Scientific Evidence of BellaVie SKINOSAL

The SKINOSAL Synbiotic from Bellavie is a broad-spectrum, high-CFU, multispecies probiotic supplement containing 10 probiotic microbial species, prebiotic, and supplement, each selected for well-documented supportive health benefits.

The formula has been developed with essential intestinal bacteria to support a more favorable balance of intestinal microbiota, atopic dermatitis, and allergic rhinitis management, and decrease allergic sensibility

The formula is completed with prebiotics and nutraceuticals which are working in synergy with probiotics and enhance their activity.

The Bellavie SKINOSAL capsules contain vitamin D3 and selenium to increase the immune function. They also contain quercetin which has antioxidant and anti-inflammatory benefits, but their main asset is their antihistamine action, which contributes to relieving allergies.

Probiotics and Allergies

Despite the availability of treatments, such as antihistamines, corticosteroids, and immunotherapy, these interventions primarily target symptom management rather than addressing the underlying immune dysregulation.

The development of allergic diseases has been linked to dysfunction of complex mucosal systems, which collectively comprise of the epithelial barrier function, immune system and a newly identified actor: the microbiota.

Emerging evidence highlights the pivotal role of the gut microbiome in immune regulation and allergic disease development. Dysbiosis, or imbalance in the gut microbiota, has been implicated in the pathogenesis of allergies, as it can disrupt immune homeostasis and promote inflammation (1).

The interest in probiotic therapeutic potential in allergic disorders stemmed from the fact that they have been shown to reduce inflammatory cytokines and improve intestinal permeability in vitro. Such effects would be desirable in treating allergic disorders. Therefore, several studies have been designed to examine the efficacy of probiotics in many allergic conditions, such as eczema, allergic rhinitis, asthma, and food allergies (2).

Benefits of Probiotics

The efficacy of probiotics has been tested in several clinical studies in the prevention and complimentary treatment of allergic diseases, including allergic rhinitis and atopic dermatitis. A recent meta-analysis, comparing the effect of probiotics to placebo showed that, the Rhinitis Quality of Life (RQLQ) global score, RQLQ nasal score and Rhinitis Total Symptom Score (RTSS) for nasal symptoms were significantly improved after probiotic supplementation. In this meta- analysis, most of the clinical studies included, used probiotics composed of Lactobacillus and Bifidobacterium strains (3). In atopic dermatitis, probiotics have been also tested in human. L. plantarum, L. salivarius, and L. acidophilus specifically showed evidence of efficacy and safety across multiple studies with a significant improvement in SCORAD scores that combines extent, severity and subjective symptoms of atopic dermatitis (4). The mechanism by which probiotics could improve allergic reactions is not fully understood. For allergic rhinitis, probiotics supplementation might modulate the secretion of mucosal IgA, antigen-specific IgE and Th2 cytokines (IL-4, IL-13) (5). Moreover, the International Consensus Statement on Allergy and Rhinology recommends considering probiotics as an adjuvant therapy for patients with AR due to their minimal harm and proven efficacy in improving symptoms (6).

BellaVie Cap Composition

Each Bellavie capsule contains a symbiotic combination (probiotic and prebiotic) along with nutraceutical elements, collectively referred to as a "synbioceutical". Within the probiotic element of the capsule, there are 10 specially selected microorganisms chosen based on scientific evidence outlining their many health benefits.

For the prebiotic component of the capsule, 2'-Fucosyllactose (2'-FL), a component of Human Milk Oligosaccharides, is used due to its ability to stimulate probiotic growth, provide a synergistic effect, and offer protection against inflammatory and allergic diseases.

For the nutraceutical component, vitamin D3, selenium, and quercetin are included for their well-documented benefits in supporting immune defense and alleviating allergy symptoms.

Probiotics

Each probiotic contained within the Bellavie SKINOSAL capsule is based on scientific research that demonstrates how each probiotic makes a positive impact on immune health. The following facts about each probiotic has been backed up by extensive research and clinical trials.

- **Bacillus Coagulans**

    - *Bacillus Coagulans* can normalize both the quantitative parameters of the immune system and immune cells' functional activity and activate human immune cells and altered the production of both immune activating and anti-inflammatory cytokines and chemokines. Thus in turn can significantly benefit the host immune system (7).

- **Lactobacilli**
  - Administration of some Lactobacillus species resulted in nasal and ocular symptom relief and improvement of quality of life in children and adults suffering from rhinitis (8).

  - Lactobacilli has demonstrated different changes in cytokine profiles, such as elevated Th1 and decreased Th2 cytokines, reduced allergy-related immunoglobulins and cell immigration have in both human and murine studies (8). Allergies are associated with a disbalance of the ratio of Th1/Th2 and tends to favor a positive Th2 ratio.

  - Positive effects on patients like less activity limitations or fewer rhinitis episodes and longer periods free from asthma or rhinitis were also described following oral administration of Lactobacillus bacteria (8).

  - A mixture of probiotic ŁOCK strains (*Lactobacillus rhamnosus* ŁOCK 0900, *Lactobacillus rhamnosus* ŁOCK 0908, and *Lactobacillus casei* ŁOCK 0918) offers benefits for children with AD and CMP allergy (9).

  - The protective effect of HN001 against eczema, when given for the first 2 years of life only, extended to at least 4 years of age. This, together with our findings for a protective effect against rhinoconjunctivitis, suggests that this probiotic might be an appropriate preventative intervention for high-risk infants (10).

  - *L. delbrueckii* is a potent inducer of proinflammatory cytokines IL-1b and TNFa. The immune-stimulatory effects of LAB are well recognised. While there is much evidence for the influence of various probiotic strains, conventional cultures are also beneficial to health as suggested by the findings described above (11).

- **Bifidobacterium**

  - After 6-month *B. bifidum* intervention, *B. bifidum* TMC3115 consumption reduced allergic scores, and improved anti-inflammatory responses and secondary outcomes in CMPA infants (12).

  - *Bifidum/infantis* reduces Th2 cytokines and act as potent inducers of interleukin (IL)-10 production in different peripheral blood mononuclear cell cultures (13).

  - Certain strains of *lactobacilli* and *bifidobacteria* modulate the production of cytokines by monocytes and lymphocytes, and may divert the immune system in a regulatory or tolerant mode (13).

- Allergic TH2-low asthma studies have shown that oral delivery of Bifidobacterium strains has the potential to alleviate disease symptoms (14).

- Administration of *B. breve* at doses of 1010, 109 and 107 CFU significantly decreases the Ovalbumin-specific IgE levels and sneezing frequency, and nasal mucosal epithelium is protected from local allergic reaction (15).

- **Streptococcus Thermophilus**

  - The probiotic *S. thermophilus* is a potent inducer of Th1 type cytokines IL-12 and IFN-γ than the probiotic Lactobacillus strains. This is crucial for the resolution of allergic-related immunopathologies (16).

  - HKBBST decreased the incidence of potentially allergic adverse event in children with family history of atopy, during the first months of life and after the formula was stopped. Oral tolerance to cow's milk in infants at high risk of atopy may therefore be improved using not hydrolysed fermented formulae (17).

Prebiotic

Prebiotics are needed to provide nutrients to create an optimal environment and support the growth of the probiotics. Inulin was chosen as the prebiotic for this capsule as inulin increases the number of good bacteria in the gut, particularly bifidobacterial and lactobacilli.

2'-Fucosyllactose (2'-FL) which is a component of Human Milk Oligosaccharides (HMO), complex carbohydrates that are naturally present in breast milk. HMO is used in infant nutrition and dietary supplements to support the digestive and immune health of consumers.

Clinical trials and preclinical studies have shown that 2'-FL contributes to (18):

- Growth of beneficial intestinal bacteria
- Building up the immune system
- Protection against inflammatory and allergic diseases
- Normalizing gut movements
- Support the development of brain functions and cognition.

Nutraceutical

Nutraceuticals are natural health supplements recognized for their effects on targeted functions. The Bellavie SKINOSAL cap contains Vitamin D3, Quercetin and Selenium as they are known for the beneficial roles that they play in the immune system and symptoms of allergies.

- **Selenium**

- Studies showed that lowered selenium status may have an important role in the pathogenesis of allergic diseases and more importantly that this decreased serum level is correlated with Th2 cytokines profile predominance (19).

- **Vitamin D3**

- It may potentially decrease the severity of asthma and allergies through a variety of mechanisms including effects on immune cells, improved handling or prevention of predisposing infections, decreased inflammatory responses, improved lung function, effects on airway smooth.

- A 2018 systematic review of 21 publications found that lower vitamin D levels were associated with eczema severity, and supplementation improved symptoms in 67% of people (20).

- It has been proposed that vitamin D insufficiency has contributed to the rise of allergic disease. The levels of Vitamin D correlated with the severity of disease. Vitamin D supplementation alters the course of Allergic Rhinitis towards clinical improvement (21).

- The immunomodulatory effects of vitamin D on allergen-induced inflammatory pathways could be linked to the fact that several immune cells (B cells, T cells, dendritic cells and macrophages) expressed the receptor for vitamin D. Another mechanism proposed is the inhibiting effect of vitamin D on both Th1 and Th2 responses (22).

- **Quercetin**

- The therapeutic effect of quercetin has been demonstrated in experimental rat models notably in allergic rhinitis, in which orally administered quercetin reduced the nasal symptoms such as sneezing, rubbing and redness as well as alleviated allergic reaction, inhibiting the inflammatory cells infiltration and improving the imbalance of Th1/Th2 and Treg/Th17 (23-24-25).

- Quercetin is effective eosinophilic inflammation suppressor for diseases like allergic rhinitis and asthma (26).

- Studies showed that quercetin inhibited the release of histamine, leukotrienes, prostaglandin D2, and granulocyte macrophage-colony stimulating factor from human cultured mast cells in a concentration-dependent manner (27).

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