OP-16
DOI: 10.14232/syrptbrs.2026.40

Controlling the drug release profile of nasal polymeric nanoparticles via hyaluronic acid

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Controlled drug release via the nasal route is a challenging area of pharmaceutical technology, yet it offers numerous benefits. As a general observation, nasal drug delivery is rapid due to the highly vascularized nasal mucosa, despite mucociliary clearance limiting residence time on the nasal surface. Mucoadhesive excipients, such as hyaluronic acid, can act in two ways: either they prolong residence time, thereby increasing the likelihood of drug release and permeation, or they can act as permeability enhancers. The current study aimed to demonstrate the concentration-dependent behavior of hyaluronic acid on the drug release profile of polymeric micelles, a novel nanocarrier used for alternative administration routes.

The nanocarriers were prepared via nano spray-drying, followed by a particle characterization using laser diffraction and scanning electron microscopy. Liquid-state characterization techniques included dynamic light scattering and the determination of solubility enhancement-related parameters. *In vitro* drug release and permeability studies were conducted in nasal conditions. Our results highlight the importance of conducting rigorous foundational research to determine whether selecting the most promising excipient yields benefits. The particle size and morphology of the spray-dried particles varied with the hyaluronic acid concentration. At lower concentrations, they exhibited smaller particles but higher polydispersity, whereas at higher concentrations, aggregation was observed. This aggregation also translated into our liquid-state studies, as larger micelles and greater polydispersity were observed. A clear and statistically significant effect was also observed in the drug release and permeability studies, as controlled drug release was observed at higher concentrations, which may be suitable for numerous therapeutic indications.

Thus, the importance of the question of which is more important: appropriate colloidal structure or fitting the potential therapeutic indication has arisen, and, as a general opinion, a structured optimization study must always be conducted to determine the potential of the developed nanocarriers.

Acknowledgement

This work was supported by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences (Recipient: Bence Sipos).