

## Letter to Editor

### **Flavonoids and sudden death in Parkinson's disease: despite evidence, the defense council must still work hard**

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We read with great interest the excellent review by Jung and Kim about the beneficial effects of flavonoids, the phytonutrients present in almost all fruits and vegetables, for Parkinson's disease (PD).<sup>1</sup> Appropriately, the authors clearly demonstrated that flavonoids regulate a number of important physiological responses, which may contribute to neuroprotective effects in PD.<sup>1</sup> Flavonoids exert their effects by its anti-inflammatory, anti-oxidative and anti-apoptotic properties, Hesperidine may attenuate the iron-induced oxidative damage and may withhold dopamine-depletion. From acacetin it is known that it inhibits the death of neurons and chrysin has a neuroprotective effect. Epigallocatechin has neuro-rescuing effects in a mouse model of PD. The relationship between PD and natural products is a world apart. In this sense, it is well evidenced in the literature that plant-derived natural products can be considered as future pharmaceutical drugs or adjuvant treatment in addition to conventional therapeutic approaches to improve their efficacy and alleviate their psychological adverse effects in the

management of PD.<sup>2</sup> Interestingly, the association between dietary flavonoid intake and the risk of mortality from all causes and cardiovascular disease (CVD) in the general population is well established.<sup>3</sup> In brief, the dose-response analysis from a recent systematic review and a meta-analysis of cohort studies demonstrated that those consuming 200mg of total flavonoids per day had the lowest risk of all-cause mortality, providing strong evidence for the recommendation to consume flavonoids-rich food to reduce risks of mortality from all causes as part of a healthy diet among adults.<sup>3</sup>

Considering these aspects together, an intriguing question emerged: Is there a possible relationship between dietary flavonoids intake, cardiac abnormalities, and even the occurrence of sudden death in individuals with PD (SUDPAR)? Obviously, this questioning sensitizes our reasoning ability and opens new perspectives for future translational research. In the last 10 years, remarkable advances in PD research from the molecular mechanisms to

modern therapeutic approaches have been achieved. Nevertheless, the mortality rates of PD patients are still higher than those of the general population and the cause of these deaths is mainly related to pneumonia, cerebrovascular, and cardiovascular diseases<sup>4,5</sup>. Unfortunately, a small portion of PD patients dies suddenly and unexplained, also described as Sudden Unexpected Death in Parkinson's Disease (SUDPAR)<sup>4</sup>. The mechanism responsible for SUDPAR is still unknown, but there are indications that the autonomic system, i.e., cardiovascular and/or respiratory system, may play a pathophysiological role.<sup>4</sup> Though the availability of pharmacological treatment of PD has increased, these drugs are still limited in clinic efficacy. In these lines, several factors such as genetic and environmental may contribute to the inefficacy of therapeutic strategies in patients with PD. Among these factors, phytochemical aspects, i.e. dietary flavonoids intake, could play an interesting role in this

context. Since some studies have demonstrated, consumption of flavonoids-rich food to have a positive effect on PD and CVD<sup>1-3</sup>, it is quite reasonable to put up the hypothesis that the use of "natural medicine" and in this specific case, the daily consumption of flavonoids, may protect the patient's heart with PD from possible cardiac dysfunctions and even SUDPAR.

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