Summary: Investigation on the In Vitro Effects of Resveratrol on Peripheral Blood Mononuclear Cells Harvested from Healthy and Atopic Dogs.

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This WFA-funded study was undertaken at the University of Florida College Veterinary Medicine by Dr. Domenico Santoro. Resveratrol is a natural polyphenol present in the skin and seeds of grapes. Notably, it is a component of red wine. This compound has antimicrobial activity as well as anti-oxidant activity. There has been great interest in studying the effects of this compound in a variety of inflammatory disorders, including atopic dermatitis. Most of the studies have looked at its effects in cell systems and mouse models, but results are encouraging. Interestingly, a metabolite of resveratrol is able to inhibit one of the critical enzymes (Janus kinase-1) mediating the itch and inflammatory pathways in atopic dermatitis. This is the same enzyme targeted by oclacitinib (Apoquel®, Zoetis). In mouse models, this metabolite has been able to reduce the inflammation, itch, and skin water loss associated with house dust mite allergy.

The purpose of Dr. Santoro's study was to examine the effects of resveratrol on canine mononuclear cells prepared from fresh blood. Mononuclear cells are lymphocytes and monocytes, both very important in immune function. Samples were taken from 10 healthy dogs and 10 atopic dogs. The cells were cultured overnight, then set up for the experiment.

Each dog's cells were set up to have a negative control (no resveratrol and no stimulant (phytohemagglutinin – PHA – a compound derived from the red kidney bean that causes lymphocytes to proliferate), from positive control (PHA), resveratrol alone, and PHA + resveratrol. After 24 hrs these cells were tested for viability, production of defensins, anti-oxidant activities, and cytokine production.

One of the important things to consider is the effect of culture on cells. Do the cells remain alive or do they die under these conditions? There were two tests for viability. One is a measurement of an enzyme that only leaks out of dying or dead cells. The other is a measurement of a specific kind of cell death called apoptosis.

The cells were assessed for their anti-oxidant activities, the product of host defense molecules (called defensins), and a number of cytokines important in atopic dermatitis and other inflammatory states

This study showed that cells from healthy dogs tended to be healthier, in that there were fewer dead cells in all the test conditions. Resveratrol tended to increase viability. Interestingly, the cells from atopic dogs had almost double the number of apoptotic cells regardless of the culture conditions. This finding is quite interesting as skin cells from atopic humans and mice tend to die by this mechanism, and that impairs the skin barrier (the very surface of the skin which holds water in and keeps allergens and microbes out).

Healthy cells had more antioxidant activity than atopic cells. Resveratrol seemed to increase the anti-oxidant activity in healthy cells, and to some extent, in atopic cells. The levels in atopic cells never reached that of healthy cells however, and the changes were not statistically significant.

Interestingly, resveratrol-treated atopic cells were able to increase their production of one of the defensins, compared to healthy cells. This is interesting because defensins are molecules that help kill pathogens. With regard to cytokines, the resveratrol had little effect on either population, and it was noted that the allergic cells tended to produce less. Possibly this effect resulted from the fact that there were more dead cells in that population.

So what can we conclude about resveratrol and atopic dermatitis? The concentrations used in this study were not high enough to warrant a recommendation of oral resveratrol for atopic dogs, but these concentrations were based on equivalency to what is safe to administer to a dog systemically. Higher levels might be more effective, but this compound at high levels can induce renal disease in dogs. It is possible that resveratrol could be used much more effectively on the skin. Much more work needs to be done to support the use of this compound.

It is important to realize that while these are negative results, they are still very valuable. Based on these results, we can say that administering resveratrol orally at doses safe for dogs is unlikely to be beneficial