

Happy Joints, Happy Life

By Kate Lloyd, Celeste Sepessy and Sandy Almendarez

An estimated one-fifth of U.S. adults suffers from doctor-diagnosed arthritis, according to the Centers for Disease Control and Prevention (CDC), and two-thirds of obese people are likely to develop symptomatic knee osteoarthritis (OA) in their lifetime, making joint health a major concern for a large chunk of the population.

Americans are reporting arthritis, joint pain and the ability to carry out activities in old age among their top concerns, according to Catherine Adams Hutt, Ph.D., RD, CFS, chief science and regulatory officer, Sloan Trends. Arthritis has been one of the country's fastest growing health concerns since 2006, she added, and compared to other major health issues, the population is most active in both arthritis management and treatment.

"Joint health represents the number one condition-specific supplement category being used by American adults," said Paul Dijkstra, CEO, InterHealth Nutraceuticals. That reach extends globally, as Global Industry Analysts predicted the bone and joint product market to reach US\$9 billion by 2017.

"In the United States, middle-aged and the early elderly are more active than ever, and are much more likely to be engaging in some form of exercise and supplementation to allow them to fulfill their active lifestyles," said Sendhil Pani, head of international marketing, Bayir Inc. "The large joints tend to lose cartilage through years of simply living, and the resulting discomfort is driving millions to seek resolution."

According to Vanessa Agnolutto, communications manager at Nexira, joint health consumers can be split up into three groups that turn to specialized ingredients:

1. Baby Boomers who hope to continue an active lifestyle;
2. Overweight/obese individuals facing joint pain; and
3. Middle-aged adults looking to proactively preserve joint health.

Due to the complex need, many joint health ingredients target three main areas—promoting healthy joint tissues, protecting against inflammation and relieving pain. In some cases, ingredients tackle all three mechanisms of action.

"In the last couple of years, there has been a great number of studies focused on preventive care for joint health using natural products," said Anurag Pande, Ph.D., vice president of scientific affairs, Sabinsa. The results have been overwhelmingly positive, he said.

Research-Backed Natural Ingredients

Over time, cartilage wears down from normal everyday activities and the effects of OA can start to cause reduced flexibility and mobility. As a result, many natural ingredients target cartilage in some form or another—whether protecting or repairing the collagen-heavy tissue.

“Daily wear and tear of the joints leads to release of pro-inflammatory cytokines and upregulation of collagenases and aggrecanases by chondrocytes, ultimately leading to the breakdown of joint cartilage and the extracellular matrix,” Dijkstra said. “Pain and stiffness soon follow.”

It comes as no surprise that undenatured type-2 collagen is a key ingredient for bolstering joint health. The ingredient has been reported to benefit both OA and healthy populations in clinical trials. After taking 40 mg of UC-II (from InterHealth Nutraceuticals) for 120 days, healthy subjects had significantly improved knee extension and exercised longer before experiencing joint pain, compared to placebo.¹ In OA populations, research has shown UC-II improves joint comfort, mobility and flexibility, reducing Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores by 33 percent.²

A randomized, double blind, placebo-controlled trial from 2012 found 2 g/d of BioCell Collagen (BCC, from BioCell Technology), a low molecular weight dietary supplement consisting of hydrolyzed chicken sternal cartilage extract, caused significant reduction of visual analogue scale (VAS) pain after 70 days of treatment, and of Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores after 35 days and 70 days of supplementation.³ The BCC group experienced a significant improvement in physical activities compared to the placebo group at both 35 and 70 days.

An additional study presented at the 2004 Experimental Biology Meeting found 1,000 mg of BioCell Collagen taken twice a day for two months reduced WOMAC scores compared to placebo in subjects with OA of the hand or knee.

In sales, collagen products experienced an increase of 33.5 percent (\$1.6 million to \$2.1 million), according to data collected by SPINS, which tracks sales of vitamins, supplements, herbs and homeopathics marketed for joint health (within the U.S. combined natural and conventional channels).

Certain joint health ingredients are certainly on the rise, but as a whole, the sector had a less-than-stellar year in terms of U.S. sales during 2014. According to data collected by SPINS, which tracks sales of vitamins, supplements, herbs and homeopathics marketed for joint health (within the U.S. combined natural and conventional channels), the segment experienced an 11.6-percent decrease from December 2013 to November 2014 (USD \$358.9 million to \$317.4 million).

Among the top primary ingredients across all channels, **glucosamine/chondroitin** combinations fell 16.7 percent (\$246.6 million to \$205.5 million), while chondroitin alone fell 26.9 percent (\$3.0 million to \$2.2 million). Traditional ingredients for joint health, such as glucosamine and chondroitin, may have experienced decreased sales due to fact they’ve been “overplayed” in the market, Hutt said. She added these ingredients are helpful for some of the population, but not all, due to studies showing they can help certain consumers with specific types of joint pain.

While sales may be slowing, glucosamine and chondroitin are still recognized as the go-to combination for restoring joint health.

“The same drivers of aging population, more active lifestyles and obesity will continue to make joint health a viable and attractive market segment,” said Mike Fleagle, brand manager for Regensure® glucosamine, Cargill. “We will continue to see different new ingredients being touted as joint health ingredients. Some will gain a marketable audience, most will not. Glucosamine is still the most widely used and discussed joint health ingredient.”

Glucosamine treatment of chondrocytes from normal human articular cartilage activated autophagy, an essential cellular homeostasis mechanism that protects against certain age-related pathologies such as OA, in a 2013 *in vitro* study.⁴ The same study examined mice *in vivo* and found administration of glucosamine markedly activated autophagy in articular cartilage. The study authors reported, “These findings suggest that glucosamine is an effective autophagy activator and should motivate future studies on the efficacy of glucosamine in modifying aging-related cellular changes and supporting joint health.”

In a 2009 study, researchers found glucosamine administration (1.5 g/d and 3 g/d for three months) significantly decreased type-2 collagen degradation in soccer players; however, the effect disappeared after withdrawal of administration.⁵ In contrast, glucosamine administration did not affect the increased level of type-2 collagen synthesis, thus, the ratio of type-2 collagen breakdown to synthesis was reduced by glucosamine administration, but returned to the pre-administration level after withdrawal of administration.

In a follow-up study from the same group of researchers, glucosamine administration (1.5 or 3 g/d) also reduced type-2 collagen degradation in bicycle racers, particularly at a dose of 3 g/d.⁶ The ratio of type-2 collagen breakdown to synthesis was also reduced by glucosamine administration and the effect of glucosamine was dose-dependent.

Fresh research from the *Annals of Rheumatic Diseases* compared glucosamine and chondroitin sulfate to celecoxib, a nonsteroidal anti-inflammatory drug (NSAID).⁷ The double blind, multi-center trial of 606 patients with knee OA found chondroitin plus glucosamine supplementation (as CosaminDS from Nutramax Laboratories) just as effective as the NSAID. “Both groups elicited a reduction [of] more than 50 percent in the presence of joint swelling; a similar reduction was seen for effusion,” the authors wrote.

Comprised of collagen, chondroitin sulfate and hyaluronic acid—basically, the building blocks of connective tissue—**natural eggshell membrane** (NEM) offers a sustainable ingredient option for joint health. In 2014, one *Journal of Arthritis*-published, six-center study touted a single 500-mg dose of NEM reduced joint discomfort and increased flexibility.⁸

As the primary component in synovial fluid, **hyaluronic acid** (HA) is a crucial player in healthy joints. The compound, which is also found in eyes, acts as a lubricant and a cushion in the joints. According to Japanese researchers, daily dosages of 200 mg of HA improved pain and stiffness in OA subjects’ knees, and daily life condition significantly improved compared to placebo throughout the study and after 12 months.⁹

Anti-inflammatory Protection

“Many consumers today live in a state of chronic inflammation, which can increase the risk of many health conditions and diseases,” said Becky Wright, marketing director, Aker BioMarine Antarctic US. And aching, painful joints are one consequence felt across the world.

In a study of 90 patients with elevated levels of C-reactive protein (CRP, a marker compound for inflammation), **krill oil** (as Neptune Krill Oil from Neptune Technology and Bioresources) reduced CRP by 29.7 percent in just 14 days, compared to an increase of 32.1 percent for the placebo group.¹⁰

Fatty acids from bovine tallow oil also offer effective and natural anti-inflammatory compounds. Patients taking **cetylated fatty acids** (as Celadrin from Proprietary Nutritionals Inc.) improved knee range of motion and overall function in patients with knee OA.¹¹ Subjects took either placebo or 350 mg/d Celadrin for 68 days.

A separate double blind, placebo-controlled study conducted by Jay Udani, M.D., medical director of Medicus Research, reported after eight weeks of taking Celadrin capsules, (894 mg/d), average walking ability increased 45 percent in subjects ranging from 40 to 86 years of age, and participants claimed a 35-percent decrease in knee discomfort.¹² These improvements were significantly better than the results seen in the placebo group, and no negative side effects were found.

Efficacious ingredients also come from the botanical kingdom. “**Curcumin** has a long history of medicinal use due to its anti-inflammatory and antioxidant properties, and the science around curcumin has increased dramatically over the years with more than 7,000 citations currently in PubMed,” said Lynda Doyle vice president of global marketing, OmniActive Health Technologies. As the bioactive component of turmeric, curcumin interacts with multiple inflammatory pathways— inhibiting pro-inflammatory cytokine release and thereby suppressing inflammation.

Research from Baqiyatallah University of Medical Sciences, Tehran, Iran, solidifies curcumin’s benefits for OA. Subjects with OA took either 1,500 mg/d of curcumin (as Curcumin C3 Complex from Sabinsa) or placebo for six weeks.¹³ Supplemented patients had significant reductions in WOMAC, VAS and Lequesne's pain functional index (LPFI) scores. Of particular note were the improvements in pain and physical function markers. “The systemic inflammation markers were also studied, and it was believed that the benefits of curcumin in osteoarthritis arise from the reduction of inflammation in the osteo-cartilagenous tissue without impacting significantly the systemic biomarkers,” Pande said.

A patented extract of **Andrographis Paniculata** (as ParActin from HP Ingredients) administered at 100f mg/d for 14 weeks decreased the intensity of joint pain in patients with rheumatoid arthritis (RA) compared to placebo in a 2009 study.¹⁴ Those who took the botanical also had fewer tender joints and number of swollen joints. Patients treated with ParActin also showed improvement in CRP from above normal to a normal level, and demonstrated an ability to normalize immunoglobulin (Ig) A and IgM. The reduction in IgA and IgM is beneficial as there is positive correlation between the grade of cartilage damage.

In another study from 2013, 300 mg/d of ParActin for four years significantly improved total grade of tender joints and quality of life in patients with various rheumatoid conditions.¹⁵ In addition, researchers found a significant reduction in Rheumatoid Factor and CRP.

In various studies, **French maritime pine bark** extract has been demonstrated to promote joint health. A double-blind, placebo-controlled study found three-month treatment with French maritime pine bark (as Pycnogenol® from Horphag Research) significantly decreased joint pain and improved joint function, as evaluated using the WOMAC score and treadmill walking performance, in patients with osteoarthritis of the knee.¹⁶ In a follow-up study, the same researchers reported three-month treatment with Pycnogenol significantly decreased plasma free radicals to 70.1 percent of baseline values and decreased CRP levels from baseline 3.9 mg/l to 1.1 mg/l in a subset of the OA patients presenting with elevated CRP and plasma-free radical levels.¹⁷ No significant changes for plasma free radicals or CRP were found in the placebo-treated group.

A third double-blind, placebo-controlled, randomly allocated trial, 150 mg/d of Pycnogenol for three months improvement of WOMAC scores and alleviated pain per the VAS measurement in patients suffering from knee OA.¹⁸

In a double blind, placebo-controlled trial of 100 subjects, **methylsulfonylmethane** (MSM) showed promise in OA support.¹⁹ After 26 weeks of 6 g/d of MSM or placebo for 26 weeks, researchers reported MSM improved all physical symptoms in the WOMAC scale without any adverse events.

“While MSM’s mechanism of action is not fully understood, in-vitro studies, along with both animal and human trials, have shown MSM helps mitigate the oxidative stress that can lead to chronic inflammation,” according to Rodney Benjamin, Bergstrom Nutrition’s director of research and development.

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