

STUDY OF THE DYNAMIC EFFECT OF CHOLESTEROL LOWERING DRUGS

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It is widely accepted that cholesterol plays an important role in the infiltration and entrapment of low density lipoprotein (LDL) in the blood vessel walls (atherogenesis). The transport of cholesterol and other lipids through the circulatory system is facilitated by their packaging into lipoprotein carriers such as LDL. In fact, LDL is the major carrier of cholesterol in human plasma, and therefore it plays a crucial role in atherosclerosis. Small and dense lipoproteins (sdLDL) are held to be particularly atherogenic.

Fibrates can be used to correct the lipoprotein metabolism disorder associated with sdLDL. Fibrates act by lowering plasma triacylglycerol and very low density lipoprotein levels (VLDL), therefore correcting the underlying metabolic disturbance that causes hypercholesterolemia.

A deeper understanding of this system is necessary in order to design more effective drugs. In this work we present a mathematical model for lipoprotein metabolism. This model was used to study the effect of Niacin, a fibrate drug, on the levels of VLDL and sdLDLs. Simulations results show that high levels of triacylglycerol are essential for VLDL accumulation and sdLDL production. Addition of Niacin reduces triacylglycerol levels. As a result of this the production of VLDL decreases, which prevents the formation of sdLDL.

MODELING OF PRECURSOR HEMATOPOIETIC STEM CELL MOBILIZATION AND APHERESIS

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Hematopoietic stem cells (HSC) travel from bone marrow to peripheral blood and vice versa. We believe that this travel process is crucial for the cells to maintain their stem characteristics and for allowing the homogeneous distribution of the cells in the bone marrow. A mathematical model was developed to describe the mechanism proposed, where stem cells leave the bone marrow upon differentiation to the peripheral blood, and subsequently return to the bone marrow. The experimental data used in this work was obtained from the process of apheresis, where stem cells (CD34⁺) are collected from peripheral blood. Experimental data from 14 healthy volunteers was used to estimate parameters required for the model and determine ranges for all the variables that characterize the apheresis process. The model describes the apheresis process and provides an initial estimate for the net transport rate of the cell from the bone marrow.