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Vibrational Spectra and Qualitative Analysis of Albendazole and Mebendazole

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In this work, vibrational spectral analysis of two broad-spectrum anthelmintic drugs albendazole and mebendazole, that fall under the category of the WHO's model list of essential drugs for the eradication of helminthiasis, has been carried out by employing FTIR, FT-Raman and UV-Visible spectroscopic techniques. The change in the quality of the drugs under various storage conditions has been studied by spectral techniques. The results are indicative of the fact that it is essential to store the drugs under the prescribed ones to maintain their quality and the alteration in quality can be assessed by spectroscopy as a tool.

Key Words: Albendazole, Mebendazole, Storage, Quality, FTIR, FT-Raman, UV-Visible.

INTRODUCTION

Human beings have always been in need of solutions to address illness, injury and various health related issues. A drug may be defined as a substance used in the prevention, diagnosis, treatment or cure of disease in man or other animals[1]. Pharmaceutical products differ considerably in their composition, so naturally, they are subject to different forms of chemical degradation and in addition, there may be several simultaneous decomposition reactions occurring in a product. Some of the physical factors that influence chemical degradation are temperature, moisture, strong sunlight and ionizing radiation[2]. By taking care of the storage condition of the drug products, these degradations could be avoided to large extent. Numerous references in the pharmaceutical literature[3-5] refer to the instability of many drug products when exposed to strong sunlight. The photochemical degradation of a sensitive material can be reduced by protecting the drugs from light by storing in light-resistant containers are used. In the preparation of solid dosage

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from drugs whose chemical stability is affected by moisture, care is taken to ensure an environment of controlled humidity in every stage like manufacturing, packaging and storage[6]. While increase in storage temperature than the labelled ones can lead to certain types of degradation, a decrease too can cause harm to the drug quality[7]. As access to medicines must be accompanied by quality assurance, there must be controls and checks to ensure that the medicines ultimately reaching the patients are of good quality, safe and effective[8].

Deworming helps meet the Millennium Development Goals of the WHO. The control of worm-induced disease is a highly effective investment in terms of health, education, poverty reduction and development which not only takes the mankind onwards, but also upwards[9]. Periodic chemotherapy with single dose anthelmintic drugs for helminth control in developing countries are in the mainstay in the public health related issues. In light of the increasing drug resistance of nematodes of livestock to anthelmintic products, assessment and monitoring of efficacy of anthelmintic drugs in areas where they are commonly used has gained importance. Moreover, the WHO has urged for the creation of a global network for monitoring anthelmintic drug efficacy and drug resistance as a needed response to this emerging threat. The choice of the most cost-effective drugs for use in helminth control is guided principally by considerations of quality, efficacy, safety and cost[10]. The study of efficacy of these drugs in biological systems, their chemotherapeutic activity needs the knowledge of biological disciplines and is a concern of pathologists and medical practitioners. Alternatively, with an eye of a spectroscopist, the current work is a study on the behaviour of albendazole and mebendazole by tracing their vibrational spectra for ensuring the presence of the basic functional groups and analyzing the change in their behaviour when stored at different conditions, thereby checking the quality of the drugs. In this paper, an attempt is made to use infrared and UV-Visible spectroscopic techniques as a tool to indicate the deterioration when albendazole and mebendazole are not stored as recommended.

EXPERIMENTAL

High grade pure samples of albendazole and mebendazole were procured from reputed pharmaceutical firms in Chennai, India and used for spectral recording as such. The FTIR spectra of the drugs were recorded with ABB Bomem Series spectrophotometer over the region 4000-400 cm^{-1} by KBr pellet technique at Dr. CEEAL Analytical Lab, Chennai, India. The FT-Raman spectra were recorded using 1064 nm line of Nd:YAG laser operating at 200 mW on Bruker FRA106 spectrophotometer in the region 50-3500 cm^{-1} with the spectral width of 4.29 cm^{-1} at SAIF, IIT, Chennai. The Indian

Pharmacopoeia recommends that albendazole and mebendazole should be stored in tightly closed, light-resistant containers[11]. To study the change in the quality, the pure drugs were (i) stored in well-sealed light resistant container, (ii) exposed to sunlight and (iii) at ice point and FTIR spectrum of each was recorded. All the spectra were recorded at the room temperature.

The UV-Visible spectral measurements were carried out using Shimadzu-160A spectrophotometer at Dr. CEEAL Analytical Lab, Chennai. For the purpose, the linearity range in which the drugs obey Beer-Lambert's law has been figured out by analyzing the sample at various concentrations. Accurately weighed 100 mg of each of the drug, albendazole and mebendazole are taken in separate 100 mL standard flasks to which 10 mL formic acid was added. The solutions are made up to the mark by adding 0.1 M HCl and sonicated to ensure thorough mixing of the contents. Each of these drug solutions are transferred into separate test tubes and further diluted to obtain drug concentrations of 2, 4, 6 … 20 μg mL^{-1}. The absorption values for various concentrations of the drugs which fall within this linearity range are used to plot the linearity curves. The absorbance values at 291 and 262 nm of albendazole are noted and the absorbance peak at 284 nm of mebendazole spectra are used to study the linearity behaviour. In order to support the qualitative analysis done by the FTIR method, UV-Visible spectroscopic approach has been adopted to study the variation in the light absorption properties of the drugs stored in various conditions.

RESULTS AND DISCUSSION

The drugs, albendazole (Fig. 1) and mebendazole (Fig. 2) belong to benzimldazole group of drugs. Albendazole has the IUPAC name methyl[(5-propyl sulfanyl-3*H*-benzo-imidazol-2-yl)amino]formate, while the Indian Pharmacopoeia mentions it as methyl 5-propylthio-1*H*-benzimidazol-2-yl-carbamate. The vibrational spectrum of a compound is the superposition of vibrational bands of the various functional groups present in it. By observing the nature, position, shape and relative intensity of the vibrational bands and comparing them with that of structurally and chemically related compounds, a satisfactory frequency assignment of these functional groups present has been done. The corresponding vibrational spectral assignments are summa-rized in Tables 1 and 2.

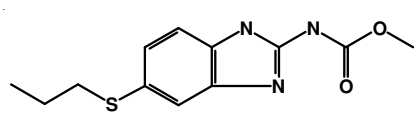

Fig. 1. Structure of albendazole

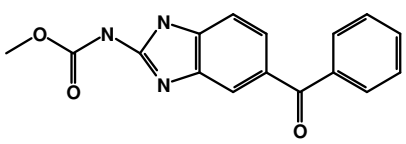

Fig. 2. Structure of mebendazole

TABLE-1
VIBRATIONAL SPECTRA AND FREQUENCY
ASSIGNMENT FOR ALBENDAZOLE

Frequency (cm^{-1})		Vibrational band assignment
FTIR	FT Raman	
3328(m)	3325(w)	N-H stretching
3142(w)	3151(w)	Aromatic C-H stretching
3104(w)	3102(w)	Aromatic C-H stretching
-	3078((w)	Aromatic C-H stretching
2980(w)	2989(w)	Aromatic C-H stretching
2957(m)	2960(m)	CH_3/CH_2 C-H stretching
2927(m)	-	CH_3/CH_2 C-H stretching
2918(w)	2917(m)	CH_3/CH_2 C-H stretching
2867(w)	2887(m)	CH_3/CH_2 C-H stretching
2845(w)	2847(m)	CH_3/CH_2 C-H stretching
2810(w)	2797(m)	CH_3/CH_2 C-H stretching
2666(m)	2647(m)	C-H stretching
1712(m)	1717(m)	Amide I band
1633(vs)	1632(m)	Aromatic ring stretching
1621(vs)	1624(m)	Aromatic $C\equiv C/C\equiv N$ stretching
1589(s)	1575(s)	Aromatic $C\equiv N$ stretching
1524(m)	1535(ms)	Amide II band /C-N stretching
1480(m)	-	Aromatic $C\equiv C/C\equiv N$ stretching
1460(ms)	1469(s)	Aromatic $C\equiv C/C\equiv N$ stretching
1441(ms)	1449(ms)	CH_2 deformation
1374(w)	1379(w)	CH_2 deformation
1325(ms)	1323(ms)	CH_2 deformation
1268(vs)	1269(vs)	Amide III band
1223(m)	1227(m)	Amide IV band
1194(ms)	1157(w)	CH_2 wagging
1122(vw)	1128(m)	CH_2 wagging
1095(s)	1090(s)	C-O/C-S stretching
958(w)	965(ms)	C-H in-plane deformation
922(w)	901(w)	C-H in-plane deformation
886(w)	-	C-H in-plane deformation
863(w)	866(w)	C-H out-of-plane deformation
847(w)	-	C-H out-of-plane deformation
806(w)	810(w)	C-H out-of-plane deformation
792(m)	-	CH_2 rocking
770(w)	777(w)	CH_2 rocking
760(w)	-	CH_2 rocking
730(w)	732(w)	CH_2 rocking
695(w)	707(w)	N-H out-of-plane deformation
640(w)	644(w)	N-H out-of-plane deformation
612(w)	612(w)	N-H out-of-plane deformation
597(w)	570(w)	C-S stretching
512(w)	518(w)	C-C out-of-plane deformation

TABLE-2
VIBRATIONAL SPECTRA AND FREQUENCY
ASSIGNMENT FOR MEBENDAZOLE

Frequency (cm^{-1})		Vibrational band assignment
FTIR	FT Raman	
3368(s)	3367(m)	N-H stretching
3086(w)	-	Aromatic C-H stretching
3071 (w)	3069 (ms)	Aromatic C-H stretching
3058 (w)	3049(w)	Aromatic C-H stretching
3024 (w)	-	Aromatic C-H stretching
2998 (w)	3004(w)	Aromatic C-H stretching
2947 (w)	2922(w)	CH_3 stretching
2867 (m)	2869(w)	CH_3 stretching
2699 (m)	2702(w)	C-H stretching
2661 (m)	2669(w)	C-H stretching
1731(s)	1730(ms)	Amide I Band
1650 (s)	1647 (s)	Benzoyl C=O stretching
1644 (s)	-	Aromatic ring stretching
1639 (s)	-	Aromatic ring stretching
1593 (s)	1600 (vs)	Aromatic C⋯C /C⋯N stretching
1574 (ms)	-	Aromatic C⋯C /C⋯N stretching
1530 (ms)	1542 (ms)	Amide II Band /C⋯N ring stretching
1456 (ms)	1452 (ms)	Aromatic ring stretching
1445 (ms)	1420 (s)	CH_2 deformation
1323 (ms)	1357 (m)	CH_2 deformation
1311 (m)	-	CH_2 deformation
1259 (s)	1269 (s)	Amide III Band
1227 (s)	1231 (ms)	Amide IV Band
1193 (s)	1193 (w)	CH_2 wagging
1119 (ms)	1120 (s)	CH_2 wagging
1089 (ms)	1033(m)	C-O stretching
1012 (w)	1006 (m)	C-H in-plane deformation
977 (w)	958 (w)	C-H in-plane deformation
884 (w)	878 (w)	C-H in-plane deformation
861 (w)	862 (w)	C-H out-of-plane deformation
825 (w)	824 (w)	C-H out-of-plane deformation
796 (m)	800(w)	CH_2 rocking
769 (m)	767 (w)	CH_2 rocking
758 (w)	-	CH_2 rocking
721 (w)	731(m)	CH_2 rocking
706 (ms)	704(w)	N-H out-of-plane deformation
641(ms)	660(w)	N-H out-of-plane deformation
541 (w)	540(w)	C-C in-plane deformation
502(w)	503(w)	C-C out-of-plane deformation

Urethane bands: Primary urethanes have a number of absorptions in the region 3450-3200 cm^{-1} due to the N-H stretching vibration. Secondary urethanes absorb near 3300 cm^{-1} if hydrogen-bonding occurs and at 3450-3390 cm^{-1} if it is absent[12]. Albendazole and mebendazole both being, N-aryl secondary urethanes exhibit a medium intensity peak at 3328 and 3368 cm^{-1}, respectively in their FTIR spectrum, that is attributed to N-H stretching. The assignment has been verified by the presence of these vibrations in the FT-Raman spectrum of these compounds.

Urethanes, also called as carbamates exhibit carbonyl frequency at somewhat higher frequency than amides and lower than esters. This band due to the carbonyl stretching vibration, termed as amide I band of urethanes occurs in the region 1740-1680 cm^{-1}. In $CHCl_3$ solution, most primary carbamates absorb at 1728-1722 cm^{-1} secondary carbamates at 1722-1705 cm^{-1} and tertiary at 1691-1683 cm^{-1}. In solid state, they are much the same, except that some primary carbamates give very broad bands which may absorb as low as 1690 cm^{-1}. N-aryl urethanes in solid phase exhibit this band in the region 1735-1705 cm^{-1}, while strong hydrogen bonding may result in band as low as 1690 cm^{-1}. In view of these, the sharp band present at 1712 and 1731 cm^{-1} in the FTIR spectrum of albendazole and mebendazole is assigned to the amide I vibration of the carbamate group present. The FTRaman spectrum of the two drugs show this vibration at 1717 and 1730 cm^{-1}, respectively.

Associated secondary urethanes absorb strongly at 1540-1530 cm^{-1} due to CNH group vibration, similar to that of secondary amides and in dilute solution this band is found at 1530-1510 cm^{-1} is termed as amide II band involves both N-H deformation and predominantly absorbs strongly near 1550 cm^{-1}. The in-plane N-H bending frequency and the resonance stiffened C-N bond stretching frequency fall close together and therefore interact. This band very characteristic for monosubstituted amides which occurs in urethanes too, can be traced as the medium strong bands present at 1524 cm^{-1} in FTIR and at 1535 cm^{-1} in the FT-Raman spectrum, respectively of albendazole. Similar peaks at 1530 and 1542 cm^{-1} of the vibrational spectra of mebendazole can be attributed to the CNH group which reflects the correctness of this assignment.

Urethanes also exhibit amide III band just like amides, but in the region 1260-1220 cm^{-1} in solid and is usually stronger than the C=O band. In this line, the very strong band present at 1260 cm^{-1} in the FTIR spectrum of mebendazole and at 1268 cm^{-1} of other three spectra is due to the combination of N-H deformation and C-N stretching vibration motion.

Amide IV band that arises due to coupling between C-N and C-O stretching vibrations occur in the region 1265-1200 cm^{-1} in urethanes. The strong band present at 1223 cm^{-1} in FTIR spectrum is allotted as amide IV

band in albendazole. While the same can be traced at 1227 cm^{-1} in its FT Raman spectrum of albendazole and as a strong peak in the FTIR spectrum of mebendazole. The amide IV band for mebendazole is located at 1231 cm^{-1} in its FT-Raman spectrum.

The band present at 1095 and 1089 cm^{-1} in the FTIR spectrum of the two drugs can be assigned to the C-O stretching of urethane group. In case of albendazole, this peak is overlapped by the band due to aryl-S linkage resulting in a higher intensity peak compared to that of mebendazole. The variation in the intensity of this peak due to the presence of aryl-S linkage is even more pronounced in the FT-Raman spectrum of the compounds. The out of plane deformation of the N-H group of urethane has resulted in weak to medium intensity peaks in 700-625 cm^{-1} region as expected.

Propyl-thio group vibrations: In general, the assignment of the band due to the C-S stretching vibration in different compounds is difficult since it is of variable intensity and may be found over the wide region 1035-245 cm^{-1}. Both aliphatic and aromatic sulphides have a weak-to-medium band due to the C-S stretching vibration in the region 710-570 cm^{-1}, primary sulphides absorbing at the higher frequency end of the range and tertiary sulphides at the lower end. While C-S stretching frequency of CH_3-S occurs in the range 710-685 cm^{-1}, R-CH_2-S moeity results in this vibration in the range 660-630 cm^{-1}, as the increase in the length of the alkyl group attached to the sulphur atom decreases the C-S stretching frequency. Moreover, this vibration does not give rise to strong bands in the infrared spectrum which makes this linkage difficult to detect in some cases, while it is a better band in Raman spectrum usually[13]. With propyl group attached to the sulphur atom, a lowering in the stretching frequency of C-S band is expected. A further decrease is expected due to the double bond conjugation of the aromatic group attached to this link. Hence C-S stretching vibrational band has been traced at 570 cm^{-1} in the vibrational spectra of albendazole, while no peak is found in this region in case of mebendazole indicating the absence of such a linkage or bond of such nature.

A band near 1090 cm^{-1} is usually characteristic for the aryl-S linkage. It is thought to be an aromatic vibration having some C-S stretching character. The presence of this vibration can be immediately noted in albendazole, which happens to be also a region of C-O stretching vibration. In case of mebendazole, the absence of C-S group can be verified from the variation in the intensity of the said band in both the molecules. The asymmetric and symmetric stretching vibration of the CH_2 group attached to the sulphur atom give rise to medium intensity bands in the region 2950-2920 and 2880-2845 cm^{-1}, respectively. In the characterization of certain mercapto-benzothiole compounds, Yadav *et al.*[14] have identified the CH_2-S methylene vibrational band at 2960 cm^{-1}. The peak at 2927 and 2867 cm^{-1} of the FTIR

and FT-Raman spectrum of albendazole is a sufficient proof for the presence of this group in albendazole and not in mebendazole. Infrared absorption bands characteristic of alkylthio groups have been discussed by Menefee *et al.*[15] who suggest that the bands near 1305 and 1420 cm^{-1} are attributed to methylene twisting and wagging vibrations in P-S-Et compounds.

Benzoyl group vibrations: Conjugation with a C⋯C bond results in delocalization of the π electrons of both the unsaturated groups. This reduces the double bond character of the C=O bond causing a decrease in force constant of this band which tends to decrease the carbonyl stretching frequency. The position of the C=O stretching and is determined by the following factors (i) the physical state, (ii) electronic and mass effects of neighbouring substituents, (iii)conjugation, (iv) intermolecular and intramolecular hydrogen bonding and (v) ring strain. Consideration of these factors leads to a considerable amount of information about the environment of the C=O group[16]. Among the title compounds, mebendazole shows a strong peak at 1644 cm^{-1} in FTIR spectrum and at 1647 cm^{-1} in FT Raman spectrum due to the ketone group vibration. A weak overtone of this vibration can be seen near 3300 cm^{-1} in both the spectra of this compound.

Benzimidazole group vibrations: Several derivatives of benzimidazoles are known to posses diverse types of biological activities. The characteristic stretching bands at about 3290-2460 cm^{-1} originating from imidazoles' N-H group were observed in the infrared spectra of all the compounds synthesized[17,18]. Very broad absorption bands near 3000 cm^{-1} have been identified as due to N-H stretching vibration of benzimidazole group by Dubey *et al.*[19]. In solid phase, five members heteroatomic compounds with two or more nitrogen atoms in the ring have a broad absorption at 2800-2600 cm^{-1} due to NH ...N bond. The FTIR band at 3328 and 3368 cm^{-1} in the spectrum of albendazole and mebendazole respectively has been already allotted to the N-H stretching vibration of the carbamate group. The same bands are re-allotted to the same mode of vibration here for the benzimidazole group N-H moeity.

The C=N stretching of this group is expected at 1560-1520 cm^{-1} region. Imidazoles have several bands of variable intensity in range 1660-1450 cm^{-1} due to C⋯N and C⋯C stretching vibrations. Report[16] shows these vibrations to occur in the region 1615-1500 cm^{-1} and the current work also shows vibrations in the same region. In case of mebendazole, the C⋯C vibrational band occurs as a doublet, which indicates the presence of carbonyl group in attached to the benzene zing. When C=O, C=C, C=N or NO_2 is directly conjugated to the benzene ring, a doublet is observed at 1625-1575 cm^{-1}. Substituent resulting in conjugation, such as C=C and C=O, increase the intensity of this doublet. The ring C⋯C and C⋯N stretching vibrations occur[19] in the region 1615-1575 cm^{-1}. Mohan *et al.*[20] have identified

the stretching frequency of C⋯N bond in benzimidazole at 1617 cm^{-1}. Chidambarathanu *et al.*[21] have observed the ring carbon-carbon stretching at 1574, 1498 and 1468 cm^{-1} in a poly-substituted pyrazole compound. Vibrational bands present at 1535, 1567, 1579 and 1581 cm^{-1} are assigned to this aromatic C⋯C stretching in diazepam, a nitrogen containing heterocyclic compound, while the band present at 1605 cm^{-1} has been attributed to C⋯N stretching vibration[22]. Referring to the above assignments, the bands present in this region have been assigned to the ring stretching vibrations.

Aromatic C-H stretching vibrations: The C-H stretching vibrations of aromatic and heteroaromatic structures of strong to medium intensity occur in the region 3100-3000 cm^{-1} which is the characteristic region for ready identification of this structure. These bands have been identified in the 3095-3055 cm^{-1} region in some pyridine type benzimidazoles. The Raman bands at 3078, 2989, 3102 and 3151 cm^{-1} of albendazole and the weak IR bands at 2980, 3104 and 3142 cm^{-1} are attributed to this vibration. In case of mebendazole, a number of weak bands are present in 3069-2945 cm^{-1} in both FTIR and FT-Raman spectrum. A band with upto five peaks may be observed in this region. As might be expected, monosubstituted benzenes usually exhibit more peaks than di- or tri-substituted benzenes. This reason may be attributed to the presence of more bands in this region in case of mebendazole due to the presence of the benzoyl group in it, but not in albendazole.

Other deformation vibrations: A number of CH in-plane deformation bands, upto six occur in the region 1290-1000 cm^{-1} the bands usually being sharp but of weak to medium intensity. However, these bands are not normally of importance for interpretation purposes much. On the other hand, the frequencies of the C-H out-of-plane deformation vibrations give an important means for determining the type of the aromatic substitution. These bands are determined mainly by the number of adjacent hydrogen atoms on the ring. Mono-substituted benzenes have a strong band in the region 770-735 cm^{-1} with an additional band observed at 745-690 cm^{-1} in the spectra. A coupling between adjacent hydrogen atoms is also observed for naphthalene, phenanthrenes, in pyridines and quinolines where the nitrogen atom being treated as a substituted carbon atom of a benzene ring and in other aromatic compounds. Overtones and combination bands due to the C-H out-of-plane deformation vibrations occur in the region 1200-1600 cm^{-1}. The absorption patterns observed are characteristic of different benzene ring substitutions.

In most hydrocarbons, CH_2 deformation occurs near 1465 cm^{-1}. Unsaturation next to the CH_2 lowers its deformation to about 1440 cm^{-1}. Sulphur, phosphorus, silicon, chlorine, bromine and iodine all lower the deformation frequency of the CH_2 group to 1450-1405 cm^{-1}. The methyl groups give rise to two vibration bands, the asymmetric deformation band

falling in the 1465-1440 cm^{-1} region and symmetric band in 1390-1370 cm^{-1} region. The former band is often overlapped by the CH_2 scissor vibration band occurring at 1480-1440 cm^{-1}. With this idea, the bands due to various deformations have been assigned.

Change in internal standard ratio: The vibrational band assignment of the two benzimidazole group of drugs albendazole and mebendazole have been made in analogy with related compounds. With the change in storage condition, the FTIR spectra recorded show changes in the intensity of the absorption pattern. The internal standard ratio is calculated among certain absorption bands of these two drugs and the results are tabulated in Tables 3 and 4. The internal standard ratios evaluated clearly states the change in the quality of drugs due to the alteration in the storage condition.

UV-Visible spectral study: UV-Visible spectral studies of the drugs show that they obey Beer's law in the concentration range 2-20 μg mL^{-1}. The linearity curves for the two drugs are represented in Figs. 3 and 4. The regression analysis by UV-Visible method done with the absorbance values for various concentrations yield the corresponding regression equations $Y = 0.0370X + 0.0035$ at $\lambda = 291$ nm and $Y = 0.0288X + 0.0231$ at $\lambda = 262$ nm for albendazole. The regression equation indicating the relationship between the concentration of the drug and absorbance values for mebendazole is found to be $Y = 0.0518X + 0.0206$ at 284 nm. The Pearson

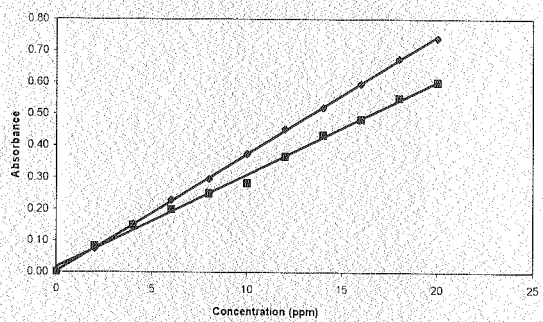

Fig. 3. Linearity curves of albendazole (◆ λ = 291 nm; ■ λ = 262 nm)

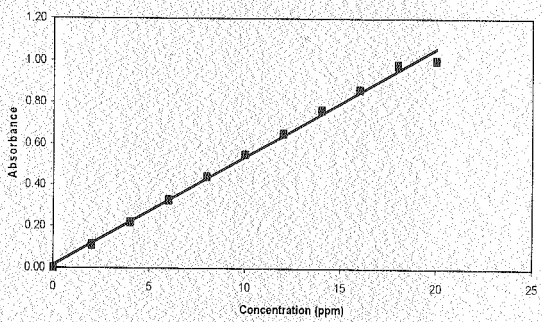

Fig. 4. Linearity curve of mebendazole (■ λ = 284 nm)

TABLE-3
INTERNAL STANDARD EVALUATION FOR ALBENDAZOLE

Conditions of exposure	Internal standard of specific modes of vibration at 3328 cm^{-1}							
	3328/ 3328	2957/ 3328	1712/ 3328	1633/ 3328	1589/ 3328	1460/ 3328	1268/ 3328	1194/ 3328
Labelled condition	1.0000	1.2397	1.1227	2.8296	2.3988	1.5569	2.7603	1.8488
Exposed to sunlight	1.0000	1.2311	1.1296	3.1464	2.5722	1.5881	3.0984	1.9281
At ice point	1.0000	1.2732	1.1311	3.5474	2.8455	1.6613	3.4912	2.0346
	Internal standard of specific modes of vibration at 2957 cm^{-1}							
	3328/ 2957	2957/ 2957	1712/ 2957	1633/ 2957	1589/ 2957	1460/ 2957	1268/ 2957	1194/ 2957
Labelled condition	0.8066	1.0000	0.9056	2.2824	1.9349	1.2559	2.2265	1.4913
Exposed to sunlight	0.8123	1.0000	0.9175	2.5557	2.0893	1.2899	2.5167	1.5661
At ice point	0.7854	1.0000	0.8884	2.7861	2.2349	1.3048	2.7420	1.5980
	Internal standard of specific modes of vibration at 1712 cm^{-1}							
	3328/ 1712	2957/ 1712	1712/ 1712	1633/ 1712	1589/ 1712	1460/ 1712	1268/ 1712	1194/ 1712
Labelled condition	0.8907	1.1043	1.0000	2.5204	2.1367	1.3868	2.4587	1.6468
Exposed to sunlight	0.8853	1.0899	1.0000	2.7854	2.2770	1.4059	2.7429	1.7069
At ice point	0.8841	1.1257	1.0000	3.1363	2.5157	1.4688	3.0866	1.7988
	Internal standard of specific modes of vibration at 1633 cm^{-1}							
	3328/ 1633	2957/ 1633	1712/ 1633	1633/ 1633	1589/ 1633	1460/ 1633	1268/ 1633	1194/ 1633
Labelled condition	0.3534	0.4381	0.3968	1.0000	0.8477	0.5502	0.9755	0.6534
Exposed to sunlight	0.3178	0.3913	0.3590	1.0000	0.8175	0.5047	0.9847	0.6128
At ice point	0.2819	0.3589	0.3188	1.0000	0.8021	0.4683	0.9842	0.5735
	Internal standard of specific modes of vibration at 1589 cm^{-1}							
	3328/ 1589	2957/ 1589	1712/ 1589	1633/ 1589	1589/ 1589	1460/ 1589	1268/ 1589	1194/ 1589
Labelled condition	0.4169	0.5168	0.4680	1.1796	1.0000	0.6491	1.1507	0.7707
Exposed to sunlight	0.3888	0.4786	0.4392	1.2233	1.0000	0.6174	1.2046	0.7496
At ice point	0.3514	0.4475	0.3975	1.2467	1.0000	0.5838	1.2269	0.7150
	Internal standard of specific modes of vibration at 1460 cm^{-1}							
	3328/ 1460	2957/ 1460	1712/ 1460	1633/ 1460	1589/ 1460	1460/ 1460	1268/ 1460	1194/ 1460
Labelled condition	0.6423	0.7963	0.7211	1.8174	1.5407	1.0000	1.7729	1.1874
Exposed to sunlight	0.6297	0.7752	0.7113	1.9812	1.6196	1.0000	1.9510	1.2141
At ice point	0.6019	0.7664	0.6808	2.1353	1.7128	1.0000	2.1015	1.2247
	Internal standard of specific modes of vibration at 1268c m^{-1}							
	3328/ 1268	2957/ 1268	1712/ 1268	1633/ 1268	1589/ 1268	1460/ 1268	1268/ 1268	1194/ 1268
Labelled condition	0.3623	0.4491	0.4067	1.0251	0.8690	0.5640	1.0000	0.6698
Exposed to sunlight	0.3227	0.3973	0.3646	1.0155	0.8302	0.5126	1.0000	0.6223
At ice point	0.2864	0.3647	0.3240	1.0161	0.8150	0.4759	1.0000	0.5828
	Internal standard of specific modes of vibration at 1194 cm^{-1}							
	3328/ 1194	2957/ 1194	1712/ 1194	1633/ 1194	1589/ 1194	1460/ 1194	1268/ 1194	1194/ 1194
Labelled condition	0.5409	0.6706	0.6073	1.5305	1.2975	0.8422	1.4930	1.0000
Exposed to sunlight	0.5186	0.6385	0.5859	1.6319	1.3340	0.8237	1.6070	1.0000
At ice point	0.4915	0.6258	0.5559	1.7436	1.3986	0.8165	1.7159	1.0000

TABLE-4
INTERNAL STANDARD EVALUATION FOR MEBENDAZOLE

Conditions of exposure	Internal standard of specific modes of vibration at 3368 cm^{-1}							
	3368/ 3368	2947/ 3368	1731/ 3368	1639/ 3368	1593/ 3368	1456/ 3368	1259/ 3368	1227/ 3368
Labelled condition	1.0000	0.5094	1.2017	1.2952	1.2697	0.9731	1.2975	1.1730
Exposed to sunlight	1.0000	0.4604	1.3973	1.8184	1.7114	0.9824	2.2556	1.3838
At ice point	1.0000	0.4807	1.3075	1.8636	1.7013	0.9508	2.0290	1.3353
	Internal standard of specific modes of vibration at 2947 cm^{-1}							
	3368/ 2947	2947/ 2947	1731/ 2947	1639/ 2947	1593/ 2947	1456/ 2947	1259/ 2947	1227/ 2947
Labelled condition	1.9631	1.0000	2.3591	2.5427	2.4926	1.9104	2.5471	2.3028
Exposed to sunlight	2.1721	1.0000	3.0351	3.9497	3.7173	2.1337	4.8994	3.0057
At ice point	2.0803	1.0000	2.7200	3.8767	3.5392	1.9779	4.2208	2.7777
	Internal standard of specific modes of vibration at 1731 cm^{-1}							
	3368/ 1731	2947/ 1731/	1731/ 1731	1639/ 1731	1593/ 1731	1456/ 1731	1259/ 1731	1227/ 1731
Labelled condition	0.8321	0.4239	1.0000	1.0778	1.0566	0.8098	1.0797	0.9761
Exposed to sunlight	0.7157	0.3295	1.0000	1.3014	1.2248	0.7030	1.6143	0.9903
At ice point	0.7648	0.3676	1.0000	1.4252	1.3012	0.7271	1.5518	1.0212
	Internal standard of specific modes of vibration at 1639cm^{-1}							
	3368/ 1639	2947/ 1639	1731/ 1639	1639/ 1639	1593/ 1639	1456/ 1639	1259/ 1639	1227/ 1639
Labelled condition	0.7721	0.3933	0.9278	1.0000	0.9803	0.7513	1.0017	0.9057
Exposed to sunlight	0.5499	0.2532	0.7684	1.0000	0.9412	0.5402	1.2404	0.7610
At ice point	0.5366	0.2579	0.7016	1.0000	0.9129	0.5102	1.0888	0.7165
	Internal standard of specific modes of vibration at 1593 cm^{-1}							
	3368/ 1593	2947/ 1593	1731/ 1593	1639/ 1593	1593/ 1593	1456/ 1593	1259/ 1593	1227/ 1593
Labelled condition	0.7876	0.4012	0.9465	1.0201	1.0000	0.7664	1.0219	0.9238
Exposed to sunlight	0.5843	0.2690	0.8165	1.0625	1.0000	0.5740	1.3180	0.8086
At ice point	0.5878	0.2825	0.7685	1.0954	1.0000	0.5588	1.1926	0.7848
	Internal standard of specific modes of vibration at 1456 cm^{-1}							
	3368/ 1456	2947/ 1456	1731/ 1456	1639/ 1456	1593/ 1456	1456/ 1456	1259/ 1456	1227/ 1456
Labelled condition	1.0276	0.5235	1.2349	1.3310	1.3048	1.0000	1.3333	1.2054
Exposed to sunlight	1.0180	0.4687	1.4224	1.8511	1.7422	1.0000	2.2962	1.4087
At ice point	1.0518	0.5056	1.3752	1.9601	1.7894	1.0000	2.1340	1.4044
	Internal standard of specific modes of vibration at 1259 cm^{-1}							
	3368/ 1259	2947/ 1259	1731/ 1259	1639/ 1259	1593/ 1259	1456/ 1259	1259/ 1259	1227/ 1259
Labelled condition	0.7707	0.3926	0.9262	0.9983	0.9786	0.7500	1.0000	0.9041
Exposed to sunlight	0.4433	0.2041	0.6195	0.8062	0.7587	0.4355	1.0000	0.6135
At ice point	0.4929	0.2369	0.6444	0.9185	0.8385	0.4686	1.0000	0.6581
	Internal standard of specific modes of vibration at 1227cm^{-1}							
	3368/ 1227	2947/ 1227	1731/ 1227	1639/ 1227	1593/ 1227	1456/ 1227	1259/ 1227	1227/ 1227
Labelled condition	0.8525	0.4343	1.0245	1.1042	1.0824	0.8296	1.1061	1.0000
Exposed to sunlight	0.7226	0.3327	1.0098	1.3141	1.2367	0.7099	1.6300	1.0000
At ice point	0.7489	0.3600	0.9792	1.3956	1.2741	0.7120	1.5195	1.0000

correlation factor in all the three cases happens to be greater than 0.99 indicating the excellent linear behaviour of the drugs in the chosen range. Overlay of the UV-Visible spectra of albendazole and mebendazole of 10 ppm, the mid-concentration level of linearity range level stored at the three conditions projected in Figs. 5 and 6. As albendazole shows two absorption peaks, the change in the quality of the drugs has been ascertained by calculating the Q-factor or the internal standard ratio by dividing the absorbance values of various peaks of the spectra of albendazole. These results projected in Table-5 and diagrammatically represented in Fig. 7 are in support of the results from vibrational spectral study on quality and indicate that the drugs have a change in their behaviour with a deviation from the prescribed storage condition.

TABLE-5
VARIATION OF ABSORBANCE OF ALBENDAZOLE AND MEBENDAZOLE AND THE INTERNAL STANDARD RATIO FOR DIFFERENT STORAGE CONDITIONS
Concentration = 10 ppm

Storage condition	Albendazole			Mebendazole
	291 nm	262 nm	A_{291}/A_{262}	284 nm
Ice point	0.3710	0.3160	1.1741	0.5560
Labelled storage condition	0.3690	0.3000	1.2300	0.5470
Exposed to sunlight	0.3560	0.2660	1.3383	0.5320

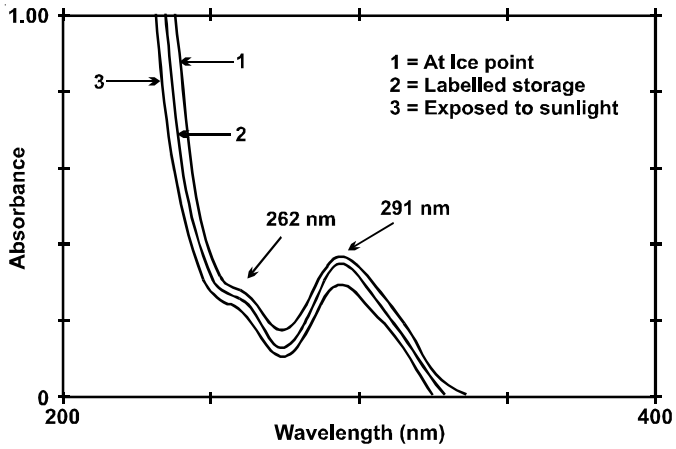

Fig. 5. A comparative representation of UV-Visible spectra of albendazole

Conclusion

FTIR, FT-Raman and UV-Visible spectroscopic techniques have been employed for the qualitative analysis of the anthelmintic drugs, albendazole and mebendazole. A satisfactory vibrational assignment of the drugs done

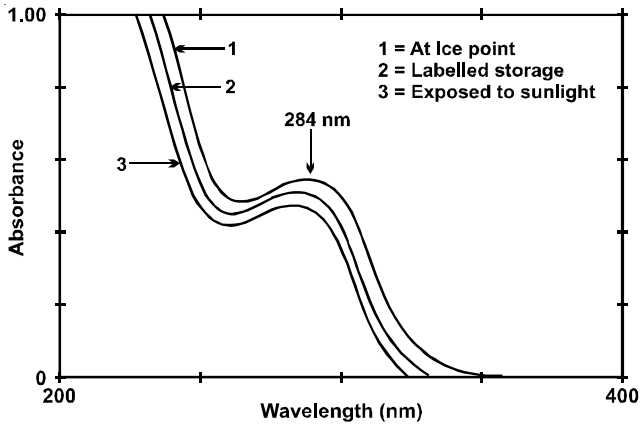

Fig. 6. A comparative representation of UV-Visible spectra of mebendazole

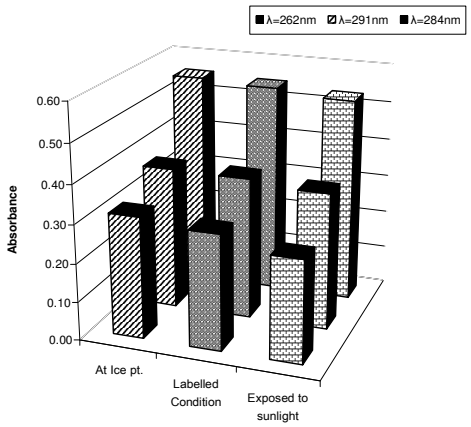

Fig. 7. Variation in absorbance of albendazole and mebendazole under different storage conditions

with the FTIR and FT-Raman spectra recorded confirms the basic functional groups present in the compounds. The intensity ratio calculation among specific modes of vibration clearly shows that some vibrational bands are altered due to sunlight exposure and storage at ice point. In both the drugs, deviations are observed clearly from the values of the labelled storage condition which denotes change in the quality of drugs due to change in the storage condition. The results insist that the drugs must be stored only in labelled condition for maintaining their quality and spectroscopy serves as an aid to check the quality of drugs.

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