THE HYPOLIPIDEMIC ACTIVITY OF POTERIUM SANGUISORBA L.

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Atherosclerosis is recognized as "non-infectious pandemic of the XXI-th century". There is a wide range of drugs for correction of hyperlipidemia, as well as for the primary and secondary prevention of atherosclerosis complications. However, all known lipid-lowering drugs have many side effects. Herbal medicines have several advantages over synthetic monodrugs. In particular, due to the complex and balanced chemical composition and the rational combination of biologically active substances they have multifaceted effects on the body: on the one hand, they affect directly on the diseased area, and on the other hand, provide pharmacological correction of various functional systems. In this regard it is interesting to study triterpenoid compounds isolated from the plant material, which have a wide range of pharmacological activities, including the lipid-lowering effect. The aim of this study was to assess the lipid-lowering properties of the ethanol extract from Poterium sanguisorba L. (burnet salad) containing triterpenoid compounds in the underground part of the plant. The ethanol extract of Poterium sanguisorba L. underground part was studied for the hypolipidemic activity in the acute model of hyperlipidemia induced by injecting a single dose of Tween-80 (250 mg/kg) intraperitoneally to rats. In 8 h the blood samples were taken, and the level of hyperlipidemia was assessed. Daily white mature Wistar rats were orally treated with the extract in two doses: 100 mg/kg and 250 mg/kg for 7 days, the last injection was together with Tween-80. As a reference drug nicotinic acid (30 mg/kg) was used. At the end of the study the serum levels of the total cholesterol, triglycerides and the total lipids were measured. Determination was performed using enzymatic methods. The results of the study conducted have confirmed the hypolipidemic activity of Poterium sanguisorba L. extract under conditions of acute hyperlipidemia.

Atherosclerosis is the traditionally known consequence of the lipid metabolism disorders (dyslipidemia, hyperlipidemia, hypertriglyceridemia) and reduction of the elasticity of vessels of different caliber [4]. Hyperlipidemia is the major risk factor for atherosclerosis. Other complications are coronary heart disease, ischemic cerebrovascular disease, hypertension, obesity and diabetes mellitus (Type II). Although many effective lipid-lowering synthetic drugs exist, none is effective for all lipoprotein disorders, and all of them are associated with some adverse effects. Therefore, it is a need of the day to search other products from natural sources that are less toxic, less expensive, and can provide better safety and efficacy when using. Natural products from plants are a rich source used for centuries to cure various ailments [12].

Today, a lipid-lowering therapy uses a wide range of drugs (statins, fibrates, cholesterol absorption inhibitors, niacin drugs) for correction of hyperlipidemia, as well as the primary and secondary prevention of atherosclerosis complications [5]. The known lipid-lowering drugs have many side effects in patients [11].

Herbal medicines have several advantages over synthetic monodrugs. In particular, due to the complex and balanced chemical composition and the rational combination of biologically active substances they have multifaceted effects on the body: on the one hand, they affect directly on the diseased area, and on the other hand, provide pharmacological correction of various functional systems [3, 13]. In this regard it is interesting to study triterpenoid compounds isolated from the plant material, which have a wide range of pharmacological activities, including the lipid-lowering effect [1, 10]. The Rosaceae family includes such interesting species as Poterium polygamum Waldst. Et Kit., P. sanguisorba L., P. lasioicarpum Boiss. Et Haukskn., which are widespread in Ukraine. Such triterpenoids as caccigenin, poteriside and tormentoside are contained in the underground part of these plants [6].

The aim of this study was to assess the antihyperlipidemic properties of the ethanol extract of P. sanguisorba L. (burnet salad) on the model of acute hyperlipidemia.

Materials and Methods

Only male albino Wistar rats weighing 200-220 g were used in this study. They were acclimatized under laboratory conditions. Animals were fed on a standard diet and water ad libitum. Thirty animals were distributed into 5 groups (six rats in each group): Group 1 – control rats, group 2 – intact rats, group 3 – standard rats, group 4-5 – test rats.

P. sanguisorba L. rhizomes were collected in the Zaporizhzhia region, dried under shade, powdered and extracted with 96% ethanol in a Soxhlet extractor. The extract was concentrated using a vacuum evaporator, and the extract residue was stored at 4°C in refrigerator for further use.
The effect of *Poterium sanguisorba* L. extract on plasma lipids on the acute model of hyperlipidemia

| Group                  | Total cholesterol (mmol/l) | Triglycerides (mmol/l) | Total lipids (g/l) |
|------------------------|-----------------------------|------------------------|--------------------|
| Intact rats            | 1.19±0.002*                 | 0.26±0.004**           | 6.56±0.209**       |
| % to control rats      | 86.86%                      | 66.66%                 | 73.29%             |
| Control group          | 1.37±0.064                  | 0.39±0.02              | 8.95±0.234         |
| PSE 100 mg/kg          | 1.12±0.075*                 | 0.28±0.003**           | 5.2±0.624**        |
| % to control rats      | 81.75%                      | 71.79%                 | 58.10%             |
| PSE 250 mg/kg          | 1.26±0.144                  | 0.31±0.009**           | 5.35±0.25**        |
| % to control rats      | 91.97%                      | 79.48%                 | 59.77%             |
| Nicotinic acid         | 1.25±0.12                   | 0.30±0.02*             | 5.02±0.471**       |
| % to control rats      | 91.24%                      | 76.92%                 | 56.09%             |

Notes: * – p<0.05; ** – p<0.01 – probability differences compared to the control group.

The model of acute hyperlipidemia is based on the ability of such surfactant as Tween-80 to bind blood plasma lipids and to form micelles isolated from the action of lipoprotein lipase. In 8-10 h after a single intraperitoneal administration of Tween-80 the level of blood triglycerides increased by 6-8 times and the level of cholesterol increased by 3-4 times.

The model of acute hyperlipidemia was induced by injecting a single dose of Tween-80 intraperitoneally in rats in the amount of 250 mg/kg per 1 ml of distilled water [8]. In eight hours the blood samples were collected to assess the level of hyperglycemia. Blood was collected by decapitation of anesthetized rats (sodium thiopental, 40 mg/kg) and centrifuged at 3000 rpm for 15-20 min. The serum samples were further subjected to biochemical analysis.

In acute toxicity studies [7] it was determined that a single oral (by gavage) introduction of *P. sanguisorba* L. extract (PSE) in the dose of 5 g/kg did not cause the death of animals and did not also contribute to the negative impact on their condition and behaviour. Thus, PSE can be referred to the IV-th class of toxicity (low-toxic compounds). In this study PSE was administered in two doses of 100 and 250 mg/kg (Group 4-5, respectively) introduced in advance within 7 days before the injection of Tween-80.

The antihyperlipidemic activity of PSE was compared to nicotinic acid (30 mg/kg) [9] administered intraperitoneally to standard rats (Group 3).

At the end of the study the total cholesterol (TC), triglycerides (TG) and the total lipids (TL) were measured in the serum. Determination was performed using enzymatic methods (Felicit, Ukraine).

Statistical analysis was performed using Student t-test. The data obtained was processed by the method of variation statistics at the significance level of p<0.05.

**Results and Discussion**

The data in Table show that a single administration of Tween-80 caused marked increase in levels of TC (13.14%, p<0.05), TG (33.34%, p<0.05) and TL (26.71%, p<0.05) in the plasma in control rats compared to intact rats.

Treatment with PSE caused decrease in these levels in both doses. But the dose of 100 mg/kg showed the highest reduction.

Thus, PSE in the dose of 100 mg/kg reduced the level of TC by 18.25% compared to the control group, while PSE in the dose of 250 mg/kg and nicotinic acid reduced the probability of the appropriate level by 8.03% and 8.76%, respectively.

Besides, administration of PSE in the dose of 100 mg/kg caused the highest TG level decrease in the blood (28.21%) and appeared to be 5.13% higher than in standard rats receiving nicotinic acid. Increase in the dose of PSE to 250 mg/kg did not result in increase of its effect (reduction of the blood TG level compared to control is 20.52%).

Under the effect of PSE the level of TL significantly decreased compared to the control to almost identical values. Thus, in Group 4 the level of TL decreased by 41.90% and in Group 5 by 40.23%. Nicotinic acid showed the more pronounced effect on overall blood lipids, thus reducing the corresponding figure by 43.91%.

Therefore, we have found that the ethanol extract of *Poterium sanguisorba* L. on the model of acute hyperlipidemia showed a pronounced hypolipidemic activity. The ability to reduce the blood lipid spectrum – the total cholesterol, triglycerides, and the total lipids – was manifested. However, a significant increase in the efficiency of PSE when increasing the dose was not found. Therefore, the dose of 100 mg/kg was determined to be the most effective lipid-lowering dose in this study. The ability of PSE to reduce the plasma levels of TC, TG and TL is close to nicotinic acid.

**CONCLUSIONS**

1. The results of the study show that *P. sanguisorba* L. has a significant antihyperlipidemic action against experimentally-induced hyperlipidemia.
2. It has been found that the most effective dose in the conditions of acute hyperlipidemia is the dose of 100 mg/kg.
3. The lipid profile under action of PSE (100 mg/kg) can be comparable with nicotinic acid.
ГІПОЛІПІДЕМІЧНА АКТИВНІСТЬ ЧОРНОГОЛОВНИКА РОДОВИКОВОГО

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Ключові слова: гіполіпідемічні засоби; екстракти з рослин; експерименти на тваринах

Атеросклероз визнаний «неінфекційною пандемією XXI століття». Існує широкий спектр лікарських засобів для корекції гіперліпідемії, а також для первинної та вторинної профілактики ускладнень атеросклерозу. Проте усі відомі гіполіпідемічні препарати мають безліч побічних ефектів. Рослинні препарати мають ряд переваг перед синтетичними монопрепаратами. Завдяки складному та збалансованому хімічному складу, раціональному поєднанню біологічно активних речовин вони чинять багатосторонню дію на організм: впливають, з одного боку, безпосередньо на вогнище ураження, а з іншого боку, забезпечують фармакологічну корекцію різних функціональних систем. Становить інтерес вивчення тритерпеноїдних сполук, виділених з рослинної сировини, які мають широкий спектр фармакологічної активності, в тому числі гіполіпідемічну дію. Мета даного дослідження полягала в оцінці гіполіпідемічних властивостей етанольного екстракту з чорноголовника родовикового (P. sanguisorba L.), який містить у підземній частині тритерпеноїдні сполуки. Білим статевозрілим щуром лінії Вістар однократно внутрішньочеревно вводили твін-80 з розрахунку 250 мг/кг в 1 мл води дистильованої. Рівень гіперліпідемії оцінювали через 8 годин після введення твіну-80, взявшисі зразки крові. Перорально вводили екстракт у 2-х дозах: 100 мг/кг та 250 мг/кг заздалегідь протягом 7 днів, проводячи останнє введення разом з твіном-80. Як препарат порівняння використали нікотинову кислоту (30 мг/кг). В кінці дослідження у сироватці були вимірювані рівні загального холестерину, тригліцеридів та загальних ліпідів. Визначення проводили з використанням ферментативних методів. Результати проведенного дослідження підтвердили наявність гіполіпідемічної активності екстракту підземних органів чорноголовника родовикового в умовах індукованої гострої гіперліпідемії.
корекцію різних функціональних систем. Представляє інтерес ізучення тритер-
пеноїдних сполук, які обладнані широким спектром фармацологічної активності, в том чисел гіпопліпідемічним дією.
Цель даного дослідження заключалась в вимірюванні гіпопліпідемічних властивостей этанольного экстракту черноголовника кровохлебкового (P. sanguisorba L.), который включає в под- 
земної часті тритерпеноїдні сполук. Белым половозрелым крысам линии Вистар однократно внутривенно вводили твин-80 из расчета 250 мг/кг в 1 мл воды дистили-
рованой. Уровень гіперліпідемії оценивали через 8 часов после введення твіна-80, взяв образцы крови. Перорально вводили экстракт у 2-x дозах 100 мг/кг и 250 мг/кг заранее в тече-
ння 7 дній, проводя степені введення вместо твин-80. В каче практіка сравне-
ния использовали никотиновую кислоту (30 мг/кг). В конце исследования в сыворотке были 
измерены уровни общего холестерина, триглицеридов і общих липидов. Определение про-
водили с использованием ферментативных методов. Результаты проведеного исследова-
ния подтвердили наличие гіпопліпідемічної дії экстракт подземних органов черноголовника кровохлебкового в умовах індукуваної острй гіперліпідемії.