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Thermosensitive polymeric micelles as nanocarriers in nasal administration

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Utilizing thermosensitive polymeric nanocarriers for the intranasal delivery of antidepressants offers a promising strategy to overcome key challenges such as delayed therapeutic onset and systemic adverse effects, which are major contributors to treatment failure. This study seeks to exploit the temperature-responsive properties of Pluronic polymers to develop and evaluate intranasal citalopram-loaded polymeric micelles (CT-PM), with the goal of improving therapeutic efficacy.

According to initial studies, rotary evaporator was utilized to create CT-PM by employing Pluronic® F127 and Poloxamer® 188 as polymeric micelles generators and freeze-drying method was applied on the aqueous product to stabilize it. Thereafter, comprehensive investigations were conducted to evaluate the final product attributes, encompassing the micelle size transformation at nasal temperature, size distribution, entrapment efficiency, thermodynamic solubility, and X-ray powder diffraction. Moreover, *in vitro* studies (drug release and diffusion) were carried out in nasal conditions and micelles stability was inspected in biological media and different storage environments.

Prepared formulation revealed a preferred LCST value (31 °C) with a monodisperse distribution (polydispersity index < 0.3), which ensures stability at ambient temperature and triggered drug release at nasal conditions. It also achieved remarkably improved drug solubility with approximately 90% entrapment efficiency and amorphous transformation. Additionally, 25-fold increase in in vitro drug release from CT-PM was observed accompanied with 4- fold enhancement in *in vitro* drug diffusion. Storage stability test demonstrated appropriate stability in both states, liquid and solid, and accepted behaviour was displayed after incubation in biological solutions. This advanced nanoscale platform represents a promising approach for targeted antidepressant delivery to the brain, offering a more rapid therapeutic effect while minimizing systemic side effects. Further studies are planned to evaluate its cytotoxicity profile and *in vivo* pharmacokinetic behaviour.

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