In Clover BioResiliant® Allergy Support for dogs, clinical data

Quercetin is a bioflavonoid that has been shown to be very effective in blocking histamines which are released when the immune system detects an allergy and are what account for uncomfortable allergy symptoms (Mlcek et al., 2016). It does this by inhibiting mast cells as well as pro-inflammatory cytokines, which are immune cells critical to triggering allergic reactions and inflammation (Kimata et al., 2000) (Park et al., 2008). Additionally, Quercetin is particularly powerful in fighting free radical damage to reduce inflammation and lessen the oxidative stress on the body (Yuan et al., 2006).

Bromelain is an anti-inflammatory enzyme that speeds up the reaction rate of quercetin. When combined with Quercetin, the antihistamine and anti-inflammatory effects are much more prominent (Lakhanpal & Kumar Rai, 2007). Bromelain also works to fight free radicals in the body and reduce symptoms of inflammation while supporting a healthy immune system (Rohn et al., 2004) (Yuan et al., 2006). Additionally, it plays a crucial role in modulating the immunological responses by regulating the activity of T cells and NK cells (Engwerda et al., 2001).

Mangosteen (*Garcinia mangostana*) is another powerful anti-inflammatory agent that supports the immune system. Mangosteen contains xanthones which are rich in antioxidants that work to reduce free radicals in the body responsible for inflammation (Tang et al., 2009) (Gutierrez-Orozco & Failla, 2013). It has also been shown to inhibit the synthesis of Prostaglandin E2, a principle mediator of inflammation as well as reduce the release of histamines which trigger allergic reactions (Nakatani et al., 2002).

Polysaccharide Krestin (PSK) and PSP found in the mycelium of a fungus known as Turkey Tail (Trametes versicolor) have been shown to enhance the functioning of the immune system (Hobbs C, 2004). Like Shiitake and Maitake mushrooms, Turkey tail works by activating the functions of NK cells in the body which play crucial roles in immunity as well as benefiting immunomodulation (Guggenheim AG et al., 2014). Furthermore, polysaccharides within the Turkey Tail mushroom have been shown to increase macrophage lysosomal enzyme activity as well as reduce T helper cell inflammatory response (Jeong SC et al., 2006) (Cortese L et al., 2015)

Curcumin found in turmeric (turmeric extract 95% curcumin) is recognized to be an effective modulator of the immune system by increasing the activation of T cells, reducing the proliferation of T cells and promoting the activity of NK cells (Jagetia GC, 2007). It has also been shown to block the release of cells that cause inflammation (Bose S et al., 2015).

Organic inulin prebiotic selectively feeds good bacteria in the gut specifically Bifidobacteria and Lactobacilli which play a crucial role in digestion and are necessary for optimal intestinal health as well as overall immune health (Wang & Gibson, 1993) (Watzl et al., 2005). Inulin only fortifies beneficial intestinal flora, starving any bad bacteria to maintain a healthy balance in the intestine. These good bacteria produce volatile and short-chain fatty acids which help to prevent colonization of pathogenic bacteria (Flamm et al., 2001). Inulin supplementation has been shown to prevent food allergies by protecting the intestine and promoting tolerance (Bouchaud et al., 2014). Studies specific to the microbiota found in cats and dogs before and after supplementation with inulin demonstrate the importance of FOS in the diet as well as the beneficial effects it has on the gut and immune system of animals (Rochus et al., 2014) (Garcia-Mazcorro et al., 2017) (Flickinger et al., 2003).

The high levels of vitamin A found in Sweet Potato (*Ipomoea batatas)* come from pro-vitamin A carotenoid beta carotenes which help to increase the activity of T cells and fight infection in the body (Chen at al., 2005). Furthermore, antioxidants found within sweet potato including vitamin A and vitamin C work to boost the immune system and prevent disease by interception of free radicals (Mohanraj & Sivasankar, 2014).

Coconut (*Cocos nucifera*) plays an important role in immunity because it contains medium chain triglycerides (MCTs) lauric acid, capric acid and caprylic acid which have antifungal, antibacterial and antiviral properties (Dayrit, 2015) (Dierick et al., 2002)(Lima et al., 2015). Coconut also contains antioxidative tocopherols and tocotrienols which fight free radicals to lessen the prevalence of infections

antioxidative tocopherols and tocotrienols which fight free radicals to lessen the prevalence of infections and diseases (Iranloye et al., 2013).

Anise stimulates the immune system by increasing the level of immunoglobins as well as beta carotene, vitamin A and vitamin C to protect the body from harmful infections (Soltan et al., 2008) (Shojaii & Fard, 2012). Anise also has antioxidant activity due to the polyphenol compounds found in the seeds along with natural antiviral and antibacterial properties to support the immune system (Barakat et al., 2016).

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