Lipoproteins in the postprandial state

Studies on the metabolism of triglyceride-rich lipoproteins using multicompartmental models

Lipoproteins are vehicles of transport of lipids; such as cholesterol and triglycerides, around the human body. Lipoproteins are secreted by the liver continuously and by the intestine, in response to feeding. So-called low-density lipoproteins (LDL) have been long recognized for their association with heart disease; an association which has been confirmed to be causal. Recent evidence also suggests that another type of lipid particle in the human blood stream; so-called triglyceride-rich lipoproteins (TRLs) are also causally associated with heart disease. Therefore, there is a need to better understand the metabolism of these particles, in relation to LDL. Here, we developed a multicompartmental model for the purpose of investigating the metabolism of both TRL- and LDL particles in the human blood stream. A multicompartmental model is a representation of the lipoprotein metabolic system and can be used for quantification of fluxes of lipoproteins. This information may increase our fundamental knowledge of the behaviour of the various lipoprotein sub-species and why they are elevated in some individuals. In the current thesis, I describe the model development process and the implementation of the model for the study of hypertriglyceridemia (high levels of TRLs) and for the study of the antidiabetic drug liraglutide and the LDL-lowering drug evolocumab. We show that the model is useful in describing the metabolism of lipoproteins and that the results may contribute to our understanding of the role of these lipoproteins in heart disease.

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