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FTIR and Raman Spectroscopic Investigations of Ofloxacin / Carbopol940 Mucoadhesive Suspension

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Abstract: At present, very few formulations are available from which the drug is absorbed uniformly, so that safe and effective blood level of Ofloxacin could be maintained for a prolonged period. Considering this limitation, a mucoadhesive suspension has been prepared for the study by ultrasonication method, using mucoadhesive Carbopol940 polymer. The chemical interaction between Ofloxacin and polymer in formulation has been studied by FTIR and Raman Spectroscopy. From the spectral interpretation, it has been found that in formulation, the carboxylic groups of Ofloxacin and hydroxyl groups of Carbopol940 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. As a result of which the formulation of Ofloxacin may give better controlled release and mucoadhesive action in the gastrointestinal tract. Hence, Carbopol940 could be considered as an effective carrier for Ofloxacin.
Keywords: Ofloxacin, C940, FTIR, Raman Spectroscopy, Mucoadhesive formulation.

INTRODUCTION

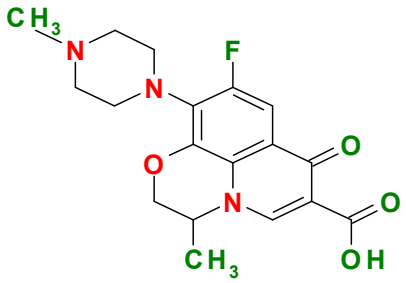
There is a demand for a dosage form that will provide a controlled release action of the drug in solution, particularly in the basic pH conditions of the intestinal lumen over the full dosage period. By achieving constant blood level, drug benefit is maximized while its potential toxicity is minimized[1]. There are several means of achieving controlled release action, such as by suspending the drug (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[2].

As frequent dosing is required to maintain the therapeutic plasma concentration, Ofloxacin (Oflox) was chosen as a model drug for the controlled release study. Ofloxacin, 9-fluro-2, 3-dihydro-3-methyl-10-(4-methyl-1-piperizinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxaine-6-carboxylic acid, is a fluoroquinolone antibacterial agent[3] (**Fig 1).**

Carbopol polymers form hydrogel that change their swelling behaviour 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, Carbopol polymer forms 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 condition of the intestine, Carbopol gels are very

highly swollen[13]. 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, the lower the contraction[14]. In the present study design, Carbopol940 (C940) is used as a polymer, which consists of chains of polyacrylic acid[15] (Fig 2). This hydrophilic polymer may form a complex with the low solubility drug like Ofloxacin. Because it is known that the solubility is the crucial factor for drug effectiveness, independence of the route of administration[16].

While the functional groups of the molecules can be determined by FTIR analysis, the backbone structures and symmetric bonds of molecules can be 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 information in detail about chemical interaction between Ofloxacin and C940, both FTIR and Raman analyses were carried out[17,18].



Ofloxacin

Figure 1: Structure of Ofloxacin

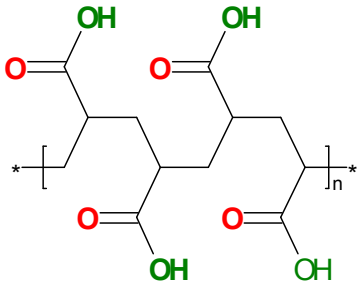


Figure 2: Structure of Carbopol Polymer (Polyacrylic acid)

MATERIALS AND METHODS

MATERIALS

The following materials were used: Ofloxacin was obtained from Dr. Reddy's Lab, Hyderabad, India, as a gift sample. C940, 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. Praparation 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. Praparation 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 C940 (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 250 mg of Oflox 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 [19-21]. 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 potable 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 AND DISCUSSION

The infrared spectra are recorded on Fourier Transform Spectrometer in the mid –infrared region (MIR) within the range (400-4500 cm^{-1})[22]. 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 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} [19,20].

In FTIR spectra of Oflox, one prominent characteristic peak was found between 3050 and 3000 cm^{-1}, which was assigned to stretching vibration of OH group and intramolecular hydrogen bonding (Fig 3). This band also suggested the NH stretching vibration of the imino-moiety of piperazinyl group which was less prominent due to intense OH stretching vibration. The peak at 2700 cm^{-1} was assigned to υCH_3 of methyl group. The band at 1750-1700 cm^{-1} represented the acidic carbonyl C=O stretching i.e., $\upsilon C{=}O$ [23]. The peak at 1650 to 1600 cm^{-1} was assigned to υN-H bending vibration of quinolones. The 1550 to 1500 cm^{-1} represented the υCH_2 of the aromatic ring. The band at 1450-1400 cm^{-1} was assigned to the stretching vibration of CH_2 confirming the presence of methylene group in benzoxazine ring. The peak at 1400-1350 cm^{-1} represented the bending vibration of hydroxyl group. The band at 1250 to 1200 cm^{-1} suggested the stretching vibration of oxo group. In addition, a strong absorption peak between 1050 and 1000 cm^{-1} was assigned to C-F group. The band at 900-800 cm^{-1} represented the out of plane bending vibration of double bonded enes or =CH groups[19,20,24-26] (Table 1a).

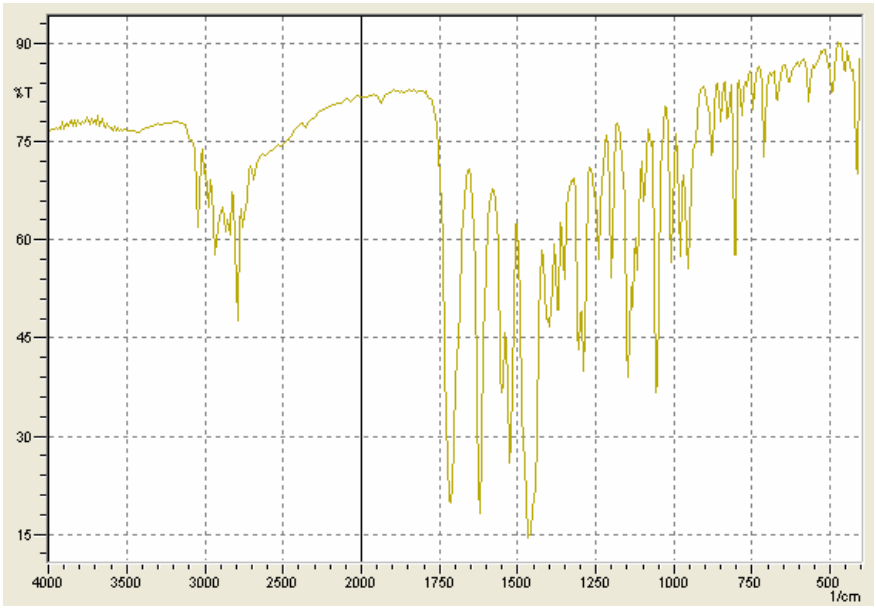


Figure 3: FTIR Spectra of Ofloxacin

In case of C940, the FTIR spectra having peak between 3000 and 2950 cm^{-1} represented OH stretching vibration, i.e., υO-H and intramolecular hydrogen bonding (Fig 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 to 1400 cm^{-1} was for υ_{C-O} / δ_{O-H}, the band at 1250 to 1200 cm^{-1} was due to υ_{C-O-C} of acrylates[20,22]. The band between 850 and 800 cm^{-1} was for out of plane bending of =C-H i.e., δ=C-H[19,22] (Table 1b).

In case of FTIR spectra of Oflox with C940, the prominent peak found at 3500-3400 cm^{-1} was assigned to polymeric υ_{O-H} group (Fig 5). The band between 3100 to 3000 cm^{-1} represented $\upsilon_{=C-H}$ (m). While the peak at 2800-2700 cm^{-1} suggested intermolecular hydrogen bonding, the band at 1750-1700 cm^{-1} was assigned to υC=O. Moreover, the bands at 1650-1600 cm^{-1} and 1500-1400 cm^{-1} indicated both asymmetric and symmetric stretching vibration of O-C-O group of carboxylic acids, respectively. The peak at 1250-1200 cm^{-1} suggested υC-O-C of acrylates and ethers. In addition, the band at 1050-1000 cm^{-1} was assigned to υ_{C-F} and at 800 cm^{-1} was for bending vibration of Ar-H groups[19,20] (Table 1c).

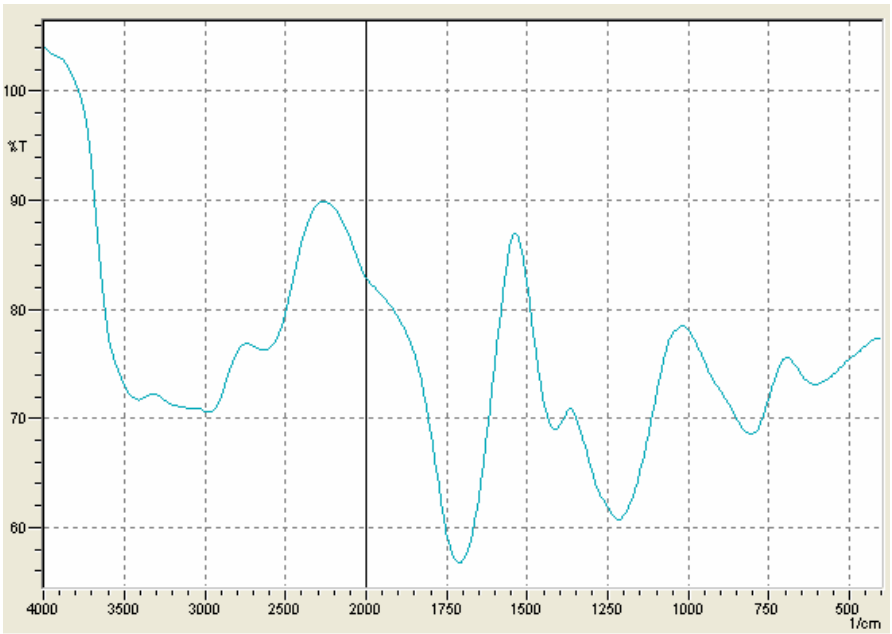


Figure 4: FTIR peaks of C940

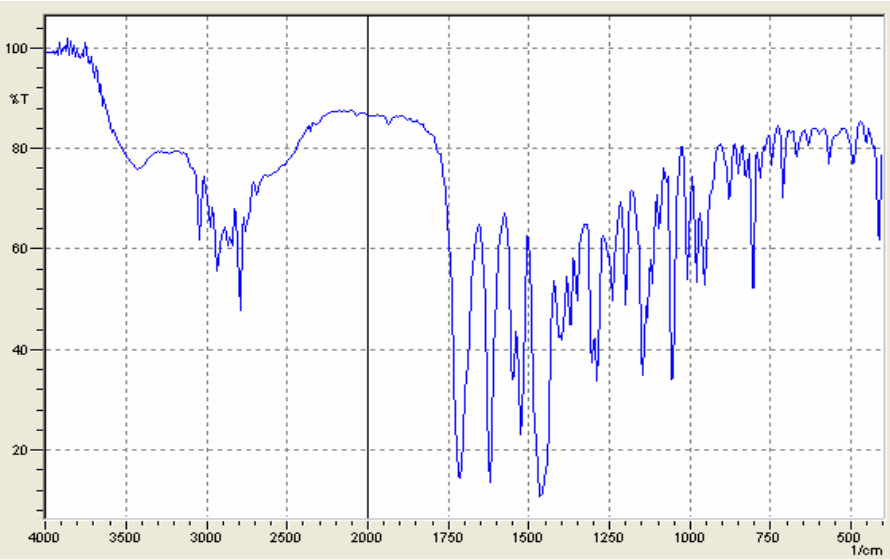


Figure 5: FTIR Spectra of Ofloxacin Mucoadhesive Formulation

Table 1: Prominent FTIR peaks of Ofloxacin, C940 and Formulation

a) Prominent FTIR peaks of Ofloxacin		
PEAKS(cm-1)	**GROUPS**	**PEAK ASSIGNMENT**
3050-3000	Hydroxyl group	O-H stretching vibration, intremolecular H-bonded
3000-2950	Aromatic, cyclic enes	υ=CH & Ar-H
2750	Alkyl groups	υCH_3
1750-1700	C=O group of acids	υC=O stretching vibration
1650-1600	Quinolines	δN-H bending vibration
1550-1500	Alkyl groups	υCH_3 and υCH_2
1450-1400	Methylene group in Benzoxazine	stretching vibration of CH_2
1400-1350	Hydroxyl group	δO-H bending vibration
1250-1200	Oxo group	C-O-C stretching vibration
1050-1000	C-F group	C-F stretching
950-800	Aromatics & enes	=C-H out of plane bending vibration
b) Prominent FTIR peaks of C940		
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
850-800	Aromatics & enes	=C-H out of plane bending vibration
c) Prominent FTIR Peaks of Ofloxacin Mucoadhesive Formulation		
3500-3400	Hydroxyl group	υ_{O-H}
3100-3000	enes	$\upsilon_{=C-H(m)}$
2800-2700	O-H groups	Intermolecular H-bonded
1750-1700	C=O groups	$\upsilon_{C=O}$
1650-1600	O-C-O group of acid	υ_{as} stretching vibration
1500-1450	O-C-O group of acid	υ_{s} stretching vibration
1300-1250	Hydroxyl group	δ_{O-H}
1250-1200	Acrylates & esters	C-O-C stretching vibration
1050-1000	C-F groups	υ_{C-F}
800	Aromatic & enes	δ_{Ar-H} & $\delta_{=C-H}$

By Raman spectroscopy of Ofloxacin, the prominent Raman shifts were observed at 518.4, 797.5, 1419.8 and 1649.6 cm^{-1} (Fig 6). The Raman shift at 518.4 cm^{-1} represented the bending vibration of aliphatic carbon atom, C-N stretching vibration of piperazinyl group and O-H torsional vibration of carboxylic acid[27-30]. The band at 797.5 cm^{-1} suggested the symmetric stretching vibration of C-F group[31]. The peak at 1419.8 cm^{-1} was for the symmetric stretching vibration of O-C-O group of carboxylic acid and methylene deformation mode of the piperazinyl group[30]. A band at 1649.6 cm^{-1} was due to symmetric stretching of the carbonyl group $\upsilon_{C=O}$ of the pyridone moiety, the stretching vibration of (C-C) aromatic ring chain. In addition, it (peak at1649.6cm^{-1}) also indicated the $N^{+}H_2$ scissoring of piperzinyl group[27,30,32-34] (Table 2a).

The characteristic prominent Raman bands for C940 were observed at 523.9, 876.8 and 1366.5 cm^{-1} (Fig 6). The bending vibration of C-C-O group was indicated by the Raman shift at 523.9 cm^{-1}. The band at 876.8 cm^{-1} was due to stretching vibration of C-O-C for acrylates and carboxylic acid. The Raman band at 1366.5 cm^{-1} was assigned to symmetric vibration of O-C-O of acids[27] (Table 2b).

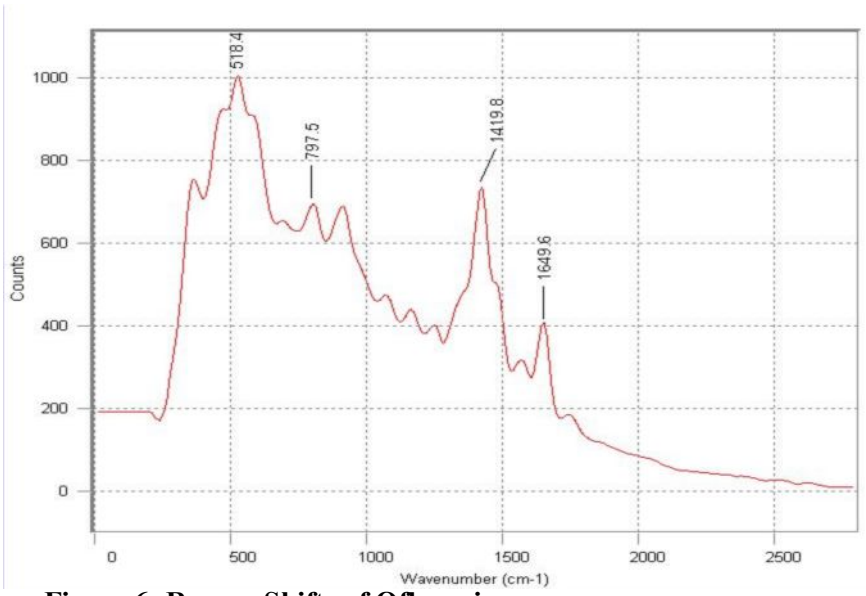


Figure 6: Raman Shifts of Ofloxacin

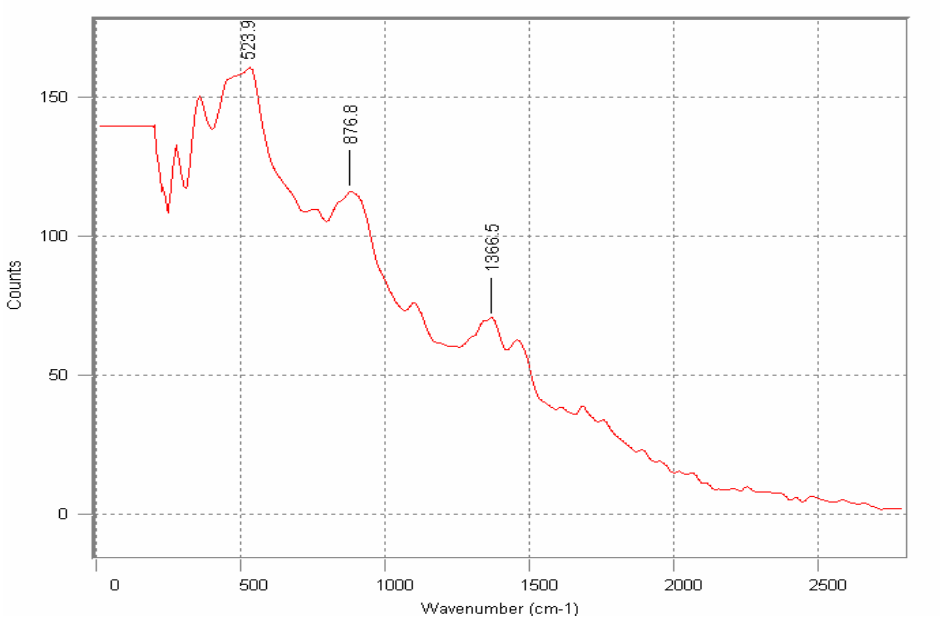


Figure 7: Raman Shifts of C940

In the formulation containing both Oflox and C940, the Raman peak at 352.9 cm^{-1} represented bending vibration of δCC of aliphatic chain (Fig 8). The band at 900 cm^{-1} was assigned to symmetric stretching vibration of both C-F group and C-O-C group for acrylates and esters. The peak at 1050 cm^{-1} represented stretching vibration of carbonyl group. The band at 1250 cm^{-1} suggested symmetric stretching vibration of O-C-O group. The band at 1800 to 1750 cm^{-1} was the characteristic of stretching vibration of carbonyl group of esters[26,33] (Table 2c).

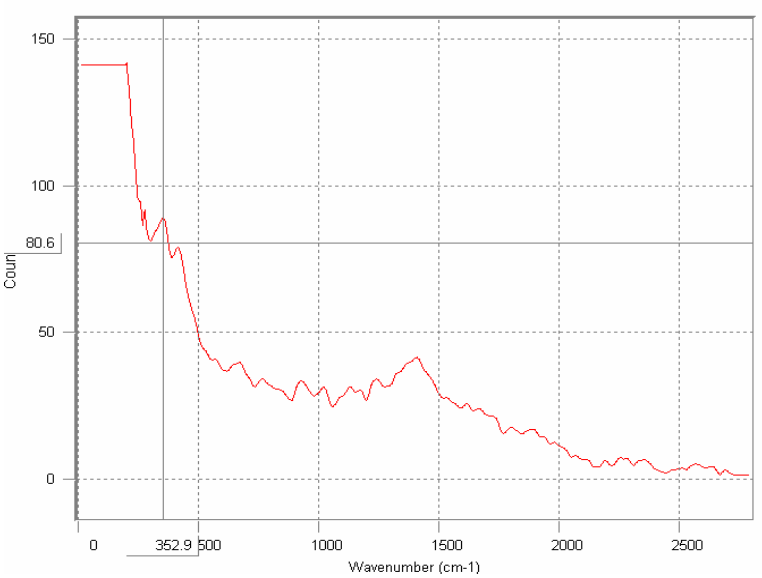


Figure 8: Raman Shifts of Ofloxacin Mucoadhesive Formulation

Table 2. Raman Shifts of Ofloxacin, C940 and Formulation

a) Prominent Raman Shifts of Ofloxacin	
Raman Shifts(cm^{-1})	**Functional Groups / Vibrations**
518.4	Strong δ (CC) aliphatic chain, C-N stretching vibration and O-H torsional vibration
797.5	Symmetric vibration of C-F bond
1419.8	υ_S O-C-O and methylene deformation of the piperazinyl group
1649.6	υs of C=O group of pyridone moiety and N^+H_2 scissoring of piperzinyl group
b) Prominent Raman Shifts of C940	
Raman Shifts(cm^{-1})	**Functional Groups / Vibrations**
450-300	Strong $\delta_{(CC)}$ aliphatic chain
523.9	C-C-O bending vibration
876.8	$\upsilon_{(C\text{-}O\text{-}C)}$ of acrylates
1366.5	$\delta_{(CH3)}$ medium
c) Prominent Raman Shifts of Ofloxacin Mucoadhesive Formulation	
Raman Shifts(cm^{-1})	**Functional Groups / Vibrations**
352.9	δ(CC) aliphatic chain
900	Symmetric stretching vibration of both C-F group C-O-C group for acrylates and esters
1050	Stretching vibration of CO
1250	υ_sO-C-O
1800-1750	υC=O medium

From the above mentioned results, it is clear that the band position of C=O group in Ofloxacin has been affected by esterification and conjugation in the formulation. The FTIR peaks assigned to υ_{C-O} and υ_{C-O-C} represented acrylates and esters, which confirmed the esterification between polymeric OH group and –COOH group of Oflox. The stretching vibration of C-F group remained nearly unaltered. The C=O group of drug lowers the stretching vibration of C=O frequency in the formulation, 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 could be deduced because the corresponding band found from 1650 to 1600 cm^{-1} and 1250-1200 cm^{-1} was due to probability of formation of β-ketoesters[35]. From the above data, it can be inferred that the carboxylic group of Oflox undergoes the interaction with the polymer, 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, ethyl 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 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[19-21]. In the formulation, the 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, represented the formation of β-ketoesters (as mentioned earlier)[20,36]. The difference Δ [$\upsilon_{(CO2)asym}$-$\upsilon_{(CO2)sym}$] is a useful characteristic for determining the involvement of the carboxylic group of Oflox. 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[33] (Table 1).

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 in the formulation. The symmetric stretching vibration of O-C-O group is found in suspension containing C940. Moreover, the Raman peak for stretching vibration of C=O is prominent in the suspension. From this it is clear that there is esterification reaction between Oflox and Carbopol polymer (Table 2).

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 Ofloxacin with Carbopol polymer (C940) following ultrasonication, there is a very good interaction between the carboxylic group of 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 Carbopol940 polymer may function as a useful carrier for the Oflox molecule. The main advantage of the present investigation is that higher Oflox drug loading would be possible in dosage forms as compared to conventional formulation strategies. The release of drug from the formulation system is very slow because the carboxylic group of Oflox interacts with polymeric OH groups. It suggests less active site of the drug is left for the attack by the water molecules for the hydration and solubilization, which gives controlled release action. In addition, the free polymeric carboxylic groups in the formulation may 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. Both these properties suggest a very good mucoadhesive property of the formulation in the gastrointestinal mucosa. Considering the above mentioned interpretation, it may be concluded that the mucoadhesive suspension would produce an effective controlled release and mucoadhesive action. The utility of the present work can be improved if their delivery rate, biodegradation and site-specific targeting of such mucoadhesive suspension would be monitored and controlled.

REFERENCES

1. (WO/2006/007354) A Drug/Polymer Complex, Preferably Ciprofloxacin/HPMC, Its Method of Manufacturing Using Lyophilisation and Its use in an Osmotic Divice; Available from *http://www.wipo.int/pctdb/en/wo.jsp*?WO=2006007354&IA=US2005020356&DISPLAY=DESC, accessed on 13.01.2010.
2. Hui H.W., Robinsion J.R. and Lee V.H.L., Controlled Drug Delivery- Fundamentals and application. 2nd ed., Marcel Dekker, Inc., New York, 2005, 373.
3. Arunachalam A., Rathinaraj B.S., Subramanian, Choudhury P.K., Reddy A.K. and Fareedullah Md., Preparation and Evaluation of Ofloxacin Microsphere Using Natural Gelatin Polymer. Int. J. Appl. Biol. Pharm. Tech. 2010; 1(1): 61-67.
4. Qiu Y. and Park K., Environment-sensitive hydrogels for drug delivery. Adv. Drug. Deliv. Rev. 2001; 53: 321-339.
5. Bettini R., Colombo P. and Peppas NA., Solubility effects on drug transport through pH sensitive, swelling-controlled release systems: Transport of theophylline and metoclopramide monohydrochloride. J. Control. Release. 1995; 37: 105-111.
6. Bromberg L.E. and Ron E.S., Temperature-responsive gels and thermogelling polymer matrices for protein and peptide delivery. Adv. Drug. Deliv. Rev. 1998; 31: 197-221.
7. Smart Polymer for Controlled Drug Delivery Protein and Peptides: A Review of Patents; Available from *http://www.ingnetaconnect.com/content/ben/pdf/2009/00000003/00000001/art00004*, accessed on 24.01.2010.
8. Galaev I.Y. and Mattiasso B., Smart' polymers and what they could do in biotechnology and medicine. Trends Biotechnol. 1999; 17: 335-340.
9. Jeong B. and Gutowska A. Stimuli-responsive polymers and their biomedical applications. Trend Biotechnol. 2001; 20: 305-311.
10. Gupta P., Vermani K. and Garg S., Hydrogels: from controlled release to pH-responsive drug delivery. Drug Discovery Today. 2002; 7: 569-579.
11. Yoshida R., Sakai K., Okana T. and Sakurai Y., Pulsatile drug delivery system using Hydrogels. Adv. Drug. Deliv. Rev. 1998; 11: 85-108.
12. Guo J.H.: Carbopol Polymer for Pharmaceutical Drug Delivery Applications.Excipient Updates.Drug Delivery Technology; Available from *http://www.drugdeliverytech.com/cgi-bin/articles.cpi?id* Article=159, accessed on 19.01.2010.
13. Pharceutical Bulletins; Available from *http://www.lubrizol.com/pharmaceutical/literature/bulletins.html*, accessed on 05.01.2010.
14. Leung S.H., Irons B.K. and Robinsion J.R., Polyanionic hydrogel as a gastric retentive System. J. Materials Sci. 1995; 4: 483-492.
15. Hosmani A.H.: Carbopol and its Pharmaceutical Significance: A Review; Available from http://www.pharmainfo.net/reviews/carbopol-and-its-pharmaceuticalsignificance-review, accessed on 20.01.2010.
16. Lakshmi P. and Kumar GA., Nano-Suspension Technology : A Review. Int. J. Pharmacy Pharm. Sci. 2010; 2(Suppl 4): 35-40.
17. Venkeirsbilck T., Vercauteren A., Baeyens W., Weken G.V.D., Verpoort F., Vergote G. and Remon JP., Applications of Raman Spectroscopy in pharmaceutical analysis.Trends Anal. Chem. 2002; 21: 869-877.
18. Clarke R.H., Londhe S., Premasiri W.R. and Womble M.E., Low-Resolution Raman Spectroscopy: Instrumentation and Application in Chemical Analysis. J. Raman Spectrosc. 1999; 30: 827-832.
19. Silverstein R.M. and Webster F.M., Spectrometric Identification of Organic Compounds. 6th ed., Jhon Wiley and Sons, New York, 2002, 71.
20. Dani V.R., Organic Spectroscopy. 1st ed., Tata McGraw-Hill Publishing Company Limited, New Delhi, 1995, 86.
21. Precautions for Making KBr Pellets; Available from http://www.chemistry.nmsu.edu/Instrumentation/KBr_New.html, accessed on 20.01.2010.
22. Hsu C.P.S.: Infrared Spectroscopy; Available from http://www.prenhall.com/settle/chapters/ch15.pdf, accessed on 20.01.2010.
23. Kulkarni P.V. and Keshavayya J., Chitosan Sodium alginate biodegradable interpenetrating polymer network (IPN) beads for delivery of ofloxacin hydrochloride.Int. J. Pharm. Sci. 2010; 2(Suppl 2): 77-82.
24. Anam A.A., Fandi Z., Gryta M. and Balcerowiak W., Synthesis and Characterization of Hydroquinone Based Benzoxazines and their Polymers Using Solventless System.Pak. J. Appl. Sci. 2002; 2(10): 940-944.
25. Pandya S.J., Bhalekar M.R., Harinarayana D., Shah S.S. and Darji D., Preparation and Characterization of Light Sensitive Ofloxacin Complexes under Accelerated Condition. Int. J. Pharm. Res. 2010; 2(3): 28-32.
26. Sahoo S., Chakraborti C.K., Mishra S.C., Nanda U.N. and Naik S., FTIR and XRD investigations

of some Fluoroquinolones. Int. J. Pharmacy Pharm. Sci. 2011; 3(3): 165-170.
27. Raman Data and Analysis; Available from *http://www.horiba.com/fileadmin/uploads/scintific/Documents/Raman/bands.pdf*, accessed on 20.01. 2010.
28. Tua Q., Eisenb J. and Changa C., Band Shifts in Surface Enhanced Raman Spectra of Indolic Molecules Adsorbed on Gold Colloids; Available fromhttp://www.icors2010.org/abstractfiles/ ICORS20101040.5375VER.5.pdf, accessed on 2.01.2010.
29. Xu J., Stangel I., Butler I.S. and Gilson D.F.R., An FT-Raman Spectroscopic Investigation of Dentin and Collagen Surfaces Modified by 2-Hydroxyethylmethacrylate. J. Dent. Res. 1997; 76: 596-601.
30. Bright A., Devi T.S.R. and Gunasekaran S., Spectroscopical Vibrational Band Assignment and Qualitative Analysis of Biomedical Compounds with Cardiovascular Activity. Int. J. Chem. Tech. Res. 2010; 2: 379-388.
31. Sharts DOSHCM and Gorelik V.S., Method and apparatus for determination of carbon-halogen compounds and applications thereof. United States Patent 6445449; Available from http://www.freepatentsonline.com/6307625.html, accessed on 20.01.2011.
32. Skoulika S.G. and Georgiou C.A., Rapid Quantitative Determination of Ciprofloxacin in Pharmaceuticals by Use of Solid-State FT-Raman Spectroscopy. Appl. Spectrosc. 2001; 55: 1259-1265.
33. Lawrence B.A., Lei Z., Liling Z., Christopher L.E. and Andrew R.B. Solid-State NMR Analysis of Fluorinated Single - Carbon Nanotubes: Assessing the extent of Fluorination. Chem. Mater. 2007; 19: 735-744.
34. Agarwal U.P., Reiner R.S., Pandey A.K., Ralpha S.A., Hirth K.C. and Atalla R.H.: Raman Spectra of Liginin Model Compounds; Available from *http://www.treesearch.fs.fed.us/pubs/20194*, accessed on 20.01.2010.
35. Gruodis A., Alkasa V., Powell D.L., Nielsen C.J., Guirgis G.A. and Durig J.R., Vibrational spectroscopic studies, conformations and ab initio calculations of 1,1,1 trifluoropropyltrifluorosilane. J. Raman Spectrosc. 2003; 34: 711-724.
36. Ramesh S., Ranganayakulu D., Reddy R.S.P. and Tejaswi E., Formulation and Evaluation of Sepia Nanaparticles Containing Ciprofloxacin Hydrochloride. J. Innovative Trends Pharm. Sci. 2010; 1: 79–85.

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