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## ЕКСПРЕСІЯ ГЕНА CHGA В ЕПІТЕЛІОЦИТАХ ДВАНАДЦЯТИПАЛОЇ КИШКИ ЗА УМОВ ТРИВАЛОЇ ГІПОАЦИДНОСТІ ШЛУНКА ТА ПРИ ВВЕДЕННІ МУЛЬТИПРОБІОТИКА СИМБІТЕР

***Показано зростання рівня експресії гена Chga в епітеліоцитах ворсинок та крипт дванадцятипалої кишки щурів за гіпоацидних умов. При введенні мультипробіотика Симбітер за тих самих умов патерн експресії вищезазначеного гена в епітеліоцитах як ворсинок, так і крипт був подібний до контролю.***

***Ключові слова: шлункова гіпоацидність, дванадцятипала кишка, щури, експресія гена Chga, мультипробіотик.***

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## ЭКСПРЕССИЯ ГЕНА *CHGA* В ЭПИТЕЛИОЦИТАХ ДВЕНАДЦАТИПЕРСТНОЙ КИШКИ КРЫС ПРИ ДЛИТЕЛЬНОЙ ЖЕЛУДОЧНОЙ ГИПОАЦИДНОСТИ И ПРИ ВВЕДЕНИИ МУЛЬТИПРОБИОТИКА СИМБИТЕР

***Показано увеличение уровня экспрессии гена Chga в эпителиоцитах ворсинок и крипт двенадцатиперстной кишки крыс в гипоацидных условиях. При введении мультипробиотика Симбитер в тех же условиях содержание мРНК Chga в эпителиоцитах как ворсинок, так и крипт было на уровне контрольных значений.***

***Ключевые слова: желудочная гипоацидность, двенадцатиперстная кишка, крысы, экспрессия гена Chga, мультипробиотик.***

**UDK 612.323+616.3**

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# THE CHANGES IN FUNCTIONING OF MUCUS BARRIER OF STOMACH IN CONDITIONS OF LONG-TERM HYPOACIDITY AND THEIR CORRECTION

***Increase in the duration of hypoacidity of gastric juice evoked by daily injection of blocker of gastric acid secretion omeprazole from 7 to 28 days accompanied by substantial rise of the level of oxiproline, fucose, N-acetylneuraminic acid and hexuronic acids in gastric mucus in rats. It is witness of intensification of degradation collagenic and noncollagenic proteins in gastric mucus. Injection of multiprobiotic Symbiter against the background of hypoacidity evoked by omeprazole led to decrease the level of studied parameters to control values in all terms of investigations.***

***Key words: gastric mucus, omeprazole, multiprobiotic.***

**Introduction.** The basis mucous layer of the stomach are polymerized structural glycoproteins of mucus. Due to its polymer structure and hydrophobic properties gel mucus protects gastric mucosa from direct contact with xenobiotics, endogenous nitroso compounds, free radicals, bacterial toxins. Long-term hypoacidity of gastric juice and anacidity are risk factors for carcinogenesis in stomach. In conditions of hypoacidity in stomach dysbiosis develops [5], this can lead to structural changes of mucus. Dysbiosis [9] and disturbance of structure of gastric mucus [4] in turn accelerate the development of neoplastic changes in stomach.

In connection with this the aim of our work was to investigate effect of multiprobiotic "Symbiter® acidophilic" as drug for prophylaxis of dysbiosis, on state of mucus barrier in stomach in conditions of hypoacidity of different duration evoked by omeprazole.

**Materials and methods.** The study was done on white rats which were divided into 12 group. To the rats of 4 groups during 7, 14, 21, 28 days consequently were injected blocker of gastric acid secretion omeprazole ("Sigma", USA) (14 mg/kg intraperitonealy once a day). To the rats of others 4 groups during the same terms simultaneously with omeprazole we injected multiprobiotic "Symbiter® acidophilic" (Symbiter) (limited company "O.D. Prolisok") (0.14 ml/kg per os once a day). To the rats of 4 control groups were injected during 7, 14, 21 and 28 days 0.2 ml $H_2O$ intraperitonealy and 0.5 ml $H_2O$ per os. Symbiter is concentrated fluid biomass of bioplasts of symbiosis of 14 microorganisms strains. The composition of one dose (10 ml) of Symbiter is concentrated biomass of bioplasts of bacterium's symbiosis CFU/cm$^3$, no less: Lactobacillus and Lactococcus – $6.0x10^{10}$, Propionic bacterium – $3.0x10^{10}$, Bifidobacterium – $1.0x10^{10}$, Acetic bacterium – $1.0x10^{6}$. For assessment of mucus barrier state in stomach in a day of last injection of drugs in parietal mucus we determined the levels of oxiproline using method as described earlier [8] ,

fucose using method as described earlier [6], N-acetylneuraminic acid using method as described previously [1] and hexuronic acids using method as described earlier [7]. All results are performed as Mean±SD by using Students t test.

**Results and discussion.** In 7, 14, 21 and 28 days of omeprasole injection the levels of oxiproline were increased respectively by 7.9% (p<0.001), 125.3% (p<0.001), 146.3% (p<0.001) and 163.2% (p<0.001) (Fig.1).

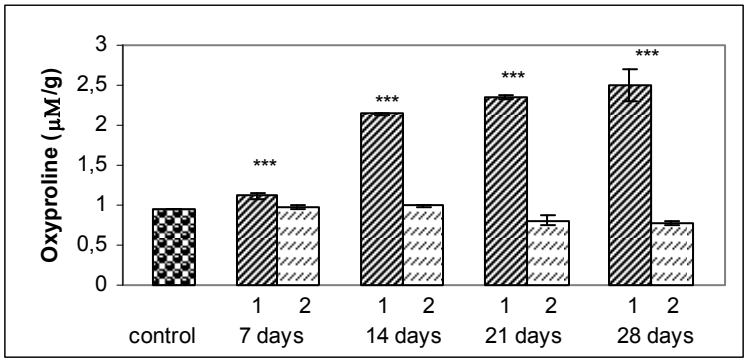


**Fig.1. Changes of oxiproline concentration in gastric mucus in rats after long-term injection of omeprazole (1) and simultaneous injection of omeprazole and multiprobiotic "Symbiter" (2). Changes that are statistically different from the control group (p<0.001 by Student t test) are indicated with stars**

This indicates that with enhance of duration of hypoacidity of gastric juice degradation of collagenic proteins in gastric mucus intensifies.

In 7, 14, 21 and 28 days of omeprasole injection the levels of fucose were increased respectively by 23.6% (p<0.001), 49.7% (p<0.001), 52.3% (p<0.001) and 107.0% (p<0.001) (Fig.2).

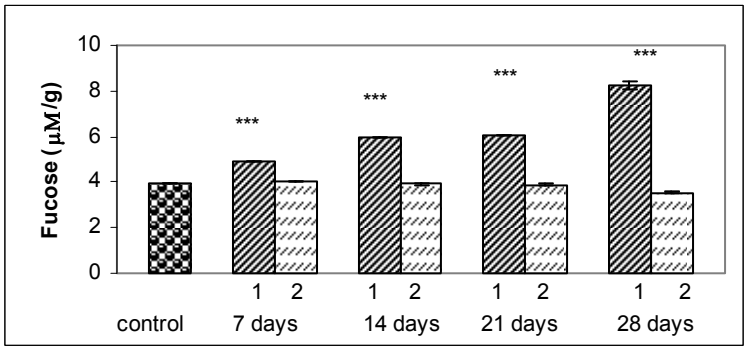


**Fig. 2. Changes of fucose concentration in gastric mucus in rats after long-term injection of omeprazole (1) and simultaneous injection of omeprazole and multiprobiotic "Symbiter" (2). Changes that are statistically different from the control group (p<0.001 by Student t test) are indicated with stars**

In 7, 14, 21 and 28 days of omeprazole injection the levels of N-acetylneuraminic acid were increased by 7.6% (p>0.05), 65.2% (p<0.001), 79.3% (p<0.001) and 111.0% (p<0.001) (Fig.3).

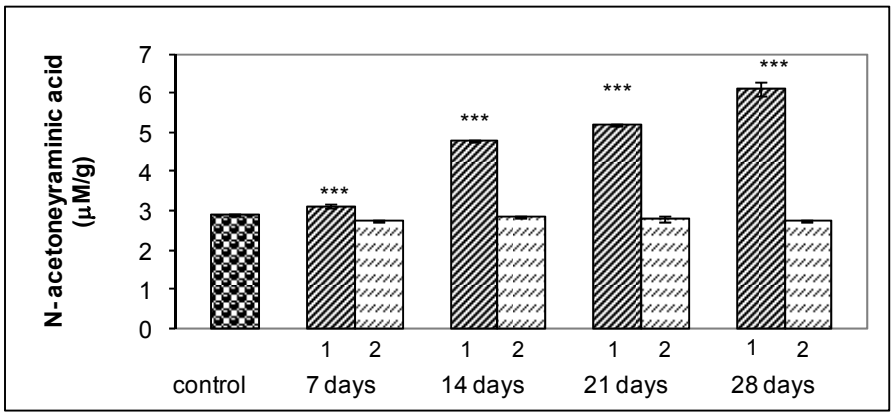


**Fig.3. Changes of N-acetylneuraminic acid concentration in gastric mucus in rats after long-term injection of omeprazole (1) and simultaneous injection of omeprazole and multiprobiotic "Symbiter" (2). Changes that are statistically different from the control group (p<0.001 by Student t test) are indicated with stars**

In 7, 14, 21 and 28 days of omeprazole injection the levels of hexuronic acids were increased by 17.2% ($p<0.001$), 33.9% ($p<0.001$), 78.5% ($p<0.001$) and 74% ($p<0.001$) compared with the control (Fig.4).

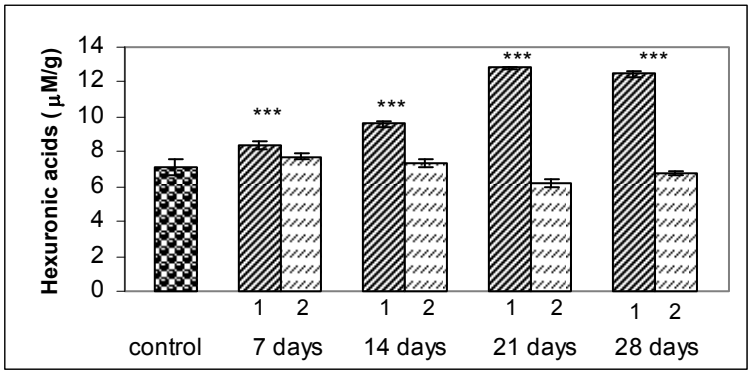


**Fig.4. Changes of hexuronic acids concentration in gastric mucus in rats after long-term injection of omeprazole (1) and simultaneous injection of omeprazole and multiprobiotic "Symbiter" (2). Changes that are statistically different from the control group ($p<0.001$ by Student t test) are indicated with stars**

The increase the levels in gastric mucus such glycoproteins as fucose, N-acetylneuraminic acid and hexuronic acids is evidence of degradation of non-collagenic proteins in gastric mucus.

Injection of multiprobiotic Symbiter against the background of hypoacidity evoked by omeprazole led to decrease the level of studied parameters to control values in all terms of investigations.

Long-term suppression of gastric acid secretion increases depolymerization of protective as collagenic and non-collagenic proteins in gastric mucus. As result the levels of oxiproline, fucose, N-acetylneuraminic acid and hexuronic acid in gastric mucus were substantially increased. Our results are in agreement with the studies of Ekambaram et al. [2] which shows that the levels of glycoproteins (hexose, hexosamine, sialic acid and fucose) were increased in rats with gastric cancer induced by N-methyl-N'-nitro-N-nitrosoguanidine. To take into account our previous date that injection of omeprazole to the rats during 28 days evoked in one group of rats hyperplasia and in other group metaplasia in gastric mucosa we supported the idea [3] that mucins are diagnostic markers in cancer. Multiprobiotic Symbiter prevented enhanced catabolism of protective proteins in gastric mucus. We hypothesize that regulation of glycoprotein levels by multiprobiotic could be associated with the regression of omeprazole-induced gastric hyperplasia and metaplasia.

**Conclusions.** Long-term inhibition of gastric acid secretion leads to degradation of protective collagenic and noncollagenic proteins in gastric mucus. Injection of multiprobiotic Symbiter against the background of hypoacidity evoked by omeprazole decreased the level of studied parameters to control values in all terms of investigations. These results shows the gastroprotective effect of multiprobiotic Symbiter and make probiotic perspective means of prophylaxis of negative consequences of hypoacidity.

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## ЗМІНИ У ФУНКЦІОНУВАННІ СЛИЗОВОГО БАР'ЄРУ ШЛУНКА В УМОВАХ ГІПОАЦИДНОСТІ ТА ЇХ КОРЕКЦІЇ

***Збільшення тривалості гіпоацидності шлункового соку, викликаної щоденним введенням блокатора секреції соляної кислоти в шлунку омепразолу, з 7 до 28 днів супроводжувалось суттєвим зростанням рівня оксипроліну, фукози, N-ацетилнейрамінової кислоти та гексуронових кислот у шлунковому слизу щурів. Це є свідченням інтенсифікації процесу деградації колагенових та неколагенових білків шлункового слизу. Введення мультипробіотика "Симбітер" на фоні гіпоацидності, викликаної омепразолом, призводило до зменшення рівня досліджуваних показників до контрольних в усі терміни експерименту.***

***Ключові слова:шлунковий слиз, омепразол, мультипробіотик.***

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## ИЗМЕНЕНИЯ В ФУНКЦИОНИРОВАНИИ СЛИЗИСТОГО БАРЬЕРА ЖЕЛУДКА В УСЛОВИЯХ ГИПОАЦИДНОСТИ И ИХ КОРЕКЦИЯ

***Увеличение продолжительности гипоацидности желудочного сока, вызванного ежедневным введением блокатора секреции соляной кислоты в желудке омепразола, с 7 до 28 дней сопровождалось существенным ростом уровня оксипролина, фукозы, N- ацетилнейраминовой кислоты и гексуроновых кислот в желудочной слизи крыс. Это является свидетельством интенсификации процесса деградации коллагеновых и неколлагеновых белков желудочной слизи. Введение мультипробиотика "Симбитер" на фоне гипоацидности, вызванной омепразолом, приводило к уменьшению уровня исследуемых показателей до контрольных во все сроки эксперимента.***

***Ключевые слова: желудочная слизь, омепразол, мультипробіотик.***