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NOVEL, SENSITIVE AND VALIDATED UV- SPECTROPHOTOMETRIC METHOD FORTHE ESTIMATION OF DEXLANSOPRAZOLE IN PURE AND FORMULATION

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ABSTRACT

Dexlansoprazole is a class of proton pump inhibitors it is a medication used to treat moderate to severe gastroesophageal reflux. A specific and economic UV spectrophotometric method has been developed using methanol. To determine the dexlansoprazole content in bulk and pharmaceutical dosage formulations at a predetermined λmax of 247nm, it was proved. Beer limits in the range of 10-100 µg/mL and exhibited good correlation coefficient (R^2 = 0.999) and the regression equation was found to be (y=0.018x+0.028). This method was successfully applied in the determination of Dexlansoprazole content in a marketed brand from the local market and the results were in good agreement with the label claim. The method was validated according to ICH guidelines for linearity, Accuracy, Precision, Robustness, and Ruggedness the obtained results proved that the method can be employed for the routine analysis of Dexlansoprazole in bulks as well as formulation.

INTRODUCTION

Dexlansoprazole chemically is (R)-(+) 2-([3-methyl-4-(2,2,2-trifluoromethoxy)pyridin-2yl] methylsulfonyl)-1H-benzimidazole (Fig. 1). It is a proton pump inhibitor[1] by healing of Erosive Esophagitis and symptomatic Non-Erosive Gastroesophageal Reflux Disease[2]. Dexlansoprazole is the R-enantiomer of lansoprazole (a racemic mixture of the R- and S- enantiomers). It is a white powder having molecular formulae C16H14F3N3O2S and a molecular weight of 369.363. It is freely soluble in methanol. The mechanism action of dexlansoprazole is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the (H+, K+)-ATPase in the gastric parietal cell. By acting specificity on the proton pump, Dexlansoprazole blocks in the final step of acid production. A detailed literature survey for Dexlansoprazole revealed That few HPLC and LC-MS[3-6] methods have been reported for the quantification of Dexlansoprazole. No author reported the UV Spectrophotometric method for the determination of Dexlansoprazole in pharmaceutical formulations. Hence an attempt was made to develop a simple, precise, accurate, and validated spectrophotometric method for the determination of Dexlansoprazole in Bulk and Capsules. Dexlansoprazole was approved by US-FDA in 2010 with a brand name DELTONE[7]. The developed method was validated as per ICH Guidelines [8-9].

MATERIALS AND METHODS

Instruments and materials: A gift sample of Dexlansoprazole with purity of 101.52% w/w was obtained by Dr. Reddy's laboratory,

Visakhapatnam. LAB INDIA (T60) double beam UV / Visible Spectrophotometer and ELITE analytical balance were the instruments used. Chemicals and reagents used are of analytical grade. Dexlansoprazole of 60mg with a brand name Deltone® was purchased from the local market.

Preparation of standard stock solution: A standard drug solution of Dexlansoprazole was prepared by adding 100mg of the drug into a 100mL volumetric flask and made up to mark with methanol to get a concentration of 1000µg/mL.

Preparation of working standard solution: From the above standard stock solution, 10mL of the sample was transferred to a 100 mL volumetric flask and made up to mark with methanol to get a concentration of 100µg/mL. It was then scanned by a UV Spectrophotometer in the range of 200-400nm using methanol as a blank. The absorbance was found to be maximum at 247 nm.

Construction of calibration curve: Aliquots ranging from10-100 µg/mL solutions were prepared by using methanol as solvent. The samples were then analyzed at a λmax of 247nm to get respective absorbance. The values [Table 1] are then plotted to get a calibration curve.

Preparation of the assay solution: The proposed method was applied to analyze the commercially available Dexlansoprazole capsules Deltone® (60mg). 5 capsules are weighed and powdered the amount powder is equivalent to 100mlof Dexlansoprazole was weighed accurately and transferred into 100 mL volumetric flask containing methanol which was further sonicated for 15 min with vigorous shaking the volume was brought up to 100mL with methanol. The solution was subjected to filtration through Whatman filter paper #44. The filtrate was diluted suitably with methanol to get a final solution of 60µg/ml concentration. This was subsequently analyzed using a Double beam UV-VIS spectrophotometer and taking methanol as blank in the UV range 200-400nm. The spectrum was recorded as 247nm. The concentrations of the drug were calculated from the linear regression equation.

Method validation: Validation is a process of establishing documented evidence, which provides a high degree of assurance that is a specific activity will consistently produce the desired result, or a product meeting its predetermined specifications and quality characteristics. The method was validated according to ICH guidelines for various parameters like Linearity, precision, Accuracy, Robustness, Ruggedness, LOD, LOQ, Range, and Sensitivity.[10-13]

Linearity: The ability of an analytical procedure is to produce test results that are directly proportional to the concentration of an analyte. Linearity should be evaluated by visual inspection of a plot of signals as a function of analyte concentration. For estimation of linearity at least 5 concentrations are required.

Accuracy: Accuracy means the expression of closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference true value and the value found. Accuracy is assessed by using 9 determinations covering a minimum of 3 concentrations.

Precision: The closeness of agreement between the obtained values by analyzing the same sample multiple times under prescribed conditions. There are 3 levels of repeatability, intermediate precision, and reproducibility. Repeatability is a measure of the exactness under the same working conditions more than a short interim of time, that is, under ordinary working states of the scientific technique with the same hardware it is also known as intraday precision. Reproducibility also is known as inter-day precision. Precision is expressed in terms of % Relative Standard Deviation. % RSD= (Standard deviation)/Mean×100

Standard deviation (SD)

$$SD = \sqrt{((\sum [(x-\bar{x})]^2)/(n-1))}$$

Where n = no of entries

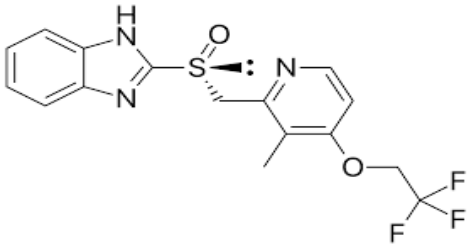

Figure 1: Chemical structure of Dexlansoprazole

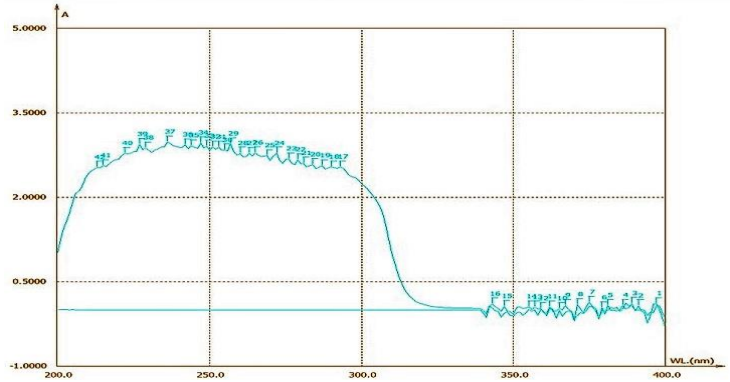

Figure 2: Determination of λ_{max} of Dexlansoprazole

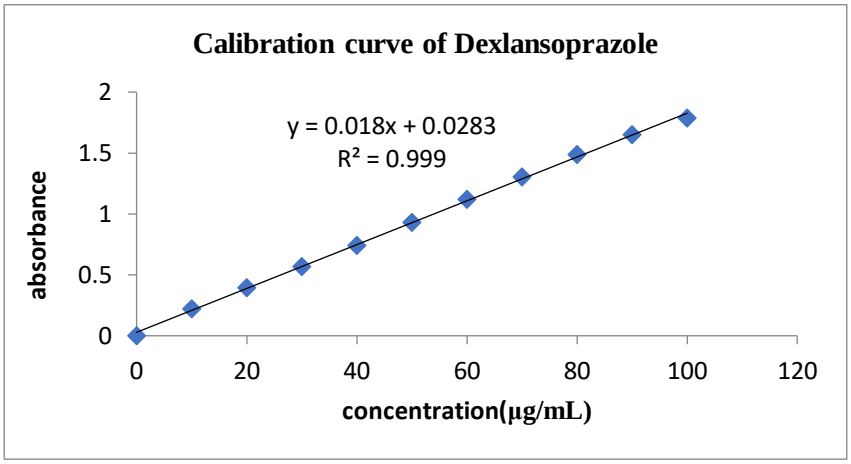

Figure 3: Standard calibration curve of Dexlansoprazole

Table 1: Linearity of working standard solutions

Concentration (µg/mL)	Absorbance
10	0.2210
20	0.3940
30	0.5660
40	0.7425
50	0.9300
60	1.1189
70	1.3065
80	1.4863
90	1.6516
100	1.7858

Table 2: Repeatability data

Concentration (µg/mL)	Absorbance	Statistical analysis
60	1.0583	Mean: 1.0584
60	1.0593	% RSD: 0.109%
60	1.0576	
60	1.0599	
60	1.0568	
60	1.0589	

Table 3: Intra-day study

Concentration (µg/mL)	%RSD			Average % RSD
	1	2	3	
60	0.29	0.14	0.064	0.1646

Table 4: Inter-day study

Concentration (µg/mL)	% RSD					Average % RSD
	Day1	Day 2	Day3	Day4	Day5	
60	0.109	0.299	0.369	0.071	0.365	0.2426

Table 5: Accuracy data

Level of Addition (%)	Amount added (µg/mL)	Amount Found (µg/mL)	%Recovery	%Mean Recovery
80	48	47.43	100.1	99.70
100	60	59.93	99.38	
120	72	71.70	99.64	

Table 6: Robustness data

Concentration (µg/mL)	Absorbance		
	246nm	247nm	248nm
60	1.0408	1.0568	1.0586
60	1.0459	1.0576	1.0669
60	1.0440	1.0583	1.0678
60	1.0439	1.0589	1.0697
60	1.0445	1.0593	1.0697
60	1.0434	1.0599	1.0699

Table 7: Ruggedness

Concentration (µg/mL)	Absorbance	
	Analyst 1	Analyst 2
60	1.0568	1.0492
60	1.0583	1.0478
60	1.0589	1.0502
60	1.0576	1.0513
60	1.0599	1.0556
60	1.0593	1.0498

Table 8: LOD & LOQ

Limit of Detection	Limit of Quantification
0.090 µg/mL	0.27 µg/mL

Table 9: Results of validated parameters

Parameters	Results
Absorption maxima (nm)	247nm
Linearity range (µg/mL)	10-100
Regression equation	y= 0.018x+0.028
Correlation coefficient (R^2)	0.999
Molar Extinction coefficient	15061.1
LOD (µg/ml)	0.09
LOQ (µg/ml)	0.27
Accuracy (% Recovery± SD)	98.38-100.10
Precision	
Intraday precision (%RSD)	0.1646
Inter-day precision (%RSD)	0.2408
Sand ell's sensitivity	0.0526
(µg/cm²/0.001 absorbance units)	

Ruggedness: The ruggedness of an analytical procedure is the degree of reproducibility of results by analyzing the same sample under a variety of conditions like laboratories, instruments, analysts, reagents, etc.

Robustness: Robustness of an analytical procedure is the capacity to remain unchanged by small but deliberate changes in parameters

Sensitivity: Limit of detection (LOD) and Limit of quantification (LOQ) of the drug was calculated by using equations according to ICH guidelines.

Limit of Detection: It is the lowest amount of the drug in a sample that can be detected, but not necessarily quantitated.

$$LOD = (3.3\times\sigma)/S$$

Where S= standard deviation

Limit of Quantification: It is an amount of analyte that can be quantitated with a specified limit of accuracy and precision.

$$LOQ = (10\times\sigma)/S$$

Linearity: Different aliquots of Dexlansoprazole were prepared from the working standard solution (100µg/mL) in the range of 10-100µg/mL. The solutions were scanned on a Double beam UV-VIS spectrophotometer in the UV range of 200-400nm using methanol as the blank. The spectrum was recorded at 247nm. The calibration plot was constructed as concentration Vs absorbance and can be shown in [Table1]. **Precision:** The precision of the method was demonstrated by intra-day and inter-day variation studies. In the inter-day variation study, the solutions of the same concentration 60µg/mL were prepared and

analyzed six times, for five consecutive days, and the absorbance was recorded[Table 4]. In the intra-day variation study, six different solutions of the same concentration 60 µg/mL were prepared and analyzed thrice a day (Morning, Afternoon, and Evening). And the % RSD was calculated and reported [Table3].

Accuracy: The accuracy of the method was determined by preparing solutions of different concentrations, i.e., 80, 100, and 120%, in which the amount of marketed formulation Deltone® was kept constant (60µg/L) and the amount of pure drug was varied, that is 48µg, 60µg, 72µg for 80, 100, and 120% respectively. The solutions were prepared in triplicate and the accuracy was indicated by % recovery was calculated and reported in the [Table 5].

Robustness: The robustness of the method was carried out by analyzing the sample using two different wavelengths (±1 of lambda max) that were and respective absorbance were recorded. The results are indicated in [Table 6].

Ruggedness: The ruggedness of the method was carried out by analyzing the sample using two different analysts and respective absorbance was recorded. The results are indicated in [Table 7].

Sensitivity: Limit of detection (LOD) and Limit of quantification (LOQ) of the drug was calculated by using equations according to ICH guidelines. They are calculated by checking absorbance using solvent and calculate using formulae and the results are shown in [Table 8].

RESULTS AND DISCUSSION

The method was developed and validated as per ICH guidelines. The method was validated in terms of linearity, precision, accuracy, robustness, ruggedness, LOD, and LOQ. Beers law obeyed over the concentration range of 10-100µg/mL, using regression analysis the linear equation y=0.018x+0.028 with a correlation coefficient of r2 0.999. The precision results show % RSD less than 2 at each level which indicates clearly that the method is precise enough for the analysis of Dexlansoprazole. The accuracy of the method was checked by recovery studies. The high recovery with values indicates the accuracy of the developed method. The robustness and ruggedness studies reveal that the method is enough robust and rugged. The LOD, LOQ values indicate that the method is more sensitive. There was no interference observed from the excipients present in the formulation, indicated that the method is specific. Determination of Dexlansoprazole in capsule formulation Deltone® showed the content of Dexlansoprazole was very close to the label amount. The% RSD values in all the parameters were within the acceptable limit (<2%) All the characteristics of the method are represented in the [Table 9].

CONCLUSION

A UV spectrophotometric method has been validated for the estimation of Dexlansoprazole in bulk as well as the pharmaceutical dosage form. The developed method was found to be simple, accurate, precise, specific, reproducible, and linear over the concentration range studied. The proposed method can be used for routine analysis of Dexlansoprazole in bulk as well as Pharmaceutical formulations.

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