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## Beta-1,3/1,6-glucans as functional ingredient for petfoods

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Evidence is presented that beta-1,3/1,6-glucans are beneficial in the treatment of canine osteoarthritis. The efficacy of a purified beta-1,3/1,6-glucans preparation has been demonstrated in a double-blind, placebo-controlled trial and there is a plausible mechanism of action. Because of their anti-inflammatory effect, it is suggested that beta-1,3/1,6-glucans might be effective in the management of inflammatory bowel disease and allergic dermatitis in dogs and cats.

### Beta-1,3/1,6-glucans

Glucans are polymers of glucose. Well-known examples of glucans are starch and cellulose, but these molecules have no specific influence on the immune system. The glucose molecules of starch and cellulose are linked together by so-called alpha- and beta-1,4-bonds, respectively. Glucan molecules that have the ability to enhance the immune system are chains of glucose molecules linked together by beta-1,3-bonds and have 'branches' of glucose molecules through beta-1,6-linkages. Beta-1,3/1,6-glucans can be isolated from the cell walls of baker's yeast (*Saccharomyces cerevisiae*). During the isolation process the mannoproteins in the surface of the cell walls can be removed in order to obtain a highly purified preparation of which the beta-1,3/1,6-glucans are exposed for optimum bioactivity.

### Regulatory activity

It has been demonstrated (unpublished data, 2008) that purified beta-1,3/1,6-glucans (MacroGard®, Biorigin/ Orffa) can bind to the so-called dectin-1 receptor on immune cells in the gut (e.g. macrophages and dendritic cells). The terminal end of the beta-1,3-linked glucan chains is recognized by the receptor. Only after removal of the outer protein layer of the yeast cell wall the betaglucans are free to interact with the receptor. Due to the presence of proteins that cover the side branches of the beta-1,3/1,6-glucans, non-purified beta-1,3/1,6-glucan products do not influence the immune system. This holds for various yeast cell wall products and mannanoligosaccharides (MOS) preparations. Non-purified betaglucans are not bound by the specific receptors on immune cells and thus cannot elicit a response in the form of the production of cytokines (unpublished observations). MOS products, which are commonly used in petfoods, have specific characteristics other than binding to the dectin-1 receptor of immune cells.

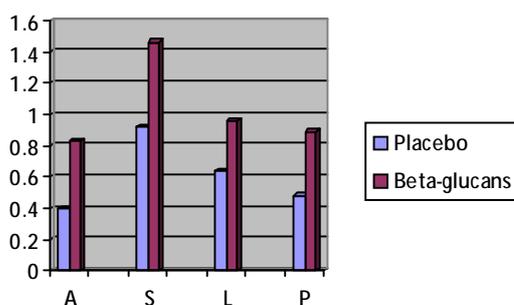
Research in pigs (Li et al., 2006) has demonstrated that the feeding of beta-1,3/1,6-glucans reduced the plasma concentrations of the pro-inflammatory cytokines, IL-6 and TNF $\alpha$ , and raised the concentration of the anti-inflammatory cytokine, IL-10. Thus, the intake of beta-1,3/1,6-glucans may reduce inflammation in canine and feline disorders such as osteoarthritis, atopy and inflammatory bowel disease. TNF $\alpha$  stimulates the production of matrix metalloproteinase-3 by chondrocytes (O'Connor and Fitzgerald, 1994), which is involved in the degradation of collagen molecules in the cartilage matrix. Possibly, ingested beta-1,3/1,6-glucans inhibit the degradation of cartilage collagen through a decreased production of TNF $\alpha$ .

## Osteoarthritis

Osteoarthritis is a joint disease that is frequently seen in veterinary practice. The condition occurs in both dogs and cats, but generally receives more attention in dogs. In various degrees of severity, osteoarthritis occurs in more than 90% of dogs older than 5 years. In severe cases, the symptoms are chronic pain, lameness and immobility. Osteoarthritis is a degenerative and inflammatory condition in which loss of cartilage matrix is associated with the release of pro-inflammatory cytokines. Osteoarthritis cannot be cured and treatment is directed towards relief of pain by inhibition of inflammatory reactions and counteracting further breakdown of cartilage.

Berge (Nordberg Veterinary Clinic, Oslo) found that the intake of purified beta-1,3/1,6-glucans improved the clinical signs of dogs with joint disorders (unpublished data, 2003). Because of the open nature of the study and the absence of a placebo group, the observation cannot be taken as proof for a beneficial effect of beta-1,3/1,6-glucans. It is well-known that placebo effects occur when evaluating the clinical signs of dogs with osteoarthritis.

To readdress the effect of beta-1,3/1,6-glucans, Beynen and Legerstee (2009) carried out a double-blind, placebo-controlled trial with privately owned, osteoarthritic dogs. With the use of a questionnaire, the clinical signs were evaluated by the owners. For a period of 8 weeks, the test dogs were fed on a complete dry food with 800 ppm beta-1,3/1,6-glucans (MacroGard<sup>®</sup>); as a placebo, the same diet without supplement was used. There were 23 dogs per treatment group. When compared with the placebo treatment, the ingestion of beta-1,3/1,6-glucans showed a greater numerical improvement as to the scores for activity, stiffness, lameness and pain (Figure 1).



*Figure 1. Improvement of clinical signs of osteoarthritis in dogs given a preparation of purified beta-1,3/1,6-glucans. The difference in change of scores between the two groups was not statistically significant. The increase (= improvement) in score (on a 0-10 scale) as induced by beta-1,3/1,6-glucans versus baseline values was statistically significant ( $P < 0.05$ ) for the variables activity (A), stiffness (S) and lameness (L) and pain (P).*

## Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a collective term referring to a group of chronic, idiopathic gastrointestinal disorders. Each of the disorders has an unknown cause and is typified by an infiltration of inflammatory cells into the intestinal mucosa. The clinical signs are non-specific so that the diagnosis of IBD is reached by ruling out other diseases. IBD in dogs and cats is associated with chronic vomiting, diarrhea and weight loss and is often considered to be the most common cause of these clinical signs.

Research in laying hens (Star et al., 2009) showed that the feeding of beta-1,3/1,6-glucans has a positive effect on intestinal health and alleviates chronic enteritis with unknown cause. The supplementation of beta-1,3/1,6-glucans (MacroGard®) resulted in significantly higher villus/crypt ratios and diminished severity of inflammation which was characterized by a significant decrease in the number of inflammatory cells. Given the results of the trial in hens with chronic enteritis and the anti-inflammatory action of beta-1,3/1,6-glucans, it could be suggested that IBD might be treated by feeding a diet containing the functional ingredient.

## Atopy

Skin disorders in dogs and cats usually are of a chronic nature and may account for about 40% of veterinary consultations. The main type of skin disorders is allergic dermatitis with symptoms such as pruritis, erythema, oedema and self-trauma. Atopy is generally caused by inhaled allergens that cannot be avoided. The treatment of atopic dermatitis involves the suppression of chronic inflammatory reactions in the skin.

Berge (Nordberg Veterinary Clinic, Oslo) found that the intake of purified beta-1,3/1,6-glucans improved the clinical signs of dogs with chronic skin disorders (unpublished data, 2003). The study was open and lacked a placebo group so that the observation should be confirmed by a double-blind, placebo-controlled trial. It would also be of interest to carry out a similar study with cats. Given the anti-inflammatory action of beta-1,3/1,6-glucans, the outcome of the study of Berge, and the reported beneficial effects of beta-1,3/1,6-glucans on ova-albumin-induced allergic reactions in mice (Kimura et al., 2007) and allergic rhinitis in human patients (Kirmaz et al., 2005), it would be anticipated that atopy in dogs and cats may be managed by feeding a diet containing the functional ingredient.

## Conclusion

This communication advances that beta-1,3/1,6-glucans beneficially affect the clinical signs of canine osteoarthritis and does so through an acceptable underlying mechanism. In addition, there is suggestive evidence that the anti-inflammatory effect of beta-1,3/1,6-glucans may be beneficial in the treatment of inflammatory intestinal disorders and allergic dermatitis in dogs and cats.

## References

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