Boron and Cancer

https://pubmed.ncbi.nlm.nih.gov/26770156/

Nothing Boring About Boron 2015

The trace mineral boron is a micronutrient with diverse and vitally important roles in metabolism that render it necessary for plant, animal, and human health, and as recent research suggests, possibly for the evolution of life on Earth. As the current article shows, boron has been proven to be an important trace mineral because it

(1) is essential for the growth and maintenance of bone;
(2) greatly improves wound healing;
(3) beneficially impacts the body's use of estrogen, testosterone, and vitamin D;
(4) boosts magnesium absorption;
(5) reduces levels of inflammatory biomarkers, such as high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor α (TNF-α);
(6) raises levels of antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase;
(7) protects against pesticide-induced oxidative stress and heavy-metal toxicity;
(8) improves the brains electrical activity, cognitive performance, and short-term memory for elders;
(9) influences the formation and activity of key biomolecules, such as S-adenosyl methionine (SAM-e) and nicotinamide adenine dinucleotide (NAD(+));
(10) has demonstrated preventive and therapeutic effects in a number of cancers, such as prostate, cervical, and lung cancers, and multiple and non-Hodgkin's lymphoma; and
(11) may help ameliorate the adverse effects of traditional chemotherapeutic agents.

In none of the numerous studies conducted to date, however, do boron's beneficial effects appear at intakes > 3 mg/d. No estimated average requirements (EARs) or dietary reference intakes (DRIs) have been set for boron-only an upper intake level (UL) of 20 mg/d for individuals aged ≥ 18 y. The absence of studies showing harm in conjunction with the substantial number of articles showing benefits support the consideration of boron supplementation of 3 mg/d for any individual who is consuming a diet lacking in fruits and vegetables or who is at risk for or has osteopenia; osteoporosis; osteoarthritis (OA); or breast, prostate, or lung cancer.

https://pubmed.ncbi.nlm.nih.gov/19912103/

Boron-containing compounds as preventive and chemotherapeutic agents for cancer. 2010

Types of cancers most frequently impacted by B-containing compounds include prostate, breast, cervical and lung cancer. Mechanisms involving B activity on cancer cells are based on the inhibition of a variety of enzymatic activities, including serine proteases, NAD-dehydrogenases, mRNA splicing and cell division, but also receptor binding mimicry, and the induction of apoptosis. Boron-enriched diets resulted in significant decrease in the risk for prostate and cervical cancer, and decrease in lung cancer in smoking women. Boron-based compounds show promising effects for the chemotherapy of specific forms of cancer, but due to specific benefits should also be included in cancer chemopreventive strategies.

https://pubmed.ncbi.nlm.nih.gov/37772231/

Boric Acid Exhibits Anticancer Properties in Human Endometrial Cancer Ishikawa Cells 2023

Concentrations up to 80 mM had no effect on cell viability and apoptosis, but BA at 80 mM concentration decreased viability and increased cytochrome c and caspase 3 levels in L929 cells. Conclusion BA inhibited cell viability, triggered apoptosis, induced oxidative stress, and suppressed inflammatory responses in endometrial cancer cells. Notably, at its IC50 concentration, BA had no cytotoxic effect on normal fibroblasts. Given its favorable properties, BA may provide a valuable therapeutic option to impede the development and progression of endometrial cancer.

https://pubmed.ncbi.nlm.nih.gov/38015327/

Boric Acid Affects Cell Proliferation, Apoptosis, and Oxidative Stress in ALL Cells

T-cell acute lymphoblastic leukemia (T-ALL) is a type of acute lymphoblastic leukemia from early T-cell progenitors. Interest grows in creating less toxic agents and therapies for chemo-resistant T-ALL cancer. Recently, elemental boron has special properties useful in the creation of new drugs. Studies have revealed the cytotoxic properties of boric acid (BA) on cancer, but not fully understood. We aimed to investigate the effect of BA on cell proliferation, apoptosis, and oxidative stress in the Jurkat cells. The effects of BA on cell viability were determined by 2,3-bis-(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide (XTT) assay for 24-48-72 h. The impact of BA on apoptosis was analyzed by acridine orange/ethidium bromide. Expression of apoptosis regulatory genes (Bcl-2, Bax, Caspase-3-8-9) and apoptotic miRNA (miR-21) was used by real-time quantitative polymerase chain reaction (RT-qPCR). The total oxidant status (TOS), total antioxidant status (TAS), and the oxidative stress index (OSI) value were calculated for oxidative stress. We determined the cytotoxic activity of BA on Jurkat cells by using XTT and defined the IC50 concentration (802.7 µg/mL) of BA. The findings clearly show that BA inhibited Jurkat cell proliferation dose-dependently. BA induced apoptosis through downregulated anti-apoptotic genes, and upregulated pro-apoptotic genes. Additionally, we found that BA significantly reduced the expression of miR-21 ($p<0.001$). Our findings demonstrated that different doses of BA increased TAS levels while decreasing TOS levels in Jurkat cells. Our study suggests that BA might be potential anti-cancer agent candidate in ALL via inhibition of cell proliferation, induced apoptosis, and reducing the amounts of anti-oxidants in cells.

https://pubmed.ncbi.nlm.nih.gov/31066018/

High Concentrations of Boric Acid Trigger Concentration-Dependent Oxidative Stress, Apoptotic Pathways and Morphological Alterations in DU-145 Human Prostate Cancer Cell Line 2020

We have concluded that boric acid caused oxidative stress, inhibition of cell growth, apoptosis, and morphological alterations in a concentration-dependent manner in DU-145 cells. Furthermore, treatments with increasing boric acid concentrations decreased the antioxidant levels in cells. We actually revealed that boric acid, known as an antioxidant, may prevent cell proliferation by acting as an oxidant in certain doses. Although the high IC50 concentration of boric acid is perceived to be negative, we think it provides important background for subsequent studies.

https://pubmed.ncbi.nlm.nih.gov/33438559/

Polymers Based on Phenyl Boric Acid in Tumor-Targeted Therapy 2021

Background: Tumors are still among the major challenges to human health. Tumor-targeted therapy is an effective way to treat tumors based on precise medical models. Sialic acid (SA) is overexpressed on the surface of tumor cells, and Phenyl Boric Acid (PBA) can specifically bind to SA. However, studies on the use of PBA in tumor-targeted therapy are few.

Objective: To summarize and analyze the characteristics and influencing factors of tumor targeted therapy in recent years, and the influencing factors of phenyl boric acid modified polymers in tumor targeted therapy, such as hydrogen ion concentration (pH), Adenosine Triphosphate (ATP), and sugars. This paper describes the application of phenyl boric acid partially functionalized nano-polymers in various types of targeted tumors, such as breast cancer, lung

adenocarcinoma, liver cancer, and so forth. In order to further improve the basic research and clinical workers' understanding of nano-preparations and tumor targeted therapy. At the same time, it is also expected to promote the development value of phenyl boric acid.

https://pubmed.ncbi.nlm.nih.gov/34175401/

Boric acid as a promising agent in the treatment of ovarian cancer: Molecular mechanisms 2021

Purpose: The aim of this study is to determine the therapeutic effects of boric acid cell proliferation, invasion, migration, colony formation, cell cycle and apoptosis mechanisms in ovarian cancer cell line under in vitro conditions.

Methods: MDAH-2774 ovarian cancer cells were employed. Real-time PCR test was used to investigate changes in genes and proteins of cell cycle and apoptosis and identified miRNAs under the addition of boric acid. The apoptosis rates were calculated by TUNEL assay. Matrigel invasion, colony formation and Wound healing tests were used to determine invasion and migration. Oxidative stress index value was calculated for oxidative stress.

Results: Boric acid inhibited cell proliferation, invasion, migration and colony formation, but induces apoptosis and oxidative stress. Also, the expression of miRNA-21, miRNA-200a, miRNA-130a and mi-RNA-224 (which are indicators of poor prognosis of ovarian cancer) decreased significantly.

Conclusion: The potential of boric acid as a natural molecule may supports its effectiveness in reducing adverse effects arising from conventional ovarian cancer treatments

https://pubmed.ncbi.nlm.nih.gov/35219976/

Boric acid suppresses cell proliferation by TNF signaling pathway mediated apoptosis in SW-480 human colon cancer line 2022

Boric acid is the most frequently observed form of boron. Some epidemiological data suggest that environmental exposure to boric acid reduces the incidence of prostate cancer in men, cervical and lung cancers in women. Experimental studies show, boric acid reduces cell proliferation and stimulates apoptosis in some prostate, melanoma, breast cancer cell lines. In this study, it was investigated whether boric acid could be a new candidate molecule that could be used in the treatment of colon cancer.

Results: We observed that boric acid suppresses cell proliferation and induces apoptosis both in 2D and 3D culture conditions. In addition, as a result of qRt-PCR studies, it was revealed that the observed apoptotic process was related to the TNF signaling pathway.

Conclusion: Boric acid can be considered as a potential anti-cancer agent candidate for colon cancer treatment.

https://pubmed.ncbi.nlm.nih.gov/37572183/

Does Boric Acid Inhibit Cell Proliferation on MCF-7 and MDA-MB-231 Cells in Monolayer and Spheroid Cultures by Using Apoptosis Pathways? 2024

The aim of this study was to investigate if boric acid could be used for treating breast cancer. The impacts of boric acid on the human breast carcinoma cell lines MCF-7 and MDA-MB-231 were studied with TUNEL, BrdU, caspase-3, and endo-G immunohistochemical studies in 3D and 2D culture systems. Furthermore, we conducted a qRT-PCR study to show changes in the expression of some genes involved in apoptosis. Suppression of cell proliferation through boric acid-inducing apoptosis was observed both in 3D and 2D culture conditions. These results are compatible with the gene expression results. The ENDOG, CASP3, CASP8, and CASP9 gene expression significantly changed at all time intervals in MCF-7 and MD-MB-231 cell lines boric acid can potentially treat breast cancer as an anti-cancer agent candidate

https://pubmed.ncbi.nlm.nih.gov/35868168/

Boric acid exert anti-cancer effect in poorly differentiated hepatocellular carcinoma cells via inhibition of AKT signaling pathway 2022

Background: The possible anti-cancer properties of boron, a trace element for humans, have been demonstrated in various experimental and epidemiological studies, although the effects of boron on liver cancer are unclear. In the present study we evaluate the effects of boric acid on the cell lines of hepatocellular carcinoma (HCC) of the liver, as the leading form of liver cancer, for which a poorly-differentiated HCC cell line (Mahlavu cell line) was used.

Methods: The anti-cancer effect of boric acid was investigated with a cell viability assay, apoptosis analysis, cell migration analysis, cell morphology analysis, colony formation assay and 3D cell culture techniques. Also, the effect of boric acid on the AKT signaling pathway was determined through a western blot analysis.

Results: Boric acid was found to reduce cell viability in a dose- and time-dependent manner, and decreased survival, colony formation ability, migration capability and HCC cell tumor spheroid growth in HCC cell lines, while also inducing apoptosis, autophagy and morphological alteration. Furthermore, boric acid inhibited AKT phosphorylation, and anticancer biological responses in HCC cells were observed only in cells in which AKT phosphorylation was suppressed by boric acid.

Conclusion: Our results suggest that boric acid might be a promising therapeutic candidate in hepatocellular carcinoma via the inhibition of AKT signaling pathway.

https://pubmed.ncbi.nlm.nih.gov/37372032/

Redox Mechanisms Underlying the Cytostatic Effects of Boric Acid on Cancer Cells-An Issue Still Open. 2023

Boric acid (BA) is the dominant form of boron in plasma, playing a role in different physiological mechanisms such as cell replication. Toxic effects have been reported, both for high doses of boron and its deficiency. Contrasting results were, however, reported about the cytotoxicity of pharmacological BA concentrations on cancer cells. The aim of this review is to briefly summarize the main findings in the field ranging from the proposed mechanisms of BA uptake and actions to its effects on cancer cells.

Part of these studies also pointed out that BA would be able to modulate the redox state of the cell, thus contributing to apoptotic cell death. A short (24 h) exposure of DU145 prostate cancer cells to millimolar concentrations of BA (6–16 mM) was able to reduce cell viability and induce oxidative stress by decreasing superoxide dismutase (SOD) and catalase (CAT) activities and the levels of intracellular glutathione. Accordingly, a significant increase in malondialdehyde (MDA) levels was also observed, with this suggesting that BA would exert major cytotoxic effects by reducing antioxidant levels [10].

In this perspective, a "bell-shaped" dose response for borate's effect on cellular growth was demonstrated in both HEK293 and HeLa cells, and the modulation of differential MAPKs' pathway was proposed to play a role.

https://pubmed.ncbi.nlm.nih.gov/36468437/

Enhancement of ferroptosis by boric acid and its potential use as chemosensitizer in anticancer chemotherapy. 2023

Ferroptosis is a form of regulated cell death (RCD) characterized by intracellular iron ion accumulation and reactive oxygen species (ROS)-induced lipid peroxidation. Ferroptosis in cancer and ferroptosis-related anticancer drugs have recently gained interest in the field of cancer treatment. Boron is an essential trace element playing an important role in several biological processes. Recent studies have described contrasting effects of boric acid (BA) in cancer cells, ranging from protective/mitogenic to damaging/antiproliferative. Interestingly, boron has been shown to interfere with critical factors involved in ferroptosis-intracellular glutathione and lipid peroxidation in the first place. Thus, the present study was aimed to verify the ability of boron to modulate the ferroptotic process in HepG2 cells, a model of hepatocellular carcinoma. Our results indicate that-when used at high, pharmacological concentrations-BA can increase intracellular ROS, glutathione, and TBARS levels, and enhance ferroptosis induced by RSL3 and erastin. Also, high BA concentrations can directly induce ferroptosis, and

such BA-induced ferroptosis can add to the cytotoxic effects of anticancer drugs sorafenib, doxorubicin and cisplatin. These observations suggest that BA could be exploited as a chemo-sensitizer agent in order to overcome cancer drug resistance in selected conditions. However, the possibility of reaching suitably high concentrations of BA in the tumor microenvironment will need to be further investigated.

https://pubmed.ncbi.nlm.nih.gov/38216793/
Boric Acid and Borax Protect Human Lymphocytes from Oxidative Stress and Genotoxicity Induced by 3-Monochloropropane-1,2-diol. 2024
In conclusion, BA and BX are safe and non-genotoxic under the in vitro conditions and can alleviate cytotoxic, oxidative, and genetic damage induced by 3-MCPD in the human blood cells. Our findings suggest that dietary boron supplements may offer a novel strategy for mitigating hematotoxicity induced by xenobiotics, including 3-MCPD.

https://pubmed.ncbi.nlm.nih.gov/34293392/
Promising potential of boron compounds against Glioblastoma: In Vitro antioxidant, anti-inflammatory and anticancer studies. 2021
We found that BA and BX led to a remarkable reduction in U-87MG cell viability in a concentration-dependent manner. We also found that boron compounds increased the total oxidative status and MDA levels along with the SOD and CAT enzyme activities and decreased total antioxidant capacity and GSH levels in U-87MG cells without inducing DNA damage. The cytokine levels of cancer cells were also altered. We verified the selectivity of the compounds using a normal cell line, HaCaT and found an exact opposite condition after treating HaCaT cells with BA and BX. BA applications were more effective than BX on U-87MG cell line in terms of increasing MDA levels, SOD and CAT enzyme activities, and decreasing Interleukin-1α, Interleukin-6 and Tumor necrosis factor- α (TNF- α) levels. We finally observed that anticancer effect of BA and BX were associated with the BRAF/MAPK, PTEN and PI3K/AKT signaling pathways in respect of downregulatory manner. Especially, BA application was found more favorable because of its inhibitory effect on PIK3CA, PIK3R1, PTEN and RAF1 genes. In conclusion, our analysis indicated that boron compounds may be safe and promising for effective treatment of GB.

https://pubmed.ncbi.nlm.nih.gov/29500724/
The Effect of Boric Acid and Borax on Oxidative Stress, Inflammation, ER Stress and Apoptosis in Cisplatin Toxication and Nephrotoxicity Developing as a Result of Toxication 2018
As a result of the treatments applied to experimental animals, it was determined that boric acid and borax reduced apoptotic damage in kidney tissue, but the decrease was statistically significant only in 200 mg/kg boric acid-administered group. In the study, low anti-apoptotic effects of borate doses with the anti-inflammatory and antioxidant effect may be due to increased ER stress at the relevant doses.

https://pubmed.ncbi.nlm.nih.gov/38713435/
Protective Effect of Boric Acid Against Ochratoxin A-Induced Toxic Effects in Human Embryonal Kidney Cells (HEK293): A Study on Cytotoxic, Genotoxic, Oxidative, and Apoptotic Effects 2024
In addition, the study shows that treatment with BA leads to a decrease in oxidative stress markers, highlighting its potential as a therapeutic intervention against the deleterious effects of OTA. These results emphasize the need for further research into the protective mechanisms of boron, particularly BA, in combating cell damage caused by OTA.

https://pubmed.ncbi.nlm.nih.gov/30885023/
Boron's neurophysiological effects and tumoricidal activity on glioblastoma cells with implications for clinical treatment 2019
Results: Discovery of novel boron compounds in treatment of glioblastoma is being actively investigated, but the majority of such studies is focused on the synthesis of boron compounds as sensitizers to Boron Neutron Capture Therapy (BNCT). Nonetheless, the translational functionality of boron compounds is not limited to BNCT as many boron compounds possess direct tumoricidal activity and there is substantial evidence that certain boron compounds can cross the blood-brain barrier. Moreover, boron-containing compounds interfere with several tumorigenic pathways including intratumoral IGF-I levels, molybdenum Fe-S containing flavin hydroxylases, glycolysis, Transient Receptor Potential (TRP) and Store Operated Calcium Entry (SOCE) channels. Conclusions: Boron compounds deserve to be studied further in treatment of systemic cancers and glioblastoma due to their versatile antineoplastic functions.

https://pubmed.ncbi.nlm.nih.gov/38536434/
The analysis of boric acid effect on epithelial-mesenchymal transition of CD133 + CD117 + lung cancer stem cells. 2024
Boric acid slightly reduced the migration of cancer cells. Increased expression of transcription factor SNAIL ($p < 0.001$), but not ZEB1, was observed in LC-SCs. mRNA expression levels of ITGB1 ($p < 0.01$), ITGA5 ($p < 0.001$), COL1A1 ($p < 0.001$), and LAMA5 ($p < 0.001$) increased; CDH1 and VIM decreased in LC-SCs. Moreover, while E-cadherin ($p < 0.001$) and Collagen-1 ($p < 0.01$) immunoreactivities significantly increased, MMP-3 ($p < 0.001$) and Vimentin ($p < 0.01$) immunoreactivities decreased in BA-treated LC-SCs. To conclude, the current study provided insights into the efficacy and effects of BA against LC-SCs regarding proliferation, EMT, and cell death for future studies.

https://pubmed.ncbi.nlm.nih.gov/38367174/
Boric Acid Affects the Expression of DNA Double-Strand Break Repair Factors in A549 Cells and A549 Cancer Stem Cells: An In Vitro Study 2024
Different concentrations of BA (at doses ranging from 1 to 100 mM) were applied to cancer stem cells. Cytotoxic activities were determined using the cell viability assay (MTT assay) at 24 and 48 h. Expression levels of DNA DSB genes that BRCA1, BRCA2, RAD51, KU70/80, ATM, and XRCC4 were evaluated by RT-qPCR. Additionally, immunofluorescence staining analysis was exploited for caspase-3 and E-cadherin. ATM expression increased significantly ($p < 0.001$). No significant change was observed in the expression of other genes. Moreover, BA up-regulated caspase-3 and E-cadherin expression. Consequently, we can say that BA affects DNA DSB and the apoptotic abilities of LC-SCs.

https://pubmed.ncbi.nlm.nih.gov/38087035/
Boric Acid Alters the Expression of DNA Double Break Repair Genes in MCF-7-Derived Breast Cancer Stem Cells. 2024
Targeting the expression of DNA double-strand break (DSB) repair genes in breast cancer stem cells (BC-SCs) is essential for facilitating their elimination with conventional therapies. This study aims to investigate the effects of boric acid (BA) on the expression of DNA DSB repair genes in BC-SCs, which has not been studied in the literature before. BS-SCs were isolated by the MACS method and characterized by flow cytometry. The effects of BA on BC-SCs' DNA DSB repair genes were deciphered by cell viability assay, inverted microscopy, and RT-qPCR. While the expression of the BRCA1 and BRCA2 was upregulated, the expression of the ATM ($p < 0.001$), RAD51 ($p < 0.001$), and KU70 ($p < 0.001$) was downregulated in dose-treated BC-SCs ($p < 0.001$) to the qPCR results. Consequently, BA affects some of the DNA DSB repair genes of breast cancer stem cells. Findings from this study could provide new insights into the potential therapeutic application of BA in BC-SC elimination and cancer intervention.

https://pubmed.ncbi.nlm.nih.gov/38963646/

Evaluation of Boric Acid Treatment on microRNA-127-5p and Metastasis Genes Orchestration of Breast Cancer Stem Cells. 2024
Our findings suggest that boric acid could induce miR-127-5p expression. However, it cannot be said that it improves the metastasis properties of breast cancer stem cells.

https://pubmed.ncbi.nlm.nih.gov/30196486/
Boric Acid Activation of eIF2α and Nrf2 Is PERK Dependent: a Mechanism that Explains How Boron Prevents DNA Damage and Enhances Antioxidant Status. 2019
Boron is abundant in vegetables, nuts, legumes, and fruit and intake is associated with reduced risk of cancer and DNA damage and increased antioxidant status. Blood boric acid (BA) levels are approximately 10 μM BA in men at the mean US boron intake. Treatment of DU-145 human prostate cancer cells with 10 μM BA stimulates phosphorylation of elongation initiation factor 2α (eIF2α) at Ser51 leading to activation of the eIF2α/ATF4 pathway which activates the DNA damage-inducible protein GADD34.

https://pubmed.ncbi.nlm.nih.gov/38494858/
Borax induces ferroptosis of glioblastoma by targeting HSPA5/NRF2/GPx4/GSH pathways. 2024
Glioblastoma multiforme (GBM) is a highly aggressive and lethal form of primary brain tumour. Borax has been demonstrated to exhibit anti-cancer activity through cell death pathways. However, the specific impact of borax on ferroptosis in GBM is not well-established, and the underlying regulatory mechanisms remain unclear. Initially, the effective concentration of borax on cell viability and proliferation in U251 and A172 cells was determined. Subsequently, the effects of borax on the wound healing were analysed. Nuclear factor erythroid 2-related factor 2 (NRF2), glutathione peroxidase 4 (GPx4), glutathione (GSH), HSP70 protein 5 (HSPA5), malondialdehyde (MDA) levels and caspase-3/7 activity were determined in borax-treated and untreated cells. Finally, the protein expression levels of HSPA5, NRF2 and GPx4 were analysed. Borax suppressed cell viability and proliferation in U251 and A172 cells in a concentration- and time-dependent manner. In addition, borax treatment decreased GPx4, GSH, HSPA5 and NRF2 levels in U251 and A172 cells while increasing MDA levels and caspase-3/7 activity. Moreover, borax reduced mRNA and protein levels of HSPA5, NRF2 and GPx4 in U251 and A172 cells. Consequently, borax may induce ferroptosis in GBM cells and regulate the associated regulatory mechanisms targeting NRF2 and HSPA5 pathways. This knowledge may contribute to the development of novel therapeutic approaches targeting ferroptosis in GBM and potentially improve patient outcomes.

https://pubmed.ncbi.nlm.nih.gov/36988300/
Borax regulates iron chaperone- and autophagy-mediated ferroptosis pathway in glioblastoma cells 2023
Glioblastoma (GBM) is classified as a stage-IV glioma. Unfortunately, there are currently no curative treatments for GBM. Poly(rC)-binding protein 1 (PCBP1) is a cytosolic iron chaperone with diverse functions. PCBP1 is also known to regulate autophagy, but the role of PCBP1 in ferroptosis, iron-dependent cell death pathway, remains unrevealed in GBM cells. Here, we investigated the effects of borax, a boron compound, on the ferroptosis signaling pathway mediated by PCBP1 and autophagy.
The result showed that borax in U87-MG cells induced reduction of the PCBP1, GSH, and GPx4 and enhancement of Beclin1, MDA, and ACSL4. Furthermore, borax triggered apoptosis by activating caspase 3/7 in U87-MG cells. Our study indicated that the borax has potential as an anticancer treatment for GBM via regulating PCBP1/Beclin1/GPx4/ACSL4 signaling pathways.

https://pubmed.ncbi.nlm.nih.gov/35007916/
Anti-cancer effect of boron derivatives on small-cell lung cancer. 2022
Background: Anti-cancer activity of boron has been reported. Although many boron derivatives such as boric acid (BA) have been discovered to have anticancer effects, there are many boron derivatives whose anticancer effects have not yet been discovered. Some of these include sodium pentaborate pentahydrate (NaB), which has had limited research on its anticancer effects, and sodium perborate tetrahydrate (SPT), whose anticancer effect has yet to be discovered. The aim of this study was to investigate the anti-cancer effects of boric acid (BA), sodium pentaborate pentahydrate (NaB), and sodium perborate tetrahydrate (SPT) against small-cell lung cancer (SCLC) cell line DMS-114 cells in vitro
Conclusions: BA, NaB and SPT show anti-cancer activity in the DMS-114 cell line without damaging MRC-5 cells, and some of the molecular mechanisms are involved in apoptosis and cell cycle arrest.

https://pubmed.ncbi.nlm.nih.gov/36940038/
Boron Derivatives Inhibit the Proliferation of Breast Cancer Cells and Affect Tumor-Specific T Cell Activity In Vitro by Distinct Mechanisms. 2023
Therefore, we aimed to investigate the potential anti-carcinogenic effect of some boron derivatives (sodium pentaborate pentahydrate (SPP) and sodium perborate tetrahydrate (SPT)), which showed a promising effect on some types of cancers in the literature, on breast cancer cell lines, as well as immuno-oncological side effects on tumor-specific T cell activity.
In conclusion, SPP, SPT, and their combination could have growth inhibitory (antiproliferative) effects and could be a potential treatment for breast cancer. However, their stimulatory effects on the PD-1/PD-L1 signaling pathway and their effects on cytokines could ultimately account for the observed repression of the charging of specifically activated effector T cells against breast cancer cells.

https://pubmed.ncbi.nlm.nih.gov/38689139/
In Vitro Effects of Boric Acid on Cell Cycle, Apoptosis, and miRNAs in Medullary Thyroid Cancer Cells. 2024
Medullary thyroid cancer (MTC) is a highly aggressive and chemotherapy-resistant cancer originating from the thyroid's parafollicular C cells. Due to its resistance to conventional treatments, alternative therapies such as boric acid have been explored. Boric acid, a boron-based compound, has shown anticarcinogenic effects, positioning it as a potential treatment option for MTC.
At 48 h, 50% inhibitory concentration (IC50) of boric acid was found to be 35 μM. Treatment with boric acid resulted in significant modulation of apoptosis-related genes and miRNAs, including increased expression of phorbol-12-myristate-13-acetate-induced protein 1(NOXA), apoptotic protease activating factor 1 (APAF-1), Bcl-2-associated X protein (Bax), caspase-3, and caspase-9. In contrast, the expression of B cell lymphoma 2 (Bcl2), B cell lymphoma- extra-large (Bcl-xl), and microRNA-21 (miR-21), which are linked to the aggressiveness of MTC, was significantly reduced. The TUNEL assay indicated a 14% apoptosis rate, and there was a 67.9% reduction in colony formation, as shown by the colony formation assay. Our study suggests that boric acid may have anticancer activity in MTC by modulating apoptotic pathways. These findings suggest that boric acid could be a potential therapeutic agent for MTC and possibly for other malignancies with similar pathogenic mechanisms.

https://pubmed.ncbi.nlm.nih.gov/36326151/
Boron- and phosphorus-containing molecular/nano platforms: exploiting pathological redox imbalance to fight cancer. 2022
In this context, redox imbalance is an undervalued characteristic of cancer. However, it may be targeted by boron- and phosphorus-containing materials to selectively or systemically fight cancer. In particular, boron and phosphorus derivatives are attractive building blocks for rational drug discovery due to their unique

and wide regioselective chemistry, high degree of tuneability and chemical stability. Thus, they can be meticulously employed to access tunable molecular platforms to selectively exploit the redox imbalance of cancer cells towards necrosis/apoptosis. This field of research holds a remarkable potential; nevertheless, it is still in its infancy.

https://pubmed.ncbi.nlm.nih.gov/37770673/
Boric Acid (Boron) Attenuates AOM-Induced Colorectal Cancer in Rats by Augmentation of Apoptotic and Antioxidant Mechanisms. 2024
Boric acid-treated rats had significantly lower pro-inflammatory cytokines (TNF-α and IL-6) and higher anti-inflammatory cytokines (IL-10) based on serum analysis. The colorectal cancer attenuation by BA is shown by the reduced ACF numbers, anticipated by its regulatory potentials on the apoptotic proteins, antioxidants, and inflammatory cytokines originating from AOM-induced oxidative damage.

https://pubmed.ncbi.nlm.nih.gov/38780503/
Borax affects cellular viability by inducing ER stress in hepatocellular carcinoma cells by targeting SLC12A5. 2024
The determined IC50 value of borax for HL-7702 cells was 40.8 mM, whereas for HepG2 cells, this value was 22.6 mM. The concentrations of IC50 (22.6 mM) and IC75 (45.7 mM) of borax in HepG2 cells did not manifest morphological aberrations in HL-7702 cells.
Moreover, SLC12A5 levels decreased following borax treatment in HepG2 cells, whereas ATF6, CHOP, GRP78, CASP3, and CYC levels exhibited a significant increase. In conclusion, our data highlight the potential therapeutic effects of borax through the regulation of ER stress in HCC by targeting SLC12A5.

https://pubmed.ncbi.nlm.nih.gov/31066018/
High Concentrations of Boric Acid Trigger Concentration-Dependent Oxidative Stress, Apoptotic Pathways and Morphological Alterations in DU-145 Human Prostate Cancer Cell Line. 2020
The objective of the present study was to assess the effects of boric acid at concentrations higher than that can be achieved in blood by dietary intake on DU-145 human prostate cancer cells for 24 h. Firstly, we determined the cytotoxic activity of boric acid (0 to 12.5 mM) on DU-145 human prostate cancer cells by using 3-(4, 5-dimethylthiazol, 2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) and defined the IC50 concentration of boric acid. Then, by employing the doses found in MTT, the levels of antioxidant-oxidant molecules and apoptotic proteins were measured and morphological changes were evaluated. We have concluded that boric acid caused oxidative stress, inhibition of cell growth, apoptosis, and morphological alterations in a concentration-dependent manner in DU-145 cells. Furthermore, treatments with increasing boric acid concentrations decreased the antioxidant levels in cells. We actually revealed that boric acid, known as an antioxidant, may prevent cell proliferation by acting as an oxidant in certain doses. Although the high IC50 concentration of boric acid is perceived to be negative, we think it provides important background for subsequent studies

https://pubmed.ncbi.nlm.nih.gov/37934369/
Investigation of cytotoxic antiproliferative and antiapoptotic effects of nanosized boron phosphate filled sodium alginate composite on glioblastoma cancer cells. 2023
The effects of nanosized boron phosphate-filled sodium alginate composite gel (SA/BP) on the biological characteristics of three types of glioblastoma multiforme (GBM) cells (C6, U87MG and T98G) were examined in this study. MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) assay was used to determine the cytotoxicity of the composite gel on GBM, which was then compared to L929 healthy cells. Furthermore, wound healing, apoptosis, and colony formation capacities were evaluated. The investigation revealed that the SA/BP composite gel was successful in all GBM cells and could be used as a treatment agent for GBM and/or other invasive cancer types.
Conclusions: In line with experimental findings, it was observed that the SA/BP composite gel system did not affect healthy fibroblast cells but had a cytotoxic effect on glioblastoma cells, significantly reduced cell migration and colony-forming capacity of cells, and significantly increased apoptosis and depolarization of cell membranes. Based on all these findings, it can be said that SA/BP composite gel has cytotoxic, antiproliferative and antiapoptotic effects on different glioblastoma cells.

https://pubmed.ncbi.nlm.nih.gov/37318308/
Organoboronic acids/esters as effective drug and prodrug candidates in cancer treatments: challenge and hope 2023
Boronic acids/esters have recently emerged in the field of medicinal and pharmaceutical research due to their exceptional oxophilicity, low toxicity, and unique structure. They are known as potent enzyme inhibitors, cancer therapy capture agents, and can mimic certain types of antibodies to fight infections. They have been designed and developed into drugs, and this approach has emerged in the last 20 years. Five boronic acid drugs have been approved by the FDA and Health Canada, two of which are used to treat cancer, specifically multiple myeloma. The purpose of this review is to investigate boronic acid/ester derivatives as potential pharmaceutical agents as well as the mechanism of action. It will concentrate on six types of cancer: multiple myeloma, prostate cancer, breast cancer, lung cancer, cervical cancer, and colon cancer. Some newly developed boron-containing compounds have already demonstrated highly promising activities, but further investigation is required before final conclusions can be drawn.

https://journals.sagepub.com/doi/full/10.1177/2156587211407638
Growing Evidence for Human Health Benefits of Boron. 2011
Both animal and human data suggest that boron intakes should be >1.0 mg/d. Many people consume less than this amount.
Cancer
After an epidemiological study found an inverse association between dietary boron and prostate cancer,45 Barranco and Eckhert initiated studies showing that boric acid completely inhibited the growth of the cultured prostate cancer cells, DU-145.46–48 Subsequently, Carper et al49 found that variable, often dose-dependent, amounts of boron gave responses indicating controlled apoptosis as opposed to a toxic or cytotoxic effect on DU-145, PC-3, and LNCaP-cultured prostate cells. Their initial studies found that 1 mmol/L boric acid markedly inhibited growth of DU-145 cells, moderately inhibited growth of cultured LNCaP cells, and had a muted effect on growth of cultured PC-3 cells. Boron analogs such as phenylboronic acid and hydroxymethylphenylboronic acid also had similar inhibitory effects on growth that were consistent with those on growth of cancer cells in vitro reported by others using boric acid.46,50 Boric acid at 1 mmol/L also was found to inhibit growth of breast cancer cells in vitro.51 Cultured SK-BR-3 and ZR-75-1 breast cells were only partially inhibited—an effect that was less than that with cultured DU-145 prostate cells. However, an apoptotic response occurred in cultured ZR-75-1 cells after 7 days of exposure to either boric acid or phenylboronic acid. Caspase 3 activities confirmed apoptotic, or programmed death, rather than a cytotoxic or necrotic death induced by the boron compounds. In contrast to $MgCl_2$, which stimulated cell attachment, boric acid and phenylboronic acid inhibited cell attachment.51 Phenylboronic acid induced a dose-dependent block in the S-phase of the cell cycle in the detached ZR-75-A cells.
Changes in focal adhesion kinase were targeted as a possible mechanism of action through which boric acid induced apoptosis in both cultured breast and cultured prostate cancer cells. Focal adhesion kinase is overexpressed in several human cancer cell lines and is essential in the integrin-mediated signal transduction pathway; it participates in cell migration, angiogenesis, and inflammation/wound healing. Through phosphorylation reactions, focal adhesion kinase conformation changes elicit both intracellular and extracellular responses that suppress apoptosis and promote cell migration. A 4-fold reduction in phosphorylated

focal adhesion kinase with concurrent increased caspase-3 occurred with boric acid treatment, which indicated apoptotic activity in the cancer cells.52
It should be noted that boron has been associated with other forms of cancer. A study of cervical smears from 472 women with a high mean boron intake (8.41 mg/d) and 587 with marginal mean boron intake (1.26 mg/d) found 15 cases of cytopathological indications of cervical cancer in boron-low women and none in the boron-high women.53 In a study of 763 women with lung cancer and 838 matched healthy controls, boron intake was inversely associated with the incidence of cancer; odds increased substantially if the women were not on hormone replacement therapy.54
Both animal and human data were used by the World Health Organization (WHO)95 to suggest that an acceptable safe range of population mean intakes of boron for adults could be 1 to 13 mg/d. This suggestion implies that intakes <1.0 mg/d is inadequate for optimal boron beneficial activity.
Safe Upper Level of Intake
Despite the large array of findings showing beneficial effects of boron in animal and human studies, the United States Institute of Medicine Food and Nutrition Board96 did not set an adequate intake level for boron. However, they set a tolerable upper intake level of 20 mg/d. The World Health Organization first suggested that 13 mg/d would be a safe upper intake level95 but later increased this to 0.4 mg/kg body weight or about 28 mg/d for a 70-kg person.97
In a population exposed to drinking water containing up to 29 mg/L boron and to boron mining and production, no adverse effects on health or fertility were found over 3 generations. In another study, no adverse effects were found in 66 men (mean age of 39 years) residing in a high boron area for 36 years who had a calculated boron excretion of 6.77 mg/L, which indicated a high intake of boron. The drinking water in the area where they resided had boron concentrations that ranged from 2.05 to 29.00 mg/L, with a mean of 10.2 ± 4.1 mg/L

https://ods.od.nih.gov/factsheets/Boron-HealthProfessional/
Boron is present in foods and beverages as inorganic borates as well as mono- or di-sugar-borate esters, such as calcium fructoborate [14,15]. Most ingested boron is hydrolyzed to boric acid within the gastrointestinal tract [6]. The body absorbs about 85%–90% of ingested boron [2,4]. However, very little is known about how or where in the gastrointestinal tract absorption occurs [8].
Boron does not accumulate in most body tissues, but bone, nails, and hair have higher boron levels than other body tissues, whereas fat has lower levels [9]. Boric acid is the main form of boron in blood, urine, and other body fluids [2,4,7]. The lack of substantial changes in blood boron levels in response to large increases in dietary intakes suggests that the body maintains boron homeostasis, likely by increasing urinary excretion, but the regulatory mechanisms for boron homeostasis have not been identified [6]. Boron is excreted mainly in the urine, and small amounts are excreted in the feces, sweat, breath, and bile [9,10].
The amount of boron in plant foods depends somewhat on the boron content of the soil and water where they were grown [7,21]. Areas of the world with limited boron in the soil include Brazil, Japan, and most of the United States, mainly because of high levels of rainfall, which leaches boron out of the soil [21]. In contrast, arid regions of the world—including California and parts of Turkey, Argentina, Chile, Russia, China, and Peru—have higher boron concentrations [21,22].
In dietary supplements, boron is present in many different forms, including sodium borate, sodium tetraborate, boron amino acid chelate, boron ascorbate, boron aspartate, boron citrate, boron gluconate, boron glycinate, boron picolinate, and calcium fructoborate [6,27]. In a small human study, boron as sodium tetraborate significantly increased plasma boron levels within 4–6 hours of consumption [5], but no data are available on the relative bioavailability of different forms of supplemental boron.

://www.researchgate.net/publication/352786926_Using_Boron_Supplementation_in_Cancer_Prevention_and_Treatment_A_Review_Article
Using Boron Supplementation in Cancer Prevention and Treatment: A Review Article. 2018
The results showed that boron supplement is a useful and essential ingredient for humans with a daily intake of about 1-3 mg per day. Its rich diets have a significant reduction in the risk of developing a variety of cancers including prostate, breast, cervix and lung, liver, melanoma. The mechanisms by which boron may influence cancer is still unknown, but evidence suggests that boron has antioxidant and anti-inflammatory properties. Proposed mechanisms related to boron activity in cancer cells include inhibition of proteasezonin enzymatic activity, dehydrogenase, mRNA modification, and cell division and induction of apoptosis.
Boron-containing compounds indicate promising effects for chemotherapy types of cancer. Its concluded that low levels of boron should be considered as a concern for health, and increasing the consumption of boron with its rich diets should be recognized as a rational and reasonable diet recommendation for the prevention and treatment of cancer, promotion of health and well-being.

https://link.springer.com/article/10.1007/s12011-018-1284-3
The Physiological Role of Boron on Health. 2018
The health benefits of boron are numerous in animals and humans; for instance, it affects the growth at safe intake. Central nervous system shows improvement and immune organs exhibit enhanced immunity with boron supplementation. Hepatic metabolism also shows positive changes in response to dietary boron intake. Furthermore, animals and human fed diets supplemented with boron reveal improved bone density and other benefits including embryonic development, wound healing, and cancer therapy.

https://link.springer.com/article/10.1007/s10552-007-9052-2
Boron intake and prostate cancer risk. 2007
Experimental studies suggest that boron may prevent prostate cancer. Only one small epidemiological study has been conducted of boron, which found that those in the highest quartile of boron intake had less than half the risk of prostate cancer versus those in the lowest quartile.

https://www.researchgate.net/publication/48855337_Dietary_boron_possible_roles_in_human_and_animal_physiology
Dietary boron: possible roles in human and animal physiology. 2008
Boron increases the level of testosterone in men, 17 is important in the immune system, 18,19 prevents osteoporosis 20 and protects against some types of cancer. 21,22 Boron contains many features such as anti-inflammatory, anticancer, disinfectant, antioxidant and antiapoptotic.
Moreover, it seems likely that dietary boron reduces prostate cancer risk through its influence on steroid hormones (especially androgens) (Scorei, 2011). Furthermore, in humans an increased boron consumption has been associated with a decreased incidence of several types of cancers (e.g., lung, cervical or breast cancer) (Hunt, 2008;Scorei, 2011). In fact, negative correlations have been found between the concentration of boron in diets and the incidence of lung cancer. .

https://www.semanticscholar.org/paper/Dietary-boron-intake-and-prostate-cancer-risk.-Cui-Winton/ea6e91bd6a5fd3573e1b3acec9fbe0acaf7c6d2e
Dietary boron intake and prostate cancer risk. 2004
Cross-sectional case-control study design was employed by comparing boron intake of 95 prostate cancer cases with that of 8,720 male controls. After controlling for age, race, education, smoking, body mass index, dietary caloric intake, and alcohol consumption, increased dietary boron intake was associated with a decreased risk of prostate cancer with a dose-response pattern. The adjusted odds ratio was 0.46 (95% confidence interval: 0.21-0.98) for the highest quartile of boron intake comparing to the lowest quartile (P for trend = 0.0525). The observed association should be interpreted with caution because of the small case sample size and the nature of the cross-sectional study design, but deserve further investigation.

https://www.lifeextension.com/magazine/2021/11/what-is-boron
Boron has been shown to have actions against specific types of malignancies, such as:
Cervical cancer: The country Turkey has an extremely low incidence of cervical cancer, and scientists partially attribute this to its boron-rich soil.1 When comparing women who live in boron-rich regions versus boron-poor regions of Turkey, not a single woman living in the boron-rich regions had any indication of cervical cancer.2 (The mean dietary intake of boron for women in this group was 8.41 mg/day.)
Boron interferes with the life cycle of the human papillomavirus (HPV), which is a contributing factor in approximately 95% of all cervical cancers.1
Considering that HPV viruses are increasingly implicated in head and neck cancers,3,4 supplementation with this ultra-low-cost mineral could have significant benefits in protecting against this malignancy that is increasing in prevalence.
Lung cancer: A study conducted at the University of Texas MD Anderson Cancer Center between 1995 and 2005 found that increased boron intake was associated with a lower risk of lung cancer in postmenopausal women who were taking hormone replacement therapy.
Prostate cancer: Studies point to boron's ability to inhibit the growth and spread of prostate cancer cells.
In one study, when mice were exposed to boric acid, their tumors shrank by as much as 38%.6 One analysis found that increased dietary boron intake was associated with a decreased risk of prostate cancer.7
In addition to its bone and anti-cancer benefits, there are nine additional reasons boron is an important trace mineral vital for health and longevity. It has been shown to:1
Greatly improve wound healing,
Beneficially impact the body's use of estrogen, testosterone, and vitamin D,
Boost magnesium absorption,
Reduce levels of inflammatory biomarkers, such as high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor α (TNF-α),
Raise levels of antioxidant enzymes, such as superoxide dismutase (SOD), catalase, and glutathione peroxidase,
Protect against pesticide-induced oxidative stress and heavy-metal toxicity,
Improve the brain's electrical activity, which may explain its benefits for cognitive performance, and short-term memory in the elderly,
Influence the formation and activity of key biomolecules, such as S-adenosyl methionine (SAM-e) and nicotinamide adenine dinucleotide (NAD+), and
Potentially help ameliorate the adverse effects of traditional chemotherapeutic agents.
Because the amount of boron varies in the soil, based on geographical location, obtaining enough boron through diet alone can be difficult.
Supplementing with low-cost boron is an effective way to maintain adequate levels of this overlooked micronutrient.
Most Life Extension® supporters obtain 3 mg to 6 mg of boron in their multi-nutrient supplements

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9409115/
New Insights into Boron Essentiality in Humans and Animals 2022
Boron (B) is considered a prebiotic chemical element with a role in both the origin and evolution of life, as well as an essential micronutrient for some bacteria, plants, fungi, and algae. B has beneficial effects on the biological functions of humans and animals, such as reproduction, growth, calcium metabolism, bone formation, energy metabolism, immunity, and brain function. Naturally organic B (NOB) species may become promising novel prebiotic candidates. NOB-containing compounds have been shown to be essential for the symbiosis between organisms from different kingdoms. New insights into the key role of NOB species in the symbiosis between human/animal hosts and their microbiota will influence the use of natural B-based colon-targeting nutraceuticals. The mechanism of action (MoA) of NOB species is related to the B signaling molecule (autoinducer-2-borate (AI-2B)) as well as the fortification of the colonic mucus gel layer with NOB species from B-rich prebiotic diets. Both the microbiota and the colonic mucus gel layer can become NOB targets. This paper reviews the evidence supporting the essentiality of the NOB species in the symbiosis between the microbiota and the human/animal hosts, with the stated aim of highlighting the MoA and targets of these species.
To date, out of all SBEs, only fructoborate (FB) has been clinically tested, proving to have beneficial and quantifiable activity in humans [18,34,35].

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6373344/
The Fructoborates: Part of a Family of Naturally Occurring Sugar–Borate Complexes—Biochemistry, Physiology, and Impact on Human Health: a Review. 2019
Sugar–borates (SBs) are mono- or di-sugar–borate esters (SBEs) comprised of one or two monosaccharide molecules linked to a boron (B) atom. SBEs occur naturally in commonly consumed herbs, vegetables, fruits, seeds, and nuts and, other than greatly varying levels of B found in local drinking water, are the primary natural dietary sources of B-containing molecules in humans. To date, the most studied SBE is calcium fructoborate (CaFB).
borates are crucial in the development of plants (for example, the normal cell wall growth, membrane functions, and the biosynthesis of lignin), but more recently, sugar–borates have been demonstrated to be potentially important modulators of human health [17, 18, 25, 26].
The identification of health benefits related to sugar–borates and the subsequent clinical validation of their significance has become an important new extension of boron science. Thus far, out of all sugar–borate esters, only fructoborate (calcium fructoborate—CaFB) has been clinically proven to have measurable activity in humans [4, 17, 19, 27–30].
FBEs are found in various vegetables and fruits that are subsequently consumed by humans and animals [16]. Plant-based materials serve as the fundamental dietary source of organic B-containing molecules. Plant-based materials
do not serve as a primary source of inorganic B-containing molecules. CaFB, the most common form of FBE, is naturally found in fresh fruits, vegetables and honey, and in dried fruits (plums, raisins, apricots) [20].
Today, CaFB is industrially manufactured in a nature-identical form using a chemical synthesis according to Miljkovic (1999) and Hunter (2016) patents [44, 45]. This industrially produced CaFB is being widely used as a dietary supplement for joint health, specifically for modulation of the symptoms of age-related joint discomfort and degeneration [17, 19]. CaFB has been presented in numerous published papers that report its chemistry [20, 33, 46, 47]. Additionally, it has been repeatedly reported to significantly reduce pain and improve flexibility in a clinical setting as evidenced by improvements in Western Ontario and McMaster Universities Arthritis Index (WOMAC) and McGill Indices [27–30].
Food itemTotal boron (μg/g)Fructoborate esters (μg/g)
Apple253.5
Apricotn.d.16
Dandelion root (Taraxaci radix)20080Figs3515
Flaxseed sprouts (Lini semen)80080
Honey (Mel)127
Raisinn.d.79
Tomato paste207
For CaFB and related compounds, the daily average sugar–borate intake was estimated to be about 35 mg (75 mg 95th percentile intake) (based on IOM

Committee's estimation of an assumed 5 mg of daily B intake). Mathematically converted, this means that the typical daily dietary intake (from fruits and vegetables) of CaFB (containing only 2.5% B by weight) and related complexes might be as high as 165 mg/individual/day. When administering an encapsulated daily dose of 216 mg of industrially produced CaFB, the B intake (5.4 mg/day) does not exceed the safe upper limits of 6–20 mg B/day [18–20, 52], according to World Health Organization (WHO) and Organization for Economic Co-operation and Development (OECD) regulations

https://pubmed.ncbi.nlm.nih.gov/26686846/

Calcium Fructoborate for Bone and Cardiovascular Health. 2016

Calcium fructoborate (CF), a natural sugar-borate ester found in fresh fruits and vegetables, is a source of soluble boron. CF contains three forms of borate (diester, monoester, and boric acid) and all are biologically active, both at the intracellular (as free boric acid) and extracellular level (as fructose-borate diester and monoester). At the cellular and molecular level, CF is superior to the boric acid/borate, exhibiting a complex "protective" effect against inflammatory response. CF is commercially available in the USA as a "nature-identical" complex, an active compound for dietary supplements.

https://pubmed.ncbi.nlm.nih.gov/28028787/

A Study on the Anticarcinogenic Effects of Calcium Fructoborate. 2017

Evidences about the preventive and therapeutic effects of boron compounds on cancer have been increasing in the last years. Although calcium fructoborate (CaFB) is used as a nutritional supplement, data about its preventive and therapeutic effects on neoplastic transformations are limited. In the present study, the various concentrations of CaFB were applied to the MDA-MB-231 metastatic breast cancer cell line.

Cell viability was significantly reduced at 50 µM CaFB treatment. pATM, p-p53, and caspase-9 levels increased significantly in all groups; furthermore, there was approximately 12.5-, 2.4-, and 10.7-fold increase, respectively, for 100 µM CaFB treatment. ATM and p53 levels did not change with CaFB treatment, but PARP levels significantly 2.5-fold decreased. While VEGF immunoreactivity decreased in all groups, significant increase in caspase-3 immunoreactivity was observed only in the group treated with 50 µM CaFB ($p < 0,001$). Our results imply that CaFB may have therapeutic potential as well as preventive benefits in cancer.

https://pubmed.ncbi.nlm.nih.gov/21196370/

Calcium fructoborate: plant-based dietary boron as potential medicine for cancer therapy. 2011

CF has been identified as Ca ((C6H10O6)2B)2o4H2O and is a natural product from plants (can be produced by chemical synthesis as well), and is efficient in the prevention and treatments (as adjuvant) of osteoporosis and osteoarthritis. CF showed inhibitory effects on MDA-MB-231 breast cancer cells as well, and enters the cell (most likely) by a co-transport mechanism via a sugar transporter. Inside cells CF acts as an antioxidant and induces the overexpression of apoptosis-related proteins and eventually apoptosis.

https://pubmed.ncbi.nlm.nih.gov/18176783/

Comparative effects of boric acid and calcium fructoborate on breast cancer cells. 2008

Recent studies suggested that **boron has a chemo-preventive role in prostate cancer.** In the present report, we investigated the effects of calcium fructoborate (CF) and boric acid (BA) on activation of the apoptotic pathway in MDA-MB-231 human breast cancer cells. Exposure to BA and CF inhibited the proliferation of breast cancer cells in a dose-dependent manner. Treatment with CF but not BA resulted in a decrease in p53 and bcl-2 protein levels. Furthermore, after the treatment with CF, augmentation of pro-caspase-3 protein expression, cytosolic cytochrome c level, and caspase-3 activity were observed, indicating apoptotic cell death induction. This was also demonstrated by terminal deoxynucleotidyl transferase-mediated 2'-deoxyuridine 5'-triphosphate nick-end-labeling assay. In conclusion, our data provide arguments to the fact that both BA and CF inhibited the growth of breast cancer cells, while only CF induced apoptosis. Additional studies will be needed to identify the underlying mechanism responsible for the observed cellular responses to these compounds and to determine if BA and CF may be further evaluated as chemotherapeutic agents for human cancer.

https://pubmed.ncbi.nlm.nih.gov/35174920/

Calcium fructoborate regulate colon cancer (Caco-2) cytotoxicity through modulation of apoptosis. 2022

Sugar-borate esters have recently been reported to have anti-cancer potential. Among the sugar-borate esters, calcium fructoborate (CaFB) possesses beneficial effects on human health. Despite the beneficial effects of CaFB, there is a lack of knowledge about their mode of action in cancer. The potential cytotoxic effects of CaFB were investigated on colon cancer cells (Caco-2). The mode of action was determined through the evaluation of Fyn and Hck expression levels together with Bcl-2, Bax, and PI3K/Akt pathway proteins. CaFB treatment was found to be most effective on Caco-2 cells at 10 mM concentration for 24 h. Decreased Bcl-2 levels and increased Bax levels at 10 mM were evaluated as an indicator of apoptotic effects of CaFB. Akt, p70S6K, and 4EBP1 levels, in general, tend to decrease following CaFB, while PTEN and TSC2 levels have been found to increase. Furthermore, CaFB upregulated Hck expression and downregulated Fyn expression. In conclusion, our results indicated that CaFB treatment at 10 mM concentration, the IC50 dose found in our study, might prevent colon cancer cell proliferation both by inducing apoptosis and presumably by activating autophagy.

https://pubmed.ncbi.nlm.nih.gov/31529243/

Calcium Fructoborate Prevents Skin Cancer Development in Balb-c Mice 2020

Recent evidence obtained from our study validated that CaFB treatment may have skin cancer-preventing effect.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8256803/

Safety of calcium fructoborate as a novel food pursuant to Regulation (EU) 2015/2283. 2021

Following a request from the European Commission, the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) was asked to deliver an opinion on calcium fructoborate as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF, produced by chemical synthesis, contains a maximum of 2.9% of boron and on average 4.7% calcium and 84.2% fructose. It is intended to be marketed as food supplements targeting the general adult population, excluding pregnant and lactating women, at a maximum level of 220 mg/day (maximum boron intake of 6.4 mg per day). The combined intake of boron from the background diet and the NF is in the range of 9.6–9.9 mg/day

https://pubmed.ncbi.nlm.nih.gov/36136913/

The dual role of boron in vitro neurotoxication of glioblastoma cells via SEMA3F/NRP2 and ferroptosis signaling pathways 2023

A certain dose of Boric acid (BA) has many biochemical effects, conspicuously over antioxidant/oxidant rates. This article sought to investigate the modifies of various doses of BA on the glioblastoma concerning cytotoxicity, ferroptosis, apoptosis, and semaphorin-neuropilin signaling pathway.

This study revealed that BA, defined as trace element and natural compound, incubated ferroptosis, total oxidant molecules, and caspase protein in a dose-dependently by disrupting SEMA3F in tumor cells.

https://www.sciencedirect.com/science/article/abs/pii/S0223523420306425

Anticancer boron-containing prodrugs responsive to oxidative stress from the tumor microenvironment 2020
Boronic acid (and ester) prodrugs targeting the overexpressed level of reactive oxygen species within tumor microenvironment represent a promising area for the discovery of new selective anticancer chemotherapy.

https://pmc.ncbi.nlm.nih.gov/articles/PMC9103596/
The inhibitory effect of boric acid on hypoxia-regulated tumour-associated carbonic anhydrase IX 2022
We tested the inhibitory effect of boric acid (BA), an inorganic Lewis acid, on CA IX as well as other isoforms (CA I, II, and XII). BA acted as a millimolar *in vitro* CAI, decreased proliferation of two cancer cell lines, although not strong correlations between the *in vitro* inhibition and *in vivo* effects were observed. The mechanism of antiproliferative action of BA should be investigated in more detail.

https://www.pnas.org/doi/10.1073/pnas.2107503118
Evaluation of borinic acids as new, fast hydrogen peroxide–responsive triggers 2021
We discovered that borinic acid is 10,000-fold more reactive than its boronic counterpart toward H_2O_2-mediated oxidation.

https://pmc.ncbi.nlm.nih.gov/articles/PMC9438760/
Cytotoxic and Apoptotic Effects of the Combination of Borax (Sodium Tetraborate) and 5-Fluorouracil on DLD-1 Human Colorectal Adenocarcinoma Cell Line 2022
Our current findings suggest that the combination of borax with 5-FU has a strong cytotoxic and apoptotic effect on the human CRC DLD-1 cells.
Boron is found abundantly in nature as boric acid (a soluble form of boron) and inorganic salts called borates.[14,15] Sodium tetraborate known as borax is a salt of boric acid.[15] A study by Wei et al.[15] revealed the anticarcinogenic effect of borax in hepatocellular carcinoma. Another boron compound, boric acid inhibited the proliferation of prostate cancer cell lines, DU-145 and LNCaP[16] and MDA-MB-231 human breast cancer cells[17] and inhibited cell growth, apoptosis, and morphological alterations of DU-145 cells.[18] Currently, bortezomib, which is made from boric acid polymers, is used as an anticancer chemotherapeutic agent for treating multiple myeloma cells.[19] Additionally, boron compounds have been used in neutron capture therapy for different types of cancer.[20,21]

https://pubmed.ncbi.nlm.nih.gov/38789899/
Boric Acid Alleviates Lipopolysaccharide-Induced Acute Lung Injury in Mice 2024
Inflammation plays a central role within ALI progress, and boric acid (BA) has demonstrated anti-inflammatory properties both in vitro and in vivo. However, its potential to mitigate lipopolysaccharide (LPS)-induced ALI remains an area awaiting exploration in research. To bridge this research gap, we created a mouse model of ALI induced by intraperitoneal LPS injection.
Our findings revealed that prophylactic treatment with BA effectively attenuated LPS-induced ALI, as supported by improved pathological alterations, decreased total protein concentration in bronchoalveolar lavage fluid (BALF), and reduced pulmonary edema. Furthermore, BA exhibited anti-inflammatory properties by suppressing inflammatory cytokines within the lung tissue. BA ingestion caused upregulation in SOD and a decrease in MDA contents in lung tissue homogenates. BA downregulated the levels of GRP78 and CHOP compared to the LPS group. Remarkably, BA also upregulated transcription and protein expression of Nrf2 and HO-1 compared to the LPS group. In conclusion, our study highlights BA's potential as a novel promising prophylactic agent for LPS-induced ALI, offering avenue for improving clinical management of this condition.

https://pmc.ncbi.nlm.nih.gov/articles/PMC2698284/
Receptor Activated Ca2+ Release Is Inhibited by Boric Acid in Prostate Cancer Cells 2009
The global disparity in cancer incidence remains a major public health problem. We focused on prostate cancer since microscopic disease in men is common, but the incidence of clinical disease varies more than 100 fold worldwide. Ca^{2+} signaling is a central regulator of cell proliferation, but has received little attention in cancer prevention. We and others have reported a strong dose-dependent reduction in the incidence of prostate and lung cancer within populations exposed to boron (B) in drinking water and food; and in tumor and cell proliferation in animal and cell culture models.
We show B causes a dose dependent decrease of Ca^{2+} release from ryanodine receptor sensitive stores. This occurred at BA concentrations present in blood of geographically disparate populations. Our results suggest higher BA blood levels lower the risk of prostate cancer by reducing intracellular Ca^{2+} signals and storage.

https://pubmed.ncbi.nlm.nih.gov/39458975/
The Potential Role of Boron in the Modulation of Gut Microbiota Composition: An In Vivo Pilot Study 2024
The administration of BA significantly altered the composition of the gut microbiota, resulting in a rise in advantageous species such as *Barnesiella* and *Alistipes*. Additionally, there was a decrease in some taxa associated with inflammation and illness, such as *Clostridium XIVb* and *Bilophila*. Notable increases in genera like *Treponema* and *Catellicoccus* were observed, suggesting the potential of boron compounds to enrich microbial communities with unique metabolic functions.
Conclusions: These findings indicate that boron compounds may have the potential to influence gut microbiota composition positively, offering potential prebiotic effects. Further research with additional analyses is necessary to fully understand the interaction between boron and microbiota and to explore the possibility of their use as prebiotic agents in clinical settings.
Colorectal cancer (CRC) is associated with intestinal dysbiosis, characterised by an elevated presence of potentially pathogenic bacteria and a concurrent decrease in the proportion of butyrate-producing bacteria among CRC patients. Studies have reported diminished production levels of *Proteobacteria*, *Bifidobacteria*, *Prevotella*, and short-chain fatty acids (SCFA), while an increase has been observed in *Firmicutes*, *Bacteroidetes*, *Enterobacteriaceae*, and *Fusobacteria* [11,21].
An increasing number of studies suggest that dysbiosis in the gut microbiota contributes to senescence, oxidative stress, cytokine production, and neuroinflammation in the early phases of Alzheimer's disease pathogenesis [23].

https://pubmed.ncbi.nlm.nih.gov/15500945/
Boric acid inhibits human prostate cancer cell proliferation 2004
The role of boron in biology includes coordinated regulation of gene expression in mixed bacterial populations and the growth and proliferation of higher plants and lower animals. Here we report that boric acid, the dominant form of boron in plasma, inhibits the proliferation of prostate cancer cell lines, DU-145 and LNCaP, in a dose-dependent manner. Non-tumorigenic prostate cell lines, PWR-1E and RWPE-1, and the cancer line PC-3 were also inhibited, but required concentrations higher than observed human blood levels. Studies using DU-145 cells showed that boric acid induced a cell death-independent proliferative inhibition, with little effect on cell cycle stage distribution and mitochondrial function.

https://pubmed.ncbi.nlm.nih.gov/17186423/

Evaluation of ecological and in vitro effects of boron on prostate cancer risk (United States) 2007
Results: Groundwater boron levels correlated with a decrease in prostate cancer incidence (R = 0.6) and mortality (R = 0.6) in state planning regions, whereas selenium did not (R = 0.1; R = 0.2). Growth inhibition was greater during combined treatments of boric acid and selenomethionine, or boric acid and genistein, versus singular treatments. 8-day boric acid pre-exposure enhanced the toxicity of ionizing radiation treatment, while dose-dependently decreasing the expression of anti-apoptotic protein Bcl-2.
Conclusions: Increased groundwater boron concentrations, across the state of Texas, correlate with reduced risk of prostate cancer incidence and mortality. Also, boric acid improves the anti-proliferative effectiveness of chemo-preventative agents, selenomethionine and genistein, while enhancing ionizing radiation cell kill.

https://pubmed.ncbi.nlm.nih.gov/34677681/
Boron Intake and decreased risk of mortality in kidney transplant recipients 2022
We determined 24 h urinary boron excretion using inductively coupled plasma mass spectrometry as a measure of boron exposure in 693 stable KTR (57% male, mean age 53y), enrolled in the TransplantLines Food and Nutrition Biobank and Cohort Study.
Cox regression analyses showed that high boron excretion was strongly associated with lower risk of mortality, independent of age, sex, estimated glomerular filtration rate and history of cardiovascular disease
Conclusion: Boron may be an overlooked target to improve long-term survival among KTR and potentially other patients, likely through pathways other than inflammation or the methionine-homocysteine cycle that were previously suggested. Interventional trials are warranted to confirm the potential of dietary boron supplementation in KTR and other patient populations.

https://pubmed.ncbi.nlm.nih.gov/18343880/
Dietary boron and hormone replacement therapy as risk factors for lung cancer in women 2008
In an ongoing case-control study in Houston, Texas (July 1995 through April 2005, end date for this analysis), 763 women were diagnosed with lung cancer, and 838 were matched healthy controls with data on both diet and HRT. Multiple logistic regression analyses were conducted to assess the associations between dietary boron and HRT with lung cancer risk.
In joint-effects analyses, compared with women with high dietary boron intake who used HRT, the odds ratio for lung cancer for low dietary boron intake and no HRT use was 2.07 (95% CI: 1.53, 2.81). Boron intake was inversely associated with lung cancer in women, whereas women who consumed low boron and did not use HRT were at substantial increased odds.

https://pubmed.ncbi.nlm.nih.gov/14713551/
Boron supplementation inhibits the growth and local expression of IGF-1 in human prostate adenocarcinoma (LNCaP) tumors in nude mice 2004
We proposed that dietary supplementation with boric acid would inhibit PSA and reduce the development and proliferation of prostate carcinomas in an animal model. We tested this hypothesis using nude mice implanted subcutaneously with LNCaP cells in Matrigel. Two groups (10 animals/group) were dosed with boric acid solutions (1.7, 9.0 mgB/kg/day) by gavage. Control group received only water. Tumor sizes were measured weekly for 8 weeks. Serum PSA and IGF-1 levels were determined at terminal sacrifice. The size of tumors was decreased in mice exposed to the low and high dose of boric acid by 38% and 25%, respectively.

https://pmc.ncbi.nlm.nih.gov/articles/PMC3216419/
Cellular changes in boric acid-treated DU-145 prostate cancer cells 2006
Epidemiological, animal, and cell culture studies have identified boron as a chemopreventative agent in prostate cancer. The present objective was to identify boron-induced changes in the DU-145 human prostate cancer cell line. We show that prolonged exposure to pharmacologically-relevant levels of boric acid, the naturally occurring form of boron circulating in human plasma, induces the following morphological changes in cells: increases in granularity and intracellular vesicle content, enhanced cell spreading and decreased cell volume.

https://pubmed.ncbi.nlm.nih.gov/18516691/
Boric acid inhibits stored Ca2+ release in DU-145 prostate cancer cells 2009
Boron (B) is a developmental and reproductive toxin. It is also essential for some organisms. Plants use uptake and efflux transport proteins to maintain homeostasis, and in humans, boron has been reported to reduce prostate cancer. Ca2+ signaling is one of the primary mechanisms used by cells to respond to their environment. In this paper, we report that boric acid (BA) inhibits NAD+ and NADP+ as well as mechanically induced release of stored Ca2+ in growing DU-145 prostate cancer cells.

https://pubmed.ncbi.nlm.nih.gov/37219712/
An Investigation into the Protective Effects of Various Doses of Boric Acid on Liver, Kidney, and Brain Tissue Damage Caused by High Levels of Acute Alcohol Consumption 2023
In this study we aim to determine whether administering boric acid (BA) can protect certain organs (liver, kidney, and brain) from the damaging effects of alcohol by reducing oxidative stress.
As a result, we found that the effect of alcohol-induced oxidative stress on liver, kidney, and brain tissues was different, and that giving boric acid reduces the increased oxidative stress in tissues due to its antioxidant effect. It was found that 100mg/kg BA administration had a higher antioxidant effect than in the 50mg/kg group.

https://aacrjournals.org/cancerres/article/67/9_Supplement/4220/535557/Boric-acid-induces-apoptosis-in-both-prostate-and
Boric acid induces apoptosis in both prostate and breast cancer cell lines 2007
Recent reports have indicated that boric acid is able to inhibit the growth of prostate cancer cell lines and tumors. Our studies confirm growth inhibition of the DU-145 and PC-3 human prostate cancer cells >lines. In addition, we have observed that boric acid is also capable >of inhibiting the growth of two human breast cancer cell lines ZR- >75-1 and SK-BR-3 but not MDA-MB-231, MDA-MB-435, T-47D >or MCF-7 breast cancer cell lines. In addition to growth inhibition >it was observed that boric acid and phenyl boric acid were able to >cause both the breast and prostate cancer cells to detach and >undergo apoptosis. Flow cytometery indicated that the floating >cells were undergoing apoptosis in a dose dependent manner. A >caspase 3 assay further confirmed apoptosis. Both boric acid and >phenyl boric acid were able to inhibit the attachment of DU-145 in >the absence or presence of MnCl2. Cell attachment is controlled >by the integrin proteins hence, our working hypothesis is that boric >and phenyl boric acids are binding to the integrin proteins, causing >the cells to detach and undergo apoptosis.

https://link.springer.com/article/10.1007/s12011-024-04274-6
Evaluation of Boric Acid Treatment on microRNA-127-5p and Metastasis Genes Orchestration of Breast Cancer Stem Cells 2024
Coregulation of microRNAs (miRNAs) and cancer stem cells (CSCs) is very important in carcinogenesis. miR-127-5p is known to be downregulated in breast

cancer. In this study, we aimed to investigate how boric acid (BA), known for its previously unstudied anti-cancer properties, would affect the expression of miR127-5p and genes responsible for breast cancer stem cells (BC-SCs) metastasis.
Our findings suggest that boric acid could induce miR-127-5p expression. However, it cannot be said that it improves the metastasis properties of breast cancer stem cells.

https://pubmed.ncbi.nlm.nih.gov/21975546/
Phenylboronic acid is a more potent inhibitor than boric acid of key signaling networks involved in cancer cell migration 2011
Previous studies from our lab have shown that both boric (BA) and phenylboronic- acid (PBA) inhibit the migration of prostate cancer cell lines, as well as non-tumorigenic prostate cells. Our results indicate that PBA is more potent than BA in targeting metastatic and proliferative properties of cancer cells. Here we focus on the impact of BA and PBA on Rho family of GTP-binding proteins and their downstream targets. Treatment with 1mM PBA and BA decreases activities of RhoA, Rac1, and Cdc42 in DU-145 metastatic prostate cancer cells, but not in normal RWPE-1 prostate cells. Furthermore, ROCKII activity and phosphorylation of myosin light chain kinase decrease as a result of either PBA or BA treatment in DU-145 cells, suggesting these compounds target actomyosin-based contractility.

https://pubmed.ncbi.nlm.nih.gov/29779163/
Discovering simple phenylboronic acid and benzoxaborole derivatives for experimental oncology - phase cycle-specific inducers of apoptosis in A2780 ovarian cancer cells 2019
Conclusion Phenylboronic acid and benzoxaborole derivatives were found to be highly promising antiproliferative and proapoptotic compounds with a cell cycle-specific mode of action. The presented data support their candidacy for further studies as a novel class of potential anticancer agents.

https://pmc.ncbi.nlm.nih.gov/articles/PMC6620035/
Effects of B2O3 (boron trioxide) on colon cancer cells: our first-step experience and in vitro results 2019
Boron oxide (B2O3) is derived from dehydration of boric acid and is a colorless, semitransparent, crystalline compound that is moderately soluble in water. On the other hand, boron oxide is chemically hygroscopic. This gives the molecule the ability to soak up water and adhere to tissues. Boron oxide can be used locally after tumor debulking in inoperable tumors and especially when the tumor-free margin distance cannot be provided.

https://pubmed.ncbi.nlm.nih.gov/21129941/
Comparative effects of daily and weekly boron supplementation on plasma steroid hormones and proinflammatory cytokines 2010
Boron possesses widespread properties in biochemistry and nutrition. Acute supplementation with 11.6 mg of boron resulted in a significant increase in plasma boron concentration. Given such a fast bioavailability, the objective was to determine whether acute (hourly or daily), and weekly supplementation could have any significant biological effects on the steroid hormones and further on some inflammatory biomarkers. Eight healthy male volunteers attended the laboratory on three occasions (days 0, 1 and 7). On the first day (day 0), a blood sample collection at 8.00 A.M was followed by ingestion of placebo with the breakfast. On the next day (supplementation-day 1), similar procedure was followed by ingestion of a capsule containing 10mg of boron. On both occasions blood was collected every 2h for the next 6h. Subjects were requested to consume a capsule of 10mg boron every day with their breakfast, and on the day 7, the blood collection was carried out at 8.00 A.M, again. Boron in plasma increased significantly following hours and weekly consumption. Six hours supplementation showed a significant decrease on sex hormone binding globulin (SHBG), high sensitive CRP (hsCRP) and TNF-α level. After one week (in samples taken at 8.00 A.M, only), the mean plasma free testosterone increased and the mean plasma estradiol decreased significantly. Dihydrotestosterone, cortisol and vitamin D was elevated. Also, concentrations of all three inflammatory biomarkers decreased after supplementation. Of note, despite decreased proinflammatory cytokines, based on recent clinical data, this must be the first human study report to show an increase level of free testosterone after boron consumption.

https://pubmed.ncbi.nlm.nih.gov/12428176/
Boron supplementation and activated factor VII in healthy men 2002
The aim of the present study was to determine whether postprandial concentrations of the active component of serine protease coagulation factor VII (VIIa) were lowered by acute boron supplementation in vivo.
Results from this study suggest that acute boron supplementation (at 11.6 mg boron) does not alter the activity of factor VIIa following consumption of a high-fat meal.

https://pubmed.ncbi.nlm.nih.gov/9197924/
The effect of boron supplementation on its urinary excretion and selected cardiovascular risk factors in healthy male subjects 1997
Supplementation with 10 mg B/d for 4 wk resulted in 84% of the supplemented dose being recovered in the urine.
Our studies suggest that the absorption efficiency of B is very high and estimation of the urinary B concentration may provide a useful reflection of B intake. In addition, the elevation of endogenous estrogen as a result of supplementation suggests a protective role for B in atherosclerosis.

https://pubmed.ncbi.nlm.nih.gov/10376277/
The significance of dietary boron, with particular reference to athletes 1999
To avoid the side-effect of drug abuse, it is suggested that the key to success is a proper athletic nutrition.
Boron is a trace element nutrient, and recently its supplements have been shown to increase the concentration of plasma steroid hormones. In a single blind cross-over trial, it resulted in a significant increase in plasma 17-B estradiol (E2) concentration ($P < 0.004$) and there was a trend for plasma testosterone (T) levels to be increased. The ratio of E2/T increased significantly. However, there was no perturbation in plasma lipids. Furthermore, the effect of boron on steroidogenesis and its mechanism was also investigated in two more studies conducted on adult male rats. The elevation of endogenous steroid hormones as a result of boron supplementation suggest that boron may be used as an ergogenic safe substance for athletes which should be further investigated.

https://pubmed.ncbi.nlm.nih.gov/27054120/
Boron Induces Early Matrix Mineralization via Calcium Deposition and Elevation of Alkaline Phosphatase Activity in Differentiated Rat Bone Marrow Mesenchymal Stem Cells 2016
Although more investigation is required, we suggest the prescription of a very low concentration of B in the form of BA or foods containing BA, in groups at high risk of osteoporosis or in the case of bone fracture.

https://pubmed.ncbi.nlm.nih.gov/39275197/
Low-Mineral Water Diminishes the Bone Benefits of Boron 2024
Boron exposure improved bone formation, microstructure, and biomechanics initially but the benefits weakened with higher levels of exposure ($p < 0.05$).

https://pubmed.ncbi.nlm.nih.gov/10050922/
The nutritional and metabolic effects of boron in humans and animals 1998
In rats, increasing the intake of B through the drinking water is reflected in the tissue concentrations, results in an increase in plasma testosterone and vitamin D, and results in a decrease in HDL cholesterol. It is clear that B has the potential to impact significantly on a number of metabolic processes.

https://pubmed.ncbi.nlm.nih.gov/37220543/
Therapeutic Efficacy of Boric Acid Treatment on Brain Tissue and Cognitive Functions in Rats with Experimental Alzheimer's Disease 2023
Discussion: Significant improvement in learning and memory abilities after BA application is promising for AD.
Conclusion: These results show that BA application positively affects learning and memory abilities, and reduces oxidative stress.

https://pubmed.ncbi.nlm.nih.gov/39139931/
A pilot study investigating the influence of dietary boron levels on osteoporosis in postmenopausal women 2024
A significant link was found between boron intake and bone mineral density highlighting the importance of nutritional and lifestyle factors affecting bone health.

https://pubmed.ncbi.nlm.nih.gov/38983826/
Boron-containing compounds as labels, drugs, and theranostic agents for diabetes and its complications 2024
Finally, it should be noted that some boron compounds appear to exert beneficial effects on diabetes complications such as accelerating wound healing while ameliorating pain in diabetic patients.

https://pmc.ncbi.nlm.nih.gov/articles/PMC8837486/
Possible therapeutic effects of boron citrate and oleoylethanolamide supplementation in patients with COVID-19: A pilot randomized, double-blind, clinical trial 2022
Patients were randomized in a 1:1:1:1 allocation ratio to 1of 4 treatment groups: (A) 5 mg of boron citrate twice a day, (B) 200 mg of oleoylethanolamide twice a day, (C) both therapies, or (D) routine treatments without any study medications.
Supplementation with boron citrate alone or in combination with oleoylethanolamide significantly improved O2 saturation and respiratory rate ($p < 0.01$). At the end of the study, significant increases in white blood cell and lymphocyte count were observed in the boron citrate and combined groups ($p < 0.001$). Boron citrate supplementation led to a significant decrease in serum lactate dehydrogenase ($p = 0.026$) and erythrocyte sedimentation rate ($p = 0.014$), compared with other groups. Furthermore, boron citrate in combination with oleoylethanolamide resulted in a significant reduction in the high-sensitivity C-reactive protein and interleukin-1β concentrations ($p = 0.031$ and $p = 0.027$, respectively).

https://www.nature.com/articles/ncomms13936
Hollow boron nitride nanospheres as boron reservoir for prostate cancer treatment 2017
Boron compounds are increasingly recognized as preventative and chemotherapeutic agents. However, systemic administration of soluble boron compounds is hampered by their short half-life and low effectiveness. Here we report on hollow boron nitride (BN) spheres with controlled crystallinity and boron release that decrease cell viability and increase prostate cancer cell apoptosis.
. The work demonstrates that hollow BN spheres may function as a new agent for prostate cancer treatment.

https://www.researchgate.net/publication/50832657_Prevalence_of_Prostate_Cancer_in_High_Boron-Exposed_Population_A_Community-Based_Study
Prevalence of Prostate Cancer in High Boron-Exposed Population: A Community-Based Study 2011
Although there was no significant difference among the groups in terms of total PSA levels, prostatic volumes were significantly lower in the study group as compared with those in the control group 2 in men whose prostates were biopsied ($p<0.012$), as detailed in Table 3.

https://pubmed.ncbi.nlm.nih.gov/28028787/
A Study on the Anticarcinogenic Effects of Calcium Fructoborate 2017
In the present study, the various concentrations of CaFB were applied to the MDA-MB-231 metastatic breast cancer cell line.
Cell viability was significantly reduced at 50 µM CaFB treatment. pATM, p-p53, and caspase-9 levels increased significantly in all groups; furthermore, there was approximately 12.5-, 2.4-, and 10.7-fold increase, respectively, for 100 µM CaFB treatment. ATM and p53 levels did not change with CaFB treatment, but PARP levels significantly 2.5-fold decreased. While VEGF immunoreactivity decreased in all groups, significant increase in caspase-3 immunoreactivity was observed only in the group treated with 50 µM CaFB ($p < 0,001$). Our results imply that CaFB may have therapeutic potential as well as preventive benefits in cancer.

https://pubmed.ncbi.nlm.nih.gov/33634364/
Therapeutic Effects of Newly Synthesized Boron Compounds (BGM and BGD) on Hepatocellular Carcinoma 2022
Boron glycine monoester (BGM) and boron glycine diester (BGD) compounds containing boron atoms were synthesized and investigated their cytotoxic, oxidative stress, and antimicrobial activities on the HepG2 cancer cell line.
Newly synthesized boron compounds, particularly BGM, with their cytotoxic, oxidative stress, and antimicrobial effects, could provide a new therapeutic approach for the treatment of hepatocellular carcinoma.

https://www.sciencedirect.com/science/article/abs/pii/S0163725823002127
Boron in cancer therapeutics: An overview 2023
Boron has become a crucial weapon in anticancer research due to its significant intervention in cell proliferation. Being an excellent bio-isosteric replacement of carbon, it has modulated the anticancer efficacy of various molecules in the development pipeline. It has elicited promising results through interactions with various therapeutic targets such as HIF-1α, steroid sulfatase, arginase, proteasome, *etc.*

https://pmc.ncbi.nlm.nih.gov/articles/PMC8590914/
Synthesis of New Boron Derived Compounds; Anticancer, Antioxidant and Antimicrobial Effect in Vitro Glioblastoma Tumor Model 2021
We synthesized boron glycine monoester (BGM) and boron glycine diester (BGD) structures containing boron atoms and determined their cytotoxic activities on glioblastoma by the MTT method.
After 48 hours of BGM and BGD application to U87MG glioblastoma cells, we found the IC50 value as 6.6 mM and 26 mM, respectively. CAT and ACP enzyme activities were decreased in BGM and BGD groups. MDA which is a metabolite of lipid peroxidation was increased in both boron compounds groups. GSH level was reduced especially in BGD group. BGM and BGD have been found to be antimicrobial effects.

Conclusion: Boron compounds, especially the BGM, can provide a new therapeutic approach for the treatment of glioblastoma with their anticancer, antioxidant, and antimicrobial effects.

https://pubmed.ncbi.nlm.nih.gov/32540741/
Pivotal role of boron supplementation on bone health: A narrative review 2020
The average daily consumption of boron in the US population was assessed by survey, in different age groups, using the "Boron Nutrient Data Base" and a two-day food diary. The average intake of boron was between 0.75 and 0.96 mg / day for school-age children and between 0.87 and 1.35 mg / day for adults [9].
Boron appears to significantly improve the absorption of magnesium and its deposition at the bone level
Conclusions: The studies considered in this narrative review have evaluated the positive effectiveness on bone, in humans, through control of calcium, vitamin D and sex steroid hormone metabolism, considering a dietary supplementation of 3 mg/day of boron (alone or with other nutrients); this supplementation is demonstrably useful to support bone health (in order to prevent and maintain adequate bone mineral density), also considering the daily dose of 3 mg is much lower than the Upper Level indicated by EFSA in the daily dose of 10 mg.

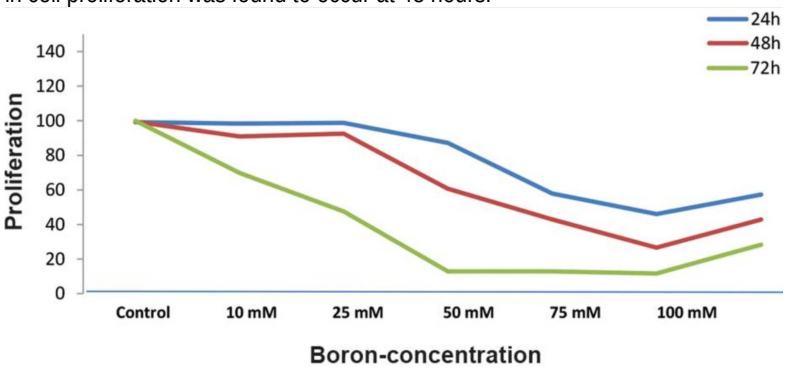
https://pubmed.ncbi.nlm.nih.gov/39358580/
Boron Salicylate Ester Compounds as Boron Therapeutics. Their Synthesis, Structural Characterizations and Anticancer Effects against MDA-MB-231 2024
Additionally, the anticancer potential of boron salicylate esters against the MDA-MB-231 human breast adenocarcinoma cell line was examined. The K-B salicylate diester molecule was found to have the most potential potency with the lowest IC_{50} value against the MDA-MB-231 cell line. The anticancer potential of boron salicylate esters can be further investigated with other cancer models with the combination of anticancer drugs.

https://pubmed.ncbi.nlm.nih.gov/38758480/
Boric Acid in Milk Replacer as a Health Enhancer and Growth Promoter for Lambs in the Suckling Period 2024
During the suckling period, 60 lambs (4 days old) were randomly given four levels of boric acid (0, 30, 60, and 90 mg/kg body weight) via milk replacer for 57 days.
In conclusion, the use of boric acid to lambs in the suckling period improved the average weekly body weight gain and feed conversion efficiency, positively affected some biochemical parameters, antioxidant system, and intestinal flora, and also affected gene expressions related to the immune system. Boric acid supplementation had a beneficial effect on the health and growth of suckling lambs.

https://pmc.ncbi.nlm.nih.gov/articles/PMC6524471/
Effects of magnesium with or without boron on headshaking behavior in horses with trigeminal-mediated headshaking 2019
Magnesium in combination with boron had the greatest decrease in headshaking.

https://aacrjournals.org/cancerres/article/67/9_Supplement/3384/537484/Mechanism-of-boric-acid-cytotoxicity-in-breast
Mechanism of boric acid cytotoxicity in breast cancer cell lines 2007
Boric acid, an essential plant element, has recently been implicated as a chemo-preventive agent in prostate cancer. However, the mechanism of action is not yet fully known. Our interest is to determine if Boric acid displays this same preventative role in breast cancer and by what mechanism it acts. Integrins are heterodimeric, glycoprotein, transmembrane molecules responsible for cell adhesion, survival, motility, growth and interaction. We hypothesize that Boric acid molecules interact with integrins through cis-diol bonds and mediate a response in breast cancer cells. To test this hypothesis we use Phenylboronic acid (PBA), a bulkier analog of Boric acid, on both breast ductal carcinoma, ZR-75-1, and breast andenocarcinoma, MCF-7.
Proliferation assays using 1mM PBA display a 68% inhibition of growth beginning on day 3 in ZR-75-1 cells and 70% inhibition of growth on day 5 in MCF-7.

https://pmc.ncbi.nlm.nih.gov/articles/PMC8405086/
Investigation of The Apoptotic and Antiproliferative Effects of Boron on CCL-233 Human Colon Cancer Cells 2021
This experimental study effect of different concentrations of boric acid on the CCl-233 human colon adenocarcinoma cell lines was investigated, by analyzing proliferation assay (proliferation was applied to the cells for 24, 48 and 72 hours).
As a result of the studies, analysis of the cell viability showed that 50 mM boric acid decreased cell proliferation after 24, 48 and 72 hours. The maximal decrease in cell proliferation was found to occur at 48 hours.



https://ar.iiarjournals.org/content/37/11/6347
Effect of Tumor Microenvironment on Selective Uptake of Boric Acid in HepG2 Human Hepatoma Cells 2017
To gain further insight, this study aimed to investigate the mechanisms of transportation and selective uptake of BA in HepG2 liver tumor cells.
The selective uptake of BA was achieved primarily by diffusion, while other factors, such as low pH and increased membrane fluidity, which are hallmarks of HCC, might further enhance BA uptake.

https://link.springer.com/article/10.1007/s12011-023-03930-7
Boric acid Increases Susceptibility to Chemotherapy by Targeting the Ferritinophagy Signaling Pathway in TMZ Resistant Glioblastoma Cells 2023
Temozolomide (TMZ) is the primary chemotherapy used for GBM, but it has limited effectiveness, with about half of the patients developing resistance.
In this study, we investigated whether boric acid increases chemosensitivity mediated by ferritinophagy via the NCOA4 and IRP2 signaling pathways in TMZ-resistant GBM cells.

According to our results, boric acid may regulate chemosensitivity in A172-R and T98G-R cells mediated by NCOA4 and IRP2. In conclusion, the manipulative effects of boric acid on the ferritinophagy pathway hold the potential to sensitize TMZ-resistant GBM cells to chemotherapy.

https://www.biorxiv.org/content/10.1101/193441v1.full.pdf

High concentrations of boric acid induce autophagy in cancer cell lines 2017

Our results demonstrate that all studied cell lines did not suffer mortality in low to medium doses of BA (up to 5mM). However, a high dose (over 25mM) could inflict significant death in all cell lines. Those high doses caused P62/SQSTM1 consumption and LC3II-B accumulation after 3 days of treatment. Using small doses of BA in combination with autophagy blockage did not improve cytotoxicity in lung cancer cell lines.

We found that low to medium concentrations of boric acid did not cause significant changes in cell growth in concordance with other studies, while effective doses were around 25mM. These doses are 700 to 3500 times higher than normal blood levels [13]. Although no reflection on health was observed when human population consumed water with Boron up to 29mg/L (equal to 2.5 mM boric acid) [23], nothing is known about concentrations as high as 25mM except that BA toxicity is not reported to be lethal [12]

It was reported that other boron based compounds exhibit better anti-cancer properties such as Phenylboronic acid and Calcium Fructoborate [5, 7]. Those compounds presented a better effect which reflects in less toxicity, and future studies are recommended to focus on them

https://www.sciencedirect.com/science/article/abs/pii/S0946672X20301383

In vitro effects of boric acid on human liver hepatoma cell line (HepG2) at the half-maximal inhibitory concentration 2020

Highlights

- •Boric acid led to growth inhibition of HepG2 cells with an estimated IC50 of 24 mM.
- •Key transcriptional changes accompany the effects of IC50-level boric acid.
- •Cell-cycle, DNA repair, and metabolic pathways were mostly downregulated.
- •Cell death and xenobiotic metabolism were mostly upregulated.
- •Transcriptional changes indicate a senescence-like profile with pro-apoptotic cues.

HepG2 cells treated with a growth-inhibitory concentration of boric acid for 24 h exhibited a senescence-like transcriptomic profile along with DNA damage.

https://pmc.ncbi.nlm.nih.gov/articles/PMC4300416/

Boric acid induces cytoplasmic stress granule formation, eIF2α phosphorylation, and ATF4 in prostate DU-145 cells 2014

Our results using physiological levels of boric acid identify the eIF2α/ATF pathway as a plausible mode of action that underpins the reported health effects of dietary boron.

https://pubmed.ncbi.nlm.nih.gov/20448936/

Assessment of the chemical changes induced in human melanoma cells by boric acid treatment using infrared imaging 2009

Boron is found in everyday foods and drinking water in trace quantities. Boron exists as boric acid (BA) within plants and animals, where low levels have been linked to cancer incidence. However, this correlation is not well characterized. In this study, we examined the chemical and morphological effects of BA on human skin melanoma cells (SK-MEL28) using Fourier Transform InfraRed Imaging (FTIRI) with a Focal Plane Array (FPA) detector. Cells were grown under concentrations of BA ranging from 0 to 50 mM.

PCA results showed an increase in beta-sheet protein at higher concentrations of BA (12.5, 25, and 50 mM). Together, these results suggest that high concentrations of BA have an anti-proliferative effect and show signs consistent with apoptosis.

https://pubmed.ncbi.nlm.nih.gov/19262119/

Phenylboronic acid selectively inhibits human prostate and breast cancer cell migration and decreases viability 2008

We compared the in vitro effect of boric acid (BA) versus phenylboronic acid (PBA) on the migration of prostate and breast cancer cell lines and non-tumorigenic cells from the same tissues. Treatment at 24 hours with BA (< or =500 microM) did not inhibit chemotaxis on fibronectin in any cell line. However, treatment over the same time course with concentrations of PBA as low as 1 muM significantly inhibited cancer cell migration without effecting non-tumorigenic cell lines. The compounds did not affect cell adhesion or viability at 24 hours but did alter morphology; both decreased cancer cell viability at eight days. These results suggest that PBA is more potent than BA in targeting the metastatic and proliferative properties of cancer cells.

https://www.researchgate.net/publication/51695649_Phenylboronic_acid_is_a_more_potent_inhibitor_than_boric_acid_of_key_signaling_networks_involved_in_cancer_cell_migration

Phenylboronic acid is a more potent inhibitor than boric acid of key signaling networks involved in cancer cell migration 2014

Previous studies from our lab have shown that both boric (BA) and phenylboronic- acid (PBA) inhibit the migration of prostate cancer cell lines, as well as non-tumorigenic prostate cells. Our results indicate that PBA is more potent than BA in targeting metastatic and proliferative properties of cancer cells. Here we focus on the impact of BA and PBA on Rho family of GTP-binding proteins and their downstream targets. Treatment with 1mM PBA and BA decreases activities of RhoA, Rac1, and Cdc42 in DU-145 metastatic prostate cancer cells, but not in normal RWPE-1 prostate cells. Furthermore, ROCKII activity and phosphorylation of myosin light chain kinase decrease as a result of either PBA or BA treatment in DU-145 cells, suggesting these compounds target actomyosin-based contractility.

https://pmc.ncbi.nlm.nih.gov/articles/PMC6010135/

In vitro and in vivo antitumour effects of phenylboronic acid against mouse mammary adenocarcinoma 4T1 and squamous carcinoma SCCVII cells 2017

After tumour transplantation in syngeneic mice, phenylboronic acid was shown to slow the growth of both tumour cell lines (4T1 and SCCVII) compared with the control. The inhibitory effects were pronounced during the application of phenylboronic acid. For both tested tumour cell lines, the most prominent antitumour effect was obtained by intraperitoneal administration, followed significantly by oral administration.