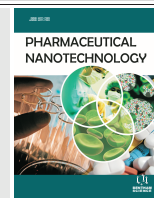




Chemistry Characterization and Application of Nanocrystals-based Drug Delivery System: Present to Future Perspective



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Abstract: With the development of new technologies, various drugs with higher efficacy have been found, but their therapeutic use is still limited owing to poor water solubility, which leads to poor systemic bioavailability. Currently, about 40% of newly discovered drugs have a solubility issue. It is a major challenge for formulation scientists to overcome this problem and make a robust and effective formulation. One such unique approach is to formulate the drug as nanocrystals which alter the physical characteristics of the drug, resulting in the development of a novel formulation strategy for poorly soluble drugs. Nanocrystals are produced by various techniques such as top-down, bottom-up, or combination methods. Nanocrystals improve the clinical application of problematic drug molecules by decreasing the particle size, enhancing the dissolution rate and reducing the dose requirement, *etc.* This approach is not only improving the bioavailability of the drug but also facilitates the drug targeting to specific sites due to its feasibility of surface modification and all administration routes. This article deals with the various aspects of nanocrystals including chemistry, production, stabilization, characterization, and application in the field of pharmacy.

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1. INTRODUCTION

Product nanonization, whether intended for medical applications, such as mini robots to cleanse arteries, or, use in the food industry, such as nano-encapsulated vitamins for use as functional food, or, for pharmaceutical applications, has become a significant factor both economically and medically [1]. Nowadays it has been found that 40% of the drug in the development pipeline and 60% of all drugs coming out of synthesis have low systemic bioavailability due to their poor solubility [2]. Most of these drugs belong to the BCS class II (low solubility and high permeability) and IV category (low solubility and low permeability). Most of the newly developed chemical entities have physicochemical properties like high molecular weight and high lipophilicity (log *p*) value and their solubility is a limiting step for further advancements [3]. Solubility is a major barrier to developing a suitable dosage form because generally compounds with low aqueous solubility possess low bioavailability, which is a primary indicator for assessing the rate and extent (amount) at which the drug reaches the systemic circulation. It is the major hurdle for formulation scientists to improve the solubility and make a robust, safe and highly effective formulation.

To improve the solubility of the drug, scientists have proposed several methods like co-solvation, solid dispersion, nanoparticle formation, micronization, Self-Emulsifying Drug Delivery System (SEDDS), complexation, and nanocrystallization. The standard formulation approach is micronization, in which powdered drugs are reduced to a size range typically between 1-10 μm . However, in several cases, they are unable to address the issue of bioavailability. The next logical step was to progress from the micronization of drugs to nanonization [4]. Out of these methods, this article deals with the overall aspects of the nanocrystallization technique [5].

Among the various nanotechnology-based strategies for solubility improvement, nanocrystals are demonstrating their potential as a substantial delivery system for addressing the solubility issues of several drugs. Nanocrystals play a significant role because of the large surface area which increases saturation solubility and decreases the diffusional path length subsequently enhancing the bioavailability. Nanocrystals are not only improving solubility but also play an important role in drug targeting since they are highly suitable for passive and active targeting because of the maximum possible drug content (nearly 100%, no carrier material) [2]. Nanocrystals have piqued researchers' interest in recent years as a way of generating colloidal particles with altered biological properties, facilitating drug delivery, and drug targeting to be modified [6]. As a result of their simplicity of formulation and

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