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Biochemical mechanisms of the gastric mucosal prevention of vitamin A, β-carotene in 4 h pylorus-ligated plus sodium-salicylate-treated rats

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Backgrounds: Sodium salicylate is a well-known chemical component, which damages the gastric mucosal damage in presence of free gastric H^+ secretion (Davenport *et al.*, 1970). After that time we proved the existence of a positive correlation between the suggested gastric H^+ backdiffusion and the decreased gastric mucosal energy metabolism (Mózsik *et al.*, 1981). We also proved the gastric mucosal preventive effects of vitamin A and beta-carotene are independent processes from the inhibitory effects their gastric acid secretion. The aims of this study were: (i) To study the gastric mucosal preventive effects of vitamin A and β-carotene in the 4 h pylorus-ligated plus sodium salicylate (200 mg/kg, i.g.)-induced gastric mucosal damage; (ii) to evaluate the changes in the gastric mucosal level of adenosine triphosphate (ATP), adenosine diphopsphate (ADP), adenosine monophosphate (AMP), adenylate pool (ATP + ADP + AMP), 'energy charge' ((ATP + 0.5 ADP)/(ATP + ADP + AMP)) and cyclic adenosine monophosphate (cAMP) in 4 h pylorus-ligated plus sodium-salicylate-treated animals in association of the development of their gastric mucosal preventive effects against sodium salicylate.

Materials and methods: The observations were carried out of Sprague–Dawley rats of both sexes,weighing 180–210 g. The animals were treated with 20 mg/kg sodium salicylate in 4 h pylorus-ligated rats without and with i.g. administration of vitamin A and β-carotene (0.01, 0.1, 1.0 and 10 mg/kg). The animals were killed 4 h after the start of the examinations. The number and severity were calculated. The severity of gastric mucosal damage was calculated using a semiquantitave scale (Mózsik *et al.*, 1982). The tissue concentrations of adenosine triphosphate (ATP), adenosine diphosphate (ADP) and adenosine monophosphate (AMP) were enzymatically measured (Boehringer-Ingelheim, Germany), while the tissue content of the gastric mucosal level of cAMP was measured by radioimmoassay (RIA, Beckton Dickinson, Orangeburg, USA). The protein content was measured by biuret reaction. The adenylate pool (ATP + ADP + AMP) and 'energy charge' ((ATP + 0.5 ADP)/(ATP + ADP + AMP)) were calculated according to Atkinson (1968). The results are expressed as means ± SEM in accordance to 1 mg protein ($n = 10–20$).

Results: The gastric secretory volume, gastric acid and gastric acid output was the same in pylorus-ligated and pylorus-ligated plus saline (2 ml, i.g.) treated animals. No ulceration was detected, and no difference was obtained between the biochemical parameters (gastric mucosal level of ATP, ADP, AMP, adenylate pool, 'energy charge' and cAMP). Also, the number and severity of gastric mucosal damage and volume of the gastric secretory volume increased significantly, meanwhile the gastric acid output, gastric mucosal levels of ATP, ADP, AMP, adenylate pool, 'energy charge' and cAMP decreased significantly in 4 h pylorus-ligated plus aspirin-treated rats; meanwhile, the value of the 'energy charge' remained unchanged. The gastric mucosal preventive effects against the sodium salicylate decreased dose-dependently. The number and severity of gastric mucosal damage, volume of gastric secretory responses (without modification of gastric

acid output), on the other hand, dose-dependently increased the gastric mucosal levels of ATP, ADP, AMP, adenylate pool and cAMP in the pylorus ligated plus sodium salicylate treated rats, meanwhile the values of 'energy charges' remained unchanged.

Conclusions: The sodium-salicylate-induced gastric mucosal damage associated with the significantly decreased adenosine phosphate metabolism in 4 h pylorus-ligated rats. Vitamin A and β-carotene dose-dependently prevent the gastric mucosal damage in association with the significant increase of adenosine phosphate metabolism. The gastric mucosal preventive effects of vitamin A and β-carotene differ from the decrease of the gastric acid secretion. The sodium-salicylate-induced gastric mucosal damage and the preventive effects of vitamin A and β carotene depend only the gastric mucosal energy metabolism. Vitamin A and β carotene dose-dependently decreased the volume of gastric secretory responses without any modification of gastric acid. This fact suggests that the carotenoids are able to modify only the volume of gastric volume (water) secretory responses. Calculation of the 'energy charge' should be considered as the research pool for use to indicate the tissue metabolism.

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