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Raman Spectroscopy for the Characterization of Multifunctional Nanoliposomes for Alzheimer's disease and Glioblastoma

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Extended Abstract

In recent years, the ongoing growing and ageing world population has led to an increased incidence of neurological disorders. Despite efforts in researching innovative therapies against various brain diseases, the main problem that still exists today is the delivery of drugs to the brain. The blood brain barrier (BBB) has unique anatomical features that mirror its protective role in maintaining the microenvironment within the brain. Thanks to its special anatomical structure, the BBB regulates the exchange of substances between blood and the cerebral parenchyma. This is very important to protect the central nervous system (CNS), but on the other hand it prevents the passage of pharmacological substances that are useful for the treatment of brain disorders. [1]

Among brain disorders, Alzheimer's disease is the most common form of dementia in the elderly population, while Glioblastoma is the primary malignant tumor involving glial cells in the CNS with a high mortality rate. These two serious disorders have in common the weakening of the immune system and the induction of a chronic neuroinflammatory condition.

For all these reasons, we propose the design and the synthesis of nanocarriers capable of transporting drugs for Alzheimer's disease and Glioblastoma in the brain in order to treat inflammation, without compromising normal immune defence mechanisms. As vehicle, we chose nanoliposomes (LPs) characterized by a double lipid layer and an aqueous interior core to host the selected drug. LPs were functionalized to improve the bioavailability of different molecules and to demonstrate their therapeutic efficacy as drug delivery systems. [2] In order to overcome bioavailability issues with the therapies currently in use, LPs were functionalized with Apolipoprotein E-modified peptide (mApoE) [3] to target and bypass the BBB, and with a peptide sequence sensitive to proteases (lipid-peptide chimera), overexpressed in diseased areas, which guarantee the effective and localized release of the candidate drugs.

To characterize and verify the repeatability of LP production and drug loading, we used Raman spectroscopy (RS), a fast, sensitive and label-free biophotonics-based technique. Through RS we first acquired the spectra of each single component of the liposome (sphingomyelin, mApoE, maleimmide, cholesterol, protease sensitive peptide sequence) and, subsequently, of functionalized and non-functionalized LPs.

The Raman spectra of both LP formulations are, as expected, the combination of the signal provided by individual components, with prominent peaks demonstrating their composition. Through a PCA-LDA analysis we showed that we

can statistically discriminate the spectra collected from LPs either functionalized or not functionalized with mApoE, from drug-loaded LPs and from empty LPs, demonstrating that RS can distinguish each LP-component.

In conclusion, our results proved the ability of this biophotonics-based technique to obtain a specific chemical fingerprint for each formulation. Furthermore, we have confirmed RS as a valid quality control tool for functionalized liposomes.

References

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