

Title: Low-molecular weight NGF mimetic attenuates insulin resistance in a high-carbohydrate diet/streptozotocin-induced rat model of type 2 diabetes

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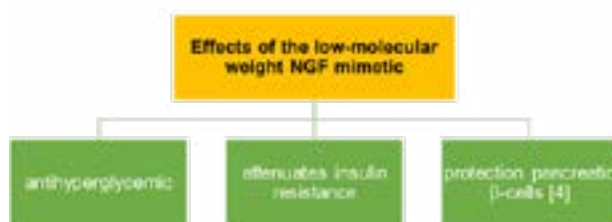
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Statement of the problem: Type 2 Diabetes Mellitus (DM2) remains one of the most important medical and social problems. The search for new effective antidiabetic drugs is an urgent task of pharmacology. Taking into account the deficiency of the neurotrophic factor NGF in DM2 and the importance of NGF for the pancreatic β -cells functioning, the low-molecular weight NGF mimetic "GK-2" (hexamethylenediamine bis-(N-monosuccinyl-L-glutamyl-L-lysine)) created in V. V. Zakusov Research Institute of Pharmacology was studied in the streptozotocin (STZ) DM2 model. The purpose of this work is to investigate the effect of GK-2 on insulin resistance in Wistar rats with DM2 induced by a high-carbohydrate diet combined with low doses of STZ.

Methodology and theoretical orientation: Rats were fed a high-carbohydrate diet based on replacing of tap water with a 10% fructose solution for 6 weeks. On the 15th day, STZ 35 mg/kg was administered. Then, the rats were divided into two groups: one group (n=10) was treated with GK-2 orally (5 mg/kg), the other (n=10) was treated with saline. The control group (n=10) received water. Blood glucose level was measured weekly. After 28 days of treatment, an oral glucose tolerance test (3 g/kg) was performed. The results of blood glucose measurement were analyzed by ANOVA.

Findings: The usage of high-carbohydrate diet in combination with STZ leads to the development of hyperglycemia up to 22.5 mmol/l and impaired glucose tolerance (AUC 2159,1 \pm 224,1 min(0-120) \cdot mmol/l in untreated diabetic rats vs. 1012,0 \pm 29,5 min(0-120) \cdot mmol/l in healthy rats, p<0.01). GK-2 therapy was shown to reduce not only basal glycemia to 12.2 \pm 1.7 mmol/l (p<0.05), but also decrease insulin resistance by 29% (AUC 1543,2 \pm 197,4 min(0-120) \cdot mmol/l, p<0.05) [Figure 1].



Conclusion: Low-molecular weight NGF mimetic GK-2 demonstrated antidiabetic activity and the ability to reduce the severity of insulin resistance in rats kept on a high-carbohydrate diet combined with low doses of STZ.

Biography

Sergei Ivanov, PhD, senior researcher of the V. V. Zakusov Research Institute of Pharmacology, 29 years old. His Research interests include the study of the anti-diabetic activity of the original cytoprotective compounds on the type 2 diabetes experimental model at the functional and morphological levels.