Optimization of diazepam-loaded nanostructured lipid carriers (NLC) for nose-to-brain delivery using the quality by design (QbD) approach

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Epilepsy requires fast and effective treatment, targeting the brain. Herein, intranasal administration of nanostructured lipid carriers (NLC) has been suggested as a promising strategy [1]. In addition, the quality-by-design (QbD) approach is a useful tool for the optimization of manufacturing variables, resulting in effective and safe pharmaceutical products [2].

The aim of this work was to use the QbD approach to optimize a NLC formulation for the nose-to-brain delivery of diazepam, improving the emergency therapy of epilepsy. The studies began with screening of excipients and assessing lipid-drug compatibility. The central composite design was used to evaluate the effects of critical material attributes (CMAs) (ratio of solid and liquid lipids and amount of emulsifiers) on the critical quality attributes (CQAs) of the NLC formulation (particle size, polydispersity index (PDI), zeta potential (ZP) and encapsulation efficiency (EE)).

The results showed that the most adequate ratios of lipids and emulsifiers were 6.65:2.85 and 4.2:0.3 (% w/w), with values of 84.92 nm, 0.18, -18.20 mV and 95.48% for particle size, PDI, ZP and EE, respectively. This formulation was selected for further studies on the optimization of critical process parameters (CPPs).