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DEVELOPMENT AND VALIDATION OF UV SPECTOPHOTOMETRIC METHOD FOR THE SIMULTANEOUS ESTIMATION OF ESOMEPRAZOLE AND DOMPERIDONE IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

A simple, accurate and precise spectrophotometric method was developed and validated for simultaneous estimation of Esomeprazole(ESO) and Domperidone(DOM) in combined dosage form. In simultaneous equation method, Esomeprazole and Domperidone were quantified using their absorptivity values at selected wavelengths, viz; 302nm and 287nm respectively. Methanol was used as the solvent. Different analytical performance parameters such as linearity, precision, accuracy, limit of detection (LOD), limit of quantification (LOQ) was determined according to ICH guidelines. The linearity range was found to be 5-15µg/ml for Esomperazole and 5-20 µg/ml for Domperidone. LOD and LOQ for Esomeprazole were found to be 1.16µg/ml and 3.52µg/ml, for Domperidone 1.94µg/ml and 5.88µg/ml respectively.

KEY WORDS

Esomeprazole, Domperidone, Spectrophotometric method, Method development, Validation.

INRODUCTION:

Esomeprazole [1-2] (Fig.1) is chemically 6-methoxy-2-[(S)-(4-methoxy-3,5-dimethylpyridin-2-yl) methylsulfinyl]-1H-benzimidazole which inhibits the gastric acid secretion. Esomeprazole is an S-isomer of omeprazole. It is a proton pump inhibitor. This inhibits the H^+/K^+-ATPase channel present in stomach or gastric parietal cells which are responsible for acid secretion.

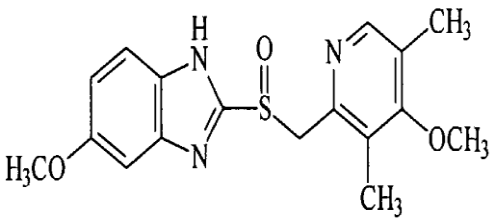

Fig.1. ESOMEPRAZOLE

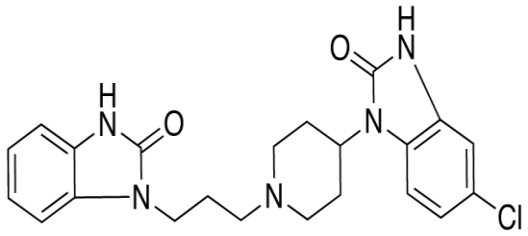

Fig.2. DOMPERIDONE

Domperidone [3-4] (Fig.2) is chemically a 6-chloro-3-[1-[3-(2-oxo-3H-benzimidazol -1yl) propyl] piperidin-4-yl]-1H-benz- imidazol-2-one which is a specific blocker of dopamine receptors. It speeds gastrointestinal peristalsis, causes prolactin release, and is used as antiemetic.

The literature review [5-12] revealed that Spectrophotometric, HPLC and HPTLC methods were already reported for estimation of Esomeprazole and Domperidone alone or in combination. Here is an attempt made to develop and validate UV spectrophotometric method for simultaneous

estimation of Esomeprazole and Domperidone in capsule dosage form.

EXPERIMENTAL:

Instruments used:

SHIMADZU double beam UV/Visible spectrophotometer model UV1800s was employed with a spectral band width of 1nm and a wavelength accuracy of 0.3nm (with automatic wavelength correction with a pair of 1cm matched quartz cells). SHIMADZU Electronic balance model AX 200 and Ultra Sonicator (Fast clean) model 2k811056 were also used during the analysis.

Chemicals and Reagents:

Pure drugs of Esomeprazole and Domperidone were obtained from KP labs (Hyderabad, India). Raciper D40 capsules manufactured by Sun Pharmaceuticals LTD., purchased from local pharmacy was used for the analysis. The label claim states that this formulation contains 40mg of Esomeprazole and 30mg of Domperidone.

Method:

Selection of solvent and wavelength:

The UV spectra of Esomeprazole(ESO) and Domperidone(DOM) differ in different solvents like ethanol, methanol and distilled water were recorded. The two drugs showed good absorbance when dissolved in methanol. Hence, methanol was selected as the solvent for the method. In this the two drugs showing good absorbances at wavelengths of 302nm and 287nm, hence selected as λ_{max} of ESO and DOM respectively (Fig.3). Simultaneous equation method was developed for the estimation of ESO and DOM in the combined dosage form.

Preparation of standard stock solutions:

Standard stock solution of Esomeprazole and Domperidone were prepared by dissolving 100 mg of each drug separately in a 100 ml volumetric flask and both the drugs were dissolved in methanol to get a concentration of 1000µg/ml.

Preparation of working standard solutions:

The working standard solutions of Esomeprazole and Domperidone were prepared by diluting 1 ml each of the standard stock solution to 10 ml with methanol in a 10 ml volumetric flask to get the concentration of 100µg/ml.

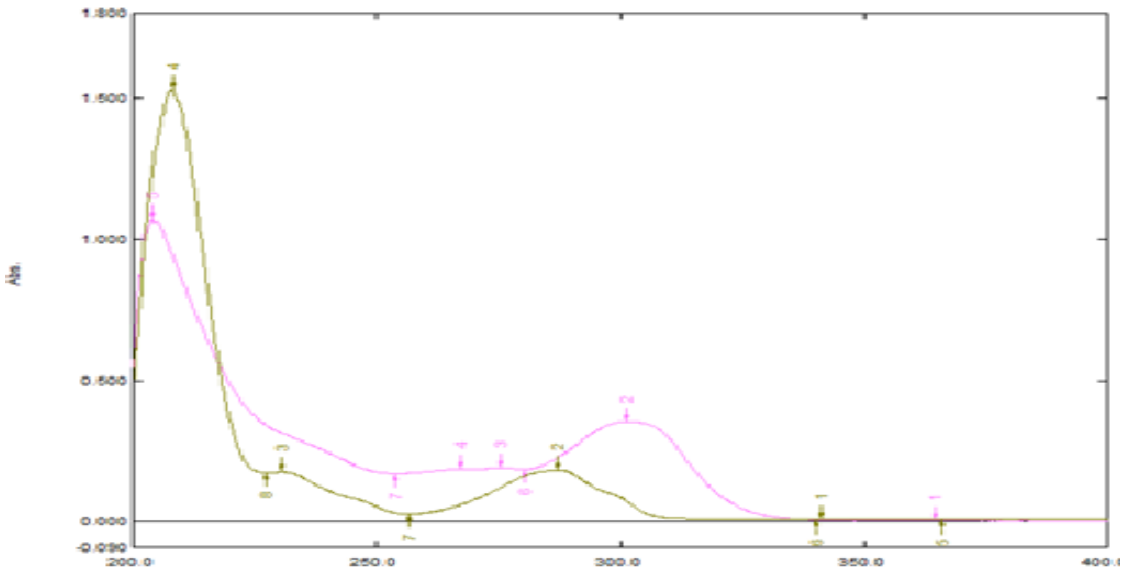

Fig.3: Overlain Normal Spectra Esomeprazole and Domperidone in methanol

The absorptivity values were determined at the two selected wavelengths. The concentration of two drugs in the sample was calculated using the following equation.

$C_{RST} = A_2ay_1-A_1ay_2/ax_2ay_1-ax_1ay_2$

$C_{EZE} = A_1ax_2-A_2ax_1/ax_2ay_1-ax_1ay_2$

Where C_{RST}, C_{EZE} are the concentrations of ESO and DOM in sample solutions. A_1, A_2 are the absorbances of sample at 302nm and 287nm respectively, ax_1, ax_2 are the absorptivity values of ESO at 302nm and 287nm, ay_1,

ay_2 are the absorptivity of DOM at 302nm and 287nm respectively.

Preparation of sample solutions:

Twenty Raciper D40 capsules each containing 40mg and 30 mg of Esomeprazole and Domperidone respectively were weighed, average weight was calculated and powdered. A quantity equivalent to 10 mg of ESO is weighed and 2.5 mg of DOM pure drug is added to it, transferred into 10 ml volumetric flask and it was dissolved in methanol. The volumetric flask was sonicated for about 15mins to affect the complete dissolution of the drugs and the solution was made up to the volume with methanol to obtain concentration of 1000µg/ml and filtered. This solution was further diluted with methanol to get a solution having concentration of 10µg/ml of both ESO and DOM. The absorbance was measured at 302nm and 287nm (Fig.4).

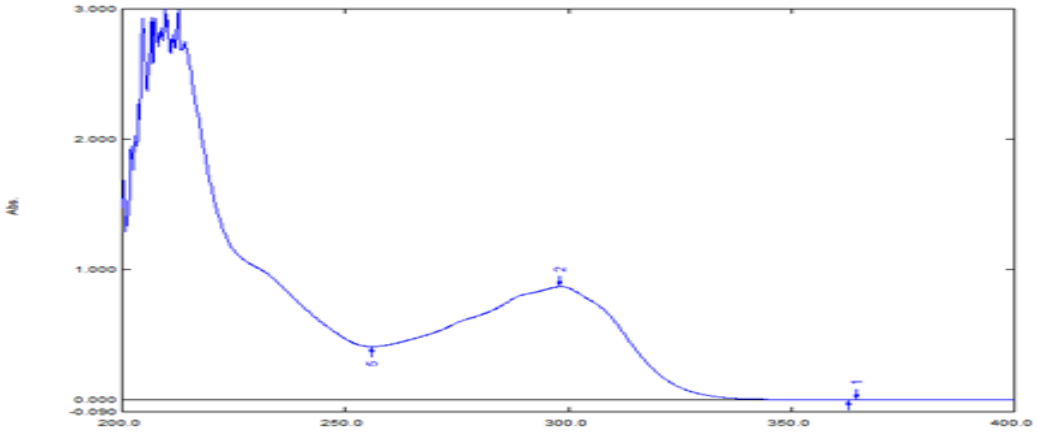

Fig.4: UV Spectra of Raciper D 40 in methanol (capsule solution)

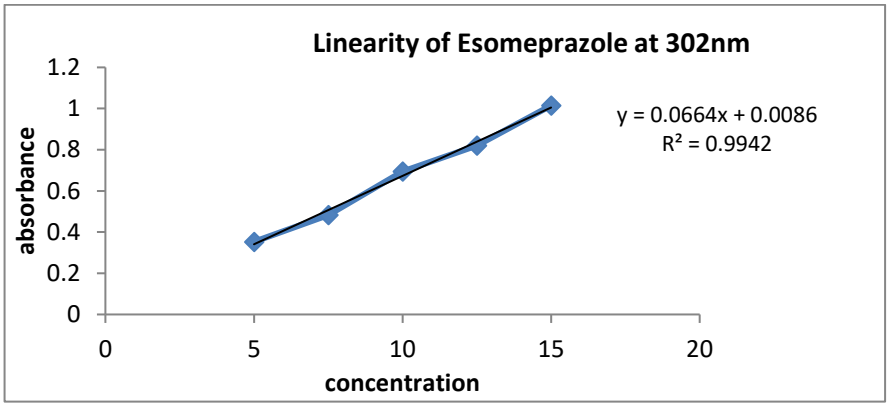

Fig. 5 Calibration graph of Rosuvastatin at 223 nm

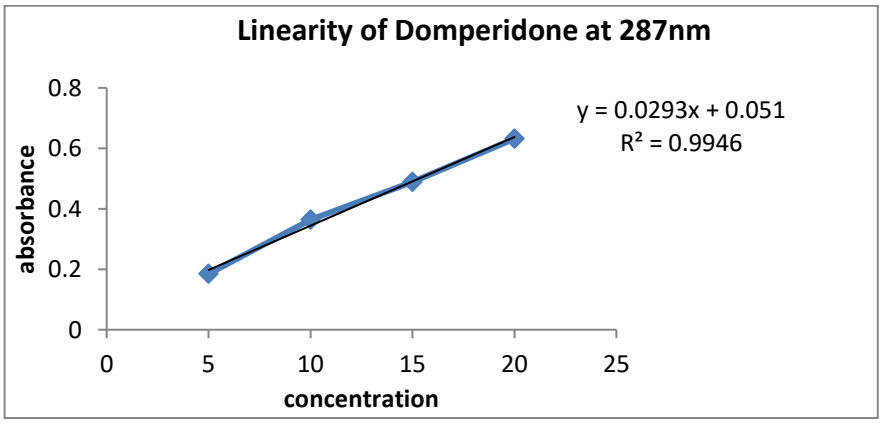

Fig. 6 Calibration graph of Rosuvastatin at 229 nm

Then the amount of drug present in the formulation was calculated by using simultaneous equation and the results are shown (Table-1).

Table 1: Analysis of marketed formulation

Drug	Amount labelled (mg)	Amount found (µg/ml)	% Assay
Rosuvastatin	40.0	40.48	101.2%
Ezetimibe	30.0	30.24	100.8%

Table 2: Linearity data of Rosuvastatin with methanol

S.No.	Concentration (µg/ml)	Absorbance at 302nm
1	5	0.353
2	7.5	0.483
3	10	0.694
4	12.5	0.820
5	15	1.015

Table 3: Linearity data of Ezetimibe with methanol

S.No.	Concentration (µg/ml)	Absorbance at 287nm
1	5	0.185
2	10	0.364
3	15	0.489
4	20	0.632

Table 4: Absorbance values of Precision at intraday

S.No.	Absorbance	
	At 302nm	At 287nm
1	0.402	0.403
2	0.433	0.442
3	0.408	0.418
4	0.443	0.453
5	0.435	0.446
6	0.439	0.451

Table 5: Absorbance values of Precision at interday

S.No.	Absorbance	
	At 302nm	At 287nm
1	0.402	0.403
2	0.410	0.413
3	0.421	0.423
4	0.431	0.438
5	0.433	0.440
6	0.433	0.442

Table 6: Intraday and interday precision

S.No.		Mean		Standard deviation		%RSD	
		302nm	287nm	223nm	229nm	223nm	229nm
1	Intraday	0.426	0.435	0.0172	0.0203	0.280	0.338
2	Interday	0.421	0.427	0.0131	0.0160	0.219	0.267

Table 7: Accuracy results for Rosuvastatin and Ezetimibe

S.No.	Amount of marketed formulation (µg/ml)	Amount of API mixture added (µg/ml)	Total amount of both the drugs (µg/ml)	Total amount of drug found (µg/ml)		% Recovery	
				ESO	DOM	ESO	DOM
1	5µg/ml	4µg/ml	9µg/ml	9.12	8.98	101.3	99.77
2	5µg/ml	5µg/ml	10µg/ml	10.08	10.12	100.80	101.20
3	5µg/ml	6µg/ml	11µg/ml	11.16	10.82	111.60	98.36

Table 8: Validation results for UV method (ESO and DOM)

S.No.	Parameters	Esomeprazole	Domperidone	Acceptance criteria
1	Linearity	R^2 = 0.994	R^2 = 0.994	Correlation coefficient (R^2 = 0.992-0.999)
2	Precision	Intraday: % RSD: 0.28 Interday: % RSD: 0.219	Intraday: % RSD: 0.338 Interday: % RSD: 0.267	%RSD = <2%
3	Accuracy	100%-102%	98%-102%	98%-102%
4	LOD	1.16 µg/ml	1.94 µg/ml	-
5	LOQ	3.52 µg/ml	5.88 µg/ml	-

RESULTS AND DISCUSSION:

Method Development:

The analytical method was developed using simultaneous equation method by taking 302nm and 287nm as λ_{max} of ESO and DOM respectively. For the capsule dosage form the %assay was found to be 101.2 for ESO and 100.8 for DOM.

Method Validation:

The analytical method was validated with respect to parameters such as linearity, precision, accuracy, limit of detection (LOD), limit of quantification (LOQ).

Linearity and range:

Linearity was established by least squares linear regression analysis of the calibration curve. For linearity a series of standard solutions of concentration 5-20 µg/ml were prepared by diluting appropriate volumes. ESO and DOM showed linearity range from 5-15 µg/ml and 5-20 µg/ml respectively (Table-2&3). Coeffcients of correlation were found to be 0.994 for both ESO and DOM (Fig.5&6).

Precision:

The precision of the analytical method was studied by multiple sampling of the homogenous sample. The precision was done at two levels (intraday and interday). Intraday precision was done by analyzing the intermediate concentration of each drug (ESO 10µg/ml and DOM 10µg/ml) for six times. Interday precision was measured over six consecutive days for the same drug concentrations. The %RSD values were calculated for each of them and the low RSD values indicate that the method is precise (Table-4,5&6). The results were found within 2% limit.

Accuracy:

Recovery studies were carried out by spiking the sample solution with standard solutions of ESO and DOM at a level of 80, 100 and 120%. At each level % recovery was determined three times (Table-7). The results were found within the limit (98-102%).

Sensitivity:

LOD and LOQ decide about the sensitivity of the method. LOD is the lowest detectable concentration of the analyte by the method while LOQ is the minimum quantifiable concentration. For these LOD and LOQ linearity values were taken and standard graphs were drawn. From the standard graphs standard deviations and slope were calculated, then LOD and LOQ values were calculated using the following formulas.

$LOD = 3.3\ S_a/b$

$LOQ = 10S_a/b$

S_a = Standard deviation

b= slope of calibration curve

CONCLUSION:

The elevation of obtained values suggests that the proposed UV spectrophotometric method provide simple, precise, accurate and economical quantitative analytical method for determination of ESO and DOM in capsule dosage form. After validating proposed method as per ICH guidelines and correlating the obtained values with the standard values, satisfactory results were obtained (Table-8). The sample recoveries in all formulations were in good agreement with their respective label claims and they suggested no interference of formulation excipients in the estimation. Hence, the method can be easily and conveniently adopted for routine estimation of ESO and DOM in capsule dosage form.

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