

CLOBETASOL PROPIONATE NANOCRYSTALS: IMPROVING DRUG SAFETY FOR TOPICAL APPLICATION

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INTRODUCTION: Inflammatory skin diseases can cause symptoms such as pain, redness, itching, and scaling, resulting from the interaction of genetic, environmental, and immunological factors. Clobetasol propionate (CP) is used as a topical treatment, but prolonged use may cause side effects. Nanotechnology is a promising alternative to improve efficacy and reduce toxicity. **MATERIALS AND METHODS:** CP nanocrystals (NC-CP) were developed by precipitation–ultrasonication using acetone as a solvent and HPMC as stabilizer. The samples were characterized in triplicate of batches regarding average particle size and size distribution, pH, zeta potential, drug content, nanocrystallization rate, and stability. *In vitro* release assays (dialysis bag) and skin permeation (Strat-M[®] membrane) were also performed, comparing NC-CP with CP classical solutions used to formulate clobetasol topical products: ethanol and propylene glycol. The cytotoxicity was evaluated (MTT and neutral red [NR] assays on 3T3 cells) comparing NC-CP with the drug solution in DMSO. **RESULTS AND DISCUSSION:** The nanocrystals presented average size of 648 ± 67.77 nm and a PDI of 0.317 ± 0.05 , drug content of 90.29%, nanocrystallization rate of 99.36%, and pH of 7.53, maintaining stability for 180 days under refrigeration. Microscopy images confirmed the efficacy of the nanocrystallization process. NC-CP showed controlled CP release over 48 h, with significantly lower CP released values than drug solution ($p < 0.05$). Regarding permeation to the receptor fluid, NC-CP presented significantly lower values of permeated CP than the drug solutions (24 h and 48 h; $p < 0.05$). These data suggest CP retention in viable layers, with reduced chance of systemic effects. NC-CP cytotoxicity assays showed viability above 80%, except at the highest nanocrystal concentration (0.5 mg/mL) in the MTT test. The drug solution, on the other side, showed cellular viability values of less than 40% (MTT) and less than 60% (NRU) for all concentrations tested. **CONCLUSION:** NC-CP was considered promising for topical application, offering controlled release, reduced skin permeation and citocompatibility, supporting its improvement of drug safety in the topical treatment of inflammatory skin diseases.

Keywords: Nanocrystals; clobetasol propionate; skin permeation; precipitation–ultrasonication; cytotoxicity.