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Benzothiazole-containing tetrazolium salts as radiochromic indicators in gel dosimetry

Kalin I Penev^{1,2} and Kibret Mequanint^{1,3}

¹Department of Chemical and Biochemical Engineering, the University of Western Ontario, London, ON, N5A 5B9, Canada

²Modus Medical Devices Inc., 1570 N Routledge Park, London, ON, N6H 5L6, Canada

³Biomedical Engineering Program, the University of Western Ontario, London, Ontario, N6A 5B9, Canada

E-mail: kmequani@uwo.ca

Abstract. Benzothiazole-containing tetrazolium salts (Bt-TS) have been previously described but have never been tested for dosimetry applications. Considering that such salts may provide higher dose sensitivity than previously tested tetrazolium salts, we synthesized a library of Bt-TS, three of which are reported here. Dosimeters based on the salts BtPP, BtNP and BtNpP were prepared in gellan gum gels, and compared to a previously-described gel dosimeter, based on bisnitrotetrazolium chloride (BNC) in the same medium. All three Bt-TS showed a higher sensitivity at their respective wavelengths of maximum optical attenuation post-irradiation. Two of the new Bt-TS (BtNP and BtNpP) were identified for further studies in large-scale samples and other gel-forming materials.

1. Introduction

Tetrazolium salts (TS) are a class of colourless or weakly coloured water-soluble compounds that have been used in a variety of dosimetry applications, owing to their ability to form coloured formazans following irradiation [1]. TS-based gel dosimetry has been reported in gelatin (5%) and gellan gum (1.25%) by our group [1] and more recently in gels containing 25% Pluronic F-127 [2]. Considering that most formazans are practically insoluble in water, the main feature of TS-based gel dosimeters is the complete lack of image diffusion over the course of hours, days and weeks post-irradiation [1, 2].

The initially reported high dose rate dependence of a commercially-available TS-gellan gum gel dosimeter (ClearView), manufactured by ModusQA (London, ON, Canada) [3] can be alleviated by increasing the concentration of the TS from 0.10 to 0.25 mM or higher (unpublished data), as also evident in the Pluronic gels which use 1.0 mM TS and show no dose rate effect [2]. However, the relatively low radiation sensitivity of ClearView and other TS-based dosimeters remains an issue.

In an effort to increase the sensitivity, we decided to extend the library of TS tested in gel dosimeters. Benzothiazole (Bt) is a side group with strong colour forming properties, which has been previously added to TS [4, 5]. However, Bt-containing tetrazolium salts (Bt-TS) are presently not widely used or commercially available, so we modified a previously-published approach [6] to obtain a library of Bt-TS in high yield (manuscript in preparation). Here we report the initial dosimetric characterization of three previously untested Bt-TS salts in gellan gum gels.



2. Materials and methods

2.1. Tetrazolium salts

Figure 1 presents the tested tetrazolium salts, including (a) 2-(benzothiazol-2-yl)-3,5-diphenyl-2*H*-tetrazolium chloride (BtPP), (b) 2-(benzothiazol-2-yl)-3-(4-nitrophenyl)-5-phenyl-2*H*-tetrazolium chloride (BtNP), (c) 2-(benzothiazol-2-yl)-3-(1-naphthyl)-5-phenyl-2*H*-tetrazolium chloride (BtNpP), and (d) 2,3-bis(4-nitrophenyl)-5-phenyl-2*H*-tetrazolium chloride, also known as “bisnitrotetrazolium chloride” (BNC). Materials (a)-(c) were synthesized in house, using a modification of [6]; the last material (BNC), used as a control, was purchased from TCI America (Portland, OR, USA) as 2,3-bis(4-nitrophenyl)-5-phenyltetrazolium chloride hydrate (cat. no: B1047).

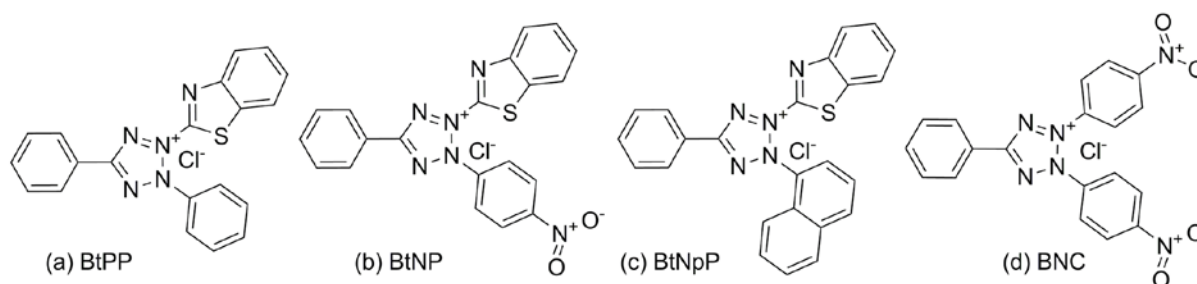


Figure 1. Evaluated tetrazolium salts. The dosimetric properties of BtPP, BtNP and BtNpP are reported here for the first time; BNC was used as a control.

2.2. Gel preparation and irradiation

Gellan gum (cat. no: J63423 from Alfa Aesar, Haverhill, MA, USA), propylene glycol (Caledon labs, Georgetown, ON, Canada) and each of the tetrazolium salts (TS) were dissolved in deionized water and mixed at 55 °C, to obtain the final composition containing 0.25 mM TS, 10% (v/v) propylene glycol and 1.25% (wt/v) gellan gum [1]. Samples were poured into polymethylmethacrylate cuvettes (4mL with 10 mm square cross-section) capped with polyethylene caps and refrigerated overnight to allowed for proper gel setting but otherwise used and stored at room temperature (21-23 °C) in the dark. Irradiation followed on the next day, using a Co-60 source (at approximately 90 cGy/min) at the London Regional Cancer Program in London, Canada. Optical readout (300 – 700 nm) was performed before and after irradiation on a GENESYS 10S UV-visible spectrophotometer (Thermo Scientific, Canada). Whereas the spectrophotometer measures optical absorbance (a unitless quantity), the results here are presented in units of optical attenuation (cm^{-1}) in order to facilitate comparison with other types of optical scanning.

3. Results and discussion

Figure 2 shows the background attenuation (0 Gy) and the attenuation after irradiation to a dose of 20 Gy for each of the four compositions. It can be seen that the BNC gels have very low optical attenuation in the visible part of the spectrum (above 380 nm), and appear colourless. The newly tested Bt-TS-based dosimeters absorb in the violet and blue part of the spectrum with a cut-off around 500 nm and appear yellow. After irradiation, additional attenuation is seen in the green part of the spectrum, causing the gels to become purple or brown to the naked eye.

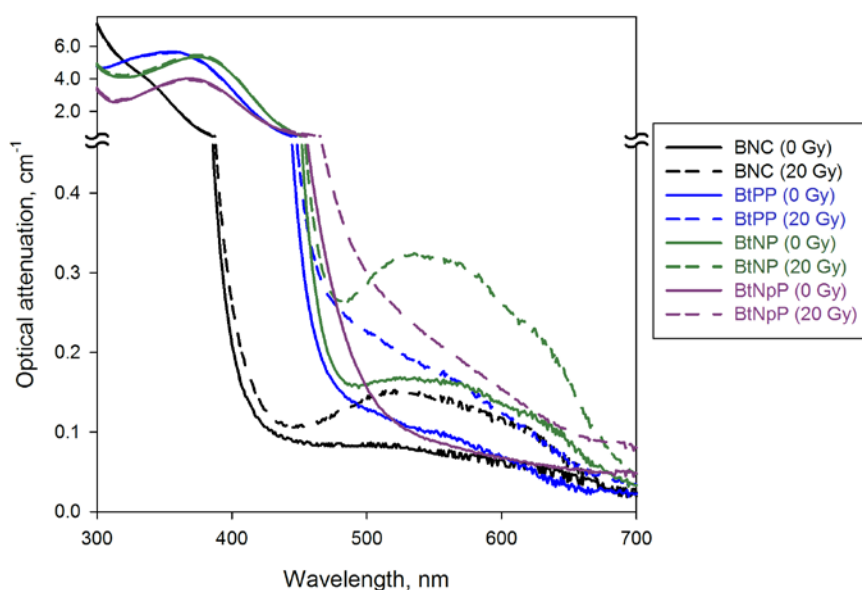


Figure 2. Optical attenuation one day after preparation with 0 and 20 Gy absorbed dose.

The wavelength of maximum attenuation (λ_{\max}) can be determined from Figure 3 which shows the change in attenuation for doses of 5, 10 and 20 Gy. It is apparent that all of tested benzothiazole-containing tetrazolium salts (Bt-TS) show higher dose response than BNC in gellan gum. However, the attenuation maximum is blue-shifted for BtPP and BtNPp, and red-shifted only for BtNP. Comparing the Bt-TS, substitution of the simple aromatic structure (phenyl) with a condensed aromatic structure (1-naphthyl) causes a moderate bathochromic shift of ~ 30 nm, but has little effect on the overall shape or intensity of the attenuation peak. By contrast, addition of a nitro group in position 4 of the phenyl ring causes both a marked bathochromic shift of (~ 60 nm) and a change of the shape and intensity of the attenuation spectrum with a secondary attenuation maximum at 575 nm. Such an effect may be beneficial from a dosimetric point of view, as at higher wavelengths both optical background and optical scatter are lower.

The magnitude of the dose response depends on the wavelength of optical readout, and is linear for all compositions within the range of approximately 450 to 650 nm. As such, choosing λ_{\max} may not always present the best dosimetric characteristics, considering factors such as background attenuation (Figure 2), lights scattering in the gel and spontaneous darkening. All gels showed some degree of spontaneous darkening at room temperature of approximate rates (at λ_{\max}): $2 \times 10^{-3} \text{ cm}^{-1} \text{ day}^{-1}$ (BNC), $1.7 \times 10^{-2} \text{ cm}^{-1} \text{ day}^{-1}$ (BtPP), $4.2 \times 10^{-2} \text{ cm}^{-1} \text{ day}^{-1}$ (BtNP) and $1.5 \times 10^{-2} \text{ cm}^{-1} \text{ day}^{-1}$ (BtNPp). Thus, BtNP forms both the most sensitive and least stable of all tested dosimeters, while BtNPp may provide the best compromise between sensitivity, stability and optical properties.

4. Summary

All of the newly tested benzothiazole-containing tetrazolium salts (Bt-TS) showed higher dose sensitivity than the previously reported BNC in gellan gum gel dosimeters. However, that is at the expense of a higher optical background and a higher rate of spontaneous darkening. Future work includes testing Bt-TS for gel dosimetry into other gel forming materials, such as gelatin and Pluronic F-127.

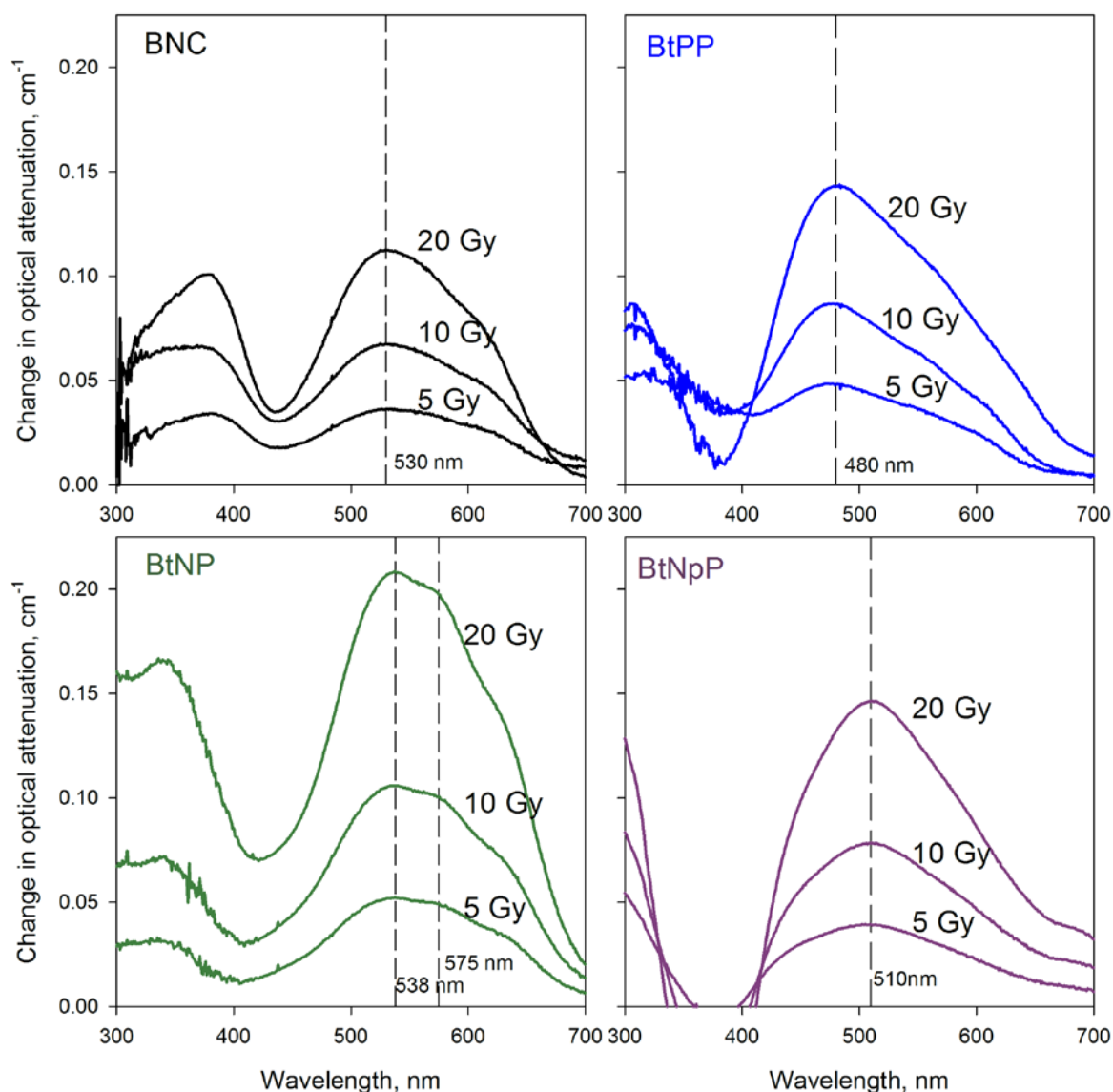


Figure 3. Change in optical attenuation for the four tested compositions following Co-60 irradiation to 5, 10 and 20 Gy, compared to 0 Gy. Same scale; λ_{max} presented with vertical dashed lines.

5. Acknowledgements

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6. References

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