SYNTHESIS OF A COMPLEX OF FERULIC ACID INCORPORATION INTO THE CAVITY OF MODIFIED β-CYCLODEXTRIN

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This study aimed to synthesize and characterize inclusion complexes of ferulic acid incorporation based on modified β-cyclodextrin (MCD). Ferulic acid (FA), a natural antioxidant with limited water solubility, is challenging to deliver effectively to the human body. Therefore, to konoenhance its stability and solubility, it was encapsulated in cyclodextrin with a modified surface. The interaction between ferulic acid and the modified β-cyclodextrin compound was confirmed through Fourier transform infrared spectrometry (FT-IR). The thermogravimetric analysis (TGA) indicated that the successful encapsulation of ferulic acid in the β-cyclodextrin cavity led to increased thermal stability of the FA-MCD inclusion complex compared to the individual components. These findings suggest that the modified β-cyclodextrin can serve as a promising carrier for improving the delivery and effectiveness of ferulic acid as an antioxidant in various pharmaceutical applications.

Keywords: ferulic acid, β-cyclodextrin, surface modification, encapsulation

Introduction. Ferulic acid is a naturally occurring substance found in many plants, including rye, rice, and wheat. It has antioxidant properties and helps protect body cells from the harmful effects of free radicals, so it is used in pharmacology to treat various diseases, such as diabetes, cardiovascular diseases, and others. Ferulic acid has a low solubility in water and other solvents, is unstable and decomposes rapidly when exposed to light and heat, which can make it difficult to deliver to the human body and reduce the effectiveness of its use as an antioxidant. One of the main applications of cyclodextrin is as a carrier for biologically active substances with low stability and poor solubility [1].

Aim. The objective of this study was to synthesize and characterize inclusion complexes of ferulic acid incorporation complex based on modified β-cyclodextrin.

Materials and methods. To study the properties and possibilities of synthesizing new cyclodextrin derivatives, studies were conducted to improve the structure by chemical and physical interactions [2]. To characterize and better understand the process of incorporating a biologically active substance as a guest molecule, various approaches are used, including analytical methods that are studied in combination and form a complete picture of the interaction process [3].

The object of the study was ferulic acid (Fig. 1, a), which is a phenolic-type biologically active substance, a natural antioxidant with antitumor activity. However, due to its limited water solubility, it is not widely used.

One of the ways is encapsulation in cyclodextrin with various surface modifications, which will facilitate the loading of the acid into the internal space of the molecule. A phenolic anhydride, cyclohexylsuccinic anhydride, was used to modify the internal surface of cyclodextrin (Fig. 1, b).

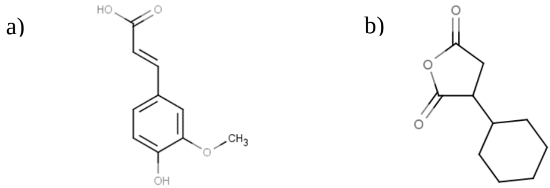

Fig. 1. Structure of ferulic acid (a) and cyclodextrin modifier - cyclohexylsuccinic anhydride (b).

To analyze the formed complex, we used the comparison of Fourier transform infrared spectra (FT-IR) and thermogravimetric analysis (TGA) graphs of the obtained samples.

Results and discussion. The samples obtained as a result of the experiments were studied by Fourier transform infrared spectrometry (FT-IR) - Fig. 2.

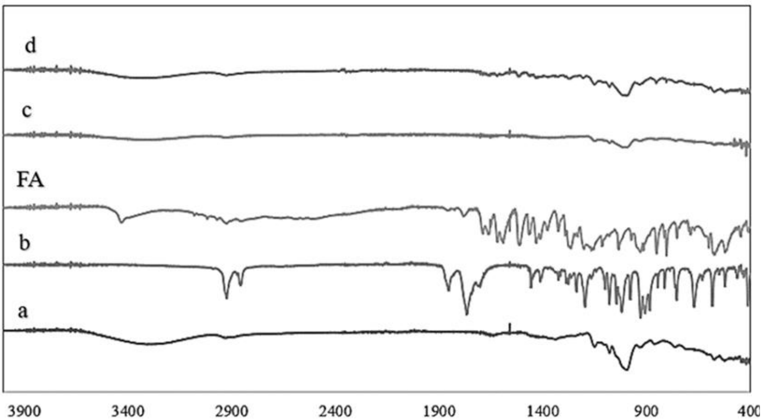

Fig. 2. Fourier transform infrared spectra (FT-IR): β-CD (a), modifier - succinic anhydride (b), MCD (c), FA-MCD (d).

The FT-IR spectra of ferulic acid, a modified β-cyclodextrin compound, and a complex of ferulic acid included in the cavity of a modified β-cyclodextrin were investigated. In comparison with the spectrum of the modified β-cyclodextrin compound using cyclohexylsuccinic anhydride and the complex-inclusion of ferulic acid in the cavity of the modified β-cyclodextrin, an increase in the intensity of the absorption bands in the ranges corresponding to the values of carboxylic acid corresponding to the values of the carboxyl group (3500 cm^{-1}, 1590-1660 cm^{-1}, 1270 cm^{-1}), as well as the aromatic ring bonds (2920 cm^{-1}, 1450-1600 cm^{-1}, at 650-900 cm^{-1}) of the ferulic acid structure.

A comparison of the β-cyclodextrin spectra and FA-MCD inclusion complex shows a clear shift of a broad peak in the absorption range of 3000-3500 cm-1 also indicates the presence of a hydroxyl bond of the carbonyl group of ferulic acid. Such a predominance of the signals of the carbonyl group may indicate its external location in relation to the ferulic acid molecule, which may be located inside the internal cavity of β-cyclodextrin.

The most common and easiest way to study the temperature resistance of a carbon material is through thermogravimetric analysis.

Thermogravimetric analysis allows determining the thermal stability of samples by changing their weight with increasing temperature. Analyzing the curve corresponding to β-cyclodextrin, two characteristic zones of mass loss can be observed. The first stage of mass loss is 8.3% in the temperature range of 20-130°C, which is explained by the evaporation of water molecules on the surface and in the cavity of β-cyclodextrin [5]. The second stage of mass loss is 70% of the total mass of the sample and begins at about 300°C, associated with the decomposition of the β-cyclodextrin molecule [6]. For ferulic acid, the total mass loss is concentrated at 250°C, which corresponds to the phase transition from the liquid state of the substance to the gaseous state.

Table 1 Weight loss values of samples according to TGA results

	Weight loss (%)			
	1	2	3	4
Ferulic acid	–	63.3	28.8	-
β-cyclodextrin	8.4	–	67.7	16.6
Modified β-cyclodextrin	0.3	–	68.4	19.6
FA-MCD inclusion complex	5.6	8.7	47.5	27.7

For the modified β-cyclodextrin sample, the first stage of mass loss about 0.3% indicates the absence of water molecules in the sample and may be due to the successful modification of the β-cyclodextrin surface with cyclohexylsuccinic anhydride. It contributes to the hydrophobic properties of the surface. The second stage of mass loss also accounts for about 70% of the total mass of the sample and begins at about 300 °C, which is characteristic of the decomposition of the β-cyclodextrin molecule.

For the thermogravimetric curve of the complex of ferulic acid incorporation into the cavity of modified β-cyclodextrin, we can see three stages of mass loss. According to the data obtained from the thermogravimetric analysis (Table 1), it can be concluded that the encapsulation of ferulic acid in the cavity of modified β-cyclodextrin was successful.

Conclusions. The obtained results of infrared spectrometry indicate that an interaction occurred between ferulic acid and the modified β-cyclodextrin compound with cyclohexylsuccinic anhydride, which could suggest the creation of a complex inclusion complex in the β-cyclodextrin cavity. According to the TGA data, a slight weight loss (8.7%) of the FA-MCD inclusion complex can be attributed to the decomposition of a small part of the free ferulic acid present in the sample. Also, the final product of the FA-MCD inclusion complex showed the highest thermal stability, it has the highest percentage of mass remaining when 500ºC was reached in the system and the thermogravimetric curves were recorded, indicating the successful encapsulation of ferulic acid in the β-cyclodextrin cavity with a modified surface.

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