Method of calculation the actual values of the parameters of drug elimination

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Statement of the Problem: The half-life $t_{1/2}$ or $t_{1/2(\beta)}$ is an indispensable characteristic to any drug, because it is one of the pharmacokinetic (PK) parameters required for the calculation of its dosage regimen. But, now in use the methods of calculation $t_{1/2}$, which are valid only for the so-called monoexponential curve. They are also subject to the rule $t_{1/2} / MRT = \ln 2$, where MRT - mean residence time. In reality, there are many cases of deviation from it: $\ln 2 > t_{1.2} / MRT > 1$.
According to the results of our investigation [1], they are logically related with the number of compartments in a PK model and mode of the drug administration, thus the relation $t_{1/2(\beta)} / MRT$ can be recommended as an additional its characteristic.
The aim of this study is to devise a method for determining an actual values $t_{1/2}$ and MRT.
Methodology & Theoretical Orientation: By analysis of mathematical tool, numerical simulation and experimental data from literature it was shown, that to the determination of the actual values $t_{1/2}$ and MRT instead PK curve of blood one must use the curve of the drug elimination from it. The problem of non-uniqueness of solutions [2-5] can be avoided by using the value $C_{10}(t)/C_0$ or its equivalent - $AUC_{0-t} / AUC_{0-\infty}$.
Findings: Based on elimination curves it is possible to calculate not only an actual values $t_{1/2}$ and MRT, but also others parameters of drug elimination: the time-t_{calc}, required for the elimination from the blood of a given fraction of administered dose of drug - $(C_{10}/C_0)_{fix}$, or, conversely, to find its value-$(C_{10}/C_0)_{calc}$ at any point in time - t_{fix} (Fig.1a and 1b).
Conclusion & Significance: The proposed method make possible properly evaluate the parameters of drug elimination, optimize the dosage regimen and, consequently, will enhance their effectiveness.

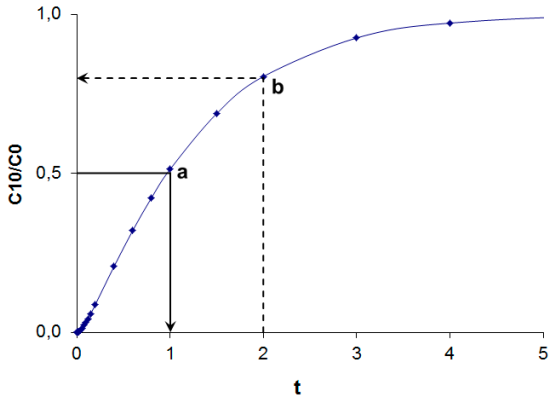


Fig. 1 - The scheme of calculation of drug elimination parameters on base of curve $C_{10}(t)/C_0 = f(t)$:
a - $(C_{10}/C_0)_{fix} \rightarrow t_{calc}$, b - $t_{fix} \rightarrow (C_{10}/C_0)_{calc}$

Recent publications

1 Asmanova N, Ilin AI (2016) The patterns of correlations between half-life – $t_{1/2}$ and mean residence time - MRT for PK models of different dimensions and mode of drug administration. //Abstracts: International Conference Mathematical modeling and High Performance Computing in Bioinformatics, Biomedicine and biotechnology MM-HPC-BBB-2016, Novosibirsk, RUSSIA, 29 August - 2 September, p 17

2 Asmanova N., Koloskov G., Ilin A (2013) Coupled solutions of one- and two-compartment pharmacokinetic models with first-order absorption. J. Pharmacokinet. Pharmacodyn. 40: 229-241

3 Asmanova N, Koloskov G, Ilin AI (2014) On Issues of Nonuniquenes of Solution to Some Problems in Pharmacokinetics and Appraisal of Excretion dates Capabilities in their Resolving. Abstracts of sectional reports Modern technologies for development of anti-infectious drug Almaty, 17-19 September, p133

4 Asmanova N, Ilin AI (2016) Flip-flop phenomenon in two-compartment models with first order absorption. Abstracts: International Conference Mathematical modeling and High Performance Computing in Bioinformatics, Biomedicine and biotechnology MM-HPC-BBB-2016, Novosibirsk, RUSSIA, 29 August - 2 September, p16

5 Asmanova N, Ilin AI (2016) Futures of solution of some inverse problems in PK models with first order absorption. Abstracts: International Conference Mathematical modeling and High Performance Computing in Bioinformatics, Biomedicine and biotechnology MM-HPC-BBB-2016, Novosibirsk, RUSSIA, 29 August - 2 September, p 15

Biography

The purpose of research, conducted by Asmanova Nazira in the last years - theory and practice of handling experimental data of pharmacokinetic studies of drugs. This is due to the fact that some properties PK models and methods of estimation the values of PK parameters are still controversial or even incorrect, which can lead to undesirable consequences.

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Ilin Aleksander I. - His research is associated with the development and creation of new drugs based on iodine-organic compounds. The main advantages of these drugs are a wide spectrum of action and a practical lack of resistance to them in microorganisms.

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