PHARMACOKINETIC MODEL OF THE EXTENDED ACTIONS OF MEDICAL DRUGS.

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Introduction. The speed and degree of absorption of a drug substance depends on many factors: the route of administration, the individual characteristics of the patient's body, the physiological and pathological state of the gastrointestinal tract, the cardiovascular system, the liver, and the kidneys. In addition, bioavailability has a pronounced effect on biopharmaceutical factors: the dosage form, its composition, and the technology of the preparation.

Aim. Most drugs are administered orally in the form of tablets, capsules. It is for these dosage forms that biopharmaceutical factors are particularly important.

On the bioavailability of the drug may have a pronounced effect of auxiliary substances used to prepare dosage forms and are part of their composition. For example, the disintegration of tablets often depends on the amount and nature of the disintegrates included in their composition. For pressing the tablets and filling the capsules, substances that can adversely affect the dissolution rate of the active compound are used. Dissolution of drugs may be hampered by the low dispersing ability of the filler particles, and surface-active agents or other substances that affect the electrostatic properties of the particles promote their disaggregation. The technology of granulation of powders in pharmaceutical plants also affects the nature of the release of the active substance from the dosage form. An important role for bioavailability of drugs is played by the nature and composition of the coating of tablets and capsules. In this regard, it is interesting to extend the effect of the drug by simultaneous administration of it in two different forms with varying degrees of bioavailability.

Materials and methods. Mathematical methods allow modeling a pharmacokinetics (behavior of medicine in an organism). The main index of a pharmacokinetics — change of concentration of medicine in a blood plasma depending on time. If medicine is taken in the form of tablets, then the corresponding dependence is described by two differential equations. To describe such a process, consider a pharmacokinetic model with a subcamera, through which the drug is administered:

$$\begin{cases} \dfrac{dM_1}{dt} = -k_{in1}\alpha M_1 - k_{in2}(1-\alpha)M_1 \\ \dfrac{dM}{dt} = k_{in1}\alpha M_1 + k_{in2}(1-\alpha)M_1 - k_{el}M \end{cases} \quad (1)$$

Here $M_1, M -$ the amount of the drug in the subcamera and the main camera that simulates blood and other tissues, $k_{in1}, k_{in2} -$ the absorption constants of the two forms of the drug from the subcamera to the main camera, $k_{el} -$is the elimination constant of the drug from the main camera, α is the relative fraction of the first drug in the administered dose, t is the time.

Integration of system of differential equations taking into account starting conditions ($M_1(0) = M_0, M(0) = 0$) allows to receive dependence of M (t):

$$M(t) = \frac{\alpha M_0 k_{in1}}{k_{in1}-k_{el}}(e^{-k_{el}t} - e^{-k_{in1}t}) + \frac{(1-\alpha)M_0 k_{in2}}{k_{in2}-k_{el}}(e^{-k_{el}t} - e^{-k_{in2}t}) \quad (2)$$

Results and discussion. Parameters of the received expression are constants of an absorption $k_{in1}, k_{in2,}$, which can be varied technologically, and the constant α determined by a ratio in an initial dose of two different forms of medicine. Let's assume that $k_{in1} < k_{in2}$, then the first item in a right member (2) provides extension of effect of medicine, and the second – regulates the speed of achievement of the necessary concentration of medicine in blood.

Conclusions. The given consideration shows that at enteral simultaneous reception of two different forms of a medicinal preparation, perhaps extensions of effect of medicine when ensuring its high quick action. Naturally, confirmation of such effect requires carrying out the corresponding experiments.