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To cite this article: N M Triana et al 2020 IOP Conf. Ser.: Earth Environ. Sci. 441 012103

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IOP Conf. Series: Earth and Environmental Science **441** (2020) 012103 doi:10.1088/1755-1315/441/1/012103

## Antiproliferation effects of *Glycine max Linn* ethanolic extract on induced mammary gland carcinoma in albino rats

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**Abstract.** This study aimed to determine the antiproliferation effect of *Glycine max Linn* ethanolic extract on Sprague Dawley albino rats induced by 7,12-dimethylbenz(á)anthracene (DMBA) on the mammary gland. This study used 20 albino rats then divided into five treatment groups, i.e., positive control (C+) induced DMBA; negative control (C-) none treatment; Treatment groups (T1; T2; T3) induced DMBA then followed extract dose (5; 10; 20 mg/day). DMBA induction was given every two days for 20 days subcutaneously. Administration of *Glycine max Linn* extract was given peroral for 14 days. It can be concluded that *Glycine max Linn* ethanolic extract inhibits the proliferation cell in mammary gland carcinoma in albino rats revealed on aspect hyperchromatization, tubular formation, and shape of the nuclei.

#### 1. Introduction

Breast cancer or mammary gland cancer is a malignant tumor in the breast or mammary tissue that occurs due to the uncontrolled growth of breast gland cells due to abnormal changes in the genes that play a role in cell proliferation. Breast cancer occurs because of cell abnormalities in the duct glands and breast tissue, which can invade tissue around the breast [1]. Mammary gland cancer was the highest percentage of cases, which was 43.3%, and the rate of deaths from mammary gland cancer was 12.9% [2].

In the last decade, the use of natural materials has been widely used both as medicine and other purposes. The study of a cancer prevention agent originating from nature is increasingly in demand by the public because natural ingredients are not harmful to the body. For this reason, an effort is needed to explore the potential of nature, especially in Indonesia, as an alternative treatment for cancer, especially as a chemopreventive agent [3].

Soybeans (*Glycine max Linn*) have several types with different content of each kind and variety. A new issue between health and soybeans is the presence of isoflavones found in soybean cotyledons, where isoflavones have the potential to become new chemopreventive agents for mammary gland cancer. One of the physiological activities of isoflavones is antioxidant activity. Generally, antioxidant compounds have the same core structure, which contains a benzene ring with a hydroxy group or an amino group. The existence of these activities is beneficial in delaying or preventing oxidation by free radicals [4]. This study aimed to determine the antiproliferation effect of *Glycine max Linn* ethanolic extract on induced mammary gland carcinoma in albino rats.

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#### 2. Material and methods

This study was approved by animal use and ethic commission, Faculty of Veterinary Medicine, Universitas Airlangga. This study used 20 albino rats then divided into five treatment groups, i.e., positive control (C+) induced DMBA; negative control (C-) none treatment; Treatment groups (T1; T2; T3) induced DMBA then followed extract dose (5; 10; 20 mg/day). DMBA induction was given every two days for 20 days subcutaneously. Administration of Glycine max Linn extract was given peroral for 14 days. Albino rats were dissected with cervical dislocation, then fixation the mammary gland used 15% formalin buffer.

Haematoxylin eosin staining preparations performed plain method [5]. Histopathological observation performed using a Trinocular microscope. The inspection was done by scoring the tissue that has pathological changes in the cells and tubules of the mammary gland. Observation of the mammary gland histopathology refers to the Misdorp method [6].

Kolmogorov-Smirnov tested the mean score of the observations for the normality test. If the data is normally distributed, then continued with a one-way ANOVA test, and if a significant difference (p<0.05) was found, the analysis was followed with Duncan's test. All analyses processes used SPSS v21 software (IBM, USA).

#### 3. Results and discussion

The results of scoring aspects of hyperchromatization, tubular formation, and shape of nuclei showed significant differences (p<0.05) between C+ with T1, T2, and T3. All treatment groups showed decreased scores compared to C+. However, it was also still significantly different (p<0.05) from C-(Table 1.). In other words, the decrease in all treatment groups approached the C-treatment.

| Table 1. The mean and standard deviation of the mammary gland carcinoma score |                         |                         |                         |
|---|-------------------------|-------------------------|-------------------------|
| Treatment   | Hyperchromatization     | Tubular formation       | Shape of nuclei         |
| C-  | $1.00^{a}\pm0.05$       | $0.10^{a}\pm0.06$       | $0.10^{a}\pm0.21$       |
| C+  | 3.30°±0.13              | 3.30°±0.18              | 3.40°±0.11              |
| T1  | $2.50^{b}\pm0.25$       | 2.60 <sup>b</sup> ±0.16 | 2.20 <sup>b</sup> ±0.32 |
| T2  | 2.40 <sup>b</sup> ±0.31 | 2.40 <sup>b</sup> ±0.16 | 2.20 <sup>b</sup> ±0.22 |
| Т3  | 2.00 <sup>b</sup> ±0.16 | 2.20 <sup>b</sup> ±0.28 | 2.10 <sup>b</sup> ±0.13 |

Note: Different superscripts in the same column indicate significant differences among treatment (p<0.05)

*Glycine max Linn* extract has antioxidant compounds that inhibit the proliferation of cancer cells. The concentration of isoflavone compounds can easily reach biologically active levels without toxic effects [4]. Through the impact of inhibiting growth factors, tyrosine kinase, and angiogenesis, genistein can be a universal inhibitor of cancer. Through modulation of drug transport, genistein can be an excellent additive to improve cancer therapy [7]. The biological effects described can also serve as prevention strategies for other diseases such as cardiovascular and osteoporosis through the estrogenic and antioxidative impact [8].

Isoflavones act as antioxidants as well as anticancer by binding to free radicals, inhibiting fat peroxidase, and inhibiting cancerous cell cells from developing into cancer cells [9]. The antioxidants in isoflavones impede the production of reactive oxygen, thereby reducing free radicals. In existing cancer cells, isoflavones can break DNA strands in apoptosis and help control cell proliferation due to loss of regulation of growth signals and suppressing growth due to DNA damage [10, 11].

The recent study on anticancer effects in soybean has been found that the compounds contained in the extract of *Glycine max Linn* are isoflavones [12]. Administration of *Glycine max Linn* in this study can reduce the rate of progression of cancer after DMBA initiated the experimental animal. The possibility of obstacles is due to the inhibition of the early stages of cancer development through modulation of cell proliferation [11]. Isoflavones in the essence of *Glycine max Linn* also inhibit the effect of DNA topoisomerase II so that the process of replication, transcription, and cell proliferation has decreased [13].

IOP Conf. Series: Earth and Environmental Science 441 (2020) 012103 doi:10.1088/1755-1315/441/1/012103

#### 4. Conclusion

In conclusion, *Glycine max Linn* ethanolic extract inhibits the proliferation cell in mammary gland carcinoma in albino rats revealed on aspect hyperchromatization, tubular formation, and shape of the nuclei.

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#### Acknowledgements

The authors acknowledge the Ministry of Research, Technology and Higher Education, Republic of Indonesia, and Faculty of Veterinary Medicine, Universitas Airlangga for providing fund support to carry out this study.