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"BIOAVAILABILITY ENHANCEMENT OF DRUGS FOR THERAPEUTIC APPROACHES AND FUTURE TREND"

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ABSTRACT

The solubility issues complicating the delivery of these new drugs also affect the delivery of many existing drugs. The various traditional and novel techniques that that can be used for solubility enhancement of BCS Class drugs. Bioavailability refers to the rate and extent of the drug absorbed in the systemic circulation after administration. Oral delivery, the most convenient mode of drug administration has certain limitation. Therapeutic effectiveness of a drug depends upon the bioavailability and ultimately upon the solubility of drug molecules. Solubility is one of the important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response to be shown. Thus, a major amount of the drug is wasted and the unabsorbed drug leads to undesired side effects in the gastrointestinal tract. Various approaches are used for bioavailability enhancement of the orally administered drugs. The present review focuses on the importance of bioavailability, for therapeutic approaches and future trend.

KEYWORDS: Therapeutic effectiveness, bioavailability enhancement, solubility.

INTRODUCTION

Bioavailability is defined as the rate and extent (amount) of absorption of unchanged drug from its dosage form. It is one of the important parameters which are required to achieve optimal concentration of drug in systemic circulation to show a pharmacological response.[1] A drug which has poor bioavailability shows poor aqueous solubility, slow dissolution rate, poor stability of dissolved drug at physiological pH, poor permeation through biological membrane, extensive first pass metabolism.[2] Solubility is one of the important parameter to increase bioavailability. Currently only 8% of new drug candidates have both high solubility and permeability. Nearly 40% of the new chemical entities currently being discovered are poorly water soluble. More than one-third of the drugs listed in the U.S. Pharmacopoeia fall into the poorly water-soluble or water-insoluble categories. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities.[3] Any drug to be absorbed must be present in the form of an aqueous solution at the site of absorption. The process of solubilization involves the breaking of inter-ionic or intermolecular bonds in the solute, the separation of the molecules of the solvent to provide space in the solvent for the solute, interaction between the solvent and the solute molecule or ion.[4]

Factors influencing bioavailability[6]

- Drug concentration at site of administration.
- Surface area of the absorptive site.
- Drug pKa.
- Drug molecule size.
- pH of the surrounding fluid.

Methods for enhancement of the bioavailability[5]

As per the definition the drug candidate which has the following properties is one with poor bioavailability. Poor aqueous solubility and/ or slow dissolution rate in the biologic fluids Poor stability of the dissolved drug at the physiologic pH Inadequate partition coefficient and thus poor permeation through the biological membrane Extensive presystemic metabolism.

There are three major approaches used to overcome the bioavailability problems.[7,11]

A) Pharmaceutics approach: It is done by modifying of formulation, manufacturing processes or physiochemical properties of the drug are done.

B) Pharmacokinetic approach: Alteration of pharmacokinetic parameters by modifying its chemical structure.

C) Biological approach: The route of administration is changed in this method. Solubility and rate of dissolution are very important factors in third approach.

Technique to enhancement of bioavalability[8]

I. Physical Modifications

Physical Modifications and Nano Particulate Strategies for Improved to enhance the solubility and thus bioavailability of numerous drugs, the bioavailability including physical adaptation, many more modification.

A. Particle size reduction

1. Micronization
2. Sonocrystalisation
3. Nanosuspension
4. Supercritical fluid process

B. Modification of the crystal habit

1. Polymorphs
2. Pseudopolymorphs

C. Drug dispersion in carriers

1. Eutectic mixtures
2. Solid dispersions
3. Solid solutions

D. Complexation Use of complexing agents

E. Solubilization by surfactants

II. Chemical Modifications[9-11]

Chemical modifications aim to improve bioavailability by increasing drug solubility. Techniques like nanomilling, spray drying, and micronization reduce particle size and increase surface area-to-volume ratio, which encourages interaction with the solvent.

1. Change in the pH
2. Use of buffer
3. Derivatization

III. Other method

1. co-crystallisation
2. co-solvency
3. Hydrotrophy
4. Solubilizing agents
5. Selective adsorption on insoluble carrier
6. Solvent deposition
7. Using soluble prodrug
8. Functional polymer technology
9. Precipitation Porous
10. microparticle technology
11. Nanotechnology approaches

Microemulsions

Particle size reduction: Particle size reduction can be achieved by

a. Micronization
b. nanosuspension
c. Sonocrystalisation
d. Supercritical fluid process

Absolute bioavailability: Absolute bioavailability measures the availability of the active drug in systemic circulation after non-intravenous administration (i.e., after oral, rectal, transdermal, and subcutaneous administration). In order to determine absolute bioavailability of a drug, a pharmacokinetic study must be done to obtain a *plasma drug concentration vs time* plot for the drug after both intravenous (i.v.) and non-intravenous administration. The absolute bioavailability is the dose-corrected area under curve (AUC) non-intravenous divided by AUC intravenous.[10]

Relative bioavailability: This measures the bioavailability of a certain drug when compared with another formulation of the same drug, usually an established standard, or through administration via a different route.

RESULT

Drug bioavailability after oral administration is affected by anumber of different factors, including physicochemical properties of the drug, physiological aspects, the type of dosage form, food intake, biorhythms, and intra- and interindividual variability of the human population. Chemical reactions that reduce absorption can decrease bioavailability. The bioavailability from water decreases with increasing lipophilicity and with increasing amount of dissolved organic carbon or colloids in the aquatic phase. Plasma drug concentration increases with extent of absorption; the maximum (peak) plasma concentration is reached. Prodrugs have proven to be an effective approach to increase oral bioavailability. In addition, they can provide long-acting pharmacokinetic profiles and increased bioavailability.

CONCLUSION

The main mechanisms that have been identified through which bioenhancers can improve the bioavailability of drug molecules include alteration of the plasma membrane fluidity to increase passive transcellular drug permeation; modulation of tight junctions to allow for increased paracellular diffusion Modification of the physicochemical properties such as salt formation and micronization of the crystalline compound to increase the surface area and thus increase bioavailability.

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