

Microdispersions of Ellagic acid and pomegranate extracts as new potential nutraceutical ingredients

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The health properties attributed to several fruits (i.e. pomegranates, raspberries, strawberries, blackberry, chestnuts, walnuts, pecan), herbs (tea) and seeds (berries seeds) are attributed to an important group of natural polyphenols classified as hydrolysable tannins (HT) named Ellagitannins (ETs), that have shown in vitro multi-target biological properties relevant to the treatment of several human diseases. In vivo, ETs are rather not absorbed, and they are hydrolysed providing mainly Ellagic acid (EA). EA is endowed with the same biological properties of ETs and it could be considered as the responsible of their health benefits. Unfortunately, EA cannot be exploited for in vivo applications because of its poor water solubility (9.7 µg/mL) and accordingly low bioavailability.

At first, aiming to increase EA solubility, an EA solid microdispersion (EA-md) was realized by employing only water and low methoxylated pectin, as a food compatible excipient, by applying spray drying technology. EA-md showed a 22% (w/w) Drug Loading (DL), a 30 times improved water solubility maintaining a remarkable radical scavenging activity [1]. It has been analytically characterised and used for in vivo pharmacological treatments in order to evaluate it as potential nutraceutical ingredient.

Adult (3-6 months old) and old (20-22 old months) male mice were chronically administered EA-md dissolved in the drinking water (about 150 mg / Kg) for 14 days. During this period, animals were monitored for the spontaneous motor activity and for curiosity before, during and at the end of the EA-md treatment. Adult and old mice were then sacrificed for “ex vivo, in vitro” analysis to test the efficiency of noradrenaline release from cortical nerve endings. It is known that noradrenaline exocytosis from cortical nerve endings is significantly impaired during ageing. We found that the chronic administration of EA-md did not alter the noradrenaline exocytosis from cortical nerve endings of adult mice, but significantly recovered the reduced noradrenaline overflow in aged mice. Further investigations are needed to explore the cellular cascade of events accounting for the beneficial effect.

In a second step, pomegranate, as a natural source of EA, has been considered to similarly prepare and investigate an analogous formulation. Since pomegranate fruit is recognized as one of the most important sources of ETs, mainly localized in the by-products obtained after industrial juice

squeezing, a method to convert the squeezing marcs into a potential nutraceutical ingredient has been explored. In particular, Pulsed Ultrasound-Assisted Extraction (PUAE), using just water as solvent, resulted to be suitable for extracting the water-soluble bioactive molecules (PEx), whose content in hydrolysable tannins, standardized in EA, has been determined. Furthermore, the already mentioned spray drying microdispersion has been employed to formulate and to stabilize it over time. This last formulation (PEx-md) will be subjected to the already mentioned pharmacological experiments in order to study its nutraceutical properties too.

[1] S. Alfei, F. Turrini, S. Catena, P. Zunin, B. Parodi, G. Zuccari, A.M. Pittaluga, R. Boggia, *New J. Chem*, 43, 2438-2448 DOI: 10.1039/C8NJ05657A