Design, Synthesis and *In Vivo* Biological Evaluation of Imidazole-5-Carboxamide Derivatives as Lipoprotein Lipase Activators

By

Haneen Muneer Abuzaid

Supervisor

Prof. Dr. Ghassan Abu Sheikha

Co-Supervisor

Dr. Suhair Hikmat Jasim

ABSTRACT

Hypertriglyceridemia is a condition in which serum triacylglycerol levels are elevated, this condition is often associated with atherosclerosis and represents one of the major risk factors for coronary artery diseases (CAD). Lipoprotein lipase (LPL) protein is a member of the lipase gene family, which includes pancreatic lipase, hepatic lipase, and endothelial lipase. It's found primarily on the surface of cells where it plays a critical role in breaking down fat in the form of triglycerides, which are carried in the blood by molecules called lipoproteins. The importance of such enzyme in lipid metabolism makes it an essential target for the synthesis of drugs that treat hyperlipidemia. Imidazole and methyl-imidazole carboxamide benzophenone derivatives were designed as possible substrates of LPL. Docking studies which were done at the modeling unit at the Faculty of Pharmacy on the tested compounds **5**,**7**,**11** and **12** against the active domain of LPL showed that all tested compounds accommodate the binding cleft. All the synthesized compounds **5**,**7**,**11**,**12**,**13** and **14** were tested *in vivo* for their

hypolipidemic activity on hyperlipedimic rats induced by Triton WR-1339. The compounds were significantly biologically active and the most active compound was **14** which reduced triglyceride serum level by 94.5% at dose of 30mg/kg. Bezafibrate was also used as reference drug for comparable reason.