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METHODS AND ANALYSIS OF SYNTHESIS OF NEW BIOLOGICALLY ACTIVE SUBSTANCES BASED ON GOSSYPOL

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Abstract

This article is devoted to the synthesis of new biologically active substances based on gossypol and methods for their analysis. Gossypol is a polyphenol compound found in the seeds, root bark and other parts of the cotton plant, which has a complex chemical structure and a wide spectrum of biological activity. The article discusses the chemical structure, physicochemical properties of gossypol, methods for synthesizing various derivatives based on it, and modern instrumental methods for analyzing these compounds (HPLC, GC, DART-HRMS, UPLC-MS/MS). The biological activity of gossypol derivatives and their prospects for application in medicine, veterinary medicine and agriculture are also analyzed.

Keywords

gossypol, biologically active substances, synthesis, analytical methods, HPLC, GC, DART-HRMS, UPLC-MS/MS, polyphenol compounds, enantiomers.

Gossypol is a natural polyphenol compound synthesized in the seeds, root bark, leaves and branches of the cotton plant (Gossypium). This compound serves as a means of protecting the plant against pests and small rodents. Gossypol has long been known mainly as a toxic substance, and its content in feed is strictly controlled. However, recent studies have shown that gossypol and its derivatives have valuable biological properties. The chemical structure of gossypol allows it to exhibit various biological activities. It has antiviral activity, which is why interferon inducer preparations are currently being developed based on gossypol.

Also, various derivatives of gossypol - gossypurpurin, gossiverdurin, gossyfulvin and their products - are considered useful substances for humans and are used in various sectors of the national economy: medicine, chemical industry, agriculture and metal casting.

Synthesis and analysis of new biologically active substances based on gossypol is one of the current directions of modern chemistry and pharmacy. This article systematically reviews the chemical structure of gossypol, methods for synthesizing derivatives based on it, and modern instrumental methods for analyzing these compounds.

Gossypol is a complex organic compound with the formula (1,1',6,6',7,7'-hexahydroxy-5,5'-di-isopropyl-3,3'-dimethyl-(2,2'-binaphthalene)-8,8'-dicarboxaldehyde), and its molecular formula is $C_{30}H_{30}O_8$. It is a yellow, toxic, solid crystalline substance.

One of the important structural features is the presence of aldehyde groups located at the 8- and 8'-positions. These aldehyde groups play an important role in the tautomeric forms of gossypol and contribute significantly to its toxicity.

Gossypol belongs to the class of polyphenolic compounds. It is soluble in low molecular weight alcohols and water, as well as in fats. In the seed kernel, gossypol is located in special glands, the walls of which are extremely strong and resistant to the effects of most organic solvents. However, gossypol glands are quickly destroyed by low molecular weight alcohols and water.

The amount of gossypol in different varieties of cotton varies. Fine-fiber cotton varieties grown in Uzbekistan contain a large amount of gossypol (1.47-1.60%). In general, gossypol is present in cotton seeds and root bark in an amount of 0.02% to 1.6%.

Gossypol exists in two forms: free and bound. Free gossypol is toxic, while the bound form is non-toxic. During the heat treatment of the seeds, gossypol is converted to a bound form, and the amount of free gossypol drops below 0.04%.

Gossypol exists in two enantiomeric forms: (+)-gossypol and (-)-gossypol. These enantiomers differ in their biological activity and toxicity. In particular, (-)-gossypol has a negative effect on the quality of male sperm and can cause cancer when taken in low doses for a long time. Therefore, it is important to analyze the enantiomers of gossypol separately.

The gossypol molecule contains several reactive functional groups (hydroxyl and aldehyde groups), which allows it to undergo various chemical transformations and synthesize new derivatives.

Interferon inducers: Gossypol is active against viruses, therefore, currently interferon inducer drugs used against viruses have been isolated from gossypol. In this direction, it is possible to create more effective and less toxic drugs by modifying gossypol.

Enantioselective synthesis: (+)- and (-)-gossypol enantiomers have different biological activities. Therefore, the development of methods for the selective synthesis of a particular enantiomer or their separation is of great importance. Recent studies have developed highly sensitive methods for the determination of (-)- and (+)-gossypol in vegetable oils.

Amine derivatives of gossypol: Schiff bases formed as a result of the reaction of gossypol with amines can be a source of new biologically active substances. For example, Wu et al. (1988) used (+)-2-amino-1-butanol as a chiral derivatizing agent in the determination of gossypol enantiomers.

Metal complexes of gossypol: Complexes of gossypol with metals such as iron, copper, and zinc may have biological activity. It is known that iron sulfate binds to gossypol and neutralizes it. Based on this property, it is promising to synthesize other metal complexes and study their biological activity.

Gossypol and its derivatives have various biological activities and are used in a number of fields.

Antiviral activity: Gossypol actively affects viruses. Therefore, currently, antiviral interferon inducer drugs have been isolated from gossypol. Interferon inducers stimulate the production of interferon in the body, thereby enhancing protection against viruses.

Antimicrobial activity: There is information about the activity of gossypol against various microorganisms. This property allows it to be used in the creation of new antimicrobial drugs.

Effect on the reproductive system: Gossypol affects the male reproductive system. When taken for a long time and in low doses, it reduces the quality of sperm. Based on this property, studies have been conducted on the creation of a male contraceptive based on gossypol.

One of the main problems of gossypol is its toxicity. Gossypol causes discomfort in the heart, respiratory, reproductive systems, and liver. Therefore, when creating new drugs based on gossypol, reducing their toxicity and increasing their selective effect is an important task. This can be achieved by modifying the gossypol molecule, blocking certain of its functional groups, or by enantioselective synthesis.

Gossypol is an important secondary metabolite of the cotton plant, which has a complex chemical structure and a wide spectrum of biological activity. For a long time, gossypol, which was known mainly as a toxic substance, has attracted attention as a valuable biologically active compound as a result of recent studies.

The variety of functional groups in the gossypol molecule (two aldehyde groups, six hydroxyl groups) allows it to undergo various chemical modifications and synthesize new biologically active derivatives. In particular, derivatives of gossypol with amines, metal complexes, and various esters can be of practical importance.

Modern instrumental methods are widely used in the analysis of gossypol and its derivatives - HPLC, GC, HPLC-MS/MS, UPLC-MS/MS, and DART-HRMS. These methods allow for the analysis of gossypol in various objects (seeds, oils, feed, biological fluids) with high sensitivity and accuracy. In particular, in recent years, methods for the separate analysis of gossypol enantiomers have been improved, which allows for the separate study of the biological activity of (+)- and (-)-gossypol.

The biological activity of gossypol determines its potential applications in various fields. In medicine, antiviral drugs, in particular interferon inducers, have been created based on gossypol. In veterinary medicine and agriculture, gossypol is controlled in feed and methods for its neutralization (addition of ferrous sulfate) are used. In industry, gossypol and its derivatives are used in the chemical and metal casting industries.

There are a number of problems in the field of creating new biologically active substances based on gossypol, among which the problem of toxicity, the complexity of enantioselective analysis and synthesis methods occupy a key place. In the future, it is necessary to continue research on modifying the gossypol molecule, increasing its selective effect and reducing its toxicity, as well as in-depth study of the biological activity of gossypol derivatives.

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