Molecular Characterization of the Antihyperlipidemic Activity of Novel Nicotinic Acid-Carboxamides Derivatives Using Rats Animal Model

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Abstract

Hyperlipidemia is characterized by increasing the level of one or more of plasma lipids such as TC, LDL-C, TGs concentration, and decrease in HDL-C, and considered as major risk factor in developing cardiovascular diseases including atherosclerosis, Lipid biosynthesis or catabolism is considered an attractive pathway target to regulate atherogenic parameters levels in blood. In this research we investigate the antihyperlipidemic effect of target new nicotinic acid-carboxamide derivatives **C1** (N-(4- benzoylphenyl) pyridine-3-carboxamide) and **C2** (3-benzoylphenyl)pyridine-3- caroxamide), which are synthesized at University of Jordan, followed by molecular characterization of their mechanism of action *invivo* in Triton WR-1339 induced hyperlipidemic rats using PCR array profiling. Analysis of gene expression profiles of fatty acid and lipoprotein signaling and cholesterol metabolism PCR arrays of **C1** and **C2** in comparison to Triton WR-1339 control group, showed that many

genes are overexpressed involved in fatty acid metabolism and transport, cholesterol and ketone body biosynthesis, such as long chain acyl COA synthetases (Acs14, Acsl5), medium acyl COA dehydrogenaeses (Acadm), acyl COA thioesterase (Acot7, Acot12), and nuclear receptors, (Nr1h2, Nr1h3). Compounds **C1** and **C2** down regulated solute-carrier 27a(Slc27a5), which is considered gene of interest, and also diminished atherogenic Apoc3, Apob, and improve antiatherogenic Apoal, Apoa2 and Apoe, also **C1** and **C2** overexpressed many genes that reduces LDL-C in circulation.