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HERBS & SUPPLEMENTS

Boron

ABSTRACT. Objective: To evaluate the scientific evidence on boron including expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing. This review serves as a clinical support tool. Methods: Electronic searches were conducted in nine databases, 20 additional journals (not indexed in common databases), and bibliographies from 50 selected secondary references. No restrictions were placed on language or quality of publications. All literature collected pertained to efficacy in humans, dosing, precautions, adverse effects, use in pregnancy/lactation, interactions, alteration of laboratory assays, and mechanisms of action. Standardized inclusion/exclusion criteria are utilized for selection. Grades were assigned using an evidence-based grading rationale. Results: There was a lack of systematic study on the safety and effectiveness of boron in humans. However, based on popular use and supportive scientific data, nine indications are discussed in this review: hormone regulation, improving cognitive function, osteoarthritis, osteoporosis, vaginitis (topical), bodybuilding aid (increasing testosterone), menopausal symptoms, prevention of blood clotting (coagulation effects), and psoriasis (topical). Conclusion: Although studies assessing the use of boron for osteoarthritis and osteoporosis are in preliminary stages, reports are promising. There is conflicting evidence to support the use of boron in hormonal regulation and cognitive function. Future randomized controlled trials are warranted. There is fair negative evidence regarding the use of boron

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as an anticoagulant, a bodybuilding aid, for menopausal symptoms, or for psoriasis. Excessive use may be harmful, and caution is advised.

KEYWORDS. trace element, micronutrient, boric acid, borax, systematic review, interactions, pharmacology, antiseptic, preservative

SYNONYMS/COMMON NAMES/RELATED SUBSTANCES

- 1-Amino-3-[(dihydoxyboryl)methyl]-cyclobutanecarboxylic acid, 2-aminoethoxydiphenyl borate (2-APB), 3-[3-(7-NH(3)(+)-nido-*m*-carboran-1-yl)propan-1-yl] thymidine, 3-carboranyl thymidine analogs (3CTA), 3-carboranlyalkyl thymidine analogs, 3-[(closo-*o*-carboranyl)methyl] thymidine, 4-META/MMA-TBBO, 10B (pure isotope), 12-dicarba-closo-dodecaboranel-carboxylate (BCH), 11B (pure isotope), alanin-boric compound acid, amine-boranes, amorphous boron (impure boron), AN-2690, Arc Dia TPX®, atomic number 5, B, BCH (12–dicarba-closo-dodecaboranel-carboxylate), BF_2 (borondifluoride), BF_3, bis-phenylboronate, bor, boracic acid [$B(OH)_3$], boracite, boracium, boranophosphate, borate transporter, borates, borax [$Na_2B_4O_5(OH)_4 \cdot 8H_2O$], Borax®, bore, boric acid [$B(OH)_3$], boric anhydride, boron 10 (pure isotope), boron 11 (pure isotope), boron aspartate, boron citrate, boron enriched cathode, boron fluoride, boron glycinate, boron hydroxide [$B(OH)_3$], boron neutron capture therapy (BNCT), boron nitride, boron oxide [B_2O_3], boron sesquioxide, boron tribromide, boronic acid, boronated aminocyclobutanecarboxylic acid, borondifluoride [BF_2], boronophenylalanine (BPA), burah [$Na_2B_4O_5(OH)_4 \cdot 8H_2O$], buraq [$Na_2B_4O_5(OH)4 \cdot 8H_2O$], C&B Metabond®, carborane (a carbon–boron compound), closododecarborate, colemanite, crystalline boron (99% pure boron), decaborane, dicarba-closo-dodecaborane, dipyrrylmethene-BF_2, furan boron ethers, kernite [$Na_2B_4O_5(OH)_4 \cdot 2H_2O$], magnesium perborate, metaboric acid, methyl methacrylate tri-*n*-butylborane (MMA-TBB), mono-phenylboronate, NH(2)-closo-*m*-carborane, NH(3)(+)-nido-*m*-carborane-substituted thymidine analogues, orthoboric acid, ortho-carborane derivative, polyhedral boron hydrides, rasorite [$Na_2B_4O_5(OH)_4 \cdot 2H_2O$], sal sedativum [$B(OH)_3$], sassolite, sodium biborate, sodium borate, sodium borocaptate, sodium metaborate, sodium perborate, sodium pyroborate, sodium tetraborate

$[Na_2B_4O_5(OH)_4 \cdot 8H_2O]$, tri-*n*-butylborane (TBB), tri-*n*-butylborane partially oxide (TBBO), tetracarboranylketone 4, thermal water, tincal $[Na_2B_4O_5(OH)_4 \cdot 8H_2O]$, tribromide, tributylborane (TBB), trifluoride-methanol $[BF_3\text{–}MeOH]$, tri-*n*-butylborane partially oxide (TBBO), ulexite $[CaB_4O_7 \cdot NaBO_2 \cdot 8H_2O]$, zwitterionic 3-carboranyl thymidine analogues.

- *Combination product example:* Vitrum® osteomag (contains 600 mg calcium (1,500 mg calcium carbonate), 200 IU of cholecalcepherol, 40 mg of magnesium, zinc (7.5 mg), copper (1 mg), manganese (1.8 mg), and boron (250 mcg)).

CLINICAL BOTTOM LINE

Brief Background

- Boron, the fifth element in the periodic table, is a trace element that is found throughout the global environment. The inorganic compound of boron (boric acid or borax) has been used for many decades as an antiseptic and a food preservative.
- Boron is a micronutrient found in plants and is thought to be essential for animal growth and development (Park, Li, Shcheynikov, Zeng, & Muallem, 2004).
- In the 1980s, boron was discovered to play a role in regulating mineral metabolism (such as calcium and magnesium) and enhancing the vitamin D activation process in humans. Boron is required for normal bone metabolism (Miggiano & Gagliardi, 2005). These discoveries led to the hypothesis of using boron both in the prevention of osteoporosis and in the treatment of osteoarthritis. Although, studies assessing these purposes are in preliminary stages, reports are promising.
- There is conflicting evidence to support the use of boron in hormonal regulation and cognitive function. There are several ongoing studies that are examining the use of boron neutron capture technology in radiation therapy for the treatment of brain tumors (Bregadze, Sivaev, & Glazun, 2006).
- Excessive use of boron has led to fatal poisonings. Boron is easily absorbed and subsequently eliminated primarily through the kidneys; it should be used cautiously in patients with renal insufficiency.

Scientific Evidence for Common/Studied Uses

Hormonal regulation	C
Improving cognitive function	C
Osteoarthritis	C
Osteoporosis	C
Vaginitis (topical)	C
Bodybuilding aid (increasing testosterone)	D
Menopausal symptoms	D
Prevention of blood clotting (coagulation effects)	D
Psoriasis (topical)	D

Historical or Theoretical Indications which Lack Sufficient Evidence

- Analgesia (Burnham, 2005), anti-inflammatory (Burnham, 2005), antiseptic, antiviral (Burnham, 2005), bone healing (Miggiano & Gagliardi, 2005), boron deficiency, cancer (Barranco & Eckhert, 2004; Bregadze, Sivaev, & Glazun, 2006; Enfissi, Prigent, Colosetti, & Capiod, 2004; Nagasawa, Uto, Kirk, & Hori, 2006; Pan, Oie, & Lu, 2004), diabetes, diaper rash (avoid due to case reports of death in infants from absorbing boron through skin or when taken by mouth), endocrine disorders (hypersensitivity to temperature), eye cleansing, high cholesterol (Burnham, 2005), increasing lifespan, leukemia, onychomycosis (Alley, Baker, Beutner, & Plattner, 2007), pain (Hu et al., 2004), prostate cancer (Barranco & Eckhert, 2004), rheumatoid arthritis, vitamin D deficiency (Miljkovic, Miljkovic, & McCarty, 2004), and wound care (Chebassier, El Houssein, Viegas, & Dreno, 2004a; Chebassier, Ouijja, Viegas, & Dreno, 2004b).

Expert Opinion and Historic/Folkloric Precedent

- Boron has historically been viewed as a poison, but more recently has been used therapeutically in humans. Oral boron supplements have been used to treat osteoarthritis or to prevent bone loss. A topical preparation is used for vaginitis and psoriasis. Other uses of boron are under study.

Brief Safety Summary

Likely Safe: When taken by otherwise healthy individuals in trace amounts similar to amounts found in foods. A recommended daily allowance for boron is not established.
Likely Unsafe: Poisoning has occurred with the ingestion of the equivalent of 0.2 g/kg boron (Linden, Hall, Kulig, & Rumack, 1986), or with exposure to boron oxide and boric acid dust at 4.1 mg/m^3 (Garabrant, Bernstein, Peters, & Smith, 1984). Safety concerns have also been raised when boron has been taken in excessive amounts for more than 3–4 days, when it has been used in patients with renal function impairment, or when used in infants and young adults. Most toxicity is due to exposure to excessive amounts of inorganic boron. The available nutritional products are boron citrate, boron aspartate, boron glycinate chelates, or sodium borax. When taken by patients with estrogen-sensitive cancers (breast, ovarian), based on anecdotal reports of increased serum estrogen concentrations.

DOSING/TOXICOLOGY

General

Recommended doses are based on those most commonly used in available trials, or on historical practice. However, with natural products it is often not clear what the optimal doses are to balance efficacy and safety. Preparation of products may vary from manufacturer to manufacturer, and from batch to batch within one manufacturer. Because it is often not clear what are the active components of a product, standardization may not be possible, and the clinical effects of different brands may not be comparable.

Standardization

- Most of the nutritional boron products available commercially are either sodium borax or a boron-chelated agent combined with aspartate, glycinate, or citrate. Boron (as boric acid or borax) can be easily absorbed by mouth, through the skin, or by breathing. Boron may also be supplied as sodium borate.

Dosing

Adult (Age ≥ 18)

Oral.

- *General:* An acute bolus of 11.6 mg boron (given as 102.6 mg sodium tetraborate decahydrate) together with a standard fat-rich meal did not alter coagulation factor profile (Wallace et al., 2002).
- *Bodybuilding aid:* Boron of 2.5 mg daily for 7 weeks was investigated in bodybuilders but no significant effects were found (Green & Ferrando, 1994).
- *Dietary intake:* The reported average boron intake in the American diet is 1.17 mg/day for men, 0.96 mg/day for women, and 1.29–1.47 mg/day for vegetarians. High boron content foods include peanut butter, wine, grapes, beans, and peaches (Rainey et al., 1999).
- *Improvement of cognitive function:* Elemental boron of 3 mg taken by mouth daily has been studied (Penland, 1994).
- *Menopausal symptoms:* Elemental boron of 2.5–3 mg daily in post-menopausal women has been used but no changes in menopausal symptoms were observed (Beattie & Peace, 1993; Nielsen & Penland, 1999). These studies were of lesser methodological quality and more research is needed before a dosing recommendation can be made (Beattie & Peace, 1993; Nielsen & Penland, 1999).
- *Osteoarthritis:* Elemental boron of 3–6 mg (as sodium tetraborate decahydrate) taken by mouth daily for up to 8 weeks has been used (Travers & Rennie, 1990; Travers, Rennie, & Newnham, 1990).
- *Osteoporosis:* Boron of 3 mg daily for 1 year has been used to increase bone mineral density but no significant effects were observed (Biquet et al. 1996).

Topical

- *Psoriasis:* A combination formula of 1.5% boric acid with 3% zinc oxide applied to the skin as needed has been studied (Limaye & Weightman, 1997).

Intravaginal

- *Vaginitis:* Boric acid powder capsules administered vaginally daily have been studied. Safety and effectiveness are not established (Sobel & Chaim, 1997; Van Slyke, Michel, & Rein, 1981a, b).

Children (Age < 18)

- *General:* There is not enough scientific data to recommend the safe use of boron in children. Case reports exist of death in infants following use of boron (taken by mouth or placed on the skin).

Toxicology

- Although boron, as boric acid and borax, is potentially toxic to all organisms, more evolved animals usually do not accumulate boron due to their ability to rapidly excrete it. However, because boron can be easily absorbed by mouth, through skin, and inhalation, incidental exposure to excessive boron may cause potentially fatal toxic reactions. The most common reactions include skin rash, desquamation, nausea, vomiting (blue-green emesis), diarrhea (in blue-green color), abdominal pain, and headache (Chao, Maxwell, & Wong, 1991; Linden et al., 1986; Litovitz, Klein-Schwartz, Oderda, & Schmitz, 1988; Schillinger, Berstein, Goldberg, & Shalita, 1982; Tangermann, Etzel, Mortimer, Penner, & Paschal, 1992). Hypotension and metabolic acidosis have also been reported (Restuccio, Mortensen, & Kelley, 1992). Chronic exposure may cause convulsions, anemia, dehydration, as well as renal and hepatic damage (Chao et al., 1991; Gordon, Prichard, & Freedman, 1973; Ishii et al., 1993; O'Sullivan & Taylor, 1983). Exposure to boric acid or boron oxide dust can cause eye irritation, dryness of the mouth and nose, sore throat, and productive cough (Garabrant et al., 1984). Excessive amounts of boron ingestion has been shown to cause testicular toxicity, decreased sperm motility, and reduced fertility in male rats (Chapin & Ku, 1994; Fukuda et al., 2000; Lee, Sherins, & Dixon, 1978). Alopecia totalis has also been reported anecdotally with boron poisoning.
- The toxic effects of boron appear to be more severe in infants. There are fatal case reports of infants who have been exposed to boron by

either oral or topical route. Historically, a honey and borax solution was used to clean infant pacifiers, and topical boric acid powder was used to prevent diaper rash. However, these practices were associated with several infant deaths due to boron toxicity (Goldbloom & Goldbloom, 1953; Valdes-Dapena & Arey, 1962).

- *Management:* Boron can be dialyzed, which shortens its half-life. In addition to charcoal and gastric lavage, hemodialysis and peritoneal dialysis have been used to treat acute boron poisoning (Litovitz et al., 1988). *N*-Acetylcysteine is effective in increasing boron excretion and shortens its half-life in rats (Banner et al., 1986). It has been recommended that patients with acidosis, renal impairment, or ingestion (greater than 6 g in adults or greater than 200 mg/kg in children) be admitted to a hospital for management.

ADVERSE EFFECTS/PRECAUTIONS/CONTRAINDICATIONS

Allergy

- Known allergy/hypersensitivity to boron, boric acid, borax, citrate, aspartate, and glycinate.

Adverse Effects/Post–Market Surveillance

- *General:* Adverse reactions in doses below 10 mg/day are believed to be unlikely. Large doses can result in acute poisoning. There are fatal case reports of infants who have been exposed to boron by either oral or topical route. Boron toxicity may cause skin rash, nausea, vomiting (may be blue-green color), diarrhea (may be blue-green color), abdominal pain, headache, hypotension, or metabolic acidosis.
- *Dermatologic:* Dermatologic reactions such as skin erythema, desquamation, and exfoliation have been reported in the literature (Valdes-Dapena & Arey, 1962). Alopecia totalis has also been reported anecdotally with boron poisoning.
- *Endocrine:* Boron has been reported to increase serum levels of 17β-estradiol and testosterone (Nielsen, Hunt, Mullen, & Hunt, 1987). Clinical effects are not clear. Boron may be associated with reduced serum calcitonin, insulin, or phosphorus, and with increased levels of vitamin D2, calcium, copper, magnesium, or thyroxine.

- *Gastrointestinal:* Boron has been noted to cause diarrhea (Valdes-Dapena & Arey, 1962). Boron neutron capture therapy (BNCT) can cause mucositis (Kouri et al., 2004).
- *Hepatic:* Chronic exposure may cause hepatic damage (Ishii et al., 1993; O'Sullivan & Taylor, 1983).
- *Genitourinary:* Ingesting large amounts of boron has been associated with infertility in male rats (Fukuda et al., 2000). There are no reports of boron-induced human infertility in the available literature.

Neurologic/CNS: Both CNS stimulation as well as CNS depression have been reported anecdotally. Specific symptoms may include hyperexcitablitiy, irritability, tremors, seizure disorder, weakness, lethargy, headache, or depression (Gordon et al., 1973). Fever and hyperthermia have been reported anecdotally. In Japan, 16 patients with malignant glioma were treated with BNCT (Kageji et al., 2004). Of those, nine died; three due to cerebrospinal fluid dissemination, one each of tumor invasion, meningitis, pneumonia, and unknown cause, and two patients died of local recurrence or radiation necrosis. Due to the high morbidity of these patients, it is not completely known which occurrences can be attributed to BNCT versus the disease itself.
Ocular/Otic: Exposure to boric acid or boron oxide dust has been reported to cause eye irritation (Garabrant et al., 1984).
Pulmonary/Respiratory: Exposure to boric acid and boron oxide dust has been reported to cause mouth and nasal passage irritation, sore throat, and productive cough (Garabrant et al., 1984).
Renal: On the basis of a review, boron exposure may cause chronic kidney disease (Pahl, Culver, & Vaziri, 2005).

Precautions/Warnings/Contraindications

- Avoid use in infants and children due to case reports of fatalities.
- Avoid use in renal failure patients who are not on dialysis, as boron is eliminated primarily via the kidneys. For patients on dialysis, however, boron supplementation may be needed because dialysis removes boron from the bloodstream. This should be discussed with the patient's nephrologist.
- Use cautiously in patients with estrogen-sensitive cancers (breast, ovarian) based on anecdotal reports of increased serum estrogen concentrations.

Pregnancy and Lactation

- There is not enough scientific evidence to recommend the safe use of boron during pregnancy or breastfeeding. There is a trace amount of boron distributed to human milk.
- Lactating mothers of premature and full-term infants living in Canada collected milk samples to establish the profile of boron metabolism in human milk (Hunt, Friel, & Johnson, 2004). Boron concentrations were stable in full-term milk, but not in preterm milk, suggesting that boron may be under homeostatic control. There were reductions in the concentrations of copper, iron, selenium, and zinc.
- A study examined the relationship between boron exposure and some key enzymes, well known for their affinity for mineral elements, such as delta-aminolevulinic acid dehydratase (ALA-D) (Huel, Yazbeck, Burnel, Missy, & Kloppmann, 2004). Researchers examined the potential effects of an environmental boron exposure on the activity of these enzymes in an urban population of 197 "normal" newborns. Placental boron levels were negatively significantly correlated to ALA-D activity.
- The toxic effects of boron appear to be more severe in infants. There are fatal case reports of infants who have been exposed to boron by either oral or topical route. Historically, a honey and borax solution was used to clean infant pacifiers, and topical boric acid powder was used to prevent diaper rash. However, these practices were associated with several infant deaths due to boron toxicity (Goldbloom & Goldbloom, 1953; Valdes-Dapena & Arey, 1962).
- Excessive amounts of boron ingestion have been shown to cause testicular toxicity, decreased sperm motility, and reduced fertility in male rats (Chapin & Ku, 1994; Fukuda et al., 2000; Lee et al., 1978).

INTERACTIONS

Boron/Drug Interactions

- *Alzheimer's agents:* In theory, boron may interact additively with Alzheimer's agents.
- *Analgesics:* Some amine-boranes may have analgesic activities (Burnham, 2005).
- *Androgens:* Use of boron with testosterone-active drugs such as Testoderm® may result in increased testosterone effects.

- *Antacids*: Magnesium may interfere with the normal physiological effects of boron in the body (Nielsen, Gallagher, Johnson, & Nielsen, 1992; Nielsen et al., 1987). Sources of magnesium may include antacids containing magnesium oxide or magnesium sulfate (milk of magnesia, Maalox®).
- *Anti-inflammatory agents:* Some amine-boranes may have anti-inflammatory activities (Burnham, 2005).
- *Antidiabetic agents:* According to anecdotal reports, supplemental boron may decrease insulin levels in the blood.
- *Antilipemic agents:* Based on mouse and rat studies, aliphatic, heterocyclic, and nucleoside amine-boranes and many boron derivatives may decrease low-density lipoprotein (LDL) cholesterol and increase high-density lipoprotein (HDL) cholesterol levels (Burnham, 2005).
- *Antineoplastic agents:* In in vitro and in vivo murine and human tumor models, borane adducts of simple aliphatic amines, heterocyclic amines, and nucleic acids showed cytotoxic properties by inhibiting DNA synthesis (Burnham, 2005).
- *Antiviral agents:* Some amine-boranes may have antiviral activities (Burnham, 2005).
- *Arthritis agents:* Some amine-boranes may have anti-arthritic activities (Burnham, 2005).
- *Dopamine agonists:* Some amine-boranes may have dopamine receptor antagonist activity (Burnham, 2005).
- *Dopamine antagonists:* Some amine-boranes may have dopamine receptor antagonist activity (Burnham, 2005).
- *Estrogens:* In theory, use of boron with estrogen-active drugs such as birth control pills or hormone replacement therapy may result in increased estrogen effects (Nielsen et al., 1987).
- *Hepatotoxic agents*: Chronic high exposure to boron may cause hepatic damage (Ishii et al., 1993; O'Sullivan & Taylor, 1983).
- *Hormonal agents:* Nutritional boron can up-regulate 17β-estradiol levels in women, including postmenopausal women receiving hormone replacement therapy.
- *Magnesium supplements:* Magnesium may interfere with the normal physiological effects of boron in the body (Nielsen et al., 1992; Nielsen et al., 1987). Sources of magnesium may include antacids containing magnesium oxide or magnesium sulfate (milk of magnesia, Maalox®).
- *Nephrotoxic agents:* Boron exposure may cause chronic kidney disease (Pahl et al., 2005).

- *Osteoporosis agents:* On the basis of animal and preliminary human studies, boron may play a role in mineral metabolism, with effects on calcium, phosphorus, and vitamin D (Burnham, 2005; Hunt, 1994; Hunt, Herbel, & Idso, 1994; Miggiano & Gagliardi, 2005; Nielsen et al., 1987).
- *Renally eliminated drugs:* Boron exposure may cause chronic kidney disease (Pahl et al., 2005).
- *Testosterone:* In theory, use of boron with estrogen-active drugs such as birth control pills or hormone replacement therapy may result in increased estrogen effects. Use of boron with testosterone-active drugs such as Testoderm® may result in increased testosterone effects.
- *Thyroid hormones:* On the basis of secondary sources, boron may alter thyroid hormone levels.

Boron/Herb/Supplement Interactions

- *Alzheimer's herbs:* In theory, boron may interact additively with herbs used to treat Alzheimer's disease.
- *Analgesics:* Some amine-boranes may have analgesic activities (Burnham, 2005).
- *Androgens:* Use of boron with testosterone-active drugs such as Testoderm® may result in increased testosterone effects.
- *Antacids:* Magnesium may interfere with the normal physiological effects of boron in the body. Sources of magnesium may include antacids containing magnesium oxide or magnesium sulfate (milk of magnesia, Maalox®).
- *Anti-inflammatory herbs:* Some amine-boranes may have anti-inflammatory activities (Burnham, 2005).
- *Antilipemics:* On the basis of mouse and rat studies, aliphatic, heterocyclic, and nucleoside amine-boranes and many boron derivatives may decrease LDL cholesterol and increase HDL cholesterol levels (Burnham, 2005).
- *Antineoplastics:* In in vitro and in vivo murine and human tumor models, borane adducts of simple aliphatic amines, heterocyclic amines, and nucleic acids showed cytotoxic properties by inhibiting DNA synthesis (Burnham, 2005).
- *Antivirals:* Some amine-boranes may have antiviral activities (Burnham, 2005).

- *Arthritis agents:* Some amine-boranes may have anti-arthritic activities (Burnham, 2005).
- *Calcium:* Boron supplementation may result in increased calcium levels in the blood, and may add to the effects of calcium or vitamin D supplementation.
- *Dopamine agonists:* Some amine-boranes may have dopamine receptor antagonist activity (Burnham, 2005).
- *Dopamine antagonists:* Some amine-boranes may have dopamine receptor antagonist activity (Burnham, 2005).
- *Hepatotoxic herbs:* Chronic high exposure to boron may cause hepatic damage (Ishii et al., 1993; O'Sullivan & Taylor, 1983).
- *Hormonal herbs and supplements:* Nutritional boron can up-regulate 17β-estradiol levels in women, including postmenopausal women receiving hormone replacement therapy.
- *Magnesium:* Magnesium may interfere with the normal physiological effects of boron in the body (Nielsen et al. 1992; Nielsen et al., 1987). Sources of magnesium may include antacids containing magnesium oxide or magnesium sulfate (milk of magnesia, Maalox®).
- *Hypoglycemics:* According to anecdotal reports, supplemental boron may decrease insulin levels in the blood.
- *Nephrotoxic agents:* Boron exposure may cause chronic kidney disease (Pahl et al., 2005).
- *Osteoporosis agents:* On the basis of animal and preliminary human studies, boron may play a role in mineral metabolism, with effects on calcium, phosphorus, and vitamin D (Burnham, 2005; Hunt, 1994; Hunt et al., 1994; Miggiano & Gagliardi, 2005; Nielsen et al., 1987).
- *Phosphates, phosphorus:* Supplemental doses of boron may reduce serum phosphorus concentrations.
- *Phytoestrogens:* In theory, use of boron with estrogen-active herbs or supplements may result in increased estrogen effects (Nielsen et al., 1987).
- *Renally eliminated herbs and supplements:* Boron exposure may cause chronic kidney disease (Pahl et al., 2005).
- *Thyroid agents:* According to anecdotal reports, boron may alter thyroid hormone levels.
- *Vitamin D:* Boron supplementation may result in increased calcium levels in the blood, and may add to the effects of calcium or vitamin D supplementation. Based on animal study, nutritional intakes of boron

have been shown to lessen the adverse consequences of vitamin D deficiency in rodents (Miljkovic et al., 2004).

Boron/Lab Interactions

- *Blood urea nitrogen (BUN):* Boron exposure may cause chronic kidney disease (Pahl et al., 2005).
- *Calcium:* Boron supplementation may result in increased calcium levels in the blood. In a comparative open trial, a combination product containing boron (Vitrum® osteomag) increased the level of general and ionized calcium in blood but did not cause hypercalcemia lowering the level of parathormone in blood (Benevolenskaia et al., 2004).
- *Creatinine:* Boron exposure may cause chronic kidney disease (Pahl et al., 2005).
- *Lipid panel:* Boron supplementation may decrease LDL cholesterol and increase HDL cholesterol levels (Burnham, 2005).
- *Liver panel:* Chronic high exposure to boron may cause hepatic damage (Ishii et al., 1993; O'Sullivan & Taylor, 1983).
- *Phosphorus:* Supplemental doses of boron may reduce serum phosphorus concentrations (Meacham, Taper, & Volpe, 1994).
- *Plasma vitamin D2:* Supplementation of boron may result in increased plasma concentrations of D2 in men and women with low-magnesium and low-copper diets (Nielsen, 1990; Nielsen, Mullen, & Gallagher, 1990).
- *Plasma ionized and total calcium:* Boron supplementation may result in increased concentrations of plasma ionized and total calcium as well as reduced serum calcitonin concentration and urinary excretion of calcium (Nielsen, 1990; Nielsen et al., 1990).
- *Plasma copper:* Boron supplementation may result in higher serum concentrations of plasma copper (Nielsen, 1990; Nielsen et al., 1990).
- *Plasma magnesium:* Boron supplementation may result in increased plasma magnesium concentrations (Hunt, Herbel, & Nielsen, 1997).
- *Plasma insulin:* According to anecdotal reports, boron may decrease plasma insulin levels.
- *Plasma thyroxine (T4):* According to anecdotal reports, boron may increase plasma thyroxine.
- *Serum estrogen:* Use of boron may result in increased endogenous estrogen (Nielsen et al., 1987).

- *Total testosterone:* Boron supplementation may increase concentrations of serum testosterone (Ferrando & Green, 1993).

MECHANISM OF ACTION

Pharmacology

- *Analgesic activity:* Some amine-boranes may have analgesic activities (Burnham, 2005).
- *Anti-arthritic activity:* Some amine-boranes may have anti-arthritic activities (Burnham, 2005).
- *Anticoagulant effects:* No significant effect of acute boron supplementation (at 11.6 mg boron) occurred on protease coagulation factor VIIa following the consumption of a high-fat meal. Factor VIIa rose significantly following the consumption of the high-fat meal (1.05 ± 0.07 vs. 1.26 ± 0.07; $p < .001$), but this increase was not altered by boron supplementation (Wallace et al., 2002).
- *Anti-inflammatory activity:* Some amine-boranes may have anti-inflammatory activities (Burnham, 2005).
- *Antineoplastic activity:* In in vitro and in vivo murine and human tumor models, borane adducts of simple aliphatic amines, heterocyclic amines, and nucleic acids showed cytotoxic properties by inhibiting DNA synthesis (Burnham, 2005). Furthermore, boric acid, the dominant form of boron in plasma, inhibited proliferation of prostate cancer cell lines, DU-145, and LNCaP, in a dose-dependent manner (Barranco & Eckhert, 2004). Nontumorigenic 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. Also, calcium entry is a component of the processes regulating the proliferative phenotype of some types of cancer (Enfissi et al., 2004). 2-Aminoethoxydiphenylborate (2-APB) completely blocked capacitative calcium entry (CCE) in thapsigargin-treated Huh-7, and inhibited cell proliferation.
- *Antiviral activity:* Some amine-boranes may have antiviral activities (Burnham, 2005).
- *Cholesterol effects:* Acute boron supplementation (at 11.6 mg boron) did not significantly alter blood lipid profiles in 15 healthy men (Wallace et al., 2002). However, in mouse and rat studies, aliphatic, heterocyclic, and nucleoside amine-boranes and many boron derivatives have decreased LDL cholesterol and increased HDL cholesterol

levels by increasing lipid excretion and inhibiting rate-limiting enzyme activities for lipid and cholesterol synthesis (Burnham, 2005).

- *Cognitive effects:* Boron may improve cognition; however the mechanism is unclear (Penland, 1994).
- *Dopamine receptor antagonist activity:* Some amine-boranes may have dopamine receptor antagonist activity (Burnham, 2005).
- *Glycemic effects:* Acute boron supplementation (at 11.6 mg boron) did not significantly alter plasma insulin and glucose concentration in healthy men (Wallace et al., 2002).
- *Osteal activity:* Animal and preliminary human studies report boron to play a role in mineral metabolism, with effects on calcium, phosphorus, and vitamin D (Burnham, 2005; Hunt, 1994; Hunt et al., 1994; Miggiano & Gagliardi, 2005; Nielsen et al., 1987). Changing boron intake from 0.33 to 3.33 mg daily had no effect on minerals, steroids, or crosslinks. However, the low (0.33 mg daily) boron diet appeared to induce hyperabsorption of calcium since positive calcium balances were found in combination with elevated urinary calcium excretion. This phenomenon may have inhibited or obscured any effect of boron (Beattie & Peace, 1993). In another study, Nielsen et al. examined the effects of aluminum, magnesium, and boron on major mineral metabolism in postmenopausal women. Twelve women between the ages of 48 and 82 housed in a metabolic unit were included. A boron supplement of 3 mg daily markedly affected several indices of mineral metabolism of seven women consuming a low-magnesium diet and five women consuming a diet adequate in magnesium; the women had consumed a conventional diet supplying about 0.25 mg boron daily for 119 days. Boron supplementation markedly reduced the urinary excretion of calcium and magnesium; the depression seemed more marked when dietary magnesium was low. Boron supplementation depressed the urinary excretion of phosphorus by the low-magnesium women, but not by the adequate-magnesium women. Boron supplementation markedly elevated the serum concentrations of 17β-estradiol and testosterone; the elevation seemed more marked when dietary magnesium was low. Neither high-dietary aluminum (1,000 mg daily) nor an interaction between boron and aluminum affected the variables presented. Researchers found that supplementation of a low-boron diet with an amount of boron commonly found in diets high in fruits and vegetables induces changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization (Nielsen et al., 1987).
- *Hormonal and bodybuilding effects:* Researchers found that 7 weeks of bodybuilding can increase total testosterone, lean body mass, and

strength in lesser-trained bodybuilders, but boron supplementation does not affect these variables at all (Green & Ferrando, 1994). Twelve subjects had boron values at or above the detection limit with median value of 25 ng/mL (16 ng/mL lower quartile and 33 ng/mL upper quartile). Out of the 10 subjects receiving boron supplements, 6 had an increase in their plasma boron. Analysis of variance indicated no significant effect of boron supplementation on any of the other dependent variables. Both groups demonstrated significant increases in total testosterone ($p < .01$), lean body mass ($p < .01$), and one repetition maximum (RM) squat ($p < .001$) and one RM bench press ($p < 0.01$). Nutritional intakes of boron have been shown to lessen the adverse consequences of vitamin D deficiency in rodents (Miljkovic et al., 2004). The effect may be mediated by an increase in serum 25-hydroxyvitamin D. Nutritional boron can upregulate 17β-estradiol levels in women, including postmenopausal women receiving hormone replacement therapy (Miljkovic et al., 2004).

- *Wound healing effects:* Intracellular MMP-9 expression in keratinocytes was induced when incubated for 6 hr with boron at 10 mcg/mL or manganese at 0.2 mcg/mL (Chebassier et al., 2004a). Gelatin zymography on keratinocyte supernatants showed an increase of gelatinase secretion after 24 hr of incubation with keratinocytes with boron or manganese, regardless of concentration. This could suggest that boron and manganese play a role in the clinical efficiency of thermal water on wound healing. A second in vitro study demonstrated accelerated wound closure using thermal water compared with control (Chebassier et al., 2004b). Boron and manganese act on wound healing mainly by increasing the migration of keratinocytes.

Pharmacodynamics/Kinetics

- *Absorption:* Both inorganic boron (i.e., borate or borax) and organic boron (i.e., boron amino acid chelate) are well absorbed orally by humans. Dermal absorption of boron is insignificant through intact skin, although boron has been demonstrated to penetrate damaged or abraded skin (Murray, 1995).
- *Distribution:* Boron gets distributed to all tissues with highest concentration in bone and lowest in adipose tissue. Boron levels generally achieve steady state in 3–4 days (Murray, 1995).

- *Metabolism:* Boric acid and borates are not well metabolized by humans. More than 90% of the administered dose is excreted unchanged primarily via the urine (50% within 12 hr and 80–100% over 5–7 days). More than 50% of the oral dose is reported to be eliminated during the first 24 hr in healthy volunteers (Jansen, Andersen, & Schou, 1984). The half-life of boron is between 13 (Litovitz et al., 1988) and 23 hr (Jansen et al., 1984). Peak CNS concentrations may occur within 3 hr (faster in other tissues); volume of distribution is reported as 0.17–0.5 L/kg.
- 2-APB, a compound used to inhibit store-operated Ca^{2+} channels and IP3 receptors, produces robust activation of recombinant TRPV3 in human embryonic kidney 293 cells with an EC_{50} of 28 mcM (Chung, Lee, Mizuno, Suzuki, & Caterina, 2004). 2-APB also sensitized TRPV3 to activation by heat, even at subthreshold concentrations. TRPV3 participates in the detection of heat by keratinocytes.

HISTORY

- The Babylonians used borax as a flux for working gold 4,000 years ago. The Egyptians then used boron as a mummifying and medicinal agent. In the eighth century, Arabs traded borax between Medina and China. The use of borax flux by European goldsmiths dates back to the 12th century (Woods, 1994). In 1702, William Homberg introduced borax into medical practice. It was purported to be a sedative, anodyne, and antispasmodic (Valdes-Dapena & Arey, 1962).
- Boron exists in nature in a hydrated form, which can be found in soil, water, vegetables, and fruits. Most boron that enters the human body comes from the ingestion of leafy vegetables, fruit, nuts, and legumes.

REVIEW OF THE EVIDENCE

DISCUSSION ON THE REVIEW OF THE EVIDENCE

Hormonal Regulation

- *Summary:* It has been suggested that boron may increase estrogen levels in women, reducing vaginal discomfort after menopause. More research is needed in humans before a conclusion can be reached.

Condition Treated	Study Type	Author, Year	N	Statistically Significant Results	Quality of Study: 0–2, poor; 3–4, good; 5, excellent	Magnitude of Benefit (how strongis the effect?)	Absolute Risk Reduction	# of Patients Needed to Treat for	Comments
Improving cognitive function	Double-blind, placebo-controlled trial	Penland, 1994	43	Yes	3	Small	NA	NA	Three separate studies; one was conducted entirely at a metabolic research unit, while the others were not as closely monitored
Osteoarthritis	Randomized, double-blind, placebo-controlled trial	Travers, 1990	20	Yes	3	Small	40%	3	8-week study
Osteoporosis	Randomized, placebo-controlled trial	Biquet et al., 1996	87	No	1	Small	NA	NA	12 months follow-up

(Continued on next page)

Vaginitis	Double-blind comparison trail	Van Slyke et al., 1981a, b	112	Yes	2	Small	28%	4	Boric acid compared with nystatin
Bodybuilding aid	Randomized, double-blind, placebo-controlled crossover trial	Green & Ferrando, 1994	19	No	3	None	NA	NA	Weight training four times a week in both groups; 7-week trial
Prevention of blood clotting (coagulation effects)	Randomized, double-blind, placebo-controlled, crossover trial	Wallace et al., 2002	15	No	3	None	NA	NA	Acute boron supplementation (at 11.6 mg boron) does not alter the activity of factor VIIa following consumption of a high-fat meal.

Improving Cognitive Function

- *Summary:* Preliminary human study reports better performance on tasks of eye–hand coordination, attention, perception, short-term memory, and long-term memory with boron supplementation. However, additional research is needed before a firm conclusion can be drawn.
- *Evidence:* Penland conducted a double-blind, placebo-controlled trial to investigate the role of dietary boron in brain function and cognitive performance (Penland, 1994). Thirteen postmenopausal women (aged 50–78) were recruited for the first study. All subjects were in good physical and psychological health, and were not on hormone replacement therapy. For a second study, 5 men and 10 postmenopausal women (five on estrogen replacement therapy) were recruited. Subjects were 44–69 years of age and right handed. For a third study, 5 men and 10 postmenopausal women (five on estrogen replacement therapy) were recruited. Subjects were 49–61 years of age. In all the studies, subjects were Caucasian and right handed (except one left-handed subject in study I and one left-handed subject in study III). Subjects in all three studies were given a conventional diet supplemented with 115 mg magnesium and 0.23 mg boron per 2,000 kcal daily, for an equilibration period of 21 days (study I) or 14 days (studies II and III). Following the equilibration period, subjects in study I were administered each of the four possible combinations of 200 mg magnesium/placebo and 3 mg boron/placebo in a double-blind, Latin squares fashion for 42 days. Subjects in study I were restricted to a metabolic research unit for the duration of the study. In studies II and III, the 14-day equilibration period was followed by a 63-day boron depletion period. The diet was then supplemented with 3 mg boron (study II) or 3 mg boron and 200 mg magnesium (study III) daily for 49 days. Subjects in studies II and III consumed meals prepared specifically for the study; compliance was ensured by feigned monitoring of blood and urine samples. Boron was supplied as sodium borate, and magnesium was supplied as magnesium gluconate. In study II, one woman who was not on estrogen replacement therapy began menstruating, and withdrew. One man withdrew from study III in the first month. Brain electrophysiology was assessed using electroencephalogram (EEG), and cognitive and psychomotor assessment was conducted using tasks selected from the Cognition Psychomotor Assessment System (CPAS) software package. Low boron intake resulted in a significant

increase in low-frequency activity and a decrease in high-frequency activity ($p < .05$). Boron restriction was also associated with poor performance on the psychomotor tests ($p < .05$) and on tests of manual dexterity in studies II and III. In all studies, boron supplementation showed improved attention, encoding, and short-term memory. Boron supplementation also coincided with improved long-term memory in study I, hand–eye coordination in study II, perception in study III, and manual dexterity in studies I and II. The most consistent observation with boron deficiency was more of lower-frequency brain activity; an effect also observed in malnutrition and heavy metal toxicity. However, there were inconsistencies in the other parameters tested, possibly due to small sample size and unknown confounding factors (possibly small amounts of dietary copper or other metals). It is not clear whether boron supplementation would benefit cognitive function in a normal diet.

Osteoarthritis

- *Summary:* Based on human population research, in a boron-rich environment, people appear to have fewer joint disorders (Newnham, 1994a, 1994b). It has also been proposed that boron deficiency may contribute to the development of osteoarthritis. However, there is no clear human evidence that supplementation with boron is beneficial as prevention against or as a treatment for osteoarthritis.
- *Evidence:* Travers et al. conducted a double-blind study to examine the effects of boron supplements in the treatment of osteoarthritis. Twenty patients were assigned to take either 6 mg of elemental boron orally (as sodium tetraborate decahydrate) or placebo (Travers & Rennie, 1990; Travers et al. 1990). To evaluate the improvement of joint conditions, patients were examined at weeks 0, 3, and 8. The authors reported “slight” improvements in 50% of patients taking boron supplementation versus 10% of patients in the placebo group. However, the small number of patients included in this study, high dropout rate (25%), and lack of use of validated measures make the results difficult to interpret.

Osteoporosis

- *Summary:* Animal and preliminary human studies report boron to play a role in mineral metabolism, with effects on calcium, phosphorus, and vitamin D (Hunt, 1994; Hunt et al., 1994; Nielsen et al., 1987). Lower quality studies may shed some light onto the physiology of boron in the human body, but they are limited by design, and comparisons were made between a very low-boron diet (less than 0.25 mg daily while average boron intake in the United States is 1–1.5 mg daily) and a high boron intake (3.25 mg daily), but bone marrow density and risk of fracture were not examined. Therefore, the clinical implications of these studies are limited (Beattie & Peace, 1993). Research of bone mineral density in women taking boron supplements does not clearly demonstrate benefits in osteoporosis. Additional study is needed before a firm conclusion can be drawn.

- *Evidence:* Biquet et al. reported the results of a randomized, placebo-controlled trial comparing bone mineral density of the lumbar spine, hip, and femoral neck regions in a group of healthy postmenopausal women taking boron supplementation (3 mg daily) versus placebo (Biquet et al. 1996). After 1 year of follow-up, no significant difference in bone marrow density between the two groups was observed, further clouding the evidence supporting the use of boron in the prevention of bone loss.
- *Studies of lesser methodological quality:* Beattie and Peace (1993) conducted a clinical study to investigate the effect of a boron supplement on bone mineral absorption and excretion, plasma sex steroid levels, and urinary excretion of pyridinium crosslink markers of bone turnover in healthy postmenopausal volunteers. The six women were accommodated in a metabolic unit, given a low-boron diet (0.33 mg daily) for 3 weeks, and were asked to take a boron supplement of 3 mg daily in addition to the low-boron diet for further 3 weeks. Changing boron intake from 0.33 to 3.33 mg daily had no effect on minerals, steroids, or crosslinks. However, the low-boron diet appeared to induce hyperabsorption of calcium since positive calcium balances were found in combination with elevated urinary calcium excretion. This phenomenon may have inhibited or obscured any effect of boron.
- *Studies using combination formulas:* Benevolenskaia et al. conducted a multicenter comparative open trial to investigate the efficacy, tolerance, and safety of the drug Vitrum® osteomag in women with osteopenia for the prevention of osteoporosis (Benevolenskaia et al., 2004). Three hundred and thirty-four postmenopausal women with osteopenia were included in the study. Endpoints of this study included bone mineral density, change of pain syndrome in bones, and index of calcium–phosphorous metabolism covered. Bone mineral density was measured in low-back spine and proximal part of the

hip with DEXA method. Patients were divided into three groups: 125 women taking two tablets of Vitrum® osteomag daily for 12 months (group 1); 111 women taking 1,500 mg calcium carbonate (group 2); and 96 women as the control group (only observation). One tablet of Vitrum® osteomag contains 600 mg calcium (1,500 mg calcium carbonate), 200 IU of cholecalcepherol, 40 mg of magnesium, 7.5 mg of zinc, 1 mg of copper, 1.8 mg of manganese, and 250 mcg of boron. According to the authors, Vitrum® osteomag relieved pain in the back and joints and had a positive effect on bone density (+1.5%) and proximal parts of the hip (0.6–0.93%) exceeding the effect of calcium carbonate, which only preserves the initial bone mineral density in low-back spine but does not prevent bone loss in the hip. Bone mineral density dynamics in patients given Vitrum® osteomag differs essentially from the control group (from −1.9 to −2.91%), which demonstrates a reliable preventive anti-osteoporotic effect of this medication, suggested the authors. The drug increased the level of general and ionized calcium in blood but did not cause hypercalcemia lowering the level of parathormone in blood. The rate of side effects in group 1 was 14.4% and did not differ much from that in group 2 (16.2%). Vitrum® osteomag contains other agents besides boron and the effects of boron alone are difficult to ascertain.

- Hunt et al. (1997) conducted a clinical study with 11 postmenopausal volunteers to evaluate the metabolic responses of postmenopausal women to supplemental dietary boron and aluminum during usual and low magnesium intake. It was found that a low-magnesium diet in addition to boron supplementation enhanced calcium preservation.
- Nielsen et al. (1987) conducted a study to examine the effects of aluminum, magnesium, and boron on major mineral metabolism in postmenopausal women. Twelve women between the ages of 48 and 82 housed in a metabolic unit were included. A boron supplement of 3 mg daily markedly affected several indices of mineral metabolism of seven women consuming a low-magnesium diet and five women consuming a diet adequate in magnesium; the women had consumed a conventional diet supplying about 0.25 mg boron daily for 119 days. Boron supplementation markedly reduced the urinary excretion of calcium and magnesium; the depression seemed more marked when dietary magnesium was low. Boron supplementation depressed the urinary excretion of phosphorus by the low-magnesium women, but not by the adequate-magnesium women. Boron supplementation markedly elevated the serum concentrations of 17β-estradiol and

testosterone; the elevation seemed more marked when dietary magnesium was low. Neither high-dietary aluminum (1,000 mg daily) nor an interaction between boron and aluminum affected the variables presented. Researchers found that supplementation of a low-boron diet with an amount of boron commonly found in diets high in fruits and vegetables induces changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization.

Vaginitis

- *Summary:* Inorganic boron (boric acid or borax) has been used as an antiseptic based on proposed antibacterial and antifungal properties. It is proposed that boric acid may have effects against candidal and non-candidal vulvovaginitis (Prutting & Cerveny, 1998). A limited amount of poor-quality research reports that boric acid capsules used in the vagina may be effective for vaginitis. Further evidence is needed before a recommendation can be made.
- *Evidence:* Van Slyke et al. (1981a, b) compared a 600 mg boric acid capsule to a nystatin vaginal capsule in the treatment of vulvovaginitis in 112 patients. After 7–10 days of therapy, the authors reported a 92% cure rate in the boric acid group and a 64% cure rate in the nystatin group. However, this study has been criticized for using a low dose of nystatin in the comparison group (Orley, 1982).

In a case series (Sobel & Chaim, 1997), 21 out of 26 patients with Torulopsis (candida) glabrata vaginitis were reported as being cured or experiencing improved symptom control with boric acid therapy.

In a case report (Shinohara & Tasker, 1997), boric acid was successfully used to treat azole-refractory candidal vaginitis in a woman with AIDS.

Bodybuilding Aid (Increasing Testosterone)

- *Summary:* There is preliminary negative evidence for the use of boron for improving performance in bodybuilding by increasing testosterone. Although boron is suggested to raise testosterone levels, in early human research, total lean body mass has not been affected by boron supplementation in bodybuilders. Additional research is necessary before a firm conclusion can be drawn.
- *Evidence:* The effect of boron supplementation (2.5 mg) was investigated in 19 male bodybuilders using a randomized, double-blind,

placebo-controlled design (Green & Ferrando, 1994). Subjects in both the boron supplemented group and the placebo group underwent 7 weeks of weight training. The authors reported that testosterone levels and total lean body mass were increased from baseline in both groups, but were unaffected by boron supplementation.

Menopausal Symptoms

- *Summary:* It has been proposed that boron affects estrogen levels in postmenopausal women. However, preliminary studies have found no changes in menopausal symptoms.
- *Studies of lesser methodological quality:* In two studies, serum 17β-estradiol levels were raised when postmenopausal women ingested boron supplements (Beattie & Peace, 1993; Nielsen et al., 1987). It appears that boron, magnesium, and other factors may play a complex role in estrogen regulation, and it is not clear that boron directly interferes with serum estrogen levels. In a follow-up study, Nielsen conducted a double-blind crossover study to examine the effects of boron in women with menopausal discomfort (Nielsen & Penland, 1999). The authors reported that more women receiving boron supplements experienced exacerbation of symptoms (46%) rather than relief (22%). As in previous investigations, estrogen levels were found to increase during the period of boron supplementation.

In a randomized, placebo-controlled trial, Volpe et al. investigated the effects of boron supplementation on hormonal levels in two groups of young women: college female athletes and sedentary women (Volpe, Taper, & Meacham, 1993). After a 10-month follow-up, the authors found no significant differences in serum 17β-estradiol and testosterone levels between the boron and placebo arms. However, the athlete group did show a significant increase in 17β-estradiol and testosterone levels compared to baseline. Nonetheless, the authors concluded that boron does not affect sex steroid levels in young women.

Prevention of Blood Clotting (Coagulation Effects)

- *Summary:* It has been proposed that boron may affect the activity of certain blood clotting factors. There is not enough evidence in this area to form a clear conclusion.

- *Evidence:* Wallace et al. conducted an acute, randomized, double-blind, placebo-controlled, crossover study of a free-living population to determine whether postprandial concentrations of the active component of serine protease coagulation factor VII (VIIa) were lowered by acute boron supplementation (Wallace et al., 2002). Fifteen apparently healthy men between the ages of 45 and 65 years were included. Subjects visited the center on two occasions, with the study days separated by a minimum of 2 weeks. Following collection of a fasting blood sample, subjects received either placebo or acute bolus of 11.6 mg boron (given as 102.6 mg sodium tetraborate decahydrate) together with a standard fat-rich meal. Blood samples were obtained 1, 2, 4, and 6 hr after the administration of the test meal, during which time subjects were at liberty to consume deionized water only. Blood samples were assayed for concentrations of insulin, glucose, lipids, and boron. Measurement of the concentration of activated factor VIIa and of factor VII antigen, and of the activity of coagulation factors VII, IX, and X was also carried out. Plasma boron concentrations were significantly higher following the consumption of the boron supplement compared with placebo (0.124 ± 0.02 mg/L vs. 0.008 ± 0.01 mg/L; $p \leq .001$). There was no significant effect of acute boron supplementation on plasma insulin and glucose concentration or on blood lipid or coagulation factor profile. Factor VIIa rose significantly following consumption of the high-fat meal (1.05 ± 0.07 vs. 1.26 ± 0.07; $p \leq 0.001$), but this increase was not altered by boron supplementation. Notably, a manufacturer of boron funded this study.

Psoriasis (Topical)

- *Summary:* Preliminary human study of an ointment including boric acid does not report significant benefits in psoriasis.
- *Study using combination formula:* An ointment consisting of boric acid, zinc oxide, starch, and petrolatum was compared to placebo in treating plaque-type psoriasis in 30 subjects (Limaye & Weightman, 1997). Although use of the boron ointment demonstrated a trend toward better performance versus placebo, this result did not reach statistical significance. A high dropout rate (14 subjects) hinders this result.

FORMULARY: BRANDS USED IN CLINICAL TRIALS/THIRD-PARTY TESTING

Brands Used in Statistically Significant Clinical Trials

- Vitrum® Osteomag. From: Benevolenskaia LI, Toroptsova NV, Nikitinskaia OA, Sharapove, EP, Korortkova TA, Rozhinskaia Lla, Marova EI, Dzeranova LK, Molitvoslovova NN, Men'shikova LV, Grudinina OV, Lesniak OM, Evstigneeva LP, Smetnik VP, Shestakova IG, Kuznetsov Slu. [Vitrum osteomag in prevention of osteoporosis in postmenopausal women: results of the comparative open multicenter trial] Ter Arkh. 2004;76(11):88–93. Russian.

Brands Shown to Contain Claimed Ingredients Through Third-Party Testing

- Consumer Lab : NA. Last accessed 02/2008.
- Consumer Reports: NA. Last accessed 02/2008.
- Natural Products Association: NA. Last accessed 02/2008.
- NSF International: NA. Last accessed 02/2008.
- U.S. Pharmacopeia: NA. Last accessed 02/2008.

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