THE STRUCTURE OF THE MONOAMMONIUM SALT OF GLYCYRRHIZIC ACID

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Glycyrrhizic acid and its salts are used in medicine in various diseases [1]. In particular, in the USSR the preparation glitsiram, consisting of the monoammonium salt of glycyrrhizic acid, is approved for medicinal use [2, 3].

In developing the technology of the production of glitsiram and the technical documentation for it, we came up against the question of the position of the ammonium group in the molecule of glycyrrhizic acid.

Glycyrrhizic acid is a diglucuronoside of glycyrrhetic acid and contains three carboxy groups, two of which are in the glucuronic acid residues while one belongs to the glycyrrhetic acid.

In the process of preparing glitsiram, on crystallization from acetic acid, the triammonium salt is converted into the monoammonium salt. It might be logical to assume that the substitution in glitsiram is at the position of the carboxy group of the glycyrrhetic acid. This is supported by the fact that the two carboxy groups of the glucuronic acid residues have the same basicity and, if after the reaction with acetic acid only one carboxy group substituted by an ammonium ion remains in glitsiram, this must relate to the glycyrrhetic acid, the acidity of which differs from that of glucuronic acid. This hypothesis was put forward by Abubakirov and Yatsyn [4].

To prove the location of the ammonium group in glitsiram, we used the method of molecular spectroscopy.

We recorded the spectra of glycyrrhetic and glycyrrhizic acids and the triammonium and monoammonium salts of glycyrrhizic acid on a UR-20 infrared spectrometer in the 1800-1600 cm^{-1} region, i.e., where the vibrations of the carbonyl groups appear.

It is known [3] that in the spectrum of glycyrrhetic acid (Fig. 1, curve 1) the absorption band at 1705-1710 cm^{-1} is due to the carbonyl in position 11 and the absorption band at 1673 cm^{-1} to the carbonyl of the carboxy group, the latter being stronger since it shows the influence of the OH group.

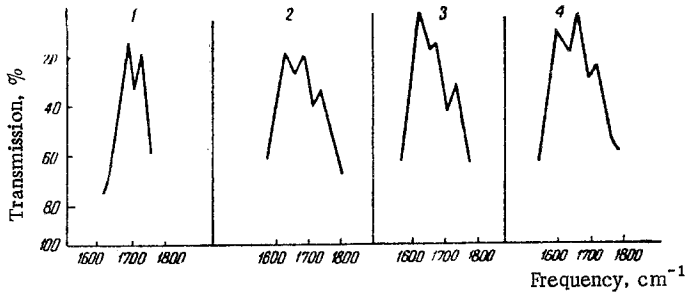

Fig. 1. IR spectra of glycyrrhetic acid (1), glycyrrhizic acid (2) and its triammonium salt (3) and monoammonium salt (4).

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The molecule of glycyrrhizic acid differs from that of glycyrrhetic acid only by the presence of two glucuronic acid residues, which also have two carbonyl groups. These carbonyl groups give an absorption maximum at about 1604 cm^{-1}, as can be well seen in the spectrum of glycyrrhizic acid (Fig. 1, curve 2).

In the process for the production of glitsiram, an intermediate is the triammonium salt of glycyrrhizic acid where the OH groups in the carboxyls are replaced by ONH_4 groups, which are more polar and, consequently, should increase the intensity of the absorption bands of the carbonyls near which they are located [5]. In the spectrum of the triammonium salt of glycyrrhizic acid (Fig. 1, curve 3) this can be clearly seen. The intensity of the absorption band of the carbonyls of the sugar part of the molecule at 1604 cm^{-1} has increased sharply as compared with glycyrrhizic acid. The intensity of the absorption band of the carbonyl of the aglycone at 1673 cm^{-1} has also increased.

The spectrum of the monoammonium salt (Fig. 1, curve 4) shows that the intensity of the absorption band of the carbonyl part of the molecules (1604 cm^{-1}) has fallen considerably, while the intensity of the absorption band of the aglycone (1673 cm^{-1}) remains unchanged as compared with the triammonium salt of glycyrrhizic acid. This shows that the most polar ONH_4 group, located in the aglycone, has remained in the molecule.

Thus, the ammonium group in glitsiram is bound to the carboxy group of glycyrrhetic acid.

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