



Research Article

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Quantitative determination of Domperidone and Paracetamol in combined dosage form by FT-IR spectroscopy

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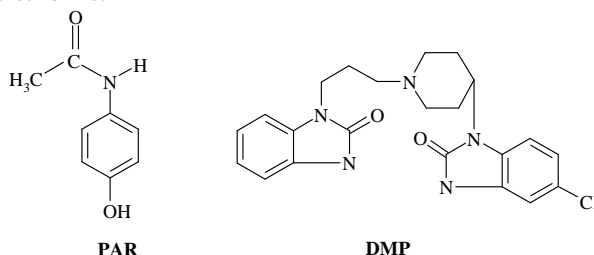
ABSTRACT

A simple and rapid method has been developed for the quantification of Domperidone (DMP) and Paracetamol (PAR) through FT-IR in combined dosage form. The method involves the measurements of peaks of carbonyl group (C=O) at 1656 cm^{-1} (PAR) and 1717 cm^{-1} (DMP). An UV-Spectrophotometric method was also described for the simultaneous determination of DMP and PAR. The analytical results obtained with FT-IR showed very good correlation with UV-Spectrophotometric method. The method was validated for pharmaceuticals in tablet form and found to be highly precise with high recovery levels (>99%).

Key words: FT-IR, UV-Spectrophotometry, Paracetamol, Domperidone, combined dosage form.

INTRODUCTION

Chemically, Paracetamol (PAR) is [N-(4-hydroxy phenyl) acetamide]. It is widely known antipyretic and analgesic drug and is available with many combinations. Domperidone (DMP) is chemically 5-chloro-1-[1-{3-(2-oxo-2, 3-dichloro-1H-benzimidazole-1-yl) propyl}-piperidine-4-yl]-1, 3-dihydro-2H-benzimidazol-2-one and is used as antiemetic drug. Both the drugs are available in combination with other drugs as combined dosage tablet forms. A recent combination of PAR (500mg) with DMP (20mg) is available as combined dosage tablet under the trade name GRENIL for clinical practice. The same combination of tablets are also available under the trade name DOMCET in the ratio, PAR (500mg) and DMP (10mg). These tablets are used for antiemetic and pain associated with gastrointestinal disorders. Many methods are available in literature for their determination in pure form [1-9] as well as in combined dosage forms [10-20]. But methods for their determination in combined dosage forms of PAR with DMP are not available except HPLC [21] and UV-spectroscopic [22] method using Vireodt's formula. An attempt was made to develop a simple, rapid and non-destructive method using FT-IR for the estimation of both these drugs in combined dosage tablet forms.



The method was compared with UV-Spectrophotometric results and found it suitable for quantitative estimation of Paracetamol and Domperidone in combined dosage formulations.

EXPERIMENTAL SECTION

Materials

FT-IR spectra were recorded on Thermo Nicolet, Model Nexus 670, USA, Spectrophotometer. KBr used for recording spectra was spectroscopic grade obtained from Sigma-Aldrich, Germany.

UV spectra were recorded on Varian UV-VISIBLE-NIR Spectrophotometer, Model-Cary 5000, Australia. Methanol used for recording spectra was A. R. grade obtained from M/s Qualigens fine chemicals, Mumbai. The reference standards of Paracetamol and Domperidone were obtained as gift samples from M/s Ipca Laboratories Ltd., Madhya Pradesh. Combined dosage form tablets Grenil and Domcet were procured from local market, Hyderabad.

FT-IR spectroscopy

Standards preparation and calibration

Fused KBr pellete spectra were recorded between 4000cm^{-1} and 400cm^{-1} , by averaging 32 scans with a resolution of 4cm^{-1} with a DTGS detector. For calibration, the spectra were recorded by compressing the standard substances PAR & DMP in the concentration range 0.25mg to 0.55mg and 0.02mg to 0.04mg respectively in spectral grade KBr.

A synthetic mixture of pure DMP & PAR was prepared in the ratio 1:25 and 1:50 similar to commercial tablet formulations, Grenil and Domcet respectively. Calibration was carried out for PAR and DMP in synthetic mixture in the concentration range mentioned for individual drugs.

Sample preparation and formulation analysis

Ten tablets of Grenil were weighed and ground to a fine powder. A known quantity of it equivalent to the concentration of the individual drug in the calibration range was compressed with spectral grade KBr. Five KBr discs of different concentrations were prepared and spectra were recorded for both PAR and DMP under similar experimental conditions as standards. In a similar manner the other tablet formulation, Domcet was also prepared and recorded the IR spectra.

UV-spectroscopy

Preparation of standard stock solutions and calibration

Standard stock solutions of pure drug $100\mu\text{g/ml}$ of PAR and DMP were prepared separately in methanol. Stock solutions were further diluted with methanol to get the working standards in the concentration range $2\text{-}10\mu\text{g/ml}$ and $1\text{-}5\mu\text{g/ml}$ of PAR and DMP respectively. UV-spectra were recorded in the range $200\text{-}400\text{nm}$.

A synthetic mixture of DMP and PAR was also prepared in a similar manner in tablet formulation ratio and recorded UV-spectra.

Preparation of sample solution

Twenty commercial tablets were weighed accurately and finely powdered. A known quantity of the powder was weighed and dissolved in 50ml of methanol. It was sonicated for 15min and filtered through whatman filter paper No. 41 and made up to 100ml after thorough washing of the filter paper with methanol. The solution was further diluted to get required concentrations of PAR and DMP.

RESULTS AND DISCUSSION

The FT-IR spectra of pure PAR and DMP by KBr pellete method is given in Figure 1. The compounds exhibited strong sharp signals at 1656cm^{-1} (PAR) & 1717cm^{-1} (DMP) which are due to the absorption of carbonyl group (C=O) and this feature is taken for the quantitative analysis.

A calibration has been carried out for PAR 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 ($0.25\text{mg} - 0.55\text{mg}$ for PAR and $0.02\text{mg} - 0.04\text{mg}$ for DMP) (Table 1).

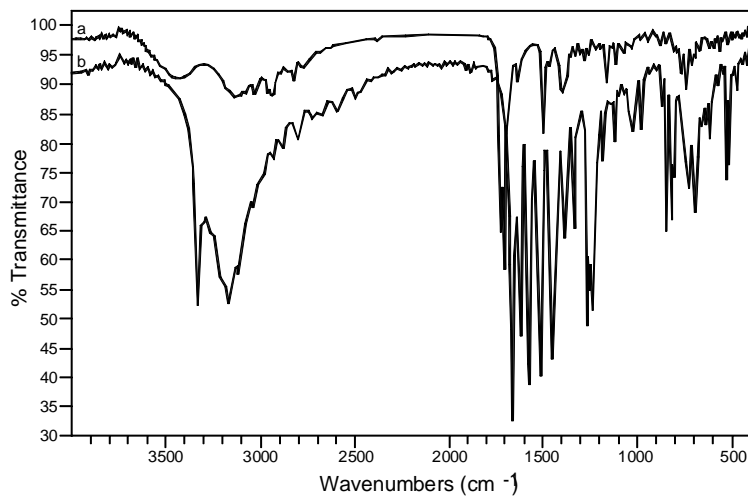


Figure 1: FT-IR spectra of pure a. DMP and b. PAR

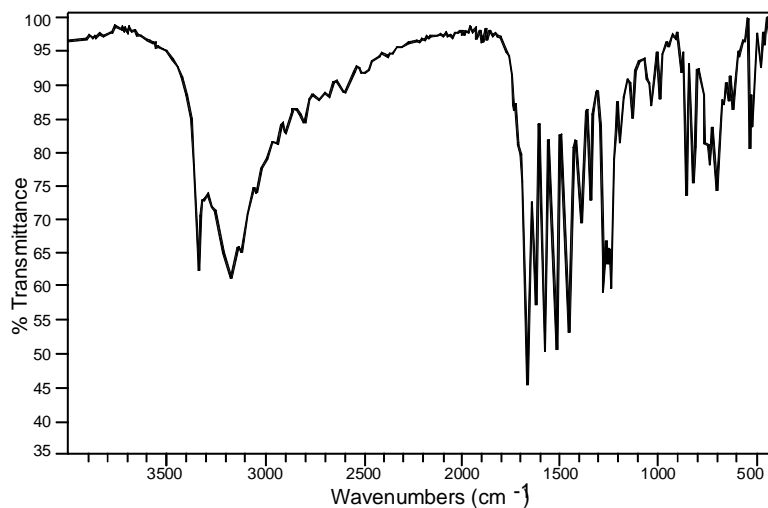


Figure 2 : FT-IR Spectrum of Synthetic Mixture

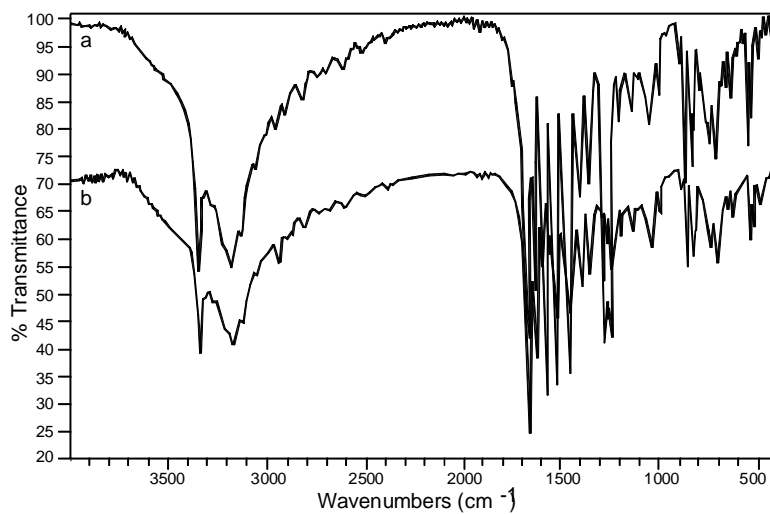


Figure 3 : FT-IR Spectra of combined dosage formulations a. GRENIL & b. DOMCET

Similarly FT-IR spectra was recorded for synthetic mixture containing 1:25 ratio of DMP and PAR respectively (Figure 2). The spectra (Figure 2) clearly shows the two peaks pertaining to PAR and DMP at the corresponding wave numbers (1656cm^{-1} , 1717cm^{-1}) without any interference. Quantification of both the drugs (PAR & DMP) in synthetic mixture was carried out using calibration method. The amount, standard deviation and % RSD were calculated and tabulated in Table. 2. The results revealed that both the drugs followed Beer-Lamberts law in the concentration range studied.

The method was applied to combined dosage formulations and the spectra were recorded for Grenil and Domcet tablets (Figure 3). From the spectra it was observed that the peaks (1656cm^{-1} and 1717cm^{-1}) were free from interferences from other compounds present in the tablet (excipients). Table 3 shows the recovery and % RSD ($\eta=5$) for commercial tablets Grenil and Domcet. The % RSD was found to be 3.33 and 3.90 for PAR and DMP (Grenil) & 0.71 and 1.32 for PAR and DMP (Domcet) respectively. The co-efficient of correlation (R^2) was calculated from the calibration and found it to be 0.9998 and 0.9980 for PAR and DMP respectively. The recovery was found to be >99%. The values of recovery, RSD and coefficient of correlation show high precision of the method. The estimation of both PAR and DMP in tablets by the proposed method yielded precise results indicating the reliability of the method.

Table 1: Optical characteristics

Parameters	Paracetamol		Domperidone	
	FT-IR	UV	FT-IR	UV
Beer's Law Limit	0.25-0.55mg	2-10 ppm	0.02-0.04mg	1-5 ppm
Limit of detection	0.001mg	0.1 ppm	0.001mg	0.1 ppm
Limit of quantification	0.01mg	1ppm	0.02mg	1ppm
Regression equation (Y*)	$Y=0.44+1.01x$	$Y=0.01+0.09x$	$Y=0.02+0.98x$	$Y=-0.06+0.37x$
Slope (B)	1.00835	0.09125	0.98021	0.36582
Intercept (A)	0.44075	0.0055	0.01743	-0.05814
Correlation coefficient (R^2)	0.99982	0.99968	0.99803	0.99954

$Y=A + Bx$, where x is the concentration of analyte and y is the absorbance value

Table 2: Quantification of PAR and DMP in Synthetic mixture

S. No	Compound	Amount of drug Taken (mg) & (ppm)		% Recovery		± %SD		%RSD	
		FT-IR	UV	FT-IR	UV	FT-IR	UV	FT-IR	UV
1.	Paracetamol	0.25	5.0	99.50	100.25	2.7094	0.5065	2.70	0.50
2.		0.37	7.0	98.65	98.75	3.19	0.6349	1.17	0.63
3.		0.56	9.0	102.86	99.82	2.655	1.0339	2.65	1.04
1.	Domperidone	0.022	1.5	99.25	102.5	1.7104	1.4919	1.73	1.48
2.		0.033	3.0	101.10	100.93	2.0702	1.2843	2.09	1.27
3.		0.044	4.5	100.42	99.97	1.2098	0.7080	1.22	0.70

A spectrophotometric method was also developed for the estimation of the above compounds and compared with FT-IR method. The UV spectra were scanned from 200-400nm for pure Paracetamol & Domperidone and peaks were observed at λ_{max} 248nm and 287nm respectively. Beer-Lamberts law was obeyed in the concentration range 2-10ppm (PAR) and 1-5ppm (DMP) (Table 1).

Synthetic mixture containing 1:25 ratio of pure DMP and PAR respectively has also scanned under similar experimental conditions. It was found that the peaks for PAR and DMP appeared at the same λ_{max} i.e., 248nm and 287nm respectively. A calibration has been carried out for both the components in standard synthetic mixture. Calibration parameters, correlation coefficient and % RSD ($\eta=5$) were calculated and are given in Table 2. The correlation coefficient (R^2) was found to be 0.9997 (PAR) and 0.9995 (DMP). The method was applied to tablet formulations for the simultaneous determination of PAR and DMP.

The quantification of PAR and DMP in combined dosage forms by FT-IR yielded similar accuracy and recovery as obtained in UV-spectroscopic method. The average % recovery by the present method was found to be 100.45 and 101.07 for PAR and DMP respectively (Table 3). Finally, the developed methods extend its use for both qualitative and quantitative analysis of active ingredient in single as well as combined dosage tablets forms.

Table 3: Recovery studies of commercial formulations

Tablet	Label claim (mg/tablet)	Amount found (mg/tablet)		Estimated label claim (%)		%RSD	
		FT-IR	UV	FT-IR	UV	FT-IR	UV
Grenil	Paracetamol 500	503.15	499.51	100.63	99.90	2.28	1.39
	Domperidone 20	19.89	20.10	99.45	100.50	1.65	1.27
Domcet	Paracetamol 500	501.42	500.80	100.28	100.16	0.84	0.88
	Domperidone 10	10.26	9.98	102.69	99.80	0.58	0.93

**Average of 4 determinations*

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 PAR and DMP in the above formulations and comparable to UV-Spectrophotometric method. The proposed FT-IR method was found to be simple, rapid and reproducible and less time consuming compared to UV-Spectrophotometric methods, which exists in literature.

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