Effect of Novel Benzylidene Thiazolidinediones (BTZDs) Derivatives on Insulin Resistance in High-Fat Fed Mice

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Thiazolidinediones are insulin-sensitizing agents that working by binding to PPAR-?, which leads to alteration in the expression of key regulators of lipid homeostasis and insulin resistance. In this study, it was evaluated the effect of treatment with novel benzylidene thiazolidinediones (BTZDs): 5-(4-chloro-benzylidene)-3-(4-methyl-benzyl)-thiazolidine-2,4-dione (GQ2), 5-(4-methoxy-benzylidene)-3-(4-methyl-benzyl)-thiazolidine-2,4-dione (GQ5), 5-(2,4-dimethoxy-benzylidene)-3-(4-methyl-benzyl)-thiazolidine-2,4-dione (GQ6), 5-(4-dimethylamino-benzylidene)-3-(4-methyl-benzyl)-thiazolidine-2,4-dione (GQ10) on insulin resistance in high-fat diet induced mice. Firstly, mice were allocated into two dietary regimens either chow diet or high fat diet, for the period of 75 days. After, the mice were randomly divided into 7 groups (n=6). The normal group (NC) and the high-fat diet control group (HFD-C) received vehicle (carboxymethylcellulose), once daily, orally for 15 days. The other groups of mice received GQ2, GQ5, GQ6, GQ10 and Rosiglitazone (all 30mg/Kg/day), respectively, once daily, orally for 15 days. All the groups of mice except the normal group were on high-fat diet throughout the period of treatment. Fasting serum glucose levels (FSG), fasting serum insulin levels (FSI) and HOMA-IR were evaluated in all groups. The elevated FSG were brought back to normal levels by BTZDs and rosiglitazone treated groups ($P<0.01$). Treatment with BTZDs and rosiglitazone significantly reduced FSI ($P<0.01$) in comparison with HFD-C group. GQ5 was 34% more potent than rosiglitazone in terms of decrease insulin levels ($P<0.05$). Insulin sensitivity, as accessed by HOMA-IR indices of BTZDs and rosiglitazone treated groups were significantly ($p<0.01$) improved when compared to the HFD-C group. These results suggest that novel BTZDs derivatives were able to improve insulin resistance. In addition, comprehensive studies are required to reveal the mechanism action of BTZDs.

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