

3. AIMS AND OBJECTIVES

The acyl-coenzyme A: cholesterol O-acyltransferases (ACAT) is a small family of enzymes comprising of three homologous members, namely acyl-coenzyme A: cholesterol O-acyltransferase 1 and 2 (ACAT-1 and ACAT-2), and acylcoenzyme A: diacylglycerol acyltransferase 1 (DGAT-1). ACAT has generated much interest as a potential means of exploring the atherosclerotic disease process by both lipid and non-lipid mechanisms. Enzymes of ACAT family perform important biological functions. ACAT-1 and ACAT-2 are critical for *in vivo* cholesterol homeostasis. At the single cell level, they prevent free excessive cholesterol from building up in the cell membranes. Under pathophysiological condition, these enzymes convert excess cholesterol into cholesteryl esters in cholesterol-loaded macrophages. The macrophages are gradually converted into foam cells, which is a hallmark of early lesions of atherosclerosis.

Despite its major importance in pathophysiology of atherosclerosis, the details about its active site remain unknown. Till date there is no enzyme structure identified for ACAT. This brings the limitations in the development of better and effective ACAT inhibitors for the treatment of atherosclerosis. On the basis of biological activity data obtained from our laboratory, it was aimed to develop a predictive pharmacophore and atom based 3D-QSAR model for ACAT inhibitors along with the development of possible ACAT enzyme structures to depict the probable active site of the enzymes for the purpose of designing of better ACAT inhibitors.