Beta-1,3/1,6-glucans

BALANCE IMMUNITY USING NUTRITION

By Pauline Rovers-Paap, Orffa Additives

The immune system has evolved during millions and millions of years as an extremely potent and efficient defence mechanism directed towards a single goal; to keep us healthy. The primary function of the immune system is to protect the body against infections by pathogenic viruses, bacteria, fungi and parasites. It also plays a key role in removing dead body cells and repairing damage caused by environmental factors like strong light, irradiation and toxins. Occasionally, the immune system may over-react or be brought out of balance. Such imbalances can result in immune disorders like arthritis, allergies or other health conditions. The immune system can be suppressed, resulting in reduced overall resistance to infections. Therefore a properly functioning immune system is essential for good health in pets.

For many years, researchers have tried to find substances which induce a controllable procedure that alerts the innate immune defences to respond quickly and effectively to infections without causing inflammation or the negative side effects associated with an infectious disease. An activated immune system is extremely effective, enhancing resistance to infections by viruses, bacteria, fungi and parasites. A natural carbohydrate structure from bakery yeast, the beta-1,3/1,6-glucan, is recognised by immune cells as a non-self or foreign molecule and can initiate a particular immune response.

The immune system

Three major principles of immunity are common to all living creatures; recognition, processing and elimination of threats. The immune system needs to recognise the invading danger (by distinguishing between self and non-self), process this information and eliminate the threat. All animals should stay healthy by employing these 'simple' principles.

An organism that can cause disease is called a pathogen. The virulence of a pathogen varies greatly and depends on their ability to evade the body defences. The body's defences includes physical barriers (e.g. skin, intestinal wall, mucous) that exclude invaders, innate immunity (a-specific) that provides rapid initial protection and adaptive (specific) immunity that provides prolonged effective immunity. A properly functioning immune system can distinguish between pathogens and their own healthy tissue.

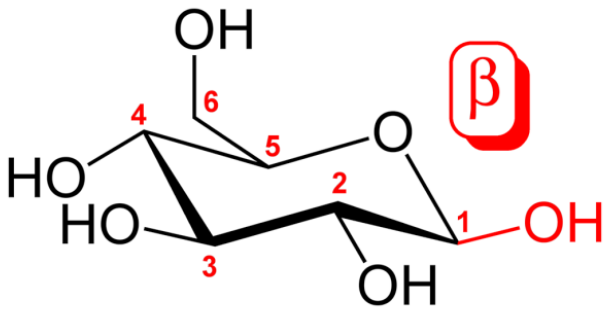
It might become clear that the immune system is not always working well enough. Immune suppression by, for example, stress, ageing or medication can make animals more susceptible to infectious diseases or other immune related problems. Imbalances can result in allergic reactions, (chronic) inflammations or auto-immune diseases. Optimisation of the immune response can be beneficial in the case of many health issues.

What is a beta-1,3/1,6-glucan?

A glucan is a carbohydrate polymer containing glucose as the only building block. The glucose molecules can be linked together via a so-called alpha- or beta-linkages; the two main types of glucan molecules. Figure 1 shows a glucose molecule with a beta-orientated binding. The numbers refer to the location where one glucose molecule can be linked to the next glucose molecule. This combination between type

of linkage (alpha- or beta linkages) and the location of the linkages (the number) provide the exact structure of the complete glucan chain. Well known examples of glucans are starch and cellulose. The glucose molecules of starch and cellulose are linked together in so-called alpha- and beta-1,4-linkages, respectively. It is obvious that cellulose (cell walls of e.g. grass) and starch do not have a particular effect in the immune system.

Figure 1: Glucose molecule, showing the carbon numbering notation and beta-orientated binding.



Yeast cell walls from the commonly used strain Saccharomyces cerevisiae contain beta-1,3/1,6-glucans. Figure 2 shows the molecular structure of a beta-1,3/1,6-glucan. The main chain or backbone of the molecule contains glucose molecules linked together via a beta-1,3-linkage. The backbone of the molecule also has side 'branches' of glucose molecules via beta-1,6-binding. Years of research indicate that the length of the backbone, the branching frequency and length of the branches determine the efficacy of stimulating the immune system.

Not every yeast cell wall product has the ability to influence the immune system. The major challenge is to remove the other components of the yeast cell wall, such as manno-proteins and lipids (attached to the end points of the side branches in the intact cell wall) without damaging the beta-1,3/1,6-glucan molecule.

It is clear that not all glucans can enhance the immune system (like cellulose and starch). The specific structure (length of the chains and branching frequency) of beta-1,3/1,6-glucans determines if the molecule can be recognised by the immune cells and stimulate a response.

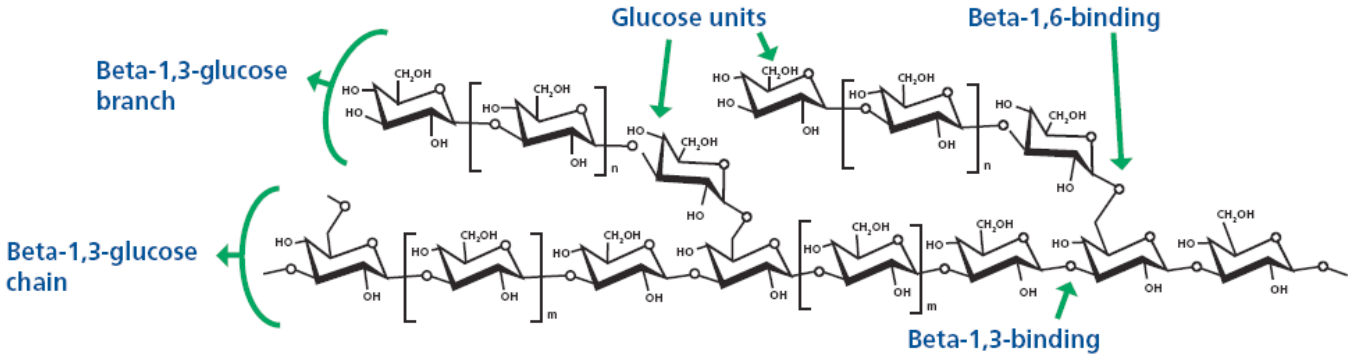
How can beta-1,3/1,6-glucans be recognised?

White blood cells (e.g. macrophages, dendritic cells) are immune cells in the front-line of the defences of the body. The white blood cells have receptors on their surface, these receptors can recognise invading pathogens (e.g. bacteria, viruses, fungi, parasites) but also beta-1,3/1,6-glucans. A highly specific 'key-in-lock' type of interaction between the beta-1,3/1,6-glucan and the receptors on the cell surface triggers the immune cell to release anti-microbial substances and alarm signals (or cytokines) into the bloodstream. To match perfectly into the receptors of white blood cells the specific structure of the beta-1,3/1,6-glucan (length of the chain and branching frequency) is for this reason, very important.

The majority of the immune cells (approximately 75%) are found in the body surfaces, particularly in gut endothelia, the largest immunological organ in the body. The activated immune cells in the gut endothelia release the alarm signals or cytokines into the bloodstream. This will not only stimulate the a-specific immune system but also the immune status of the whole body (specific immune response) will be activated by orally ingested beta-1,3/1,6-glucans. This leads to an enhanced phagocytosis by macrophages, activation of the production of specific immunoglobulins and the counteraction of harmful side effects of the immune system. Activation of immune cells in the gut by beta-1,3/1,6-glucans do not only have a positive influence on gut health, scientific evidence supports that it can also reduce immune disorders in the rest of the body.

Does an activated immune cell always provide the same immune responses? No, immune cells are equipped with several surface

Figure 2: structure of the beta-1,3/1,6-glucan molecule. A main chain of beta-1,3-linked glucose molecules, with side branches of glucose molecules via a beta-1 ,6-binding.



receptors that discriminate between different substances. Beta-1,3/1,6-glucans stimulate anti-microbial activity, cellular defence and an anti-inflammatory response. Bacteria and other pathogens bind to other receptors on the same immune cells and stimulate other immune responses; bacterial lipopolysaccharides (LPS) for example interact with another receptor on the macrophages which induce inflammation and fever.

MacroGard, the most researched betaglucan

The product MacroGard (produced by Biorigin and distributed in major European markets by Orffa Additives) is the most well known beta-1,3/1,6-glucan product for animal nutrition. There is a large scientific dossier available that shows the beneficial effects of MacroGard. Both in vitro trials and in vivo research with several animal species has shown the beneficial effects on immune parameters and animal health.

In vitro trials show that the source and type of beta-glucan is extremely important for efficacy. Several Universities worldwide, including the University of Ghent, carried out extensive in vitro research where different sources and types of betaglucans were evaluated for their capacity to modulate several different immune cells. Research showed the high efficacy of MacroGard on immune cells.

In vivo research by several universities and research institutes show that MacroGard has beneficial effects on the health status of animals during pathogenic pressure as well as during (chronic) inflammatory situations. For example, in pet animals it is shown that dietary MacroGard reduces the clinical signs of arthritic disorders and atopic dermatitis. It supports the natural defences and protection in young puppies. Latest research has shown beneficial effects of MacroGard on the metabolism and appetite control in obese dogs with insulin resistance.

Conclusion

Beta-1,3/1,6-glucans have several beneficial properties and many useful applications. Beta-1,3/1,6-glucans, found in the cell wall of yeast, are known for their ability to optimise immune response. In vitro work shows that it is very important to have the correct type and structure of beta-1,3/1,6-glucan. Commonly used yeasts, yeast cultures or complete yeast cell wall products do not have this particular ability to stimulate immune response. MacroGard is the most researched beta-1,3/1,6-glucan. The product has been investigated intensively and has proven to be very efficient in both in vitro trials and animal trials in pets, horses, livestock and aquatic species.