

Boron and Cancer Treatment

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ABSTRACT

Boron (B), atomic number 5, atomic weight 10.81g density 2.84g / cm³, melting point 2300 °C, is a semiconductor between metal and non-metal. Boron is an essential element for human and animal health. Although boron has toxic effects at high concentrations, it has a wide variety of physiological effects on biological systems at low concentrations, and there are many studies related to this. The most common forms of boron uptake into metabolism are sodium borate, boron citrate, boron aspartate and boron glycinate. It is known that boron and boron compounds have antioxidant effects. Cancer is a pathological condition that occurs as a result of a disorder in the mechanisms regulating cell growth and division (cell cycle). Malignant tumours show metastasis features by spreading to tissues after originating. All cancers are caused by some abnormalities in the DNA sequence. 10-15% of cancers are inherited, that is, inherited by genes from the parents, and the remaining 85-90% is shaped by exposure to mutagens in living cells, slight progressive changes in cell DNA, and errors in replication. is considered Cancer is multifactorial, and many factors, from bacteria to viruses, radiation to inheritance, environmental factors, dietary habits and chemicals, are blamed in cancer formation. The boron neutron capture therapy (BNCT) method, which has come to the fore, especially recently, has been a ray of hope for cancer treatment. This method, which has been tried in many cancer treatments, has been a treatment mainly used in the treatment of brain cancer and is known as a method in which the damage of healthy cells is at the lowest level in addition to the destruction of cancerous cells. It has also been observed that boric acid prevents cancerous prostate cells growth and the proliferation of cancerous cells. It has also been observed that boron taken into the body with diet is inversely proportional to lung and cervical cancers. In some experiments in animals and humans, boron has been shown to positively affect the central nervous system and be a bioactive element associated with a reduced risk for some types of cancer. This compilation; the significant effects of boron on human health and the use of boron in new treatments are mentioned.

Keywords: Boron; Cancer; DNA; Treatment methods

Introduction

Boron (B), atomic number 5, atomic weight 10.81g, density 2.84g / cm³, and melting point 2300 °C are semiconductors between metal and non-metal. Boron is a micronutrient element in living nutrition. Boron is mostly in the form of boric acid in tissues and body fluids. 98.4% of the amount of boron in human blood is boric acid, and 1.6% is borate anion. Boron is an essential element for human and animal health. Although boron has toxic effects at high concentrations, it has a wide variety of physiological effects on biological systems at low concentrations, and there are many studies related to this [1]. The World Health Organization has rearranged the safe and sufficient boron value for healthy people from its former value of 1 mg/day to 1-13 mg/day [2].

The American Toxic Substances and Diseases Association (ATSDR) have established a minimum risk level of 0.01 mg/kg/day for orally ingested boron in humans [3]. It has also been found that boron has very beneficial effects on the human body. Boron is found in many metabolic pathways such as bone development, hormones, psychological activities, antioxidant system in human tissues and is an important element for many biochemical events [4-6]. It can also be taken into the body externally by consuming fruits, vegetables (potatoes and avocados), legumes, nuts, eggs, milk, wine and dried foods [7,8]. Boron taken orally is completely absorbed, but enters the body easily without being metabolized. Boron entering the body in this way is eliminated from the body in a short time. The daily amount of boron that an adult human will receive from natural sources is approximately 1-4 mg [9,10].

Table 1: Boron Content of Some Foods/Food Groups and Beverages ($\mu\text{g}/100\text{g}$). Rainey, et al.1999 [11].

Nutrients (Foods)	Boron Content ($\mu\text{g}/100\text{g}$)
Avacado	1212
Oil Seeds	1214
Milk	18
Raw Apple	360
Raw Banana	135
Potatoes, unfried	62
Potatoes, fried	147
Peach and Nectarine	352
Dried legumes	400
Grapes	490
Broccoli	250
Tomato	63
Carrot	230
Onions	190
Rice	32
White Bread	46
Drinks	
Coffee	34
Wine	566
Tea	9
Soda	6

Boron has been determined that boron plays a role in regulating body minerals such as calcium and vitamin D and protects the bone structure by preventing calcium and magnesium's decrease. It also contributes to the improvement of learning, talent and school skills of minors; It is known that boron is taken in tablet form to develop sports performance and athletic structure [12]. No matter how it enters the body, 90-95% of it is immediately excreted with urea without accumulating in the body. In other words, it is not kept in the body. It only accumulates somewhat in bones, nails, hair, and organs such as the liver and spleen. Approximately 1-10 mg of boron intake per day will be appropriate and safe. In some literature, it is emphasized that 3 mg boron's daily information will be sufficient. Boron tablets in the market have been prepared in 3 or 6 mg doses. The most common forms of boron uptake into metabolism are sodium borate, boron citrate, boron aspartate and boron glycinate.

Boron oxide and boric acid are also the most common boron compounds, especially boric acid, which evaporates from the oceans and mixes into the air, descends into the soil with rain and snow, and disperses groundwater. Studies to determine the carcinogenic effect of boron on animals have shown that boric acid and borax are not genotoxic [13]. It has been proven that contact with boron compounds does not cause cancer, does not change genes, and does not cause chromosomal irregularity even at high concentrations. It is known that boron and boron compounds have antioxidant effects. Boron element increases the amount of reduced glutathione in the body's cells, thus reducing oxidative stress. Again, in some sources, it is stated that it increases glutathione and reduces the oxidative damage that may occur in the body [14].

It is a pathological condition that occurs due to a disorder in the mechanisms regulating cell growth and division (cell cycle). Malignant tumours show metastasis feature by spreading to tissues after originating. Some abnormalities in the DNA

sequence cause all cancers. 10-15% of cancers are inherited, that is, inherited by genes from the parents, and the remaining 85-90% is shaped by exposure to mutagens in living cells, slight progressive changes in cell DNA, and errors in replication is considered. Sometimes one of these mutations causes the cell in which it is located to grow and the formation of a cancer clone derived from this cell.

Cancer is multifactorial, and many factors, from bacteria to viruses, radiation to inheritance, environmental factors, dietary habits and chemicals, are blamed in cancer formation. Today, boron is used quite frequently in the health field. Boron and its compounds are used in medicines and ointments used in many treatment areas such as wound therapy, burn treatment, rheumatoid treatment, solutions we use for lens cleaning, eye drops, etc. [15]. Boron neutron capture therapy (BNCT) is a newly emerging method of practically improving healing for those who are difficult to treat. BNCT boron agents to give recipients an alphanule for growth-7 and after continued exposure with them. It has an alpha-related range, that more than normal tissues affect short school tissues. up to and including BNCT, glioblastoma multiforme, meningiomas, head and neck cancers, target cancer cancers, hepatocellular carcinoma, hepatocellular carcinoma, sarcomas, cutaneous malignancies, extramammary Pages report, recurrent cancers, pediatric cancers and metastatic disease. We aim to provide a review of the BNCT non-delivery, along with an up-to-date and review of his overall general examination of this disease episode, We aim to provide a review of the BNCT non-delivery, along with an up-to-date and review of his overall general examination of this disease episode, Malouff, et al. [16] there has been significant interest in targeted therapies, with the goal of selectively treating tumor cells while sparing normal tissues. Boron neutron capture therapy (BNCT) is an emerging treatment modality aimed at improving the therapeutic ratio for traditionally difficult to treat tumors. BNCT was first proposed by Gordon Locher in 1936 [17], who suggested that, if boron were able to be concentrated in the tumor and then exposed to thermal neutrons, the tumor would selectively receive a higher dose compared to normal tissues [18].

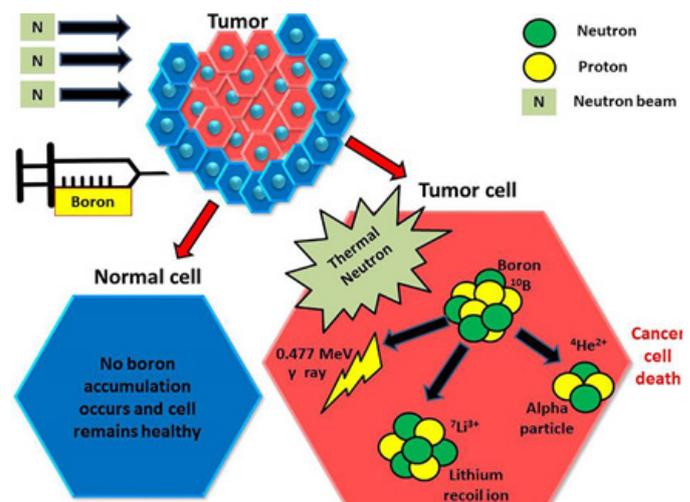


Figure 1: Injected boron compounds are preferentially found in tumor cells, which are then irradiated with thermal neutrons. The boron then undergoes a reaction, giving an alpha particle and an inert lithium ion. The alpha particle then damages the tumor cell with a finite range.

The general requirements for successful boron delivery agents includes high tumor uptake, low normal tissue uptake, rapid clearance from tissue after treatment, and low toxicity [16,19]. Boron delivery has been achieved typically with two

agents: sodium borocaptate (BSH) and boronophenylalanine (BPA), with the latter complexed with fructose to form the more soluble BPA-[16,20]. BNCT evolved through 60 years of research and clinical progress, but faced n-number of problems including lack of controlled, prospective trials, need of nuclear research reactors for clinical irradiation and disappointment regarding the evolution of ideal boron compounds. The re-emergence of BNCT took place in the 1990s in USA at Brookhaven [21] and Cambridge, MA [22], then in Europe at Petten [20], in Finland [23], Sweden[24], the Czech Republic [25] and Japan [26, 27], and finally in Argentina [28] and Taiwan [29].

Materials and Methods

In the experiments, half of the boron taken orally appeared in the urine after 24 hours and the other half within four days. Even after 23 days, large amounts of boron compounds were found in the urine. The body's boron level can be measured by performing a blood or urine test. Today, there are many methods used for the Determination of boron; atomic absorption spectrometry (AAS), Inductively coupled plasma-atomic emission spectrometry (ICP-AES), Inductively coupled plasma-mass spectrometry (ICP-MS) are some of them. Briefly, boron has been determined in various samples by volumetric, spectroscopic, chromatographic, nuclear reaction-based analytical methods and electroanalytical methods [3].

Discussion

Boron is an essential element for living things and was used for medical treatment thousands of years ago [30]. The boron neutron capture therapy (BNCT) method, which has come to the fore, especially recently, has been a ray of hope for cancer treatment. This method, which has been tried in many cancer treatments, has been a treatment mainly used in the treatment of brain cancer and is known as a method in which the damage of healthy cells is at the lowest level in addition to the destruction of cancerous cells [31,32].

It has also been observed that boric acid prevents cancerous prostate cells growth and the proliferation of cancerous cells. It has also been observed that boron taken into the body with diet is inversely proportional to lung and cervical cancers [33].

In some experiments in animals and humans, boron has been shown to positively affect the central nervous system and be a bioactive element associated with a reduced risk for some types of cancer [34].

In cases where the antioxidant capacity is insufficient to respond to this situation with the increase of free radical production, the resulting stress causes direct damage to proteins, DNA and lipids in the cell. Oxidative stress is a state of instability between the production of free radicals in tissues and organs and the body's ability to counteract its harmful effects through neutralization by antioxidants [35]. It is an imbalance between oxidants (reactive oxygen and nitrogen species) and antioxidants that tend towards the oxidative state [36] and the increase of free reactive oxygen radicals, which are called SOR when hemostatic processes fail, are caused by the disruption of oxidative balance due to antioxidant insufficiency. It is the type of damage that causes molecules to be damaged or cells to die [37]. Free reactive oxygen radicals are produced excessively to maintain standard tissue integration and functions. These overproduced free oxygen radicals are endogenous glutathione (GSH), glutathione peroxidase (GPO), glutathione reductase (GRx), glutathione-s transferase (GST), superoxide dismutase (SOD), catalase (CAT)

and other antioxidants (A, C, E) vitamins) are detoxified by defence systems. In the physiological conditions of the body, the oxidant-antioxidant balance is in favour of the antioxidants. Still, if the antioxidants cannot detoxify the oxidants, this balance is disrupted and shifts in favour of the oxidant. When the balance is disturbed, tissues undergo oxidative stress, become damaged and cause many disease conditions [35]. These diseases are many diseases such as DNA, carbohydrates, proteins, neurodegenerative diseases, cardiovascular diseases, chronic obstructive pulmonary disease, namely COPD and cancer [37].

In treating brain tumours with neutron capture, 20 g of borax is given to patients. In terms of its chronic effect on humans, it has been determined that 3 g boric acid or 5 g borax per day has no effect, and 5-10 g borax only increases protein metabolism and the amount of nitrogen in the urine. When the dose of 4-5 g per day was repeated, anorexia and disease were observed, but there was no incapacity to work [38].

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Cancer Treatment BNCT method: In this type of cancer treatment, neutron bombardment is performed by administering p-boronophenylalanine, the drug form of boron, to the tumour tissue.



He andLi stay in the body for a concise time while emitting energy over a wide area. With total kinetic energy of 2.3-2.8 MeV, these emitted particles scatter in a radius of 10 µm, which is about cell size. Thus, only cancerous cells are destroyed, and other healthy cells are not damaged [39].

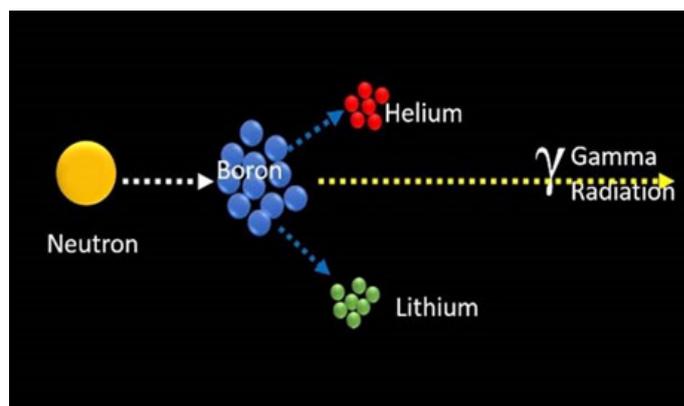
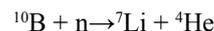


Figure 2: Nuclear reaction.



BNCT utilizes boronated agents to preferentially deliver boron-10 to tumors, which, after undergoing irradiation with neutrons, yields lithium-7 and an alpha particle. The alpha particle has a short range, therefore preferentially affecting tumor tissues while sparing more distal normal tissues. To date, BNCT has been studied clinically in a variety of disease sites, including glioblastoma multiforme, meningioma, head and neck cancers, lung cancers, breast cancers, hepatocellular carcinoma, sarcomas, cutaneous malignancies, extramammary Paget's disease, recurrent cancers, pediatric cancers, and metastatic disease. We aim to provide an up-to-date and comprehensive

review of the studies of each of these disease sites, as well as a review on the challenges facing adoption of BNCT [16].

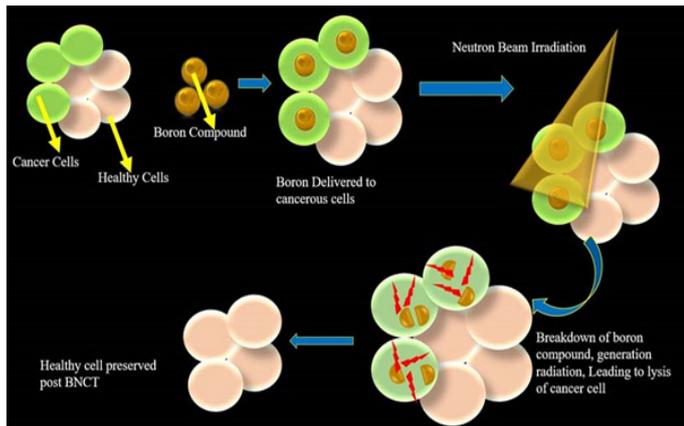


Figure 3: BNCT eliminates tumour cells.

These particles provide high energy along their very brief pathway (<10 μ m), Hence, their energy deposition is limited to the diameter of a single cell. Thus, only neoplastic cells with ¹⁰B are ravaged following thermal neutron irradiation. Hypothetically, any normal cells abutting the cancer cells are saved from high LET irradiation by ⁴He and ⁷Li particles [Table/Figure 3],[17].

It has been observed that environmental factors are influential in prostate cancer rather than genetic factors. Nutrition is one of the most critical environmental factors. Low dose boron intake with diet reduces the risk of prostate cancer. High doses of boron intake have the opposite effect.

In the research on “Effects of Boron Minerals on Human Health” conducted by Ankara University Faculty of Medicine, when the findings obtained from people living on or near mineral deposits and people who are still working in boron factories and quarries or retired from these workplaces are examined, boron has It is concluded that there is no effect. Within the scope of the research project titled “Effects of Boron and Its Compounds on Human Health and the Environment”, it was investigated whether the primary and secondary sexual power and reproductive abilities of people exposed to boron are affected children’s health during and after pregnancy. As a result of the research, it was observed that 10-12 ppm boron intake per day did not affect primary and secondary sexual performance. It has been determined that exposure to boron and boron compounds does not pose any danger for the inhabitants of boron regions and employees of boron production [2].

BNCT is emerging as a hopeful tool in treating cancer, by selectively concentrating Boron compounds in tumour cells and then subjecting the tumour cells to epithermal neutron beam radiation which selectively destroys the tumour cells. As a result of the studies carried out, it is seen that boron is an essential mineral. However, like any substance that has a toxic effect, excess boron, of course, has a poisonous effect. In the near future, BNCT will provide the opportunity to use it with safer and advanced technology in the field of oncology treatment.

More clinical studies are needed for this.

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