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# Accelerate Drug Development with Pharmacokinetic Softwares

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***Abstract***

*During continuously evolving technologies and mechanized equipments, there has beena tremendous growth in the pharmaceutical sector over the past few decades. New technologies,software, devices, and techniques are being developed or researched upon with each passing day. By leveraging pharmacokinetic software, researchers can efficiently analyze vast datasets from preclinical and clinical studies, extracting actionable insights that inform decision-making early in the development cycle. This predictive capability not only accelerates the identification of promising drug candidates but also minimizes the risks associated with unexpected pharmacokinetic profiles in later stages of development. This set of software is medication development based on a model that seeks to increase the rate at which scientist's analyzes data supplying thorough interpretation of reusable streamlined processes, excellent reporting, and presentations. In this review, some commonly used software intended for pharmacokinetic studies have been focused on. Some examples of used software include APIS, AUC-RPP, Biokmod, DATAKINETICS, Edsim++, etc. Using these softwares one may perform pharmacokinetic parameters, pharmacodynamic parameters (PK/PD), and non-compartmental analysis demographics, modelling, bioequivalence, IVIVC, superposition without parameters. One such example of technological advancement in the pharma sector is the development of numerous software to aid in the processes like drug manufacturing, inventory management, management of all types of records, and Pharmacokinetic and Pharmacodynamic studies. These softwares are briefly explained together with the parameters they are used for and their importance in simplifying pharmacokinetic calculations. A basic description of pharmacokinetic studies is also presented to thoroughly understand software employed for these studies. By continuously refining and optimizing pharmacokinetic models based on emerging data, these tools empower pharmaceutical companies to make informed decisions that drive innovation and improve patient outcomes in drug development.*

**Keywords:** Software, pharmacokinetic, pharmacodynamic, bioequivalence, drug development

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## INTRODUCTION

Pharmacokinetics is a pathway of how chemicals interact with a particular organism which involves uptake of drug substances by a living body, the biotransformation they undergo, their distribution and formation of metabolites in the tissues, and their elimination from the body over a specific period. It refers to a branch of pharmacology which determines how substances administered to living organisms will behave once they are administered. The concerned substance is termed as a xenobiotic which is defined as any

 

foreign material entering an ecological or living system. It includes chemicals like carcinogens, food additives, essential amino acids, drugs, etc. Pharmacokinetic studies focus on how a living body responds to a particular chemical substance from the moment it is administered to the body till the time it is fully eliminated from that body. These studies comprise of Absorption, Metabolism, Distribution, and Elimination (ADME) processes and the parameters governing these mechanisms which determine the overall course of action of that drug/chemical substance in that living organism.

Several metabolic and enzymatic reactions take place from administration to elimination and different stages are representative of specific pharmacokinetic parameters at that stage.To study and determine these parameters accurately, various pharmacokinetic software have been developed. The type of software to be used depends on the PK parameter intended for evaluation. The results of these software-based studies overall depend on several factors which are discussed in the following sections [1–4].

**Factors Affecting Pharmacokinetic Parameters/Studies**

a. Dosage regimen of the individual.
b. Age, sex, and weight of the person.
c. Time of drug administration.
d. Dietary routine and habits.
e. Route of drug administration.
f. Physical and chemical properties of drug/chemical substance.
g. Drug-drug, drug-food, and drug-excipient interaction studies.
h. Pathophysiology of the patient.
i. Genetic factors.
j. Environmental factors.

**Pharmacokinetic Parameters Governing Pharmacokinetic Studies [5, 6]**

Pharmacokinetic parameters are evaluated to ensure a dynamic equilibrium between the amount of drug substance administered, and the amount eliminated from the body. Ideally, the amount of ingested dose should be in accordance with the amount eliminated from the body and this condition is termed as steady state (ss). This can only be achieved in ideal conditions and if all the reactions and equations are accurately assessed from administration to elimination. Some of the most important pharmacokinetic parameters are listed in the following Table 1.

**Pharmacokinetic Modeling**

Pharmacokinetic modeling is the mathematical derivation and depiction of absorption, distribution, metabolism, and elimination parameters expressed using mathematical equations and graphs. The consequences of the transformations that a drug undergoes in an organism and the factors that determine this fate depend on a few interrelated factors. Therefore, several functional models have been designed to simplify the study of pharmacokinetics. Pharmacokinetic modeling is carried out by either of the two methods – compartmental models or non-compartmental models (Figure 1) [7–10].

**Pharmacokinetic Software**

The advancements in pharmaceutical sector have led to development of new computerized technologies which have further led to our codependence on these technologies. Several pharmacokinetic softwares have been designed to provide much more accurate results and reduce human efforts. Software programs are a sophisticated set of instructions developed using computer coding languages. The designed software code should be in accordance with the computer's operating system and the programming language used. Over the last two decades, computers with huge storage capacities and processors have been developed to withhold complex software and support software-based studies. The outbreak of several pharmacokinetic software globally has greatly enhanced the quality of work and has made research and development much more easy, convenient, and time saving [2, 11, 12].

 

**Table 1.** Pharmacokinetic parameters.

| S. N. | PK Parameter and Its Symbol | Description | Unit |
|---|---|---|---|
| 1 | Dose (D) | Amount of dug/xenobiotic administered. | mol |
| 2 | Dosing interval (T) | Time difference between two consecutive doses. | h |
| 3 | Concentration (C0) | Amount of drug present in given volume ofplasma. | mmol/L |
| 4 | Maximum concentration ($C_{max}$) | Highest amount (peak) of drug concentration in plasma after administration. | mmol/L |
| 5 | Maximum time ($T_{max}$) | Time taken to achieve $C_{max.}$ | h |
| 6 | Minimum concentration($C_{min}$) | Lowest concentration (trough) of drug in plasma indicative of requirement of administration of next dose. It is also referred to as 'offset' of action. | mmol/L |
| 7 | Steady state concentration ($C_{ss}$) | Concentration of drug in plasma whichconsistently persists. | h (mmol/L) |
| 8 | Volume of distribution ($V_d$) | Also known as apparent volume of distribution, it is the ratio of total amount of drug administered (dose) to the concentration of drug in blood plasma and tissue fluids. | L |
| 9 | Absorption half-life ($t_{1/2a}$) | Time required by administered dose of drug to get 50% absorbed in the systemiccirculation. | H |
| 10 | Absorption rate constant ($k_a$) | Rate at which a drug substance enters the system. | $H^{-1}$ |
| 11 | Elimination half-life ($t_{1/2}$) | Time required for amount of drug in plasma to remain half of its administered amount. | H |
| 12 | Elimination rate constant ($k_e$) | Rate of drug removal from the body. | $H^{-1}$ |
| 13 | Rate of infusion or dosing rate ($k_{in}$) | Desired rate of drug administration necessary to achieve a steady state and the dose should be therapeutically effective. | mol/L |
| 14 | Area under the curve ($AUC_{0-\infty}$) | It is the area under plasma drug concentration-time curve which denotes the exposure of living body towards administered drug. | Mg * h/L |
| 15 | Bioavailability(f) | Amount of administered drug dose that reaches the systemic circulation. It is the rate and extent of drug absorption. | Unitless |
| 16 | Peak-to-trough ratio (PTR) | Also known as 'peak-to-trough fluctuations', it is the ratio of $C_{max}$ (peak) and $C_{min}$ (trough) over a dosing interval. It occurs in steady state. | % |
| 17 | Clearance(CL) | It is the measure of drug elimination rate divided by plasma concentration of that drug. In other words, it is equal to the volume of drug free plasma per unit time. | $M^{3/8}$ |

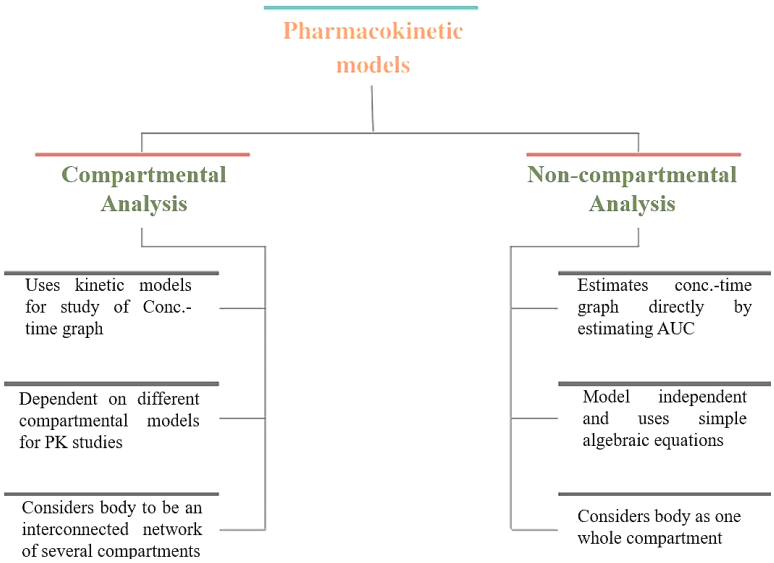


 

**Figure 1.** Basic differences between the two PK models.

**Advantages of Pharmacokinetic Software [2, 11–14]**

1. Calculations have become less time-consuming and easier.
2. Studies can be carried out simultaneously.
3. Results are much more accurate than in conventional methods.
4. New experimental models can be easily developed along with statistical data, graphical representations, and simulations of pharmacokinetic models.
5. In-vitro in-vivo correlation (IVIVC) studies have become less complex to perform.
6. Accurate prediction of drug action, dosage regimen, and appropriate route of drug administration.
7. Drug toxicity studies can be easily carried out thus reducing the risk of toxic effects.
8. Software studies have built a link between pharmacokinetic and pharmacodynamic studies, allowing the researcher to analyze both parameters simultaneously and derive PK/PD models.
9. The possible effect of a drug substance in-vivo can be accurately predicted with the help of simulated software-based models, graphs, and mathematical equations.
10. Software-based teaching has overtaken conventional teaching.
11. The need for trial-and-error methodology is reduced as studies have become software specific and thus more accurate.
12. Drug-drug, drug-food, and drug-excipient interaction studies can be precisely estimated.
13. Optimization of formulations to obtain desired properties can be successfully achieved.

**Limitations of Pharmacokinetic Software [2, 13, 14]**

1. Highly skilled and expert personnel are required to operate such complicated software and carry out complex calculations.
2. Software-based studies demand high monetary investment in terms of computers and software installations and appropriate workspace.
3. Machines are only reliable as far as they are in proper working condition. Once they crash down, a lot of resources would be required to re-establish all the systems and data as well.
4. Technical teams must be on alert all the time.

**Commonly used Pharmacokinetic Software [11–25]**

1. *ABSPLOTS* – It is a simple python package; LOTUS 123 spreadsheet used to estimate and plot drug absorption rates in multi-compartmental models via series of equations.
2. *ADAPT 5* – This software is mainly employed for simulation modeling, non-linear regression modeling, and sample optimization including Bayesian optimization. Models are presented in the form of differential or integral equations using FORTRAN statements.
3. *APIS* – It is a software package for mathematical modeling in drug therapy optimization. It is an extremely important software in clinical and experimental pharmacokinetic studies. This provides an approach for determination of dosage regimen based on patient specific parameters to optimize drug therapy according to the patient's therapeutic requirements.
4. *AUC-RPP* – It is a non-complex software used for estimation of pharmacokinetic parameters based on non-compartmental modeling.
5. *Bear (BE/BA for R)* – This software package is meant for analyzation of bioequivalence and bioavailability studies of a single or multiple dosage regimen. This software employs simple non-compartmental models using AUC values for study.
6. *Berkeley Madonna* – This software is a general-purpose equation solver program built for the purpose of solving differential equations corresponding to the best suited model.
7. *Biokmod* – It is a mathematical toolbox for solving various equations corresponding to the linear and non-linear models for biokinetic systems.
8. *BIOPAK* – It is a software package for statistical analysis of bioequivalence and bioavailability.
9. *Boomer* – This program includes Bayesian optimization, simulation modeling, and non-linear regression studies via a series of equations.
10. *CalcuSyn* – It is an important software for studying and quantifying drug-drug interaction

 

phenomena like synergism, antagonism, and inhibition.

11. *CombiTool* – It is a Microsoft windows program designed for experimental studies for combination medications and biologically active agents. It evaluates combination effects of two or more agents Loewe additivity and Bliss independence criteria.
12. *CXT* – This program can run under MS DOS or Windows and is developed for evaluation of linear dynamic systems using various frequency models.
13. *Cyber Patient*™ - It is a Windows operated program designed for the purpose of developing of multimedia pharmacokinetic simulations for setting up random of PK models and evaluating them for patient case studies.
14. *DATAKINETICS* – It is drug monitoring and data management software.
15. *DESIGN* – This software is a McIntosh production and is provided as a FORTRAN source code within the text. It is used for mathematical modeling and sampling.
16. *DDI Predict* – It provides immediate graphical reports of all possible drug-drug interactions between a specific drug and all its available or banned marketed formulations.
17. *DoseAssist* – As the name suggests, it helps in dosing related documentation and models.
18. *DoseMe* – It is a simple, convenient, and useful software that allows healthcare professionals to decide dosing strategies and schedules for each patient depending on that patient's pathophysiology and physical responses.
19. *Edsim++* – It is a PK/PD modeling software based on the concept of object-oriented modeling. It is user friendly and offers easy teaching and learning procedures through a variety of objective models required for research purposes. Users can also create new objects and models and their own personal custom-built applications.
20. *ERDEM* – It is a physiologically-based PK/PD modeling software for assessing risk factors associated with individual's exposure and dosage regimen.
21. *GastroPlus*™ – It is a physiologically based software package that offers a wide range of functions like assessing drug interaction studies, deriving IVIVC data and metabolic pathways, and PK/PD model simulations.
22. *INTELLIPHARM PK* – It is designed for the basic purpose of PK parameters involving absorption kinetics and drug dissolution.
23. *ivivc for R* – This software is one of the many R (a free software for graphical and statistical analysis) packages developed specifically for obtaining and validation of IVIVC models.
24. *Kinetica* – It is a fast operating, high accuracy, PK analysis program for advanced data analysis of clinical, preclinical, and ADME parameters.
25. *MacDope* – It displays how a drug substance and its every metabolite allocates in the body with respect to time and route of administration. Patient and drug properties are used to develop simulating models.
26. *Manchester PBPK* – It is an open-source software used to study all the equations related to derivation of concentration-time profiles in specific organs.
27. *Maxsim2* – It consists of a collection of numerous PK/PD exemplar models and what-if situations. These visuals help in simulating a variety of profiles, for example, volume of drug distribution, drug clearance, dosing amount, drug solubility, etc.
28. *MedRoc-A* – It is a simple and free program used to perform ROC studies and from these studies conclude diagnostic methodology, drug therapies, drug potency, etc.
29. *MLXPlore* – It is a digital visualization software that allows user to explore model variabilities and orientational varieties.
30. *MEDICI-PK* – It is an open source, user friendly, app-specific software package that allows easy assessment of PK/PD models.
31. *MetidaNCA* – It is a software package for non-compartmental model analysis.
32. *MONOLIX* – It is reliable software for population analysis and for generating PK/PD models along with several physicochemical processes.
33. *MwPharm++* – This software is very convenient as it provides Therapeutic Drug Management facility. PK models up to three compartments are analyzed by simulation.

 

34. *NCOMP* – It is a free software program for analysis of non-compartmental PK models.
35. *NONMEM* – It stands for Non-Linear Mixed Effects Model. It is a widely used software program that involves non-linear regression analysis of either population or individual data.
36. *PAVA* – Physiological and Anatomical Visual Analytics is a simple and easily available browser application used to view physiologically annotated data (POD) from different sources.
37. *PDx-Pop* – It works together with NONMEM and other accessible software used for population analysis and modeling.
38. *PharmaCalc v02 and PharmaCalcCL* – It is a Java based OS used for simulation of PK curves in correspondence to patient's dosage regimen and missed doses.
39. *Pharmacokinetic Modeling Program (PKMP)* – It is a multi-functional complete package for performing most of the PK studies.
40. Phoenix WinNonlin – It is simple software for designing tables and graphs and for data management of PK/PD models as well as for non-compartmental models.
41. *Physiological parameters for PBPK modeling version 1.0 ($P^3M$)* – It is an extremely useful software as it provides facility to manage and study every individual's complete physiological data and models are governed as per the records.
42. *PKfit for R* – It is a software package for data analysis in R which provides tools for solving all differential PK equations, algorithms, and a wide variety of criteria.
43. *PKMP* – It offers a wide range of features like IVIVC, simulation of PK/PD models, non-compartmental and compartmental analysis, combined PK/PD analysis, method validation, etc.
44. *PK-Sim* – It is useful in studying model specific and organ specific functions depending on the bioavailability studies and optimized PK simulation models.
45. *POP3CM* – It is a free Visual Compartmental Population Analysis Program having a graphical UI for three compartmental analyses. The equations and solutions corresponding to the parameter are in-built.
46. *PsN* – It aids in the development of NONMEM analysis.
47. *RIDO and RIDO plus* – It is a comprehensive training software intended for fathoming dose development studies of a newly developed drug with the aid of PK/PD models.
48. *SAAM II* – It is a kinetic modeling software based on developing and then analyzing a prototype model for compartmental study.
49. *Scientist for Windows* – It is an equation solver software providing best suited parameters for solving a particular equation.
50. *Simcyp* – It includes a whole system for developing simulated PB/PK models from in-vitro and IVIVC studies. It is also beneficial in determining drug interaction studies and predicting results.
51. *SimPHARM* – It is based on simulating in-vivo conditions to in-vitro mathematical models and thus produces a realistic clinical approach.
52. *stab for R* – It is designed to estimate formulation and drug stability studies.
53. *TCIWorks* – It is developed with the purpose of dose optimization for patients undergoing regular medication routines.
54. *USC * PACK – This program set contains several modules for clinical and R&D based studies.*
55. *Xpose – This is R based program meant for aiding and enhancing NONMEM model development studies.*

## CONCLUSION

In conclusion, pharmacokinetic software represents a transformative tool in modern drug development, offering substantial benefits across the entire pharmaceutical pipeline. By enabling precise modeling, simulation, and analysis of drug behavior within biological systems, these software solutions empower researchers to make informed decisions faster and more efficiently. The recent advancements pharmaceutical sector has provoked humans to indulge in various research and developmental projects. Numerous software has been designed and developed to reduce human workload and to provide much more accurate results. Pharmacokinetic software has been proven to minimize manual efforts as studies now-a-days are largely completely software dependent. The

 

pharmaceutical sector has immensely revolutionized with the help of such software-based studies which continue to flourish day by day. Pharmacokinetic and pharmacodynamic modeling with the aid of software has initiated several new researches and has increased disease recovery rates globally. In essence, the adoption of pharmacokinetic software is not merely a technological advancement but a strategic imperative for pharmaceutical companies seeking to innovate and compete in a dynamic healthcare landscape. Its role in enhancing efficiency, reducing costs, and improving patient outcomes underscores its significance as a cornerstone of modern drug development strategies.

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