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## Particle size's role in drug delivery

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### ABSTRACT

Developing new dosage forms has always required consideration of the state of subdivision of a medicine. As physical pharmacy has developed, pharmaceutical researchers and medical experts have begun to explore this characteristic more carefully in order to comprehend how particle size impacts not only physical systems but also biological systems. In this we had tried to understand and explain what role particle size plays in drug delivery by using various databases. Solid medication delivery techniques are crucial formulations for oral administration. In these pharmacological systems, particle size has a substantial impact on drug absorption, dissolution and crossing the blood brain barrier. The ability of a medicine to dissolve in water has a substantial impact on how efficiently it is absorbed when administered orally. It is helpful for modifying and testing pharmacological qualities as a drug is being developed and produced. It also indicates whether a medication may be administered parentally.

### Keywords:

Particle size, drug delivery, absorption, distribution, treatment

### 1. INTRODUCTION

It has always been important to take a drug's state of subdivision into account when creating aesthetically pleasing, elegant, and stable dosage forms. Pharmaceutical researchers and medical professionals have started to examine this attribute more closely as physical pharmacy has advanced in order to understand not just how it affects physical systems but also how particle size affects biological systems. It is also indicated in Ayurvedic science also, methods like *Bhavana* (wet grinding) and *Maranaa* (incineration) are employed to create dosage forms with microscopic particle sizes. These nanosized formulations are allegedly said to be more potent and quick-acting. This article focuses mostly on current developments in biopharmaceutics regarding medication

particle size. Since 1963, a number of review articles addressing particle size in various contexts have been published [1].

The medication is mainly absorbed from particulate matter after it has dissolved. The particle size of the drug is crucial in the transport from the GI tract to the site of action via the blood and lymph via the dissolution rate being the rate-limiting step, that is, if the dissolution rate is less than the diffusion rate to the site of absorption and the absorption rate itself. The physiological availability of a drug must be taken into account when its solubility is less than 0.1 mg/ml, and the impact of particle size may be crucial. Others assert that if the solubility is 1 mg/ml, particle size should be taken into account [1].

Taking all these fact in consideration, it was decided to explore the role of particle size in drug delivery. In this review, studies are collected and assed for the fact that how particle size reduction helps enhancing the drug potency.

## 2. METHODOLOGY

A number of widely used databases, including SciFinder, Google Scholar, MEDLINE, EMBASE, Scopus, PubMed, and Science Direct, were utilised to retrieve published papers (up until April 2023). We looked for and extracted published literature relating to particle size role in drug delivery using the keywords “particle size”, “absorption”, “distribution”, “drug discovery”, “therapeutic”, and “treatment”. The language of searches was limited to English.

## 3. RESULT

For oral administration, solid drug delivery methods are essential formulations. Particle size has a significant effect on medication absorption and dissolution in such pharmacological systems.

### 3.1. Role in absorption

#### 3.1.a. Noyes-Whitney equation

Noyes-Whitney equation, the modified form by Nerst-Brunner, and the cube root equation, its function in the dissolution rate is explained. According to these equations, the rate-limiting step in both drug dissolution and absorption is the diffusion of solute through a boundary layer surrounding the particles. This process is dependent on the specific (external) surface area of the particles, the solute’s diffusion coefficient, the thickness of the boundary layer, and the solute’s solubility. In this regard, sufficient particle dispersion and proper wetting of the particle surface by the surrounding liquid are crucial [2].

In this regard, sufficient particle dispersion and proper wetting of the particle surface by the surrounding liquid are crucial. According to information on dissolution rates, the thickness of the boundary layer is dependent on particle size for smaller particles but constant for bigger ones. The focus is on nanosystems and their significance to the bioavailability of poorly soluble medicines due to the increased surface area of smaller particles.

#### 3.1.b. Freundlich-Ostwald equation

According to the Freundlich-Ostwald equation, a second benefit of such drug delivery systems is that solubility rises with decreasing particle size. The effect of particle size on drug absorption is discussed because dissolution and absorption are closely related [2].

### 3.2. Role in dissolution rate

In solid organ transplantation, Cyclosporin A (CsA), a hydrophobic medicine, is frequently utilised as an immunosuppressant and anti-rejection medication. A study was carried out to develop oral Cyclosporin A nanosuspensions (CsA-NSs) and examine the impact of particle size on CsA-NSs absorption. Wet bead milling was used to create CsA-NSs with diameters of 280 nm, 522 nm, and 2967 nm. Results show that the form of CsA-NSs with lower size was similar to that of spheres. These studies looked at the *in vitro* dissolution, intestinal absorption qualities, and pharmacokinetic analysis of CsA-NSs. Also, CsA's crystallinity in nanocrystals was decreased. The disintegration rate of CsA-NSs (280 nm) was higher than that of CsA-NSs (522 nm) and CsA-NSs (2967 nm). CsA-NSs (280 nm) demonstrated higher [3].

CsA-NSs (280 nm) had a higher dissolving rate than CsA-NSs (522 nm) and CsA-NSs (2967 nm). In contrast to CsA-NSs (522 nm) and CsA-NSs (2967 nm), CsA-NSs (280 nm) demonstrated better effective permeability coefficients ( $P_{eff}$ ) and absorption rate constants ( $K$ ) of various intestinal segments. The AUC<sub>0-48h</sub> of 280 nm CsA-NSs was approximately 1.12 times that of 522 nm CsA-NSs and approximately 1.51 times that of 2967 nm CsA-NSs. Particularly, CsA-NSs had nanoscale particle size, and their bioavailability was bioequivalent to that of marked self-microemulsion (Sandimmun Neoral®). The study found that lowering size improved CsA-NSs' dissolving rate, gastrointestinal transport characteristics, and oral absorption. There should be a suitable range of particle sizes in terms of price, effectiveness, and energy consumption [3].

Solubility, dissolution, and gastrointestinal permeability have all been extensively discussed as being the major determinants of the rate and volume of drug absorption as well as its bioavailability [4]. How well a medicine is absorbed when given orally is significantly influenced by its capacity to dissolve in water. It also determines if a medication may be given parenterally, and it is useful for changing and testing pharmacological properties as a medication is being created and produced. When the dissolving time is limited, it's also critical to take into account how quickly the drug departs or dissolves from a solid dosage form [5].

Another study looked into the impact of drug particle size on the physicochemical characteristics, complexation, and dissolution of  $\beta$ -cyclodextrin inclusion complexes. The drug model used in this study was ibuprofen, which comes in sizes of 3  $\mu\text{m}$  and 45  $\mu\text{m}$  (ibuprofen 3 and ibuprofen 45). Studies on the kinetics and effectiveness of the complexation of ibuprofen with  $\beta$ -cyclodextrin in water were carried out. The solid cyclodextrin inclusion complexes were made using the kneading process, and they were examined using optical microscopy, dissolution testing, differential scanning calorimetry, X-ray powder diffractometry, and Fourier transform-infrared spectroscopy. In a study of complexation kinetics, ibuprofen with smaller particle size demonstrated a greater complexation rate with  $\beta$ -cyclodextrin.

The apparent stability constant,  $K_c$ , and the effectiveness of complexation also showed that smaller drug particles interact with  $\beta$ -cyclodextrin more effectively than bigger ones. Complexes with limited solubility are indicated by the Bs type of the phase solubility diagram. It was proven by Fourier Transform-infrared spectroscopy, differential scanning calorimetry, X-ray powder diffractometry, and optical microscopy investigations that ibuprofen 3 or ibuprofen 45 can form  $\beta$ -cyclodextrin inclusion complexes. In contrast to physical mixtures and

pure medicines, inclusion complexes showed a faster rate of dissolution in the dissolution study. Additionally, the dissolution rate of the inclusion complexes made with ibuprofen in tiny particle size was higher than in large particle size.

### 3.3.Role in blood brain barrier

Brain pathologies, among which multiple sclerosis, Alzheimer's disease, Parkinson's disease, and brain cancer are some of the most common, are currently inadequately treated because of the challenges involved in drug discovery, delivery, and targeting to the brain. Due to the blood-brain barrier, which shields the brain from outside chemicals, drug targeting and delivery to the brain present significant obstacles. But new methods for improved blood-brain barrier crossing need to be discovered. In order to cross the blood-brain barrier and deliver the right dosage of medication to the particular brain region, nanotechnology-based techniques are now being investigated in great detail. Additional study is required to comprehend and mediate the mechanisms that pass the blood-brain barrier [6].

## 4. CONCLUSION

Particle size plays a major role in increasing the potency of drug absorption, its distribution and dissolution rate. So by using various methods to reduce the particle size of medication, they are processed into novel formulations which are fast acting medications. Still there are lack of well established scientific studies, which proves this fact more effectively. Also, in order to enhance the effectiveness of brain delivery techniques using nanotechnology, more study is required to comprehend and mediate the blood-brain barrier crossing mechanisms.

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