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Synthesis and spectral characterization of fluoroquinolone-ofloxacin

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Abstract
The vibrational spectroscopy, such as FTIR has been used to measure the vibrational modes of fluoroquinolones, provides information about structural differences of its individual members. From the interpreted spectral data Ofloxacin has been distinguished by the presence of different substituents in their parent nucleus. FTIR study provides the most direct and definitive identification of fluoroquinolones and offer a means for qualitative analysis of newly synthesized fluoroquinolone-ofloxacin.

Keywords: Synthesis, Characterization, fluoroquinolone, vibrational

1. Introduction
Fluoroquinolones have been associated with a significant number of serious adverse drug reactions such as tendon damage [1] and peripheral neuropathy, such as reactions may manifest long after therapy had been completed and in severe cases may result in lifelong disabilities [2]. They are associated with severe psychiatrie [3, 4] adverse reactions. The reaction was detailed within Stephen Fried's book Bitter Pills (1999). Hepatotoxicity has also been reported with the use of some fluoroquinolones [5, 6].
Ofloxacin, one of the fluoroquinolones, has not been shown to be effective in the treatment of syphilis [7, 8] like other fluoroquinolones. Some fluoroquinolones are effective for the treatment of certain sexually transmitted diseases due to bacterial resistance. Some of them are broad spectrum antibiotic that is active against both gram-positive and Gram-negative bacteria. They act by inhibiting DNA gyrase a type-II topoisomerase and topoisomerase-IV [9] which is an enzyme necessary to separate replicated DNA thereby inhibiting bacterial cell division. The fluoroquinolones interfere with DNA replication by inhibiting an enzyme complex called DNA gyrase. This can also affect mammalian cell replication. Some fluoroquinolones may cause injury to the chromosome of eukaryotic cells [10].

Materials and Methods
Materials
All chemicals are analytical grade purchased from CDH and Merck. Melting points are determined in an open capillary tube and are uncorrected. An infrared spectrum has been recorded in KBr on Perkin-Elmer RXI spectrometer at CDRI, Lucknow. The ^{1}H-NMR were measured in $CDCl_3$ solution on a brucker DRX-300 MHz spectrometer using tetramethyl silane (TMS) as an internal reference and chemical shift in ppm at CDRI, Lucknow. Elemental analyses were carried out with elementar vario El, III elemental analyser at department of biotechnology IIT, Kharagpur.

Synthesis of Ofloxacin
The compound-11 was refluxed in autoclave at 150 ^{0}C for two hours. Sodium hydroxide was with continuous stirring for 10 minutes. Thereafter, 10 g of N-methylpiperazine was added and the mixture was added and the mixture was refluxed for 30 hrs in a 250 ml of three necked flask equipped wath a reflux condenser and mechanical stirrer. Sodium carbonate was added until the mixture was alkaline. The excess solvent was removed by steam distillation. The residual solution was kept in a refrigerator until crystallization was completed. The solution was filtered on a Buchner funnel and washed with 10 ml of saturated sodium chloride solution.
Now, the solution of 40 g of sdium hydroxide in 160 ml of water was added in a one liter round bottomed flask equipped with a reflux condenser. The mixture was heated to boil until the compound was disappeared. The reaction mixture was diluted with an equal volume of water. When cold, the reaction product was poured with vigorous stirring into 125 ml of concentrated hydrochloric acid. Then, it was allowed to cool at room temperature. The compound was filtered at the pump and washed with a little water and characterized. It is crystalline in nature.

Table 1: elemental analysis (in %)

	C	H	N
Found	59.83	5.54	11.63
Calculated	59.82	5.52	11.62

Pure samples of ofloxacin ($C_{18}H_{20}FN_3O_4$) and ciprofloxacin ($C_{17}H_{18}FN_3O_3$) were obtained from external agency. The drugs were of 99.8% to 98.0% purity.

Methods
FTIR Spectroscopy is an important analytical 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. Here KBr pellet method was used for sample preparation for FTIR study13. 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.

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) [11]. 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 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} 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 [12] in the region of 3300 to 2800 cm^{-1}.

In FTIR spectra of Ofloxacin, 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. This band also suggested the NH stretching vibration of the imino-moiety of piperazinyl groups 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., $\upsilon C=O$ [13]. 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 the 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 [14, 15].

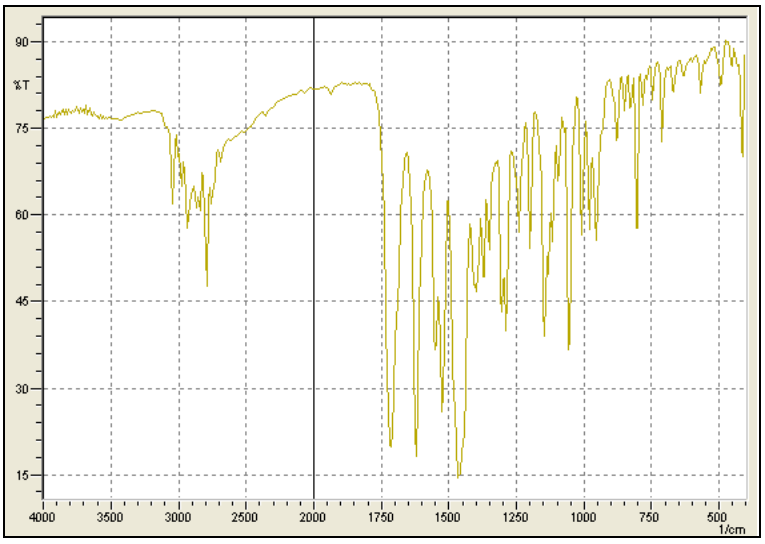
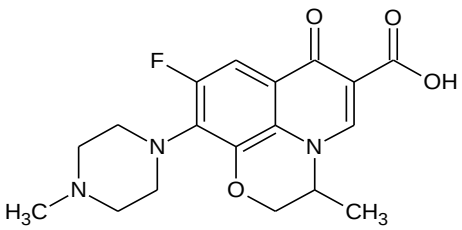


Fig 1: IR Spectrum of Ofloxacin

Conclusion

On the basis of FTIR spectral analysis of Ofloxacin, the structure of fluoroquinolone-ofloxacin may be drawn as:



Ofloxacin

Fig 2

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