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Research Article

DEVELOPMENT AND VALIDATION OF A STABILITY INDICATING REVERSE PHASE-HIGH PERFORMANCE LIQUID CHROMATOGRAPHY METHOD FOR SIMULTANEOUS DETERMINATION OF CLINDAMYCIN, METRONIDAZOLE, AND CLOTRIMAZOLE IN PHARMACEUTICAL COMBINED DOSAGE FORMS

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ABSTRACT

Objective: The objective of present work was to develop and validate a simple, fast, precise, selective, and accurate reverse phase high-performance liquid chromatography method for the simultaneous determination of Clindamycine, Metronidazole and Clotrimazole in a pharmaceutical dosage form.

Methods: The separation of these three drugs was achieved on ODS 250×4.6 mm, 5 µm C_{18} column. Mobile phase containing 0.1% ortho phosphoric acid buffer and acetonitrile in the ratio of 55:45 v/v was pumped through column at a flow rate of 1 ml/minute. Temperature was maintained at 30°C and ultraviolet detection at 238 nm.

Results: The retention times were observed to be 2.591, 3.584, and 4.221 minutes for Clindamycine, Metronidazole, and Clotrimazole, respectively. Linearity was found to be 25-150 µg/ml Clindamycine, Metronidazole, and Clotrimazole, respectively. The method was statistically validated for linearity, recovery, the limit of detection (LOD), limit of quantification (LOQ), accuracy, and precision. The stress testing of the drugs individually and their mixture are carried out under acidic, alkaline, oxidation, photostability, and thermal degradation conditions and its degradation products are well resolved from the analyte peaks.

Conclusion: This method was successfully validated for accuracy, precision, and linearity, LOD, and LOQ.

Keywords: Clindamycine, Metronidazole, Clotrimazole, Reverse phase-high performance liquid chromatography, Simultaneous determination, Degradation studies.

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INTRODUCTION

Clindamycine [1-3] is a semisynthetic lincosamide antibiotic that has largely replaced lincomycin due to an improved side effect profile. Clindamycine inhibits bacterial protein synthesis by binding to bacterial 50S ribosomal subunits. It may be bacteriostatic or bactericidal depending on the organism and drug concentration. The International Union of Pure and Applied Chemistry (IUPAC) name is (2S,4R)-N-{2-chloro-1-[(2R,3R,4S,5R,6R)-3,4,5-trihydroxy-6-(methylsulfanyl)oxan-2-yl]propyl}-1-methyl-4 propylpyrrolidine-2-carboxamide. Structure was shown in Fig. 1. Metronidazole [4-7] is a prodrug. Unionized Metronidazole is selective for anaerobic bacteria due to their ability to intracellularly reduce Metronidazole to its active form. This reduced Metronidazole then covalently binds to deoxyribonucleic acid, disrupt its helical structure, inhibiting bacterial nucleic acid synthesis, and resulting in bacterial cell death. IUPAC name is 2-(2-methyl-5-nitro-1H-imidazol-1-yl) ethan-1-ol. The structure was shown in Fig. 1. Clotrimazole [8-10] is an imidazole derivative and an antifungal compound and a CYP (cytochrome P450) inhibitor. Clotrimazole has been shown to block the intermediate conductance, IK1 channels (Ca^{2+} activated K^+ channels), in cells such as erythrocytes. *In vitro* studies of various yeast strains have demonstrated susceptibility to Clotrimazole. Clotrimazole is an activator of MB67 and an inhibitor of CYP3A4 and CYP51A1. IUPAC name is 1-[(2-chlorophenyl)diphenylmethyl]-1H-imidazole. The structure was shown in Fig. 1.

The literature survey reveals that so far there are only two analytical methods are reported for simultaneous estimation of Clindamycine, Metronidazole, and Clotrimazole [11,12]. The first method reported by Seethalakshmi *et al.* [11] utilizes a mobile phase flow rate of 2.3 ml/minute with 40 minutes runtime.

The second method reported by Raendar *et al.* is the only one stability indicating method published for the simultaneous estimation of Clindamycine, Metronidazole, and Clotrimazole [12] having phosphate buffer pH 4.5:methanol:acetonitrile in the ratio of 30:20:50% V/V as mobile phase, pH 4.5 adjusted by using 0.1M ortho phosphoric acid (OPA) with runtime of 10 minutes. The LOD and LOQ of Metronidazole, Clindamycin, and Clotrimazole were found to be 1.77 and 5.35 µg/ml, 2.55 and 7.77 µg/ml, and 1.28 and 5.25 µg/ml, respectively.

Hence, we have planned to develop a simple, precise, economic, and accurate stability indicating reverse phase-high performance liquid chromatography (RP-HPLC) method for the estimation of Clindamycine, Metronidazole, and Clotrimazole in bulk and pharmaceutical dosage form according to the International Conference on Harmonization (ICH) [13-18] Guidelines.

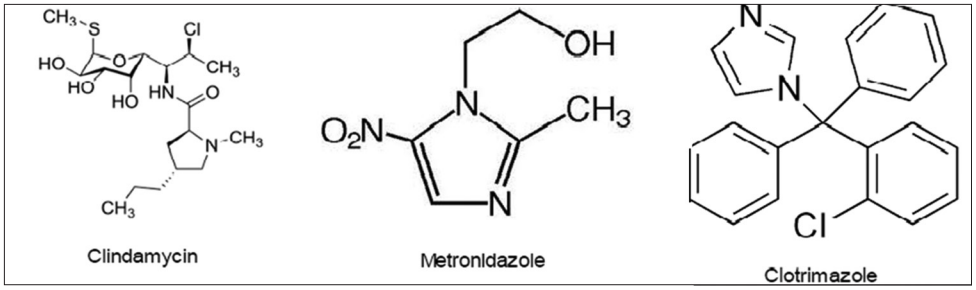

Fig. 1: Structures of Clindamycine, Metronidazole, and Clotrimazole

Finally, developed and validated the method with the comparative betterment of following parameters. Mobile phase containing 0.1% OPA buffer and acetonitrile in the ratio of 55:45 v/v was pumped through column at a flow rate of 1 ml/minute (8 minutes runtime). The LOD and LOQ of Metronidazole, Clindamycine, and Clotrimazole were found to be 0.095 and 0.290 µg/ml, 0.19 and 0.589 µg/ml, and 0.135 and 0.12 µg/ml, respectively. [19-22].

Importance of analytical method, presented in this publication, is an application to the assay of Vagi CL formulation. Vagi CL having lot of advantages for treating of amoebiasis, anaerobic infections, and antibiotic-associated colitis. Till date, no official methods developed for combination of Vagi CL. Hence, this method can be used for routine analysis of Vagi CL in industries.

METHODS

Active pharmaceutical ingredients Clindamycine, Metronidazole, and Clotrimazole were obtained as a gift sample from Spectrum Pharma Research Solutions, Hyderabad. The pharmaceutical dosage form (Vagi CL [Vaginal Pessary] from Rekvina Pharmaceuticals India Pvt., Ltd) was purchased from local pharmacy. The solvents used in this work were of HPLC grade and obtained from the Merck Specialties Private Limited, Mumbai.

Instrumentation and chromatographic conditions

The analysis was performed on a HPLC system consists of waters 2695 with 2996 module Photo Diode Array detector equipped with a quaternary solvent delivery pump, automatic sample injector, and column thermostat. The data acquisition and analysis was performed using Empower2 software. The chromatographic separation was performed on ODS C_{18} column (250×4.6 mm×5 µ). The flow rate was kept at 1 ml/minute. The column temperature was maintained at 30°C. The mobile phase was made of 0.1% OPA buffer and acetonitrile in 55:45 ratio had gave acceptable retention time and good resolution between Clindamycine, Metronidazole, and Clotrimazole. The method was optimized at 238 nm. Data acquisition and processing was performed using Empower2 system software. The run time was taken as 8 minutes. All the determinations are carried out at an ambient temperature.

Sample processing

Preparation of standard stock solutions

Accurately weighed 10 mg of Clindamycine, 10 mg of Metronidazole, and 10 mg of Clotrimazole and transferred to three 10 ml volumetric flasks separately. 7 ml of diluent was added to flasks and sonicated for 15 minutes. Flasks were made up with diluent and labeled as standard stock solution 1, 2, and 3.1 ml from each stock solution was pipette out and taken into a 10 ml volumetric flask and made up with diluent.

Preparation of sample stock solutions

5 pessaries were weighed and calculated the average weight of each pessary, then the weight equivalent to one pessary and transferred into a 100 ml volumetric flask, 70 ml of diluent added and sonicated for 25 minutes, further the volume made up with diluent and filtered. From the filtered solution, 1 ml was pipette out into a 10 ml volumetric flask and made up to 10 ml with diluent.

Preparation of buffer

Buffer: (0.1% OPA)
About 1 ml of OPA in a 1000 ml of volumetric flask adds about 100 ml of milli-Q water and final volume make up to 1000 ml with milli-Q water.

Method validation
The method was validated according to the ICH guidelines. The different validation characteristics which were performed are following: Linearity, accuracy, precision, limit of detection (LOD), limit of quantification (LOQ), robustness, and the stability indicating capability.

System suitability parameters
The system suitability parameters were determined by preparing standard solutions of Clindamycine, Metronidazole, and Clotrimazole, and the solutions were injected 6 times and the parameters such as peak tailing, resolution, and the United States Pharmacopeia (USP) plate count were determined.

Linearity
The linearity of the method is determined by preparing three individual series of solutions in the range of Clindamycine (25-150 µg/ml), Metronidazole (25-150 µg/ml), and Clotrimazole (25-150 µg/ml). The obtained peak areas are plotted against concentration.

Preparation of linearity solutions

Preparation of standard stock solutions

Accurately weighed 10 mg of Clindamycine, 10 mg of Metronidazole, and 10 mg of Clotrimazole and transferred to three 10 ml volumetric flasks separately. 7 ml of diluent was added to flasks and sonicated for 15 minutes. Flasks were made up with diluent and labeled as standard stock solution 1, 2, and 3. From three stock solutions pipette out 0.25, 0.5, 0.75, 1.0, 1.25, and 1.50 ml into 10 ml volumetric flask to get 25%, 50%, 75%, 100%, 125%, and 150%, respectively, of standard solutions.

Precision

Method precision (repeatability)
The method precision/repeatability can be determined by injecting six working standard solutions and six sample injections. The areas of all the injections were taken and standard deviation (SD), %relative standard deviation (%RSD), and %assay were calculated.

Intermediate precision
The intermediate precision can be determined by injecting six working standard solutions and six sample injections on different days by different operators or by different instruments. The areas of all the injections were taken and SD, %RSD, and %assay were calculated. The results obtained were within the acceptance criteria.

Accuracy

Accuracy is tested by the standard addition method at three different levels 50%, 100%, and 150%. The percentage recoveries

of Clindamycine, Metronidazole, and Clotrimazole present in the pharmaceutical dosage form were calculated.

Preparation of 50% spiked solution
5 pessaries were weighed and calculated the average weight of each pessary, then the weight equivalent to one pessary and transferred into a 100 ml volumetric flask, 70 ml of diluent added, and sonicated for 25 minutes, further the volume made up with diluent and filtered. 1 ml from each standard stock solution was pipette out and taken into a 10 ml volumetric flask to that 0.5 ml of filtered accuracy standard stock solution was spiked and made up with diluents.

Preparation of 100% spiked solution
5 pessaries were weighed and calculated the average weight of each pessary, then the weight equivalent to one pessary and transferred into a 100 ml volumetric flask, 70 ml of diluent added, and sonicated for 25 minutes, further the volume made up with diluent and filtered. 1 ml from each standard stock solution was pipette out and taken into a 10 ml volumetric flask to that 1 ml of filtered accuracy standard stock solution was spiked and made up with diluents.

Preparation of 150% spiked solution
5 pessaries were weighed and calculated the average weight of each pessary, then the weight equivalent to one pessary and transferred into a 100 ml volumetric flask, 70 ml of diluent added, and sonicated for 25 minutes, further the volume made up with diluent and filtered. 1 ml from each standard stock solution was pipette out and taken into a 10 ml volumetric flask to that 1.5 ml of filtered accuracy standard stock solution was spiked and made up with diluents.

LOD and LOQ
LOD and LOQ of Clindamycine, Metronidazole, and Clotrimazole were determined by calibration curve method. Solutions of Clindamycine, Metronidazole, and Clotrimazole were prepared in linearity range and injected in triplicate. Average peak area of three analyses was plotted against concentration.

Method robustness
The robustness can be determined by varying the following parameters:

Robustness of the developed method was determined by making small deliberate changes in flow rate (±0.1 ml/minute), column temperature (±5%), organic mobile phase ratio (±10%), along with the optimized method.

Forced degradation studies

Oxidation

To 1 ml of stock solution of Clindamycine, Metronidazole, and Clotrimazole, 1 ml of 20% hydrogen peroxide (H_2O_2) was added separately. The solutions were kept for 30 minutes at 60°C. For HPLC study, the resultant solution was diluted to obtain 100, 100, and 100 µg/ml of all components, and 10 µl was injected into the system and the chromatograms were recorded to assess the stability of sample.

Acid degradation studies
To 1 ml of stocks solution Clindamycine, Metronidazole, and Clotrimazole, 1 ml of 2N hydrochloric acid was added and refluxed for 30 minutes at 60°C. The resultant solution was diluted to obtain 100, 100, and 100 µg/ml of all components, and 10 µl solutions was injected into the system and the chromatograms were recorded to assess the stability of sample.

Alkali degradation studies
To 1 ml of stock solution Clindamycine, Metronidazole, and Clotrimazole, 1 ml of 2N sodium hydroxide was added and refluxed for 30 minutes at 60°C. The resultant solution was diluted to obtain 100, 100, and 100 µg/ml of all components, and 10 µl was injected into the system and the chromatograms were recorded to assess the stability of sample.

Dry heat degradation studies
The standard drug solution was placed in oven at 105°C for 6 hrs to study dry heat degradation. For HPLC study, the resultant solution was diluted obtain 100, 100, and 100 µg/ml of all components, and 10 µl was inject d into the system and the chromatograms were recorded to assess the stability of the sample.

Photostability studies
The photochemical stability of the drug was also studied by exposing 1000, 1000, and 1000 µg/ml solution to ultraviolet (UV) light by keeping the beaker in UV chamber for 7 days or 200 W h/m^2 in photostability chamber. For HPLC study, the resultant solution was diluted to obtain 100, 100, and 100 µg/ml of all components, and 10 µl was injected into the system and the chromatograms were recorded to assess the stability of sample.

Neutral degradation studies
Stress testing under neutral conditions was studied by refluxing the drug in water for 6 hrs at a temperature of 60°. For HPLC study, the resultant solution was diluted to obtain 100, 100, and 100 µg/ml of all components, and 10 µl was injected into the system and the chromatograms were recorded to assess the stability of the sample.

RESULTS AND DISCUSSIONS

Development and optimization of HPLC method
The present work was focused to develop a stability indicating RP-HPLC method for the simultaneous estimation of Clindamycine, Metronidazole, and Clotrimazole in pharmaceutical dosage form. The solubility of the active pharmaceutical ingredient was checked in different solvents such as methanol, water, acetonitrile, and in different ratios, but finally, the standard is soluble in water:acetonitrile (50:50), so it was chosen as a diluent. The different mobile phases such as acetonitrile and water, acetonitrile and 0.01N potassium dihydrogen ortho phosphate buffer, and acetonitrile and sodium dihydrogen phosphate buffer were used in compositions with a flow rate of 1 ml/minute, but the peak resolution, retention time, and tailing factor were not satisfactory, so at last OPA and acetonitrile was selected as a buffer at flow rate of 1 ml/minutes. Initially, "kromosil®" (250×4.6 mm×5 µ) and "BDS®" (150×4.6 mm×5 µ) columns with different temperatures such as 30°C, 35°C, 40°C, and 45°C were used, but the retention time, run time, and peak resolution were not exact and the problem was get rid using ODS C_{18} column (250×4.6 mm×5 µ) kept at 30°C with a run time of 8 minutes. Finally, the method was optimized by altering the mobile phase composition/ratio and the optimized wavelength of three drugs Clindamycine, Metronidazole, and Clotrimazole was found to be at 238 nm.

System suitability parameters
The system suitability tests were conducted before performing the validation, and the parameters were within the acceptance criteria such as retention times were 2.591, 3.584, and 4.221 minutes for Clindamycine, Metronidazole, and Clotrimazole; plate count was >2000; peak tailing was <2; the %RSD of peak areas of six injections were ≤2% (Table 1). Hence, the proposed method was successfully applied to routine analysis without any problems.

Linearity range
The linearity range was in the interval of Clindamycine (25-150 µg/ml), Metronidazole (25-150 µg/ml), and Clotrimazole (25-150 µg/ml), respectively. These were represented by a linear regression equation as follows: Y (Clindamycine)=13873x+1140. (r^2=0.999), y (Metronidazole)=16591x+886.2 (r^2=0.999), and y (Clotrimazole)=13335x+786.5. Regression line was established by least squares method and correlation coefficient (r^2) for Clindamycine,

Metronidazole, and Clotrimazole were found to be greater than 0.999. Hence, the curves established were linear (Table 2). Chromatograms were shown in Fig. 2.

Precision

Six replicates injections at the same concentration were analyzed on the same day and two different days for verifying the variation in the precision and the %RSD for Clindamycine, Metronidazole, and Clotrimazole were within acceptable limit of ≤2. Hence, the method is reproducible on different days with different analyst and column. This indicates that the method is precise (Table 3).

Accuracy

The percentage recoveries for Clindamycine, Metronidazole, and Clotrimazole were found to be 100.98%, 100.72%, and 100.69%, respectively (Tables 4-6). The results of the recovery studies undoubtedly demonstrate the accuracy of the proposed method.

LOD and LOQ

The determined values of LOD and LOQ were calculated using slope and Y-intercept. The LOD and LOQ values for Clindamycine were found to be 0.19 and 0.58 µg/ml; Metronidazole were found to be 0.09 and 0.29 µg/ml; Clotrimazole were found to be 0.13 and 0.41 µg/ml, respectively (Table 7).

Robustness

Robustness of the proposed method demonstrated a nonsignificant alteration through analysis of the sample and standard Clindamycine, Metronidazole, and Clotrimazole solution (Table 8). After this, the results obtained were compared with that of optimized method. It was confirmed that by the deliberate changes in the parameters there was no any significant changes in SD, RSD, theoretical plates, retention time, and USP tailing factor.

Assay

The content of Clindamycine, Metronidazole, and Clotrimazole in the pharmaceutical dosage form were found using the developed method. The percentage purity of Clindamycine, Metronidazole, and Clotrimazole was found to be 100.78%, 100.84%, and 100.54% and %RSD values for Clindamycine, Metronidazole, and Clotrimazole in were within the limit of ≤2.

Forced degradation studies

The forced degradation studies were conducted and all the parameters for Clindamycine, Metronidazole, and Clotrimazole were within the limits. Clindamycine, Metronidazole, and Clotrimazole have shown significant sensitivity toward the treatment of HCl, NaOH, and peroxide solutions. The drugs gradually undergone degradation with time and prominent degradation was observed. Clindamycine, Metronidazole,

Table 1: System suitability parameters for Clindamycine, Metronidazole, and Clotrimazole

S. No	Clindamycine			Metronidazole			Clotrimazole		
Injection	Retention time (minute)	Number of theoretical plates	Tailing factor	Retention time (minute)	Number of theoretical plates	Tailing factor	Retention time (minute)	Number of theoretical plates	Tailing factor
1	2.575	6367	1.49	3.566	9984	1.19	4.194	10826	1.11
2	2.582	6326	1.39	3.586	10152	1.19	4.216	11163	1.12
3	2.591	6514	1.48	3.591	11029	1.22	4.225	10818	1.12
4	2.597	6601	1.36	3.599	10184	1.18	4.236	10771	1.11
5	2.598	6333	1.4	3.601	10055	1.2	4.238	10895	1.13
6	2.601	6429	1.36	3.749	9646	1.18	4.466	10476	1.1
Mean % recovery	2.591	6428	1.41	3.615	10175	1.19	4.263	10825	1.12
Standard deviation	0.0102	109.9776	0.0579	0.0667	460.5753	0.0151	0.1010	220.8669	0.0105
Relative standard deviation in %	0.39	1.71	4.09	1.84	4.53	1.26	2.37	2.04	0.94

Table 2: Linearity table for Clindamycine, Metronidazole, and Clotrimazole

Clindamycine		Metronidazole		Clotrimazole	
Concentration (µg/ml)	Peak area	Concentration (µg/ml)	Peak area	Concentration (µg/ml)	Peak area
25	341795	25	404896	25	303196
50	705870	50	833160	50	696015
75	1043871	75	1253991	75	1025053
100	1386674	100	1672361	100	1326643
125	1725579	125	2072055	125	1656382
150	2087619	150	2480096	150	1999226

Table 3: Determination of repeatability and intermediate precision

Drug name	Repeatability			Intermediate		
	Peak area	SD	%RSD	Peak area	SD	%RSD
Clindamycine	1395906	9591	0.69	1380208	6542.5	0.5
Metronidazole	1683511	20795.4	1.24	1664365	7445.1	0.4
Clotrimazole	1313833	11668.4	0.89	1301211	4174	0.3

SD: Standard deviation, RSD: Relative standard deviation

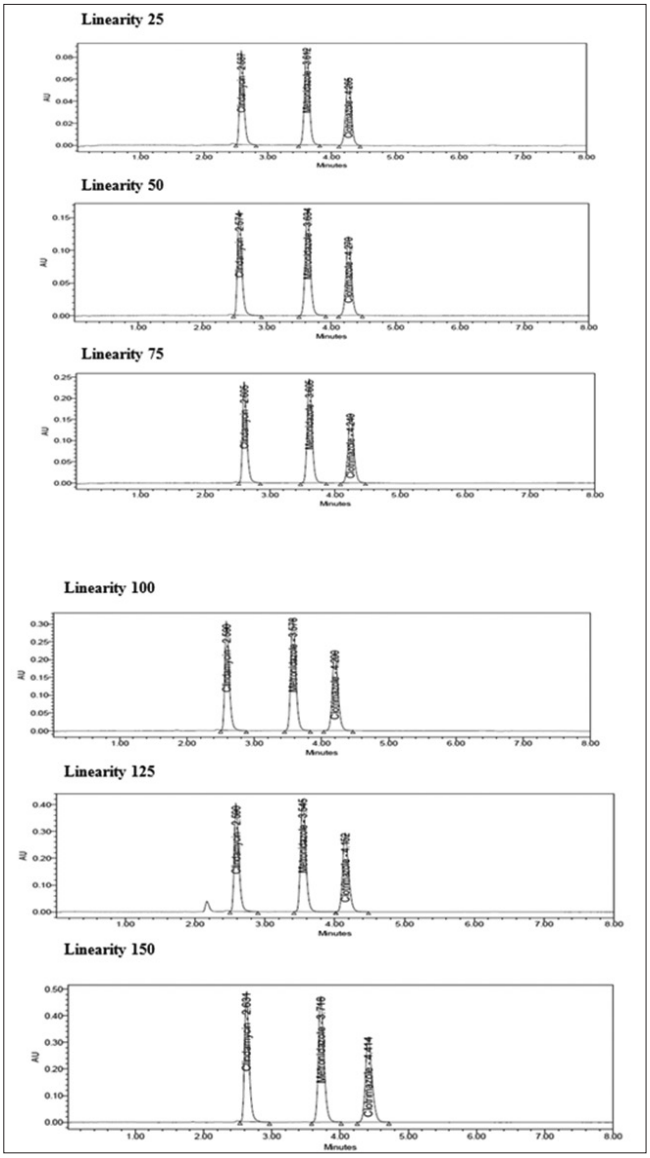

Fig. 2: Linearity chromatograms

and Clotrimazole were stable under forced thermal degradation, photolytic, and neutral degradations. From the degradation studies, Peak purity test results derived from PDA detector confirmed that the Clindamycine, Metronidazole, and Clotrimazole peaks were homogeneous and pure in all the analyzed stress samples (Table 9). The mass balance of stressed samples was close to 94.50%. Purity plots were shown in Fig. 3. Forced Degradation results are tabulated in Table 9.

CONCLUSION

Finally, we are successful in developing and validating a new, simple, rapid, and precise stability indicating HPLC method was for the simultaneous estimation of Clindamycine, Metronidazole, and Clotrimazole in pharmaceutical dosage form, with less complex mobile phase and runtime compared to available (published) methods.

Applied the validated method for estimating assay of Clindamycine, Metronidazole, and Clotrimazole in the formulation of Vagi CL. Formulation of Vagi CL having a lot of advantages for treating of amoebiasis, anaerobic infections, and antibiotic-associated colitis. Till date, no official methods developed for a combination of Vagi CL. Hence, this method can be applied

Table 4: Determination of accuracy of Clindamycine

% Level	Amount spiked (µg/ml)	Amount recovered (µg/ml)	% Recovery
50	50	49.86	99.72
		50.67	101.34
		49.95	99.89
100	100	102.09	102.09
		101.75	101.75
		100.80	100.80
150	150	152.65	101.76
		150.79	100.52
		151.47	100.98
Mean %recovery			100.98
Standard deviation			0.8354
Relative standard deviation in %			0.83

Table 5: Determination of accuracy of Metronidazole

% Level	Amount spiked (µg/ml)	Amount recovered (µg/ml)	% Recovery
50	50	50.76	101.52
		50.09	100.18
		50.38	100.76
100	100	101.34	101.34
		100.93	100.93
		100.19	100.19
150	150	148.97	99.31
		151.39	100.92
		152.05	101.36
Mean %recovery			100.72
Standard deviation			0.7137
Relative standard deviation in %			0.71

Table 6: Determination of accuracy of Clotrimazole

% Level	Amount spiked (µg/ml)	Amount recovered (µg/ml)	% Recovery
50	50	50.02	100.03
		50.95	101.91
		50.46	100.92
100	100	101.19	101.19
		100.59	100.59
		100.76	100.76
150	150	149.09	99.39
		151.36	100.91
		150.77	100.51
Mean %recovery			100.69
Standard deviation			0.7073
Relative standard deviation in %			0.70

Table 7: Sensitivity table of Clindamycine, Metronidazole, and Clotrimazole

Molecule	LOD (µg/ml)	LOQ (µg/ml)
Clindamycine	0.194	0.589
Metronidazole	0.095	0.290
Clotrimazole	0.135	0.412

LOD: Limit of detection, LOQ: Limit of quantification

Table 8: Robustness data for Clindamycine, Metronidazole, and Clotrimazole

S. No	Condition	%RSD of Clindamycine	%RSD of Metronidazole	%RSD of Clotrimazole
1	Flow rate (−) 0.9 ml/minutes	0.6	0.6	0.4
2	Flow rate (+) 1.1 ml/minutes	0.2	0.2	0.3
3	Mobile phase (−) 50b: 50a	1.1	0.4	0.2
4	Mobile phase (+) 40b: 60a	0.4	0.4	0.4
5	Temperature (−) 25°C	0.8	0.8	0.8
6	Temperature (+) 35°C	0.3	0.4	0.2

RSD: Relative standard deviation

Table 9: Forced degradation results of proposed RP-HPLC method

Degradation condition	Clindamycine			Metronidazole			Clotrimazole		
	% Drug degraded	Purity angle	Purity threshold	% Drug degraded	Purity angle	Purity threshold	% Drug degraded	Purity angle	Purity threshold
Acid	3.97	0.13	0.37	3.64	0.11	0.31	3.03	0.18	0.35
Alkali	2.52	0.18	0.42	2.94	0.10	0.33	2.12	0.13	0.36
Oxidation	5.50	0.15	0.39	5.21	0.19	0.35	4.41	0.21	0.44
Thermal	0.70	0.10	0.47	0.89	0.22	0.53	0.75	0.34	0.79
UV	0.89	0.17	0.44	0.93	0.09	0.33	0.93	0.14	0.37
Water	0.40	0.19	0.39	0.94	0.10	0.35	0.72	0.16	0.42

RP-HPLC: Reverse phase-high performance liquid chromatography, UV: Ultraviolet

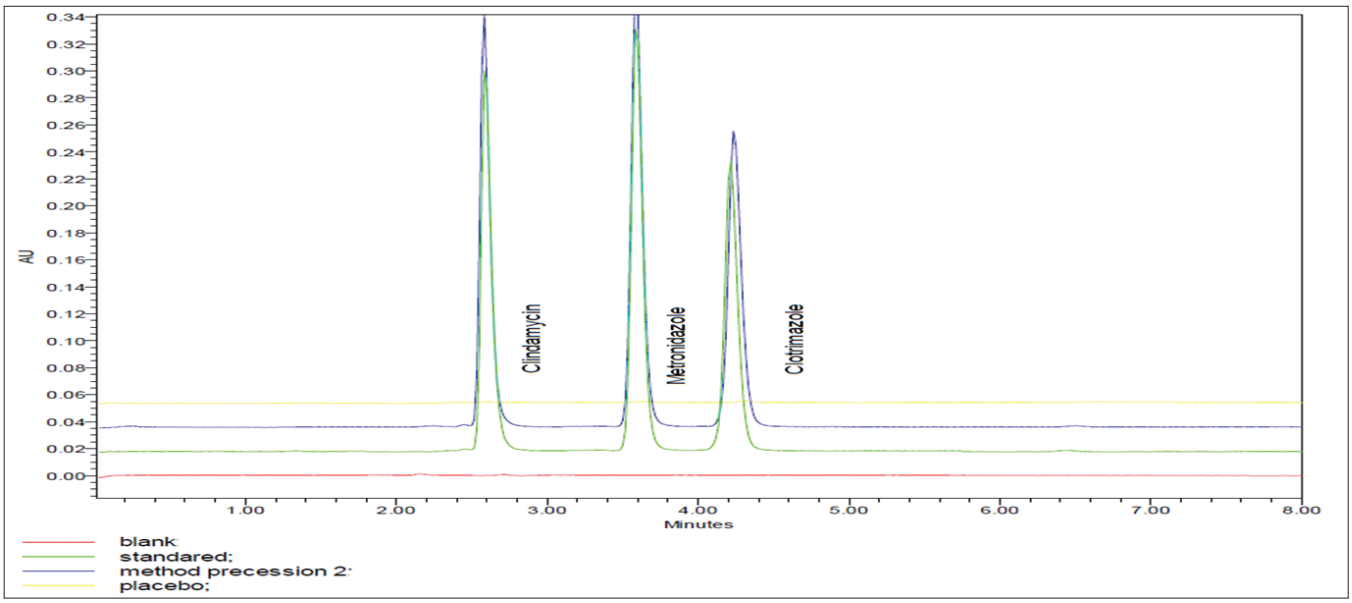

Fig. 3: Specificity overlay chromatogram of blank, standard, placebo, and marketed sample of Clindamycine, Metronidazole, and Clotrimazole

for the estimation of Clindamycine, Metronidazole, and Clotrimazole in drug testing laboratories and pharmaceutical industries.

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