

The cytoprotective effect of thymohexin in experimental gastric lesions in rats under conditions of COX-2/5-LOX inhibition and L-arginine supplementation

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Thymic peptides due to their potent antioxidant and immunomodulatory properties may be perspective for the cytoprotective purposes in gastroenterology. But there is limited knowledge on the interactions of the thymic peptides with the systems of cyclooxygenase (COX)/lipooxygenase (LOX) and nitric oxide (NO), responsible for the maintenance of gastric mucosa integrity.

Aim: To evaluate the cytoprotective effect of thymohexin (Arg- α -Asp-Lys-Val-Tyr-Arg) under conditions of dual COX-2/5-LOX inhibition and introduction of NO precursor L-arginine.

Material & Methods: Gastric lesions in rats were induced by adrenaline (2 mg/kg) injected intraperitoneally. 15 mins before the exposure to adrenaline the rats were pretreated with thymohexin (10 μ g/kg) alone (n=10) and combined with COX-2/5-LOX blockage by 2-amino-5-(3,5-ditertbutyl-4-hydroxybenzylidene)-thiazol-4 (2A5DHT) – 10 mg/kg (n=10) and 2A5DHT+L-arginine (300 mg/kg, n=10). 24 hours later the rats were sacrificed and in gastric mucosa the activity of NOS, nitrite anion and MDA content as well as superoxide dismutase (SOD) and catalase activity were determined and L-arginine concentration in blood plasm.

Results: Pretreatment with thymohexin caused 41% decrease (p<0.05) of the area of adrenaline-induced gastric lesions, 32% decrease of total NOS activity (p<0.05), 40% decrease of iNOS (p<0.05) and 24% (p<0.05) decrease of nitrite anion content in gastric mucosa, whereas L-arginine concentration in plasm rose for 39% (p<0.05) compared to the effect adrenaline. MDA content, indicative for the activity of lipid peroxidation decreased for 22% (p<0.05), SOD for 41% (p<0.05) and catalase did not change significantly.

COX-2/5-LOX blockage by 2A5DHT caused tendency to exacerbation of the ulcerogenic effect of adrenaline, which was reversed by thymohexin administration although the isolated effect of thymohexin provided higher cytoprotection than noted under conditions of COX-2/5-LOX inhibition. The cytoprotective effect of thymohexin in experimental gastric ulceration in rats was enhanced by L-arginine supplementation, accompanied by decrease of nitro-oxidative stress in gastric mucosa, although it was inferior to the combined effect of thymohexin and L-arginine without COX-2/5-LOX inhibition.

Conclusion: Thymohexin exerts cytoprotective effect in experimental gastric lesions in rats, mediated by inhibition of iNOS and oxidative damage. COX-2/5-LOX blockage by 2A5DHT did not enhance the cytoprotective effect of thymohexin, but the area of lesions and NOS activity in rats pretreated with thymohexin was lower compared to the isolated effect of 2A5DHT in epinephrine-induced stress. The processes of cytoprotection in gastric mucosa in epinephrine-induced gastric lesions were enhanced by L-arginine supplementation.

Biography

Christina Nasadyuk in 2012 completed her Ph.D. in Biochemistry, devoted to the gastroprotective effects of oligopeptides. Currently, she is continuing her research on the prevention of the ulcerogenic effects of NSAIDS towards gastrointestinal tract.

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