Research Article

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Spectroscopic Investigation and Vibrational Assignments on Life Saving Pharmaceutical Compounds

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ABSTRACT

The present investigation presents the vibrational spectra and analysis of anti-bacterial pharmaceutical compounds viz., Tetracycline and Ampicillin. These compounds of pharmaceutical interest are frequently used for the treatment of fatal bacillary coccal infections. The spectra of these pharmaceutical compounds are complex and exhibited sever group vibrational frequencies. The characteristic vibrational frequencies of these drugs have been identified and assigned on the basis of their relative intensity, characteristic position and correlation with vibrational band of related compounds.

KEYWORDS: Chemotherapeutic agent; Bacteria viruses; Gram positive; Gram negative; Chloroform; C-H Stretching; Dimethyl bending and hetero-cyclic

INTRODUCTION

There is general possible way to determine the standard regimen of drug which will have reasonable effect and will be provided based on the age and weight of the administered. Most drugs act by combining specific receptors acted on the cells within the larger tissue. Only a very small portion of the total drug reaches the receptor. The remaining portions are lost by the processes of absorption, distribution and elimination. These processes determine the concentration of the drug in the given tissue at any particular time administration. Pharmaco-dynamics applies to the study of those aspects of drug behavior which relate to its actions or effect. The term Pharmaco-kinetics applies to the study of the factors that determine its effective concentration at the site of action. According to Pharmaco-kinetics, the variability of response to drugs it due to the differences in the blood and tissue concentrations from one person to another.

Many drugs fall into one to two broad categories, chemotherapeutic and compound action on the central nervous system. Chemotherapeutic agent is a substance that inhibits or destroys a infectious organism such as pathogenic bacteria or parasites which have invaded the host. Antibiotics are chemotherapeutic agent that are produced by micro- organisms and are toxic to other organisms, particularly bacteria and viruses. Tetracycline and ampicillin are the major drugs and since they become available in 1945 it has saved thousands of human lives from fatal bacillary infection like plague.

Tetracyclines are characterized by their exceptional chemotherapeutic efficacy against a wide range of Gram Positive and Gram-negative bacteria, rickettsia, spirochetes and large viruses, such as members of the lymphogranuloma group. Tetracycline inhibits a lot of enzyme reactions essential for vital processes of bacterial cells. The most sensitive biochemical reaction that is inhibited is the synthesis of proteins. Tetracycline works by binding specifically to the 30S ribosome of the bacteria, preventing attachment of the aminacyl tRNA to the RNA ribosome complex. It simultaneously inhibits other steps of the protein biosynthesis. Tetracycline can also alter the cytoplasmic membrane and this in turn causes leakage of nucleotides and other compounds out of the cell. This does not directly kill bacteria but instead inhibit.

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Ampicillin is an antibiotic in the penciling group of drugs. It fights bacteria in your body. Ampicillin is used to treat many different types of infections caused by bacteria, such ear infections, bladder infections, pneumonia, gonorrhea and *E.coli* or *salmonella* infection. Ampicillin is an antibiotic useful for the treatment of number of bacterial infections. It is taken orally or intravenously. It is active against many gram positive and gram negative bacteria.

Experimental

The high pure pharmaceutical compounds of tetracycline and ampicillin are procured in a tablet form standard medical shop. All of the pharmaceutical compounds that are fabricated are in the powered form. Description and solubility of the compounds under present investigation are referred from pharmaceutical data. Ampicillin is a white crystalline powder soluble in 170 parts of water. It is practically insoluble in ethanol, in chloroform and in acetone. Tetracycline is a white crystalline powder soluble in water and insoluble in ethanol. Infrared spectra of these compounds are recorded over regions of 450-1000 cm^{-1},1000-1800 cm^{-1} and 1800 -4000 cm^{-1} using Perkin Elmer FTIR-ATR Spectrophotometer.

Vibrational Band Assignments

The fabrication and production of life savings drugs play an important role in our daily life. The purity of the drugs become very important. Hence, during the fabrication of the drugs, various raw materials that are available for quality checking. For checking the quality of raw materials spectroscopist needs a sophisticated instruments like Infrared and UV-Visible absorption spectrophotometers. Usually after fabrication, the drugs are tested at the laboratory by its description, colour identification and by observing its characteristic melting point. Hence, the drugs in the present investigations have proper identification test.

(i) Ampicillin is (6R) -6- (a-Phenyl -D-Glycylamino-pencillin acid). Infrared spectrum has a characteristic vibrational band that are concordant with reference spectrum of ampicillin drug. It is identified by its melting point. It is also identified by suspending 10mg of tetracycline in 1 ml of water and 2ml of mixture of potassium cupri-tartrate solution and 6ml of its added. A magnets-violet colour is produced. It has light absorption at about 325 nm.

(ii) Tetracycline is (4S,4aR,5aR,6S,12aS)-4-dimethylamino 1-4,4a,5,5a,6,11,12a-octohydro-3,6,10,12,12a-Pentahydroxy-6-methyl-1,11dioxynapthacene -2-carboxaminde. It can be identified by adding 2 ml of Sulphuric acid with 0.2 mg of tetracycline, intense violet colour is produced. Further addition of 1 ml of water changes violet colour to deep yellow colour. This confirms the test.

Further, a qualitative test of the drugs has been made by recording infrared spectra in the region of 450-1000 cm^{-1},1000-1800 cm^{-1} and 1800-4000 cm^{-1}. The frequencies observed in the spectra of the drugs are summarized and their band assignment are presented in the Table 1,2 and the spectra are shown in Figure 1,2.

Table 1: Fourier transform infrared spectrum and vibrational frequencies of tetracycline.

Infrared Frequency (Cm^{-1})	Intensity	Description
464	S	C-C-out of plane bending
488	S	C-C-out of plane bending
520	VW	C-C-out of plane bending
572	M	C-C out –of-plane
639	M	C-C in plane bending/ aromatic
		C-C out of plane bending
669	VS	Aromatic C-H out-of-plane bending
692	S	Aromatic C-H out-of-plane bending
744	M	Aromatic C-H out-of-plane bending /C-C stretching/ C-C stretching of breath type
771	M	C-C stretching / aromatic C-H out of plane bending / C-C stretching /C-C stretching / C-C stretching / C-C stretching of breath type.
796	W	C-C stretching / aromatic C-H out of plane bending /C-C stretching /C-C stretching of breath type.
823, 839	M	C-N Stretching
862	VS	C-N Stretching
949	M	C-N Stretching
964	S	C-N Stretching
1003	S	C-O stretching /C-H in plane bending
1034, 1060	S	C-O stretching/ C-N stretching / C-H in plane bending
1112	M	C-C stretching/ C-N stretching/ C-H in plane bending
1139	M	C-N stretching / C-C stretching
1175	W	C-N stretching / C-C stretching
122,712,471,278	S	C-N stretching / C-C stretching
1355	VS	C-O stretching /Symmetric CH3 bending / Terminal gem dimethyl bending
1376	W	C-O stretching/ symmetric CH3 bending /terminal gem dimethyl bending
1449	M	Unsymmetrical CH3 bending/ ring C=C stretching

1552	W	N-H in plane bending (Sci) / ring C=C stretching
1580	S	Ring C=C stretching/ C=O stretching
1614	S	Ring C=C stretching/ C=O stretching
1669	W	Ring C=C stretching/ C=O stretching
2657	M	C-H stretching of Methyl group
2757	M	C-H stretching of Methyl group
2860	W	Symmetrical stretching of methyl group
2982	S	Anti-symmetrical stretching of methyl group / C-H vibration of phenyl group
3301	VS	Associated hydroxyl group adsorption/ N-H. Vibrations
3676	W	Associated hydroxyl absorption

Note: VS: Very Strong; S: Strong; M: Medium; W: Weak; VVW: Very Very Weak

Table 2: Fourier transform infrared spectrum and vibrational frequencies of ampicillin.

Infrared Frequency (Cm^{-1})	Intensity	Description
499	S	C-C out of-plane bending
572	W	C-C out –of plane bending
589	S	C-C out –plane bending
645	s	S-C stretching / N-H wagging
696	S	S-C stretching / N-H wagging
721	M-S	Anti-symmetric S-C stretching / C-C stretching / N-H wagging / C-C out –of – plane bending type.
736	M-S	Anti-symmetric S-C stretching /C-C stretching/ N-H wagging / C-C out-of-plane bending
807	W	C-C stretching / N-H wagging / C-H out-of-plane bending
847	M	C-C stretching / C-N stretching
874	M	C-C stretching / C-O-H stretching
929	M	C-C stretching / C-O-H stretching
1020	M-W	C-C stretching / C-H in –plane bending
1079	M-S	C-C stretching / C-H in- plane bending
1118	W	C-C stretching
1155	S	C-C stretching / C-H in plane bending
1169	S	C-H in -plane bending / C-N stretching /C-O stretching
1263	S	C-O stretching /interaction band of C-N-H
1306	S	C-O stretching
1372	S	Symmetrical bending of gem dimethly group/C-OH in-plane bending /C-N stretching of peptide
1385	M	Symmetrical bending of gem dimethly group/C-OH in plane bending /C-N stretching of peptide.
1457	M	Unsymmetrical bending of CH3 group /C=C ring stretching/C-N stretching of peptide
1493	VS	Unsymmetrical bending of CH3 group /C=C ring stretching.
1572	S	N-H in plane bending / interaction band C-N-H/C=C ring stretching
1605	S	Carbonyl absorption of peptide
1686	S	Carbonyl absorption COO group
1769	VS	Carbonyl absorption of 4 mem.ring
2656	W	Characteristic absorption of carboxylic acids, 1118 X 1217
2744	W	Symmetric stretching of CH3 group
2969	S	Anti-symmetric stretching of CH3 group
3036	M-W	Aromatic C-H stretching
3441	M	N-H symmetric stretching
3500	W	O-H stretching

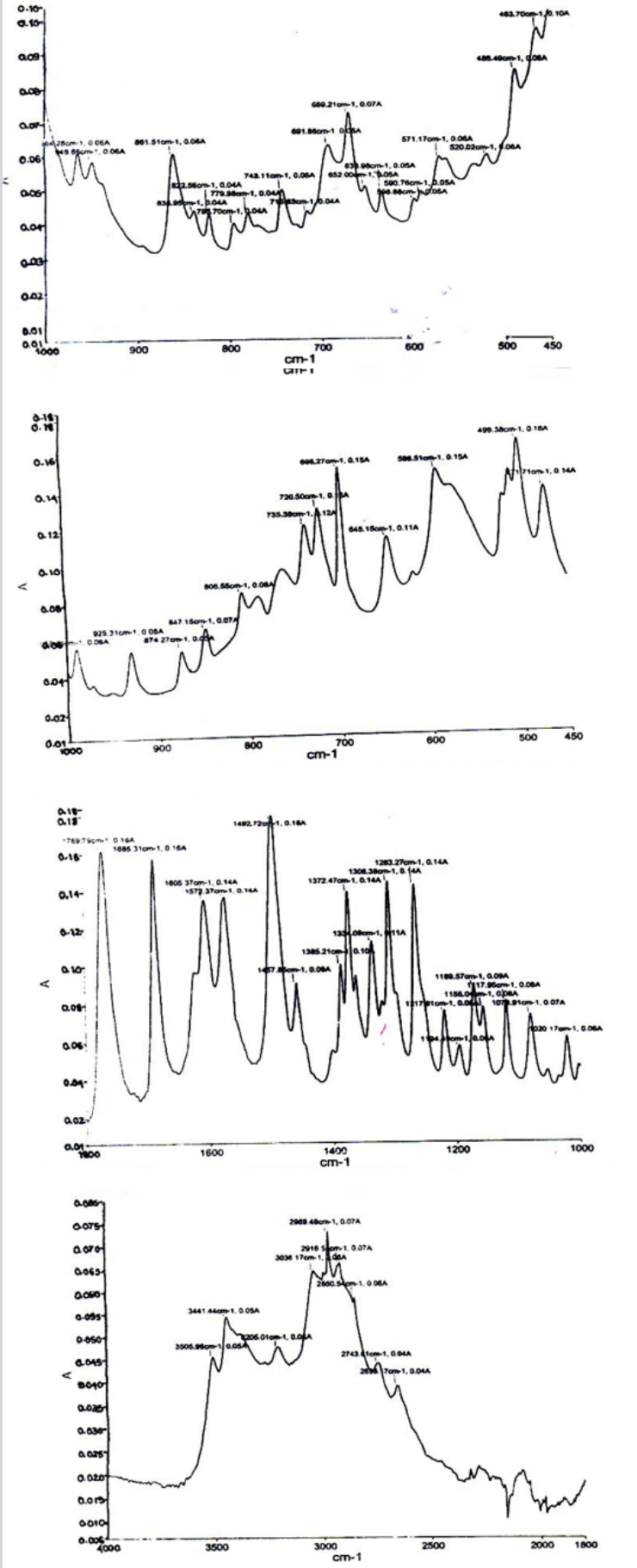

Figure 1: FTIR-ATR spectra of tetracycline.

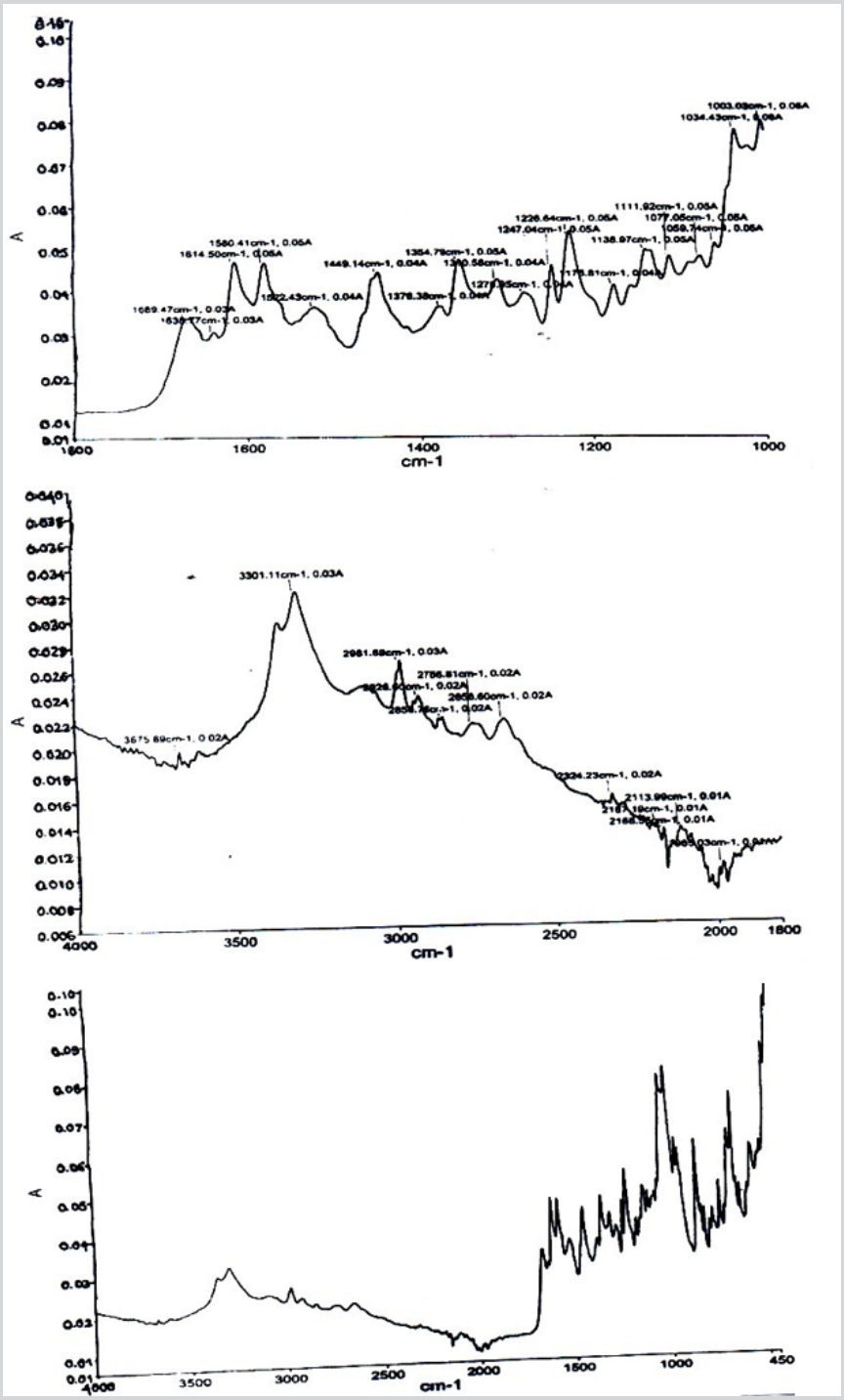

Figure 2: FTIR-ATR spectra of ampicillin.

Tetracycline

Aromatic ring vibrations: The most of the mononuclear and polynuclear aromatic compounds have three or four peaks in the region 3080-3010 cm^{-1}. This is being due to stretching vibrations of the ring C-H bonds and these have strong – medium intensity [1]. A strong band observed at 2982 is assigned to C-H vibrations of the phenyl ring.

A number of C-H in plane deformation bands occur in the region 1290-1000 cm^{-1} the band are usually being sharp but of week to medium intensity [1,2]. However, these bands are not important for interpretation purpose although they can be used quantitatively. In fact, a number of interactions are possible, thus necessitating a great care in the interpretation of bands in the region. The additional difficulties may also arise due to the presence of the other bands in the region. The frequencies of C-H out-of-plane deformation vibrations are mainly determined the type of aromatic substitute. The band gives important means for determining the type of aromatic substitution. These C-H in-plane bending vibrations and the out –of-plane bending vibrations are tabulated in the Table 1.

The ring carbon -carbon stretching vibrations occur in the region 1625-1530cm^{-3} [3-6]. For six-member ring there are two or three bands in this region is due to skeletal vibrations, the strong usually

being at 1500 cm^{-1} in general, the bands are of variable intensity are observed at 1625-1530 cm^{-1}, 1590-1575 cm^{-1}, 1525-1470 cm^{-1} and 1465-1430 cm^{-1} 1590-1575 cm^{-1}, 1525-1470 cm^{-1} and 1465-1430 cm^{-1} for substituted benzene. In the spectrum of tetracycline several aromatic phenyl ring vibrations are observed. In line with the above statement, the band observed at 1449 cm^{-1}, 1552, 1580, 1614, and 1669 cm^{-1} are assigned to C=C ring stretching. The bands in the aromatic ring deformation region are quite sensitive to the change in the nature and position of substituent's although other bands depend mainly on the distribution and number of substitute's rather than on their chemical mature or mass. So that these latter vibrations together with the out-of-plane vibration of the ring of hydrogen atoms are extremely useful in determining the position of substituent's [7-10]. For mono substituted aromatics, the bands due to the out-of-plane ring deformation vibration occur in the region 410-550 cm^{-1} hence the bands observed at 464, 488, and 520 cm^{-1} are due to out-of-plane ring deformation of aromatic phenyl ring.

Methyl group vibrations: Methyl group has two types of stretching vibrations, one is symmetrical contraction of the C-H bonds (or) expansion of C-H bonds (or) expansion of C-H bonds and another is anti -symmetrical contraction or expansion of C-H bonds. These vibrations as always occur below 3000 cm^{-1} [11]. Hence, the bands of medium intensity are observed at a frequency of 2860 cm^{-1} and 2982 cm^{-1} are assigned to anti- symmetrical and symmetrical stretching vibrations of methyl respectively. The bands observed at 1449, 1355 and 1376 cm^{-1} are attributed to unsymmetrical and symmetrical bending vibrations of C-H group respectively. It is possible for us to assign tentatively a band at 1358 cm^{-1} may due to terminal dimethyl bending vibration, since terminal dimethyl group absorb at around 1347-1360 cm^{-1} [12, 13].

The most reliable absorption bands below 1500 cm^{-1} are deformations. Methyl group has two deformations, the symmetrical (-- 1380) and the anti- symmetrical (-- 1450) [11]. The band observed at 1449 cm^{-1} is assigned to anti-symmetrical bending of C-H group and the bands observed at 1355 and 1376 cm^{-1} are assigned to symmetrical bending of C-H group.

Carbonyl vibrations: The carbonyl group is important in organic chemistry and its characteristic frequency has been extensively studied in a wide range of compounds [13]. It is necessary to exercise some caution since, we have assumed a very simple picture of the carbonyl vibration. The carbonyl vibration is not located entirely within the carbonyl bond but involves some of the other atoms in the molecule. Changes in the composition and stricture on the rest of the molecule will therefore ester a mechanical effect which is primarily responsible for the observed met-erase in the carbonyl frequency as the ring size decreases below six atoms. The carbonyl group in the four membered ring will have a strong absorption at around 1775 cm^{-1} and 1669 cm^{-1} (12-13). Hence, the bands observed at 1614 and 1664 cm^{-1} is assigned to carbonyl vibration. The strong band at 1580 cm^{-1} is assigned to carbonyl vibrations of carboxylic group (COO-) and peptide.

Vibrations of carboxylic acids of heterocyclic: The most diagnostic feature of a carboxylic acid spectrum is a very broad absorption frequency extending from 2500 cm^{-1} to 3300 cm^{-1} [11]. The factor which is responsible for the diffuse shape and relatively low frequency is hydrogen bonding. This importance characteristic features are observed over a region of 3250 -2750 cm^{-1}. the important recognizable absorption of carboxylic acids is

a) C-O stretch

b) C-O-H in-plane

c) C-O-H out-of-plane bend

d) C=O stretching

N-H Stretching and its bending vibrations: The frequency of the N-H stretching is reduced by hydrogen bonding. The overlapping occurs in the observed position of N-H and O-H stretching frequency so that an unequivocal differentiation s in structures is sometimes impossible. The dilute solutions in non-polar solvents, amides show two moderately intense N-H stretching frequency, corresponding to anti-symmetrical and symmetrical N-H stretching vibrations. These bands occur near 3520 cm^{-1} and 3400 cm^{-1} respectively. But, in the spectra of solid sample, these bands are observed near 3450 cm-1 and 3180 cm^{-1} because of hydrogen bonding. In the FTIR spectrum of tetracycline, O-H stretching vibrations occur at the regions of N-H stretching vibration, makes interpretation very difficult. In line with the above reference there might be a possibility that N-H stretching vibration are shifted, being a solid sample. Hence band at 3301 cm^{-1} is stretching in N-H vibration band has been demented by O-H band in the region. The band at 3676 cm^{-1} having weak intensity have been assigned to O-H stretching vibration.

Ampicillin

Methyl group vibration: Methyl group has three stretching vibrations. However, only two absorption bands are normally observed in the spectra. In practice, there are two anti-symmetric vibrations, but they cannot be distinguished and so the methyl group is commonly observed to have two C-H stretching absorption bands at 2962 cm^{-1} and 2872 cm^{-1}. In the spectrum of ampicillin two anti-symmetric stretching vibrations of C-H are observed at 2969 cm^{-1}. The band observed at 2744 cm^{-1} is due to symmetric stretching of methyl group.

The two bands arising from C-O Stretching and C-O in plane bending appear in the spectra of carboxylic acids near 1320-1210 cm^{-1} and near 1440-1395 cm^{-1} respectively. Both of these bands involve some interaction between C-O stretching and in-plane C-O-H bending. The bands observed at 1263, 1306 cm^{-1} and 1334 cm^{-1} are assigned to C-O stretching vibration of carboxylic group. The bands observed at 1372 cm^{-1} and 1385 cm^{-1} are assigned to C-O-H in plane bending vibration. A string band at 1684 cm^{-1} is due to carbonyl absorption of carboxylic group in the heterocyclic (Five Member) nucleus.

Heterocyclic vibrations: Usually, hetero cyclic compounds may be five membered ring or six membered rings. Containing hetero atoms like oxygen and Sulphur. In the synthetic hetero cyclic compound like Ampicillin, S-C stretching vibration are observed in the region of 650, 750 cm^{-1}. Hence the bands of medium to weak intensity at 645, 696 and 721 cm^{-1} are assigned to Heterocyclic S-C stretching vibration. The other heterocyclic vibrations are C-C stretching vibration. These vibrations are presented in the Table 2.

Aromatic ring vibrations: The C-H stretching vibration of most of the aromatic compounds are found in the region of 3080 -3010 cm^{-1} (11). A strong band observed at 3036 cm^{-1} is assigned to C-H stretching vibration of the phenyl ring carbon -carbon stretching vibration. Generally, the bands due to ring carbon

-carbon stretching vibration have strong to medium intensity. They are observed at 1625, 1590 cm^{-1}, 1590-1575 cm^{-1}, and 1457 cm^{-1} are attributed to C-C ring stretching. Remaining bending vibration of the aromatic ring and O-H stretching are presented in the Table 2.

CONCLUSION

Fabrication of several drugs need a qualitative test on various raw materials. Hence a pharmaceutical persons / spectroscopist need a powerful instrument like, infrared, Raman and UV spectrophotometers to check the quality of the raw materials available on manufacturing. The present investigation emphasizes on the vibrations band assignment of life saving compounds of pharmaceutical importance of day- to- day life viz., tetracycline, and ampicillin, through infrared spectroscopy.

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