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Raman investigation of some polymeric gels of pharmaceutical interest

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The behavior of the hydrogels obtained from the poly(ethylene oxide) (PEO) and from the polyacrylic acid (Carbopol 940 and 980) under the repeated action of the water was investigated by Raman spectroscopy. The analyze of the spectra shows a reversible action of the water on the polymeric matrix.

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1. Introduction

The use of the polymeric gels as matrix for some medical drugs in the treatment of the skin disease is one of the important directions of the developing of the new pharmaceutical products [1]. The important advantage is the possibility to obtain a long time contact between the active substance and the skin and the possibility to control the delivery rate of the drugs [2, 3]. During the medical application the polymeric matrix is submitted to the long and repeated action of the biological tissues that is characterized by a great content of water. It is essential that the polymer keep unaffected its initial properties. The possible modifications of the properties of the polymeric matrix on the microscopic scale can be observed by spectroscopic methods. Our interest was to observe the behavior of the some polymeric matrix under the repeated action of the water.

2. Experimental

We used for ours investigations the poly(ethylene oxide) PEO 750 with the molecular mass 75000 g/mol and the polyacrylic acid with two molecular mass (Carbopol 940 and 980). In dried state, all these polymers are solid powders but they have great affinity towards the water. The polymeric gel is prepared by mixing slowly the polymer and the pure water during 3-4 hours. We investigated the sample with the polymeric concentrations 6%. The gels were deposed on thin films on the microscope glass plates. The first type of measurement was done on these samples. After the water was removed from the samples by evaporation during 48 hours at room temperature and a new series of measurements was performed. The samples were hydrated again at the initial water concentration and a new series of measurements was performed. The samples were investigated by Raman spectroscopy in the domain 200-2000 cm^{-1}, using a co focal Raman microscope (Witec CRM 200), at the room temperature. All Raman spectra were excited with 100mW of 633 nm light produced by a He-Ne laser and the spectra were recorded in backscattering geometry. A digital acquisition data is performed by the PC computer of the system.

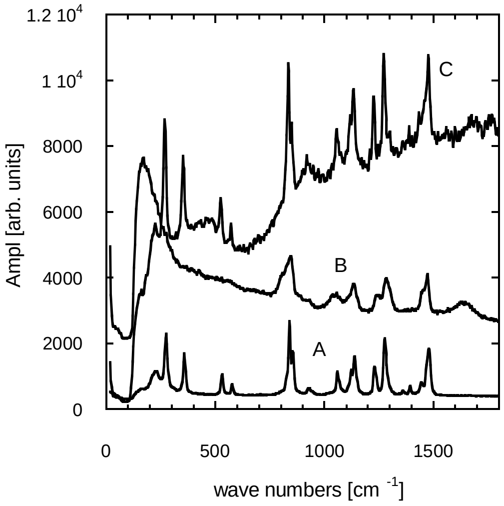

Fig. 1. Raman spectra of the PEO in solid state (curve A); in the aqueous state (gel), (curve B); and in dried gel, (curve C).

3. Results and discussion

The poly(ethylene oxide) and the polyacrylic acid were selected due to theirs stability and hydrogel forming capacity. These polymers have a good compatibility with a great category of medical drugs. The poly(ethylene oxide) (PEO) has a repeated unit consisting on three linkages along the backbone, the O-C, C-C, and C-O bonds that can adopt many conformations. The most probable conformation of the monomer is the trans conformation, designed *ttt* that corresponds to the minimum of the potential interaction energy between the atoms of the repeat unit. In crystalline state the most stable atomic arrangement includes a gauche conformation, designed as *tgt* [4]. In the molten state the local structure of the polymer contains all the possible arrangements allowed by the chemical bonds between these conformations (from *tgt* to *ttt*). The local organization of the monomer is responsible by the specific spectrum observed by Raman spectroscopy. The spectrum of the PEO in powder state, before forming the gel, contain a fine structure, corresponding to different vibrations of the chemical bonds of the monomer, (Fig. 1, curve A). In the presence of the water, in the gel state, the spectrum is broad, and without well defined structure, but it contains approximately the same bands as the spectrum of the solid sample, (Fig. 1, curve B).

The conformation distribution for poly(ethylene oxide) contains a variety of conformer sequences *ttt, tgt. tgg'*, *ttg* [4, 5, 6]. Each conformation give rise to its characteristic vibration spectrum, determinate by the mechanical coupling coordinates of the monomer. For a large distribution of the conformations, the recorded spectrum is a superposition of the individual spectra corresponding to each conformation.

Computer simulation, reported in the literature, of combinations of these conformations, extended to few neighboring monomers, shows that in function of the contribution of each conformation to the distribution function it is possible to obtain almost any shape of the spectrum [9].

For example, the simulated Raman spectra computed for backbone stretching mode of three identical rotameric sequences *tgt* - *tgt* - *tgt* and *tgg* – *tgg* – *tgg* contain a strong band around 860 cm^{-1}, and the simulated spectra of the sequences *tgg'* – *tgg'* – *tgg'* contain a band around at 840 cm^{-1}, in accord with our experimental data. These bands appear in solid state as well as in aqueous state of PEO, but they are very net and well defined in the solid state, whereas in the aqueous state they are broad and without clear structure (Fig. 1)**.** Other possible sequences as *ttt* – *tgt* – *tgt* or *tgt* – *tgt* – *tgt* have simulated bands in the domain 230 – 280 cm^{-1}, in accord with our data observed in the solid PEO. These bands merge into a large broad band in the aqueous state observed in this domain (Fig. 1).

In solid state, the fluctuations of the polymeric conformations are much reduced, and the spectrum is characterized by well-defined and narrow vibration bands.

In the aqueous state the dynamics of the polymeric chain is more important than in the solid state, and the number of possible local conformations and the fluctuations of these conformations are more important than in the solid state. Each conformation is characterized by its own spectrum giving a contribution to the total spectrum. As result, the spectrum is broad, without fine structure. In the domain of 700-1500 cm^{-1} the spectrum of the aqueous solution contains approximately the same bands as the spectrum of the solid sample, but the vibration bands are broad and with reduced amplitude. The most intense band at 840 cm^{-1} of the spectrum of the solid PEO, that is assigned to the C-O stretching for the *tgt* conformer, appears also in the spectrum of the aqueous solution, but this band is broad and its intensity is strongly reduced. Great differences appear in the domain 200-700 cm^{-1}. There we can observe an important broadening of the spectrum of the aqueous solution and a leak of some bands by rapport to the spectrum of solid PEO. This behavior is determined by the large distribution of the conformations and by the important fluctuation of these conformations in the aqueous state compared to the solid state.

After removing the water from the gel, by evaporation, we obtain again the initial spectrum of the powder sample, but the amplitude of the bands is reduced and the noisy is much important, (Fig. 1, curve C). This result demonstrates that the water has a reversible action on the local structure of the polymer.

Similar measurements were performed on the polyacrylic acid. We utilized two polymers with different molecular mass, the carbopol 940 with the molecular mass 94000 g/mol and the carbopol 980 with the molecular mass 98000 g/mol. The interest was focused on the observation of the influence of the molecular mass on the local structural behavior of the monomer. The spectra of these polymers are very similar (Fig. 2). This behavior demonstrates that the local vibrations of the chemical bonds of the monomer are not influenced by the molecular mass. The number of the monomers along the chain can affect the long-range polymeric fluctuations but they have very weak influence on the local dynamics of the chemical bonds of the monomer [7, 8, 10]. In the aqueous solution the spectrum of the polyacrylic acid gel is very broad, practically without structure, (Fig. 3, curve A). Only the large band at 1650 cm^{-1} appears in both the spectra of the gel and polymeric powder. As in the case of the poly(ethylene oxide) this broadening is determined by the large distribution of the conformations and by the important time fluctuation of these conformations. In the presence of water the dynamics of entire chain is amplified which fact facilitate the rapid rearrangements of the segmental bonds of the chain. A large distribution of the conformations is allowed by the increased dynamics of the polymeric chain. The spectrum is a superposition of the spectra corresponding to each conformation and became broad.

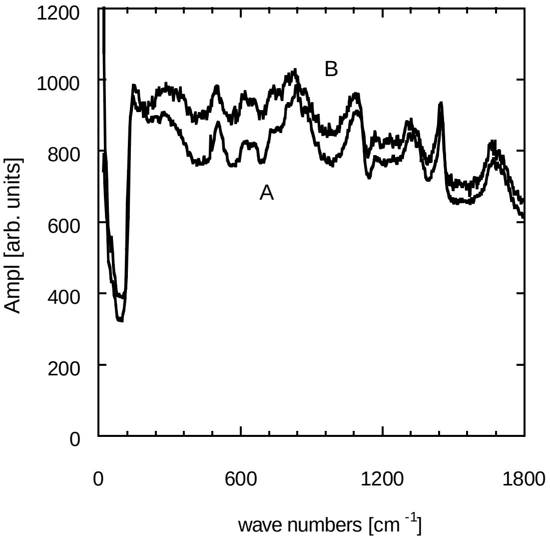

Fig. 2. The spectra of the polyacrylic acid (carbopol) with different molecular mass. Curve A, the carbopol 940 and curve B, the carbopol 980 in powder state.

The next step of our experiment is concerned with the observation of the Raman spectra after removing the water from the gel, by evaporation. Except an important reduction of the amplitude of the observed bands and the presence of the noisy, the spectrum of the dried gel is very similar with the spectrum of the polymer in powder state (Fig. 3 curve C). In the domain 800-1500 cm^{-1} the vibration bands are clear and well defined in both the spectra. We can assume that the conformations responsible for these bands are identically in both the samples, and they have almost the same distribution. In the domain 200-800 cm^{-1} the bands appear in both the spectra at the same wave numbers, but the amplitude of the bands of the dried gel is much reduced. This fact indicates the existence of the same conformations responsible for these bands in both the samples, but their contributions to the total spectrum is reduced in the dried gel compared with the solid state.

The rising of the vibration bands of the dried gel at the same wave numbers as for the powder polymer demonstrates that the water have not induced irreversible modification on the local structure of the polymer. The cycle adding-removing of the water is a reversible process. This result is very important for the applications in the biological liquids, with great water contents, when we are interested for a reversible interaction between the polymer and the biological tissues.

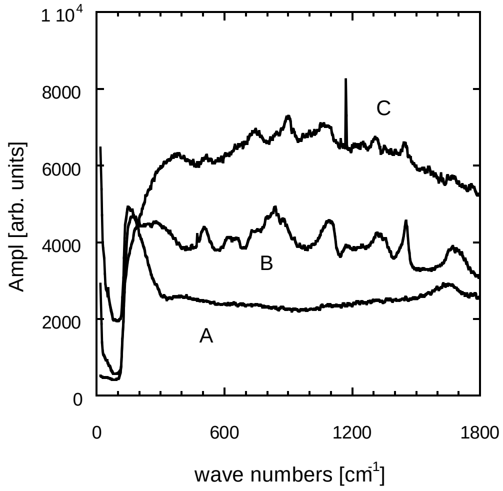

Fig. 3. The spectra of the polyacrylic acid in different states. Curve A, the polyacrylic acid in aqueous gel state; Curve B, the polyacrylic acid in powder state; Curve C, the polyacrylic acid gel after the evaporation of the water.

5. Conclusions

The Raman spectroscopy is a powerful tool for the investigation of the possible interactions between the polymeric matrix with pharmaceutical applications, and the aqueous medium of the biological liquids.

The polymeric matrix is obtained from two polymers with great affinity towards the water, the poly(ethylene oxide) and the polyacrylic acid. The samples were investigated in powder state, in aqueous gel state, and in dried state after removing the water. For PEO the Raman spectra of the solid polymer and of the gel contain almost the some vibration bands in the domain 800-1500 cm^{-1}, but they are different in the domain 200-700 cm^{-1}. The spectrum of the solid polymer contains narrow lines, whereas the spectrum of the aqueous solution is broad and without well-defined structure. This behavior indicates a broad dispersion of the local conformation of the polymer in the aqueous state and important time fluctuation of these conformations compared to the solid state. In dried state, after removing the water from the gel, the observed spectrum is identical to those of the polymer in powder state. This fact indicates a reversible interaction between the polymer and the water.

For the polyacrylic acid the Raman spectra of the samples with different molecular mass are identically, that indicates no influence of the length of the chain on the local conformation of the polymer. The spectrum of the aqueous solution is very broad, without structure, which indicates a large distribution of conformations compared to the solid state of the polymer. The spectrum of the dried gel contains almost the same bands, but with different amplitudes, that the spectrum of the powder. The local conformations of the chain, characteristic for the powder polymer, are also presents in the dried gel, but theirs distribution is different, that explain the modification of the amplitude. This behavior indicates a little influence of the water on the local distribution of the conformation of the polymeric chain.

Acknowledgments

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