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# METABOLIC EFFECTS OF GOUTWEED (AEGOPODIUM PODAGRARIA L.) PREPARATIONS IN RATS TREATED WITH A SINGLE DOSE OF ETHANOL

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***Abstract.*** The search of the herbal drugs exerting favourable metabolic effects and decreasing xenobiotics toxicity has intensified recently. This study addressed the influence of goutweed extract and tincture on carbohydrate and protein metabolism as well as uricemia and plasma enzymes activity in rats treated with a single dose of ethanol (9 g/kg intragastrically). For the 7 days before the animals received intragastrically the extract (100 mg/kg and 1 g/kg), the tincture (1 and 5 ml/kg), the reference drug fenofibrate (100 mg/kg), in the groups of the intact and untreated control drinking water was given. Basal glycemia was measured 7 h after ethanol administration, other values – after 8 h, in plasma of the anesthetized animals. Hypoglycemia was not manifested in ethanol-treated rats (and not caused by the studied drugs), but the tendency to the exhaustion of liver glycogen was seen. The tincture at both doses increased glycemia, while glycogen reserves did not undergo exhaustion, the changes in same direction were registered in rats receiving fenofibrate. Activity of enzymes in plasma in did not indicated cytolisis caused by ethanol. The extract (1 g/kg) reduced ALT activity, the tincture exerted a dose-dependent influence on γ-glutamyl transferase activity decreasing it at a dose of 5 ml/kg, the tincture and fenofibrate moderately increased ALP activity. Goutweed drugs did not induce unfavourable shifts in total protein, albumin, uric acid, and creatinine content (a moderate increase in urea level was seen in the groups receiving extract (100 mg/kg) and the tincture (5 ml/kg)). The results confirm the safety of goutweed preparations and substantiate the further study of their pharmacodynamics.

***Keywords:*** Aegopodium podagraria L., ethanol, rats, glycemia

Biologically active substances of herbal origin are able to decrease xenobiotics toxicity and exert a favourable influence in metabolic disorders. The drugs obtained from the aerial part of Aegopodium podagraria L. (goutweed, GW), namely the water extract and the tincture, are promising in this context as they demonstrate organoprotective activity reducing the effects of nephro- and hepatotoxins including ethanol [1–5]. Furthermore, these preparations normalize the disorders of carbohydrate, lipid, purine metabolism, which are pathogenetically important in the "diseases of civilization" [1,2,6,7], and the studies in ethanol-treated rats allowed clarifying the influence of GW preparations on the lipid exchange [4]. Taking into account the possible use of GW drugs in chronic diseases, their coadministration with ethanol is also of practical interest. It has been shown that GW extract reduces the duration of ethanol-induced narcosis in mice, it is able to counteract the negative metabolic effects of this agent in rats not causing hypoglycemia [3,8]. The influence of GW preparations on the carbohydrate metabolism and activity of marker enzymes in plasma of the ethanol-treated animals has not been described in detail and the changes of the protein and uric acid exchange have not been studied on this model.

Therefore, the objective of this research is to characterize the influence of Aegopodium podagraria L. extract and tincture on the values of carbohydrate and protein metabolism as well as activity of marker enzymes in plasma of the ethanol-treated rats.

***Materials and methods.***

All the experimental protocols were approved by the Bioethics Commission of the National University of Pharmacy and were in accordance with "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."

The model recommended for the investigation of ethanol-induced metabolic shifts was used [9]. Male rats with 190 to 230 g body weight were randomly divided into 7 groups (n=6–8 in each group) as follows:

intact control (IC),

ethanol (untreated);

ethanol + GW extract, 100 mg/kg intragastrically;

ethanol + GW extract, 1 g/kg intragastrically;

ethanol + GW tincture, 1 ml/kg intragastrically;

ethanol + GW tincture, 5 ml/kg intragastrically;

ethanol + fenofibrate, 100 mg/kg intragastrically.

Fenofibrate ("Tricor," Laboratoires Fournier Solvay Pharmaceuticals Group, France) was used as a recommended reference drug influencing on the pathogenesis of ethanol-induced metabolism disorders [9] at a dose of 100 mg/kg recommended for rats [10].

The animals were treated for 7 days, after this a single dose of ethanol (9 g/kg intragastrically as a 30% solution) was given. The rats of the IC group received the same volume of the drinking water. After 7 hours glycemia was determined in the samples obtained from a cut at the tip tail and after 8 hours, as recommended in [9], the rats were taken out of the experiment under barbiturate-induced anaesthesia, blood heparinized plasma was separated. Liver samples were taken from which glycogen was isolated through precipitation with ethanol after alkaline hydrolysis, and determined as glucose after acid hydrolysis as described in [6]. Glucose concentration in plasma samples was determined using the glucose oxidase method, total protein concentration – by biuret method, albumin level – by the bromcresol green procedure, creatinine – by Jaffe reaction, uric acid – by the enzymatic method, urea – by the reaction with diacetyl monooxime. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity was determined according to the method of Reitman and Frankel and De Ritis ratio was calculated. Alkaline phosphatase (ALP) was assayed by measurement of the amount of phenol liberated from the hydrolysed substrate, gamma-glutamyl transferase (γ-GT) activity – by the kinetic method using γ-L-glutamyl-3-carboxy-4-nitroanilide as a substrate and glycylglycine as an acceptor. Commercially-available kits from Filisit-Diagnostika (Ukraine) and Erba Lachema s.r.o. (Czech Republic) were used.

Medians, 25% and 75% percentiles (upper and lower quartiles) were calculated as well as arithmetic means and their standard errors (M±m). The comparison of the central tendencies of independent samples was performed by the Mann-Whitney U-criterion. To determine the relationship between the individual parameters, the Spearman's correlation coefficient of ρ was used.

***Results and discussion.***

Ethanol did not cause hypoglycemia during the observation period, on the contrary, a tendency towards the increase in basal blood glucose level was seen in the untreated group (Table 1), while this value under the conditions of anaesthezia did not change significantly.

Table 1.

Influence of goutweed preparations and fenofibrate on carbohydrate metabolism values in ethanol-treated rats and Spearman's correlation coefficients of ρ between the biochemical parameters (n=6–8), M±m; $Q_{50}$ ($Q_{25}$–$Q_{75}$)

| Indices | | Intact control | Ethanol (untreated) | GW extract, 100 mg/kg, + ethanol | GW extract, 1 g/kg, + ethanol | GW tincture, 1 ml/kg, + ethanol | GW tincture, 5 ml/kg, + ethanol | Fenofibrate, 100 mg/kg, + ethanol |
|---|---|---|---|---|---|---|---|---|
| Basal glycemia, mmol/l | | 3.80±0.27<br>**3.80**<br>(3.30–4.15) | 4.70±0.45<br>**4.45**<br>(3.98–4.98) | 4.53±0.55<br>**4.05**<br>(3.70–5.38) | 4.71±0.40^<br>**4.70**<br>(3.85–5.50) | 5.55±0.27**<br>*#<br>**5.30**<br>(5.20–6.08) | 5.32±0.43*<br>**5.70**<br>(5.08–5.88) | 5.75±0.28**<br>*#<br>**5.75**<br>(5.18–6.18) |
| Glycemia in anaesthetized rats, mmol/l | | 7.42±0.33<br>**7.77**<br>(7.10–7.90) | 7.85±0.59<br>**8.07**<br>(6.62–8.94) | 6.41±0.40^<br>**5.85**<br>(5.80–7.21) | 8.19±0.43<br>&<br>**8.28**<br>(7.59–8.65) | 9.12±0.37**<br>*<br>**8.97**<br>(8.51–9.55) | 8.14±0.40<br>**8.20**<br>(7.56–8.97) | 8.31±0.57<br>**8.06**<br>(7.94–8.50) |
| Liver glycogen, mg/g | | 18.3±5.81<br>**15.9**<br>(6.74–22.4) | 11.7±3.46<br>**6.90**<br>(4.98–15.8) | 9.96±3.05^<br>**6.84**<br>(5.99–14.7) | 13.9±2.64<br>**12.4**<br>(11.4–18.8) | 17.4±2.69<br>**19.4**<br>(12.6–22.0) | 17.6±2.87<br>**19.3**<br>(13.8–22.7) | 22.6±2.30<br>**20.7**<br>(19.9–20.9) |
| Coefficients of correlation | liver glycogen – plasma glucose | **+0.54**<br>NS | **+0.25**<br>NS | **1.0** | **–0.71**<br>NS | **+0.26**<br>NS | **+0.83**<br>p<0.05 | **–0.40**<br>NS |
| | Liver triglycerides–liver glycogen | **–0.57**<br>NS | **–0.18**<br>NS | **+0.09**<br>NS | **+0.90**<br>p<0.05 | **+0.90**<br>p<0.05 | **+0.50**<br>NS | **+0.38**<br>NS |
| | Liver cholesterol–liver glycogen | **–0.50**<br>NS | **–0.02**<br>NS | **–0.26**<br>NS | **–0.66**<br>NS | **–0.94**<br>p<0.05 | **–0.50**<br>NS | **–0.35**<br>NS |

*Note.* * – p<0.05 compared to intact control; *** – p<0.01 compared to intact control; # – p<0.05 compared to the untreated group receiving ethanol; ^ – p<0.05 compared to the group receiving fenofibrate; & – p<0.05 compared to the group receiving the extract at a dose of 100 mg/kg. NS – not significant. GW – goutweed. Medians are highlighted in bold.

It is noted that there is considerable inconsistency in the literature for the changes in glucose metabolism induced by ethanol (since different species, time intervals, doses etc. are used) [11,12]. Our data indicating the decreased glycogen reserves with glycemia unchanged are in accordance with the continuum described in [11]: after acute ethanol administration under fed or short-term fasted conditions hypoglycemia does not develop due to the stimulation of hepatic glycogenolysis and a depletion of glycogen reserves evolves because of the inhibition of gluconeogenesis (through the suppression of de novo synthesis of glucose from glycerol and from alanine, while gluconeogenesis from pyruvate is unaltered or even elevated) [11,13]. These changes are the consequence of the oxidative metabolism of alcohol via alcohol dehydrogenase with the increment in the $NADH/NAD^+$ ratio, also leading to the increase in acetate quantity and intensified synthesis of fatty acids as well as cholesterol while their utilization and transport are suppressed [11]. These changes result in the accumulation of lipids in the liver and a significant elevation of liver triglycerides and cholesterol was registered in our study [4].

GW extract did not change the studied carbohydrate metabolism values (Table 1). The influence on glycemia in anaesthetized rats appeared to be dose-dependent with its higher level against the background of a dose of 1 g/kg. Glycogen content in the liver did not differ between the untreated animals and rats receiving the extract, but the direction of the relationship between glycemia and glycogen changed with the increase in the dose, and at a dose of 1 g/kg higher glycemia was seen in animals with the most exhausted glycogen reserves.

It has been shown that the extract (in contrast to the tincture) at a dose of 1 g/kg, but not 100 mg/kg, significantly reduces the duration of ethanol-induced narcosis in mice [8] and this effect could be associated with the favourable influence on metabolic processes in the liver. The data obtained in the present study do not directly support this concept, although the absence of hypoglycemia and glycogen exhaustion under the influence of the effective dose of 1 g/kg might be favourable for CNS functioning in an intoxication by ethanol.

Hypoglycemic effect of GW tincture (that is dose dependent and also depends on the model used) [3,6,7] was not manifested in ethanol-treated rats. On the contrary, in animals receiving the tincture at both doses blood glucose was higher than in the intact rats (and at a low dose basal glycemia was also higher than in the untreated group, Table 1). Since hypoglycemia is a generally known consequence of ethanol intoxication, these properties of the tincture might be advantageous. Besides, a regulatory mode of action on carbohydrate metabolism may be supposed: hypoglycemic activity of the tincture is seen in dexamethasone-treated rats [6] with the upregulated gluconeogenesis and increase in blood glucose occurs in ethanol treated animals, in which this process is suppressed, as discussed above (still further verification is needed).

Glycogen content in the liver was maintained, being higher than in the untreated group (the absence of statistical significance is connected with inter-individual differences of this value). There was no dose-dependence in the effects of the tincture, except for the strengthening of the relationship between glycemia and glycogen (approximating it to the intact control value) with the increment in the dose. At the same time, its normalizing influence in regard to the lipid metabolism in the liver increased with the dose [4].

Inverse relationship between liver triglyceride content and liver glycogen content (associated with insulin resistance) was registered in high-fat-fed rats [14]. In mice chronically affected by ethanol, it also has been shown that glycogen metabolism changes are closely linked to ethanol-induced liver injury and fatty liver formation [15] The authors of this work substantiate that during the fed state acetyl-CoA generated from ethanol mainly goes to the lipid synthesis pathway as glycogen synthesis from glucose formed within the liver is inhibited by ethanol. Furthermore, it appeared possible to prevent hepatic steatosis by elevation of liver glycogen content (through overexpression of protein phosphatase 1 R3G inhibiting glycogen phosphorylase) thus reducing glucose usage for lipogenesis. A link in this process is realized through the restoration of PPARα signaling pathway [15]. PPARα activator fenofibrate under the conditions of our study counteracted the increase in liver triglycerides level as reported in [4] (still the data concerning PPARα agonists efficacy in regards to hepatic steatosis are controversial [16,17]). The decrease of lipids accumulation in the liver of fenofibrate-treated rats was accompanied with the maintenance of relatively high glycogen reserves and glycemia (Table 1). The similar changes were seen in animals receiving GW tincture. In the mentioned groups there was a change in the direction of the relationship between liver triglycerides and glycogen content. The inverse (albeit moderate) relationship between these parameters was seen in intact rats (Table 1), in contrast to the data in [14], the reason for this inconsistency may be in the differences between fed and food-deprived animals in accordance with the period of the studies. The correlation between liver cholesterol and glycogen was restored under the influence of GW drugs, except for the extract at a low dose. The reference drug showed the similar tendency not reaching the level of significance.

Our results do not allow elucidating the molecular mechanisms of GW preparations action. It can be noted that PPARα agonists (selective or PPARα+γ agonists, such as flavonoids) are found among the substances of herbal origin [18], where-

in the other sites of action are also possible, as discussed in [4,6].

Proceeding from the enzymes activity in plasma (Table 2), no signs of severe damage of hepatocytes were evident in the untreated group. Indeed, acute use of ethanol might not result in increased fermentemia (such situation was even confirmed clinically [19]). γ-GT activity tended to increase (Table 2) but it was characterized by high inter-individual variability. The positive interrelation between γ-GT and ALT activity inherent in intact control group ($\rho = +0.82$; $p<0.05$) disappeared in all groups treated with ethanol, this might indicate the early phase of hepatocytes injury with the beginning of γ-GT leakage while the transaminases (being not membrane-localized) were still unchanged. The tincture exerted a dose-dependent influence on γ-GT activity (the effective dose was also capable of preventing lipids accumulation in the liver [4]), the extract decreased it only at a low dose (significant when compared to fenofibrate group). γ-GT is also known to participate in prooxidative/ antioxidant processes, which are changed by ethanol, but we have not directly addressed them.

As seen in Table 2, the tincture did not change ALT activity, AST activity and de Ritis ratio. GW extract dose-dependently decreased ALT activity with the corresponding changes in De Ritis ratio (previously briefly reported in [3]) and elimnated the significant correlation between the activity of AST and ALT (ρ equalled +0.46 compared with +0.97 ($p<0.05$) in the untreated group

Table 2.

Influence of goutweed preparations and fenofibrate on the activity of enzymes in blood plasma of the ethanol-treated rats (n=6–8), M±m; $Q_{50}$ ($Q_{25}$–$Q_{75}$)

| Indices | Intact control | Ethanol (untreated) | GW extract, 100 mg/kg, + ethanol | GW extract, 1 g/kg, + ethanol | GW tincture, 1 ml/kg, + ethanol | GW tincture, 5 ml/kg, + ethanol | Fenofibrate, 100 mg/kg, + ethanol |
|---|---|---|---|---|---|---|---|
| AST activity, μcat/l | 1.06±0.03<br>**1.03**<br>(1.00–1.08) | 1.18±0.12<br>**1.11**<br>(0.96–1.16) | 1.00±0.06<br>**0.99**<br>(0.87–1.07) | 1.03±0.04<br>**1.06**<br>(1.00–1.10) | 1.21±0.08<br>**1.14**<br>(1.11–1.34) | 1.12±0.08<br>**1.21**<br>(0.99–1.22) | 1.13±0.07<br>**1.21**<br>(1.02–1.22) |
| ALT activity, μcat/l | 0.60±0.06<br>**0.59**<br>(0.51–0.70) | 0.79±0.25<br>**0.57**<br>(0.46–0.80) | 0.50±0.14^<br>**0.43**<br>(0.39–0.48) | 0.37±0.03**<br>^^^<br>**0.36**<br>(0.31–0.39) | 0.77±0.10<br>**0.83**<br>(0.65–0.98) | 0.72±0.17<br>**0.74**<br>(0.51–0.86) | 0.90±0.09*<br>**0.87**<br>(0.85–1.07) |
| De Ritis ratio | 1.88±0.20<br>**1.84**<br>(1.56–2.03) | 1.94±0.27<br>**1.83**<br>(1.47–2.36) | 2.61±0.66^<br>**2.23**<br>(2.05–2.48) | 2.84±0.23**#^<br>^^<br>**2.76**<br>(2.47–3.17) | 1.69±0.20<br>**1.53**<br>(1.44–1.72) | 1.91±0.42<br>**1.63**<br>(1.42–1.95) | 1.30±0.13*<br>**1.13**<br>(1.13–1.45) |
| ALP activity, μcat/l | 5.94±0.55<br>**6.19**<br>(4.93–7.10) | 7.08±0.94<br>**5.73**<br>(5.28–8.96) | 8.26±1.48^<br>**6.62**<br>(5.89–9.24) | 8.01±1.41<br>**7.17**<br>(5.32–10.3) | 10.4±1.48*<br>**9.98**<br>(9.16–11.7) | 8.75±1.58<br>**9.73**<br>(5.66–11.7) | 15.3±3.21***#<br>**15.4**<br>(8.34–21.1) |
| γ-GT activity, μcat/l | 0.023±0.01<br>**0.011**<br>(0.009–0.036) | 0.030±0.004<br>**0.035**<br>(0.022–0.035) | 0.024±0.01^<br>**0.020**<br>(0.017–0.025) | 0.031±0.01<br>**0.031**<br>(0.017–0.039) | 0.048±0.01<br>**0.044**<br>(0.044–0.052) | 0.024±0.004$<br>**0.026**<br>(0.023–0.026) | 0.038±0.01<br>**0.031**<br>(0.026–0.044) |

*Note.* * – $p<0.05$ compared to intact control; ** – $p<0.02$ compared to intact control; *** – $p<0.01$ compared to intact control; # – $p<0.05$ compared to the untreated group receiving ethanol; ^ – $p<0.05$ compared to the group receiving fenofibrate; ^^^ – $p<0.01$ compared to the group receiving fenofibrate; $ – $p<0.05$ compared to the group receiving the tincture at a dose of 1 ml/kg. GW – goutweed. Medians are highlighted in bold

and +0.66 in the intact control). The opposite change in ALT activity under the influence of fenofibrate was also accompanied with the elimination of the significance of AST–ALT correlation. Besides, the reference drug increased ALP activity, that is an unexpected result given the known ability of fibrates to reduce this value in clinics [20]. However, there are experimental data supporting our findings: increased transaminases activity was seen in the serum of rats receiving fenofibrate at the dose used in our study (still these data were obtained in spontaneously hypertensive rats expressing human C-reactive protein [21]); increment of ALP activity in the serum was also seen in hyperlipidemic mice treated with this drug at a dose of 40 mg/kg [22]. At the same time, fenofibrate did not show significant influence on γ-GT activity in plasma (Table 2). The tincture at a high dose also increased ALP activity, while in the other groups of the treated rats this elevation was not significant.

Total protein and albumin level in plasma remained practically unchanged in all of the experimental groups (Table 3), that is consistent with the data confirming the unaltered protein metabolism in acute ethanol exposure [23]. A decrease in albumin content was registered only against the background of the tincture at a dose of 5 ml/kg. Urea level tended to reduction in the untreated rats receiving ethanol and increased under the influence of the tincture at a dose of 5 ml/kg but not 1 ml/kg. The influence of the extract on blood urea level

appeared to be dose-dependent (increment was seen at a low dose). It has been shown in vitro and ex vivo [12,23] that ethanol is able to suppress urea synthesis by the liver. GW drugs might counteract this suppression or influence aminoacid catabolism directly. Renal origin of the changes in plasma urea level are possible but hardly believable proceeding from the extract pharmacodynamics.

The stability of plasma creatinine concentration indicates the absence of the severe disorders of the kidney function in all groups. That is in accordance with the data [24] concerning the absence of nephrotoxicity of ethanol even at doses considered as hepatotoxic. Fibrates are able to increase serum urea and creatinine levels [20], but such changes were not evident in our study, while GW preparations tended to reduce creatininemia. It is well known and clinically confirmed that fenofibrate significantly lowers uricemia, this effect is independent of any changes in lipid metabolism and partially realized through enhanced renal urate excretion [20]. This ability was clearly seen in ethanol-treated rats (Table 3), while in the other groups uricemia did not change significantly. It has been established before that GW preparations do not cause the shifts in blood uric acid level of the normouricemic animals (while normalize purine metabolism in its disorders) [1].

Table 3.

Influence of goutweed preparations and fenofibrate on the biochemical marker in blood plasma of the ethanol-treated rats (n=6–8), , M±m; $Q_{50}$ ($Q_{25}$–$Q_{75}$)

| Indices | Intact control | Ethanol (untreated) | GW extract, 100 mg/kg, + ethanol | GW extract, 1 g/kg, + ethanol | GW tincture, 1 ml/kg, + ethanol | GW tincture, 5 ml/kg, + ethanol | Fenofibrate, 100 mg/kg, + ethanol |
|---|---|---|---|---|---|---|---|
| Urea, mM/l | 2.28±0.24<br>**2.33**<br>(1.77–2.67) | 1.81±0.18<br>**1.98**<br>(1.47–2.16) | 3.44±0.40*##^^<br>**3.10**<br>(2.95–3.64) | 2.24±0.31&&<br>**1.98**<br>(1.68–2.63) | 2.31±0.23<br>**2.33**<br>(1.88–2.65) | 2.70±0.35#<br>**2.63**<br>(2.18–3.10) | 2.15±0.15<br>**2.07**<br>(2.03–2.19) |
| Total protein, g/l | 52.4±1.92<br>**50.6**<br>(48.8–54.3) | 51.1±1.00<br>**51.6**<br>(49.4–52.1) | 53.5±2.08<br>**51.5**<br>(49.7–55.7) | 49.8±1.12<br>**49.5**<br>(48.2–51.0) | 50.1±0.47<br>**50.7**<br>(49.3–50.8) | 50.0±0.69<br>**50.3**<br>(49.8–50.9) | 49.6±0.75<br>**49.9**<br>(49.5–50.1) |
| Albumin, g/l | 28.0±1.85<br>**26.6**<br>(25.7–30.9) | 24.7±1.68<br>**23.8**<br>(22.1–27.4) | 25.3±1.65<br>**24.6**<br>(23.6–27.4) | 25.6±1.46<br>**26.6**<br>(23.3–27.9) | 25.6±1.26<br>**24.7**<br>(24.3–26.9) | 20.4±2.58*<br>**19.5**<br>(15.3–24.2) | 25.3±0.47<br>**25.4**<br>(25.0–25.7) |
| Uric acid, mM/l | 0.067±0.004<br>**0.068**<br>(0.061–0.070) | 0.081±0.006<br>**0.082**<br>(0.069–0.088) | 0.078±0.007^^^<br>**0.068**<br>(0.066–0.085) | 0.069±0.006^^<br>**0.063**<br>(0.059–0.073) | 0.074±0.005^^^<br>**0.068**<br>(0.068–0.070) | 0.080±0.009^^^<br>**0.073**<br>(0.064–0.094) | 0.054±0.002*#<br>**0.054**<br>(0.054–0.054) |
| Creatinine, μM/l | 58.5±1.57<br>**56.0**<br>(56.0–61.6) | 83.0±11.9<br>**82.1**<br>(56.0–97.0) | 62.6±4.38<br>**63.4**<br>(57.9–63.4) | 63.4±7.81<br>**56.0**<br>(48.5–74.6) | 65.1±7.96<br>**59.7**<br>(55.6–74.6) | 56.0±5.78<br>**56.0**<br>(50.4–67.2) | 69.4±6.42<br>**70.9**<br>(63.4–78.4) |

*Note.* * – p<0.05 compared to intact control; # – p<0.05 compared to the untreated group receiving ethanol; ## – p<0.01 compared to the untreated group receiving ethanol;
^^ – p<0.02 compared to the group receiving fenofibrate; ^^^ – p<0.01 compared to the group receiving fenofibrate; && – p<0.02 compared to the group receiving the extract at a dose of 100 mg/kg. GW – goutweed. Medians are highlighted in bold.

**Conclusions and further prospects of the research in the discussed direction.** The obtained data lead to the conclusions as follows:

A single dose of ethanol (9 g/kg intragastrically) did not induce hypoglycemia after 8 hours, but the tendency to the exhaustion of liver glycogen was seen. Goutweed tincture (1 and 5 ml/kg) increased glycemia, while glycogen reserves did not undergo exhaustion, the changes in same direction were seen under the influence of the reference drug fenofibrate. Ethanol at the investigated term did not cause a significant elevation of the activity of marker enzymes in plasma. Goutweed extract (1 g/kg) reduced plasma ALT activi-

ty, goutweed tincture as well as fenofibrate increased plasma ALP activity and exerted a dose-dependent influence on γ-GT activity decreasing it at a dose of 5 ml/kg.

Proceeding from the total protein, albumin, uric acid, and creatinine content in plasma, all of the investigated goutweed preparations did not show a negative influence on protein and purine metabolism as well as excretory kidney function in ethanol-treated rats. The extract (100 mg/kg) and the tincture (5 ml/kg) moderately increased plasma urea concentration that might be associated with the metabolic shifts.

Further in-depth study of GW preparations mechanisms of actions as well as possibility of their combined use with the conventional drugs is expedient.

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**МЕТАБОЛИЧЕСКИЕ ЭФФЕКТЫ ПРЕПАРАТОВ СНЫТИ ОБЫКНОВЕННОЙ (AEGOPODIUM PODAGRARIA L.) У КРЫС НА ФОНЕ ОДНОКРАТНОГО ВВЕДЕНИЯ ЭТАНОЛА.**

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***Резюме.*** Возрастает интерес к фитопрепаратам с благоприятными метаболическими эффектами, способных уменьшать токсичность ксенобиотиков. В настоящей работе изучено влияние экстракта и настойки сныти обыкновенной на углеводный и белковый обмен, а также урикемию и активность ферментов в плазме крови крыс, которым однократно вводили этанол (9 г/кг внутрижелудочно). В течение 7 дней до этого животные получали внутрижелудочно экстракт (100 мг/кг и 1 г/кг), настойку (1 и 5 мл/кг), препарат сравнения фенофибрат (100 мг/кг), крысам групп интактного контроля и модельной патологии вводили питьевую воду. Определяли базальную гликемию – через 7 ч после введения этанола, другие показатели – через 8 ч, в плазме наркотизированных животных. Гипогликемия на фоне этанола не развивалась (исследуемые препараты также ее не вызывали), однако проявлялась тенденция к исчерпанию резервов гликогена печени. Настойка в обоих дозах повышала гликемию, истощения резервов гликогена при этом не происходило, изменения такой же направленности зарегистрированы у крыс, получавших фенофибрат. Активность ферментов в плазме крови не указывала на развитие цитолиза на фоне этанола. Экстракт (1 г/кг) уменьшал активность АлАТ, настойка оказывала дозозависимое влияние на активность γ-глутамилтрансферазы, снижая ее в дозе 5 мл/кг, настойка и фенофибрат умеренно увеличивали активность щелочной фосфтазы. Препараты сныти не вызывали неблагоприятных сдвигов уровня общего белка, альбуминов, мочевой кислоты, креатинина (умеренное повышение содержания мочевины наблюдали в группах, получавших экстракт (100 мг/кг) и настойку (5 мл/кг)). Результаты подтверждают безопасность препаратов сныти и обосновывают целесообразность дальнейшего изучения их фармакодинамики.

***Ключевые слова:*** Aegopodium podagraria L., этанол, крысы, гликемия

**МЕТАБОЛІЧНІ ЕФЕКТИ ПРЕПАРАТІВ ЯГЛИЦІ ЗВИЧАЙНОЇ (AEGOPODIUM PODAGRARIA L.) У ЩУРІВ НА ТЛІ ОДНОРАЗОВОГО ВВЕДЕННЯ ЕТАНОЛУ.**

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***Резюме.***Зростає інтерес до фітопрепаратів із сприятливими метаболічними ефектами, здатних зменшувати токсичність ксенобіотиків. У даній роботі досліджено вплив екстракту та настойки яглиці звичайної на вуглеводний та білковий обмін, а також урикемію та активність ферментів плазми крові щурів, яким одноразово вводили етанол (9 г/кг внутрішньошлунково). Протягом 7 днів до цього тварини одержували внутрішньошлунково екстракт (100 мг/кг та 1 г/кг), настойку (1 та 5 мл/кг), препарат порівняння фенофібрат (100 мг/кг), щурам груп інтактного контролю та модельної патології вводили питну воду. Базальну глікемію визначали за 7 год після введення етанолу, інші показники – через 8 год (у плазмі наркотизованих тварин). Гіпоглікемія не була наявною на тлі етанолу (досліджувані препарати також жо неї не призводили), однак виявлялася тенденція до вичерпання резервів глікогену печінки. Настойка в обох дозах підвищувала глікемію, тимчасом як виснаження резервів глікогену не відбувалося, зміни такої спрямованості зареєстровано також у щурів, що одержували фенофібрат. Активність ферментів у плазми крові не вказувала на розвиток цитолізу на тлі етанолу. Екстракт (1 г/кг) зменшував активність АлАТ, настойка чинила дозозалежний вплив на активність γ-глутамілтрансферази зі зменшенням її в дозі 5 мл/кг, настойка та фенофібрат помірно збільшували активність лужної фосфатази. Препарати яглиці не спричиняли несприятливих зсувів рівня загального білка, альбумінів, сечової кислоти, креатиніну (помірне підвищення вмісту сечовини спостерігали в тварин на тлі екстракту (100 мг/кг) та настойки (5 мл/кг)). Результати підтверджують безпечність препаратів яглиці та обґрунтовують доцільність подальшого вивчення їх фармакодинаміки.

***Ключові слова:*** Aegopodium podagraria L., етанол, щури, глікемія.

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