April 30, 2021

PharmacologyOnLine

Archives • 2021 • vol.1 • 456-463

# PHARMACOLOGICAL ACTIVITY OF SUNFLOWER HEADS DRY EXTRACT (Helianthus annuus L.)

Moeen Dababneh
Middle East University, Amman, Jordan

*moeen_dababneh2006@hotmail.com

**Abstract**

Introduction. The therapeutic improvement of hepatobiliary system pathologies associated with cholestatic syndrome using phytomedicines is a pressing issue of modern experimental and clinical pharmacology.

The aim of this study was to investigate the phytochemical composition of dry extract of Sunflower heads (Helianthus annuus L.) (DESH) and investigate the presence of choleretic and cholekinetic activity in case of complex experimental hepatic injury with tetrachloromethane combined with alcohol.

Materials and methods. The pathology was modeled by injection of 50% of oleic solution of carbon tetrachloride (at a dose of 0.4 mL/100 g subcutaneously) and 40% ethanol solution (at a dose of 1.3 mL/100 g intragastrically). The studied DESH was administered in a therapeutic-prophylactic regimen at doses 15, 25, 50, 75, and 100 mg/kg. The DESH effect was accessed by changes of biligenic (content of bile acids (BA) and cholesterol) and bile secretory (bile secretion rate (BSR)) processes under pathology conditions.

Results. Administration of DESH at doses of 75 and 100 mg/kg initiates a 1.7 and 1.5-fold increase of BSR respectively ($p < 0.05$). At same dosages under DESH action synthesis of BA and cholesterol was normalized in liver: BA content was 1.4 times higher ($p<0.05$) in both cases, cholesterol content - 1.7 times with DESH dosages 75 mg/kg and 1.5 times higher with dose 100 mg/kg. Probably the biliary-synthetic and choleretic effect of the studied extract is due to flavonoids (quercetamethrin) and coumarin glycoside scopolin, which are part of it, and the experimentally effective dose of DESH is in the range from 75 to 100 mg/kg.

Summary. The determined biliary-synthetic and choleretic action is the basis for the development of a phytomedicine, based on Sunflower heads extract (Helianthus annuus L.) with bile-secretory action of adjuvant nature in complex treatment of hepatobiliary diseases accompanied by cholestasis.

**Keywords**: *Annual sunflower (Helianthus annuus L), phytochemical composition, choleretic activity*

## Introduction

The use of phytopreparations in medicine has recently increased significantly, both in qualitative and quantitative terms, which is due to the complex pharmacological activity of herbal preparations, their relative safety, and breadth of therapeutic action [1, 2]. In particular, according to the WHO, almost 75% of patients prefer herbal medicines [3]. This, in turn, determines a relevant task of the modern scientific and practical medical community - to ensure the adaptation and integration of modern herbal medicine to the needs of practical medicine.

To date, the number of hepatobiliary system diseases is rapidly increasing and the number of cases is second only to diseases of the cardiovascular system [4, 5, 6]. In Ukraine, the registration of chronic hepatitis and liver cirrhosis cases has increased on average 2.5 times over the past twenty years [7]. Special attention needs to be paid to the correction of liver diseases comorbid with biliary tract pathology [8, 9]. Quite often with the deposition of stones in the gallbladder, cholestasis syndrome is clearly diagnosed and in accordance with the clinical picture of the pathology, a cholagogue product should be chosen according to its pharmacological effect [10]. It is not always rational to prescribe a drug with a pronounced choleretic effect [11]. Given the above, improving the treatment of hepatobiliary system diseases associated with cholestatic syndrome through phytopreparations is a topical issue of modern experimental and clinical pharmacology and hepatology in particular.

According to the sources of scientific literature, the leaves and ligulate flowers of the common sunflower (Helianthus annuus L.) contain betaine, choline, arnidiol, faradiol, flavonoids (quercimetrine and cyanidin glycoside), carotenoids, and pectin. Also, the leaf contains solanthic, succinic, fumaric, and citric acids, resinous substances (up to 3%); in ligulate flowers - saponins, phenolic acids (chlorogenic, neochlorogenic, caffeic, salicylic). Sunflower oil contains glycerides of oleic, palmitic, stearic, arachidic, and lignoceric acids and carotenoids [12, 13].

Thus, the literature analysis of phytochemical components of the common sunflower (Helianthus annuus L.) allows predicting the presence of bile-forming and choleretic activities in this medicinal plant, which led to further targeted receipt and study of extracts from this plant: dry extract of heads of the common sunflower (Helianthus annuus L.).

The aim of this work was to study the phytochemical composition of the dry extract of common sunflower heads (Helianthus annuus L.) and substantiation of its positive influence on the processes of bile formation and bile secretion under the conditions of complex experimental liver damage with carbon tetrachloride in combination with alcohol.

## Methods

Dry extract of Sunflower heads (DESH) was produced from common sunflower (Helianthus annuus L.) and its phytochemical composition has been studied at the Department of Botany of the NUPh by postgraduate student Olga Sokolova under the supervision of professor, doctor of pharmaceutical sciences - Gontova Tatiana.

DESH represents a dark-brown dry powder, without a specific odor, obtained by the following technology. Pre-dried to air-dry state and crushed heads of Helianthus annuus L. are subjected to three-fold extraction with 40% ethyl alcohol solution at a ratio of raw material to extractant of 1:10 and the total duration of extraction - 16 hours at room temperature. The first extraction is carried out for 12 hours, the second and third - for 2 hours each. The obtained aqueous extracts are combined and kept in the refrigerator for 1 day to precipitate mechanical inclusions. After settling, the extract is evaporated to 1/3 of its volume and purified from lipophilic fractions with chloroform. Then the chloroform residues are removed by heating and the polysaccharides are precipitated with a 96% solution of ethyl alcohol. The polysaccharide precipitate is filtered off and the supernatant is dried under vacuum to dryness [12, 14].

To achieve the aim, a study of the bile-forming and choleretic activity of the studied extract has been carried on a model of subchronic hepatitis modeled by the introduction of carbon tetrachloride

in combination with alcohol. Control pathology was modeled following the guidelines of the SEC of the Ministry of Health of Ukraine for experimental study of choleretic, cholelytic and hepatoprotective activities of medicinal products[15]. The model of subchronic (subacute) liver damage was reproduced by a single subcutaneous (s/c) injection of 50% oil solution of carbon tetrachloride in a dose of 0.4 mL/100 g of rat, followed by intragastric (i/g) administration of 40% ethyl alcohol. The above mode of administration of toxicants was repeated for 4 days.

The extract under study was administered intradermally in a therapeutic and prophylactic mode in the following doses: 15, 25, 50, 75, and 100 mg/kg of rat 7 days before the simulation of control pathology once a day (preventive mode). During the modeling of the control pathology, the extract was administered 1 h before the introduction of carbon tetrachloride and 2 h after its administration (therapeutic and prophylactic). After the last injection of the toxin (on the 4th day of modeling the pathology), DESH was administered once a day, the last time an hour before the manipulation in rats.

As a reference drug, "Carsil" (coated tablets containing 22.5 mg of milk thistle flavonoids) by JSC "Sopharma", Bulgaria has been chosen, a plant hepatoprotector based on milk thistle flavonoids, which has a choleretic effect. In determining the experimental dose of "Carsil" we were guided by the guidelines of the Federal State Budgetary Institution "Scientific Centre for Expert Evaluation of Medicinal Products" of the Ministry of Health of the Russian Federation (FSBI "SCEEMP" of the Ministry of Health of the Russian Federation) [16], as well as data from experimental studies which indicate the effectiveness of the dose of 100 mg/kg [17, 18].

72 hours after the last injection of toxins, the animals were anesthetized with 1% barbamyl solution, fixed on the operating table, and performed laparotomy (an incision of the anterior abdominal wall), slightly below the chest of size 1.5-2.0 cm. Identified the duodenum and the confluence of the bile duct. One of two ligatures fixed the location of the duct into the intestine, and the other - tube-cannula, inserted into the incised bile duct [19]. To make the process of bile secretion as close as possible to physiological conditions, the operated area was sutured. Over the next three hours, bile was collected, recording the hourly volume excreted, and the average bile excretion rate (mg/min/100 g of rat weight) was calculated. The content of cholesterol and bile acids was studied in the obtained bile by the method of VP Miroshnichenko [19].

The obtained results were processed statistically using the program "Statistica 8.0", using the non-parametric Mann-Whitney test (the significance level $p < 0.05$ was taken when comparing the statistical indicators) [20].

The research was conducted in the CentralScientific-Research Laboratory of NUPh, which is certified by the SEC of the Ministry of Health of Ukraine (Certificate No. 058/15 dated 08.12.2015, effective until 07.12.2019). Work with animals was carried out under GLP requirements, recommendations of the SEC of the Ministry of Health of Ukraine, National General Ethical Principles of Animal Experiments (Ukraine, 2001), Law of Ukraine No. 3447-IV dated 21.02.2006, amended "On protection of animals from cruel treatment" and "European Union Directive 2010/63 / EU on the protection of animals used for scientific purposes" [21].

## Results and Discussion

Carrying out of phytochemical researches (by postgraduate student Olga Sokolova under the supervision of professor Tatyana Gontova at the Botany Department of the NUPh) has allowed identifying in heads of Helianthus annuus L. flavonoids (quercetamitrin), coumarin glycoside scopolin, triterpene saponins, sterols (sitosterol glycoside), carotenoids (β-carotene, cryptoxanthin, taraxanthin), phenolic acids (chlorogenic, neochlorogenic, caffeic), anthocyanins [12].

The research of DESH effect on bile-forming and bile-secretory functions of the liver under the conditions of simulated subchronic hepatitis was performed by assessing the rate of bile secretion (BSR) and its qualitative and quantitative components: the content of bile acids (BA) and

cholesterol. Tetrachloromethane is a classic hepatotropic poison that causes severe liver damage, based on the activation of lipid peroxidation (LPO) processes [22, 23, 24, 25]. Toxic effects of alcohol on the liver are associated with the metabolism of ethyl alcohol in this organ and the formation of acetaldehyde, which exceeds ethanol in hepatotoxicity, and the mechanism of the destructive action of the latter is based on changes in the activity of microsomal enzymes and cytochrome P 450 content, which leads to the development of cytolysis and cholestasis [15, 23].

Modeling of subchronic hepatitis in rats impaired bile-forming and bile-secretory function of the liver, which is confirmed by a 1.6 times decrease in BSR ($p < 0.05$) and quantitative change of bile components: the content of BA decreased by 1.4 times (p0.05) and cholesterol by 1.6 times (table. 1).

So, under conditions of subchronic carbon tetrachloride hepatitis, there was a violation of the BA and cholesterol synthesis and their excretion with bile, ie there was a syndrome of cholestasis [27, 25].

The introduction of dry extract of sunflower heads was characterized by a dose-dependent manifestation in the restoration of functional parameters of bile-forming and bile-secretory function of the liver. In particular, the use of DESH at a dose of 15 and 25 mg/kg did not contribute to significant changes in BSR, content of BA, and cholesterol in it. At administration of DESH at a dose of 50 mg/kg a 1.4 times increase of BSR was observed (p <0.05) and the tendency to normalize the content of BA and cholesterol: 1.1 and 1.3 times, respectively. The introduction of the studied extract at a dose of 75 and 100 mg/kg was characterized by a significant increase in BSR 1.7 and 1.5 times ($p < 0.05$) respectively. Also, taking DESH at a dose of 75 and 100 mg/kg contributed to the normalization of the synthesis of BA and cholesterol in the liver, as the content of BA increased 1.4 times (p <0.05) in both cases, and the cholesterol content increased 1.7 times at the dose of DESH 75 mg/kg and 1.5 times at a dose of DESH 100 mg/kg (table. 1).

The studied extract of common sunflower heads when administered at a dose of 75 and 100 mg/kg provided effect at the level of the comparison drug - carsil, which contributed to a significant increase in BSR 1.6 times and a pronounced tendency to increase the content of BA and cholesterol in bile in 1.2 and 1.4 times, respectively. Under the exposure to DESH (doses of 75 and 100 mg/kg), there was a slightly more pronounced increase in the content of BA (on average by 15%) than with the use of carsil, but these data were not statistically significant.

Thus, based on the obtained experimental results on the positive effect of DESH on the processes of bile formation and bile secretion under cholestasis, which develops against the background of simulated subchronic hepatitis and taking into account the phytochemical composition of the studied extract, it can be argued that the ability of DESH to normalize bile formation and bile secretion processes is due to complex composition of biologically active substances that are part of it. DESH contains: flavonoids (quercemerithrine); coumarin glycoside scopolin [28, 29]; phenolic acids: chlorogenic [30, 31], neochlorogenic, caffeic [32, 33] and other BAS [34]. The studies conducted have allowed establishing an experimentally effective dose of DESH, which is in the range from 75 to 100 mg/kg. The obtained data indicate the prospect of further studies of DESH, for hepatoprotective and other pharmacological activities, and the established cholagogic action is the basis for the development of Helianthus extract-based phytopreparation of biliary secretive action of adjuvant nature for use in complex treatment of diseases associated with cholestasis.

It has been found that the use of the dry extract of Helianthus annuus heads in doses of 75 and 100 mg/kg helps to restore the formation and secretion of bile in subchronic hepatitis, which is confirmed by increasing the rate of bile secretion (1.5-1.7 times) and increasing the content of bile acids (1.4 times) and cholesterol (1.5-1.7 times). Further experimental studies of dry extract of sunflower heads at a dose of 75-100 mg/kg are recommended to develop a promising phytopreparation of bile-secretory action based on this extract, and it is additionally recommended to investigate it for hepatoprotective activity to expand the pharmacodynamics of this extract.

**Acknowledgments.** The author would like to express gratitude to the head of the Botany

Department of NUPh, Doctor of Pharmaceutical Sciences, professor Tetyana Gontova and postgraduate student Olga Sokolova for obtaining the extract and studying its phytochemical composition. And also to the doctor of medical sciences, the professor of pharmacology and pharmacotherapy department of NUPh Lyudmyla Derymedvid for the help in carrying out experimental researches.

## References

1. Antiviral activity of silymarin against chikungunya virus / Rafidah Lani et al. Sci Rep. 2015. No. 5. P. 11421.
2. Sokar S. S., El-Sayad M. E., Ghoneim M. E., Shebl A. M. Combination of Sitagliptin and Silymarin ameliorates liver fibrosis induced by carbon tetrachloride in rats. Biomed Pharmacother. 2017. No. 89. P. 98–107.
3. Elena Yu Enioutina, Emma R Salis, Kathleen M Job, Michael I. Gubarev, Lubov V Krepkova & Catherine MT Sherwin (2016): Herbal Medicines: Challenges in the Modern World. Part 5. Status and current directions of complementary and alternative herbal medicine worldwide., Expert Review of Clinical Pharmacology. http://dx.doi.org/10.1080/17512433.2017.1268917
4. Hepatotropic drugs: organoprotective action (review of the literature) / G.A. Pogotova, N.O. Gorchakova, I.F. Belenichev, I.S. Chekman. Bulletin of problems of biology and medicine. 2015. Vol. 1. Pp. 19 - 27.
5. Mann DA Epigenetics in Liver Disease. Hepatology. 2014. Vol. 60, No. 4. P. 1418 - 1425.
6. Tacke F, Kroy DC, Barreiros AP, Neumann UP. Liver transplantation in Germany. Liver Transpl. 2016 Aug;22(8):1136-42. doi: 10.1002/lt.24461. PMID: 27082951.
7. Kalko K.O. Chronopharmacological study of the of hepatoprotective agents activity .... cand. pharm. Science: 14.03.05 / NUPh. Kh., 2017. 195 p.
8. Huang RX, Wang BC, Fan JG. [Research advances of relationship between non-alcoholic fatty liver disease and biliary tract diseases]. Zhonghua Gan Zang Bing Za Zhi. 2017 Aug 20; 25 (8): 633-636. Chinese. doi: 10.3760 / cma.j.issn.1007-3418.2017.08.016. PMID: 29056017.
9. Peng SY, Wang XA, Huang CY, Li JT, Hong DF, Liu YB, Cai XJ. [The new classifications of biliary tract diseases based on actual anatomy]. Zhonghua Wai Ke Za Zhi. 2019 Jun 1; 57 (6): 412-417. Chinese. doi: 10.3760 / cma.j.issn.0529-5815.2019.06.004. PMID: 31142064.
10. Gossard AA, Talwalkar JA. Cholestatic liver disease. Med Clin North Am. 2014 Jan;98(1):73-85. doi: 10.1016/j.mcna.2013.09.002. Epub 2013 Oct 20. PMID: 24266915.
11. Stulic, M., Culafic, D., Boricic, I., Stojkovic Lalosevic, M., Pejic, N., Jankovic, G., ... Culafic, M. (2019). Intrahepatic Cholestasis of Pregnancy: A Case Study of the Rare Onset in the First Trimester. Medicina, 55(8), 454. doi:10.3390/medicina55080454
12. Sokolova O.O. Pharmacognostic study of raw sunflower (Helianthus annuus L.) and development of herbal medicines based on it. ... cand. pharm. sci.: 15.00.02 / NUPh. Kh., 2019. 257 p.
13. Common sunflower (Helianthus annuus). Access mode: https://lektrava.ru/encyclopedia/podsolnechnik-odnoletniy/
14. Sokolova OO, Gontova TM Method of obtaining dry extract from common sunflower heads: pat. № 121462 Ukraine, № u 201705217; declared 29.05.2017; publ. 11.12.2017, Bull. No. 23. 3 p.
15. Preclinical studies of medicinal products (guidelines) / Ed .: Corresponding Member. Academy of Medical Sciences of Ukraine O.V Stefanov. K.: Avicenna Publishing House, 2001. 528 p
16. Guide to conducting preclinical studies of medicines/ A.N Mironov [et al.]. M.: Grif and Co., 2012. 944 p.
17. A screening study of hepatoprotective activity of liquid extract from Common Tansy Tanacetum vulgare L. herb in the setting of subchronic hepatitis in rats / Kalko K. O., Mishchenko O. Ya., Derymedvidet L. V. et al. Research J. Pharm. and Tech. 2018. No. 11(10).

P. 4393-4396. DOI: 10.5958 / 0974-360X.2018.00803.X
18. Chronopharmacological features of hepatoprotectors action in the experiment / Bunyatyan N.D, Kalko E.A, Drogovoz S.M, Kononenko A.V Bulletin of Experimental Biology and Medicine. 2018. No. 6 Pp. 712-715 DOI: 10.1007 / s10517-018-4258-8.
19. Skakun N.P Clinical pharmacology of hepatoprotectors / N.P Skakun, V.V Shmanko, L.M. Okhrimovich. Ternopil, 1995. 272 p.
20. Trukhacheva N.V Mathematical statistics in biomedical research using the Statistica package. M.: GEOTAR-Media, 2012. 379 p.
21. Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. Official Journal of the European Union. 2010. No. L276. P. 33–79.
22. Li N, Li B, Zhang J, Liu X, Liu J, Li K, Pan T, Wang S, Diao Y. Protective effect of phenolic acids from Chebulae Fructus immaturus on carbon tetrachloride-induced acute liver injury via suppressing oxidative stress, inflammation, and apoptosis in mouse. Nat Prod Res. 2020 Nov; 34 (22): 3249-3252. doi: 10.1080 / 14786419.2018.1553174. Epub 2019 Jan 8. PMID: 30618288.
23. The effect of Acorus calamus extract on indicators of cholestasis and biliary function of the liver in experimental hepatitis / Derimedvid L.V, Korang L.A, Kalko K.O, Vereitinova V.P Pharmacology, and drug toxicology. 2020. No. 14 (2). Pp. 114-121.
24. Hozzein WN, Al-Khalaf AA, Mohany M, Al-Rejaie SS, Ali DMI, Amin AA. The potential protective effect of two actinomycete extracts against carbon tetrachloride-induced hepatotoxicity in rats. Environ Sci Pollut Res Int. 2019 Feb; 26 (4): 3834-3847. doi: 10.1007 / s11356-018-3904-z. Epub 2018 Dec 11. PMID: 30539391.
25. Nwidu LL, Oboma YI, Elmorsy E, Carter WG. Alleviation of carbon tetrachloride-induced hepatocellular damage and oxidative stress with a leaf extract of Glyphae brevis (Tiliaceae). J Basic Clin Physiol Pharmacol. 2018 Nov 27; 29 (6): 609-619. doi: 10.1515 / jbcpp-2017-0058. PMID: 30157032.
26. Hepatoprotective and choleretic activity of dried extract of Tanacetum vulgare flowers / Mishchenko O. Ya., Kalko K. O., Zolotaikina M. Yu. et al. Thai Journal of Pharmaceutical Sciences. 2019. No. 43 (1). P. 30-35.
27. Xu G, Han X, Yuan G, An L, Du P. Screening for the protective effect target of deproteinized extract of calf blood and its mechanisms in mice with CCl4-induced acute liver injury. PLoS One. 2017 Jul 10; 12 (7): e0180899. doi: 10.1371 / journal.pone.0180899. PMID: 28700704; PMCID: PMC5507287.
28. Nugroho A, Lim SC, Karki S, Choi JS, Park HJ. Simultaneous quantification and validation of new peroxynitrite scavengers from Artemisia iwayomogi. Pharm Biol. 2015 May; 53 (5): 653-61. doi: 10.3109 / 13880209.2014.936022. Epub 2014 Dec 4. PMID: 25474707.
29. Yoo A, Narayan VP, Hong EY, Whang WK, Park T. Scopolin ameliorates high-fat diet-induced hepatic steatosis in mice: potential involvement of SIRT1-mediated signaling cascades in the liver. Sci Rep. 2017 May 22; 7 (1): 2251. doi: 10.1038 / s41598-017-02416-6. PMID: 28533555; PMCID: PMC5440403.
30. Lu H, Tian Z, Cui Y, Liu Z, Ma X. Chlorogenic acid: A comprehensive review of dietary sources, processing effects, bioavailability, beneficial properties, mechanisms of action, and future directions. Compr Rev Food Sci Food Saf. 2020 Nov; 19 (6): 3130-3158. doi: 10.1111 / 1541-4337.12620. Epub 2020 Sep 4. PMID: 33337063.
31. Xu Y, Chen J, Yu X, Tao W, Jiang F, Yin Z, Liu C. Protective effects of chlorogenic acid on acute hepatotoxicity induced by lipopolysaccharide in mice. Inflamm Res. 2010 Oct; 59 (10): 871-7. doi: 10.1007 / s00011-010-0199-z. Epub 2010 Apr 20. PMID: 20405164.
32. Mangrulkar S, Shah P, Navnage S, Mazumdar P, Chaple D. Phytophospholipid Complex of Caffeic Acid: Development, In vitro Characterization, and In Vivo Investigation of Antihyperlipidemic and Hepatoprotective Action in Rats. AAPS PharmSciTech. 2021 Jan 6; 22 (1): 28. doi: 10.1208/s12249-020-01887-7. PMID: 33404939.
33. Bispo VS, Dantas LS, Chaves AB Filho, Pinto IFD, Silva RPD, Otsuka FAM, Santos RB,

Santos AC, Trindade DJ, Matos HR. Reduction of DNA damages, Hepatoprotective Effect and Antioxidant Potential of the Coconut Water, ascorbic and Caffeic Acids in Oxidative Stress Mediated by Ethanol. An Acad Bras Cienc. 2017 Apr-Jun; 89 (2): 1095-1109. doi: 10.1590/0001-3765201720160581. Epub 2017 May 15. PMID: 28513780.

34. Boseila AA, Abdel-Reheem AY, Basalious EB. Design of bile-based vesicles (BBVs) for hepatocytes specific delivery of Daclatasvir: Comparison of ex-vivo transenterocytic transport, in-vitro protein adsorption resistance and HepG2 cellular uptake of charged and β-sitosterol decorated vesicles. PLoS One. 2019 Jul 16; 14 (7): e0219752. doi: 10.1371/journal.pone.0219752. PMID: 31310613; PMCID: PMC6634393.

**Table 1.** Effect of dry extract of Helianthus heads on the bile-forming and bile-secretory function of the liver in subchronic hepatitis (n = 6), (M ± SEM)

| Experimental conditions | BSR, mg/min/100 | Bile acids, mg% | Cholesterol, mg% |
|---|---|---|---|
| IC | 4.47 ± 0.12 | 832.96 ± 74.17 | 29.72 ± 4.92 |
| CP | 2.75±0.23* | 581.78 ± 56.56* | 18.29 ± 5.21 |
| CP + Carsil, 100 mg/kg | 4.48 ± 0.18 ** | 707.65±53.44 | 25.38±6.71 |
| CP + DESH, 15 mg/kg | 3.20±0.22 | 607.24 ± 55.92 | 16.68 ± 4.51 |
| CP + DESH, 25 mg/kg | 3.29 ± 0.19 | 616.36 ± 48.28 | 18.89±3.91 |
| CP + DESH, 50 mg/kg | 3.78 ± 0.31 ** | 664.24 ± 92.80 | 23.85 ± 3.81 |
| CP + DESH, 75 mg/kg | 4.61 ± 0.22 ** | 818.52 ± 32.87 ** | 31.10 ± 6.80 |
| CP + DESH, 100mg/kg | 4.23 ± 0.26 ** | 807.12 ± 47.96 ** | 27.37 ± 3.73 |

Notes:

IC - group of intact control animals;

CP - a group of animals, in which control pathology was modeled;

n - the number of rats in one experimental group;

M - average value in the population;

SEM - standard error of the average value in the population;

* - deviation of the indicator is significant relative to the rate of intact animals ($p < 0.05$);

** - deviation of the indicator is significant relative to the indicator in the control pathology group ($p < 0.05$).