

IMMUNIS

Feed supplement for cats and dogs in tablet form, intended to support immune function

IMMUNIS <I-MU-NIS

The name is inspired by the Latin word « immūnis », which means « free from, devoid of, without »

Andrews EA, Freund W, Lewis CT, Short C. *A Latin dictionary*. Oxford: Clarendon Press; 1879.

Generally, the immune system has short- and long-term pathogen response capabilities which are mediated by the innate and adaptive segments of the immune system. To broadly categorize the capabilities of feed or feed additives to alter immune function, components can be broken into intervention agents, such as vitamins, zinc, or omega-3 fatty acids, and functional foods such as probiotics, phytogenics, essential oils, or smaller components of a feedstuff such as epigallocatechin gallate (EGCG) of tea¹. Immunis is a carefully selected combination of vitamins, zinc, phytogenics (*Echinacea purpurea* extract, green tea extract) and prebiotics (Larch wood arabinogalactan) to actively modulate the immune deficiency due to life stage (neonate or old age) or natural stress.

Vitamins: C, B6, B12 and folic acid

Supplementation with vitamin C enhances T- and B-cell proliferation and bacterial phagocytosis by macrophages².

The B-vitamins are generally considered as a “complex,” however, with regard to having a specific impact on immune function, there is one B-vitamin, pyridoxine (B6), whose deficiency is associated with impaired cell-mediated and humoral immune responses².

Zinc

Zinc is a mineral required for key biological processes that affect normal growth, development, repair, metabolism, cell integrity/functionality, and immune tolerance in both innate and adaptive immune systems³. The reaction of the immune system to zinc depends on zinc concentration, where zinc can have both positive and negative effects on immune function. Zinc depletion leads to function compromise in nearly every class of immune cells and also results in thymus involution⁴.

Green tea extract

The most notable and abundant immunomodulatory component of green tea is epigallocatechin-3-gallate (EGCG). EGCG induces IL-10 production and Treg (T regulatory cell) differentiation and reduces neutrophil migration while also slowing

Dendritic cells maturation. EGCG also alters forkhead box P3 (FOXP3) signaling, the master regulator in T cell development, and promotes Tregs, which turn the immune system down to reduce inflammation^{4,5}.

In a model of high fat diet induced gut dysbiosis and inflammation in dogs⁶, green tea polyphenols supplementation exhibited significant protective effects against obesity and dysbiosis. The anti-obesity and anti-inflammatory effects of GTPs involve numerous mechanisms, including intestinal microbiota composition, proinflammatory cytokine expression, and inhibition of the TLR4 signaling pathway.

Larch arabinogalactan

Larch arabinogalactan is a long, densely branched, high-molecular-weight polysaccharide derived from *Larix laricina* and *Larix occidentalis* (North American Larix species). The role played by larch arabinogalactan on the innate immune system is further substantiated by an *in vivo* study on dogs, demonstrating that oral administration of larch arabinogalactan (at doses of 0.55 g/day or 1.65 g/day for 10 days) increases the number of circulating white blood cell counts, namely neutrophils and eosinophils⁷. The effect of larch arabinogalactan on the adaptive immune system has also been studied. Grieshop et al.'s study on dogs⁷ showed that the number of lymphocytes (CD4+T helper, CD8+ cytotoxic T cells or B CD19+) was not affected by larch arabinogalactan administration. Serum IgG, IgM and IgA were also unaffected⁷. However, in an *in vitro* study⁸, the treatment of mice splenic lymphocytes with arabinogalactan increased their cytotoxic activity against tumor cells.

Studies of the specific modes of action of larch arabinogalactan support in part the two pathways: it can possibly act indirectly through microbiota-dependent mechanisms (i.e., rebalancing microbiota composition in the gut, production of short-chain fatty acids) and/or have a direct effect on the immune system after passage from the gut lumen through the gut-associated lymphoid tissue⁹.

Echinacea purpurea extract

An open multi-centered veterinary clinical trial¹⁰, comparing conditions before and after treatment with a herbal preparation, containing the powdered root of *Echinacea purpurea*, was conducted by 6 practicing veterinarians in Switzerland. The plant-based immune stimulant was administered to 41 dogs with manifestations of chronic and seasonal upper respiratory tract infections, including pharyngitis /tonsillitis, bronchitis and kennel cough. Echinacea powder (1:3) was administered with the food at a dose of 1.0 g/10 kg body weight once daily for 8 weeks. Overall efficacy showed significant improvement for 92% of 39 dogs after 4 weeks of treatment and this was confirmed after 8 weeks.

In another study performed on 14 dogs that were referred to the veterinary clinic, *Echinacea* extracts were found to exhibit appreciable immunostimulatory activity¹¹. The results showed that in the group which received *Echinacea* packed cell volume (PCV), haemoglobin (Hb), red blood cell (RBC) count, white blood cell (WBC) count, lymphocytes (Lym), counting neutrophils (Nut), the per cent of phagocytosis and IgM significantly increased ($P < 0.05$).

References

1. Bobeck EA. Nutrition and health: Companion animal applications: Functional nutrition in livestock and companion animals to modulate the immune response. *J Anim Sci.* 2020;98(3): 1–8
2. Baumgartner TG, Henderson G, Baumgartner SL. Micronutrients in clinical nutrition. In: Shikora SA, Blackburn GL, editors. *Nutrition support. Theory and therapeutics*. New York: Chapman & Hall; 1997. p. 66–90.
3. Ibs, K. H., L. Rink. 2003. Zinc-altered immune function. *J. Nutr.* 133:1452S–1456S.
4. Wu, D., Lewis E. D., Pae M., Meydani S. N. Nutritional modulation of immune function: analysis of evidence, mechanisms, and clinical relevance. *Front. Immunol.* 2018. 9:3160
5. Grimble, R. F. Nutritional modulation of immune function. *Proc. Nutr. Soc.* 2001. 60:389–397
6. Li Y, Rahman SU, Huang Y, Zhang Y, Ming P, Zhu L, Chu X, Li J, Feng S, Wang X, Wu J. Green tea polyphenols decrease weight gain, ameliorate alteration of gut microbiota, and mitigate intestinal inflammation in canines with high-fat-diet-induced obesity. *J Nutr Biochem.* 2020;78:108324
7. Grieshop CM, Flickinger EA, Fahey Jr GC. Oral administration of arabinogalactan affects immune status and fecal microbial populations in dogs. *J Nutr.* 2002;132(3):478–82
8. Choi EM, Kim AJ, Kim YO, Hwang JK. Immunomodulating activity of arabinogalactan and fucoidan *in vitro*. *J Med Food.* 2005;8(4):446–53.
9. Dion, C., Chappuis, E. & Ripoll, C. Does larch arabinogalactan enhance immune function? A review of mechanistic and clinical trials. *Nutr Metab (Lond)*, 2016, 13, 28
10. Reichling J, Fitzi J, Fürst-Jucker J, Bucher S, Saller R. Echinacea powder: treatment for canine chronic and seasonal upper respiratory tract infections. *Schweiz Arch Tierheilkd.* 2003;145(5):223–31.
11. Torkan S, Khamesipour F, Katsande S. Evaluating the effect of oral administration of *Echinacea* hydroethanolic extract on the immune system in dog. *Aut Autac Pharmacol.* 2015;35(1-2):9-13.