



GIVING IMMUNITY

Stress and impaired immune function go hand-in-hand; here's why formulating for immune health with an eye on increasingly stressed-out populations is a winning idea.

By Lisa Schofield

Everyone would love immunity. More specifically, consumers, more active and engaged than ever, are seeking higher functioning immunity, and they are beginning to realize (thankfully) that promoting their immune health status is indeed a year-round initiative with year-round payoffs that accumulate in multifarious ways (from fewer bouts of colds/flu, to better energy, to better sleep, less mental fog, better mood, etc.). Healthy immunity is a golden ticket to a vibrant, sprightly life.

There was a time not too long ago when Americans only linked immune health with winter viruses. Now, for example, more consumers are aware that the gut plays an active, presiding role in immune status. More sophisticated knowledge on the part of consumers has created a platform for accelerated research and development activities in the past several years, leading to ingredient innovation for immune support.

"Strengthened immunity will benefit

everyone because many factors may contribute to a weakened immune defense, such as: stress, pollution, poor diet, allergens, medications, sleep deprivation, medical procedures/surgery and aging," noted Hank Cheatham, vice president of Daiwa Health Development (Gardena, CA).

"Immune support is an area of supplementation that holds both great opportunity and great risks," commented Nena Dockery, technical services manager for Missouri-based Stratum Nutrition. Researchers continue to learn more about how food and supplement ingredients influence human immune response, particularly in the digestive tract, as well as how our indigenous bacteria and microorganisms consumed as probiotics can protect from harmful microbes. Recently, she pointed out, there has been more investigation into the health benefits of bacteria that reside elsewhere in the body. "We know that most pathogens enter the body through the

nose and mouth, and we now can begin to appreciate the role that bacteria in the oral cavity play in helping provide a protective barrier against these invaders," she said.

As an example, Dockery pointed to research on the indigenous bacterial strain, *Streptococcus salivarius* K12. This rare human strain has been shown in multiple studies to provide strong protection against microbes that cause upper respiratory infections, such as strep throat, and middle ear infections.

With antibiotic-resistant bacteria on the rise, and people dealing with overflowing lives, it's a great time to formulate immune-support products.

"Health care costs are rising rapidly making the prevention of infections by microorganism more important than ever," said Guy Woodman, general manager with Pennsylvania-based Euromed USA. The medical community has been warning about the possibility of multiple antibiotic-resistant pathogenic organisms

taking hold in the coming years, which he said underscores the importance of a responsive immune system.

According to a recent survey conducted by the Natural Marketing Institute (NMI) and commissioned by New Jersey-based Lonza Consumer Health & Nutrition (CH&N), 36 percent of U.S. supplement users look for products that help boost immunity, cited Juliana Erickson, senior marketing manager, Lonza Consumer Health & Nutrition.

In the viewpoint of Don Cox, director of R&D for Wellmune and GanedenBC³⁰, Ohio-based Kerry Functional Ingredients & Actives, immune health is the foundation of a better quality of life and is increasingly becoming the cornerstone of consumers' holistic approach to wellness. "As such, it's no surprise that research from Global Data shows supporting immune function is the leading health concern among consumers, with 87 percent of them expressing an interest in buying food and beverage products that deliver this benefit," he said.

Melanie Bush, chief science officer for Artemis International, Inc. in Indiana, observed that there are pharmaceuticals, treatments, supplements and functional foods and beverages that address nearly every possible health condition "but immune health is arguably the most important category; its relevance spans consumers from every walk of life and health status. Regardless of age, race, gender or lifestyle, the ability to remain healthy and free from illness is high on everyone's priority list—all year long."

However, she added, immune health isn't just about fending off a cold—the immune system, if imbalanced, is integrally tied to other conditions like gut dysbiosis and inflammation. Further, these conditions can lead to a whole host of health conditions ranging from free radical oxidative damage, cardiovascular insufficiency, cognitive deterioration and premature aging. "It's all connected with the immune system at the core," she stated.

And that core is influenced and altered primarily through stress—and it may not be enough to just focus on directly addressing immune biochemistry, your formulas or mini-line may need to consider tackling stress adaptation and symptom relief as well.

To a degree, stress is largely subjective and tolerance varies between individuals, especially in cases of emotional impacts (such as relationship issues, social anxiety and deadline stress). However, there are

physical stressors that are universally damaging—poor diet (fried foods, fatty meats, sugars), polluted environment, use of chemically laden HBA products and over-exercising.

And every day brings some stressors to everyone; Woodman noted that daily stress increases the level of cortisol in the body. Ironically, he pointed out, elevated cortisol reduces the amount of inflammation in the short term, but over time the body adapts to excessive cortisol which leads to increased systemic inflammation. This chronic inflammation impairs immune response as it lowers white blood cell counts and thus, hampers ability to fight off infections effectively.

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Bush elaborated, "Since the immune system is so interconnected with other body systems, it makes sense that it also can be affected by numerous factors." Seasonal allergies strain the immune system, and everyday stressors like lack of sleep or a significant work project deadline can impact the effectiveness and responsiveness of a healthy immune system.

Immune Solutions

Consider the following for formulating the next generation of immune solutions for consumers who are beginning to demand all-year support.

When consumed, said Cox, Kerry's Wellmune is taken up in the body by the Peyer's patches in the intestines. Macrophages in the Peyer's patches ingest Wellmune and travel to immune organs throughout the body.

Macrophages disassemble Wellmune into smaller fragments that bind to neutrophils, (the most immune cells), which are then primed to recognize and disable foreign invaders.

Wellmune has several clinical studies showing immune support benefits for specific populations—children, athletes and individuals with high stress. A published, clinical study with children in a daycare setting showed that Wellmune helped decrease episodes of common childhood illnesses and symptoms of illness, with 62 percent of children taking Wellmune reported to have "good" health versus 15 percent of children who did not consume Wellmune.

In a clinical study with medical students, participants taking Wellmune experienced a reduction in URTI (upper respiratory tract infection) symptoms. A clinical study with stressed women showed a significant decrease in URTI symptoms as well as an 8.3 percent improvement in overall well-being and 26 percent increase in vigor. Another published clinical study with stressed adults found a 71 percent reduction in those reporting URTI symptoms and a 38 percent decrease in fatigue.

In a clinical study with marathon runners, participants taking Wellmune experienced a 40 percent reduction in upper respiratory tract infection (URTI) symptoms. Another study with both recreational and elite athletes showed that participants taking Wellmune had less risk of immune system suppression than typically follows high-intensity exercise.

For both immune and sports nutrition products, research on OptiMSM, methylsulfonylethane, suggests the supplement supports the innate immune system following exhaustive exercise, according to Tim Hammond, vice president of sales and marketing for Bergstrom Nutrition in Washington. Consumers may still be confused, "does it or doesn't it," meaning does exercise lower immunity? Hammond explained, "While exercise may boost immune function, strenuous training can exhaust the immune system and hinder the innate immune response. Viruses and bacteria may gain a foothold during this open window of altered immunity and lead to potential illness or downtime away from training."

He added that research on OptiMSM has shown that it bolsters immune response after exhaustive exercise—a time in which athletes are prone to decreased immune function. The researchers indicated that participants

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taking MSM showed lower serum levels of inflammatory markers post-exercise. This response indicated that OptiMSM conserved a healthy immune system after physical stress.

OptiMSM, Hammond described, supports immune function by lessening chronic inflammation through reducing levels of inflammatory cytokines and supporting a healthy inflammatory response. MSM also supports levels of glutathione, an antioxidant fundamental for immune function, and prevents immunosuppression caused by exhaustive and strenuous activity.

Berry flavonoids have been shown to boost the body's natural immune response, and also ameliorate cold and flu symptoms, according to Bush, who specified that black elderberry has been strongly linked to cytokine modulation, which protects against influenza. Bush reported in a recent randomized, double-blind, placebo-controlled human clinical trial long-haul international flight passengers who are especially prone to illness consumed Artemis' Black Elderberry prior to and during the flight. "Consumption of the elderberry supplement resulted in 35 percent less incidence of infections, a one-third shorter duration of the cold occurrences, a reduction in severity of cold symptoms, and three times better overall health reported by all passengers taking elderberry," she said. This study supported preliminary studies that showed direct antiviral and antibacterial properties of Artemis' black elderberry extract.

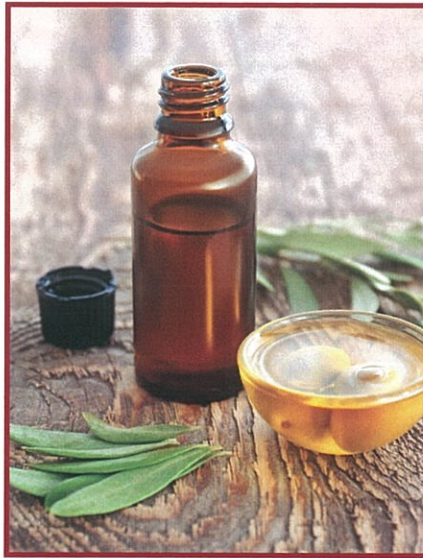
Another botanical extract with immune-boosting properties is olive leaf. Woodman explained that olive trees are naturally resistant to plant microorganisms and are particularly rich in oleuropein, a phenolic compound. Oleuropein has been shown in scientific studies to have antimicrobial activity against foodborne pathogens, such as *E. coli*, salmonella and listeria.

Researchers at the USDA (U.S. Department of Agriculture) have tested Euromed's Spanish olive leaf extract (SOLE), 18 to 20 percent oleuropein compared to four other commercially available olive leaf extracts, finding that

Euromed's olive leaf extract was the most potent of the five products tested, and inhibited *Listeria* growth at a concentration of 7.8 mg/ml, Woodman noted.

"Olive leaf extracts have been shown to provide an additive immune response with antibiotic administration to infection," he said. "One proposed mechanism of action is that oleuropein increases nitric oxide production in white blood cells that subsequently has a greater cytotoxic (cell-killing) effect on pathogenic organisms."

Woodman added that other studies have demonstrated the efficacy of pomegranate extracts against the growth of gram-positive bacteria and gram-negative bacteria suggesting it would be a good complementary ingredient. Euromed's Pomanox whole fruit pomegranate extract has been shown to have a prebiotic effect by decreasing the amount of two pathogenic bacteria, clostridium and bacteroids in human subjects.



According to Dockery, Stratum Nutrition's BLIS K12 is an oral-cavity probiotic that provides a physical barrier and deterrence to the entry of ingested pathogens. BLIS K12 is the probiotic form of *Streptococcus salivarius* K12, which is indigenous in only approximately 2 percent of the population. It works synergistically with other beneficial oral bacteria to competitively inhibit the colonization of undesirable bacteria.

She elaborated that BLIS K12 produces specialized substances called bacteriocin-like-inhibitory substances (BLIS) that target and destroy specific harmful bacterial species, becoming part of the body's clever arsenal of self-protection. BLIS K12 has been also shown to help

protect the oral cavity and upper respiratory area from inflammation caused by pathogens.

Stratum also markets Ahiflower oil, an omega-3,6,9 fatty acid ingredient from *Buglossoides arvensis*. Omega-3 fatty acids have been well-researched for their benefits in supporting a healthy immune response," and Ahiflower is a source of stearidonic acid, an omega-3 fatty acid that converts in the body much more readily than other vegan omega-3 sources to the beneficial long-chain polyunsaturated fatty acid, eicosapentaenoic acid," she described.

Lonza CH&N's ResistAid, a proprietary ingredient provides natural immune support, is produced via a patented water-based extraction process from North American larch trees, the ingredient consists of arabinogalactan (soluble polysaccharide) and bioactive polyphenolic flavonoids. It offers the ability to modulate and support the appropriate immune response based on the immune stressor, helping to enhance antioxidant capacity.

According to Erickson, ResistAid has three mechanisms of action: indirect action via gut microbiota-dependent pathways, direct action on the immune system via the gut-associated lymphoid tissue (GALT), and antioxidant action attributed to polyphenolic flavonoids, such as taxifolin and quercetin. "Research highlights that it can support the body's adaptive immune response in amounts that are safe and well-tolerated," she said.

GanedenBC³⁰ (*Bacillus coagulans* GBI-30, 6086) is a probiotic that Cox said has been shown to support digestive and immune health. In a controlled study, Ganeden BC³⁰ was shown to help increase immune response to a viral challenge. "Studies have shown that when the body is challenged—by colds and the flu, for example—GanedenBC³⁰ helps regulate the protective cytokines that help to fight this challenge," he related. "When the body is challenged by overactive cytokines—inflammation related to arthritis, for example—it helps down-regulate these cytokines."

Daiwa Health Development's Rice Bran Arabinoxylan Compound (RBAC), said Cheatham, was shown to triple natural killer (NK) cell activity, increase helper T cells, and demonstrate vital antioxidant and immune balancing activity. In pre-clinical studies, it was shown to increase the T cell levels up to 200 percent. Accelerated helper T cell activity supports the proliferation of cytotoxic T and



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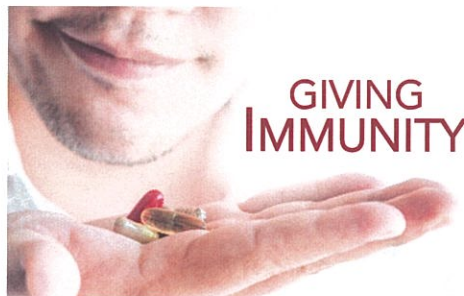
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B cells. B cells promote a healthy production of antibodies to combat viral and bacterial infections. RBAC has been studied in two cancer populations (breast and liver) with standard chemotherapy compared to standard chemotherapy only, and the results showed that both RBAC groups had better outcomes than those patients that received only standard chemo protocol.

Cheatham reported that there is currently a study underway at the University of Texas confirming that RBAC is efficacious in relieving the negative side effects of chemotherapy by increasing the activity of the natural killer (NK) cells of the other white blood cells to enhance the immune response. So far, the results are extremely positive.

Innovations for Immunity

The industry has, of course, evolved to make dietary supplements more accessible for more people to take and to promote higher compliance. Bush explained that berries “lend themselves to a variety of fun and innovative product options due to their friendly and familiar nature, natural red-purple color ranges, unique sweet to tart flavor profiles, and incredible science-backed functionality.”

One of the newest delivery options Bush observed is extremely popular is “popping crystals” that are enjoyed by kids and adults alike. Product developers have been challenged to meet the demand of consumers who are looking for alternative deliveries to conventional capsules and tablets so they can better enjoy their healthy food and supplement products. “Popping crystals can add a bit of whimsy to a therapeutic dose of elderberry for immune promoting benefits,” she commented.

Oleuropein in Euromed’s Spanish olive leaf extract, said Woodman, naturally provides the bitter note to olives and potentially to the palate; therefore it is best consumed in a tablet or capsule dosage form. The latest innovation in this extract, he reported, is an organic certified olive leaf extract produced from young leaves from a well-controlled grove in Southern Spain containing a high oleuropein content.

Wellmune can be found in hundreds of products in more than 60 countries; in the U.S., said Cox, it has been incorporated in a variety of innovative product applications, including these recent launches:

- Olly Kids Mighty Immunity: Children’s gummy for immune system support.
- V-Coffee (Brazil): Coffee capsule with immune health benefits
- Gold Standard BCAA Train + Recover: Sports nutrition bulk powder for endurance, immunity and muscle recovery.
- Isagenix Shake Booster Immune Shake booster for immune health that can be blended into any Isagenix shake.
- GanedenBC³⁰ is in more than 900 products currently on shelves, more than 350 of which launched in 2017. Some recent U.S. product launches GanedenBC³⁰ include:
 - Lola Bars: A range of plant protein + probiotic snack bars
 - ThinkThin Protein & Probiotics Hot Oatmeal: Oatmeal cup with probiotics to support overall wellness and digestion
 - Organic India: A wellness hot tea beverage
 - Betty Lou’s: Probiotic bites (nutritional bars) that support digestive health.
- Erickson observed that consumers are increasingly taking active measures to help keep their immune systems in top condition. As people lead increasingly busy, hectic lives, day-to-day stress can leave people feeling run down and low on energy—therefore, she concluded, “there is an opportunity to develop products that support immune function, while meeting the need for convenience, such as on-the-go beverages or gummies.” **NIE**

Extra! Extra!

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