Zhang J, Park Y-D, Bae W-J, El-Fiqi A, Shin S-H, Lee E-J, Kim H-W and Kim E-C 2015 Effects of bioactive cements incorporating zinc-bioglass nanoparticles on odontogenic and angiogenic potential of human dental pulp cells *J. Biomater. Appl.* **29** 954–64

Chapter 9

[1] Zafar M S, Khurshid Z, Najeeb S, Zohaib S and Rehman I U 2017 Nanostructures for oral medicine, micro and nano technologies, *Therapeutic Applications of Nanotechnology in Dentistry* ed E Andronescu and A M Grumezescu (Amsterdam: Elsevier), pp 833–62

[2] Roy I, Stachowiak K and Bergey E J 2008 Non-viral gene transfection nanoparticles: function and applications in brain *Nanomedicine* **4** 89–97

[3] Li X, Feng Q, Cui R, Liu W, Sun L, Yu B, Fan Y, Feng Q, Cui F and Watari F 2013 The use of nanoscaled fibres or tubes to improve biocompatibility and bioactivity of biomedical materials *J. Nanomater.* **2013** 728130

[4] Salas M, Lucena C, Herrera L J, Yebra A, Bona A B and Pérez M M 2018 Translucency thresholds for dental materials *Dent. Mater.* **34** 1168–74

[5] Mirghani I, Mushtaq F, Allsop M J, Al-Saud L M, Tickhill N, Potter C and Manogue M 2018 Capturing differences in dental training using a virtual reality simulator *Eur. J. Dent. Educ.* **22** 67–71

[6] Burns J, McGoldrick N and Muir M 2018 Oral health literacy, oral health behaviours and dental outcomes *Evid. Based. Dent.* **19** 69–70

[7] Coutinho I F, Aras M A and D'souza K M 2018 Nanomaterials and their application in prosthodontics: a review *J. Res. Dent.* **6** 124–31

[8] Price C A 1994 A history of dental polymers *Aust. Prosthodont. J.* **8** 47–54

[9] Lessa F C R, Enoki C, Ito I Y, Faria G, Matsumoto M A N and Nelson- Filho P 2007 In-vivo evaluation of the bacterial contamination and disinfection of acrylic baseplates of removable orthodontic appliances *Am. J. Orthod. Dentofacial. Orthop.* **131** 705.e11

[10] Gad M M, Abualsaud R, Al-Thobity A M, Baba N Z and Al-Harbi F A 2020 Influence of addition of different nanoparticles on the surface properties of poly(methylmethacrylate) denture base material *J. Prosthodont.* **29** 422–28

[11] Mohammed B D S D and Mudhaffar B D S M 2012 Effect of modified zirconium oxide nano-fillers addition on some properties of heat cure acrylic denture base material *J. Bagh. Coll. Dent.* **24** 1–7

[12] Cooper C A, Ravich D, Lips D, Mayer J and Wagner H D 2002 Distribution and alignment of carbon nanotubes and nanofibrils in a polymer matrix *Compos. Sci. Technol.* **62** 1105–112

[13] Fouda S M, Gad M M, Ellakany P, Al-Thobity A M, Al-Harbi F A, Virtanen J I and Raustia A 2019 The effect of nanodiamonds on candida albicans adhesion and surface characteristics of pmma denture base material—an in-vitro study *J. Appl. Oral. Sci* **27** e20180779

[14] Bacali C *et al* 2020 Flexural strength, biocompatibility, and antimicrobial activity of a polymethyl methacrylate denture resin enhanced with graphene and silver nanoparticles *Clin. Oral. Investig.* **24** 2713–25

[15] Acosta- Torres L S, Lopez- Marin L M, Nunez- Anita R E, Hernandez-Padron G and Castano V M 2011 Biocompatible metal oxide nanoparticles: nanotechnology improvement of conventional prosthetic acrylic resins *J. Nanomater.* **2011** 941561

[16] Acosta- Torres L S, Mendieta I, Nunez- Anita R E and Castano V M 2012 Cytocompatible antifungal acrylic resin containing silver nanoparticles for dentures *Int. J. Nanomed.* **7** 4777–86

[17] Monteiro D R, Gorup L F, Takamiya A S, de Camargo E R, Filho A C and Barbosa D B 2012 Silver distribution and release from an antimicrobial denture base resin containing silver colloidal nanoparticles *J. Prosthodont.* **21** 7–15

[18] Totu E E, Nechifor A C, Nechifor G, Aboul- Enein H Y and Cristache C M 2017 Polymethymethacrylate with TiO_2 nanoparticles inclusion for stereographic complete denture—the future in dental care for elderly edentulous patients? *J. Dent.* **59** 68–77

[19] Gad M M, Fouda S M, Al-Harbi F A, Näpänkangas R and Raustia A 2017 PMMA denture base material enhancement: a review of fiber, filler, and nanofiller addition *Int. J. Nanomedicine.* **12** 3801–12

[20] Arun Kumar C, Ravi Kumar C, Vamshikiran K, Deepthi G, Naveen Kumar G and Akhilesh M 2019 Evaluation of impact strength of dental acrylic resins by incorporation of TiO_2 nanoparticles using two different processing techniques *J. Contemp. Dent. Pract.* **20** 1184–89

[21] Zidan S, Silikas N, Alhotan A, Haider J and Yates J 2019 Investigating the mechanical properties of ZrO_2-impregnated PMMA nanocomposite for denture-based applications *Materials (Basel)* **12** 1344

[22] Gad M M, Abualsaud R, Rahoma A, Al- Thobity A M, Al Abidi K S and Akhtar S 2018 Effect of zirconium oxide nanoparticles addition on the optical properties of polymethyl methacrylate denture base material *Int. J. Nanomedicine.* **13** 283–92

[23] Ahmed M A and Ebrahim M I 2014 Effect of zirconium oxide nanofillers addition on the flexural strength, fracture toughness and hardness of heat polymerized acrylic resin World *J. Nano. Sci. Eng.* 4 50–7

[24] Zidan S, Silikas N, Haider J, Alhotan A, Jahantigh J and Yates J 2020 Assessing tensile bond strength between denture teeth and nano-zirconia impregnated PMMA denture base *Int. J. Nanomed.* 15 9611–25

[25] Gad M, ArRajaie A S, Abdel-Halim M S and Rahoma A 2016 The reinforcement effect of nano-zirconia on the transverse strength of repaired acrylic denture base *Int. J. Dent.* **2016** 7094056

[26] Gad M M, Al-Thobity A M, Shahin S Y, Alsaqer B T and Ali A A 2017 inhibitory effect of zirconium oxide nanoparticles on candida albicans adhesion to repaired polymethyl methacrylate denture bases and interim removable prostheses: a new approach for denture stomatitis prevention *Int. J. Nanomed.* **12** 5409–19

[27] Opdam N J M, Collres K, Hickel R, Bayne S C, Loomans B A, Cenci M S and Wilson N H F 2018 Clinical studies in restorative dentistry: new directions and new demands *Dent. Mater.* **34** 1–12

[28] Donovan T E, Marzola R, Murphy K R, Cagna D R, Eichmiller F, McKee J R and Troeltzsch M 2018 Annual review of selected scientific literature: a report of the committee on scientific investigation of the American Academy of Restorative Dentistry *J. Prosthet. Dent.* **120** 816–78

[29] Chen M H 2010 Update on dental composites *J. Dent. Res.* **89** 549–60

[30] Mitra S B, Wu D and Holmes B N 2003 An application of nanotechnology in advanced dental materials *J. Am. Dent. Assoc.* 134 1382–90

[31] Pal K S, Ranganath L M, Gaikwad A V, Sarapur S and Jain S K 2015 Nanoparticles in prosthodontics—boon or bane *IJOCR.* **3** 32–9
[32] Swift E J 2005 Ask the experts-nanocomposites *J. Esthet. Restor. Dent.* **17** 3–4
[33] Xia Y, Zhang F, Xie H and Gu N 2008 Nanoparticle—reinforced resin based dental composites *J. Dent.* **36** 450–5
[34] Al-Haik M, Hanson C, Luhrs C, Tehrani M and Miltenberger S 2009 Mechanical performanance of dental fillers based on alumina nanoparticles *Proc. SEM. Ann Conf.* (Albuquerque, NM: Society for Experimental Mechanics Inc.), 1992–99
[35] Vollenweider M, Brunner T J, Knecht S, Grass R N, Zenhder N, Imfeld T and Stark W J 2007 Remineralisation of human dentine using ultrafine bioactive glass particles *Acta Biomater.* **3** 936–43
[36] Xu H H K, Weir M D and Sun L 2007 Nanocomposites with Ca and PO_4 release, effects of reinforcement, di-calcium phosphate particle size and silanization *Dent. Mater.* **23** 1482–91
[37] Xie X, Wang L, Xing D, Arola D D, Weir M D, Bai Y and Xu H H K 2016 Protein-repellant and antibacterial functions of a calcium phosphate rechargeable nanocomposite *J. Dent.* **52** 15–22
[38] Jardim R N, Rocha A A, Rossi A M, Neves A A, Portela M B, Lopes R T, Dos Santos T M P, Xing Y and da Silva E M 2020 Fabrication and characterization of remineralizing dental composites containing hydroxyapatite nanoparticles *J. Mech. Behav. Biomed. Mater.* **109** 103817
[39] Li L, Pan H, Tao J, Xu X, Mao C, GuX and Tang R 2008 Repair of enamel by using hydroxyapatite nanoparticles as the building blocks *J. Mater. Chem.* **18** 4079–84
[40] Malathi S, Sujatha V and Mahalaxmi S 2014 Nanotechnology: an asset to dentistry!!! *Int. J. Comm. Dent.* **5** 27–31
[41] Kolb C, Gumpert K, Wolter W and Sextl G 2020 Highly translucent dental resin composites through refractive index adaption using zirconium dioxide nanoparticles and organic functionalization *Dent. Mater.* **36** 1332–42
[42] Chandki R, Kala M, Kumar K N, Brigit B, Banthia P and Banthia R 2012 Nanodentistry —exploring the beauty of the miniature *J. Clin. Exp. Dent.* **4** e119–124
[43] Bai X, Lin C, Wang Y, Ma J, Wang X, Yao X and Tang B 2020 Preparation of Zn doped mesoporous silica nanoparticles (Zn-Msns) for the improvement of mechanical and antibacterial properties of dental resin composites *Dent. Mater.* **36** 794–807
[44] Zhang Y, Huang C and Chang J 2018 Ca-doped mesoporous SiO_2/dental resin composites with enhanced mechanical properties, bioactivity and antibacterial properties *J. Mater. Chem. B.* **6** 477–86
[45] Barszczewska-Rybarek I and Chladek G 2018 Studies on the curing efficiency and mechanical properties of Bis-GMA and TEGDMA nanocomposites containing silver nanoparticles *Int. J. Mol. Sci.* **19** 3937
[46] Hanif A and Ghani F 2020 Mechanical properties of an experimental resin based composite containing silver nanoparticles and bioactive glass *Pak. J. Med. Sci.* **36** 776–81
[47] Odermatt R, Par M, Mohn D, Wiedemeier D B, Attin T and Taubock T 2020 Bioactivity and physico-chemical properties of dental composites functionalized with nano- vs. micro-sized bioactive glass *J. Clin. Med.* **9** 772
[48] Ilie N, Sarosi C, Rosu M C and Moldovan M 2021 Synthesis and characterization of graphene oxide-zirconia (GO-ZrO_2) and hydroxyapatite-zirconia (HA-ZrO_2) nano-fillers for resin-based composites for load-bearing applications *J. Dent.* **105** 103557

[49] Roshanali M, Nodehi A and Atai M 2020 Synthesis and characterization of core–shell nanoparticles and their application in dental resins *Mech. Behav. Biomed. Mater.* **110** 103926
[50] Lotfi L, Javadpour J and Naimi-Jamal M R 2018 Biological and nano-indentation properties of polybenzoxazine-based composites reinforced with zirconia particles as a novel biomaterial *Biomed. Mater. Eng.* **29** 369–87
[51] Liao W, Zheng S, Chen S, Zhao L, Huang X, Huang L and Kang S 2020 Surface silanization and grafting reaction of nano-silver loaded zirconium phosphate and properties strengthen in 3D-printable dental base composites *J. Mech. Behav. Biomed. Mater.* **110** 103864
[52] Jung J H, kim D H, Yoo K H, Yoon S Y, kim Y, Bae M K, Chung J, Ko c.c., Kwon Y H and Kim Y L 2019 Dentin sealing and antibacterial effects of silver-doped bioactive glass/mesoporous silica nanocomposite: an in-vitro study *Clin. Oral. Investig.* **23** 253–66
[53] Ranjbar M, Noudeh G D, Hashemipour M A and Mohamedzad I 2019 A systematic study and effect of PLA/Al_2O_3 nanoscaffolds as dental resins: mechanochemicalproperties *Artif. Cells. Nanomed. Biotechnol.* **47** 201–9
[54] Ranjbar M, Pardakhty A, Tahmipour B and Mohamadzadeh I 2019 Novel Cao/polylactic acid nanoscaffold as dental resin nanocomposites and the investigation of physicochemical properties *Luminescence* **34** 360–67
[55] Rodriguesa M C, Chiaria M D S, Alaniaa Y, Natalea L C, Arana- Chaveza V E, Mierb M M, Fadalb V S, Vichic F M, Hewerd L R and Bragaa R R 2018 Ion-releasing dental restorative composites containing functionalized brushite nanoparticlesfor improved mechanical strength *Dent. Mater.* **34** 746–55
[56] Hesaraki S, Karimi M and Nezafati N 2020 The synergistic effects of SrF_2 nanoparticles, YSZ nanoparticles, and poly-ε-L-lysin on physicomechanical, ion release, and antibacterial-cellular behavior of the flowable dental composites *Mater. Sci. Eng. C. Mater. Bio. Appl.* **109** 110592
[57] Silikas N, Masouras K, Satterthwaite J and Watts D C 2007 Effects of nanofills in adhesives and aesthetic properties of dental resin composites *Int. J. Nano. Biomater.* **1** 116–27
[58] Abiodun-Solanke I M F, Ajayi D M and Arigbede A O 2014 Nanotechnology and its applications in dentistry *Ann. Med. Health. Sci. Res.* **4** S171–77
[59] Azad E, Atai M, Zandi M, Shokrollahi P and Solhi L 2018 Structure—properties relationships in dental adhesives: effect of initiator, matrix monomer structure, and nano-filler incorporation *Dent. Mater.* **34** 1263–70
[60] Zhang L, Weir M D, Hack G, Fouad A F and Xu H H 2015 Rechargeable dental adhesive with calcium phosphate nanoparticles for long term ion release *J. Dent.* **43** 1587–95
[61] Florez F L, Hiers R D, Larson P, Johnson M, O'Rear E, Rondinone A J and Khajotia S S 2018 Antibacterial dental adhesive resins containing nitrogen-doped titanium dioxide nanoparticles *Mater. Sci. Eng. C. Mater. Biol. Appl.* **939** 31–43
[62] Gutiérrez M F *et al* 2019 Biological, mechanical and adhesive properties of universal adhesives containing zinc and copper nanoparticles *J. Dent.* **8** 245–55
[63] Jowkar Z, Shafiei F, Asadmanesh E and Koohpeima F 2019 Influence of silver nano-particles on resin-dentin bond strength durability in a self-etch and an etch-and-rinse adhesive system *Restor. Dent. Endod.* **44** e13
[64] Solhi L, Atai M, Nodehi A and Imani M 2020 Poly (methacrylic acid) modified spherical and platelet hybrid nanoparticles as reinforcing fillers for dentin bonding systems: synthesis and properties *J. Mech. Behav. Biomed. Mater.* **109** 103840

[65] Wang W, Liao S, Liu M, Zhao Q and Fu Y 2015 Recent applications of nanomaterials in prosthodontics *J. Nanomater.* **2015** 408643
[66] Persson C, Unosson E, Ajaxon I, Engstrand J, Engqvist H and Xia W 2012 Nano grain sized zirconia-silica glass ceramics for dental applications *J. Eur.Ceram. Soc.* **32** 4105–10
[67] Raj V and Sirajudeen M M 2014 Formation and surface characterization of nanostructured Al_2O_3–Tio_2 coatings *Bull. Mater. Sci.* **37** 1141–48
[68] Fujii Y, Okada M, Taketa H and Matsumoto T 2021 Coating method for smooth and reinforced surface layer of highly translucent zirconia *Dent. Mater. J.* **40** 532–37
[69] Li C H, Hou Y L, Liu Z R and Ding Y C 2011 Investigation in temperature field of nano-zirconia ceramics precision grinding *Int. J. Abras. Technol.* **4** 77–89
[70] An J W, You D H and Lim D S 2003 Tribological properties of hot-pressed alumina-CNT composites *Wear* **255** 677–81
[71] Chen C, Trinidade F Z, de Jager N, Kleverlaan C J and Feilzer A J 2014 The fracture resistance of a CAD/CAM resin nano ceramic (RNC) and a CAD ceramic at different thickness *Dent. Mater.* **30** 954–62
[72] Koller M, Arnetzl G V, Holly L and Arnetzl G 2012 Lava ultimate resin nanoceramic for CAD/CAM: customization case study *Int. J. Comput. Dent* **15** 159–64
[73] Azari A, Jamnani S N, Yazdani A, Atri F, Rasaie V and Yazdi A F 2017 Deposition of crystalline hydroxyapatite nanoparticles on Y-TZP ceramic: a potential solution to enhance bonding characteristics of Y-TZP ceramics *J. Dent.* **14** 62
[74] Karthikeyan V, Chander N G, Reddy J R and Muthukumar B 2019 Effectsof incorporation of silver and titanium nanoparticles on feldspathic ceramic toughness *J. Dent. Res. Dent. Clin. Dent. Prospects.* **13** 98–102
[75] Magalhães A P, Ramos-Tonello C M, Galli M Z, Gomes O P, Pacheco L E, Fortulan C A, Lisboa-Filho P N, Furuse A Y and Borges A F 2020 Yttria-stabilized tetragonal zirconia polycrystal/resin luting agent bond strength: influence of titanium dioxide nanotubes addition in both materials *J. Prosthodont. Res.* **64** 408–16
[76] Nam K Y 2011 In vitro antimicrobial effect of the tissue conditioner containing silver nanoparticles *J. Adv. Prosthodont.* **3** 20–4
[77] Habibzadeh S, Omidvaran A, Eskandarion S and Shamshiri A R 2020 Effect of incorporation of silver nanoparticles on the tensile bond strength of a long term soft denture liner *Eur. J. Dent.* **14** 268–73
[78] Samaranayake Y H and Samaranayake L P 2001 Experimental oral candidiasis in animal models *Clin. Microbiol. Rev.* **14** 398–429
[79] Krevel S, Oliveira V C, Bachmann L, Alves O L and Dos Reis A 2019 Influence of $AgVO_3$ Incorporation on antimicrobial properties, hardness, roughness and adhesion of a soft denture liner *Sci. Rep.* **9** 11889
[80] Homsiang W, Komankhantikul K, Arksornnukit M and Takahashi H 2021 Effect of zinc oxide nanoparticles incorporated into tissue conditioner on antifungal, physical, and mechanical properties *Dent. Mater. J.* **40** 481–86
[81] Mousavi S A, Ghotaslou R, Akbarzadeh A, Azima N, Aeinfar A and Khorramdel A 2019 Evaluation of antibacterial and antifungal properties of a tissue conditioner used in complete dentures after incorporation of Zno–Ag nanoparticles *J. Dent. Res. Dent. Clin. Dent. Prospects.* **13** 11–18

[82] Mousavi S A, Ghotaslou R, Kordi S, Azin, Khoramdel A, Aeenfar A, Kahjough S T and Akbarzadeh A 2018 Antibacterial and antifungal effects of chitosan nanoparticles on tissue conditioners of complete dentures *Int. J. Biol. Macromol.* **118** 881–5

[83] Mousavi S A, Ghotaslou R, Khorramdel A, Akbarzadeh A and Aeinfar A 2020 Antibacterial and antifungal impacts of combined silver, zinc oxide, and chitosan nanoparticles within tissue conditioners of complete dentures *in vitro* IR *J. Med. Sci.* **189** 1343–50

[84] Garner S J, Nobbs A H, McNally L M and Barbour M E 2015 An antifungal coating for dental silicones composed of chlorhexidine nanoparticles *J. Dent.* **43** 362–72

[85] Ataol A S, Ergun G, Cekic-Nagas I, Alas M O and Genc R 2020 The effects of adding fluorescent carbon nanoparticles on variousmechanical properties of denture liners *Dent. Mater. J.* Dec **24** Online ahead of print

[86] Elsaka S E, Hamouda I M and Swain M V 2011 TiO_2 nanoparticles addition to conventional glass ionomer restoratives: influence on physical and antibacterial properties *J. Dent.* **34** 589–98

[87] Cibim D D *et al* 2017 Novel nanotechnology of TiO_2 improves physical-chemical and biological properties of glass ionomer cement *Int. J. Biomater.* **2017** 7123919

[88] Najeeb S, Khurshid Z, Zafar M S, Khan A S, Zohaib S, Martí J M N, Sauro S, Matinlinna J P and Rehman I U 2016 Modifications in glass ionomer cements: nano-sized fillers and bioactive nanoceramics *Int. J. Mol. Sci.* **17** 1134

[89] Moshavernia A, Ansari S, Movasaghi Z, Billington R W, Darr J A and Rehman I U 2008 Modification of conventional glass ionomer cements with n-vinylpyrrolidone containing polyacids, nano-hydroxy and fluoroapatite to improve the mechanical properties *Dent. Mater.* **24** 1381–90

[90] Xie D, Weng Y, Guo X, Hhao J, Gregory R L and Zheng C 2011 Preparation and evaluation of a novel glass-ionomer cement with antibacterial functions *Dent. Mater.* **27** 487–96

[91] Baheti M J and Toshniwal N G 2014 Nanotechnology: a boon to dentistry *J. Dent. Sci. Oral. Rehab.* **5** 78–88

[92] Dola S, Kumar T V, SubbaRao P S, Ravikumar R V S S N and Gopala Krishna A 2017 Green synthesis and characterization of Ag nanoparticles from mangifera indica leaves for dental restoration and antibacterial application *Prog. Biomater.* **6** 57–66

[93] Yoshida K, Tanagawa M, Matsumoto S, Yamada T and Atsuta M 1999 Antibacterial activity of resin composites with silver containing materials *Euro. J. Oral. Sci.* **107** 290–96

[94] Habekost L V, Camacho G B, Lima G S, Ogliari F A, Cubas G B and Moraes R R 2012 Nanoparticle loading level and properties of experimental hybrid resin luting agents *J. Prosthodont.* **21** 540–45

[95] Ramos-Tonello C M, Lisboa-Filho P N, Arruda L B, Tokuhara C K, Oliviera R C, Furuse A Y, Rubo J H and Borges A F S 2017 Titanium dioxide nanotubes addition to self-adhesive resin cement: effect on physical and biological properties *Dent. Mater.* **33** 866–75

[96] Karimi M A, Roozbahani S H, Reza A, Hatefi A, Mashhadizadeh M H, Behjatmanesh-Ardakani R, Mohammad M A, Kargar H and Zebarjad S 2011 Synthesis and characterization of nanoparticles and nanocomposites of ZnO and MgO by sonochemical method and their application for zinc polycarboxylate dental cement preparation *Int. Nano. Lett.* **1** 43–51

[97] AlSahafi R, Balhaddad A A, Mitwalli H, Ibrahim M S, Melo M A S, Oates T W, Xu H H K and Weir M D 2020 Novel crown cement containing antibacterial monomer and calcium phosphate nanoparticles *Nanomaterials (Basel)* 10 2001

[98] Padmasree S, Vaishnavi R and Sridharan R 2018 OSC45: comparative evaluation of physical properties of nanoparticle incorporated addition silicone with other elastomeric impression materials *J. Indian. Prosthodont. Soc.* **18** S27–8

[99] Jhaveri H M and Balaji P R 2005 Nanotechnology: the future of dentistry *J. Indian. Prosthodont. Soc.* **5** 15–17

[100] Ginjupalli K, Shaw T, Tellapragada C, Alla R, Gupta L and Perampalli N U 2018 Does the size matter? Evaluation of effect of incorporation of silver nanoparticles of varying particle size on the antimicrobial activity and properties of irreversible hydrocolloid impression material *Dent. Mater.* **34** e158–65

[101] Matos G R M 2021 Surface roughness of dental implant and osseointegration *J. Maxillofac. Oral. Surg.* **20** 1–4

[102] Chopra D, Gulati K and Ivanovski S 2021 Understanding and optimizing the antibacterial functions of anodized nano-engineered titanium implants *Acta. Biomater.* **127** 80–1

[103] Yeo I L 2019 Modifications of dental implant surfaces at the microand nano-level for enhanced osseointegration *Materials (Basel)* 13 89

[104] Yao C, Slamovich E B and Webster T J 2008 Enhanced osteoblast functions on anodized titanium with nanotube-like structures *J. Biomed. Mater. Res.* A **85** 157–66

[105] Puckett S, Pareta R and Webster T J 2008 Nano rough micron patterned titanium for directing osteoblast morphology and adhesion *Int. J. Nanomed.* **3** 229–41

[106] Praveena C, Chaughule R S and Satyanarayana K V 2021 Advances in dental implantology using nanomaterials and allied technology applications *Nanotechnology in Implant Dentistry* ed R S Chaughule and R Dashaputra (Cham: Springer), pp 9–17

[107] Souza J C M, Sordi M B, Kanazawa M, Ravindran S, Henriques B, Silva F S, Aparicio C and Cooper L F 2019 Nano-scale modification of titanium implant surfaces to enhance osseointegration *Acta. Biomater.* **94** 112–31

[108] Yazdani J, Ahmadian E, Sharifi S, Shahi S and Maleki Dizaj S 2018 A short view on nanohydroxyapatite as coating of dental implants *Biomed. Pharmacother.* **105** 553–7

[109] Souza J G S *et al* 2020 Targeting pathogenic biofilms: newly developed superhydrophobic coating favors a host-compatible microbial profile on the titanium surface *ACS Appl. Mater. Interfaces.* **12** 10118–29

[110] Huang Y, Shen X, Qiao H, Yang H, Zhang X, Liu Y and Yang H 2018 Biofunctional Sr- and Si-loaded titania nanotube coating of Ti surfaces by anodization-hydrothermal process *Int. J. Nanomed.* **13** 633–40

[111] Zayed S M, Alshimy A M and Fahmy A E 2014 Effect of surface treated silicon dioxide nanoparticles on some mechanical properties of maxillofacial silicone elastomer *Int. J. Biomater.* **2014** 750398

[112] Han Y, Kiat-amnuay S, Powers J M and Zhao Y 2008 Effect of nanooxide concentration on the mechanical properties of a maxillofacial silicone elastomer *J. Prosthet. Dent.* **100** 465–73

[113] Akay C, Cevik P, Karakis D and Sevim H 2018 In vitro cytotoxicity of maxillofacial silicone elastomers: effect of nano-particles *J. Prosthodont.* **27** 584–87

[114] Abdalqadir M, Faraj S and Azhdar B 2021 An evaluation of a technique to improve the mechanical properties of maxillofacial silicone elastomers with zinc oxide nanoparticles *J. Prosthet. Dent.* in press

[115] Shakir D A and Abdul-Ameer F M 2018 Effect of nano-titanium oxide addition on some mechanical properties of silicone elastomers for maxillofacial prostheses *J. Taibah. Univ. Med. Sci.* **13** 281–90 Erratum in: *J. Taibah. Univ. Med. Sci.***13** 407
[116] Abdul-Ameer F M 2020 Impact of a mixture of nanofiller and intrinsic pigment on tear strength and hardness of two types of maxillofacial silicone elastomers *Dent. Res. J. (Isfahan)* **17** 251–57
[117] Meran Z, Besinis A, De Peralta T and Handy R D 2018 Antifungal properties and biocompatibility of silver nanoparticle coatings on silicone maxillofacial prostheses *Vitro J. Biomed. Mater. Res. B. Appl. Biomater.* **106** 1038–51
[118] Barman A, Rashid F, Farook T H, Jamayet N B, Dudley J, Yhaya M F B and Alam M K 2020 The influence of filler particles on the mechanical properties of maxillofacial prosthetic silicone elastomers: a systematic review and meta-analysis *Polymers (Basel)* **12** 1536
[119] Arafa K A O 2016 Comparing the effects of titanium alloy and chrome cobalt in removable partial denture connectors on tooth mobility, bone loss and tissue reaction *Saudi. J. Dent. Res.* **7** 112–7
[120] Moradpoor H, Safaei M, Rezaei F, Golshah A, Jamshidy L, Hatam R and Abdullah R S 2019 Optimisation of cobalt oxide nanoparticles synthesis as bactericidal agents *Open. Access. Maced. J. Med. Sci.* **7** 2757–62
[121] Iravani S and Varma R S 2020 Sustainable synthesis of cobalt and cobalt oxide nanoparticles and their catalytic and biomedical applications *Green. Chem.* **22** 2643–61
[122] Joiner A 2006 The bleaching of teeth: a review of the literature *J. Dent.* **34** 412–19
[123] Kurzmann C, Verheyen J, Coto M, Kumar R V, Divitini G, Shokoohi-Tabrizi H A, Verheyen P, De Moor R J G, Moritz A and Agis H 2019 *In vitro* evaluation of experimental light activated gels for tooth bleaching *Photochem. Photobiol. Sci.* **18** 1009–19
[124] Lima F V, Mendes C, Zanetti-Ramos B G, Nandi J K, Cardoso S G, Bernardon J K and Silva M A S 2019 Carbamide peroxide nanoparticles for dental whitening application: characterization, stability and *in vivo*/*in situ* evaluation *Colloids. Surf.* B **179** 326–33
[125] Wang Y, Wen X, Jia Y, Huang M, Wang F, Zhang X, Bai Y, Yuan G and Wang Y 2020 Piezo-catalysis for nondestructive tooth whitening *Nat. Commun.* **11** 1328
[126] Vildosola P, Bottner J, Avalos F, Godoy I, Martin J and Fernandez E 2017 Teeth bleaching with low concentrations of hydrogen peroxide (6%) and catalyzed by LED blue (450 ± 10 nm) and laser infrared (808 ± 10 nm) light for in-office treatment: randomized clinical trial 1-year follow-up *J. Esthet. Restor. Dent.* **29** 339–45
[127] Zhang F, Wu C, Zhou Z, Wang J, Bao W, Dong L, Zhang Z, Ye Jing, Liao L and Wang X 2018 Blue-light-activated nano-TiO_2@PDA for highly effective and nondestructive tooth whitening *ACS. Biomater. Sci. Eng.* **4** 3072–77

Chapter 10

[1] Taniguchi N 1974 Proc. Int. Conf. Prod. Eng., Part II, Japan Society of Precision Engineering, Tokyo *J. Jpn. Soc. Precis. Eng.* **40** 516–21
[2] El-Sayed I 2010 Nanotechnology in head and neck cancer: the race is on *Curr. Oncol. Rep.* **12** 121–8
[3] Karatutlu A, Barhoum A and Sapelkin A 2018 Liquid-phase synthesis of nanoparticles and nanostructured materials *Micro and Nano Technologies, Emerging Applications of Nanoparticles and Architecture Nanostructures* (Amsterdam: Elsevier), pp 1–28

[4] de Souza Rastelli A N, Carreira E T, Dias H B and Hamblin M R 2016 Nanobiomaterials in dentistry *Nanobiomaterials in Dentistry* (Boston, MA: William Andrew Publishing), pp 1–25
[5] AZoNano 2020 Classification of nanomaterials, the four main types of intentionally produced nanomaterials https://www.azonano.com/article.aspx?ArticleID=1872
[6] Abbasi E, Aval S, Akbarzadeh A, Milani M, Nasrabadi H, Joo S, Hanifehpour Y, Nejati-Koshki K and Pashaei-Asl R 2014 Dendrimers: synthesis, applications, and properties *Nanoscale Res. Lett.* **9** 247
[7] Mayer A, Johnson R, Hausner S and Mark J 1999 Colloidal silver nanoparticles protected by water-solublenonionic polymers and 'soft' polyacids *J. Macromol. Sci., Part* A **36** 1427–41
[8] Zhao C-Y, Cheng R, Yang Z and Tian Z-M 2018 Nanotechnology for cancer therapy based on chemotherapy *Molecules* **23** 826
[9] Poonia M, Ramalingam K, Goyal S and Sidhu S K 2017 Nanotechnology in oral cancer: a comprehensive review *J. Oral Maxillofac. Pathol.* **21** 407–14
[10] Chen X J, Zhang X Q, Liu Q, Zhang J and Zhou G 2018 Nanotechnology: a promising method for oral cancer detection and diagnosis *J. Nanobiotechnol.* **16** 52
[11] Ghosh P, Han G, De M, Kim C and Rotello V 2008 Gold nanoparticles in delivery applications. *Adv. Drug Delivery Rev.* **60** 1307–15
[12] Cho K, Wang X, Nie S, Chen Z and Shin D 2008 Therapeutic nanoparticles for drug delivery in cancer *Clin. Cancer Res.* **14** 1310–16
[13] Choi H and Frangioni J 2010 Nanoparticles for biomedical imaging: fundamentals of clinical translation *Mol. Imag.* **9** 291–310
[14] Nie S, Xing Y, Kim G and Simons J 2007 Nanotechnology applications in cancer *Annu. Rev. Biomed. Eng.* **9** 257–88
[15] Frangioni J 2008 New technologies for human cancer imaging *J. Clin. Oncol.* **26** 4012–21
[16] Klaassen C D 2001 *Casarett and Doull's Toxicology: The Basic Science of Poisons* (New York: McGraw-Hill)
[17] Cheng W, Ping Y, Zhang Y, Chuang K H and Liu Y 2013 Magnetic resonance imaging (MRI) contrast agents for tumor diagnosis *J. Healthc. Eng.* **4** 23–45
[18] Bennett K M, Jo J, Cabral H, Bakalova R and Aoki I 2014 MR imaging techniques for nano-pathophysiology and theranostics *Adv. Drug. Deliv. Rev.* **74** 75–94
[19] Brigger I, Dubernet C and Couvreur P 2002 Nanoparticles in cancer therapy and diagnosis *Adv. Drug Deliv. Rev.* **54** 631–51
[20] Pande P, Shrestha S, Park J, Gimenez-Conti I, Brandon J and Applegate B E *et al* 2016 Automated analysis of multimodal fluorescence lifetime imaging and optical coherence tomography data for the diagnosis of oral cancer in the hamster cheek pouch model *Biomed. Opt. Express* **7** 2000–15
[21] Kim C S, Wilder-Smith P, Ahn Y C, Liaw L H, Chen Z and Kwon Y J 2009 Enhanced detection of early-stage oral cancer *in vivo* by optical coherence tomography using multi-modal delivery of gold nanoparticles *J. Biomed. Opt.* **14** 034008
[22] Sharma A, Jain N and RashmiSareen 2013 Nanocarriers for diagnosis and targeting of breast cancer *BioMed Res. Int.* **2013** 960821
[23] Tomsia A P, Launey M E, Lee J S, Mankani M H, Wegst Ulrike G K and Saiz E *et al* 2011 Nanotechnology approaches for better dental implants *Int. Oral Maxillofac. Implants.* **26** 25–44
[24] Zheng M *et al* 2003 Structure-based carbon nanotube sorting by sequence-dependent DNA assembly *Science* **302** 1545–8

[25] Shvedova A A *et al* 2008 Inhalation vs. aspiration of single-walled carbon nanotubes in C57BL/6 mice: inflammation, fibrosis, oxidative stress, and mutagenesis *Physiol. Lung Cell. Mol. Physiol.* **295** L552–65
[26] Sargent L M *et al* 2012 Single-walled carbon nanotube-induced mitotic disruption *Mutat. Res.* **745** 28–37
[27] Akerman M E, Chan W C, Laakkonen P, Bhatia S N and Ruoslahti E 2002 Nanocrystal targeting *in vivo Proc. Natl Acad. Sci. USA* **99** 12617–21
[28] Paciotti G F, Myer L and Weinreich D *et al* 2004 Colloidal gold: a novel nanoparticle vector for tumor directed drug delivery *Drug Deliv.* **11** 169–83
[29] Goldman E R, Clapp A R, Anderson G P, Uyeda H T and Mauro J M *et al* 2004 Multiplexed toxin analysis using four colors of quantum dot fluororeagents *Anal. Chem.* **76** 684–8
[30] Ahamed M, AlSalhi M S and Siddiqui M K J 2010 Silver nanoparticle applications and human health *Clin. Chim. Acta* **411** 1841–8

Chapter 11

[1] Mallanagouda P, Dhoom Singh M and Sowjanya G 2008 Future impact of nanotechnology on medicine and dentistry *J. Ind. Soc. Periodontol* **12** 34–40
[2] Reshma R 2021 Review article nanotechnology in interdisciplinary dentistry *Indian J. Med. Sci.* **73** 226–9
[3] Freitas R Jr 2005 Nanotechnology: nanomedicine and nanosurgery *Int. J. Surg.* **3** 243–46
[4] Chen H F, Clarkson B H, Sunk and Mansfield J F 2005 Self-assembly of synthetic hydroxyaptite nanorods into enamel prism like structure *J. Colloid Interf. Sci.* **188** pp 97–108
[4] Maryam M 2013 Review future of dentistry, nanodentistry, ozone therapy and tissue engineering *J. Develop. Biol. Tissue Eng.* **5** 1–6
[5] Cao W and Zhang Y 2018 Novel resin-based dental material with anti-biofilm activity and improved mechanical property by incorporating hydrophilic cationic copolymer functionalized nanodiamond *J. Mater. Sci. Mater. Med.* **29** 162
[6] Amini H, Shenkin J D and Chi D L 2019 Dental public health issues in pediatric dentistry *Pediatr. Dent.* **617** 159–68
[7] Thomas N, Blake S, Morris C and Moles D R 2018 Autism and primary care dentistry: parents' experiences of taking children with autism or working diagnosis of autism for dental examinations *Int. J. Paediatr. Dent.* **28** 226
[8] Loke K F, Mohammad M F, Armita F M and Mohadeseh S *et al* 2020 Review article: applications of nanomaterials in diverse dentistry regimes *RSC Adv.* **10** 15430–60
[9] Saafan A and Zaazou M H 2018 Assessment of photodynamic therapy and nanoparticles effects on caries models *Open Access Maced. J. Med. Sci.* **6** 1289–95
[10] Magalhaes A P and Moreira F C 2016 Silver nanoparticles in resin luting cements: antibacterial and physiochemical properties *J. Clin. Exp. Dent.* **8** 415–22
[11] Bhuvaneswarri J, Nazish Alam M, Chandrasekaran S C and Sathya M S 2013 , Future impact of nanotechnology in dentistry—a review Int. J. Nanotechnol. Appl. *(IJNA)* **3** 15–20
[12] Abiodun-Solanke I M F, Ajayi D M and Arigbede A O 2014 Nanotechnology and its application in dentistry *Ann. Med. Health Sci. Res.* **4** 171–77
[13] Robert A F 2005 Progress in nanomedicine and medical nanorobotics https://researchgate.net/publication/241612132

[14] Shaeesta K B 2014 Current applications of nanotechnology in dentistry: a review *Gen. Dent.* **62** 72–7
[15] Neetha J S, Swati P and David K 2013 Review article, nanorobots: future in dentistry *Saudi Dent. J.* **25** 49–52
[16] Banu V 2012 Applications of nanomedicine in oral cancer *Oral Health Dent. Manag.* **11** 62–68
[17] Nikalje A P 2015 Nanotechnology—its applications in medicine *Med. Chem.* **5** 81–89
[18] Hatziantoniou S and Demetzos C 2006 An introduction to nanotechnology in health care *Pharmakeftiki* **19** 86–88
[19] Himanshu A, Varun K, Shashank U and Pooja T 2015 Nanodentistry: is just a fiction or future *J. Oral Biol. Craniofac. Res.* **5** 207–11
[20] Freitas R Jr 2005 Nanotechnology, nanomedicine and nanosurgery *Int. J. Surg.* **3** 243–46
[21] Sneha S, Sashi R A and Vidya S 2013 Review article: nanodentistry *Indian J. Sci. Res.* **4** 233–38
[22] Rybachunk A V and Chelkman I S 2009 Nanotechnology and nanoparticles in dentistry *Pharmacol. Pharm.* **1** 18–21
[23] Rita C, Kala M, Kiran B, Priyank B and Ruchi B 2012 Review article: 'Nanodentistry': exploring the beauty of miniature *J. Clin. Exp. Dent.* **4** 119–24
[24] Zohaib K, Muhammad Z, Saad Q, Sana S, Mustafa N and Ammar A R 2015 Advances in nanotechnology for restorative dentistry *Mater. Eng.* **8** 717–31
[25] Shellart W C and Oesterle I J 1999 Uprighting molars without extrusion *JADA* **130** 38
[26] Bumb S S, Bhaskar D J and Punia H 2013 Nanorobots and challenges faced by nanodentistry *Guident.* pp 67–69
[27] Neeta S and Swati P 2013 Nanorobots: future in dentistry *Saudi Dental J.* **25** 49–52
[28] Upadhyay Y 2013 Current state and future perspectives of nanotechnology in dentistry *Int. Organ. Sci. Res. J. Pharm.* **3** 68–71
[30] Hernandez J D, Perez M A and Valenzuela M C 2011 Use of new technologies in dentistry *Rev. Odontol. Mex.* **15** 158–63
[31] Fakruddin M, Hossain Z and Afroz H 2012 Prospects and applications of nanobiotechnology: a medical perspective *J. Nanobiotechnol.* **10** 1–8
[32] Rao K V and Kumar J S 2013 Nanotechnology in dentistry *Kerala Dent. J.* **36** 56–59
[33] Lainovic T, Vilotic M, Blazic L, Kakas D, Markovic D and Ivanisevic A 2013 Determination of surface roughness and topography of dental resin-based nanocomposites using AFM analysis *Bosn. J. Basic. Med. Sci.* **13** 35–43
[34] Wang W, Liao S, Zhu Y, Liu M, Zhao Q and Fu Y 2015 Recent applications of nanomaterials in prosthodontics *J. Nanomater.* **2** 1–11
[35] Ozak S T and Ozkan P 2013 Nanotechnology and dentistry *Eur. J. Dent.* **7** 145–51
[36] Rathee M and Bhoria M 2014 Nanodentistry: the emerging tiny tools—a review *Int. J. Biosci. Nanosci.* **1** 63–67
[37] Saravana K R and Vijaylakshmi R 2006 Nanotechnology in dentistry *Indian J. Dent. Res.* **17** 62–65
[38] Kong L X, Peng Z, Li S and Mark P 2000 Nanotechnology and its role in the management of periodontal diseases *Periodontology* **40** 184–96
[39] Jesitus J Nanotechnology accelerates wound healing http://dermatologytimes.modernmedicine.com

[40] Priyadarsini S, Mukherjee S and Mishra M 2018 Nanoparticles used in dentistry: a review *J. Oral Biol. Craniofac. Res.* **8** 58–67
[41] Business Wire 2019 Global $36+ billion toothpaste market, 2024: growth, trends and forecast analysis from 2019 https://businesswire.com/news/home/20190509005698/en/Global-36-Billion-Toothpaste-Market-2024-Growth-Trends-and-Forecast-Analysis-from-2019---ResearchAndMarkets.com
[42] European Commission 2018 Catalogue of nanomaterials in cosmetic products placed on the market https://ec.europa.eu/docsroom/documents/38284
[43] Florence C, Stephane V, Livia O, Cedric G and Denis B 2020 Review nanoparticles as antimicrobial, anti-inflammatory, and remineralizing agents in oral care cosmetics: a review of the current situation *Nanomaterials* **10** 1–32
[44] Loke K F, Mohammad M F, Armita F M and Mohadeseh S *et al* 2020 Applications of nano materials in diverse dentistry regimes *RSC Adv.* **10** 15430–60
[45] Resnik D B and Tinkle S S 2007 Ethics in nanomedicine *Nanomedicine* **2** 345–50
[46] Eman M O 2019 Environmental and health safety considerations of nanotechnology: nano safety *Biomed. J. Sci. Techn. Res. BJSTR* **19** 14501–15
[47] Hester K, Mullins M, Murphy F and Tofail S A M 2015 Anticipatory ethics and governance (AEG): towards a future care orientation around nanotechnology *Nano Ethics* **9** 123–36
[48] Brey P A 2012 Anticipatory ethics for emerging technologies *NanoEthics* **6** 1–13
[49] Khushf G 2006 An ethic for enhancing human performance through integrative technologies *Managing Nano-Bio-Info Cogno Innovations* (Berlin: Springer), pp 255–78
[50] Gupta N, Fischer A R and Frewer L J 2015 Ethics, risk and benefits associated with different applications of nanotechnology: a comparison of expert and consumer perceptions of drivers of societal acceptance *NanoEthics* **9** 93–108
[51] Kurzweil R 2006 The singularity is near: when humans transcend biology *Technol. Forecast. Soc. Change* **73** 95–127
[52] Macnaghten P, Kearnes M B and Wynne B 2005 Nanotechnology, governance, and public deliberation: what role for the social sciences *Sci. Commun.* **27** 268–91
[53] Erik F and Roop L M 2006 Contradictory intent? US federal legislation on integrating societal concerns into nanotechnology research and development *Sci. Public Policy* **33** 5–16
[54] Leo S and Louis T 2011 Environmental implications of nanotechnology—an update *Int. J. Environ. Res. Public Health* **8** 470–79
[55] Rawan N A 2018 The Implications and applications of nanotechnology in dentistry: a review *Saudi Dental J.* **30** 107–16
[56] Stone V, Hankin S, Aschberger R K, Anders B, Christensen F and Fernandes T *et al* 2010 Engineered nanoparticles: review of health and environmental safety (ENRHES) *Project Final Report, European Commission* http://nmi.jrc.ec.europa.eu/documents/pdf/ENRHES%20Review.pdf
[57] Jyoti G 2011 Review Article: dental biomaterials nanotechnology applications in medicine and dentistry *J. Investig. Clin. Dent.* **2** 81–88
[58] Karlsson H L, Cronholm P, Gustafsson J and Möller L 2008 Copper oxide nanoparticles are highly toxic: a comparison between metal oxide nanoparticles and carbon nanotubes *Chem. Res. Toxicol.* **21** 1726–32
[59] Rafal P, Krzysztof P and Agnieszka M 2018 Nanomaterials in dentistry: a cornerstone or a black box *Nanomedicine* **3** 639–67

[60] Kopera D, Soyer H P and Kopera H 1998 Nonprecious metal tattoos (amalgam tattoos) of the oral mucosa can be successfully removed with the Q-switched Ruby laser *Laser in Medicine* (Berlin: Springer), pp 453–55
[61] Buchner A 2004 Amalgam tattoo (amalgam pigmentation) of the oral mucosa: clinical manifestations, diagnosis and treatment *Refuat Hapeh Vehashinayim* **21** 25–8
[62] Medina C, Inkielewicz S I, Santos M J and Radomski M W 2014 Pharmacological and toxicological effects of co-exposure of human gingival fibroblasts to silver nanoparticles and sodium fluoride *Int. J. Nanomed.* **9** 1677
[63] Zielinska E, Tukaj C, Radomski M W and Inkielewicz-Stepniak I 2016 Molecular mechanism of silver nanoparticles-induced human osteoblast cell death: protective effect of inducible nitric oxide synthase inhibitor *PLoS One* **11** e0164137
[64] Gaillet S and Rouanet J M 2015 Silver nanoparticles: their potential toxic effects after oral exposure and underlying mechanisms—a review *Food Chem. Toxicol.* **77** 58–63
Gunduz N, Ceylan H, Guler M O and Tekinay A B 2017 Intracellular accumulation of gold nanoparticles leads to inhibition of macropinocytosis to reduce the endoplasmic reticulum stress *Sci. Rep.* **7** 1–10
[65] Jia G, Zhi A, Lai P F H, Wang G, XiaY, Xiong Z, Zhang H, Che N and Ai L 2018 The oral microbiota—a mechanistic role for systemic diseases *Br. Dent. J.* **224** 447–55
[66] Gunduz N, Ceylan H, Guler M O and Tekinay A B 2017 Intracellular accumulation of gold nanoparticles leads to inhibition of macropinocytosis to reduce the endoplasmic reticulum *Stress. Sci. Rep.* **7** 1–10
[67] Sung J H, Ji J H, Park J D, Song M Y, Song K S, Ryu H R, Yoon J U, Jeon K S, Jeong J and Han B S *et al* 2011 Subchronic inhalation toxicity of gold nanoparticles *Part. Fibre Toxicol.* **8** 16
[68] Agarwal H, Nakara A and Shanmugam V K 2019 Anti-inflammatory mechanism of various metal and metal oxide nanoparticles synthesized using plant extracts: a review *Biomed. Pharmacother. Biomed. Pharmacother.* **109** 2561–72
[69] Lynch E, Brauer D S, Karpukhina N, Gillam D G and Hill R G 2012 Multi-component bioactive glasses of varying fluoride content for treating dentin hypersensitivity *Dent. Mater.* **28** 168–78
[70] Kachoei M Y, Divband B, Tabriz F D, Helali Z N and Esmailzadeh 2018 A comparative study of antibacterial effects of mouthwashes containing Ag/ZnO or ZnO nanoparticles with chlorhexidine and investigation of their cytotoxicity *Nanomed. J.* **5** 102–10
[71] Karlsson H L, Cronholm P, Gustafsson J and Moller L 2008 Copper oxide nanoparticles are highly toxic: a comparison between metal oxide nanoparticles and carbon nanotubes *Chem. Res. Toxicol.* **21** 1726–32
[72] Geraets L, Oomen A G, Krystek P, Jacobsen N R, Wallin H, Laurentie M, Verharen H W, Brandon E F and de Jong W H 2014 Tissue distribution and elimination after oral and intravenous administrationof different titanium dioxide nanoparticles in rats *Part. Fibre Toxicol.* **11** 30
[73] Rompelberg C, Heringa M B, van Donkersgoed G, Drijvers J, Roos A, Westenbrink S, Peters R, vanBemmel G, Brand W and Oomen A G 2016 Oral intake of added titanium dioxide and its nanofraction from food products, food supplements and toothpaste by the Dutch population *Nanotoxicology* **10** 1404–14
[74] Baranowska-Wójcik E, Szwajgier D, Oleszczuk P and Winiarska-Mieczan A 2019 Effects of titanium dioxidenanoparticles exposure on human health—a review *Biol. Trace Elem. Res.* **193** 118–29

[75] Niska K, Knap N, Kedzia A, Jaskiewicz M, Kamysz W and Inkielewicz-Stepniak I 2016 Capping agent-dependent toxicity and antimicrobial activity of silver nanoparticles: an in vitro study, concerns about potential application in dental practice *Int. J. Med. Sci.* **13** 772–82

[76] Geng H, Poologasundarampillai G and Todd N *et al* 2017 Biotransformation of silver released from nanoparticle coated titanium implants revealed in regenerating bone *ACS Appl. Mater. Interfaces* **9** 21169–80

[77] Pokrowiecki R, Zareba T and Szaraniec B *et al* 2017 In vitro studies of nanosilver doped Ti-implants for oral and maxillofacial surgery *Int. J. Nanomed.* **12** 4285–97

[78] Pauksch L, Hartmann S and Rohnke M *et al* 2014 Biocompatibility of silver nanoparticles and silver ions in primary human mesenchymal stem cells and osteoblasts *Acta Biomater.* **10** 439–49

[79] Hsiao I L, Hsieh Y K, Wang C-F, Chen I C and Huang Y J 2015 Trojan-Horse mechanism in the cellular uptake of silver nanoparticles verified by direct intra- and extracellular silver speciation analysis *Environ. Sci. Technol.* **49** 3813–21

[80] Aruoja V, Dubourguier H C, Kasemets K and Kahru A 2009 Toxicity of nanoparticles of CuO, ZnO and TiO_2 to microalgae *Pseudokirchneriella Subcapitata Sci. Total Environ.* **407** 1461–68

[81] McShan D, Ray P C and Yu H 2014 Molecular toxicity mechanism of nanosilver *J. Food Drug Anal.* **22** 116–27

[82] Kaplan J H and Maryon E B 2016 How mammalian cells acquire copper: an essential butpotentially toxic metal *Biophys. J.* **110** 7–13

[83] Lyons T and Eide D 2007 Transport and storage of metal ions in biology *Biological Inorganic Chemistry—Structure and Reactivity* (Sausolito, CA: University Science Books), pp 57–78

[84] Park E J, Yi J, Kim Y, Choi K and Park K 2010 Silver nanoparticles induce cytotoxicity by a Trojan-horse type mechanism *Toxicol. in Vitro* **24** 872–78

[85] Jiravova J, Tomankova K B and Harvanova M *et al* 2016 The effect of silver nanoparticles and silver ions on mammalian and plant cells *in vitro Food Chem. Toxicol.* **96** 50–61

[86] Shang L, Nienhaus K and Nienhaus G U 2014 Engineered nanoparticles interacting with cells: size matter *J. Nanobiotechnol.* **12** 5

[87] Zhang X-F, Shen W and Gurunathan S 2016 Silver nanoparticle-mediated cellular responses in various cell lines: an *in vitro* model *Int. J. Mol. Sci.* **17** 1603

[88] Cheng X, Tian X and Wu A *et al* 2015 Protein corona influences cellular uptake of gold nanoparticles by phagocytic and nonphagocytic cells in a size-dependent manner *ACS Appl. Mater. Interfaces* **7** 20568–75

[89] Dobrovolskaia M A, Patri A K and Zheng J *et al* 2009 Interaction of colloidal gold nanoparticles with human blood: effects on particle size and analysis of plasma protein binding profiles *Nanomed. Nanotechnol. Biol. Med.* **5** 106–17

[90] Corbo C, Molinaro R, Parodi A, Toledano Furman N E, Salvatore F and Tasciotti E 2016 The impact of nanoparticle protein corona on cytotoxicity, immunotoxicity and target drug delivery *Nanomedicine* **11** 81–100

[91] Gaillet S and Rouanet J-M 2014 Silver nanoparticles: their potential toxic effects after oral exposure and underlying mechanisms—a review *Food Chem. Toxicol.* **77C** 58–63

[92] Konstantinova V, Ibrahim M and Lie S A *et al* 2017 Nano-TiO_2 penetration of oral mucosa: *in vitro* analysis using 3D organotypic human buccal mucosa models *J. Oral Pathol. Med.* **46** 214–22

[93] Walczak A P, Fokkink R and Peters R *et al* 2013 Behavior of silver nanoparticles and silver ions in an *in vitro* human gastrointestinal digestion model *Nanotoxicology* **7** 1198–210
[94] Roblegg E, Frohlich E, Meindl C, Teubl B, Zaversky M and Zimmer A 2012 Evaluation of a physiological *in vitro* system to study the transport of nanoparticles through the buccal mucosa *Nanotoxicology* **6** 399–413
[95] Laffleur F, Hintzen F, Shahnaz G, Rahmat D, Leithner K and Bernkop-Schnurch A 2014 Development and *in vitro* evaluation of slippery nanoparticles for enhanced diffusion through native mucus *Nanomedicine* **9** 387–96
[96] Teubl B J, Leitinger G and Schneider M *et al* 2014 The buccal mucosa as a route for TiO_2 nanoparticle uptake *Nanotoxicology* **5390** 1–9
[97] Fröhlich E and Roblegg E 2016 Oral uptake of nanoparticles: human relevance and the role of *in vitro* systems *Arch. Toxicol.* **90** 2297–314
[98] Wang B, Feng W and Wang M *et al* 2008 Acute toxicological impact of nano- and submicro-scaled zinc oxide powder on healthy adult mice *J. Nanoparticle Res.* **10** 263–76
[99] Ebabe Elle R, Gaillet S and Vide J *et al* 2013 Dietary exposure to silver nanoparticles in Sprague–Dawley rats: effects on oxidative stress and inflammation *Food Chem. Toxicol.* **60** 297–301
[100] Liu H, Ma L, Liu J, Zhao J, Yan J and Hong F 2010 Toxicity of nano-anatase TiO_2 to mice: liver injury, oxidative stress *Toxicol. Environ. Chem.* **92** 175–86
[101] Subhashree P, Sumit M and Monalisa M 2018 Review article nanoparticles used in dentistry: a review *J. Oral Biol. Craniofac. Res.* **8** 58–67
[102] Besinis A, De Peralta T, Tredwin C J and Handy R D 2015 A review of nanomaterials in dentistry: interactions with the oral microenvironment, clinical applications, hazards and benefits *ACS Nano* **9** 2255–89

Chapter 12

[1] Rabilloud T, Chevallet M, Luche S and Leong C 2010 Two-dimensional gel electrophoresis in proteomics: past, present and future *J. Proteomics* **73** 2064–77
[2] Fabian T, Hermann P, Beck A, Fejerdy P and Fabian G 2012 Salivary defense proteins: their network and role in innate and acquired oral immunity *Int. J. Mol. Sci.* **13** 4295–320
[3] Garcia-Godoy F and Hicks M 2008 Maintaining the integrity of the enamel surface. The role of dental biofilm, saliva and preventive agents in enamel demineralization and remineralization *J. Am. Dent. Assoc.* **139** 25S–34S
[4] Paine M and Snead M 2005 Tooth developmental biology: disruptions to enamel-matrix assembly and its impact on biomineralization *Orthod Craniofac. Res.* **8** 239–51
[5] Vitorino R, Guedes S, Manadas B, Ferreira R and Amado F 2012 Toward a standardized saliva proteome analysis methodology *J. Proteom.* **75** 5140–65
[6] He L and Swain M 2008 Understanding the mechanical behavior of human enamel from its structural and compositionalcharacteristics *J. Mech. Behav. Biomed. Mater.* **1** 18–29
[7] Zenobio M, Tavres M, Zenobio E and Silva T 2011 Elemental composition of dental biologic tissues: study by means of different analytical techniques *J. Radioanal. Nucl. Chem.* **289** 161–6
[8] Hu J, Chun Y, A L, Hazzazzi T and Simmer J 2007 Enamel formation and amelogenesis imperfecta *Cells Tissues Organs* **186** 78–85

[9] Lee J, Lee D, Choung H, Shon W, Seo B, Lee E, Cho J and Park J 2011c Odontogenic differentiation of human dental pulp stem cells induced by preameloblast-derived factors *Biomaterials* **32** 9696–706
[10] Dusevich V, Xu C, Wang Y, Walker M and Gorski J 2012 Identification of a protein-containing enamel matrix layer which bridges with the dentine-enamel junction of adult human teeth *Arch. Oral Biol.* **57** 1585–94
[11] Webb E, Amarasiriwardena D, Tauch S, Green E, Jones J and Goodman A 2005 Inductively coupled plasma-mass (ICP-MS) and atomic emission spectrometry (ICP-AES): versatile analytical techniques to identify the archived elemental information in human teeth *Microchem. J.* **81** 201–8
[12] Sharma V, Srinivasan A, Roychoudhury A, Rani K, Tyagi M, Dev K, Nikolaje F and Kumar S 2019 Characterization of protein extracts from dierent types of human teeth and insight in biomineralization *Sci. Rep.* **9** 9314
[13] Cook J, Layrisse M, Martinez-Torres C, Walker R, Monsen E and Finch C 1972 Food iron absorption measured by an extrinsic tag *J. Clin. Invest.* **51** 805–15
[14] Jágr M, Eckhardt A, Pataridis S and Miksik I 2012 A comprehensive proteomics analysis of human dentin *Eur. J. Oral Sci.* **120** 259–68
[15] Lee K, Kang H, Yoo S, Lee J, Hwang Y, Nam K, Kim J S, Park J and Kim J 2011 Novel dentin phosphoprotein frameshift mutations in dentinogenesis imperfecta type II *Clin. Genet.* **79** 378–84
[16] Foster B *et al* 2011 The progressive ankylosis protein regulates cementum apposition and extracellular matrix composition *Cells Tissues Organs* **194** 382–405
[17] Byers M and Taylor P 1993 Effect of sensory denervation on the response of rat molar pulp to exposure injury *J. Dent. Res.* **72** 613–8
[18] Couve E, Osorio R and Schmachtenberg O 2013 The amazing odontoblast: activity, autophagy, and aging *J. Dent. Res.* **92** 765–72
[19] Hannig C, Hannig M and Attin T 2005 Enzymes in the acquired enamel pellicle *Eur. J. Oral Sci.* **113** 2–13
[20] Fabian T, Fejerdy P and Csermely P 2008 Salivary genomics, transcriptomics and proteomics: the emerging content of the oral ecosystem and their use in the early diagnosis of cancer and other diseases *Curr. Genom.* **9** 11–21
[21] Hubbard M and Kon J 2002 Proteomic analysis of dental tissues *J. Chromatogr.* B **771** 211–20
[22] Paine M and Snead M 2005 Tooth developmental biology: disruptions to enamel-matrix assembly and its impact on biomineralization *Orthodon. Craniofac. Res.* **8** 239–51
[23] Butler W, Brunn J and Qin C 2003 Dentin extracellular matrix (ECM) proteins: comparison to bone ECM and contribution to dynamics of dentinogenesis *Connect Tissue Res.* **44** 171–8
[24] Hu J, Yamakoshi Y, Yamakoshi F, Krebsbah P and Simmer J 2005 Proteomics and genetics of dental enamel *Cells Tissues Organs* **181** 219–31
[25] Tsuchiya S, Simmer J, Hu J, Richarddson A, Yamakoshi F and Yamakoshi Y 2011 Astacin proteases cleave dentin sialophosphoprotein (Dspp) to generate dentin phosphoprotein (DPP) *J. Bone Miner. Res.* **26** 220–8
[26] Smith A, Scheven B, Takahashi Y, Ferracane J, Shelton R and Cooper P 2012 Dentine as a bioactive extracellular matrix *Arch. Oral Biol.* **57** 109–21
[27] Bar-On B and Wagner H 2013 Structural motifs and elastic properties of hierarchical biological tissues—a review *J. Struct. Biol.* **183** 149–64

[28] Mckee M, Hoac B, Addison W, Barros N, Millan J and Chaussain C 2013 Extracellular matrix mineralization in periodontal tissues: noncollagenous matrix proteins, enzymes, and relationship to hypophosphatasia and x-linked hypophosphatemia *Periodontology* **2000** 102–22

[29] Linde A 1989 Dentin matrix proteins, composition and possible functions in calcification *Anatom. Rec.* **224** 154–66

[30] Myllyharju J and Kivirikko K 2004 Collagens, modifying enzymes and their mutations in humans, flies and worms *Trends Gen.* **20** 33–43

[31] Yamakishi Y, Hu J, Iwata T, Kobayashi K, Fuake M and Simmer J 2006 Dentin sialophosphoprotein is processed by MMP-2 and MMP-20 *in vitro* and *in vivo J. Biol. Chem.* **281** 38235–43

[32] Mazzoni A, Pashley D, Ay F, Gobbi P, Orsisni G, Ruggeri A, Carrilho M, Tjaderhane L, Dilenarda R and Breschi L 2009 Immunohistochemical identification of MMP-2 and MMP-9 in human dentin,correlative FEI-SEM/TEM analysis *J. Biomed. Mater. Res.* A **88** 697–703

[33] Park E, Cho H, Kwon T, Jang S, Lee S, An C, Shin H, Kim J and Cho J 2009 Proteomics analysis of human dentin reveals distinct protein expression profiles *J. Proteome Res.* **8** 1338–46

[34] Lee S-K, Lee K-E, Song J S, Hyun H-K, Lee S-H and Kim J-W 2013 A DSPP mutation causing dentinogenesis imperfecta and characterization of the mutational effect *Biomed. Res. Int.* **2013** 948181

[35] Qin C, Brunn J, Baba O, Wygant J, Mcintyre B and Butler W 2003 Dentin sialoprotein isoforms, detection and characterization of a high molecular weight dentin sialoprotein *Eur. J. Oral Sci.* **111** 235–42

[36] Gibson M, Zhu Q, Liu Q, D´souza R, Feng J and Qin C 2013 Loss of dentin sialophosphoprotein leads to periodontal diseases in mice *J. Periodontal Res.* **48** 221–7

[37] Qin C, Brunn J, Jones J, George A, Ramachandran A, Gorski J and Butler W 2001 A comparative study of sialic acid-rich proteins in rat bone and dentin *Eur. J. Oral Sci.* **109** 133–41

[38] Suzuki S, Sreenath T, Haruyama N, Honeycutt C, Terse A, Cho A, Kohler T, Muller R, Goldberg M and Kulkarni A 2009 Dentin sialoprotein and dentin phosphoprotein have distinct roles in dentin mineralization *Matrix Biol.* **28** 221–9

[39] Beniash E, Deshpande A, Fang P, Lieb N, Zhang X and Sfeir C 2011 Possible role of DMP1 in dentin mineralization *J. Struct. Biol.* **174** 100–6

[40] Ma D, Zhang R, Sun Y, Rios H, Haruyama N, Han X, Kulkarni A, Qin C and Feng J 2011 A novel role of periostin in postnatal tooth formation and mineralization *J. Biol. Chem.* **286** 4302–9

[41] Papagerakis P, Berdal A, Mesbah M, Peucmaur M, Malaval L, Nydegger J, Simmer J and Macdougall M 2002 Investigation of osteocalcin, osteonectin, and dentin sialophosphoprotein in developing human teeth *Bone* **30** 377–85

[42] Embery G, Hall R, Waddington R, Septier D and Goldberg M 2001 Proteoglycans in dentinogenesis *Critic. Rev. Oral Biol. Med.* **12** 331–49

[43] Haruyama N, Sreenath T, Suzuki S, Yao X, Wang Y, Honeycutt C, Iozzo R, Young M and Kulkarni A 2009 Genetic evidence for key roles of decorin and biglycan in dentin mineralization *Matrix Biol.* **28** 129–36

[44] Petersson U, Hultenby K and Wendel M 2003 Identification, distribution and expression of osteoadherin during toothformation *Eur. J. Oral Sci.* **111** 128–36

[45] Bosshardt D and Selvig K 1997 Dental cementum: the dynamic tissue covering of the root *Periodontology* **13** 41–75
[46] Nanci A 1999 Content and distribution of noncollagenous matrix proteins in bone and cementum: relationship to speed of formation and collagen packing density *J. Struct. Biol.* **126** 256–69
[47] Wei X, Wu L, Ling J, Liu L, Liu S, Liu W, Li M and Xiao Y 2008 Differentially expressed protein profile of human dental pulp cells in the early process of odontoblast-like differentiation *in vitro J. Endodontol.* **34** 1077–84
[48] Sawa Y, Kuroshima S, Yamaoka Y and Yoshida S 2005 Intracellular distribution of desmoplakin in human odontoblasts *J. Histochem. Cytochem.* **53** 1099–108
[49] Sandanayake N *et al* A combination of serum leucine-rich alpha-2-glycoprotein 1, CA 19-9 and interleukin-6 differentiate biliary tract cancer from benign biliary structures *Br. J. Cancer* **105** 1370–8
[50] Siqueira W, Zhang W, Helmerhorst E, Gygi S and Oppenheim F 2007 Identification of protein components in *in vivo* human acquired enamel pellicle using LC-ESI-MS/MS *J. Proteom. Res.* **6** 2152–60
[51] Lee Y, Zimmerman J, Custodio W, Xiao Y, Basiri T, Hatibovic-Kofman S and Siqueira L 2013 Proteomic evaluation of acquired enamel pellicle during *in vivo* formation *PLoS One* **8** e67919
[52] Sahlberg C, Aukhil I and I T 2001 Tenascin-C in developing mouse teeth: Expression of splice variants and stimulation by TGF and FGF *Int. Eur. J. Oral Sci.* **109** 114–24
[53] Tucker R and Degen M 2019 The expression and possible functions of Tenascin-W during development and disease *Front. Cell Develop. Biol.* **7** 53
[54] Kaur J and Reinhardt D 2015 Extracellular Matrix (ECM) molecules *Stem Cell Biology and Tissue Engineering in Dental Sciences* (Amsterdam: Elsevier)
[55] Salmon C, Tomazela D, Rui K, Foster B, Leme A, Sallum E, Somerman M and Nociti F 2013 Proteomic analysis of human dental cementum and alveolar bone *J. Proteomics* **91** 544–55
[56] Farah R, Monk B, Swain M and Drummond B Protein content of molar-incisor hypomineralization enamel *J. Dent* **38** 591–6
[57] Ohshima H, Nakakura K, Yamamoto H and Haeda T 2001 Alteration in the expression of heat shock protein (Hsp) 25-immunoreactivity in the dental pulp of rat molars following tooth replantation *Arch. Histol. Cytol.* **64** 425–37
[58] Iohara K, Zheng L, Ito M, Tomokiyo A, Matsushita K and Nakashima M 2006 Side population cells isolated from porcine dental pulp tissue with self-renewal and multipotency for dentinogenesis, chondrogenesis, adipogenesis, and neurogenesis *Stem Cells* **24** 2493–503
[59] Paakkonen V and Tjaderhane L 2010 High-throughput gene and protein expression analysis in pulp biologic research: review *J. Endodontol.* **36** 179–89
[60] Paakkonen V, Ohelmeir S, Bergmann U, Larmas M, Salo T and Tjäderhane L 2005 Analysis of gene and protein expression in healthy and carious tooth pulp with cDNA microarray and two-dimensional gel electrophoresis *Eur. J. Oral Sci.* **113** 369–79
[61] Mclachlan J, Sloan A, Smith A, Landini G and Cooper P 2004 S100 and cytokine expression in caries *Infect. Immun.* **72** 4102–8
[62] Mclachlan J, Smith A, Bujalska I and Cooper P 2005 Gene expression profiling of pulpal tissue reveals the molecular complexity of dental caries *Biochim. Biophys. Acta* **1741** 271–81

[63] Smith A, Scheven B, Takahashi Y, Ferracane J, Shelon R and Cooper P 2012 Dentine as a bioactive extracellular matrix *Arch. Oral Biol.* **57** 109–21
[64] Qin Y, Zhong Y, Zhu M, Dang L, Yu H, Chen Z, Chen W, Wang X, Zhang H and Li Z 2013 Age- and sexassociated differences in the glycopatterns of human salivary glycoproteins and their roles against influenza A virus *J. Proteome Res.* **12** 2742–54
[65] Grandin H, Gemperli A and Dard M 2012 Enamel matrix derivative: a review of cellular effects *in vitro* and a model of molecular arrangement and functioning *Tissue Eng. Part B Rev.* **18** 181–202
[66] Cairo F, Pagliaro U and Nieri M 2008 Treatment of gingival recession with coronally advanced flap procedures: a systematic review *J. Clin. Periodontol.* **35** 136–62
[67] Lallier T, Yukna R, St Marie S and Moses R 2001 The putative collagen binding peptide hastens periodontal ligament cell attachment to bone replacement graft materials *J. Periodontol.* **72** 990–7
[68] Yukna R, Salinas T and Carr R 2002 Periodontal regeneration following use of ABM/P-15: a case report *Int. J. Periodontics Restorative Dent.* **22** 146–55
[69] Hollinger J, Hart C, Hirsch S, Lynch S and Friedlaender G 2008 Recombinant human platelet-derived growth factor: biology and clinical applications *J. Bone Joint Surg. Am.* **90** 48–54
[70] Morotome Y, Goseki-Sone M, Ishikawa I and S O 1998 Gene expression of growth and differentiation factors-5, -6, and -7 in developing bovine tooth at the root forming stage *Biochem. Biophys. Res. Commun.* **244** 85–90
[71] Stavropoulos A, Windisch P, Gera I, Capsius B, Sculean A and Wikesjo U 2011 A phase IIa randomized controlled clinical and histological pilot study evaluating rhGDF-5/beta-TCP for periodontal regeneration *J. Clin. Periodontol.* **38** 1044–54
[72] Aspenberg P, Genant H, Johansson T, Nino A, See K and Krohn K 2010 Teriparatide for acceleration of fracture repair in humans: a prospective, randomized, double-blind study of 102 postmenopausal women with distal radial fractures *J. Bone Miner. Res.* **25** 404–14

Chapter 13

[1] Priyadarsini S, Mukherjee S and Mishra M 2018 Nanoparticles used in dentistry: a review *J. Oral Biol. Craniofac. Res.* **8** 58–67
[2] Priyadarsini S, Mukherjee S, Bag J, Nayak N and Mishra M 2020 *Nanoparticles in Medicine* (Berlin: Springer), pp 55–98
[3] Feng X, Chen A, Zhang Y, Wang J, Shao L and Wei L 2015 Application of dental nanomaterials: potential toxicity to the central nervous system *Int. J. Nanomed.* **10** 3547
[4] Shahi S, Özcan M, Maleki Dizaj S, Sharifi S, Al-Haj Husain N, Eftekhari A and Ahmadian E 2019 A review on potential toxicity of dental material and screening their biocompatibility *Toxicol. Mech. Methods* **29** 368–77
[5] Xiaoli F and Longquan S 2018 Neurotoxicity of nanomaterials *Emerging Nanotechnologies in Dentistry* ed K Subramani and W Ahmed (Amsterdam: Elsevier), ch 20 421–44
[6] Teleanu D M, Chircov C, Grumezescu A M and Teleanu R I 2019 Neurotoxicity of nanomaterials: an up-to-date overview *Nanomaterials* **9** 96
[7] Manzo L, Artigas F, Martínez E, Mutti A, Bergamaschi E, Nicotera P, Tonini M, Candura S M, Ray D E and Costa L G 1996 Biochemical markers of neurotoxicity. A review of mechanistic studies and applications *Human Exp. Toxicol.* **15** S20–35

[8] Nanda R, Panda P and Mishra M 2020 *Nanomaterials in Diagnostic Tools and Devices* (Amsterdam: Elsevier), pp 479–523
[9] Mishra M and Panda M 2021 Reactive oxygen species: the root cause of nanoparticle-induced toxicity in *Drosophila melanogaster Free Radical Res.* **55** 1–17
[10] Jang H J, Lee E C, Kwon G J and Seo Y K 2020 The effect of coated nano-hydroxyapatite concentration on scaffolds for osteogenesis *J. Biomater. Appl.* **34** 827–39
[11] Samanipour F, Bayati M, Golestani-Fard F, Zargar H, Mirhabibi A, Shoaei-Rad V and Abbasi S 2011 Innovative fabrication of ZrO_2–HAp–TiO_2 nano/micro-structured composites through MAO/EPD combined method *Mater. Lett.* **65** 926–8
[12] Soundrapandian C, Bharati S, Basu D and Datta S 2011 Studies on novel bioactive glasses and bioactive glass–nano-HAp composites suitable for coating on metallic implants *Ceram. Int.* **37** 759–69
[13] Teixeira J A, Santos Júnior V E d, Melo Júnior P C d, Arnaud M, Lima M G, Flores M A P, Stamford T C M, Dias Pereira J R, Ribeiro Targino A G and Galembeck A 2018 Effects of a new nano-silver fluoride-containing dentifrice on demineralization of enamel and *Streptococcus mutans* adhesion and acidogenicity *Int. J. Dent.* **2018** 1351925
[14] Bapat R A, Joshi C P, Bapat P, Chaubal T V, Pandurangappa R, Jnanendrappa N, Gorain B, Khurana S and Kesharwani P 2019 The use of nanoparticles as biomaterials in dentistry *Drug Discov. Today* **24** 85–98
[15] Galvez A M, Ramos K M, Teja A J and Baculi R 2021 Bacterial exopolysaccharide-mediated synthesis of silver nanoparticles and their application on bacterial biofilms *J. Microbiol. Biotechnol. Food Sci.* **2021** 970–8
[16] Espinosa-Cristóbal L F, López-Ruiz N, Cabada-Tarín D, Reyes-López S Y, Zaragoza-Contreras A, Constandse-Cortéz D, Donohué-Cornejo A, Tovar-Carrillo K, Cuevas-González J C and Kobayashi T 2018 Antiadherence and antimicrobial properties of silver nanoparticles against Streptococcus mutans on brackets and wires used for orthodontic treatments *J. Nanomater.* **2018** 9248527
[17] Spriano S, Yamaguchi S, Baino F and Ferraris S 2018 A critical review of multifunctional titanium surfaces: new frontiers for improving osseointegration and host response, avoiding bacteria contamination *Acta Biomater.* **79** 1–22
[18] Simon A P, Santos V A Q, Rodrigues A, Santos J S, Trivinho-Strixino F, Pereira B L, Lepienski C M and Sikora M d S 2019 Enhancement of mechanical properties and wettability of TiO_2NT arrays formed in simulated body fluid-based electrolyte *Adv. Eng. Mater.* **21** 1900813
[19] Netti P A 2014 *Regenerative Medicine Applications in Organ Transplantation* (Amsterdam: Elsevier), pp 137–50
[20] Yuan Q, He G, Tan Z, Gong P, Li X Y, Chen Z Q, Ban Y, Tang H, Wang F F and Man Y 2007 Biocompatibility of nano-TiO_2/HA bioceramic coating for nerve regeneration around dental implants *Key Engineering Materials* (College Park, MD: TransTech Publ), pp 1393–6
[21] Salehi P, Babanouri N, Roein-Peikar M and Zare F 2018 Long-term antimicrobial assessment of orthodontic brackets coated with nitrogen-doped titanium dioxide against Streptococcus mutans *Prog. Orthod.* **19** 1–6
[22] Cao B, Wang Y, Li N, Liu B and Zhang Y 2013 Preparation of an orthodontic bracket coated with an nitrogen-doped $TiO_{2-x}N_y$ thin film and examination of its antimicrobial performance *Dent. Mater. J.* **32** 311–6

[23] Jiang Y, Zhang L, Wen D and Ding Y 2016 Role of physical and chemical interactions in the antibacterial behavior of ZnO nanoparticles against E. coli *Mater. Sci. Eng.* **C69** 1361–6
[24] Jiang J, Pi J and Cai J 2018 The advancing of zinc oxide nanoparticles for biomedical applications *Bioinorg. Chem. Appl* **2018** 1062562
[25] Windiasti G, Feng J, Ma L, Hu Y, Hakeem M J, Amoako K, Delaquis P and Lu X 2019 Investigating the synergistic antimicrobial effect of carvacrol and zinc oxide nanoparticles against *Campylobacter jejuni Food Control* **96** 39–46
[26] Feris K, Otto C, Tinker J, Wingett D, Punnoose A, Thurber A, Kongara M, Sabetian M, Quinn B and Hanna C 2010 Electrostatic interactions affect nanoparticle-mediated toxicity to gram-negative bacterium *Pseudomonas aeruginosa* PAO1 *Langmuir* **26** 4429–36
[27] Wang S, Wu J, Yang H, Liu X, Huang Q and Lu Z 2017 Antibacterial activity and mechanism of Ag/ZnO nanocomposite against anaerobic oral pathogen *Streptococcus mutans J. Mater. Sci.: Mater. Med.* **28** 1–8
[28] Toledano M, Vallecillo-Rivas M, Aguilera F S, Osorio M T, Osorio E and Osorio R 2021 Polymeric zinc-doped nanoparticles for high performance in restorative dentistry *J. Dent.* **107** 103616
[29] Kraipok A, Mamanee T, Ruangsuriya J and Leenakul W 2021 Investigation of phase formation and mechanical properties of lithium disilicate glass-ceramic doped CeO_2 *J. Non-Cryst. Solids* **561** 120772
[30] Garcia I M, Leitune V C B, Takimi A S, Bergmann C P, Samuel S M W, Melo M A and Collares F M 2020 Cerium dioxide particles to tune radiopacity of dental adhesives: Microstructural and physico-chemical evaluation *J. Funct. Biomater.* **11** 7
[31] Augustine R, Hasan A, Patan N K, Dalvi Y B, Varghese R, Antony A, Unni R N, Sandhyarani N and Moustafa A-E A 2019 Cerium oxide nanoparticle incorporated electrospun poly (3-hydroxybutyrate-co-3-hydroxyvalerate) membranes for diabetic wound healing applications *ACS Biomater. Sci. Eng.* **6** 58–70
[32] Augustine R, Zahid A A, Hasan A, Dalvi Y B and Jacob J 2020 Cerium oxide nanoparticle-loaded gelatin methacryloyl hydrogel wound-Healing patch with free radical scavenging activity *ACS Biomater. Sci. Eng.* **7** 279–90
[33] Kaze R C, Beleuk à Moungam L M, Cannio M, Rosa R, Kamseu E, Melo U C and Leonelli C 2018 Microstructure and engineering properties of Fe_2O_3 (FeO)-Al_2O_3-SiO_2 based geopolymer composites *J. Clean. Prod.* **199** 849–59
[34] Gad M M and Abualsaud R 2019 Behavior of PMMA denture base materials containing titanium dioxide nanoparticles: a literature review *Int. J. Biomater.* **2019** 6190610
[35] Xu Z-l, Yu L-y and Han L-f 2009 Polymer-nanoinorganic particles composite membranes: a brief overview *Front. Chem. Sci. Eng. China* **3** 318–29
[36] Hossen M M, Chowdhury F, Gafur M, Hakim A A and Nasrin S 2014 Investigation of mechanical properties of $Al_2O_{3–20}$ wt% ZrO_2 composites as a function of sintering temperature *Eur. Sci. J.* **10**
[37] Sonin D L, Korolev D V, Postnov V N, Naumysheva E B, Pochkaeva E I, Vasyutina M L and Galagudza M M 2016 Silicon-containing nanocarriers for targeted drug delivery: synthesis, physicochemical properties and acute toxicity *Drug Deliv.* **23** 1747–56
[38] De Cremer K, Braem A, Gerits E, De Brucker K, Vandamme K, Martens J, Michiels J, Vleugels J, Cammue B and Thevissen K 2017 Controlled release of chlorhexidine from a mesoporous silica-containing macroporous titanium dental implant prevents microbial biofilm formation *Eur. Cells Mater.* **33** 13–27

[39] Barot T, Rawtani D and Kulkarni P 2021 Nanotechnology-based materials as emerging trends for dental applications *Rev. Adv. Mater. Sci.* **60** 173–89
[40] Gulati K, Maher S, Findlay D M and Losic D 2016 Titania nanotubes for orchestrating osteogenesis at the bone–implant interface *Nanomedicine* **11** 1847–64
[41] De Aza A, Chevalier J, Fantozzi G, Schehl M and Torrecillas R 2002 Crack growth resistance of alumina, zirconia and zirconia toughened alumina ceramics for joint prostheses *Biomaterials* **23** 937–45
[42] Gautam C, Joyner J, Gautam A, Rao J and Vajtai R 2016 Zirconia based dental ceramics: structure, mechanical properties, biocompatibility and applications *Dalton Trans.* **45** 19194–215
[43] Behnaz M, Davani S T, Abdi A, Azadi G and Goudarzi M 2018 Efficacy of antimicrobial agents in orthodontic adhesive systems and brackets: a narrative review *J. Dent. Sch.* **37** 112–7
[44] Ahmed B, Solanki B, Zaidi A, Khan M S and Musarrat J 2019 Bacterial toxicity of biomimetic green zinc oxide nanoantibiotic: insights into ZnONP uptake and nanocolloid–bacteria interface *Toxicol. Res.* **8** 246–61
[45] Pelling H, Nzakizwanayo J, Milo S, Denham E, MacFarlane W, Bock L, Sutton J and Jones B 2019 Bacterial biofilm formation on indwelling urethral catheters *Lett. Appl. Microbiol.* **68** 277–93
[46] Son N T, Oda M, Hayashi N, Yamaguchi D, Kawagishi Y, Takahashi F, Harada K, Cuong N M and Fukuyama Y 2018 Antimicrobial activity of the constituents of Dalbergia tonkinensis and structural-bioactive highlights *Nat. Prod. Commun.* **13**
[47] Fatfat M, Abou Merhi R, Rahal O, Stoyanovsky D A, Zaki A, Haidar H, Kagan V E, Gali-Muhtasib H and Machaca K 2014 Copper chelation selectively kills colon cancer cells through redox cycling and generation of reactive oxygen species *BMC Cancer* **14** 1–12
[48] Vimbela G V, Ngo S M, Fraze C, Yang L and Stout D A 2017 Antibacterial properties and toxicity from metallic nanomaterials *Int. J. Nanomed.* **12** 3941
[49] Olteanu D, Filip A, Socaci C, Biris A R, Filip X, Coros M, Rosu M C, Pogacean F, Alb C and Baldea I 2015 Cytotoxicity assessment of graphene-based nanomaterials on human dental follicle stem cells *Colloids Surf.* B **136** 791–8
[50] He J, Zhu X, Qi Z, Wang C, Mao X, Zhu C, He Z, Li M and Tang Z 2015 Killing dental pathogens using antibacterial graphene oxide *ACS Appl. Mater. Interfaces* **7** 5605–11
[51] Konar M, Nayak N, Priyadarsini S, Mishra M and Sahoo H 2019 Antimicrobial activity of nanoparticle-based dental fillers on novel chromogenic bacteria *Enterobacter ludwigii Mater. Res. Exp.* **6** 085407
[52] Kulshrestha S, Khan S, Meena R, Singh B R and Khan A U 2014 A graphene/zinc oxide nanocomposite film protects dental implant surfaces against cariogenic *Streptococcus mutans Biofouling* **30** 1281–94
[53] Wang C, Hu H, Li Z, Shen Y, Xu Y, Zhang G, Zeng X, Deng J, Zhao S and Ren T 2019 Enhanced osseointegration of titanium alloy implants with laser microgrooved surfaces and graphene oxide coating *ACS Appl. Mater. Interfaces* **11** 39470–83
[54] Ge Z, Yang L, Xiao F, Wu Y, Yu T, Chen J, Lin J and Zhang Y 2018 Graphene family nanomaterials: properties and potential applications in dentistry *Int. J. Biomater.* **2018** 1539678
[55] Sarosi C, Biris A R, Antoniac A, Boboia S, Alb C, Antoniac I and Moldovan M 2016 The nanofiller effect on properties of experimental graphene dental nanocomposites *J. Adhesion Sci. Technol.* **30** 1779–94

[56] Toledano M, Osorio R, Osorio E, Medina-Castillo A L, Toledano-Osorio M and Aguilera F S 2017 Ions-modified nanoparticles affect functional remineralization and energy dissipation through the resin-dentin interface *J. Mech. Behav. Biomed. Mater.* **68** 62–79
[57] Li Y, Hu X, Xia Y, Ji Y, Ruan J, Weir M D, Lin X, Nie Z, Gu N and Masri R 2018 Novel magnetic nanoparticle-containing adhesive with greater dentin bond strength and antibacterial and remineralizing capabilities *Dent. Mater.* **34** 1310–22
[58] Vitt A, Sofrata A, Slizen V, Sugars R, Gustafsson A, Gudkova E, Kazeko L, Ramberg P and Buhlin K 2015 Antimicrobial activity of polyhexamethylene guanidine phosphate in comparison to chlorhexidine using the quantitative suspension method *Ann. Clin. Microbiol. Antimicrob.* **14** 1–9
[59] Curtis A R, Palin W M, Fleming G J, Shortall A C and Marquis P M 2009 The mechanical properties of nanofilled resin-based composites: characterizing discrete filler particles and agglomerates using a micromanipulation technique *Dent. Mater.* **25** 180–7
[60] Satpathy A, Ranjan R, Priyadarsini S, Gupta S, Mathur P and Mishra M 2019 *Medical Imaging Methods* (Berlin: Springer), pp 59–95
[61] McCabe J F and Walls A W 2013 *Applied Dental Materials* (New York: Wiley)
[62] Buzea C, Pacheco I I and Robbie K 2007 Nanomaterials and nanoparticles: sources and toxicity *Biointerphases* **2** MR17–71
[63] Pachter J S, de Vries H E and Fabry Z 2003 The blood-brain barrier and its role in immune privilege in the central nervous system *J. Neuropathol. Exp. Neurol.* **62** 593–604
[64] Stadelmann C, Wegner C and Brück W 2011 Inflammation, demyelination, and degeneration—recent insights from MS pathology *Biochim. Biophys. Acta (BBA)-Molecular Basis of Disease* **1812** 275–82
[65] Wolburg H, Noell S, Mack A, Wolburg-Buchholz K and Fallier-Becker P 2009 Brain endothelial cells and the glio-vascular complex *Cell Tissue Res.* **335** 75–96
[66] Xiao G and Gan L-S 2013 Receptor-mediated endocytosis and brain delivery of therapeutic biologics *Int. J. Cell Biol.* **2013** 703545
[67] Curtis J, Greenberg M, Kester J, Phillips S and Krieger G 2006 Nanotechnology and nanotoxicology *Toxicol. Rev.* **25** 245–60
[68] Al-Lamki R S, Bradley J R and Pober J S 2017 Human organ culture: updating the approach to bridge the gap from in vitro to in vivo in inflammation, cancer, and stem cell biology *Front. Med.* **4** 148
[69] Li Y, Fan J and Ju D 2019 *Brain Targeted Drug Delivery System* (Amsterdam: Elsevier), pp 377–408
[70] Kumar V, Sharma N and Maitra S 2017 In vitro and in vivo toxicity assessment of nanoparticles *Int. Nano Lett.* **7** 243–56
[71] Figueroa-González G and Pérez-Plasencia C 2017 Strategies for the evaluation of DNA damage and repair mechanisms in cancer *Oncol. Lett.* **13** 3982–8
[72] Blanco A and Blanco G 2017 *Apoptosis Medical Biochemistry* (New York: Elsevier), ch 32 pp 791–6
[73] Lovisolo D, Dionisi M, Ruffinatti F A and Distasi C 2018 Nanoparticles and potential neurotoxicity: focus on molecular mechanisms *AIMS Molecul. Sci.* **5** 1–13
[74] Weksler B, Romero I A and Couraud P-O 2013 The hCMEC/D3 cell line as a model of the human blood brain barrier *Fluids Barriers CNS* **10** 1–10
[75] Greiffenberg L, Goebel W, Kim K S, Weiglein I, Bubert A, Engelbrecht F, Stins M and Kuhn M 1998 Interaction of Listeria monocytogenes with human brain microvascular

endothelial cells: InlB-dependent invasion, long-term intracellular growth, and spread from macrophages to endothelial cells *Infect. Immun.* **66** 5260–7

[76] Al Ahmad A, Gassmann M and Ogunshola O 2009 Maintaining blood–brain barrier integrity: pericytes perform better than astrocytes during prolonged oxygen deprivation *J. Cell. Physiol.* **218** 612–22

[77] Guttenplan K A and Liddelow S A 2019 Astrocytes and microglia: models and tools *J. Exp. Med.* **216** 71–83

[78] Nakagawa S, Deli M A, Kawaguchi H, Shimizudani T, Shimono T, Kittel A, Tanaka K and Niwa M 2009 A new blood–brain barrier model using primary rat brain endothelial cells, pericytes and astrocytes *Neurochem. Int.* **54** 253–63

[79] Arakha M, Roy J, Nayak P S, Mallick B and Jha S 2017 Zinc oxide nanoparticle energy band gap reduction triggers the oxidative stress resulting into autophagy-mediated apoptotic cell death *Free Radic. Biol. Med.* **110** 42–53

[80] Choi J, Zheng Q, Katz H E and Guilarte T R 2010 Silica-based nanoparticle uptake and cellular response by primary microglia *Environ. Health Persp.* **118** 589–95

[81] Larner S F, Wang J, Goodman J, O'Donoghue Altman M B, Xin M and Wang K K 2017 *In vitro* neurotoxicity resulting from exposure of cultured neural cells to several types of nanoparticles *J. Cell Death* **10** 1179670717694523

[82] Bhattamisra S K, Shak A T, Xi L W, Safian N H, Choudhury H, Lim W M, Shahzad N, Alhakamy N A, Anwer M K and Radhakrishnan A K 2020 Nose to brain delivery of rotigotine loaded chitosan nanoparticles in human SH-SY5Y neuroblastoma cells and animal model of Parkinson's disease *Int. J. Pharm.* **579** 119148

[83] Xu L J, Zhao J X, Zhang T, Ren G G and Yang Z 2009 *In vitro* study on influence of nano particles of CuO on CA1 pyramidal neurons of rat hippocampus potassium currents *Environ. Toxicol.* **24** 211–7

[84] Lapiz M and Morilak D 2006 Noradrenergic modulation of cognitive function in rat medial prefrontal cortex as measured by attentional set shifting capability *Neuroscience* **137** 1039–49

[85] Kreyling W G, Holzwarth U, Haberl N, Kozempel J, Hirn S, Wenk A, Schleh C, Schäffler M, Lipka J and Semmler-Behnke M 2017 Quantitative biokinetics of titanium dioxide nanoparticles after intravenous injection in rats: part 1 *Nanotoxicology* **11** 434–42

[86] Sun C, Yin N, Wen R, Liu W, Jia Y, Hu L, Zhou Q and Jiang G 2016 Silver nanoparticles induced neurotoxicity through oxidative stress in rat cerebral astrocytes is distinct from the effects of silver ions *Neurotoxicology* **52** 210–21

[87] Valdiglesias V, Fernández-Bertólez N, Kiliç G, Costa C, Costa S, Fraga S, Bessa M J, Pásaro E, Teixeira J P and Laffon B 2016 Are iron oxide nanoparticles safe? Current knowledge and future perspectives *J. Trace. Elem. Med. Biol.* **38** 53–63

[88] Song B, Zhang Y, Liu J, Feng X, Zhou T and Shao L 2016 Unraveling the neurotoxicity of titanium dioxide nanoparticles: focusing on molecular mechanisms *Beilstein J. Nanotechnol.* **7** 645–54

[89] Zhou M, Xie L, Fang C-J, Yang H, Wang Y-J, Zhen X-Y, Yan C-H, Wang Y, Zhao M and Peng S 2016 Implications for blood-brain-barrier permeability, in vitro oxidative stress and neurotoxicity potential induced by mesoporous silica nanoparticles: Effects of surface modification *RSC Adv.* **6** 2800–9

[90] Shi D, Mi G and Webster T 2017 *Neurotoxicity of Nanomaterials and Nanomedicine* (Amsterdam: Elsevier), pp 259–84

[91] Dusinska M, Rundén-Pran E, Schnekenburger J and Kanno J 2017 *Adverse Effects of Engineered Nanomaterials* (Amsterdam: Elsevier), pp 51–82
[92] Pappus S A and Mishra M 2018 A drosophila model to decipher the toxicity of nanoparticles taken through oral routes *Cell. Mol. Toxicol. Nanopart.* **1048** 311–22
[93] O'Brown N M, Pfau S J and Gu C 2018 Bridging barriers: a comparative look at the blood–brain barrier across organisms *Genes Devel.* **32** 466–78
[94] Song B, Zhang Y, Liu J, Feng X, Zhou T and Shao L 2016 Is neurotoxicity of metallic nanoparticles the cascades of oxidative stress? *Nanoscale Res. Lett.* **11** 1–11
[95] Barik B K and Mishra M 2019 Nanoparticles as a potential teratogen: a lesson learnt from fruit fly *Nanotoxicology* **13** 258–84
[96] Presland R B, Boggess D, Lewis S P, Hull C, Fleckman P and Sundberg J P 2000 Loss of normal profilaggrin and filaggrin in flaky tail (ft/ft) mice: an animal model for the filaggrin-deficient skin disease ichthyosis vulgaris *J. Investig. Dermatol.* **115** 1072–81
[97] Vilella A, Tosi G, Grabrucker A M, Ruozi B, Belletti D, Vandelli M A, Boeckers T M, Forni F and Zoli M 2014 Insight on the fate of CNS-targeted nanoparticles. Part I: Rab5-dependent cell-specific uptake and distribution *J. Control. Release.* **174** 195–201
[98] Amara S, Ben-Slama I, Mrad I, Rihane N, Jeljeli M, El-Mir L, Ben-Rhouma K, Rachidi W, Sève M and Abdelmelek H 2014 Acute exposure to zinc oxide nanoparticles does not affect the cognitive capacity and neurotransmitters levels in adult rats *Nanotoxicology* **8** 208–15
[99] Ze Y, Hu R, Wang X, Sang X, Ze X, Li B, Su J, Wang Y, Guan N and Zhao X 2014 Neurotoxicity and gene-expressed profile in brain-injured mice caused by exposure to titanium dioxide nanoparticles *J. Biomed. Mater. Res. Part A* **102** 470–8
[100] Marano F, Hussain S, Rodrigues-Lima F, Baeza-Squiban A and Boland S 2011 Nanoparticles: molecular targets and cell signalling *Arch. Toxicol.* **85** 733–41
[101] Shrivastava R, Raza S, Yadav A, Kushwaha P and Flora S J 2014 Effects of sub-acute exposure to TiO_2, ZnO and Al_2O_3 nanoparticles on oxidative stress and histological changes in mouse liver and brain *Drug Chem. Toxicol.* **37** 336–47
[102] Win-Shwe T-T and Fujimaki H 2011 Nanoparticles and neurotoxicity *Int. J. Mol. Sci.* **12** 6267–80
[103] Zhang Y, Yu C, Huang G, Wang C and Wen L 2010 Nano rare-earth oxides induced size-dependent vacuolization: an independent pathway from autophagy *Int. J. Nanomed.* **5** 601
[104] Yuan Z-Y, Hu Y-L and Gao J-Q 2015 Brain localization and neurotoxicity evaluation of polysorbate 80-modified chitosan nanoparticles in rats *PLoS One* **10** e0134722
[105] Raj A, Shah P and Agrawal N 2017 Dose-dependent effect of silver nanoparticles (AgNPs) on fertility and survival of Drosophila: an in-vivo study *PLoS One* **12** e0178051
[106] Perez R G and Hastings T G 2004 Could a loss of α-synuclein function put dopaminergic neurons at risk? *J. Neurochem.* **89** 1318–24
[107] Tian H, Eom H-J, Moon S, Lee J, Choi J and Chung Y D 2013 Development of biomarker for detecting silver nanoparticles exposure using a GAL4 enhancer trap screening in Drosophila *Environ. Toxicol. Pharmacol.* **36** 548–56
[108] Vecchio G, Galeone A, Brunetti V, Maiorano G, Rizzello L, Sabella S, Cingolani R and Pompa P P 2012 Mutagenic effects of gold nanoparticles induce aberrant phenotypes in Drosophila melanogaster *Nanomed.: Nanotechnol. Biol. Med.* **8** 1–7
[109] Huang N, Yan Y, Xu Y, Jin Y, Lei J, Zou X, Ran D, Zhang H, Luan S and Gu H 2013 Alumina nanoparticles alter rhythmic activities of local interneurons in the antennal lobe of Drosophila *Nanotoxicology* **7** 212–20

[110] Sabat D, Patnaik A, Ekka B, Dash P and Mishra M 2016 Investigation of titania nanoparticles on behaviour and mechanosensory organ of Drosophila melanogaster *Physiol. Behav.* **167** 76–85

[111] Vales G, Demir E, Kaya B, Creus A and Marcos R 2013 Genotoxicity of cobalt nanoparticles and ions in Drosophila *Nanotoxicology* **7** 462–8

[112] Carmona E R, Inostroza-Blancheteau C, Rubio L and Marcos R 2016 Genotoxic and oxidative stress potential of nanosized and bulk zinc oxide particles in Drosophila melanogaster *Toxicol. Indus. Health* **32** 1987–2001

[113] Mallick T, Karmakar A, Bag J, Sahu S, Mishra M and Begum N A 2020 Carbazole analog anchored fluorescent silica nanoparticle showing enhanced biocompatibility and selective sensing ability towards biomacromolecule *Dyes Pigment.* **173** 107994

[114] Priyadarsini S, Sahoo S K, Sahu S, Mukherjee S, Hota G and Mishra M 2019 Oral administration of graphene oxide nano-sheets induces oxidative stress, genotoxicity, and behavioral teratogenicity in Drosophila melanogaster *Environ. Sci. Pollut. Res.* **26** 19560–74

[115] Anand A S, Gahlot U, Prasad D N, Amitabh and Kohli E 2019 Aluminum oxide nanoparticles mediated toxicity, loss of appendages in progeny of Drosophila melanogaster on chronic exposure *Nanotoxicology* **13** 977–89

[116] Mishra M, Sabat D, Ekka B, Sahu S, Unnikannan P and Dash P 2017 Oral intake of zirconia nanoparticle alters neuronal development and behaviour of Drosophila melanogaster *J. Nanoparticle Res.* **19** 1–12

[117] Sahu S and Mishra M 2020 Hydroxyapatite nanoparticle causes sensory organ defects by targeting the retromer complex in Drosophila melanogaster *NanoImpact* **19** 100237

[118] Liu X, Vinson D, Abt D, Hurt R H and Rand D M 2009 Differential toxicity of carbon nanomaterials in Drosophila: larval dietary uptake is benign, but adult exposure causes locomotor impairment and mortality *Environ. Science Technol.* **43** 6357–63

[119] Li T, Shi T, Li X, Zeng S, Yin L and Pu Y 2014 Effects of nano-MnO_2 on dopaminergic neurons and the spatial learning capability of rats *Int. J. Environ. Res. Public Health* **11** 7918–30

[120] Kim E-M, Palmer P, Howard V, Elsaesser A, Taylor A, Staats G and O'Hare E 2013 Effect of Intracerebroventricular injection of TiO_2 nanoparticles on complex behaviour in the rat *J. Nanosci. Nanotechnol.* **13** 8325–30

[121] Sorce S and Krause K-H 2009 NOX enzymes in the central nervous system: from signaling to disease *Antioxid. Redox. Signal.* **11** 2481–504

[122] Schäppi M G, Jaquet V, Belli D C and Krause K-H 2008 Hyperinflammation in chronic granulomatous disease and anti-inflammatory role of the phagocyte NADPH oxidase *Seminars in Immunopathology* (Berlin: Springer), pp 255–71

[123] Thomas M P, Chartrand K, Reynolds A, Vitvitsky V, Banerjee R and Gendelman H E 2007 Ion channel blockade attenuates aggregated alpha synuclein induction of microglial reactive oxygen species: relevance for the pathogenesis of Parkinson's disease *J. Neurochem.* **100** 503–19

[124] Hu R, Gong X, Duan Y, Li N, Che Y, Cui Y, Zhou M, Liu C, Wang H and Hong F 2010 Neurotoxicological effects and the impairment of spatial recognition memory in mice caused by exposure to TiO_2 nanoparticles *Biomaterials* **31** 8043–50

[125] Flora S 2017 *Neurotoxicity of Nanomaterials and Nanomedicine* (Amsterdam: Elsevier), pp 179–203

[126] Das M, Ghosh M, Gharami K and Das S 2018 Thyroid hormone and astrocyte differentiation *Vitamins Hormones* **106** 283–312

[127] Gholamine B, Karimi I, Salimi A, Mazdarani P and Becker L A 2017 Neurobehavioral toxicity of carbon nanotubes in mice: focus on brain-derived neurotrophic factor messenger RNA and protein *Toxicol. Indus. Health* **33** 340–50