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DEVELOPMENT AND VALIDATION OF HPTLC METHOD FOR SIMULTANEOUS ESTIMATION OF DOMPERIDONE IN COMBINATION WITH ESOMEPRAZOLE MAGNESIUM IN SOLID DOSAGE FORM

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ABSTRACT

The present work describes high performance thin layer chromatographic method for simultaneous estimation of domperidone in combination with esomeprazole magnesium in capsule formulation. Chromatography was performed on (10 × 10 cm) silica gel F_{254} TLC plates using mobile phase chloroform : methanol (9 : 1 v/v) with 30 min time of saturation with filter paper. Chromatographic conditions were found to effectively separate domperidone (Rf –0.25) and esomeprazole magnesium (Rf-0.46). Standard calibration curve was found to be linear in the range 0.06-0.3 µg/spot for domperidone and 0.08-0.4 µg/spot for esomeprazole magnesium, respectively. The proposed method was found to be accurate, precise, reproducible, economic, reliable and specific and can be used for simultaneous analysis of these drugs in capsule formulation.

Key words : Domperidone, Esomeprazole Magnesium, HPTLC

INDRODUCTION

Domperidone (DOM) is 5-chloro-1-[1-{3-(2-oxo-2, 3-dihydro-1H-benzimidazol-1-yl) propyl}-piperidin-4-yl]-1, 3-dihydro-2H-benzimidazole-2-one and esomeprazole magnesium (ESO) is 5-methoxy 2- { (s) – [(4- methoxy – 3, 5- dimethyl – 2- pyridyl) methyl] sulfinyl}benzimidazole magnesium (2 : 1) trihydrate.

Domperidone is an antiemetic drug usually given in combination with either rabeprazole or esomeprazole, respectively. The combination is useful in treatment of Gastro Esophageal Reflux Disease (GERD). The marketed capsule formulations contain

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domperidone and esomeprazole magnesium in the ratio 3 : 4 (Sompraz D 40, domperidone 30 mg and Esomeprazole Mg 40 mg, manufactured by Sun Pharmaceuticals).

Literature survey revealed spectrophotometric[3] and RPHPLC methods for estimation of domperidone alone and in combination with other drugs in pharmaceutical preparations.

Esomeprazole magnesium alone and in combination is reported to be estimated by RPHPLC[9] and LCMS[10] methods.

So far no analytical method is reported for simultaneous determination of domperidone with esomeprazole magnesium in pharmaceutical formulation and hence, the present work describes validated HPTLC method for simultaneous determination of these drugs in capsule formulation

EXPERIMENTAL

Materials and method

Instruments

(i) CAMAG HPTLC system comprising of

- CAMAG Linomat V semiautomatic sample applicator,
- Hamilton syringe 100 µL
- CAMAG TLC Scanner 3,
- CAMAG twin trough chamber (10 × 10 cm) and

(ii) Sonicator

Pure drug samples of domperidone and esomeprazole magnesium were procured from Abbott Pharma, Mumbai, India and Blue Cross Labs, Nasik, India, respectively. Silica gel 60 F_{254} TLC plates (10 × 10 cm) with thickness 0.25 mm, E. Merck, Mumbai) were used as stationary phase. All chemicals and reagents used were of analytical grade.

The capsule formulations Sompraz D 40 (manufactured by Sun Pharmaceutical), with a labeled claim of 30 mg domperidone and 40 mg esomeprazole magnesium respectively, were obtained from local drug stores.

Standard preparation

Accurately weighed quantity of domperidone (30 mg) and esomeprazole magnesium (40 mg) was weighed and transferred to a standard 100 mL volumetric flask, dissolved and diluted to the mark with methanol. The so prepared stock solution was further diluted with mobile phase to get concentration range of 60-300 ng/spot and 80-400 ng/spot for domperidone and esomeprazole magnesium, respectively. Plotting a graph of peak area Vs concentration allowed the checking of linearity of detector response.

HPTLC method and chromatographic conditions

TLC plates were prewashed with methanol. The chromatographic conditions maintained were precoated silica gel 60 F_{254} aluminium sheets (10 × 10 cm) as stationary phase, chloroform : methanol (9 : 1 v/v) as mobile phase. Chamber saturation time was kept 30 minutes and migration distance allowed was 80 mm, wavelength scanning was done at 284 nm keeping slit dimension at 6.0 × 0.3 mm.

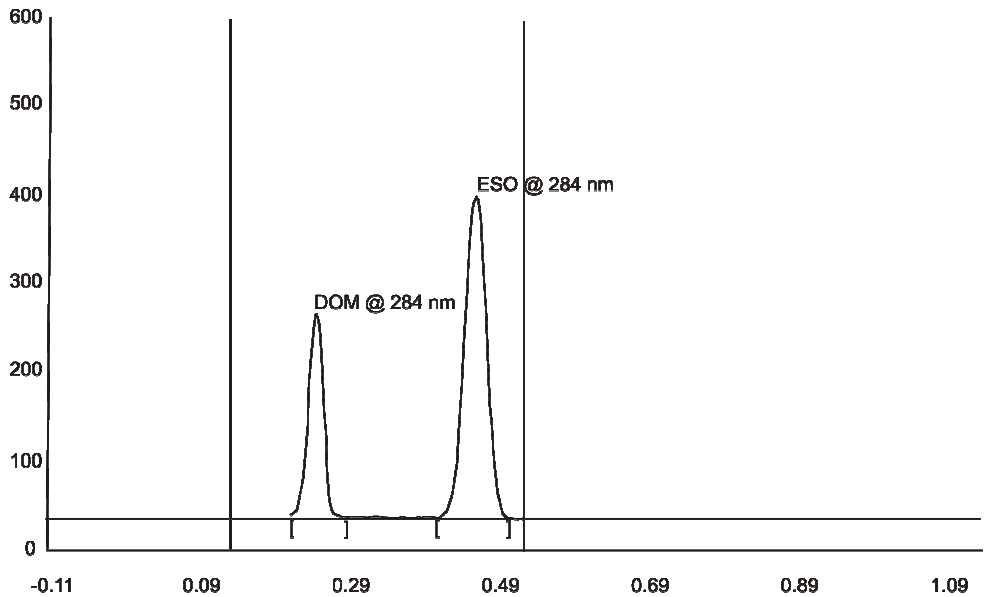

Fig. 1 : Chromatogram of domeperidone (R_f = 0.26) and esomeprazole magnesium (R_f = 0.46)

Analysis of marketed formulation

About 6 microliters of sample solutions of marketed formulation were spotted on to

TLC plate and developed. The analysis was repeated in triplicate. The content of drug was calculated from peak area recorded.

Recovery studies

To study the accuracy of proposed method, recovery experiments were carried out. About 6 µL of sample solution was applied as 6 mm bands; these were then spiked with 5, 6 and 7 µL of standard solution of each drug. Peak areas were recorded.

Validation of method

The developed method was validated in terms of linearity, accuracy, limit of detection, limit of quantitation, inter day and intra day precision.

RESULTS AND DISCUSSION

Table 1 : Results of analysis of capsule formulation

Capsule formulation	Label claim (mg/capsule)		Amount of drug estimated (mg)		% of label claim* ±SD	
	DOM	ESO	DOM	ESO	DOM	ESO
Sompraz D 40	30	40	29.99	9.84	99.98 ± 0.97	99.60 ± 0.81

*Mean of six determinations

Table 2 : Results of recovery studies

Solution of pure drug spiked each (µL)		% of drug found on preanalysed basis		% recovery	
DOM	ESO	DOM	ESO	DOM	ESO
5	5	99.16	99.58	98.34	98.31
6	6	99.23	100.94	99.23	97.93
7	7	99.44	100.92	99.44	98.65

Table 3 : Method validation parameters

Parameter	ESO	DOM
Accuracy : Recovery studies	98.30 % ± 0.64	99.003 % ± 0.58
Precision (RSD, n = 6)	0.00723	0.0082
Linearity and range	80-400 ng/spot	60-300 ng/spot
Regression equation	Y = 38491x + 35.048	Y = 18728x-11.929
Slope (m)	38491	18728
Intercept (c)	35.048	11.929
Correlation coefficient (r^2)	0.9989	0.9997
Limit of detection (ng)	0.4151	0.3150
Limit of quantitation (ng)	1.2453	0.945
Intra-day precision (RSD, n = 3)	0.0006	0.0028
Inter-day precision (RSD, n = 3)	0.0036	0.0092
Different analysts (RSD, n = 3)	0.0077	0.0078

A solvent system that would give dense and compact spots with significant R_f values was desired for quantification of domperidone and esomeprazole magnesium.

The mobile phase consisting of chloroform : methanol (9 : 1 v/v) gave R_f values of 0.25 ± 0.014 for DOM and 0.46 ± 0.0261 for ESO, respectively. The linear regression data (n = 5) showed good linear relationship over a concentration range of 60-300 ng/spot for DOM and 80-400 ng/spot for ESO, respectively.

To confirm specificity of proposed method, the solution of formulation was spotted on the TLC plate, developed and scanned. It was observed that the excipients present in the formulation did not interfere with the peaks of domperidone and esomeprazole magnesium. Validation of proposed method was carried out by using validation parameters.

CONCLUSION

The proposed HPTLC method is simple, precise, accurate, reliable, economic and validated and can be used for routine analysis of these drugs in Quality Control Laboratory

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