University of Naples Federico II
Department of Pharmacy
Doctoral Course in Pharmaceutical Sciences XL Cycle

MOLECULAR AND PHARMACOLOGICAL REPURPOSING OF A NEW CLASS OF ORAL ANTIDIABETIC DRUGS TARGETING CARDIOMETABOLIC DISEASES.

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Metabolic Syndrome (MS) is a cluster of interconnected risk factors that increase the likelihood of developing cardiovascular diseases, type 2 diabetes, and other health complications. A combination of factors, including obesity, high blood pressure, high blood glucose levels, abnormal lipid profiles, and insulin resistance characterizes this condition. Recently, the incidence of MS has been dramatically increasing, principally due to the global epidemics of diabetes and obesity. Many therapeutic options are available, however, the research of alternative/additive molecular targets to manage this multifaced condition is currently under investigation. Sodium-glucose co-transporter 2 inhibitors are new anti-hyperglycemic drugs. They inhibit renal glucose and sodium reabsorption in the proximal convoluted tubule, leading to increased glucose excretion and lower blood glucose levels through an insulin-independent mechanism. Another class of hypoglycemic drugs is the incretin mimetics that act like incretin hormones such as glucagon-like peptide-1 (GLP-1). By binding to GLP-1 receptors, these drugs stimulate glucose-dependent insulin release. Growing evidence suggests that both of these antidiabetic medications provide several benefits in patients with cardiometabolic disease, beyond their hypoglycemic effects. Therefore, the current project will evaluate the molecular mechanisms underlying the beneficial action of these antidiabetic drugs in MS-associated multiorgan failure (skeletal muscle, kidney, heart, vessels). To do so, in vitro, ex vivo, and in vivo approaches will be used, coupled with transcriptomic, proteomic, and post-translational modification analysis. MS-induced multiorgan failure will be evaluated in both genetically modified mouse models of MS and high-fat diet-induced MS. Additionally, gene silencing strategies and/or selective drug treatments for altered genes and/or proteins related to MS-associated multiorgan failure will be performed.

References:

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