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Research Article

SPECTROSCOPIC INVESTIGATIONS OF A CIPROFLOXACIN / HPMC MUCOADHESIVE SUSPENSION

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ABSTRACT

Introduction: Very few formulations are available, at present, from which the drug is absorbed uniformly, so that safe and effective blood level of the drug could be maintained for a prolonged period. Considering this limitation, a suspension of Ciprofloxacin (drug) has been prepared for the present study using mucoadhesive HPMC as a polymer.

Materials and Methods: The ultrasonication method has been used for the preparation of mucoadhesive suspension of Ciprofloxacin in which HPMC has been incorporated. The chemical interaction between Ciprofloxacin and polymer in the formulation has been studied by FTIR and Raman Spectroscopic analyses.

Results: From the spectral interpretation, it has been found that in formulation, the carboxylic groups of Ciprofloxacin and hydroxyl groups of HPMC undergo chemical interaction, leading to esterification and hydrogen bonding.

Conclusion: The formation of micellies due to esterification and hydrogen bonding causes more drug entrapment and a stable formulation. Due to that the formulation of Ciprofloxacin may give better controlled release and mucoadhesive action in the gastrointestinal tract. Hence, HPMC could be considered as an effective carrier for Ciprofloxacin.

Keywords: Ciprofloxacin, HPMC, FTIR, Raman Spectroscopy, Mucoadhesive suspension

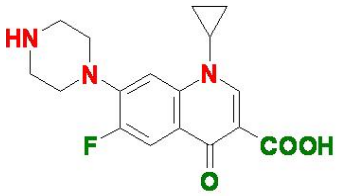
INTRODUCTION

There is a demand for a dosage form that would provide a controlled release action of the drug in solution, particularly in the basic pH conditions of the intestinal lumen over the full dosage period. By achieving constant blood level, drug benefit is maximized while its potential toxicity is minimized[1]. There are several means of getting controlled release action; one of them is by utilizing interaction between the drug and a polymer[2].

As frequent dosing is required to maintain the therapeutic plasma concentration, Ciprofloxacin (Cipro) was chosen as a model drug for the controlled release study. Ciprofloxacin, 1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid, is a fluoroquinolone antibacterial agent [Fig. 1][3].

Hydroxypropyl methylcellulose (HPMC) is a propylene glycol ether of methyl-cellulose [Fig. 2][4]. It 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 inducing a pseudofed state, thereby reducing peristaltic contraction, which contributes to overall drug release[5-9]. 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. It may form a complex with the low solubility drug like Ciprofloxacin.

The interaction between Cipro and HPMC can be determined by several methods such as Fourier Transform Infrared (FTIR) Spectroscopy, Raman Spectroscopy, etc. To know the different functional groups and highly polar bonds of pure Ciprofloxacin and HPMC, and chemical interactions in the mucoadhesive suspension, FTIR analysis was conducted. However, their backbone structures and symmetric bonds were checked by Raman spectroscopy. Although it is known that Raman and FTIR are complementary vibrational spectroscopic techniques, there are band intensity differences between the two techniques. Therefore, to obtain more detailed information about chemical interaction between Ciprofloxacin and HPMC, both FTIR and Raman analyses were carried out[10,11].



Ciprofloxacin

Fig. 1: Structure of Ciprofloxacin

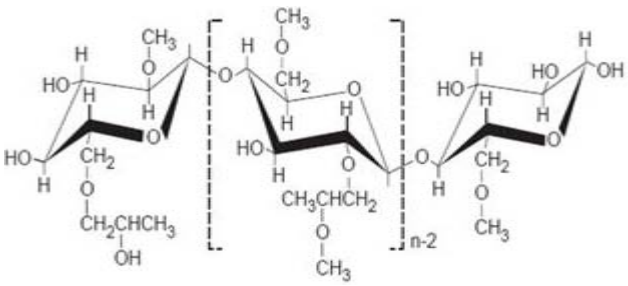


Fig. 2: Structure of Hydroxypropyl methylcellulose

MATERIALS AND METHODS

Materials

The following materials were used for the study: Ciprofloxacin was obtained from Dr. Reddy's Lab, Hyderabad, India, as a gift sample. Hydroxypropyl methylcellulose (HPMC E15 LV Premium) was supplied by Loba Chemie Pvt. Ltd., India. It was having methoxy (23.8%) and hydroxypropoxy groups (8.3%). Pluronic F 68 and Soya lecithin were purchased from Himedia Laboratories Pvt. Ltd., India. Glycerol, Methyl praraben sodium, Propyl paraben sodium, Sorbitol solution I.P. and Sucrose were supplied by Cosmo Chem. Laboratory, Pune, India. Ultra pure water was obtained from a Millipore Milli-Q UV water filtration system.

Methods

Preparation of Formulation-

1. Preparation of Bulk A

In a beaker, 6 ml water was heated up to 80° C. Sucrose (10 gm) was added under continuous stirring. The temperature was monitored in such a way so that it should not fall below 70° C, till the sucrose was completely dissolved. The prepared syrup was cooled properly at room temperature and kept overnight. Syrup was filtered using 120 mesh nylon cloth.

2. Preparation of Bulk B

Five millilitre of Ultra pure water was taken in a beaker to which 1.8 ml of sorbitol solution and 0.2 ml glycerin were added. The mixture was stirred properly. To this solution, pluronic F 68 (5%), soya lecithin (1%) and HPMC (5%) in w/w of drug were added with continuous stirring.

3. Preparation of Mucoadhesive Suspension and Ultrasonication

Five millilitre of water was taken in another beaker to which 1.25 gm of Cipro was added. To the drug suspension, the bulk B and bulk A were added with continuous stirring. Methyl paraben sodium (0.015%w/v) and Propyl paraben sodium (0.08%w/v) were added as preservatives. The volume was made up to 25 ml by Ultra pure water. The pH was adjusted to 5.5. Homogenization was carried out for at least 20 min by ULTRASONIC HOMOZENIZER LABSONIC^R M (SARTORIUS), having operating frequency 30 KHZ and line voltage 230 V/50 HZ, using the probe made up of Titanium of diameter 7 mm and length 80 mm. The setting knob "cycle" was adjusted to 0.8, indicating sound was emitted for 0.8 s and paused for 0.2 s. In this manner, we could expose our sample with 100% amplitude, while reducing the heating effect to 80%. This LABSONIC^{R}M generates longitudinal mechanical vibrations with a frequency of 30,000 oscillations / s (30 KHZ). The probes bolted to the sound transducer were made of high-strength Titanium alloys, built as λ /2 oscillators. It amplified the vertical oscillation, and transferred the ultrasonic energy via its front surface with extremely high power density into the sample that was to be subjected to ultrasonic waves. In our study, stress applied was sound wave and in addition, mild rise in temperature of the sample occurred during ultrasonication which helped in the homogenization of the suspension. The sample was then divided into two parts –one part was for FTIR analysis and the other part was used for Raman spectroscopy.

Fourier Transform Infrared Spectroscopic Analysis-

After ultrasonication, the polymeric suspension was sprayed on to an aluminum slip with the aid of an atomizer. The fine droplets were dried overnight at room temperature and the solid samples were then collected and powdered. This powder sample was used for FTIR analysis. The Fourier transform infrared analysis was conducted to verify the possibility of interaction of chemical bonds between drug and polymer. FTIR analysis was performed by FTIR Spectrophotometer interfaced with 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 the x and y directions. Solid powder samples were oven dried at around 30°C, finely crushed, mixed with potassium bromide (1:100 ratio by weight) and pressed at 15000 psig (using a Carver Laboratory Press, Model C, Fred S. carver Inc., WIS 53051) to form disc. The detector was purged carefully using clean dry nitrogen gas to increase the signal level and reduce moisture. The spectra were collected in the 400 cm^{-1} to 4000 cm^{-1} region with 8 cm^{-1} resolution, 60 scans and beam spot size of 10 µm-100 µm[12-14]. The FTIR imaging in the present investigation was carried out using a Perkin Elmer Spectrum RX.

Raman Spectroscopic Analysis-

The Raman system R-3000 instrument (Raman systems INC.USA), a low resolution portable Raman Spectrometer using a 785 nm solid state diode laser, was adjusted to deliver 250 mw to the sample having spectral resolution 10 cm^{-1} and 12 v dc/5A power supplies and USB connectivity. The solid powder samples i.e., both pure drug and polymers were enclosed in plastic poly bags and tested directly. For our study, the fibre optic sampling probe was directly dipped into the formulation (prepared as per the above-mentioned procedure) to collect the spectra 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 2400 cm^{-1}.

RESULTS

The infrared spectra are recorded on Fourier Transform Spectrometer in the mid –infrared region (MIR) within the range (400-4500 cm^{-1})[15]. Due to the 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 characteristic 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. Thus, the spectral interpretations should not be confined to one or two bands only; actually, the whole spectrum should be examined.

While the FTIR bands at 4000-1300 cm^{-1} represented functional group region, the appearance of strong absorption bands in the region of 4000 to 2500 cm^{-1} was due to stretching vibrations between hydrogen and some other atoms with a mass of 19 or less. The O-H and N-H stretching frequencies were in the 3700 to 2500 cm^{-1} region with various intensities. Hydrogen bonding had a significant influence on the peak shape and intensities, generally causing peak broadening and shifts in absorption to lower frequencies. The C-H stretching vibration occurred in the region of 3300 to 2800 cm^{-1}[12,13].

In FTIR spectra of Cipro, one prominent characteristic peak was found between 3500 and 3450 cm^{-1}, which was assigned to stretching vibration of OH groups and intermolecular hydrogen bonding [Fig. 3]. Another band at 3000-2950 cm^{-1} represented alkene and aromatic C-H stretching, mainly $\upsilon_{=C-H}$. The 1950 to 1450 cm^{-1} region exhibited FTIR absorption from a wide variety of double-bonded functional groups. The band at 1750 to 1700 cm^{-1} represented the carbonyl C=O stretching i.e., $\upsilon_{C=O}$. The peak between 1650 and 1600 cm^{-1} was assigned to quinolones. The band from 1450 to 1400 cm^{-1} represented υ_{C-O} and at 1300 to 1250 cm^{-1} suggested bending vibration of O-H group which proved the presence of carboxylic acid. A strong absorption peak between 1050 and 1000 cm^{-1} was assigned to C-F group [Table 1a] [12,13,16,17].

From FTIR spectra of HPMC, it was found that the peak at 3500 to 3400 cm^{-1} which indicated OH vibrational stretching [Fig. 4][12,13]. The symmetric stretching mode of υ_sMe and $\upsilon_s$hydroxypropyl groups was found at 2900 cm^{-1} in which all the C-H bonds extend and contract in phase[13]. The peak at 2550-2500 cm^{-1} was assigned to OH stretching vibration, i.e., υ_{O-H} and intramolecular hydrogen bonding[12,13]. The band between 1650 and 1600 cm^{-1} indicated the presence of stretching vibration of υ_{C-O} for six membered cyclic rings. Two bending vibrations might occur within a methyl group. Firstly, the symmetric bending vibration of δ_sMe was involved the in-phase bending of the C-H bonds. Secondly, the asymmetric bending mode of δ_{as}Me was due to out-of-phase bending of the C-H bonds. While the asymmetric bending vibrations of the methoxy group appeared in the region of 1500-1450 cm^{-1}, the symmetric vibrations were mostly displayed in the range of 1400-1350 cm^{-1} [18,19]. The band between 1400 and 1350 cm^{-1} suggested υ_{C-O-C} of cyclic anhydrides. The peak at 1300-1250 cm^{-1} was due to

υ_{C-O-C} cyclic epoxide. The band at 1100-1000 cm^{-1} was for stretching vibration of ethereal C-O-C groups. The peak at 1000-950 cm^{-1} was due to υ_{as} of pyranose[20]. The rocking mode of CH_2 was found in the range of 850-800 cm^{-1} [Table 1b][18]. The computed frequencies of HPMC were in a good agreement with experimental frequencies for carbohydrate region as well as OH and CH regions.

Fig. 3: FTIR Spectra of Ciprofloxacin

Fig. 4: FTIR Spectra of HPMC

In the FTIR spectra of the mucoadhesive suspension containing Cipro and HPMC, the peak from 3500 to 3400 cm^{-1} was assigned to polymeric υ_{O-H} and hydrogen bonding while the band between 3000 and 2600 cm^{-1} represented the stretching vibration of υ_{O-H} i.e., strong intermolecular hydrogen bonding [Fig. 5]. The band from 1650 to 1600 cm^{-1} was assigned to $\upsilon_{C=O}$ i.e., carbonyl stretching vibration. A prominent peak at 1500-1450 cm^{-1}(w) was for υ_{C-O} / δ_{O-H}. The band from 1400-1350 cm^{-1} was assigned to δC-O-C representing esters and symmetric bending of methoxy groups. The peak between 1100 and 1000 cm^{-1} represented υ_{C-F} group[12,13]. The band at 1000-950 cm^{-1} was assigned to υ_{as} of pyranose ring of HPMC [Table 1c][20].

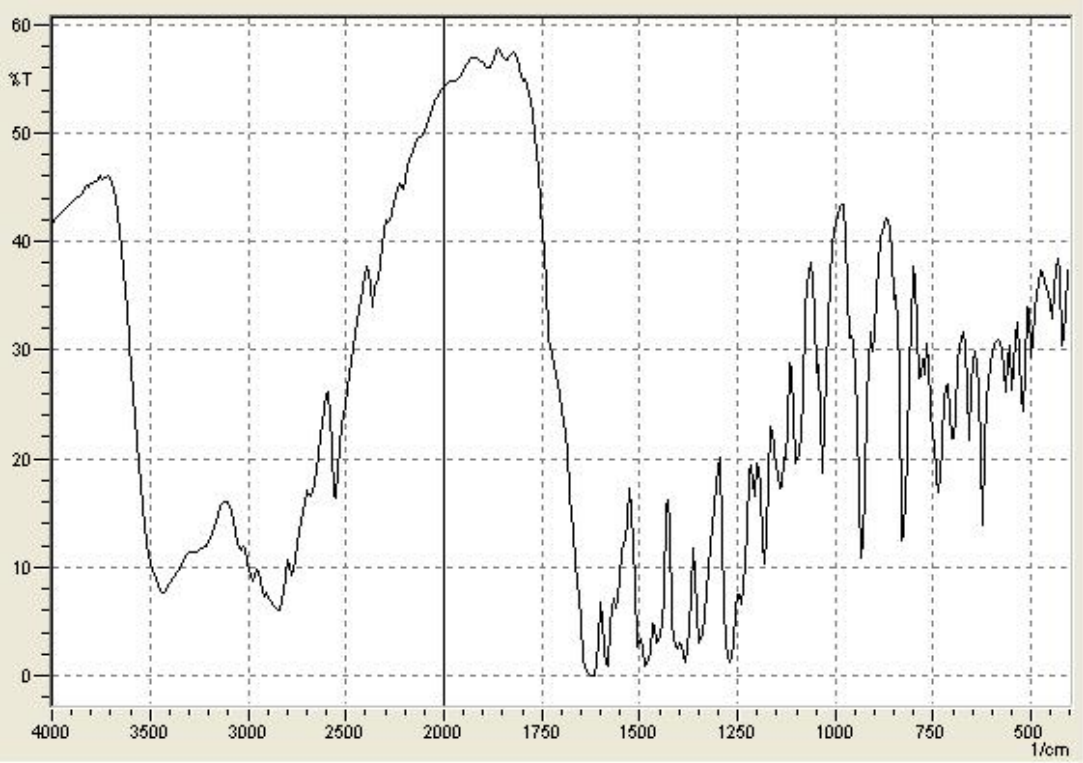


Fig. 5: FTIR Spectra of Ciprofloxacin Mucoadhesive Formulation

Table 1: FTIR Peaks of Ciprofloxacin, HPMC and Ciprofloxacin Mucoadhesive Formulation

a) Prominent FTIR Peaks of Ciprofloxacin		
PEAKS(cm-1)	**GROUPS**	**PEAKS ASSIGNMENT**
3500-3450	Hydroxyl group	O-H stretching vibration, intermolecular H-bonding
3000-2950	Aromatics,cyclic enes	υ=CH & Ar-H
1750-1700	CO group of acid	C=O stretching vibration
1650-1600	Quinolines	δN-H bending vibration
1450-1400	Carbonyl group	υC-O
1300-1250	Hydroxyl group	δO-H bending vibration
1050-1000	Fluorine group	C-F stretching
b) Prominent FTIR peaks of HPMC		
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	cylic υC-O-C
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
c) Prominent FTIR Peaks of Ciprofloxacin Mucoadhesive Formulation		
3500-3400	Hydroxyl group	O-H stretching vibration, polymeric H-bonded
3000- 2600	Hydroxyl group	O-H stretching vibration, intremolecular H-bonded
1650-1600	O-C-O group of acids	υ_{as} stretching vibration of acids
1500-1450	O-C-O group of acids	υ_s stretching vibration of acids, $\upsilon_{C\text{-}O}$ / $\delta_{O\text{-}H}$
1400-1350	Esters and Methoxy groups	δC-O-C symmetric bending of esters and methoxy groups
1100-1000	C-F group	C-F stretching of Cipro
1000-950	Pyranose ring	υ_{as} of pyranose ring of HPMC

In case of Ciprofloxacin, the prominent Raman shifts were observed at 484.22, 771.47, 1411.63 and 1655.11 cm^{-1} [Fig. 6]. The Raman shifts at 484.22 cm^{-1} indicated strong bending vibration of C-C of the aliphatic chain of cyclopropyl group and C-N stretching vibration of piperazinyl group[21-23]. While the band at 771.47 cm^{-1} represented the symmetric stretching vibration of C-F group[24], the peak at 1411.63 cm^{-1} was due to symmetric stretching vibration of O-C-O group of carboxylic acid and methylene deformation mode of the piperazinyl group[25]. A band at 1655.11 cm^{-1} was for symmetric stretching of the carbonyl group $\upsilon_{C=O}$ of the pyridone moiety[16]. In addition, it (peak at1655.11 cm^{-1}) also indicated the $N^{+}H_2$ scissoring of piperazinyl group [Table 2a] [16,21,25-28].

In case of HPMC, the prominent Raman shifts were found at 504.7, 908.3 and 1384.3 cm^{-1}

[Fig. 7] The peak at 504.7 cm^{-1} was assigned to C-H out of plane bending vibration and C-C-O bending vibration of β D-glucose monomer of HPMC. The band at 908.3 cm^{-1} was 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} was assigned to C-C stretching vibration [Table 2b][18,19,21,29].

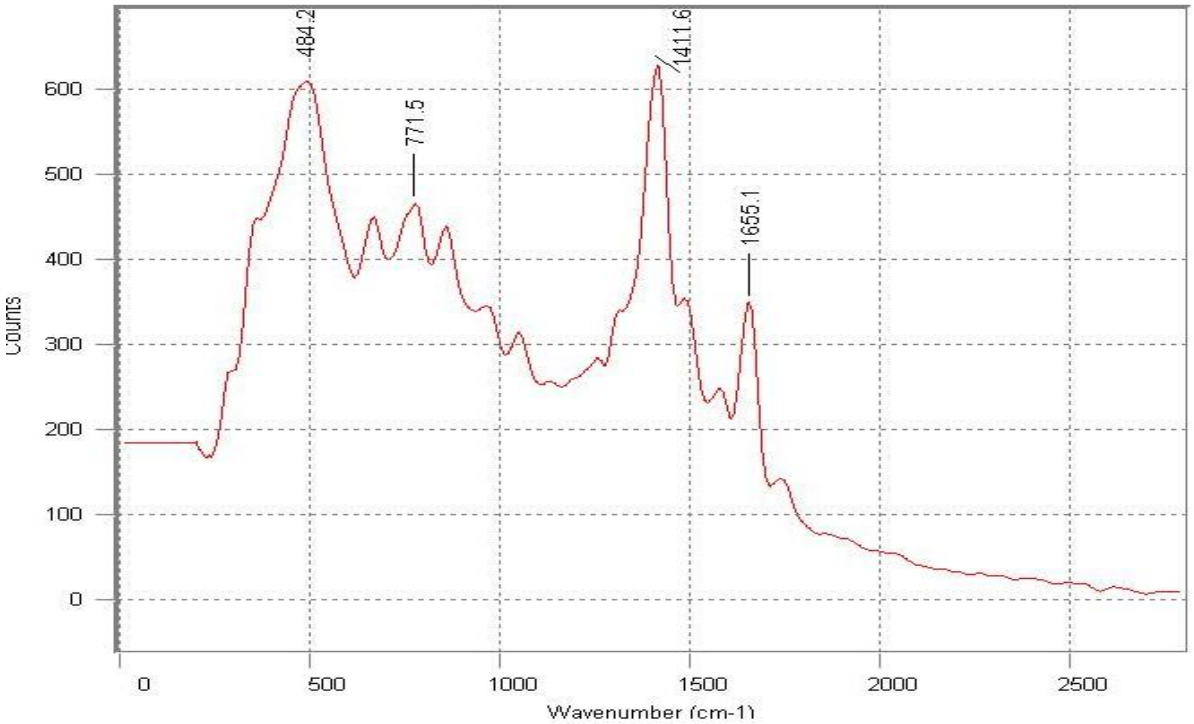


Fig. 6: Raman Shifts of Ciprofloxacin

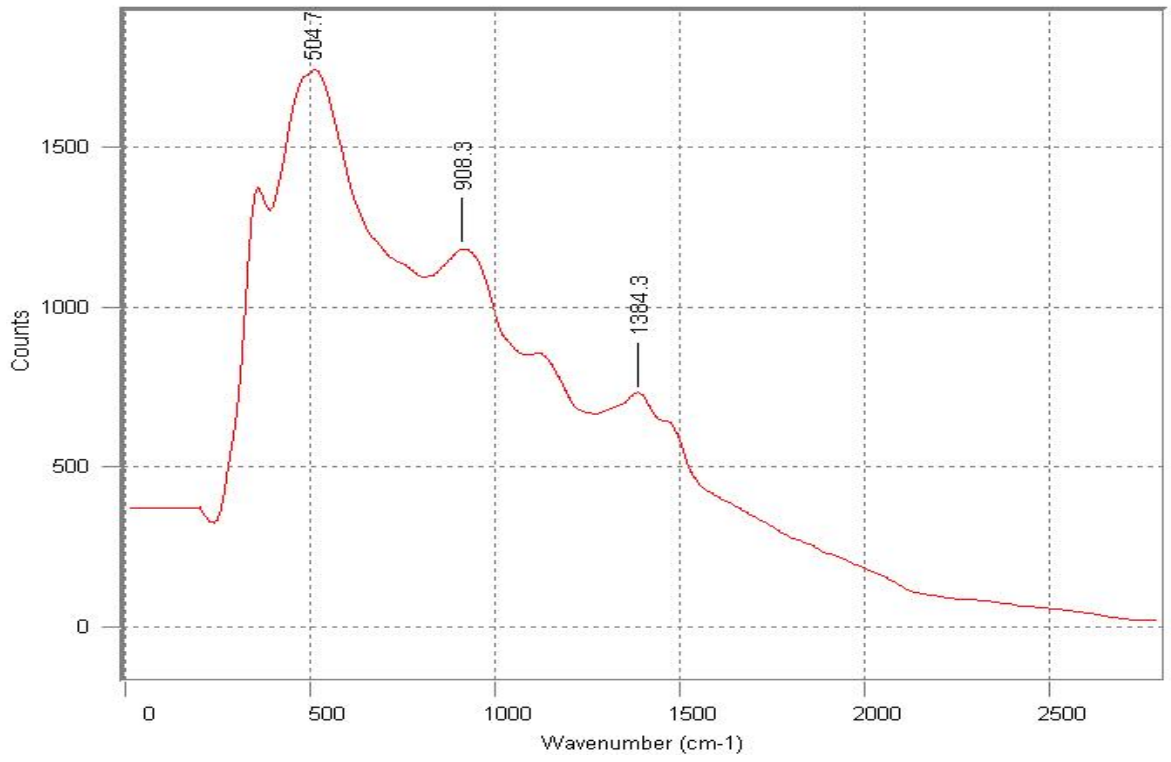


Fig. 7: Raman Shifts of HPMC

The characteristics Raman peaks of mucoadhesive suspension containing both Cipro and HPMC were observed at 352.9, 900-800, 1376.1 and 1850-1700 cm^{-1} [Fig. 8]. The band at 352.9 cm^{-1} was assigned to C-C-C out of plane bending of pyranose ring[19]. The peak at 900-800 cm^{-1} was due to symmetric stretching vibration of C-F bond and symmetric COC stretching vibration for esters. The band at 1376.1 cm^{-1} respesented δCCH and δOCH bending vibration of methoxy group[18]. The peak at 1850-1700 cm^{-1} was assigned to C=O stretching vibration of carbonyl groups of esters [Table 2c][19].

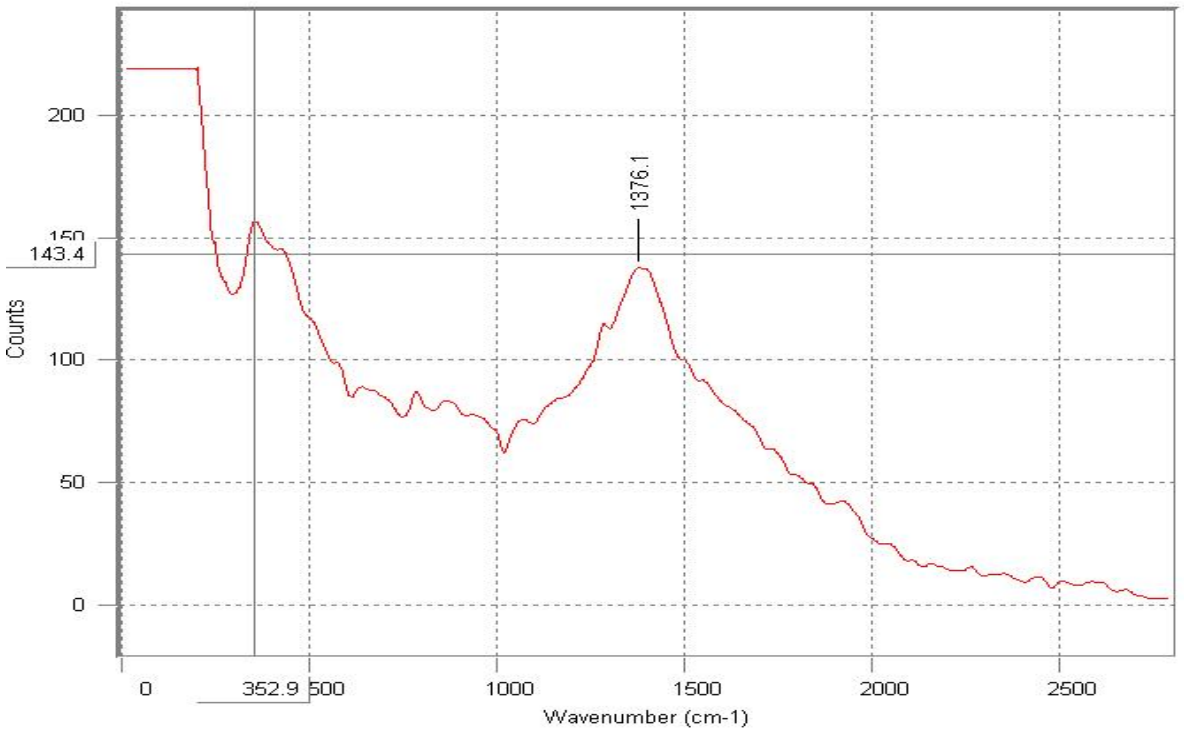


Fig. 8: Raman Shifts of Ciprofloxacin Mucoadhesive Formulation

Table 2: Raman Shifts of Ciprofloxacin, C940 and Ciprofloxacin Mucoadhesive Formulation

a) Prominent Raman Shifts of Ciprofloxacin	
Raman Shifts(cm^{-1})	**Functional Groups / Vibrations**
484.22	Strong δ (CC) aliphatic chain and C-N stretching vibration
771.47	Symmetric vibration of C-F bond
1411.63	υ_sO-C-O and methylene deformation of the piperazinyl group
1655.11	υs of C=O group of pyridone moiety and N^+H_2 scissoring of piperazinyl group
b) Prominent Raman Shifts of HPMC	
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
c) Prominent Raman Shifts of Ciprofloxacin Mucoadhesive Formulation	
352.9	δ(CC) aliphatic chain
900-800	Symmetric stretching vibration of both C-F group C-O-C group for esters
1376.1	υ_sO-C-O
1850-1700	υC=O medium

DISCUSSION

When Infrared (IR) radiation falls on a molecule, it may be absorbed, reflected or transmitted. Absorption leads to the FTIR spectrum, while reflection leads to scattering which is utilized in Raman Spectroscopy[12]. In addition, 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[12,13].

In case of FTIR spectra of Cipro, prominent peaks for $\upsilon_{C\text{-}O}$ / $\delta_{O\text{-}H}$ and $\upsilon_{C=O}$ indicated the presence of –CO-, -CHO and -COOH groups [Fig. 3]. The involvement of above groups may be confirmed by fermi resonance bands for –CHO; $\upsilon_{C\text{-}O\text{-}C}$ peaks for esters; and absence of these two for ketones. This suggests the existence of –COOH group in Cipro [Table 1a].

From FTIR spectral analysis it has been found that 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 cyclic anhydride, methoxy and hydroxypropoxy groups along with epoxide helps in the identification of HPMC [Table 1b][12,13,18,19,25].

While comparing the FTIR spectra among pure Cipro and HPMC, and the mucoadhesive suspension containing both Cipro and HPMC, it is clear that the band position of C=O group has been affected by esterification and conjugation involving C=O group. Here, the stretching vibration of C=O in pure Cipro was found from 1750 to 1700 cm^{-1}, which was lowered to 1650-1600 cm^{-1} in this suspension. This might be due to formation of β-ketoesters [Figs. 3-5]. The FTIR peaks assigned to $\upsilon_{C\text{-}O}$ and $\upsilon_{C\text{-}O\text{-}C}$ groups representing esters confirm the esterification between polymeric OH group and COOH group of

drug (Cipro). The stretching vibration of C-F group remains more or less unaltered.

The C=O group of drug (present in the formulation) lowers the stretching vibration of C=O frequency indicating deprotonation and probably interaction of the said carboxylic C=O moiety with the polymer. However, a definite conclusion about the keto group in the bonding to the polymer can be deduced because the corresponding band found from 1650 to 1600 cm^{-1} is probably due to the formation of β-ketoesters[29]. From the above data it can be inferred that the carboxylic group of Cipro undergoes the interaction with the polymer, as would be expected chemically. Thus, the nitrogen atoms are not likely to be involved in binding or the interaction. Actually, the nitrogen atom of the quinolone ring, 1-ortho to fluorine, is less electron rich due to electron deficient fluoroquinolone ring. In addition, methoxy and piperazinyl groups sterically hinder the reaction. The possibility of involvement of imino moiety of the piperazinyl group is also less prominent due to intense OH stretching vibration. The bands in the region of 3500-2600 cm^{-1} can be assigned to the asymmetric and symmetric stretching vibrations of the OH groups present in the inner and outer sphere of polymer. The shift in the characteristic bands of the FTIR spectra suggests change in their intensity leading to the appearance of several absorbance bands of the asymmetric and symmetric stretching vibrations and overtone of the deformation vibrations. This indicates the confirmation of the hydrogen bonding[12,13]. By comparing the FTIR spectra among the pure drug, HPMC polymer and the mucoadhesive suspension containing both drug and polymer, it has been noted that the FTIR peak of Cipro from 1750 to 1700 cm^{-1} has not been detected in the formulation, probably due to interaction with the polymer. The missing peak has been replaced by two very strong characteristic bands in the range of 1650-1600 cm^{-1} and at 1450 cm^{-1}. These are assigned to $\upsilon_{(O\text{-}C\text{-}O)}$ asymmetric and symmetric stretching vibrations, respectively[13]. The difference $\Delta[\upsilon_{(CO2)asym} - \upsilon_{(CO2)sym}]$ is a useful characteristic for determining the involvement of the carboxylic group of Cipro. The Δ value for the interaction falls in the range of 183 - 250 cm^{-1} indicating the deprotonation of the carboxylic acid group and interaction between drug and polymer [Table 1][29].

By comparing the Raman spectra of pure drug with the drug incorporated in the Ciprofloxacin containing mucoadhesive suspension, it has been found that the peak at 1411.63 cm^{-1} representing symmetric stretching vibration of O-C-O group is not prominent. Moreover, the symmetric stretching vibration of C-O-C group and stretching vibration of C=O group are noticeable in our mucoadhesive formulation. From this it is clear that there is esterification reaction between Cipro and HPMC polymer [Table 2].

The results of FTIR and Raman spectra indicate that both the spectra show prominent peaks for the stretching vibration of C-O-C and C=O groups, which prove the formation of the esters between the drug and polymer. Moreover, both the intermolecular and polymeric hydrogen bondings are also remarkable from the FTIR spectra of the suspension.

CONCLUSION

Due to very good interaction between the carboxylic group of the drug and hydroxyl group of the polymer, esterification and intermolecular hydrogen bonding occur in the formulation, which may lead to a stable controlled release formulation. Moreover, the drug polymer complex may aggregate forming a micelle like structure, which can absorb and solubilize more drugs. As a result of which HPMC polymer may function as a useful carrier for the Ciprofloxacin molecule. The main advantage of the present investigation is that higher Ciprofloxacin drug loading would be possible in dosage forms as compared with alternate formulation strategies, such as conventional solid dispersions. Here, Ciprofloxacin interacts with the polymer monomerically. The release of the drug from the formulation is very slow because the carboxylic group of Ciprofloxacin has already interacted with polymeric OH groups. It suggests less active sites of the drug are left for the attack by water molecules for the hydration and solubilization, which may give controlled release action. In addition, the free polymeric carboxylic groups form hydrogen bonding with the polysaccharides and proteins of mucosa. Due to the presence of HPMC, the formulation is highly swollen and stiffened showing a very good mucoadhesive property in the gastrointestinal mucosa. This may lead to a better bioadhesive and controlled release action. The utility of the present work may be improved, if delivery rate, biodegradation and site-specific targeting of such formulation would be monitored and controlled.

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