Analytical Characterization of a Gelling Biodegradable Polymer

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The present study was undertaken for the analytical characterization of a hydrophilic biodegradable polymer, Hydroxypropyl methylcellulose (HPMC). Purity and the crystalline nature of the polymer were evaluated. Fourier Transform Infrared (FTIR) analysis was performed by FTIR Spectrophotometer interfaced with infrared (IR) microscope operated in reflectance mode. The spectra were collected over the wave number from 400 to 4000 cm^{-1} at room temperature. Raman spectroscopic analysis for the polymer was performed by a low resolution portable Raman Spectrometer (Raman system R-3000), using 785 nm solid state diode laser, with fiber optic sampling probe. The Raman spectra were collected over the wave number from 140 to 2500 cm^{-1} at room temperature. X-ray powder diffraction (XRD) data for HPMC polymer were obtained using a powder diffractometer. The polymer was scanned from a Bragg angle (2θ) between 10^0 and 70^0. The obtained data were tabulated in terms of the lattice spacing (Å) and relative peak intensities (I/I_0). From the spectral interpretation, it has been found that the FTIR and Raman spectroscopic analysis help in determining the back bone structure of HPMC i.e., the pyranose ring with beta-linked D-glucose units. Moreover, sharp peaks with respect to different 2θ values obtained from XRD study indicate its crystalline nature. From our results, it can be concluded that the FTIR study, Raman Spectroscopic analysis, and XRD study help in the analytical characterization of the HPMC. This information is very important for the preformulation study to prepare any novel drug delivery system having bioadhesive property.

Key words: HPMC, FTIR, Raman spectroscopic analysis, XRD study

INTRODUCTION

Hydroxypropyl methylcellulose (HPMC) is one of the most commonly used hydrophilic biodegradable polymers for developing controlled release formulations, because it works as a pH-independent gelling agent. Swelling as well as erosion of it occurs simultaneously and contributes to overall drug release. It is a widely accepted pharmaceutical excipient, because HPMC is available in a wide range of molecular weights and the effective control of gel viscosity is easily possible [1-5].

HPMC has many pharmaceutical uses as a drug carrier, a coating agent, a tabletting agent, and it is also used in ophthalmic solutions and in personal care products, such as KY Jelly [6]. It is the most important hydrophilic carrier material used for the preparation of oral controlled drug delivery systems. One of its most important characteristics is the high swellability, which has a significant effect on the release kinetics of an incorporated drug. Upon contact with water or biological fluid, the latter diffuses into the device, resulting in polymer chain relaxation with volume expansion. Subsequently, the incorporated drug diffuses out of the system [1].

HPMC is propylene glycol ether of methyl-cellulose. Its chemical structure is

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Received 30-03-2011; **Accepted** 25-04-2011

illustrated in Figure.1[7]. The physicochemical properties of this polymer are strongly affected by: (i) the methoxy group content; (ii) the hydroxypropoxy group content; and (iii) the molecular weight [1]. Considering the importance of HPMC, its qualitative test and analytical characterization are highly essential. To know the different functional groups and highly polar bonds of pure HPMC polymer, FTIR analysis was conducted. Their backbone structures and symmetric bonds were checked by Raman spectroscopy. It is known that Raman and FTIR are complimentary vibrational spectroscopic techniques. There are band intensity differences between the two techniques. Therefore, to obtain the more detailed chemical information both FTIR and Raman analyses were carried out [8, 9].

Since we know the wavelength λ of the incident X-ray beam, and can measure the angle of incidence of the X-ray beam θ, we can calculate the distance between adjacent planes of atoms, *d*-spacings, using Bragg's Law. The characteristic set of d-spacings generated in a typical X-ray scan provides a unique "fingerprint" of the HPMC polymer. When properly interpreted, by comparing this "fingerprint" of pure polymer as reference, the identification and change in crystallinity of polymer present in the polymeric composites can be determined [10]. So, to check the crystalline/amorphous nature of pure HPMC polymer, XRD study was performed. It is known that the identification of a structure from its powdered diffraction pattern is based upon the position of peaks and their relative intensities. Each XRD pattern is characterized by the interplanar d- spacing and the relative intensities (I/I_0) [11]. Nevertheless, complete diffraction patterns are still characteristics of the samples.

Considering all the above mentioned reasons, the qualitative analysis of HPMC was performed by FTIR, Raman Spectroscopy and X-Ray diffractometry. This study is very important before incorporating the polymer into the novel drug delivery systems.

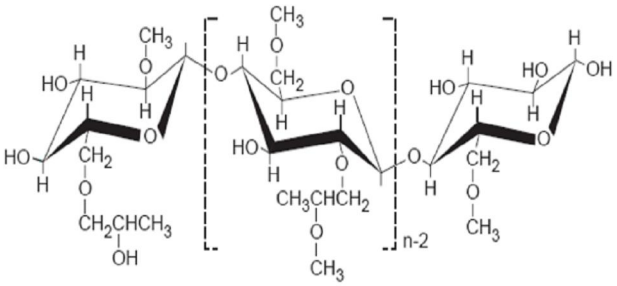

Figure.1: Chemical structure of Hydroxypropyl methylcellulose (HPMC)

MATERIAL AND METHODS

Materials:

Hydroxypropyl methylcellulose (HPMC E15 LV Premium) was supplied by Loba Chemie Pvt. Ltd., India. It was having methoxy group (23.8%) and hydroxypropoxy group (8.3%).

Methods:

Fourier Transform Infrared (FTIR) Spectroscopy:

FTIR analysis was performed with an FTIR spectrophotometer interfaced with an infrared (IR) microscope operated in reflectance mode. The microscope was equipped with a video camera, a liquid nitrogen-cooled mercury cadmium telluride (MCT) detector and a computer controlled translation stage, programmable in x and y directions. 2 mg of each sample was taken with dry IR-grade KBr at about 2% sample to KBr ratio. KBr pellet of the samples were prepared [12]. Normally background was first scanned by using blank potassium bromide pellet. Then the samples were scanned. The spectra were obtained in the 400 cm^{-1} to 4000 cm^{-1} region with 8 cm^{-1} resolution, 60 scans and beam spot size of 10-100µm. FTIR imaging was carried out using Perkin Elmer Spectrum RX.

Raman Spectroscopy:

The Raman system R-3000 instrument, manufactured by Raman systems INC.USA, is a low resolution portable Raman Spectrometer using a 785nm solid state diode laser adjusted to deliver 250mw to the sample having spectral resolution 10 $cm^{-1}$and 12 v dc/5A power supplies and USB connectivity. This Raman Spectrometer is having fibre optic sampling probe with safety shutter and automatic focusing caps for both solid and liquid samples. The solid powder samples i.e., pure polymers were enclosed in plastic poly bags and tested directly at room temperature. The interference of the outside light was also prohibited to prevent photon shot noise. The spectra were collected over the wave number range from 140 to 2500 cm^{-1}.

X-Ray Diffractometry:

XRD measurements were made using Philips X'Pert powder diffraction system (Philips Analytical, The Netherlands) equipped with a vertical goniometer in the Bragg-Brentano focusing geometry. The X-ray generator was operated at 40kV and 50mA, using the CuKα line at 1.54056 Å as the radiation source. Each powdered specimen was packed in a specimen holder made of glass. In setting up the specimen and apparatus, co-planarity of the specimen surface with the specimen holder surface, and the setting of the specimen holder at the position of symmetric reflection geometry were ensured. The powders were passed through a 100 mesh sieve and were placed into the sample holder by the side drift technique [11, 13]. The holder consisted of a central cavity. In order to prepare a sample for analysis, a glass slide was clipped to the top face of the sample holder so as to form a wall. The powder sample was filled into the holder, gently tapped and used for XRD measurement. Ten milligram of each sample was scanned at 25°C from 10˚ to 70˚ (2θ) and in step size of 0.020 and count time of 2.00 s, using an automatic divergence slit assembly and a proportional detector. Relative intensities were read from the strip charts and corrected to fixed slit values.

RESULTS

FTIR Spectroscopic Analysis:

Assignments of FTIR frequencies are achieved by comparing the band positions and intensities observed in FTIR spectra with wave numbers and intensities. The peak at 3500 to 3400 cm^{-1} is due to OH vibrational stretching (Figure. 2) [12, 14]. The symmetric stretching mode υ_sMe and $\upsilon_s$hydroxypropyl group are found in the range 2900 cm^{-1} in which all the CH bonds extend and contract in phase [15]. The peak at 2550-2500 cm^{-1} is assigned to OH stretching vibration, i.e., $\upsilon_{O\text{-}H}$ and intramolecular hydrogen bonding [12, 14]. The band between 1650 and 1600 cm^{-1} indicates the presence of stretching vibration of $\upsilon_{C\text{-}O}$ for six membered cyclic rings. Two bending vibrations can occur within a methyl group. The first of these, the symmetric bending vibration δ_sMe involves the in-phase bending of the C-H bonds. The second, the asymmetrical bending mode δ_{as}Me is due to out-of-phase bending of the C-H bonds. While the asymmetric bending vibrations of the methoxy group normally appear in the region 1500-1450 cm^{-1}, the symmetric vibrations are mostly displayed in the range 1400-1350 cm^{-1} [15, 16]. The band between 1400 and 1350 cm^{-1} suggests $\upsilon_{C\text{-}O\text{-}C}$ of cyclic anhydrides [12, 14]. The peak at 1300-1250 cm^{-1} is due to $\upsilon_{C\text{-}O\text{-}C}$ cyclic epoxide. The band at 1100-1000 cm^{-1} is for stretching vibration of ethereal C-O-C groups. The peak at 1000-950 cm^{-1} is due to υ_{as} of pyranose [17]. The rocking mode of CH_2 is found in the range 850-800 cm^{-1} (Figure 2 and Table 1) [15]. The computed frequencies of HPMC are in a good agreement with experimental frequencies for both carbohydrate region as well as OH and CH region.

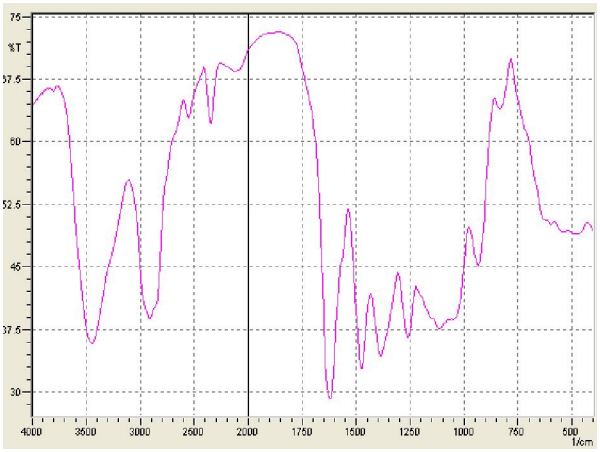

Figure 2: **FTIR Spectra of HPMC**

Raman Spectroscopy:

In case of HPMC, the prominent Raman shifts are found at 504.7, 908.3 and 1384.3 cm^{-1} (Figure 3). However, the OH stretching is not observed. The peak at 504.7 cm^{-1} is assigned to C-H out of plane bending vibration and C-C-O bending vibration of β D-glucose monomer of HPMC [16, 17]. The band at 908.3 cm^{-1} is due to C-C-C in-plane bending and $\upsilon_{(C\text{-}O\text{-}C)}$ stretching vibration of pyranose ring. The peak at 1384.3 cm^{-1} is assigned to C-C stretching vibration (Table 2) [15-18].

Peaks (cm^{-1})	Groups	Peak Assignments
3500-3400	Hydroxyl group	O-H stretching vibration, intermolecular H-bonding
2900	Methyl and hydroxypropyl group	$\upsilon_{s\text{-}CH}$ stretching of methyl and propyl group
2550-2500	Hydroxyl group	O-H stretching vibration, intramolecular H-bonding
1650-1600	Six membered cyclic	$\upsilon_{C\text{-}O}$
1500-1450	δCH, δOCH, δCCH	Assymmetric bending vibration of methyl group in CH_3O
1400-1350	Cyclic anhydrides	υC-O-C and symmetric bending of methoxy group
1300-1250	epoxides	υC-O-C cylic
1100-1000	Ethereal C-O-C group	Stretching vibration of C-O-C group
1000-950	Pyranose ring	υ_{as} of pyranose ring
850-800	CH_2 group	rocking mode of CH_2 group

Table 1: Prominent FTIR Peaks of HPMC

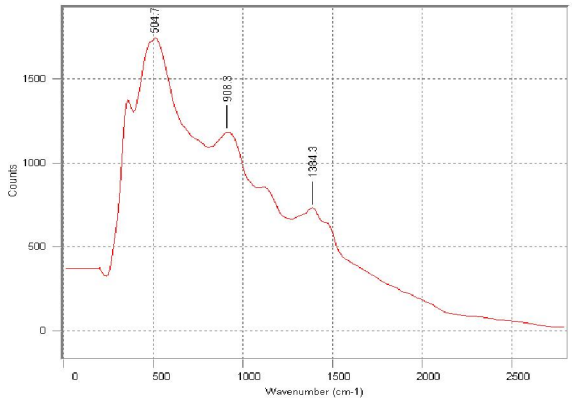

Figure 3: Raman Shifts of HPMC

Raman Shifts (cm^{-1})	Functional Groups / Vibration
504.7	C-H out plane bending and C-C-O bending vibration
908.3	C-C-C in plane bending and stretching vibration of $\upsilon_{(C\text{-}O\text{-}C)}$ in pyranose ring
1384.3	C-C stretching vibration

Table 2: Prominent Raman Shifts of HPMC

X-Ray Diffraction Study:

The powder X-ray diffraction patterns for the pure HPMC are given in Figure 4. The XRD pattern of HPMC shows sharp peaks. X-ray diffraction data in terms of lattice spacing (Å) and relative intensities (I/I_0) for HPMC polymer are represented in Table 3. Both peaks and their relative intensities were determined because the identification of a structure from its powdered diffraction pattern is based upon the position of peaks and their relative intensities. Although each XRD pattern is characterized by the interplanar d- spacing (Å) and the relative intensities (I/I_0) of the three strongest peaks in the pattern under the Hanawalt system [11], complete diffraction patterns are still characteristics of the samples as can be seen from Table 3. In our study, it has been found that the three prominent peaks of pure HPMC having relative intensities 28.42, 100.00 and

5.4 % corresponding to d-spacing 5.03, 4.46 and 2.83 Å, respectively. Corresponding to Bragg's angle of 19.90 with d-spacing 4.46 Å between the planes in the atomic lattice, our sample shows relative intensity of 100% and peak height of 406 cps, which are the characteristics of HPMC polymer.

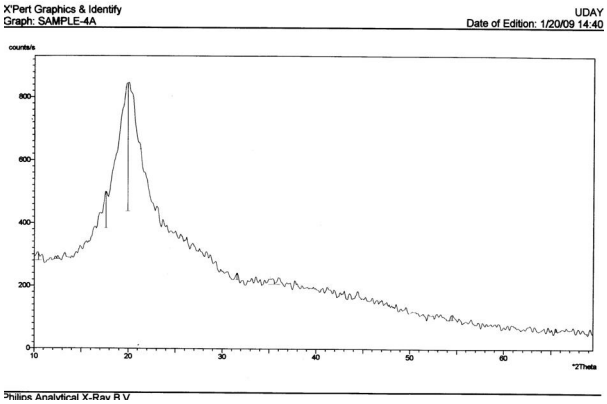

Figure 4: X-ray diffraction patterns of HPMC

S.No.	d-spacing (Å)	Relative intensity (I/I_0) (%)	Angle (2θ)	Peak Height (cps)
1	8.47	4.81	10.44	20
2	7.13	1.52	12.40	6
3	5.03	28.42	17.60	115
4	4.46	100.00	19.90	406
5	2.83	5.40	31.54	22
6	2.53	2.42	35.50	10
7	1.68	3.90	54.48	16
8	1.42	2.50	65.51	10

Table 3: X-ray diffraction data in terms of lattice spacing (Å) and relative intensity (I/I_0) and peak height for HPMC polymer

DISCUSSION

It is known that the infrared spectra are recorded on Fourier Transform Spectrometer in the mid –infrared region (MIR) within the range (400-4500 cm^{-1}) [12, 14]. Due to complex interaction of atoms within the molecule, IR absorption of the functional groups may vary over a wide range. However, it has been found that many functional groups give characteristics IR absorption at specific narrow frequency range. Multiple functional groups may absorb at one particular frequency range but a functional group often gives rise to several characteristic absorptions. That is why the spectral interpretations should not be confined to one or two bands; actually, the whole spectrum should be examined. Accordingly, in our study, whole FTIR spectra of two grades of the polymer were taken into consideration for spectral interpretation.

From FTIR spectral analysis it has been found that the HPMC shows both intramolecular and intermolecular hydrogen bonding. The presence of pyranose ring of β D-glucose monomers has been confirmed. The stretching vibration of the cyclic anhydride, methoxy and hydroxypropoxy groups along with epoxide helps in the identification of HPMC [12, 14-17].

From the nondestructive Raman spectroscopic analysis of HPMC, the C-H out of plane bending vibration and C-C-O bending vibration of β D-glucose monomers have been confirmed. The presence of pyranose ring is also determined by the Raman shift at 908.3 cm^{-1} .The Raman shift for C-C stretching vibration strengthens the FTIR results for the characterization of HPMC polymeric chain [15-18].

It has already been mentioned that Raman and FTIR are complimentary vibration spectroscopic techniques. However, there are band intensity differences between the two techniques. Therefore, to obtain the more detailed chemical information both FTIR and Raman analyses have been carried out [8, 9]. Most of the characteristic peaks in the XRD patterns are prominent and sharp, so measurement of the angles and hence of d-values was accurate. Proper sample preparation helps to attain exact peak positions for qualitative analysis.

From the XRD patterns of HPMC it is clear that HPMC is fully crystalline in nature due to its sharp prominent peaks (Figure 4). From the Table 3 it has been found that the three prominent peaks of both pure HPMC having relative intensities 28.42, 100.00 and 5.4 % corresponding to d-spacing 5.03, 4.46 and 2.83 Å, respectively. This variation in relative intensities of these peaks is probably due to change in atomic densities in that particular plane of crystal lattice. Like Parameswara et al (2008), our maximum relative peak intensity was found at more or less similar 2θ value, which is also the characteristic of pure HPMC polymer (Table 3) [19]. It is known that the highest peak and maximum relative intensity with respect to particular d-spacing at certain 2θ value is the characteristics of a crystalline compound. In our work, we have also seen that at particular Bragg's angle 19.90 with d-spacing 4.46 Å between the planes in the atomic lattice, our sample shows maximum relative intensity (100%) and highest peak height of 406 cps, which are the characteristics of crystalline HPMC polymer.

From the above discussion, it may be concluded that the FTIR and Raman spectroscopic analysis help in determining the back bone structure of HPMC having pyranose ring with beta-linked D-glucose units. Moreover, XRD study suggests its crystalline nature of the polymer. Thus, FTIR, Raman spectroscopic analysis and XRD study help in the analytical characterization of the HPMC polymer. This information is essential in the preformulation study for the preparation of any novel drug delivery system having bioadhesive property. Such investigation may be extended further by performing more analytical methods for the detail characterization of HPMC polymer, which would give us better idea about the polymer.

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Source of support: Nil, Conflict of interest: None Declared