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The importance of bile circulation in cholesterol homeostasis - A three-compartment mathematical model analysis

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The analysis of the two-compartment model of cholesterol homeostasis has shown a significant influence of the amount of cholesterol carried by the bile on the total cholesterol concentration in the second compartment, i.e. peripheral blood. To study the influence of bile circulation on the cholesterol homeostasis, we have developed a three-compartment model by the addition of a new compartment, describing changes of the bile amount in the gallbladder. Now our model allows to consider: Chole-sterol synthesis in the liver, cholesterol exchange kinetics between compartments, the rate of cholesterol entry and loss with bile, the loss of cholesterol due to the conversion into cholic acid, cholesterol consumption by tissues, dietary cholesterol, gallbladder filling and emptying rates and gallbladder bile accumulation ability. Our model consists of three equations (ODE) and fourteen parameters. All parameters in our model can be divided into five groups:

1. Parameters whose values result directly from physiological knowledge: The tissues demand for cholesterol, volume of blood serum in the liver and in the blood stream, total amount of bile, loss of cholesterol with feces, time of gallbladder filling and emptying.

2. Parameters whose values result indirectly from physiological knowledge through equations describing particular processes. This group includes: Parameter describing the rate of cholesterol synthesis, parameters responsible for the rate of cholic acid synthesis and the medium rate of cholic acid flow from the liver into the gallbladder.

3. Parameters which are bound together by postulated equations to describe known physiological changes.

4. Parameters estimated on the basis of a case study.

5. Parameters which could be described as effective rate constants responsible for multistep processes of cholesterol exchange between two compartments: Blood in the liver and peripheral blood.

The model allows us to perform the analysis with different gallbladder physiological conditions, i.e. differences in bile accumulation, patency of the bile ducts and gallbladder motility. Based on the obtained results we speculate that inter-individual features regulating the bile circulation might result in different responses to the dietary cholesterol (hypo- and hyper responders).

Biography

Krystian Kubica is Biochemist and Physicist, Head of the Computer Simulation team of Biological Systems at the Department of Biomedical Engineering, Wroclaw University of Technology. Research interests: Biophysics of biological membranes (lipid phase behaviour, interaction between biologically active compounds and membranes, the influence of molecular probes on membrane properties, the influence of lipid oxidation on membrane properties, membrane electroporation, physiological process modelling cholesterol homeostasis, molecular mechanism of thermoregulation, bone remodelling, pharmacokinetic). He has published 37 research papers. He is also the author of 7 patents. He has an experience in:

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• Theoretical modeling of biological systems.

• Biochemical techniques of isolation, separation and characterization of biological compounds.

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Page 27