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Method Development and Validation for Simultaneous Estimation of Esomeprazole and Domperidone by RP-HPLC in pharmaceutical dosage form

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ABSTRACT

A reverse phase HPLC method is developed for the determination of Esomeprazole and Domperidone in pharmaceutical dosage forms. Chromatography was carried out on a C18 column [4.6 x 100mm, 5µm, Make: BDS] using a mixture of potassium di hydrogen ortho phosphate buffer and acetonitrile (65:35 v/v) as the mobile phase at a flow rate of 1.3 ml/min. Detection was carried out at 298 nm .The retention time of Domperidone and Esomeprazole was 2.788 min and 3.485 min. The linearity was observed In range of 50-130 µg/ml and 60-140 µg/ml with a correlation coefficient of Domperidone and Esomeprazole were 0.999 and 0.999.the proposed method was validated for its linearity, accuracy, precision and robustness .The proposed method is simple, accurate, precise, and reproducible hence it can be applied for routine quality control analysis of Esomeprazole and Domperidone in pharmaceutical dosage form.

Keywords: HPLC, Domperidone and Esomeprazole, Estimation, capsules.

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INTRODUCTION

Esomeprazole magnesium trihydrate 1 (ESO) is chemically bis(5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl- 2 -pyridinyl)methyl]sulfinyl] - 1-H - enzimidazole - 1 -yl) magnesium trihydrate , a compound that inhibits gastric acid secretion . Esomeprazole is cost effective in the treatment of gastric esophageal reflux diseases. It is S-isomer of omeprazole and is the first single optical isomer proton pump inhibitor. It provides better acid control than current racemic proton pump inhibitors and has favorable pharmacokinetic profile relative to omeprazole. Domperidone3 (DOMPE) chemically, [5- chloro-1-[1, 3-(2, 3-dihydro-2-oxo-1H-benzmidazole-1yl) propyl)-4piperdinyl-1, 3 dihydro -2Hbenzimidazole-2-one] is a dopamine antagonist. Detailed surveys of literature revealed a number of methods have been published for the estimation of above said analysts. Spectrophotometric estimation of Domperidone and Esomeprazole, TLC, and several HPLC methods However, no references have been found for simultaneous determination of ESO and DOMPE in pharmaceutical dosage form. A successful attempt has been made to estimate two drugs simultaneously by RP-HPLC.

MATERIALS AND METHOD

Equipment and apparatus

Different kinds of equipment's via analytical weighing balance (shimadzu AUX 200), High performance liquid chromatography (waters, separation module 2695) equipped with Auto Sampler and DAD (Dual Absorbance Detector) detector ,pH meter, Vacuum filter pump (model XI 5522050 of Millipore), Millipore filtration kit, mobile phase reservoir, Sample filtration assembly and glassware's were used throughout the experiment.

Chemicals and Solvents Used

Potassium di hydrogen ortho phosphate and Orthophosphoric acid (AR grade) were used for preparing the buffer. HPLC grade acetonitrile (Qualigens) was used for diluent preparation. Pure sample Of Domperidone and Esomeprazole was a gift sample from a local pharmaceutical industry.

PREPARATION OF SOLUTIONS

Preparation of mobile phase

Mix a mixture of above buffer 650 ml (65%) and 350 ml of Acetonitrile HPLC (35%) and degas in ultrasonic water bath for 5 minutes. Filter through 0.45 µ filter under vacuum filtration

Diluent Preparation

Use the Mobile phase as Diluent.

Preparation of standard solutions:

Accurately weighed and transfer 10 mg of Domperidone and Esomeprazoleworking standard into a 10ml clean dry volumetric flask add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. Further pipette 0.9ml&1.0ml of Domperidone and Esomeprazole from the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent.

Preparation of sample solutions:

Accurately weigh and transfer equivalent to 10 mg of Domperidone and Esomeprazolesample in to a 10mL clean dry volumetric flask and add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent. Further pipette 0.9ml&1.0ml of Domperidone and Esomeprazole the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent

METHOD VALIDATION

The method was validated as per International Conference on Harmonization (ICH) guidelines

Method application (Assay)

The validated high performance liquid chromatography method was applied to simultaneous determination ofEsomeprazole and Domperidone. Locally available capsule dosage form (SOMPRAZ-D) contains Domperidone 30mg, and Esomeprazole 40 mg. Accurately weigh and transfer equivalent to 10 mg of Domperidone and Esomeprazolesample into a 10mL clean dry volumetric flask add about 7mL of Diluent and sonicate for 20 min to dissolve it completely and make volume up to the mark with the same solvent and then filtered the solution through 0.45µm membrane filter. Further pipette out 0.9ml&1.0ml of Domperidone and Esomeprazole from the above stock solution into a 10ml volumetric flask and dilute up to the mark with diluent and 20µLof this solution was injected for HPLC analysis. The analyte peaks were identified by comparisons with those of respective standard for their retention time. The peak areas were used to calculate the drugs. The assay results, expressed as % of the label claim, are in table.1.

Linearity

Under the experimental conditions described above, linear calibration curves for the drugs were obtained throughout the concentration ranges studied. Regression analysis was done on the peak areas of the drugs (y) v/s concentration (x). The linear ranges of Domperidone and Esomeprazole are 50-140µg/ml respectively showed in table.2.

Precision

The assay was carried out of the drugs using proposed method in five replicates. The value of

relative standard deviation lie well within the limits (1.86% for Domperidone, 1.98% for Esomeprazole), it indicates the sample repeatability of the method enclosed in table 3.

Accuracy

The accuracy was done by recovery study. Sample solutions were prepared by spiking at about 50 %, 100% and 150 % of specification limit to Placebo and analyzed by the proposed HPLC method. Results are shown in table4, 5.

ROBUSTNESS:

As part of the Robustness, deliberate change in the Flow rate, Mobile Phase composition, Temperature Variation was made to evaluate the impact on the method. Results are shown in (Table 6, 7.8, 9.)

RESULTS AND DISCUSSION

In the present work, an attempt was made to provide a newer, sensitive, simple, accurate, and less time consuming HPLC new method. It is successfully applied for the determination of Domperidone and Esomeprazolein pharmaceutical preparations.

Table 1: Method application (Assay)

S.No	Parameters	Drug	
		Domperidone	**Esomeprazole**
1	Label claim (mg)	30mg	40mg
2	Drug content (%)	100.8%	100.1%
3	%RSD	0.27	0.31

Table 2: Linearity Regression data for Domperidone and Esomeprazole

S.No	Parameters	Domperidone	Esomeprazole
1	Linear Range(µg/ml)	50-130 µg/ml	60-140 µg/ml
2	Correlation coefficient (r^2)	0.999	0.999
3	LOD	3.02	9.95
4	LOQ	3.04	9.97
5	Tailing Factor	1.4	1.3

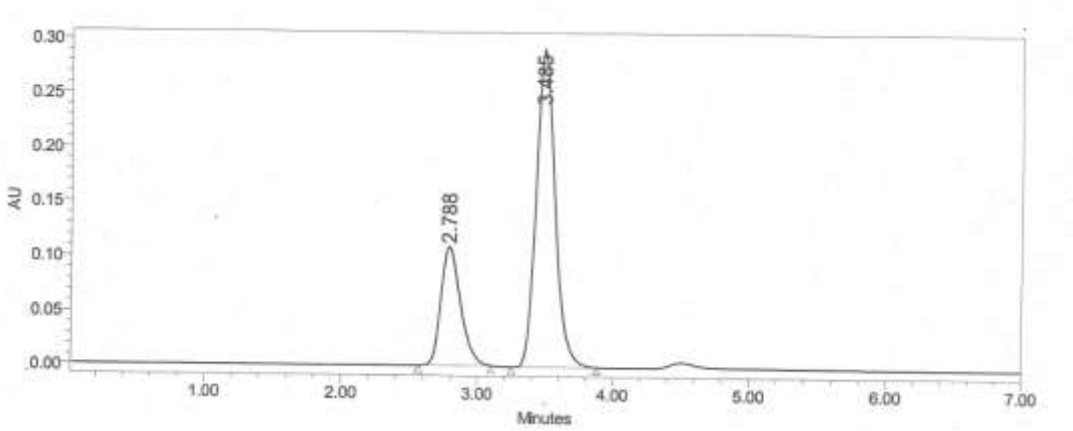

Figure 1: Domperidone and Esomeprazole standard chromatogram

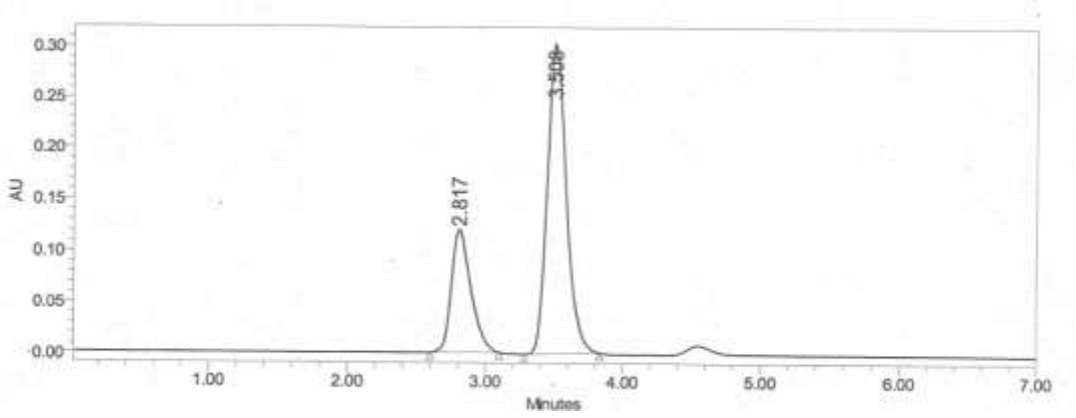

Figure 2: Domperidone and Esomeprazole sample chromatogram

Table 3: Method Precision of Domperidone and Esomeprazole

S.No	Domperidone		Esomeprazole	
	AREA	RT	AREA	RT
1	1130933	2.787	2901501	3.489
2	1135720	2.789	2929818	3.480
3	1172575	2.789	2841624	3.488
4	1171126	2.786	2978022	3.484
5	1174056	2.792	2980190	3.489
AVG	1156882		2926231	
SD	21594.5		57828.7	
%RSD	1.86		1.98	

Table 4: Accuracy-%recovery of each Domperidone

%Concentration (at specification Level)	Area	Amount Added (mg)	Amount Found (mg)	% Recovery	Mean Recovery
50%	534199	4.96	4.87	98.2%	99.9%
100%	1109488	10.0	10.1	101.2%	
150%	1647166	15.0	15.0	100.2%	

Table 5: Accuracy-%recovery of each Esomeprazole

%Concentration(at specification Level)	Area	Amount Added(mg)	Amount Found(mg)	% Recovery	Mean Recovery
50%	1361098	4.92	4.82	98.0%	100.4%
100%	2852643	10.0	10.1	101.0%	
150%	4867723	16.9	17.2	102.0%	

Table 6: System suitability results forDomperidone:

S.No	Flow Rate (ml/min)	System Suitability Results	
		USP Plate Count	USP Tailing
1	1.2	2712.7	1.3
2	1.3*	2756.6	1.4
3	1.4	2700.6	1.3

Table 7: System suitability results forEsomeprazole:

S.No	Flow Rate (ml/min)	System Suitability Results	
		USP Plate Count	USP Tailing

1	1.2	2925.3	1.3
2	1.3*	3035.8	1.3
3	1.4	2826.0	1.3

Table 8: System suitability results for Domperidone

S.No	Change in Organic Composition in the Mobile Phase	System Suitability Results USP Plate Count	USP Tailing
1	10% less	2216.0	1.3
2	*Actual	2756.5	1.4
3	10% more	2021.8	1.3

Table 9: System suitability results for Esomeprazole:

S.No	Change in Organic Composition in the Mobile Phase	System Suitability Results USP Plate Count	USP Tailing
1	10% less	3817.7	1.2
2	*Actual	3035.8	1.3
3	10% more	3786.8	1.4

In HPLC method, HPLC conditions were optimized to obtain, an adequate separation of eluted compounds. Initially, various mobile phase compositions were tried, to get good optimum results. Mobile phase and flow rate selection was based on peak parameters (height, tailing, theoretical plates, capacity factor), run time etc. The system with Buffer: Acetonitrile (65:35 v/v) with 1.3 ml/min flow rate is quite robust. The optimum wavelength for detection was 298 nm at which better detector response for drug was obtained. The average retention time for Domperidone and Esomeprazolewere found to be 2.788 and 3.485 min. System suitability tests are an integral part of chromatographic method. They are used to verify the reproducibility of the chromatographic system. To ascertain its effectiveness, system suitability tests were carried out on freshly prepared stock solutions. The calibration was linear in concentration range of 50-140 µg/ml with Correlation Coefficient of 0.999 to Domperidone and Esomeprazole. The low values of % R.S.D indicate the method is accurate. Sample to sample precision and accuracy were evaluated using, three and of five samples of three different concentrations respectively, these results show the accuracy and reproducibility of the assay. Ruggedness of the proposed methods was determined by analysis of aliquots from homogeneous slot by different analysts, using similar operational and environmental condition; the % R.S.D reported was found to be less than 2 %. The proposed method was validated in accordance with ICH parameters Thus it was show that proposed methods could be successfully applied to estimate commercial pharmaceutical products containing Domperidone and Esomeprazole.

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