

Drugs Acting on Imidazoline Receptor are Still in Infancy for Treating the Diabetes Mellitus

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Imidazoline receptors (*I*) are distributed in the central nervous system and in peripheral tissue. They involved in the regulation of the blood pressure and secretion of hormones, including adrenocorticotrophic hormone and insulin. Drugs that are selectively act on *I*-receptor showed pleotropic effects, including anti-inflammatory; protection of central nervous system against stress, pain, convulsion and depression; regulation of body fat; and cell protection against apoptosis and adhesion. Several studies found that there is a heterogenous group of substances that served as a ligand for imidazoline receptors. Canavanine activates the *I*-2 and thereby reduced the hyperglycemia that induced by streptozocin in animal [1]. Allantoin, a byproduct of uric acid and is the primary active substance of the Yam (*Dioscorea* spp.) activates the *I*-3 receptors and it ameliorates the apoptotic changes in the pancreatic beta-cell that induced by streptozocin and thereby attenuates the hyperglycemia [2]. Li, *et al.* [3] found that agmatine an endogenous substance that activates the *I*-3 receptors and protects the beta-cell of the pancreas from the damage that induced by streptozocin [3]. Chronic administration of selective *I*-1 receptor agonists improved the insulin sensitivity and exerted favorable effects upon the components of the metabolic syndrome like metformin [4,5]. Drugs acting on the *I*-receptors improved insulin sensitivity by inhibiting the sympathetic nervous system, stimulation of adiponectin release and activation of the adenosine monophosphate activated protein-kinase (AMPK) pathways in the peripheral tissue [4]. Morin is an active substance of the guava that related to the flavonoids and found to activate the *I*-3 receptors at β -cell of pancreas and thereby increases the release of insulin [6]. Chen, *et al.* [7] found that metformin, the anti-diabetic biguanide-related drug, enhanced the uptake of glucose by peripheral tissue by acting on the *I*-2 receptor and inducing phosphorylation of adenosine monophosphate protein-kinase. Preclinical studies documented the anti-diabetic effects of *I*-receptor agonists, but the researchers did not carry clinical studies to assess the efficacy of these compounds as anti-diabetic and specify the mechanism of action. It is important to mention here that these compounds reduced the blood pressure, therefore, they will be promising agents in the management of metabolic syndrome as they act at least on the two components of metabolic syndrome.

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