

Formulation and Characterization of Ursodeoxycholic Acid Nanosuspensions Based on Bottom-up Technology and Box Behnken Design †

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Abstract: Ursodeoxycholic acid (UDCA) is a low-water solubility therapeutic agent used to treat cholestatic hepatobiliary diseases. This work aimed to design and optimize UDCA nanosuspensions using the precipitation-ultrasonication method. A three-factor, three-level Box-Behnken design was used, such as stabilizer (X_1), amplitude (X_2), and sonication time (X_3). A cryoprotection effectiveness test was carried out to evaluate the efficiency of lyophilization. Particle size (PS), polydispersity index (PDI), and Z potential (ZP) were evaluated by DLS, and residual solvent content by GC-FID-MS. Physicochemical stability was evaluated at 25°C and 4°C at intervals of 7, 14, 30, and 60 days. The content of UDCA was determined by HPLC-UV. Values with a significant effect on the developed nanosuspension were 0.3% for stabilizer concentration, 5 min sonication time, and 50% for the suitable operative amplitude. The optimal UDCA nanosuspension showed a PS of 352.4 nm, a ZP of -4.30 mV, and a PDI of 0.11. For lyophilization, 10% maltose (cryoprotectant) and -80°C (freezing temperature) were selected, the absence of acetone was observed, and the nanosuspension presented adequate physicochemical stability throughout the study. The UDCA nanosuspension formulation may be an alternative to improve UDCA's oral administration, dosage, and bioavailability.

Keywords: ursodeoxycholic acid; nanosuspensions; stability study; Box-Behnken design.

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Conflicts of Interest

The authors declare no conflict of interest.