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Bioavailability & Bioequivalence Studies – Pharmaceutical Importance

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Research Article

ABSTRACT

Pharmacokinetics has now emerged as an important part of drug development especially in the development of new drugs. The combined studies of Pharmacodynamics and pharmacokinetics present a thorough understanding on how the drug affects the body and how the body affects the drug.

Bioavailability is the study of the rate and extent to which the active ingredient is absorbed from a dosage form and it is available at the required action site. Bioequivalence is that there should not be any significant difference in bioavailability between two products.

Bioavailability (BA) and bioequivalence (BE) studies play a key role during the phase of drug development for both innovator drugs and generic drugs and thus have gained great attention over the past few decades. BE is used to introduce generic drugs of innovator drugs at a lower cost. So a thorough understanding of these BA/BE studies is required.

INTRODUCTION

Generic products need to be of the same standards of quality, efficacy and safety as that of the original product. The Generic product should be therapeutically equivalent and interchangeable with the innovator product [1-3]. Such comparative studies are termed as Bioavailability & Bioequivalence Studies which have emerged as very important issues in the evaluation studies of drug products [3]

The expiry of patent of many biopharmaceutical drugs which are the block buster drugs for many chronic diseases encourage the evolution of generic drugs in the market with reduced costs and so BABE studies becomes an emerging are of study in the development of generic drugs [4-6].

Studies used to define bioequivalence between two different products are important especially for drugs that require fast absorption and onset of action [7].

The European Medicines Agency (EMA) and FDA have released guidance for the bioequivalence (BE) [8] FDA publishes a list approved products with their Equivalents in a book called "Orange Book".

BIOAVAILABILITY

According to FDA, Bioavailability is the rate and extent to which the active ingredient or is absorbed from the dosage form and is available at the required site of action [9].

Types

1. Relative bioavailability [10]

When the systemic bioavailability of a drug after administered orally is compared with that of an oral standard of the same drug (aqueous or non aqueous solutions). It is denoted by symbol (Fr).

2. Absolute bioavailability [11]

It compares the bioavailability of the active drug administered through non intravenous routes such as after oral route, rectal route, transdermal route, subcutaneous route, or sublingual route of administration and comparing the bioavailability of the same drug administered intravenously.

BIOEQUIVALENCE

According to FDA, Bioequivalence is the similarity in the rate and extent of active ingredient in pharmaceutical equivalents available at the site of action [12,13].

Bioequivalence studies are as vital concern in drug development process, which are required for small changes in drug products that develop during drug development to ensure that the dosage forms prove to be safe and effective. Moreover, bioequivalence has proven even more significant in case of drugs with narrow therapeutic index

Types

1. Chemical equivalence

When two or more drug products contain the same chemical substances as active ingredients in the same ratios [14,15]

2. Therapeutic equivalence

Drug substances are pharmaceutical equivalents when their bioavailability profiles are similar and their safety and efficacy can be assumed to be equal [16]

3. Pharmaceutical equivalence

Drug products that are identical in strength, quality, purity, content uniformity and disintegration and dissolution characteristics are said to be Pharmaceutical equivalents [17].

CLASSIFICATION OF BA-BE STUDIES

1. Pharmacokinetic endpoint studies
2. Pharmacodynamic endpoint studies
3. Clinical endpoint studies
4. In vitro endpoint studies

REQUIREMENT OF BABE STUDIES

- During the administration of new drugs parenterally which contain the same active substance as that of the innovator drug.
- During the administration of new drugs orally which contain the same active substance as that of the innovator drug.
- During the administration of a new drug in the form of a gas

- During the administration of a new drug in the form of a powder to be reconstituted before usage
- During the introduction of new drugs for ophthalmic purposes
- During the administration of a new drug used as inhalations

WORKFLOW OF BA-BE STUDIES

- Study design and protocol
- Bioanalysis
- Selection of appropriate analyte
- BE metrics and data treatment
- Statistical approaches and analysis

STUDY DESIGNS FOR BABE STUDIES

1. Randomization [18]
2. Replication and Error control [19]
3. Cross over designs [20]

FEATURES STUDIED DURING BABE STUDIES

- Enantiomers show different pharmacodynamic characteristics
- Enantiomers show different pharmacokinetic characteristics
- Primary safety resides
- Nonlinear absorption

SOME EXAMPLES OF BABE STUDIES

1. Bioequivalence of Flogofin® & Profenid ® in Latin American Volunteers [21].
2. Bioequivalence of Canagliflozin/Metformin Combination Tablets Compared with simultaneous administration of Single Components of Canagliflozin and Metformin [22].
3. Bioequivalence of Omeprazole Delayed-Release Capsules [23].
4. Bioequivalence comparison of Generic Formulation of Erlotinib Hydrochloride Tablets versus Tarceva [24-25].

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