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PreKinetix: web application for pharmacokinetic analysis in preclinical drug research

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The aim. Development and validation of domestic software for non-compartmental analysis (NCA) of pharmacokinetic data, comparable in accuracy and functionality to the recognized foreign software Phoenix WinNonlin (USA).

Materials and methods. The PreKinetix web application is implemented in the Python programming language using the Streamlit framework. Algorithms for calculating pharmacokinetic parameters (maximum concentration [C_{max}], area under the pharmacokinetic curve [AUC], half-life [$T_{1/2}$], mean residence time [MRT], etc.) are based on the methods of the reference software Phoenix WinNonlin (Certara, USA), used for comparison and are widely used in international practice. Three models of single drug administration are supported: intravenous bolus, intravenous infusion, and extravascular administration. Literary and experimental data covering more than 450 pharmacokinetic profiles were used for verification.

Results. Calculations performed using PreKinetix showed complete agreement with the results of Phoenix WinNonlin with a relative error of less than 0.0001% for all main parameters. The program stably processes zero and missing values, automatically excludes incorrect records, visualizes pharmacokinetic profiles in linear and semi-logarithmic scales, and generates reports in .xlsx* and .docx* formats. The application interface allows it to be used not only by specialists but also by less trained users.

Conclusion. PreKinetix is a domestic tool for NCA that combines accuracy, automation, accessibility, and convenience. It can be used in preclinical and early phases of clinical trials, as well as in educational settings for training specialists in pharmacokinetics and biopharmaceutics.

Keywords: pharmacokinetic analysis; preclinical studies; non-compartmental analysis; pharmacokinetics; biopharmaceutical research; software; pharmaceutical development

List of abbreviations: adjusted R^2 — adjusted coefficient of determination; ADME — absorption, distribution, metabolism, excretion; AUC — area under the concentration–time curve; AUMC — area under the first moment curve; C_0 — initial concentration (for bolus administration only); Cmax — maximum drug concentration in blood; C_{max}/D — C_{max} to dose ratio; GLP — Good Laboratory Practice; GUI — graphical user interface; $K_{el/\lambda z}$ — terminal elimination rate constant; MRT — mean residence time of the drug in the body; PBPK — physiologically based pharmacokinetics; RE/REi — relative error; sparse sampling — sparse sampling; $T_{1/2}$ — half-life; T_{max} — time to reach maximum concentration; NCA — non-compartmental analysis; PK — pharmacokinetics/pharmacokinetic.

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PreKinetix: веб-приложение для проведения фармакокинетического анализа в доклинических исследованиях лекарственных препаратов

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Цель. Разработка и валидация отечественного программного обеспечения для некомпартментного анализа (НКА) фармакокинетических данных, сопоставимого по точности и функциональности с признанным зарубежным программным обеспечением Phoenix WinNonlin (США).

Материалы и методы. Веб-приложение PreKinetix реализовано на языке программирования Python с использованием фреймворка Streamlit. Алгоритмы расчёта фармакокинетических параметров (максимальная концентрация [C_{max}], площадь под фармакокинетической кривой [AUC], период полувыведения [$T_{1/2}$], среднее время пребывания [MRT] и др.) основаны на методиках референсного программного обеспечения Phoenix WinNonlin (Certara, США), использованного для сравнения и широко применяемого в международной практике. Поддерживаются три модели однократного введения лекарственного средства: внутривенное болюсное, внутривенная инфузия и внесосудистое введение. Для верификации использованы литературные и экспериментальные данные, охватывающие более 450 фармакокинетических профилей.

Результаты. Расчёты, выполненные с помощью PreKinetix, показали полное совпадение с результатами Phoenix WinNonlin с относительной ошибкой менее 0,0001% по всем основным параметрам. Программа устойчиво обрабатывает нулевые и пропущенные значения, автоматически исключает некорректные записи, визуализирует фармакокинетические профили в линейной и полулогарифмической шкалах, формирует отчёты в форматах .xlsx* и .docx*. Интерфейс приложения позволяет использовать его не только специалистам, но и менее подготовленным пользователям.

Заключение. PreKinetix представляет собой отечественный инструмент для НКА, объединяющий точность, автоматизацию, доступность и удобство. Он может применяться в доклинических и ранних фазах клинических исследований, а также в образовательных целях для подготовки специалистов в области фармакокинетики и биофармацевтики.

Ключевые слова: фармакокинетический анализ; доклинические исследования; некомпартментный анализ; фармакокинетика; биофармацевтические исследования; программное обеспечение; фармацевтическая разработка

Список сокращений: adjusted R^2 — скорректированный коэффициент детерминации; ADME — абсорбция, распределение, метаболизм, экскреция; AUC — площадь под кривой «концентрация–время»; AUMC — площадь под кривой первого момента времени; C_0 — начальная концентрация (только для болюсного введения); C_{max} — максимальная концентрация препарата в крови; C_{max}/D — отношение C_{max} к дозе; GLP — надлежащая лабораторная практика; GUI — графический пользовательский интерфейс; $K_{el/\lambda z}$ — терминальная константа скорости элиминации; MRT — среднее время пребывания препарата в организме; PBPK — физиологически обоснованная фармакокинетика; RE/REi — относительная ошибка; $T_{1/2}$ — период полувыведения; T_{max} — время достижения максимальной концентрации; ЛС – лекарственное средство; НКА — некомпартментный анализ; ПО — программное обеспечение; ФК — фармакокинетика/фармакокинетический.

INTRODUCTION

The main aim of pharmacokinetic (PK) studies is to study the kinetic properties of drugs, including the processes of absorption, distribution, metabolism, and excretion (ADME — absorption, distribution, metabolism, excretion) [1]. One of the simplest and most effective methods for studying these processes is non-compartmental analysis (NCA). NCA includes various approaches for calculation of the area under the pharmacokinetic curve (AUC — area under the curve) — a graph of the dependence of the concentration of drugs in a biological material on the sampling time [1–4]. The non-compartmental approach includes calculation of key PK parameters, such as the maximum observed drug concentration (C_{max}), AUC, time to reach peak concentration (T_{max}), half-life ($T_{1/2}$), area under the first moment curve (AUMC — area under the first moment curve), and others[1] [1, 3].

PK studies are increasingly faced with the need to work with sparse sampling, especially in preclinical and phase trials, where multiple sampling enquiries may be ethically and logistically difficult. At low density of time points, classical NCA demonstrates high error in estimation of key pharmacokinetic parameters, such as $T_{1/2}$ and AUC exposure, which can negatively affect the accuracy of pharmacotherapeutic decisions [5]. This necessitates reliable tools for processing sparse data, while maintaining the accuracy of calculations even with limited measurements.

At the same time, there is a noticeable increase in the preference for open-source software in pharmacokinetics and physiologically based modeling (PBPK). According to the works of Rajput et al. (2023) and Aldibani et al. (2023), the proportion of publications using open-source platforms has significantly increased due to their transparency, flexibility, and the ability to be expanded by research groups [6, 7]. However, most existing tools focus on compartmental analysis or PBPK modeling, and available NCA toolkits remain either commercial or require significant programming skills. This underscores the importance of developing user-friendly, verifiable, and user-oriented domestic software, such as PreKinetix, capable of ensuring the independence and reproducibility of PK studies.

Modern software solutions for PK analysis using the NCA method are represented by both commercial (e.g., Phoenix WinNonlin, CPhaMAS, PKanalix) and freely distributed tools (PKSolver, Pkweb, R-packages NonCompart and ncar). However, free software has a number of limitations. For example, the NonCompart and ncar packages lack a graphical user interface, which makes them difficult to use by non-specialists. In addition, some PKSolver algorithms (in particular, the estimation of the elimination rate constant — λz) are unstable and give discrepancies in results compared to commercial solutions. Moreover, most free software does not meet the validation requirements established by regulatory authorities [1, 2, 8]. Commercial solutions for NCA are currently represented mainly by foreign software; similar products are not yet offered on the territory of the Russian Federation[2], [3] [9]. In this regard, the development of domestic software is relevant, which would ensure the technological independence of research organizations in the field of PK analysis.

In response to this need, we have developed the PreKinetix web application, focused on conducting NCA in preclinical and phase I clinical PK studies. The current version supports the analysis of a single dose administration with modeling of three main methods of administration: intravenous bolus, intravenous infusion, and extravascular administration, using data on the concentration of the drug in the blood. Algorithms for calculating and visualizing the results of studies of absolute and relative bioavailability, the distribution of drugs in the organs and tissues of laboratory animals, dose linearity, etc. have also been implemented. Thus, **THE AIM** of this work was to create and initially validate the PreKinetix program and present its capabilities for PK analysis.

MATERIALS AND METHODS

Software development

The Python programming language was chosen to implement the web application, as it is one of the most popular languages in scientific research due to its simplicity, flexibility, and extensive ecosystem of tool libraries. Python is widely used in various fields — from data analysis to modeling and visualization — which is confirmed by many works [10–12]. The Streamlit[4] framework (open-source Python framework) was used to speed up the development of the web interface and simplify testing the application with data.

The main computational logic of PreKinetix is implemented using a number of Python libraries: pandas (version 1.5.3) [13], numpy (1.24.2) [14], matplotlib (3.7.1) [15], seaborn (0.12.2) [16], SciPy (1.10.1) [17], scikit-learn (1.3.1) [18], statsmodels (0.14.0) [19], cycler (0.11.0)[5], python-docx (0.8.11)[6],

[1] Certara. Phoenix WinNonlin User Guide — Noncompartmental Analysis. Available from: https://onlinehelp. certara.com/phoenix/8.2/topics/nca.htm

[2] Certara. Phoenix WinNonlin User Guide – Noncompartmental Analysis. Available from: https://onlinehelp.certara.com/phoenix/8.2/topics/nca.htm

[3] Lixoft. PKanalix. Available from: https://pkanalix.lixoft.com/

[4] Streamlit. Streamlit – The fastest way to build and share data apps. Available from: https://streamlit.io/

[5] Droettboom M. Cycler: composable style cycles. GitHub repository. Available from: https://github.com/ matplotlib/cycler

[6] Canny S. python-docx: Create and update Microsoft Word .docx files. 2013. Available from: https://github. com/python-openxml/python-docx

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networkx (3.4.2) [20] and pyvis (0.3.2)[7]. The Visual Studio Code software platform (version 1.99.3)[8] was used as the development environment.

Microsoft Excel 2016 (Microsoft Office package, Microsoft Corporation, USA)[9] was used to build certain graphs and diagrams when analyzing data for vizualization of the comparative analysis results described below.

Reference software

The Phoenix WinNonlin program (version 8.3.4.295, Certara, USA) was applied as a reference system used for comparison.

Data sets for comparative analysis

450 PK profiles were analyzed as part of the initial scientific testing of the PreKinetix web application. Three data groups were used to assess the correctness of calculations: open reference sets of PK data from the PKanalix software distribution (version 2024R1, Lixoft, France[10]; PKanalix data were obtained by downloading statistical collections) and the Rdatasets collection prepared by Arel-Bundock et al.[11, 12], experimental data obtained in our scientific organization, as well as specially constructed examples for verifying individual boundary cases.

The following medicines M2000, cefamandole[13] and indomethacin[14] were randomly selected as demonstration examples for calculating statistical parameters, NCA, visualizing the obtained results of comparing Prekinetix and Phoenix WinNonlin (Table 1).

Algorithm for calculating of statistical parameters

To implement the algorithms for calculating statistical parameters, principles similar to Phoenix WinNonlin were used according to the documentation of the reference software[15].

The criterion of compliance was the relative difference between the values of each statistical parameter calculated by the two systems, in which the maximum deviation did not exceed 10^{-6}. Thus, in all tested cases, the calculations of PreKinetix and Phoenix WinNonlin showed complete coincidence of results, confirming the correctness of the algorithmic implementation.

Algorithm for calculating of pharmacokinetic parameters

To implement the algorithms for calculating NCA, principles similar to Phoenix WinNonlin were used according to the documentation of the reference software[16].

PreKinetix calculates a complete set of PK parameters based on the results of NCA, similar to Phoenix WinNonlin. The designations of key parameters used in our software and their correspondence to the designations of Phoenix WinNonlin are given in Table 2 with a brief description of each indicator.

As you can see, most parameters have identical designations in both software, and some differ slightly (for example, $AUC_{0\to t}$ as AUC_{last}, etc.).

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Visualization of results of comparative analysis

To assess the accuracy of the coincidence of PreKinetix results with the reference software, we used an approach similar to that described in [9]. The relative error of determining the i-th parameter (RE_i — Relative Error,%) was introduced, calculated by the formula:

$$RE_i = \left(\frac{P_i - R_i}{R_i} \right) \times 100\%$$

where Pi is the value of the parameter obtained by the tested algorithm; and Ri is the corresponding value calculated using Phoenix WinNonlin.

This indicator allows you to quantitatively assess the accuracy of the developed algorithm and identify possible systematic bias in the calculation of one or another pharmacokinetic indicator. Negative RE values indicate a slight underestimation of the PreKinetix result relative to Phoenix, positive values indicate an overestimation. The criterion of acceptability was a relative error of less than 0.0001% for most parameters.

[7] Rémy P. pyvis: Python library for interactive network visualization. 2019. Available from: https://github. com/WestHealth/pyvis

[8] Microsoft. Visual Studio Code. Available from: https://code.visualstudio.com/

[9] Microsoft. Microsoft Office. Available from: https://www.microsoft.com/en-us/download/details.aspx?id=49164

[10] Lixoft. PKanalix. Available from: https://pkanalix.lixoft.com/

[11] Arel-Bundock V. Cefamandole // Rdatasets: A collection of datasets originally distributed with R and some of its packages. Available from: https://vincentarelbundock.github.io/Rdatasets/doc/nlme/Cefamandole.html

[12] Arel-Bundock V. Indometh; Rdatasets: A collection of datasets originally distributed with R and some of its packages. Available from: https://vincentarelbundock.github.io/Rdatasets/doc/medicaldata/indometh.html

[13] Arel-Bundock V. Cefamandole; Rdatasets: A collection of datasets originally distributed with R and some of its packages. Available from: https://vincentarelbundock.github.io/Rdatasets/doc/nlme/Cefamandole.html

[14] Arel-Bundock V. Indometh; Rdatasets: A collection of datasets originally distributed with R and some of its packages.

[15] Certara. Phoenix WinNonlin User Guide – Noncompartmental Analysis. Available from: https://onlinehelp.certara.com/phoenix/8.2/topics/nca.htm

[16] Ibid.

Visualization of pharmacokinetic profiles

In addition PreKinetix provides convenient tools for vizualization of PK profiles. The application's user interface allows to customize the display of graphs: change the scale of the axes, the division step, the location of the legend, and other parameters.

To build graphs of PK profiles using the developed software, data from subject No. 271 of the M2000[17] drug were used (Table 1).

RESULTS

Software implementation results

The PreKinetix web application was developed and designed for conducting NCA in preclinical studies and phase I clinical trials. The current version supports the analysis of PK data after a single administration of a drug with three main methods of administration: intravenous bolus, intravenous infusion, and extravascular administration, based on measurements of drug concentration in the blood. In addition to calculating standard NCA parameters, the system implements algorithms for evaluating and visualizing the results of studies of absolute and relative bioavailability, the distribution of a drug in the organs and tissues of laboratory animals, checking dose linearity, and other PK analysis tasks.

Python scripts with open-source code are available at https://github.com/FimaLab/prekinetix.

Calculation of pharmacokinetic parameters

The general principles and sequence for calculation statistical indicators and PK parameters in the developed software were based on the algorithms of the commercially available validated software Phoenix WinNonlin (version 8.3.4.295), which is considered as the "gold standard" in the international market of PK analysis[18]. In particular, PreKinetix implements standard methods for calculating AUC and AUMC. There are several main methods for calculating AUC / AUMC: the linear trapezoid method, the log-linear trapezoid method, as well as a combined method involving linear interpolation at the stage of increasing concentration and logarithmic interpolation at the stage of decreasing[19] [3, 21]. PreKinetix includes two of the most popular approaches: linear trapezoidal and combined methods for calculating the area under the curve [21, 22].

[17] Lixoft. PKanalix. Available from: https://pkanalix.lixoft.com/
[18] Certara. Phoenix WinNonlin User Guide – Noncompartmental Analysis. Available from: https://onlinehelp.certara.com/phoenix/8.2/topics/nca.htm
[19] Ibid.

Assessment of the terminal constant elimination (λz)

The terminal elimination constant λz (K_{el}) is estimated using linear regression on the final section of the PK profile, corresponding to a monoexponential decrease in concentration [21]. PreKinetix implements an automatic algorithm for estimating λz according to the approach used in Phoenix WinNonlin. Automatic Kel estimation in Phoenix is performed by the best fit method, sequentially iterating through different sized sets of points on the terminal section of the curve. In our software, this algorithm is implemented as follows:

1. Linear regression of the dependence of the logarithm of concentration on time is performed, starting from the last 3 positive points (from 2 points for the bolus model).
2. The number of points used in the regression is gradually increased to 4, 5, etc., excluding in each such analysis data up to the time of reaching C_{max}, the C_{max} point itself (for non-bolus models), as well as points with C_0.
3. For the intravenous infusion model, points before the end of the drug administration are additionally excluded if C_{max} is observed earlier than the end of the infusion.
4. For each regression performed, the adjusted coefficient of determination (adjusted R^2) is calculated. The option with the maximum value of this indicator is selected. If several options give close values (difference ≤ 0.0001), preference is given to the option with a larger number of points.
5. The minimum number of points for calculating λz is 3 for non-bolus models and 2 for bolus administration. The condition for the correctness of the result is a negative value of the angular coefficient (i.e., a negative slope of the regression line)[20].

Correction of the initial concentration

The calculation of the initial concentration C_0 is performed only for the intravenous bolus administration model. The initial concentration is taken equal to the first observed concentration value if it is measured at the time of drug administration; otherwise, C_0 is calculated by back extrapolation using linear regression. This indicator affects the calculation of a number of PK parameters (AUC and AUMC) in the bolus administration model, so the user is given the opportunity to include the back extrapolation algorithm if necessary for correct accounting of C_0 in calculations[21].

[20] Ibid.
[21] Ibid.

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Features of calculation with infusion administration

For the intravenous infusion model, it is necessary to take into account the infusion time when calculating some parameters. For example, when calculating the mean residence time of the drug in the body (MRT — mean residence time), the duration of the infusion affects the result[22] [23]. The value of the infusion time is entered by the user through the corresponding interface field, and it is used by the program when calculating MRT and related parameters.

The developed algorithms for calculating statistical indicators and PK parameters stably process zero concentration values that may be present in the initial data array. Records with missing time or concentration values are automatically excluded from the analysis[23]. This ensures the correctness of the results even if there are missing or zero points in the pharmacokinetic profile.

Statistical parameters

First, the correctness of calculating basic statistical indicators was checked. When comparing the values of statistical parameters calculated by PreKinetix with the corresponding results of Phoenix WinNonlin, it was shown that the differences were less than 10^{-6}. Table 3 shows data on a number of such indicators using the example of calculating the elimination constant λz of M2000[24], cefamandole, and indomethacin.

It may be concluded that both software products give identical values for all statistical parameters (number of observations, mean, standard deviation, etc.).

Pharmacokinetic parameters

To assess the correctness of the calculation of PK parameters in general, as well as to check for the absence of systematic deviations, a series of comparative calculations were performed on various data sets. Table 4 shows the results of calculating the main PK parameters for some of these data sets (using the example of the M2000, cefamandole, and indomethacin)[25].

In this example, the analysis was performed for the intravenous bolus administration model (single dose). As in the case of statistical indicators, the difference in the values of all PK parameters calculated by PreKinetix compared to Phoenix WinNonlin was less than 10^{-6}.

The results of the comparative analysis of PK parameters were demonstrated by calculating the RE and constructing the corresponding graphs. Figure 1 reflects the relative error (RE_i,%) for the main calculated PK parameters (according to Table 4).

All detected discrepancies between the programs were random and extremely small in magnitude (less than 0.0001% for most parameters). This indicates that the developed tool does not introduce systematic errors in calculations and can reproduce results at the accuracy level of the reference software. The results of comparing NCA calculations using intravenous infusion and intravascular administration methods were also satisfying.

Visualization of pharmacokinetic profiles

Figures 2 and 3 show an example of a graphical representation of an individual PK profile in the blood, constructed by PreKinetix using the example of the drug M2000: in linear coordinates (Fig. 2) and in semi-logarithmic coordinates (Fig. 3).

Such graphs are generated automatically and can be included in a .docx* report, which facilitates data presentation and interpretation.

It should be noted that all graphic materials created by the program can be saved by the user for its subsequent application in reports or scientific publications and help to improve the clarity of the results, as well as the convenience of their analysis.

DISCUSSION

The development and validation of the PreKinetix program were aimed to confirm its equivalence with the generally accepted means of NCA of PK data. Phoenix WinNonlin (Phoenix 64, version 8.3.4.295) is historically known as the “gold standard” for NCA and is widely used for scientific and regulatory purposes. PreKinetix calculations for 3 experimental drugs (M2000, cefamandole, indomethacin) showed almost complete agreement with the results obtained using Phoenix WinNonlin. All major pharmacokinetic parameters — maximum concentration (C_{max}), time to maximum (T_{max}), area under the curve (AUC), half-life ($T_{1/2}$), elimination rate constant (λz), etc. — were identical when using both software tools, with a relative difference of less than 0.0001%. For example, for bolus intravenous administration of M2000, PreKinetix and Phoenix give the same absence of time delay in reaching Cmax (T_{max}=0 h) at a high initial concentration (C_{max}≈2950 ng/mL), while for extravascular administration of indomethacin, both tools show the expected delay in reaching the peak (T_{max}≈0.25 h) at a comparatively smaller C_{max} value (≈1.5 μg/mL). The complete match of parameters throughout the profile (including, for example,

[22] Ibid.
[23] Ibid.
[24] Lixoft. PKanalix. Available from: https://pkanalix.lixoft.com/
[25] Ibid.

AUC_{0-t}=4126.36 for M2000, 3740.5 for cefamandole and 1.741 for indomethacin; $T_{1/2}$=6.40, 56.04 and 4.38 h, respectively) indicates the correctness of PreKinetix algorithms and the absence of systematic error in calculations. As can be seen in Figure 1, a graphical analysis of relative errors did not reveal a systematic bias, which confirms the correctness of the algorithms implemented in PreKinetix. Thus, PreKinetix provides calculation accuracy at the level of the reference software, which confirms the successful verification of the developed tool using the example of drugs with different PK properties.

The results obtained are consistent with similar publications of recent years devoted to the validation of various NCA tools. For example, in a recent study by Zang et al. (2010) presented the PKSolver add-in for Microsoft Excel, the calculation results of key PK parameters of which showed a satisfactory degree of correspondence to the results of Phoenix WinNonlin [2]. In the work of Kim et al. (2018) compared calculations between Phoenix and the R-package NonCompart, which underlies the online tool PKWeb, which also confirmed the identity of the output parameters [1]. In addition, a recent article by Kyang et al. (2024) presented the CPhaMAS cloud platform, designed for the analysis of PK data, including NCA and bioequivalence; the authors showed that CPhaMAS calculations are in close agreement with Phoenix WinNonlin results in *in vivo* modeling and parameter analysis [9]. The totality of these independent validations confirms that when using the same algorithmic approaches, different NCA software tools give practically indistinguishable results.

Table 1 – Part of the initial data of M2000, cefamandole and indomethacin with information about ID (subject), dose, time and concentration

M2000				cefamandole				indomethacin			
ID	Dose (mg)	Time (h)	Concentration (ng/mL)	ID	Dose (mg)	Time (min)	Concentration (μg/mL)	ID	Dose (mg)	Time (h)	Concentration (μg/mL)
271	100	0	2950	1	15	0	0	1	50	0	0
271	100	0.17	2164	1	15	10	127	1	50	0.25	1.5
271	100	0.25	1884	1	15	15	80	1	50	0.5	0.94
271	100	0.5	1366	1	15	20	47.4	1	50	0.75	0.78
271	100	1	844	1	15	30	39.9	1	50	1	0.48
271	100	1.5	625	1	15	45	24.8	1	50	1.25	0.37
271	100	2	478	1	15	60	17.9	1	50	2	0.19
271	100	4	256	1	15	75	11.7	1	50	3	0.12
271	100	6	147	1	15	90	10.9	1	50	4	0.11
271	100	8	88	1	15	120	5.7	1	50	5	0.08
271	100	10	58	1	15	150	2.55	1	50	6	0.07
271	100	12	48	1	15	180	1.84	1	50	8	0.05
271	100	16	26	1	15	240	1.5	–	–	–	–
271	100	24	13	1	15	300	0.7	–	–	–	–
–	–	–	–	1	15	360	0.34	–	–	–	–

Table 2 – Key pharmacokinetic parameters: correspondence of designations in PreKinetix and Phoenix WinNonlin

PreKinetix	WinNonlin	Description
C_{max}	C_{max}	Maximum observed concentration
T_{max}	T_{max}	Needed time to reach C_{max}
AUC_{0-t}	AUC_{last}	Area under the pharmacokinetic curve from the time of dosing to the last measured concentration (T_{last})
K_{el}	Lambda_z	Terminal elimination rate constant, estimated from the final part of the pharmacokinetic profile
$T_{1/2}$	HL_Lambda_z	Half-life in the terminal phase
Cl (Cl/F)	Cl_obs (Cl_F_obs)	Total drug clearance
Vz (Vz/F)	Vz_obs (Vz_F_obs)	Volume of distribution in the terminal phase (for non-stationary data)
$AUMC_{0-t}$	AUMClast	Area under the concentration×time curve to T_{last}
$MRT_{0\to t}$	MRTlast	Mean residence time of the drug in the body to T_{last}
V_{ss}	Vss_obs	Volume of distribution at steady state (for non-stationary data)

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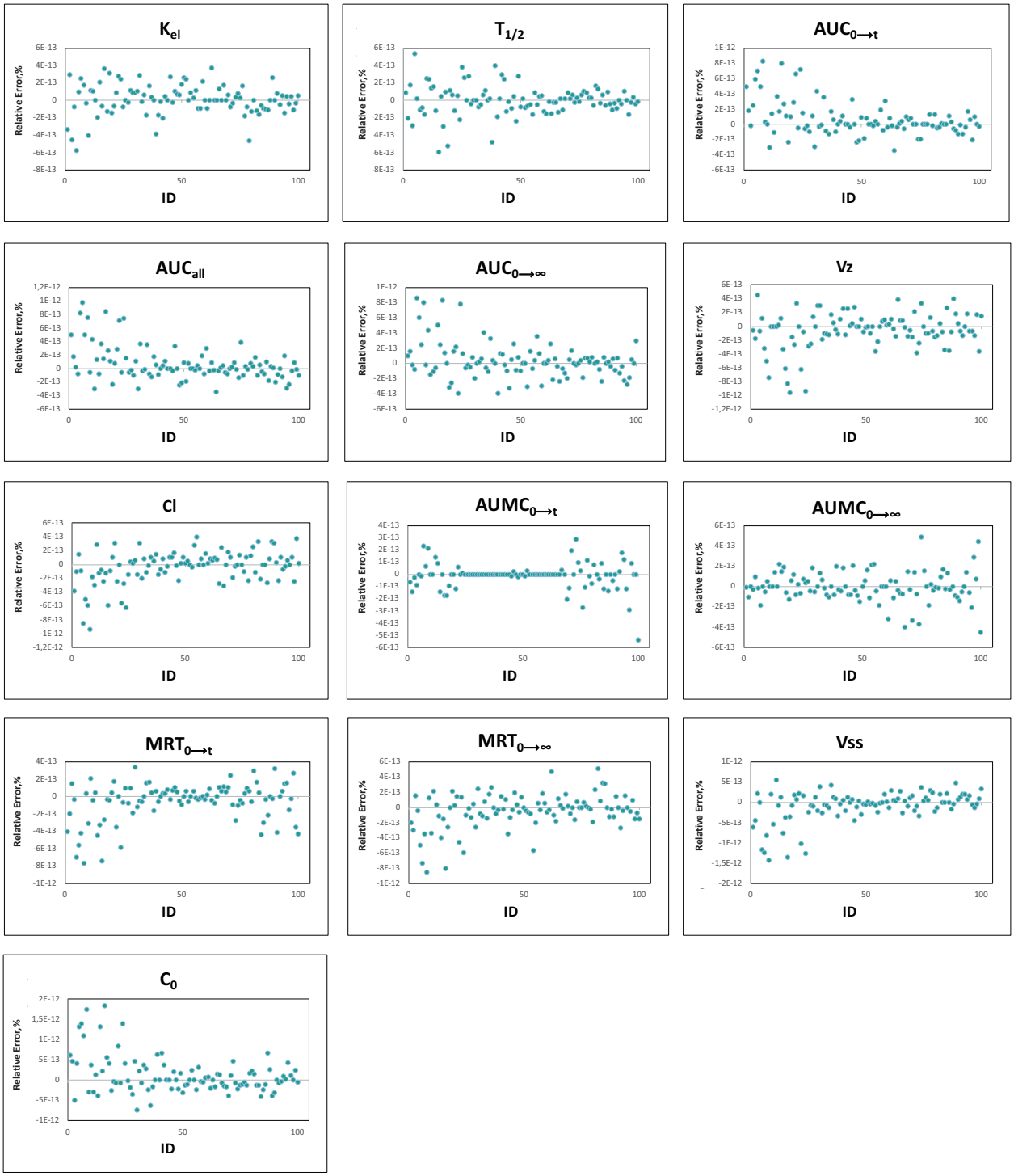

Figure 1 – Relative error (RE_i,%) for a number of key pharmacokinetic parameters calculated using PreKinetix algorithms (intravenous bolus administration model, single dose, linear trapezoidal method, without extrapolation of initial concentration) compared to Phoenix WinNonlin results.

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Table 3 – Comparison of the results of calculating statistical parameters (using the example of the λz parameter of M2000, cefamandole, and indomethacin)

Medicine		M2000		Cefamandole		Indomethacin	
Parameter	Description	WinNonlin	PreKinetix	WinNonlin	PreKinetix	WinNonlin	PreKinetix
N	Number of non-missing observations	12	12	6	6	6	6
NMiss	Number of observations with missing data	0	0	0	0	0	0
NObs	Number of observations	12	12	6	6	6	6
Mean	Arithmetic mean	0.11888	0.11888	0.011296	0.011296	0.324034	0.324034
SD	Standard deviation	0.016801	0.016801	0.00083	0.00083	0.11021	0.11021
SE	Standard error	0.00485	0.00485	0.000339	0.000339	0.044993	0.044993
Variance	Unbiased sample variance	0.000282	0.000282	0.000001	0.000001	0.012146	0.012146
CVPercent	Coefficient of variation	14.132647	14.132647	7.34997	7.34997	34.011658	34.011658
Min	Minimum value	0.10525	0.10525	0.01004	0.01004	0.15832	0.15832
Median	Median — based on the results of calculating percentiles, the 50th percentile	0.110571	0.110571	0.011238	0.011238	0.3279	0.3279
Max	Maximum value	0.156808	0.156808	0.012369	0.012369	0.455445	0.455445
Range	Sample range (difference between the maximum and minimum values)	0.051558	0.051558	0.002329	0.002329	0.297125	0.297125
MeanLog	Arithmetic mean of natural logarithms of observations	-2.13801	-2.13801	-4.485572	-4.485572	-1.184033	-1.184033
SDLog	Standard deviation of natural logarithms of observations	0.132149	0.132149	0.074198	0.074198	0.388093	0.388093
GeometricMean	Geometric mean	0.117889	0.117889	0.01127	0.01127	0.306042	0.306042
GeometricSD	Geometric standard deviation of natural logarithms of observations	1.141278	1.141278	1.07702	1.07702	1.474167	1.474167
GeometricCVPercent	Geometric coefficient of variation	13.272787	13.272787	7.430046	7.430046	40.31756	40.31756
CI95PercentLower	Lower limit of the 95% confidence interval for the data	0.081901	0.081901	0.009162	0.009162	0.040732	0.040732
CI95PercentUpper	Upper limit of the 95% confidence interval for the data	0.155858	0.155858	0.01343	0.01343	0.607337	0.607337
CI95PercentLowerMean	Lower limit of the 95% confidence interval for the arithmetic mean value	0.108205	0.108205	0.010425	0.010425	0.208377	0.208377
CI95PercentUpperMean	Upper limit of the 95% confidence interval for the arithmetic mean value	0.129555	0.129555	0.012167	0.012167	0.439692	0.439692
CI95PercentLowerVar	Lower limit of the 95% confidence interval for the variance	0.000142	0.000142	0	0	0.004733	0.004733
CI95PercentUpperVar	Upper limit of the 95% confidence interval for the variance	0.000814	0.000814	0.000004	0.000004	0.073063	0.073063
CIGEO95PercentLower	Lower limit of the 95% confidence interval for the logarithmized data, reduced to the original scale	0.088137	0.088137	0.009313	0.009313	0.112854	0.112854
CIGEO95PercentUpper	Upper Upper limit of the 95% confidence interval for the logarithmized data, reduced to the original scale	0.157686	0.157686	0.013639	0.013639	0.829936	0.829936
CI95PercentLowerGEOMean	Lower limit of the 95% confidence interval for the geometric mean value	0.108395	0.108395	0.010426	0.010426	0.203658	0.203658
CI95PercentUpperGEOMean	Upper limit of the 95% confidence interval for the geometric mean value	0.128215	0.128215	0.012183	0.012183	0.459897	0.459897
P1	P-th percentile divides the distribution into points in such a way that P percent of the distribution is below this point.	0.10525	0.10525	0.01004	0.01004	0.15832	0.15832
P2.5		0.10525	0.10525	0.01004	0.01004	0.15832	0.15832
P5		0.10525	0.10525	0.01004	0.01004	0.15832	0.15832
P10		0.105356	0.105356	0.01004	0.01004	0.15832	0.15832
P25		0.107117	0.107117	0.010662	0.010662	0.229141	0.229141
P50		0.110571	0.110571	0.011238	0.011238	0.3279	0.3279
P75		0.130099	0.130099	0.012109	0.012109	0.430281	0.430281
P90		0.152636	0.152636	0.012369	0.012369	0.455445	0.455445
P95		0.156808	0.156808	0.012369	0.012369	0.455445	0.455445
P97.5		0.156808	0.156808	0.012369	0.012369	0.455445	0.455445
P99		0.156808	0.156808	0.012369	0.012369	0.455445	0.455445
IQR	Interquartile range (difference between the first and third quartiles).	0.022982	0.022982	0.001448	0.001448	0.20114	0.20114

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Table 4 — Comparison of the results of non-compartmental analysis for the intravenous bolus administration model (single dose, linear trapezoid method, without extrapolation of the initial concentration) using the example of M2000, cefamandole and indomethacin

Drug	M2000		Cefamandole		Indomethacin	
Parameter	WinNonlin	PreKinetix	WinNonlin	PreKinetix	WinNonlin	PreKinetix
N_Samples	14	14	15	15	12	12
Dose	100000000	100000000	15000	15000	50000	50000
Rsq	0.984143	0.984143	0.999758	0.999758	0.997067	0.997067
Rsq_adjusted	0.976215	0.976215	0.999516	0.999516	0.994133	0.994133
Corr_XY	-0.99204	-0.99204	-0.999879	-0.999879	-0.998532	-0.998532
No_points_lambda_z	4	4	3	3	3	3
K_{el}	0.108265	0.108265	0.012369	0.012369	0.15832	0.15832
Lambda_z_intercept	5.116786	5.116786	3.367347	3.367347	-1.724211	-1.724211
Lambda_z_lower	10	10	240	240	5	5
Lambda_z_upper	24	24	360	360	8	8
$T_{1/2}$	6.402296	6.402296	56.039261	56.039261	4.378127	4.378127
Span	2.186716	2.186716	2.141356	2.141356	0.685225	0.685225
T_{max}	0	0	10	10	0.25	0.25
C_{max}	2950	2950	127	127	1.5	1.5
C_{max}/D	0.00003	0.00003	0.008467	0.008467	0.00003	0.00003
C_0	2950	2950	0	0	0	0
T_{last}	24	24	360	360	8	8
C_{last}	13	13	0.34	0.34	0.05	0.05
AUC_{0-t}	4126.36	4126.36	3740.5	3740.5	1.74125	1.74125
AUC_{0-t}/D	0.000041	0.000041	0.249367	0.249367	0.000035	0.000035
AUC_{all}	4126.36	4126.36	3740.5	3740.5	1.74125	1.74125
$AUC_{0\to\infty}$	4246.435284	4246.435284	3767.988172	3767.988172	2.057065	2.057065
$AUC_{0\to\infty}/D$	0.000042	0.000042	0.251199	0.251199	0.000041	0.000041
AUC_%Extrap	2.827673	2.827673	0.729519	0.729519	15.352703	15.352703
AUC_%Back_Ext	0	0	0	0	0	0
Vz	217513.271517	217513.271517	321.84641	321.84641	153527.034923	153527.034923
Cl	23549.163784	23549.163784	3.980904	3.980904	24306.47423	24306.47423
$AUMC_{0-t}$	14317.575	14317.575	190453.5	190453.5	3.27125	3.27125
$AUMC_{0-\infty}$	18308.464419	18308.464419	202571.593629	202571.593629	7.792554	7.792554
AUMC_%Extrap	21.798057	21.798057	5.982129	5.982129	58.020826	58.020826
$MRT_{0\to t}$	3.469783	3.469783	50.916589	50.916589	1.878679	1.878679
$MRT_{0\to\infty}$	4.31149	4.31149	53.761207	53.761207	3.78819	3.78819
V_{ss}	101531.990574	101531.990574	214.018217	214.018217	92077.554608	92077.554608

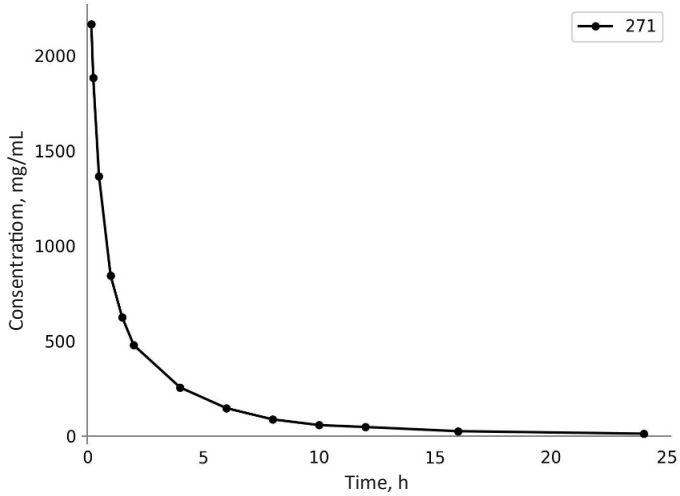

Figure 2 — Individual pharmacokinetic profile in blood (in linear scale), after intravenous bolus administration of M2000.

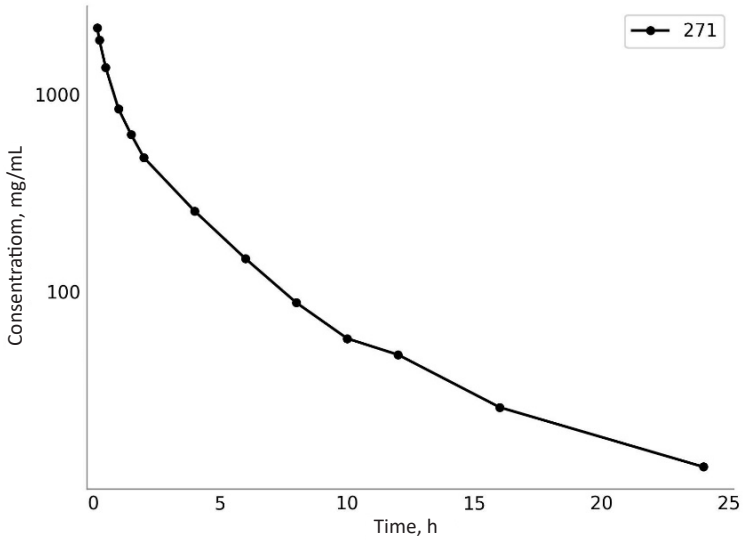

Figure 3 — Individual pharmacokinetic profile in blood (in semi-logarithmic scale) after intravenous bolus administration of M2000.

It should be noted that the fundamental algorithms for calculating PK parameters implemented in PreKinetix correspond to industry-accepted approaches similar to Phoenix WinNonlin. In particular, the area under the curve (AUC) is calculated using the trapezoidal method, if necessary, in a combined mode — with linear interpolation at the stage of increasing concentration and logarithmic at the stage of decreasing. The estimation of the elimination rate constant λz and the associated $T_{1/2}$ in PreKinetix is performed by automatically selecting the points of the terminal phase based on maximizing the coefficient of determination R^2 (usually for the last sequential points with decreasing concentration), which is similar to the built-in Phoenix WinNonlin algorithm. In our calculations, all programs (PreKinetix, Phoenix, etc.) showed the same $T_{1/2}$ values with high statistical quality of approximation of the terminal section, which confirms the equivalence of the methods. As for missing points or concentrations below the limit of quantification, PreKinetix processes them according to generally accepted practice: such values are excluded from the AUC calculation (i.e., do not contribute to the area under the curve) or, if necessary, replaced by conditional zeros — similar to the default settings in Phoenix WinNonlin. Thus, the choice of algorithms for integrating the "concentration–time" profile and estimating λz in PreKinetix is consistent with the approaches implemented in recognized NCA tools, which ensures comparability of results even in non-standard cases.

In numerous studies, Phoenix WinNonlin is used as a reliable tool for NCA calculations on in vivo data. Thus, in the analysis of the PK of the monoclonal antibody WBP216, the authors report that all PK parameters were calculated using Phoenix WinNonlin and used in dose establishment and exposure assessment [24]. The use of Phoenix in early-phase clinical trials confirms its practical significance and compliance with regulatory standards. In addition, a number of other publications describe the use of Phoenix for NCA in the analysis of the effect of food on the PK of various drugs [25]. Thus, the use of Phoenix WinNonlin in this study as a reference for comparing the results obtained using PreKinetix is methodologically justified and consistent with international practice for validating pharmacokinetic software.

From a practical point of view, PreKinetix has a number of advantages. First, the application has an intuitive web interface, which favorably distinguishes it from some existing freely distributed solutions (for example, R-packages without GUI) and facilitates its use by a wide range of users. Secondly, the program integrates a full cycle of PK data analysis — from loading and statistical processing of raw data to calculating PK parameters and visualizing profiles. The results are automatically formatted as easy-to-read reports (Excel tables and Word documents with graphs), which reduces the researcher's labor costs for data formatting. Finally, PreKinetix is based on open technologies (Python, Streamlit, etc.), which provides flexibility in refining and expanding functionality in the future. At the same time, the existing analogues of PreKinetix software that use a similar methodology for calculating PK still have a number of disadvantages.

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Comparison of PreKinetix with other available solutions shows that our application successfully overcomes a number of limitations inherent in them. Unlike tools without a graphical interface [1], our web application provides interactivity and clarity. In terms of the set of implemented models and parameters, PreKinetix is at the level of modern commercial packages (Phoenix, PKanalix, etc.), while being more accessible. Thus, PreKinetix can be used as a reliable alternative to commercial software for NCA tasks in preclinical studies, and also fills a significant gap in the market of software tools for pharmacokinetic analysis in Russia and can contribute to strengthening technological sovereignty in this area.

Study limitations

The limitations of this study include the focus of the current version of PreKinetix primarily on the analysis of PK data with a single administration of the drug. Support for multiple dosing, as well as the possibility of conducting population PK analysis, has not yet been implemented. In addition, the validation of algorithms was carried out mainly on literary and local experimental data, without the involvement of external independent centers, which may require additional confirmation of reproducibility in multicenter studies. Also, at the time of preparation of the article, the application had not undergone official certification or registration as a software tool for use in conditions regulated by the standards of good laboratory practice (GLP). Visualization and export of graphs are implemented with limited flexibility, which may require refinement when used in complex reporting formats.

Further prospects

Modern studies demonstrate a growing interest in hybrid approaches that combine traditional NCA and machine learning methods. Thus, in the work of Hughes et al. (2024) [26] it was shown that MAP-Bayesian methods can significantly increase the accuracy of busulfan dosing compared to classical NCA, despite the close AUC values. In addition, the Deep-NCA model [3], based on deep learning algorithms, demonstrated improved accuracy in predicting C_{max} and AUC compared to classical methods.

This underscores the prospect of expanding PreKinetix in the future by adding machine learning modules to improve the accuracy of algorithms and adapt to large and complex data.

CONCLUSION

During the work, a new web application PreKinetix was created and tested for conducting statistical and NCA PK data. The program supports the main types of preclinical PK experiments (bolus intravenous administration, intravenous infusion, extravascular single-dose administration) and calculates a wide range of PK parameters that fully comply with international standards. The results of the comparative analysis showed that PreKinetix provides high calculation accuracy, not inferior in this respect to the recognized commercial software Phoenix WinNonlin. The introduction of PreKinetix into practice will allow Russian research organizations to reduce the time and financial costs of PK data analysis, automate routine calculations and visualize results with high quality. Thus, PreKinetix is an effective and accessible tool that has great potential for use in preclinical and clinical PK studies, as well as in the educational process for training specialists in the field of biopharmaceutical analysis.

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Research and development objective: “Development of digital models for predicting drug organotoxicity based on data from metabolomic analysis using an alternative biological model”.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS’ CONTRIBUTION

Pavel M. Rezvanov — software development, statistical processing of the results, writing of the draft of the manuscript; Natalia E. Moskaleva — conducting the experiment, statistical processing of the results; Ksenia M. Shestakova — creation of software architecture, statistical processing of the results; Vadim V. Tarasov — analysis of the results with interpretation and conclusions, approval of the final version of the manuscript; Elena A. Smolyarchuk — analysis of literature data on the study aim and results; Dmitry A. Kudlay — analysis of the results with their interpretation and conclusions, approval of the final version of the manuscript; Svetlana A. Appolonova — development of the concept, approval of the final version of the manuscript. All authors confirm that their authorship meets the international ICMJE criteria (all authors made a significant contribution to the development of the concept and preparation of the article, read and approved the final version before publication).

REFERENCES

1. Kim H, Han S, Cho YS, Yoon SK, Bae KS. Development of R packages: 'NonCompart' and 'ncar' for noncompartmental analysis (NCA). Transl Clin Pharmacol. 2018;26(1):10–5. DOI: 10.12793/tcp.2018.26.1.10 Erratum in: Transl Clin Pharmacol. 2018;26(3):141. DOI: 10.12793/tcp.2018.26.3.141
2. Zhang Y, Huo M, Zhou J, Xie S. PKSolver: An add-in program for pharmacokinetic and pharmacodynamic data analysis in Microsoft Excel. Comput Methods Programs Biomed. 2010;99(3):306–14. DOI: 10.1016/j.cmpb.2010.01.007
3. Liu G, Brooks L, Canty J, Lu D, Jin JY, Lu J. Deep-NCA: A deep learning methodology for performing noncompartmental analysis of pharmacokinetic data. CPT Pharmacometrics Syst Pharmacol. 2024;13(5):870–9. DOI: 10.1002/psp4.13124
4. Benet LZ. Benet L Z and Galeazzi R L: noncompartmental determination of the steady-state volume of distribution, J Pharm Sci 68, 1071-1074, 1979 – the backstory. AAPS J. 2012;14(2):164–7. DOI: 10.1208/s12248-012-9326-9
5. Yu YP, Yan XY, Yao C, Xia JL. Bioequivalence Assessment of Topical Ophthalmic Drugs Using Sparse Sampling Pharmacokinetics Data. Biomed Environ Sci. 2019;32(10):788–92. DOI: 10.3967/bes2019.099
6. Rajput AJ, Aldibani HKA, Rostami-Hodjegan A. In-depth analysis of patterns in selection of different physiologically based pharmacokinetic modeling tools: Part I – Applications and rationale behind the use of open source-code software. Biopharm Drug Dispos. 2023;44(3):274–85. DOI: 10.1002/bdd.2357
7. Aldibani HKA, Rajput AJ, Rostami-Hodjegan A. In-depth analysis of patterns in selection of different physiologically-based pharmacokinetic modeling tools: Part II – Assessment of model reusability and comparison between open and non-open source-code software. Biopharm Drug Dispos. 2023;44(4):292–300. DOI: 10.1002/bdd.2360
8. Dong Zh, Fan X, Fan W, Chang H, Xu Y, Li T, Su M. Pkweb: An online application for pharmacokinetic data analysis. Environmental Technology & Innovation. 2020;19:100838. DOI: 10.1016/j.eti.2020.100838
9. Kuang Y, Cao D, Zuo Y, Yuan J, Lu F, Zou Y, Wang H, Jiang D, Pei Q, Yang G. CPhaMAS: An online platform for pharmacokinetic data analysis based on optimized parameter fitting algorithm. Computer Methods and Programs in Biomedicine. 2024;248:108137. DOI: 10.1016/j.cmpb.2024.108137
10. Hau NP. Data analysis in Python using Pandas and Matplotlib. Ekonomika i upravlenie: problemy, resheniya. 2024;8(12):91–7. DOI: 10.36871/ek.up.p.r.2024.12.08.011
11. Taiirbekova R, Kochkonbaeva B, Kalbaeva D. Data Analysis using Python Programming Language. Bulletin of Science and Practice. 2025;11(5):139–44. DOI: 10.33619/2414-2948/114/20
12. Kumar A, Sharma PK, Tyagi MK. The High Demanding Programming Language for Data Science-Python. International Journal of Scientific Research in Engineering and Management. 2024;8(6):1–6. DOI: 10.55041/IJSREM34913
13. McKinney W. Data Structures for Statistical Computing in Python. Proc. of the 9th Python in science conf. (SCIPY 2010). 2010:56–61. DOI: 10.25080/Majora-92bf1922-00a
14. Harris CR, Millman KJ, van der Walt SJ, Gommers R, Virtanen P, Cournapeau D, Wieser E, Taylor J, Berg S, Smith NJ, Kern R, Picus M, Hoyer S, van Kerkwijk MH, Brett M, Haldane A, Del Río JF, Wiebe M, Peterson P, Gérard-Marchant P, Sheppard K, Reddy T, Weckesser W, Abbasi H, Gohlke C, Oliphant TE. Array programming with NumPy. Nature. 2020;585(7825):357–62. DOI: 10.1038/s41586-020-2649-2
15. Hunter JD. Matplotlib: A 2D Graphics Environment. Computing in Science & Engineering. 2007;9(3):90–5. DOI: 10.1109/MCSE.2007.55
16. Waskom ML. Seaborn: statistical data visualization. Journal of Open Source Software. 2021;6(60):3021. DOI: 10.21105/joss.03021
17. Virtanen P, Gommers R, Oliphant TE, Haberland M, Reddy T, Cournapeau D, Burovski E, Peterson P, Weckesser W, Bright J, van der Walt SJ, Brett M, Wilson J, Millman KJ, Mayorov N, Nelson ARJ, Jones E, Kern R, Larson E, Carey CJ, Polat İ, Feng Y, Moore EW, VanderPlas J, Laxalde D, Perktold J, Cimrman R, Henriksen I, Quintero EA, Harris CR, Archibald AM, Ribeiro AH, Pedregosa F, van Mulbregt P; SciPy 1.0 Contributors. SciPy 1.0: fundamental algorithms for scientific computing in Python. Nat Methods. 2020;17(3):261–72. DOI: 10.1038/s41592-019-0686-2 Erratum in: Nat Methods. 2020;17(3):352. DOI: 10.1038/s41592-020-0772-5
18. Pedregosa F, Varoquaux G, Gramfort A, Michel V, Thirion B, Grisel O, Blondel M, Prettenhofer P, Weiss R, Dubourg V, Vanderplas J, Passos A, Cournapeau D, Brucher M, Perrot M, Duchesnay É. Scikit-learn: Machine Learning in Python. J Mach Learn Res. 2011;12(85):2825–2830.
19. Seabold S, Perktold J. Statsmodels: Econometric and Statistical Modeling with Python. Proc. of the 9th Python in science conf. (SCIPY 2010). 2010:92–6. DOI: 10.25080/Majora-92bf1922-011
20. Hagberg AA, Schult DA, Swart PJ. Exploring network structure, dynamics, and function using NetworkX. Proceedings of the 7th Python in Science Conference (SciPy 2008). 2008:11-16. DOI: 10.25080/TCWV9851
21. Platova AI. Population pharmacokinetics analysis in Lixoft Monolix softwares. Pharmacokinetics and Pharmacodynamics. 2021;(3):36–51. DOI: 10.37489/2587-7836-2021-3-36-51
22. Archakova OA, Bagaeva NS, Komarov TN, Rogov AV, Shchelgacheva DS, Suvorova AV, Karnakova PK, Karpova PA, Shohin IE. Pharmacokinetics Study of the Long-acting Antiarrhythmic Drug of Lappaconitine Hydrobromide (Allaforte®, JSC "Pharmcenter VILAR", Russia). Drug development & registration. 2022;11(1):140–7. DOI: 10.33380/2305-2066-2022-11-1-140-147
23. Yamaoka K, Nakagawa T, Uno T. Statistical moments in pharmacokinetics. J Pharmacokinet Biopharm. 1978;6(6):547–58. DOI: 10.1007/BF01062109
24. Leng X, Tang X, Hu P, Guan X, Li Q, Huang C, Zhang Q, Chen R, Zeng X. Safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of WBP216, a novel IL-6 monoclonal antibody, in patients with rheumatoid arthritis: A phase Ia randomized placebo-controlled study. Front Immunol. 2023;13:1110992. DOI: 10.3389/fimmu.2022.1110992
25. Cheng Y, Lin BJ, Guo JH, Huang BL, Fang LP, Que WC, Liu MB, Chen XF, Qiu HQ. The Effect Of Food On The Pharmacokinetic Properties and Bioequivalence of Two Formulations of Levocetirizine Dihydrochloride in Healthy Chinese Volunteers. Drug Des Devel Ther. 2019;13:3625–34. DOI: 10.2147/DDDT.S215316 Erratum in: Drug Des Devel Ther. 2019;13:3835. DOI: 10.2147/DDDT.S236661
26. Hughes JH, Long-Boyle J, Keizer RJ. Maximum a posteriori Bayesian methods out-perform non-compartmental analysis for busulfan precision dosing. J Pharmacokinet Pharmacodyn. 2024;51(3):279–88. DOI: 10.1007/s10928-024-09915-w

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