Nose to brain delivery and nanomedicine: a brief journey through successes and setbacks

Teresa Musumeci
Rosario Pignatello, Claudia Carbone, Angela Bonaccorso
Department of Drug and Health Science, University of Catania, Via Valdisavoia 5, Catania, Italy
NANOMED, Research Centre for Nanomedicine and Pharmaceutical Nanotechnology, University of Catania, Catania, Italy
teresa.musumeci@unict.it

Nose-to-brain (N2B) drug delivery constitutes a compelling alternative to conventional oral and parenteral administration routes for achieving therapeutically relevant concentrations of drugs within the central nervous system (CNS). The anatomical features of the nasal cavity facilitate a noninvasive and rapid transport mechanism, which minimizes systemic exposure and associated adverse effects reducing dosing requirements. This enhances the overall safety profile of the therapy. The N2B delivery exploits systemic pathway and/or the olfactory and trigeminal nerve pathways to bypass the blood–brain barrier (BBB), with the possibility of direct drug delivery to the brain for the treatment of CNS diseases. N2B drug delivery shows challenges, due to the physiological properties of the nasal cavity.

To overcome these limits nanomedicine is being explored to enhance drug retention, absorption, and direct delivery to the CNS while minimizing systemic distribution and degradation. In our ten years of investigation to design suitable nano-formulations to achieve the brain we met success but also many obstacles. We studied several molecules, from natural compounds (such as curcumin, resveratrol), fluorescent molecules for imaging to antipepilectic drugs (oxcarbazepine and carbamazepine) to load into polymeric, lipid or hybrid nanoparticles and/or use nanonization technology to overcome the challenges encountered [1-3].

Nanoparticles allowed to protect drugs and/or increase residence time when coated with mucoadhesive materials. Moreover, nanonization technology represents a useful strategy for drugs belonging to the II or IV class of the BCS, since it allows to reduce particle size to the nano-scale increasing particle surface area, saturation solubility and dissolution rate. This strategy overcome in some case the limit correlate with low volume and therapeutic drug dose. We focused our studies on different neurological diseases (epilepsy, neurodegenerative diseases, metabolic syndrome (MetS) associated to cognitive impairment).

The quality by design (QbD) approach was used as a strategy for factorial planning and protocol development to obtain the suitable nanoformulations for our goal [4-5].

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