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RESEARCH PAPER

Box–Behnken Optimization of a Probe-Ultrasonicated Paracetamol Nanosuspension: Colloidal Characterization and Dissolution Enhancement

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ABSTRACT

Generally conventional paracetamol suspensions contain coarse particles (10–90 µm) that sediment rapidly. This has a risk of dose variability in successive dose during usage; especially, paracetamol is given to children on basis of weight to avoid liver toxicity. In this work, suspension of paracetamol was prepared at nano level by ultrasonication method and stabilized by Carbopol 71G NF and poly sorbate 80. The resultant nano scale suspension was evaluated to produce stable nanosuspension in physical and dissolution terms. A three-factor, three-level Box–Behnken design (BBD) address the effects of Carbopol 71G NF (X_1), Polysorbate 80 (X_2) and sonication amplitude (X_3) on Z-average diameter (Y_1), polydispersity index (Y_2) and zeta potential (Y_3). All three quadratic models were significant ($R^2 \geq 0.95$; $p < 0.0001$); Carbopol was the dominant variable, and the $X_1 \times X_3$ interaction was significant ($p < 0.05$). Desirability optimization (D = 0.847) identified 0.38% w/v Carbopol, 0.062% w/v Polysorbate 80, and 48% amplitude, and the validation batch matched predictions within 2% (341 ± 12 nm; PDI 0.186; zeta potential −29.7 mV). HPLC content (22.93 ± 0.75 mg mL^{-1}) comply well with limits in USP. The optimized formula released 92.4% of the dose within 15 min against 69.8% for unprocessed powder ($f_2 = 31.7$) HCl (pH=1.2). The formulation was physically and chemically unchanged after 21 days at −4, 24, and 40 °C. The Carbopol–Polysorbate 80 electrostatic network preserved colloidal integrity, and the BBD exposed a Carbopol–amplitude synergy that one-variable-at-a-time screening cannot detect.

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INTRODUCTION

Paracetamol is the first-line analgesic-antipyretic in children under six because aspirin is contraindicated owing to the risk of Reye's syndrome [1]. Generally, the pediatric dose of paracetamol is 15mg/Kg q.i.d. because children below five years cannot swallow solid dosage forms, so oral liquids are the only practical option. Accordingly, as much as uniformly distributed liquid system, the safer precise dose given [2]. The dose accuracy is achieved by uniform distribution of medicine in that particular milliliters -dose given

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