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PHARMACOLOGICAL STUDY OF ORIGINAL EXTRACTS OF CORN SILK

Naboka Olga, Liliia Vyshnevska, Inna Pasynchuk, Olga Filiptsova, Oksana Tkachenko, Olha Vislous

Aim: *the aim of the research is a pharmacological study of the original extracts of corn silk.*
Materials and methods. *The object of the study were 4 original extracts of corn silk, obtained by extraction with water and ethanol of different concentrations, namely: aqueous extract of corn silk (ACSE), extract of corn silk, extracted with ethanol 30 % (ECSE 30 %) , extract of corn silk, extracted with ethanol 50 % (ECSE 50 %), extract of corn silk, extracted with ethanol 70 % (ECSE 70 %). A screening study of the antioxidant properties of corn silk extracts was carried out in vitro using models of spontaneous and ascorbate-induced lipid peroxidation (LPO) in rat liver homogenate.*
Results. *As can be seen from the given data, ECSE 50 % at a dose of 20 mg/kg showed a pronounced protective effect on the hepatotoxicity of TCM. Its use led to a probable restoration of the bile-forming function of the liver against the background of tetrachloromethane hepatitis: in response to an increase in the cholesterol content (by 43 %, $p<0.05$), the content of bile acids increased 2 times ($p<0.05$), as a result of which cholate -cholesterol ratio approached the level of indicators of intact animals, the rate of bile secretion normalized. Based on the analysis of the results of the study, it can be concluded, that in terms of bile-forming and choleretic activity on the tetrachloromethane hepatitis model, ECSE 50 % was not inferior to silibor and superior to quercetin ($p<0.05$).*
Conclusions. *Biologically active substances of corn silk affect not only the diffusion and filtration processes of the liver parenchyma, but also the biosynthesis and transport of its organic components, that is, they affect the bile-forming function.*
Keywords: *corn silk extracts, lipid peroxidation, antioxidant activity, choleretic activity, acute toxicity, Drosophila melanogaster Meig. test system, hepatoprotectors.*

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1. Introduction

Under modern conditions, it is relevant to create medicinal products based on plant raw materials for the prevention and treatment of pathological conditions, associated with an increase in the content of free radicals in the body under the influence of various stressor agents [1]. Data from scientific sources indicate that a large number of stressors, such as emotional stress, poisoning by xenobiotics, alcohol, intake of essential microelements in quantities exceeding physiological ones, cause a shift in the balance in the prooxidant-antioxidant system and the development of oxidative stress [2]. According to the authors [3], the antioxidant properties of polyphenols are associated with their ability to serve as a trap for active oxygen metabolites, free radicals, bind metal ions that are inducers of LPO and inhibit the activity of a number of redox-sensitive transcription factors, in particular, NFkD (nuclear factor kappa B), AP-1 (activator protein 1) and pro-oxidant enzymes [4].

The above and the results of the analysis of literature data regarding the features of the chemical composition of the investigated extracts of corn silk (the presence of a significant amount of saikosaponins, polyphenols, tannins of the pyrocatechin group (11–13 %), sugars, silica compounds, fatty oil (1.88–2.55 %), which contains linoleic and arachidonic acids, volatile oil (0.1–0.2 %), as well as potassium, magnesium, calcium, sitosterol and stigmasterol, retinol, thiamine, riboflavin, ascorbic acid, phylloquinones, α-tocopherol, pantothenic acid) became the basis for studying their antioxidant and protective properties in vitro and in vivo [5].

The aim of the research is the pharmacological study of original extracts of corn silk.

2. Materials and methods

The object of the study were 4 original extracts of corn silk, obtained by extraction with water and ethanol of different concentrations, namely: aqueous extract of corn silk (ACSE), extract of corn silk extracted with ethanol 30 % (ECSE 30 %) , extract of corn silk, extracted with ethanol 50 % (ECSE 50 %), extract of corn silk, extracted with ethanol 70 % (ECSE 70 %). The investigated plant extracts were obtained at the Department of Pharmacy Technology of Medicines of the National Pharmaceutical University (NPU) under the supervision of the head of the department, Doctor of Pharmaceutical

Sciences, Professor Vishnevska L.I. Pharmacological studies were carried out at the Department of Biological Chemistry of the National Academy of Sciences under the supervision of Doctor of Biological Sciences, Professor Naboka O. I.

A screening study of the antioxidant properties of corn silk extracts was carried out in vitro using models of spontaneous and ascorbate-induced lipid peroxidation (LPO) in rat liver homogenate [6].

Studies of the acute toxicity of plant extracts were carried out when administered intragastrically to sexually mature mice in the dose range of 1000–5000 mg/kg. The route of administration is chosen in accordance with the intended method of use of the medicinal product in clinical practice. Mice of the first group were the intact control, 2–5 groups of experimental animals were injected intragastrically with the corresponding studied extracts at a dose of 1000 mg/kg, 3000 mg/kg and 5000 mg/kg (dose of class IV toxicity). The degree of toxicity of plant extracts was assessed by lethality, changes in the general condition of animals, influence on the dynamics of animal body weight and mass coefficients of internal organs.

The study of the toxic properties of the extract of corn silk, extracted with 50 % ethanol, was carried out using the Drosophila melanogaster Meig test system. The toxic effect of the studied extract was evaluated by the total productivity of Drosophila - the number of adult offspring. The rate of imago output is integral [7]. At the embryonic and post-embryonic stages of development, its components are considered to be the fertility of the parents and the viability of the offspring. The research was carried out on the classic object of genetic research – the fruit fly Drosophila melanogaster Meig, which, according to the recommendations of the World Health Organization (WHO), is effectively used in modern pharmacological research [8].

In the work, there was used the outbred line of the wild type Canton-S (C-S) from the collection of the Department of Genetics and Cytology of the Kharkiv National University named after V. N. Karazin. Flies were grown on a standard sugar-yeast medium at a temperature of 24 ± 0.5 ^{o}C in a thermostat. Drosophila cultures were grown in sugar cups with a diameter of 2.0 cm and a height of 10.0 cm. The volume of the nutrient medium was 5.0 ml. ECSE 50 % was added to the nutrient medium, in which Drosophila larvae developed in concentrations of 10^{-3} mg/ml, 10^{-2} mg/ml, 10^{-1} mg/ml, 1 mg/ml, 10 mg/ml. Egg laying time is 5 days. The yield of imago was estimated by taking into account the number of adult females and males in the period from the beginning to the end of the flight of flies [9]. To account for recessive, sex-linked lethal mutations, the Meller-5 method was used [10].

The study of the effect of plant extracts on the bile-forming function was determined on the model of acute hepatitis in rats, caused by tetrachloromethane (TCM) [11]. ECSE 50 % was administered intragastrically, once a day at a dose of 20 mg/kg for 14 days. As comparison drugs, silibor and quercetin, which are analogs in terms of pharmacological action, were chosen in a similar regimen in doses of 100 mg/kg and 50 mg/kg, respectively.

On the 14th day, 1 hour after the last injection of the studied plant extracts, animals were injected intragastrically with TCM at a dose of 0.8 ml/100 g of animal weight in the form of a 50 % oil solution. Controls were intact rats and rats with the reproduced pathology, which were injected with water in an equivalent volume [12].

On the 15th day of the experiment, the animals were anesthetized with a 1 % solution of barbamil, which does not affect the formation of bile. Bile was collected in hourly portions for 3 hours. The intensity of bile secretion was assessed by the rate of bile secretion, which was calculated for 3 hours of observation in ml/100g according to the method of Miroshnichenko V.P. et al. [13]. The concentration of bile acids and cholesterol was determined in the bile, the level of which allows assessing the synthetic function of the liver. After collection of bile, the animals were removed from the experiment by decapitation, the liver was removed and weighed. The LMC was calculated, which allows characterizing the state of general trophic processes, the degree of swelling and alteration of the organ [14].

Vitamin E ("Tocopherol" (Vitamin E) capsules, 0.1 g, PJSC "Kyiv Vitamin Plant", Ukraine), quercetin ("Quercetin granules", 2.0, PJSC "Borshchagivskyi KhFZ", Ukraine) in a dose of 50 mg/kg, silymarin (Silibor, tablets, 35 mg, FC Zdorovya, Ukraine) in a dose of 100 mg/kg were selected as comparison drugs. The experiments were carried out in accordance with the "General ethical principles of animal experiments" (Kyiv, 2001), which are consistent with the provisions of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Scientific Purposes" (Strasbourg, 1986 with amendments, 1998) [15]. Experimental data were also processed by parametric (Newman-Keuls) and non-parametric (Mann-Whitney) methods of variational statistics, using the Statistica 6.0 statistical software package, differences were considered statistically significant at $p<0.05$ [16].

3. Research results and their discussion

In the first series of experiments, the oxidant status of rat liver homogenate in vitro against the background of TCM administration [17] and the effect of the addition of extracts of corn silk, extracted with water and ethanol (30 %, 50 %, 70 %) on these indicators were studied.

According to the research results (Fig. 1), during the incubation of the liver homogenate in a buffer solution at a temperature of 37 °C, a significant accumulation of TBA-reactants (TBA-R) was observed, which indicates an intensive course of LPO processes.

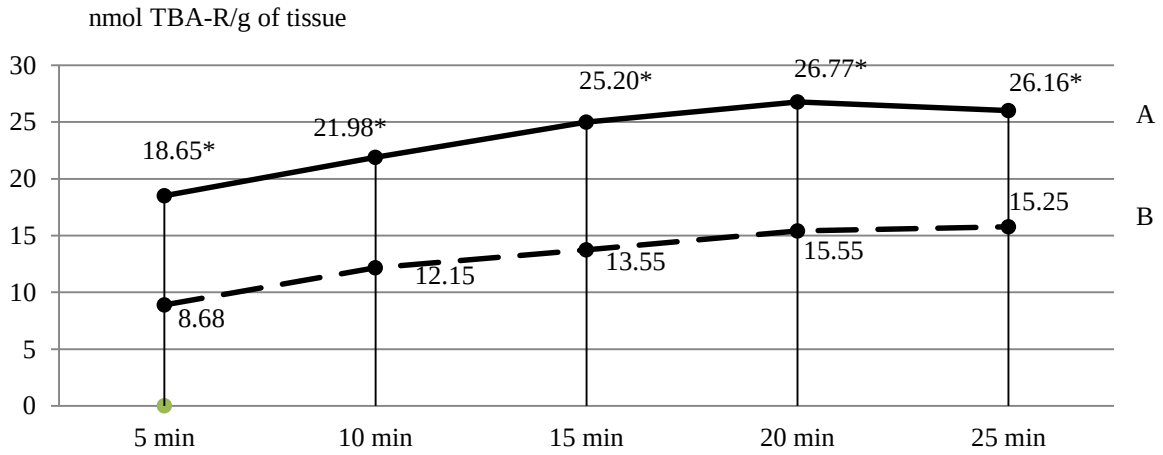

Fig. 1 Dynamics of TBA-R accumulation during incubation of rat liver homogenate (t 37 °C) with spontaneous and ascorbate-induced LPO, n=7: A – spontaneous LPO, B – ascorbate-induced LPO; * – the difference is significant relative to spontaneous LPO, $p<0.05$; n – the number of samples

At the same time, an increase in the content of TBA-R was observed during the first 20 minutes of incubation. After 20 minutes, the content of TBA-R did not change. This fact can be associated with the depletion of LPO substrates. It should be noted, that the accumulation of TBA-R was less pronounced when ascorbate, a powerful inducer of non-enzymatic LPO, was added to the incubation medium. Thus, the rate of accumulation of TBA-R with spontaneous LPO in the first 20 minutes of incubation was 0.54 nmol/l per 1 min, with ascorbate-induced – 0.46 nmol/l per 1 min.

The obtained data indicate the ability of the studied plant extracts to block LPO processes already in the first minutes after the start of incubation. Obviously, this is due to the presence of a significant amount of polyphenols, which are part of the investigated plant extracts. It is known from literary sources, that polyphenols are capable of binding active oxygen metabolites, which in the early stages are inducers of POL [18].

When adding to the medium of incubation the studied extracts of corn silk (ECSE 50 %, ECSE 30 %, ECSE, ECSE 70 %), in concentrations of 0.5 mg/g of liver, the content of TBA-reactants 20 minutes after the start of incubation was lower in comparison with control at 3.9; 3.1; 2.1; 2.4 times ($p<0.05$) respectively (Fig. 2) for spontaneous LPO and 3.5; 3.1; 2.2; 2.4 times ($p<0.05$) for acorbate-induced LPO (Fig. 3). At the same time, an increase in the content of TBA-reactants after 5 minutes of incubation was not observed both under the conditions of spontaneous and ascorbate-induced LPO.

The ability of experimental plant extracts to inhibit ascorbate-induced LPO may also be related to the binding of iron ions by polyphenols, which are necessary for the induction of LPO by ascorbate [19]. When extracts of corn silk, extracted with 50 % and 70 % ethanol in concentrations of 0.5 mg/g of liver were added to the incubation medium, a less pronounced accumulation of TBA-R was recorded ($p<0.05$) in comparison with the samples, to which this extract, received with water and ethanol 70 %, was added

When α-tocopherol was added to the incubation medium at a concentration of 0.5 mg/g of liver, the accumulation of TBA-R was also less pronounced ($p<0.05$) compared to the control group of animals, but more pronounced compared to incubation with the extract, received with 50 % ethanol in a concentration of 0.5 mg/g of liver. Thus, with spontaneous LPO, the content of TBA-R during the studied time (20 minutes) when α-tocopherol was added to the incubation medium was on average 1.3 times higher ($p<0.05$), and with ascorbate-induced LPO by 1.5 times higher ($p<0.05$) in comparison with the samples, to which 50 % ECCE was added.

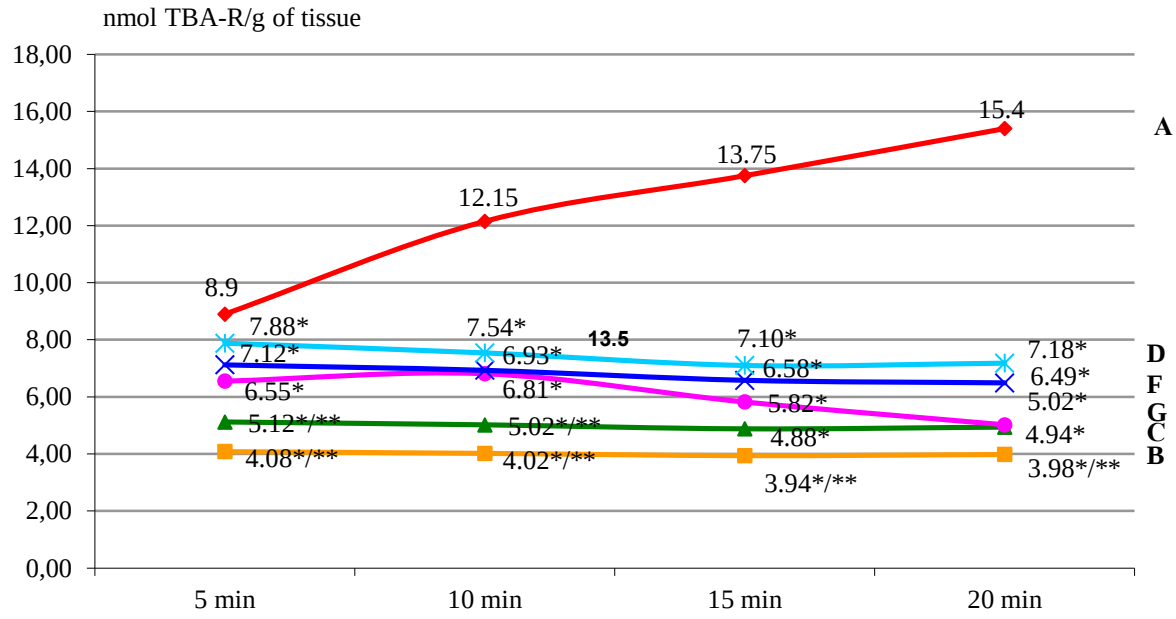

Fig. 2 Influence of extracts from corn silk and α-tocopherol on the course of spontaneous LPO during incubation of rat liver homogenate at t 37°C, n=7: A – control pathology, B – ECSE 50 %, C – ECSE 30 %, D – ACSE , F – ECSE 70 %, G – α-tocopherol); * – the difference is significant relative to the control pathology, p<0.05; ** – the difference is significant relative to α-tocopherol, p<0.05; n – number of samples

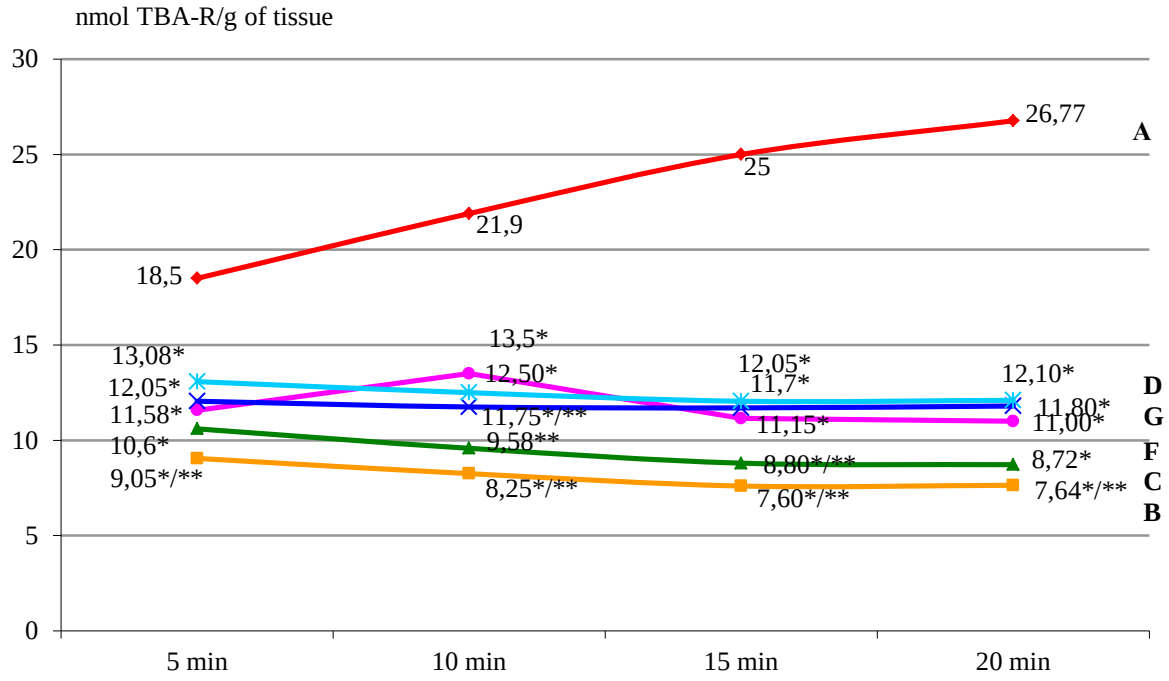

Fig. 3 Influence of extracts from corn silk and α-tocopherol on the course of ascorbate-induced LPO during incubation of rat liver homogenate at t 37 °C with the addition of ascorbate, n=7: A – control pathology, B – ECSE 50 %, C – ECSE 30 % , D – ACSE, F – ECSE 70 %, G – α-tocopherol); * – the difference is significant relative to the control pathology, p<0.05; ** – the difference is significant relative to α-tocopherol, p<0.05; n – the number of samples

Thus, the obtained data indicate that all the studied extracts are able to block both spontaneous and ascorbate-induced activation of LPO processes in vitro, which indicates their antioxidant properties. The most pronounced antioxidant activity was found in the extract from corn silk, extracted with 50 % ethanol.

Taking into account that the safety of potential medicinal products is one of the most important characteristics, the acute toxicity of 4 original plant extracts was studied at the next stage of experiments.

The results of the research are shown in Table 1.

Table 1

Indicator of acute toxicity after intragastric administration of extracts of corn silk, extracted with water and ethanol to sexually mature mice (n=7)

Animal group	Dose, mg/kg	Lost animals number	Survived animals number	Lethality, %
Intact control	–	0	7	0
ACSE	1000	0	7	0
	3000	0	7	0
	5000	0	7	0
ECSE 30 %	1000	0	7	0
	3000	0	7	0
	5000	0	7	0
ECSE 50 %	1000	0	7	0
	3000	0	7	0
	5000	0	7	0
ECSE 70 %	1000	0	7	0
	3000	0	7	0
	5000	0	7	0

Note. n – number of animals in the group

The results of the research showed that against the background of 14-day observation of experimental mice, since the administration of the studied extracts in doses of 1000 mg/kg, 3000 mg/kg and 5000 mg/kg, not a single animal died. The general condition and behavior of the animals of these groups did not differ from the intact control. Only in the first hours after the introduction of the studied extracts, the appetite of the animals decreased slightly compared to the intact control. However, at the end of the first day, normalization of the general condition of the experimental animals was recorded: they had a satisfactory appetite, skin of a normal color. During the entire period of observation, the animals were tidy, had a satisfactory appetite, responded adequately to sound and light stimuli, the processes of urination and defecation were normal, breathing disorders and convulsions were not observed, and no signs of intoxication were visually detected. The skin, motor and reflex excitability were normal. The results of the acute toxicity study of the considered plant extracts also indicate that the administration of a higher dose (>5000 mg/kg) was difficult, making it impossible to establish an average lethal dose for mice. According to the generally Accepted classification of toxicity by K.K. Sydorov, ACSE, ECSE 30 %, ECSE 50 % and ECSE 70 % can be attributed to the V class of toxicity [20].

In previous studies on the model of acute tetrachloromethane hepatitis in rats, it was established, that the investigated plant extracts from corn silk show antioxidant properties of varying degrees of severity, suppress the course of peroxide destructive processes, reduce the severity of cytolytic syndrome, and significantly improve the state of the own antioxidant system. In terms of antioxidant and anticytolytic activity, in conditions of acute oxidative stress, these extracts are superior to the reference drugs silibor and quercetin. As part of these studies, ECSE 50 % was selected, its conditionally effective dose was determined – 20 mg/kg, which became the subject of further experimental studies.

Tables 2–3 show data from the experimental studies of changes in the viability of Drosophila under the influence of 50 % ECSE.

The obtained data indicate that the magnitude and direction of changes in the general productivity indicator of Drosophila depend on the type of extraction and the concentration of 50 % ECSE in the nutrient medium. Thus, it was shown, that all tested concentrations of the extract did not have a significant toxic effect and did not have a significant influence on the output of Drosophila imago. Scientific papers [21] show the dependence of the Drosophila imago output on physical, chemical, and biological factors. Informative are the data on the study of 50 % ECSE on the overall productivity of Drosophila. All studied concentrations of the extract did not have a toxic effect, and concentrations of 10^{-3} and 10^{-1} mg/ml showed a pronounced stimulating effect, which was manifested in an increase in the total productivity of Drosophila by 22.91 % and 58.25 %, respectively, compared to the control. Based on the obtained data, further preclinical analysis of 50 % ECSE for mutagenicity is advisable – the ability of the tested substance and its metabolic products to induce gene mutations in Drosophila germ cells in accordance with WHO recommendations [22].

Table 2

The total productivity of Drosophila when cultivated in the environment, containing an extract from corn silk, extracted with 50 % ethanol (M±m)

50 % ECCE concentration, mg/ml	Imago output	Imago output	
		Females	Males
Control (0 mg/ml)	94.58±5.24	45.40±4.34	48.40±2.81
10^{-3} mg/ml	117.25±6.44*	59.25±2.66*	59.50±5.63
10^{-2} mg/ml	110.25±12.22	55.50±7.08	52.75±5.86
10^{-1} mg/ml	149.67±17.32*	77.67±10.84*	71.75±6.84*
1 mg/ml	91.25±11.81	48.50±5.57	41.55±6.58
10 mg/ml	92.00±11.7	48.50±6.83	43.60±5.19

*Note: * – difference from the control (p<0.05)*

Table 3

The total productivity of Drosophila when cultivated in the environment, containing an extract from corn silk, extracted with 50 % ethanol (M±m)

ECCE 50 % concentration, mg/ml	Imago output	Imago output	
		Females	
Control (0 mg/ml)	108.4±10.33	55.9±4.28	52.9±7.37
100 mg/ml	93.6±20.13	49.6±15.06	44.20±6.34
250 mg/ml	131.8±16.17*	73.2±9.27*	58.30±9.63

*Note: * – difference from the control (p<0.05)*

One of the stages of the preclinical study of the safety of the use of new pharmacological agents and auxiliary components of dosage forms is the study of their mutagenicity. This fragment of research involves the assessment of the drug's ability to induce various types of mutations. For the purpose of initial screening of possible mutagenicity of new pharmacological agents, experiments usually use short-term tests for gene mutation detection in microorganisms (Ames test), Drosophila fruit fly (detection of recessive, sex-linked lethal mutations or somatic mosaicism) or mammalian cell culture in vitro. If positive results are obtained at the second stage, the substance is subjected to research using mainly methods of accounting for mutations on somatic and germ cells of mammals and humans in order to identify the dose-effect relationship for the regulation of the studied genotoxicant [23].

A subsequent series of experiments evaluated the potential ability of 50 % ECSE (at a concentration of 250 mg/ml, previously identified as LD_{50}) and its metabolites to induce recessive, sex-linked, lethal mutations in Drosophila.

Research results (Table 4) show that using the test system Drosophila melanogaster Meig. in the test for accounting for recessive, sex-linked lethal mutations (Meller-5 method), 50 % ECSE, in a semi-lethal dose (250 mg/ml) and the products of its metabolism do not induce recessive, sex-linked lethal mutations

Table 4

Accounting for recessive, sex-linked, lethal mutations in Drosophila

50 %ECCE concentration, mg/ml	Analyzed cultures number F_2	Non-fertile males number F_2	Recessive lethal mutations		Significance level
			Number	%	
0 mg/ml	1000	31	8	0.83±0.29	p<0.95
250 mg/ml (LD_{50})	1000	13	3	0.30±0.18	

The next stage of the work was the study of the effect of 50 % ECSE on the bile-forming function of the liver in the conditions of tetrachloromethane hepatitis in rats. The experiment showed that an increase in the liver weight ratio in the control pathology group indicates the development of edema. A violation of the biliary secretory function of the liver was registered, as evidenced by a decrease in bile secretion by 40 % (p<0.05) and changes in the chemical composition of bile, in particular, a 2.2-fold increase in cholesterol content (p<0.05). Intrahepatic cholestasis is indicated by a 3.2-fold decrease in the cholate-cholesterol ratio compared to the intact control (Table 5).

Table 5

The effect of corn silk extract, received with ethanol 50 % (ECSE 50 %) on the bile-forming function of the liver against the background of TCM-induced hepatitis in rats (M±m), n=7

Animals group	Intact control	Control pathology	ECSE 50 %, 20 mg/kg	Quercetin, 50 mg/kg	Silibor, 100 mg/kg
LMC, g/100g	3.0±0.1	4.3±0.2 *	3.5±0.1 **	4.0±0.3 *	4.1±0.2 *
Bile secretion speed, ml/min·100^{-1}	1.00±0.07	0.60±0.05*	1.05±0.03**/α	0.67±0.06*/**	0.96±0.09**
Bile acids in bile mg/100g	532±35	353±48*	728±72 **/α/#	345±55*	584±81**
Cholesterol in bile, mg/100g	11.5±1.7	24.8±4.5*	12.3±3.3**/α	16.7±2.8**	15.1±1.9**
Cholate-cholesterol coefficient	51±6	16±1*	55±15 **/α	29±6*	41±7**

*Note: * – statistically significant differences relative to the intact control group, p<0.05; ** – statistically significant differences relative to the control pathology group, p<0.05; # – statistically significant differences relative to the silibor group, p<0.05; α – statistically significant differences relative to the quercetin group, p<0.05; n – the number of animals in the group*

As can be seen from the given data, ECSE 50 % at a dose of 20 mg/kg showed a pronounced protective effect on the hepatotoxicity of TCM. Its use led to a probable restoration of the bile-forming function of the liver against the background of tetrachloromethane hepatitis: in response to an increase in the cholesterol content (by 43 %, p<0.05), the content of bile acids increased 2 times (p<0.05), as a result of which cholate -cholesterol ratio approached the level of indicators of intact animals, the rate of bile secretion normalized. Based on the analysis of the results of the study, it can be concluded, that in terms of bile-forming and choleretic activity on the tetrachloromethane hepatitis model, ECSE 50 % was not inferior to silibor and superior to quercetin (p<0.05).

Prospects for further research are the creation of a new drug with hepatoprotective action.

4. Conclusions

1. Plant extracts of corn silk, extracted with water and ethanol, are able to effectively inhibit both spontaneous and ascorbate-induced LPO process in vitro, which indicates their antioxidant activity. The most pronounced antioxidant activity was found in the extract of corn silk, extracted with 50 % ethanol.

2. The studies of the acute toxicity of 4 original plant extracts of corn silk showed that, according to the generally Accepted toxicological classification of substances, when administered intragastrically to sexually mature mice, they belong to the V class of toxicity – practically harmless substances (LD_{50}>5000 mg/kg).

3. Cultivation of Drosophila on a medium with corn silk extract, received with 50 % ethanol did not have a toxic effect within all studied concentrations ($10\text{-}3^{-3}$, $10\text{-}2^{-2}$, $10\text{-}1^{-1}$, 1, 10, 50, 100 mg/ml), and in concentrations of $10\text{-}3^{-3}$ mg/ml and $10\text{-}1^{-1}$ mg/ml a pronounced stimulating effect is shown.

4. In the test of accounting for recessive, sex-linked lethal mutations using the Drosophila melanogaster Meig test system, it was established, that the extract of corn silk, received with 50 % ethanol, in a semi-lethal dose (250 mg/ml) and the products of its metabolism do not induce recessive, sex-linked lethal mutations.

5. Biologically active substances of corn silk affect not only the diffusion-filtration processes of the liver parenchyma, but also the biosynthesis and transport of its organic components, that is, they affect the bile-forming function.

Conflict of interest

The authors declare that they have no conflict of interest in relation to this research, including financial, personal, authorship, or any other nature that could affect the research and its results, presented in this article.

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References

1. Naboka, O. I., Khouari, S., Glushchenko, A. V., Georgiyants, V. A. (2014). Antioxidant properties of extracts of aerial part of Bupleurum aureum, hill-growing saltwort herb, Fumaria schleicheri and Cynara scolymus in vitro and in vivo. Journal of Chemical and Pharmaceutical Research, 6 (7), 172–177.

2. Kulkarni, S. R., Ravindra, K. P., Dhume, C. Y., Rataboli, P., Rodrigues, E. (2019). Levels of plasma testosterone, antioxidants and oxidative stress in alcoholic patients attending deaddiction centre. Biology and Medicine, 1 (4), 11–20.

3. Manach, C., Scalbert, A., Morand, C., Rémésy, C., Jiménez, L. (2004). Polyphenols: food sources and bioavailability. The American Journal of Clinical Nutrition, 79 (5), 727–747. doi: https://doi.org/10.1093/ajcn/79.5.727

4. Baraboi, V. A., Sutkovoi, D. A.; Zozuli, Iu. A. (Ed.) (1997). Okislitelno-antioksidantnyi gomeostaz v norme i patologii. Kyiv: Chernobylinterinform, 257.

5. Tkachenko, M. F., Kovalov, V. M., Kononenko, A. G., Maloshtan, L. M. (2009). Vivchennia flavonoidnogo skladu listkiv kukurudzi su-1. Zbirnik naukovikh pratc spivrobitnikiv NMAPO im. P. L. Shupika, 18, 497–502.

6. Vladimirov, Iu. A., Archakov, A. I. (1972). Perekisnoe okislenie lipidov v biologicheskikh membranakh. Moscow: Nauka, 252.

7. Khouari, S., Naboka, O. I. (2016). Toxicity of Bupleurum Aureum extracts in Drosophila melanogaster Meig. Study. Topical issues of new drugs development. Kharkiv: NUPh, 20.

8. Shkorbatov, Yu. H., Pasiuha, V. N., Shakyna, L. A., Hrabyna, V. A. et al. (2007). Vlyianye mahnytnoho polia y mykrovolnovoho yzluchenyia na zhyznesposobnost drozofyli. Dosiahnennia i problemy henetyky, selektsii ta biotekhnolohii. Zbirnyk naukovykh prats. Vol. 1. Kyiv: Lohos, 334–338.

9. Shkorbatov, Yu. H., Shakina, L. O., Pasiuha, V. M., Rybalchenko, T. V. (2010). Doslidzhennia vplyvu riznometalichnykh kompleksnykh spoluk na stan khromatynu v klitynakh liudyny i zhyttiezdatnist drozofily. Problemy ekolohichnoi ta medychnoi henetyky i klinichnoi imunolohii. Kyiv-Luhansk, 4, 354–364.

10. Zhuravlova, L., Strashniuk, V., Shakhbazov, V. (2004). Vplyv shchilnosti kultury na proiav efektu heterozysu u Drosophila melanogaster. Visnyk Lvivskoho universytetu. Biolohichna seriia, 35, 102–109.

11. Marchyshyn, S. M., Kovalova, Ye. O., Berdei, T. S. (2013). Vyvchennia zhovchohinnoi dii sukhoho ekstraktu travy chornobryvtsiv. Naukovo-tekhnichnyi prohres i optymizatsiia tekhnolohichnykh protsesiv stvorennia likarskykh preparativ. Ternopil: Ukrmedknyha, 373.

12. Arutiunian, A. V., Dubynyna, E. E., Zibyna, N. N. (2000). Metodi otsenky svobodnoradykalnoho okyslenyia y antyoksydantnoi systemi orhanyzma. Saint Petersburg: YKF «Folyant», 104.

13. Drohovoz, S. M., Hubskyi, Yu. I., Skakun, M. P., Kovalenko, V. M., Derymedvid, L. V.; Stefanov, O. V. (Ed.) (2001). Eksperymentalne vyvchennia zhovchohinnoi, kholelitiaznoi ta hepato-protektornoi aktyvnosti novykh likarskykh zasobiv. Doklinichni doslidzhennia likarskykh zasobiv. Kyiv, 334–351.

14. Kamyshnikov, V. S. (Ed.) (2013). Metody klinicheskikh laboratornykh issledovanii. Moscow: MEDpress-in form, 736.

15. European convention for the protection of vertebrate animals used for experimental and other scientific purpose (1986). Council of Europe 18.03.1986. Strasbourg, 52.

16. Lapach, S. N., Chubenko, A. V., Babich, P. N. (2001). Statisticheskie metody v mediko-biologicheskikh issledovaniiakh s ispolzovaniem Excel. Kyiv: Morin, 320.

17. Kononenko, A. G., Maloshtan, L. M., Tkachenko, M. F., Kovalov, V. M. (2009). Vivchennia gepatoprotektornoi aktivnosti ekstraktu listkiv kukurudzi v umovakh gostrogo tetrakhlormetanovogo gepatitu. Zaporozhskii meditcinskii zhurnal, 11 (5), 115–117.

18. Shkarina, E. I., Maksimova, T. V., Nikulina, I. N. et al. (2008). O vliianii biologicheski aktivnikh veshchestv na antioksidantnuiu aktivnost fitoprep-reparatov. Khimiko-farmatcevticheskii zhurnal, 35 (6), 40–47.

19. Kurkin, V. A. (2002). The flavonoids as the bioantioxidants. Polyphenols Communications 2002. Morocco, 285–286.

20. Sidorov, K. K. (1973). O klassifikatcii toksichnosti iadov pri parenteralnykh sposobakh vvedeniia. Toksikologiia novykh promyshl. khim. v-v. Moscow: Meditcina, 47–51.

21. Strashniuk, V. Yu., Shakina, L. O., Skorobahatko, D. O. (2014). Pat. No. 90336 UA. Sposib vyznachennia henotoksychnoi dii khimichnoho abo fizychnoho chynnyka. MPK (2013.01) G01N 33/554. № u201313929; declareted: 02.12.2013; published: 26.05.2014, Bul. No. 10, 4.

22. Otsenka mutahennosty novikh lekarstvennikh sredstv. Moscow, 20.

23. Rukovodstvo po kratkosrochnym testam dlia vyiavleniia mutagennykh i kantcerogennykh khimicheskikh veshchestv. Gigienicheskie kriterii sostoianiia okruzhaiushchei sredy (1989). Vsemirnaia organizatciia zdravookhraneniia. Zheneva, 212.

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Olga Naboka*, Doctor of Biological Sciences, Professor, Department of Biochemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Liliia Vyshnevska, Doctor of Pharmaceutical Sciences, Professor, Head of Department, Department of Pharmaceutical Technology of Drugs, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Inna Pasynchuk, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Olga Filiptsova, Doctor of Biological Sciences, Professor, Department of Cosmetology and Aromology, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Oksana Tkachenko, PhD, Associate Professor, Department of Biological Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

Olha Vislous, PhD, Assistant, Department of Medical Chemistry, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002

***Corresponding author**: Olga Naboka, e-mail: olganaboka2012@gmail.com*