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MECHANOCHEMICAL INTERACTION OF FENASAL WITH NATURAL AND SYNTHETIC POLYMERS

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The mechanochemical interaction of medicinal substances (MSs) with polymers is one of the most effective methods of creating new drugs: it may change the physicochemical characteristics of the substances and, naturally, their pharmacological action [1, 2].

Fenasal (niclosamide) — 5-chlorosalicylic acid 2-chloro-4-nitrophenylanilide — is a highly active antihelminthic preparation that is widely used in medical practice for the treatment of taeniarhynchosis and taeniasis, and in veterinary medicine for the treatment of the monieziasis of sheep.

In order to increase the solubility and prolong the action of fenasal we have obtained compositions of it with synthetic polymethacrylic acid (PMAA) and microcrystalline cellulose (MCC) and the natural biopolymers pectic acid (PA) and enzymatic apple pectin (EAP) in a ratio of 1:2 by the mechanochemical method (Gefest AGO-2U, 10 min, energy stress 60 g).

In view of the fact that the infrared spectral method has proved to be the most informative on the reactivity of the active centers of molecules interacting with one another [3], we studied the IR spectra of fenasal and its compositions obtained by the mechanochemical method.

In the IR spectrum of fenasal—PMAA (1:2) compositions we observed a displacement of the 1070 cm^{-1} absorption band characterizing the stretching vibrations of the carbonyl group by 18 cm^{-1} in the low-frequency direction as compared with ν_{COOH} for polymethacrylic acid and the appearance in the ν_{OH} and ν_{NH} substituent absorption regions of an intense broad absorption band in the frequency range of 3050—3100 cm^{-1} in place of the 3240 and 3100 cm^{-1} absorption bands that are present in the IR spectrum of fenasal.

The above-mentioned changes in the IR spectral frequencies in the case of the fenasal—PMAA (1:2) composition as compared with the corresponding parameters of the initial components permit the assumption that the interaction of the two molecules takes place through the formation of a hydrogen bond between a COOH group of the PMAA and the proton of the phenolic hydroxyl of fenasal (OH···O-C).

In the IR spectrum of the fenasal—MCC (1:2) composition the frequencies of the absorption bands of the amide carbonyl and the nitro group retained their values relative to the corresponding frequencies for fenasal. However, in the 3100—3500 cm^{-1} region the maximum corresponding to the absorption of the hydroxy groups in the MCC had disappeared and an absorption band had appeared in the frequency interval of 3000—3300 cm^{-1}.

The appearance in the IR spectrum of the fenasal—EAP (1:2) composition of an absorption band at 1618 cm^{-1} absent from the initial components, obviously witnesses the participation of some part of the molecules in the formation of a HB between CO (carboxyl, ester) and the OH acceptor groups of the EAP with the phenolic hydroxyl of fenasal.

This experimental fact indicates, in all probability, that the fenasal—MCC (1:2) complex is formed through a hydrogen bond between the phenolic hydroxy of fenasal, the proton-donating properties of which are enhanced by the chlorine atom present in the *para*-position to it, with an alcoholic OH group of the MCC.

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A comparison of the IR spectral pattern of the fenasal—PA (1:2) composition and the corresponding IR spectra of fenasal and pectic acid showed that the frequency of the 1733 cm^{-1} absorption band corresponding to the stretching vibrations of a carboxy group was 10 cm^{-1} lower than in PA (1743 cm^{-1}) and there was also a shift in the low-frequency direction by 148 cm^{-1} of the absorption band of a hydroxyl group relative to its value for pectic acid (3392 cm^{-1}). Obviously, in this example, the observed anomaly of the frequencies may be considered as evidence of the most probable participation of the OH substituent of fenasal in the formation of a HB with the carboxy group and the alcoholic hydroxyl of pectic acid.

On the basis of the IR spectral information obtained it is possible to conclude that the interaction of fenasal with PMAA, MCC, PA, an EAP takes place through a hydrogen bond between the proton-donating phenolic hydroxyl of fenasal and proton-accepting COOH (PMAA, PA, EAP) and OH (MCC, PA, and EAP) substituents.

Attention is attracted by the retention of the frequencies of the absorption bands of the nitro group (1570 cm^{-1}), the chlorine atom (740 cm^{-1}), and the amide carbonyl (1654 cm^{-1}) of fenasal, and this shows that these functional groups do not participate in the formation of hydrogen bonds.

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