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Characterization of Mucoadhesive Norfloxacin suspensions by fourier transform Infrared Spectroscopy

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Abstract

Till now very few formulations are available from which the drug is absorbed uniformly so that safe and effective blood level of Norfloxacin could be maintained for a prolonged period. To fulfill this requirement a controlled release mucoadhesive suspension was prepared using mucoadhesive polymers. The chemical interaction between Norfloxacin and different polymers in suspensions has been studied to know their compatibility by Fourier Transform Infrared Spectroscopy (FTIR). Ultrasonication method was used for the preparation of different formulations, taking Carbopol934, Carbopol940 and Hydroxypropyl methyl cellulose polymers. FTIR (400 cm^{-1} to 4000 cm^{-1} region) Spectroscopic study was carried out and its spectra were used for interpretation. From the spectral interpretation, it was found that in formulations, the carboxylic groups of Norfloxacin and hydroxyl groups of respective polymers encountered chemical interaction leading to esterification and hydrogen bonding (both intermolecular and polymeric). It may be concluded that Norfloxacin is compatible with three polymers used. Formation of micellies due to esterification and intermolecular hydrogen bonding causes more drug entrapment. In addition, stable suspensions are formed without hampering the C-F bond of the quinolone nucleus, which is responsible for the antibacterial activity of the drug. As a result, stable mucoadhesive suspensions of Norfloxacin could be produced and hence, these polymers may be considered as effective carriers for Norfloxacin.

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INTRODUCTION

Norfloxacin (Norflox) is a second generation fluoroquinolone, IUPAC name being 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-

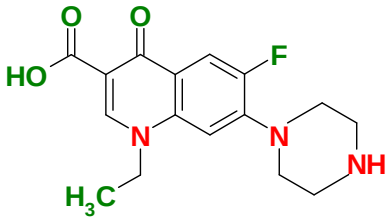
quinolone carboxylic acid (Fig. 1). It inhibits the enzyme deoxyribonucleic acid (DNA) gyrase preventing DNA and protein synthesis. It requires multiple administration of drug leading to fluctuation in plasma concentration of the drug [1].

The demand always remains for a dosage form that will provide a drug at a sustained and constant level in solution, 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 [2]. For this reason, dosage forms that incorporate such low solubility drugs provide a major challenge for sustained release technologists.

Taking into consideration of above factors, different polymeric suspensions of Norfloxacin were prepared by using two grades of mucoadhesive biodegradable Carbopol polymers i.e., Carbopol934 (C934) and Carbopol940 (C940); and Hydroxypropyl methylcellulose (HPMC). This was done to protect the drug from the physiological environment leading to improvement in its stability *in vivo*. Both C934 and C940 consist of chains of polyacrylic acid and they differ by the cross linking agents like allyl ethers of sucrose in C934 and allyl ethers of pentaerythritol in C940 (Fig. 2)[3,4]. Carbopol polymers are pH sensitive,[5,6] environmentally responsive polymer or considered as smart gels[7]. They have recently attracted considerable interest in the field of drug delivery as a means of providing an on-off release by shrinking and swelling in response to the change in pH[8-11].

Hydroxypropyl methylcellulose (HPMC) is propylene glycol ether of methyl-cellulose. Its chemical structure has been illustrated in Figure 3[12]. 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. 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[13-17]. It has many pharmaceutical uses, such as a drug carrier, a coating agent, a tabletting agent, etc [12]. 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. Moreover, the physicochemical properties of HPMC are strongly affected by: (i) the methoxy group content; (ii) the hydroxypropoxy group content; and (iii) the molecular weight.[13] It may form a complex with the low solubility drug like Norfloxacin.

To know the different functional groups and highly polar bonds of pure Norfloxacin and different polymers, and their chemical interactions in the mucoadhesive suspensions, FTIR analysis was conducted[18,19].



Norfloxacin

Figure 1: Chemical structure of Norfloxacin

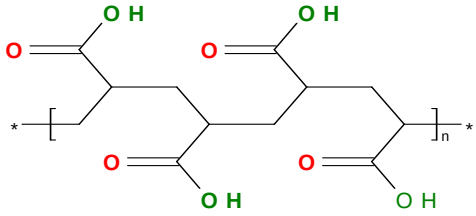


Figure 2: Chemical Structure of Carbopol Polymer

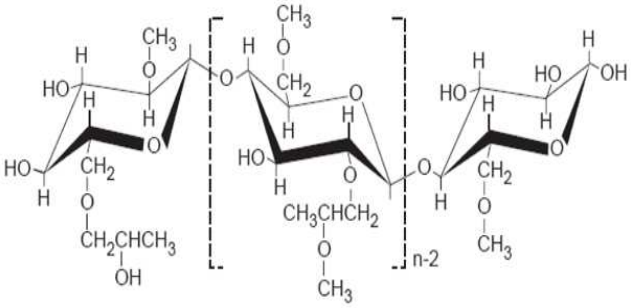


Figure 3: Chemical structure of Hydroxypropyl methylcellulose

MATERIALS AND METHODS

Materials:

The following materials were used for the study: Norfloxacin 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 group (23.8%) and hydroxypropoxy group (8.3%). Pluronic F 68 and Soya lecithin were purchased from Himedia Laboratories Pvt. Ltd., India. C934, C940, Glycerol, Methyl praraben sodium, Propyl paraben sodium, Sorbitol solution I.P. and Sucrose were supplied by Cosmo Chem. Laboratory, Pune, India. Tri-sodium citrate dehydrate purified was obtained from Merck Specialities Private Limited, Mumbai, 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. Then sucrose (10 gm) was added to it 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 C934/C940/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 500 mg of Norfloxacin 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 p^H was adjusted by adding citrate buffer (0.75M) to p^H5.5. 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.

Fourier Transform Infrared Spectroscopy-

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[18-20]. The FTIR imaging in the present investigation was carried out using a Perkin Elmer Spectrum RX.

RESULTS

In FTIR spectra of Norfloxacin, one prominent characteristic peak was found between 3550 and 3500 cm^{-1}, which was assigned to stretching vibration of OH group and intermolecular hydrogen bonding by single bridge. A band at 3500 to 3300 cm^{-1} suggested the NH stretching vibration of the imino-moiety of piperazinyl groups. The peak at 2750-2700 cm^{-1} indicated the presence ethyl group. The band at 2500 cm^{-1} was due to the υOH group of the carboxylic acid. The peak at 1700 cm^{-1} represented the carbonyl C=O stretching i.e., $\upsilon_{C=O}$. The band at 1650 to 1600 cm^{-1} was assigned to υN-H bending vibration of quinolones. The peaks at 1500 to 1450 cm^{-1} represented υ_{O-C-O} of acids and at 1300 to 1250 cm^{-1} suggested bending vibration of O-H group, which indicated the presence of carboxylic acid. In addition, a strong absorption band between 1050 and 1000 cm^{-1} was assigned to C-F group. The peak in the region 950-900 cm^{-1} suggested the δNH bending vibration of amines. The band at 800 cm^{-1} was due to the meta distribution of the aromatic protons (Fig. 4 and Table 1)[18, 21, 22].

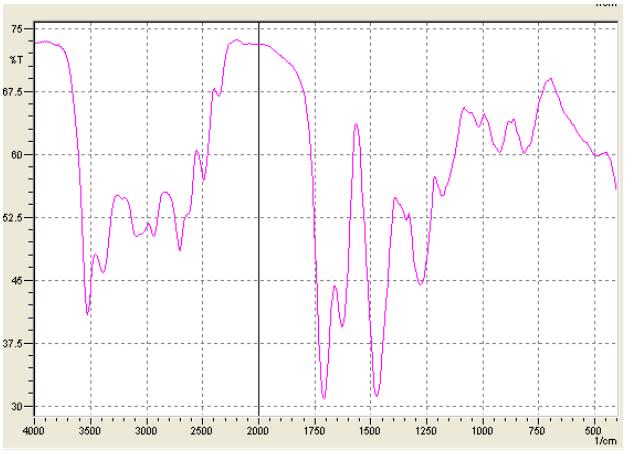


Figure 4: FTIR Spectra of Norfloxacin

Table 1: Prominent FTIR peaks of Norfloxacin

PEAK(cm-1)	GROUP	PEAK ASSIGNMENT
3550-3500	Hydroxyl group	Intermolecular H -bonding by single bridge
3500-3300	Imino-moiety of Piperazinyl groups	NH stretching vibration
3000-2950	Aromatic,cyclic enes	υ=CH & Ar-H
2750-2700	Ethyl group	υCH_2
2500	Acid group	υOH group
1700	Carbonyl of acids	υC=O stretching vibration
1650-1600	Quinolones	υN-H bending vibration
1500-1450	O-C-O group of acid	υ_s stretching vibration of O-C-O group
1300-1250	Hydroxyl group	δO-H bending vibration
1050-1000	C-F groups	υC-F
950-900	Amines	δNH bending vibration
800	Aromatic m – distribution	δAr-H

In case of C934, the FTIR spectrum having peak between 3000-2950 cm^{-1} represented OH stretching vibration, i.e., υ_{O-H} and intramolecular hydrogen bonds (Fig. 5). The prominent band between 1750 to 1700 cm^{-1} was assigned to carbonyl C=O stretching band i.e., $\upsilon_{C=O}$. The peak at 1250 to 1200 cm^{-1} represented υ_{C-O-C} for acrylates [18,19]. The ethereal cross linking, was proved by prominent peak at 1160 cm^{-1}, indicated stretching vibration of υ_{C-O-C} group. The band at 1450 to 1400 cm^{-1} was assigned to υ_{C-O} / δ_{O-H} and between 850 and 800 cm^{-1} was for out of plane bending of C=CH i.e., $\delta_{=C-H}$ (Table 2a) [18,19].

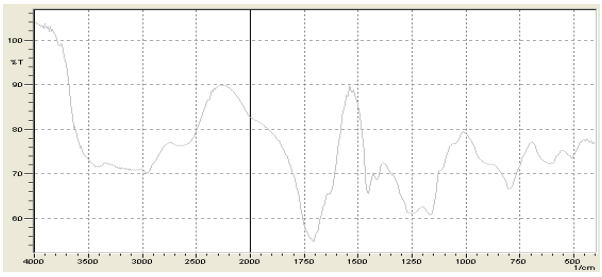


Figure 5: FTIR Spectra of C934

In case of FTIR spectrum of C940, peaks were more or less similar to those of C934 (Fig. 6). The FTIR band at 2960.73 cm^{-1} was assigned to υ_{O-H} i.e., intermolecular hydrogen bonding. While the peak at 1712.79 cm^{-1} represented $\upsilon_{C=O}$, the bands at 1452.40 cm^{-1} and 1246.02 cm^{-1} were assigned to υ_{C-O} / δ_{O-H} and υ_{C-O-C} (for acrylates), respectively. The ethereal cross linking, proved by prominent peak at 1172.72 cm^{-1}, indicated stretching vibration of υ_{C-O-C} group and finally the band at 800.46 cm^{-1} was assigned to $\delta_{=C-H}$ i.e., out of plane bending of C=CH group (Table 2b)[18,19].

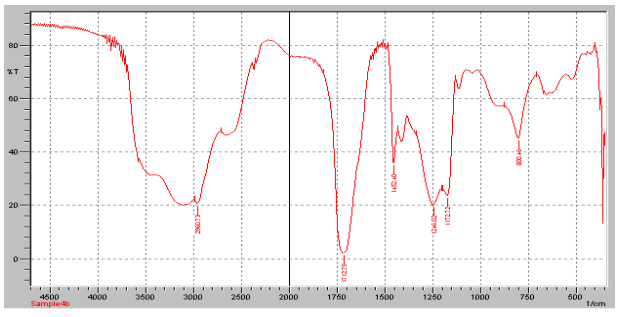


Figure 6: FTIR Spectra of C940

From FTIR spectra of HPMC, it was found that the peak at 3500 to 3400 cm^{-1} indicated OH vibrational stretching (Fig. 7)[18,19]. 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[19]. The peak at 2550-2500 cm^{-1} was assigned to OH stretching vibration, i.e., υ_{O-H} and intramolecular hydrogen bonding[18,19]. 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 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} [23,24]. 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[25]. The rocking mode of CH_2 was found in the range of 850-800 cm^{-1} (Table 2c)[23]. The computed frequencies of HPMC were in a good agreement with experimental frequencies for both carbohydrate region as well as OH and CH regions.

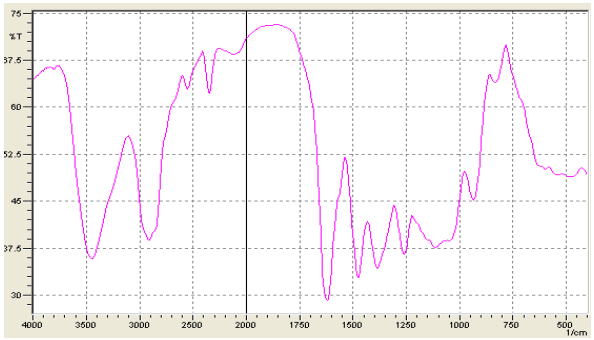


Figure 7: FTIR Spectra of HPMC

Table 2: Prominent FTIR Peaks of Polymers

PEAK(cm^{-1})	GROUP	PEAK ASSIGNMENT
a) Prominent FTIR Peaks of C934		
3000-2950	Hydroxyl group	O-H stretching vibration, intramolecular H-bonded
1750-1700	C=O group of acids	$\upsilon_{C=O}$ stretching vibration
1450-1400	Carbonyl group of acids	υ_{C-O}
1250-1200	Acrylates	C-O-C stretching vibration
1160	Ethereal C-O-C group	Stretching vibration of C-O-C group
850-800	Aromatics & enes	=C-H out of plane bending vibration
b) Prominent FTIR Peaks of C940		
2960.73	Hydroxyl group	O-H stretching vibration, intramolecular H-bonded
1712.79	C=O group of acids	$\upsilon_{C=O}$ stretching vibration
1452.40	Carbonyl group of acids	υ_{C-O}
1246.02	Acrylates	C-O-C stretching vibration
1172.72	Ethereal C-O-C group	Stretching vibration of C-O-C group
800.46	Aromatics & enes	=C-H out of plane bending vibration
c) 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	υ_{C-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

In the FTIR spectra of formulation containing both Norflox and C934, the prominent band, found between 3550 and 3400 cm^{-1}, was assigned to υ_{O-H} and polymeric hydrogen bonding (Fig.8). The peak at 2600-2500 cm^{-1} represented υ_{O-H} of carboxylic acid i.e., strong intermolecular hydrogen bonding. 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 1300 to 1250 cm^{-1} was assigned to υ_{C-O-C} of acrylates. The peak between 1100 and 1000 cm^{-1} represented υ_{C-F} groups. The band at 800 cm^{-1} indicated the meta distribution of δ_{Ar-H} group [19, 20, 23] (Table 3a).

In the FTIR spectra of formulation containing both Norflox and C940, the prominent band, found between 3550 and 3500 cm^{-1}, was assigned to υ_{O-H} and polymeric hydrogen bonding (Fig 9). The peak at 2600-2500 cm^{-1} represented the υ_{O-H} of carboxylic acid i.e., strong intermolecular hydrogen bonding. 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 1300 to 1250 cm^{-1} was due to υ_{C-O-C} of acrylates. The peak between 1100 and 1000 cm^{-1} represented υ_{C-F} groups. The band at 800 cm^{-1} indicated the meta distribution of δ_{Ar-H} group [18, 19] (Table 3b).

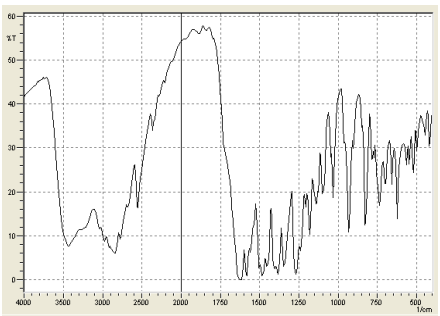


Figure 8: FTIR Spectra of Polymeric Suspension containing Norflox and C934

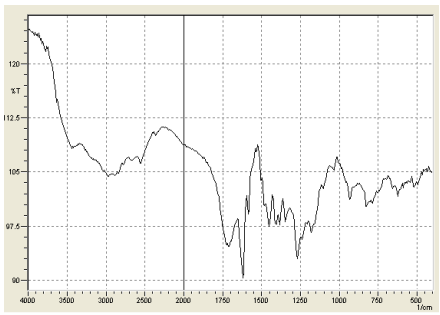


Figure 9: FTIR Spectra of Polymeric Suspension containing Norflox and C940

In the FTIR spectra of the mucoadhesive suspension containing Norflox and HPMC, the peak from 3500 to 3400 cm^{-1} was assigned to υ_{O-H} and single bridge hydrogen bonding, the band between 3000 and 2800 cm^{-1} represented the stretching vibration of υ_{O-H} i.e., strong intermolecular hydrogen bonding (Fig. 10). 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} suggested υ_{C-F} groups [18,29,23]. The band at 950-900 cm^{-1} was assigned to υ_{as} of pyranose ring of HPMC [26] (Table 3c).

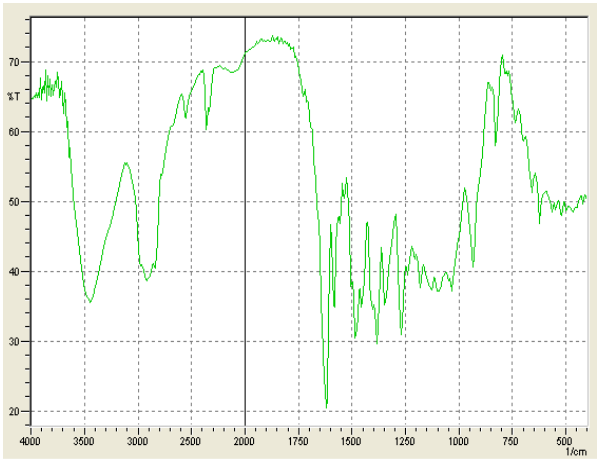


Figure 10: FTIR Spectra of Polymeric Suspension containing Norflox and HPMC

Table 3: Prominent FTIR Peaks of Norfloxacin Polymeric Suspensions

PEAK(cm^{-1})	GROUP	PEAK ASSIGNMENT
a) Polymeric Suspension containing Norflox and C934		
3550-3400	Hydroxyl group	Polymeric H -bonding
2650-2500	Hydroxyl group of acid	Strong Intermolecular H- bonding
1650-1600	O-C-O group of acid	υ_{as} stretching vibration of O-C-O group
1500-1450	O-C-O group of acid	υ_{s} stretching vibration of O-C-O group
1300-1250	Acrylates & esters	C-O-C stretching vibration
1100-1000	C-F groups	υC-F
800	Aromatic m – distribution	δAr-H
b) Polymeric Suspension containing Norflox and C940		
3550-3500	Hydroxyl group	Polymeric H -bonding
2600-2500	Hydroxyl group of acid	Strong intermolecular H- bonding
1650-1600	O-C-O group of acid	υ_{as} stretching vibration of O-C-O group
1500-1450	O-C-O group of acid	υ_{s} stretching vibration of O-C-O group
1300-1250	Acrylates & esters	C-O-C stretching vibration
1100-1000	C-F groups	C-F stretching of Ofloxacin
800	Aromatic m – distribution	δAr-H
c) Polymeric Suspension containing Norflox and HPMC		
3500-3400	Hydroxyl group	single bridge H-bonded
3000- 2800	Hydroxyl group	intermolecular 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, υ_{C-O} / δ_{O-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 Ofloxacin
950-900	Pyranose ring	υ_{as} of pyranose ring of HPMC

DISCUSSION

Infrared (IR) absorption of the functional groups may vary over a wide range. However, it has been found that many functional groups give characteristic IR absorptions at specific narrow frequency ranges[18,19].

In case of FTIR spectra of Norflox, prominent peaks for υ_{C-O} / δ_{O-H} and $\upsilon_{C=O}$ indicated the presence of –CO-, -CHO and -COOH groups (Fig. 3). The presence of above groups could be confirmed by fermi resonance bands for –CHO, υ_{C-O-C} bands for esters and absence of these two for ketones. This suggested the existence of –COOH group in Norflox molecule (Table 1).

In case of FTIR spectra of Carbopol polymers, there were prominent peaks for intramolecular hydrogen bonding, υ_{OH} stretching vibration, carbonylic C=O and C-O stretching vibration, and stretching vibration for the C-O-C, which confirmed the presence of acrylates (Figs. 5 and 6). The peak for out of plane bending vibration of =C-H was found between 850 and 800 cm^{-1} (Tables 2a and 2b). On the other hand, from FTIR spectral analysis of HPMC, it was found that there were both intramolecular and intermolecular hydrogen bondings. In addition, the presence of pyranose ring of β D-glucose monomers was confirmed. The stretching vibration of the cyclic anhydride, methoxy and hydroxypropoxy groups along with epoxide helped in the identification of HPMC (Table 2c)[18,19,23-25].

While comparing the FTIR spectra among the pure Norflox and polymers like C934, C940 and HPMC, and the suspensions containing both Norflox and polymers , it was clear that the band position of C=O group was affected by esterification and conjugation involving C=O group. Here, the stretching vibration of C=O in pure Norflox was found from 1750 to 1700 cm^{-1} which was lowered to 1650-1600 cm^{-1} in the formulations, might be due to formation of β-ketoesters (Figs. 4 and 8-10). The FTIR peaks assigned to υ_{C-O} and υ_{C-O-C}, representing acrylates and esters confirmed the esterification between polymeric -OH and -COOH groups of drug (Norflox). The stretching vibration of C-F group of the drug remained nearly unaltered which indicated that the antibacterial activity of the drug was not affected appreciably in different suspensions. Another probability of interaction was hydrogen bonding i.e., intermolecular hydrogen bonding due to prominent FTIR peaks between 3550 and 3500 cm^{-1}, 3450 and 3400 cm^{-1}, and 2650 and 2600 cm^{-1} represented single bridge O-H...O, polymeric O-H...O-H...O-H and strong hydrogen bonding, respectively. The hydrogen bonded -OH stretching vibration occurred over a wide range, 3550-2600 cm^{-1}. In case of intramolecular hydrogen bonding, FTIR bands were sharp while in intermolecular hydrogen bonding they were broad. However, it was less broad than which was required for chelation. The bending vibration of O-H group gave medium to strong bands in the region around 1450 cm^{-1}. The FTIR peak at 800 cm^{-1} suggested the probability of out of plane bending of –ene bond and m-substitution of δ_{Ar-H} hydrogen atom (Tables 1 and 3)[18,19].

The C=O group of drug lowered the stretching vibration of C=O frequency indicating deprotonation and probably interaction of the said carboxylic C=O moiety with the polymers. However, a definitive conclusion about the keto group in the bonding to the polymer could be deduced because the corresponding band found from 1650 to 1600 cm^{-1} was due to probability of the formation of β-ketoesters[27]. From the above data, it can be inferred that the carboxylic group of Norflox undergoes the interaction with the polymers, as would be expected chemically. Thus the nitrogen atoms aren't likely to be involved in binding or the interaction. The nitrogen atom of the quinolone ring, 1-ortho to fluorine, is less electron rich due to electron deficient fluoroquinolone ring. In addition, cyclopropyl 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 3500-2700 cm^{-1} could be assigned to the asymmetric and symmetric stretching vibrations of the OH groups of the inner and outer sphere of polymers. 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 confirms the presence of the hydrogen bonds [18,19,27]. By comparing the FTIR spectra among the pure drug, polymers and the suspensions containing drug and polymer, the FTIR peak of Norflox from 1750 to 1700 cm^{-1} was not detected in the formulations probably due to interaction with polymers. The missing peak was replaced with two very strong characteristic bands, in the range of 1650-1600 cm^{-1} and at 1450 cm^{-1}, were assigned to $\upsilon_{(O\text{-}C\text{-}O)}$ asymmetric and symmetric stretching vibrations, respectively[26, 28]. The difference Δ $[\upsilon_{(CO2)asym}\text{-}\upsilon_{(CO2)sym}]$ is a useful characteristic for determining the involvement of the carboxylic group of Norflox. 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 polymers (Table 1 and 3) [28].

On the basis of the above interpretation, it can be concluded that by preparing mucoadhesive suspensions of Norfloxacin with these three polymers following a novel method of ultrasonication, there is a very good interaction between the carboxylic group of drug and hydroxyl group of polymers. This leads to esterification and intermolecular hydrogen bonding, by virtue of which stable mucoadhesive suspensions could be produced.

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