By connecting a synthetic scaffold and a natural shell of Gallic acid: an innovative double-acting antioxidant device to figh «oxidative stress»

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Oxidative stress (OS) is involved in the onset and developing of most degenerative diseases hard to fight with exsisting synthetic drugs without adverse side effects. Gallic acid (GA) (Figure 1), a natural triphenolic acid present in several plants, fruits and common foodstuffs, is provided both with the basic nutritional values and with several extra health benefits such as a remarkable antioxidant power. GA exhibited abilities in protecting cells from OS via a number of pathways without triggering unpleasant side effects.[1] GA several potentials could be exploited both in industry and in medicine but unfortunately its clinical application is limited by its pharmacokinetic drawbacks, poor bioavailability, slow GIT absorption, fast metabolism and short half-life. Dendrimer nanoparticles, thanks to their nonpareil physicochemical properties are extensively exploited in nanomedicine to control molecular weight, hydrophilicity, solubility,[2-4] bioavailability and pharmacokinetic behaviour of drugs as well as to protect them from early degradation or fast metabolism. With the aim at minimizing GA's limitations for medical purposes, in this study, a G5 polyester-based dendrimer was prepared and subsequently, it was peripherally further esterified with bioactive GA (Figure 1).

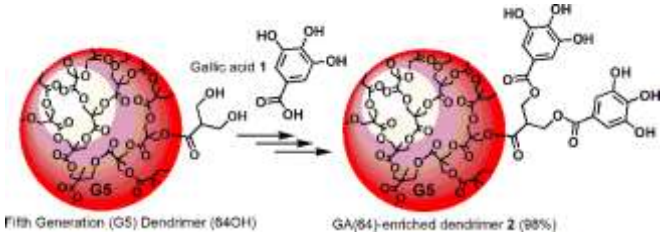

Figure 1. Representations as close as possible to the reality of dendrimers matrix and shell including the structure of Gallic acid **1**

Once the structure of the achieved GA-enriched dendrimer **2** was confirmed by FT-IR, NMR and Elemental analysis, it was evaluated to ascertain its antioxidant power (RSA %) and to establish its behaviour and fate once inside the cells. **2** showed an antioxidant power four time higher than free GA. Besides, it proved to work as a GA delivering device able to carry several bioactive GA units at once and in physiological condition, i.e. once inside the cells, to degrade by cell esterases hydrolytic action to non cytotoxic small molecules setting free the bioactive GA units.

References

1. Dalla Pellegrina, C. ; Padovani, G. et al. *Cancer Lett.*, **2005**, *226*, 17.
2. Alfei, S. Taptue, G. B. et al. *Chinese J. Polym. Sci.*, **2018**, *36*, 999.
3. Alfei, S. ; Catena, S. et al., *Eur. J. Pharm. Sci.*, **2018**, *124*, 153.
4. Alfei, S. ; Turrini, F. et al. *New J. Chem.*, **2019**, *43*, 2438.