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Bioavailability – Challenges and Advances in Drug Targeting

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Abstract

It has been a very challenging task in drug development to handle bioavailability of drug molecules during targeting. Foremost challenges include the time span involved apart from various complexities, wrong methods or failure in outcome, increasing manual and financial requirements to be managed in the drug discovery process. Among this bioavailability is one of the biggest challenges handled to successfully identify druggability in a molecule. Various methods of administration and targeting has been used including co-crystallization, micro emulsion, micellar solubilization and other traditionally which has also expanded to other methods as morphous solid dispersion, liposomes, and complexions. To enable precision in availability of drug molecule at the targeted site. There has been an increase in bioavailability of potential drugs. This review comprehensively determines challenges and methods used in drug targeting based on their bioavailability.

Keywords: Drug; Bioavailability

Introduction

Challenges Faced in Bioavailability of Drugs in Human Body

There are numerous factors which determine the bioavailability of drug molecules, which determines a crucial phase of drug development. The physicochemical properties of the drug affect the passage into solution and affects or guides transfer across membranes includes the pKa, solubility in lipids, dissociation rate of the drug, and the potential of the compound to form complexes. These factors also have an influence on the dosage form in which the drug is administered. The solubility and dissolution rate are two factors which are under the influence of pH and environment that impacts dissolution of drug and controlled by surface area of the drug.

Solubility in lipids is prime indicator of availability of drug molecules across membranes. Absorption is influenced by the rate of dissolution of drugs. This in turn affects the usage and form of excipient used with active ingredients in drug delivery [1,2].

The physiological aspects in drug availability in the human body have also had profound effects on druggability of molecules. The factors that are influential are diseases, genetics, and age of the diseased. Differences are also evident based on the other parameters as health and nutrition intake, sex, hormonal health, and changes that happen in body as in condition due to pregnancy, circadian rhythm of body and its influences. Tolerance and body defense to toxic substances not only affects the individuals but also the dependent fetus in case of pregnancy. Diseases also have a profound influence on drug metabolism, its absorption and excretion. This highlights the importance of food intake and significance of fulfilling nutritional requirements of the body. Previous experiences in the body along with the toxicology of the drug molecule also affect the disease state and administration of the drug [2,3].

The form of administration can vary and influence dosage of drug and bioavailability. The administration of oral drugs in solid forms as tablets, suspensions, or capsules is highly studied and commonly used form of bioavailability. Intramuscular administrations, or intravenous, vary from each other in their bioavailability [4]. The bioavailability of intravenous route of administration is found to be 100% in comparison to other forms as intramuscular, subcutaneous, oral., inhalation, transdermal or subcutaneous. The characteristics of administration differ from rapid onset for inhalation, most rapid for intravenous to slow absorption in transdermal [5]. Some form of administration is found to be greater bioavailability than others. The antibiotic, Chloramphenicol, administered through intravenous route is less bioavailable than when provided orally as it exists in preform and has to be activated in the intestines [5,6].

It's a highly variant but dependent factor of drug path in the body from absorption, distribution, metabolism, and excretion which affects the availability of drug molecules. Studies indicate a time-dependent variation in pharmacokinetics of most classes of drug molecules, which are also found to occur based on underlying changes related to physiological functions. The high and low values of the variation are also found to vary based on time, indicating a time dependent variation in bioavailability of drug molecules [7]. The ethnic, environmental and individual variations in population across all human races are found to vary in having a difference in availability of drugs biologically.

The variations in genetic, physiological, and pathological aspects between ethnic/racial populations have been associated with racial or ethnic differences in both pharmacokinetics and pharmacodynamics. These pharmacokinetic/pharmacodynamic variations are also known to be influenced by a number of external elements, including socioeconomic status, culture, nutrition, and environment. When conducting or analyzing pharmacokinetic/pharmacodynamic studies in connection to ethnicity or race, it should be highlighted that other aspects linked to dosing regimen and dosage form have generally been ignored or omitted [8]. The wide variation leads to optimizing the biological availability of drugs based on few factors which can be generically controlled across populations [1].

Methods of used in Drug Delivery and Bioavailability

Different methods have been used for administration of drugs which traditionally also was done by swallowing, inhalation, skin absorption or injection. Local administration of drugs was sometimes preferred over general administration to reduce treatment impact. However, carriage of drugs is being done using 'packaging' of micelle or nanoparticles which also protects drugs from degradation and enable better site targeting. Studies have advance on physiological barriers for efficient drug delivery.

Use of microscopic needles in large numbers as dozens of needles each much thinner than the human hair carrying medicine is used. Their efficiency is such that without penetrating nerves, they deliver medicine after penetrating the skin. The advanced pills, the robotic pills, carry complex, liquid drugs are carried directly to stomach. The drug is then injected into the stomach tissue whereas the pill gets excreted through the gastrointestinal tract. The delivery modes of micelles, liposomes or nanoparticles also help improve targeting of drug by helping the precise delivery of drug in destination site [9].

There are further challenges in certain cases of pathological conditions where Nano vesicles mimicking neutrophils are used to deliver anti-inflammatory drugs to target lungs. The method of delivery system is in early stage of development [9]. Malate dehydrogenase 1 and 2 are effectively inhibited by AC1497, a dual inhibitor that targets cancer metabolism. Its low bioavailability due to poor water solubility, however, prevents clinical development. The components of SNEDDS (self-nanoemulsifying drug delivery system) were taken to be Capryol 90, Kolliphor RH40, and Transcutol HP based on the solubility of AC1497 in various oils, surfactants, and cosurfactants.

The most effective SNEDDS-F4 was found to comprise 20% Capryol 90, 45% Kolliphor RH40, and 35% Transcutol HP. It had a narrow size distribution (17.8 0.36 nm) and a high encapsulation efficiency (93.6 2.28%). As much as 80% of AC1497 was released from SNEDDS-F4 in just 10 minutes, with only a negligible (2%) amount of the drug powder dissolving. Additionally, oral absorption of AC1497 was greatly enhanced by SNEDDS-F4 [10].

Assessing Bioavailability

The area under the curve (AUC) is a definite integral of a drug's blood plasma concentration as a function of time in the field of pharmacokinetics [11]. AUC is the most trustworthy indicator of a drug's bioavailability (Area under the curve). The total amount of medication that enters systemic circulation unmodified is directly inversely related to AUC. If the curves for a drug product's plasma concentration are essentially superimposable, then the extent and rate of absorption may be deemed to be bioequivalent.

Chemical equivalency asserts that drug products contain the exact active ingredient in the same quantity and adhere to predetermined standards, although inactive substances may

vary. In case of bioequivalence, the drug products produce equal drug concentrations in plasma and tissues when administered to the same patient according to the same dose regimen.

Therapeutic equivalence suggests that drug items have the same beneficial and harmful effects when administered to the same patient under the same dosing regimen [12].

Conclusion

From drug formulation, drug administration, drug absorption, through drug pharmacokinetics in the body, managing a disease situation as a biological deviation from normalcy or pathogenicity is difficult.

There are numerous physical, biological, and mechanical challenges to overcome. In order to control the dosage requirement while keeping an eye on the body's physiological status, it is necessary to combine the effective bioavailability of the medicine with a drug formulation that targets a disease or pathologic condition.

The development of bio friendly creative approaches to synchronise the treatment of disease with optimal targeting using new drug delivery systems, providing greater bioavailability, and the advancement of technology are thus crucial to increasing the bioavailability of drugs. Despite these developments, however, maintaining healthy cells or tissues is a task that must be successfully addressed.

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