Bioavailability and Metabolism of Raspberry Ellagitannins

Studies have shown that raspberry ellagitannins can have a positive health influence on the cardiovascular system. However, raspberry ellagitannins have never been detected at biologically relevant levels in the bloodstream in any test subject. How can a substance help protect the cardiovascular system if it never enters into it? The answer lies with an important series of metabolic products of ellagitannins that are known as urolithins.

The consumption, absorption, and metabolism of raspberry ellagitannins are quite well studied. It is known that ellagic acid is poorly bioavailable. Ellagitannins are stable (surprisingly) in the acidic environment of the stomach but begin to break down upon entering the small intestine. Eventually the ellagitannins will break down into ellagic acid. The raspberry ellagitannins themselves are not absorbed into the blood stream at all. Ellagic acid, being poorly bioavailable, continues through the intestines and into the colon where many important bacteria live. Some of these bacteria metabolize ellagic acid and form compounds called urolithins. These urolithins are bioavailable and can be detected in the bloodstream at micromolar concentrations, which is considered to be quite high.

Figure 1 – General scheme showing the metabolism of ellagitannins into urolithins. Once consumed, the ellagitannins lambertianin C and sanguin H-6 pass through the stomach and into the small intestine.
Once inside the small intestine, the ellagitannins are hydrolyzed to release ellagic acid. Ellagic acid then passes into the colon where it is metabolized into urolithins (primarily UroB) by colonic bacteria.

Depending on what kinds of intestinal bacteria are present, urolithins may or may not form in high levels in vivo (in humans). Some people have gut bacteria that produce large amounts of urolithins, while others do not. The exact bacterial strains that are responsible for this metabolism are as of yet unidentified.

Once in systemic circulation, the urolithins exist as a combination of glycosylated derivatives and their aglycone form. What this means is that the body will attach a sugar molecule to the urolithin in order to increase its water solubility. At any given moment, the urolithins in the blood stream will be a combination of these “sugar-on” and “sugar-off” forms. The urolithins will exert their effects until they are excreted from systemic circulation.

The urolithin that is produced in the highest amounts from raspberry ellagitannins is urolithin B (UroB). This compound has been studied both in vitro and in vivo and a variety of biological effects have been observed including antioxidant, antimalarial, anti-inflammatory, and anticancer activities. Urolithins are much more bioavailable than ellagic acid and have been reported to reach many tissues in the body. Thus, it has been proposed that many of the health benefits derived from the consumption of raspberries may be due to the colonic metabolism of ellagic acid to form urolithins.

References: