REVIEW

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY

Terpenoids and phenolic compounds as biologically active compounds of medicinal plants with diuretic effect

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Received 20 Oct 2023 After peer review 18 Nov 2023 Accepted 23 Dec 2023

The aim of the study was to summarize and systematize the literature data, as well as the results of the carried out research in the field of medicinal plants used as diuretics in the Russian Federation and abroad.

Materials and methods. During the search for this review article materials, the abstract databases of PubMed, Google Scholar, as well as the ResearchGate and elibrary.ru were used. The search was carried out according to the publications for the period from 2005 to 2023. The keywords were as follows: herbal diuretics, diuretic drugs, kidney diseases, types of medicinal plant raw materials. The data from the authors' previous scientific research on the analysis of the diuretic properties of certain types of medicinal plant raw materials, as well as individual substances of a phenolic nature isolated from them (simple phenols, flavonoids), were also reviewed.

Results. It was determined that the diuretic activity of most of the medicinal plants used, is due to such groups of biologically active compounds as terpenoids (essential oils and saponins), simple phenols, flavonoids and anthracene derivatives related to the secondary metabolites. It has been shown that, despite the fact that many herbal diuretics have concomitant anti-inflammatory, antimicrobial, antiviral, antihistamine and other properties relevant from the point of view of etiology and pathogenesis of the disease, it is reasonable to use them as part of collections of medicinal plants and other combined medicinal herbal preparations, as this is in accordance with the global trend. The types of medicinal plant raw materials that can be a promising source of new diuretic herbal medicines, have been examined in this review.

Conclusion. It has been determined that terpenoids and phenolic compounds make the greatest contribution to the manifestation of the diuretic activity of medicinal herbal preparations, among which the greatest structural diversity is noted for flavonoids. It has been established that in the composition of any drug, taking into account the peculiarities of etiology and pathogenesis of the disease, herbal diuretics can be both the main drug and an auxiliary component. The expediency of using medicinal plant raw materials with a diuretic effect as part of collections of medicinal plants and other combined preparations used in the treatment of kidney and urinary tract diseases has been also substantiated.

Keywords: diuretic effect; diuretic drugs; medicinal plants; medicinal plant raw materials; biologically active compounds; flavonoids; excretory system; diseases of the excretory system

Abbreviations: MPRMs – medicinal plant raw materials; BAFAs – biologically active food additives; BACs – biologically active compounds; MP – medicinal product; EOs – essential oils.

For citation: V.A. Kurkin, O.E. Pravdivtseva, E.N. Zaitseva, A.V. Dubishchev, A.S. Tsibina, A.V. Kurkina, S.V. Pervushkin, A.V. Zhdanova. Terpenoids and phenolic compounds as biologically active compounds of medicinal plants with diuretic effect. *Pharmacy & Pharmacology.* 2023;11(6):446-460. **DOI:** 10.19163/2307-9266-2023-11-6-446-460

Для цитирования: В.А. Куркин, О.Е. Правдивцева, Е.Н. Зайцева, А.В. Дубищев, А.С. Цибина, А.В. Куркина, С.В. Первушкин, А.В. Жданова. Терпеноиды и фенольные соединения как биологически активные соединения лекарственных растений, обладающих диуретическим действием. *Фармация и фармакология.* 2023;11(6):446-460. **DOI:** 10.19163/2307-9266-2023-11-6-446-460

Научно-практический журнал
ФАРМАЦИЯ И ФАРМАКОЛОГИЯ

ОБЗОР
DOI: 10.19163/2307-9266-2023-11-6-446-460

Терпеноиды и фенольные соединения как биологически активные соединения лекарственных растений, обладающих диуретическим действием

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Получена 20.10.2023 После рецензирования 18.11.2023 Принята к печати 23.12.2023

Цель. Обобщение и систематизация литературных данных, а также результатов собственных исследований лекарственных растений, применяемых в качестве диуретических средств на территории Российской Федерации и за рубежом.

Материалы и методы. При поиске материалов для написания обзорной статьи использованы реферативные базы данных PubMed, Google Scholar, ResearchGate и elibrary.ru. Поиск осуществлялся по публикациям за период с 2005 по 2023 гг. с использованием ключевых слов: растительные диуретики, диуретические лекарственные препараты, заболевания почек, виды лекарственного растительного сырья. Также были использованы данные собственных научных исследований по анализу диуретических свойств некоторых видов лекарственного растительного сырья, а также выделенных из них индивидуальных веществ фенольной природы (простые фенолы, флавоноиды).

Результаты. Определено, что диуретическая активность большинства применяемых лекарственных растений обусловлена такими группами биологически активных соединений, как терпеноиды (эфирные масла (ЭМ) и сапонины), простые фенолы, флавоноиды и антраценпроизводные, относящиеся к вторичным метаболитам. Показано, что несмотря на то, что многие растительные диуретики обладают сопутствующими противовоспалительными, антимикробными, противовирусными, антигистаминными и другими свойствами, актуальными с точки зрения этиологии и патогенеза заболевания, целесообразно использование их в составе сборов лекарственных растений и других комбинированных лекарственных растительных препаратов, что находится в соответствии с общемировой тенденцией. В настоящем обзоре рассмотрены виды лекарственного растительного сырья, которые могут быть перспективным источником новых диуретических лекарственных растительных препаратов.

Заключение. Определено, что наибольший вклад в проявление диуретической активности лекарственных растительных препаратов вносят терпеноиды и фенольные соединения, среди которых значимое структурное разнообразие отмечено для флавоноидов. Установлено, что растительные диуретики могут являться как основным лекарственным средством, так и вспомогательным компонентом в составе какого-либо препарата с учетом особенностей этиологии и патогенеза заболевания. Обоснована также целесообразность использования лекарственного растительного сырья, обладающего диуретическим эффектом, в составе сборов лекарственных растений и других комбинированных препаратов, применяемых при лечении заболеваний почек и мочевыводящих путей.

Ключевые слова: растительные диуретики; диуретические лекарственные препараты; заболевания почек; лекарственное растительное сырье; биологически активные соединения

Список сокращений: ЛРС – лекарственное растительное сырье; БАД – биологически активная добавка к пище; БАС – биологически активные соединения; ЛП – лекарственный препарат; ЭМ – эфирные масла.

INTRODUCTION

Medicinal plants used as sources of diuretics are widely used in both scientific and folk medicine [1–4]. These drugs are used both in our country [5, 6] and abroad [7–10]. The diseases of the human urinary system are quite common and require special attention [11–14]. Moreover, the degree of severity of the disease, as well as the nature of this pathology manifestation, differs greatly from patient to patient [15–18]. In addition, kidney diseases are often accompanied by pathologies of the heart and blood vessels [19–21], the nervous system and endocrine diseases [22–25]. Therefore, a necessary condition for successful treatment is the use of a wide range of herbal diuretics, taking into account the characteristics of the disease and the patient population. It should be noted that herbal diuretics

ISSN 2307-9266 e-ISSN 2413-2241

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are most often prescribed to the elderly, children, and women during pregnancy [6, 26–28].

It is important to emphasize that most types of medicinal plant raw materials (MPRMs) used to enhance diuresis also have some concomitant effects, for example, anti-inflammatory, antimicrobial, antispasmodic and other properties [6, 29–31]. All this makes it possible to use diuretic plants for a wide variety of diseases, especially chronic ones [32–35]. It should be noted that universal herbal diuretics with all the above-mentioned properties do not exist. Therefore, it is more expedient to use MPRMs with a diuretic action not in the form of monophytotherapy, but as a part of a combined drug, where the main diuretic effect is complemented by anti-inflammatory, antimicrobial, antiviral, antihistamine and other properties relevant from the point of view of the etiology and pathogenesis of the disease [26, 30, 36]. Therefore, it is advisable to use aqueous extraction not from one type of a MPRMs, but from a composition consisting of several plant components, or a ready-made preparation of a plant origin [30, 37–39].

However, along with diuretics of the plant origin, there are drugs with a diuretic effect that are not directly related to diuretics. E.g., these are medicinal herbal preparations containing cardiac glycosides [40]. They include foxglove leaves (*Digitalis* L.), adonis herb (*Adonis vernalis* L.), flowers, herb and leaves of lily of the valley (*Convallaria majalis* L.), as well as some other plants. These drugs are characterized by a pronounced diuretic effect, which is not due to a specific effect on the kidneys, but is a consequence of the redistribution of the blood circulation in the human body.

It should be also noted that diuretic plants should be used not only for treatment, but also for prevention [41–44]. At the same time, it should be remembered that some types of MPRMs can have an undesirable effect on the kidneys [45, 46]. The examples of the nephrotoxic plant components in biologically active food additives (BAFAs) have been known for a long time. In review, only medicinal plants that do not contain high concentrations of toxic substances, have been considered [47–49].

The diuretic effect of MPRMs may not be the main, but concomitant effect. It should be noted that an increase in diuresis is welcome in the case of the use of many medicinal plants [5, 6, 50]. This is due to the fact that an increased kidney function leads to the early removal from the body of various, contributes to the early onset of recovery [15, 21, 28]. An increased water excretion helps to get rid of edema and accelerate the healing process of soft tissues [6, 30, 35, 46].

In this review, medicinal plants that have a diuretic effect, we will be considered. However, the presence of this effect, in the authors' opinion, will contribute more to the positive dynamics of various diseases treatment, especially since the plants being considered, do not contain such dangerous biologically active compounds (BACs) as cardiac glycosides.

THE AIM of the study was to summarize and systematize the literature data, as well as the results of the carried out research in the field of medicinal plants used as diuretics in the Russian Federation and abroad.

MATERIALS AND METHODS

During the search for this review article materials, the abstract databases PubMed, Google Scholar, ResearchGate scientific information network and elibrary.ru were used. The search was carried out according to the publications for the period from 2005 to 2023. The keywords were as follows: herbal diuretics, diuretic drugs, kidney diseases, types of MPRMs. Over 400 sources were found, from the total, the articles on medicinal plants with diuretic properties and containing terpenoids and phenolic compounds were selected. The data from the authors' previous scientific research on the analysis of the diuretic properties of certain types of MPRMs, as well as individual substances of a phenolic nature isolated from them (simple phenols, flavonoids), were also reviewed.

RESULTS AND DISCUSSION

Medicinal plants with diuretic effect, as well as their biologically active compounds

The diuretic activity of medicinal plants is due to such groups of BACs as terpenoids (the components of essential oils (EOs) and saponins), simple phenols, flavonoids, anthracene derivatives (Table 1). The greatest structural diversity of active substances is observed in the group of flavonoids, which are most often represented by derivatives of apigenin, kaempferol and quercetin [51–54].

In the discussion of medicines, herbal diuretics with a pronounced effect, such as buds and birch leaves (*Betula pendula* Roth. (*Betula verrucosa* Ehrh.), bearberry leaves (*Arctostaphylos uva-ursi* Spreng.) and cranberries (*Vaccinium vitis-idaea* L.), juniper cones (*Juniperus communis* L.), are primarily referred to [52, 56, 68, 69]. These drugs, being effective herbal uroantiseptics along with a diuretic effect, have a pronounced antimicrobial effect. Birch buds and leaves, as well juniper cones, contain EOs as the leading group of BACs. In addition, birch buds and leaves also contain flavonoids as the second group of active substances [57]. Bearberry and cranberry leaves are characterized by a high content of phenolic components belonging to simple phenolic compounds, among which arbutin dominates [52, 70, 71]. These drugs are more often used as a part of compositions of MPRMs in combination with other plant components [5, 6].

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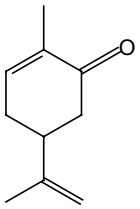
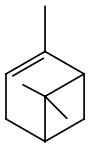
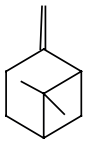
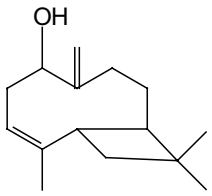
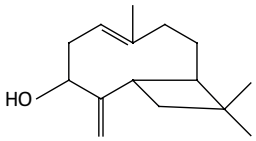
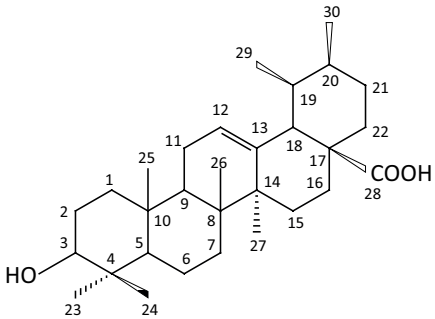
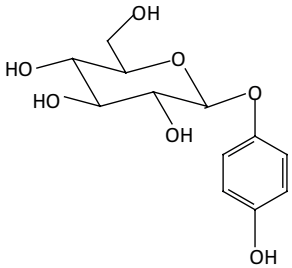
DOI: 10.19163/2307-9266-2023-11-6-446-460

Table 1 – Chemical formulas of the most important biologically active compounds with diuretic activity and some of their herbal sources

Connection name	Chemical structure	Medicinal plant raw materials containing this component	References
	Terpenoids		
(+)-Carvon		Dill fruits (*Anethi graveolentis fructus*)	[55]
∝-Pinene		Common juniper fruits (*Juniperi communis fructus*)	[56]
β-Pinene			
α-Belulenol		Buds and leaves of hanging birch and fluffy birch *Betulae gemmae, Betulae folia*	[57]
β-Belulenol			
	Saponins		
Ursolic acid		Orthosiphon leaves (*Orthosiphonis staminei folia*)	[58}
	Simple phenols		
Arbutin		Bearberry and cowberry leaves (*Arctostaphylos uvae-ursi folia, Vaccinii vitis-idaeae folia*)	[52]

ISSN 2307-9266 e-ISSN 2413-2241

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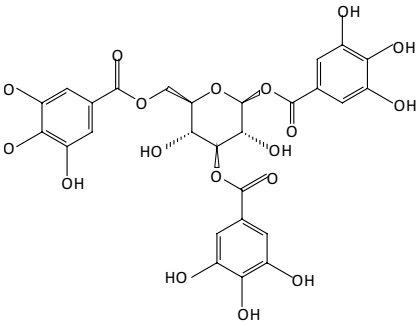
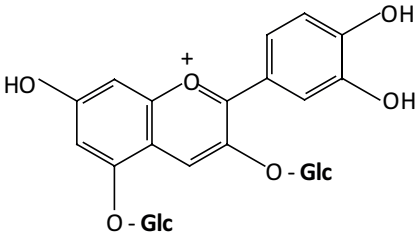
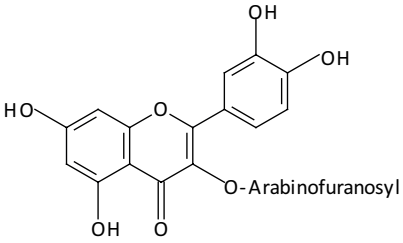
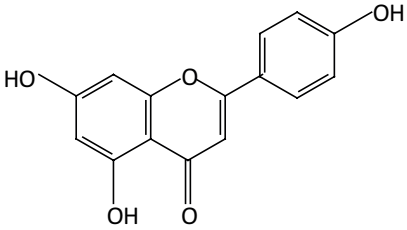
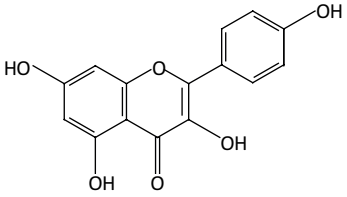
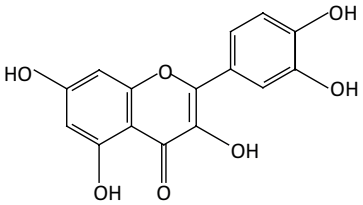
Connection name	Chemical structure	Medicinal plant raw materials containing this component	References
1,3,6-trigalloyl glucose		Common bearberry leaves of (*Arctostaphylos uvae-ursi folia*)	[52]
	Flavonoids		
Cyanine (cyanidin-3,5-diglucoside)		Cornflower blue flowers (*Centaureae cyani flores*)	[59]
Avicularin		Knotgrass herb (*Polygoni avicularis herba*)	[30, 60]
Apigenin		Horsetail herbs (*Equiseti arvensis herba*)	[61]
Kaempferol		Canadian Goldenrod herbs (*Solidaginis canadensis herba*)	[62]
Quercetin			

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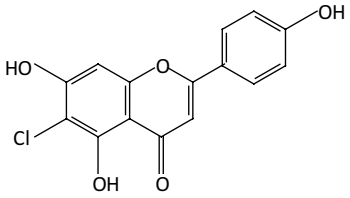
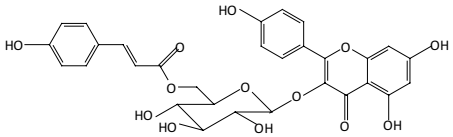
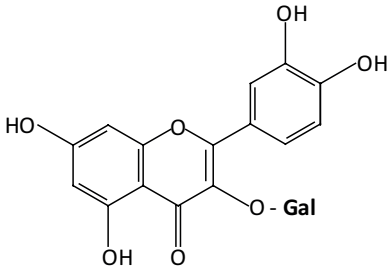
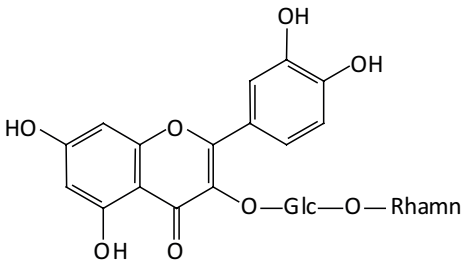
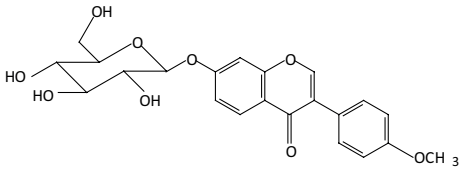
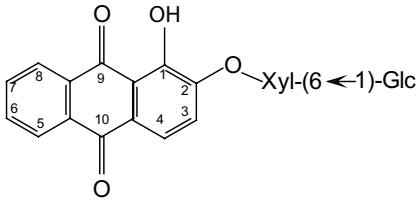
DOI: 10.19163/2307-9266-2023-11-6-446-460

Connection name	Chemical structure	Medicinal plant raw materials containing this component	References
Chlorapigenin		Horsetail herbs (*Equiseti arvensis herba*)	[61]
Tiliroside		Aerva Woolly herbs (*Aervae lanatae herba*)	[63]
Hyperoside		Birch leaves, St. John's wort herbs (*Betulae folia, Hyperici herba*)	[57, 63]
Routine		Wild strawberries leaves and fruits, St. John's wort herbs (*Fragariae vescae folia, Hyperici herba*)	[63, 64]
Ononin		Plowed steelworm roots (*Ononidis arvensis radices*)	[65]
Anthracene derivatives			
Ruberitric acid		European madder rhizomes and roots (*Rubiae rhizomata et radices*)	[54, 66, 67]

ISSN 2307-9266 e-ISSN 2413-2241

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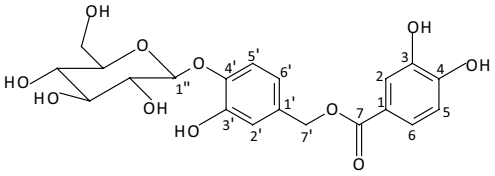
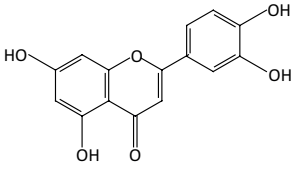
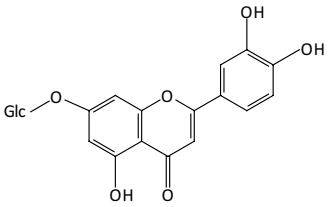
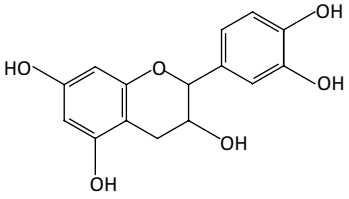
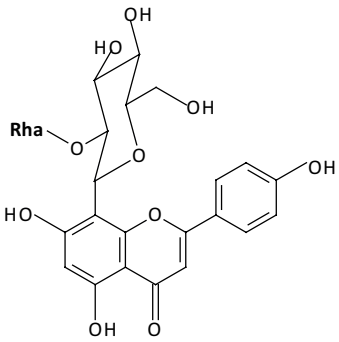
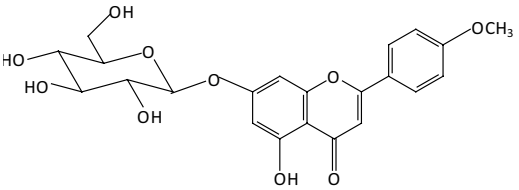
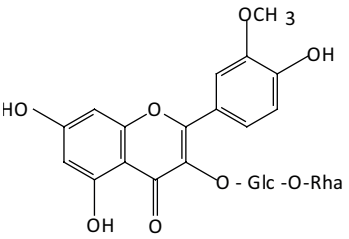
Table 2 – Chemical formulas of some biologically active compounds of pharmacopoeial medicinal plant raw materials promising for diuretics production

Name of compound	Chemical structure	Medicinal plant raw materials	References
	Simple phenolic compounds		
Oregano A		Oregano herbs (*Origani vulgaris herba*)	[77]
	Flavonoids		
Luteolin		Melissa officinalis herb, dandelion officinalis herb (*Melissae officinalis herba, Taraxaci officinalis herba*)	[78, 79]
Cynaroside			
Catechin		Blood-red hawthorn fruits (*Crataegi sanguinea fructus*)	[80]
2''-O-vitexin rhamnoside		Blood-red hawthorn leaves (*Crataegi sanguinea folia*)	[81, 82]
Tilianin		Common tansy flowers (*Tanaceti vulgaris flores*)	[83]
Narcissin		Calendula officinalis flowers (*Calendulae officinalis flores*)	[84]

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DOI: 10.19163/2307-9266-2023-11-6-446-460

Table 3 – Chemical composition of non-pharmacopoeial MPRMs promising for diuretics production

Medicinal plant	Type of medicinal plant raw materials	Chemical composition	References
Blood-red hawthorn (*Crataegus sanguinea* Pall.)	Leaves	Flavonides: vitexin, 2''-O-rhamnoside of vitexin, quercetin, hyperoside, trifolin Phenylpropanoids: caffeic acid	[80–82]
Medicinal dandelion (*Taraxacum officinale* Web.)	Herb	Phenylpropanoids: caftaric acid, chlorogenic acid, caffeic acid Flavonoids: luteolin, cynaroside, etc.	[79, 93]
Blessed milk thistle (*Silybum marianum* (L.) Gaertn)	Herb	Phenylpropanoids: *p*-coumaric acid, caffeic acid, chlorogenic acid Flavonoids: apigenin	[89]

Herbal diuretics also include horsetail (*Equisetum arvense* L.) and knotgrass herb or door-weed (*Polygonum aviculare* L.) [60, 61]. These two types of MPRMs, along with flavonoids, contain silicic acid derivatives. Medicinal preparations based on horsetail and knotweed, have a diuretic effect and contribute to the loosening and excretion of renal calculi in the treatment of a kidney stone disease. It is advisable to include them in diuretics to harmonize the therapeutic effect. It is also desirable to include fruits of fragrant dill (*Anethum graveolens* L.) in diuretic compositions of medicinal plants, which are pronounced urospasmodic and nephrolytic agents [55]. The fruits of the garden dill should be included in the compositions intended for the treatment of a kidney stone disease. Aqueous extracts based on kidney tea leaves (*Orthosiphon stamineus* Benth.), cornflower flowers (*Centaurea cyanus* L.), Aerva woolly herbs (*Aerva lanata* Juss.), leaves and fruits of wild strawberries (*Fragaria vesca* L.) and roots of field stalks (*Ononis arvensis* L.), are also used as herbal diuretics [30, 58, 59, 64]. Diuresis is characteristic of Chinese tea leaves (*Thea sinensis* L.) due to the presence of flavonoids (catechin, etc.), as well as alkaloids (caffeine) [72]. The shoots of dicolor Lespedeza (*Lespedeza bicolor* Turcz.), a Canadian goldenrod herb (*Solidago canadensis* L.), rhizomes and European madder roots (*Rubia tinctorum* L.) are used to obtain ready-made medicines [54, 62, 73]. Being diuretics, these drugs contribute to a better excretion of nitrogen metabolism products (urates), as well as phosphates, and in some cases even oxalates from the human body with the kidneys [6, 51, 74].

Plant raw materials with diuretic effect in compositions of domestic medicines

Oral drops "Urolesan" (ART-FARM, Russia) contain a Siberian fir needles oil, a peppermint oil, a liquid extract of wild carrot seeds, a liquid extract of common hop coplodia, a liquid extract of wild marjoram, castor seeds oil [75]. This drug has antispasmodic and anti-inflammatory effects. It is most often prescribed in the treatment of a kidney stone disease with stones of a different chemical nature. Similar in composition to the drug "Urohol" (VIFITECH, Russia), it is also intended for the treatment of various urological diseases in humans. The combined drug "Marelin" (VIFITECH, Russia) is intended for the treatment of a kidney stone disease [73]. In its composition, it contains an extract of rhizomes with madder roots, an extract of Canadian goldenrod, an extract of horsetail, cardiac glycosides of lily of the valley and kellin. "Marelin" is available in tablets for the oral administration. The preparation of "Madder roots extract" is also produced in tablets as diuretic and antispasmodic agents [54]. It should be noted that madder roots preparations are advisable for the treatment of a kidney stone disease with the formation of phosphate stones. The solution for the oral administration of "Lespefril" (VIFITECH, Russia) and "Lespeflan" (Dalkhimpharm, Russia) is obtained on the basis of bicolor lespedecia with the addition of the anise fruit EO. Both drugs have a hypo-azotemic effect [37]. The tablet preparation of "Bearberry extract" (VIFITECH, Russia) contains an extract from the leaves of bearberry and is intended for the use as a diuretic and uroantiseptic drug [52].

As diuretics in our country, "Birch buds" (Krasnogorskleksredstva, Russia), "Birch leaves" (Krasnogorsklex means, Russia), "Bearberry leaves" (Krasnogorskleksredstva, Russia), "Lingonberry leaves" (Krasnogorskleksredstva, Russia), "Juniper fruits" (Krasnogorsklex means, Russia), "Horsetail field grass" (Krasnogorskleksredstva, Russia), "Mountain bird (knotweed) grass" (Krasnogorskleksredstva, Russia), "Dill fragrant fruits" (Krasnogorskleksredstva, Russia), "Orthosiphon staminate (Kidney tea) leaves" (Krasnogorskleksredstva, Russia) and "Aerva woolly herbs" (Krasnogorskleksredstva, Russia) [70].

The collections based on MPRMs, are also used. The composition of the collection "Brusniver" (Krasnogorskleksredstva, Russia) includes leaves of cranberries, St. John's wort herb, rosehip fruits, bur-marigold. The collection of urological "Phytonephrol" (Krasnogorskleksredstva, Russia) is also used [74, 76]. It contains bearberry leaves, marigold flowers, fragrant dill fruits, rhizomes and roots of Siberian ginseng,

ISSN 2307-9266 e-ISSN 2413-2241

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peppermint leaves. In the authors' opinion, these charges are not fully optimal in terms of the composition of the components. The collection of "Brusniver" can be supplemented with antispasmodic and nephrolytic components. In the collection of "Phytonephrol", the presence of rhizomes and roots of Siberian ginseng, the BACs of which are poorly extracted by water, is not entirely clear.

It should be noted that these drugs do not cover the entire range of prescriptions for the excretory system diseases. It can be also concluded that the effect of diuretics used in our country is primarily due to terpenoids, simple phenolic compounds, flavonoids and anthracene derivatives [6, 30, 52, 54].

Plant raw materials with diuretic effect in the compositions of foreign medicines

In the treatment of various pathologies of the kidneys and urinary tract, the drug "Kanefron N" (Bionorica CE, Germany) is used [32, 37]. These medicines are available in a solution and tablets. "Kanefron N" contains an extract of the herb of the golden thousandth, leaves of rosemary and the root of the medicinal lovage. It should be noted that only the herb of the golden thousandth is a pharmacopoeial raw material in the Russian Federation, and it is used in the treatment of appetite disorders. All three types of raw materials included in the preparation contain EOs. The drug "Cystone" (Himalaya Drug Co., India) can be also used in the treatment of kidney stones [44]. It consists of extracts of flowers of dicotyledonous stalk, an extract of saxifrage stems, an extract of madder cordial stems, an extract of rhizomes of filmy sativa, an extract of rough strawflower, an extract of the aboveground part of *Onosma polychroma*, an extract of the whole vernonia ashy plant, as well as steam-treated extracts of the aboveground part of basil, horse bean seeds, fruits of the creeping anchor, a whole plant of fragrant swamp mallow, a whole plant of horsetail and teak seeds. All types of MPRMs, with the exception of horsetail, are not pharmacopoeial in our country. Phytolysin paste (Herbapol Warsaw, Poland) is also often used *per os* [35]. It contains condensed extracts of European goldenrod, horsetail, bird's knotweed grass, creeping wheatgrass rhizomes, birch leaves, fenugreek seeds, parsley roots, lovage roots. At the same time, the rhizomes of creeping wheatgrass, parsley roots and fenugreek seeds are not used in the Russian Federation. This preparation also contains EOs of sweet orange, clary sage and peppermint. The drug Lespenefril (USB Helskea, France) is obtained from the aboveground part of the head lespedecia with aniseed oil [37]. This drug is available in the form of an oral solution.

It should be noted that diuretic medicines manufactured abroad contain extracts of MPRMs, the chemical composition of which is not fully known. The vast majority of these drugs are not included in the Russian Pharmacopoeia. The diuretic effect of MPRMs, which is the main one for diuretic drugs of a foreign production, is mainly due to terpenoids, flavonoids and anthracene derivatives [29, 37, 44, 49].

Promising medicinal plants and MPRMs for new diuretic drugs production

Diuretics of the plant origin should be used not only in the treatment of the cardiovascular system diseases [53]. It is possible to use herbal diuretics in the treatment of liver and metabolic diseases [22, 24, 85]. Diuretics of the plant origin should be prescribed for the treatment of certain bronchopulmonary diseases, especially in cases where patients are prescribed copious drinking for medicinal purposes [13]. Herbal diuretics will also be useful in the treatment of musculoskeletal diseases, skin diseases and in neurological practice [24, 86]. It should be noted that most of the herbal diuretics contribute to the preservation of potassium in the body [6, 78, 79].

Consequently, in some cases, diuretic medicinal plants act as the main or specific component of treatment, in other cases – as a symptomatic remedy, complementing and harmonizing the main treatment with a number of concomitant pharmacological effects, including anti-inflammatory, antimicrobial, litholytic, etc. In the world medical practice, diuretic properties are noted in medicines from many medicinal plants, such as St. John's wort herb (*Hypericum perforatum* L.) and Melissa officinalis herb (*Melissa officinalis* L.) [78, 87]. Both types of raw materials contain flavonoids: hyperoside and rutin are found in the herb of St. John's wort, and cinaroside in the herb of melissa officinalis (Tables 1, 2).

The diuretic activity of blood-red hawthorn (*Crataegus sanguinea* Pall.), tansy flowers (*Tanacetum vulgare* L.) flowers and fruits, calendula flowers (*Calendula officinalis* L.), blueberry (*Vaccinium myrtillus* L.) fruits and shoots were also studied [82–84, 88]. A diuretic activity was also detected in the BAC of the oregano herb (*Origanum vulgare* L.) – oreganol A [77]. Diuretic properties were also noted in the raw materials of some non-pharmacopoeial raw materials: blood-red hawthorn (*Crataegus sanguinea* Pall.) leaves, dandelion herbs (*Taraxacum officinale* Web.), milk thistle herbs (*Silybum marianum* (L.) Gaertn.) (Table. 3) [79, 82, 89].

In the study of oreganol A from the oregano herb at a dose of 0.5 mg/kg, an increase in diuresis was noted by 73% in 4 h of the study and by 47% in 24 h of the study. There was also an increase in creatininuresis by 47% in 24 h of the study [77].

In the diuretic activity study of the extracts based on blood-red hawthorn flowers and fruits, it was shown that the infusion of blood-red hawthorn flowers 100 µl/kg for 4 h, contributed to a significant increase in diuresis

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DOI: 10.19163/2307-9266-2023-11-6-446-460

by 28%, in Na uresis by 62%, in K uresis by 93% and in creatinineuresis by 70%, while in 24 h, the same drug increased diuresis by 48%, Na uresis by 91%, K diuresis by 74%, creatinine diuresis (by 69%). A decoction of blood-red hawthorn fruits at a dose of 100 µl/kg caused an isolated significant increase in creatinine clearance by 52% in 4 h of the experiment. In the 24 h of the experiment, the same drug significantly stimulated the excretion of water by 48%, sodium by 78% and potassium by 53%. In addition, a thick extract of blood-red hawthorn fruits had a diuretic effect. It was also established that in 24 h, the intragastric administration of a thick extract of blood-red hawthorn fruits at a dose of 20 mg/kg significantly stimulated diuresis by 58%, Na uresis by 42%, potassium diuresis by 25% and creatinine diuresis by 48% in the experimental group compared with the aqueous control [80–82]. At the same time, the flowers and fruits of the blood-red hawthorn contain flavonoids and are used in modern medical practice as cardiotonic agents [80].

Tansy flowers contain terpenoids (thujone, thujol), flavonoids (tilianin, acacetin, cosmosiin, apigenin) and phenylpropanoids (chlorogenic acid). They are used to obtain the drug “Tanacehol” (VILAR Pharmaceutical Center, Russia), as well as collections of MPRMs “Phytohepatol” (Krasnogorskleksredstva, Russia) (Choleretic collection No. 3). Tansy flowers have a choleretic effect and are used in the complex therapy of liver and gallbladder diseases. The developed drug “Tansy of flowers syrup” at a dose of 50 µl/kg has the ability to increase diuresis by 49%, Na uresis by 62%, potassium diuresis by 40%, and creatinine diuresis by 25% [83, 90].

Blueberry fruits contain tannins, have an astringent effect, and can also serve as a source of vitamins and anthocyanins. Blueberry fruits can be used fresh and dried. Fresh fruits can be a source of juice. Juice and an infusion of dried fruits at a dose of 50 ml/kg in the experiment increases diuresis by 49%, sodium diuresis by 76%, potassium diuresis by 44% in 4 h of the experiment, as well as diuresis by 85% in 24 h of the experiment. At the same time, blueberry shoot extract obtained with 70% ethyl alcohol in a similar dose increases a renal excretion of water in 4 h (62%) and 24 h (59%) of the experiment [88, 91].

Calendula officinalis flowers contain carotenoids and flavonoids and are used primarily as an external remedy with anti-inflammatory and wound healing effects. Less often, calendula flowers are used *per os* as a part of urological and choleretic collections of MPRMs. A calendula flowers tincture obtained with 70% ethyl alcohol at a dose of 50 µl/kg increases diuresis by 75%, Na uresis – by 81%, K uresis – by 59%, and creatinine by – 35% in 4 h of the experiment. Herewith, in 24 h, only diuresis increased by 27% and Na uresis by 39% [84].

In the authors’ opinion, the types of MPRMs that are not currently pharmacopoeial, however, are also noteworthy and very promising. Blood-red hawthorn leaves are currently not a pharmacopoeial MPRM (Table 3). It was also noted that an alcohol-aqueous blood-red hawthorn leaves extraction at a dose of 100 µl/kg in 4 h of experience, contributed to a significant increase in diuresis by 20%, Na uresis by 38% and K uresis by 77%. Herewith, in 24 h of the experiment, the extraction of blood-red hawthorn leaves led to an increase in the renal excretion of water by 29%, sodium by 30% and creatinine by 36% relative to the control parameters, which indicates the presence of diuretic and saluretic effects [82]. In addition, the present studies show that the thick extract obtained on the basis of flowering shoots of blood-red hawthorn at a dose of 10 mg/kg, increased creatinine by 67% in 4 h and by 35% in 24 h of the study [81]. It should be noted that hawthorn leaves contain flavonoids [81, 82, 92].

In the medical practice of the Russian Federation, dandelion roots are used as a digestive aid, as well as a choleretic and appetite-inducing bitterness. A dandelion herb containing flavonoids and phenylpropanoids is currently not used, although it can be used for food purposes. It was shown that a dandelion herb tincture, obtained on 70% ethyl alcohol, administered to animals at a dose of 50 ml/kg increased diuresis by 63%, Na uresis by 111% and potassium diuresis by 37% for 4 h of the study. Herewith, the same drug had a significant increase in diuresis by 38% and creatinine clearance by 34% for 24 h of the experiment [79, 93].

Blessed milk thistle (*Silybum marianum* (L.) Gaertn.) contains flavolignans and a fatty oil. On the basis blessed milk thistle fruits, medicines with both hepatoprotective and choleretic activities are obtained. The blessed milk thistle herb containing flavonoids and phenylpropanoids is currently not used. At the same time, it was shown that the infusion of the blessed milk thistle herb increases diuresis by 20%, sodium diuresis by 43% and potassium diuresis by 38% in 4 h. The same drug increased diuresis by 28% in 24 h, and sodium and potassium diuresis by 34%. In the authors’ opinion, the diuretic effect of the blessed milk thistle herb could harmoniously complement the hepatoprotective effect of the fruits of the same plant when obtaining complex preparations based on them [89].

Thus, it can be noted that there are many types of MPRMs that have a mild diuretic effect. The leading group of active substances in most of the promising types of MPRMs are flavonoids [94, 95], as well as terpenoids [96]. All the types of raw materials listed by the authors, can further become the basis for the creation of domestic effective medicines with a diuretic effect.

ISSN 2307-9266 e-ISSN 2413-2241

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CONCLUSION

MPRMs and preparations based on them with a diuretic effect, are important means for the treatment of kidney and urinary tract diseases, as well as many concomitant diseases. The diuretic effect of herbal diuretics is due, most often, to the content of the substances of terpene and phenolic nature, among which flavonoids are of particular importance.

A huge structural diversity of BACs of medicinal plants, as well as the combination of various active substances in each particular plant, as a rule, provides not only the main diuretic effect, but also such effects as anti-inflammatory, antimicrobial, antispasmodic and others that contribute to achieving a therapeutic effect. The severity of the disease, as well as the nature of the pathology of the urinary system, differ greatly from patient to patient. This indicates the necessary to pay attention to the issue of creating new effective domestic herbal diuretics.

FUNDING

This study didn't receive any support from outside organizations.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

All the authors confirm that their authorship meets the ICMJE international criteria (all the authors have contributed substantially to the conceptualization, research and preparation of the article, read and approved of the final version before the publication). Vladimir A. Kurkin – the idea of writing the article and systematization of the materials, methodology and a scientific guidance for compiling the review; Olga E. Pravdivtseva, Elena N. Zaitseva, Anastasia S. Tsibina – search for scientific literature, formulation of the concept of the review and systematization of the data block on the diuretic activity of terpenoids and phenolic compounds, writing the article; Anna V. Kurkina, Sergey V. Pervushkin, Alina V. Zhdanova – formation of a block of medicinal plants with a diuretic activity, writing the chemical block of the article, selection and critical analysis of the material, design of the article.

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