

Review Article

Using Boron Supplementation in Cancer Prevention and Treatment: A Review Article

Somayeh Nikkhah^{1,*}, Mohammad Reza Naghii²

ABSTRACT

Cancer is a multistage and multifactorial process in which genetic and environmental factors contribute to it. The results of the studies indicate the effective role of micronutrients, vitamins, and minerals in the treatment of malignancies. One of these elements, endorsed by the American Food and Drug Administration, is boron supplements. The present study reviews the role of boron supplementation in the prevention and treatment of cancer. At ISI, Pub Med, Science Direct, Google Scholar, Scopus, Iranmedex and Magiran databases, we examined 41 studies conducted in the years 1988-2018 regarding the effect of boron supplementation on cancer. 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.

Keywords: Boron Supplement, Cancer, Treatment, Prevention

Cancer incidence continues to be a major health problem possibly because cancer is a complex system comprising many agents (1), so that various genetic factors such as fat-rich diets free from fruits and vegetables and the wrong life style can contribute to the development of various types of

Author Information

1. *Department of Midwifery, Faculty of Nursing and Midwifery, Kerman Branch, Islamic Azad University, Kerman, Iran.*
2. *Department of Nutrition, Health School, Baqiyatallah (a.s.) University of Medical Sciences, Tehran, Iran.*

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cancer (2). Cancer is the third most common cause of death in Iran (3). Gastrointestinal cancers are the most frequent cancer among Iranian males and second to breast cancer among females (3, 4). Significant progress has been made in detection and early treatment of cancer recently which has improved its prediction. But long-term treatments for cancer, in addition to physical complications, affect the quality of life of these patients (5, 6). There is considerable evidence to support dietary recommendations for prevention of cancer as well as for patients undergoing or recovering from cancer treatment (7). The results of some studies

indicate a positive effect of micronutrients, vitamins and minerals intake in the treatment of malignancies (8-10), so that nutritional supplements are widely used among patients with cancer who perceive them to be anticancer and antitoxicity agents (11), and often cancer survivors tend to start taking dietary supplements after receiving a diagnosis of cancer (12). The most commonly reported reasons for dietary supplement use were to improve health (e.g., immune system) and prevent disease (13), and manage the side effects of chemotherapy (14), also supplements could support the body to overcome the treatment-

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related- toxicities - and the relative oxidative stress in cancer patients (15).

One of these proposed micronutrients is boron. The evidence indicates that boron is a useful and possibly essential element for humans (16, 17). Boron is a metalloid element with atomic number 5(18), and in nature is not freely available in elemental form and is found as compounds. Boric acid (19) and calcium fructoborate are two boron-containing compound that compared with other boron compounds have allocated most of the studies performed (20). People constantly intake boron from drinking water and food (21). The daily intake of boron is about 1-3 mg per day for

most adults (18), and maximum level of boron intake recommended for all adults is 20 mg/day (22). The daily intake of boron depends on type of food stuffs, and the amount boron of water. Nuts and vegetables have higher concentration of boron than fruits and legume (18). About 85 percent of the consumed boron is absorbed (23). Since the regulation of plasma levels of boron is through the renal excretion, the effect of boron toxicity in animals and humans is rare (24, 25). Boron-rich diets significantly reduce the risk of developing a variety of cancers including prostate, breast, cervix, lung, liver, melanoma, bone marrow cancer, ovarian, pancreas and lymphoma (26). The mechanisms by which boron may influence cancer

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is still unknown, but evidence suggests that boron acts through anti-oxidant and anti-inflammatory properties (9, 27, 28), inhibition of serine protease enzymatic activity, dehydration, mRNA processing, cell division and induction of apoptosis. Boron-based compounds indicate promising effects for chemotherapy types of cancer (26).

Considering the increasing prevalence of cancer in Iran and the non-invasive nature of complementary and boron medicine, we consider here implications from human, animal and in vitro studies of the effects of boron on cancer.

Materials and Methods

In order to investigate the related studies on the effects of boron on cancer, keywords **cancer** and **Boron supplementation** was searched in the databases including ISI, Pub Med, Science Direct, Google Scholar, Scopus, Iranmedex and Magiran from 1998 to 2017. Out of 148 articles by high search strategy, 41 studies were investigated in this study. Out of 41 articles obtained based on the keywords used, 28 interventional articles and 13 descriptive articles are included in this study, which

we deal with some.

Results

Boron compounds in cancer prevention

A diet with low boron has been found to lead to a number of general health problems and to increase cancer risk (26). Both animal and human data indicate that an intake of less than 1.0 mg/day inhibits the health benefits of boron. Dietary surveys indicate such an intake is not rare (29). The most common symptoms of boron deficiency include arthritis, memory loss, osteoporosis, degenerative and soft cartilage diseases, hormonal disequilibria and a drop in libido (30).

Boron and breast cancer prevention

Today, breast cancer is the most common cancer type diagnosed in women (31). Breast cancer patients appear to have relative sex steroid hormone imbalance, in favour of estrogens (32). High bio-available testosterone counteracts the proliferative effects of estrogens on the mammary tissues and exerts a protective role to the breast, inhibiting cancer development and/or tumour

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growth (33). Naghii et al. reported that after one week, supplementation of healthy males with 10 mg boron/day resulted in a significant rise in the plasma free testosterone concentration (34). Calcitriol is a coordinate regulator of proliferation, differentiation and survival of breast cancer cell (35). Calcium Fructoborate increases the level of calcitriol in the blood, thus increases the level of protection against breast cancer (36).

Boron and prostate cancer prevention

A diet containing boric acid prevents the growth and transcription of prostate tumors (18), so that the increase in boron in the environment and diet is negatively correlated with hyperplasia and prostate cancer (26, 37). Prostate enlargement is an important risk factor for prostate cancer. Muezzinoğlu et al. in Turkey have measured the level of prostate specific antigen (PSA) and used sonography to measure men's prostate volume. These people lived in two villages with different levels of boron in water resources. Men living in a village with high boron had significantly smaller

prostate glands than men who lived in the village with low boron. However, there was no significant difference between the two groups in terms of PSA (37).

Boron and cervical cancer prevention

Korkmaz et al. reported that using high levels of boron in drinking water reduces the pathological risk of cervical cancer by conducting research in rich and deprived areas of boron in Turkey. The function of boron in preventing cervical cancer is not clear, but it seems that boron acts by inhibiting the HPV receptors involved in cervical cancer (38).

Boron and lung cancer prevention

In a study by Mahabir et al., they measured boron levels in women with lung cancer compared to healthy people over the past 10 years, and found that for women with lung cancer, low consumption of boron has a reverse relationship with the chance of lung cancer (39).

Boron and liver cancer prevention

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After induction of Hepatocellular carcinoma (HCC) in rats, Zafar and Ali observed that boron consumption (4 mg / kg body weight) orally for 122 days significantly reduced proliferating cell nuclear antigen (PCNA) and ameliorated oxidative stress in mice exposed to cancer (40).

Boron-mediated chemoprevention of cancer

Cancer chemoprevention uses natural, synthetic or biological chemical agents to reverse, suppress or prevent carcinogenic progression (41). Compounds of boron, which have an anticancer effect, include boric acid, borate, borate esters, boranes, borinic esters (26). Boric acid is one of the most studied boron-containing chemicals. Boric acid has been demonstrated to control the proliferation of some

Table: Clinical practice studies on boron and cancer

Authors	Year	Type of study design	Number of samples	Findings
Müezzinoğlu et al.	2011	Prostate sonography, measuring PSA level	159 intervention groups: 159 people with high levels of boron(>1 mg /L) and 63 people with low-boron sources(<1mg/L) Control group: 234 men without boron	There was a significant difference in prostate size between the two groups There was no significant difference between the intervention and control groups at PSA level
Korkmaz et al.	2007	Pap smear	Intervention group: 472 women in the boron-rich region Control group: 87 women in the deprived area	Significant differences in cytological changes in cervix between the two groups
Mahabir et al.	2008	Measuring the level of boron	Intervention group: 763 women with lung cancer Control group: 38 healthy women	There was a significant difference between the two groups for boron consumption
Zafar and Ali	2013	Measuring the level of PCNA	Intervention group: 68 mice suffered from HCC receiving 221 days of boron Control group: 80 mice suffered from HCC receiving 122 days of placebo	Boron reduced PCNA and ameliorated oxidative stress in rats exposed to cancer

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cancer cell types (19). Calcium fructoborate is a natural product that is extracted from plants, but it can also be produced by chemical synthesis (26). Calcium fructoborate is efficient in the prevention and treatment of cancer (25). Bortezomib is a borate ester that slows the

growth of breast cancer cells and induces apoptosis in bone marrow, prostate, lung, ovary, pancreas, lymphoma and head and neck squamous cell carcinoma (SCC) (30).

Conclusion

Most of the in vitro and animal studies confirm the positive effects of supplementary boron on the prevention and treatment of cancer. Studies show that diets with low boron are common. And increasing in the consumption of boron by diets rich in fruits, vegetables, crops and legumes should be recognized as a rational diet recommendation to prevent and treat cancer, promote health and well-being. Physicians should be encouraged to more routinely discuss supplements use with their cancer patients and increase of clinical research on boron and cancer prevention seems necessary.