

## PROTECTIVE ROLE OF ANTHOCYANINS IN DIABETIC NEPHROPATHY

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Diabetic nephropathy (DN) is a common microvascular complication occurring in approximately 20-40% of patients with type 2 diabetes mellitus (T2DM). It is characterized by the progressive impairment of glomerular function leading to end-stage renal failure (1). Hyperglycaemia, kidney inflammation and oxidative stress are crucial in promoting the development and progression of DN and several factors play a key role in the onset of the disease and its progression (2). Anthocyanins are one class of flavonoid compounds, showing high anti-oxidant and anti-inflammatory activity since their constant intake seems to correlate with a reduction of global oxidative state and with a reduction of inflammation markers (3). A standardized new extract, obtained by properly mixing anthocyanins and other polyphenols, recovered from red orange processing wastes, and eriocitrin and other flavanones, recovered from lemon peel has been developed and used in this study.

We have characterized the pathophysiology of DN in a T2DM/DN animal model and the effect of the anthocyanins in the prevention of DN by evaluating the cause-to-effect relationship between the anthocyanins intake and protection from renal damage. Zucker fa/fa rats and Zucker fa/+ rats (healthy controls) were sacrificed after 6 weeks (T2DM rats without renal damage); 15 weeks (T2DM rats with incipient renal damage) and after 30 weeks (rats with DN). Furthermore, the same groups of Zucker rats were treated by oral intake with specific formulations of anthocyanins to ascertain the protective effect of anthocyanins on the progression of DN.

We have demonstrated in the Zucker fa/fa rat, through the clearance of inulin, that the glomerular filtration rate (GFR) is significantly increased after 15 weeks, while after 30 weeks this value is drastically reduced compared to the control. The analysis of Reactive Oxygen Species (ROS), through the dihydroethidium assay and through the Klotho assessment have shown a significant increase of ROS after 15 and 30 weeks. Treatment with anthocyanins have shown, after 15 weeks, value of GFR similar to the control and a similar reparatory effect we have also found in ROS production. Instead, we have not noticed significant differences between diabetic rats and control rats in inflammatory markers, as such as IL-2, IL-6 and TNF $\beta$  before and after treatment.

In conclusion, the use of anthocyanins could reduce the nephrotoxic effect in course of DN through the modulation of ROS productions and open new perspectives in the treatment of patients with T2DM.

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