World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:14, No:12, 2020

Therapeutic Effect of Indane 1,3-Dione Derivatives in the Restoration of Insulin Resistance in Human Liver Cells and in Db/Db Mice Model: Biochemical, Physiological and Molecular Insights of Investigation

Authors : Gulnaz Khan, Meha F. Aftab, Munazza Murtaza, Rizwana S. Waraich

Abstract : Advanced glycation end products (AGEs) precursor and its abnormal accumulation cause damage to various tissues and organs. AGEs have pathogenic implication in several diseases including diabetes. Existing AGEs inhibitors are not in clinical use, and there is a need for development of novel inhibitors. The present investigation aimed at identifying the novel AGEs inhibitors and assessing their mechanism of action for treating insulin resistance in mice model of diabetes. Novel derivatives of benzylidene of indan-1,3-dione were synthesized. The compounds were selected to study their action mechanism in improving insulin resistance, in vitro, in human hepatocytes and murine adipocytes and then, in vivo, in mice genetic model of diabetes (db/db). Mice were treated with novel derivatives of benzylidene of indane 1,3-dione. AGEs mediated ROS production was measured by dihydroethidium fluorescence assay. AGEs level in the serum of treated mice was observed by ELISA. Gene expression of receptor for AGEs (RAGE), PPAR-gamma, TNF-alpha and GLUT-4 was evaluated by RT-PCR. Glucose uptake was measured by fluorescent method. Microscopy was used to analyze glycogen synthesis in muscle. Among several derivatives of benzylidene of indan-1,3-dione, IDD-24, demonstrated highest inhibition of AGESs. IDD-24 significantly reduced AGEs formation and expression of receptor for advanced glycation end products (RAGE) in fat, liver of db/db mice. Suppression of AGEs mediated ROS production was also observed in hepatocytes and fat cell, after treatment with IDD-24. Glycogen synthesis was increased in muscle tissue of mice treated with IDD-24. In adipocytes, IDD-24 prevented AGEs induced reduced glucose uptake. Mice treated with IDD-24 exhibited increased glucose tolerance, serum adiponectin levels and decreased insulin resistance. The result of present study suggested that IDD-24 can be a possible treatment target to address glycotoxins induced insulin resistance.

Keywords : advance glycation end product, hyperglycemia, indan-1,3-dione, insulin resistance
Conference Title : ICSRD 2020 : International Conference on Scientific Research and Development
Conference Location : Chicago, United States
Conference Dates : December 12-13, 2020