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MRI Study of Fickian, Case II and Anomalous Diffusion of Solvents into HPMC

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1. Introduction

The interest in hydrophilic polymers, especially hydroxypropylmethyl cellulose (HPMC) is due to the increasing use of this polymer in pharmaceutical industry for production of controlled drug delivery systems [1-3]. The main issue of such systems is to predict the mechanism of the drug release. One of the important mechanisms that govern the release of drug is the diffusion of water solvent or body fluids into a dry hydrophilic polymer. During hydration of HPMC the gel layer is formed around the dry core of polymer and swelling of polymer occurs.

2. Experimental

The hydroxypropylmethyl celluloses HPMC80-120 (M_w = 12000); HPMCE4M (M_w = 86000) and HPMC100M (M_w = 120000) were purchased from FLUKA as powders and used as supplied. For Magnetic Resonance Imaging (MRI) studies the samples were prepared in the form of cylindrical tablets (8 mm × 5 mm) by compressing the powders under hydraulic pressure of 100 MPa. MRI experiments were carried out with a Bruker AVANCE 300 MHz spectrometer equipped with a micro imaging probehead, magnetic field gradients, and Para Vision software. A Bruker Micro 2.5 imaging probehead was used with a 20 mm birdcage coil. The MRI measurements were performed at 37 ^{0} C as a function of the hydration time and for acidic (pH = 2), neutral (pH = 7) and alkaline (pH = 12) solvent. The hydration process started when the HPMC tablet was immersed in the particular solvent. At different hydration time, the solvent was removed from the sample tube, the tube was placed in the magnet, and then the images were taken. In our MRI experiments, the images of the slices taken in radial direction from the middle of the sample were acquired with a repetition time T_R of 3000 ms. The acquisition parameters were a field–of–view (FOV) of 1.5 mm × 1.5 mm digitized into 128 × 128 pixels with a slice thickness of 2 mm (i.e. each voxel = 117 μm × 117 μm × 2mm).

3. Results

The swelling properties of the HPMC hydrated in the neutral, alkaline and acidic solvents were studied through the diffuse solvent molecules. The spatially resolved spin-spin relaxations times, spin densities and diffusion coefficients together with the change in the dimension of the glass core of the polymer were determined for HPMC tablets as a function of hydration time.

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The 1D profiles of the studied parameters taken after 210 minutes of hydration of the HPMC matrices in the solvents with pH = 2, 7, and 12 are presented in Figs. 1, 2 and 3, respectively.

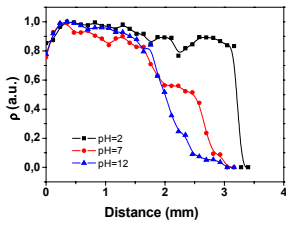

Fig.1. The spin-density ρ profiles of solvent protons within the gel layer of HPMC

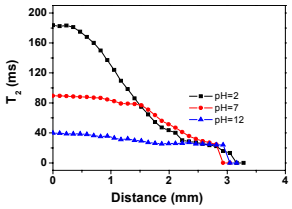

Fig.2. The spin-spin T_2 profiles of solvent protons within the gel layer of HPMC

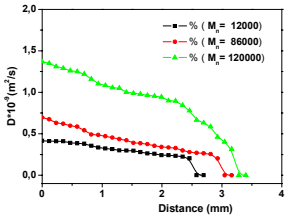

Fig.3. The diffusion profiles within the gel layer of HPMC taken along radial direction

4. Conclusion

Our MRI measurements allow determination of the diffusion mechanisms to be Fickian or Case I (for solvent with pH = 12), Case II for solvent with pH = 2 and an anomalous for water solvent of neutral pH = 7 [4-6]. From T_2 and D parameters the mobility of the solvent molecules within the gel layer of HPMC was estimated. It is worth to point out that MRI is the only method, which allows distinguishing anomalous diffusion.

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