

## **ALTERNATIVE APPROACHES OF PATHOLOGY'S MODELING IN PHARMACOLOGICAL STUDIES OF MEDICINES**

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Introduction of new medicines in clinical practice is impossible without preclinical studies in which are used a lot of laboratory animals. According to Council Directive of EU (86/609/EEC) of 1986, following ethical norms must be considered during holding studies on animals: reduction of number of studies, improvement of studies' severity and used species, also replacement of studies on animals that is a final goal of this Directive. Alternative of preclinical studies of medicines on animals is using of appropriate cell cultures and tissues for these goals. Modern toxicology and pharmacological laboratories use standardized cell cultures for holding screening toxicology studies, determining orientation of new biologically active substances and first evaluations of dependence "dosage - effect". But the metabolism of organism's tissue differ from one of the cell culture that prevents fully evaluate effect of medicine on all organs and systems of biological organism. Considering this, the full toxicology and pharmacological study can't be holded without using of laboratory animals.

Another alternative side of pharmacological study of new drugs is computer modeling of biochemical, pharmacokinetic and pharmacodynamic processes in human body, its organs and systems in general. Herewith, different processes of organism can be introduced with the help of number of mathematical models given with possible variations of physiological indexes. Also there can be simulated pathologies that are needed for study. The complexities of implementation of such kind of modeling pharmacological effects of medicine are wide variation of indexes under study, multifactorial effects under study and complicated correlation, interrelatedness and interaction of systems under study. Besides, verification on traditional pathology models in animals needs to be holded for conformation of their reliability and introduction into the pharmacological studies of medicines.

Especially interesting for pharmacological studies of medicines is developing and verification of kidney's mathematical model, because the most of drugs are excreting through them, so this process can be changed or broken at kidneys' diseases. Kidney anatomy and its functions are rather complicated research problem, realization of which should include several stages. Mathematical models of single processes in kidney should be created first, then they should be verified on animals and after that the model of the whole kidney can be done.

Glomerular filtration is the most important process among ones in kidneys, but it is hard to verify its pathology because of complexity of creating physiological pathology model exactly of this process. Tubular reabsorption has a lot of ways of modeling on animals exactly its pathology. In our future research it is planned to simulate tubular reabsorption and pyelonephritis as its pathology via mathematical modeling with the following their verification on animals.