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GEL BASED ON MICROCRYSTALLINE CELLULOSE AND AZIDIN

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The structure of a gel based on microcrystalline cellulose (MCC) and the antiprotozoic preparation azidin is studied. Intense ultrasonic irradiation produces a physicochemical reaction in the MCC:azidin system that lengthens the effective lifetime of the drug.

Microcrystalline cellulose (MCC) is promising as a polymeric carrier for drugs [1, 2]. This unique material has specific properties owing to its high degree of crystallinity, irregular particle shape, hydrophilic nature, etc.

The goal of the present work is to investigate the possibility of reacting the antiprotozic drug azidin [4,4′-(diazoamino)dibenzamidine diaceturate] with the MCC polymeric carrier to produce a gel and to study the MCC properties.

We used x-ray diffraction, IR spectroscopy, and dialysis to study the hydrogel obtained by mechanical mixing of MCC, azidin, and water in a given proportion with subsequent irradiation by ultrasound.

The x-ray studies of the starting materials showed that both components are distinctly crystalline materials. Four equatorial reflections are clearly observed in the diffraction pattern of MCC (Fig. 1, curve 1). These are characteristic of the cellulose-I structural modification with 2θ = 14.7, 16.5, 22.4, and 34.5° and correspond to reflections from the crystallographic planes (101), (10$\bar{1}$), (002), and (040). The diffraction pattern of azidin (Fig. 2) contains several reflections (about 15) of moderate strength that are rather sharp and narrow. This is characteristic of a low-molecular-weight substance. The strongest reflections occur at 2θ = 14.0, 26.6, 20.1, 15.7, and 28.4°.

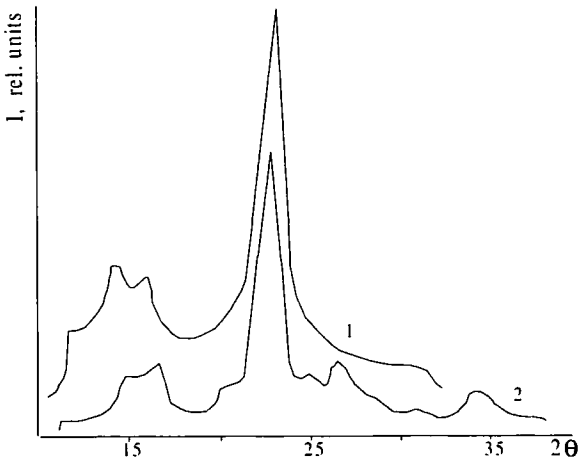

Fig. 1

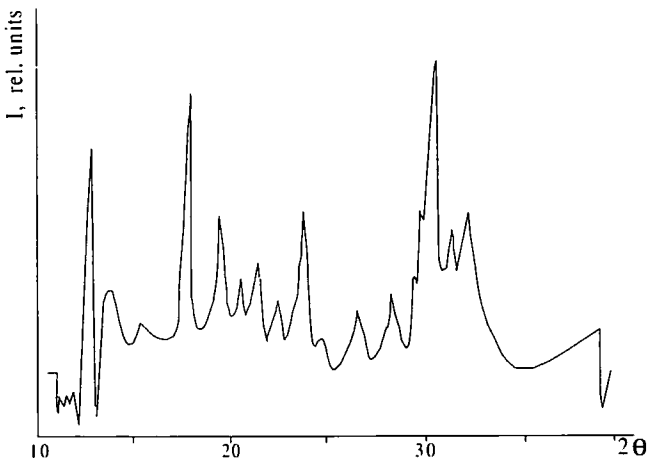

Fig. 2

Fig. 1. X-ray diffractograms: MCC (1), MCC:azidin (1:3) (2).
Fig. 2. X-ray diffractogram of azidin.

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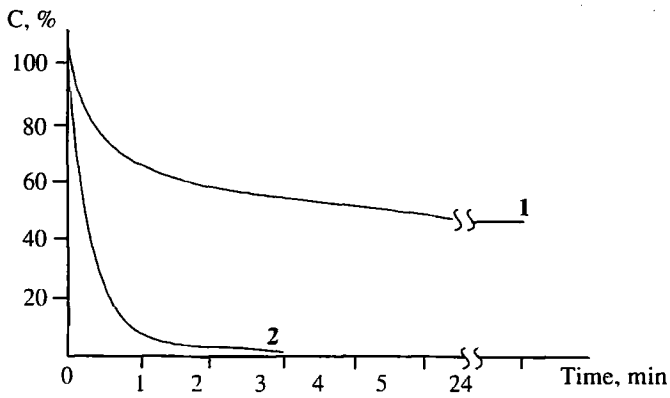

Fig. 3. Kinetics of samples desorption: MCC:azidin (1:1) (1), azidin (starting) (2).

The x-ray diffraction patterns of the MCC-azidin mixture (Fig. 1, curve 2) clearly shows all the MCC reflections at the angles noted above. However, peaks corresponding to azidin are poorly visible. The mixture containing 30% azidin exhibits weak broad reflections at $2\theta = 26.7$ and 28.4°. These same reflections, slightly stronger, are observed in the sample with a 1:1 ratio of components. The intense ultrasonic irradiation of the liquid phase during preparation of the gel may cause the azidin to become somewhat amorphous, which would weaken most of its reflections and lead to their disappearance. This supposition is fully justified because other mixtures of biologically active substances (BAS) with cellulose that have a 1:1 ratio of components produce very clear BAS reflections (if the BAS is crystalline).

The IR spectrum of the MCC—azidin composition is not a simple superposition of the two individual spectra. The changes in the frequencies of the mixture absorption bands can be estimated. Frequency differences in the range 1000-1300 cm^{-1} in the spectrum of the gel relative to those of MCC and azidin are a reliable criterion of polycomplex formation.

The most important changes in the IR spectra of azidin and MCC are observed in the range 3000-3100 cm^{-1}, which corresponds to NH and OH stretching vibrations. The spectrum of the composition contains a band at 3344 cm^{-1}, which is absent in the spectra of MCC and azidin. This may indicate formation of new types of H-bonds between MCC and azidin.

Thus, the following conclusions can be made based on the investigations of the molecular and supramolecular structure of the MCC—azidin mixture. On the supramolecular level, no interactions (e.g., epitaxial growth, formation of joint lattices, etc.) occur although such phenomena were noted for the reaction of cellulose with certain BAS. On the molecular level, MCC and azidin do not form covalent bonds to each other but most likely form rather strong H-bonds to each other under the appropriate conditions (swelling in water, ultrasonic irradiation).

A study of the kinetics of azidin desorption from its MCC mixture showed (Fig. 3) that the fraction of azidin released from the hydrogel and passed through a semipermeable membrane after 24 h was 55% (curve 1). However, the amount passed through the membrane from an aqeous solution of azidin (without MCC) is 99% after 3 h (curve 2). These data confirm the hypothesis that ultrasonic irradiation of a MCC—azidin mixture produces H-bonds, the presence of which facilitates the slower release of azidin from the polymer matrix and the passage through the semipermeable membrane. This lengthens the effective lifetime.

EXPERIMENTAL

MCC was prepared according to the literature [3]. Commercial azidin was supplied by Akrikhin plant (Moscow).

The MCC—azidin hydrogel composition was prepared by adding successively to a beaker MCC (1.5 g), azidin (1.5 g), and distilled water (27.0 g). The mixture was irradiated with ultrasound (15 kHz) for 20 min in an UZDN-1 apparatus.

X-ray diffraction patterns were taken on a DRON-3M diffractometer using monochromatized Cu Kα-radiation produced at 20 kV and 15 mA. Patterns were recorded for $2\theta = 10$-40°. Diffraction patterns of the MCC—azidin hydrogel were recorded after drying the preparation.

IR spectra were recorded on a Perkin—Elmer 2000 Fourier-IR spectrophotometer. The kinetics of azidin desorption

from the hydrogel were studied by dialysis and photocolorimetry. The optical density of the azidin solutions was measured on a KFK-3 instrument.

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