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EFFECT OF GLITAZONE A1 4-[(Z)-(2,4-DIOXO-1,3-THIAZOLIDINO-5-YLIIDENE)METHYL]-N-PHENYLBENZOSULFONAMIDE IN A FRUCTOSE-INDUCED METABOLIC SYNDROME MODEL

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INTRODUCTION

Metabolic syndrome (MS) is characterized as a set of interrelated risk factors that contribute to the emergence of cardiovascular diseases (CVD) and type 2 diabetes mellitus (DM2), with its prevalence associated with excessive consumption of sugars used by the food industry. Guidelines recommend that the treatment of obesity is the main target for the reduction of MS. Drugs from the Thiazolidinedione class can increase insulin sensitivity, reduce adipose tissue inflammation, and promote the reduction of visceral fat. In this context, the present work evaluated the effect of glitazone A1 on fructose-induced obesity in mice.

MATERIAL AND METHODS

Swiss, male mice were used and the control of growth and body weight, water and food consumption were evaluated. The naive group (n=8) received water and chow *ad libitum*, the other groups received a 20% fructose solution and chow *ad libitum* for a period of 12 weeks to induce MS. Nociception was assessed using the Von Frey test every 7 days. After this period, treatment with Pioglitazone (10 mg/kg p.o.) or glitazone A1 (1, 3 or 10 mg/kg p.o.) was started for 4 weeks. Hematological and biochemical tests were performed, macroscopic and microscopic evaluation of the liver, kidneys, pancreas, adipose tissue, brain, and spinal cord for cytokine measurement.

RESULTS

In the obesity induction model, animals that received 20% fructose showed a significant increase in body weight gain and water consumption, in addition to a decrease in food consumption and glucose tolerance, and an increase in insulin resistance. In the groups treated with A1 (1, 3 or 10mg/kg), a significant weight loss, reduced food consumption and increased water consumption and insulin resistance were observed. In the mechanical hypersensitivity assay, there was a reduction in the percentage of inhibition of A1 (1, 3 and 10 mg/kg). Liver and spinal cord levels of interleukin 6 (IL-6) and TNF were reduced by A1 (3mg/kg and 10mg/kg respectively). There was no significant change in glucose, lipids, renal and hepatic function, suggesting no toxicity. Glitazone A1 did not change the weight of the liver, kidneys, and pancreas, but it promoted a decrease in body weight. No histological

changes were observed in the groups treated with glitazone A1.

CONCLUSIONS

The results obtained showed a reduction in fructose-induced chronic hypersensitivity through the PPARγ pathway, in addition to a low toxicological profile. This new glitazone appears to be a promising pharmacological tool in the treatment of central obesity, insulin resistance, and changes present in the metabolic syndrome.

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