April 30, 2021

PharmacologyOnLine

Archives • 2021 • vol.1 • 96-105

ANTI-DYSBIOTIC AND RENOPROTECTIVE ACTION OF PLANT REMEDIES WITH METABOLIC SYNDROME

[1]Stepan, V. T.; [1]Fedoruk, O. S.; [2]Badiuk, N. S.*; [1]Vasiuk, V. L.; [3]Gozhenko, A. I.; [4]Stepan, B. T.; [1]Stepan, N. A.

[1]Bukovina State Medical University, Chernovtsy, Ukraine

[2]International European University, Kyiv, Ukraine

[3]State Enterprise Ukrainian Research Institute of Transport Medicine of the "Ministry of Health of Ukraine", Odesa, Ukraine

[4]Lesya Ukrainka Volyn National University, Lutsk, Ukraine

*badiuk_ns@ukr.net

Abstract

In recent years a number of patients suffering from metabolic syndrome have considerably increased. Metabolic syndrome includes metabolic disorders of lipid and carbohydrate metabolism, insulin resistance and development of hypertension.

Nephropathy develops with different forms of metabolic syndrome at the expense of lipotoxicity, hyperglycemia, and endotoxemia.

To prevent nephrotic complications in patients with metabolic syndrome a number of medicinal means are suggested: hepatoprotectors, bioflavonoid quercetin, the drug of soy-bean isoflavons «EKCO», and essential polyunsaturated fatty acids.

Plant extracts are most widely used among all the renoprotective means. Objective. Objective of the study is investigation of a therapeutic-preventive action of the two plant extracts from grape husks and oak wood produced on the kidneys of rats with experimental metabolic syndrome, as well as renoprotective action of the oral applications of anti-dysbiotic plant gels with simulated dysbiosis.

Materials and methods. The study was conducted under experimental conditions completely keeping to the current international and Ukrainian bioethical requirements. Metabolic syndrome (MS) was simulated in albino Wistar rats (females, 11 months, body weight of 258-279 g). Intestinal dysbacteriosis was caused by means of introduction of the antibiotic Lincomycin into drinking water in the dose of 60 mg/kg during the first five days. Immune deficiency was simulated by means of the cytostatic Cyclophosphan in the dose of 21 mg/kg administered into the peritoneum on the 1st, 7th, 14th and 21st days of the experiment.

Results and discussion. The study conducted demonstrated that under conditions of metabolic syndrome systemic inflammation, bacteremia and multiple organ failure develop. According to the data obtained hepatitis and obvious nephropathy develop with the signs of inflammatory-dystrophic process.

One of the causes of MS pathological signs can be insufficient protective body systems (immune and antioxidant), and the main thing is development of dysbiotic syndrome.

Administration of plant remedies possessing anti-dysbiotic properties can considerably improve therapeutic-preventive including renoprotective functions under conditions of metabolic syndrome.

Conclusions. Anti-dysbiotic plant remedies produce renoprotective function, which is evidenced by the results of administration of grape and oak extracts, and the latter appeared to be considerably more active.

The use of oral applications of mucous-adhesive gels containing anti-dysbiotic means performs renoprotective function under conditions of experimental dysbiosis.

Key words: metabolic syndrome, plant extracts, dysbiosis, hepatoprotectors, bioflavonoid quercetin, plan gel «Quertulin»

Introduction

In recent years a number of patients suffering from metabolic syndrome have considerably increased. Metabolic syndrome includes metabolic disorders of lipid and carbohydrate metabolism, insulin resistance and development of hypertension [1-4]. According to the scientific literary data endogenous microbiota plays an important role in the development of metabolic syndrome. It provokes systemic inflammation, bacteremia, and multiple organ failure [5-7].

Nephropathy develops with different forms of metabolic syndrome at the expense of lipotoxicity, hyperglycemia, and endotoxemia [8-11].

To prevent nephrotic complications in patients with metabolic syndrome a number of medicinal means are suggested: hepatoprotectors [12, 13], bioflavonoid quercetin [14-19], the drug of soy-bean isoflavons «EKCO» [20], and essential polyunsaturated fatty acids [21-23].

Plant extracts are most widely used among all the renoprotective means. They contain a complex of biologically active substances (vitamins, trace elements, adaptogens, and many other compounds). Their total action can considerably increase therapeutic-preventive action of separately taken substances [24, 25]. «Oak» extract contains a number of phenolic compounds of an oak-tree which have been used as stabilizers of wine and cognac for a long time. Grape husks contain great amount of polyphenolic compounds, and physiologically active bioflavonoids in particular (Vitamin P) [26]. The above mentioned is indicative of potentialities to apply these substances with a therapeutic purpose in case of various pathological processes.

In its turn, dysbiotic syndrome in the body is characterized by the signs of systemic inflammation and multiple organ failure [1-3]. The kidneys are extremely sensitive to dysbiotic condition, which is evidenced by numerous data published in the scientific literature [2-4]. A great amount of anti-dysbiotic means are suggested which contain pro- and prebiotics, antioxidants, membrane protectors, and adaptogens [5, 6]. Administration of oral mucous-adhesive gels containing anti-dysbiotic means performs renoprotective action under conditions of experimental dysbiosis [3, 7].

Objective of the study is investigation of a therapeutic-preventive action of the two plant extracts from grape husks and oak wood produced on the kidneys of rats with experimental metabolic syndrome, as well as renoprotective action of the oral applications of anti-dysbiotic plant gels with simulated dysbiosis.

Methods

«Grape» extract was obtained from grape husks of the grape breed «Odessa Black» by means of infusion of the husks with 60% isopropanol solution during 5 days mixing periodically. After filtration the extract was 2/3 boiled out, and practically all the isopropanol was evaporated. The residue was completed to 10% concentration of dry substances and used for feeding animals. «Oak» extract (the content of dry substances – 9,3 %) was obtained from «Sercial» company. «Oak» extract is allowed to be used in food industry in order to be added to alcohol beverages.

The study was conducted under experimental conditions completely keeping to the current international and Ukrainian bioethical requirements. Metabolic syndrome (MS) was simulated in albino Wistar rats (females, 11 months, body weight of 258-279 g). For this purpose they were kept on a high-fat diet (20 % palm oil). Intestinal dysbacteriosis was caused by means of introduction of the antibiotic Lincomycin into drinking water in the dose of 60 mg/kg during the first five days. Immune deficiency was simulated by means of the cytostatic Cyclophosphan in the dose of 21 mg/kg administered into the peritoneum on the 1st, 7th, 14th and 21st days of the experiment.

All the rats were distributed into 4 equal groups including 8 animals: 1 group – control, kept under standard vivarium diet, the 2nd, 3rd and 4th groups received high fat diet to simulate MS. In addition to diet rats from the 3rd group received «Grape» extract in the dose of 50 mg/kg of the live weight, and rats from the 4th group in addition to drinking water received «Oak» extract in the dose of 50 mg of dry extract per 1 kg of live weight.

Euthanasia of animals was performed on the 41st day of the experiment under Thiopental narcosis (20 mg/kg) by means of the total bleeding from the heart. Blood serum was obtained, the kidneys were removed. Activity of elastase (marker of

inflammation) [27], urease (parameter of bacterial contamination) [28], lysozyme (indicator of nonspecific immunity) [29], and alanine aminotransferase (ALT) [29] was determined in the blood serum.

The level of biochemical markers of inflammation was determined in the kidney homogenates: activity of elastase and content of Malone dialdehyde (MDA), antioxidant enzyme catalase. Antioxidant-prooxidant index (API) was calculated by the ratio of catalase activity and MDA content [27].

Experiments concerning investigation of the effect of oral applications of the plant gel «Quertulin» on the condition of kidneys in rats with experimental dysbiotic syndrome were conducted on 40 albino Wistar rats (males, 12 months, average live weight 380±17 g), distributed into 5 equal groups: 1 – control (intact animals), 2-5 groups – with experimental immune deficiency every day the 3rd group received oral applications of the plan gel «Quertulin» in the dose of 0,3 ml per one rat.

The plan gel «Quertulin» contains quercetin , inulin and calcium citrate [10].

Experimental immune deficiency was simulated by means of Prednisolone [11], adminsitered *per os* in the dose of 10 mg/kg (the first two days), followed by the dose 5 mg/kg during 17 days. The experiment lasted 20 days.

Euthanasia of animals was performed on the 41st day of the experiment under Thiopental narcosis (20 mg/kg) by means of the total bleeding from the heart. Blood serum was obtained, the kidneys, liver, mucous membrane of the cheeks and mucosa from the small intestine were removed.

The level of inflammation markers were determined in the kidney homogenate [12]: activity of elastase [13] and content of Malone dialdehyde (MDA) [14], activity of the antioxidant enzyme catalase [15], as well as activity of the bacterial enzyme urease [16], activity of the antimicrobial enzyme lysozyme [17].

Activity of urease and lysozyme was determined in the homogenates of the mucous membranes of the cheeks and small intestine, liver, and blood serum. Dysbiosis degree was calculated by their ratio according to A. P. Levytskyi [18].

Antioxidant-prooxidant index (API) was calculated by the ratio of catalase activity and MDA content [12].

The results of the experiment were processed statistically by means of standard methods of variation statistics [19]. Normalcy of distribution was checked by means of the method of direct visual estimation of distribution histograms of the obtained values. To perform statistical analysis of the results obtained the software package Microsoft Excel 2016 (USA) was applied.

Results

Table 1 contains the results determining biochemical markers of inflammation in the blood serum (elastase), microbial contamination (urease), nonspecific immunity (lysozyme), and hepatitis (ALT). These data illustrate that elastase activity increases reliably (32 %) in rats with metabolic syndrome, and after the action of plant remedies it decreases: after «Grape» extract – 15 % ($p<0,05$), after «Oak» extract – 22 % ($p<0,05$).

Urease activity in rats with MS increases more than twice as much, and after administration of plant remedies it 12,5 % decreases («Grape» extract) and 50 % («Oak» extract).

Lysozyme activity in rats with MS 44% decreases, and after administration of plant remedies it increases – 37 % («Grape» extract) and 42 % («Oak» extract).

ALT activity in rats with MS 36% increases ($p<0,01$), and after administration of «Grape» and «Oak» extracts it 14% and 19% decreases respectively.

The data obtained are indicative of the fact that rats with MS develop systemic inflammation, which is evidenced by a considerable increase of elastase activity, bacteremia (increased urease activity), reduced level of nonspecific immunity (considerable decrease of lysozyme activity) and development of hepatitis, which is proved by a reliable increase of the liver marker ALT activity. Both plant extracts produce a positive action on biochemical parameters, and «Oak» extract appeared to be more effective.

Table 2 presents the results determining inflammation markers degree in the kidneys of rats, that is, elastase activity and MDA content. The level of both markers is seen to increase reliably in rats with MS: 27% of elastase and 82% of MDA. In rats receiving plant medicines the indices of both inflammation markers decrease reliably: after administration of «Grape» extract elastase activity

18% decreased and MDA content – 22 %, after administration of «Oak» extract elastase activity 16% decreased and MDA content – 43 %.

Table 3 contains the results determining catalase activity and API in the kidneys. In rats with MS catalase activity 3,7 % decreases and plant remedies return it to the norm, though in all the cases p>0,05.

API appeared to be more significant, which 47% decreased in rats with MS. After administration of «Grape» extract it 32 % increased, and after «Oak» extract – 82 %.

Table 4 presents the results determining activity of urease, lysozyme in the kidneys and dysbiosis degree. Urease activity in rats with MS is seen 32 % increase (p<0,05), though after administration of plant remedies it decreases reliably practically to the control level. On the contrary, lysozyme activity in rats with MS decreases considerably – 41%. In rats receiving «Grape» extract it 24 % increased, and in rats receiving «Oak» extract – 39 %. Dysbiosis degree calculated by the indices of urease and lysozyme activity in rats with MS was 2,23, while in rats with MS receiving «Grape» extract it was 1,48, and those receiving «Oak» extract – 1,32.

Thus, the study conducted demonstrated that under conditions of metabolic syndrome systemic inflammation, bacteremia and multiple organ failure develop. According to the data obtained hepatitis and obvious nephropathy develop with the signs of inflammatory-dystrophic process.

One of the causes of MS pathological signs can be insufficient protective body systems (immune and antioxidant), and the main thing is development of dysbiotic syndrome [31].

Administration of plant remedies possessing anti-dysbiotic properties can considerably improve therapeutic-preventive including renoprotective functions under conditions of metabolic syndrome.

Table 5 contains the results determining dysbiosis markers, that is, activity of urease, lysozyme and dysbiosis degree in the liver, mucous membrane of the intestine and blood serum. These data demonstrate that urease level increases in the liver of rats with experimental dysbiosis 2,3 times, in the mucous membrane of the stomach – twice as much, and in the blood serum – 2,3 times which is indicative of a considerable increase of bacterial contamination of these tissues. On the contrary, lysozyme activity in these tissues decreases in rats with dysbiosis: 42% in the liver, 36% in the stomach and 32% in the blood serum, which is indicative of a considerable decrease of nonspecific immunity level.

As a result, dysbiosis degree in the liver of rats 4 times increases, in the stomach – 3,1 times, and in the blood serum – 3,9 times. The data obtained are indicative of the development of generalized dysbiosis, that is, dysbiotic syndrome [24].

Oral applications of plant gel «Quertulin» normalize to certain degree the levels of urease and lysozyme. Though reliably decreased dysbiosis degree did not return to the control level. It might be associated with an inadequate period of treatment (3 days only).

Table 6 presents the results determining activity of urease and lysozyme, and dysbiosis degree in the kidney homogenate of rats with experimental dysbiosis. These results demonstrate that in rats after administration of Lincomycin and Epinephrine urease activity 76 % increases, and lysozyme activity 33 % decreases, which stipulates 2,6 times increase of dysbiosis degree.

Oral applications of the plan gel «Quertulin» decrease urease activity by 20% (p>0,3), increase lysozyme activity by 18,5% (p>0,05) and decrease dysbiosis degree by 33% (though, p>0,05).

Dysbiotic process in the kidneys is seen to develop less than in other organs. It might be at the expense of very high activity of antimicrobial enzyme lysozyme. The kidneys contain its highest level in comparison with other organs and tissues of the body [6].

Dysbiosis results in (Table 7) a considerable increase of biochemical markers of inflammation in the kidneys: elastase – 79,5 % and MDA – 18%. Oral applications of the plan gel «Quertulin» decrease (practically to the control level) both indices of inflammation.

Table 8 contains the results determining catalase activity and API in the kidneys. In rats with dysbiosis catalase activity decreases reliably (6%) and API decreases (21%). Oral applications of the plan gel «Quertulin» normalize both indices.

Conclusions

1. Under conditions of metabolic syndrome nephropathy is observed which is manifested by the development of inflammation, dysbiosis and

decreased level of nonspecific immunity and antioxidant protection.

2. A possible causative agent promoting development of nephropathy can be dysbiotic syndrome.

3. Anti-dysbiotic plant remedies produce renoprotective function, which is evidenced by the results of administration of grape and oak extracts, and the latter appeared to be considerably more active.

4. Dysbiotic syndrome in the body is characterized by the signs of systemic inflammation and multiple organ failure.

5. The use of oral applications of mucous-adhesive gels containing anti-dysbiotic means performs renoprotective function under conditions of experimental dysbiosis.

Prospects of further studies

A comprehensive estimation of dysbiosis factors on the state of the pro- and antioxidant systems under conditions of metabolic syndrome.

Acknowledgments (optional)

The authors declare that there are no conflicts of interest.

References

1. Sokolenko A, Sydorchuk L, Sydorchuk A, Ursuliak J, Sydorchuk R. Association of dismetabolic disorders in hypertension with polymorphism of PPAR-gamma2 (Pro12Ala) and ACE (I/D) genes. *J Hypertension*. 2011; 29(Suppl A): 476.
2. Rzheshevsky AV. Deadly "triad": lipotoxicity, oxidative stress. Biochemistry. 2013; 78(9: 1265-1277. (in Russian)
3. Sydorchuk A, Boychuk T, Sydorchuk L, Sydorchuk R, Sydorchuk I. Immune and metabolic disorders in obese patients with hepatic steatosis and hypertension associate with PPAR-gamma2 Pro12Ala and ACE I/D genes' polymorphisms. *UEGJ*. 2015; 3(Suppl 1): A59.
4. Labeznik LB, Konev YV. Colon microbiota and components of metabolic syndrome. Experimental and Clinical Gastroenterology. 2014; 5: 33-39. (in Russian)
5. Cani P.D, Bibiloni R, Knauf C, et al. Changes in gut microbiota control metabolic endotoxemia-induced inflammation in high-fat diet-induced obesity and diabetes in mice. *Diabetes*. 2008; 57(6): 1470-1481.
6. Kaydashev IP. NF-kB signaling as a basis for the development of systemic inflammation, insulin resistance, lipotoxicity, type 2 diabetes mellitus and atherosclerosis. International Endocrinological Journal. 2011; 3(35): 35-45. (in Russian)
7. Titov VN. Phylogenetic theory of general pathology. Pathogenesis of metabolic pandemics. Diabetes mellitus: monograph. M .: INFRA-M, 2015. 223. (in Russian)
8. Maleki A, Montazeri M, Rashidi N, et al. Metabolic syndrome and its components associated with chronic kidney disease. *J Res Med Sci*. 2015; 15(5): 465-469.
9. Bavbek N, Isik B, Kargili A, et al. Association of obesity with inflammation in occult chromic kidney disease. *J Nephrol.* 2008; 21(5): 761-767.
10. Kravchun NO, Dorosh OG, Romanova SP, etc. Diagnosis of diabetic nephropathy in patients with type 2 diabetes mellitus in combination with non-alcoholic fatty liver disease (literature review and own data). International Journal of Endocrinology. 2015; 5(69): 156-166. (in Ukrainian)
11. Zhang K, Li Q, Chen Yi, et al. Visceral adiposity and renal function: an observational study from SPECT-China. *Lipids in Health and Disease*. 2017; 16: 205.
12. Zamorsky II, Drachuk VM, Goroshko OM. The effect of ademethionine on the state of prooxidant-antioxidant balance in rats with glycerol acute renal failure. Medical and clinical chemistry. 2015; 17(3): 34-37. (in Ukrainian)
13. Kvasnytska OB. Opportunities for medical correction of free radical processes in patients with chronic hepatitis and renal dysfunction. Bull. XVIII readings named after VV Podvysotsky, May 21-22, 2019, Odessa. 7-8.
14. Gomes IBS, Porto ML, Santos MC, et al. Renoprotective, anti-oxidative and anti-apoptotic effects of oral low-dose quercetin in the CS7BL/GJ model of diabetic nephropathy. *Lipids in Health and Disease*. 2014; 13: 184.
15. Goroshko OM, Zamorsky II, Gerush OV, etc. Changes in proteolytic activity of blood plasma, urine and kidney tissue of rats in experimental renal failure and its correction by corvitin.

Medical chemistry. 2010; 12(4): 22-25. (in Ukrainian)
16. Goroshko OM, Overseas II. Therapeutic efficacy of a single injection of the liposomal drug quercetin "Lipoflavone" in experimental acute renal failure. Bulletin of Pharmacy. 2008; 1(53): 67-71. (in Ukrainian)
17. Levitskiy AP, Pustovoit IP, Makarenko OA, et al. Renoprotective effect of quertulin in experimental immunodeficiency in rats. Actual problems of transport medicine. 2013; 4(34): 129-132. (in Russian)
18. Zupanets IA, Shebeko SK, Kharchenko DS. Experimental study of the pharmacological properties of the parenteral form of quercetin in the development of chronic renal failure. Bulletin of Pharmacy. 2009; 2(58): 75-78. (in Ukrainian)
19. Kharchenko DS, Zupanets IA, Shebeko SK, etc. The effect of quercetin when administered parenterally on the functional parameters of the kidneys of rats with renal insufficiency on the background of chronic glomerulonephritis. Clinical pharmacy. 2009; 13(2): 50-53. (in Ukrainian)
20. Voloshchuk NI. Comparative evaluation of nephrotoxic effects of diclofenac sodium, nimesulide and celecoxib in male and female rats and nephroprotective effect of flavonoids and isoflavonoids. Pharmacology and drug toxicology. 2008; 5-6(6-7): 68-74. (in Ukrainian)
21. Lenin M, Latha LM, Nagaraj M, et al. Mitigation of free radical toxicity in hyperoxaluric condition by a novel derivative eicosapentaenoate-lipoate. *Hum and Exp Toxicol*. 2002; 21(3): 153-158.
22. Banach M, Aronow WS, Serban M-C, et al. Lipids, blood pressure and kidney update 2015. *Lipids Health. Disease*. 2015; 14: 167.
23. Sampaio LS, da Silva PA., Ribeiro VS, et al. Bioactive lipids are altered in the kidney of chronic andemonriched rats: is there any correlation with the progression of prevalent nephropathies? *Lipids Health. Disease*. 2017; 16: 245.
24. Wardle E. N. Antioxidants in the prevention of renal disease. *Renal Failure*. 1999; 21(6): 581-591.
25. Popkov VA, Fetisova AN, Nesterova OV, et al. Experience in the use of phytopreparations based on edible plant materials for the prevention and correction of inflammatory pathologies of the genitourinary system. RAMS Bulletin. 2001; 2: 11-13. (in Russian)
26. Levitsky AP. Treatment-and-prophylactic dental elixirs: a tutorial. Odessa: KP OGT, 2010. 246. (in Russian)
27. Levitsky AP, Makarenko OA, Demyanenko SA. Experimental dentistry methods. Simferopol: Tarpan, 2018. 78. (in Russian)
28. Levitsky AP, Makarenko OA, Selivanskaya IA, et al. Enzymatic method for determining oral dysbiosis for screening pro- and prebiotics: guidelines. K .: GFC MZU, 2007. 22. (in Russian)
29. Goryachkovsky AM. Clinical biochemistry in laboratory diagnostics. Ed. 3rd rev. and add. Odessa: Ecology, 2005. 616. (in Russian)
30. Trukhacheva NV. Mathematical statistics in biomedical research using the Statistica package. M .: GEOTAR-Media, 2012. 379. (in Russian)
31. Levitsky AP. Dysbiotic syndrome: etiology, pathogenesis, clinical picture, prevention and treatment. Dentistry bulletin. 2019; 10 (special release):14-20. (in Russian)

Table 1. Biochemical indices of the blood serum in rats with experimental metabolic syndrome (n=8 in all the groups)

№№	Groups	Elastase, mc-cat/L	Urease, mc-cat/L	Lysozyme, units/L	ALT, mc-cat/L
1	Control	138±12	0,3±0,2	131±8	0,47±0,03
2	Metabolic syndrome (MS)	182±11 p<0,05	0,8±0,2 p<0,05	73±10 p<0,01	0,64±0,06 p<0,01
3	MS + «Grape» extract	155±10 p>0,2 p_1>0,05	0,7±0,4 p>0,3 p_1>0,5	100±6 p<0,05 p_1<0,05	0,55±0,02 p<0,05 p_1>0,05
4	MS + «Oak» extract	142±12 p>0,5 p_1<0,05	0,4±0,2 p>0,3 p_1>0,3	104±11 p<0,05 p_1>0,05	0,52±0,04 p>0,3 p_1>0,05

Notes: p – in comparison with group 1; p_1 – in comparison with group 2.

Table 2. Therapeutic-preventive action of plant remedies on the level of biochemical inflammation markers in the kidneys of rats with experimental metabolic syndrome (n=8 in all the groups)

№№	Groups	Elastase, mc-cat/L	MDA, mmol/kg
1	Control	440±32	24,8±1,5
2	Metabolic syndrome (MS)	559±14 p<0,05	45,1±1,7 p<0,01
3	MS + «Grape» extract	458±14 p>0,3; p_1<0,05	35,3±2,4 p<0,05; p_1<0,05
4	MS + «Oak» extract	471±16 p>0,3; p_1<0,05	25,8±1,2 p>0,3; p_1<0,01

Notes: similar to those of Table 1.

Table 3. Catalase activity and API in the kidneys of rats with experimental metabolic syndrome (n=8 in all the groups)

№№	Groups	Catalase, mc-cat/kg	API, un.
1	Control	6,42±0,02	2,59±0,14
2	Metabolic syndrome (MS)	6,18±0,08 p<0,05	1,37±0,12 p<0,01
3	MS + «Grape» extract	6,40±0,06 p>0,3; p_1>0,05	1,81±0,10 p<0,05; p_1<0,05
4	MS + «Oak» extract	6,40±0,05 p>0,3; p_1>0,05	2,48±0,13 p>0,3; p_1<0,05

Notes: similar to those of Table 1.

Table 4. Activity of urease and lysozyme, and dysbiosis degree in the kidneys of rats with experimental metabolic syndrome (n=8 in all the groups)

№№	Groups	Urease, mc-cat/kg	Lysozyme, un/kg	Degree of dysbiosis, un.
1	Control	0,25±0,02	6395±386	1,00±0,16
2	Metabolic syndrome (MS)	0,33±0,02 p<0,05	3774±414 p<0,05	2,24±0,29 p<0,05
3	MS + «Grape» extract	0,27±0,01 p>0,3; p_1<0,05	4681±531 p<0,05; p_1>0,05	1,48±0,19 p>0,05; p_1<0,05
4	MS + «Oak» extract	0,27±0,02 p>0,3; p_1>0,05	5258±437 p>0,05; p_1<0,05	1,32±0,20 p>0,05; p_1<0,05

Notes: similar to those of Table 1.

Table 5. Effect of oral applications of the plant gel «Quertulin» on the activity urease and lysozyme, and dysbiosis degree in different organs of rats with experimental dysbiotic syndrome

№	Organs and groups	Urease	Lysozyme	Degree of dysbiosis
	Liver			
1	Control	0,26±0,09	179±13	1,00±0,15
2	EDS	0,61±0,10 p<0,05	104±12 p<0,05	4,05±0,38 p<0,01
3	EDS + «Quertulin»	0,42±0,11 p>0,05 p_1>0,05	140±20 p>0,05 p_1>0,05	2,06±0,24 p<0,05 p_1<0,05
	Gastric mucosa			
1	Control	0,21±0,05	149±8	1,00±0,18
2	EDS	0,42±0,10 p<0,05	95±15 p<0,05	3,12±0,29 p<0,01
3	EDS + «Quertulin»	0,26±0,07 p>0,3 p_1>0,05	132±10 p>0,05 p_1<0,05	1,39±0,21 p>0,05 p_1<0,05
	Blood serum			
1	Control	0,66±0,21	107±8	1,00±0,17
2	EDS	1,51±0,28 p<0,05	73±5 p<0,05	3,87±0,42 p<0,01
3	EDS + «Quertulin»	1,23±0,20 p>0,05 p_1>0,3	100±7 p>0,3 p_1<0,05	2,00±0,23 p<0,05 p_1<0,05

Notes: p – in comparison with group 1; p_1 – in comparison with group 2, EDS – experimental dysbiotic syndrome

Table 6. Effect of oral applications of the plant gel «Quertulin» on the activity urease and lysozyme, and dysbiosis degree in the kidneys of rats with experimental dysbiotic syndrome

№	Groups	Urease, mc-cat/kg	Lysozyme, un/kg	Degree of dysbiosis, un.
1	Control	0,17±0,09	9846±629	1,00±0,20
2	Experimental dysbiotic syndrome (EDS)	0,30±0,10 p>0,05	6621±475 p<0,05	2,63±0,45 p<0,05
3	EDS + «Quertulin» gel	0,24±0,10 p>0,05 p_1>0,3	7847±399 p<0,05 p_1>0,05	1,76±0,28 p<0,05 p_1>0,05

Notes: similar to those of Table 1.

Table 6. Effect of oral applications of the plant gel «Quertulin» on the level of inflammation markers in the kidneys of rats with experimental dysbiotic syndrome

№№	Groups	Elastase, mc-cat/kg	MDA, mmol/kg
1	Control	0,44±0,07	35,5±1,2
2	Experimental dysbiotic syndrome. (EDS)	0,79±0,17 p<0,05	41,9±1,9 p<0,05
3	EDS + «Quertulin» gel	0,46±0,16 p>0,3; p_1>0,1	37,1±1,4 p>0,3; p_1<0,05

Notes: similar to those of Table 1.

Table 8. Effect of oral applications of the plant gel «Quertulin» on the level of inflammation markers in the kidneys of rats with experimental dysbiotic syndrome

№№	Groups	Catalase, mc-cat/kg	API, un.
1	Control	6,30±0,05	1,78±0,08
2	Experimental dysbiotic syndrome. (EDS)	5,93±0,10 p<0,05	1,41±0,09 p<0,05
3	EDS + «Quertulin» gel	6,09±0,09 p>0,05; p_1>0,05	1,64±0,11 p>0,05; p_1>0,05

Notes: similar to those of Table 1.