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TECHNOLOGY OF GASSIPOL ACIC ACID (GSK) FROM TECHNICAL GOSSIPOL

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ABSTRACT

This article provides information on the biological characteristics and technical Gossipol (Gossypium) isolation of Gossipol acetic acid (GSK) based on the fact that all species of cotton belong to the genus Gossipium and belong to the family Malvaceae.

KEYWORDS: Cotton, Gossipium, rosemary, technical Gossipol, Bactericide, Antiseptic, Antibacterial, antioxidant. Gossypol acetic acid (GSK).

INTRODUCTION

In the treatment of various diseases, plant-derived substances are characterized by high biological sensitivity to synthetic substances, low toxicity and no side effects. Cottonseed oil is obtained from cotton seeds by pressing and extraction. The oil is used for food and technical purposes. It is used in the manufacture of soap, alif, lacquer, enamel and other products. The seeds contain gossypol pigment (a toxic organic compound), which is extracted during the oil extraction process and various synthetic substances are produced from it. Residual tar in oil production is also sent to the national economy for use. In addition to cotton clothes, bedding, artificial cotton, plastic, lacquer, paper, explosives are used for production. In addition to animal feed, the industry produces potash, preservatives, alcohol, paper, cardboard and many other products from seed husks and husks. Even cottonseed meal

separates phytin and food protein. More than 100 compounds can be obtained from cotton stalks.[1]

THEORETICAL PART

All species of cotton belong to the same genus: Gossipium, and belong to the family Malvaceae. The genus Gossipium includes 35 species, and 5 of them are cultural: 1. G. hirsutum (Mexican) Mexican or ordinary (medium-fiber) cotton 2.G.barbadenze (G.barbadenze) Peruvian cotton or long (fine-fiber), 3. G. herbaceum, African Asian or herbaceous cotton, 4. G. arboreum Indo-Chinese or woody cotton, 5. G. tricuspidatum, West India-three (bowl) is called toothed cotton. The last West Indian species is considered a minor species because it is morphologically close to xirzutum. Cotton, its seeds and oil products are shown in Figure 1.[1]

Figure 1: Cotton, seeds and oilseeds.

The ripe seeds are ovoid or pear-shaped. The seed consists of a spike and two surrounding skins, the inner skin is curved, the outer skin is hardened with wood. The outer surface of the seed coat is covered with hairs, these hairs are called fibers, in some of them there are short hairs along with the long hairs, which are called lint (linter). The wide side of the seed is called the aunt, and the thin side is called the micropile. The seeds can be 12-14 mm long, 6-8 mm in diameter and weigh 50-50 mg depending on the growing conditions. The seed pod consists of two seed pods and the beginning of the main organs of the plant. The oil in the kernel bud averages 20-25% of the seed weight. The seed coat is very strong, reaching a thickness of 0.25 mm. The development period of the seed lasts 50-60 days. The earlier the cotton ripens and the more favorable the growing conditions, the faster and better the seed will grow.[1]

The importance of cotton in the national economy is immense. This is because there is no economic sector in which cotton and its products are not used in one way or another. Unlike

other agricultural crops, cotton is a valuable product of three types at once; that is, it provides raw materials for textiles, oil for food, pet food - kunjara and shellux. Cotton is grown mainly for fiber. An average of 320-340 kg of fiber and 560-580 kg of seeds are obtained from 1 ton of raw cotton. 340 kg of fiber produces 3500-4000 m^2 of fabric, and 580 kg of seeds produce 112 kg of oil, 10 kg of soap, 270 kg of kunjara, 170 kg of silkworm and 8 kg of lint. Cotton fiber also differs from man-made fibers in the production of high-quality textile and technical products (articles) and belongs to the group of natural fibers that provide universal raw materials.[1]

Gossypol belongs to the triterpene aldehyde group, the presence of OH and CH_3-radicals determines its biological activity. Substances synthesized on the basis of gossypol have been found to have interferon-inducing, immunosuppressive properties against various harmful viruses.[1]

Many drugs derived on the basis of gossypol are now widely used in medicine. Examples include 3% gossypol liniment used for viral diseases, 3% megosin ointment for herpes, Ragosin tablets used in the treatment of hepatitis B, and other drugs.[2]

Gossypol (Gossypium) is a natural polyphenol, a yellow pigment in seeds, which is an inhibitor of a number of enzymes, dehydrogenases. The maximum amount of gossypol is in the cotton roots and seed kernel, to a lesser extent in the leaves, in the bark of the stems. Gossypol is present in nature in two enantiomeric forms: (+) levorotator positive and (-) dextrorotator negative. In the cotton plant, gossypol occurs as a mixture of both stereoisomers. Gossypol is a very active chemical compound. Gossipol according to the systematic nomenclature is 2.21 di (1,6,7- trioxy 3 methyl 5 isopropyl 8 naphthaldehyde) chemical gross formula $C_{30}N_{30}O_8$, physical properties, light yellow to orange crystalline substance, molar mass 518,563 g / mol, density 1.4 g / cm^3, liquefies at 177-182 ° C (by decomposition), boils at 707 ° C, dissolves better in polar solvents, almost insoluble in non-polar ones. The gossypol molecule has a large number of polar groups, for example, six hydroxyl groups. But the presence of two heavy dialkylnaphthalene groups makes it insoluble in water. Therefore gossypol is insoluble in water. Gossypol is well soluble in methyl, ethyl, isopropyl, butyl alcohols, diethylene glycol, dioxane, acetone, diethyl ether, ethyl acetate, chloroform, carbon tetrachloride, dichloroethane, phenol, pyridine, diluted naphthalene, heated vegetable oil. Gossypol is poorly soluble in glycerin, cyclohexane, benzene, benzene, and petroleum ether, and its solubility in gasoline is higher than that of petroleum ether.

Gossypol is sparingly soluble in liquid oils, so it is partially transferred to the mistletoe when the oil is extracted from cottonseed using gasoline. The literature does not give median indicators of the solubility of gossypol in extractants. Only a few figures are available: the solubility of gossypol in benzene is 0.5%, in petroleum ether - 0.06%. The solubility of gossypol in aqueous-acetone mixtures depends on the concentration of acetone in the mixture at 40 0C, expressed in g / ml as 1,165 g / ml in 60% acetone, 9.505 g / ml in 70%, 12.155 g / ml in 80%, 97.62% g / ml solubility is given.The formula for the structure and configuration of Gossypol is shown in Figure 1.

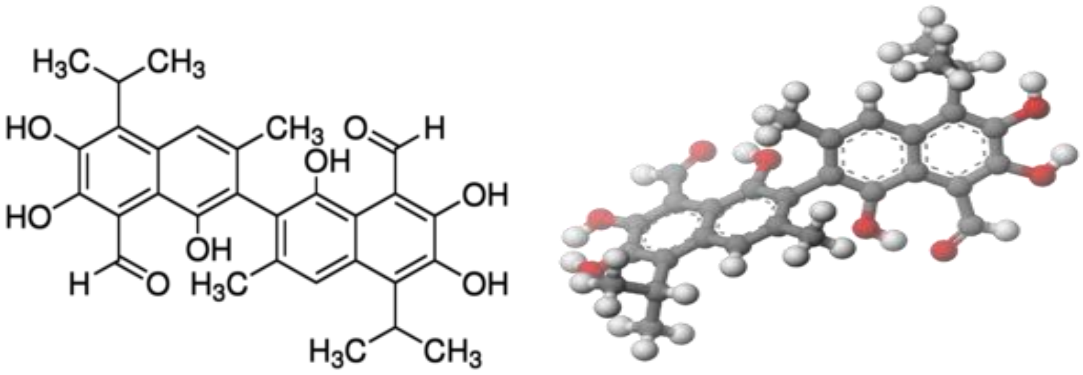


Figure 2: Gossypol structure and configuration formula.

In nature, gossypol serves to protect the plant from pests and diseases and is present in the plant composition mainly in free form. Gossypol is also involved in a number of other mechanisms that ensure the plant's high resistance to the adverse effects of the environment. Gossypol has antiviral, antimicrobial, antiprotozoal, antioxidant properties. The ability of gossypol and a number of its derivatives to block the reproduction of some pathogenic animal viruses was discovered in studies conducted by Soviet virologists using a model of influenza infection. Scientists also later determined the ability of gossypol to induce interferon synthesis. These data have been confirmed by several research groups.[3]

The antifertile effect of gossypol is based on the ability of sperm to bind to enzymes of epithelial cells (lactate dehydrogenase and glutathione-alpha-transferase) involved in maturation processes. Gossypol has a direct inactivating effect on viruses by interacting with harmful proteins and cytoplasmic membranes of virus-sensitive cells, as well as through indirect interferons and other protective cytokine induction mechanisms.[3]

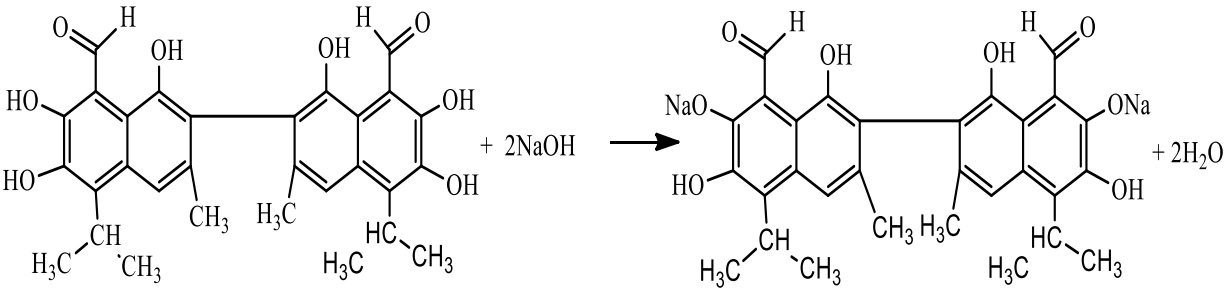
Separation of gossypol from different organs of the cotton plant in different ways has been reported in the literature. These methods are mainly carried out by extracting the raw material containing gossypol in solvents and precipitating gossypol in the form of gossypol acetic acid using acetic acid or by bonding it with amines to form shingle bases.[4]

PROCESSING OF EXPERIMENTAL RESULTS

Gossypol is well soluble in oils. Using this feature, the seed is transferred directly to the oil by gossipol pigment located in the nodules in the nucleus by cold pressing. In this case, in order to reduce the adhesion and decomposition of free gossypol to proteins at high temperatures, the temperature of the oil leaving the press should not exceed 60 ^{0}C. Cold-pressed polygossipol oil contains 1.0 % -3.5 % free gossypol.

Gossypol acetic acid (GSK), which is currently produced on an industrial and semi-industrial scale, is first separated from the cold-crushed kupgosssipol oil in the form of technical gossypol. The content of pure gossypol in this technical gossypol powder ranges from 10 % to 40 %.[4]

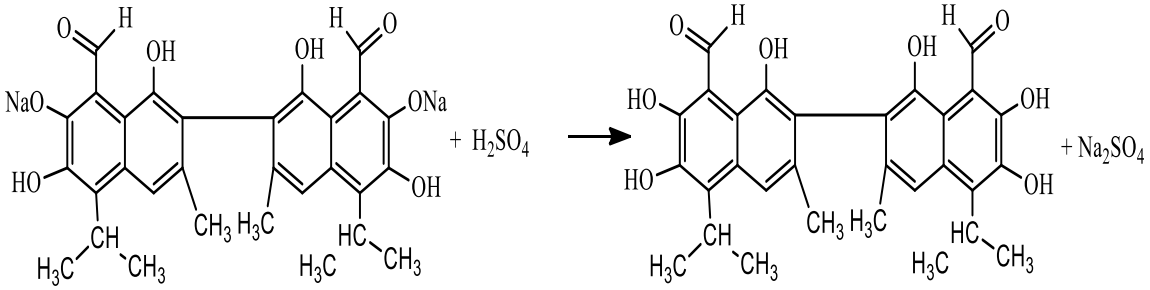
For technical gossypol extraction, a gentle refining-forrafination of the oil is carried out with a liquid solution of sodium hydroxide (NaOH) calculated according to the acid number of the cupgosypol oil. This process results in the formation of a liquid soapistok, which contains the sodium salt of gossypol, soap phosphatides and other satellite substances. The liquid soapistok is separated from the oil and decomposed using a solution of sulfuric acid, resulting in the decomposition of the sodium salt of gossypol into the gossypol free state and floating on the surface of the water when mixed with fatty acids, phosphatides and other satellite substances. This wet, oily, gossypol-containing mass is filtered, degreased in gasoline extract, dried and ground. This method is carried out in two stages. In the first stage, a water-soluble sodium salt is formed in the presence of gossypol sodium hydroxide. This chemical process is shown in Scheme 1.



Free gossypol in cottonseed oil **Sodium salt of gossypol**

Scheme 1. Formation of water-soluble sodium salt of gossypol in the presence of sodium hydroxide.

In the second stage, free gossypol is formed as a result of the decomposition of the sodium salt of gossypol in the presence of sulfuric acid. The chemical reaction of this process is carried out according to Scheme 2 below.



Sodium salt of gossypol **gossipol**

Scheme 2. Formation of free gossypol when the sodium salt of gossypol is broken down in the presence of sulfuric acid.

To obtain gossypol acetic acid (GSK) from technical gossypol Free gossypol containing technical gossypol is transferred to the solvent-acetone by extraction method, the collected acetone solution is placed in a vacuum evaporator and concentrated glacial acetic acid is used using gossypol acetic acid: The mixture is then washed in hexane and dried, while the sung is crushed. The amount of the main substance in the 1-GSK obtained in the first precipitation is around 50-80 %.1-GSK purification process; it is dissolved again in acetone and re-precipitated using glacial acetic acid, and in the process of filtering the precipitate it is washed, dried and ground in a mixture of acetic acid and acetone.[2] The purity level of GSK 2 should not be less than 92%. When the obtained substances were tested by thin-layer chromatography (YKX) in benzene: acetone (5: 1) and hexane: acetone (3: 1) systems, the Rf values of these substances in the benzene: acetone (5: 1) system were 0.7-0.8 and hexane: in

the acetone (3: 1) system in the range of 0.26-0.33. The structural formula of gossypol acetic acid is shown in Figure 3.[5-7]

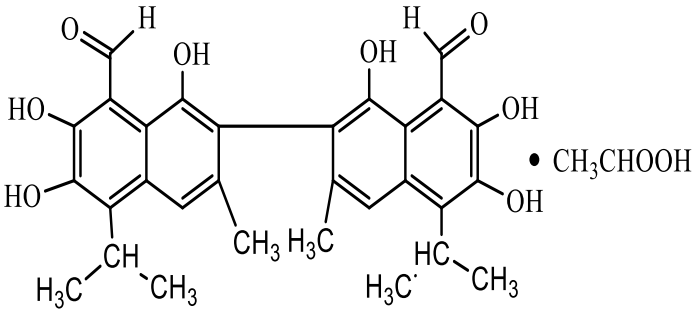


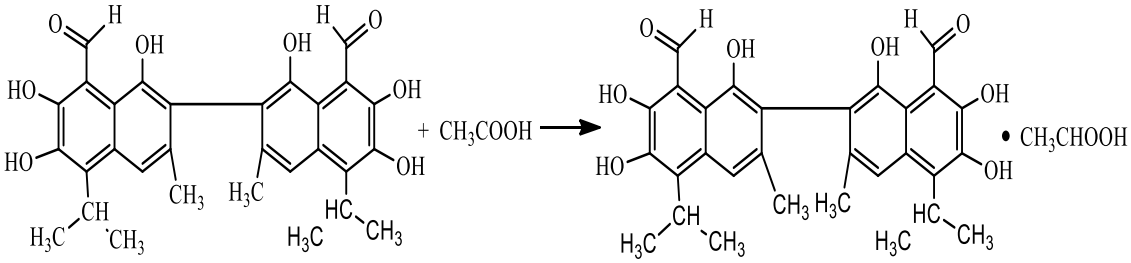
Figure 3: Structural formula of gossypol acetic acid.

To obtain a pharmacopoeial GSK, a recrystallization process of GSK 2 was performed and the purity of GSK 3 formed after all stages was 98-99%. The appearance of degreased technical gossypol and its derivatives 1-GSK, 2-GSK is shown in Figure 4 below.

technical gossipol **1- GSK** **2- GSK**

Figure 4. 1-GSK, 2-GSK formed after degreasing technical gossypol crystallization steps.

The chemical reactions of precipitation of gossypol with acetic acid are shown in Scheme 3.



gossypol **gossypol acetic acid**

Scheme 3: Infusion of gossypol with acetic acid.

The structures of the IK spectra of the obtained gossypol acetic acid were studied and shown in Figure 5.

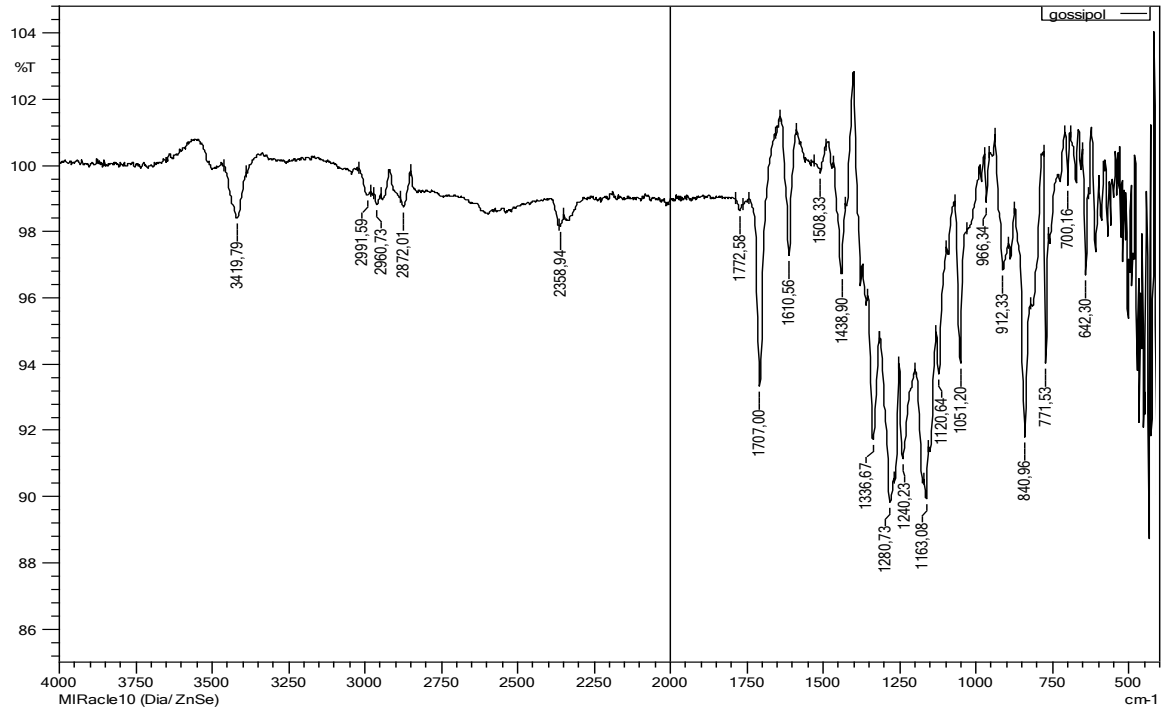


Figure 5: IK spectra of gossypol acetic acid.

In the IK spectrum of gossypol acetic acid, the valence oscillation frequencies of the OH groups were observed at 3420 cm-1, while the valence oscillation frequencies of the SN, SN2, SN3 groups were observed at 2991, 2961, 2872 cm-1. The valence oscillation frequency of the aldehyde group (-S = O) in the molecule was observed at 1610 cm-1. Deformation vibration frequencies of groups SN, SN2, SN3 were observed at 1439, 1337, 1281, 1240, 1163 cm-1. At 841, 771, 700, 642 cm-1, the valence oscillation frequencies of the aromatic ring were observed. Furthermore, the fact that the valence oscillation frequency corresponding to the carbonyl (S = O) part of the carboxyl group of acetic acid in GSK is intense at 1707 cm-1 indicates that this substance is indeed GSK.

EXPERIMENTAL SECTION

Separated from the unrefined black oil of cottonseed and degreased, technical gossypol powder was weighed on a scale and extracted with acetone in a flat tube. The collected extracts were filtered, condensed by distillation of the solvent, and precipitated to 1-GSK by adding the required amount of ml of glacial acetic acid. The first acetic acid gossypol 1-GSK precipitated was composed of lemon-yellow crystals, which were filtered and recrystallized to 2-GSK to make the 1-GSK substance more pure. To do this, we took a little 1-GSK,

dissolved it in acetone and concentrated, added ice acetic acid to it in a mixed state, and the solution was filtered after two hours. The resulting precipitate was filtered, acetic acid was washed in hexane in a 1: 1 mixture of acetone, dried and ground. The yield of GSK 1 to GSK 2 is 65-75% and the purity is 92-97%. To obtain a pharmacopoeial GSK, the 2nd GSK was recrystallized again as in the previous step. The yield of GSK from GSK 2 was 75-85% and the purity level was 98-99%.

CONCLUSION

The technical gossypol extracted and degreased from the unrefined black oil of cottonseed was recrystallized in ice acetic acid and the purity level of gossypol acetic acid (3-GSK) was brought to 98-99%. The main oscillation frequencies in the IK spectrum were studied.

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