ANTHOCYANIN RESEARCH PRECLINICAL STUDY ON THE EFFECT OF ANTHOCYANINS ON INTESTINAL HEALTH

The peer-reviewed study results summarized below were published in the journal *Redox Biology* in 2019.

BACKGROUND

The gastrointestinal tract plays a major role in health and wellness, and it contributes significantly to overall metabolic health. Many lifestyle factors can impact how well it functions, including a high fat diet, being overweight, and being sedentary. High fat diets, where unhealthy fat consumption is excessive, are associated with measurable disruptions to the gastrointestinal tract, including changes to the microbiome (gut bacteria), decreased intestinal barrier function, and increased inflammation. Therefore, a high fat diet also serves as an established method of studying gastrointestinal disruption and protective effects of dietary factors found in fruits and vegetables as means to address our modern lifestyles.

One class of compounds of particular interest is anthocyanins, which are responsible for the deep blue-purple colors of berries, black rice, and other colored fruits and vegetables. Our previous work established that two specific anthocyanins, cyanidin and delphinidin, were very effective at mitigating inflammation and intestinal barrier disruption in an *in vitro* intestinal cell model. These anthocyanins were then shown to mitigate insulin sensitivity and the buildup of fat in the liver of mice. The purpose of this study was to further investigate the mechanisms supporting these beneficial metabolic effects by determining whether a blend of anthocyanins rich in cyanidin and delphinidin had a protective effect on the gastrointestinal tract of mice fed a high fat diet.

METHODS

Healthy mice were divided into groups and fed one of four diets for fourteen weeks. The first group was fed a standard diet; this was the Control (C) group. The second group was fed a standard diet plus anthocyanins (CA group). The third group was fed a high fat diet (HF group). Lastly, the fourth group was fed a high fat diet plus anthocyanins (HFA group). The dose of anthocyanins given to the mice was equivalent to an intake of about 225 mg of anthocyanins per day in humans (about what 1 cup of berries would provide).

Researchers measured intestinal permeability, endotoxin levels in the blood plasma, and intestinal hormones as measurements of gastrointestinal health. Additionally, they also looked at the impact on pathways involving tight junction structure and function in cells in the digestive tract and sources of oxidative stress. Changes in microbiome composition were measured as well.

RESULTS

Researchers measured intestinal permeability using FITC-dextran. FITC-dextran is used to measure how much of an unwanted substance is transported from the gut through the cells lining the gastrointestinal tract into the body. Higher transport levels indicate greater intestinal permeability, which is undesirable. HF mice had five times more FITC-dextran transport than the control group. However, the HFA group had levels similar to the control group (Figure 1A). Additionally, researchers measured plasma endotoxin levels and found similar patterns: endotoxins were higher in the blood of the HF group, while the HFA group had levels that were similar to the control group (Figure 1B). Increased intestinal permeability can lead to greater levels of endotoxins in the blood, so these results are consistent and demonstrate a postive effect of specific anthocyanins to attenuate the negative effects of the high fat diet.

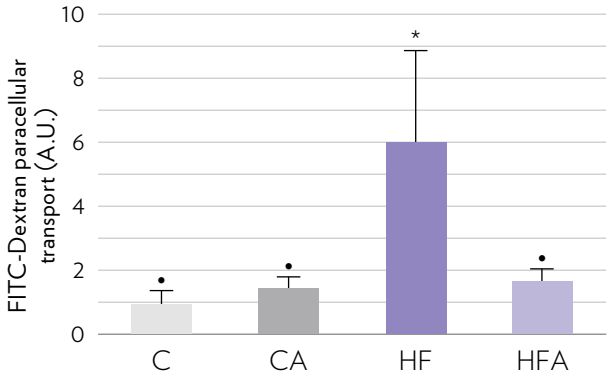

Figure 1A

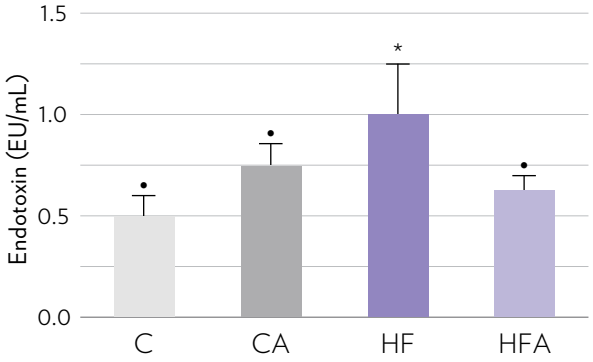

Figure 1B

Researchers also measured GLP-2, an intestinal hormone that has important protective effects on tight junctions between epithelial cells in the gastrointestinal tract. Tight junctions are specialized multiprotein complexes that help to prevent the leakage of compounds into the body; they also impact cell permeability. They found that mice fed with anthocyanins showed a significant increase in plasma GLP-2 levels compared to the groups that were not fed anthocyanins (Figure 2).

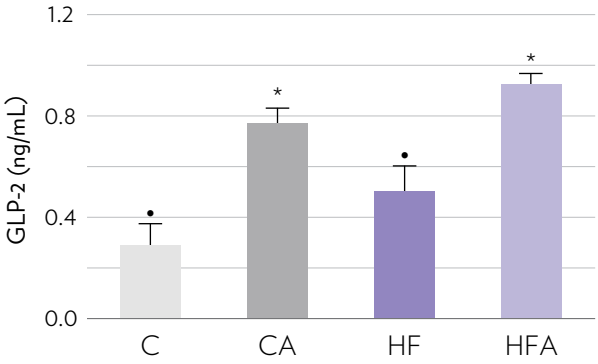

Figure 2

The researchers found further evidence that anthocyanins provide a protective effect when looking at three other pathways involved in tight junction structure and function. The negative effects of a high fat diet on these pathways were prevented in groups given anthocyanins (Figure 3A). Additionally, the researchers also found that anthocyanin supplementation offsets oxidative stress caused by NADPH oxidases, like NOX1 and NOX4 (Figure 3B). Oxidative stress is commonly observed in conjunction with intestinal permeability as a result of a high fat diet, so these results further support the protective effects of anthocyanins. This research was done by measuring protein levels as a marker of some of the sources of tight junction production and oxidative stress.

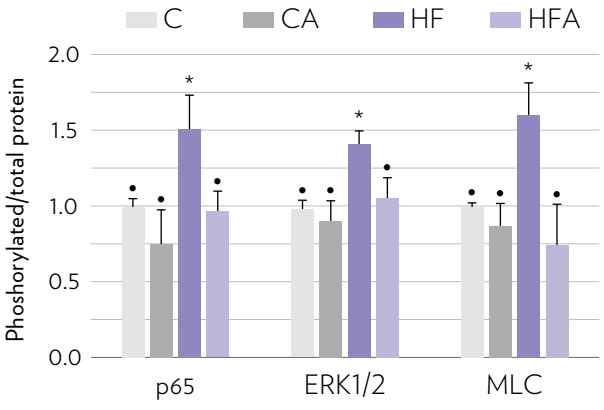

Figure 3A

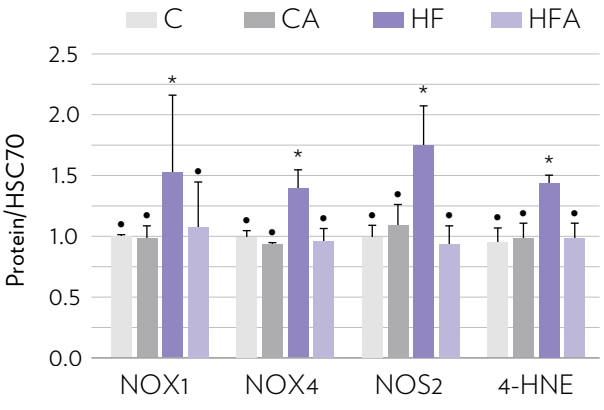

Figure 3B

The researchers also investigated differences in the composition of the microbiota (gut bacteria) of each group of mice. They found that mice in the HF group had a significantly higher ratio of *Firmicutes/Bacteroidetes* bacteria, along with a decrease in *Akkermansia* bacteria, which aligns with what other research has found on the impacts of a high fat diet on bacterial composition in the gut. Interestingly, anthocyanin supplementation prevented both changes from occurring in the HFA group (Figures 4A & 4B).

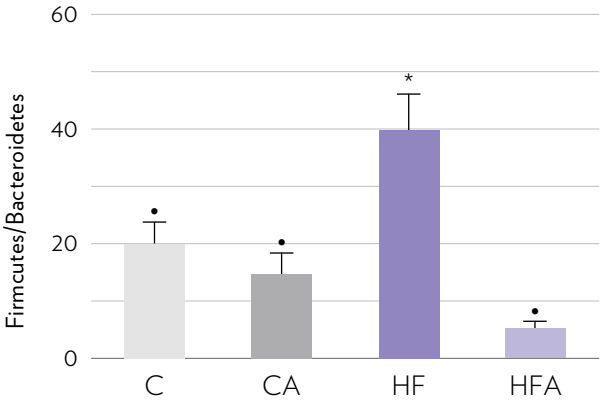

Figure 4A

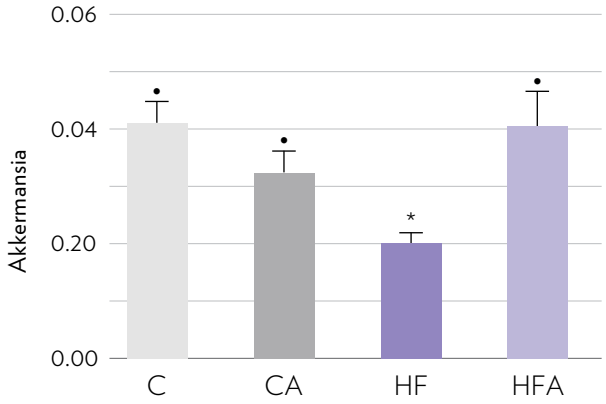

Figure 4B

DISCUSSION

The major finding of this study is that the beneficial effects of anthocyanins can contribute to the protection of intestinal barrier function, prevention of endotoxemia (thus resulting in a healthier inflammatory response), and enhancement of metabolic control. Anthocyanins were able to partially (or in some cases completely) prevent negative changes to the gastrointestinal barrier caused by a high fat diet. Additionally, anthocyanins played a significant role in preventing negative changes to the microbiome composition associated with a high fat diet.

These findings support the concept that anthocyanins can help mitigate the negative effects of an unhealthy lifestyle, and one of the mechanisms by which it does so is through its impact on intestinal health.

(Feb 2021)

REFERENCE

Cremonini E, Daveri E, Mastaloudis A, et al. Anthocyanins protect the gastrointestinal tract from high fat diet-induced alterations in redox signaling, barrier integrity and dysbiosis. Redox Biol. 2019;26:101269.

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