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Investigation of the nasal applicability and the effect of mucoadhesive excipients on thermosensitive polymeric micelles

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Neuropsychiatric disorders like depression and schizophrenia present significant therapeutic challenges because the blood-brain barrier limits drug access to the brain. Additionally, conventional oral drugs often cause systemic side effects. This study aimed to develop and compare intranasal thermosensitive polymeric micelles using Pluronic F127, Poloxamer 188, and tocophersolan for the delivery of citalopram (CT) and risperidone (RIS). The primary goal is to improve brain targeting. To increase mucosal adhesion and structural stability, the micelles were loaded in two different gelling polymers: Chitosan (CH) and Hyaluronic Acid (HyA).

CT and RIS-loaded micelles were prepared using the thin-film hydration method. Different concentrations of CH and HY, ranging from 0.1% to 1%, were investigated. The effects of these adhesive polymers on the Z-average, polydispersity index (PdI), and lower critical solution temperature (LCST) were measured using dynamic light scattering (DLS). *In vitro* drug-release profiles were investigated for all samples under simulated nasal conditions at 35 °C to ensure the system operates at nasal-cavity temperature.

The LCST results for CT-CH (0.1 and 0.5%) and CT-HyA (0.1 and 1%) showed preferred values of 28, 33, 29, and 27 °C, respectively, with PdI < 0.3. In contrast, the RIS-CH formulation exhibited undesirable LCST and PdI values, whereas RIS-HyA at 0.25% and 0.75% demonstrated favorable LCST values of 29 °C and 28 °C, respectively, along with a homogeneous size distribution. Moreover, drug release studies revealed a significant enhancement compared to raw drug suspensions.

These findings confirm that loading thermosensitive polymeric micelles in gelling polymers is an effective strategy to improve the nasal delivery of both citalopram and risperidone. Further studies are required to assess *in vitro* and *in vivo* permeability, mucoadhesive characteristics, and cytotoxicity.

References:

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