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ARTICLE

Fourier Transform Infrared Spectrophotometry: An Eco-Friendly Green Tool for Simultaneous Quantification of Aspirin and Omeprazole in Pharmaceutical Formulation

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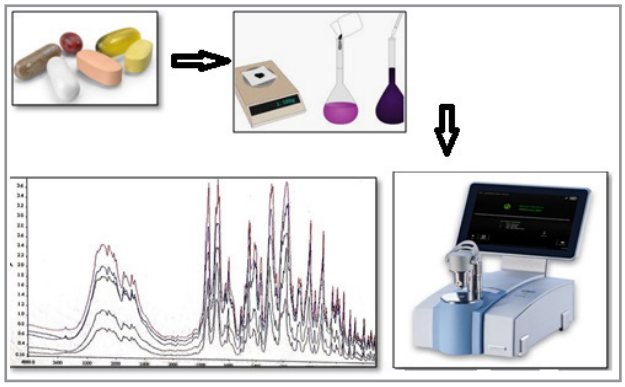

An eco-friendly method for quantification of Aspirin and Omeprazole in pharmaceutical solid dosage form has been developed using Fourier transform infrared spectrophotometry. The proposed method avoids the use of solvents which are commonly used for other methods of quantification e.g. Liquid Chromatography, UV spectrophotometry, etc. The developed method has been validated for the quantification of Aspirin and Omeprazole in a marketed formulation as per ICH Topic Q 2 (R1) guidelines. The method is based on Beer-Lamberts' law. For the proposed method C=O stretch at 1754 cm^{-1} was selected for Aspirin between 1750 – 1730 cm^{-1} and C=N stretch at 1627 cm^{-1} was selected for Omeprazole in the range of 1690 – 1620 cm^{-1}. Linearity was obtained in the concentration range of 10 – 50 mg g^{-1} and 5 – 25 mg g^{-1} with an R^2 value of 0.999 and 0.997 for Aspirin and Omeprazole respectively. The % recovery was calculated with intra and inter day precision study.

Keywords: FTIR spectrophotometry, Aspirin, Omeprazole, C=O stretching peak, C=N stretching peak.

INTRODUCTION

Yosprala® (Aralez Pharmaceuticals R&D Inc.), a fixed dose combination of 81 mg Aspirin and 40 mg of Omeprazole, which was approved by USFDA in 2016 [1], was selected for the proposed method. Aspirin produces gastric ulcer as a side effect in some patients with the age > 55 years, so Omeprazole is added to reduce the side effect of Aspirin in this combination. Aspirin ($C_9H_8O_4$), chemically 2-(acetyloxy) benzoic acid is used as an anti-inflammatory, antipyretic and analgesic. It decreases the formation of precursors of thromboxane and prostaglandin from arachidonic acid by inhibiting the activity of COX-1 and COX-2 enzymes [2]. Omeprazole ($C_{17}H_{19}N_3O_3S$), chemically 5-methoxy-2-[[(4-methoxy-3, 5-dimethyl pyridine-2yl) methyl] sulfinyl]-1H-benzoimidazole is a proton pump inhibitor used in gastric and duodenal

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ulcers, nonsteroidal anti-inflammatory drug (NSAID) associated ulceration and gastroesophageal reflux disease (GERD) [3]. The structural formulas of Aspirin and Omeprazole are presented in Figures 1 and 2 respectively.

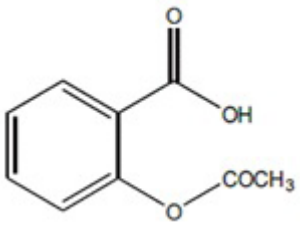

Figure 1. Structural formula of Aspirin.

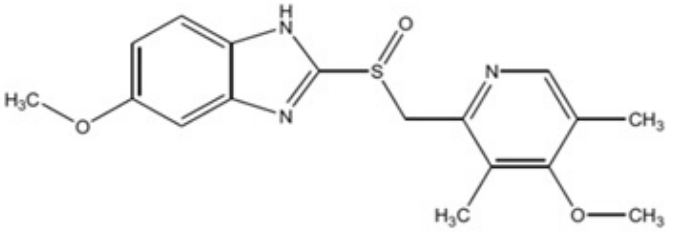

Figure 2. Structural formula of Omeprazole.

Omeprazole is used to inhibit acid secretions [4]. Studies have reported analytical methods for quantitative estimation in which Omeprazole can be determined in a solution form e.g UV [5] and HPLC [6-8]. One UV spectrophotometric method for simultaneous quantification of Aspirin and Omeprazole is reported [8] and one HPLC method [10] is reported. The earlier reported methods required the preparation of solutions using different solvents. Fourier Transform Infrared (FTIR) spectrophotometry uses molecular vibrations with the help of which Aspirin and Omeprazole can be quantified in a solid form [11-15]. The present study was aimed to develop an FTIR spectrophotometric method which is more advantageous, green, simple and rapid as compared to the other available methods. Individual identical Infrared (IR) spectra are given in Figures 3 and 4.

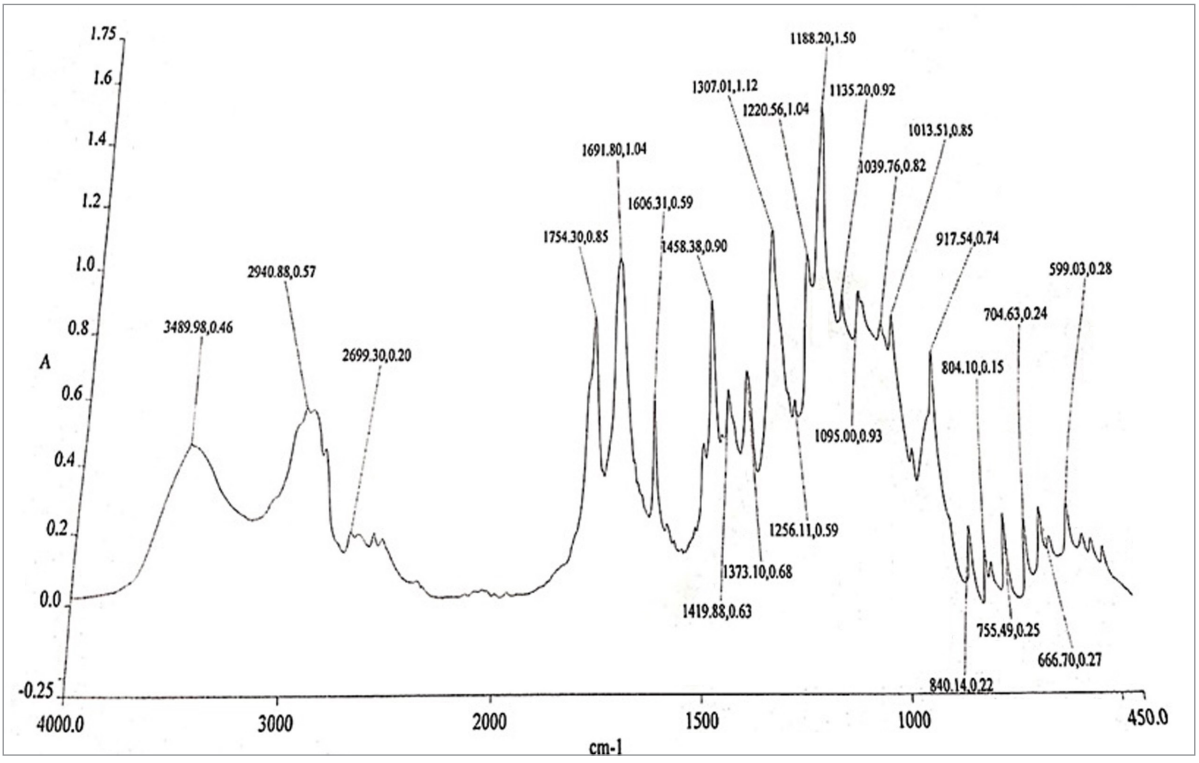

Figure 3. Spectra of standard Aspirin.

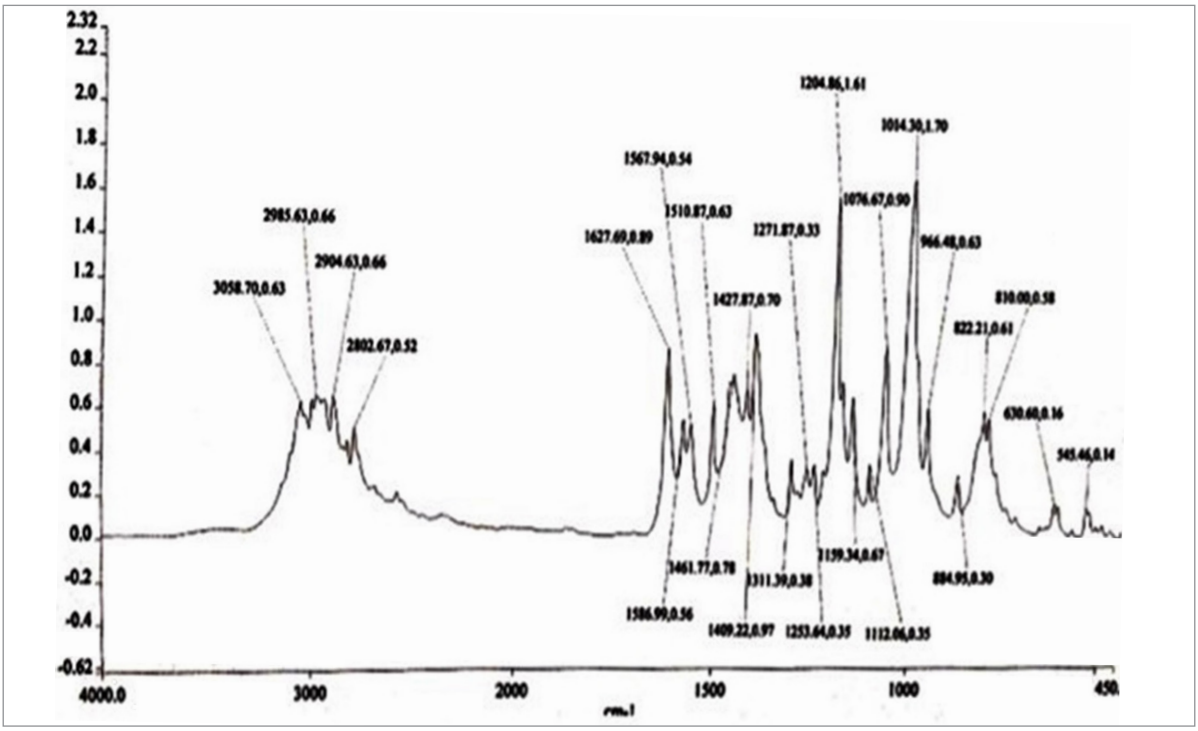

Figure 4. Spectra of standard Omeprazole.

MATERIALS AND METHODS

Chemicals and Reagents

The standard sample of Aspirin was procured from Sidmak, Valsad, India and Omeprazole from Mangalam drugs, Vapi. Potassium bromide was procured from the Axiom chemicals PVT. Ltd., Vadodara, India.

Instrument

The analysis was performed on Bruker Optics Alpha-Fourier transform infrared spectrophotometer. For the collection and analyses of data, OPUS software was used. The optimised IR conditions are given in Table I. The interpretation of the Aspirin IR spectra is given in Table II and the interpretation of the Omeprazole IR spectra is given in Table III.

Table I. Optimised infrared conditions for proposed study

Parameters	Optimised conditions
Method of making pellets	Direct mixing (press pellet) method
Mode of measurement	Absorbance mode
Final mass of pellet	200 mg
Peak selection	1754 cm^{-1} for aspirin and 1627 cm^{-1} for omeprazole
No. of scans	16 scans
Resolution	4 cm^{-1}

Table II. Interpretation of IR spectrum of Aspirin

Wave number (cm^{-1})	Functional group
3489	O-H streching
2700	C-H streching
1754	C=O streching (ester)
1691	C=O streching (carboxylic acid)
1458	CH_3 bending
1306	C-O stretching
917, 840	C=C bending in ring

Table III. Interpretation of IR spectrum of Omeprazole

Wave number (cm^{-1})	Functional group
2903	C-H streching
1627	C=N streching
1271	C-N streching
1204	C-O streching
101	S=O stretching
1567	N-H bending
965, 629	C=C aromatic ring

Calibration Curve

To plot a calibration curve, solid pellets of Aspirin and Omeprazole were prepared by the Pressed Pellet Technique using Polymer Press. Five different concentrations were selected in the range of 10 – 50 mg g^{-1} and 5 – 25 mg g^{-1} for Aspirin and Omeprazole respectively. Appropriate quantities (2, 4, 6, 8 and 10 mg) of Aspirin and (1, 2, 3, 4 and 5 mg) of Omeprazole were separately mixed with potassium bromide and triturated to get a homogenous solid solution which was converted to solid pellets ensuring the final mass of 200 mg for each pellet. Each concentration was used in replicates of six to record and analyze the data. For quantification, absorbance of C=O stretch cantered at 1754 cm^{-1}, between wave number of 1750 – 1730 cm^{-1} was selected for Aspirin and absorbance of C=N stretch cantered at 1627 cm^{-1}, between 1690 – 1620 cm^{-1} was used for Omeprazole. Results are reported in Figure 5.

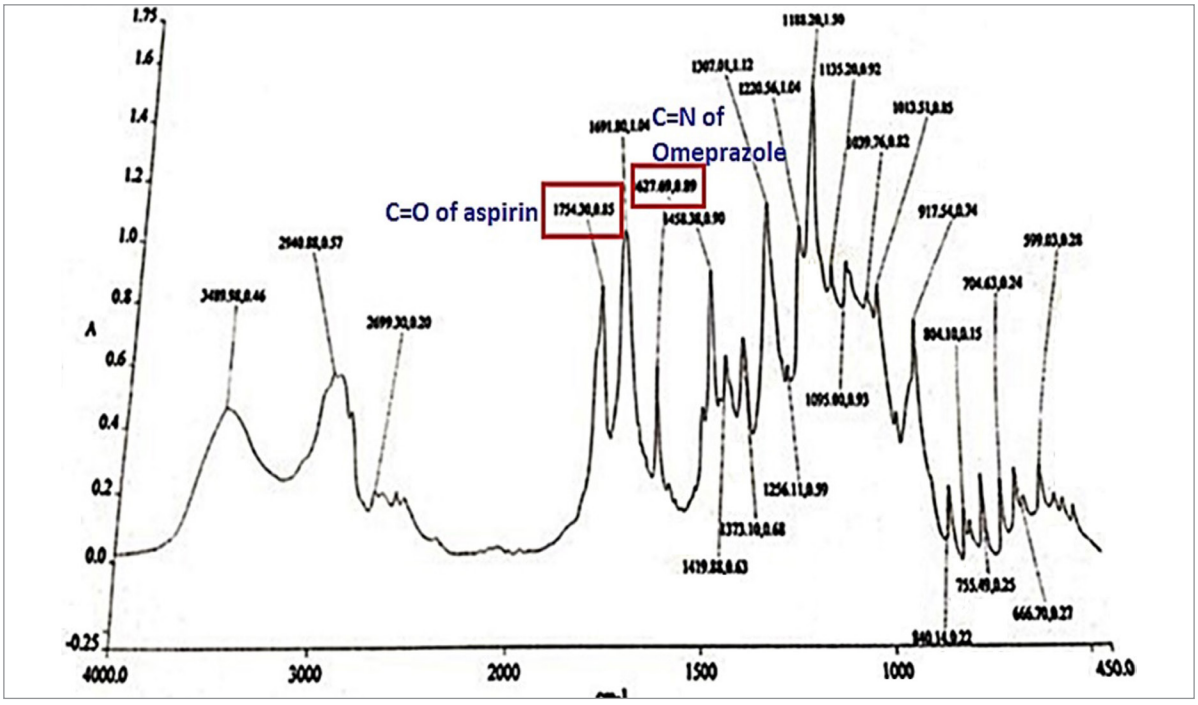

Figure 5. Spectra of standard Aspirin (10 mg g^{-1}) and Omeprazole (5 mg g^{-1}).

Method Validation

Parameters like linearity, specificity, precision, accuracy and robustness were evaluated for validation of the developed method.

Specificity

The wave number (cm^{-1}) selected for the study was specific for Aspirin and Omeprazole. Results are reported in Figures 6 and 7.

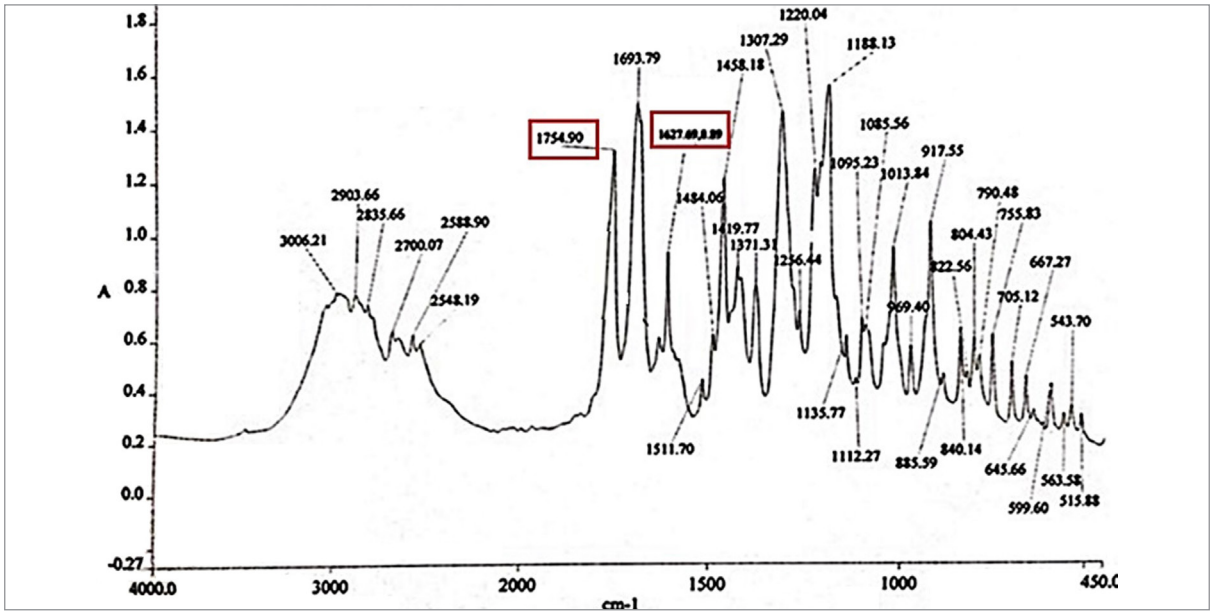

Figure 6. Spectra of test Aspirin (10 mg g^{-1}) and Omeprazole (5 mg g^{-1}).

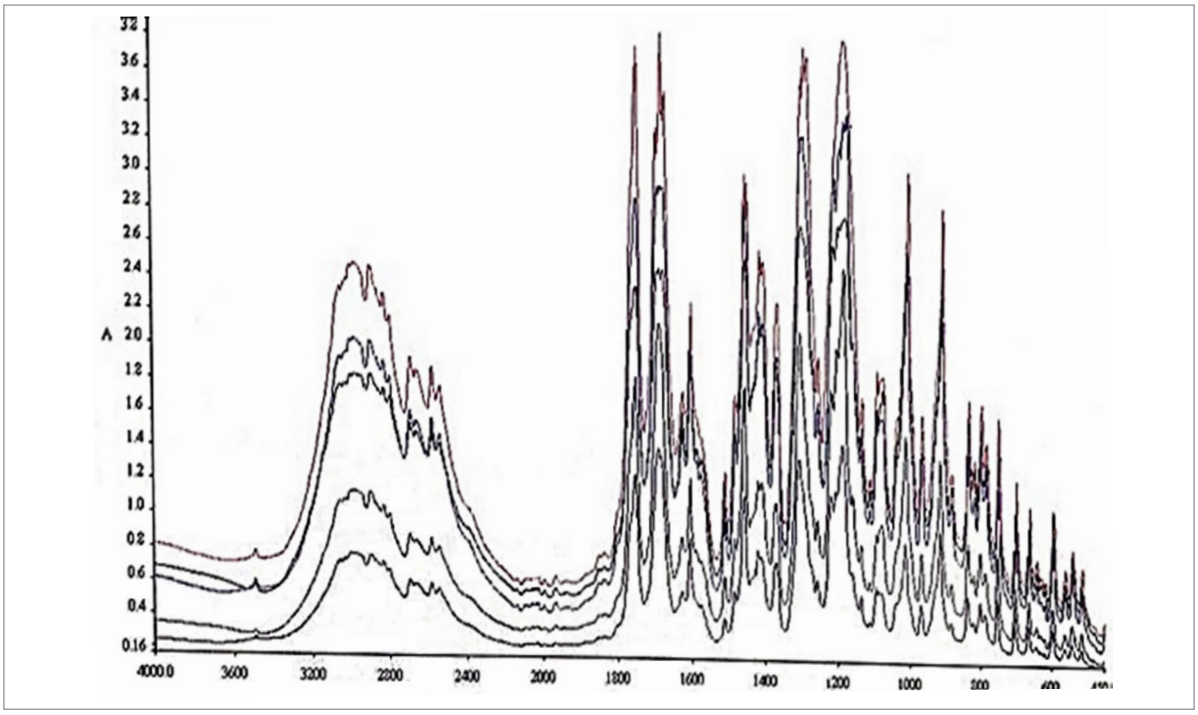

Figure 7. Overlain spectra of Aspirin (10 – 50 mg g^{-1}) and Omeprazole (5 – 25 mg g^{-1}) of linearity.

Linearity, Limit of Detection (LOD) and Limit of Quantitation (LOQ)

The linearity study was performed by plotting absorbance *vs*. concentration in the range of 10 – 50 mg g^{-1} for Aspirin and 5 – 25 mg g^{-1} for Omeprazole at selected wave numbers respectively. As it follows Beer-Lambert's law, an increase in absorbance with concentration for the selected peak was analysed. LOD and LOQ were calculated in the same concentration range. Results were reported in Figures 8 and 9 and Table IV.

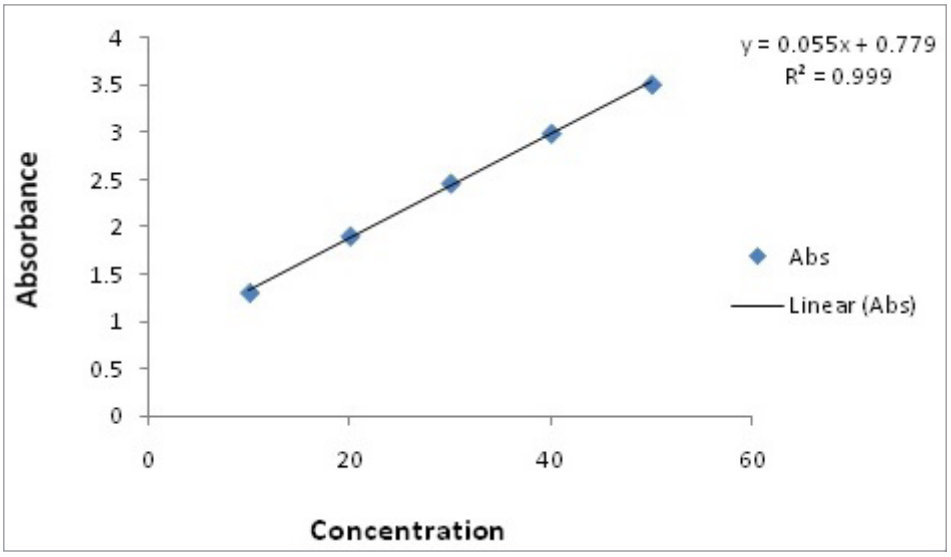

Figure 8. Calibration curve of Aspirin (10 – 50 mg g^{-1}).

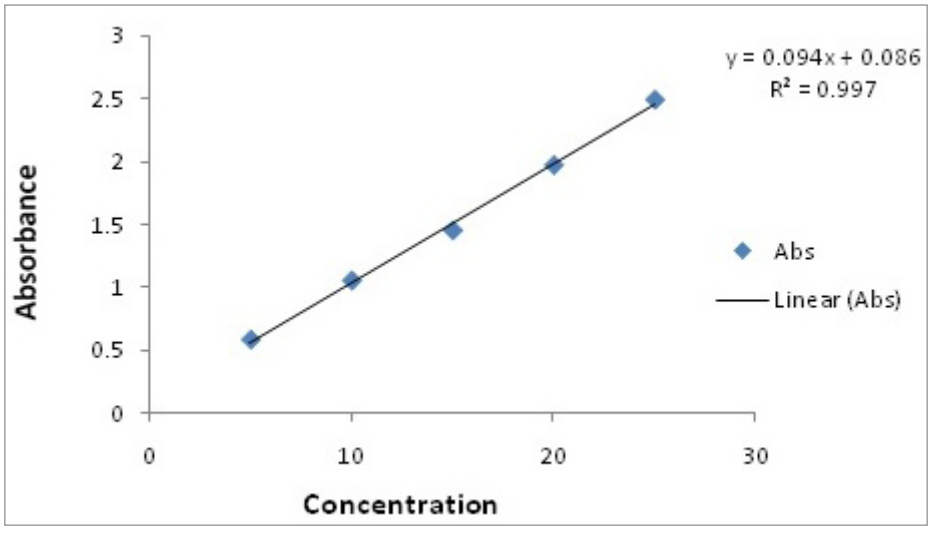

Figure 9. Calibration curve of Omeprazole (5 – 10 mg g^{-1}).

Table IV. LOD and LOQ data of Aspirin and Omeprazole by FT-IR method

Parameters	Results of ASP	Results of OME
S.D. of Y intercept of calibration curve	0.0115	0.015
Mean slope of the calibration curve	0.055	0.095
LOD	0.69	0.05
LOQ	2.09	0.15

Accuracy

Accuracy was recorded at 3 different concentration levels (50%, 100%, 150%). Known amounts of standard Aspirin (15, 30 and 45 mg g^{-1}) and Omeprazole (7.5, 15 and 22.5 mg g^{-1}) were added to a test sample containing 10 mg g^{-1} of Aspirin and 5 mg g^{-1} of Omeprazole. The results of this study are ported in Table V. The percentage recovery for both drugs was calculated at each level using the formula: (Measured value/ True value) x 100.

Table V. Accuracy data of Aspirin and Omeprazole by FT-IR method

Drug	Level (%)	Sample (mg g^{-1})	Standard (mg g^{-1})	Spiked (mg g^{-1})	Found (mg g^{-1})	% Recovery (Avg.)
Aspirin	50	10	15	25	24.57	98.29
	100		30	40	40.34	100.85
	150		45	55	54.53	99.15
Omeprazole	50	5	7.5	12.5	12.71	101.70
	100		15	20	19.65	98.27
	150		22.5	27.5	27.5	100

Precision

Precision was carried out by repeatability and intermediate study at 3 different concentration levels (50%, 100%, and 150%) for a test sample. The concentrations of Aspirin and Omeprazole were kept the same as the accuracy study (15, 30 and 45 mg g^{-1} for Aspirin and 7.5, 15 and 22.5 mg g^{-1} for Omeprazole.) %RSD was calculated. Results of the precision studies are reported in Table VI.

Table VI. Results of the precision studies of the proposed FT-IR method

Drug	Concentration (mg g^{-1})	Intraday (at 10 am) (%RSD)	Intraday (at 4 pm) (%RSD)	Interday (Day 2) (%RSD)	Interday (Day 3) (%RSD)
Aspirin	15	0.0293	0.0783	0.0228	0.4963
	30	0.0227	0.0359	0.0412	0.0239
	45	0.0061	0.0046	0.5207	0.0991
Omeprazole	7.5	0.0483	0.1158	0.0587	0.1302
	15	0.0943	0.7878	0.0864	0.0555
	22.5	0.0710	0.7687	0.3034	0.0903

Robustness

The robustness study was performed by changing parameters such as different analysts (analyst 1, analyst 2), different solvent (NaCl) and changing scanning time (16 s, 24 s). To perform this study, the same standard solutions with 30 mg g^{-1} Aspirin and 15 mg g^{-1} Omeprazole (six measurements were taken), and a sample solution of the same concentration (two measurements were taken) were tested and the %RSD was calculated for both the drugs. The results of this study are reported in Table VII.

Table VII. Results of the Robustness studies by changing solvent and scan time

	Average			
Parameters	**Absorbance of Aspirin**	**Absorbance of Omeprazole**	**% RSD of Aspirin**	**% RSD of Omeprazole**
Solvent	2.4700	1.4614	0.028	0.1995
Scanning time	2.4701	1.4577	0.030	0.0258
Analyst	2.4681	1.4561	0.1091	0.0488

Analysis of tablets

Twenty tablets were accurately weighed and made into the powder form by trituration. Quantity of tablet powder equivalent to 10 mg g^{-1} of Aspirin was taken and diluted with potassium bromide to get a pellet with about 200 mg. The pellets were analyzed to determine the % of Aspirin and Omeprazole. The results are reported in Table VIII.

Table VIII. Analysis of Marketed Formulation by FT-IR Method

Formulation	**Drug**	**Concentration (mg g^{-1})**	**Mean of absorbance**	**Label claim (mg)**	**Amount obtained (mg)**	**% Assay**
Yosprala	Aspirin	30	2.9665	81	80.93	99.92
	Omeprazole	15	1.4575	40	40.01	100.04

RESULTS AND DISCUSSION

This method is based on the measurement of absorbance for Aspirin at C=O stretching vibration centred at 1754 cm^{-1}, which is typically in the range of 1750 – 1730 cm^{-1} and for Omeprazole at C=N stretch vibration at 1627 cm^{-1} between 1690 – 1630 cm^{-1}. The proposed developed method was validated as per ICH Topic Q 2 (R1) guidelines [16]. The validation was started by specificity study and the results are described in the Figures 6 and 7. Figure 6 presents the spectra of the standard mixture of Aspirin and Omeprazole and Figure 7 presents the spectra of the formulation. By comparing both the spectra it was observed that there was no interference from other excipients at wave number of 1754 cm^{-1} for Aspirin and 1627 cm^{-1} for Omeprazole. The overlain plot was obtained in the range of 10-50 mg g^{-1} and 5-25 mg g^{-1} for Aspirin and Omeprazole respectively. The linear regression coefficient correlation value for Aspirin was found to be 0.999 and for Omeprazole was found to be 0.997 whose values for both drugs meet the acceptance criteria. The precision study was performed at intraday as well as inter day. The calculated % RSD for intermediate precision and repeatability was within the acceptance limit of ± 2.0%. The accuracy study was performed by recovery study. The accuracy was found to be within the acceptance criteria of 98 – 102%. The result of the accuracy study was described in Table V. The results of the robustness studies show that the developed method is consistent for small changes. The developed and validated method was applied to the assay of marketed formulation of Yosprala (81 mg Aspirin and 40 mg Omeprazole) and the results were in agreement with the reported values.

CONCLUSION

The proposed FTIR spectrophotometric method for the simultaneous determination of Aspirin and Omeprazole was found to be a novel, simple and rapid method. The proposed method was found to be Eco-friendly as well as environmentally friendly compared to the UV and HPLC methods, as it requires only one specifically selected solid solvent. This method was found to be less time consuming compared to other analytical methods. This method can be used as a green tool and can be applied to other pharmaceutical ingredients too.

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