ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 49. 23
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 4, Issue – 1, January - 2019, Page No. : 312 - 315

Pharmacokinetic Software: Current Practices

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Type of Publication: Review Paper

Conflicts of Interest: Nil

Abstract

The Almighty god blessed humans with the hands of a hard worker and with the brain of a scientist. One such advancement in software technology correlated with human life is " Pharmacokinetic Software". Computer - assisted learning played an important role in the teaching of pharmacokinetics as it transfers the emphasis from mathematical expression to experimental demo using graphical and symbolic tools. This software package is based on model -based drug development aiming to improve scientific productivity during analysis of data providing comprehensive interpretation of reusable workflows and high quality reports and presentation. Using this software one can perform pharmacokinetic parameters, Non Compartmental Analysis, PK/PD modeling, bioequivalence, Demographics, IVIVC, Nonparametric superposition. It highlights the importance of modeling and simulation to understand and optimize key decisions related to safety, efficacy and dosing. Software had proven its efficiency in interpreting PK/PD analysis results. This software made analyst expertise in his work, reducing the load of problem solving manually. The user can visualize results using graphical workflows, e.g., data processing, tables, figures, plots. The salient features of this software include empowerment of the user, avoiding user mediated errors, storage of the work in a single file.

Keywords: PK/PD; software; bioequivalence; efficacy, nonparametric superposition, validation suite.

Introduction

Our world population is always facing chronic disease. With the hands of technology, legends made resolutions; substance to cure i.e., drugs. Drugs are chemical substances used to prevent, diagnose and for the treatment of ill. Drugs mainly intended to modify or explore the physiological or pathological state for the benefit of the recipient. The branch of biomedical science concerned with the effects of pharmaceuticals on livings systems is pharmacology. Clinical pharmacology is concerned with how to use medicines and how to treat diseases and improve the life of the wellbeing.[1] The heart and soul of pharmacology is the pharmacokinetics and pharmacodynamics.[3]

Pharmacokinetics

It deals with "what the body does to the drug". Focusing mainly on the rate and extent to which drugs are absorbed upon administration, its distribution to various cells and tissues. Drug metabolism and the elimination of the

inactive metabolites. Monitoring plasma drug concentration in accordance with time. The time course of drug concentration in the body after its administration can be defined by a number of pharmacokinetic parameters. The application of pharmacokinetic principles mainly aim to control or cure the ill condition using minimum dose of drug over shorter duration of time with minimum side-effects. The importance of pharmacokinetics are ADME of drugs.(A---Absorption--Distribution--Metabolism--Excretion), impact of drug use, toxicology, drug dose, medicinal formulation, routes of administration[4]

Applications of pharmacokinetics

1. **C**alculation of Dosage regimen: dosage regimen is the frequency of administration of a drug in a particular dose. It depends on dose and frequency of dose. It is calculated on the basis of patient -related factors like age, sex, weight, other diseases etc
2. Drug switching: drug change during therapy, from one to another cause difference in plasma drug concentration. These differences can n be studied using pharmacokinetic parameters.
3. Determination of efficient route of administration.[5]
4. Drug dose calculation: to achieve effective drug concentration in plasma.
5. Drug-drug and food-drug interactions.
6. Protein binding: the rate and extent of drug accumulation.
7. To know about the physiological functions in the patient.
8. Designing formulations to achieve maximum therapeutic response.
9. To increase therapeutic benefit to the patient.
10. To decrease drug toxicity.[6]
11. Drug design and development with greatly improved therapeutic effectiveness.[7].

Pharmacokinetic Parameters/Variables

Parameters that govern a pharmacokinetic process. There are 2 types of variables.

- Independent variables: not affected by any other factor. e.g.: time
- Dependent variables: depend on independent variables e.g.: time dependent -plasma drug concentration.

1. Dose: amount of drug administrated.
2. Dosing interval: time between drug dose administrations.
3. C_{max}: the peak concentration of drug in plasma after administration.
4. T_{max}: time taken to reach C_{max}.
5. Volume of distribution: apparent volume in which drug is administrated.
6. Concentration: amount of drug in plasma.
7. Half life: time required for the concentration of drug to reach half.
8. Elimination rate: rate at which a drug is removed from the body.[8,9]
9. Area Under Curve: the integral of the concentration -time curve after a single dose.
10. Clearance: volume of drug in plasma cleared per unit time.
11. Bioavailability: the rate and extent of absorption of a drug.[10,11]

The pharmacokinetics of a drug can be determined by Non-Compartmental Analysis (NCA) using Pharmacokinetic Software.

- A software package for model-based drug development. Software designed to make efficient and faster Non-Compartmental analysis, pharmacokinetic/pharmacodynamic modelling to be possible.
- Non -linear modeling tool. It is suitable for PK/PD modeling and non-Compartmental analysis[12] for evaluating data from bioavailability and clinical

pharmacological studies.

- Supports creation of custom models to enable fitting and analysis of clinical data.[13]
- Generation of graphs, tables' output summaries, figures for submission of data.
- Visual presentation of results enables clear understanding of data.[13]
- Use of text-based modeling language enable user to describe, fit and simulate models. Powerful graphics engine
- Facilitate 90% reduction of analyst memory utilization, thus improve user experience when working with large data or projects.
- Quick and correct interpretation of results.
- Easy to calculate pharmacokinetic parameters
- Correct answers thereby reducing the load of analyst.
- For estimation of total drug exposure.
- Improve scientific productivity during critical drug development with reusable workflows and high quality outputs.
- Easy to validate, accurate, reproducible and traceable results.

Significance: [14]

To perform

- **Non-Compartmental Analysis**

NCA is not based on any specific compartment model. It is based on the assumption that drug follows linear kinetics. Software performs NCA on both predicted and observed PK data, averages the AUC and C_{max} for each formulation and displays the percentage error and the ratio of the predicted to observed data as measures of prediction error.

(Tab: 1) NCA MODELS - USING SOFTWARE

Type of Data	Dose Output
plasma	extra-vascular
plasma	Iv bolus
plasma	Constant infusion
urine	Extra vascular
urine	Iv bolus
urine	Constant infusion
drug effect	any

Predicting PK parameters: Once an acceptable In Vitro In Vivo Correlation model is generated, software can predict PK data based on dissolution data for new formulations. It uses IVIVC Model to predict absorption.

Non parametric superposition: its aim to predict drug concentrations after multiple dosing at steady state and is based on non compartmental results describing single dose data.

Benefits: [14]

- Saves time manual work; it has an intuitive graphical user interface that is easy to learn.
- Avoid risk-Microsoft excel is prone to user-generated errors, but with phoenix, the user can re-execute the entire analysis with a single click.
- Empower researcher: researchers can spend more time on their work with less time doing manual data manipulation. Visualize data with graphics engine save more time.
- Facilitates collaboration-entire project can be stored in a single file that can be easily shared.
- Supports validation environment: a validation suite automatically validate saving weeks or months of time. Since computer programs used in pharmaceutical industry must be validated to assure proper performance. So companies spend more time performing validation. But validation Suite contains a set of detailed test scripts that accelerate validation saving time and reduce error.

Conclusion

With no doubts, we conclude that the software proven to be the most trusted industrial software standard for PK/PD modeling, compartmental and non compartmental analysis. Owing to its accuracy, less human effort, high valid data without errors, these software standard give away the world population to access and interpret information regarding their health status , by analyzing the various parameters .This innovative software helps the finders and researchers approach and solve pharmaceutical ,biopharmaceutical aspects.

Acknowledgement

Both Arunima G and Saritha A Surendran contributed by understanding the literatures and in the manuscript writing. Amrita school of pharmacy is gratefully acknowledged for carrying out the literature works.

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