

MOVING ON UP

Protecting bone and joint function is a priority for almost everyone today. Here's how to formulate products that keep us all moving up, down or sideways.

By Lisa Schofield

A common item that makes everyone shudder and say, "not me" is the wheelchair. It is the paramount symbol for loss of mobility (broken bones or joints that won't work).

But it also serves as a motivator for reasonably healthy adults of all ages to take care of themselves and be proactive about bone and joint health. This category has grown and morphed in numerous ways, which should impact R&D for mobility support.

According to Annie Eng, CEO, HP Ingredients, Florida, this supplement sector has improved dramatically in ingredient research and availability. It has moved beyond the staples of calcium and vitamin D to include botanicals with compelling studies showing bone and joint support benefits. In addition, "such botanicals can work synergistically with traditional bone and joint supplement ingredients (such as calcium, vitamin D, omega-3 EFAs) to provide opportunities for product distinction in the marketplace."

Ingredients themselves are shifting the wave of change for this category. "Longtime

joint health headliners glucosamine and chondroitin are fading in popularity, perhaps because it's hard for consumers to feel immediate results from these products," observed Eric Anderson, managing director, NXT-USA, New Jersey. Agreeing with Eng, he stated, "As consumers look for alternatives, sales of botanical blends are growing rapidly."

In the viewpoint of Shil Kothari, CEO, Nevada-based IminoTech, Inc., one trend occurring in the past few years is the growing consumer awareness and recognition of alternatives to glucosamine and chondroitin that still dominates the market. These include collagens, turmeric, SAME, boswellia and emerging ingredients such as iminosugars.

For bone health, the trajectory has been strong and distinct, according to Jeff Lind, executive vice president, Synergia Life Sciences-US (a Novozymes One Health company), New Jersey. "First there was calcium for bones, then there was vitamin D3 for calcium absorption, and now there's vitamin K2 for proper utilization of calcium

to the bones and away from the heart and soft tissue," he summarized.

Newer research points to managing homocysteine as a factor in preserving bone health. According to Silvia Pisoni, market manager, reproduction & women's health, Gnosis by Lesaffre, France, the regulation of homocysteine levels and the modulation of the inflammatory markers could represent additional therapeutic approaches for bones, as suggested by recent research revealing a link between hyperhomocysteinemia and low bone mineral density (BMD). Hyperhomocysteinemia was also associated with high inflammatory marker C-reactive protein levels and low vitamin D, vitamin B12 and folate levels in 252 post-menopausal women.

Homocysteine, inflammation, bone-resorption markers and prevalence of C677T polymorphism were higher, whereas vitamin D, B12, folate and bone formation markers were lower in women with decreased BMD compared to those with normal BMD. Furthermore, 77 percent of women with low BMD presented with the C677T MTHFR

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polymorphism, while only 37 percent of women with normal BMD presented with the mutation. "Taken together," she concluded, "these results suggest an association between the C677T MTHFR polymorphism and elevated homocysteine levels and inflammation, which may further influence the onset of compromised bone health."

The target audience has evolved as well—it isn't just for "gran and gramps" with their walking canes anymore. Jacqueline Rizo, digital engagement & communications specialist, Stratum Nutrition, Missouri, said, "An aging population is certainly a significant contributing factor to the growing need for joint health solutions. However, the 21st century senior citizen is not just content with being active. These individuals remain vibrant and busy and competitive in all aspects of their lives."

Angie Rimel, marketing communications

manager, Gelita, agreed, expounding, "We see an increase in the sports nutrition market as the worldwide wellness and fitness industry is booming. From barbell classes to CrossFit to high-intensity interval training, to running to cycling, physical activity can take a toll on your bone/joint health status. Consumers, she pointed out, are increasingly realizing both overuse and increasing age make tendons, ligaments and joints more injury prone and put bones at increased risk of stress fractures. "White tissue injuries account for more than 70 percent of time away from exercise regimens, indicating that there is a real need for nutritional strategies to strengthen the white connective tissue."

On the bone-health side, she added, stress fractures from an active/fitness lifestyle account for up to 20 percent of all injuries seen in sports medicine clinics. Sports of non-weight bearing nature, such as endurance cycling, also put many well-trained athletes and active lifestyle consumers at risk of low bone mineral density, at premature age.

Relatedly, Anderson observed that recovery has become important in the active nutrition community, as today, most people are aware of the need to both train

and recover safely as well as effectively. Most consumers, depending on their level of training, will more than likely experience joint-related issues, such as pain or connective tissue problems. And rather than wait until the point of no return, they are taking supplements as a preemptive action to support their joint health.

Other growth aspects in the bone and joint support category include, according to Kothari, the increasing number of combination products supporting both bone and joint health. "Consumers increasingly want these twin benefits in a single product even though this requires multiple ingredients that specifically benefit bones, articular cartilage and connective tissues." However, he added, combination products can present a formulation challenge because effective amounts of some ingredients require very large dose amounts.

Yet, some in the industry believe that bone and joint health may be most effective if left singular. Said Francis Foley, president, New Jersey-based Xsto Solutions, LLC, "While bone health and joint health supplements may make sense and come together at the consumer level, the science behind these two areas differs. Historically these

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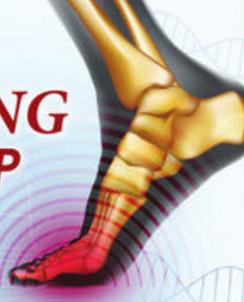
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were two separate categories, but they are moving together and now arguably overlap. It may never be a total eclipse, but there is demand from consumers who want one product to address both health concerns."

According to Tanja Budde, consumer goods director innovation & technical marketing, Omya International AG, Switzerland, global launches of new products targeting bone and joint health in supplements, food and beverages are stable. "According to Innova Market Insights, supplements with bone and joint health claims accounted for 49 percent of new product launches worldwide in 2020," she noted. And, added Anderson, the joint relief category has been shown to hold the highest price per unit of any nutraceutical category, at a 34 percent premium.

There is another opportunity for R&D in the bone health category that is rapidly emerging: babies and children. As young-

er moms are prompted to support bone health to enjoy an active life in their elderly years, they are also primed to consider ensuring their kids are on the right path as well. Bone support beginning in childhood is critical. "We reach our peak bone mass in our 20s-30," explained Hogne Vik, chief medical officer, Gnosis by Lesaffre. "Once that peak is reached, that is all we get. From there it is about staving off a steady decline of our bone mass, and women's bone mass takes a sharper decline once they reach their menopausal years due to hormone changes. One in two women is expected to incur future bone fractures due to poor bone metabolism, whereas the risk to men is one in three."

Lind agreed, emphasizing that bone loss is conventionally associated with getting old, but it should be addressed during childhood and young adulthood. "If we can build a solid 'bone bank' early on, the foundation will have been laid for better bone health as we get older," he stated.

The concept of staving off bone (and joint) deterioration in elderly years was the initial driver for this category but it has evolved rather dramatically and is directly relevant for a much wider consumer base.

According to Anderson, more than 92 million adults experience joint discomfort. This is not just a problem for adults over 65; nearly one in three people aged 18 to 64 report joint discomfort. "Beyond this, masses of adults seek ways to maintain healthy joints to experience the liberation of enjoying active lifestyles, be they serious athletes, weekend warriors or people simply wanting to move in comfort on the lifelong wellness journey," he commented.

Indeed, underscored Rizo, bone-joint health supplements are no longer being marketed solely to Baby Boomers. Marketers should not underestimate the extent of potential joint problems among younger generations. More Millennials are invested in their health and wellness for the long haul and should certainly be considered a main target for brands developing bone and joint products. According to Goldman Sachs, "For Millennials, wellness is a daily, active pursuit. And this is one space where they're willing to spend money on compelling brands."

She added that Millennials and Generation Z consumers are driving transformation in dosage forms by increasingly incorporating supplements into their health

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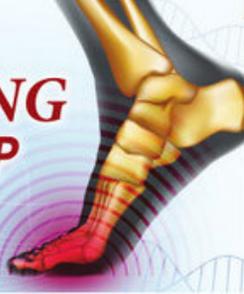
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regimens—and in the “Age of Me,” they seek convenience in tandem with an overall pleasant experience.

Now nearing 40 years old and soon to be the largest, living adult generation, many Millennials are beginning to feel the sense of loss when it comes to invincibility and youthfulness, and this makes them a high-value demographic for supplement brands.

Younger adults have a desire for portable products, such as ready to drink supplements, stick packs, gummies and more, “so brand marketers and product formulators need to be able to formulate with ingredients that have good taste, are soluble, and have proven efficacy,” stated Patrick Stano, brand manager, Stauber USA, California.

When considering formulating bone and joint support products aimed at younger adults, Foley advised starting with the mindset differentiating factor—“risk reduction” for younger adults vs. “repair” for older consumers.

“Bone and joint health products are not the supplements for elderly consumers only, but in fact today, this category attracts more younger consumers who are following active lifestyle and regular gym goers. The joint and bone health products are not only meant for managing the joint health but also for better recovery and delaying or inhibiting the onset of DOMS or delayed onset of muscle soreness,” said Anurag Pande, PhD, Sabinsa Corporation, New Jersey.

Ingredients to Consider

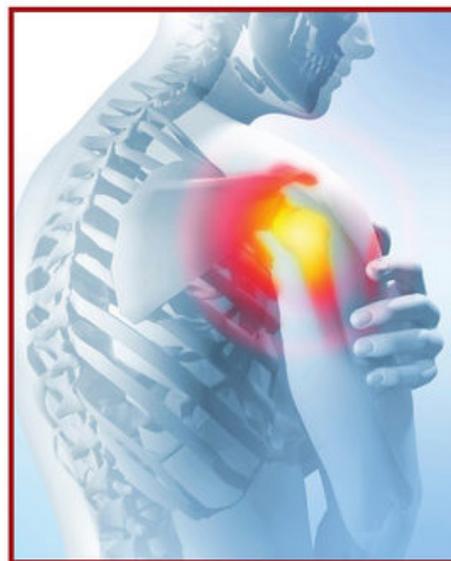
Bone health and calcium go hand in hand, and with calcium now, K2 menaquinone-7 is generating much buzz.

Gnosis by Lesaffre’s MenaQ7 has a breakthrough three-year study. The trial of 244 healthy post-menopausal women taking 180 mcg dose of MenaQ7 Vitamin K2 as MK-7 daily yielded unprecedented results, according to Dr. Vik. “Clinically statistically significant protection of the vertebrae and the femoral neck (hip) against bone loss was the result of a daily nutritional dose of MenaQ7. After three years of supplementation, maintenance in both bone mineral content and bone mineral density were statistically significant in the MenaQ7 group, as well as statistically improved bone strength,” he explained.

Synergia’s MenaquinGold Natural Vitamin

K2-7 is a fermented, natural vitamin K2 in its most bioactive form, Menaquinone-7 (MK-7). MenaquinGold, made from chickpea, is patented and backed by more than 50 clinical studies and papers, is non-GMO (genetically modified organism), and is FDA (U.S. Food and Drug Administration) GRAS (generally recognized as safe) for children, according to Lind.

Stauber USA offers Aquamin, calcified red algae rich in calcium and 73 other minerals. According to Stano, Aquamin has been shown in numerous studies to enhance bone mineralization in osteoblast formation and also to reduce discomfort and stiffness as well as improve walking distance while reducing reliance on NSAID (non-steroidal anti-inflammatory drug) medications.



Aquamin has been tested against widely recognized materials such as glucosamine and has been shown to be more efficacious. For example, a 2020 study showed that Aquamin significantly reduced pain levels and NSAID intake in human subjects/patients with OA (osteoarthritis) and did so to a greater extent than glucosamine, he noted.

Omya’s Calcipur and Omyapure are natural calcium carbonates, and well-established for calcium fortification, according to Budde. Natural calcium carbonates have a high level of elemental calcium at 39 percent and thus only 770 mg of Omyaforte is required to satisfy 30 percent of the RDA (recommended daily allowance). “Omyaforte has an innovative new mineral composition and structure based on high-purity natural calcium carbonate which has been functionalized via our patented re-crystallization process,” she described. “This unique feature ensures optimum calcium solubility in the gastrointestinal tract for enhanced bioavailability.”

Stratum Nutrition supplies ESC, a natural

calcium ingredient derived from chicken eggshells. ESC is low in heavy metals, 50 times lower than California’s strict Proposition 65 minimum levels, according to Rizo. “Also, ESC contains a high level of elemental calcium, 35 percent or higher, and it is readily absorbable through the intestinal tract.”

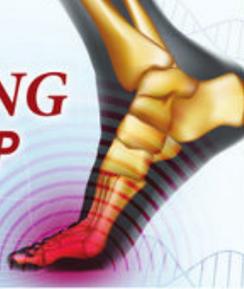
Collagen in bones is essential for bone flexibility and elasticity, according to Rimel. The peptides in FORTIBONE stimulate bone cells to increase the synthesis of bone components such as collagen to improve bone mass density and support bone stability and flexibility. The peptides signal osteoblasts to trigger collagen synthesis and thus counterbalance the collagen degradation in the extracellular bone matrix, which is the essential framework for bone mineralization. “FORTIBONE influences degenerative processes in bones by reducing osteoclast activity. The result is a considerably higher synthesis of collagenous bone matrix.”

Quatrefolic from Gnosis by LeSaffre, said Pisoni, can help postmenopausal women to normalize homocysteine, which contributes to bone health, and provides a form of folate that is biologically active and not dependent on the metabolization of the MTHFR enzyme. Quatrefolic may lower and normalize homocysteine levels as shown in a randomized clinical trial where hypertensive subjects at low cardiovascular risk received 400 µg/day for two months versus a conventional vitamin supplementation with highly dosed folic acid (5 mg/day). “Quatrefolic supplementation was more effective in reducing homocysteine serum level than folic acid, normalizing homocysteine in 55.8 percent of cases, significantly higher than in the control,” she said.

Stratum Nutrition’s NEM partially hydrolyzed eggshell membrane is, said Rizo, “exceptionally suited” to joint health applications. Through a patented enzymatic process, the natural eggshell membrane is predigested enough to begin digesting the fibrous membrane and release the nutrients within, allowing the components to benefit joint health in two different ways. One is enhancing optimal bio-accessibility for absorption through the intestinal wall and utilization in joint tissue. Second, the pre-digestion releases collagen peptides, that interact with the gut immune system and help facilitate NEM’s functioning systemically via oral tolerance. This two-prong functioning would not be possible if NEM were either fully hydrolyzed or unhydrolyzed.

There have been two significant developments in recent months related to research on NEM, both on healthy adult populations. One evaluates the effects of joint thera-

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peutics on cartilage turnover in healthy subjects while the other assesses the effects of NEM supplementation on joint cartilage breakdown as well as the pain and stiffness associated with a new exercise regimen was also completed in recent months.

Also for joint health, NXT-USA's TamaFlex is a patented standardized plant-based synergistic blend of two ayurvedic ingredients historically used for joint discomfort and newly recognized benefits—tamarind seed (*Tamarindus indica*) and turmeric root (*Curcuma longa*). According to Anderson, TamaFlex "utilizes the world's first tamarind seed extract, newly recognized for its efficacy as an anti-inflammatory, enabled by the antioxidant-rich seed of the tamarind plant for joint care and digestive support. TamaFlex offers a three-pronged approach to exercise recovery by inhibiting inflammation through the COX and LOX pathways and preserving tissue and cartilage integrity."

He added that TamaFlex is also supported by two clinical studies—one in healthy subjects and a second in subjects with mild knee osteoarthritis. TamaFlex was shown to support joint comfort, function and mobility in both studies, and in as few as five days in the second study. In the second study, biomarker analysis found significant reductions in biomarkers of systemic inflammation, and inflammation of synovial joints. TamaFlex also significantly reduced Matrix metalloproteinase-3 (MMP-3), the compound that degrades connective tissue.

HP Ingredients' ParActin, said Eng, "is the most researched *Andrographis paniculata* extract with a unique standardization profile." Patented ParActin's benefits arise from its powerful ability to manage the body's primary inflammation pathway via inhibition of NF- κ B, which has direct impact on joint comfort and flexibility.

ParActin is a patented extract of *Andrographis paniculata*, standardized to andrographolide, 14 deoxyandrographolide, and neo-andrographolide. ParActin inhibits NF- κ B activity, by reducing its natural inclination to bind to DNA, thereby reducing pro-inflammatory cytokines such as COX-2 and prostaglandins that cause joint discomfort. *In-vitro* research showed ParActin to be a natural COX-2 inhibitor without the typical side effects associated with prescription COX-2 inhibitors.

Newer research shows that ParActin

significantly increases Nrf2 activity, unbind Nrf2 from Keap1, and activates the Antioxidant Response Element (ARE) signal pathways, increasing antioxidant enzymes such as glutathione, superoxide dismutase (SOD), heme oxygenase-1 and catalase (CAT). Andrographolide also activates both the Nrf2-p62 signaling pathway as well as autophagy-related genes and proteins (Beclin-1 and LC3) to get rid of damaged and/or senescent cells.

Xsto's Cuvitus is shown to support joint health by reducing pro-inflammatory cytokines, and according to Foley, is synergistic with its K2Quest vitamin K2 MK7. "The metabolic activity of K2Quest is unique and different than our novel cucumber-sourced Cuvitus, so we see a place for both in this overlapping space of bone and joint health," he commented.



IminoTech Inc. offers Q-actin, a patented cucumber extract that clinical research shows can help support healthy joints, according to Kothari. Q-actin is an iminosugar, a biologically active class of carbohydrates that helps modulate certain cellular functions.

Ex-vivo research shows Q-actin works through complementary mechanisms. It reduced LPS-induced tumor necrosis factor alpha (TNF- α), an inflammatory cytokine that can increase metalloproteinases, enzymes that lead to a breakdown in cartilage. Q-actin also inhibits α -L-iduronidase and sialidases, enzymes involved in the inflammatory process that can enable microorganisms to degrade glycosaminoglycans that support connective tissues, including articular cartilage and tendons.

A newly published clinical study shows that Q-actin improves joint function and reduces discomfort significantly better than glucosamine-chondroitin. In the six-month study 122 subjects with mild to moderate joint complaints took either 20 mgs of

Q-actin daily or glucosamine/chondroitin. According to Kothari, the Q-actin group showed significant improvement over those consuming 2,700 mgs of glucosamine-chondroitin.

"We are particularly excited to see products hitting the shelves that combine OptiMSM with collagen—specifically Type II collagen—and its inclusion in products with hyaluronic acid and botanicals such as curcumin, boswellia and ashwagandha, related Tim Hammond, vice president of sales and marketing for Bergstrom Nutrition (Vancouver, WA). "Studies also suggest MSM has potential to be used as a therapeutic agent to treat bone-depleting conditions, such as osteoporosis, where the mineralization of bone is impaired due to decreased osteoblast differentiation."

Sabinsa offers three botanical-based ingredients for supporting healthy joints and bones.

Curcumin C3 Complex supports healthy joints, healthy levels of inflammation, antioxidant and supports joint mobility, according to Pande. Boswellin Super supports healthy joints, healthy levels of inflammation, joint mobility, helps manage stiffness associated with exercise, and helps improve joint function. Sabinsa's Acticissus supports healthy bones, healthy inflammation levels and healthy bone density.

These ingredients represent a handful of the cache of science-backed products for supporting bone structure and joint structure and function. The possibilities and opportunities to help support overall mobility as we age abound. **NIE**

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