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Spectrophotometric Methods for Simultaneous Estimation of Esomeprazole Magnesium and Domperidone from Pharmaceutical Dosage Form

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Three simple, accurate, economical and reproducible UV spectrophotometric methods for simultaneous estimation of two components drug mixture of domperidone and esomeprazole magnesium from combined capsule dosage form have been developed. First developed method involves formation and solving of simultaneous equations at 285.6 and 301.2 nm. Second method was developed making use of first order derivative spectroscopy using 300.8 and 311.2 nm as zero crossing points for estimation of domperidone and esomeprazole magnesium, respectively. Third method is based on two wavelength calculation, wavelengths selected for estimation of domperidone were 284.4 and 313.2 nm and for esomeprazole magnesium 275.2 and 293.2 nm. The results of analysis have been validated statistically and by recovery studies.

Key Words: Domperidone, Esomeprazole magnesium, Spectrophotometric, Simultaneous estimation.

INTRODUCTION

Domperidone, chemically 5 chloro-1-[1-[3-(2,3-dihydro-2-oxo-1H-benzimidazole -1-yl) propyl]-4-piperidinyl]-1,3 dihydro 2H- benzimidazole-2-one is an antiemetic agent[1]. Literature survey reveals that for domperidone, spectrophotometric[3-7] and HPLC[8], methods have been reported. Esomeprazole magnesium, chemically S-*bis*(5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl]sulfinyl]-1H benzimidazole-1-yl) magnesium is an proton pump inhibitor[2]. One LC[9], one HPLC[10] and one spectrophotometric[3] methods have been reported in literature for estimation of esomeprazole magnesium. However no spectrophotometric method is yet reported for simultaneous analysis of two drugs from combined pharmaceutical dosage form.

EXPERIMENTAL

A systronics UV/Visible spectrophotometer (model 2101) with 1 cm matched quartz cells was used for spectrophotometric analysis. Spectra's were recorded using specific program of instrument, having specifications as, spectral band width 2 nm, wavelength accuracy ± 0.5 nm, wavelength readability 0.1 nm increment. The capsule samples of combined dosage form of domperidone and esomeprazole magnesium [Sompraz-D (Mankind Laboratories), were procured from the local market.

Method-I: Employing simultaneous equations

Pure drug sample of domperidone and esomeprazole magnesium were dissolved separately in methanol so as to give six dilutions of standard in concentration range of 5-50 µg/mL of domperidone and 5-35 µg/mL of esomeprazole magnesium. All solutions were scanned in wavelength range of 220 and 380 nm. Two wavelengths selected for formation and solving of simultaneous equations were 285.6 and 301.2 nm. Absorptivity coefficients of both the drugs were determined at selected wavelengths. Absorptivity coefficient for domperidone at 285.6 and 301.2 nm were 301.81 and 90.45 $cm^{-1}g^{-1}$ L, respectively while respective values for esomeprazole magnesium were 284.14 and 452.18 cm^{-1} g^{-1} L. Set of two simultaneous equations thus formed are

$$A_1 = 301.81C_1 + 284.14C_2 \quad (1)$$

$$A_2 = 90.45C_1 + 452.18C_2 \quad (2)$$

where A_1 and A_2 are absorbance of sample solution at 285.6 and 301.2 nm, respectively. C_1 and C_2 are concentration of domperidone and esomeprazole magnesium, respectively in sample solution in g/L.

Validity of above formed equations was checked by preparing five mixed standards using pure drug sample of two drugs, results of which are reported in Table-1.

TABLE-1
RESULTS OF VALIDATION STUDIES FOR METHOD I, II AND III USING MIXED STANDARDS

Sample no.	Conc. present (mcg/mL)		Conc. Found (%)					
			Method I		Method II		Method III	
	DOM	ESO	DOM	ESO	DOM	ESO	DOM	ESO
01	15	35	99.67	98.16	99.70	99.45	99.82	99.12
02	20	30	98.25	98.84	99.13	98.50	98.29	98.48
03	25	25	99.20	98.25	100.55	100.36	98.96	98.72
04	30	20	98.66	98.27	100.56	99.35	100.20	100.45
05	35	15	98.31	98.50	100.30	100.40	99.02	98.75

Analysis of commercial formulation: For analysis of formulation contents of 20 capsules were accurately weighed and average weight of powder per capsule was determined. The contents were powdered and powder equivalent to 100 mg of esomeprazole magnesium was accurately weighed and extracted four times with 20 mL portions of methanol and filtered through Whatmann filter paper No.41 into 100 mL volumetric flask. The filter paper was washed with methanol adding washings to the filtrate and volume was made up to the mark with the same. From above filterate 5 mL was diluted to 50 mL and finally 2 mL was further diluted up to 10 mL. Absorbance of this final diluted solution was measured at 285.6 and 301.2 nm, respectively and concentration of two drugs in the sample were calculated using above formed simultaneous eqns. 1 and 2. Results of analysis of capsule formulation are reported in Table-2.

TABLE-2
RESULTS OF ANALYSIS OF COMMERCIAL FORMULATION

Method	Batch	Label claim (mg/tablet)		Label claim estimated* (%)		Standard deviation		Recovery** (%)	
		ESO	DOM	ESO	DOM	ESO	DOM	ESO	DOM
Method I	A	40	30	98.25	98.73	0.541	0.557	99.93	100.33
	B	40	30	98.70	99.12	0.613	0.419	99.51	100.45
	C	40	30	99.48	99.51	0.467	0.253	100.58	99.01
Method II	A	40	30	100.32	100.65	0.708	0.413	99.17	99.70
	B	40	30	100.44	101.54	0.624	0.614	99.84	100.28
	C	40	30	101.12	99.66	0.651	0.381	100.25	99.76
Method III	A	40	30	99.60	100.02	0.217	0.364	99.76	101.12
	B	40	30	98.95	99.60	0.714	0.219	100.75	100.27
	C	40	30	99.56	100.17	0.569	0.527	99.73	100.14

*Average of five determinations.
** Average of determinations at three different concentration levels.

Method-II: Employing first order derivative spectroscopy

From first derivative spectra of domperidone and esomeprazole magnesium in methanol, zero crossing points 300.8 and 311.2 nm were selected for simultaneous estimation of two drugs. Accurately weighed pure drug sample of domperidone and esomeprazole magnesium were dissolved in methanol so as to give six dilutions in range of 5-50 μg/mL of domperidone and 5-35 μg/mL of esomeprazole magnesium. The absorbance of these solutions was recorded in first derivative mode at 300.8 nm for estimation of domperidone and 311.2 nm for estimation of esomeprazole magnesium and respective calibration curves were prepared.

Validity of proposed method was checked by preparing five mixed standards using pure drug sample of two drugs and absorbance was measured at respective selected zero crossing points and determined concentration of two drugs using respective calibration curve. Results of validation studies are reported in Table-1. Capsule sample solution was prepared in similar manner as for method I, absorbance of final dilution of sample was recorded at 300.8 and 311.2 nm from first derivative spectra of sample and amount of two drugs were calculated using respective calibration curve. Results of analysis are reported in Table-2.

Methods-III: Using two wavelength calculation

From absorption spectra of domperidone and esomeprazole magnesium, set of two wavelengths λ_1 (284.4 nm) and λ_2 (313.2 nm) for estimation of domperidone and λ_3 (275.2 nm) and λ_4 (293.2 nm) for estimation of esomeprazole magnesium were selected on basis of principle that absorbance difference between two points on a mixture spectra is directly proportional to concentration of component of interest and independent of interfering component. Five mixed standard containing different concentration of pure drug sample of two drugs were prepared in methanol. All standards were scanned at respective set of selected wavelengths. Absorbance difference was measured and respective calibration curve was plotted. Results of validation studies are reported in Table-1. Capsule sample solution was prepared in similar manner as for method I, final dilution was analyzed by scanning at respective set of wavelength and absorbance difference values were noted, the concentration of domperidone and esomeprazole magnesium was calculated from the respective calibration curve. Result of analysis is reported in Table-2.

Recovery studies: To study the accuracy, reproducibility and precision of the above developed methods recovery studies were carried out by addition of standard drug solution to pre-analyzed sample at three different concentration levels. Results of recovery studies were found to be satisfactory and are reported in Table-2.

RESULTS AND DISCUSSION

Three spectrophotometric methods have been developed for simultaneous estimation of domperidone and esomeprazole magnesium from combined capsule dosage form. The first developed method involving formation and solving of simultaneous equations is very simple and requires only the accurately determined absorptivity of the two drugs at two selected wavelengths. The method just requires recording of absorbance and few calculations that can be manually done, thus method can be used with any model of spectrophotometer. Once the equations are framed the method is very fast. Framed equations were validated using laboratory prepared mixed standards of two drugs which gave satisfactory results.

Second developed method for simultaneous analysis of domperidone and esomeprazole magnesium from combined dosage form make use of first derivative ultraviolet spectrophotometry based on principle that at zero crossing point of one component the other component have substantial absorbance.

Third developed method for simultaneous analysis of domperidone and esomeprazole magnesium make use of two wavelength calculation so as to remove interference between two components. Proper selection of two wavelengths for estimation of a component is critical.

The results of analysis of two drugs from capsule formulation using all the three developed methods were found close to 100 % for both domperidone and esomeprazole magnesium, standard deviation was satisfactorily low indicating accuracy and reproducibility of the methods. Recovery studies were satisfactory which shows that there is no interference of excipients. The developed methods were found to be simple, rapid, accurate and can be used for routine analysis of two drugs from capsule formulations.

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