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GLYCYRRHIZA GLABRA PLANT PROPERTIES, USES IN FOLK MEDICINE AND PREPARATION AND CHEMICAL STRUCTURES OF GLYCYRRHIZIN ACID SALTS

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Annotation: *In this article, the biology, properties, uses in folk medicine of Glycyrrhiza glabra plant and the preparation of technical glycyrrhizic acid (TGK), glycyrrhizic acid triammonium (GKUAT), glycyrrhizic acid monoammonium (GKMAT), glycyrrhizic acid monopotassium (GKMKT) salts from its dark root extract and their chemical Information about the composition and structure is provided.*

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

INTRODUCTION.

The root of the licorice plant is a medicine known in folk medicine since ancient times. Licorice root has been used in folk medicine in Chinese medicine for 2800 years. Its tinctures and decoctions are used for inflammation of the upper respiratory tract and as an expectorant. Shirinmia is used in the treatment of stomach ulcers. It is used in gall bladder and black spleen, liver diseases, as a diuretic, and as an antidote to snakebite poisoning. Licorice root is the second most rejuvenating medicine after ginseng and is more recommended for the elderly. Licorice root, which is rich in biologically active compounds, contains potassium and calcium salts of GK. Mixed salts of GK with sodium and potassium are highly effective stimulators of reparative skin regeneration. In order to obtain effective immunomodulators, immunostimulators, a number of GK derivatives were synthesized based on the amino acid content of certain peptide molecules, and when they were administered to animals once, they were found to have primary immunostimulatory properties.

LITERATURE ANALYSIS AND METHODOLOGY

Glycyrrhiza glabra L.; Licorice (sweet licorice, sweet licorice), legumes - belongs to the Fabaceae family. Licorice is a perennial, 50-100 cm tall herbaceous plant with a strongly developed underground part. The rhizome is cup-headed, short, thick, horizontally underground from all sides, ending with a bud, and one main vertical root growing downwards. The length of the main shoot root is 4 - 5 m. The stem is several, erect, unbranched or sparsely branched, hairy, covered with small point glands or small spines. The

leaf is composed of 3-7 pairs of leaflets. The leaf is elliptic, oblong-ovate or lanceolate, flat-edged, covered with sticky glands. Additional leaves are small, lanceolate, and become dull. The flowers are clustered in a peduncle emerging from the axils of the leaves. The calyx is tubular, with 5 lanceolate, sharp-toothed corollas, purple in color, and has the structure typical of butterfly florets. there are 10 paternity nodes, 9 of which are connected to each other, and the tenth is not connected to the maternal node. The fruit is a pod that does not open when ripe or opens when the stem dries. It blooms in June-August and fruits in August-September. [1] (Figure 1).

Fig. 1. Glycyrrhiza glabra plant and its root and waste

The plant Glycyrrhiza glabra grows in marshes with saline soil, ditches, canals and riverbanks in marshes, as a weed in cultivated fields. It is found abundantly in the desert and semi-desert regions of Urta Osnyo, Kazakhstan, the North Caucasus, Transcaucasia, Ukraine, Moldova, Belarus, and the south of Europe (along the Sea of Azov, in the lower and middle parts of the Don and Volga rivers). The product is produced in the valley of the Ural River, in Dagestan, Turkmenistan and Uzbekistan (along the Amu Darya and Syrdarya Rivers) and in South Kazakhstan.

Licorice root contains glycosides, sucrose, flavonoids, essential oil, vitamin E, mineral salts and pectin substances. Liquorice plants accumulate triterpene glycosides in their roots and rhizomes. One of the main glycosides is glycyrrhizic acid.

Glycyrrhizic acid is found in more than ten species of licorice, and among them, bare licorice (Glycyrrhiza glabra.L), Ural licorice (Glycyrrhiza uralensis Fish) and Korzhinsky's licorice (Glycyrrhiza Korshinski G) are the most studied. The amount of GK in licorice root can reach 24%, and it is found in the form of potassium-calcium-magnesium mixed salts, which give a sweet-tart taste [2].

Its solubilization property is one of the main factors in the creation of drugs based on GK and its derivatives. It has been shown that many drugs that are poorly soluble or not at all soluble in water (aspirin, indomethacin, etc.) form molecular complexes with GC and its salts and become water-soluble.

Many studies are known about the structure of GK and its derivatives According to the information presented in these sources, the GK structure is 3-O-(2'-O-β-D-glucurono-pyranosyl)-β of 3β-hydroxy-11-oxo-12-ene-18β-N, 20β-olean-30 acid. The structure corresponding to -D-glucuronopyranoside is correct (Figure 2).

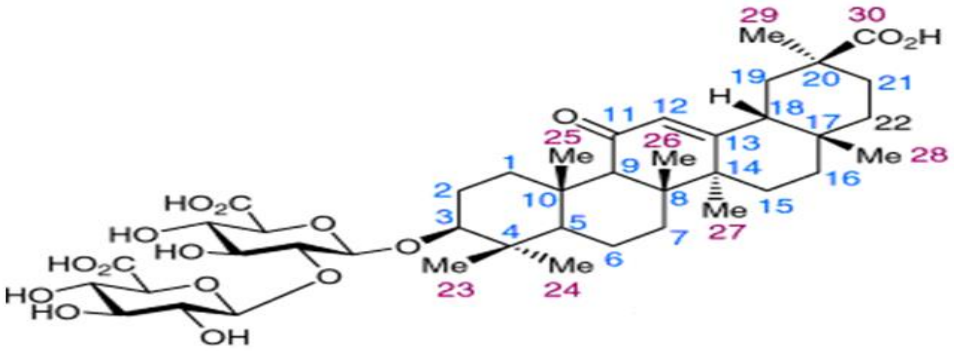
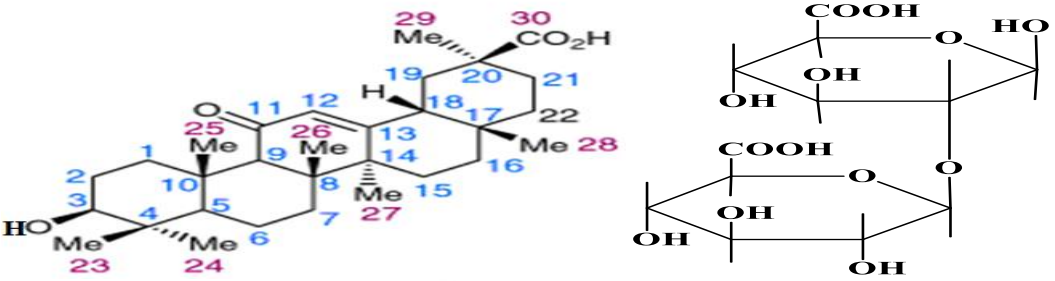


Figure 2. Chemical structure of glycyrrhizic acid

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



a b

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

In terms of the aglycon structure, there is some similarity to glucocorticoid hormones. According to this feature, GK and its salts have the properties of coordination of salt exchange (in Addison's disease) and anti-inflammatory effect. In addition, GK is a synergist of corticosteroid hormones [3].

Derivatives of GK on glucuronic acid part were obtained to study anti-ulcer activity. For this, GK is glycosidated with peracetyl derivatives or its 30 methyl ester in the presence of Ag2CO3, 2,3,4,6-tetra-O-acetyl or α-D-galactosopyranosyl bromide in dichloroethane. In order to study the anti-ulcer activity, compared to GK, D-galactosopyranosyl containing GK saponin was found to have a higher anti-ulcer activity than GK at a dose of 25mg/kg [4-10].

The amazing physicochemical properties of GK consisting of hydrophobic (triterpene) and hydrophilic (glucuron) parts, surfactant and gel formation are related to its structural features, and the cyclic conformation of GK is found by 13S NMR method [11], but scientists did not provide information about the favorable energy of this state conformation. The spatial structure of glycyrrhizic acid is shown below (Figure 4) [12].

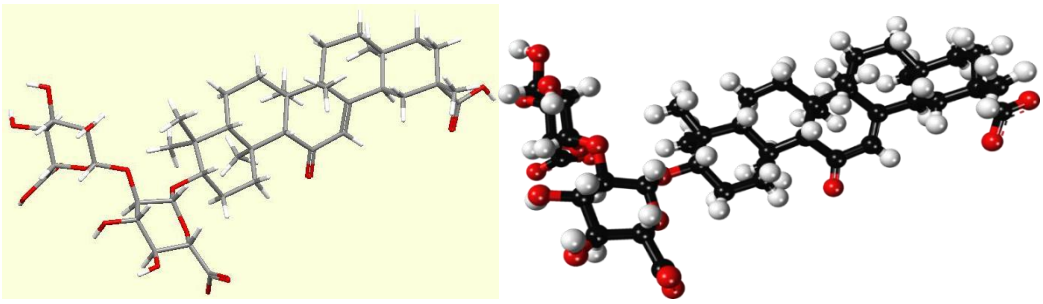


Figure 4. Spatial structure of glycyrrhizic acid

Licorice root (around 4%) contains flavonoids (liquiritin, lnkviritoside, 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 surface part of licorice is rich in flavone glycosides. In addition to flavonoids, the top part contains sapoins, essential oil, flavoring and other substances. If the solution of glycyrrhizin in water 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 hemolysis reaction. The amount of glycyrrhizic acid in the product should not be less than 6%. [13-14].

Decoctions and decoctions of Glycyrrhiza glabra plant are used in folk medicine as an expectorant for respiratory tract infections, and as a mild expectorant for chronic constipation. Medicinal preparations prepared from the root are used in the treatment of asthma, eczema, allergic dermatitis and other diseases. Preparations obtained from plants and glycyrrhizin and glycyrrhetinic acids regulate water-salt exchange in the body and have a similar effect to deoxycorticosterone. Liquiriton, a sum of flavonoids extracted from the root, is used as an anti-inflammatory, antispasmodic and antiseptic agent, and for the treatment of gastric and duodenal ulcers. Licorice powder, cut root and dry extract are used in pharmaceutical practice as a basis for preparation of medicine and to improve the taste of potions and teas. Licorice root is widely used in the food industry (to sweeten the taste of beer, lemonade and kvass) and in technology (for the preparation of flammable liquid). [13-14].

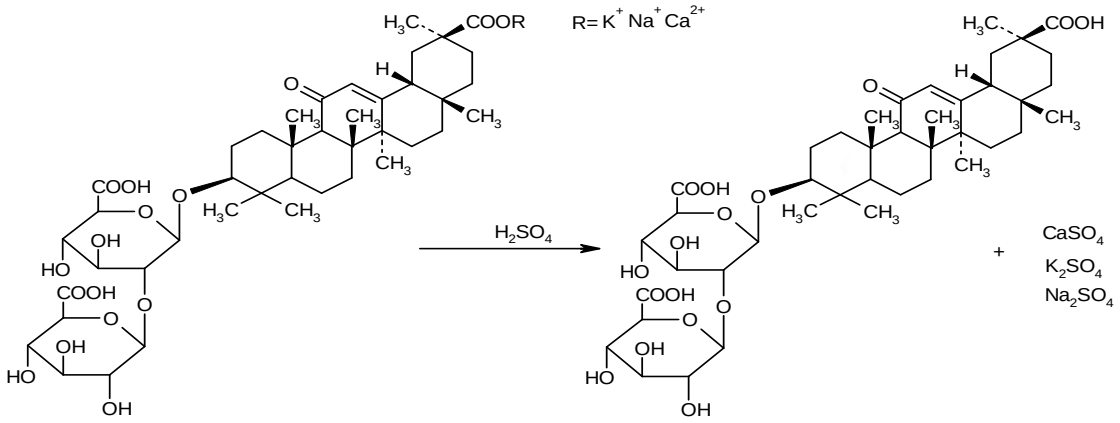
RESULTS AND DISCUSSION

According to information in the literature, the amount of GK in the root of "Glycyrrhiza glabra" reaches 2-24%. Many methods have been proposed for the extraction of HC, most of which are based on the precipitation of HC from the aqueous extract of the root with the help of mineral acids. The nature and concentration of the mineral acid plays an important role in the precipitation of HC, for example, when concentrated H2SO4 is used for its precipitation, HC precipitates quickly and easily, but the main product is precipitated in a tarry solid, and the amount of ballast substances in the precipitate is much higher. A large amount of water is used to transform the resinous precipitate into an amorphous state, resulting in a significant reduction in product yield. The use of diluted mineral acids in the deposition of GC: firstly, if it ensures the deposition of the product in an amorphous state; secondly, it causes a decrease in the amount of ballast material that is added to the sediment. It is also necessary to pay attention to the fact that concentrated H2SO4 should be added dropwise to the aqueous extract, otherwise the yield of the obtained substance will be drastically affected. If rN is in the range of 2.5-3.5, TGK is highly productive. Extraction of TGK also depends on the amount of conc H2SO4. The reason is that GK is in salt form in the extract, so we need to add enough acid to it. The method of extracting TGK from the dark extract of sweet potato root is carried out according to the following reaction. 700 g of dark licorice root extract was dissolved in water in a ratio of 1:4, and concentrated sulfuric acid was added with 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 600S. TGK brown amorphous powder Unum 135 g (17-19%). Tcuyuq=1250S. Extracting TGK from the roots of Glycyrrhiza glabra (liquorice) plant

by sulfuric acid and obtaining the next final product GKMAT was carried out in the following step-by-step manner shown in Figure 5.

Fig. 5. TGK brown amorphous powder of Glycyrrhiza glabra plant and GKMAT

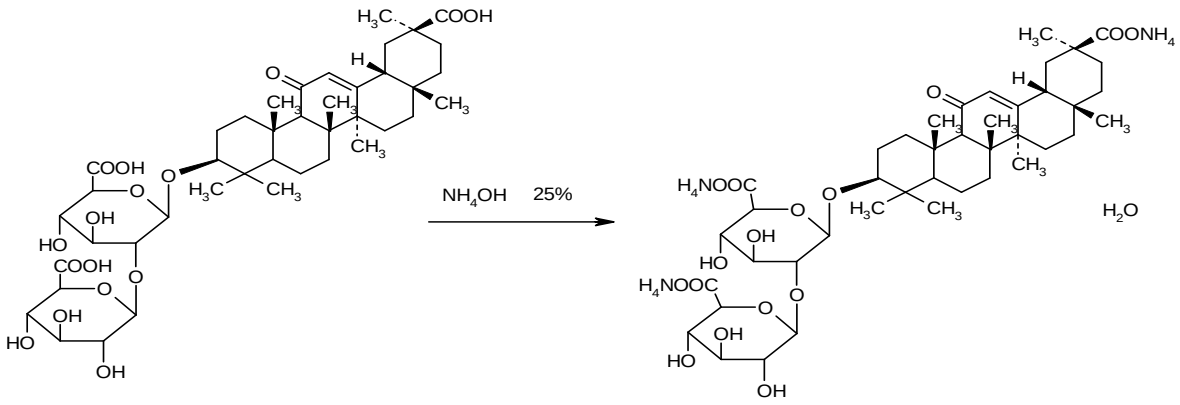
The method of extracting TGK from the dark extract of sweet potato root is carried out according to the following reaction. 700 g of dark licorice root extract is dissolved in water in a ratio of 1:4, and concentrated sulfuric acid is added while stirring until the precipitation of technical GK stops. 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 and then dried in a drying cabinet at 600S. The method for the precipitation of technical glycyrrhizic acid (TGC) from the dark extract of licorice root is presented in Scheme 1.



Licorice root dark extract TGK

Scheme 1. Precipitation of technical glycyrrhizic acid (TGK) from licorice root dark extract.

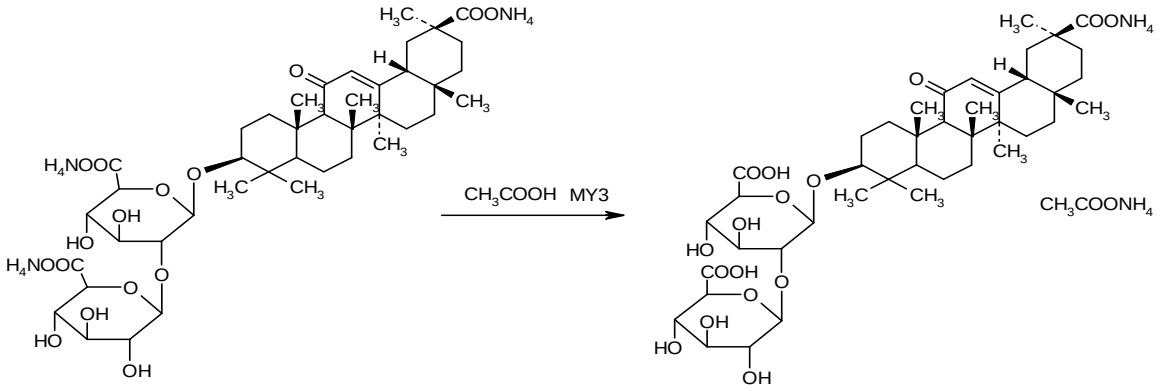
The method of obtaining triammonium salt of glycyrrhizic acid (GKUAT) from technical glycyrrhizic acid (TGK) is carried out according to the following reaction. 300 g of technical glycyrrhizic acid was placed in a 3000 ml 3-necked flask equipped with a reflux condenser, a mechanical stirrer and a thermometer, and it was extracted with 2 l of dry acetone at 50-60 0C for 3 hours. After the acetone extract was filtered, it was further extracted with 2 L of acetone. A concentrated solution of 25% NH4OH was added to the combined acetone extracts with stirring until pH 8-9 was weakly alkaline. The yellow precipitate of glycyrrhizic acid triammonium salt was filtered off and washed with acetone. and dried at room temperature.T_{liq}=135^{0}C. The method of obtaining triammonium salt of glycyrrhizic acid by NH_4OH effect on technical glycyrrhizic acid (TGA) is presented in scheme 2.



TGK GKUAT

Scheme 2. Preparation of triammonium salt of glycyrrhizic acid

To obtain monoammonium salt of glycyrrhizic acid (GKMAT) from triammonium salt of glycyrrhizic acid (GKUAT), 40g of triammonium salt of GK was added to a flask with a volume of 1000 ml (1l) and 400 ml of glacial acetic acid was added in a ratio of 1:10. It was heated in a water bath at 90-95oC until complete dissolution. When a homogenous system was obtained, the solution was filtered while hot and left at room temperature for 12 hours overnight. The precipitated GKMAT crystals were filtered in a Buchner funnel and washed three times with glacial acetic acid and then with ethyl alcohol. The wet technical GKMAT was air-dried and recrystallized in 80% ethyl alcohol (1:3 ratio). Light yellow amorphous powder. Liquid= 225-227°C, $[\alpha]_D^{25}$= +40 (50% ethanol), the method of obtaining GKMAT by hydrolysis of glycyrrhizic acid triammonium salt (GKUAT) with glacial acetic acid is presented in scheme 3.



GKUAT GKMAT

Scheme 3. Obtaining GKMAT by hydrolysis with glacial acetic acid.

Extraction of TGK from the root of Glycyrrhiza glabra (liquorice) plant by sulfuric acid and obtaining the next final product GKMAT was carried out in the following step-by-step manner, shown in Scheme 4.

Scheme 4. Extraction of GK, GKMAT and GKMKT from the root extract of Glycyrrhiza glabra (liquorice)

Figure 6 shows the IR spectrum of GKMAT obtained by hydrolysis of glycyrrhizic acid triammonium salt (GKUAT) with glacial acetic acid.

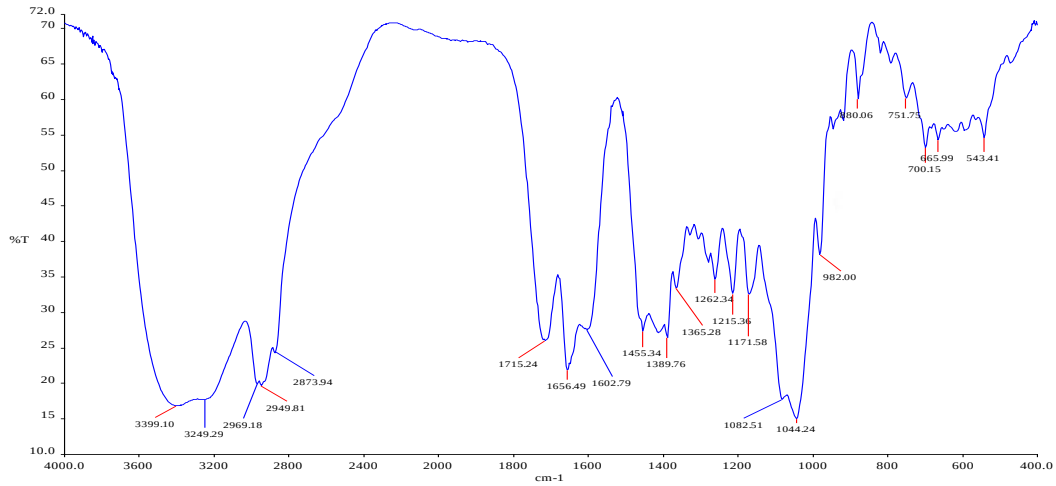


Figure 6. GKMAT IK-spectrum 80-82%

In the IR-spectrum of GKMAT, in the form of a broad shoulder related to the OH groups in the sugar part, the valence vibration is in the range of 3200-3400 cm^{-1}, the valence vibration related to the C=O bond in the free carboxyl groups is in the area of 1710-1680 cm^{-1}, O=CO–, which participated in the formation of salt In the form of a broad shoulder corresponding to NH_4^+ carbonyl groups, the valence vibration was observed in the region of 1651 cm^{-1}. If in the spectrum, the valence vibration related to C–O–C bonds is visible in the region between 1200-1000 cm^{-1}, the valence vibration related to the adjacent carbonyl group O=C–C=C– was recorded in the region 1643 cm^{-1} (Fig. 6) [15- 22].

CONCLUSIONS Technical glycyrrhizinic acid (TGK), glycyrrhizinic acid triammonium (GKUAT), glycyrrhizinic acid monoammonium (GKMAT), glycyrrhizinic acid monopotassium (GKMKT) salts were isolated from the sweet root extract.

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