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High Performance Thin Layer Chromatographic Determination of Famotidine and Domperidone in Combined Tablet Dosage Form

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ABSTRACT

A new simple High Performance Thin Layer Chromatographic (HPTLC) method for determination of Famotidine (FAM) and Domperidone (DOM) in combined tablet dosage form has been developed and validated. The mobile phase selected was Toluene: Methanol: Triethylamine (6: 3: 0.5 v/v/v) with UV detection at 290 nm. The retention factor for FAM and DOM were found to be 0.23±0.102 and 0.67±0.123. The method was validated with respect to linearity, accuracy, precision and robustness. Results found to be linear in the concentration range of 100-500 ng/band for both FAM and DOM. The method has been successfully applied for the analysis of drugs in pharmaceutical formulation. The % assay (Mean±S.D.) was found to be 98.63±0.257 for FAM and 98.87±0.654 for DOM.

Key words: Famotidine, Domperidone, High Performance Thin Layer chromatography, Tablet dosage form

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INTRODUCTION

Famotidine (FAM) {3-[[[2-[diaminomethylene) amino] thiazole-4-yl] methyl] sulphanyl]-N'sulphamoyl propanimidamide} is a histamine H_2-receptor antagonist that inhibits stomach acid production and is commonly used in the treatment of peptic ulcer disease and gastro esophageal reflux disease [1]. Domperidone (DOM) chemically 5-chloro-1-[1-[3-(2-oxo-2, 3-dihydro-1H-benzimidazol-1-yl) propyl]-piperidin-4-yl]-1, 3-dihydro-2H-benzimidazol-2-one is a peripheral dopamine-2 receptor antagonist used as antiemetic drug [2].

Literature survey reveals High Performance Liquid Chromatographic (HPLC) [3] and High Performance Thin Layer Chromatographic (HPTLC) [4] methods for determination of FAM in tablet dosage form. Spectrophotometric methods [5] for quantification of FAM are also reported. British pharmacopoeia describes HPLC method for determination of DOM [2]. HPLC [6, 7, 8], UPLC [9] Spectrophotometry [10, 11] methods have been reported for the determination of DOM either in single or in combination with other drugs. Spectrophotometric methods have been reported for determination of FAM and DOM in combined tablet dosage form [12].

No work has been reported for the determination of the FAM and DOM in combined dosage form by HPTLC method. This paper presents HPTLC method for determination of Famotidine and Domperidone in combined tablet dosage form. The proposed method is optimized and validated as per the International Conference on Harmonization (ICH) guidelines [13].

MATERIALS AND METHODS

Reagents and chemicals

Analytically pure samples of FAM (98.75 % pure) and DOM (99.12 % pure) were kindly supplied by Cadila Healthcare Ltd. (Vadodara, Gujrat) and Themis Laboratories Pvt. Ltd. (Mumbai, India), respectively. Toluene, Triethylamine and Methanol (all AR grade) were used for the method development. The pharmaceutical dosage form used in this study was Famotidine-20 tablets (Progene Pharma Pvt. Ltd., Turbhe, Navi Mumbai, India) labeled to contain 20 mg of Famotidine and 10 mg of Domperidone/tablet were procured from local market.

EXPERIMENTAL

Instrumentation and chromatographic conditions

The samples were spotted in the form of bands of width of 6 mm with space between bands of 5 mm, with a 100µl sample syringe (Hamilton, Bonaduz, Switzerland) on precoated silica gel aluminium plate 60 F_{254} (10 ×10) with 250µm thickness (E. MERCK, Darmstadt, Germany) using a CAMAG Linomat V sample applicator (Switzerland). The plates

were prewashed with methanol and activated at 110 ^{0}C for 5 min., prior to chromatography. The slit dimensions 5mm×0.45mm and scanning speed of 20mm/sec was employed.

The linear ascending development was carried out in 10 cm×10 cm twin trough glass chamber (CAMAG, Muttenz, Switzerland) using mobile phase. The optimized chamber saturation time for mobile phase was 15 min. The length of chromatogram run was 9 cm and development time was approximately 15 min. TLC plates were dried in a current of air with the help of a hair drier. Densitometric scanning was performed on CAMAG thin layer chromatography scanner 3 at 290 nm for all developments operated by WINCATS software version 1.4.2. The source of radiation utilized was deuterium lamp emitting a continuous UV spectrum between 200 to 400 nm.

Preparation of standard stock solutions

Standard stock solution of FAM and DOM was prepared by dissolving 10 mg of each drug in 10 ml of methanol separately to get concentration of 1mg/ml from which 0.5 ml was further diluted to 10 ml to get stock solution of 50ng/µl of each drug.

Selection of detection wavelength

After chromatographic development bands were scanned over the range of 200-400 nm and the spectra were overlain. It was observed that both drugs showed considerable absorbance at 290 nm. So, 290 nm was selected as the wavelength for detection (Fig 1).

Preparation of calibration curve

The standard stock solutions of FAM and DOM (50ng/µl each) were applied by overspotting on TLC plate in range of 2 – 10 µl with the help of CAMAG 100 µl sample syringe, using Linomat V sample applicator. The plate was developed and scanned under above established chromatographic conditions. Each standard in five replicates was analyzed and peak areas were recorded. Calibration curves of FAM and DOM were plotted separately of peak area vs respective concentration of FAM and DOM.

Analysis of tablet formulation

Twenty tablets were weighed accurately and finely powdered. A quantity of powder equivalent to 20 mg of FAM (10 mg of DOM) was weighed and dissolved in 10 ml of methanol. The solution was filtered using Whatman paper No. 41 and 0.5 ml of filtrate was further diluted to 10 ml. Two µl volume of this solution was applied on TLC plate to obtain final concentration of 200ng/band for FAM and 100ng/band for DOM. After chromatographic development peak areas of the bands were measured at 290 nm and the amount of each drug present in sample was estimated from the respective calibration curves. Procedure was repeated six times for the analysis of homogenous sample.

Robustness studies

In the robustness study, the influence of small, deliberate variations of the analytical parameters on peak area of the drugs was examined. Factors varied were development distance (± 5 %), time from application to development (0, 10, 20, and 30 min) and from development to scanning (0, 30, 60, and 90 min). One factor at a time was changed to estimate the effect. Robustness of the method was checked at a concentration level of 200ng/band and 100ng/band for FAM and DOM respectively.

Recovery studies

To check the accuracy of the method, recovery studies were carried out by addition of standard drug solution to pre-analyzed sample solution at three different levels 50, 100 and 150 %. Chromatogram was developed and the peak areas were noted. At each level of the amount, three determinations were carried out.

RESULTS AND DISCUSSION

Different mobile phases containing various ratios of Toluene, Methanol, Triethylamine were examined (data not shown). Finally the mobile phase containing Toluene: Methanol: Triethylamine (6: 3: 0.5 v/v/v) was selected as optimal for obtaining well defined and resolved peaks. The optimum wavelength for detection and quantitation used was 290 nm. The retention factors for FAM and DOM were found to be 0.23±0.102 and 0.67±0.123 respectively. Representative densitogram of mixed standard solution of FAM and DOM is shown in Fig 2.

Straight-line calibration graphs were obtained for FAM and DOM in the concentration range 100-500ng/band for both the drugs with high correlation coefficient > 0.998. The proposed method was also evaluated by the assay of commercially available tablets containing FAM and DOM. The % assay (Mean±S.D.) was found to be 98.63±0.257 for FAM and 98.87±0.654 for DOM. Robustness of the method checked after deliberate alterations of the analytical parameters showed that areas of peaks of interest remained unaffected by small changes of the operational parameters (% RSD < 2). The results are given in Table No. 1.

For FAM, the recovery study results ranged from 98.89 to 100.06 % with % RSD values ranging from 0.346 to 0.574. For DOM, the recovery results ranged from 98.73 to 99.98 % with % RSD values ranging from 0.357 to 0.469. Results of recovery studies are reported in Table No. 2.

CONCLUSION

The validated HPTLC method employed here proved to be simple, fast, accurate, precise and robust, thus can be used for routine analysis of FAM and DOM in combined tablet dosage form.

[1]

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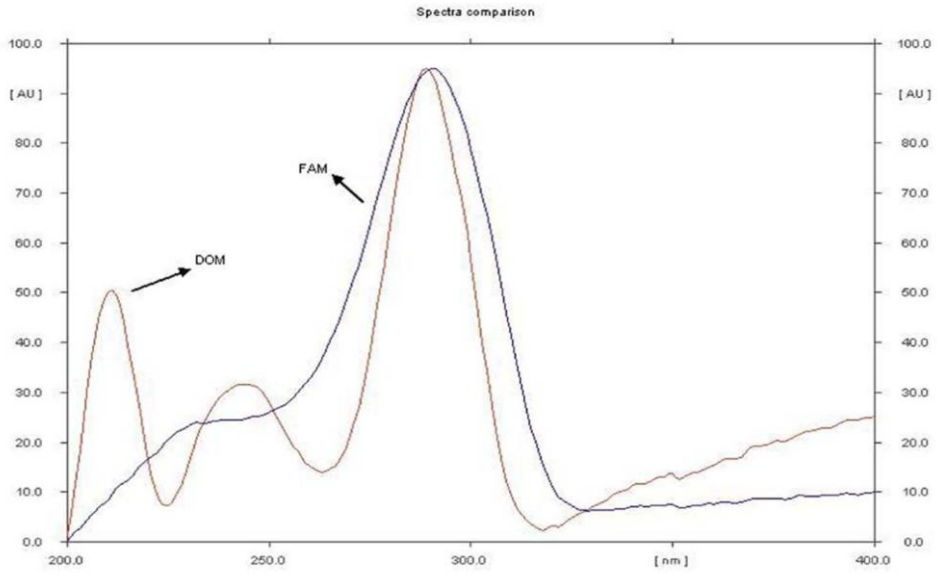

Figure No. 1: Overlain spectra of Famotidine and Domperidone

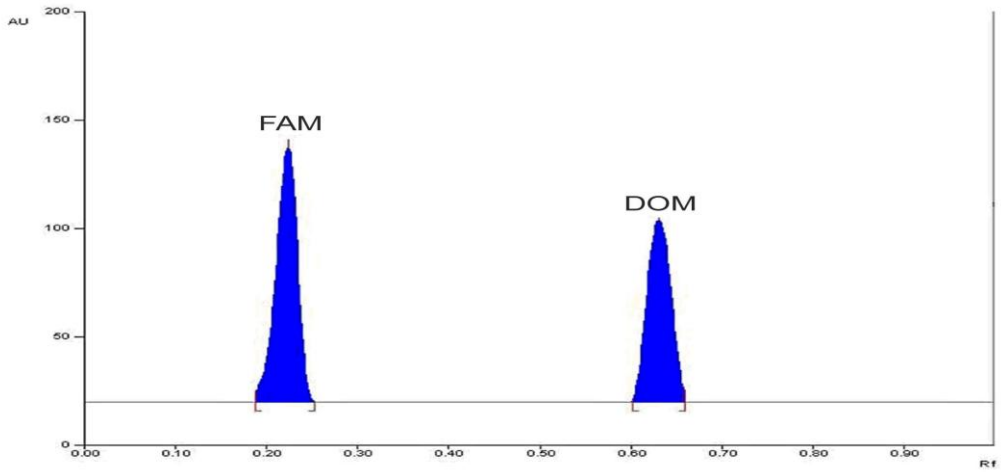

Figure No. 2: Representative chromatogram of mixed standard solution of FAM (200 ng/band, R_f = 0.23 ± 0.102) and DOM (100 ng/band, R_f = 0.67 ± 123).

Table No. 1: Robustness Data in Terms of Peak Area (% RSD)

Sr. No.	Parameter Varied	FAM	DOM
1	Development distance	0.88	0.72
2	Time from application to development (Mins.)	0.73	0.56
3	Time from development to scanning (Mins.)	1.23	0.75

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Table No. 2: Recovery Studies of FAM and DOM

Drug	Amount taken (ng/band)	Amount added (ng/band)	Total amount found (ng/band)	% Recovery	% RSD[a]
FAM	200	100	296.670	98.89	0.346
	200	200	396.240	99.06	0.574
	200	300	500.312	100.06	0.396
DOM	100	50	148.095	98.73	0.357
	100	100	199.680	99.84	0.469
	100	150	249.950	99.98	0.364

[a] Average of three determinations

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