

## **Electrical Nutrition For Physically Active People**

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The skeletal system of humans is constantly undergoing continual degradation that in ideal situations is balanced by new bone synthesis. Because bone is a dynamic tissue, it can adapt by strengthening when subjected to mechanical stress, such as repetitive physical activity. In athletic exercise the extremities of the body are subjected to repeated mechanical stress creating a condition where bone turnover (bone remodeling) is accelerated. The process of bone remodeling is dependent on numerous factors including levels of exercise, hormone levels and tissue availability of certain vitamins and minerals.

When bone repair processes are suboptimal, bone repair cannot keep up with accelerated bone degradation resulting in loss of bone strength and stress fractures. Strenuous physical training in young adults will result in either a rapid increase in bone density as a result of adaptive bone remodeling or bone mineral loss, which can result in stress fractures (1).

Bone mineral loss is a condition involving multiple interacting factors. Numerous variables including age, gender, hormonal status, heredity, amount of exercise, medication use, smoking, alcohol consumption, inactivity due to illness or injury, and nutritional factors such as the level of intake of protein, calcium, magnesium, sodium, potassium, zinc, phosphorus and trace minerals, which all affect bone mass, bone strength and muscle strength (2-4).

Clinicians recognize that regular strenuous exercise could contribute to nutritional deficiencies due to mineral loss in sweat and increased urinary excretion (5-7); but most dieticians believe that any emergent deficiencies are easily corrected by ingestion of a well balanced diet. From my review of the literature, it is apparent to me that the conventional thinking, in regards to bone density and bone health is wrong, since a significant proportion of athletes will develop stress fractures as a result of training (8-9). In one study of 95 track and field athletes there was an over all frequency of stress fractures of 21% with low bone density identified as a significant risk factor especially in women (10). Researchers have implicated bone mineral loss secondary to estrogen deficiency, testosterone deficiency, nutritional insufficiency of calcium and vitamin D and trace mineral deficiencies as a contributing factor in the causation of stress fractures in individuals who are involved in athletic training programs (11-13). Despite an adequate diet many athletes will still develop bone mineral loss not bone strength with training (14-16). I believe part of the solution can be the use of nutrients such as mineral transporters that support the bioelectric regenerative processes involved in bone formation.

Regeneration is a healing process where the body can replace damaged tissues. Some of the most important biophysical factors implicated in musculoskeletal repair and regeneration involve natural electrical properties of the body's tissues and cells (17), such as cell membrane potential (capacitance) and protein semiconduction of electricity. The body utilizes these fundamental bioelectronic features to naturally produce electrical currents that are involved in repair and regeneration (18-22).

Becker has shown in his research that the flow of endogenous electrical currents in the body is not a secondary process, but in fact is an initiator and control system used by the body to regulate healing in bone and other tissues (20, 23-24). The proper production and conduction of endogenous electrical currents is required to stimulate primitive precursor cells to differentiate to osteoblasts and chondroblasts (23-24). Once the bone forming osteoblasts are created, they must maintain a healthy cell membrane electrical potential and have available certain critical nutrients in order to form the polysaccharide and collagen components of osteoid. Endogenous bone electrical currents created through piezoelectricity (25-26) are

also required for deposition of calcium crystals (27). When the biophysical electrical properties of bone are considered, then it makes sense to develop a nutritional bone support formula that supports the body's biophysical electrical processes to potentiate the healing of injured musculoskeletal tissue.

Bone and other connective tissues are organized living liquid crystals that have the ability to remodel themselves in response to stress. Bone calcium crystals are deposited in orderly arrays in protein liquid crystal fibers in proportion to the compressional load placed on the bone. This is why athletes with healthy mineral nutrition generally have thicker bones and stronger bones as compared to nonathletes.

When bone is compressed it will generate electrical potentials (28). Bone forming cells will deposit calcium crystals at the point of compressional stress. Researchers, particularly Robert O. Becker, have determined that this calcium deposition is caused by a piezoelectric effect (24). When bone is compressed the compressed area will develop a negative potential with positive potential present in uncompressed areas. When there is a difference in electrical potential an electric current will flow in liquid crystal protein fibers and in and just above the bone cell membranes, which will stimulate bone formation (osteoblastic activity) at the negative end of the current flow. For such a system to work the cell membranes of the osteoblasts must act as biological capacitors that are able to hold electrical charges and allow for the flow of electric currents. Capacitors are well known electronic components that are composed of two conducting sheets or metal plates separated by a thin layer of insulating material. Cells contain several forms of biological capacitors, which consist of an insulating material (the membrane) covered on both sides by collections of charged dissolved minerals, which serve the same function as a conducting metal plate. Because the exterior cell membrane and the membranes of cell organelles like the mitochondria in animals and the chloroplasts in plants are biological capacitors they have the capacity to accumulate and store charge and hence energy to be given up when needed.

Bone formation in part depends on having healthy osteoblast cell membrane capacitance (29). A healthy cell membrane in turn depends on having the proper lipid composition, which in turn is dependent on adequate dietary sources of essential lipid compounds. Since energy is needed to run any type of machinery be it mechanical or biological it makes sense that nutrients that can enhance energy production and energy storage can have profound biological effects. Nutrients that support protein synthesis, cell membrane capacitance and the electrical properties can facilitate bone regeneration and bone mineralization.

Bone matrix, a composite specialized connective tissue framework made up of collagen and noncollagenous proteins, is biologically hardened by the deposition of minerals, the primary one being calcium (30). Bone is not a static tissue. It is continually being deposited and reabsorbed. The initial stage in bone production is the secretion of collagen molecules by bone forming cells called osteoblasts. The collagen strands secreted by the osteoblasts then spontaneously organize themselves into triple helix structures. The stability of collagen requires vitamin C, which is necessary for the amino acid proline to form cross linkages between the three strands of collagen. Vitamin C is therefore an essential nutrient in bone formation. Collagen now binds to molecules called proteoglycans (chondroitin sulfate and hyaluronic acid), which are also made by bone osteoblasts, forming a composite connective tissue matrix called osteoid. The formation of osteoid traps the osteoblasts in the matrix where they now secrete calcium salts on the surface of the collagen these salts eventually crystallize into calcium hydroxyapatite crystals hardening the matrix.

Because bone becomes brittle with age and because the body is continually being subjected to mechanical stress, the old bone matrix and calcium crystals are removed by bone cells called osteoclasts. Osteoclasts are needed to reabsorb old bone so new bone can be made in its place. When osteoporosis and bone degeneration occur the reabsorption of bone outpaces the deposition of new bone.

Any nutritional program designed to support bone health must address the different processes that go into bone formation and the starting point is to insure that: healthy bone matrix is formed, osteoblasts are able to maintain a healthy capacitance charge and adequate amounts of key structural minerals, trace mineral cofactors and enzyme coenzymes (vitamins) are delivered to and into osteoblast cells.

All living cells have a membrane potential (of about -70mV). In healthy tissue the inside of the cell is negative relative to its external surface, but when tissues are injured sodium and water flows in to the cells and potassium, magnesium and zinc are lost from the cell interior. The change in mineral content of the cell is one of the major factors causing injured cells to have lower membrane potential. A healthy cell membrane potential is strongly linked to the control of cell membrane transport mechanisms as well as DNA activity and protein synthesis. Therefore injured cells, which cannot maintain normal membrane potential, will have electronic dysfunction that will impede repair and rejuvenation processes. A key component of bone repair and rejuvenation is to reestablish a healthy membrane potential in bone forming cells (31-36).

The electrical charge of the cell membrane is maintained both by the structure of the membrane and its associated minerals, however these minerals must be in the proper location at the proper concentration for optimization of cellular potential and metabolic activity. Mineral transporters serve the function of special delivery vehicles placing minerals in optimal cellular and subcellular locations (37-39).

As medical doctors have come to understand the electrical properties of tissues and the role of electricity in repair and rejuvenation, use of electrotherapy is becoming commonplace in health care. Since the application of electrotherapy modalities is now being used in repairing wounds (40-41), nonhealing fractures (23) and other conditions. It makes logical sense to investigate, find and utilize nutrient compounds that can support the production of the body's own natural electrical properties. From the point of view of bone my bone support recommendations are designed to facilitate intracellular mineral levels, cell membrane capacitance, cell protein production, normal collagen structure and calcium crystal deposition. This supplement approach is specifically designed to support the electrical processes involved in bone formation.

Nutritional approaches designed to support bone health should include components that provide the required building materials as well as the cofactors needed by the body. Almost everyone knows calcium is needed to build bone, but it is less well known that zinc, magnesium, trace minerals, vitamin C and vitamin D are also essential nutrients in the production of bone particularly bone matrix (42). Animals given trace mineral deficient diets show bone loss identical to osteoporotic bone loss in humans (43). Studies have shown that individuals with deficiencies of the mineral magnesium and the trace minerals boron, zinc, copper and manganese have lower bone mineral density and bone strength (44).

## **Biological Role of Mineral Transporters In Bone Formation**

Biological utilization of a mineral encompasses far more than just mineral absorption. Biological utilization of minerals includes mineral absorption, mineral transport in the blood stream and mineral delivery into the tissues. Most mineral supplements generally break apart during the processes of digestion releasing ionized minerals into the lumen of the digestive tract, which are then moved into the bloodstream. Just getting a mineral into the blood stream doesn't guarantee that the mineral can be directed to any particular tissue or be transported across the cell membrane to the cell interior (31,45).

The joining of carrier molecules with minerals forms electrically neutral compounds that have different transport properties than unbound ionized minerals (39). Calcium orotate, calcium arginate, calcium aspartate, calcium 2-AEP, magnesium orotate, zinc orotate and zinc aspartate are mineral transporters. When these mineral transporters are properly manufactured to be acid resistant, they deliver minerals still bound to the transporter into the alkaline environment of the small intestine where the mineral compounds are absorbed relatively intact from the digestive tract into the blood stream with the mineral still bound to the transporter (37-39).

The mineral-transporter complex remains stable in the blood stream with low dissociation, and the minerals are not released until the mineral-transporter complex enters the target tissues/cells. The attachment of minerals to carrier molecules forms electrically neutral stable complexes that allow selective direction of minerals to particular tissues that metabolically use the carrier molecules. This form of directed mineral

nutrition even enhances mineral entry even into cells that have disturbed cell membranes. Use of mineral transporters can increase the bioavailability of minerals to bone tissue (31-36, 46-51).

Calcium orotate, calcium aspartate, calcium arginate, calcium 2-AEP, magnesium orotate, zinc orotate and zinc aspartate are all efficient mineral transporters for conditions associated with mineral loss in bone tissue (32, 36, 39, 46-47, 49) and are excellent vehicles for delivering bioavailable minerals to bone tissue undergoing decalcification. Because these mineral transporters can penetrate through cell membranes they can compensate for impaired calcium, magnesium and zinc transport through cell membranes and be effective delivery compounds for intracellular supplementation of these minerals (36-39).

The pentose pathway is involved in the metabolic processes of cartilage, blood vessels, the cardiac conduction system, connective tissue, lymphatics, bone matrix, blood brain barrier, keratin building tissues (skin, hair and nails), liver and ligaments (39, 46, 49-51). Because orotic acid is a substrate in the pentose phosphate pathway, orotate mineral transporters are able to bioaccumulate in tissues, such as bone, that use this pathway (52). In addition, orotic acid is a naturally occurring substance that is a key intermediate in the biosynthetic pathway of pyrimidines (53).

Pyrimidines are important constituents of nucleic acids, which are required for the synthesis of DNA and RNA molecules. An under appreciated feature of bone stress is stress induced depletion of bone cell pyrimidine levels. Dietary mineral orotates are metabolic supplements that can potentially correct depleted bone cell pyrimidine levels. This explanation illustrates that minerally bound orotic acid can facilitate formation of DNA and RNA, which in turn controls protein formation in repair and regeneration of tissues (54). One of the critical features of bone enhancement with nutrients is to insure that the protein components of bone matrix are produced. Mineral orotates have stimulating effects on cell protein production, in growing tissue (54). Any improvement in cellular protein synthesis in bone forming cells and increase in calcium, magnesium and zinc bioavailability to bone forming cells, in active remodeling bone tissue, can reduce these rate-limiting factors in bone formation and bone mineralization (39, 46-49).

Magnesium orotate is a mineral transporter where magnesium is bound orotic acid (52). Magnesium orotate can help assure delivery of magnesium intracellularly into bone forming cells (39). This is important since intracellular magnesium is required for transport of ionized calcium into cells through the cell membranes. Intracellular magnesium not only plays a role in intracellular calcium transport, but it is also needed for energy production and along with zinc is needed for protein synthesis and for the activation of the enzyme required for production of hydroxyapatite, the calcium crystal that creates bone hardness.

Calcium orotate, calcium aspartate, calcium arginate and calcium 2-AEP are valuable food supplements that can deliver calcium to bone tissue without creating excessive blood calcium levels. These compounds are beneficial in assuring calcium delivery to bone in conditions, such as trauma due to strenuous exercise or accidents, where damaged cell membranes and reduced cellular capacitance can impair cellular calcium entry, protein synthesis and calcium crystal formation and deposition.

Calcium 2-AEP plays a dual role both as a mineral carrier that releases calcium on the cell membrane surface and as a cell membrane repair material. Calcium 2-AEP was considered by Dr. Hans Nieper to be a cell membrane integrity factor (29). When the AEP is incorporated into cell membranes it helps in the repair of membrane structure and membrane functions (32). The incorporation of AEP molecules into cell membranes helps bind electrically charged calcium ions to the exterior surface of the cell membranes. By rebuilding cell membrane structure and binding of electric charges to cell membranes, AEP helps normalize the electric charge of cell membranes, particularly in diseased and damaged tissues.

Calcium 2-AEP enhances normal membrane activity by assisting the cell membrane in maintaining its electronic function allowing for proper production of cellular capacitance (37-39). The capacitance of cell membranes is a reflection of the amount of charge in the membrane. Healthy cells are able to maintain their membrane charge. Unhealthy and damaged cells have structural membrane abnormalities and imbalances of intracellular mineral concentrations, which result in lower membrane capacitance. One of the most important electronic roles of the cell membrane is creation of charge, maintenance of charge and the

transfer of that charge to genetic material, which facilitates cellular protein synthesis. Reestablishing cell membrane structure in damaged cells and maintaining a healthy capacitance of the cell membranes of osteoblast cells is critical in the repair of damaged bone tissue and in supporting remodeling processes in bone.

Proper crystallization of calcium salts in bone formation is dependent on maintaining a healthy electromagnetic potential in the cell membranes of bone forming cells (osteoblasts). Supplementation with calcium 2-AEP can be helpful in maintaining and rebuilding bone density in osteoporosis and in traumatic injury to the bone (29). Calcium 2-AEP is included in bone support to support the membrane capacitance in osteoblast cells, since a healthy capacitance is needed for bone formation. Calcium 2-AEP is a useful repair compound in traumatic and inflammatory conditions where bone cells are damaged (55). Calcium 2-AEP is combined with calcium aspartate, calcium arginate and calcium orotate in bone nutrition because these other calcium mineral transporters have an affinity for the connective tissue of bone and intervertebral discs making them particularly beneficial in improving bone density and bone remodeling processes (39, 46-47).

Zinc aspartate and calcium aspartate are mineral transporters where the minerals are bound to the amino acid aspartic acid. Aspartate mineral transporters are able to penetrate the cell membrane and deliver minerals intracellularly (37-39). In the process of the aspartic acid being metabolized, the minerals are released on the inner layer of the cell membrane. Aspartic acid is a non-essential amino acid that can be synthesized from oxaloacetate. Aspartic acid is itself the precursor of orotic acid, lysine, methionine and threonine.

Zinc is included my bone support approach, since zinc depletion and deficiency can develop during physical or emotional stress, especially if it is prolonged. Individuals who have had trauma or surgery will also use and lose large amounts of zinc, lysine, glutamine and vitamin C as the body mobilizes these nutrients in order to repair itself.

A number of minerals and trace elements other than calcium are involved in skeletal strength (56). In addition strenuous exercise will accelerate body excretion of minerals and create increased demands for certain critical nutrients involved in maintenance of bone density. Low calcium along with low magnesium, boron, copper, manganese, zinc and vitamins C, D, K, B12, B6 and folic acid are nutritional factors that may pre-dispose to osteoporosis (57-58) Since calcium supplementation alone may reduce absorption of magnesium and zinc further compromising potential deficiencies of these minerals it is prudent to also supplement these minerals (59-60). While copper deficiency is relatively uncommon, it can occur in people who supplement with zinc and vitamin C without also increasing copper intake, since both of these essential nutrients can interfere with copper absorption (61-62).

The use of a bone support program that addresses not only calcium metabolism, but also the biophysical aspects of bone formation may be beneficial for individuals at risk for exercise related bone calcium loss and osteoporosis. I have found that this approach is particularly beneficial in hastening the recovery of orthopedic injuries and in individuals with osteoporosis. I believe the use of mineral transporters is the best way to deliver bioavailable minerals to bone tissue.

## References

1. Margulies JY, Simkin A, Leichter I, et al. Effect of intense physical activity on the bone-mineral content in the lower limbs of young adults. *J Bone Joint Surg Am* 1986 Sep;68(7):1090-3.
2. Giladi M, Milgrom C, Simkin A, Danon Y. Stress fractures: identifiable risk factors. *American Journal of Sports Medicine* 1991;19(6):647-652.
3. Casez JP, Fischer S, Stussi E, et al. Bone mass at lumbar spine and tibia in young males - Impact of physical fitness, exercise, and anthropometric parameters: A prospective study in a cohort of military recruits. *Bone* 1995 Sep;17(3):211-219.
4. Heinonen A, Oja P, Kannus P, et al. Bone mineral density in female athletes representing sports with different loading characteristics of the skeleton. *Bone* 1995 Sep;17(3):197-203.

5. Anderson RA, Polansky MM, Bryden NA. Strenuous running: Acute effects on chromium, copper, zinc and selected variables in urine and serum of male runners. *Biol Trace Elem Res* 1984;6:327-336.
6. Clarkson PM. Minerals: exercise performance and supplementation in athletes. *J Sports Sci* 1991 Summer;9 Spec No:91-116.
7. Dolev E, Burstein R, Wishnitzer R, Lubin F, Chetriet A, Shefi M, Deuster PA. Longitudinal study of magnesium status of Israeli military recruits. *Magnes Trace Elem* 1991-92;10(5-6):420-6.
8. Myburgh, KH, Hutchins, J, Fataar, AB, et al. Low bone density is an etiologic factor for stress fractures in athletes. *Ann Intern Med*;113:10(Nov 15), 1990, 754-9.
9. Lauder TD, Dixit S, Pezzin LE, et al. The relation between stress fractures and bone mineral density: evidence from active-duty Army women. *Arch Phys Med Rehabil* 2000 Jan;81(1):73-9.
10. Bennell KL, Malcolm SA, Thomas SA, et al. The incidence and distribution of stress fractures in competitive track and field athletes: a twelve-month prospective study. *Am J Sports Med* 1996;24(2):211-217.
11. Brunet ME, Cook SD, Brinker MR, et al. A survey of running injuries in 1505 competitive and recreational runners. *J Sports Med Phys Fitness* 1990;30:307-315.
12. Lloyd T, Andon MB, Rollings N, et al. Calcium supplementation and bone mineral density in adolescent girls. *JAMA* 1993;270:841-844.
13. Lane JM. Biology of Stress Fractures. In: *Stress Fractures of the Lower Extremity Etiology, Diagnosis and Treatment(s) Symposium*, Moderator: Lane JM, New York, NY Friday, March 2, 2001.
14. Pouilles JM, Bernard J, Tremollieres F, Louvet JP, Ribot C. Femoral bone density in young male adults with stress fractures. *Bone* 1989;10(2):105-8.
15. Klesges RC, Ward KD, Shelton ML, et al. Changes in bone mineral content in male athletes. Mechanisms of action and intervention effects. *JAMA* 1996 Jul 17;276(3):226-30.
16. Voss LA, Fadale PD, Hulstyn MJ. Exercise-induced loss of bone density in athletes. *J Am Acad Orthop Surg* 1998 Nov-Dec;6(6):349-57.
17. Brighton CT, Black J, Pollack SR. *Electrical Properties of Bone and Cartilage*. New York: Grune & Stratton, 1979.
18. Becker RO. The bioelectric factors in amphibian limb regeneration. *Journal of Bone and Joint Surgery* 1961;43A:643-656.
19. Becker RO. The electrical control of growth processes. *Medical Times* 1967;95: 657-669.
20. Becker RO, Murray DG. The electrical control system regulating fracture healing in amphibians. *Clin Orthop Rel Res* 1970;73:169.
21. Becker R). Stimulation of partial limb regeneration in rats. *Nature* 1972;235:109-111.
22. Becker RO. The basic biological data transmission and control system influenced by electrical forces. *Ann N Y Acad Sci* 1974;238: 236-241.
23. Becker RO. *Cross Currents*. London, England: Bloomsbury Publishing, 1990.
24. Becker R, Selden. *The Body Electric*. New York: W. Morrow and Company Inc, 1985.
25. Fukada E, Yasuda I. On the piezoelectric effect in bone. *J Physiol Soc Japan* 1957;12:1198.
26. Fukada E. Piezoelectricity of natural biomaterials. *Ferroelectrics* 1984;60:285-296.
27. Becker RO, Bassett CAL, Bachman CH. Bioelectric factors controlling bone structure. In: *Bone Biodynamics*, ed. H. Frost. New York: Little Brown, 1964.
28. Bassett CAL, Becker RO: Generation of electrical potentials by bone in response to mechanical stress. *Science* 1962;137:1063.
29. Nieper HA. The colamine phosphate salts as membrane integrity factor. *Raum and Zeit* 1988 Aug;35:4-9.
30. Termine JD. Bone matrix proteins and the mineralization process. In: Favus MJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism*. Richmond, VA: William Byrd Press; 1996:16-18.
31. Nieper HA, Blumberger K. Electrolyte transport therapy of cardiovascular disease in: *Electrolytes and cardiovascular disease*. Ed. Bajusz E. Vol 2: 141-173, Basel/ New York: S. Karger, 1966a.
32. Nieper HA. Experimentation clinique de transporteurs de calcium. 1966b;7(6): 623-639.
33. Nieper HA. Clinical experimentation with calcium transport agents. Calcium DL, L-aspartate and calcium-aminoethyl phosphate, 2 powerful anti-inflammatory and antiallergic agents. *Aggressologie* 1966c Nov;7(6):623-639.

34. Nieper HA. A clinical study of Ca-2-aminoethanolphosphate (2<sup>nd</sup> communication). *Aggressologie* 1967a;7(4):4-16.
35. Nieper HA. A clinical study of the calcium transport substances Ca-1, dl-aspartate and Ca-2-aminoethanol phosphate as potent agents against autoimmunity and other anticytological aggressions. *Aggressologie* 1967b; 8(4):395-406.
36. Nieper HA. Comparative study of the clinical effect of dl- aspartate (calciretard), of ca-2- calcium aminoethanol phosphate (Ca-EAP) and of the cortisones. *Aggressologie* 1968;9(3):471-475.
37. Alexander AD. Calcium 2-AEP and calcium orotate found essential in the prevention and treatment of osteoporosis. *INI Newsletter* June 1997a.
38. Alexander AD. The healthy cell: Its structure and functions that are so essential to disease prevention and treatment. *INI Newsletter* June 1997b.
39. Nieper HA, Alexander AD, Eagle-Ogden GS. *The Curious Man: The Life and Works of Dr. Hans Nieper*. Garden City Park, NY: Avery Publishing Group; 1999.
40. Foulds I, Barker A. Human skin battery potentials and their possible role in wound healing. *British J Derm* 1983;109: 515-522.
41. Carley P, Wainapel S. Electrotherapy for acceleration of wound healing: Low intensity direct current. *Arch Phys Med Rehabil* 1985;66: 443-446.
42. Saltman PD, Strause LG. The role of trace minerals in osteoporosis. *J Am Coll Nutr* 1993;12:384-389.
43. Underwood E. *Trace Elements in Human and Animal Nutrition*. New York: Academy Press, 1977.
44. Howard G, Andon M, Bracker M, et al. Serum trace mineral concentrations, dietary calcium intake and spinal bone mineral density in postmenopausal women. *J Trace Elem Exp Med* 1992;5:23-31.
45. Nieper H A. Experimental bases and clinical use of electrolyte carrier compounds. *Arztl Forsch* 1961;15: 510-514.
46. Nieper HA. The anti-inflammatory and immune-inhibiting effects of calcium orotate on bradytrophic tissues. *Aggressologie* 1969;10(4):349-357.
47. Nieper HA. Recalcification of bone metastases by calcium- diorotate. *Aggressologie* 1970;11(6):495-503.
48. Nieper HA. Therapeutically effective calcium diorotate US Patent 3,621,024, filed Nov. 13, 1968, pat. Nov. 16, 1971.
49. Nieper HA The clinical effect of calcium- diorotate on cartilaginous tissue, the specific function dependent upon the pentose- metabolism of bradytrophic tissue. *Geriatric* 1973; 3(4): 82-89.
50. Buist R. *Biological Applications of Orotates: Orotates Mineral Salts of Vitamin B13*. Sydney: Colprint Press, 1972.
51. Buist R. *Orotates: The Ultimate in Mineral Transportation*. Sydney: Colprint Press, 1978.
52. Williams JF, Donohoe JA, Rosenfeldt FL, Munsch CM. Biochemistry and functional roles of orotic acid for support of the infarcted heart during open heart surgery. In: *Orotic Acid in Cardiology: International Symposium on Orotic Acid and Magnesium Orotate*, Nov., 1991.
53. Rosenfeldt FL. Metabolic supplementation with orotic acid and magnesium orotate. *Cardiovasc Drugs Ther* 1998 Sep;12 Suppl 2:147-52.
54. Cihak A, Reutter W. *Orotic Acid*. Lancaster, England: MTP Press Limited, 1980.
55. Haltiwanger SG. Clinical use of mineral transporters and their effects on cell membrane capacitance: Second International Congress of BioEnergetic Medicine, Institute of Quantum and Molecular Medicine, Daniel G. Clark, President, February 20-22, 1998.
56. Branca F, Valtuena S, Valtuena S. Calcium, physical activity and bone health--building bones for a stronger future. *Public Health Nutr* 2001 Feb;4(1A):117-23.
57. Bunker VW. The role of nutrition in osteoporosis. *Br J Biomed Sci* 1994 Sep; 51(3): 228-40.
58. Gaby AR. *Preventing and Reversing Osteoporosis*. Rocklin, CA: Prima Publishing, 1994.
59. Cohen L, Laor A, Kitzes R. Magnesium malabsorption in postmenopausal osteoporosis. *Magnesium* 1983;2:139-43.
60. Sahap AO. Zinc and senile osteoporosis. *J Am Geriatr Soc* 1983;31:790-1.
61. Jacob RA, Skala JH, Omaye ST, Turnlund JR. Effect of varying ascorbic acid intakes on copper absorption and ceruloplasmin levels of young men. *J Nutr* 1987;117:2109-15.
62. Broun ER, Greist A, Tricot G, Hoffman R. Excessive zinc ingestion. A reversible cause of sideroblastic anemia and bone marrow depression. *JAMA* 1990;264:1441-3.