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PROPERTIES OF THE GLYCYRRHIZA GLABRA PLANT AND THE OBTAINMENT OF GLYCYRRHIZIC ACID SALTS AND THEIR CHEMICAL STRUCTURES

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Abstract
This article presents information on the biology, properties, folk medicinal uses of the plant Glycyrrhiza glabra, and the extraction of technical glycyrrhizic acid (TGK), triammonium glycyrrhizic acid (GKUAT), monoammonium glycyrrhizic acid (GKMAT), and monopotassium glycyrrhizic acid (GKMKT) salts from the liquid extract of its roots, as well as their chemical composition and structure.

Keywords: Glycyrrhiza glabra, licorice, licorice, liquid extract, technical glycyrrhizic acid (TGK),, glycyrrhizic acid (GK), triammonium glycyrrhizic acid (GKUAT), monoammonium glycyrrhizic acid (GKMAT), monopotassium glycyrrhizic acid (GKMKT).

Introduction

Infusions and decoctions of the root of Glycyrrhiza glabra L are used for inflammation of the upper respiratory tract and as an expectorant, in the treatment of stomach ulcers. It is used in diseases of the gallbladder and spleen, liver, as a diuretic, and as an antidote for snakebites. The root of Glycyrrhiza glabra L is considered the second most effective drug after ginseng in rejuvenating the body and is recommended more for the elderly. The root of Glycyrrhiza glabra L, which is rich in biologically active compounds, contains potassium and calcium salts of GK. Sodium and potassium mixed salts of GK are highly effective stimulants in the reparative regeneration of the skin. In order to obtain effective immunomodulators and immunostimulants, a number of GK derivatives were synthesized based on the amino acids in the molecule of certain peptides, and it was found that they have primary immunostimulating properties when administered once to animals.

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LITERATURE ANALYSIS AND METHODOLOGY

Glycyrrhiza glabra L.; Licorice (Licorice, Licorice)., belongs to the Fabaceae family. Licorice is a perennial herb, reaching a height of 50 - 100 cm, with a strongly developed underground part. The rhizome is multi-headed, short, thick, with horizontal underground branches on all sides, ending with a tip bud, and one main vertical taproot growing downwards. The length of the main taproot is 4 - 5 m. The stem is several, erect, unbranched or sparsely branched, hairy, covered with small pointed glands or small spines. The leaf blade is compound, consisting of 3 - 7 pairs of leaflets. The leaf is elliptic, oblong-ovate or lanceolate, with smooth edges, covered with sticky glands. The accessory leaves are small, lanceolate, and pubescent. The flowers are arranged in a raceme that emerges from the leaf axils. The calyx is tubular, 5-lanceolate, and the corolla is purplish-purple in color, typical of butterfly inflorescences. There are 10 stamens, 9 of which are united with each other, and the tenth is not united, located above the maternal node. The fruit is a pod that does not open when ripe or opens after the peduncle dries. It flowers in June-August, and the fruit ripens in August-September. [1] (Figure 1).

Figure 1. Glycyrrhiza glabra plant and its roots and waste

The plant Glycyrrhiza glabra grows in saline soil, along ditches, canals, and rivers in the grasslands, and as a weed in crops. It is found in large quantities mainly in the arid and semi-arid regions of Central Asia, Kazakhstan, the North Caucasus, Transcaucasia, and large areas of Ukraine, Moldova, Belarus, and the south of the European part of Russia (along the Sea of Azov, in the upper and middle reaches of the Don and Volga rivers). The product is produced in the Ural River valley, Dagestan, Turkmenistan, and Uzbekistan (along the Amu Darya and Syr Darya rivers), as well as in Southern Kazakhstan.

The root of Glycyrrhiza glabra L contains glycosides, sucrose, flavonoids, essential oil, vitamin E, mineral salts and pectin substances. Plants of the genus Glycyrrhiza glabra L accumulate triterpene glycosides in their roots and rhizomes. One of the main glycosides is glycyrrhizic acid.

More than ten species of the plant Glycyrrhiza glabra L contain glycyrrhizic acid, of which the most studied are the naked licorice (Glycyrrhiza glabra.L), the Ural licorice (Glycyrrhiza uralensis Fish) and the Korshinski licorice (Glycyrrhiza Korshinski G). The amount of GK in licorice root can reach 24% and is found in the form of mixed potassium-calcium-magnesium salts, which give it a sweet-sour taste [2].

In the development of drugs based on GK and its derivatives, its solubilization property is one of the main factors. It has been shown that many poorly or completely insoluble drugs (aspirin, indomethacin, etc.) form molecular complexes with GK and its salts, becoming water-soluble. Many studies are known about the structure of GK and its derivatives

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According to the data presented in these sources, the structure of GK is considered to be the correct structure corresponding to 3-O-(2'-O-β-D-glucurono-pyranosyl)-β-D-glucuronopyranoside of 3β-hydroxy-11-oxo-12-ene-18β-H, 20β-olean-30 acid (Fig. 2)

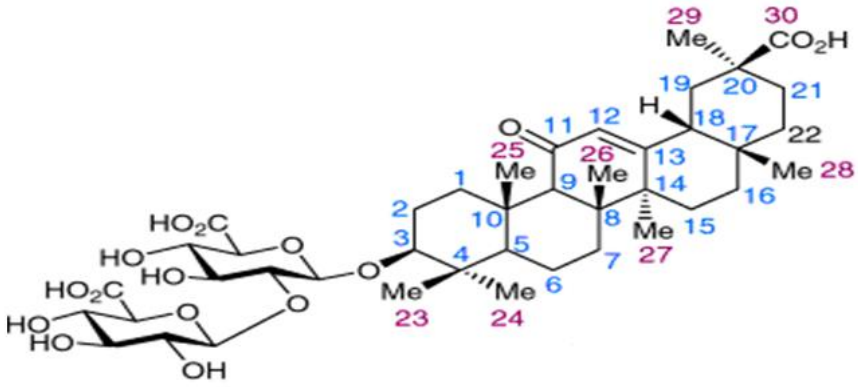

Figure 2. Chemical structure of glycyrrhizic acid

Glycyrrhizic acid (GK) consists of two parts: hydrophobic (aglycone triterpene) glycyrrhetic acid (a) and hydrophilic (2 sugar molecules, glucuronic acid).si(b). Figure 3.

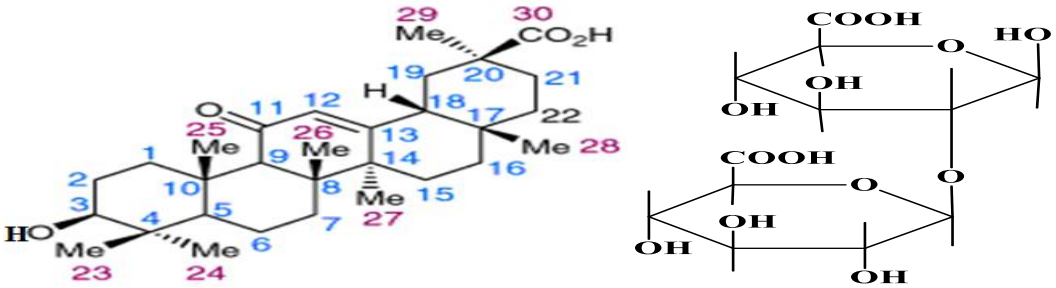

Figure 3. (a) Hydrophobic (aglycone triterpene) glycyrrhetic acid and (b) Hydrophilic (2 sugar molecules, glucuronic acid)

In terms of aglycone structure, it has some similarities with glucocorticoid hormones. Due to this property, GK and its salts have the properties of regulating salt metabolism (in Addison's disease) and anti-inflammatory effects. In addition, GK is a synergist of corticosteroid hormones [3].

To study the antiulcer activity, derivatives of GK with the glucuronic acid moiety were obtained. For this, peracetyl derivatives of GK or its 30 methyl ester were glycosylated in dichloroethane with 2,3,4,6-tetra-O-acetyl or α-D-galactopyranosyl bromide in the presence of Ag_2CO_3. In order to study the antiulcer activity, when compared with GK, it was found that the D-galactopyranosyl-containing GK saponin had a higher antiulcer activity than GK at a dose of 25 mg/kg [4-10].

The fact that GK is composed of hydrophobic (triterpene) and hydrophilic (glucuronide) parts, its excellent physicochemical properties, such as surfactant and gel formation, are related to its structural features. The ^{13}C NMR method has shown the existence of a cyclic conformation of GK [11], but scientists have not provided information on the favorable energy of this conformation. The phase structure of glycyrrhizic acid is presented below (Figure 4) [12].

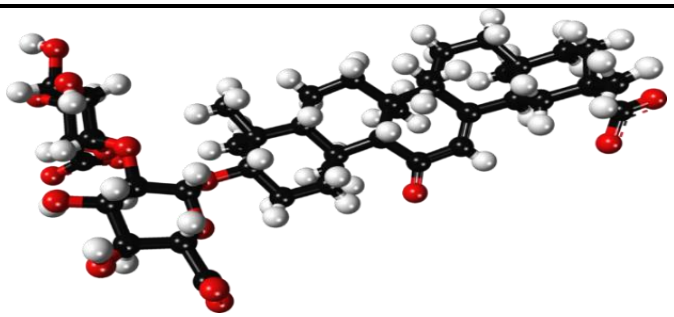

Figure 4. Spatial structure of glycyrrhizic acid

The root of Glycyrrhiza glabra L contains (about 4%) flavonoids (liquiritin, linquiritoside, glabroside and other glycosides and their aglycones), 2-4% bitter substance, triterpenoid-oleanan, vitamin C, asparagine, 6-34% starch, up to 20% mono- and disaccharides, pectin and other substances. The above-ground part of licorice is rich in flavone glycosides. In addition to flavonoids, the above-ground part also contains saponins, essential oil, sweeteners and other substances. When a solution of glycyrrhizin is shaken, it forms a stable foam, like saponins, but it does not dissolve red blood cells, that is, it does not hemolyze blood, only the aglycone glycyrrhetinic acid formed as a result of hydrolysis gives a hemolytic reaction. According to X DF, the content of glycyrrhizin acid in the product should not be less than 6%. [13-18].

In folk medicine, tinctures and decoctions of the plant Glycyrrhiza glabra are used as an expectorant for respiratory diseases and as a mild laxative for chronic constipation. Medicinal preparations prepared from the roots of Glycyrrhiza glabra L., glycyram, are used for asthma, eczema, allergic dermatitis, and other diseases. The plant-derived preparations, as well as glycyrrhizin and glycyrrhetinic acids, regulate water-salt metabolism in the body and have an effect similar to deoxycorticosterone. Liquiriton, a flavonoid compound obtained from the roots of Glycyrrhiza glabra L., is used as an anti-inflammatory, antispasmodic, and antiseptic agent, and for the treatment of gastric and duodenal ulcers. Glycyrrhiza glabra L root powder, grated root, and dry extract are used in pharmaceutical practice as a base for the preparation of herbal medicines and to improve the taste of mixtures and teas. Glycyrrhiza glabra L root is widely used in the food industry (to sweeten the taste of beer, lemonade, and kvass) and in technology (to prepare a foaming agent for extinguishing fires). [18-22].

RESULTS AND DISCUSSION

According to the literature, the content of GK in the root of "Glycyrrhiza glabra" reaches 2-24%. Many methods for isolating GK have been proposed, most of which are based on the precipitation of GK from an aqueous extract of the root with the help of mineral acids. The nature and concentration of the mineral acid play an important role in the precipitation of GK, for example, when concentrated H_2SO_4 is used for its precipitation, GK precipitates quickly and easily, but the main product precipitates in a tarry state, and the amount of ballast substances in the precipitate is much higher. A large amount of water is consumed to bring the tarry precipitate to an amorphous state, as a result of which the product yield is significantly reduced. The use of diluted mineral acids in the precipitation of GK: firstly, ensures the precipitation of the product in an amorphous state; Secondly, it leads to a decrease in the amount of ballast substances that precipitate together with the precipitate. It is also

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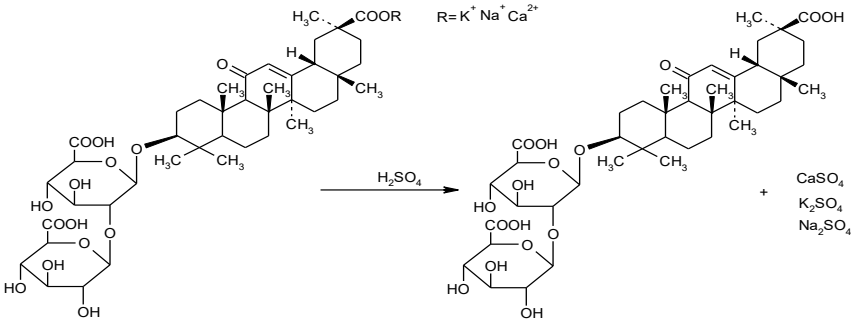
important to note that concentrated H_2SO_4 should be added dropwise to the aqueous extract, otherwise it will drastically affect the yield of the substance being obtained. If the pH is in the range of 2.5-3.5, TGK is produced in high yield. The extraction of TGK also depends on the amount of concentrated H_2SO_4. This is because the extract contains HC in the form of salts, so we need to add a sufficient amount of acid to it. The method of extracting TGK from the liquid extract of Glycyrrhiza glabra L root is carried out according to the following reaction. 700 g of liquid extract of licorice root was dissolved in water in a ratio of 1:4, and concentrated sulfuric acid was added while stirring until the precipitation of technical GK stopped. The precipitate was filtered through a dense gray cloth. The filtrate was washed with water until neutral. The precipitate was dried first in the open air, then in a drying cabinet at 60^0C. TGK brown amorphous powder Yield 135 g (17-19%). Melting point = 1250C. The extraction of TGK from the roots of Glycyrrhiza glabra (licorice) by the action of sulfuric acid and the subsequent preparation of the final product GKMAT was carried out step by step according to the following method, which is presented in Figure 5.

Figure 5. Brown amorphous powder of TGK and GKMAT from the plant Glycyrrhiza glabra

The method for extracting TGK from the liquid extract of the root of Glycyrrhiza glabra L is carried out according to the following reaction. 700 g of liquid extract of the root of Glycyrrhiza glabra L is dissolved in water in a ratio of 1:4, and concentrated sulfuric acid is added with stirring until the precipitation of technical glycyrrhizic acid stops. The precipitate is filtered through a dense gray cloth. The filtrate is washed with water until neutral. The precipitate is first dried in the open air, then in a drying cabinet at 600C. The method for extracting technical glycyrrhizic acid (TGK) from the liquid extract of the root of Glycyrrhiza glabra L is presented in Scheme 1.

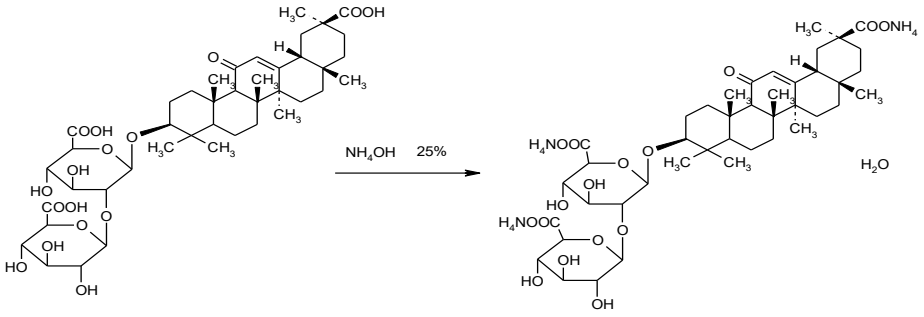


Root of Glycyrrhiza glabra L dark extract

TGK

Scheme 1. Precipitation of technical glycyrrhizic acid (TGK) from the liquid extract of the root of Glycyrrhiza glabra L.

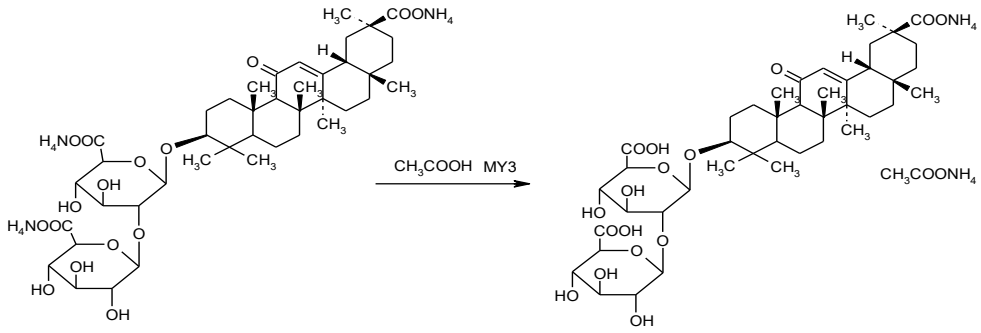
The method for obtaining triammonium salt of glycyrrhizinic acid (TGK) from technical glycyrrhizinic acid (GKUAT) is carried out according to the following reaction. 300 g of technical glycyrrhizinic acid was placed in a 3-necked flask with a volume of 3000 ml, equipped with a reflux condenser, mechanical stirrer and thermometer, and extracted with 2 l of dry acetone for 3 hours at 50-60 0C. After filtering the acetone extract, it was extracted with another 2 l of acetone. A concentrated solution of 25% NH_4OH was added to the combined acetone extracts with stirring until the pH reached a weak alkaline environment of ~ 8-9. The yellow precipitate of triammonium salt of glycyrrhizinic acid was filtered and washed with acetone. and dried at room temperature. Tsyuyq = 1350C. The method for obtaining the triammonium salt of glycyrrhizinic acid by reacting technical glycyrrhizinic acid (TGK) with NH_4OH is presented in Scheme 2.



TGK GKUAT

Scheme 2. Preparation of the triammonium salt of glycyrrhizic acid

To obtain the monoammonium salt of glycyrrhizinic acid (GKUAT) from the triammonium salt of glycyrrhizinic acid (GKMAT), 40 g of the triammonium salt of glycyrrhizinic acid were placed in a 1000 ml (1 l) flask and 400 ml of glacial acetic acid were added in a 1:10 ratio. It was heated in a water bath at 90-95°C until completely dissolved. When a homogeneous system was obtained, the solution was filtered hot and left at room temperature overnight for 12 hours. The precipitated crystals of GKMAT were filtered on a Buchner funnel and washed three times with glacial acetic acid and then with ethyl alcohol. The wet Technic GKMAT was dried in the open air and recrystallized from 80% ethyl alcohol (1:3 ratio). A pale yellow amorphous powder. Liquid = 225-227ºC, [α]D25 = +40 (50% ethanol), The method for obtaining glycyrrhizinic acid triammonium salt (GKMAT) by hydrolysis with glacial acetic acid is presented in Scheme 3.



GKUAT GKMAT

Scheme 3. Hydrolysis with glacial acetic acid to obtain GCMAT.

The IK spectrum of glycyrrhizinic acid triammonium salt (GKUAT) obtained by hydrolysis of glycyrrhizinic acid triammonium salt (GKMAT) with glacial acetic acid is shown in Figure 6.

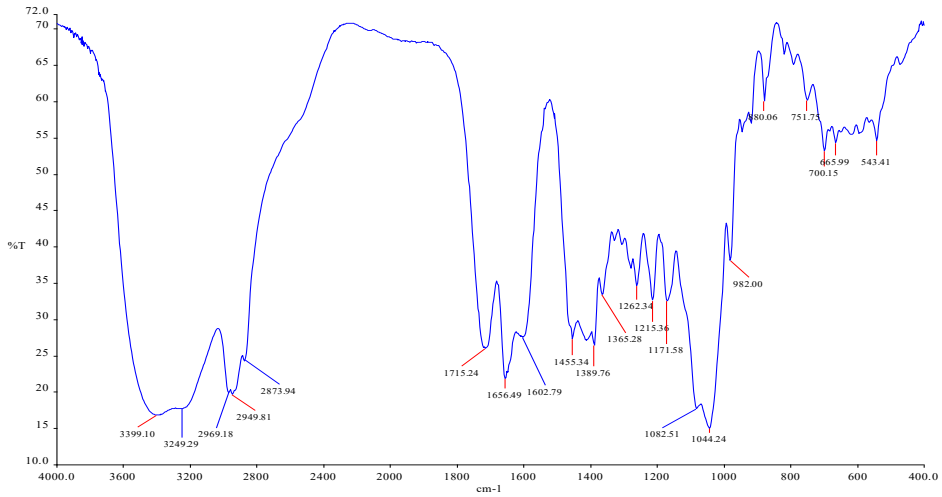


Figure 6. IR spectrum of GCMAT 80-82%

In the IR spectrum of GCMAT, the valence vibration in the form of a broad shoulder corresponding to the ON groups in its sugar moiety was observed in the region between 3200-3400 cm-1, the valence vibration corresponding to the C=O bond in the free carboxyl groups was observed in the region between 1710-1680 cm-1, and the valence vibration in the form of a broad shoulder corresponding to the O=CO–NH4+ carbonyl groups involved in salt formation was observed in the region between 1200-1000 cm-1. While the valence vibration corresponding to the C–O–C bonds was visible in the spectrum in the region between 1200-1000 cm-1, the valence vibration corresponding to the adjacent carbonyl group O=C–C=C– was observed in the region between 1643 cm-1 (Figure 6) [15-22].

CONCLUSIONS

Technical glycyrrhizic acid (TGK), triammonium glycyrrhizic acid (GKUAT), monoammonium glycyrrhizic acid (GKMAT), and monopotassium glycyrrhizic acid (GKMKT) salts were isolated from the liquid extract of the root of Glycyrrhiza glabra L.

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