Design of nanosized carbamazepine for nose-to-brain delivery

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Epilepsy is one of the most common neurological disorders in the world. The therapeutic treatment is challenging since conventional drugs have limited efficacy and several side effects that impair patient management (1). Efforts are being made to find innovative strategies to control epileptic seizures. Intranasal administration provides a convenient route to deliver drug to the brain. However, it shows limits due the anatomic structure of the site (the drug dose should fit into 100–200 µL) and the intrinsic properties of the molecule that has to be delivered (2). Carbamazepine (CBZ) is an anticonvulsant characterized by poor water solubility (BCS class II) and nanonization can improve the bioavailability of this molecule. Therefore, the design of CBZ nanocrystals (NCs) was assessed to obtain a formulation suitable for nose-to-brain delivery. CBZ NCs were prepared by sonoprecipitation following the Quality by Design approach to identify the impact of process and formulation variables on the critical quality attributes of the final product. Response surface methodology was a reliable tool (error % 2.6) to optimize CBZ NCs with size ≤300 nm. The formulation was characterized by a technological point of view (thermotropic behavior, crystallinity, morphology). Stability study of CBZ NCs in artificial cerebrospinal fluid at 37°C revealed the absence of aggregation and degradation. The suspension was successfully converted into a powder. Highly concentrated formulation can be obtained, providing the possibility to administer the maximum dose of the drug in the lowest volume. Biological studies revealed the biocompatibility of CBZ NCs towards Olfactory Ensheating Cells.

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