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Simultaneous estimation of esomeprazole and levosulpiride in solid dosage form

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ABSTRACT

A simple, precise and highly selective analytical method was developed for simultaneous estimation of Esomeprazole 40 mg and Levosulpiride SR 75 mg in capsules dosage form. Estimation was carried out by multi-component mode of analysis at selected wavelength of 277 nm and 283 nm for Levosulpiride and Esomeprazole respectively in methanol. The method was found to be linear in the range of 1-40 µg/ml for Levosulpiride and 1-30 µg/ml for Esomeprazole while accuracy of the method was confirmed by recovery studies of solid dosages forms and was found to be for batch-A 98.33% and 98.44% for Batch-B 99.24% and 98.77% for Levosulpiride and Esomeprazole respectively. Initially lab samples were utilized to validate developed method according to ICH guidelines followed by determination of % concentration of Levosulpiride and Esomeprazole in marketed formulation that was found to be for Batch-A 98.07 ±0.51 and 96.81± 0.51 for Batch-B 98.23 ±0.65 and 9 7.98± 0.65 respectively. The values of precision and robustness lie within acceptable limit. Thus the proposed method can be successfully applied for simultaneous determination of Levosulpiride and Esomeprazole respectively in routine analytical work.

Key words: Levosulpiride, Esomeprazole, λ_{max}, spectrophotometric method.

INTRODUCTION

Levosulpiride is a *N*-[[(2*S*)-1-Ethylpyrrolidin-2-yl]methyl]-2-methoxy-5-sulfamoylbenzamide; it is a new orally effective anti-psychotic and a prokinetic agent reported to be a selective antagonist of dopamine D_2 receptors activity on both central and peripheral levels. It is an atypical neuroleptic (*S*)-enantiomer of sulpiride having molecular formula $C_{15}H_{23}N_3O_4S$ with molar mass 341.43 g/mol. Levosulpiride is also claimed to have mood elevating property and used in the treatment of psychoses[1], particularly negative symptoms of schizophrenia, anxiety disorders, dysthymia, vertigo, dyspepsia, irritable bowel syndrome and premature ejaculation[2].

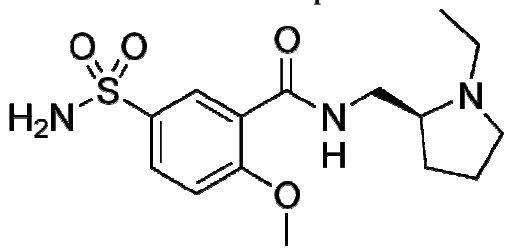
Esomeprazole is an *S*-enantiomer of omeprazole that inhibits gastric acid secretion. Chemically Esomeprazole is a (*S*)-5-methoxy-2- [(4-methoxy-3,5-dimethyl pyridin-2-yl) methyl sulfinyl]-3*H*-benzoimidazole [3]. Esomeprazole is a white to slightly yellowish-white solid having empirical formula of $C_{17}H_{19}N_3O_3S$ and a molecular weight of

345.41. It is cost effective in the treatment of gastric esophageal reflux diseases [4-5].

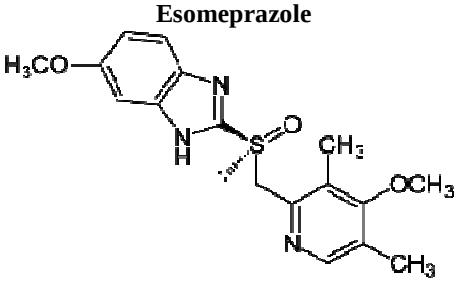
Several method were reported for the simultaneous estimation of Esomeprazole or its derivatives with combination of several drugs by using UV-spectrophotometry[6-7], derivative spectrophotometer, assay using HPTLC [8] while few methods were available for Levosulpiride estimation by UV-spectroscopy[9], using RP-HPLC [10]in plasma.

A comprehensive literature research reveals the lack of a spectrophotometric analytical method for simultaneous estimation of Levosulpiride and Esomeprazole in pharmaceutical formulations. A successful attempt was made to develop accurate, precise and sensitive developed method is simple, rapid, selective, less expensive and less time consuming. The purpose of present study was to develop and validate spectrophotometric analytical methods for simultaneous estimation of Levosulpiride and Esomeprazole in their combined solid dosage form.

Levosulpiride



Esomeprazole



MATERIALS AND METHODS

The present work was carried out on double beam UV – 1700 spectrophotometer (Shimadzu, Japan) of 1 cm quartz cell having spectral band width of 0.1 nm to development analytical method over the range of 230-400 nm. Standard gift sample of Levosulpiride and Esomeprazole was provided from FDC Ltd (India) and Unichem Lab. Ltd (India).

Marketed formulation Sompraz-L containing Levosulpiride SR 75 mg and Esomeprazole 40 mg was used as sample; purchased from local pharmacy Indore. Calibrated glassware's were used throughout the work.

Standard stock and sub stock solution

Analysis was done by using standard stock solution of 1000 µg/ml of each Levosulpiride and Esomeprazole by dissolving 10 mg of standard Levosulpiride and 10 mg of standard Esomeprazole separately in 10 ml methanol with vigorous shaking. Aliquot in the range of 1-40 µg/ml (Levosulpiride) and 1-30 µg/ml (Esomeprazole) were prepared using this stock solution, for the preparation of calibration curve.

Procedure

Spectral characteristics of Levosulpiride and Esomeprazole

Aliquots of sub stock solution equivalent to 100 µg/ml of Levosulpiride and Esomeprazole were transferred separately into 10 ml volumetric flask and the volume was made with methanol. The absorption spectra of both the drugs were recorded from 230-400 nm.

Wavelength selection

For estimation of both the drugs, the wavelength maxima of Levosulpiride and Esomeprazole were determined and found to be 277 nm (λ_1) and 283 nm (λ_2) respectively where there was no interference among the drugs. Calibration curve was plotted between absorbance and its nominal concentration in the range of 0-40 µg/ml for Levosulpiride and 0-30 µg/ml for Esomeprazole at their respective maxima. Calibration curve equation was utilized by multi-component mode to calculate the concentration of laboratory samples.

Linearity and molar Absorptivity

The linearity of UV-Spectrophotometric method was established for Levosulpiride and Esomeprazole with absorbance in the range of 1-40 µg/ml and 1-30 µg/ml at their respective λ_{max}, which were validated by least square method. Coefficient of correlation was found to be 0.995 for Levosulpiride and 0.994 for Esomeprazole.

Preparation of mix standards

Four mixed standards containing Levosulpiride (100 µg/ml) and Esomeprazole (10 µg/ml) were prepared within linearity range and scanned over the wavelength range of 400-230 nm at slow scan speed and spectra was recorded as shown in Fig.-1.

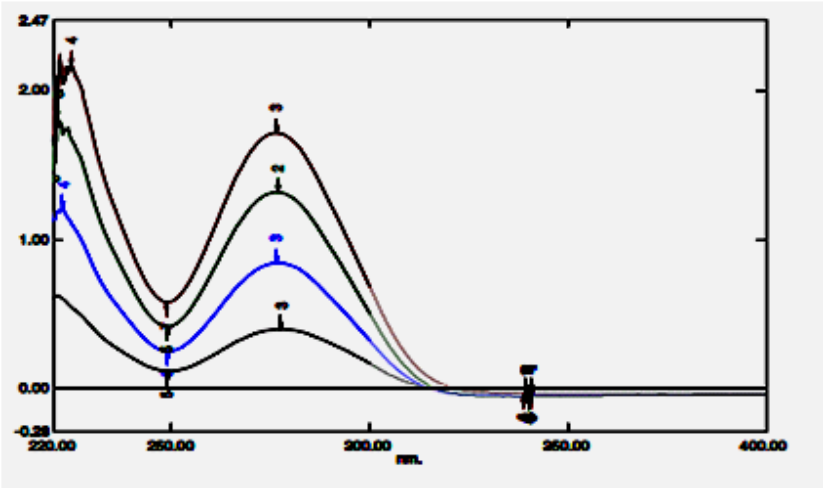


Fig.-1:- Overlain spectra in multi-component mode

All mixed standards were scanned in multi-component mode between 400 to 220 nm using methanol as blank at medium speed and the concentration of mixed standard was evaluated as shown in Table-1 at their respective λ_{max}.

Table-1:- Concentration of Levosulpiride and Esomeprazole in Mixed Standard.

Standard No.	1	2	3	4	5
Levosulpiride	7.5	15	22.5	30	37.5
Esomeprazole	4	8	12	16	20

Validation of proposed method using laboratory samples:

The developed analytical method was validated according to ICH guidelines using different concentration of mixed standard as shown in Table-2 and accuracy was determined by recovery studies.

Table -2:- Analysis Data of Laboratory Mixed Standards

S. No.	Expected concentration (mcg/ml)		Concentration found (mcg/ml)		Percentage found (%)	
	LSP	EPZ	LSP	EPZ	LSP	EPZ
1	7.5	4	7.35	3.92	97.94	97.95
2	15	8	15.09	8.13	100.61	101.60
3	22.5	12	22.10	11.78	98.20	98.20
4	30	16	29.49	15.73	98.31	98.33
5	37.5	20	37.17	19.98	99.12	99.92

Analysis of commercial formulation:

Twenty capsules were accurately weighed and its contents crushed to fine powder. Powder equivalent to 10 mg of Levosulpiride and 5.33 mg of Esomeprazole was weighed and dissolved in methanol, sonicated for 10 min and filtered through Whatman's filter paper no.41. After rejecting first few ml, different concentrations of Capsule sample were prepared by serial dilution technique and scanned over the range of 400-220 nm in multi-component mode and analyzed at 277 and 283 nm wavelength.

Recovery studies:

Accuracy of analytical method was evaluated by fortifying capsule samples through recovery studies which was

carried out by spiking the preanalysed sample of capsule with different known concentration of standard Levosulpiride and Esomeprazole and concentration of resulting solution was determined through multi-component mode of analysis. Precision for assay was determined by repeatability, interday, intraday precision for both drugs (each in three replicate).

RESULTS AND DISCUSSION

The analytical method was developed in Multi-component mode of analysis and validated according to ICH guidelines for determination of Levosulpiride and Esomeprazole in their combined capsule dosage form at selected wavelength 277 nm (λ_1) and 283 nm (λ_2) respectively where there was no interference among the drugs as shown in overlain spectra (Fig. 2).

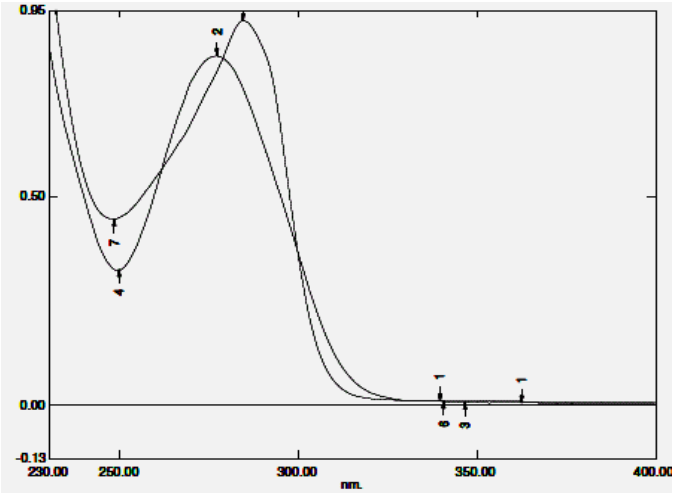


Fig.2:- Overlain spectra of Levosulpiride and Esomeprazole

Linearity

Developed analytical method shows linearity response over the range of 1-40 µg/ml for Levosulpiride and 1-30 µg/ml for Esomeprazole at their selected wavelength.

Table-3:- The Linearity of Levosulpiride and Rabeprazole Sodium

Drugs	Linearity
Levosulpiride	1-40
Esomeprazole	1-30

LOD and LOQ of Levosulpiride were found to be 0.044 µg/ml and 0.132 µg/ml respectively whereas for EsomeprazoleLOD and LOQ were found to be 0.046 µg/ml and 0.139 µg/ml. Statistical Data of Linearity and coefficient of correlation was shown in Table-4.

Table-4:- Statistical Data of Linearity of Levosulpiride and Rabeprazole Sodium

Analytes	Regression parameters		Coefficient of correlation	LOD (µg/ml)	LOQ (µg/ml)
	Slope	Intercept			
LSP	0.039	0	0.995	0.044	0.132
RBZ	0.037	0	0.994	0.046	0.139

Assay

The analytical method was validated by scanning the laboratory samples and the percent composition of drugs in laboratory mixture was determined with ±S.D and was found to be 99.30 ± 0.47 and 98.07 ±0.27 for Levosulpiride and Esomeprazole respectively. The percent composition of drug in marketed formulation (Sompraz-L) was also determined with ±S.D and found to be for Batch-A 98.07 ±0.51 and 96.81± 0.51 for Batch-B 98.23 ±0.65 and

97.98± 0.65 respectively. The values of precision and robustness lie within acceptable limit.

Table-5:- Concentration of Levosulpiride (LSP) and Esomeprazole (EPZ) Found in Marketed Formulation Sompraz-L

Formulation	S. No.	Label Claim (mg/Cap)		Concentration found (mg/Cap)		Percentage found	
		LSP	EPZ	LSP	EPZ	LSP	EPZ
Batch A (10:1)	1	75	40	73.92	38.92	98.56	97.30
	2	75	40	73.16	38.52	97.54	96.29
	3	75	40	73.58	38.74	98.11	96.85
Batch B(10:1)	1	75	40	73.91	39.32	98.55	98.30
	2	75	40	73.11	38.89	97.48	97.23
	3	75	20	74.00	19.68	98.66	98.41

Recovery studies

The accuracy of the proposed method was evaluated by percentage recovery (by standard addition method) of two drugs. The average recovery of marketed formulation was found to be for batch-A 98.33% and 98.44% for Batch-B 99.24% and 98.77% for Levosulpiride and Esomeprazole respectively as shown in Table-6 & 7.

Table -6:- Recovery studies data for Levosulpiride (LSP) and Esomeprazole (EPZ) in marketed formulation

Formulation	% Drug added	Expected concentration (mcg/ml)		Concentration found (mcg/ml)		Percentage found %	
		LSP	EPZ	LSP	EPZ	LSP	EPZ
Batch-A	80%	18 (10+8)	1.8 (1+0.8)	17.926	1.775	99.58	98.66
	100%	20 (10+10)	2 (1+1)	19.741	1.955	98.70	97.78
	120%	22 (10+12)	2.2 (1+1.2)	21.942	2.173	99.71	98.78
Batch-B	80%	18 (10+8)	1.8 (1+0.8)	17.732	1.764	98.51	98.05
	100%	20 (10+10)	2 (1+1)	19.916	1.982	99.58	99.11
	120%	22 (10+12)	2.2 (1+1.2)	21.922	2.181	99.64	99.16

Table -7:- Result of Statistical Analysis

Statistical Parameters	Lab. Mixed Standard		Recovery Studies	
	LSP	EPZ	LSP	EPZ
Mean	99.30	98.07	99.33	98.40
Standard Deviation	0.470	0.558	0.549	0.546
Standard error	0.271	0.322	0.317	0.315

CONCLUSION

The developed spectrophotometric method is simple, accurate, precise and reliable for the simultaneous estimation of Levosulpiride and Esomeprazole in combined dosage form. The relative std. deviation (RSD) for all parameters was found to be less than one, which indicates the validity of method and assay results are also within the limit so the proposed method can be used for routine quantitative simultaneous estimation of both the drugs in multi-component pharmaceutical preparation.

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