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NEW SOURCE OF SYNTHESIS OF PHYSIOLOGICALLY ACTIVE SUBSTONCES

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ABSTRACT:

Fiziological active flavinoids and possibilities for sintesis medical drugs used in medicine. In a result of our work excreted flawing Vexibinol and identified the configuration with IR-, UF-PMR-KD- With alanisys methods

KEYWORDS: Flavinoids, soforamin, cofokarpin, matrin, sitozin, alaprin,karotinids, kumarins, rutin, izobavahin, glabrol, trifolirizin, veksibinol.

INTRODUCTION:

Relevance of the problem: From medical scientific literature it is known that more than 45% of medicinal products used in medicine are isolated from plants. The need for these drugs is growing annually, since drugs obtained by synthesis cannot be used for a long time, because in most cases they have side effects in the human body. From this it is clear 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 these 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 processes of growth and development, immunity and adaptation of plants.

With a wide range of pharmacological activity, flavonoids are used in medicine as choleretic, hepatoprotective, antiulcer, 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, a number of substances with antitumor, hypoazotemic, and tonic properties have been identified among them.

OBJECTIVE:

Plants of the legume family (Fabaceae) are a rich source of flavonoids that are diverse in structure and interesting in biological properties. Isolation and establishment 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) is a perennial weed plant 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. It grows in groups in steppes, clay semi-deserts,

along the banks of rivers and lakes, among tugai plants, sometimes in the foothill zone, and also as a weed plant in crops of rainfed cotton crops / / 1, 2 /. It is widespread in our republics and its massifs 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 aerial parts I345-I530 tons, operational - I050-I250 tons / 3 /.

Vexibia foxtail in the All-Union State Quarantine as a poisonous, harmful and dangerous weed. A fresh plant is not eaten by cattle at all, its large admixture in the hay causes poisoning. The plant has a strong insecticidal and repellent effect, a powder made from a dry plant kills insects ./4/.

In traditional 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, venereal diseases, and also used as an antipyretic, antitussive, and general strengthening agent. The aerial part is used for pulmonary tuberculosis, rheumatism, diseases of the throat, eyes and as an anti-fever remedy ./5/.

Sophoramine, sofocarpine, matrine, L-sophoridine, cytisine, aloperin and other quinolysidine alkaloids were isolated from fox-tail vesibia at various periods of vegetation. / 6.7 /. Organic acids, carotenoids, coumarins, triterpene saponins, vitamins were found in the aerial parts, and fatty oil was found in the seeds. / 5,6,7 / In the leaves and fruits, rutin (I, 35 and I, 27%, respectively) and tannins were found. / 5 /.

In our available literature, there was no information about a deep chemical study of the flavonoids of this plant. Preliminary studies of extracts of individual organs of vexibia foxtail using TLC showed that flavonoid compounds are mainly concentrated in the roots.

Materials and research methods: The plant material for this study was the roots harvested in the Samarkand and Tashkent regions. The substances were isolated by ethanol extraction, 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 were found in the chloroform and ethyl acetate fractions, their main fraction being in the first fraction.

To isolate individual substances, the chloroform fraction of the alcoholic extract, as well as the chloroform extract from the roots of Vexibia foxtail, were separated by silica gel column chromatography 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 isobavachine, glabrol, ammotamnidine and trifolirizin, and vexibinol and vexibidine were new.

THE STRUCTURE OF VEXIBINOL:

RESULTS AND DISCUSSION:

Vexibinol was isolated from the chloroform fraction of the alcoholic root extract in the form of an optically active fine-crystalline creamy powder. When reduced with magnesium in hydrochloric acid, it forms yellow, and with a solution of ferric chloride - a dark blue color. On the chromatograms, vexibinol appears as an orange-red spot after spraying with a solution of vanillin in sulfuric acid. Φ (3366 cm-1), a carbonyl group conjugated to the aromatic nucleus (I 604; I 519 cm-1).

The UV spectrum of vexibinol has a maximum absorption at 293, 340 * (kink) nm, characteristic of flavonones and dihydro flavonols.

The fact that compound I belongs to flavonones is indicated by the presence 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 in the PMR spectrum 41.4 ppm) in the 13C NMR spectrum (77.78).

The table shows the physicochemical properties of flaxon vexibia foxtail

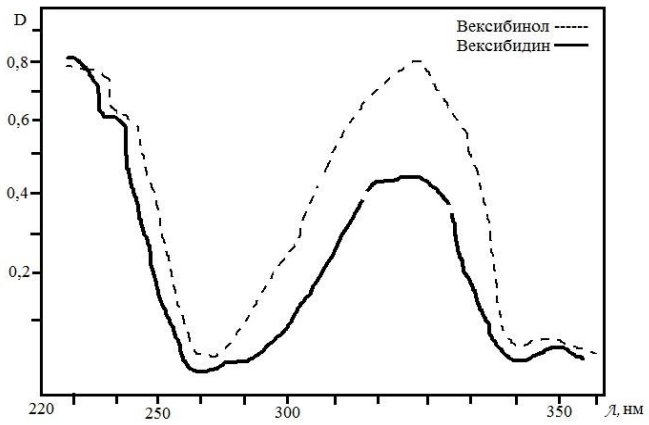
№	Connection Names	Elemental composition	temperature ^{0}C	/α/D grad.
1	Izobavakhin	$C_{20}H_{20}O_4$	203-204	-45,3 (э)*
2	Glabrol	$C_{25}H_{28}O_4$	136-137	-39,2 (м)
3	Ammotamnidine	$C_{25}H_{28}O_4$	112-114	+4,5(м)
4	Vexibinol	$C_{25}H_{28}O_6$	174-176	-36,5(м)
5	Vexibidine	$C_{26}H_{30}O_6$	157-158	-43,6(м)
6	Trifolirizin	$C_{21}H_{24}O_{10}$	140-142	-180,7(п)

Designations: e – ethanol, m-methanol, p-pyridine.

Acetylation of vexibinol with acetic anhydride in pyridine gave the tetraacetyl derivative II, in the NMR spectrum of which proton signals of four acetoxyls appeared at 2.23 (9H, s) and 2.29 ppm. (ZN, s). Therefore, substance I contains four phenolic hydroxyl groups. Indeed, in the 1H-NMR spectrum of vexibinol recorded in DMSO α6, 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 of the six oxygen atoms of molecule I, four belong to phenolic hydroxyl groups, and the remaining two are part of the пир-pyrone ring. This conclusion is also confirmed by the study of the 13C 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 carbon of the carbonyl group resonate (194.4 ppm) The bathochromic shifts of the absorption maxima in the UV spectrum with aluminum chloride and sodium acetate / 34.35 /, as well as the chemical shift of the carbon signal of the carbonyl group in the 17C / 2.7 NMR spectrum, indicate the presence of free hydroxyl groups at C-5.7.

Methylation of I with an ether solution of diazomethane leads to the formation of trimethyl ether III (PMR spectrum: 3.74; 3.75; 3.76 ppm, each in 3H, s). Signals of protons of three vinyl methyl groups, a terminal methylene group, an olefin proton, a methylene group attached to an aromatic nucleus, and three more aliphatic protons appear in the 1H-NMR spectra of compounds I-III.

UV spectra of vexibinol (I) and vexibidine (YI)



Judging by the composition, data of the PMR spectrum and the presence of intense peaks of ions with m / z 301 (M-C9H15) + and m / z 124 (C9H16) + vexibinol in the mass spectrum should 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 production of tetrahydrovexibinol (IV), which, according to the PMR spectrum, contains two isopropyl groups. In contrast to the spectra of compounds I-III, the signals of olefin protons are absent in spectrum IV.

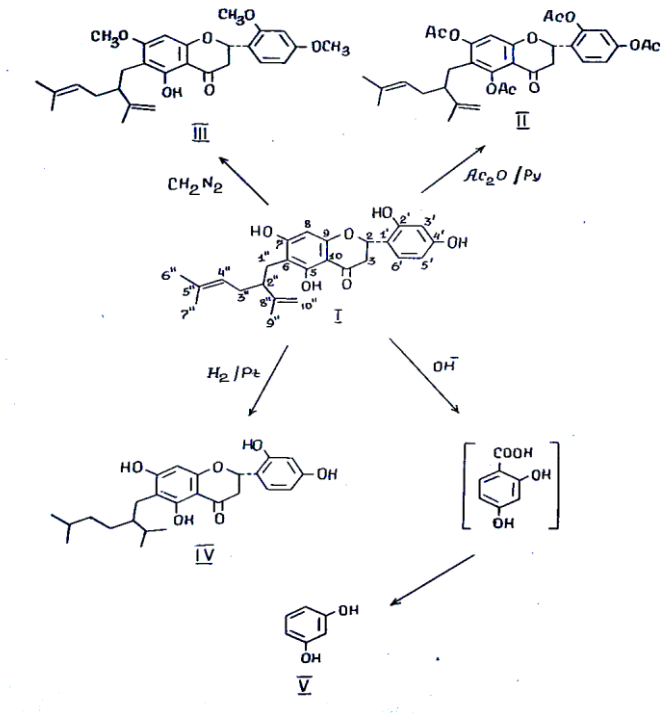
The above data and a comparative analysis of the 1 H NMR and 13 C NMR spectra of lavenderulol (2-isopropenyl-5-methylhex-4-enol), cuchenols A, E, F / 6.7 / and vesibinol showed that the latter contains 2-isopropenyl-5 -methylhex-4-enyl (lavender) side chain attached to the aromatic nucleus of a CC bond.

BIOLOGICAL ACTIVITY OF ISOLATED FLAVONOIDS:

It was found that flavexan in small doses lowers cholesterol, β-lipoproteins and triglycerides in the blood serum of experimental animals under 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 action, the drug we developed exceeds the widely used drug clofibrate (miskleron). Unlike clofibrate, flavexan is a low-toxic drug; administering it in doses of 1000-2000 mg / kg to mice orally 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 OF VEXIBINOL:



CONCLUSIONS

1. The chemical composition of the flavonoids of plants of the family Fabacea: Vexibia alopecuraides was studied.
2. The new flavanone and vexibinol, as well as the well-known isobavachin, glabrol, ammotamnidine and trifolirizin, were isolated from the roots of vexibia foxtail:
3. The structure and configuration of vexibinol-(2 S) - 5,7,2I, 4I-tetrahydroxy-6- (2II-isopropenyl-5II methylhex-4II-enyl) -flavanone - were established as a result of chemical transformations and analysis of IR, UV -, mass, PMR-YNR13-, CD spectra;
4. A laboratory method has been developed to obtain the sum of flaxon vexibia foxtail, with pronounced hypolipidemic and antiatherosclerotic activity.

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