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FTIR and Raman Spectroscopic Investigations of a Norfloxacin/ Carbopol934 Polymeric Suspension

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ABSTRACT

Till now very few formulations are available from which the drug is uniformly absorbed, so that the 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 by using a mucoadhesive carbopol934 polymer. The chemical interaction between norfloxacin and the polymer in formulation (prepared by an ultrasonication method) has been studied by FTIR and Raman spectroscopy. From the spectral interpretation, it has been found that in formulation, the carboxylic groups of norfloxacin and hydroxyl groups of carbopol934 undergo chemical interaction, leading to esterification and hydrogen bonding. The formation of micellies due to esterification and hydrogen bonding causes more drug entrapment and a stable formulation. From this it can be concluded that the formulation of norfloxacin may give a better controlled release and mucoadhesive action in the gastrointestinal tract. Hence, carbopol934 could be considered as an effective carrier for norfloxacin.

Key words: C934, FTIR, mucoadhesive formulation, Norfloxacin, Raman spectroscopy

INTRODUCTION

Norfloxacin, 1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolone carboxylic acid, is a second generation fluoroquinolone antibacterial [Figure 1]. It inhibits the enzyme deoxyribonucleic acid (DNA) gyrase preventing DNA and protein synthesis. It requires multiple administration of drug, leading to fluctuation in the plasma concentration of the drug.[1]

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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 the constant blood level, the drug benefit is maximized while its potential toxicity is minimized.[2]

There are several ways of achieving sustained release, such as by suspending the drug in the suspension (at a concentration exceeding the solubility), by formulating the drug as micro- or nanospheres, by distributing the drugs to the liposome or surfactant aggregates, or by utilizing interaction between the drug and the polymer.[3]

Carbopol polymers form hydrogel that changes their swelling behavior upon exposure to an external stimulus such as change in pH,[4,5] temperature,[6] light, or electric

field, and are known as "environmentally responsive polymers" or "smart gels".[7,8] 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.[9-12] In stomach, the carbopol polymer forms the hydrogen bond with the drug and also with the polysaccharides or proteins of mucosa, which is probably the major mechanism for bioadhesion. In addition, under alkaline conditions of the intestine, carbopol gels are very highly swollen.[13] The carbopol polymer in mucoadhesive formulation may provide a gastric retention system by swelling in the stomach and inducing a pseudofed state, thereby reducing peristaltic contraction. This phenomenon is dependent on viscosity—the higher the viscosity, lower is the contraction.[14] In this study design, the polymer used is carbopol934 (C934) which consists of chains of polyacrylic acid [Figure 2].[15] The hydrophilic polymers may form a complex with the low solubility drug-like norfloxacin.

The backbone structures and symmetric bonds of molecules can be checked by Raman spectroscopy. Although it is known that Raman and Fourier transform infrared (FTIR) spectroscopy are complementary vibrational spectroscopic techniques, there are band intensity differences between the two techniques. Therefore, to obtain more information in detail about chemical interaction between norfloxacin and C934, both FTIR and Raman analyses were carried out.[16,17]

MATERIALS AND METHODS

Materials

The following materials were used: Norfloxacin (Norflox) was obtained from Dr. Reddy's Lab, Hyderabad, India, as a gift sample. C934, 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 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 taken and heated up to 80 °C. Sucrose (10 g) 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 a 120 mesh nylon cloth.
2. Preparation of bulk B: Five milliliters 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 (5%) in w/w of drug were added with continuous stirring.
3. Preparation of mucoadhesive suspension and ultrasonication: Five milliliters 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 and the pH was adjusted to 5.5. Homogenization was carried out for at least 20 min using a Ultrasonic Homozenizer LABSONIC® 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

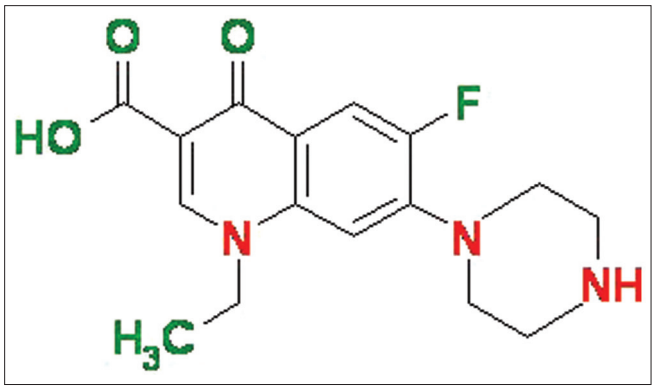

Figure 1: Structure of norfloxacin

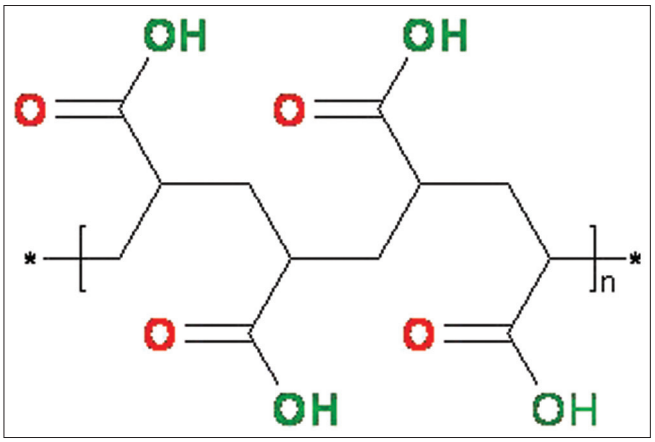

Figure 2: Structure of carbopol polymer (polyacrylic acid)

to 80%. This Homozenizer generates longitudinal mechanical vibrations with a frequency of 30,000 oscillations per second (30 kHz). The probes bolted to the sound transducer were made of high-strength titanium alloys, built as $\lambda/2$ 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 FTIR analysis was conducted to verify the possibility of interaction of chemical bonds between drug and polymer. FTIR analysis was performed by a FTIR spectrophotometer interfaced with a 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 a 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 to 4000 cm^{-1} region with 8 cm^{-1} resolution, 60 scans and a beam spot size of 10–100 μm.[18-20] 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/5 A 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 fiber 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 a Fourier Transform Spectrometer in the mid-infrared region (MIR) within the range (400–4500 cm^{-1}).[21] 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 a functional group region, the appearance of strong absorption bands in the region of 4000–2500 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 3700–2500 cm^{-1} region with various intensities. Hydrogen bonding has 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}.[18,19]

In FTIR spectra of norfloxacin, one prominent characteristic peak was found between 3550 and 3500 cm^{-1}, which was assigned to stretching vibration of the OH group and intermolecular hydrogen bonding by a single bridge. A band at 3500–3300 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 υ_{OH} 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 1650–1600 cm^{-1} was assigned to υN–H bending vibration of quinolones. The peaks at 1500–1450 cm^{-1} represented υ_{O-C-O} of acids and at 1300–1250 cm^{-1} suggested bending vibration of the 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 the C–F group. The peak in the region 950–900 cm^{-1} suggested the δ_{NH} bending vibration of amines. The band at 800 cm^{-1} was due to the meta distribution of the aromatic protons [Figure 3 and Table 1].[19,22,23]

In the case of C934, the FTIR spectra having peak between 3000 and 2950 cm^{-1} represented OH stretching vibration, i.e., υ_{O-H} and intramolecular hydrogen bonding [Figure 4]. The prominent band between 1750 and 1700 cm^{-1} was assigned to carbonyl C=O stretching vibration i.e., $\upsilon_{C=O}$. While the peak at 1450–1400 cm^{-1} was for υ_{C-O}/ δ_{O-H}, the band at 1250–1200 cm^{-1} was assigned to υ_{C-O-C} of acrylates.[19,21] The ethereal cross linking, proved by a prominent peak at 1160 cm^{-1}, indicated stretching vibration of the υ_{C-O-C} group. The band between 850 and 800 cm^{-1} was for out of plane bending of =C–H, i.e., $\delta_{=C-H}$ [Table 2].[18,21]

In the FTIR spectra of formulation containing both norfloxacin and C934, the prominent band, found between 3550 and 3400 cm^{-1}, was assigned to υ_{O-H} and polymeric hydrogen bonding [Figure 5]. 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 $\upsilon_{C-O}/\delta_{O-H}$. 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 the δ_{Ar-H} group [Table 3].[18,19,21] Figure 6 indicates comparative FTIR peaks of the pure drug, polymer and formulation.

By Raman spectroscopy of norfloxacin, the prominent Raman shifts have been observed at 485.6, 872.7, 1418.5, and 1655.1 cm^{-1} [Figure 7]. The Raman shifts at 485.6 cm^{-1} indicated strong bending vibration of C–C of the aliphatic chain and C–N stretching vibration of the piperazinyl group.[24-26] The band at 872.7 cm^{-1} represented the symmetric stretching vibration of the C–F group.[27] The peak at 1418.5 cm^{-1} was due to symmetric stretching vibration of the O–C–O group of carboxylic acid and methylene deformation mode of the piperazinyl group.[28] A band at 1655.1 cm^{-1} was for symmetric stretching of the carbonyl group $\upsilon_{C=O}$ of the pyridone moiety, the stretching vibration of the (C–C) aromatic ring chain. In addition, it (peak at 1655.1 cm^{-1}) also indicated the $N^{+}H_2$ scissoring of the piperzinyl group [Table 4a].[24,28-31]

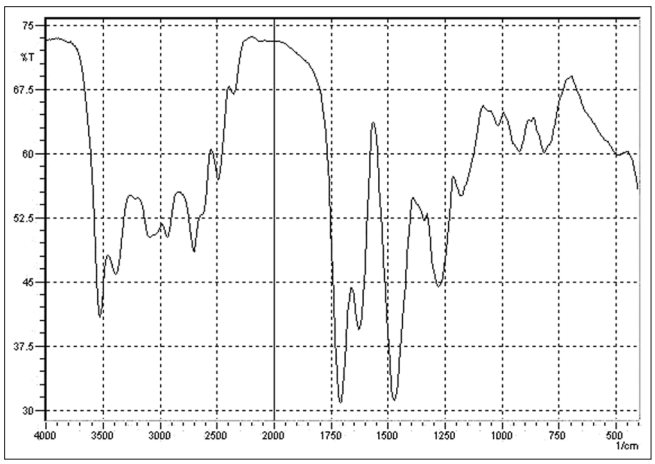

Figure 3: FTIR spectra of norfloxacin

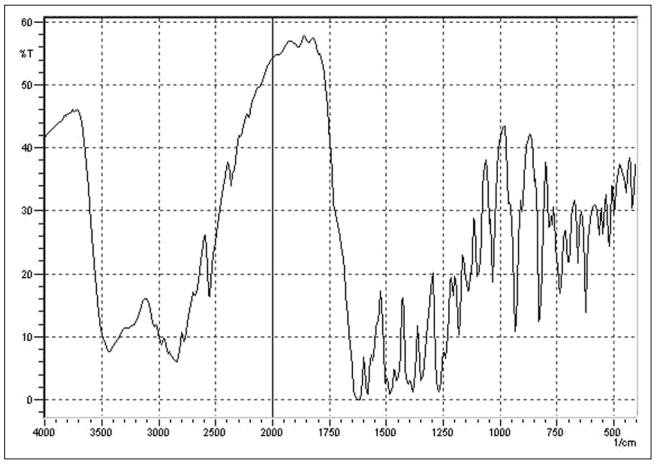

Figure 5: FTIR spectra of mucoadhesive formulation

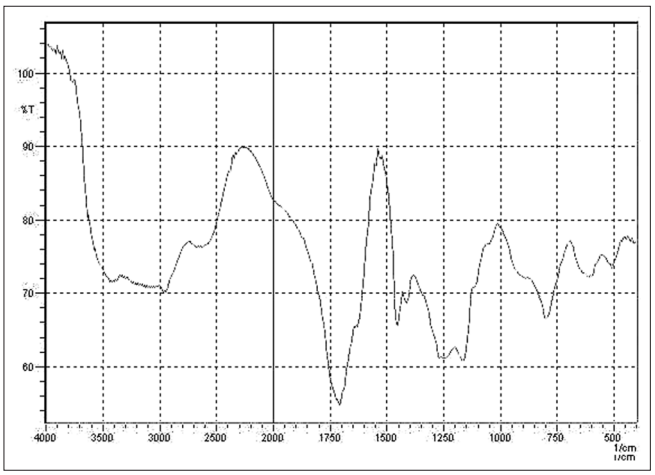

Figure 4: FTIR spectra of carbopol934

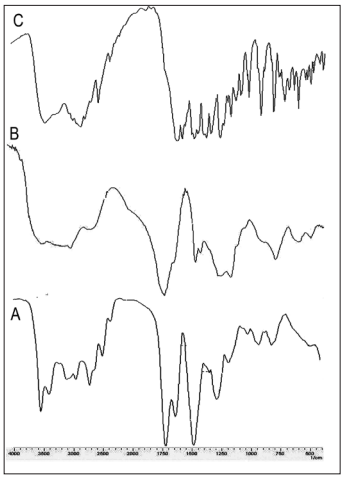

Figure 6: Comparative FTIR spectra of norfloxacin (A), C934 (B), and formulation (C)

The characteristic prominent Raman bands for C934 were observed at 350, 514.31, 872.69, and 1335.03 cm^{-1} [Figure 8]. The bending vibration of the C–C–O group was indicated by the Raman shift at 514.31 cm^{-1}. The band at 872.69 cm^{-1} was due to the stretching vibration of C–O–C for acrylates and carboxylic acid. The Raman band at 1335.03 cm^{-1} was assigned to symmetric vibration of O–C–O of acids [Table 4b].[24]

In the formulation containing both norfloxacin and C934, the Raman peak at 338.8 cm^{-1} represented bending vibration of δ_{CC} of the aliphatic chain [Figure 9]. The band at 900–850 cm^{-1} was assigned to symmetric stretching vibration of both the C–F group and C–O–C group for acrylates and esters. The peak at 1343.2 cm^{-1} suggested for symmetric stretching vibration of the O–C–O group. The band at 1550 cm^{-1} was due to asymmetric vibration of the O–C–O group. The peak at 1850–1700 cm^{-1} was the characteristic of stretching vibration of the carbonyl group of esters [Table 4c].[24,31] Figure 10 indicates comparative Raman shifts of the pure drug, polymer and formulation.

Table 1: Prominent FTIR peaks of norfloxacin

Peaks (cm^{-1})	Groups	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 and Ar–H
2750–2700	Ethyl group	υCH_2
2500	Acid group	Acidic 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 the 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

Table 3: Prominent FTIR peaks of mucoadhesive formulation

Peaks (cm^{-1})	Groups	Peak assignment
3550–3400	Hydroxyl group	Polymeric H-bonding
2650–2500	Hydroxyl group of carboxylic acid	Strong intermolecular H-bonding
1650–1600	O–C–O group of acid	υ_{as} stretching vibration of the O–C–O group
1500–1450	O–C–O group of acid	υ_s stretching vibration of the O–C–O group
1300–1250	Acrylates and esters	C–O–C stretching vibration
1100–1000	C–F groups	υC–F
800	Aromatic *m*-distribution	δAr–H

DISCUSSION

When FTIR 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.[18] In addition, infra-red (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 a specific narrow frequency range.[18,19] Infra-red (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 a specific narrow frequency range.[18-20]

In the case of FTIR spectra of norfloxacin, prominent peaks for $\upsilon_{C\text{-}O}/\delta_{O\text{–}H}$ and $\upsilon_{C=O}$ indicated the presence of –C-O, –CHO, and –COOH groups [Figure 3]. The presence of above groups can be confirmed by fermi resonance

Table 2: Prominent FTIR peaks of C934

Peaks (cm^{-1})	Groups	Peak assignment
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	$\upsilon_{C\text{–}O}$
1250–1200	Acrylates	C–O–C stretching vibration
1160	Ethereal C–O–C group	Stretching vibration of the C–O–C group
850–800	Aromatics and enes	=C–H out of plane bending vibration

Table 4: Raman shifts of norfloxacin, C934, and mucoadhesive formulation

Raman shifts (cm^{-1})	Functional groups/vibrations
a. Prominent Raman shifts of norfloxacin	
485.6	Strong $\delta_{(CC)}$ aliphatic chain and C–N stretching vibration
872.7	Symmetric vibration of the C–F bond
1418.5	$\upsilon_{S\ O\text{–}C\text{–}O}$ and methylene deformation of the piperazinyl group
1655.1	υ_s of the C=O group of the pyridone moiety and N^+H_2 scissoring of the piperzinyl group
b. Prominent Raman shifts of C934	
350	Strong $\delta_{(CC)}$ aliphatic chain
514.31	C–C–O bending vibration
872.69	$\upsilon_{(C\text{–}O\text{–}C)}$ of acrylates
1335.03	$\delta_{(CH3)}$ medium
c. Prominent Raman shifts of mucoadhesive formulation	
338.8	δ(CC) aliphatic chain
900–800	Symmetric stretching vibration of both the C–F group and C–O–C group for acrylates and esters
1343.2	υ_sO–C–O
1550	υ_{as}O–C–O
1850–1700	υC=O medium

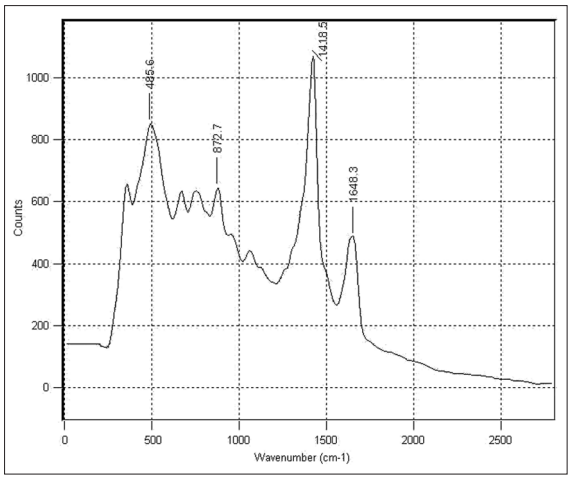

Figure 7: Raman shifts of norfloxacin

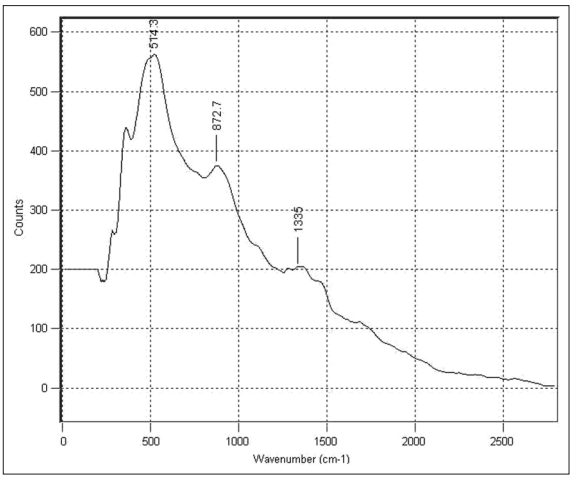

Figure 8: Raman shifts of carbopol934

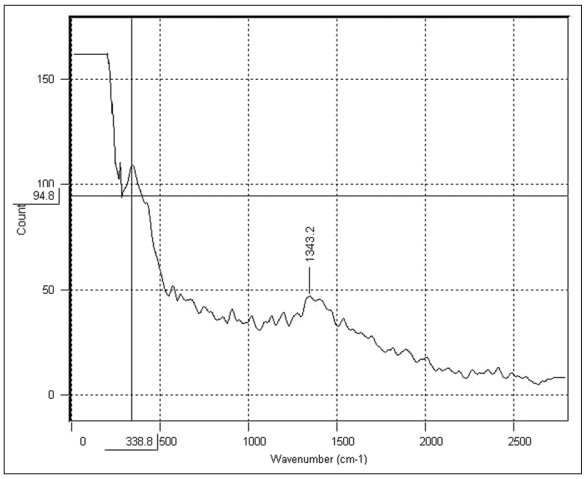

Figure 9: Raman shifts of mucoadhesive formulation

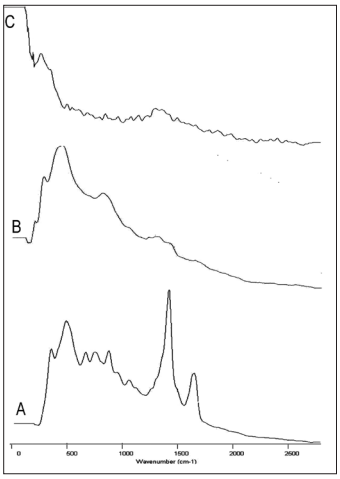

Figure 10: Comparative Raman shifts of norfloxacin (A), C934 (B), and formulation (C)

bands for –CHO, $\upsilon_{C–O–C}$ bands for esters and the absence of these two for ketones. This suggested the existence of the –COOH group in a norfloxacin molecule. In addition, its prominent FTIR peaks indicated the presence of intermolecular hydrogen bonding, quinolone moiety, and piperazinyl, ethyl, COOH, NH and C-F groups (mentioned earlier) [Table 1].[18,19,22,32,33] This C–F group takes a major role in its antibacterial activity.

In the case of FTIR spectra of C934, 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 [Figure 4 and Table 2].

While comparing the FTIR spectra among the pure norfloxacin and C934, and the formulation containing both norfloxacin and C934, it is clear that the band position of the C=O group has been affected by esterification and conjugation involving the C=O group. Here, the stretching vibration of C=O in pure norfloxacin was found at 1700 cm^{-1}, which was lowered to 1650–1600 cm^{-1} in this formulation that might be due to formation of β-ketoesters [Figure 6]. The FTIR peaks assigned to υ_{C-O} and υ_{C-O-C} represent acrylates and esters confirm the esterification between polymeric the OH group and the –COOH group of norfloxacin. The stretching vibration of the C–F group remains nearly unaltered. Another probability of interaction is hydrogen bonding, i.e., intermolecular hydrogen bonding due to prominent FTIR peaks between 3550 and 3400 cm^{-1}, and 2650 and 2500 cm^{-1} represented polymeric O–H….O–H…..O–H and strong carboxylic OH hydrogen bonding, respectively [Table 3].[18,19,21]

The C=O group of drug 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 definitive 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} was due to probability of formation of β-ketoesters.[27]

From the above data, it can be inferred that the carboxylic group of norfloxacin 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. The nitrogen atom of the quinolone ring, 1-ortho to fluorine, is less electron-rich due to an electron deficient fluoroquinolone ring. In addition, ethyl and piperazinyl groups sterically hinder the reaction. The possibility of involvement of the imino moiety of the piperazinyl group is also less prominent due to intense OH stretching vibration. The bands in the region 3550–2500 cm^{-1} could be assigned to the asymmetric and symmetric stretching vibrations of the OH groups of 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.[34] By comparing the FTIR spectra among the pure drug, carbopol polymer (C934) and the formulation containing both drug and polymer, the FTIR peak of norfloxacin at 1700 cm^{-1} was not detected in the mucoadhesive system probably due to interaction with polymer. The missing peak was replaced with two very strong characteristic bands in the range of 1650–1600 cm^{-1} and at 1500–1450 cm^{-1}, which were assigned to $\upsilon_{(O–C–O)}$ asymmetric and symmetric stretching vibrations, respectively.[19,35] The difference $\Delta[\upsilon_{(CO2)\ asym} - \upsilon_{(CO2)sym}]$ is a useful characteristic for determining the involvement of the carboxylic group of norfloxacin. The Δ value for the interaction falls in the range of 183–250 cm^{-1} indicates the deprotonation of the carboxylic acid group and interaction between drug and polymer [Tables 1–3].[30]

In the case of Raman spectra of Norflox, different bands represented the stretching vibrations of ethyl and C–F groups; and the carboxylic acid group was confirmed by $\upsilon_{O–C–O}$ and $\upsilon_{C=O}$ groups (mentioned earlier) [Table 4a]. By comparing the Raman spectra of pure drug with the drug incorporated in the carbopol suspension, the peak at 1418.5 cm^{-1}, assigned to the $\upsilon_{s\ O-C-O}$, is not prominent. Both symmetric and asymmetric stretching vibrations of the O–C–O group are found in suspension containing C934. The Raman peak for stretching vibration of C=O is prominent in the suspension. From this, it is clear that there is an esterification reaction between norfloxacin and carbopol polymer [Table 4]. The results of both FTIR and Raman spectra indicate that both the spectra show prominent peaks for the stretching vibration of O–C–O and C=O groups, which prove the formation of the esters between the drug and polymer. Moreover, both the intermolecular and polymeric hydrogen bonding are also prominent from the FTIR spectra of the formulation.

CONCLUSION

On the basis of above interpretation, it can be concluded that by preparing mucoadhesive suspension of norfloxacin with carbopol polymer (C934) following a novel method of ultrasonication, there is a very good interaction between the carboxylic group of the drug and hydroxyl group of polymer. This leads to esterification and intermolecular hydrogen bonding, by virtue of which a stable formulation would be produced. Moreover, the drug polymer complex may aggregate, forming a micelle-like structure which can absorb and solubilize more drugs. As a result of which carbopol polymer may function as a useful carrier for the norfloxacin molecule. The main advantage of the present investigation is that higher norfloxacin drug loading would be possible in dosage forms as compared to conventional formulation strategies. Here, norfloxacin interacts with the polymer monomerically. Release of the drug from the formulation system is very slow because the carboxylic group of norfloxacin interacts with polymeric OH groups. It suggests that a less active site of the drug is left for the attack by the 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 in the acidic condition of the stomach. On the other hand, mucoadhesive suspension is highly swollen and stiffened in an alkaline condition of the intestine showing a very good mucoadhesive property of the formulation 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 their delivery rate, biodegradation and site-specific targeting of such mucoadhesive suspension would be monitored and controlled.

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