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FTIR AND RAMAN SPECTROSCOPY AS A TOOL FOR ANALYZING SUSTAINED RELEASE HYDROGEL OF CIPROFLOXACIN/CARBOPOL POLYMER

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ABSTRACT

Purpose: Ciprofloxacin, an antibacterial agent, is having low solubility in aqueous solution and high rate of absorption from the stomach. It is precipitated at alkaline pH which leads to erratic absorption of the drug from small intestine. To overcome these difficulties, many researchers have prepared different formulations of Ciprofloxacin. But till now very few formulations are available from which the drug is absorbed uniformly, so that safe and effective blood level of Ciprofloxacin can be maintained for a prolonged period. To fulfill this requirement, in the present study, a sustained release drug delivery system (hydrogel) has been designed and chemical interaction between Ciprofloxacin and polymer in hydrogel has been studied by FTIR and Raman Spectroscopy. Methods: Ultrasonication method was used for preparation of hydrogel of the Ciprofloxacin, taking Carbopol 934 polymer with drug to polymer weight ratio 1:5. FTIR (400 cm^{-1} to 4000 cm^{-1} region) and Raman (140 to 2400 cm^{-1} region) Spectroscopic studies were carried out and spectra were used for interpretation. Results: From the spectral interpretation, it has been found that in hydrogel, the carboxylic groups of Ciprofloxacin and hydroxyl groups of Carbopol934 undergo chemical interaction leading to esterification and hydrogen bonding (both intermolecular and polymeric). Conclusions: The formation of micelles due to esterification and hydrogen bonding causes more drug entrapment and formation of a stable hydrogel, as a result of which, the hydrogel of Ciprofloxacin gives better controlled release and mucoadhesive action in the gastrointestinal tract and hence Carbopol934 can be considered as an effective carrier of Ciprofloxacin.

INTRODUCTION: Ciprofloxacin (Cipro) is a second generation fluoroquinolone, IUPAC name being 1- cyclopropyl- 6- fluoro- 1, 4- dihydro- 4- oxo- 7- (1- piperazinyl)- 3- quinoline carboxylic acid (**Fig. 1**). It inhibits the enzyme deoxyribonucleic acid (DNA) gyrase preventing DNA and protein synthesis. The drug is limited to the treatment of proven bacterial infections, such as urinary tract infection, acute uncomplicated cystitis in females, chronic bacterial prostatis, lower respiratory tract infection, acute sinusitis, skin infections, bone and joint infections, infectious diarrhoea, enteric fever caused by *Salmonella typhi*, complicated intra abdominal infections (in combination with metronidazole), empirical therapy for febrile neutropenic patients (in combination with piperacillin), etc [1-6].

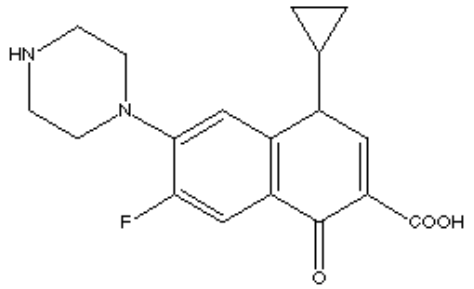

FIG. 1: STRUCTURE OF CIPROFLOXACIN

It was first patented by Bayer A.B in 1983. Ciprofloxacin has low solubility in aqueous solution and high rate of absorption from the stomach. It is precipitated in small intestine at alkaline pH which causes erratic absorption of the drug. The commercial Cipro products are designed to deliver high dosage of the drug but the problem of drug precipitation at alkaline pH remains unsolved. 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. For this reason, dosage forms that incorporate such low soluble drugs provide a major challenge for sustained release technologist. A controlled drug delivery system is usually designed to deliver the drug at a particular rate. A safe and effective blood level of the drug is maintained as long as the system continues to deliver the drug at that rate. By achieving constant blood level, drug benefit is maximized while its potential toxicity is minimized[7].

The polymer in the hydrogel formulation interacts with the mucosal component increasing the contact time with the mucosa at the site of absorption. The prolonged contact time has been attributed to rheological properties of formulation, which delays its clearance from the mucosa [8]. The polymer network is of little hindrance and the drug is likely to diffuse out of the gel rather rapidly. There are several ways of achieving sustained release, e.g., by suspending the drug in the gel (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 [9].

In the present study design, the polymer used is Carbopol934 (C934) which consists of chains of polyacrylic acid [10] (**Fig. 2**). Carbopol polymers form hydrogel that change their swelling behavior upon exposure to an external stimulus such as change in pH [11, 12], temperature [13], light, or electric field, and are known as “environmentally responsive polymers” or “smart gels” [14, 15].

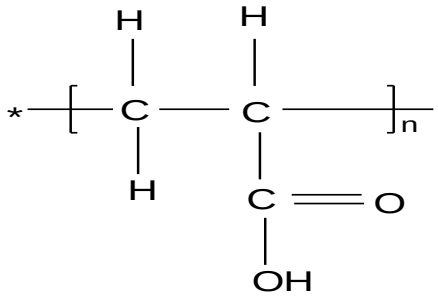

FIG. 2: STRUCTURE OF CARBOPOL POLYMER

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 [16-19]. In stomach,

Carbopol polymer forms hydrogen bonding 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, the Carbopol gels are very highly swollen [20].

Carbopol polymer hydrogel 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 [21]. The hydrophilic polymers may form a complex with the low solubility drug like Ciprofloxacin. The interaction between the Cipro and hydrophilic osmo-polymer C934 can be determined by several methods such as Fourier Transform Infrared (FTIR) Spectroscopy, Raman Spectroscopy, etc. In both methodologies, the interaction can be interpreted by comparing the spectra of the drug in presence and absence of the hydrophilic polymer.

MATERIALS AND METHODS: The work has been carried out jointly at National Institute of Technology, Rourkela and Kanak Manjari Institute of Pharmaceutical Sciences, Rourkela, in 2009.

Materials: The following materials were used: Ciprofloxacin Hydrochloride was obtained from Dr. Reddy's Lab, Hyderabad, India, as a gift sample. Carbopol934 was kindly supplied by Cosmo Chem. Laboratory. Ultra pure water obtained from a Millipore Milli-Q UV water filtration system.

Methods:

Sample preparation: Ciprofloxacin and Carbopol were added slowly to water with drug to polymer weight ratio being 1:5 and homogenized to produce a uniform hydrogel. Homogenization was carried out for at least 15 min by ULTRASONIC HOMOZENIZER LABSONIC^{R} M (SARTORIUS) having operating frequency 30 KHZ and line voltage 230V/50HZ, using the probe made up of Titanium having 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 are made of high-strength Titanium alloys, built as λ/2 oscillator. It amplifies the vertical oscillation, and transfers the ultrasonic energy via its front surface with extremely high power density into the sample that is to be subjected to ultrasonic waves. Here, stress applied was sound wave and mild rise in temperature of the sample occurred during ultrasonication.

FTIR Spectroscopic Analysis: FTIR Spectroscopy is an important analysis technique which detects various characteristic functional groups in molecules of any matter. On interaction of an infrared light with the matter, chemical bonds would stretch, contract and bend and as a result each chemical functional group tends to absorb infrared radiation in a specific wavelength range regardless of the structure of the rest of the molecule. Based on this principle, functional groups present in composite materials are identified. It is performed in a FTIR Spectrophotometer interfaced with infrared (IR) microscope operated in reflectance mode. The microscope is 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. The FTIR imaging in the present investigation was carried out using a Perkin Elmer Spectrum RX (1). Here KBr pellet method was used for sample preparation for FTIR study. 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 (**Fig. 3, 4 and 5**).

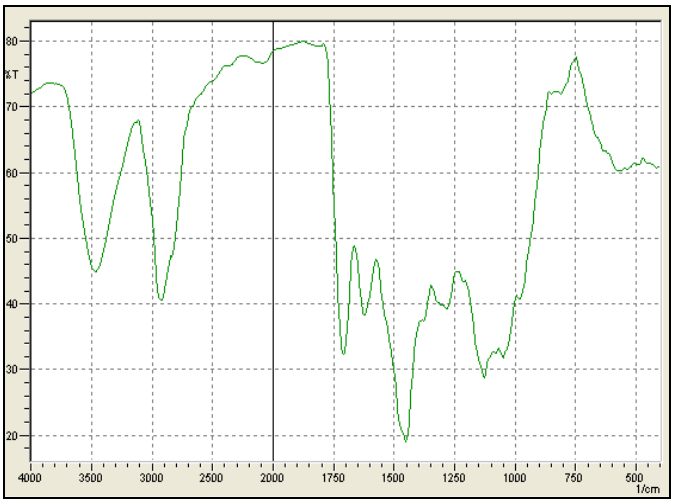

FIG. 3: FTIR SPECTRA OF CIPRO

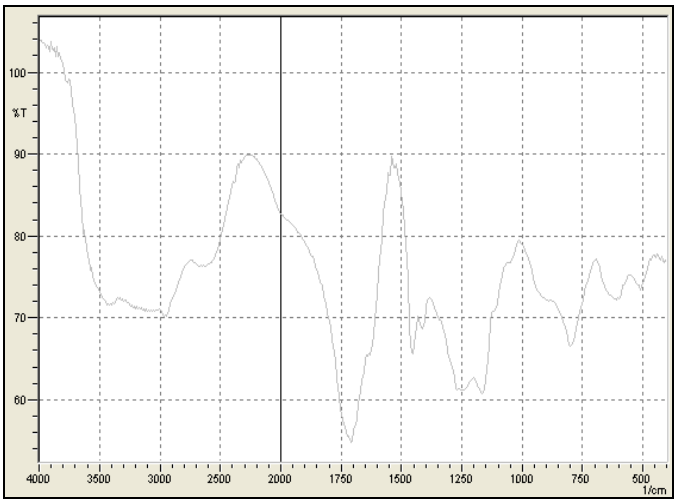

FIG. 4: FTIR SPECTRA OF C934

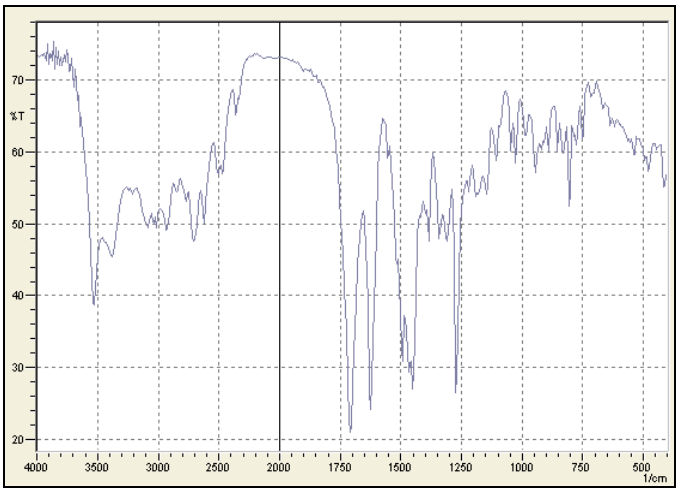

FIG. 5: FTIR SPECTRA OF HYDROGEL CONTAINING CIPRO AND C934

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, is 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. In case of hydrogel formulation, the probe directly dipped into hydrogel 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} (**Fig. 6, 7 and 8**).

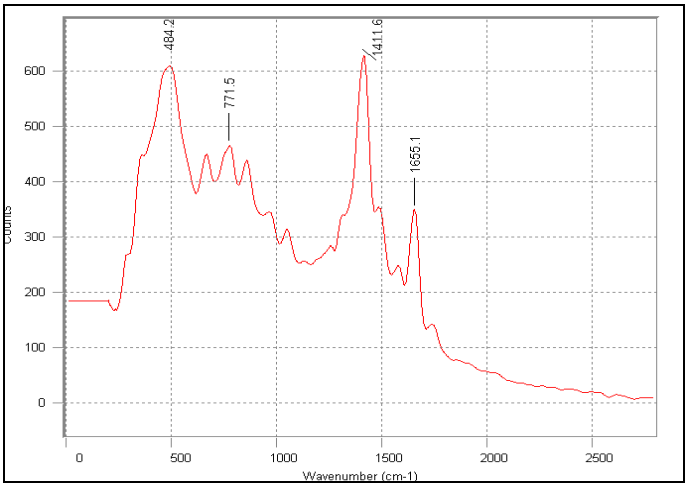

FIG. 6: RAMAN SPECTRA OF CIPRO

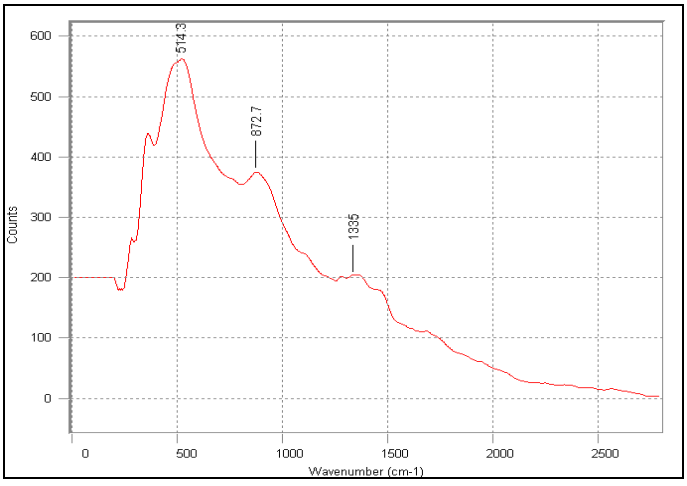

FIG. 7: RAMAN SPECTRA OF C934

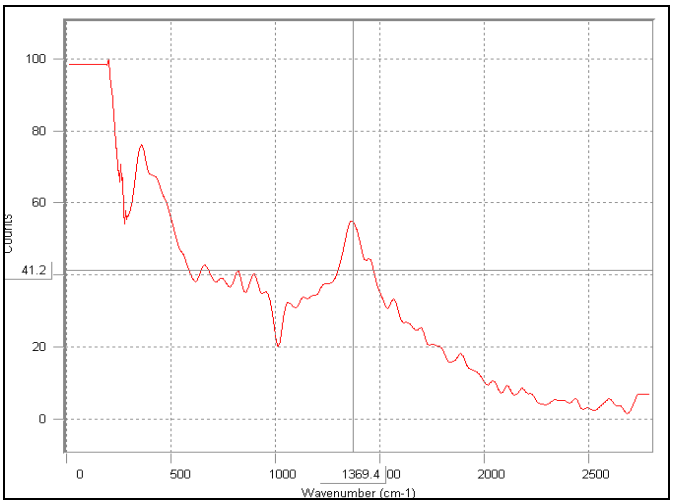

FIG. 8: RAMAN SPECTRA OF HYDROGEL CONTAINING CIPRO AND C934

RESULTS AND DISCUSSION:

Results of FTIR Study: While the FTIR band at 4000-1300 cm^{-1} represented functional group region, the appearance of strong absorption bands in the region of 4000 to 2500 cm^{-1} were 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 shifting in absorption to lower frequencies. The C-H stretching bands occurred in the region of 3300 to 2800 cm^{-1} [22] (**Table 1**).

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 the alkenes 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 bands at 1750 to 1700 cm^{-1} represented the carbonyl C=O stretching i.e., $\upsilon_{C=O}$. The peak at 1650 to 1600 cm^{-1} was assigned to quinolones. The bands at the 1450 to 1400 cm^{-1} represented υ_{C-O} and at 1300 to 1250 cm^{-1} suggested bending vibration of O-H group which indicates the presence of carboxylic acid. In addition, a strong absorption peak between 1050 and 1000 cm^{-1} was assigned to C-F group [23, 24] (**Table 1[a]**).

In case of C934, the FTIR spectra having peak between 3000-2950 cm^{-1} represented -OH stretching vibration, i.e., υ_{O-H} and intramolecular hydrogen bonding (Fig. 4). The prominent peak between 1750 and 1700 cm^{-1} was assigned to carbonyl C=O stretching band i.e., $\upsilon_{C=O}$. While the peak at 1450 to 1400 cm^{-1} was assigned to υ_{C-O} / δ_{O-H}, the band at 1250 to 1200 cm^{-1} was assigned to υ_{C-O-C} of acrylates [23, 25]. The ethereal cross linking, is proved by prominent peak at 1160 cm^{-1}, indicates stretching vibration of υ_{C-O-C} group. The band between 850 and 800 cm^{-1} was for out of plane bending of C=CH i.e., $\delta_{=C-H}$ [23, 26] (**Table 1[b]**).

In the FTIR spectra of hydrogel containing both Cipro and C934, the prominent band found between 3550 and 3500 cm^{-1} was assigned to υ_{O-H} and hydrogen bonding by single bridge (Fig.5).While the peak from 3450 to 3400 cm^{-1} was assigned to polymeric υ_{O-H} and hydrogen bonding, the band between 2650 and 2600 cm^{-1} represented the υ_{O-H} i.e., strong 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 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 [22, 23] (**Table 1[c]**).

Results of Raman Spectroscopic Study: Raman and FTIR are complimentary vibrational spectroscopic techniques. This aspect has been illustrated in the present study as well. There are band intensity

differences between the two techniques. Therefore, to obtain the more detailed information about chemical interaction both FTIR and Raman spectroscopic analyses are carried out [27, 28]. The results of Raman Spectroscopy of Ciprofloxacin showed the prominent bands at 484.22, 771.47, 1411.63 and 1655.11 cm^{-1} (Fig. 6). The peak at 1411.63 cm^{-1} was due to symmetric stretching vibration of O-C-O group of carboxylic acid [24]. A band at 1655.11 cm^{-1} was for symmetric stretching of the carbonyl group $\upsilon_{C=O}$ of the pyridone moiety. In contrast, the use of Raman Spectroscopy to quantify the presence of fluorine substituent was clearly suspected [29-33] (**Table 2[a]**).

Similarly the characteristic prominent Raman bands for C934 were observed at 350, 514.31, 872.69 and 1335.03 cm^{-1} (Fig. 7). The band at 872.69 cm^{-1} was due to 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 [33] (**Table 2[b]**).

The characteristics Raman peaks of hydrogels containing both Cipro and C934 were observed at 334.75, 812.50, 906.25, 1369.4, 1562.5 and 1703.12 cm^{-1} (Fig. 8). The band at 812.50 cm^{-1} was assigned to symmetric stretching vibration of C-O-C for acrylates and esters. The asymmetric stretching vibration of C-O-C was assigned to 906.25 cm^{-1}. The band at 1703.12 cm^{-1} was the characteristic of stretching vibration of carbonyl group of esters [34] (**Table 2[c]**).

TABLE 1: COMPARATIVE STUDY OF FTIR PEAKS

(a) Prominent FTIR Peaks of Ciprofloxacin		
PEAKS (cm^{-1})	**GROUPS**	**PEAK ASSIGNMENT**
3500-3450	Hydroxyl group	O-H stretching vibration, intermolecular H-bonded
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 C934		
PEAKS (cm^{-1})	**GROUPS**	**PEAK ASSIGNMENT**
3000-2950	Hydroxyl group	O-H stretching vibration, intramolecular
1750-1700	C=O group of acids	H-bonded
1450-1400	Carbonyl group of	υC=O stretching vibration
1250-1200	acids	C-O stretching vibration
1160	Acrylates	C-O-C stretching vibration
850-800	Etherial C-O-C group	Stretching vibration of C-O-C group
	Aromatics & enes	=C-H out of plane bending vibration
(c) Prominent FTIR Peaks of Hydrogel Containing Cipro and C934		
PEAKS (cm^{-1})	**GROUPS**	**PEAK ASSIGNMENT**
3550-3500	Hydroxyl group	H -bonding by single bridge
3450-3400	Polymeric OH groups	υO-H, H-bonding
2650-2600	Strong H- bonding	O-H stretching vibration
1650-1600	O-C-O group of acid	υ_{as} stretching vibration of O-C-O group
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

TABLE 2: COMPARATIVE STUDY OF RAMAN SHIFTS

(a) Prominent Raman Shifts of Ciprofloxacin	
RAMAN SHIFTS (cm^{-1})	**FUNCTIONAL GROUPS/VIBRATION**
484.22	Strong δ(CC) aliphatic chain
771.47	υ(CC) Alicyclic chain vibration
1411.63	υ_sO-C-O
1655.11	υ_s of C=O group of pyridone moiety
(b) Prominent Raman Shifts of C934	
RAMAN SHIFTS (cm^{-1})	**FUNCTIONAL GROUPS/VIBRATION**
350	Strong δ(CC) aliphatic chain
514.31	C-C-O bending vibration
872.69	υ(C-O-C) of acrylates
1335.03	υ_sO-C-O of acids
(c) Prominent Raman Shifts of Hydrogel Containing Cipro and C934	
RAMAN SHIFTS (cm^{-1})	**FUNCTIONAL GROUPS/VIBRATION**
334.75	δ(CC)aliphatic chain
812.5	υ(C-O-C) of acrylates/esters
906.25	υ(C-O-C) asymmetric
1369.4	υ_sO-C-O
1562.5	υ_{as}O-C-O
1703.12	υC=O medium

DISCUSSION: 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 specific narrow frequency range [23, 25, 35]. In case of FTIR spectra of Cipro, 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 can 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 Cipro (Table 1[a]).

In case of FTIR spectra of Carbopol934, 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 (Fig. 4). The peak for out of plane bending vibration of =C-H was found between 850 and 800 cm^{-1} (Table 1[b]).

While comparing the FTIR spectra among the pure Cipro and polymer C934, and the hydrogel containing both Cipro and polymer C934, 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 hydrogel might be due to formation of β-ketoesters (Fig. 3, 4 and 5). The FTIR peaks assigned to υ_{C-O} and υ_{C-O-C} representing acrylates and esters confirm the esterification between polymeric OH group and –COOH group of drug (Cipro). The stretching vibration of C-F group remains nearly unaltered. The another probability of interaction is 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} represent 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 are sharp while in intermolecular hydrogen bonding bands are broad. However, it is less broad than which is 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} gave the probability of out of plane bending of –ene bond and m-substitution of δ_{Ar-H} hydrogen atom [22, 23, 25] (Table 1[c]).

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} is due to probability of formation of β-ketoesters [36]. 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 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 3500-2700 cm^{-1} can 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 of 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 [24]. By comparing the FTIR spectra among the pure drug, Carbopol polymer (C934) and the hydrogel containing both drug and polymer, the FTIR peak of Cipro from 1750 to 1700 cm^{-1} was not detected in the hydrogel system probably due to interaction with polymer. The missing peak has been replaced with two very strong characteristic bands, in the range of 1650-1600 cm^{-1} and at 1450 cm^{-1}, were assigned to $\upsilon_{(O-C-O)}$ asymmetric and symmetric stretching vibrations respectively [23, 25]. 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} indicates the deprotonation of the carboxylic acid group and interaction between drug and polymer [37] (Table 1).

In case of Raman spectra of Cipro, the Raman band at 771.47 cm^{-1} is assigned to the stretching vibration of cyclopropyl group. The presence of carboxylic acid group was confirmed by υ_{O-C-O} and $\upsilon_{C=O}$ groups vibration at 1411.63 cm^{-1} and 1655.11 cm^{-1} respectively (Table 2[a]).

By comparing the Raman spectra of pure drug with the drug incorporated in the Carbopol hydrogel, the peak at was 1411.63 cm^{-1} was assigned to the $\upsilon_{s\ O-C-O}$ is not prominent. However, both symmetric and asymmetric stretching vibrations of O-C-O group are found in hydrogel containing C934. The Raman peak for stretching vibration of C=O is prominent in the hydrogel. From this it is clear that there is esterification reaction between the Cipro 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 bondings are also prominent from the FTIR spectra of the hydrogels.

CONCLUSION: On the basis of above interpretation, it can be concluded that by preparing hydrogel of Ciprofloxacin with Carbopol polymer (C934) following a novel method of 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 hydrogel 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 Carbopol934 polymer may function as a useful carrier for the Cipro molecule. The main advantage of the present investigation is that higher Cipro drug loading would be possible in dosage forms as compared to alternate formulation strategies, such as conventional solid dispersions.

Here, Cipro interacts with the polymer monomerically. The release of drug from the hydrogel system is very slow because the carboxylic group of Cipro has already interacted 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 form hydrogen bonding with the polysaccharides and proteins of mucosa in the acidic condition of the stomach.

On the other hand, hydrogel is highly swollen and stiffened in an alkaline condition of the intestine showing a very good mucoadhesive property of the hydrogel in the gastrointestinal mucosa. This leads 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 hydrogel would be monitored and controlled.

REFERENCES:

1. Petri WA (Jr): Goodman and Gilman's the Pharmacological Basis of Therapeutics. Mc Graw-Hill, New York, Tenth Edition, 2001: 1179-1183.
2. Mitscher LA: Principle of Medicinal Chemistry. B. I. Warverly Pvt.Ltd, New Delhi, Fifth Edition, 1995: 759-802.
3. Federico P, Rosanna M, Massimo B, Emilio L, Giovanni T and Mario F: Ciprofloxacin Disposition in Elderly Patients with LRTI Being Treated with Sequential Therapy (200mg Intravenously Twice Daily Followed by 500 mg Per Os Twice Daily): Comparative Pharmacokinetics and the Role of Therapeutic Drug Monitoring. Therapeutic Drug Monitoring 2000; 22(4): 386-391.
4. Wilton LV, Pearce GL and Mann RD: A comparison of ciprofloxacin, norfloxacin, ofloxacin, azithromycin and cefixime examined by observational cohort studies. British Journal of Clinical Pharmacology 2003; 41(1): 277-284.
5. Kumar S, Jeevangi R, Manjunath S and Wali VK: A case of Ciprofloxacin induced erythema multiform. Indian Journal of Pharmacology 2008; 40(1): 45-46.
6. Ciprofloxacin; Available from http://en.wikipedia. Org/wiki/ciprofloxacin, accessed on 13.01.2010.
7. (WO/2006/007354) A Drug/Polymer Complex, Preferably Ciprofloxacin/HPMC, its method of manufacturing using lyophilization and Its use in an Osmotic Device; Available fromhttp://www.wipo.int/pctdb/en/wo.jsp?WO=2006007354&IA=US2005020356&DISPLAY=DESC, accessed on 13.01.2010.
8. Satyanarayana S and Babu K: Advances in Controlled and Novel Drug Delivery. CBS Publisher and Distributors, New Delhi**,** First Edition (Reprint), 2005**:** 98-101.
9. Hui HW, Robinsion JR and Lee VHL: Controlled Drug Delivery-Fundamentals and Application. Marcel Dekker, Inc., New York, Second Edition, 2005: 373-432.
10. Hosmani AH: Carbopol and its Pharmaceutical Significance: A Review; Available from http://www. pharmainfo.net/reviews/carbopol-and-its-pharmaceutical significance- review, accessed on 20.01.2010.
11. Qiu Y and Park K: Environment-sensitive hydrogels for drug delivery. Advanced Drug Delivery Reviews 2001; 53(3): 321-339.
12. 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. Journal of Controlled Release 1995; 37(1-2): 105-111.
13. Bromberg LE and Ron ES: Temperature-responsive gels and thermogelling polymer matrices for protein and peptide delivery. Advanced Drug Delivery Reviews 1998; 31: 197-221.
14. 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.

15. Galaev IY and Mattiasso B: 'Smart' polymers and what they could do in biotechnology and medicine. Trends in Biotechnolology 1999; 17(8): 335-340.
16. Jeong B andGutowska A: Stimuli-responsive polymers and their biomedical applications. Trend in Biotechnology 2001; 20: 305-311.
17. Gupta P, Vermani K and Garg S: Hydrogels: from controlled release to pH-responsive drug delivery. Drug Discovery Today 2002; 7: 569-579.
18. Yoshida R, Sakai K, Okana T and Sakurai Y: Pulsatile drug delivery system using hydrogels. Advanced Drug Delivery Reviews 1993; 11: 85-108.
19. Guo JH: 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.
20. Pharmaceutical Bulletins; Available from http://www.lubrizol.com/pharmaceutical/literature/bulletins.html, accessed on 05.01.2010.
21. Leung SH, Irons BK and Robinsion JR: Polyanionic hydrogel as a gastric retentive system. Journal of Materials Science 1995; 4(5): 483-492.
22. Hsu CPS: Infrared Spectroscopy; Available from http://www.prenhall.com/settle/chapters/ch15.pdf, accessed on 20.01.2010.
23. Dani VR: Organic Spectroscopy. Tata McGraw-Hill Publishing Company Limited, New Delhi, First Edition, 1995: 86-168.
24. Tom RT, Suryanarayana V, Reddy PG, Baskaran S and Pradeep T: Ciprofloxacin protected gold nanoparticles. Langmuir 2004; 20(5): 1909-1914.
25. Silverstein RM and Webster FX: Spectrometric Identification of Organic Compounds, Jhon Wiley and Sons, New York, Sixth Edition 2002: 71-109.
26. Gruodis A, Alkasa V, Powell DL, Nielsen CJ, Guirgis GA and Durig JR: Vibrational spectroscopic studies, conformations and ab initio calculations of 1, 1, 1 trifluoropropyltrifluorosilane. Journal of Raman Spectroscopy 2003; 34: 711-724.
27. Venkeirsbilck T, Vercauteren A, Baeyens W, Weken GVD, Verpoort F,Vergote G and Remon JP: Applications of Raman Spectroscopy in pharmaceutical analysis. Trends in Analytical Chemistry 2002; 21(12): 869-877.
28. Clarke RH, Londhe S, Premasiri WR and Womble ME: Low-Resolution Raman Spectroscopy: Instrumentation and Application in Chemical Analysis. Journal of Raman Spectroscopy 1999; 30: 827-832.
29. Curman D, Zivec P, Leban I, Turel I, Polishchuk A, Klika KD, Karaseva E and Karasev V: Spectral properties of Eu(II) compound with antibacterial agent ciprofloxacin(cfqH). Crystal structure of $[Eu(cfqH)(cfq)H_2O)_4]Cl_2$ $.4.55H_2O$. Polyhedron 2008; 27: 1489-1496.
30. Skoulika SG and Georgiou CA: Rapid Quantitative Determination of Ciprofloxacin in Pharmaceuticals by Use of Solid-State FT-Raman Spectroscopy. Applied Spectroscopy 2001; 55(9): 1259-1265
31. Georgiou CA: Analytical Raman Spectroscopy; Available from http://www.aua.gr/georgiou/page82.html, accessed on 20.01.2010.
32. Lawrence BA, Lei Z, Liling Z, Christopher LE and Andrew RB: Solid-State NMR Analysis of Fluorinated Single - Carbon Nanotubes: Assessing the extent of Fluorination. Chemistry of Materials 2007; 19(4): 735-744.
33. Raman Data and Analysis; Available from http://www.horiba.com/fileadmin/uploads/scintific/Documents/Raman/bands.pdf, accessed on 20.01.2010.
34. Agarwal UP, Reiner RS, Pandey AK, Ralpha SA, Hirth KC and Atalla RH: Raman Spectra of Liginin Model Compounds; Available from http://www.treesearch.fs.fed.us/pubs/20194, accessed on 20.01.2010.
35. CRC Handbook of Chemistry and Physics, (Ed: Lide DR), CRC Press, Boca Raton, Eightyfourth Edition 2003-2004, 9-79.
36. Garrido NJ, Perello L, Ortiz R, Alzuet G, Alvarez MG, Canton E, Gonzalez ML, Granda SG and Priede MP: Antibacterial studies, DNA oxidative cleavage, and crystal structure of Cu(II) complexes with two quinolone family members, ciprofloxacin and enofloxacin. Journal of Inorganic Biochemistry 2005; 99: 677-689.
37. Efthimiadou EK, Psomas G, Sanakis Y, Katsaros N and Karaliota A: Metal complexes with the quinolone antibacterial agent N-propyl-norfloxacin: Synthesis, structure and bioactivity. Journal of Inorganic Biochemistry 2007; 101: 525-535.

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