APPLICATION OF 3D MODELING METHODS TO STUDY THE SPATIO-TEMPORAL DISTRIBUTION OF PARACETAMOL

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Paracetamol, also known as N-acetyl-p-aminophenol, is a widely available over-the-counter pain reliever that belongs to the analgesic family. It has antipyretic, analgesic, and mild anti-inflammatory properties. However, paracetamol can also cause accidental and intentional poisonings [1].

Assessment and prediction of changes in the concentration of conjugated and toxic metabolites of paracetamol in the liver and in the body are extremely important. However, due to the high cost and duration of invasive assessments of concentrations in tissues, computer modeling methods have become the most widely used approach. The object of modeling is the complexly branched vascular network of the liver, including its parenchymal tissue, within the framework of one structural and functional unit of the organ.

The blood flow modeling is based on solving the unsteady Navier-Stokes equation, which take into account the non-Newtonian properties of blood and its incompressibility. The dynamic viscosity was modeled using the Carreau model [2]. The equations describing the process of paracetamol diffusion from the blood vessels to the tissues and its metabolism are the reaction-diffusion and Michaelis-Menten equations.

As a result of simulating the processes of hemodynamics, diffusion, and metabolism of paracetamol, we obtained the spatio-temporal distribution of the drug and its metabolites in the vascular network and liver tissue. Additionally, we showed the significant effect of heterogeneous distribution and activity of hepatocyte enzyme systems on the concentration gradients of paracetamol and its metabolites, indicating the need to consider this factor in modeling.

Literature

1. *J. G. Diaz Ochoa, J. Bucher, A. R. Pery, J. M. Zaldivar Comenges, J. Niklas, and K. Mauch*, "A multi-scale modeling framework for individualized, spatiotemporal prediction of drug effects and toxicological risk," // *Front Pharmacol,* **vol. 3**, p. 204, 2012.
2. *Y. R. Nartsissov,* "Application of a multicomponent model of convectional reaction-diffusion to description of glucose gradients in a neurovascular unit," // *Front Physiol,* **vol. 13**, p. 843473, 2022.