An innovative nanocarrier for neuroprotection

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In the last decades, the incidence of age-related neurodegenerative diseases (ARND) has gained relevance due to the progressive increase of average life expectancy and the limited therapeutic solutions available [1]. The multifactorial etiology of ARND suggests the benefit of investing in the study of multi-target active compounds, such as plant polyphenols [2,3]. Within polyphenols sources, the *Curcuma* genus have acquired great importance mainly due to the presence of curcumin, a compound with anti-inflammatory and antioxidant properties, recognised as valuable for the treatment/prophylaxis of ARND [2,3]. In a first step of our research, using a multi-technique biophysical study, curcumin revealed a weak pharmacokinetic profile with low bioavailability and solubility, bioac-cumulation, high affinity to human serum albumin, as well as a tendency to induce membrane biophysical changes [4]. Therefore, to improve the bioavailability of curcumin and consequently its therapeutic benefit, this study aimed to encapsulate curcumin in stealth nanocarriers (NC) of dioctadecyldi-methylammonium bromide (DODAB) and 1-oleoyl-*rac*-glycerol (MO) (1:2) (Figure 1).

The NC present high encapsulation efficiency. Also, by dynamic/electrophoretic light scattering and nanoparticle tracking analysis, the NC developed exhibited sizes lower than 200 nm, high stability when stored up to 4 months and a positive superficial charge, allowing the permeation of the blood-brain barrier by absorption-mediated transcytosis, which increases their interest for ARND biomedical purposes.

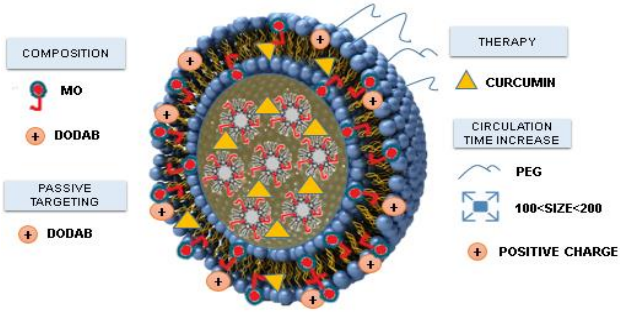

Figure 1: Schematic representation of the developed formulation.

An *in vitro* biphasic controlled release, of 94,5% of curcumin (R^2=0,998) after 50 h was also observed. Furthermore, after successful PEGylation, the ability to prevent interactions with plasma proteins, was also confirmed. Moreover, by fluorescence decay of a lipophilic probe (DPH-PA) under the action of a peroxyl radical generator (AAPH) the antioxidant activity was confirmed.

To study *in vitro* the efficiency of NC we are performing studies in neuronal cells, and analysing the concentration-toxicity curves of curcumin, empty NC and curcumin loaded NC in human SH-SY5Y cells using two cytotoxicity assays: dimethylthiazol diphenyltetrazolium (MTT) reduction and neutral red (NR) uptake.

References

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