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SPECTROSCOPICAL VIBRATIONAL BAND ASSIGNMENT AND QUALITATIVE ANALYSIS OF BIOMEDICAL COMPOUNDS WITH CARDIOVASCULAR ACTIVITY

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Abstract: Spectroscopic methods such as FTIR and Raman spectroscopy were used for the vibrational band analysis of biomedical compounds with cardiovascular activity such as metoprolol tartarate and trimetazidine hydrochloride. Metoprolol is a cardio selective beta 1-adrenoreceptor blocking agent in the treatment of hypertension, angina pectoris, and myocardial infarction. Trimetazidine is a clinically effective antianginal agent that has no negative inotropic or vasodilator properties. The vibrational bands of these compounds were assigned using the FTIR and Raman spectrum of the pure samples of these drugs. By employing FTIR and UV-Visible spectral techniques the change in the quality of the drugs when stored in different conditions have been studied. The assay of tablets of these drugs were done using UV-Visible spectroscopy and compared with the labeled amount.

Keywords: FTIR spectroscopy, Raman spectroscopy, UV-Visible spectroscopy cardiovascular drug, vibrational frequency, Drug assay.

1. INTRODUCTION

Metoprolol tartrate 1-(Isopropylamino)-3-(p-(2-methoxyethyl)phenoxy)-2propanol(2:1) Dextro-tartrate salt is known as a cardio selective beta adrenergic receptor blocker [1]. It is widely used in the treatment of angina pectoris, arrhythmias and hypertension. This drug is highly soluble and its enhanced therapeutic efficacy through the provision of constant rate input and maintenance of steady-state blood levels is well documented [2]. Early pharmacokinetic studies have established that it has a relatively short plasma half-life of 3-4 h and its absorption is rapid as well as consistent throughout the gastrointestinal tract including the distal region [3]. A combination of both these properties makes metoprolol tartrate a suitable candidate for development into controlled release formulation.

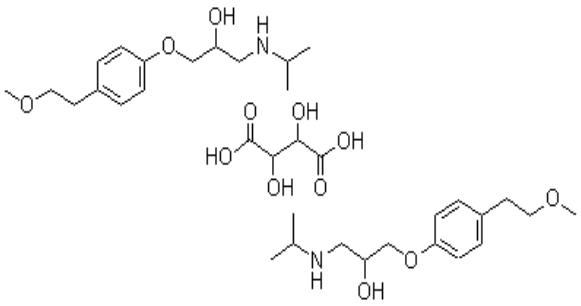


Fig 1 (a) Metoprolol tartrate

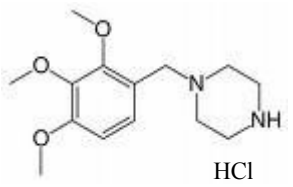


Fig 1(b) Trimetazidine Hydrochloride

Trimetazidine 1-[(2,3,4-trimethoxyphenyl) methyl]piperazine hydrochloride is a clinically effective antianginal agent that has been used in the prophylaxis and management of angina pectoris, and in ischemica of neurosensorial tissues as in Menier's disease [4]. The antianginal efficacy of trimetazidine is comparable to propranolol but it does not reduce cardiac rare-pressure product or coronary blood flow [5]. Trimetazidine exhibits some cytoprotective effects on myocardial energy metabolism and exerts an antianginal effect in the absence of significant hemodynamic effects [6]. For these clinical successes, it has become unique among the antianginal agents, and it has been clinically used throughout many counties worldwide [7].

It is very essential to design pharmaceutical products that consistently deliver the intended performance, which demands monitoring of their quality incessantly. Quality of drug plays a very vital role indicating the suitability of drug product for its intended use. In this work, a quality analysis of cardiovascular drugs metoprolol tartarate and trimetazidine hydrochloride has been carried out by employing FTIR and FT-Raman spectroscopic techniques. The change in quality of these drugs when stored under various conditions has been studied. Based on the structure of these drug molecules and other similar molecules, vibrational band assignment has been made from the FTIR and FT-Raman vibrational spectra.

2. EXPERIMENTAL

2.1 Materials

Metoprolol tartrate and trimetazidine hydrochloride of the pharmaceutical grade were procured for Orchid Chemicals, Mumbai, India and were used as received.

2.2 FTIR, FT- Raman and UV-Visible spectroscopy

The FTIR spectra of the drugs metoprolol tartrate and trimetazidine hydrochloride were recorded with ABB Bomem Series spectrophotometer over the region of 400 – 4000cm^{-1} by adopting KBr pellet technique at Dr. CEEAL Analytical Lab, Chennai, India. The FT-Raman spectra were recorded over the region 100 – 3700 cm^{-1} by Raman spectrophotometer Nexus 670 at CECRI, Karaikudi, India. The UV-visible spectral measurements were carried out using Shimadzu-160A spectrophotometer at DR. CEEAL Analytical Lab, Chennai. All the spectra were recorded at the room temperature. The frequencies of all the sharp vibrational bands are accurate to ±1 cm^{-1}.

3. RESULTS AND DISCUSSION

3.1 Vibrational Spectral Analysis

The IR spectrum of a compound is the superposition of the absorption bands of specific functional groups. By observing the position, shape and relative intensities of the vibrational bands in FTIR and FT Raman spectra of the drug molecules metoprolol tartrate and trimetazidine hydrochloride, a satisfactory vibrational band assignment has been made and summarized in Tables 1 and 2.

In the analysis of Metoprolol tartrate the band at 3459 cm^{-1} and 3033cm^{-1} is attributed to the N-H and O-H stretching vibrations respectively. The ring characteristic band appears at 1440cm^{-1} [8]. The band at 1358 cm^{-1} corresponds to the deformation of CH_3. It is a well known fact that the tartaric acid molecule is asymmetric. The carboxyl and hydroxyl groups are arranged in different planes and have different geometrical parameters. The OH, CH, and C=O stretching vibrations are characteristic with regard to their shape and frequency (1700 – 3600 cm^{-1} region). The deformation vibrations in the spectrum of tartaric acid, belonging to the carboxyl and alcohol groups, are strongly delocalized. The absorption bands observed in the spectra of carboxylic acid [9] are assigned to the O-H deformation and C-O valence vibrations of the carboxyl group in the 1200 cm^{-1} and 1300cm^{-1} to 1400cm^{-1} regions respectively. The absorption band at 1164cm^{-1} belongs to the asymmetric stretching vibration of the C-O of the secondary alcohol group [10]. The deformation vibration of the O-H, C-H of the alcohol group of the tartaric acid (1460 cm^{-1}, 1300cm^{-1}, 1250cm^{-1}) is mixed. Hence we speak of the vibrations belonging to the HCOH group [11]. The band 1460cm^{-1} belongs to C-H deformation vibration of low intensity. The band appearing at 1054cm^{-1} and 1014cm^{-1} are assigned to the C-O stretching and deformation vibrations respectively. The band at 967cm^{-1} is assigned to O-H deformation vibration of the carboxyl group. The bands at 935cm^{-1} and 821cm^{-1} are assigned to out of plane O-H vibration of the carboxyl group. There is a weak band detected at 780 cm^{-1} in both FTIR and Raman spectrum due to the liberation of H_2O [12]. At lower frequencies the vibrations are dominated by the O-H band. The bands at the 680cm^{-1} and 605cm^{-1} with their corresponding Raman bands are assigned to the out of plane O-H vibration of the alcohol. The bands at 542cm^{-1} and 508cm^{-1} are assigned to O-H torsional vibration and CO_2 deformation respectively [13].

Table 1 Vibrational band assignment for Metoprolol Tartrate

Frequency (cm^{-1})		Vibrational band assignment
FTIR	**FT Raman**	
3459(w)	3419(s)	N-H stretching
3033(w)	-	O-H stretching
2983(m)	2987(vs)	N-H/C-H symmetric stretching
2938(w)	-	C-H stretching
2875(m)	-	C-H stretching
2813(w)	-	C-H stretching of CH_2 group
2745(vw)	-	N-H symmetric stretching
2572(vw)	-	N-H stretching
2552(w)	2556(m)	N-H stretching
2452(w)	-	O-H stretching
1590(s)	-	CO_2 antisymmetric stretching
1514(s)	-	CO_2 asymmetric stretching
1460(m)	1455(m)	O-H/C-H deformation
1400(m)	-	Aromatic ring stretching
1358(m)	-	CH_3 deformation
1300(m)	-	O-H deformation
1250(s)	1279(w)	O-H deformation
1235(m)	1245(m)	C-N stretching
1181(m)	-	C-O stretching
1164(m)	-	C-O antisymmetric stretching
1112(s)	-	C-O symmetric stretching
1074(w)	1081(w)	Aromatic ring stretching
1054(m)	-	C-O stretching
1014(m)	-	C-O deformation
967(m)	-	O-H deformation
935(m)	904(m)	Out of plane O-H vibration of carbonyl group
821(s)	819(s)	Out of plane O-H vibration of carbonyl group
780(w)	780(w)	Liberation of H_2O
686(m)	680(m)	Out of plane O-H vibration of alcohol
605(m)	621(w)	Out of plane O-H vibration of alcohol
542(m)	539(m)	O-H torsional vibration
508(m)	515(m)	CO_2 deformation

s-strong, m-medium, w-weak, vs-very strong, vw-very weak

Table 2 Vibrational band assignment for Trimetazidine hydrochloride

Frequency (cm^{-1})		Vibrational band assignment
FTIR	**FT Raman**	
3565(vw)		N-H symmetric stretching
3489(vw)	3421(w)	N-H symmetric stretching
3009(w)	3007(w)	C-H stretching
2984(m)	2988(s)	C-H stretching
2939(m)	2965(m)	N^+H_2 asymmetric stretching
2832(w)	-	C-H stretching of N bonded CH_3 group
2775(w)	-	N^+H_2 symmetric stretching
2709(m)	-	CH_2 symmetric stretching
1602(s)	1601(m)	N^+H_2 scissoring
1547(w)	-	Aromatic ring stretching
1504(s)	-	N-H bending deformation
1474(ms)	-	CH_3/CH_2 asymmetrical scissoring
1455(m)	1454(m)	CH_3 asymmetric deformation
1436(vw)	-	CH_2/NH_2 symmetric deformation
1417(s)	-	CH_2 symmetric scissoring

1377(vw)	-	CH_2 wagging
1363(w)	-	C-C stretching
1301(m)	-	CH_2 wagging
1290(s)	1289(m)	CH_2 twisting
1235(m)	1244(w)	C-N stretching
1210(m)	-	CH_3 twisting
1167(m)	-	C-H deformation
1102(vs)	-	C-N stretching
1070(m)	-	CH_2 twisting
1040(m)	1041(w)	Aromatic ring deformation
1031(w)	-	Aromatic ring deformation
1012(m)	-	Aromatic ring deformation
976(w)	-	C-S stretching
958(w)	956(w)	C-H twisting
919(w)	907(w)	Aromatic ring deformation
892(w)	-	C-H stretching
858(w)	-	C-H out of plane bending
841(m)	840(m)	C-H out of plane bending
832(w)	-	C-H twisting
692(w)	696(w)	N-H twisting
669(m)	-	Aromatic ring stretching
579(m)	-	Aromatic ring stretching

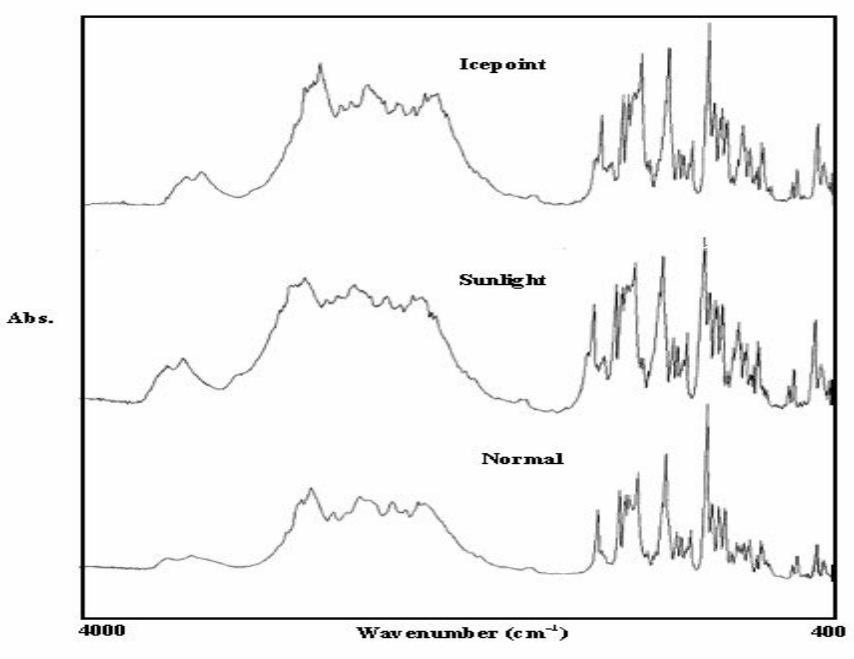
s-strong, m-medium, w-weak, ms-medium strong, vs-very strong, vw-very weak

In the case of trimetazidine starting from high wave numbers, the first feature observed in the vibrational spectra is the stretching vibration of the only N-H bond present in the molecule. This band is intense in the infrared spectra but shows only low intensity in the Raman spectra. The broad band shape and the shift toward lower wave numbers, pointed out the involvement of this band in hydrogen bonds in excellent agreement with the reported crystalline structure [14]. At lower wave numbers, the bands associated with the C-H stretching are observed. The first group corresponds to the C-H stretching of the thiophene and benzene rings [15], whereas the remaining bands are the symmetric and antisymmetric modes of the two methyl groups and the methylene functionalities of the piperazine ring [16]. It is interesting to notice that more bands are observed in this region than expected by considering the molecular structure; however the extra bands may be associated with overtones and combinations of lower energy modes. Proceeding to lower energy, the region between 1600 and1500 cm^{-1} is dominated by the bands associated with the double bonds, which are partially coupled to C-H and N-H bending deformations. The next spectral region (1500–1300 cm^{-1}) is mainly dominated by the deformations of the methyl, methylene and C-H groups. In the case of coupling, it is usually between neighboring groups (e.g. methylene deformation of the piperazinyl group coupled to the methyl at 1474 cm^{-1}). Between 1300 and 1100 cm^{-1}, the contribution of the C-C and C-N stretching is dominant and the vibrational modes are spread over the complete molecule having contributions of different moieties, as may be observed in Table 2. Below 1100 cm^{-1}, vibrational modes recover some localization and the corresponding bands are less overlapped. In this region, some relevant features are identified, such as the Raman band at 1040 cm^{-1}, characteristic of the in plane bending deformation of the benzene [17]. The deformations of the piperazinyl group coupled to other moieties are well identified in the infrared spectra. At lower wave numbers, the main components of the vibrational modes are the deformation and torsions of the rings giving rise to highly coupled movements [18]. Finally, the low energy vibrational modes originate from the deformations of the skeleton of the molecule and the lattice vibrations.

3.2 Qualitative Analysis using FTIR spectroscopy

The Indian Pharmacopoeia recommends that metoprolol and trimetazidine should be stored in tightly closed, light-resistant containers [19]. The behavior of these drugs that were stored under the prescribed storage with those stored at altered conditions has been compared. The FTIR spectra of the samples have been recorded for the pure drugs stored in (i) well-sealed light resistant container (ii) exposed to sunlight and (iii) at ice point. Fig 2 gives a comparison of the FTIR spectra of trimetazidine at different storage conditions.

Fig 2. Overlay of FTIR spectra of trimetazidine stored at different conditions



Tables 3 and 4 compares the absorbance values of some selected specific modes of vibration for both the molecules. These tables indicate change in the absorbance values with change in storage condition.

Table 3 Absorbance for certain modes of vibration under different conditions of storage for Metoprolol Tartrate

Frequency (cm^{-1})	Absorbance			Assignments
	Labeled condition	Exposed to sunlight	At ice point	
2983(m)	0.3882	0.2615	0.4888	N-H/C-H symmetric stretching
2552(w)	0.2426	0.1847	0.3377	N-H stretching
1460(m)	0.3090	0.2329	0.3741	O-H/C-H deformation
1250(s)	0.5296	0.3648	0.5697	O-H deformation
1074(w)	0.2116	0.1664	0.2791	Aromatic ring stretching
935(m)	0.1770	0.1591	0.2339	Out of plane O-H vibration of carboxyl group
686(m)	0.1540	0.1391	0.2035	Out of plane O-H vibration of alcohol
542(m)	0.1705	0.1509	0.2186	O-H torsional vibration

Table 4 Absorbance for certain modes of vibration under different conditions of storage for Trimetazidine Hydrochloride

Frequency (cm^{-1})	Absorbance			Assignments
	Labeled condition	Exposed to sunlight	At ice point	
3009(w)	1.1114	1.0119	0.5302	C-H stretching
2832(w)	0.9805	0.9145	0.4483	C-H stretching of N bonded CH_3 group
1602(s)	0.9353	0.8978	0.4770	N^+H_2 scissoring
1417(m)	1.5053	1.2023	0.7269	CH_3 symmetric scissoring
1102(vs)	1.9030	1.3495	1.1786	C-N stretching
958(w)	0.5145	0.5959	0.2710	C-H twisting
892(w)	0.7262	0.6249	0.2933	C-H stretching
669(m)	0.5087	0.4469	0.1909	Aromatic ring stretching

The internal standard ratio is calculated among the various absorption bands of these two drugs and the results are tabulated in Table 5 and Table 6. The internal standard ratios evaluated clearly states the change in the quality of drugs due to the alteration in the storage condition.

Table 5 Internal standard evaluation for Metoprolol Tartarate

Condition of Exposure	$A_{2983/2983}$	$A_{2552/2983}$	$A_{1460/2983}$	$A_{1250/2983}$	$A_{1074/2983}$	$A_{935/2983}$	$A_{686/2983}$	$A_{542/2983}$
	Internal Standard of specific modes of vibration at 2983 cm^{-1}							
Labeled condition	1.0000	0.6249	0.796	1.3642	0.545	0.4559	0.3967	0.4392
Exposed to sunlight	1.0000	0.7063	0.8906	1.395	0.6363	0.6084	0.5319	0.577
At ice point	1.0000	0.6909	0.7653	1.1655	0.5709	0.4785	0.4163	0.4472
	Internal Standard of specific modes of vibration at 2552 cm^{-1}							
	$A_{2983/2552}$	$A_{2552/2552}$	$A_{1460/2552}$	$A_{1250/2552}$	$A_{1074/2552}$	$A_{935/2552}$	$A_{686/2552}$	$A_{542/2552}$
Labeled condition	1.6001	1.0000	1.2737	2.183	0.8722	0.7296	0.6348	0.7028
Exposed to sunlight	1.4158	1.0000	1.261	1.975	0.9009	0.8613	0.7531	0.817
At ice point	1.4474	1.0000	1.1078	1.687	0.8265	0.6926	0.6026	0.6473
	Internal Standard of specific modes of vibration at 1460 cm^{-1}							
	$A_{2983/1460}$	$A_{2552/1460}$	$A_{1460/1460}$	$A_{1250/1460}$	$A_{1074/1460}$	$A_{935/1460}$	$A_{686/1460}$	$A_{542/1460}$
Labeled condition	1.2563	0.7851	1.0000	1.7139	0.6848	0.5728	0.4984	0.5518
Exposed to sunlight	1.1228	0.793	1.0000	1.5663	0.7145	0.6831	0.5973	0.6479
At ice point	1.3066	0.9027	1.0000	1.5229	0.7461	0.6252	0.5441	0.5843
	Internal Standard of specific modes of vibration at 1250 cm^{-1}							
	$A_{2983/1250}$	$A_{2552/1250}$	$A_{1460/1250}$	$A_{1250/1250}$	$A_{1074/1250}$	$A_{935/1250}$	$A_{686/1250}$	$A_{542/1250}$
Labeled condition	0.733	0.4581	0.5835	1.0000	0.3995	0.3342	0.2908	0.3219
Exposed to sunlight	0.7168	0.5063	0.6384	1.0000	0.4561	0.4361	0.3813	0.4137
At ice point	0.858	0.5928	0.6567	1.0000	0.4899	0.4106	0.3572	0.3838
	Internal Standard of specific modes of vibration at 1074 cm^{-1}							
	$A_{2983/1074}$	$A_{2552/1074}$	$A_{1460/1074}$	$A_{1250/1074}$	$A_{1074/1074}$	$A_{935/1074}$	$A_{686/1074}$	$A_{542/1074}$
Labeled condition	1.8346	1.1465	1.4603	2.5028	1.0000	0.8365	0.7278	0.8058
Exposed to sunlight	1.5715	1.101	1.3997	2.1923	1.0000	0.9561	0.8359	0.9066
At ice point	1.7513	1.21	1.3404	2.0412	1.0000	0.7873	0.7291	0.7832
	Internal Standard of specific modes of vibration at 935 cm^{-1}							
	$A_{2983/935}$	$A_{2552/935}$	$A_{1460/935}$	$A_{1250/935}$	$A_{1074/935}$	$A_{935/935}$	$A_{686/935}$	$A_{542/935}$
Labeled condition	2.1932	1.3706	1.7458	2.992	1.1955	1.0000	0.8701	0.9633
Exposed to sunlight	1.6436	1.1609	1.4639	2.2929	1.049	1.0000	0.8743	0.9485
At ice point	2.0398	1.4438	1.5994	2.4357	1.1932	1.0000	0.87	0.4472
	Internal Standard of specific modes of vibration at 686 cm^{-1}							
	$A_{2983/686}$	$A_{2552/686}$	$A_{1460/686}$	$A_{1250/686}$	$A_{1074/686}$	$A_{935/686}$	$A_{686/686}$	$A_{542/686}$
Labeled condition	2.5208	1.5753	2.0065	3.4389	1.374	1.1494	1.0000	1.1071
Exposed to sunlight	1.8799	1.3278	1.6743	2.6226	1.1963	1.1438	1.0000	1.0848
At ice point	2.402	1.6595	1.8383	2.7995	1.3715	1.1494	1.0000	1.0742
	Internal Standard of specific modes of vibration at 542 cm^{-1}							
	$A_{2983/542}$	$A_{2552/542}$	$A_{1460/542}$	$A_{1250/542}$	$A_{1074/542}$	$A_{935/542}$	$A_{686/542}$	$A_{542/542}$
Labeled condition	2.2768	1.4229	1.8123	3.1062	1.2411	1.0381	0.9032	1.0000
Exposed to sunlight	1.1329	1.2239	1.5434	2.4175	1.1027	1.0699	0.9218	1.0000
At ice point	2.236	1.5448	1.7113	2.6061	1.2768	1.07	0.9309	1.0000

Table 6 Internal standard evaluation for Trimetazidine Hydrochloride

Condition of Exposure	Internal Standard of specific modes of vibration at 3009 cm^{-1}							
	$A_{3009/3009}$	$A_{2832/3009}$	$A_{1602/3009}$	$A_{1417/3009}$	$A_{1102/3009}$	$A_{958/3009}$	$A_{892/3009}$	$A_{669/3009}$
Labeled condition	1.0000	0.8822	0.8416	1.3544	1.1712	0.4629	0.6534	0.4577
Exposed to sunlight	1.0000	0.9037	0.8872	1.1882	1.336	0.5889	0.6176	0.4416
At ice point	1.0000	0.8455	0.8997	1.371	2.223	0.5111	0.5532	0.3601
	Internal Standard of specific modes of vibration at 2832 cm^{-1}							
	$A_{3009/2832}$	$A_{2832/2832}$	$A_{1602/2832}$	$A_{1417/2832}$	$A_{1102/2832}$	$A_{958/2832}$	$A_{892/2832}$	$A_{669/2832}$
Labeled condition	1.1335	1.0000	0.9539	1.5352	1.9408	0.5247	0.7406	0.5288
Exposed to sunlight	1.1065	1.0000	0.9817	1.3147	1.4757	0.6516	0.6833	0.4887
At ice point	1.1827	1.0000	1.064	1.6215	2.629	0.6045	0.6542	0.4258
	Internal Standard of specific modes of vibration at 1602 cm^{-1}							
	$A_{3009/1602}$	$A_{2832/1602}$	$A_{1602/1602}$	$A_{1417/1602}$	$A_{1102/1602}$	$A_{958/1602}$	$A_{892/1602}$	$A_{669/1602}$
Labeled condition	1.1883	1.0483	1.0000	1.6094	2.0346	0.5501	0.7764	0.5439
Exposed to sunlight	1.127	1.0186	1.0000	1.3392	1.5031	0.6637	0.696	0.4978
At ice point	1.1115	0.9399	1.0000	1.5239	2.4709	0.5681	0.6149	0.4002
	Internal Standard of specific modes of vibration at 1417 cm^{-1}							
	$A_{3009/1417}$	$A_{2832/1417}$	$A_{1602/1417}$	$A_{1417/1417}$	$A_{1102/1417}$	$A_{958/1417}$	$A_{892/1417}$	$A_{669/1417}$
Labeled condition	0.7383	0.6514	0.6213	1.0000	1.2612	0.3418	0.4824	0.3379
Exposed to sunlight	0.8416	0.7606	0.7467	1.0000	1.1224	0.4956	0.5198	0.3717
At ice point	0.7293	0.6167	0.6562	1.0000	1.6214	0.3728	0.4035	0.2626
	Internal Standard of specific modes of vibration at 1102 cm^{-1}							
	$A_{3009/1102}$	$A_{2832/1102}$	$A_{1602/1102}$	$A_{1417/1102}$	$A_{1102/1102}$	$A_{958/1102}$	$A_{892/1102}$	$A_{669/1102}$
Labeled condition	0.584	0.5152	0.4915	0.791	1.0000	0.2704	0.3816	0.2673
Exposed to sunlight	0.7498	0.6777	0.6653	0.8909	1.0000	0.4416	0.4631	0.3316
At ice point	0.4499	0.3804	0.4047	0.6168	1.0000	0.23	0.2489	0.162
	Internal Standard of specific modes of vibration at 958 cm^{-1}							
	$A_{3009/958}$	$A_{2832/958}$	$A_{1602/958}$	$A_{1417/958}$	$A_{1102/958}$	$A_{958/958}$	$A_{892/958}$	$A_{669/958}$
Labeled condition	2.1602	1.9058	1.8179	2.9258	3.6987	1.0000	1.4115	0.9887
Exposed to sunlight	1.6981	1.5347	1.5066	2.0176	2.2646	1.0000	1.0487	0.75
At ice point	1.9565	1.6542	1.7601	2.6822	4.3491	1.0000	1.0823	0.7044
	Internal Standard of specific modes of vibration at 892 cm^{-1}							
	$A_{3009/892}$	$A_{2832/892}$	$A_{1602/892}$	$A_{1417/892}$	$A_{1102/892}$	$A_{958/892}$	$A_{892/892}$	$A_{669/892}$
Labeled condition	1.5304	1.3502	1.2879	2.0728	2.6205	0.7085	1.0000	0.7005
Exposed to sunlight	1.6193	1.4634	1.4367	1.924	2.1595	0.9536	1.0000	0.7152
At ice point	1.8077	1.5285	1.6263	2.4783	4.0184	0.924	1.0000	0.6509
	Internal Standard of specific modes of vibration at 669 cm^{-1}							
	$A_{3009/669}$	$A_{2832/669}$	$A_{1602/669}$	$A_{1417/669}$	$A_{1102/669}$	$A_{958/669}$	$A_{892/669}$	$A_{669/669}$
Labeled condition	2.1848	1.9275	1.1839	2.9591	3.7409	1.0114	1.4276	1.0000
Exposed to sunlight	1.9892	2.0463	2.009	2.6903	3.0197	1.3334	1.3982	1.0000
At ice point	2.6359	2.3483	2.4987	3.8018	6.1739	1.4196	1.5364	1.0000

3.3Qualitative Analysis using UV-Visible spectroscopy

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. 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. The standard procedure for analyzing metoprolol and trimetazidine as described in the Indian Pharmacopia has been adopted. The absorption values for various concentrations of the drugs which fall within the linearity range of were used to plot the linearity curves

(Fig. 3). Drug concentrations of 100mcg/ml, 200mcg/ml...500mcg/ml were used for this purpose. The variation in the absorbance of the drugs at a concentration of 300mcg/ml stored at three different conditions was studied. The overlay of the UV-Visible spectra of metoprolol shown in Fig. 4 illustrates the change in the absorption characteristic of the compound due to the change in storage condition. Metoprolol and trimetazidine, each show two absorption peaks respectively. The change in the quality of the drugs has been ascertained by calculating the internal standard ratio of the two drugs. The results are summarized in table 7. They substantiate the results obtained from vibrational spectral study indicating the fact that the drug's chemical composition changes when the prescribed storage condition is altered. Hence it is very essential to store the drugs under the prescribed condition to maintain their quality.

Table 7 Variation of absorbance of Metoprolol and Trimetazidine and the internal standard ratio for different storage conditions.

Storage condition	Metoprolol tartrate			Trimetazidine hydrochloride		
	274nm	222nm	$A_{274/222}$	362nm	270nm	$A_{362/270}$
Ice point	0.4287	2.3578	0.1818	0.0906	0.3262	0.2777
Labeled storage condition	0.4159	2.2078	0.1884	0.0873	0.3176	0.2746
Exposed to sunlight	0.3405	1.7407	0.1956	0.0891	0.2909	0.3063

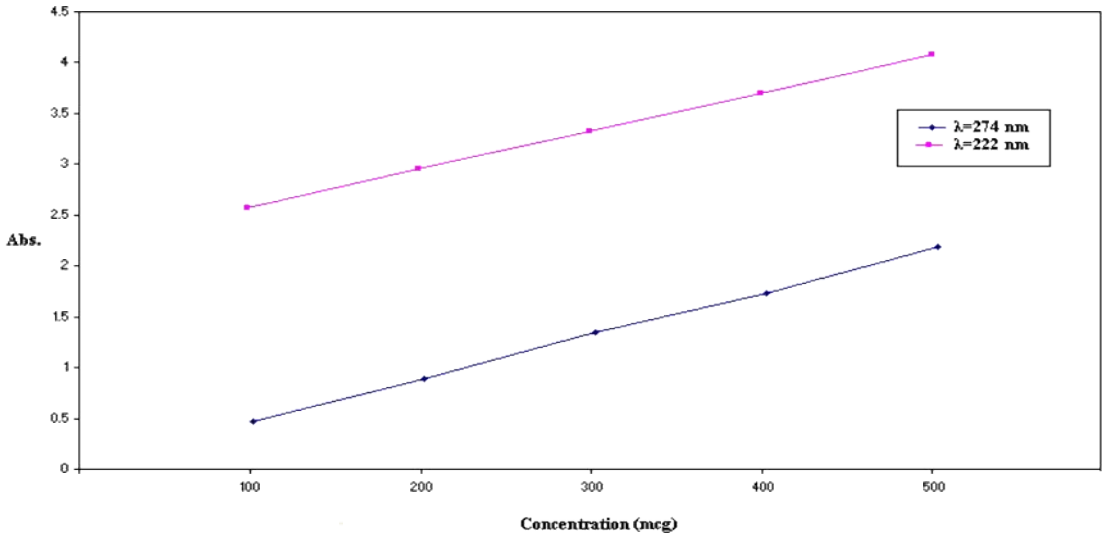


Fig. 3 Linearity curves of Metoprolol tartrate

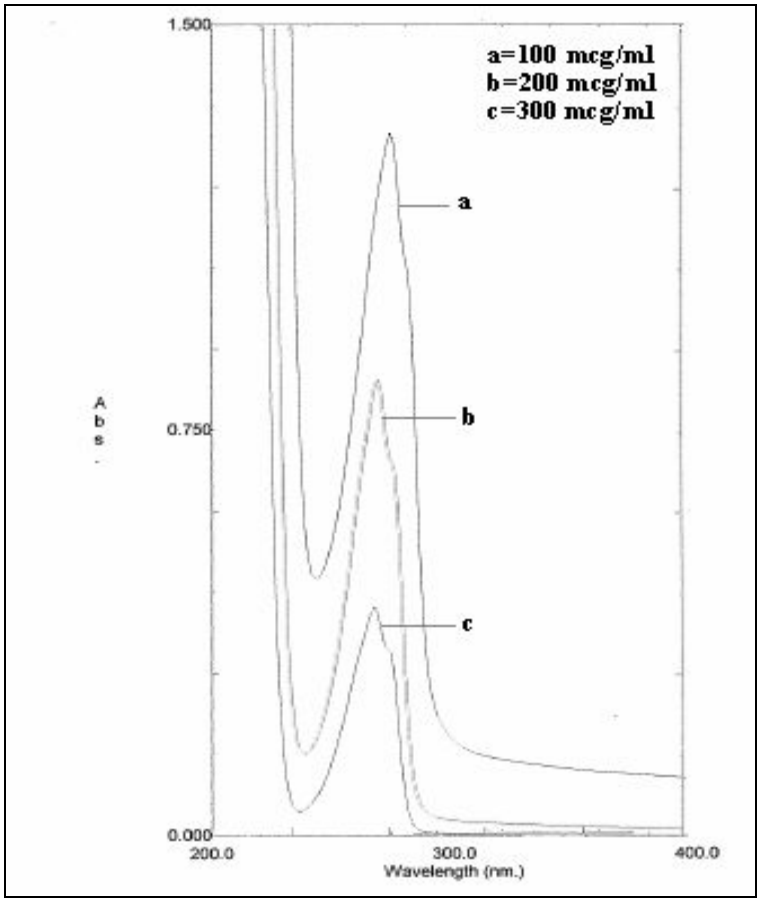


Fig. 4 Comparative representation of UV-Visible spectra of Metoprolol

3.4 Assay of tablets – UV-visible spectroscopy

Tablets are the popular form of dosage because of their cost effective preparation, stability and convenience in packaging, transporting and dispensing. It is popular among patients for accuracy of dosage, compactness, portability, blandness of taste and ease of administration [20]. Quantitative spectrometry is an extension of calorimetry and many pharmacopical substances are assayed spectrophotometrically [21].

In the present work medicines of metoprolol and trimetazidine in the form of tablets were subjected to quantitative estimation of the drug substance in the tablet using UV-visible spectroscopic technique. The tablets Meto-Er 50mg and Taz 20mg containing metoprolol and trimetazidine as the active ingredient were obtained from a leading pharmaceutical company. The drug content is determined by preparing a stock solution of the test sample and the solution is diluted to the same concentration as that of the standard sample and the absorbance of the resulting solution under UV-visible radiation was measured [22]. The drugs were found to obey Beer's law. The drug content of the tablet is calculated as given below.

Drug content of the tablet/assay=

$$\frac{\text{Test absorption}}{\text{Standard absorption}} \times \frac{\text{Standard weight}}{\text{Test weight}} \times \text{Average weight of one tablet}$$

The UV spectral recording of the pure samples metoprolol and trimetazidine and tablets Meto-Er 50mg and Taz-20mg were carried out for concentrations of 100mcg, 200mcg, 300mcg, 400mcg and 500mcg. The UV-visible spectra of metoprolol exhibits wavelength maximum at 274nm. The average weight of one tablet it found to be 259.6mg. The UV-visible spectra of trimetazidine exhibits wavelength maximum at 270 nm. The average weight of one tablet it found to be 205.8mg. The estimation of assay in tablets Meto-Er 50mg and Taz-20mg is shown in Tables 8 and 9 respectively.

Table 8 Estimation of assay in Meto-Er 50mg

Wavelength (nm)	Concentration (mcg)	Average absorbance of wavelength maximum		Estimation of assay (mg) Meto-Er	Percentage of the labeled amount
		Pure	Meto-Er		
274	100	0.4160	0.4191	50.03	100.06
274	200	0.8451	0.8453	50.05	100.10
274	300	1.2943	1.2961	50.06	100.12
274	400	1.6572	1.6584	50.06	100.12
274	500	2.4131	2.4152	50.06	100.12

Table 9 Estimation of assay in Taz-20mg

Wavelength (nm)	Concentration (mcg)	Average absorbance of wavelength maximum		Estimation of assay (mg) Taz	Percentage of the labeled amount
		Pure	Taz		
270	100	0.3052	0.3043	20.00	100.00
270	200	0.6104	0.6109	20.07	100.35
270	300	0.9092	0.9142	20.08	100.40
270	400	1.2433	1.2488	20.08	100.40
270	500	1.5145	1.5195	20.10	100.50

4. CONCLUSION

FTIR, FT-Raman and UV-Visible spectroscopic techniques have been employed for the qualitative analysis of the two cardiovascular drugs metoprolol tartarate and trimetazidine hydrochloride. A satisfactory vibrational assignment of the two drugs has been done from the FTIR and FT-Raman spectra of the drugs. They confirm the basic functional groups present in the compound. The intensity ratio calculated among specific modes of vibrations clearly shows that some vibrational bands are more altered due to sunlight exposure and storage at ice point. This clearly denotes that a change in the quality of the drugs has taken place due to the change in storage condition. This was further confirmed using the UV-Visible spectroscopic method. The UV-Visible spectroscopic method was also employed to find the amount of drug present in tablet formulations.

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