PROMISING LEAD COMPOUNDS AS ANTI-DIABETIC Α-GlUCOSIDASE INHIBITORS

Mohammad Hossein Mehraban*
*Shiraz University of Medical Sciences, Shiraz, Iran

In our ongoing program aimed at the design, synthesis and biological evaluation of novel and selective α-glucosidase inhibitors, 8 new pyrimidine fused heterocycles were synthesized and found to be potent and selective inhibitors of mouse and yeast α-glucosidases. The action of these agents would reduce the liberation of glucose in the blood stream which in turn decrease the post prandial hyperglycemia in diabetic patients. Enzyme kinetic assays proved that these compounds have an IC50 in micro molar range and since they have no significant inhibitory activity upon porcine amylase they may be the specific and selective inhibitors of α-glucosidase enzyme which in medical usage means it may result in less side effects for diabetic patients. The addition of different substructures to the pyrimidine fused core significantly altered the action of the compounds ranging from zero to considerable inhibitory action. It is noteworthy, that the inhibitory activity of these pyrimidine fused derivatives on yeast α-glucosidase are far more better than the acarbose which is a widely used anti-diabetic drug and was used as a positive control. However, the inhibition mode of these ligands are mostly the same as acarbose, as they use a competitive mechanism of inhibition against this enzyme. Hence, in search of new, selective and easily accessible anti-diabetic α-glucosidase inhibitors pyrimidine fused derivatives proved to be a new scaffold for potent and specific α-glucosidase inhibitors that can efficiently decrease the blood glucose levels and result in less side effects.