

LAY ABSTRACT

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC) affect almost two million people in the US. IBD is characterized by an exacerbated inflammatory condition in the gastrointestinal tract. Although inflammation is a normal mechanism that the organism uses to protect itself from external aggressors, chronic inflammation in IBD results in tissue damage, dysfunction and disease. Because the origin of IBD is still not known, there is no cure, and scientists are trying to develop new therapies to control the progression of the disease. Both, genetic and environmental factors, including diet, contribute to the development of IBD. We propose that the consumption of diets with high content of select flavonoids can be very important in decreasing the inflammation, in protecting the intestinal mucosa from damage, and as a consequence, in improving the quality of life of patients with IBD. Considering that the existing therapy, that can include surgery, can partially control the symptoms (diarrhea, abdominal pain secondary to intestinal ulcers and fistulas, weight loss), the possibility of a quality of life improvement through dietary changes emerge as a significant step in IBD management.

The **long term goal** of this proposal is to elucidate if diets rich in foods (grapes, red wine, cranberries, cocoa, apples) containing select flavonoids, epicatechin (EC) and its polymers (procyanidins): can prevent the onset or ameliorate the progression of IBD. Given the fact that these flavonoids, although chemically related, have their individual characteristics, they can be protective through different mechanisms, but at the same time act in a synergistic way. We plan to investigate the mechanisms underlying the anti-inflammatory and cytoprotective effects of EC and procyanidins in cell and animal models of IBD.

In the studies done in cells from the intestinal epithelium and the immune system, we will obtain information on the action of the individual compounds. We will learn which are the active compounds, how they function, their potency and their capacity to act synergistically. We propose that they will protect the intestinal epithelium through the blockage of cell signals that are responsible for triggering the chronic inflammation.

In animal models, we will obtain direct information of the beneficial effect regarding the consumption of a diet rich in EC and procyanidins (grape seed extract) in preventing the spontaneous development of CD. We need to assess these protective effects in mice, to plan future studies that will treat IBD patients with diets rich in EC and procyanidins.

Since the availability of pharmacological therapies for IBD is limited, our project is very relevant because, if successful, will lead to an improvement of the prognosis and the general quality of life of IBD patients, simply through the inclusion in their diet of foods rich in select flavonoids.