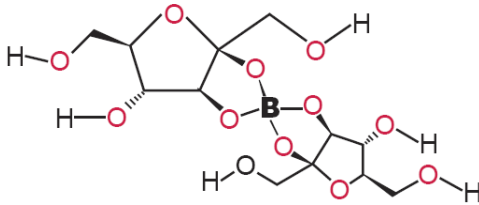


Fructo Borate Complex

Monograph



Epidemiologic Relationship Between Osteoporosis, Arthritis and Low Boron Exposure

Twenty-five million plus Americans have osteoporosis and another thirty-four million people have bone density low enough to be at risk of fractures. In America 1 out of every 2 individuals over the age of 70 will suffer a bone fracture as a result of osteoporosis with 1 in 5 diagnoses being in men (this is not only a “woman’s disease”). Women over 50 are more likely to get osteoporosis than breast cancer, heart disease, and ovarian cancer combined. Over a million people every year will have a hip or spinal fracture. In the case of hip fractures, one-third of those patients die of complications within one year, and another third never return to independent living. Over an average lifetime a woman loses 30% to 40% of her total bone mass, and a man about 20% to 30%. By age 80, many women have lost two-thirds of their skeleton. Men lose about 25% of their total bone.

In areas of the world where **boron dietary intakes** usually were 1mg or less/day, the estimated incidence of arthritis ranged from 20% to 70%. On the other hand, in areas of the world where boron dietary intakes were usually 3mg to 10 mg, the estimated incidence of arthritis ranged from 0% to 10%.

A Preventable and Reversible Disease- It’s not too early or too late to begin protecting your bones

The good news is that osteoporosis and arthritis are preventable diseases, and like in most of our Complex Diseases, life style plays a major role in prevention and/or correction. People need to understand that they are at risk without any outward

signs and they need to get truly motivated to make changes before symptoms appear. Diet, nutritional supplements and exercise can stop, prevent and even reverse bone loss.

Bone Remodeling- A Brief Physiology Reminder

Over the course of our life, we go through four phases of bone development. In the first phase bone is being built, peaking in our mid to late 20s. In the second phase there is a short plateau of bone maintenance. The third phase occurs at age of 35 where resorption overtakes formation. The fourth phase also deals with bone loss, but with the additional complication of formation and deposition slowing down. The key to preventing Osteoporosis is to build as much healthy bone mass as possible during the bone growth phases of our life, and then to minimize bone loss during the resorption phase of life. The primary modulators of the remodeling process are parathyroid hormone and vitamin D, some important secondary regulators of calcium homeostasis are estrogens, DHEA and testosterone. All of these hormones and processes are modulated by boron.

Fructo Borate: A New Form of Boron Supplementation

A new natural "food-form" of boron duplicates dietary boron, potentiating bone health. Boron occurs naturally in fruit, vegetables and nuts that humans have been consuming for many millennia. Consequently, human beings have adapted to obtaining the required amount of boron from natural food forms. Food-form boron is always chelated to carbohydrates such as fructose, mannitol and sorbitol. **Fructo Borate** is identical to these natural forms of boron. **Fructo Borate** is a rather "strong" complex of fructose with boron with an association constant of about 6000. Boron carbohydrate complexes are the only boron complexes detected so far in natural food sources.

Science Meets Nature

Fructo Borate is a synthesized copy of the naturally occurring compound. This patent describes the preparation of B-complexes with D-Fructose, D-Mannitol and D-Sorbitol, among other naturally occurring sugars. The composition of matter and B-

complexes structures are identical to naturally occurring Boron complexes in fruit. The patent is protected world-wide (US Patent #5,962,049 issued 10/5/99).

A Natural Advantage in Using Fructo Borate

Until now a natural complexed form of boron has not been available for supplementation. Currently marketed boron supplements such as boron glycinate, boron aspartate are chemically speaking, at worst, simple physical mixtures of boric acid (borax) and citric acid/citrate, glycine/glycinates or aspartic acid/aspartates respectively, or at best, these substances are rather “weak” boron complexes since these ligands in regard to boron have very low association constants. Weak complexes of boron tend to be more toxic. Additionally, boric acid is a strong electrophile and therefore binds in a non-selective way to many biomolecules that can bind boron. Consequently, boron is distributed non-selectively among too many diverse biomolecules; thus, boron with a low association constant is less biologically beneficial.

Conversely, boron complexes with high association constants (boron carbohydrate complexes) are highly selective and their boron content can only be transferred to biomolecules that have an even higher affinity for boron (such as specific receptor sites on cell surfaces). Thus superior safety and more beneficial biological activity compared to other marketed boron nutritional supplements.

On the Cusp of a Major Scientific Discovery

It has been observed in current scientific research that the **Fructo Borate** molecule is absorbed intact across the GI tract barrier into the systemic circulation. Researchers are now excitedly seeking for the actual cell membrane receptor site that receives this entire Fructo borate molecule. This makes sense considering food derived boron comes only in this bound carbohydrate package and our bodies systemically receive it in this form.

Studies Using Fructo Borate

First Study: “Osteoarthritis and Calcium Fructo Borate Supplementation: An Open-Label Pilot Study”. This study was authored by Natasa D. Miljukovic, MD, Dusan A.

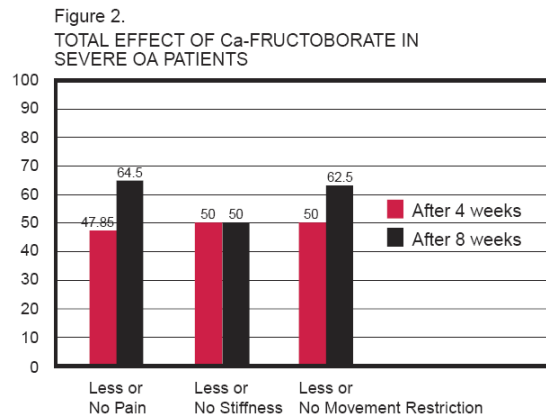
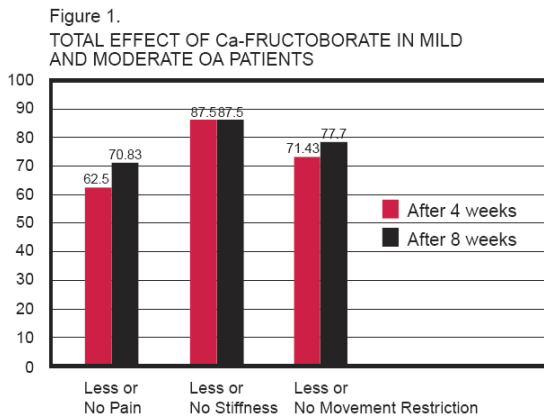
Miljkovic, PhD and Goran M. Ercegan, MD, PhD. It was conducted in the Department of Orthopedic Medicine, University of Novi Sad, Novi Sad, Yugoslavia. Jan. 15, 2002.

Purpose: The purpose of the study was to investigate the effects of Fructo Borate on OA symptoms. 20 participants with clinical and radiographic signs of OA were

included in this study. Patients were divided into two groups based on the severity of their condition. One group was given a single dose of 6mg of Fructo Borate daily. The second group was given a single daily dose of 12mg. Patients were assessed at the beginning of the study, again after 4 weeks, and finally after 8 weeks. Two criteria for assessment were used: WOMAC index and Newnham criteria.

Results: Major pain-management or comfort improvements in most patients were observed within 5 days to two weeks. Total effect of Fructo Borate in mild and moderate OA patients were (1) less or no pain after 4 weeks- 62.5% and after 8 weeks- 70.83%; (2) less or no stiffness after 4 weeks- 87.5% and after 8 weeks- 87.5%; (3) less or no movement restriction after 4 weeks- 71.43% and after 8 weeks- 77.7%. Total effect of Fructo Borate in severe OA patients were (1) less or no pain after 4 weeks- 47.85% and after 8 weeks- 64.5%; (2) less or no stiffness after 4 weeks- 50% and after 8 weeks- 50%, (3) less or no movement restriction after 4 weeks- 50% and after 8 weeks- 62.5%.

Conclusion: Fructo Borate is particularly effective in reducing pain and improving physical function of range-of-joint movement. It is becoming clear that boron's beneficial effect on OA is partially due to an indirect antioxidant activity in addition to its anti-inflammatory activity. Boron diminishes the level of oxidative bursts of neutrophils. Unfortunately, in the arthritic condition, neutrophils are attracted to the site of the damaged joint and excessively secrete their load of powerful oxidants (hydrogen peroxide, hydroperoxy radical-HO₂, hydroxyl radical HO and hypochlorous acid). Boron down regulates this process. Additionally boron increase SOD levels and enhances the glutathione level that is responsible for neutralizing at least part of the created ROS. Finally, boron may beneficially act in OA by stimulation of collagen biosynthesis and its secretion into the extra cellular matrix of cartilage.



Study Two: "Vitamin D/Steroid Hormone Homeostasis and Calcium Fructo Borate Supplementation" by Natasha Miljkovic, MD. Department of Orthopedic Medicine, University of Nov Sad, Yugoslavia. March 03, 2002 .

Purpose: The primary purpose of this study was to investigate the inter-relationship between boron supplementation with Fructo Borate and the level of serum 25-(OH)- Vitamin D-3 in 25 (OH) Vitamin deficient subjects. The additional purpose of the study was to investigate the potential inter-relationship between boron intake and other steroid hormone levels such as testosterone, estrogen and DHEA.

Method: 13 participants took one capsule, 6 mg Fructo Borate daily in the morning for 60 consecutive days and blood samples were taken on Day 1 and then again on Day 60.

Results: Average increase after 60 days of supplementation: 25-(OH)- Vitamin- D-3 (relatively more abundant intermediate of the active 1,25-dihydroxy- Vitamin D-3) +19.6%, DHEA-S +56%, Free Testosterone +29.5%, Estradiol levels varied greatly and no trend was established. The group of females was quite heterogeneous, and a study needs to be done on a more homogenous group, preferably of post-menopausal women.

Conclusion: A relationship exists between supplementation with Fructo Borate and levels of hormone homeostasis. It is believed that optimum boron supplementation regulates catabolic enzymatic hydroxylation. The significance of boron's ability to regulate hormone catabolism is far reaching particularly in the areas of calcium and

phosphate absorption, heart disease and cancer prevention and natural hormone support.

Fructo Borate- The Master Mineral

A substantial number of metabolic processes in humans and animals are beneficially affected by physiologic amounts of **dietary boron**. Boron modulates Vitamin D systems, and because of the established role of Vitamin D in maintaining calcium homeostasis, steroid hormone homeostasis and in maintaining normal physiological bone density, it is instrumental in bone health. In fact there is study evidence that boron, even in the relative absence of Vitamin D can elevate mineral concentrations in bone. Because menopausal and post-menopausal women are populations generally at risk to incur lowered levels of steroid hormone, plasma Vitamin D and

bone minerals, it logically follows that **Fructo Borate Complex** would be of great help. **Fructo Borate**, having been demonstrated as being more bioavailable, effective and safe than other forms of boron, should be used as an adjunct to, and potentiator for, calcium supplementation in the prevention and/or reversal of bone resorption in medium- to high-risk osteopenic subjects.

Additionally, chronic inflammation is a major complication in today's Complex Disease patterns. There is emerging evidence that dietary boron influences immune function. Specifically, there is evidence that dietary boron helps control the normal inflammatory process and may do so by serving as a signal suppressor that down-regulates specific enzymatic activities typically elevated during inflammation at the inflammation site. Suppression, but not elimination, of these enzyme activities by boron is hypothesized to reduce the incidence and severity of inflammatory disease. Vigorous attempts are underway to examine the effects of dietary boron on the serine proteases which are a sub-class of hydrolases and are major proteolytic enzymes released by activated leukocytes. Boron compounds inhibits the activity of many serine proteases. PSA is a serine protease and a well-established marker of prostate cancer. In a study by Zhang et al, men who ingested the greatest amount of boron were 64% less likely to develop prostate cancer. In a study by Gallardo-

Williams et al, boron supplementation decreased PSA levels by 87% and reduced tumor size in the prostate cancer mouse model.

Prevent and Even Reverse the Accelerating Rise of Today's Complex Diseases

Due to dietary habits, Americans like most other developed countries have an epidemic of low dietary boron consumption, the average intake being 1mg or less a day, while minimally we need at least 3mgs to support our bodies. Boron is found in fruits, vegetables, nuts and seeds. The *5 A Day For Better Health* government/industry campaign intends to help people eat 5 servings of fruits and vegetables a day. The National Cancer Institute found that 42% eat less than 2 servings a day. For the first time we can now offer a natural organic form of boron equivalent to food-derived boron. One vegetarian capsule of **Fructo Borate Complex** provides 6mg of elemental boron which is 100% more than the minimum dietary requirement.

Fructo Borate Complex is 100% Pure

BioImmersion Inc. manufactures and encapsulates **Fructo Borate Complex** without any added excipients: fillers, binders and flowing agents (such as magnesium stearate). Each vegetarian capsule is only filled with 240mg of Fructo Borate and 260mg of calcium ascorbate.

BioImmersion Inc. technologically advanced Therapeutic Foods range of products responds to the reality of today's negligible dietary patterns and answers the required nutritional needs to achieve and preserve good health. Our products are extensively and properly analyzed and documented to ensure consistent delivery of the highest levels of active ingredients. **Fructo Borate Complex** is therefore a better, safer and more effective therapeutic dietary supplement.

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