Nose to Brain delivery of NiR labelled PEG-PLGA/ PHEA-Dy700-PLA nanoparticles

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ABSTRACT

In the field of drug delivery, the nano-scale carriers offer unique advantages in terms of enhanced drug solubility, controlled release, improved bioavailability, and specific targeting. Their small size also allows the potential crossing of biological barriers. Thanks to these properties, nanostructured carriers have recently been proposed for the delivery of drugs to the Central Nervous System (CNS) through the Nose-to-Brain (N2B) route of administration, which offers a feasible passage from the olfactory or trigeminal pathways to the CNS, bypassing the blood-brain-barrier (BBB) (Musumeci et al., 2018). Polymeric nanoparticles (NPs) represent ideal release systems as they can be suitably designed and manufactured with features such as biocompatibility, stimuli-responsivity, dual or multiple drug loading, labelling with fluorescent dyes or specific ligands to increase their in vivo specific targeting/localization. In the present work, fluorescent polymeric NPs were prepared from two copolymers, the FDA approved polyethylene glycol-poly lactic acid-co-glycolic acid (PEG-PLGA), and the amphiphilic graft polyaspartamide/poly(lactide) copolymer, labelled by a near infrared (NIR) probe, the PHEA-g-Dy700-g-PLA (Craparo et al., 2021). The latter allows, thanks to the PHEA backbone, to stably conjugate molecules with various functions, such as markers and targeting agents. Furthermore, thanks to its amphiphilicity, by varying its concentration it is possible to modulate the characteristics of the particle core to optimise the drug loading of the incorporated drugs. The chemical-physical characterization showed that these NPs possess suitable mean size for administration through the N2B route (<200 nm), as well as good colloidal stability within 40 days after preparation, at different temperature, and stability in simulated biological fluids (such as simulated nasal fluid and cerebrospinal fluid). DSC analysis also revealed amorphous

characteristics of prepared nanocarriers. By means of Fluorescence Molecular Tomography (FMT, Perkin Elmer) pre-clinical in vivo fluorescence imaging analysis were carried out in the near-infrared spectral window to evaluate the localization of nanocarriers *in vivo* biological study on health mice after intranasal administration.

References

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SHORT CV OF THE PRESENTING AUTHOR

Sonya Salamone graduated in Pharmacy in April 2023 at University of Catania, with a score of 110/110 and honors and proposed for the “Ordine dei Farmacisti Catania” prize. During her experimental thesis, which had as its object the development and characterization of polymeric nanoparticles for imaging applications, she has deepened the study of nanomedicine for the nose to brain route of administration and their preparation methods. She experimented with well-known techniques for the characterization of nanoparticles.

From June 2023 to today, she's collaborating voluntarily at the research activity at the laboratory of pharmaceutical technology of the Department of Drug and Health Sciences (UNICT, Catania). She is co-author of one publication.