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SPECIAL EDITION: INFLAMMATION

Are we set to see an increase in demand for anti-inflammatory formulations?

By Stephen Daniells+, 16-Nov-2015

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Healthy aging and increasing coverage by the mainstream media could help drive demand for products addressing inflammation over the next few years, say experts.

"We are seeing an increase [in demand for anti-inflammatory bioactives/formulations]," Patrick Morris, communications manager – Fortitech Premixes, DSM Nutritional Products, told NutraIngredients-USA. *"If we had to surmise as to why, I would have to say that it's due to more awareness being placed on health issues among consumers. The mainstream media has definitely brought attention to how our health can be related to inflammation. And, you're always seeing blurbs about an anti-inflammatory diet and its benefits."*

"I think that over the next five years, we will see an uptick in requests for formulations and products on the market addressing inflammation," added Morris. *"I think that will be due to the increasing presence of Millennials and their desire to proactively maintain their overall health and wellness, as well as boomers such as myself that embrace the healthy aging concept and will actively look for products to address inflammation. And, among these products, I think there will be many that are formulated using botanical ingredients."*

Inflammation comes in two forms: acute and chronic. The former is part of a healthy immune response. Chronic, low-grade inflammation is brought about by an over-expression or lack of control of the normal protective mechanisms.

In a review in *Nutrition, Metabolism & Cardiovascular Diseases* (2004, Vol. 14, pp. 228-232), Katherine Esposito and Dario Giugliano from the Department of Geriatrics and Metabolic Diseases at the Second University of Naples in Italy noted that *"obesity, insulin resistance, and diabetes are associated with a pro-inflammatory state, which in turn is associated with increased cardiovascular risk"*.

Chronic inflammation has also been linked to a range of conditions linked to heart disease, osteoporosis, cognitive decline and Alzheimer's, type-2 diabetes, and arthritis.

Biomarkers

A list of established biomarkers for inflammation exists, with commonly touted markers including C-reactive protein (CRP), interleukin-6 (IL-6), IL-10, IL-18, monocyte chemoattractant protein-1 (MCP-1), and tumor necrosis factor-alpha (TNF-alpha).

The link between inflammation and chronic disease has been strengthened by identification and acceptance of these biomarkers. Indeed, an article in the *New England Journal of Medicine* (2004, Vol. 351, pp. 2599-2610) evaluated the role of inflammatory markers heart disease risk in women, and concluded: *"Elevated levels of inflammatory markers, particularly C-reactive protein, indicate an increased risk of coronary heart disease"*.

Drivers

Fortitech Premixes by DSM released a white paper on the topic of *Fighting Inflammation with Fortification*, by Kevin Krall, associate scientist, and Cathy Arnold, regional manager.

"The opportunity to use nutrients to address inflammation could complement the growing market for anti-inflammatory drugs, which is substantial and is likely to grow in the future," wrote Krall and Arnold.

The authors added that an aging population and the growing obesity epidemic across the world represent a huge potential market for products that can deliver efficacious doses of anti-inflammatory bioactives.

Leading the pack of anti-inflammatory ingredients are the omega-3s DHA (docosahexaenoic acid) and EPA

(eicosapentaenoic acid). A study by Professor Manohar Garg from the University of Newcastle in New South Wales found that increased blood levels of the omega-3s DHA (docosahexaenoic acid) and EPA (eicosapentaenoic acid) were associated with reduced levels of CRP (*European Journal of Clinical Nutrition*, 2009, Vol. 63, pp.1154-1156).

Two paper published in 2012 in the *American Journal of Clinical Nutrition* indicated that increased intakes of omega-3 fatty acids may reduce a specific marker of inflammation and confer heart and anti-cancer benefits.

The papers focused on the effects of omega-3 on levels of inflammatory biomarkers that are involved in damage to cells called soluble adhesion molecules, particularly soluble intercellular adhesion molecule-1 (sICAM-1). It is generally accepted that low circulating level of sICAM-1 is good.

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The first of the papers was a meta-analysis by Yang et al. from the Bethune First Hospital of Jilin University in China. The analysis indicated that omega-3 supplements were associated with reduced levels of sICAM-1, which may contribute to a decrease in the risk of atherosclerosis.

The second study, by Touvier et al. from the National Institute of Health and Medical Research in Paris, indicated that increased levels of omega-3 may counteract the pro-carcinogenic action of sICAM-1.

Omega-7

There is also compelling evidence to support the anti-inflammatory potential of palmitoleic acid. Results of a randomized clinical trial from the Cleveland Clinic indicated that supplements containing the omega-7 fatty acid may slash levels of CRP by a whopping 44%. The study used supplements containing the Provinal-branded purified palmitoleic acid ingredient from Ohio-based Tersus Pharmaceuticals.

"We demonstrate that supplementation with purified palmitoleic acid in adults with dyslipidemia and systemic inflammation, 2 risk factors for cardiometabolic disease, leads to improved serum lipids and decreased inflammation," wrote the researchers in the *Journal of Clinical Lipidology* .

"Thus, purified palmitoleic may be a therapeutic approach in helping maintain lipid levels within a healthy range as well as improving inflammatory markers in patients with mild dyslipidemia and inflammation."

Vitamins

The link between oxidative stress and inflammation pulls in a few of the vitamins, notably vitamins A, C and E, stated Fortitech's Krall and Arnold. *"Antioxidant vitamins and other carotenoids may help prevent free radical damage and to help maintain healthy inflammation,"* they wrote.

A 2015 meta-analysis published in the *European Journal of Clinical Nutrition* (Vol. 69, pp. 867-873) on vitamin E and CRP concluded that both alpha- and gamma-tocopherol were capable of reducing serum CRP levels.

"It seems that vitamin E supplementation may be a good strategy for decreasing inflammatory conditions in susceptible people, although large well-designed randomized controlled trials are needed to confirm these results, which are based on a total sample of less than 500 subjects," wrote the meta-analysis authors.

Niacin (vitamin B3) has been reported to reduce CRP levels, and there is also data to support the potential anti-inflammatory potential of nicotinamide riboside, with a paper published in the *Journal of Medicinal Foods* (doi: 10.1089/jmf.2015.3439) reporting that NR may attenuate low grade chronic inflammation in lab mice.

While there have been reports of the potential anti-inflammatory potential of vitamin D, a recent paper published in *British Journal of Nutrition* (doi:10.1017/S0007114515002366) reported no link between vitamin D and inflammatory biomarkers in elderly subjects.

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Botanicals

Fortitech-DSM lists the main anti-inflammatory botanicals as lemon verbena, curcumin, and grape seed extract.

The anti-inflammatory potential of curcumin is becoming increasingly well-known among consumers to the point that the mere name on the label is enough to market its many benefits, Cheryl Myers, Europharma's head of education and scientific affairs, told NutraIngredients-USA at Expo East.

Curcumin has been shown to modulate the activity of NfKb, the signaling molecule that helps to switch on so to speak the inflammatory response in the nuclei of cells, she said.

"With curcumin you have the best natural support for inflammation," she said.

Bioactives & Antioxidants

Among the bioactives and antioxidants listed by Fortitech-DSM were CoQ10, quercetin, EGCG, soy isoflavones, L-carnitine, and polyphenols.

Pycnogenol, a polyphenol-rich extract from French maritime pine bark. In a 2006 study , German and Slovak scientists reported that a 200 mg dose of the pine bark extract for five days was associated with a 25 percent reduction in matrix metalloproteinase 9 (MMP-9) levels (*Journal of Inflammation*, 2006, **3**:1).

Minerals

Among the minerals, the most widely cited anti-inflammatory is magnesium, with NHANES data indicating that low consumption of the mineral (lower than the RDA) was associated with increased levels of CRP, compared with people who consumed adequate magnesium levels.

Indeed, a review in *Current Opinion in Clinical Nutrition & Metabolic Care* (2014, Vol. 17, pp. 525-530) concluded: "*Subclinical magnesium deficiency caused by low dietary intake often occurring in the population is a predisposing factor for chronic inflammatory stress that is conducive for chronic disease. Magnesium deficiency should be considered a nutrient of significant concern for health and well-being."*

Probiotics

An interesting developing area of research is how the gut microbiota may affect a person's inflammatory state.

A recent paper published in *MBio* described how *Lactobacillus rhamnosus* GG ATCC 53103 may stimulate anti-inflammatory activities of microbes already resident without changing the host's gut microbiota.

Another study using 'underappreciated' *Lactococcus lactis* bacteria found that a fermented milk with *L. lactis* I-1631 may help reduce intestinal inflammation and oxidative stress in lab mice with inflammatory bowel disease (*Proceedings of the National Academy of Sciences of the USA* , doi: 10.1073/pnas.1501897112).

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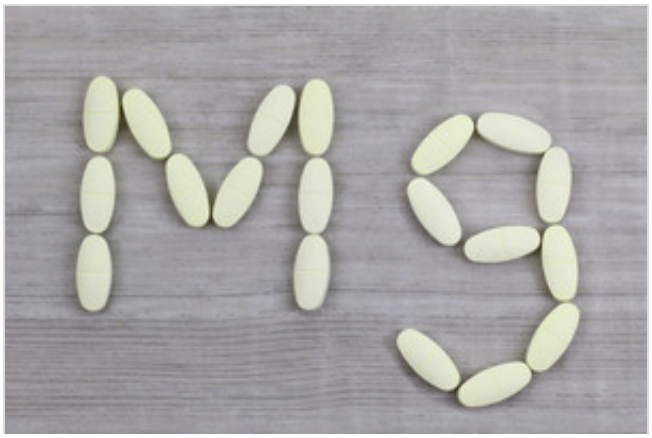

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There has also been some data to support synbiotics – a combination of pre- and probiotics. Data from a trial with obese children indicated that daily supplements containing seven probiotic bacterial strains and a prebiotic fiber may reduce markers of inflammation.

Writing in the *Jornal de Pediatria* , a bimonthly publication of the Brazilian Society of Pediatrics, researchers reported that eight weeks of supplementation resulted in significant reduction in TNF-alpha and IL-6, with the changes dependent on weight reduction.

"This trial was the first of its kind in the pediatric age group to investigate the effect of synbiotic supplementation on inflammatory factors in overweight and obese children and adolescents," explained the authors from the Isfahan University of Medical Sciences in Iran.

Editor's note: This list is not intended to be exhaustive and we apologize for any nutrients, bioactives, nutraceuticals that have been omitted.