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Formulation and optimizationof pH-sensitive nanocrystalsforimproved oral delivery

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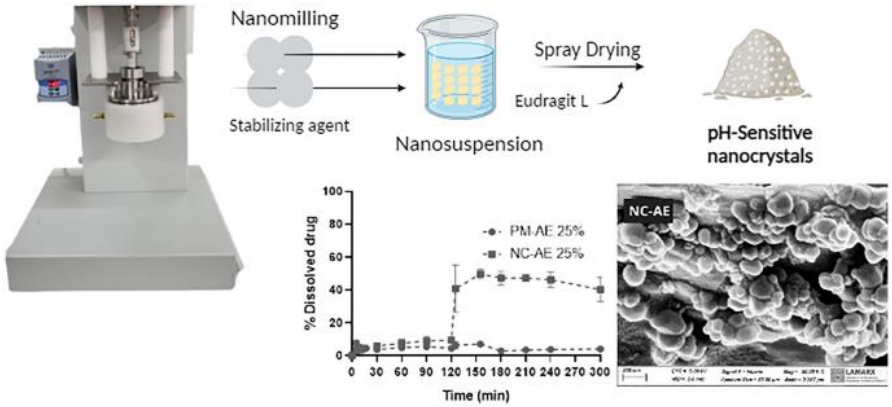
Abstract

The challenge of low water solubility in pharmaceutical science profoundly impacts drug absorption and therapeutic effectiveness. Nanocrystals (NC), consisting of drug molecules and stabilizing agents, offer a promising solution to enhance solubility and control release rates. In the pharmaceutical industry, top-down techniques are favored for their flexibility and cost-effectiveness. However, increased solubility can lead to premature drug dissolution in the stomach, which is problematic due to the acidic pH or enzymes. Researchers are exploring encapsulating agents that facilitate drug release at customized pH levels as a valuable strategy to address this. This study employed wet milling and spray drying techniques to create encapsulated NC for delivering the drug to the intestinal tract using the model drug ivermectin (IVM). Nanosuspensions (NS) were efficiently produced within 2 h using NanoDisp®, with a particle size of 198.4 ± 0.6 nm and a low polydispersity index (PDI) of 0.184, ensuring uniformity. Stability tests over 100 days at 4 °C and 25 °C demonstrated practical viability, with no precipitation

or significant changes observed. Cytotoxicity evaluations indicated less harm to Caco-2 cells compared to the pure drug. Furthermore, the solubility of the NC increased by 47-fold in water and 4.8-fold in simulated intestinal fluid compared to the pure active compound. Finally, dissolution tests showed less than 10% release in acidic conditions and significant improvement in simulated intestinal conditions, promising enhanced drug solubility and bioavailability. This addresses a long-standing pharmaceutical challenge in a cost-effective and scalable manner.



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