Asian Journal of Chemistry Vol. 19, No. 1 (2007), 315–327

Qualitative Analysis of Some Antidiabetic Drugs by Spectroscopic Measurements

S. GUNASEKARAN*, R.K. NATARAJAN† and V. RENGANAYAKI†
PG & Research Department of Physics, Pachaiyappa's College, Chennai-600 030, India

Diabetes mellitus is an age-old disease plaguing mankind even today. Many oral antidiabetic drugs are available now-a-days to control the metabolic disorder in diabetes. The aim of the present work is to make a spectral investigation on some antidiabetic drugs, namely, glibenclamide and rosiglitazone maleate. The infrared, Raman and UV-Vis spectroscopic methods are employed for the qualitative analysis of these antidiabetic drugs. The different functional groups present in the compounds are identified and assigned satisfactorily using FTIR and FT Raman spectra. The UV-Vis spectral measurements carried out on the compounds identify the wavelength maxima. Using FTIR and UV-Vis spectral measurements, a comparison between the set of internal standards arrived at for the drugs stored in suitable storage conditions and exposed to environmental hazards is made.

Key Words: Vibrational spectra, UV-Vis spectra, Antidiabetic drugs, Glibenclamide, Rosiglitazone maleate, Qualitative analysis.

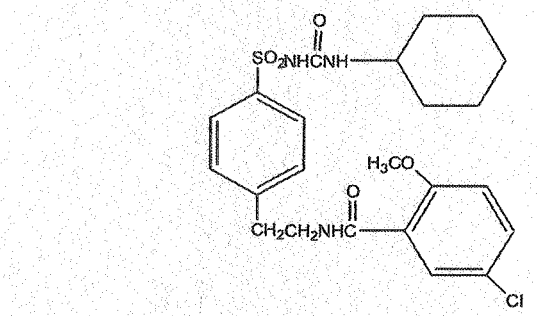
INTRODUCTION

Diabetes mellitus is a metabolic disorder affecting all age groups irrespective of the sex. It is arising due to the disorder of carbohydrate metabolism caused by the deficiency of insulin. Consequently, the blood sugar level either increases (hyperglycemia) or decreases (hypoglycemia) from the normal level. Under clinical terminology, diabetes can be categorized as (i) Type 1: Insulin dependent diabetes mellitus (IDDM) (ii) Type 2: Non-insulin dependent diabetes mellitus (NIDDM). The World Health Organization (WHO) had predicted 3 years ago that nearly 150 million people worldwide are suffering from diabetes and the number will be doubled by the end of this year[1]. This disease is a silent killer being asymptomatic till an advanced stage and cripples the vital organs of the human body. Since a large number of people are suffering from this disorder, great interest is taken in the study of these drugs. In NIDDM, the build up of sugar in the blood is due not to a lack of insulin, but to the body's inability to make proper use of it. Now-a-days oral antidiabetic drugs are used to treat NIDDM because they are effective, non-toxic and correct the basic metabolic disorder in diabetes[2, 3]. Current therapy for the treatment of hyperglycemia of type 2 diabetes includes the following groups of OHAs (oral hypoglycemic agents) sulfonylureas, biguanides, α-glucosidase inhibitors, meglitinides and thiazolidinediones[4].

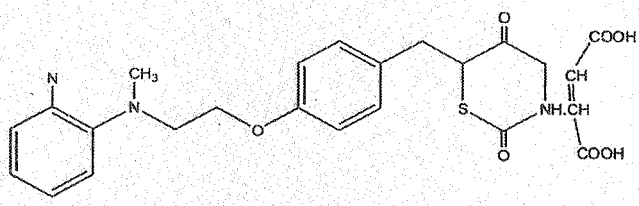
Glibenclamide ($C_{23}H_{28}ClN_3O_5S$) is of sulphonylurea category and is chemically described as 1-[[4-[2-[(5-chloro-2-methoxy benzoyl) amino) ethyl] phenyl] sul-

†PG & Research Department of Physics, Presidency College, Chennai-600 005, India.

phonyl]-3-cyclohexylurea[5]. It is a white crystalline powder, practically insoluble in water, soluble in ethanol, methanol, chloroform and dilute solutions of alkali hydroxides[6]. Glibenclamide works primarily by stimulating pancreatic insulin secretion, which in turn reduces hepatic glucose output and increases peripheral glucose disposal. It is a potassium channel blocker whose effect on the pancreatic β-islet cells is to allow an influx of calcium into the cell, which causes an increase in the release of insulin[4]. It is available in the form of tablets and should be stored in tightly closed light resistant containers[5, 6].



Glibenclamide



Rosiglitazone maleate

Fig. 1. Molecular structures of glibenclamide and rosiglitazone maleate

Rosiglitazone maleate belongs to thiazolidinediones, a new class of oral antidiabetic agents, commercially known as glitazones. This drug was introduced in the year 1999 in the international market[4]. Within a short span of time after the launch, the drug has been prescribed for a number of type-2 diabetes patients as it reduces cardiac risk factors and blood pressure[7]. This drug does not stimulate the pancreas to produce more insulin, but decreases insulin resistance by increasing glucose uptake and metabolism in muscle and fat[4]. It reduces plasma glucose, lipid and insulin in twice daily dosage. It can be used as monotherapy or with sulphonylurea, biguanide and insulin[8]. Rosiglitazone maleate is chemically described as 5-[[4-[2-(methyl-2-pyridinyl amino) ethoxy] phenyl] methyl]-2,4-thiazolidine dione[9]. Its molecular formula is $C_{18}H_{19}N_3O_3S$ and molecular weight is 357.4. Also it is a white to off-white solid which should be stored in airtight, light-resistant containers.

An extensive research work has been carried out by several investigators with different oral hypoglycemic pharmaceutical compounds[4, 10–12]. During the course of investigation on these drugs, our attention has been turned towards antidiabetic drugs namely glibenclamide and rosiglitazone maleate.

EXPERIMENTAL

High-grade pure samples of glibenclamide and rosiglitazone were procured from a reputed pharmaceutical company, Sun Pharmaceutical Industries Limited, Mumbai, India and were used as such. The FTIR spectra were recorded in the range 4000–400 cm^{-1} using Brucker IFS 66 V spectrophotometer in the solid state and the FT Raman spectra were observed using Brucker FRA 106 FT Raman spectrophotometer at Sophisticated Analytical Instrumentation Facility, IIT, Chennai, India. The FT-IR module has globar and mercury vapour lamp as the sources and the interferometer chamber has KBr and Mylar beam spitters. The sampling technique used was KBr pellet method. Both the FTIR and FTR spectrometers have a resolution of 0.1 cm^{-1}. They have the facilities of signal averaging, signal enhancement, baseline correction and other spectral manipulations are also possible with multitasking OPUS software on the dedicated PC/INTEL-4.

UV-Vis spectral measurements of the drugs were carried out using Elico SL 159 UV-Visible spectrophotometer at Spectrophysics Research Laboratory, Pachaiyappa's College, Chennai, India. The sources that produce ultraviolet rays in the spectrometer were deuterium and tungsten halogen lamps with the monochromator as Czerny-Turner type with 1200 lines/mm holographic grating. The detector had a wide range of photodiodes with greater efficiency and stray light loss is about 0.1% at 220 nm with NaI 10 g/L. The scanning range capability of the device was 200–1000 nm with an accuracy of ± 0.5 nm. Quartz cuvettes of 10 mm path length were used. The one normal solution of the drugs under investigation was prepared initially and by successive dilution, the other concentrations were got. Methanol was used as solvent. The amount of absorption of UV-Vis radiation was measured for each concentration at the characteristic wavelength maximum λ_{max}.

RESULTS AND DISCUSSION

Vibrational spectral analysis: The infrared spectrum of a compound is essentially the superposition of the absorption bands of specific functional groups. The structures of the drugs chosen, *viz.*, glibenclamide and rosiglitazone are presented in Fig. 1. The functional groups present in the drugs were identified and a satisfactory vibrational band assignment was made by observing the nature, shape and intensity of the vibrational bands in the FTIR and FT Raman spectra. The vibrational band assignments of glibenclamide and rosiglitazone maleate are presented in Tables 1 and 2 respectively.

A detailed discussion on the vibrational frequencies is given as follows:

(i) Glibenclamide

N—H Vibration: For primary amides two sharp bands of medium intensity are observed due to the asymmetric and symmetric stretching vibrations at about 3500–3300 cm^{-1}.[13, 14] In the case of primary aromatic amines, N—H stretching vibrations are of medium intensity in the region 3520–3350 cm^{-1}.[15] In the solid phase, primary sulphonamides[16] have strong bands due to their N—H stretching

vibrations in the region 3390–3245 cm^{-1}. Also N-mono-substituted sulphonamides have their N—H stretching vibrations at 3320–3250 cm^{-1}. The strong band observed at 3315 cm^{-1} in the FTIR spectrum is assigned as N—H stretching vibration. This band is present in the Raman spectrum as a weak band at 3314 cm^{-1}.

TABLE-1
VIBRATIONAL SPECTRAL ASSIGNMENT OF GLIBENCLAMIDE

Frequency (cm^{-1})		Assignment	Component group of structure
FTIR	FT Raman		
3315 s	3314 w	N—H stretching	Amine
2930 m	2937 w	C—H asymmetric stretching	Cyclohexane
2839 w		C—H symmetric stretching	Cyclohexane
1715 vs	1719 m	C=O stretching	Urea
1617 vs		C=O stretching/C=C stretching	Urea/Benzene
1591 m		C=C stretching	Benzene
1524 vs	1524 m	C=C stretching	Benzene
1479 s		N—C—N asymmetric stretching	Urea
1459 s		N—C—N asymmetric stretching	Urea
1342 s	1352 m	SO_2 asymmetric stretching	Sulphonyl group
1277 s		C—H in-plane deformation	Benzene
1245 m	1255 s	C—H in-plane deformation	Benzene
1158 vs	1162 s	SO_2 symmetric stretching	Sulphonyl group
1123 m	1100 w	C—C stretching	Cyclohexane
1012 m		N—C—N symmetric stretching/ C—C stretching	Urea/Cyclohexane
905 m	912 w	C—H— out-of-plane deformation	Benzene
820 m		C—H out-of-plane deformation	Benzene
685 m		C—H out-of-plane deformation	Benzene
573 s		C—C skeletal stretching/In-plane SO_2 deformation	Cyclohexane/Sulphonyl group
541 s	548 w	C—C skeletal stretching	Cyclohexane

Ring Vibrations: The band due to C—H asymmetric stretching vibrations of cyclohexane[17] usually occurs in the region 2940–2915 cm^{-1}.[18] In view of this, the absorption band of medium intensity occurring at 2930 cm^{-1} and a weak band at 2839 cm^{-1} in the FTIR spectrum are assigned as C—H asymmetric and symmetric stretching vibrations respectively. The C—H asymmetric stretching band occurs at 2937 cm^{-1} as a weak band in the FT Raman spectrum.

Cyclohexane derivatives[18] have bands of variable intensity in the region 1055–950 cm^{-1} and 570–435 cm^{-1} for the C—C skeletal stretching vibrations. The bands of weak intensity due to C—C stretching occur at 1055–950 cm^{-1} and the bands of strong intensity due to the same vibration occur at 570–435 cm^{-1}. In the FTIR

spectrum, the bands of medium intensity at 1123, 1094 and 1012 cm^{-1} and the bands of strong intensity at 573 and 541 cm^{-1} are due to C—C skeletal stretching of the cyclohexane group. The same bands occur as weak bands at 1100 and 548 cm^{-1} in the FT Raman spectrum of glibenclamide confirming the presence of cyclohexane functional group.

TABLE-2
VIBRATIONAL SPECTRAL ASSIGNMENT OF ROSIGLITAZONE MALEATE

Frequency		Assignment	Component group of structure
FTIR	FT Raman		
3107 w	3110 w	Aromatic C—H stretching	Pyridine
1749 s	1755 m	C=O stretching	Imide group
1700 vs	1724 m	C=O stretching	Imide group
1645 m	1686 w	C=C stretching	Pyridine
1622 s	1618 w	C=C stretching	Pyridine
1589 s	1552 w	C=C stretching	Pyridine
1510 vs		C=N stretching	Pyridine
1361 s		C—N stretching	Imide group
1332 m	1341 m	C—N stretching	Imide group
1264 m	1268 m	C—H in-plane deformation	Benzene
1237 s		C—H in -plane deformation	Benzene
1166 m	1155 w	C—H in-plane deformation	Pyridine
1142 m		C—H in-plane deformation	Pyridine
864 m		C—H out-of-plane deformation	Benzene
842 w	833 w	C—H out-of-plane deformation	Benzene
764 s	747 m	C—H out-of-plane deformation	Pyridine
604 w	613 m	In-plane ring deformation	Pyridine

The fundamental studies on benzene vibrations have the characteristic skeletal stretching modes of the carbon-carbon bonds leading to the appearance of bands of strong intensity between 1650 and 1450 cm^{-1}. For di- and tri-substituted benzene rings[14], strong bands due to C=C stretching occur at 1625–1590 and 1525–1480 cm^{-1}. In the present investigation, the bands of very strong intensity at 1617, 1524 cm^{-1} and bands of strong intensity at 1591 and 1479 cm^{-1} in the FTIR spectrum of glibenclamide are due to C=C stretching vibrations. These vibrations occur as medium intensity bands at 1534 cm^{-1} in the FT Raman spectrum.

For 1,4-disubstituted benzenes[16], the aromatic C—H in-plane deformation occurs in the range 1270–1125 cm^{-1} and the bands will be of strong to medium intensity. A strong band at 1277 cm^{-1} and a medium intensity band at 1245 cm^{-1} are due to C—H in-plane deformation vibration in the FTIR spectrum of glibenclamide, which is present in FT Raman spectrum at 1255 cm^{-1} as a strong band.

The out-of-plane C—H deformation[14] occurs in the range 900–675 cm^{-1} and the bands exhibited at 905, 820 and 685 cm^{-1} in the FTIR spectrum are allotted as C—H out-of-plane deformations and they are confirmed by FT Raman bands.

SO_2 Vibrations: In the solid phase, sulphonamides have a very strong, broad absorption band at 1360–1315 cm^{-1}, which is due to asymmetric stretching vibration of the SO_2 group[17].

In solution, this band is about 10–20 cm^{-1} higher. Also, a very strong band due to symmetric stretching vibration of the SO_2 group occurs at 1180–1140 cm^{-1} when in the solid phase. The medium intense band observed at 1342 cm^{-1} in the FTIR spectrum of the compound has been considered to be due to SO_2 asymmetric stretching. The very strong band at 1158 cm^{-1} is due to SO_2 symmetric stretching. A strong intensity band due to in-plane SO_2 deformation vibration occurs in the frequency range 610–565 cm^{-1}.[16, 18] In the FTIR spectrum of glibenclamide, this vibration occurs at 573 cm^{-1} as a strong intensity band.

C=O Vibrations: Ketones and aldehydes show a strong C=O stretching absorption band in the region 1870–1540 cm^{-1}.[19] The band due to the stretching of the carbonyl group of urea[16, 17] occurs at 1705–1635 cm^{-1}. Its relatively constant position, high intensity and relative freedom from interfering bands make this one of the easiest bands to recognize in the infrared spectra. Also the presence of ring strain and strongly electron accepting groups on the nitrogen tend to increase the frequency of these vibrations. The bands of strong intensity in the FTIR spectrum of glibenclamide at 1715 cm^{-1} and 1617 cm^{-1} are thus assigned as (C=O) vibrations. This band is in FT Raman spectrum at 1719 cm^{-1} as a medium intensity band.

N—C—N Vibrations: Ureas have a strong, characteristic band at 1490–1465 cm^{-1} due to the asymmetric stretching vibration of the (N—C—N) group[17] and the band due to symmetric stretching vibration being of medium intensity occurs at about 1010 cm^{-1}. The strong and medium intense bands at 1479, 1459 and 1012 cm^{-1} in the FTIR spectrum of glibenclamide are due to the (N—C—N) asymmetric and symmetric stretching vibrations. The same bands are present in the FT Raman spectrum at 1534 and 1100 cm^{-1} as medium and weak intensity bands.

(ii) Rosiglitazone maleate

C=O Stretching: A strong absorption band due to C=O stretching occurs in the region 1850–1550 cm^{-1}. Because of high intensity and the relatively interference free region in which it occurs, this band is easy to identify[20]. Also the carbonyl bands of the imide group[18] are strong bands at 1750–1730 cm^{-1}. The band of very strong intensity at 1749 cm^{-1} in the FTIR spectrum of rosiglitazone is assigned as C=O stretching and the very same vibration is present in the FT Raman spectrum at 1755 cm^{-1} as a medium intensity band.

C—N Vibrations: Strong bands occur in the region 1360–1250 cm^{-1} due to C—N stretching vibrations for primary aromatic amines absorb the infrared radiation strongly in this frequency range[21]. Also the C—N stretching vibrations of imides produce strong and medium intensity bands in the range 1365–1340 cm^{-1}.[15] The strong and medium intense bands at 1361 cm^{-1} and 1332 cm^{-1} in the FTIR spectrum are assigned as C—N stretching whereas the same band is present as a medium intense band at 1341 cm^{-1} in the FT Raman spectrum.

Ring Vibrations: The aromatic C—H stretching vibrations of nitrogen het-

erocyclic aromatic compounds give rise to a band at 3100–3010 cm^{-1}.[15] Being a compound having six-membered heterocyclic pyridine ring, the weak bands at 3107 and 3110 cm^{-1} in the FTIR spectrum of rosiglitazone are assigned as C—H stretching vibration.

The spectral region 1615–1575 cm^{-1} is occupied by a number of strong to medium intensity C=C stretching vibrations. Interactions between ring C=C and C=N stretching vibrations result in two strong to medium intensity absorptions about 100 cm^{-1} apart[20]. These absorptions occur at 1615–1575 and 1520–1465 cm^{-1}, the higher frequency band often has another medium intensity band on its low frequency side, which is found at 1590–1555 cm^{-1}. As a result, the strong to medium intense bands occurring at 1645, 1622 and 1589 cm^{-1} in the FTIR spectrum and the bands at 1618, 1552 cm^{-1} in the FT Raman spectrum are assigned as C=C stretching vibrations. The very strong band occurring at 1510 cm^{-1} in the FTIR spectrum is due to C=N stretching.

The spectral region 1290–1000 cm^{-1} is occupied by a number of C—H in-plane deformation vibrations[14] which are sharp and weak to medium in intensity. The bands present at 1264, 1237, 1166, 1142, 1059, 1044 and 1038 cm^{-1} in the FTIR spectrum of rosiglitazone are allotted to be due to C—H in-plane deformations. These vibrations occur at 1268, 1213, 1155 and 1044 cm^{-1} as weak intensity bands in the FT Raman spectrum of the drug.

Strong bands are observed in the region 850–600 cm^{-1} due to C—H out-of-plane deformations of pyridine ring[17]. In the FTIR spectrum of the compound, the strong to medium intense bands at 842, 764, 717, 654 and 604 cm^{-1} are due to C—H out-of-plane deformation and these are present in FT Raman spectrum at 833, 747 and 613 cm^{-1} as medium and weak intensity bands.

Thus a qualitative analysis on the vibrational bands in the FTIR and FT Raman spectra of glibenclamide and rosiglitazone have been made for different functional groups present and the results obtained have been briefly discussed.

Qualitative analysis on the drugs by internal standard calculations

The pharmaceutical activity of a drug is solely dependent on the preservative environmental condition; FTIR spectroscopic investigation being a powerful tool for qualitative analysis is used in pharmaceutical industry to study the stability of the drugs under different storage conditions. FTIR spectra of the drugs glibenclamide and rosiglitazone exposed to sunlight for a stipulated period of 6 h were recorded and the quality of the drugs was analyzed by comparing the sets of internal standards that were arrived at from absorbance ratios of the sample kept at suitable storage conditions at specific modes of vibration[22] with those of the samples exposed to sunlight.

Fig. 2 represents the normalized overlay FTIR spectra of glibenclamide and rosiglitazone at different storage conditions. Table-3 provides the internal standards calculated for glibenclamide and rosiglitazone at specific modes of vibration. From the bar diagrams in Fig. 3, it is observed that the internal standard of glibenclamide exposed to environmental hazards shows marked changes from that stored at suitable storage conditions. Also, no peaks are detected in the FTIR spectrum of exposed rosiglitazone. This undoubtedly explains the complete decomposition of the drug when it is exposed to environmental hazards[23].

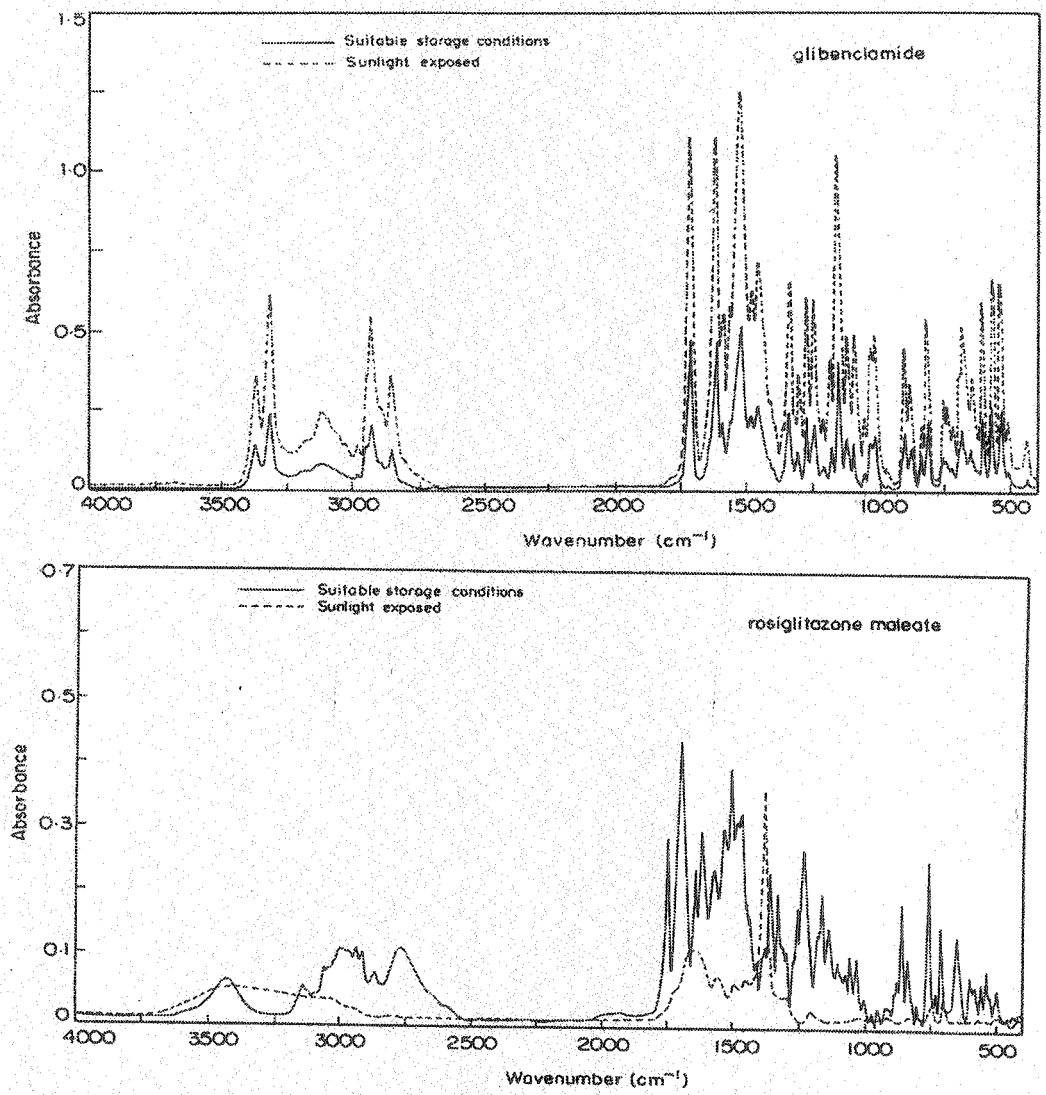


Fig. 2. FTIR overlay spectra of glibenclamide and rosiglitazone maleate

TABLE-3
INTERNAL STANDARDS AT SPECIFIC MODES OF VIBRATION

Conditions of exposure	Internal standards at specific modes of vibration of glibenclamide							
	3315/1524	2931/1524	1524/1524	1246/1524	1159/1524	906/1524	686/1524	542/1524
LRC	2.16	2.415	1	2.415	1.204	2.736	2.56	1.954
Sunlight	1.025	1.133	1	0.921	0.621	0.686	1.214	0.9

Conditions of exposure	Internal standards at specific modes of vibration of rosiglitazone maleate							
	2938/864	1750/864	1622/864	1238/864	864/864	717/864	654/864	542/864
LRC	1.555	0.629		0.683	1	1.223	1.4	2.333
Sunlight	0.1	0.075	0.1	0.1	0.075	0.1	0.125	0.1

The UV-Visible spectroscopic measurements of glibenclamide and rosiglitazone have been made over the region 200–400 nm for different concentrations and hence the light absorption characteristics of the wavelength maxima for these drugs have been analyzed. The wavelength maxima for glibenclamide were

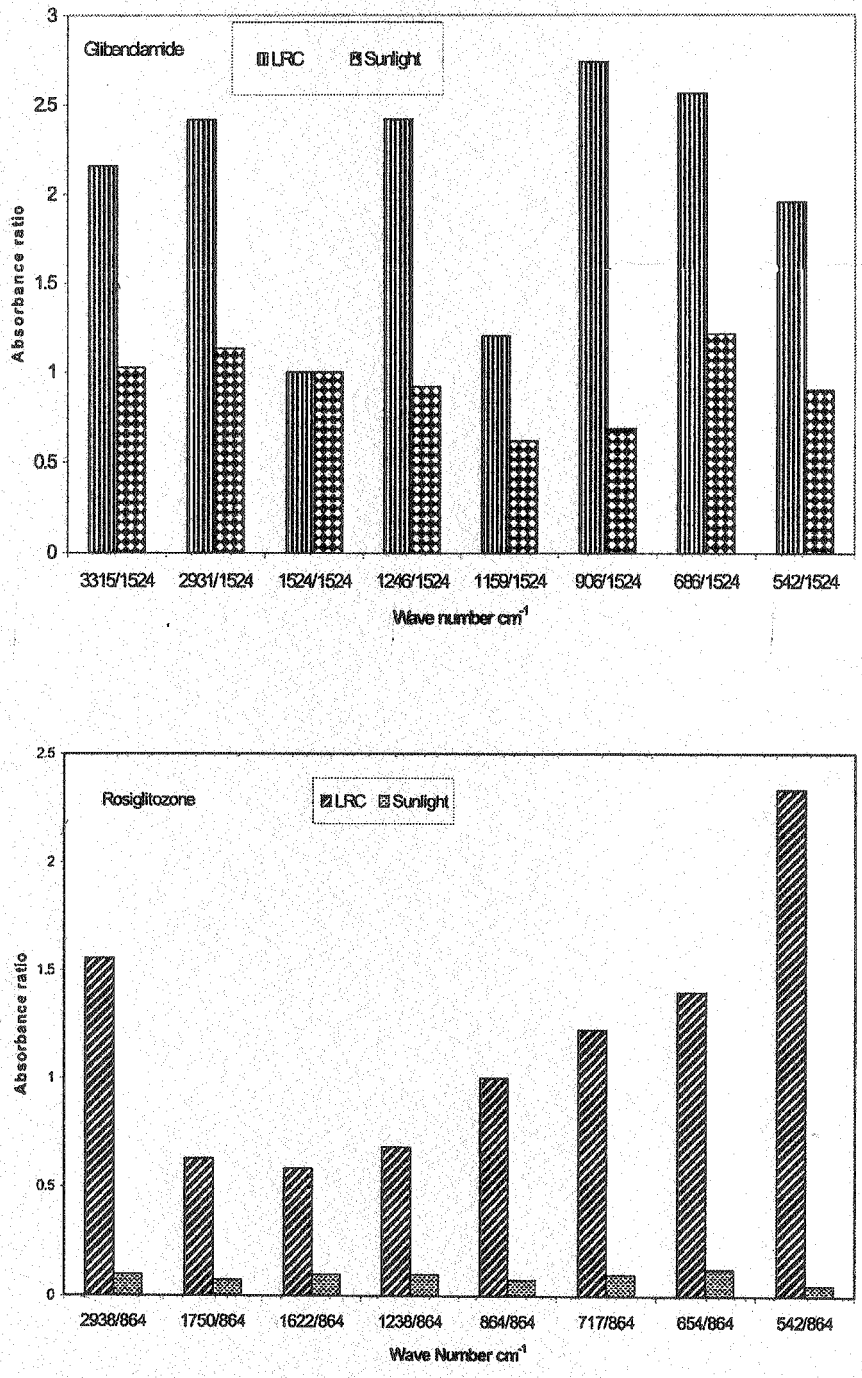


Fig. 3. Bar diagrams representing internal standards using FTIR spectra

observed at around 274 nm and 301 nm[5, 6]. Similarly, for the drug rosiglitazone, there were 3 λ_{max} observed in the UV-Vis spectrum at 250 nm, 279 nm and 316 nm[9] and the spectra of the two samples are presented in Fig. 4.

Table-4 summarizes the absorbance values obtained in the UV-Vis spectral measurements for the samples at different storage conditions and it also gives the ratio of absorbance among the peaks of the λ_{max} of the drugs. The constancy of

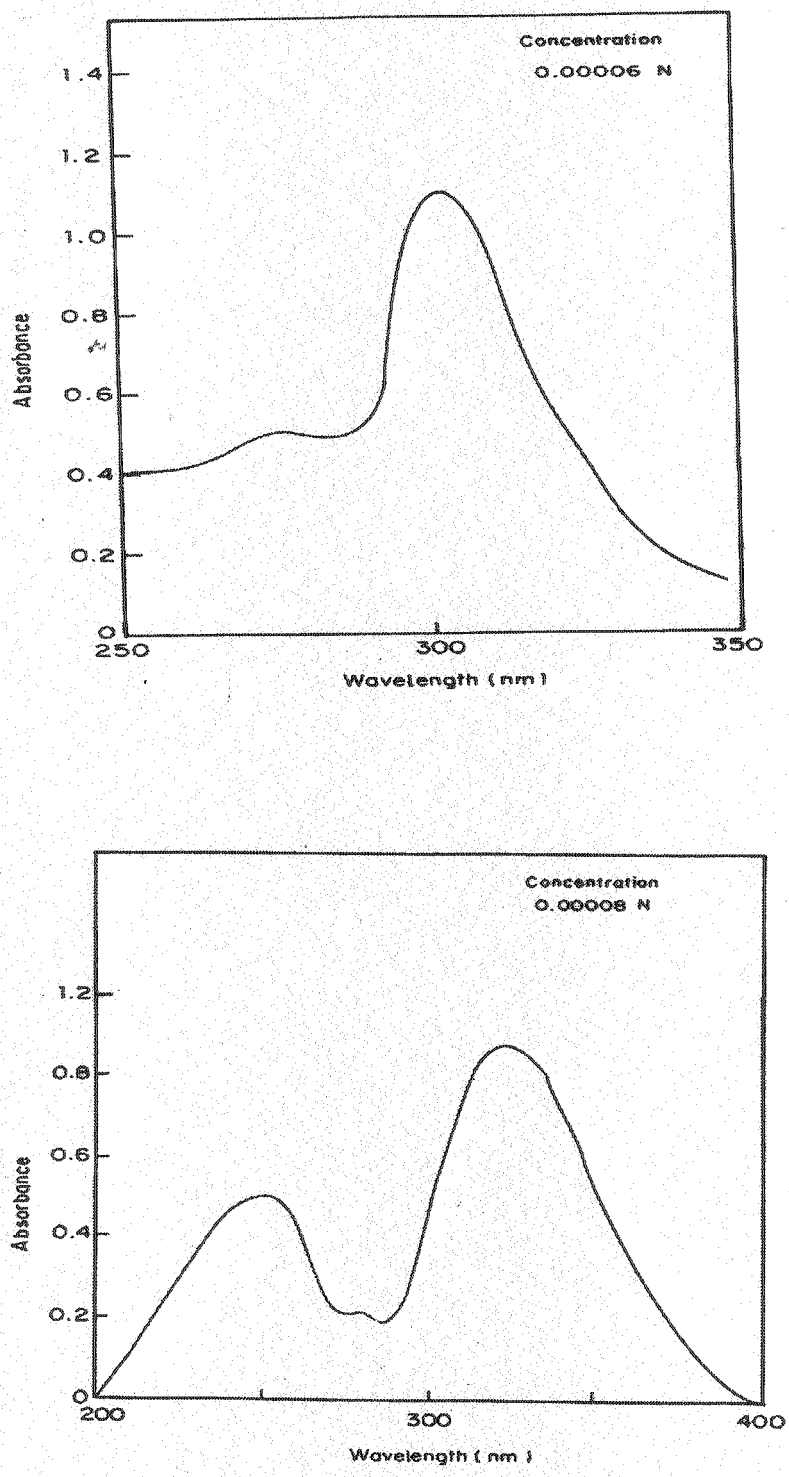
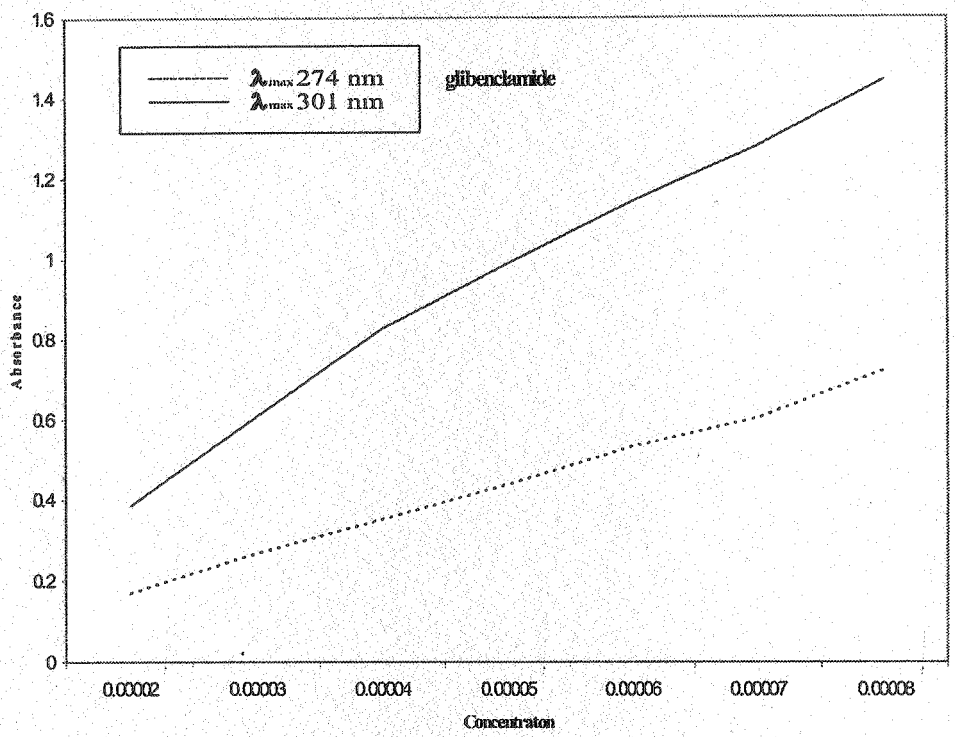


Fig. 4. UV-Visible spectra of the drugs at suitable storage conditions

the internal standard assures the stability of the drug under suitable storage conditions. A graph of concentration *vs.* absorption at λ_{max} is drawn (Fig. 5) and the slopes of the straight lines are calculated and used as a quality-checking factor for the compounds. The absorbance ratio varies markedly when the drugs were exposed to environmental hazards.



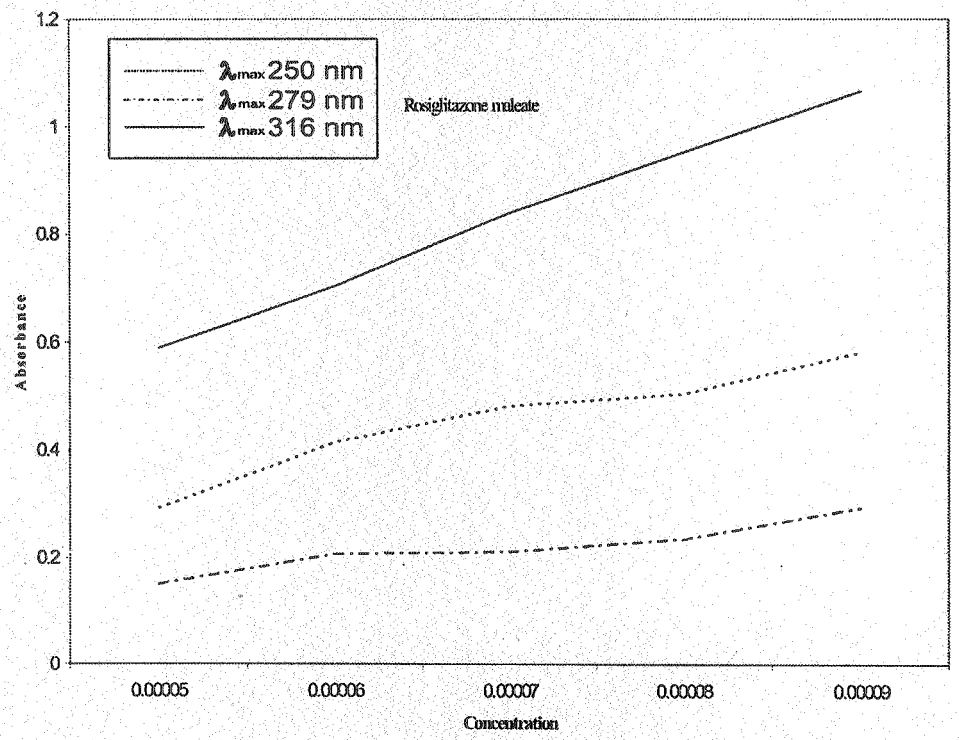


Fig. 5. Variation of absorbance with concentration at suitable storage conditions

TABLE-4
LIGHT ABSORPTION CHARACTERISTICS OF GLIBENCLAMIDE AND ROSIGLITAZONE MALEATE AT DIFFERENT STORAGE CONDITIONS

Conditions of exposure of glibenclamide	Concentration (N)	Wavelength maxima (nm)		Absorbance ratio A_1/A_2
		274.8	301.2	
		Absorbance (A)		
		A_1	A_2	
Suitable storage condition	0.00008	0.721	1.443	0.4997
	0.00007	0.603	1.279	0.4715
	0.00006	0.532	1.142	0.4658
	0.00005	0.428	0.988	0.4433
	0.00004	0.352	0.826	0.4261
	0.00003	0.269	0.607	0.4432
	0.00002	0.170	0.384	0.4427
Sunlight exposed	0.00008	0.338	0.651	0.519
	0.00007	0.317	0.601	0.527

Conditions of Exposure of rosiglitazone	Concentration (N)	Wavelength maxima (nm)			Absorbance ratio		
		250	279	316.5			
		Absorbance (A)					
		A_1	A_2	A_3	A_1/A_2	A_2/A_3	A_1/A_3
Suitable storage condition	0.00009	0.582	0.294	1.067	1.9796	0.2755	0.5455
	0.00008	0.505	0.236	0.954	2.1398	0.2474	0.5294
	0.00007	0.482	0.212	0.841	2.2736	0.2521	0.5731
	0.00006	0.415	0.208	0.704	1.9952	0.2955	0.5894
	0.00005	0.292	0.152	0.589	1.9211	0.2580	0.4958

Conclusion

A satisfactory vibrational band assignment has been made for the drugs glibenclamide and rosiglitazone using FTIR and FT Raman spectroscopy. The overlay spectra clearly show that the absorbance of the drugs exposed to environmental hazards changes to a greater extent than the drugs stored in the light resistant containers. Though the internal standards of specific modes of vibration at all wavenumbers were calculated, only two sets each for one drug are focussed here in the bar diagrams. From the FTIR spectral studies of glibenclamide and rosiglitazone maleate, it can be concluded that glibenclamide is more stable than rosiglitazone, when the drugs are exposed to environmental hazards. There was a complete degradation of rosiglitazone, when it was exposed to sunlight. Evidently, no peaks were detected in the FTIR spectrum of the sunlight-exposed sample.

In the UV-Vis spectral studies, the theoretically linear relationship between the concentration of the absorbing species in the light path and the absorbance, known as Beer-Lambert law is obeyed by both glibenclamide and rosiglitazone maleate for their λ_{max} values. As the efficacy of the drugs was lost when they were exposed

to different storage conditions, the law is violated. Also the ratio of absorbance for two λ_{max} at various concentrations was found to be a constant only at the suitable storage conditions. The ratio was not a constant for the drugs exposed to environmental hazards. Thus UV-Vis spectral results are found well in accordance with the FTIR spectral interpretations.

It is seen that the efficacy of the drugs is lost when they are not stored properly. From the comparative study, it is suggested that keeping these drugs in light-resistant, airtight containers may help in retaining their pharmaceutical properties.

REFERENCES

1. J. Marks, *J. Science*, **296**, 686 (2002).
2. R.S. Satoskar, S.D. Bhandarkar and S.S. Ainapure, Pharmacology and Pharmacotherapeutics, 15th Edn., Popular Prakashan, Mumbai (1997).
3. S. Gunasekaran and M.K. Devi, *Acta Ciencia Ind.*, **29**, 355 (2003).
4. J.Ketz, A review of Oral Antidiabetic Agents, Pharmacotherapy Update, Vol. IV, No. 3 (2001).
5. The Pharmaceutical CODEX: Principles and Practice of Pharmaceutics, 12th Edn., Pharmaceutical Press Publications, London, UK (1994).
6. Indian Pharmacopoeia, Vol. I, Controller of Publications, New Delhi, p. 347 (1996).
7. M.C. Granberry and V.A. Fonseca, *Am. J. Cardio Vasc Drugs.*, **3**, 201 (2005).
8. A.J. Wagstaff and K.L. Goa, *Treat Endocrinol.*, **1**, 411 (2002).
9. K. Parfitt, Martindale: The Complete Drug Reference, 36th Edn., Pharmaceutical Press Publications, London, UK (1999).
10. S.A. Weinzimer, *Best Practice of Medicine* (Feb. 2002).
11. U.K. Prospective Diabetes Study Group, *ACP J. Club*, **3**, 130 (1999).
12. S. Gunasekaran and M.K. Devi, *Asian J. Chem.*, **16**, 183 (2004).
13. S. Gunasekaran, P. Kumaresan, K. Manoharan and S. Mohan, *Asian J. Chem.*, **6**, 82 (1994).
14. S. Gunasekaran and G. Sankari, *Acta Ciencia Indica*, **31**, 61 (2005).
15. S. Gunasekaran, R.K. Natarajan, R. Rathikha and D. Syamala, *Indian J. Phys.*, **5**, 79 (2005).
16. G. Socrates, Infrared Characteristic Group Frequencies, John Wiley & Sons, New York (1980).
17. L.J. Bellamy, The Infrared Spectra of Complex Molecules, Methuen, London (1958).
18. N.B. Colthup, L.H. Daly and S.E. Wiberly, Introduction to Infrared and Raman Spectroscopy, 2nd Edn., Academic Press, New York (1975).
19. S. Gunasekaran and L. Abraham, *Indian J. Phys.*, **78**, 485 (2004).
20. S. Gunasekaran, R.K. Natarajan, R. Rathikha and D. Syamala, *Indian J. Pure Appl. Phys.*, **43**, 503 (2005).
21. G. Ramanarao, *J. Raman Spectrosc.*, **20**, 529 (1989).
22. R.M. Silverstein, C.G. Bassler and T.C. Morrill, Spectrometric Identification of Organic Compounds, 4th Edn., Wiley, New York (1991).
23. S. Gunasekaran and P. Abitha, *Asian J. Chem.*, **15**, 1764 (2003).

(*Received*: 21 September 2005; *Accepted*: 5 June 2006) AJC-4942