THE FIRST REPORT ON THE GASTROPROTECTIVE EFFECT OF TRIPEPTIDE T-34 UNDER CONDITIONS OF WATER-IMMOBILISATION STRESS IN RATS

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UNITED EUROPEAN GASTROENTEROLOGY ueg week
22nd United European Gastroenterology Week
October 18 - 22, 2014 | Vienna, Austria

Introduction

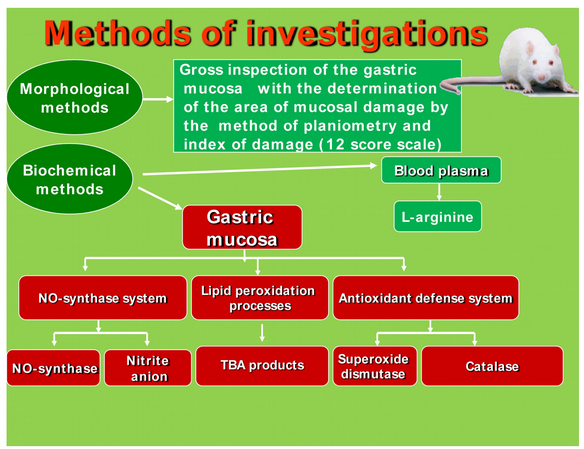
Recent literature gives accumulating evidence that a number of oligopeptides play an important role in the regulation of the function of gastrointestinal tract and their synthetic analogues were reported to be effective in the prevention and treatment of gastric ulceration.

Objectives

Aim of our research was to explore the effect of **tripeptide T-34 (H-Glu-Asp-Gly-OH),** synthesized in St-Petersburg Institute of Bioregulation and Gerontology on the area of water-immobilisation stress (WIS)-induced gastric lesions in rats and activities of NO-synthases (NOS) and lipid peroxidation processes in gastric mucosa.

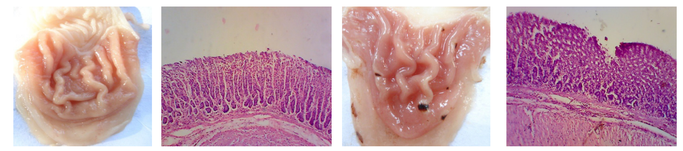
Methods

The studies were conducted on white male rats. 30 min before the exposure to WIS rats were pretreated with T-34 induced intragastrically in dose 10μg (n=5) or intraperitoneally - 2μg (n=5). Control rats were injected 0.5 ml of saline (n=5). After 5 hours of WIS, rats were sacrificed, gross inspection of stomach mucosa was conducted, its tissue samples were taken for histological studies and in gastric mucosa homogenates NO-synthases activity, NO and MDA content were determined. In blood plasma L-arginine concentration was measured.

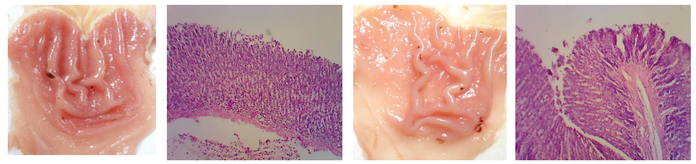


Results

THE INFLUENCE OF T-34 ON THE MORPHOLOGICAL PARAMETERS OF STOMACH MUCOSA IN WIS-INDUCED GASTRIC LESIONS IN RATS

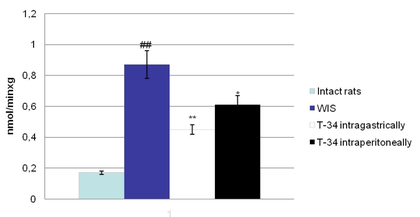


Control WIS

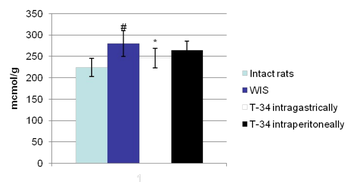


T-34 + WIS intragastrically T-34 + WIS intraperitoneally

Influence of T-34 on iNOS activity in stomach mucosa in WIS-induced gastric lesions



Influence of T-34 on MDA level in stomach mucosa in WIS-induced gastric lesions



- p < 0.05 compared to intact animals;
- p < 0.01 compared to intact animals;
* - p < 0.05 compared to WIS-exposed animals;
** - p < 0.01 compared to WIS-exposed animals.

WIS caused the formation of gastric lesions (18±1.9 mm), accompanied by acute rise of NO-synthase activity ($p<0.05$), in particular its inducible isoform – iNOS ($p<0.01$), increased production of NO and MDA ($p<0.05$) in stomach mucosa compared to intact rats. The concentration of L-arginine, NO precursor, in blood plasma decreased ($p<0.05$). Pretreatment with T-34 intragastrically caused 27% ($p<0.05$) decrease of ulceration area, at that NOS activity decreased for 45% ($p<0.05$), iNOS activity diminished for 60% ($p<0.01$) compared to control rats. Decrease of NO ($p<0.05$) and tendency to decrease of MDA content in gastric mucosa were also noted, whereas L-arginine concentration in plasma increased ($p<0.05$). Pretreatment with T-34 IP also resulted in the decrease of iNOS activity in gastric mucosa ($p<0.05$) but no statistically significant difference of the area of stomach mucosa damage was evaluated compared to saline-treated rats exposed to WIS

Conclusions

T-34 decreased the indices of nitrooxidative stress in stomach mucosa under the conditions of WIS-induced gastric lesions in rats. Intragastrical administration of T-34 was superior to intraperitoneal injection of this compound towards reduction of gastric mucosa damage. Deeper studies on the elucidation of the cytoprotective effect of tripeptide T-34, optimization of dosage and route of application are required.

References

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Acknowledgement

Tha authors express gratitude to the Institute of Bioregulation and Gerontology in St-Petersburg for the synthesis and providement of tripeptide T-34.