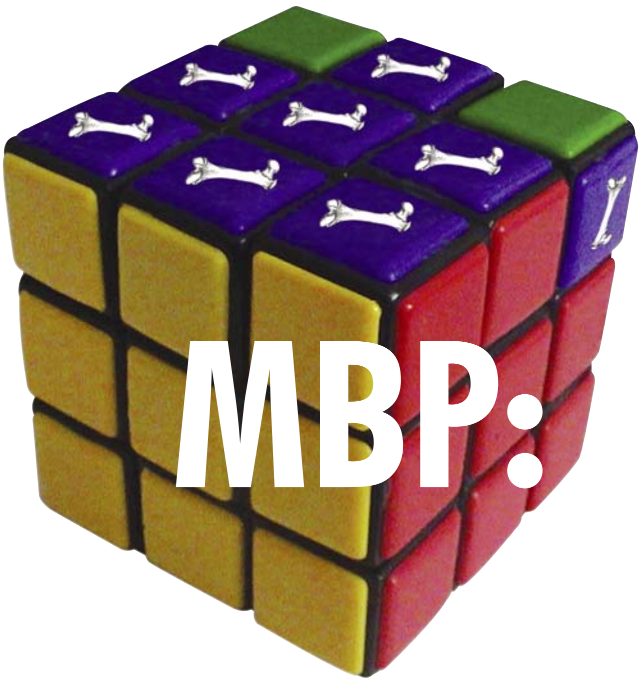


Another Piece of the Bone Health Puzzle

Finding A Place In A Crowded Room

Bone health. It is arguably one of the most scrupulously studied health conditions known. This is due in no small part to its fundamental nature, and that same fundamental nature has produced a body of dietary knowledge for bone health that is both long-established and widely accepted. Calcium comprises over 40% of bone mass, making its supplementation essential. Calcium cannot be absorbed adequately without vitamin D, which in turn depends intrinsically on a steady supply of magnesium for its active transport. These essential vitamins and minerals, as well as a handful of other nutrients, have earned a place as staples in the bone health regimen, with a myriad of advanced delivery systems manifesting around them.

Over and above these staples for the optimal sustenance of bone health, certain research-based organizations have introduced innovations such as strontium to help those whose needs exceed that of preventative maintenance. One therefore cannot be faulted for at least questioning the need for yet further nutraceutical developments in the area of bone health. One such development is Milk Basic Protein, or MBP(r).

What Is Milk Basic Protein ?

The simplicity of the name is deceiving. It is well-known that bovine milk is rich in calcium and vitamin D (the latter being mainly a synthetic addition from the 1930's to fight rickets), but it has recently yielded yet another bone-building nutrient to science.

Milk in general (and bovine milk in particular) arguably contains more growth factors than any other single food source. Growth factors are specific proteins which act as intracellular signaling molecules by affixing themselves to the receptors of certain categories of cells and promoting their differentiation and growth. Transforming Growth Factor (TGF-ß), Insulin-like Growth Factor 1 (IGF-1), and Vascular Endothelial Growth Factor (VEGF) are among the more well-known of these proteins that are particularly present in mammalian milk. Nearly all of the growth factors in milk possess what are called basic isoelectric points.[2]

Basic isoelectric points are derived from one of the most common techniques used for separating mixtures of proteins, namely the two-dimensional polyacrylamide gel. In these gels, proteins are separated in one dimension which is determined by their molecular weights and in another dimension which is determined by the pH level at which they take on a negative charge. That pH level constitutes the isoelectric point of that protein.

Scientists in Japan used this method to isolate the biologically active components of whey protein which they had determined to have positive metabolic effects on bone health. These determinations included studies reporting whey's ability to suppress osteoclast (bone teardown) cell formation and resorption[3] as well as stimulate the proliferation and differentiation of osteoblast (bone building) cells.[4]

Protein constitutes less than 3.5% of the molecular weight of milk, and less than one-fifth of that amount (0.6% of milk's molecular weight) consists of whey. The remaining 2.9% majority consists of casein, but it was within the minority whey fraction that the scientists found what they were looking for.

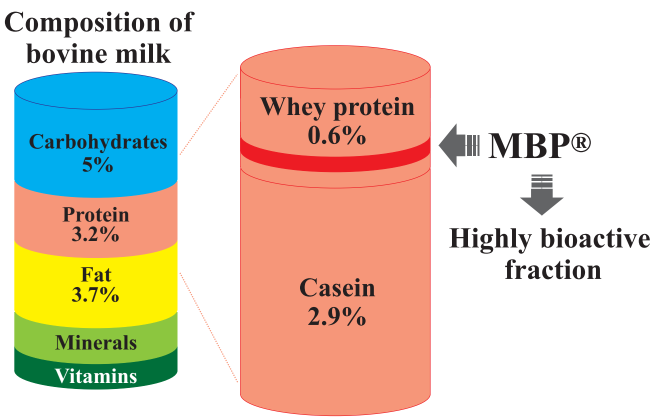
MBP is a compounded protein fraction separated from bovine whey.

What they found, using the isoelectric points as bioactivity markers, were the compound alkaline fractions most directly responsible for the bone-enhancing properties of whey protein. The Japanese scientists designated this series of fractions as a proprietary discovery known as Milk Basic Protein, or MBP. The terms 'milk' and 'protein' refer to the source and type of nutrient respectively, while the term 'basic' refers to its alkaline nature. The protein strains within MBP have basic isoelectric points ranging from 7.0 to 10.5 and contain much higher amounts of the essential amino acid lysine and the conditionally essential amino acid arginine than casein does.[5]

The Science of MBP

At first glance, the mechanism of action through which MBP exerts its effects seems remarkably similar to that of its bone-enhancing nutrient predecessors. For example, MBP assists in the absorption and retention of calcium, just as vitamin D does. Unlike vitamin D, MBP does so via the inhibition of cystein protease due to the presence of the protein strain known as cystatin C, which is part of the structure of MBP itself.[6] Cystatin C also inhibits the release of calcium from bones stimulated by thrombin, interleukin-1 and prostaglandin E2.[7] The essential nature of this function cannot be understated, as calcium is the "mortar" for the collagen matrix- together contributing to form the complex that is bone.

Cystein protease also digests collagen in the bone matrix, further testimony to the benefit of its inhibitory effect from the cystatin C in MBP.[8] The collagen factor brings us to another interesting link between MBP and its predecessors, namely MBP's effect on the relationship between osteoblast cells and osteoclast cells. Like strontium, MBP cultivates both the proliferation and activity of the bone-building osteoblasts while conversely bridling the same proliferation and activity among the osteoclasts responsible for the resorption (breakdown) of older bone tissue.[9] Even more revealing is the extent of MBP's inhibition of osteoclasts, suppressing the activity of even the most isolated osteoclast cells.[10]



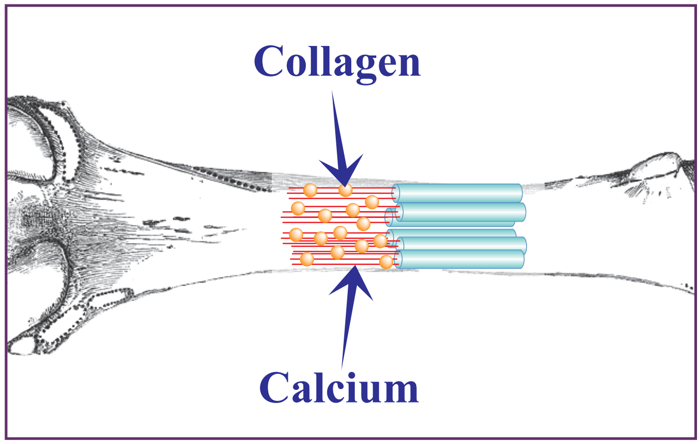
The association between the osteoblast/osteoclast relationship and collagen lies in the ability of osteoblasts to produce collagen, and it is here where MBP comes in to its own. The ability to specifically manipulate osteoblasts into producing more collagen in a manner that is more pronounced than that of its osteo-nutrient predecessors is an additional factor that makes MBP unique. Furthermore, MBP also increases serum concentrations of osteocalcin (BGP, also called Gla protein), which is the major non-collagenous protein in bone.[11]

A Brief Summary of the Effects of MBP

- Stimulates the activity and proliferation of bone-building osteoblast cells
- Stimulates collagen production
- Suppresses the activity and proliferation of osteoclast cells responsible for bone resorption
- Greatly improves the absorption and retention of calcium within bones

Science In Action: What The Studies Say

The recent scientific isolation and practical procurement of MBP has lead to numerous studies with excitingly impressive results.



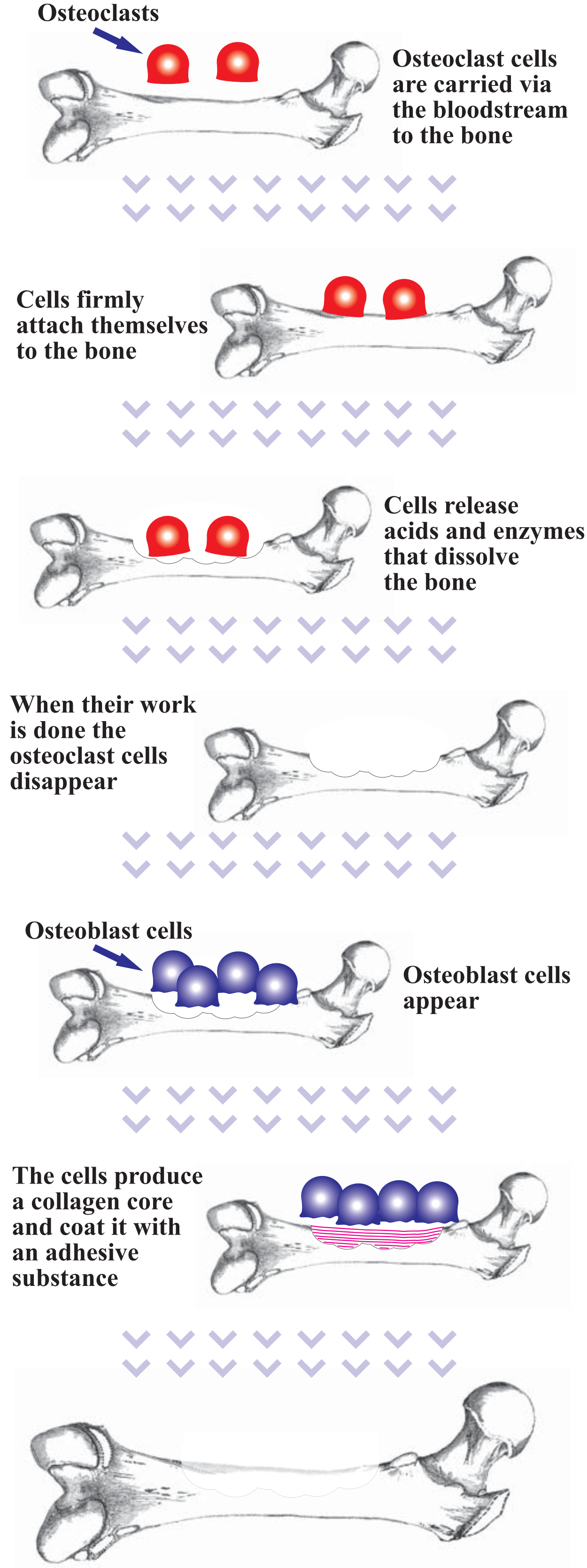
The latest among these studies examined the effects of MBP on the demographic that is undoubtedly the most vulnerable to the onset of osteopenia/osteoporosis, namely menopausal women. In this study, thirty-two healthy menopausal women were randomly assigned to treatment with either a placebo or MBP (40 mg per day) for 6 months. The bone mineral density (BMD) of the lumbar vertebrae of each subject was measured by dual-energy X-ray absorptiometry (DXA) at 0 and 6 months of treatment. Serum and urine indicators of bone metabolism were measured at 0, 3 and 6 months. Twenty-seven subjects who completed the study in accordance with the protocol were included in the analysis. The MBP group had a bone mineral density (BMD) increase of 1.21% while the placebo group lagged significantly behind with a 0.66% BMD decrease.[12] When compared with the placebo group, urinary markers indicating a loss of type-I collagen were significantly decreased in the MBP group at 6 months. The urinary excretion markers were found to be related to serum osteocalcin in the MBP group at 3 and 6 months, indicating that MBP maintained the balance of bone remodeling. These results suggested that MBP supplementation 'was effective in preventing bone loss in menopausal women'.[13]

MBP was eventually identified as a result of in-vitro studies that were done to identify more accurate methods of measuring the effects of various interventions on osteoclast formation and activation.[14] The more effective interventions were identified and sequestered for further study. Whey protein quickly emerged as superior, and was further investigated to isolate the source (MBP) of its influence on the osteoblast/osteoclast dynamic. A 1996 study revealed that whey protein increased the incorporation of the nucleotide thymidine as well as the overall DNA content within osteoblast cells.[15] More revealingly, it had a particularly enhancing effect on the hydroxyproline content of those cells, as hydroxyproline is a major constituent of collagen.[16]

The authors of this study began a process to isolate the bioactive ingredients in whey protein which were responsible for these and numerous other biological actions. This trend continued in another study conducted the following year, when in addition to fortifying osteoblasts, whey protein was also shown to suppress osteoclast-mediated bone resorption and osteoclast cell formation.[17] This was done using the highly reliable method of evaluating the number and area of pits formed on the surface of the bone by the osteoclasts.[18] This in-vitro research showed that the area of the pits formed in those treated unfractionated bone cell cultures were up to 2.4 times smaller than those of the untreated control group on a dose-dependent basis.[19]

The isolation process continued until the active component of whey protein that the Japanese scientists were looking for was determined to have an amino-terminal sequence identical to that of bovine high mobility group protein (HMG).[20] HMG is a family of proteins involved with the structure of chromatin and thus plays a precursory role in DNA replication. This led to the short-term designation 'HMG-like protein', a name that lasted until a successful in-vivo study involving laboratory rats took place in 2000, when the term 'Milk Basic Protein' was coined.

The Interaction of Osteoblasts, Osteoclasts, Collagen, Calcium and Bones



Calcium adheres to the collagen, forming new bone tissue

After further success with laboratory animals, the first study among humans was finally conducted the following year. In it, thirty-three healthy women were randomly assigned to treatment with either a placebo or MBP (40 mg per day) for six months. The bone mineral density (BMD) of the left heel bone of each subject was measured at the beginning of the study and at the end. Serum and urine indices of bone metabolism were measured at the base line, three-month intervals, and again at the end of the study. Daily intake of nutrients was monitored by a three-day food record made at three and six months.[21] When standard BMD testing was conducted at the end of the study, the women in the MBP group gained approximately 70% more bone mineral density than the control group.[22] Furthermore, urinary markers of bone loss - in this case, cross-linked type-I collagen/creatinine and deoxypyridinoline/creatinine, were 'significantly decreased' in the MBP group.[23]

A study among healthy adult men was similarly impressive,[24] as well as another study among healthy adult women in 2002. This particular double-blind, placebo-controlled trial measured radial bone mineral density, and once again the mean BMD value of the MBP group was 'significantly higher' than that of the placebo group.[25]

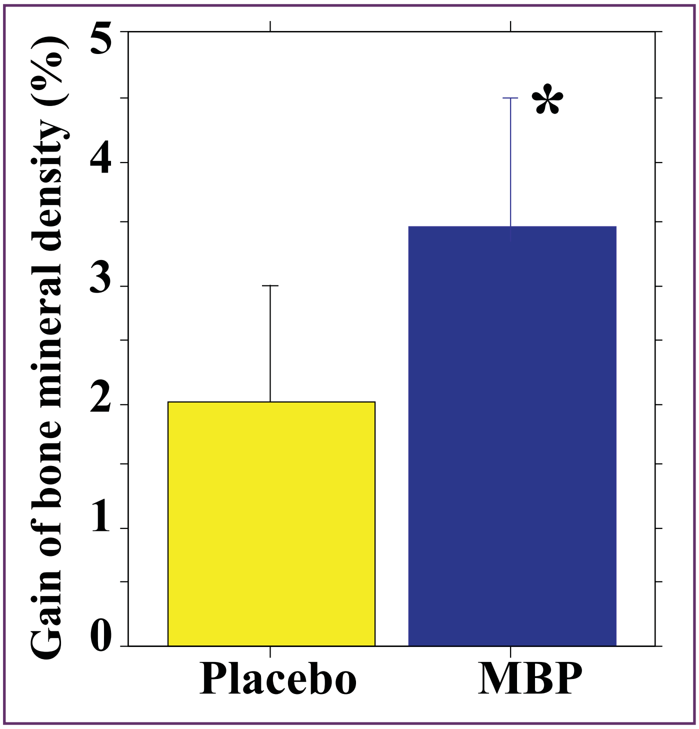
A Brief Summary of the Results of MBP Studies

- In a study among healthy menopausal women, the MBP group reported a bone mineral density (BMD) increase of 1.21% while the placebo group recorded a 0.66% BMD decrease.[26]
- In another study among healthy adult women, the MBP group gained approximately 70% more bone mineral density than the control group.[27]
- MBP reduced the number of pits on the bone surface caused by bone resorption by approximately 85% in an in-vitro study.[28]
- In yet another study among healthy adult females, the MBP group displayed a 3% increase in the BMD of the radius (a forearm bone near the wrist) compared to a 1.3% BMD decrease in the placebo group.[29]

In Conclusion

Milk Basic Protein offers certain advantages some over other osteo-nutrients. The following is a brief summary of these advantages.

- MBP can be taken with or without food.
- MBP can be taken with calcium.
- MBP comes in very small capsules, making it convenient and easy to swallow
- MBP utilizes different mechanisms of action than its osteo-nutrient predecessors, making it an augmentable or even synergistic addition to any osteo-protective protocol.
- MBP has no known interactions and can be safely consumed by anyone who is not lactose intolerant.



Gain of Bone Mineral Density in Healthy Adult women Given Placebo or MBP Supplementatin for Six Months.
Error bars represent 95% confidence intervals. Significant differences between the groups are indicated by asterisks (P<0.05).

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