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Abstract

Optimization of Lipid-Based Ceftriaxone Delivery System via Machine Learning †

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Abstract: Ceftriaxone (CTX) a third-generation cephalosporin, is a broad-spectrum antibiotic that can be administered via intramuscular or intravenous routes to treat various types of infection. However, CTX has poor cellular penetration and poor diffusion due to its high molecular weight and high hydrophilicity. To address these problems, we propose an innovative nanotherapy based on the encapsulation of CTX in a nanostructured lipid carrier. Usually, several attempts must be made, on a trial-and-error basis, before a formulation that guarantees high drug encapsulation and suitable physicochemical properties is found. Machine Learning (ML) has recently stirred great interest as a tool to model and predict nanoparticles' biological activity. Herein, for the first time, the use of ML for the optimization of a nanoformulation is explored. Several variables were optimized simultaneously, namely, the amount of solid lipid, the percentage of liquid lipid, the surfactant solution, the water volume, the sonication amplitude, and the sonication time. To define the best nanoformulation, three different outcomes were considered: the encapsulation efficiency of CTX, the size of the nanoparticles, and their zeta potential. Our ML approach was able to find, with a low number of experiments, the conditions that provided formulations with the highest encapsulation efficiency of CTX and nanoparticles with suitable size and adequate zeta potential. Besides the impressive acceleration of the optimization process that was achieved, the optimization guided by our ML model also provided insights into the optimization of other nanoformulations.

Keywords: lipid-based nanocarriers; ceftriaxone; optimization; machine learning

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