DOI 10.26724/2079-8334-2021-1-75-115-119
UDC 65.012.1[615.454.1-616.31]616-092.4:616.314.17-008.1

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STUDY OF THE MOOMIYO-CONTAINING ORAL GEL EFFECT ON THE ACTIVITY OF THE ANTIOXIDANT DEFENSE SYSTEM IN EXPERIMENTAL PERIODONTITIS

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One of the important links in the study of pathogenesis indices in chronic generalized periodontitis is the intensity of lipid peroxidation and protective antioxidant systems that ensure a balance between the formation and metabolism of reactive oxygen species in cells. The purpose of our work was an experimental study of the oral cavity moomiyo-containing gel's periodontal protection properties in the toxic calcium-deficient model. In order to simulate the pathology of periodontal disease, the laboratory white rats were given an EDTA solution (2 %) daily with drinking water, and three times a week the "Warfarin Orion" drug within 30 days. In total, 4 groups of animals were formed: group 1 – intact; group 2 – model reproduction; group 3 – model reproduction and application of "Placebo" gel to the mucous membrane of the alveolar process; group 4 – reproduction of the model and application of the moomiyo-containing gel to the mucous membrane of the alveolar process. Periodontal protective efficacy of the oral moomiyo-containing gel was shown against the background of a toxic calcium-deficient state: preservation (restoration) of protective antioxidant systems and inhibition of lipid peroxidation processes in the blood serum at the systemic level.

Key words: lipid peroxidation, antioxidant protection, experiment, periodontitis, oral gel.

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ДОСЛІДЖЕННЯ ВПЛИВУ ГЕЛЮ ДЛЯ РОТОВОЇ ПОРОЖНИНИ, ЩО МІСТИТЬ МУМІЄ, НА АКТИВНІСТЬ СИСТЕМИ АНТИОКСИДАНТНОГО ЗАХИСТУ В УМОВАХ ЕКСПЕРИМЕНТАЛЬНОГО ПАРОДОНТИТУ

Метою дослідження було: експериментальне вивчення на токсичній кальцій-дефіцитній моделі пародонтопротекторних властивостей гелю для ротової порожнини з муміє. Для моделювання патології пародонту білим лабораторним щурам щоденно із питною водою давали розчин ЕДТА (2 %) і три рази на тиждень вводили per os препарат, який містить муміє, на протязі 30 діб. Було сформовано 4 групи тварин: 1 група - інтактні; 2 група – відтворення моделі; 3 група – ввідтворення моделі і аплікація на слизову оболонку альвеолярного відростку гелю «Плацебо; 4 група – ввідтворення моделі та аплікація на слизову оболонку альвеолярного відростку гелю з муміє. Показано пародонтопротекторну ефективність застосування гелю, який містить муміє, на тлі токсичного кальцій-дефіцитного стану збереження (відновлення) захисних антиоксидантних систем та на системному рівні гальмування процесів перекисного окислення ліпідів в сиворотці крові.

Ключові слова:перекисне окислення ліпідів, антиоксидантний захист, експеримент, пародонтит, гель ротової порожнини.

The study is a fragment of the research project: "To elaborate therapeutic and preventive complexes for the patients with stomatological diseases concomitant to somatic pathology", state registration No. 0117U000403.

According to the WHO, periodontal tissue pathology ranks second in the structure of dental morbidity [12, 14]. One of the important links in the study of pathogenesis indices in chronic generalized periodontitis is the intensity of lipid peroxidation and protective antioxidant systems that ensure a balance between the formation and metabolism of reactive oxygen species in cells [6, 13].

Currently, antioxidants play a significant role in the treatment of periodontal diseases [7, 13]. Therefore, the search for effective biooxidants is among the herbal supplements for the possibility of their use in prevention and treatment of diseases associated with the development of oxidative stress [7, 13].

An important stage in the algorithm for treatment of chronic generalized periodontitis is local medical intervention and, more and more frequently, there is a tendency towards the use of gels for the oral cavity. The purpose of using gels is a prolonged effect of the main active ingredient on the periodontal tissues. The main component of the moomiyo-containing gel is an organic-mineral product of predominantly natural biological origin. This wax is a mixture of plant and animal components. The preferred pharmacological properties of "Moomiyo" are those of anti-inflammatory, adaptogenic, regenerating and anticoagulant effect [10]. Despite the diverse properties of moomiyo, its application in dentistry is still very limited.

The purpose of the work was to study the periodontal protection properties of the moomiyo-containing gel for the oral cavity in a toxic calcium-deficient model in experiment.

Materials and methods. The experiments were performed on white laboratory male rats weighing 160–180 g. The animals were kept on a standard diet with free access to water and food [9].

Experimental studies were carried out in compliance with the Law of Ukraine "On the Protection of Animals from Cruelty" and the national "General Ethical Principles of Experiments on Animals", which are consistent with the provisions of the "European convention for the protection of vertebrate animals used for experimental and other scientific purposes (1985)" [11]. The animals were sacrificed after

preliminary anesthesia (injections of 2.5 % 2.2.2–tribromomethanol ("Aldrich", USA in 2-methylbutanol; 1:50 in PBS, 300 mg/kg into the abdominal cavity).

Experimental modeling of periodontal pathology in experimental animals against the background of a toxic calcium-deficient state was carried out according to the following scheme: the animals were given the EDTA solution (2 %) daily with drinking water and three times a week, they were administered per os with the "Warfarin Orion" drug (Vitamin K antagonist) manufactured by Orion Corporation, Finland, at the dose of 5 mg/kg (in terms of the active ingredient – warfarin sodium, 0.01mg/kg) within 30 days.

Experimental studies were carried out with 4 groups of animals:

Group 1 – intact animals (8 specimens);

Group 2 – administration of the "Warfarin Orion" drug and 2% EDTA solution (8 specimens);

Group 3 – administration of the "Warfarin Orion" drug and 2% EDTA solution and starting from the 7th day, daily for 3 weeks, application of the "Placebo" gel, without biologically active components to the mucous membrane of the alveolar process (8 specimens);

Group 4 – administration of the "Warfarin Orion" drug and 2% EDTA solution and starting from the 7th day, daily for 3 weeks, application of the "Moomiyo" gel to the mucous membrane of the alveolar process (8 specimens).

The "Moomiyo" (Expert opinion No. 1378/16 dated 10.12.2019) was developed in the "Laboratory for the development and research of oral hygiene products of the State Institution "Institute of Dentistry and Maxillofacial Surgery of the Academy of Medical Sciences" [5].

After animals sacrificing, in compliance with the rules of bioethics, blood was sampled and periodontal tissues were isolated. Serum was obtained by centrifuging blood at 3000 rpm within 20 minutes, the samples were divided into appropriate aliquots and frozen at –20° C for further work. Periodontal tissues were isolated and a homogenate was prepared (25 mg of tissue per 1 ml of 0.25 M sucrose solution), centrifuged at 3000 rpm for 10 minutes. A number of marker enzymes were examined in the supernatant fraction of homogenates and blood serum.

In order to obtain ideal lipid peroxidation (LPO), it is advisable to determine diene conjugates [3] (appears at the initial stages of LPO) and malondialdehyde – one of the most important end products of LPO [8].

The enzymes of the antioxidant defense system (ADS) – superoxide dismutase (SOD) [4], catalase (CA) [2], glutathione peroxidase (GP) [8], glutathione reductase (GR) [8] – control all types of non-enzymatic free radical oxidation.

Statistical processing of the experimental study results was carried out by the methods of variation analysis using the Student's (*t*) test. Differences in the groups were considered significant at $n=k_1(8)+k_2(8)-2=14$, $p<0.05$ and $t\geq2.15$, with $p<0.01$, $t\geq2.98$, with $p<0.001$, $t\geq4.14$ [1].

Results of the study and their discussion. A week after the start of drug administration, nasal bleeding and local hemorrhagic effects in the ears were observed in individual specimens out of the total sample of test animals. In the more distant periods of observation, a decrease in these manifestations was recorded; the death of the experimental animals during the experiment was not recorded.

Simulation of periodontitis against the background of the of calcium deficiency development in animals of all groups revealed an increase in the DC level by 1.56–1.94 times ($p<0.01$) in the blood serum (table 1).

The level of MDA in the blood serum increased significantly only in animals of groups 2 and 3 by 1.31–1.42 times ($p<0.01$), and in group 4 – it had only a slight tendency to increase ($p>0.05$).

Table 1

Study of the pro- and antioxidant systems state in blood serum of experimental animals

Group No.	Indices				
	DC, RU/ml	MDA, μmol/ml	SOD, U/ml* min.	CAT, RU/ ml* min.	SOD/ CAT
Group 1 – intact animals (n=8)	1.37±0.09	0.36±0.02	191.3±11.7	0.69±0.03	277
Group 2 – model (n=8)	2.67±0.34 ($p<0.01$; t=3.70)	0.51±0.04 ($p<0.01$; t=3.33)	239.6±14.3 ($p<0.05$; t=2.61)	0.81±0.04 ($p<0.05$; t=2.40)	296
Group 3 – model +"Placebo" gel (n=8)	2.22±0.21 ($p<0.01$; t=3.72)	0.47±0.02 ($p<0.01$; t=3.89)	251.3±13.0 ($p<0.01$; t=3.43)	0.79±0.03 ($p<0.05$; t=2.36)	318
Group 4 – model + "Moomiyo" gel (n=8)	2.14±0.23 ($p<0.01$; t=3.12)	0.41±0.03 ($p>0.05$; t=1.39)	228.6±10.2 ($p<0.05$; t=2.40)	0.84±0.04 ($p<0.01$; t=3.00)	272

Note: – changes are significant compared to group 1 ($p<0.05$); ($p<0.01$).

A study of the antioxidant enzymes activity in the blood showed that the activity of SOD, which belongs to the primary link of antioxidant protection, increased in all groups by 19.5–31.4 % ($p<0.05$), which indicates an increase in the formation of reactive oxygen species in organism. The activity of CAT

increased by 14.5–21.7 % (p<0.05). A certain ratio of SOD/CAT activity is important for cell viability, as its disruption can cause the development of cytotoxic effects. As it can be seen in table 1, the ratio of SOD/CAT in groups 2– 3 exceeds the control values by 1.1–1.2 times, and in group 4, it is almost no different from the control group.

The study of glutathione-antioxidant protection enzymes showed that the activity of GP was significantly reduced in the serum only in animals of groups 2–3 – by 21.6–24.6 % (p<0.05), in the group of animals to which the "Moomiyo" gel was applied – the activity of the enzyme was at the level of the control group (p<0.05) (table 2).

Table 2

Study of the glutathione-antioxidant system state in the serum of experimental animals

Group No.	Indices		
	GP, μmol oxid. glutathione / ml*min	GR, μmol $NADPH_2$/ ml*min	G6PDH, μmol $NADPH_2$/ ml*min
Group 1 – intact animals (n=8)	4.22±0.32	6.43±0.54	1.92±0.14
Group 2 – model (n=8)	3.31±0.21 (p<0.05; t=2.38)	4.85±0.32 (p<0.05; t=2.52)	1.37±0.18 (p<0.05; t=2.41)
Group 3 – model + "Placebo" gel (n=8)	3.18±035 (p<0.05; t=2.19)	4.83±0,30 (p<0,05; t=2.54)	1.63±0.16 (p>0.05; t=1.36)
Group 4 – model + "Moomiyo" gel (n=8)	4.13±0.22 (p>0.05; t=0.23)	5.94±0.40 (p>0.05; t=0.73)	1.99±0.19 (p>0.05; t=0.30)

Note: – changes are reliable compared to group 1 (p<0.05); (p<0.01).

At the same time, in animals of groups 2–3, a decrease in the activity of GR, a key enzyme, restores the pool of glutathione, more than by 1.2 times (p<0.05), and in group 2 and G6PDH – by 1.4 times (p<0.05), respectively. In group 4 animals, the index did not differ significantly from the control.

The most informative indices of the pathological process development and the efficacy of the use of "Moomiyo" gel for treatment is the study of the pro- and antioxidant systems state directly in the tissues of the periodontium. The obtained data, given in table. 3, indicate an increase in the MDA content in animals of group 2 by 21.2 % (p<0.01) and the simultaneous activation of SOD and CAT by 38.5 % (p<0.05) and 88.2 % (p<0.001), respectively. In the group of animals treated with the "Placebo" gel, a similar activation of this system was observed.

The daily application of the therapeutic "Moomiyo" gel prevented the development of lipid peroxidation and did not cause the activation of the studied antioxidant enzymes.

Table 3

Study of the pro- and antioxidant system state in periodontal tissues of experimental animals

Group No.	Indices		
	MDA, μmol/g of tissue	SOD, un/ g of protein * min.	CAT, un/ g of protein * min.
Group 1 – intact animals (n=8)	42.33±1.17	127.4±10.6	0.17±0.02
Group 2 – model (n=8)	51.31±1.83 (p<0.001; t=4.16)	176.4±15.5 (p<0.05; t=2.61)	0.32±0.03 (p<0.001; t=4.16)
Group 3 – model + "Placebo" gel (n=8)	50.20±3.26 (p<0.05; t=2.27)	171.8±1.5 (p<0.05; t=2.58)	0.28±0.02 (p<0.01; t=3.89)
Group 4 – model + "Moomiyo" gel (n=8)	42.20±2.20 (p>0.05; t=0.05)	137.0±12.6 (p>0.05; t=0.58)	0.16±0.01 (p>0.05; t=0.45)

Note: – changes are reliable compared to group 1 (p<0.05); (p<0.01); (p<0.001).

Against the background of LPO processes activation, in periodontal tissues in animals in groups 2 – 3 (table 4), changes in the activity of enzymes of the GAOP system (glutathione antioxidant protection) were also revealed – the activity of the key enzyme GR decreased by more than 26.0 %, and the supplier of reduced equivalents (G6PDH) – by 35.6 and 29.9 %, respectively (p<0.05). At the same time, GP activity in these groups increased compensatory by almost 1.5 times (p<0.01). That is, the balance of reduced / oxidized glutathione in the tissues was disturbed, which indicates the depletion of the antioxidant defense system's reserves.

When using the therapeutic "Moomiyo" gel there was no activation of LPO in periodontal tissues, while the activity of GR and GPDH increased by 1.4 and 1.3 times, respectively, compared to the control (p<0.05).

The intensification of lipid peroxidation processes in the simulated periodontitis in animals was accompanied by an increase in the level of DC and MDA in the blood serum by 1.56–1.94 times and by 1.31–1.42 times (p<0.01), respectively, compared to the control and proceeded against the background of suppressed activity of antioxidant defense enzymes: GP, GR and G6PDH by more than 1.2–1.4 times (p<0.05), and a compensatory increase in catalase activity by 14.5–21.7 % (p<0.05). However, it was found that the SOD/CAT ratio was by 1.2 times higher than that in the control, which can lead to the development of cytotoxic effects in tissues, and the deepening of the hypoxic conditions development.

The study of the "Placebo" gel periodontal protection properties during the periodontitis modeling did not reveal any positive changes in the condition of the animals compared to the animals of group 2 (the model of periodontitis). At the same time, significant changes in all studied biochemical parameters remained compared to the control group, both at the systemic level and in the periodontal tissues: the state of the pro–and antioxidant systems both in serum and in periodontal tissues maintained a pronounced imbalance throughout the experiment – an increase in DC and MDA ($p<0.05$), which was accompanied by a decrease in the activity of glutathione-antioxidant protection enzymes (GP, GR, G6PDH–a decrease by 1.2–1.3 times ($p<0.05$)) and a compensatory increase in catalase activity by 1.4 times ($p<0.05$); there were also no significant changes in the stabilization of redox processes directly in the periodontal tissues.

Table 4

Study of the glutathione-antioxidant system state in periodontal tissues of experimental animals

Group No.	Indices		
	GP, μmol oxid. glutathione/ mg protein * min.	GR, μmol $NADPH_2$/ mg protein * min.	G6PDH, μmol $NADPH_2$/ mg protein * min.
Group 1–intact animals (n=8)	1.35±0.11	2.04±0.09	4.61±0.33
Group 2–model (n=8)	2.03±0.15 ($p<0.01$; t=3.66)	1.56±0.13 ($p<0.01$; t=3.04)	2.97±0.39 ($p<0.01$; t=321)
Group 3–model + "Placebo" gel (n=8)	1.98±0.15 ($p<0.01$; t=3.39)	1.51±0.149 ($p<0.05$; t=2.52)	3.23±0.24 ($p<0.01$; t=3.38)
Group 4 - model + "Moomiyo" gel (n=8)	1.44±0.10 ($p>0.05$; t=0.61)	2.83±0.22 ($p<0.01$; t=3.32)	6.12±0.50 ($p<0.05$; t=2.52)

Note: – changes are reliable compared to group 1. ($p<0.05$); ($p<0.01$); ($p<0.001$).

Changes in the activity of ADS enzymes in blood and tissues are important indicators of the body's nonspecific resistance in various types of pathology and can be used for diagnostic and prognostic purposes [2]. The system of reduced glutathione – oxidized glutathione – is considered as a buffer, that protects cell membranes and other structures from oxidants. A decrease in the content of reduced glutathione as a result of its oxidation, disruption of its synthesis, an increase in the rate of its decay, or due to a change in the rate of enzyme systems that regulates its level in the cell, can lead to the development of pathological processes [4].

The obtained research data correlate with the previously obtained results on the modeling of experimental periodontitis [6, 13].

Conclusions

1. The applied model of periodontitis with the combined administration of the "Warfarin" drug and 2 % EDTA solution caused the development of inflammatory processes in the blood and periodontal tissues in animals, which is confirmed by changes in the pro- and antioxidant defense system.

2. Study of the periodontal protection properties of the "Moomiyo" therapeutic gel for the oral cavity in modeling periodontitis against the background of calcium deficiency states has shown the efficacy of its use, the preservation (restoration) of protective antioxidant systems in the periodontal tissues (an increase in the activity of GP and G6PDH by almost 1.3 times compared to the control ($p<.05$)). At the systemic level, positive dynamics was also noted for certain indices, a decrease in the MDA content in the blood serum, while the level of diene conjugates remained significantly higher than the control indices by almost 1.5 times ($p<0.01$); at the same time, stabilization of the enzyme glutathione marker's activity, antioxidant protection in blood serum (GP, GR, G6PDH) was noted with reliable activation of SOD and CAT activity by 1.2 times ($p<0.05$) with stabilization of the SOD/CAT ratio.

References

1. Antomonov MY. Matematicheskaya obrabotka i analiz mediko-biologicheskikh dannykh. 2-e izd. Kiev: MICz Medinform; 2017. 578 s. [in Russian]

2. Gnid RM. Rezultaty doslidzhennya aktyvnosti fermentiv antioksidantnoho zakhystu rotovoyi ridyny u khvorykh na parodontyt, yaki prozhyvayut na terytoriyi zabrudneniy sirkoyu. Visnyk problem biolohiyi i medytsyny. 2016; 1(2) (127): 224–227. [in Ukrainian]

3. Danilova LA. Analiz krovi, mochi i drugikh biologicheskikh zhidkostey v raznye vozrastnye periody. Sankt-Peterburg. Specz – Lit. 2014. 111s. [in Russian]

4. Devyatkin AA, Boriskin PV, Gulenko ON, Karimova RG, Leonov VV. Korreliatsiya kontsentratsii fermentov sistemy POL-AO v syvorotke krovi i tkanyakh pecheni krys. Mezhdunarodnyj nauchno-issledovatelskiy zhurnal [International research journal]. 2020; 7 (97) 2:15–20. DOI: 10.23670/ IRJ.2020. 100.10.013 [in Russian]

5. Drum MB, Gorbatovska NV, Novitska IK, Novitskiy VB, Nikolayeva GV, Kosenko DK et al. Patent na korisnu model N 143336, Ukrayina, MPK 2020.01, A61K 6/60. Gel dlya rotovoyi porozhnyny "Moomiyo". u 2020 00404, Zayavl. 24.01.2020; Opubl. 27.07.2020. Byul. N 14. [in Ukrainian]

6. Mokrenko EV, Shabanov PD. Otsenka effektivnosti lecheniya zubnymi pastami vospalitelno-degenerativnykh porazheniy myagkikh tkaney parodonta po pokazatelyam oksidativnogo statusa krovi i tkaney krys. Obzory po klinicheskoy farmakologii i lekarstvennoy terapii. 2015; 3(13):24–28. [in Russian]

7. Nikitin YeV, Vereshchagina OI. Okyslyuvalnyi stres yak odyn z vazhlyvishykh chynnykiv hostroho urazhennya endoteliyu. Infektsiyni khvoroby. 2019; 2(96): 22–28. [in Ukrainian]
8. Nikolaeva AV. Razrabotka modeli eksperimentalnogo parodontita u krys v usloviyakh deystviya antagonista vitamina K. Journal of Education, Health and Sport (Polsha). 2015;5:151–158. [in Russian]
9. Razhabova GKh, Khoshimova N, Amonov MK. Mumie v meditsine (Obzor literatury). Elektronnyy nauchnyy zhurnal "Biologiya i integrativnaya meditsina". 2017; 3:130–144.4. [in Russian]
10. Khaidar DA. Gipoksiya tkanei parodonta pri khronicheskom parodontite. Elektronnyi nauchno-obrazovatelnyj vestnik "Zdorovye i obrazovanie v XX1veke". 2017; 12: 292–295. [in Russian]
11. Mc Gonigle P, Ruggeri B. Animal models of human desease: challenges in enabling translation. Biochem. Pharmacol. 2014; 87(1): 162–171. doi.org/ 10.1016ĵ.bcp.2013.08.006
12. Papapanou PN, Susin C. Periodontitis epidemiology:is periodontitis under- recognized, over-diagnosed, or both? Periodontology. 2017; 1(75):45–51. doi.org:10.1111/prd.12200
13. Saulin MP, Bolevich S, Silina E, Orlova A, Raicevic N, Vorobiev S et al. Influence of the Local and Systemic Oxidative Stress on Periodontitis: Role of Antioxidant Therapy, Serbian Journal of Experimental and Clinical Research. 2018; 4: 365–372. doi:10.2478/SJTCR–2018–0078
14. Slots J. Periodontitis:facts, fallacies and the future. Periodontology. 2017; 1(75):7–23. doi.org:10.1111/prd.12221

Стаття надійшла 28.03.2020 р.

DOI 10.26724/2079-8334-2021-1-75-119-124
UDC 616.24:616.329.-002-071

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CURRENT ISSUES IN DIAGNOSING THE RESPIRATORY MANIFESTATION OF GASTROESOPHAGEAL REFLUX DISEASE

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The purpose of the study was to determine the leading extraesophageal symptoms, disturbance of spirometric indices, changes in the immune system and production of nitric oxide in patients with gastroesophageal reflux disease. Bronchopulmonary manifestation of gastroesophageal reflux disease was a cough syndrome, which was characterized by the presence of non-intensive, unproductive cough with a small amount of mucous sputum and was combined, in most cases, with the hoarseness of the voice. Cough syndrome during gastroesophageal reflux disease was characterized by a lack of obstructive changes in the study of external respiration indices and elevated levels of proinflammatory cytokines in the blood serum. It was determined the higher nitric oxide content in platelets in patients with respiratory manifestations of gastroesophageal reflux disease.

Keywords: gastroesophageal reflux disease, cough syndrome, proinflammatory cytokines, chronic obstructive pulmonary disease

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АКТУАЛЬНІ ПИТАННЯ ДІАГНОСТИКИ РЕСПІРАТОРНИХ ПРОЯВІВ ГАСТРОЕЗОФАГЕАЛЬНОЇ РЕФЛЮКСНОЇ ХВОРОБИ

Метою роботи було визначення провідних респіраторних позазастравохідних симптомів, порушення спірометричних показників, змін в імунній системі та продукції оксиду азоту у хворих на гастроезофагеальну рефлюксну хворобу. Для вирішення поставленої мети було обстежено 94 військовослужбовці чоловічої статі, які звернулися за медичною допомогою з приводу наявності синдрому кашлю. Основним респіраторним проявом гастроезофагеальної рефлюксної хвороби був неінтенсивний малопродуктивний кашель із виділенням невеликої кількості мокроти слизового характеру, який поєднувався, у більшості випадків, із осиплістю голосу. Синдром кашлю характеризувався відсутністю обструктивних змін при дослідженні показників функції зовнішнього дихання та підвищеним рівнем прозапальних цитокінів у сироватці крові. Було встановлено високий рівень оксиду азоту в тромбоцитах у хворих із респіраторними проявами гастроезофагеальної рефлюксної хвороби.

Ключові слова: гастроезофагельна рефлексна хвороба, синдром кашлю, прозапальні цитокіни, хронічне обструктивне захворювання легень

The study is a fragment of the research project "Epidemiological, therapeutic and pharmacoeconomic features of topical therapeutic pathology in servicemen and employees of the Armed Forces of Ukraine in the conditions of the Joint Forces Operation, "Vydnokray", state registration No. 0120U101854.

The worldwide organization of gastroenterologists has recognized gastroesophageal reflux disease (GERD) as a leading disease in the 21st century, which afflicts 20 to 50 % of the population of different countries, which also causes a decrease in the life quality, work capacity and the development of a number of complications, such as Barrett's esophagus [1, 3].