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Quantitative determination of domperidone and omeprazole in combined dosage form by FT-IR spectroscopy

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ABSTRACT

There is a tremendous growth in pharmaceutical industry in the recent years due to rapid drug discovery and development of new drug processes. This has increased the frequency of release of newer drugs in to the pharmaceutical market and proportionally demanded the development of newer analytical methodologies using various analytical techniques. A simple Fourier Transform Infrared (FT-IR) spectroscopic method has been developed for the quantification of Domperidone (DMP) and Omeprazole (OMP) in combined dosage formulations. The method involves the measurement of peak absorbance of carbonyl group (C=O) at 1717 cm^{-1} for domperidone and imine group (C=N) at 1627 cm^{-1} for omeprazole. The method was found to be highly precise with %RSD less than 2 and % recovery levels >99. The developed method can be adopted for routine analysis in pharmaceutical industry.

Key words: FT-IR, Omeprazole, Domperidone, combined dosage form

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INTRODUCTION

Chemically, Omeprazole (OMP) is 6-methoxy-2-((4-methoxy-3,5-dimethylpyridin-2-yl) methyl sulfinyl)-1*H*-benzo[*d*]imidazole. It is a proton pump inhibitor and recommended for the treatment of peptic ulcers. Domperidone (DMP) is chemically 5-chloro-1-(1-[3-(2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazol-1-yl)propyl]piperidin-4-yl)-1*H*-benzo[*d*]imidazol-2(3*H*)-one and is used as antiemetic drug. Both the drugs are available in combination with other drugs as combined dosage tablet and capsule forms. A recent combination of OMP (20mg) with DMP (30mg) is available as combined dosage capsule under the trade name OMEZ-D for clinical practice. The capsule is used for antiemetic and peptic ulcer disorders. Many methods are available in literature for their estimation either individually [1-8] or in combined dosage form [9-20] using different analytical techniques.

In the present investigation, an attempt was made to develop a simple, rapid and non-destructive method using FT-IR for the estimation of both the drugs in combined dosage capsule form.

EXPERIMENTAL SECTION

Materials

OMP API was obtained from M/s Dr. Reddy's Laboratory, Hyderabad and DMP was kindly gifted by M/s Ipca Laboratories Ltd., Madhya Pradesh. Potassium Bromide (KBr) used was a spectroscopic grade obtained from

Sigma-Aldrich, Germany. Combined dosage form capsules OMEZ-D were procured from local market, Hyderabad, India having a label claim 20mg of OMP and 30mg of DMP.

Methods

FT-IR Instrumentation

Highly sophisticated bench top Thermo Nicolet, Model Nexus 670 USA, FT-IR, Consisting of Helium – Neon laser Class IIa, DTGS Detector was used. Full length spectral range ($4000cm^{-1}$ to $400cm^{-1}$) was used during the experiment. All the spectra were recorded by averaging 32 scans with a resolution of $4cm^{-1}$. Data collection was automated using OMNIC software.

Standards preparation and calibration

For calibration, the spectra were recorded by compressing the standard substances OMP & DMP in the concentration range 0.10mg to 0.25mg and 0.15mg to 0.37mg respectively in spectral grade KBr.

A synthetic mixture of pure DMP & OMP was prepared in the ratio 2:3 similar to commercial capsule formulation, OMEZ-D. Calibration was carried out for OMP and DMP in synthetic mixture in the concentration range mentioned for individual drug.

Sample preparation and formulation analysis

Ten capsules of OMEZ-D were taken for sample preparation. The capsules were carefully opened and collected the material in to a clean dry weighing bottle. The material was weighed and ground to a fine powder in an agate mortar. A known quantity of it equivalent to the concentration of the individual drug in the calibration range was compressed with spectral grade KBr. Four KBr discs of different concentrations were prepared and spectra were recorded for both OMP and DMP under similar experimental conditions as standards.

FT-IR spectral measurements

After scanning all the pellets auto smoothing is done in order to remove noise without broadening peaks excessively. Auto baseline correction is used to correct spectra with sloped or varying baselines. The peak absorbance at $1717cm^{-1}$ (C=O) and $1627cm^{-1}$ (C=N) is linearly proportional to the concentration of DMP & OMP respectively.

Linearity

Standard samples of OMP and DMP were prepared in different concentration range from 0.10mg - 0.25mg (OMP) and 0.15mg - 0.37mg (DMP). The linearity of the investigation was done by measuring the peak absorbance of individual drug at different concentrations as mentioned above. Calibration plots were constructed for both the drugs by plotting peak absorbance against the concentration of the drug.

The limit of detection (LOD) is the lowest concentration of an analyte in a sample that can be detected and the limit of quantification (LOQ) is the lowest concentration of an analyte in a sample that can be quantitated. Both LOD and LOQ were experimentally verified and calculated using the following equation.

LOD = 3.3 (SD/Slope)

LOQ = 10 (SD/Slope)

Precision

Precision study was performed by taking four readings for each concentration and %RSD was calculated.

Accuracy

Recovery studies were carried out by the addition of known amount of pure drug to the preanalysed capsule powder and analysed by the proposed method at two different concentration levels 50% and 100%.

RESULTS AND DISCUSSION

The FT-IR spectra of pure OMP and DMP by KBr pellet method are given in Figure 1. The compounds exhibited intense vibrations at $1717cm^{-1}$ (DMP) & $1627cm^{-1}$ (OMP) which are due to carbonyl (C=O) and imine (C=N) groups respectively. This feature is taken for the quantitation of the drugs.

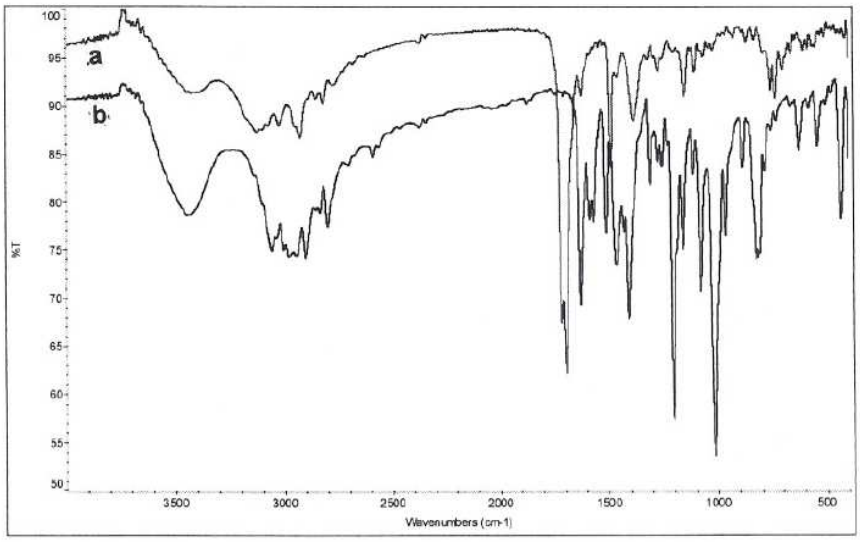

Fig. 1: FT-IR spectra of Pure a. DMP b. OMP

A calibration has been carried out for OMP and DMP using known quantities of standards as mentioned in the experimental section. It was found that the compounds followed the linearity in the concentration range studied [0.10mg – 0.25mg (OMP) and 0.15mg - 0.37mg (DMP)]. The intensity of the infrared peaks corresponding to the drug molecules shown a concentration dependent change and found to be linear. The validation parameters are mentioned in Table 1.

Table 1: Validation parameters for developed FT-IR spectroscopic technique

Parameters	OMP	DMP
Linearity (mg)	0.10-0.25	0.15-0.37
R2	0.99769	0.99985
Linear Regression Equation	Y= -0.00611+ 1.04096 x	Y= -0.01793 + 1.11667 x
Slope (B)	1.04096	1.11667
Intercept (A)	-0.00611	-0.01793
LOD (mg)	0.006	0.01
LOQ (mg)	0.02	0.034
Repeatability (% RSD)*	1.027	0.9306
% Recovery	99.35	99.54

**Four determinations, LOD = Limit of detection, LOQ = Limit of Quantification, RSD = Relative Standard Deviation, OMP = Omeprazole, DMP = Domperidone*

The accuracy of the present method was estimated in terms of % recovery of both OMP and DMP from the marketed capsule formulation and incorporated in Tables 2 and 3. The % RSD values were found to be less than 2, which indicate that developed method is precise for simultaneous estimation of OMP and DMP.

Table 2: Accuracy studies of OMP

Level (%)	Std Conc. (mg)	Amount added (mg)	Total amount (mg)	Amount recovered (mg)	Mean % recovery* ±SD
50	20	10	30	30.24	100.81 ± 0.95
	20	10	30	30.01	
	20	10	30	30.29	
	20	10	30	30.42	
100	20	20	40	40.04	100.35 ± 0.42
	20	20	40	40.25	
	20	20	40	40.32	
	20	20	40	39.94	

**Mean of 4 determinations, OMP=Omeprazole*

Table 3: Accuracy studies of DMP

Level (%)	Std Conc. (mg)	Amount added (mg)	Total amount (mg)	Amount recovered (mg)	Mean % recovery * ±SD
50	30	15	45	44.66	99.62± 1.11
	30	15	45	45.12	
	30	15	45	44.89	
	30	15	45	44.63	
100	30	30	60	60.06	100.15 ± 0.55
	30	30	60	60.16	
	30	30	60	60.04	
	30	30	60	60.07	

**Mean of 4 determinations, DMP=Domperidone*

FT-IR spectra were recorded for synthetic mixture containing 2:3 ratio of pure DMP and OMP respectively (Figure 2). The spectrum clearly shows the two peaks pertaining to OMP and DMP at the corresponding wave numbers (1627cm^{-1}, 1717cm^{-1}) without any interference. Quantification of both the drugs (OMP & DMP) in synthetic mixture was carried out using calibration method. The amount, standard deviation and % RSD were calculated and tabulated in Table. 4. The results revealed that both the drugs followed Beer-Lamberts law in the concentration range studied.

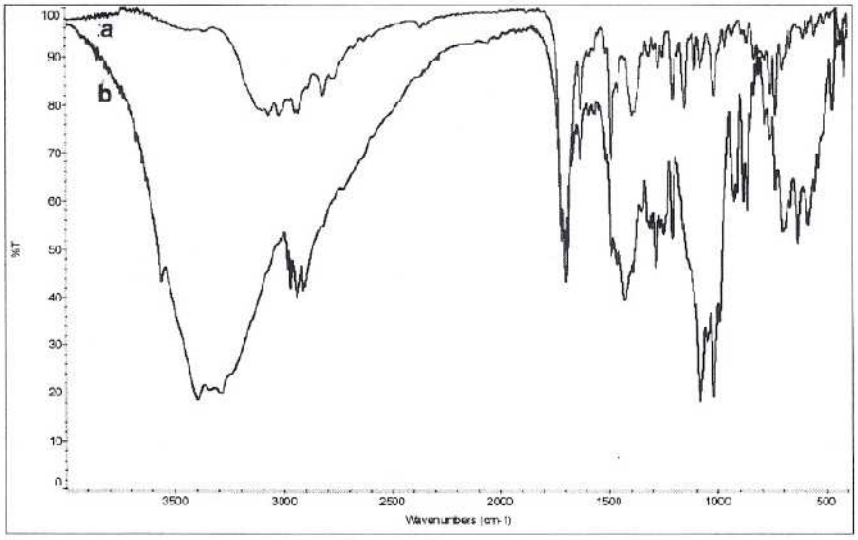

Fig 2: FT-IR spectra of a. Synthetic Mixture b. OMEZ-D

Table 4: Quantification of OMP & DMP in synthetic mixture

Compound	Amount of drug taken (mg)	%Recovery	Mean% recovery ± SD
OMZ	0.1	97.89	99.35 ± 1.102
	0.15	99.35	
	0.20	100.55	
	0.25	99.62	
DMP	0.15	99.67	99.54 ± 1.125
	0.224	97.95	
	0.299	100.58	
	0.373	99.96	

The method was applied to combined dosage formulation and the spectra were recorded for OMEZ-D capsule (Figure 2). From the spectra it was observed that the peaks (1627cm^{-1} and 1717cm^{-1}) were free from interferences from other compounds present in the capsule (excipients). Table. 5 shows the assay and % RSD (η=4) for commercial capsule OMEZ-D. The % RSD was found to be 0.995 and 0.570 for OMP and DMP respectively. The assay was found to be >99% (Avg). The values of %assay and %RSD depicts high precision of the method. The

estimation of both OMP and DMP in the capsule by the proposed method yielded precise results indicating the reliability of the method.

Table 5: Recovery studies of commercial formulations

Marketed	Label claim		% assay ± SD			
Formulation	OMP	DMP	OMP	%RSD	DMP	%RSD
			99.00 ± 0.952	0.961	99.39 ± 0.476	0.479
OMEZ-D	20	30	102.33 ± 0.859	0.84	99.82 ± 1.104	1.106
			101.55 ± 1.476	1.461	98.52 ± 0.098	0.099
			99.42 ± 0.716	0.72	98.53 ± 0.587	0.596

CONCLUSION

In the present investigation, we have studied the possibility of quantification of drug components in combined dosage formulations using FT-IR. From the data it is clear that FT-IR is capable of direct determination of OMP and DMP in the above formulations. The proposed FT-IR method was found to be simple, rapid and reproducible and less time consuming compared to other analytical methods which exists in literature.

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