International Journal of Scientific Research in Physics and Applied Sciences
Vol.9, Issue.3, pp.11-14, June (2021)
Research Paper
E-ISSN: 2348-3423

Spectroscopic study of Enalapril Maleate and Hydrochlorothiazide

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Available online at: www.isroset.org

Received: 20/Apr/2021, Accepted: 26/May/2021, Online: 30/Jun/2021

***Abstract*—** In this work, Raman and Fourier Transform Infrared (FTIR) Spectroscopic techniques are utilized. For the study, Q-Pil 5 and Aquazide tablets were collected from the Banepa Hospital and Education Pvt. Ltd., Banepa, Kavre, which were the merchandise of Quest Pharmaceuticals P. Ltd., Birgunj, Nepal. The Q-Pil 5 and Aquazide contain enalapril maleate and hydrochlorothiazide, respectively, as active ingredients. Spectra of those samples are obtained with help of the EnSpectr Raport instrument (Raman) and FTIR instrument. The main peaks are obtained within the range 1000 -1700 cm^{-1} in Raman spectra and therefore the range 500 -1800 cm^{-1} in FTIR spectra. The functional groups corresponding to the main peaks are assigned. These functional groups observed in Raman and FTIR spectra were discovered to be present in the tablets' molecular structure. Hence, this study confirms the reliability of those products available within the market.

***Keywords*—** Raman spectroscopy, Fourier transform infrared spectroscopy, Enalapril Maleate, Hydrochlorothiazide

I. INTRODUCTION

1.1 Hydrochlorothiazide

Aquazide tablet contains hydrochlorothiazide as active ingredients. The thiazide medication prototype is hydrochlorothiazide (6-chloro-3, 4-dihydro-2H-1,2,4-benzothiadiazine-7-sulphonamide-1,2 -dioxide). These medications are part of an important class of diuretics. Hydrochlorothiazide is used to treat edemas of the gastrointestinal tract (congestive heart failure), liver (hepatic cirrhosis), and kidneys (nephrotic syndrome, chronic kidney failure, acute glomerulonephritis). It has also been used for all levels of hypertension, and it is equally effective as other antihypertensive medications. [1]. Chemical formula of hydrochlorothiazide is $C_7H_8ClN_3O_4S_2$, its relative molecular mass is 492.525 g/mol and its molecular structure is given in figure 1 below.

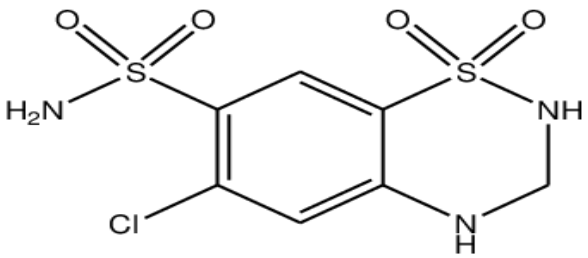

Figure 1. Molecular Structure of Hydrochlorothiazide.

1.2 Enalapril Maleate

Q-pil tablet contains enalapril maleate as the active ingredients. enalapril maleate is the maleate salt of enalapril, the ethyl ester of enalaprilat, a long-acting angiotensin-converting enzyme inhibitor. Enalapril maleate is chemically described as (S)-1-[N-[1-(ethoxy carbonyl)-3-phenylpropyl]-L-alanyl]-L-proline, (Z)-2-butenedioate salt (1:1). Enalapril is used to treat high sign (hypertension) in adults and kids who are a minimum of 1 month old. Enalapril is also used to treat adult congestive heart failure. It is also used to treat ventricular disfunction (problems with the lower chambers of the gut that allow blood to enter the heart). This disease has the potential to damage the ability of heart to pump blood throughout the body. [2]. Its formula is $C_{20}H_{28}N_2O_5{\cdot}C_4H_4O_4$ and its relative molecular mass is 297.73 g/mol and its molecular formula is shown in figure 2 below.

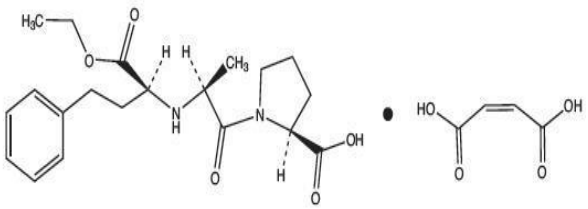

Figure 2. Structural formula of Enalapril Maleate.

II. RELATED WORK

Spectroscopic studies were mainly focused to determine the fingerprint of materials. Several research works were carried out on the spectroscopic study of different materials. In 1928, Chandrasekhara Venkata Raman (C.V. Raman) discovered inelastic scattering of light, also known as the Raman effect. [3] The mercury arc became the principle light source, first with photographic detection and then with spectrometric detection.

Skoulika [4] and coworkers quantified methyl-parathion, fethion, and diazinon in pesticide formulations, as well as ciprofloxacin in pharmaceutical solid dosage forms. L. S. Taylor and F.W. Langkilde [5] conducted research on Evaluation of solid-state forms present in tablets by Raman spectroscopy in enalapril maleate of form I and form II polymorphs. In the study, the FT-Raman spectroscopy is a beneficial supplement to or alternative to existing techniques for investigating the solid-state form of a medication contained in intact tablets.

This research work is to collect and record the spectrum of enalapril maleate (Q-pil) and hydrochlorothiazide (Aquazide), to determine the position and relative intensity of Raman spectra and Infrared spectra: thereby, proposing its internal identification and spectral examination of the results and finally comparison of the results.

III. METHODOLOGY

3.1 Materials

Enalapril maleate (Q-pil) and hydrochlorothiazide (Aquazide) in tablet form were converted into powder form and used. Banepa Hospital and Education Pvt. Ltd., Banepa, Kavre, kindly offered it. Then the spectral analysis of those pharmaceuticals products was administered.

3.2 Raman Spectroscopy

Raman spectra were recorded using EnSpectrRaport Instrument. This device is employed to live analysis of the spectra and is additionally utilized in the identification of drugs by a comparative study of spectra. EnSpectr enables not only to live Raman spectra of diverse substances but also recognize them by the comparative study of the spectra. It takes few seconds to live the spectrum of an unknown substance, to work out the position and relative intensity of Raman lines. It has spectrum range of 90−4000 cm^{-1} and a focal distance of 50 mm. EnSpectrRaport is provided with a coffee noise 3648-element linear array of CCD detectors for the measurement of intensity and spectral parameters of scattered light. It is connected to a laptop to rework the obtained data. For this work, we expose the sample under analysis to the visible range beam. The light that has been dispersed is collected and its spectrum is evaluated. EnSpectrRaport Instrument allows in measuring and recognizing the spectrum of the substance and compares measured spectrum with reference spectra stored during a spectral database, if available, and thus recognizes acquired spectra [6]. Based upon the spectra we will determine the functional group present within the compound.

3.3 Infrared Spectroscopy

The Fourier Transform Infrared Spectrometer was used to record the infrared spectra of the sample. When IR radiation is applied to the sample, part of the radiation is absorbed by the sample and some goes through. The resulting signal at the detector might be a spectrum displaying the chemical "fingerprint" of the sample. Infrared spectroscopy is useful because different chemical structures (molecules) produce different spectral fingerprints. The Fourier Transform converts a readable spectrum from the detector output. The FTIR generates spectra that contain patterns that provide structural information. The FTIR employs interferometry to collect data from a few materials put within the IR beam. The Fourier Transform produces spectra which could be used by analysts to identify or quantify the item. To create an FTIR spectrum, interferograms are 'decoded' into recognizable spectra. Because molecules have distinct infrared fingerprints, patterns in spectra help in sample identification.

IV. RESULTS AND DISCUSSION

4.1 Raman spectral analysis of Enalapril Maleate (Q-Pil)

Enalapril maleate contains functional groups such as amine, alcohol, alkane carbonyl, and so on. Various peaks were obtained between Raman shifts of 100-4000 cm^{-1}. Several peaks were observed in the frequency range 200-1600 cm^{-1}, figure 3.

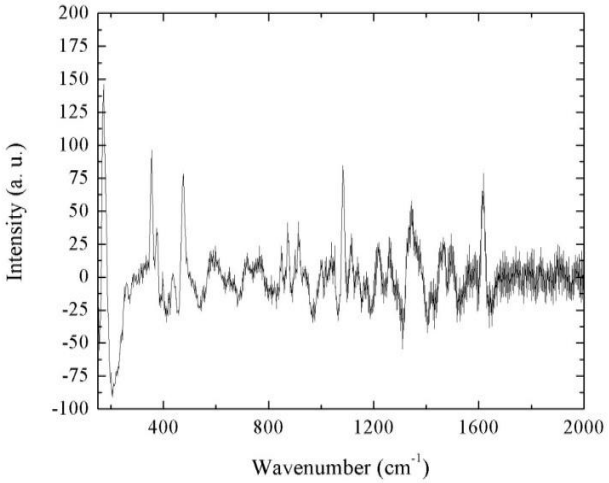

Figure 3. Raman spectrum of Enalapril Maleate (Q-Pil)

The Raman shift of 1660-1740 cm^{-1} is due to the vibration of the benzene ring (aromatic Compounds), or due to the vibration of C=O group (carbonyl group), or COOH group (carboxylic acid), or C=C group (alkene). The Raman shift of 1500-1600 cm^{-1} is due to the vibration of the N-H bond (amine). The Raman shift of 1000-1250 cm^{-1} was due to the vibration of the C-N bond (amine). The Raman shift of 1200-1400 cm^{-1} was due to the vibrations of the C-H group (alkane) ([7].

4.2 Raman spectral analysis of Hydrochlorothiazide (Aquazide)

Hydrochlorothiazide contains functional groups such as amine, alcohol, alkane, carbonyl, and so on. Various peaks were obtained between Raman shifts of 100-4000 cm^{-1}, figure 4.

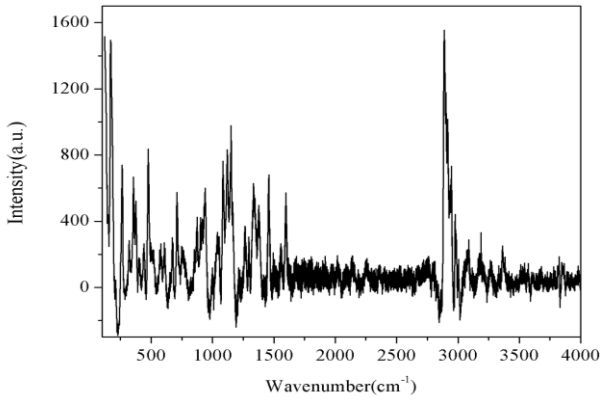

Figure 4. Raman spectrum of Hydrochlorothiazide (Aquazide)

The Raman shift of 1615-1590 cm^{-1} is due to the vibration of the benzene ring (aromatic compound). Raman shift of 1500-1600 cm^{-1} was due to the vibration of the N-H bond (amine) present in hydrochlorothiazide. Raman shift of 1000-1250 cm^{-1} and 750-833 cm^{-1} was due to the vibration of the C-N bond (amine). Raman shift of 1200-1400 cm^{-1} is due to the vibrations of the C-H group (alkane). Raman shift of 1615-1590 cm^{-1} and was due to the vibration of the Aromatic-hetero ring. Raman shift of 1050–1210 cm^{-1} was due to the vibrations of the Sulfonamide group [8].

4.3 FTIR spectral analysis of Enalapril Maleate (Q-Pil)

FTIR spectra observe in Q-pil are shown in figure 5. The sharp absorption peak just below 1550-1640 cm^{-1} was due to the presence of the N-H bond (amine group) present in the enalapril maleate molecule. The peak at around 1670-1820 cm^{-1} is due to the absorption of IR by C=O (carbonyl group). The absorption band at 1070-1150 cm^{-1} was due to C-O (ether group). The peak at 1080-1360 cm^{-1} was due to C-N amine (stretch). The peak at 1610-1640 cm^{-1} was due to C=C (alkene). The peak at 1210-1230 cm^{-1} was due to the benzene ring and at 980-1040 cm^{-1} was due to the carbon ring [9].

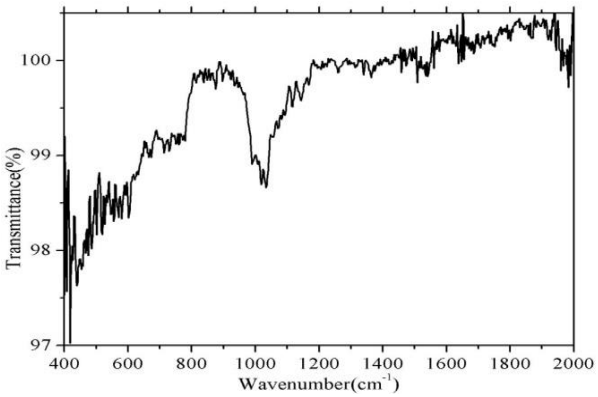

Figure 5. FTIR spectra of Enalapril Maleate (Q-Pil).

4.4 FTIR spectral analysis of Hydrochlorothiazide (Aquazide)

The FTIR spectra observe in hydrochlorothiazide are shown in figure 6. The sharp peak just below 1550-1640 cm^{-1} was due to the presence of the N-H bond (amine group) present in the hydrochlorothiazide molecule. The peak at around 980-1225 cm^{-1} was due to the absorption of IR by S=O (sulfoxides group). The absorption band at 570-710 cm^{-1} was due to C-S (sulfides group). The peak at 1080-1360 cm^{-1} was due to C-N (amine group). The peak at 1610-1640 cm^{-1} was due to the C=C (alkene group) of aromatic compounds. The peak at 1210-1230 cm^{-1} was due to the benzene ring and at 980-1040 cm^{-1} was due to the carbon ring. The peak at around 700 cm^{-1} is due to S-N (sulfonamide group) [10].

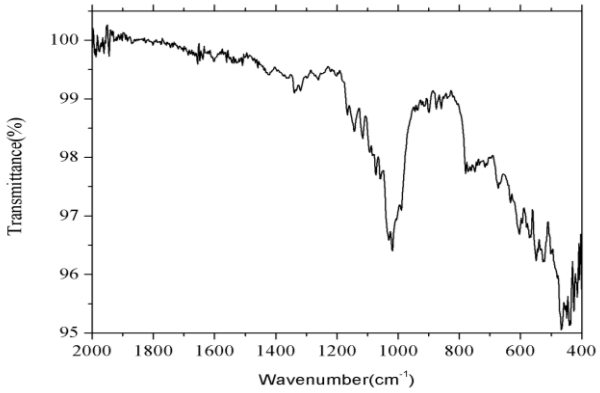

Figure 6. FTIR spectra of Hydrochrolothiadize (Aquidize)

V. CONCLUSION

In enalapril maleate, from Raman spectroscopy, we see that the major groups present are carbonyl (C=O), alkene (C=C), carboxylic acid (COOH), benzene ring (Aromatic compound), and amine (C-N). From FTIR measurement, the groups such as carbonyl and amine are observed. In addition, the absorption bands of the C-O group, carbon ring, and benzene ring are also observed which were unidentified by the Raman method. The comparison of observed Raman and FTIR spectra of Enalapril Maleate is presented in table 1.

Table 1: Comparison of observed Raman and FTIR spectra of Enalapril Maleate

Proposed assignment (Functional group)	Wavenumber (cm^{-1}): [Raman]	Proposed assignment (Functional group)	Wavenumber (cm^{-1}): [FTIR]
N-H Amine	1500-1650	N-H amine (bending)	1550-1640
C-N Amine	1000-1300	C-N amine (stretch)	1080-1360
Benzene ring (aromatic compounds)	1615-1590	-	-
C-H Alkane	1200-1400	-	-
C=O Carbonyl	1600-1700	C=O carbonyl (stretch)	1670-1820
C=C Alkene	1600-1660	C=C alkene (stretch)	1610-1640
COOH Carboxylic acid	1610-1740	-	-

-	-	Benzene ring	1210-1230
-	-	Carbon ring	980-1040
-	-	C-O ether (stretch)	1070-1150

In hydrochlorothiazide, from Raman spectroscopy, we see that major groups detected are alkane(C-H), amine(C-N), benzene ring (aromatic compounds), and aromatic hetero-ring. From FTIR spectroscopy, we see that the major groups present are sulphides (C-S), sulfoxide (S=O), carbon ring, and benzene ring. The observed Raman and FTIR spectra of hydrochlorothiazide are compared in table 2.

Table 2: Comparison of observed Raman and FTIR spectra of Hydrochlorothiazide

Proposed assignment (Functional group)	Wavenumber(cm^{-1}): [Raman]	Proposed assignment (Functional group)	Wavenumber (cm^{-1}): [FTIR]
C-N Amine	1000-1300	C-N Amine (stretch)	1080-1360
N-H Amine	1500-1650	N-H Amine(bending)	1550-1640
Sulfonamide	1050–1210	S-N Sulfonamides (stretch)	Around 700
Aromatic-hetero ring	1550–1610	-	-
Benzene ring (aromatic compounds)	1615-1590	-	-
C-H Alkane	1200-1400	-	-
-	-	Carbon ring	980-1040
-	-	C-S Sulphides	570-710
-	-	S=O Sulfoxide (stretch)	980-1225
-	-	Benzene ring	1210-1230

From the comparison of Raman and FTIR spectroscopy, the additional groups are also identified, this is due to the difference of basic principle in which they work. The Raman spectroscopy is due to the inelastic scattering of radiation by the molecule and the FTIR spectrum is due to the absorption of the Infrared spectrum by the molecule. It is found that these functional groups observed in Raman and FTIR spectra are as expected by the molecular structure of the tablets. Hence, this study confirms the reliability of these products available in the market.

ACKNOWLEDGMENT

We would like to acknowledge The World Academy of Sciences for the grant support to purchase the Raman Spectrometer used to obtain the Raman spectra and Central Department of Chemistry, Tribhuvan University for the FTIR instrument to take FTIR spectra.

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