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Systemically active NGF mimetic GK-2 demonstrates anti-diabetic activity on C57Bl/6 mice

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Original dimeric dipeptide mimetic GK-2 (hexamethylenediamide bis-(N-monosuccinyl-glutamyl-lysine) was synthesized based on the structure of β-turn of NGF loop 4 at the V V Zakusov Institute of Pharmacology. The purpose of this study was to investigate whether it affects the effects of diabetogenic toxin, streptozotocine (STZ). Experiments were carried out on C57/Bl6 mice that were divided into four groups: Passive control treated with saline, active control treated with STZ 100 mg/kg, animals treated with GK-2 0.5 mg/kg i.p. for 14 days before and 14 days after STZ, animals treated with 5 mg/kg of GK-2 p.o. at the same schedule. After this experiment, percentage of animals able to find the invisible platform in Morris water maze and the immobility duration in Porsolt test has been estimated. Then the content of MDA as a sign of oxidative stress was measured in plasma. GK-2 was shown to be able to overcome hyperglycemia, body weight loss and to diminish MDA accumulation caused by STZ. While STZ diminished the percentage of mice that are able to find the platform to 9% comparing to passive control which is 14% whereas, GK-2 treated mice demonstrated the figures as high as 27.3 and 50% for i.p and p.o routes of administration correspondingly. GK-2 also ameliorated the signs of depression. Therefore, GK-2 was shown to antagonize the main effects of STZ and these effects also lasted after the discontinuation of the treatment.

Biography

Yagubova S represents the research of group of V V Zakusov Institute of Pharmacology, Moscow, Russia. This group is working with the problems of diabetes accompanying by behavioral disorders and their correction with original peptide mimetics of NGF and BDNF designed.

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