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Estimation of Domperidone and Esomeprazole by Area under Curve method

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ABSTRACT

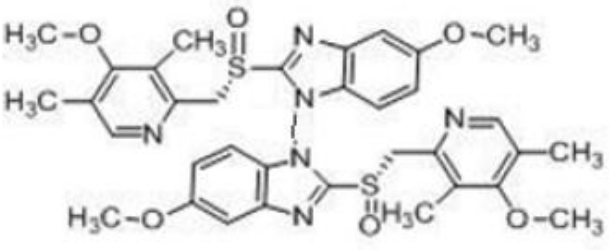
Esomeprazole is an ulcer healing drug that inhibits gastric acid by blocking the proton pumps of the gastric parietal cells. Esomeprazole is used for short term treatment of gastric and duodenal ulcer. It is also used in combination with antibacterial for the eradication of Helicobacter pylori. Domperidone is a D_2 – receptor antagonist used as an antiemetic. Chemically it is 5-chloro-1-[1-[3-(2,-3-dihydro-2-oxo-1H-benzimidazol-1-yl)-propyl]-4-piperidinyl]-1,3-dihydro-2Hbenzimidazol-2-one. The accurate and economic AUC method has been described for the simultaneous spectrophotometric estimation of Esomeprazole and Domperidone in tablet dosage form. Absorption maxima of Domperidone and Esomeprazole in methanol were found to be 286.0 nm and 301.0 nm respectively. Beer's law was obeyed in the concentration range 20-120 µg/ml for Esomeprazole and Domperidone. The analysis of binary pharmaceutical formulation was carried. The value of standard deviation was satisfactorily low and recovery was close to 100 % indicating the reproducibility and accuracy of the method.

1.1 INTRODUCTION

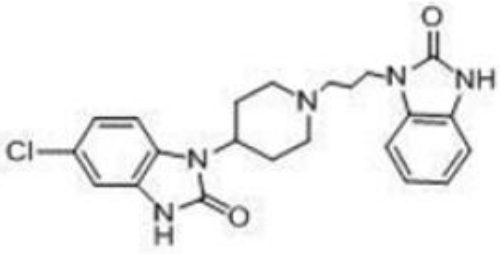
Esomeprazole is an ulcer-Healing drug that inhibits gastric acid by blocking the proton pump (Hydrogen potassium ATPase enzyme system) of the gastric parietal cells. Esomeprazole is used for short term treatment of Gastric and duodenal ulcer and in gastroesophageal reflux disease with severer symptoms. Esomeprazole is also used in combination with antibacterial for the eradication of Helicobacter pylori. Chemically it is 5-metoxy-2[(R)-[(4methoxy-3,5-dimethylpyridin-2-yl)methane]sulfinyl] -1H1,3-benzodiazole. Esomeprazole blocks the final step in acid production, thus reducing gastric acidity.

Domperidone acts as a gastrointestinal emptying adjunct and peristaltic stimulant. The gastroprokinetic properties of domperidone are related to its peripheral domperidone receptor blocking properties. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure. The antiemetic properties of domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for both D2 and D3 receptor, which are found in chemoreceptor trigger zone, located just outside the blood brain barrier, which among others- regulates nausea and vomiting. Chemically it is 5-chloro-1-{1-[3-(2-oxo-2,3-dihydro-1H1,3-benzodiazol-1yl)propyl]piperidin-4-yl}-2,3-dihydro 1H-1,3-enzodiazol-2-one.

Domperidone (Motilium™) is a drug that has, as a side effect, stimulating or increasing milk production, probably by increasing prolactin production by the pituitary gland. Prolactin is the hormone that stimulates the cells in the mother's breast to produce milk. Domperidone increases prolactin secretion indirectly, by interfering with the action of dopamine whose action is to decrease the secretion of prolactin by the pituitary gland. Domperidone is generally used for disorders of the gastrointestinal tract (gut) and has not been released in Canada for use as a stimulant for milk production.



Esomeprazole



Domperidone

1.2 MATERIALS AND METHODS

1.2.1. Instrument:

A Shimadzu UV-1700 UV/VIS Spectrophotometer was used with 1 cm matches quartz cell.

1.2.2. Materials:

Gift samples of Esomeprazole and Domperidone were procured from Emcure Pharmaceutical LTD, Pune. Tablets containing both drugs i.e. Esomeprazole and Domperidone were purchased from local pharmacy of commercial brand Torrent Nexpro.

1.2.3. Apparatus

Jasco model V-530 UV-Visible double beam spectrophotometer with single monochromator with spectra manager software, and Perkin Elmer UV-Visible double beam spectrophotometer with UV Winlab Software were used. Sartorius ADD-BL-02 balance was used. Calibrated glasswares were used for the study. Trans-o-sonic ultrasonicator, 0.45 µ filter papers (PVDF/Nylon filters) also used.

1.2.4. Selection of solvent

Methanol was selected as the solvent for dissolving Esomeprazole and Domperidone.

1.2.5. Preparations of drug stock solutions: Stock solution of Esomeprazole and Domperidone were prepared separately by dissolving 5 mg of Esomeprazole and 5 mg of Domperidone in 25 ml of Methanol. Then the volume was made up to the mark with methanol to give the drug stock solution of concentration 100 µg/mL.

1.2.6. Preparations of working standard solutions: From the stock solution of Domperidone appropriate volumes were pipetted out and transferred to 10 ml volumetric flasks. The volume was made up to the mark with methanol to give the samples of desired concentrations like 4, 8, 12 up to 32 µg/mL.

1.2.7. Determination of λmax

Both the standard solutions were scanned separately between 400 nm to 200nm. The overlain spectrum of both drugs was recorded, Fig. 3; from the overlain spectrum, two wavelengths 301 nm (λmax of Esomeprazole) and 286 nm (λmax of Domperidone) were selected for estimation of drugs.

1.2.8. Selection of analytical wavelength range (Area under the curve) for analysis: Suitable concentrations of solutions were prepared accurately to determine the range of Domperidone for analysis. The standard solutions were scanned in the spectrum mode of the instrument from 400 nm to 200 nm. The absorbance maxima of these solutions were obtained at wavelength 286 nm. The area under the curve between 276 nm to 290 nm was selected (Fig3.) for domperidone and 292 nm -310 nm was selected for Esomeprazole because the linearity was obtained within these areas with good reproducibility of results.

1.3 Application of proposed method for estimation of DOM and ESO in tablet dosage forms

20 tablets were weighed and powdered, quantity of sample powder containing equivalent to 30 mg of DOM and40 mg of ESO was transferred to 100 ml volumetric flask. Sufficient quantity of Methanol was added, and sonicated for 15 minutes and diluted upto mark with methanol. The solution was filtered through 0.45µ membrane filter paper. A 1 ml of filtrate was further diluted to 10 ml with Distilled water to get final concentration of about 10 µg/ml DOM and 10µg/ml ESO. The absorbance of resulting solutions was calculated by measuring area under curve in the range of 276.0-290.0 nm (for DOM) and 292.0-310.0 nm (for ESOMG) (Table no.5 & 6).

1.4 Method validation:

1.4.1 Accuracy

It was done by recovery study. Sample solutions were prepared by spiking at about 80 %, 100 % and 120 % of specification limit to Placebo and analyzed by the proposed method. % Recovery was determined using the formula. Results are shown in Table 1 & 2.

1.4.2. Precision

Precision study was carried out for the repeatability of sample measurement and the result was expressed as % RSD. Variability of the method was studied by analyzing aliquots of standard solutions of (20, 40, 60, 80, 100, 120 µg /ml) each of Domperidone and Esomeprazole, on the same day (intra-day precision) and on different days (inter-day precision), and the results were expressed as % RSD (Table 3& 4).

1.4.3. Linearity and Range

The six-point calibration curves that were constructed were linear over the selected concentration range for both DOM and ESOMG ranging between 20-120 µg /mL. Each concentration was repeated 3 times. The assay was performed according to the experimental conditions previously described.

1.5. RESULTS AND DISCUSSION

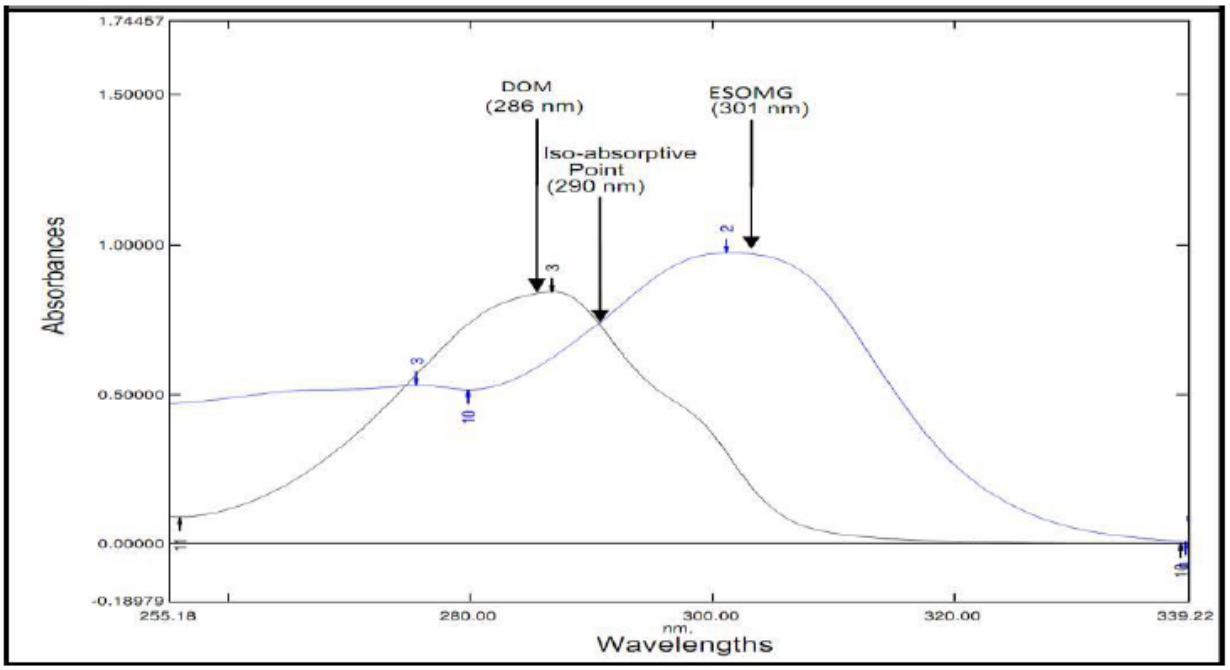


Fig 2: Overlain Spectra of DOM and ESOMG

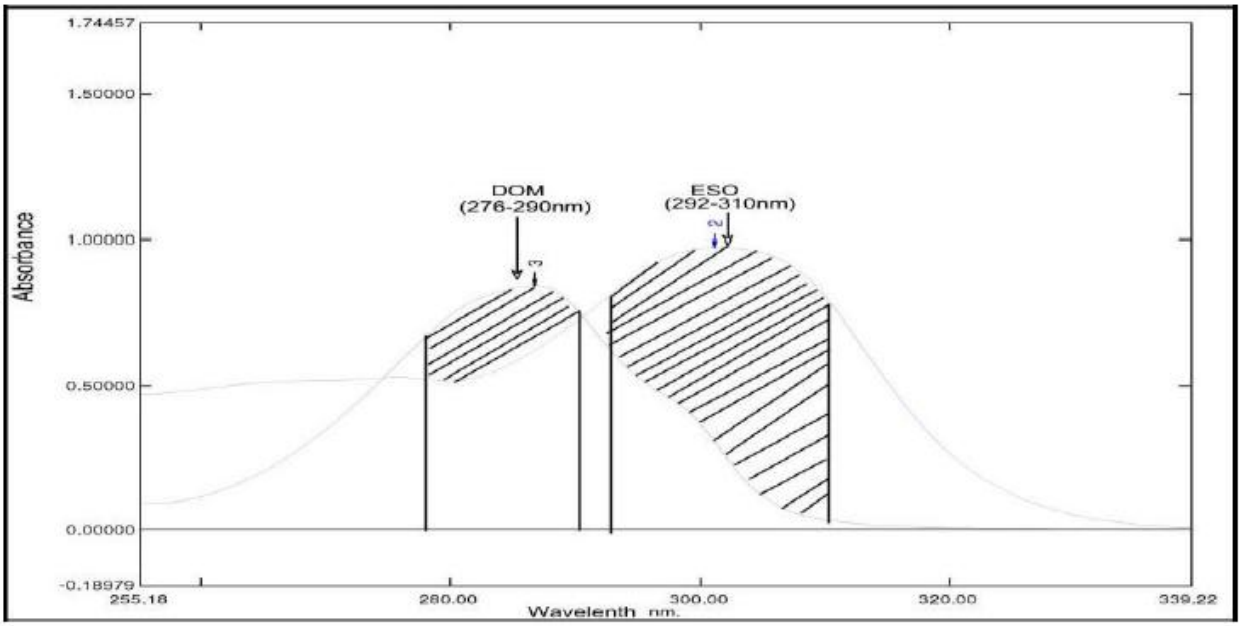


Fig. 3: Overlain of DOM and ESOMG Showing Area Under Curve

Table no. 1: Standard addition technique for determination of Domperidone and Esomeprazole using Area under curve method

Tablet Sample	Level of Recovery (%)	Amount present (mg/tab)	Amount of Std. added (mg)	Total amount recovered (mg)	% Recovery
TORRENT NEXPRO	80	10	8	17.94	99.75
		10	8	17.98	99.91
		10	8	17.97	99.87
	100	10	10	19.99	99.95
		10	10	19.84	99.21
		10	10	19.89	99.45
	120	10	12	21.82	99.22
		10	12	22.00	100
		10	12	21.94	99.75

Table no.2: Statistical data for recovery studies

Sr.No.	Tablet Sample	Type of Recovery (%)	%Mean*	S.D.	C.O.V.	S.E.
1	Torrent Nexpro	80	99.84	0.083	0.083	0.048
2		100	99.45	0.377	0.379	0.218
3		120	99.65	0.398	0.399	0.230

Precision:

The result of repeatability and intermediate precision experiments are shown. The developed method was found to be precise for repeatability and intermediate precision studies.

Table no. 3: Precision studies of Esomeprazole and Domperidone by Area under curve method

Drug	Conc µg/ml	Intraday found conc±SD	RSD (%)	Intraday found conc±SD	RSD(%)
Domperidone	40	39.87±0.082	0.438	39.89±0.098	0.299
	60	59.86±0.016	0.027	59.82±0.024	0.190
	80	79.91±0.029	0.036	80.01±0.028	0.082
Esomeprazole	40	39.89±0.043	0.108	39.99±0.045	0.245
	60	60.07±0.045	0.075	60.04±0.049	0.082
	80	80.07±0.025	0.031	80.04±0.029	0.036

Table no. 4: Statistical data for precision studies

Sr.No.	Component	Mean *	S.D.*	C.O.V.*	S.E.
1	Intra-Day	99.93	0.01000	0.010007	0.005774
2	Inter-Day	99.90	0.04000	0.04004	0.02309

Where *n = 3

Table no. 5: Analysis of Marketed formulations

Sr.No.	Tablet Sample	Label claim (mg/tab)	Label claim found (mg/tab)	% drug found
1	TORRENT NEXPRO	30	29.99	99.9
2		30	29.91	99.7
3		30	29.98	99.9
4		30	29.88	99.6
5		30	29.85	99.5
6		30	29.96	99.8

Torrent Nexpro is brand of tablet formulation

Table no. 6: Statistical data for analysis of marketed formulation

Sr.No.	Tablet	% mean *	S.D.*	C.O.V.*	S.E.*
1	Torrent Nexpro	99.73	0.1633	0.1636	0.0667

CONCLUSION

Area under curve method was developed and validated as per ICH guidelines for estimation of Domperidone and Esomeprazole. This method was applied for estimation of these compounds in the marketed formulation. The method has been evaluated for the linearity, accuracy, precision and Robustness in order to ascertain the suitability of the method. It has been proved that the developed method was linear in the concentration range of 20-120 µg/ml.

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