2-PHENYL-2H-1,2,3-TRIAZOLES AS LEAD COMPOUNDS CLASS TO TREAT DIABETES

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INTRODUCTION: More than 310 million people suffer from type 2 diabetes mellitus (DM-2) in the world. In DM-2, insulin secretion by the pancreas may be normal, but the glucose entrance into cells is compromised due to reduced number of receptors for insulin, increasing blood glucose levels. Alpha-glycosidase inhibitors (GLs) are capable of slowing down carbohydrate assimilation by humans playing an important role in DM-2 control. In this report, we disclose easily accessible synthetic triazoles as oral anti-diabetic lead compounds. OBJECTIVES: Evaluate three most active triazoles as glycosidases inhibitors using an in vivo model and determine their inhibition modality. MATERIAL AND METHODS: The 60 compounds obtained in this work had their synthesis, pharmaceutical composition and methods of treatment protected in the INPI (BR10201402751). The porcine pancreatic α-amylase and yeast maltase assays were performed as described previously, by our group, using 4-nitrophenyl based substrates (Senger et al., 2012, Gonzaga et al., 2014). For in vivo testing we selected the three most potent compounds observed in biochemical assays described above that were not derived from carboxaldehydes. Compounds (20b, 20h and 20i) and acarbose (positive control) were administered via oral gavage at a concentration of 10 mg/kg together with 4 g/kg of a maltose solution. Employing 100 fold normal enzyme and 10 fold inhibitors concentrations during 15 minutes, triazoles inhibition modality were elucidated. RESULTS AND DISCUSSION: Mice treated with the compound 20i and acarbose demonstrated a significant reduction in the peak postprandial blood glucose when compared to control animals which received only maltose solution. Furthermore those oral tested triazoles displayed reversible inhibition. CONCLUSIONS: Our results demonstrated the in vivo anti-hyperglycemic activity of a 2-phenyl-2H-1,2,3-triazole. This compound is non-glycosidic molecule obtained by molecular simplification that can be used as a lead compound for the treatment of DM-2.

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