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The cytotoxic and wound closure inhibitory effects of disodium octaborate tetrahydrate on A549 lung and DU145 prostate cancer cells

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ARTICLE INFO

Article History:
Received February 2, 2026
Accepted May 20, 2026
Available online June 30, 2026

Review Article

DOI: 10.30728/boron.1904399

Keywords:
549
Boron
DU145
Cytotoxicity
Wound closure inhibition

ABSTRACT

Disodium octaborate tetrahydrate (DOT) ($Na_2O.4B_2O_3.4H_2O$) is an inorganic salt form of boron, used in agriculture, insecticides, and antifungal in wood protection. As an important fine boride, DOT is non-toxic for humans. The antimicrobial and wound-healing properties, as well as the cytotoxicity of DOT against glioblastoma cells, were investigated in other studies. Although there are no studies about the cytotoxic potential of other cancer types of this compound. This is the first study to investigate the cytotoxic and wound closure inhibition effects of DOT on A549 lung and DU145 prostate cancer cell lines. Cytotoxicity was assessed using the MTT assay, and the IC_{50} values for A549 and DU145 cells were calculated as 58.78 mM and 109.33 mM, respectively, indicating a dose-dependent reduction in cell viability. The effect on wound closure was evaluated using an *in vitro* scratch assay. At IC_{50} concentrations, DOT significantly inhibited wound closure in both cell lines after 24 hours compared to controls. Although the relatively high IC_{50} values limit direct therapeutic applicability, these preliminary findings demonstrate, for the first time, that DOT possesses biological activity against lung and prostate cancer cells. Further studies are warranted to explore its potential applications..

1. Introduction

Studies with boron (B) compounds have shown that these compounds have significant physiological effects on various biological functions [1,2]. The antimalarial, antibacterial, antifungal, and anticancer activities of some boron compounds have been reported [3,4]. Boron compounds are used in many products, including fertilizers, pesticides, cosmetics, pharmaceuticals, food supplements, cleaning products, and personal care products [5-7]. Due to the misconception that boron compounds may have serious toxic effects, they have not been researched for clinical properties. However, recent *in vitro* and *in vivo* studies have shown that boron compounds are not toxic to healthy cells [8,9].

The anticancer activities of various boron derivatives have been investigated [10-13]. Various boron compounds can inhibit the cancer progression, and these compounds have been shown to reduce cancer risk in several cancers, including lung cancer [11,14-16], cervical cancer [17], prostate cancer [11,18], breast cancer [19], oral cancer [20], colon cancer [21], and endometrial cancer [22].

Lung and prostate cancers are the leading causes of cancer-related deaths. Although lung cancer has many treatment options, the mortality is extremely high [23]. Prostate cancer is one of the most common cancers in men, and it is important for global health [24].

Boron compounds can reduce prostate cancer proliferation and increase the production of anticancer metabolites [25]. Boric acid inhibits tumor growth and metastasis by inhibiting the expression of cyclin proteins [3]. In lung cancer, boron compounds exhibit antioxidant and anti-inflammatory effects by increasing estrogen levels [26].

Disodium octaborate tetrahydrate (DOT) is the most widely used preservative form of boron. DOT is an inorganic salt (non-volatile), having a near-neutral pH, has low toxicity on mammals, is non-corrosive, highly toxic to insects and fungi, and is colorless and odorless [27]. DOT is used in agriculture as a fertilizer and in veterinary medicine for dust mite and flea control [28]. It is also preferred as an insecticide and for protecting wood materials from fungi [29]. Recent studies have shown that DOT, an important fine boride, is a good antibacterial and flame retardant and is non-toxic and non-irritating to humans [30].

In one study, the antimicrobial activity of DOT against *C. albicans*, *S. aureus*, and *E. coli*, and its cytotoxicity on NIH-3T3 cells were determined (IC_{50}: 41.84 mM). The

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in vitro wound healing capacity was also determined in the same study [31]. In another study, the antimicrobial activity of DOT supplemented with gelatin and pectin was investigated [32]. In one study, the cytotoxicity of DOT on glioblastoma cells and found that DOT was more effective than boric acid in inhibiting glioblastoma cells were determined [33].

The rationale for investigating DOT in lung and prostate cancer stems from several observations. First, epidemiological studies have suggested an inverse relationship between boron intake and prostate cancer risk [11,18]. Second, boron compounds have been shown to modulate estrogen metabolism, which plays a role in lung cancer pathogenesis [26]. Third, the enhanced bioactivity of DOT compared to boric acid in glioblastoma cells [33] suggests that the tetrahydrate form may possess unique biological properties. Given the high global incidence of lung and prostate cancers [23,24] and the absence of studies examining DOT's effects on these specific cancer types, this investigation addresses a significant gap in the literature.

2. Materials and Methods

2.1. The Cell Culture

The human lung carcinoma epithelial cell line A549 (ATCC® CCL-185™) and the human prostate carcinoma cell line DU145 (ATCC® HTB-81™) were purchased directly from the American Type Culture Collection (ATCC, USA). Cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) with high glucose (4.5 g/L) (Sigma-Aldrich, USA) supplemented with 10% fetal bovine serum (FBS) (Gibco, Thermo Fisher Scientific, USA) and 1% penicillin-streptomycin solution (10,000 units/mL penicillin and 10,000 µg/mL streptomycin) (Sigma-Aldrich, USA). Cultures were maintained at 37°C in a humidified atmosphere containing 5% CO_2. The medium was refreshed every 2-3 days, and cells were subcultured upon reaching 80-90% confluence using 0.25% trypsin-EDTA solution.

2.2. Determine the Cytotoxic Activity

The cytotoxic activity of DOT on A549 lung and DU145 prostate cancer cells was determined using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) colorimetric assay [34].

Cells were counted using the Trypan blue exclusion method and seeded into 96-well microplates at a density of 1×10^4 cells per well in 200 µL of DMEM culture medium. Plates were incubated for 24 hours at 37°C in a humidified atmosphere containing 5% CO_2 to allow cell attachment. After incubation, the culture medium was removed, and cells were treated with varying concentrations of DOT prepared in DMEM for 24 hours. Control wells received fresh DMEM without DOT.

DOT (disodium octaborate tetrahydrate, $Na_2B_8O_{13}\cdot4H_2O$) was obtained from Eti Maden (Ankara, Türkiye). A stock solution of 200 mM DOT was prepared fresh in sterile DMEM culture medium and serially diluted to working concentrations (200, 100, 50, 25, 12.5, and 6.25 mM). Solvent-only controls (DMEM without DOT) were included in all experiments.

At the end of the incubation, the wells were emptied and washed with 100 µL of Dulbecco's Phosphate Buffered Saline (D-PBS), and 100 µL of fresh DMEM medium (per well) containing 10 µL of MTT solution (5 mg/mL in PBS, final concentration 0.5 mg/mL) was added and incubated for 3 hours at 37°C under 5% CO_2 and 98% humidity. After incubation, the medium was removed, and 100 µL of DMSO was added to each well, and the plates were shaken at room temperature for 25 minutes. Then the absorbance was measured at 540 nm [35,36] and the percentage of inhibition was calculated using the following equation:

$$\% \text{ Inhibition} = 100 - [100 \times (\text{Sample}_{abs})/(\text{Control}_{abs})] \quad (1)$$

2.3. Determining the Wound Closure Inhibition Effect

The wound closure inhibition effect of DOT was determined using an *in vitro* scratch assay [37]. A549 and DU145 cells were seeded into 6-well microplates at a density of 5×10^5 cells per well in 2.5 mL of DMEM culture medium supplemented with 10% FBS and 1% antibiotic solution. This seeding density was optimized to achieve approximately 90-100% confluence within 24-48 hours. Cell confluence prior to scratching was visually assessed using an inverted microscope. After incubation, a linear wound was created in the cell layer using a sterile 100 µL pipette tip. The wells were washed with D-PBS, and the cellular debris was removed. Thereafter, cells were treated with IC_{50} doses of DOT (59.55 mM for A549, 109.33 mM for DU145), and a control group was included, with cells cultured without DOT.

Images of the scratched areas in each well were captured at 0 and 24 hours using a Leica IL inverted microscope equipped with a digital camera. For quantitative analysis, wound areas were measured using ImageJ software (National Institutes of Health, USA). The percentage of wound closure was calculated using the following equation:

$$\% \text{ Wound Closure} = [(\text{Area at 0h} - \text{Area at 24h}) / \text{Area at 0h}] \times 100 \quad (2)$$

2.4. Statistical Analysis

All data were expressed as mean ± standard deviation (SD) of at least three independent experiments. Statistical analyses were performed using GraphPad Prism (GraphPad Software, USA). For cytotoxicity assays, differences between multiple groups were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test for multiple comparisons. For wound closure assays, comparisons

between control and treatment groups were performed using Student's t-test. For IC_{50} determination, non-linear regression analysis was employed using a four-parameter logistic (variable slope) model.

3. Results

3.1. The Cytotoxic Activity

The cytotoxic activity of DOT on A549 lung and DU145 prostate cancer cells was determined with the MTT method, and the inhibition percentages are given in Figures 1 and 2.

For A549 cells (Figure 1), DOT exhibited a concentration-dependent reduction in cell viability. The highest cytotoxic effect was observed at 200 mM concentration, with cell viability reduced to 18.3% (81.7% inhibition). Non-linear regression analysis of the dose-response curve yielded an IC_{50} value of 58.78 mM. Statistical analysis using one-way ANOVA revealed significant differences between treatment groups, and Tukey's post-hoc test indicated that concentrations of 50 mM and above significantly reduced cell viability compared to the control.

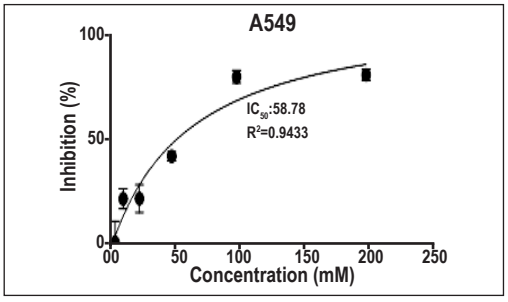


Figure 1. Cytotoxic effect of DOT on A549 lung cancer cells. (A) Dose-response curve showing percentage cell viability after 24-hour treatment with increasing concentrations of DOT (6.25-200 mM). Data points represent mean ± SD from three independent experiments (n=3). (B) Log-transformed dose-response curve used for IC_{50} calculation via non-linear regression. Statistical significance was determined by one-way ANOVA with Tukey's post-hoc test.

For DU145 cells (Figure 2), DOT also exhibited a concentration-dependent reduction in cell viability. The highest cytotoxic effect was observed at 200 mM concentration, with cell viability reduced to 22.3% (77.7% inhibition). Non-linear regression analysis yielded an IC_{50} value of 109.33 mM (95% confidence interval: 98.7-121.1 mM). One-way ANOVA followed by Tukey's post-hoc test confirmed that concentrations of 100 mM and above significantly reduced cell viability compared to the control ($p < 0.05$ for 100 mM, $p < 0.01$ for 200 mM).

3.2. The Wound Closure Inhibition Effect

The wound closure inhibition effect of DOT on A549 lung and DU145 prostate cancer cells at IC_{50} concentrations is shown in Figures 3 and 4. The images were observed at 0. and 24. hours, and the scratches were compared with those of the control group.

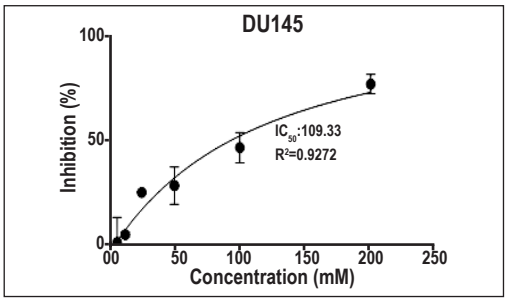


Figure 2. Cytotoxic effect of DOT on DU145 prostate cancer cells. (A) Dose-response curve showing percentage cell viability after 24-hour treatment with increasing concentrations of DOT (6.25-200 mM). Data points represent mean ± SD from three independent experiments (n=3). (B) Log-transformed dose-response curve used for IC_{50} calculation via non-linear regression. Statistical significance was determined by one-way ANOVA with Tukey's post-hoc test.

The effect of DOT on wound closure in A549 and DU145 cells at IC_{50} concentrations was evaluated using an in vitro scratch assay (Figures 3 and 4). In A549 cells (Figure 3), control cultures exhibited progressive wound closure over 24 hours, with near-complete closure observed in some areas. In contrast, DOT-treated cultures showed markedly reduced wound closure, with the wound edges remaining clearly visible at 24 hours. A similar pattern was observed in DU145 cells (Figure 4).

Quantitative analysis using ImageJ software confirmed these observations. In A549 cells, wound closure at 24 hours was 76.6 ± 8.2% in control cultures compared to 21.5 ± 5.1% in DOT-treated cultures ($p < 0.01$). In DU145 cells, wound closure was 81.3 ± 7.6% in control cultures versus 28.7 ± 4.3% in DOT-treated cultures ($p < 0.01$) (Figure 5).

It is important to note that these experiments were conducted using IC_{50} concentrations in the presence of 10% FBS. Therefore, the observed inhibition of wound closure likely reflects a combination of cytotoxic effects, and potential direct inhibition of cell migration, rather than isolated antimigratory activity.

4. Discussion

This study investigated, for the first time, the cytotoxic and wound closure-inhibitory effects of disodium octaborate tetrahydrate (DOT) on A549 lung and DU145 prostate cancer cells. The results demonstrate that DOT reduces cell viability in a dose-dependent manner and significantly impairs wound closure in both cell lines at IC_{50} concentrations.

The IC_{50} values obtained for A549 (58.78 mM) and DU145 (109.33 mM) cells are notably higher than those typically reported for conventional chemotherapeutic agents. For comparison, cisplatin, a standard chemotherapy drug used in lung cancer treatment, exhibits IC_{50} values in the range of 5-20 μM in various cancer cell lines [38]. This substantial difference (approximately 3,000-20,000-fold higher concentrations required for DOT) raises important

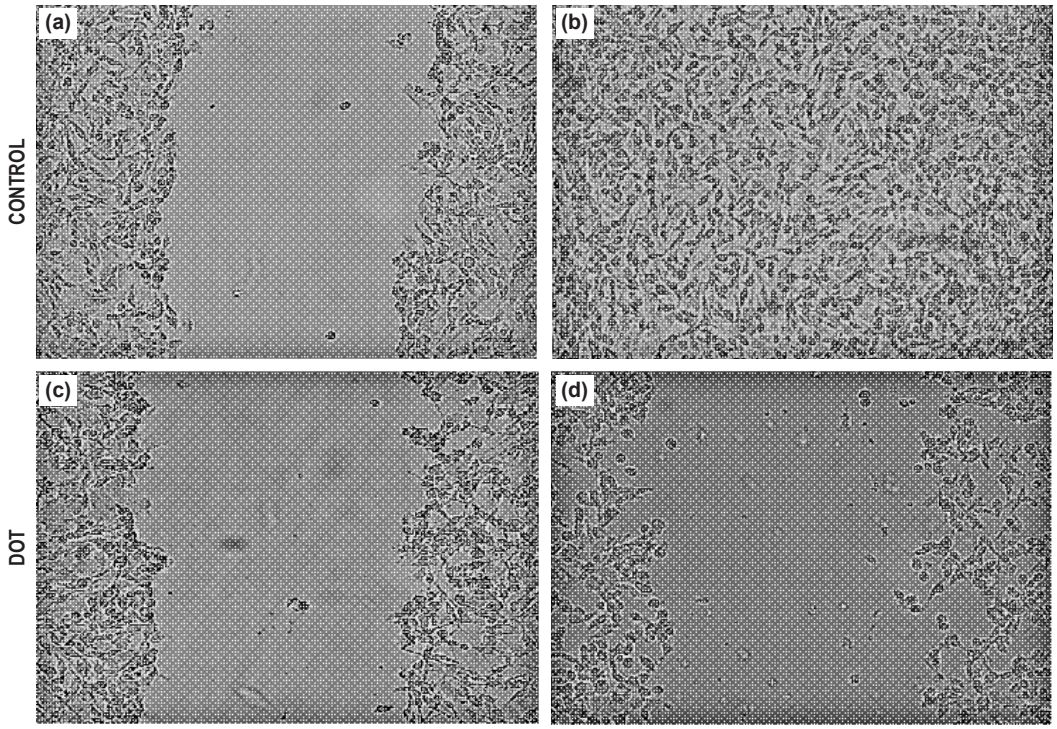


Figure 3. Representative images of wound closure in A549 cells. (A) Control group at 0 h. (B) Control group at 24 h showing near-complete wound closure. (C) DOT-treated group (58.78 mM) at 0 h. (D) DOT-treated group at 24 h showing minimal wound closure.

questions about the pharmacological relevance of our findings.

Several considerations should be taken into account when interpreting these results. First, the relatively high IC_{50} values suggest that DOT is unlikely to be suitable for systemic administration as a conventional chemotherapeutic agent due to the high doses that would be required and the associated risk of non-specific toxicity. Second, the lack of selective toxicity towards cancer cells is concerning when compared to previous findings. One study reported an IC_{50} value of 41.84 mM for DOT on healthy NIH/3T3 mouse fibroblasts, which is actually lower than the IC_{50} we

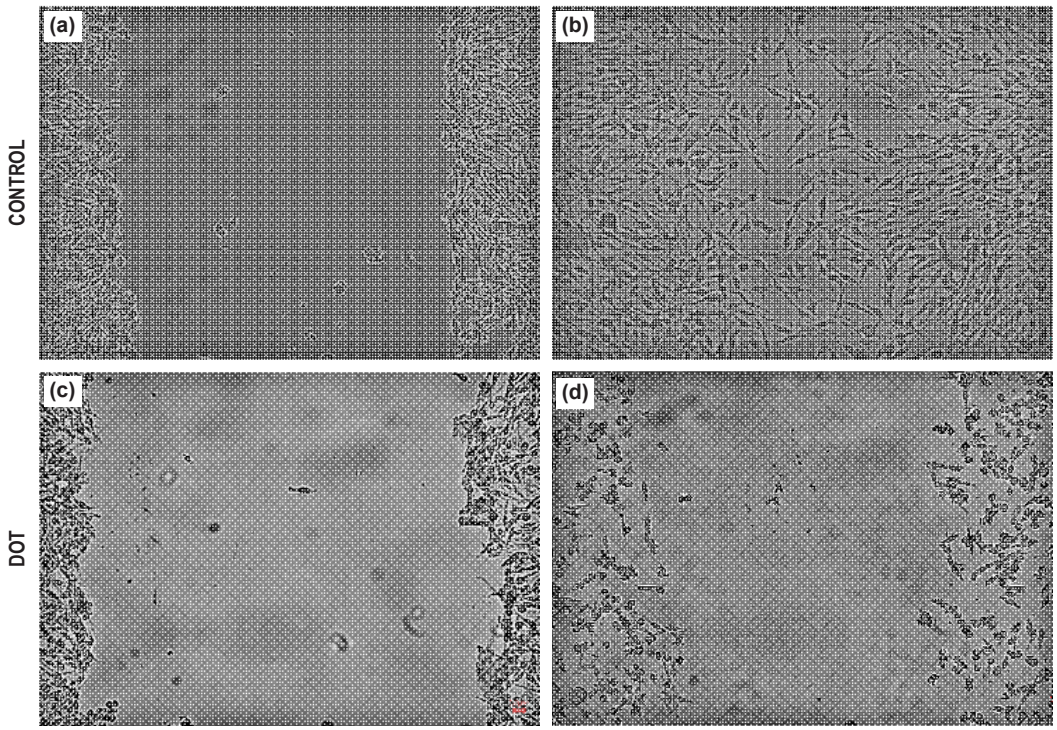


Figure 4. Representative images of wound closure in DU145 cells. (A) Control group at 0 h. (B) Control group at 24 h showing substantial wound closure. (C) DOT-treated group (109.33 mM) at 0 h. (D) DOT-treated group at 24 h showing minimal wound closure.

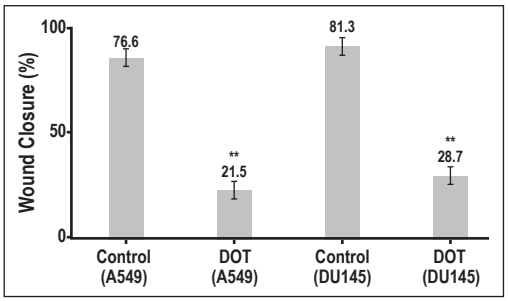


Figure 5. Quantitative analysis of wound closure at 24 hours. Percentage wound closure was calculated using ImageJ software from at least three independent experiments. Data represent mean ± SD. $p < 0.01$ compared to respective control (Student's t-test).

obtained for A549 cells (58.78 mM) and considerably lower than that for DU145 cells (109.33 mM) [31]. This indicates that healthy fibroblasts may be more sensitive to DOT than the cancer cell lines tested, precluding any claim of cancer cell selectivity.

Despite these limitations, our findings may have relevance in specific therapeutic contexts. Boron neutron capture therapy (BNCT) is a binary cancer treatment modality that relies on the selective accumulation of boron-10 compounds in tumor tissue followed by neutron irradiation [39]. In BNCT, millimolar concentrations of boron within tumors are desirable, and compounds with limited intrinsic cytotoxicity can still be therapeutically useful if they exhibit tumor-selective accumulation. DOT's lack of intrinsic potency might be circumvented through targeted delivery strategies, such as encapsulation in nanoparticles or conjugation with tumor-specific ligands [40].

The observed inhibition of wound closure at IC_{50} concentrations warrants careful interpretation. The experimental design employed (IC_{50} doses with serum-containing medium) does not allow us to distinguish between reduced wound closure due to cell death, or direct blockade of migratory capacity. The use of sub-cytotoxic doses (e.g., IC_{10}-IC_{30}) under low-serum conditions (0.5-1% FBS) would be required to specifically assess anti-migratory effects [41]. Future studies employing trans-well migration assays or incorporating proliferation inhibitors such as mitomycin-C would help elucidate the mechanisms underlying the observed effects.

The potential mechanisms by which boron compounds exert biological effects have been explored in previous studies. The one study demonstrated that DOT induces apoptosis in glioblastoma cells more effectively than boric acid, suggesting that the tetrahydrate form may possess enhanced bioactivity [33]. Boron compounds have been shown to inhibit proteasome activity [21], modulate estrogen metabolism [27], and interfere with cyclin protein expression [26]. Whether similar mechanisms operate in A549 and DU145 cells remains to be determined and represents an important direction for future research.

Several limitations of this study should be acknowledged. First, the absence of a normal control cell line (e.g., bronchial epithelial cells for lung or RWPE-1 for prostate) limits our ability to assess the therapeutic window and selectivity of DOT. Second, the lack of mechanistic studies (e.g., apoptosis assays, cell cycle analysis) precludes conclusions about the mode of cell death. Third, the wound closure assay design does not permit distinction between effects on migration versus proliferation. Finally, the relatively high IC_{50} values raise concerns about non-specific osmotic or pH effects at millimolar concentrations, although DOT's near-neutral pH and use of appropriate vehicle controls mitigate this concern to some extent.

Despite these limitations, this study makes an important contribution by providing the first evidence that DOT possesses biological activity against lung and prostate cancer cells. These preliminary findings establish a foundation for future investigations aimed at enhancing the therapeutic potential of DOT through structural modification, formulation optimization, or application in specialized treatment modalities such as BNCT.

5. Conclusions

The present study demonstrates that disodium octaborate tetrahydrate (DOT) exhibits concentration-dependent cytotoxic activity against A549 lung and DU145 prostate cancer cells, with IC_{50} values of 58.78 mM and 109.33 mM, respectively. Furthermore, DOT significantly inhibits wound closure in both cell lines at IC_{50} concentrations. Although these relatively high IC_{50} values and the lack of selective toxicity towards cancer cells (compared to previously reported IC_{50} of 41.84 mM on healthy fibroblasts) limit the potential for direct systemic therapeutic application, this study provides the first evidence of DOT's biological activity against lung and prostate cancer cells. These preliminary findings warrant further investigation with optimized delivery systems, structural analogs, or in specialized applications such as boron neutron capture therapy. Future studies should include normal cell controls, mechanistic analyses, and *in vivo* evaluation to fully assess the therapeutic potential of DOT in oncology.

6. Acknowledgements

A part of this publication is a part of a project supported by the Muğla Sıtkı Koçman University Scientific Research Projects Coordination Unit under project number 21/123/02/1/4. We thank them for their support.

7. Author Contribution Statement

Nurdan Saraç: Supervision, experimental design, cell culture investigations, writing and revising the manuscript.

Muammer Ceylan: Determination of cytotoxic activity and wound closure inhibition effect.

Sevil Yeniocak: Determination of wound closure inhibition effect.

Gizem Genç: Execuation of experimental procedures.

İrem Demir: Execuation of experimental procedures.

Aysel Uğur: Writing and revising the manuscript, statistical analysis.

8. Conflict of Interest

Authors have no conflict of interest.

References

[1] Khaliq, H., Juming, Z., & Ke-Mei, P. (2018). The physiological role of boron on health. *Biological Trace Element Research*, *186*(1), 31-51. https://doi.org/10.1007/s12011-018-1284-3

[2] Uluisik, I., Karakaya, H. C., & Koc, A. (2018). The importance of boron in biological systems. *Journal of Trace Elements in Medicine and Biology*, *45*, 156-162. https://doi.org/10.1016/j.jtemb.2017.10.008

[3] Scorei, I. R., & Popa, R. (2010). Boron-containing compounds as preventive and chemotherapeutic agents for cancer. *Anti-Cancer Agents in Medicinal Chemistry*, *10*(4), 346-351. https://doi.org/10.2174/187152010791162289

[4] Romero-Aguilar, K. S., Arciniega-Martínez, I. M., Farfán-García, E. D., Campos-Rodríguez, R., Reséndiz-Albor, A. A., & Soriano-Ursúa, M. A. (2019). Effects of boron-containing compounds on immune responses: Review and patenting trends. *Expert Opinion on Therapeutic Patents*, *29*(5), 339-351. https://doi.org/10.1080/13543776.2019.1612368

[5] Turkez, H. (2008). Effects of boric acid and borax on titanium dioxide genotoxicity. *Journal of Applied Toxicology*, *28*(5), 658-664. https://doi.org/10.1002/jat.1318

[6] Hosmane, N. S., Maguire, J. A., Zhu, Y., & Takagaki, M. (2011). Future perspectives for boron and gadolinium neutron capture therapies in cancer treatment. *Boron and gadolinium neutron capture therapy for cancer treatment*. World Scientific, 165-170. https://doi.org/10.1142/9789814338684_0009

[7] Hosmane, N. S., & Eagling, R. D. (Eds.). (2018). *Handbook of boron science: With applications in organometallics, catalysis, materials and medicine* (Vols. 1-4). World Scientific. https://doi.org/10.1142/q0130

[8] Turkez, H., & Geyikoglu, F. (2010). Boric acid: A potential chemoprotective agent against aflatoxin b1 toxicity in human blood. *Cytotechnology*, *62*(2), 157-165. https://doi.org/10.1007/s10616-010-9272-2

[9] Alak, G., Parlak, V., Yeltekin, A. Ç., Ucar, A., Çomaklı, S., Topal, A., … & Türkez, H. (2019). The protective effect exerted by dietary borax on toxicity metabolism in rainbow trout (Oncorhynchus mykiss) tissues. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *216*, 82-92. https://doi.org/10.1016/j.cbpc.2018.10.005

[10] Lawler A. (1995). Cancer therapy. Brookhaven prepares for boron trials. Science (New York, N.Y.), 267(5200), 956. https://doi.org/10.1126/science.7695774

[11] Cui, Y., Winton, M. I., Zhang, Z. F., Rainey, C., Marshall, J., De Kernion, J. B., & Eckhert, C. D. (2004). Dietary boron intake and prostate cancer risk. *Oncology Reports*, *11*(4), 887-892.

[12] Yinghuai, Z., & Hosmane, N. S. (2013). Applications and perspectives of boron-enriched nanocomposites in cancer therapy. *Future Medicinal Chemistry*, *5*(6), 705-714. https://doi.org/10.4155/fmc.13.47

[13] Ferreira, T. H., Marino, A., Rocca, A., Liakos, I., Nitti, S., Athanassiou, A., …& Ciofani, G. (2015). Folate-grafted boron nitride nanotubes: Possible exploitation in cancer therapy. *International Journal of Pharmaceutics*, *481*(1-2), 56-63. https://doi.org/10.1016/j.ijpharm.2015.01.048

[14] Schabath, M. B., Wu, X., Vassilopoulou-Sellin, R., Vaporciyan, A. A., & Spitz, M. R. (2004). Hormone Replacement Therapy And Lung Cancer Risk: A Case-Control Analysis. *Clinical Cancer Research*, *10*(1), 113-123. https://doi.org/10.1158/1078-0432.ccr-0911-3

[15] Wang, Y., Zhao, Y., & Chen, X. (2008). Experimental study on the estrogen-like effect of boric acid. *Biological Trace Element Research*, *121*(2), 160-170. https://doi.org/10.1007/s12011-007-8041-3

[16] Cebeci, E., Yüksel, B., & Şahin, F. (2022). Anti-cancer effect of boron derivatives on small-cell lung cancer. *Journal of Trace Elements in Medicine and Biology: Organ of the Society for Minerals and Trace Elements*, *70*, 126923. https://doi.org/10.1016/j.jtemb.2022.126923

[17] Korkmaz, M., Uzgören, E., Bakırdere, S., Aydın, F., & Ataman, O. Y. (2007). Effects of dietary boron on cervical cytopathology and on micronucleus frequency in exfoliated buccal cells. *Environmental Toxicology: An International Journal*, *22*(1), 17-25. https://doi.org/10.1002/tox.20229

[18] Gonzalez, A., Peters, U., Lampe, J. W., & White, E. (2007). Boron intake and prostate cancer risk. *Cancer Causes & Control*, *18*(10), 1131-1140. https://doi.org/10.1007/s10552-007-9052-2

[19] Scorei, R., Ciubar, R., Ciofrangeanu, C. M., Mitran, V., Cimpean, A., & Iordachescu, D. (2008). Comparative effects of boric acid and calcium fructoborate on breast cancer cells. *Biological Trace Element Research*, *122*(3), 197-205. https://doi.org/10.1007/s12011-007-8081-8

[20] Portu, A., Molinari, A. J., Thorp, S. I., Pozzi, E. C. C., Curotto, P., Schwint, A. E., & Saint Martin, G. (2015). Neutron autoradiography to study boron compound microdistribution in an oral cancer model. *International Journal of Radiation Biology*, *91*(4), 329-335. https://doi.org/10.3109/09553002.2014.995381

[21] Dick, L. R., & Fleming, P. E. (2010). Building on bortezomib: Second-generation proteasome inhibitors as anti-cancer therapy. *Drug Discovery Today*, *15*(5-6), 243-249. https://doi.org/10.1016/j.drudis.2010.01.008

[22] Tülüce, Y., Lak, P. T. A., Koyuncu, İ., Kılıç, A., Durgun, M., & Özkol, H. (2017). The apoptotic, cytotoxic and genotoxic effect of novel binuclear boron-fluoride complex on endometrial cancer. Biometals: *An International Journal on the Role of Metal Ions in Biology, Biochemistry, and Medicine*, *30*(6), 933-944. https://doi.org/10.1007/s10534-017-0060-8

[23] Suda, K., & Mitsudomi, T. (2014). Successes and limitations of targeted cancer therapy in lung cancer. In S. Peters & R. A. Stahel (Eds.), *Successes and limitations of targeted cancer therapy* (Progress in Tumor Research, Vol. 41, pp. 62-77). S. Karger AG.

https://doi.org/10.1159/000355902

[24] Rawla, P. (2019). Epidemiology of prostate cancer. *World Journal of Oncology, 10*(2), 63-89. https://doi.org/10.14740/wjon1191

[25] Gallardo-Williams, M. T., Chapin, R. E., King, P. E., Moser, G. J., Goldsworthy, T. L., Morrison, J. P., & Maronpot, R. R. (2004). Boron supplementation inhibits the growth and local expression of IGF-1 in human prostate adenocarcinoma (LNCaP) tumors in nude mice. *Toxicologic Pathology*, *32*(1), 73-78. https://doi.org/10.1080/01926230490260899

[26] Mahabir, S., Spitz, M. R., Barrera, S. L., Dong, Y. Q., Eastham, C., & Forman, M. R. (2008). Dietary boron and hormone replacement therapy as risk factors for lung cancer in women. *American Journal of Epidemiology*, *167*(9), 1070-1080. https://doi.org/10.1093/aje/kwn021

[27] Thévenon, M. F., Tondi, G., & Pizzi, A. (2010). Friendly wood preservative system based on polymerized tannin resin-boric acid for outdoor applications. *Maderas. Ciencia y tecnología*, *12*(3), 253-257. http://dx.doi.org/10.4067/S0718-221X2010000300009

[28] Sayin, Z., Ucan, U. S., & Sakmanoglu, A. (2016). Antibacterial and antibiofilm effects of boron on different bacteria. *Biological Trace Element Research*, *173*(1), 241-246. https://doi.org/10.1007/s12011-016-0637-z

[29] Pratt, J. E., & Quill, K. (1996). A trial of disodium octaborate tetrahydrate for the control of Heterobasidion annosum. *European Journal of Forest Pathology*, *26*(6), 297-305. https://doi.org/10.1111/j.1439-0329.1996.tb01075.x

[30] Codina, R., Lockey, R. F., Diwadkar, R., Mobly, L. L., & Godfrey, S. (2003). Disodium octaborate tetrahydrate (DOT) application and vacuum cleaning, a combined strategy to control house dust mites. *Allergy*, *58*(4), 318-324. https://doi.org/10.1034/j.1398-9995.2003.00100.x

[31] Sarac, N., Baygar, T., Ugur, A., Ceylan, O., & Boran, R. (2019). Determining the antimicrobial activity and wound healing capacity of disodium octaborate tetrahydrate. In *International Symposium on Boron Proceedings* (pp. 112-118). Nevşehir, Turkey

[32] Gülerim, M. (2017). *Development and characterization of antimicrobial gelatin and pectin films with boron derivatives* (Thesis Number: 450550) [Master's thesis, Yeditepe University].

[33] Dalmizrak, A., Erbaykent Tepedelen, B., Ersoz, E., Celik, B., & Korkmaz., M. (2018). Investigating the effects of boric acid and disodium octaborate tetrahydrate on cell dath in glioblastoma cell lines. *FEBS Open Bio*, *8*(S1), 311. https://doi.org/10.1002/2211-5463.12453

[34] Mosmann, T. (1983). Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. *Journal of Immunological Methods*, *65*(1-2), 55-63. https://doi.org/10.1016/0022-1759(83)90303-4

[35] Abdul Ghafoor, N., Galatali, S., Yeniocak, S., Kaya, E., Sarac, N., & Ugur, A. (2022). Investigating anticancer potency of in vitro propagated endemic Thymus cilicicus Boiss. & Bal. extract on human lung, breast, and prostate cancer cell lines. *Biologia*, *77*, 3229-3239. https://doi.org/10.1007/s11756-022-01168-7

[36] Yeniocak, S., Galatalı, S., Demir, İ., Uğur, A., Saraç, N., & Kaya, E. (2025). Investigation of biological activities of in vitro grown Sesamum orientale plant extract on the cell cultures: wound healing and antiproliferation. *Advances in Traditional Medicine, 25*, 233-246. https://doi.org/10.1007/s13596-024-00791-w

[37] Justus, C. R., Leffler, N., Ruiz-Echevarria, M., & Yang, L. V. (2014). In vitro cell migration and invasion assays. *Journal of Visualized Experiments*, *88*, 51046. https://doi.org/10.3791/51046

[38] Dasari, S., & Tchounwou, P. B. (2014). Cisplatin in cancer therapy: Molecular mechanisms of action. *European Journal of Pharmacology*, *740*, 364-378. https://doi.org/10.1016/j.ejphar.2014.07.025

[39] Barth, R. F., Mi, P., & Yang, W. (2018). Boron delivery agents for neutron capture therapy of cancer. *Cancer Communications*, *38*(1), 35. https://doi.org/10.1186/s40880-018-0299-7

[40] Luderer, M. J., de la Puente, P., & Azab, A. K. (2015). Advancements in tumor targeting strategies for boron neutron capture therapy. *Pharmaceutical Research*, *32*(9), 2824-2836. https://doi.org/10.1007/s11095-015-1718-y

[41] Liang, C. C., Park, A. Y., & Guan, J. L. (2007). In vitro scratch assay: A convenient and inexpensive method for analysis of cell migration in vitro. *Nature Protocols*, *2*(2), 329-333. https://doi.org/10.1038/nprot.2007.30