

---

## 6. CONCLUSION

Atherosclerosis is a disease of medium and large arteries characterized by deposition of lipid-rich plaques into the inner walls of the arteries. This progressive process silently and gradually blocks arteries, setting blood flow at risk. The acyl-coenzyme A: cholesterol O-acyltransferases (ACAT), also known as Sterol O-acyltransferase (SOAT), is a small family of enzymes comprising three homologous members, namely acyl-coenzyme A: cholesterol O-acyltransferase 1 and 2 (ACAT-1/SOAT-1 and ACAT-2/SOAT-2), and acylcoenzyme A: diacylglycerol acyltransferase 1 (DGAT-1).

ACAT-1 and ACAT-2 are critical for *in vivo* cholesterol homeostasis. At the single cell level, they prevent free excess 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. The known receptor structure of any enzyme always helps in the design of novel drugs. Although the importance of ACAT in atherosclerosis is widely known, the enzyme structure is not reported till date. In this study, we have reported possible 3D structures of ACAT-1 and ACAT-2 enzymes and identified the active binding sites in each. To develop the 3D structure of ACAT-1, I-TASSER was used for threading technique and by using this ACAT-1 model the ACAT-2 model was developed in MODELLER by homology modeling.

Further, by using molecules previously synthesized in this laboratory we have developed a pharmacophore and 3D-QSAR models to understand the structure activity relationship. The most active compound was docked in the receptor active site of both the developed enzyme structures.

Here, the pharmacophore based 3D-QSAR study and docking study based on the proposed 3D model of ACAT-1 and ACAT-2 offer important structural insights for the designing of novel potent ACAT inhibitors very important feature requirements for the development of novel ACAT inhibitors.