QUANTIFICATION OF THE MR IMAGES OF HYDROGELS BY NMR RELAXATION MEASUREMENTS

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Abstract: Layers of hydrogel represent a diffusional barrier that retards the process of drug release. For better prediction of drug release, a method for evaluating the polymer concentration profile was developed.

Key Words: NMR**,** MRI, Matrix Tablets, Hydrogel.

INTRODUCTION

Tablets that enable diffusion-controlled drug delivery are one of the promising solutions for new drugs. These tablets swell on contact with water as a layer of hydrogel forms by polymer hydration and polymer chain relaxation. It has been found that this layer represents a diffusional barrier that retards further water uptake and hence drug release [1]. Since the kinetics of drug release must match the required concentration profile, detailed information about the dynamics of gel formation is needed for the proper profiling of drug release [2].

MATERIAL AND METHODS

Tablets were prepared by direct compression of polymer powder (Hydroxypropyl-cellose:HPC HXF (Klucel 99-HXF, Aqualon, Hercules)). The tablets were covered with an impermeable hydrophobic polymer, so that only one circular surface was open for water penetration. Sequential magnetic resonance images (MRI) were taken with a standard spin-echo sequence (Fig.1).

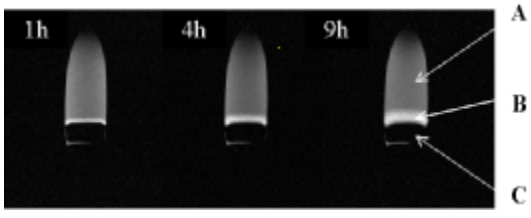

Fig.1. Two-dimensional MRI images of the gel layer at the polymer tablet/water interface: **A** – water, **B** – hydrated polymer, **C** – dry polymer**.**

A series of model samples - homogenous hydrogels with known polymer concentrations - were prepared. T_1 (spin-lattice relaxation time) and T_2 (spin-spin relaxation time) were measured for each of these at the same temperature and frequency.

RESULTS AND DISCUSSON

Each tablet's gel layer thickness was calculated as a function of time from MRI images. However, the polymer concentration in the gel layers was found not to be homogenous. A procedure for determining the polymer concentration profile was developed. Average brightness as a function of the distance from the surface of the tablet was calculated for each image. For each model sample with a different polymer concentration, the theoretical MRI signal (S) was calculated for the actual imaging parameters as follows

$$S= K.\rho.e^{(-TE/T2)}.(1-e^{(TR/T1)}) ,$$

where K is a constant independent of the polymer, and ρ is proton density. The graph of polymer concentration versus the calculated signal (Fig.2) was fitted to a parabola

$$S=a[C]^2+b[C]+c,$$

where a, b, and c are parameters typical for the hydrogel, and C is the mass concentration of the polymer in hydrogel.

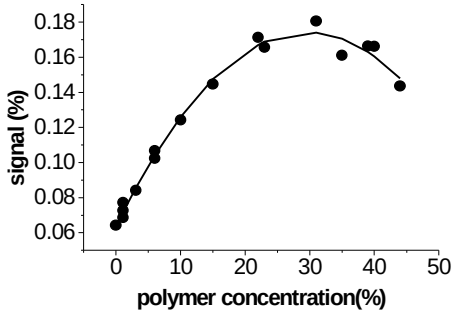

Fig. 2. Signal dependence on polymer concentration

The average image brightness was normalized and multiplied by the maximum of the calculated parabola. By putting these values into the parabola formula, the polymer concentrations can be obtained. In the experiment, we applied this procedure to obtain the polymer concentration profile through the whole swelled tablet as a function of time. (Fig.3)

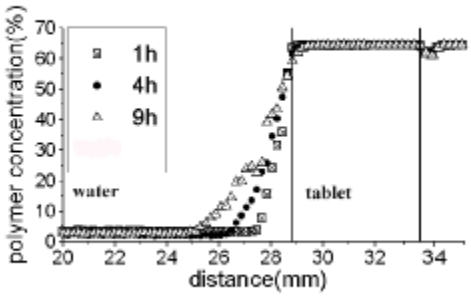

Fig. 3. Concentration profile after 1h, 4h and 9h.

For a good prediction of drug release time, it is important that, in addition to the thickness of the gel layer around the tablet, its polymer concentration profile is also known. This procedure could also be used for other kinds of gels where polymer concentration changes with distance, or time, and hence structural information about the gel layers is needed.

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