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ОЛИЙ ВА ЎРТА МАХСУС ТАЪЛИМ ВАЗИРЛИГИ

ФАРҒОНА ДАВЛАТ УНИВЕРСИТЕТИ

FarDU. ILMIY XABARLAR-

1995 йилдан нашр этилади
Йилда 6 марта чиқади

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SOME MEDICINAL COMPOUNDS OBTAINED FROM KOVRAK (FERULA)PLANT WASTE

КОВРАК (*FERULA*) ЎСИМЛИГИНИНГ ЧИҚИНДИСИДАН ОЛИНАДИГАН АЙРИМ ДОРИВОР БИРИКМАЛАР

НЕКОТОРЫЕ ЛЕКАРСТВЕННЫЕ СОЕДИНЕНИЯ, ПОЛУЧАЕМЫЕ ИЗ ОТХОДОВ КУЗИНИИ МЕЛКОПЛОДНОЙ (ФЕРУЛА)

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Аннотация

Мақолада коврак ўсимлиги чиқиндиларидан сульфаниламид доривор бирикмасини ажратиб олиш ва унинг ферроцен билан диазотирлаш реакциясини ўрганиш бўйича олиб борилган тадқиқот натижалари келтирилган.

Аннотация

В статье представлены результаты исследования экстракции лекарственного соединения сульфаниламида из отходов кузинии мелкоплодной и изучения его реакции диазотирования с ферроценом.

Annotation

This paper presents the results of a study on the extraction of a sulfanilamide drug compound from kovrak plant wastes and the study of its diazotizing reaction with ferrocene.

Таянч сўз ва иборалар: *коврак, ўсимлик чиқиндиси, лигнин, 1,3,5-триметоксибензальдегид, сульфаниламид, ферроцен, диазотирлаш, квант-кимёвий ҳисоблаш.*

Ключевые словаи выражения: *кузиния мелкоплодная, растительные отходы, лигнин, 1,3,5-триметоксибензальдегид, сульфаниламид, ферроцен, диазотирование, квантово-химический расчет.*

Keywords and expressions: *ferula, plant wastes, lignin, 1,3,5-trimethoxybenzaldehyde, sulfanilamide, ferrocene, diazotization, quantum chemical calculation.*

It is known that various drugs have been developed and put into practice around the world for the treatment and prevention of diseases that afflict mankind. Of particular importance among these compounds are medicinal compounds derived from plant raw materials, including kovrak - Ferula plant. Nowadays, the extraction of drugs from various parts of the plant, such as leaves, flowers, stems, especially from its waste, or the preparation of effective medicinal compounds as a result of chemical and biological processing of the extracted substances has become one of the most pressing issues.

It is known that after the separation of useful compounds from the composition of the brittle plant, wastes are formed, which contain mainly cellulose, hemicellulose and lignin. As a result of chemical and biological processing of waste, lignin and other natural compounds are separated. Lignin separation is performed as follows:

The wastes of the plant includes some chemicals such as H_2SO_3, Na_2SO_3, NaOH which should be melted in a sulfate solution with pH=1,5-13 for four to twelve hours at the temperature of 135-150^oC under high pressure. In this case, 90% of the lignin in the waste is converted into an alkaline solution. The medium of the solution is increased to pH 8–9 and lignin is precipitated. In this process, lignin is also removed from some additives. Sulfonation of lignin in an alkaline solution results in the formation of water-soluble lignosulfonates. They can be converted to other compounds as a result of nitration, chlorination,

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oxidation, demethylation reactions under simple or complex ether conditions. The resulting lignosulfonates are polydispersed products with a molecular mass of 100 to 200,000 and higher. Different salts of lignosulfonates are obtained by replacing calcium with other metals such as Zn, Mg, Fe. In the later stages, calcium lignosulfonates are often used. Their chemical processing produces phenol, aromatic aldehydes, 3,4,5-trimethoxybenzaldehyde. As a result of chemical changes based on the resulting 3,4,5-trimethoxybenzaldehyde, it is possible to separate trimethoprim and sulfamethoxazole compounds and mix them in different mass ratios to prepare antibacterial, antimicrobial bacterium, biseptol and other drugs [1,2].

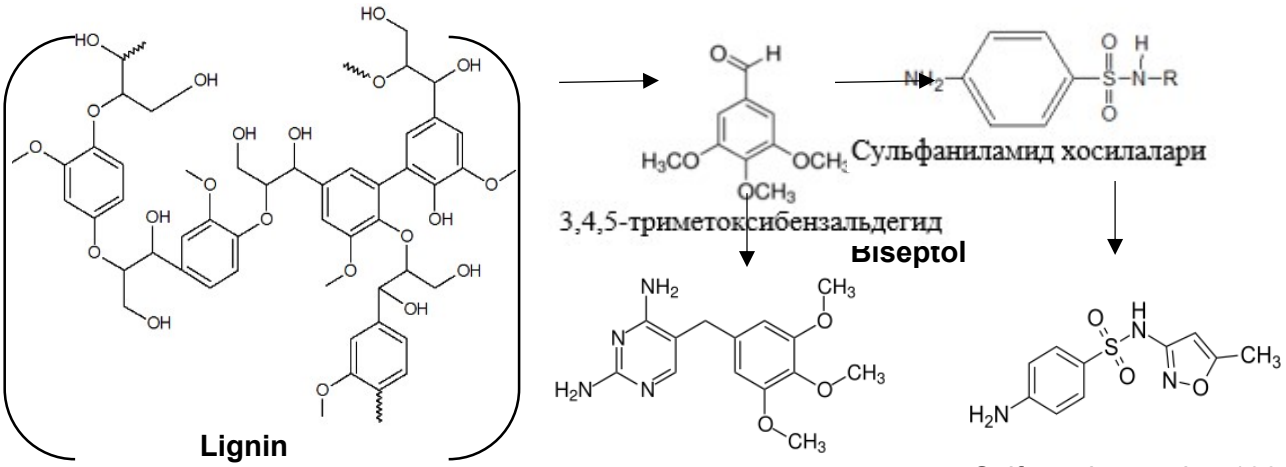

Illustration 1. The scheme of reaction on how medical compounds are obtained from lignin

In addition, sulfanilamide can be obtained from 3,4,5-trimethoxybenzaldehyde, on the basis of which it is possible to form a number of medicinal compounds containing sulfanilamide residues. These include streptocide (antibacterial compound) [3], sulfaguanidine (antimycotic, antibacterial (antidysenteric) compound) [4], sulfapyridine (strong chemotherapeutic active compound), sulfadimethoxine (antibacterial, long-acting compound) [5], sulfasalazine (rheumatoid arthritis therapeutic compound) [6] and others.

In the literature, it has been reported that some of the sulfanilamide and its derivatives listed above are indirectly bound to the compounds containing the nobenzoid aromatic ring, including ferrocene, by certain substituents in order to enhance the existing pharmacological properties (Illustration 2). It was observed that the physiological activity of the compound is further enhanced by the introduction of ferrocenyl radical into the molecule [7,8].

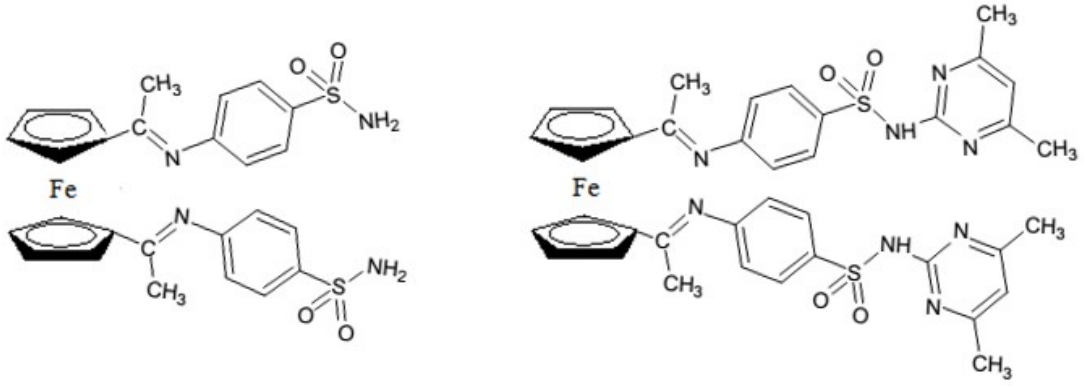

Illustration 2. Sulfanilamide derivatives with increased biological activity as a result of ferrocene accumulation

However, to date, derivatives of sulfanilamide directly bound to ferrocene have not been obtained, and their properties have not been studied. Given the sharp increase in the biological activity of sulfanilamide and its derivatives as a result of the introduction of ferrocene in the study, in this study it was theoretically studied to obtain derivatives of sulfanilamide directly associated with ferrocene. The diazotizing reaction inherent in the primary aromatic amines cited in the literature [9] can easily be said to be the most optimal way of directly binding sulfanilamide to ferrocene. It is known that the diazotization reaction is carried out under acidic conditions; first sulfanilamide is converted to diazonium salt using a solution of sodium nitrite and hydrochloric acid, and then bound to one or both of the aromatic rings of ferrocene by electrophilic exchange. However, it is not yet theoretically and practically justified by which amino group of sulfanilamide this reaction occurs.

Theoretical quantum chemical calculations were performed in order to study which amino group of the diazotization reaction of sulfanilamide with ferrocene occurs and the structure of the product (s) that can be formed as a result of the reaction. At the same time, using the currently widely used software package Gaussian 98 [10], the molecules of substances were energetically optimized on the basis of the program's DFT / B3LYP hybrid method 3-21G.

Initially, the determination of the entry point (amino group) of sulfanilamide in the diazotization reaction was studied. To do this, its molecular structure was energetically optimized using the above quantum chemical calculation program, and the charge distribution of the atoms in the molecule was calculated. The results of quantum chemical calculations are given in Table 1 below:

Table 1.

Hartry energy of a sulfanilamide molecule and charge distribution of atoms

atom	**charge**	**atom**	**charge**	**atom**	**charge**	**atom**	**charge**	**atom**	**charge**	**atom**	**Charge**
1C	-0,18	5C	-0,18	8H	+0,23	11N	-0,82	14S	+1,5	17H	+0,31
2C	-0,15	6C	+0,35	9H	+0,23	12H	+0,31	15N	-0,81	18O	-0,57
3C	-0,50	7H	+0,18	10H	+0,18	13H	+0,31	16H	+0,31	19O	-0,57
4C	-0,15	Hartry energy of the molecule, J					-886,73				

The results of the calculations showed that the sulfur in sulfanilamide (14S) had a strong positive effect (+1.5). This explained that the electron density (negative effect) in the benzene ring shifted in the direction of the sulfur bond and that the negative effect of sulfur-bound nitrogen (15N) (2) decreased, and that the hydrogen in it became mobile and formed an acid center (Illustration 2). This theoretically confirms that it is the acid center (15N) involved in the reaction of sulfanilamide with the bases. The calculations also showed that the positive effect of carbon (6C) on the benzene ring directly attached to the amino group (1) is much smaller than that of sulfur (14C), forming the relative freedom of the undistributed pair of electrons in the amino group bound to it, i.e. the base. This theoretically confirmed that the diazotization reactions of sulfanilamide and similar compounds occur mainly due to the amino group directly bound to benzene, but this does not rule out that the diazotization reaction also occurs due to the amino group 2

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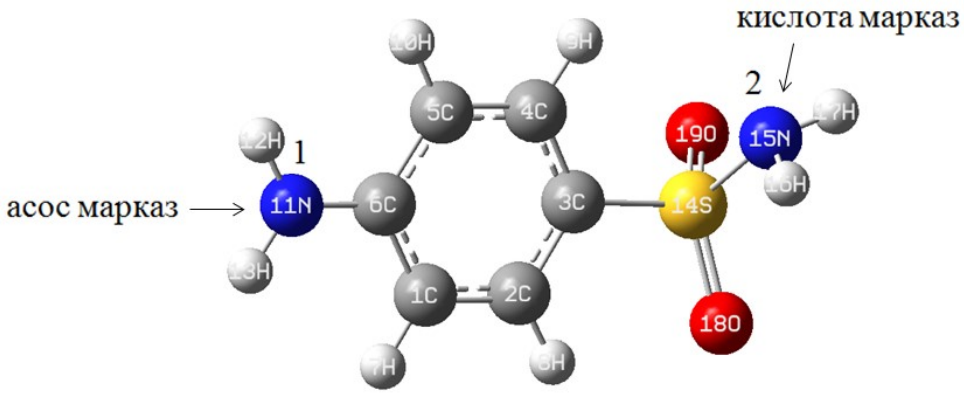

Illustration 2. Optimized molecular structure of sulfanilamide.

The diazotization reaction of sulfanilamide with ferrocene can occur in the presence of amino groups 1 or 2 in sulfanilamide, or both amino groups, resulting in the formation of mainly A, B, C (Illustration 3) and very small amounts of di-, tri, poly-exchange products:

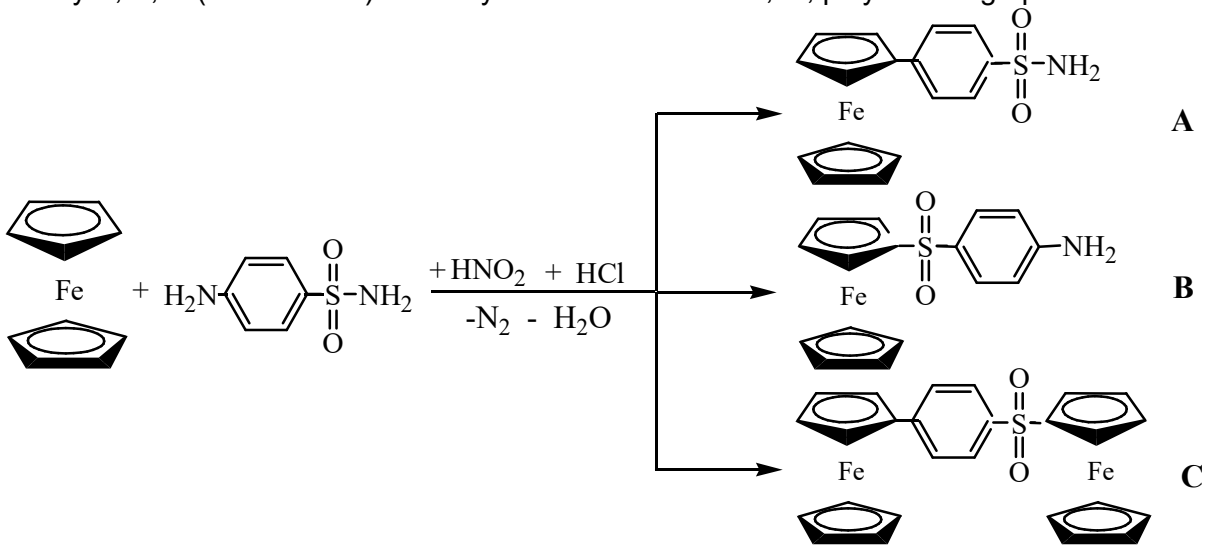

Illustration 3. Scheme of diazotization reaction of sulfanilamide with ferrocene.

In order to verify the results of the above study, i.e. to evaluate which substance is more likely to be formed as a result of the diazotization reaction of sulfanilamide with ferrocene, the Hartry energies of the main products A, B and C that were formed as a result of this reaction were calculated by the above quantum chemical method. The results of quantum chemical calculations are given in Table 2 below:

Table 2.

Hartry energies found by the quantum chemical calculation method of molecules of matter A, B and C.

Molecule	A	B	C
Hartry energy of the molecule, J	-2473,172	-2473,172	-4059,634

From the table above, it can be seen that the potential for the formation of products A and B as a result of the diazotization reaction of sulfanilamide with ferrocene is energetically equal (-2473,127). Also, the high Hartry energy of product C relative to A and B (-4059,634) indicates that its chance of formation is very low.

The results of the study showed that the diazotization reaction of sulfonamides with ferrocene obtained from the processing of fracture plant waste occurs at the expense of amino groups (1) directly bound to the benzene ring in sulfanilamide, although the energy potentials of products A and B are equal which can be considered to

be the basis for the conclusion. This is because the charge distribution of the atoms in the sulfanilamide molecule plays an important role in the course of this diazotization reaction. However, this does not rule out that this diazotization reaction may occur both at the expense of the amino group 2 of sulfanilamide, as well as the formation of substances B and C.

Moreover, the research allowed to theoretically assess the possibility of synthesizing a new type of compounds with strong effects on the basis of sulfanilamide and ferrocene, which are physiologically active compounds, and their derivatives. It can also be seen that the products formed by the combination of sulfonamides with ferrocene obtained from the processing of kovrak waste contain effective functional groups found in drugs used in the treatment of some serious diseases, including hepatitis B. This suggests that ferrocene derivatives of sulfanilamide may have therapeutic properties in diseases such as hepatitis B. In this regard, it can be concluded that scientific research on chemical or biological processing of fennel plant waste and preparation of new types of compounds with physiological activity and cost-effectiveness on the basis of obtained compounds and ferrocene gives promising results.

References:

1. Грибков Иван Владимирович. Дисс.: Химический состав и строение технического гидролизного лигнина. -Санкт-Петербург, 2008.

2. https://compendium.com.ua/info/9535/

3. Фармакология [Электронный ресурс]: учебник / Д. А. Харкевич. – 11-е изд., испр. и доп. – Электрон. дан. – Москва: ГЭОТАР–Медиа, 2015. – URL: http://www.studmedlib.ru/book/ISBN9785970434123.html. (Дата обращения: 29.01.2018).

4. Фармакология [Электронный ресурс]: учебник / под ред. Р. Н. Аляутдина. – 5–е изд., перераб. и доп. – Электрон. дан. – Москва: ЭОТАР–Медиа, 2016. – URL: http://www.studmedlib.ru/book/ISBN9785970437339.html. (Дата обращения: 29.01.2018).

5 *Машковский, М. Д.* Лекарственные средства: пособие для врачей / М. Д. Машковский, науч. ред.: С. Д. Южаков. – Изд. 15-е, перераб., испр. и доп. – Москва: Новая Волна, 2008. – 1206 с.

6 Государственный реестр лекарственных средств [Электронный ресурс]. – Электрон. дан. – URL: http://grls.rosminzdrav.ru/GRLS.aspx. – (Дата обращения 29.01.2018). Источник: https://petrsu.ru/notices/2018/42119/dlya-studentov-4-kur#t20c

7. Zahid H. Chohan (2009) Synthesis of organometallic-based biologically active compounds: *In vitro* antibacterial, antifungal and cytotoxic properties of some sulfonamide incorporated ferrocences, Journal of Enzyme Inhibition and Medicinal Chemistry, 24:1, 169-175, DOI: 10.1080/14756360801948766

8. K. Chanawanno, T.S.Blesener, B.R. Schrage, V.N. Nemykin, R.S. Herrick, C.J.Ziegler. Amino acid ferrocene conjugates using sulfonamide linkages. J Organomet Chem. 2018 September 1; 870: 121–129. doi:10.1016/j.jorganchem.2018.06.018.

9. Реутов, О. А. / Органическая химия [Текст]: в 4 ч. / О. А. Реутов, А.Л.Курц, К. П. Бутин. – М. : Бином. Лаборатория знаний, 2010. – Ч. 3. – 544 с.

10. Frisch M. J., Trucks G. V., Schlegel H. B. at all. Gaussian 98, Revision A.5, Gaussian Inc., Pittsburgh (PA), 1998.