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Vexibia Alopecroides - How to New Source for the Synthesis of Physiologically Active Substances Used in Medicine

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Abstract
This work is devoted to the isolation of Vexibia alopecia des from the Fabacea family e physiologically active flavonoids and the possibility of synthesizing drugs used in medicine on their basis. As a result of the work, a flavonoid was isolated – in exibinol, its structure and properties were studied, and identified by IR, UV, PMR, NMR ^{13} methods of analysis.

Keywords: Flavonoids, soforamine, sofocarpine, matrine, cytosine, aloprin, carotenoids, coumarins, rutin isobavaquine, glabrol, trifolirizine, vexibinol.

Relevance of the problem

It is known from the medical scientific literature that more than 45% of medicinal preparations used in medicine are isolated from plants. The need for these drugs is growing every year since drugs obtained by synthesis cannot be used for a long time because in most cases they have side effects in the human body. It follows from this that the isolation of physiologically active substances and the synthesis of their derivatives on their basis makes it possible to create new highly effective drugs used in medical practice.

The Decree of the President of the Republic of Uzbekistan dated November 7, 2017 PF - 5229 “On measures to radically improve the management of the pharmaceutical industry” is also focused on this problem.

One of the possible such plants from which physiologically active compounds can be isolated are plants capable of synthesizing phenolic compounds. Among them, flavonoids play an important role in the process of growth and development, immunity and adaptation of plants.

With a wide range of pharmacological activity, flavonoids are used in medicine as choleretic, hepatoprotective, anti-ulcer, and capillary strengthening agents. The successful combination of low toxicity and high pharmacological activity makes them extremely promising for the prevention and treatment of a number of serious diseases. In recent years, several substances with antitumor, hypoazotemic, and tonic properties have been identified among them.

Purpose of the study

Plants of the legume family (Fabaceae) are a rich source of flavonoids that are diverse in structure and interesting in biological properties. The isolation and determination of the chemical structure of flavonoids of plants of this family, as well as the search for ways to use them in medicine and the national economy, is an urgent task.

Vexibia alopecuroides (L.) Yakovl. (vexibia foxtail) - a perennial weed with a simple or somewhat branched stem. It blooms in April-May, bears fruit in June-July, and in September the cycle of its annual development ends. Grows in groups in the steppes,

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clayey semi-deserts, along the banks of rivers and lakes, among tugai plants, sometimes in the foothills, and also as a weed plant in rainfed cotton crops [1,2]. It is widespread in our republic and its arrays occupy vast areas. The total area of its massifs in the republics of Central Asia is more than 2200 hectares, the total reserve of the above-ground part is I 345- I 530 tons, operational - I 050- I 250 tons [3].

Vexibia foxtail is included in the All-Union State quarantine as a poisonous, harmful and dangerous weed. A fresh plant is not eaten by livestock at all; a large admixture of it in hay causes poisoning. The plant has a strong insecticidal and repellent action, the powder made from the dry plant kills insects [4].

In folk medicine, crushed seeds are recommended for poor digestion and lack of appetite./2/. In Tibetan medicine, the roots are part of complex medicinal mixtures used for cardiovascular, gastrointestinal, oncological, and venereal diseases, as well as used as an antipyretic, antitussive and general tonic. The aerial part is used for pulmonary tuberculosis, rheumatism, diseases of the throat, and eyes, and as an anti-febrile agent./5/.

from vexibia soforamine, sofocarpine, matrine, L - sophoridin, cytisine, aloperine and other quinolizidine alkaloids were isolated in different periods of the growing season. /6.7/. Organic acids, carotenoids, coumarins, triterpene saponins, vitamins were found in the aerial part, and fatty oil was found in the seeds. /5,6,7 / Rutin (I, 35 and I, 27% respectively) and tannins were found in the leaves and fruits. /5/.

In the literature available to us, there was no information on a deep chemical study of the flavonoids of this plant. Preliminary studies of extracts of individual organs of vexibia foxtail, using thin-layer chromatography, it was shown that flavonoid compounds are mainly concentrated in the roots.

Materials and methods

The material for this study was the roots made in the Samarkand and Tashkent regions. Substances were isolated by extraction with ethanol, followed by separation of the condensed extract into petroleum ether, chloroform, and ethyl acetate fractions. Lipids, sterols, waxes and other non-polar compounds pass into petroleum ether. Flavonoids are found in chloroform and ethyl acetate fractions, and their main share falls on the first fraction.

For the isolation of individual substances, the chloroform fraction of the alcohol extract, as well as the chloroform extract from the roots of vexibia foxtail were separated by partition column chromatography on silica gel in a chloroform-methanol gradient system. Further purification of the selected fractions was carried out by rechromatography on silica gel and recrystallization from suitable solvents. As a result, 6 individual flavonoids were isolated, 4 of them were identified with isobavaquine, glabrol, ammotamnidine and trifolirizine, while vexibinol and vexibidin were new.

Results and discussion

Vexibinol isolated from the chloroform fraction of the alcoholic extract of the roots in the form of an optically active fine-crystalline powder of cream colour. When reduced with magnesium in hydrochloric acid, it forms a yellow, and with a solution of ferric chloride - a dark blue colour. On chromatograms, vexibinol appears as an orange-red spot after spraying with a solution of vanillin in sulfuric acid.

F (3366 cm $^{-1)}$, a carbonyl group conjugated with an aromatic nucleus (I 604; I 519 cm $^{-1)}$.

The U F spectrum of vexibinol has an absorption maximum at 293, 340 * (inflexion) nm, characteristic of flavonones and dihydro flavonols.

The fact that compound I belongs to flavonones is indicated by the presence in the PMR spectrum of diagnostic signals of protons of the heterocyclic ring C - H-2 AND H-3 /34-36/ and signals of carbon atoms C-2 (73.7 ppm) C-3 (41.4 ppm) in the ^{13}C NMR spectrum /77.78/.

Table 1. Physico-chemical properties of flavonoids vexibia foxtail

No.	*Compound names*	*Elemental composition*	*M.p. _ °C*	*/ α /D deg.*
1	Isobavachin	$C_{20}H_{20}O_4$	203-204	-45.3 (e)*
2	Glabrol	$C_{25}H_{28}O_4$	136-137	-39.2 (m)
3	Ammotamnidin	$C_{25}H_{28}O_4$	112-114	+4.5(m)
4	Vexibinol	$C_{25}H_{28}O_6$	174-176	-36.5(m)
5	Vexibidin	$C_{26}H_{30}O_6$	157-158	-43.6(m)
6	Trifolirizine	$C_{21}H_{24}O_{10}$	140-142	-180.7(p)

Designations: e - e tanol, m-methanol, p-pyridine.

Acetylation vexibinol with acetic anhydride in pyridine received tetraacetyl derivative II, in the PMR spectrum of which signals of four acetoxy protons appear at 2.23 (9H, s) and 2.29 ppm. (ZN,s). Therefore, substance I contains four phenolic hydroxyl groups. Indeed, in the PMR spectrum of vexibinol, proton signals are observed at 9.37; 9.63; 10.67 and 12.13 ppm due to the presence of four phenolic hydroxyl groups in its composition. The above data indicate that out of the six oxygen atoms of the I molecule, four belong to phenolic hydroxyl groups, and the remaining two are part of the pyrone ring. This conclusion is also confirmed by the study of the ^{13}C NMR spectrum of vexibinol, where the signals of five aromatic carbon atoms (155.2; 158.0; 160.5; 160.8; 164.4 ppm) associated with oxygen and carbonyl carbon group (194.4 ppm) Bathochromic shifts of the absorption maxima in the UV spectrum with aluminium chloride and sodium acetate /34.35/, as well as the chemical shift of the carbonyl group signal in the 17C NMR spectrum /2.7/ indicate the presence free hydroxyl groups at C-5.7.

Methylation I with ethereal solution of diazomethane leads to the formation of trimethyl ester III (NMR spectrum: 3.74; 3.75; 3.76 ppm, each at 3H, s). In the PMR spectra of compounds I - III, signals of protons of three vinylmethyl groups, a terminal methylene group, an olefinic proton, a methylene group attached to the aromatic nucleus, and three more aliphatic protons appear.

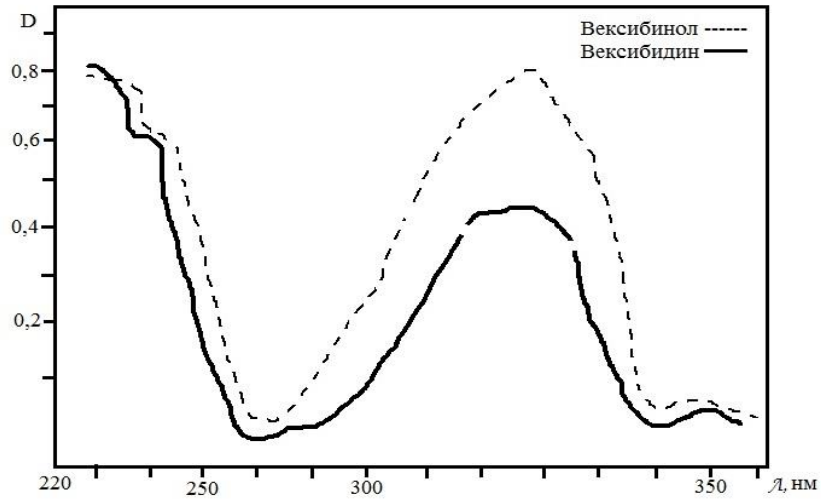


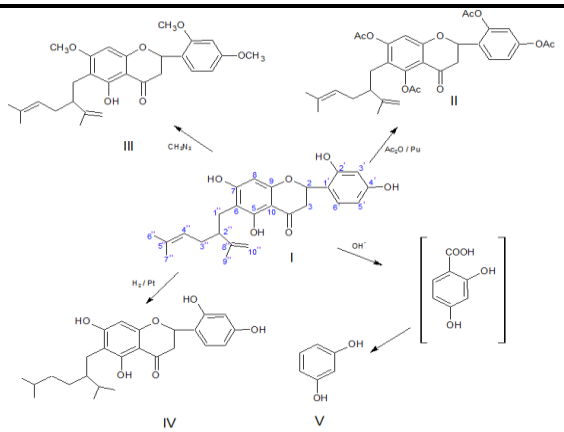
Fig.1 UV spectra vexibinol (I) and vexibidin (YI)

Judging by the composition, the data of the PMR spectrum and the presence in the mass spectrum of intense peaks of ions with m / z 301 (M- $C_9H_{15})^+$ and m / z 124 ($C_9H_{16})^+$, vexibinol must contain an unsaturated aliphatic side chain, consisting of ten carbon atoms and having two double bonds. Hydrogenation of compound I according to Adams leads to the formation of tetrahydrovexibinol (IV), which, according to the data of the PMR spectrum, contains two isopropyl groups. In contrast to the spectra of compounds I - III, the spectrum of IV contains no signals of olefinic protons.

The above data and a comparative analysis of the PMR and ^{13}C NMR spectra of lavandulol (2-isopropenyl-5-methylhex-4-enol), kushenols A, E, F /6,7/ and vexibinol showed that the latter contains 2-isopropenyl -5-methylhex-4-enyl (lavandull) side chain attached to the aromatic core by a C-C bond the biological activity of isolated flavonoids that flavexan in small doses lowers the level of cholesterol, β- lipoproteins and triglycerides in the blood serum of experimental animals under conditions of experimental hyperlipidemia and atherosclerosis.

In experiments on rabbits with experimental atherosclerosis, a clear protective effect of flavexan was found, characterized primarily by a decrease in atherosclerotic lesions of the aorta. In its anti-atheromatous effect, the drug developed by us surpasses the widely used drug clofibrate (miscleron). Unlike clofibrate Flavexan is a low-toxic drug; oral administration of it in doses of 1000-2000 mg/kg to mice did not cause any deviations in the behavior of experimental animals. In addition, flavexan is characterized by a decrease in vascular permeability when using various irritating agents (histamine, xylene, ovalbumin, etc.) and an antioxidant effect, which is especially important in the treatment of cardiovascular diseases

Chemical transformations vexibinol



Conclusions

1. The chemical composition of flavonoids of plants of the Fabacea e family was studied: Vexibia alopecuraides.
2. From the roots of vexibia foxtail isolated a new flavanone - vexibinol and also known e- isobavaquine, glabrol, ammotamnidine and trifolirizine:
3. As a result of chemical transformations and analysis; And K-, UV-, mass-, PMR-NMR ^{13} -, spectra established the structure and configuration of vexibinol.
4. A laboratory method has been developed for obtaining the sum of flavonoids vexibia foxtail, which has a pronounced hypolipidemic and anti-atherosclerotic activity.

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