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DEXLANSOPRAZOLE: A REVIEW OF ANALYTICAL METHODS FOR ESTIMATION IN PHARMACEUTICAL FORMULATION

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Abstract: Dexlansoprazole was approved by the U.S. Food and Drug Administration (FDA) in 2009. Dexlansoprazole (DSP) is a proton pump inhibitor, it used to treat GERD and ulcer colitis. DSP works by decreasing the volume of acid in the stomach. DSP is an acid-labile medication that may be destroyed in the stomach's acidic pH. A coating technique was used to postpone drug release in the stomach, which can extend pharmacological activity. There have been numerous methods developed so far for quantitative estimation of Dexlansoprazole in bulk and pharmaceutical dosage form. Pharmaceutical analytical methods include UV Visible Spectrophotometry, High Pressure Thin Layer Chromatography, Reversed Phase High Performance Liquid Chromatography and hyphenated techniques like Liquid chromatography- Mass Spectrometry.

Index Terms - UV – Visible Spectrophotometry, HPTLC, RP-HPLC, LC-MS, Validation, stability indicating methods.

Introduction:
Dexlansoprazole chemically is (R)-(+) 2-([3-methyl-4-(2, 2, 2-trifluoromethoxy) pyridin2yl] methyl sulfinyl)-1H-benzimidazole (Fig. 1). It is a proton pump inhibitor by the healing of Erosive Esophagitis and symptomatic Non-Erosive Gastroesophageal Reflux Disease.(1) Dexlansoprazole is the R-enantiomer of lansoprazole (a racemic mixture of the Rand S- enantiomers). It is a white powder having a molecular formula 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.(1,2)

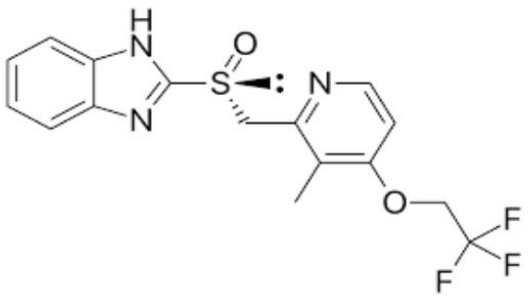

Figure 1 : Chemical Structure of Dexlansoprazole

Dexlansoprazole is the active drug compared with its enantiomer; this drug will be the therapeutic category of gastric acid secretion inhibitor. Gastroesophageal refux disease (GERD) is characterized by refux of gastric contents that causes persistent symptoms such as heartburn, cough, epigastric pain, vomiting, and regurgitation. In 2009, the PPI dexlansoprazole (DEXILANT®, Takeda Pharmaceuticals U.S.A., Inc.) capsule was approved at a 30-mg daily dose for adults to relieve heartburn, to maintain healed EE, and for relief of heartburn for up to 6 months, and to treat heartburn associated with symptomatic non-erosive GERD for 4 weeks. Dexlansoprazole is an enantiomer of lansoprazole with a unique dual delayed-release formulation designed to extend the duration of drug exposure and resulting gastric acid suppression.(3)

In this review article a new simple, precise, accurate, isocratic mode RP-HPLC method for the determination of Dexlansoprazole in Bulk and Capsules UV spectrophotometric and LCMS was studied.

Method validation: The process of creating documented evidence, or validation, offers a high level of assurance that a particular action will consistently yield the intended outcome or a product that satisfies its set quality characteristics and requirements. Many metrics, including linearity, precision, accuracy, robustness, ruggedness, LOD, LOQ, range, and sensitivity, were validated for the method by ICH recommendations.(4)
Linearity: An analytical process can yield test findings that are exactly proportionate to the analyte concentration. Visual examination of a plot of signals as a function of analyte concentration is the best method for determining linearity. It takes at least five concentrations to estimate linearity.(2,5)
Accuracy: The degree of agreement between the value found and the value that is recognized as either a conventional true value or an acceptable reference true value is known as accuracy. Nine determinations encompassing a minimum of three concentrations are used to evaluate accuracy.(2,6)
Precision: The degree of agreement between values acquired by repeated analysis of the same sample under specified conditions. Repeatability, intermediate accuracy, and reproducibility are all divided into three categories. Repeatability, also referred to as intraday precision, is a measurement of accuracy under the same working settings for a longer period of time than a brief interval; that is, during regular working conditions of the scientific technique with the same hardware. Another name for reproducibility is inter-day precision. Precision is expressed in terms of % Relative Standard Deviation. % RSD= (Standard deviation)/Mean×100
Standard deviation(2,4)

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

Analytical methods for estimation

1. **UV – Visible Spectrophotometry:**
   UV/V Spectrophotometric method is used to as an analytical method of estimation of Dexlansoprazole. UV/ V spectrophotometry is employed as it is ease to handle and accurate. It has accuracy, speed, gives sensitive and precise results. However, UV–Visible Spectrophotometry method is not able to give broad spectra for estimation of certain drugs. It consists of calculating and plotting first order and second order derivative of the mathematical expression of a spectral curve.(2)

Method	Solvent	λmax (nm)	Linearity (µg/ml)	r^2	% Recovery	Reference
Area under curve	Methanol	247	10-100ug/ml	0.999	99.70	1
Area under curve by Quinalizarin	Methanol	558	1-12ug/ml	0.9998	99.77 ± 0.67	7
	Methanol	542	1-16ug/ml	0.9994	99.20 ± 0.20	

Anthracene sulfonic acid (ARS)						

Table 1: UV/V Spectrophotometric Summary

Lakshmi Keerthi B, Deepthi R, Srinivasa Rao Y, Vara Prasada Rao K, Rama Rao B have developed spectrophotometric method using methanol. It was proved to determine the dexlansoprazole content in bulk and pharmaceutical dosage formulations at a predetermined λmax of 247nm. Beer limits in the range of 10-100 µg/mL and exhibited good correlation coefficient (R2 = 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.(1,2)

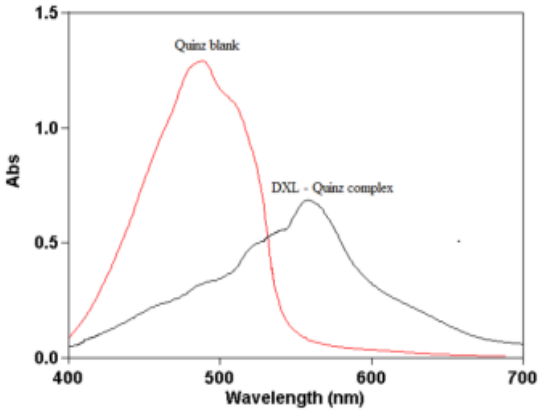

Figure 2: Absorption spectra of charge transfer complexes of 15 µg mL^{-1} DXL with (1.0 x 10^{-3} mol L^{-1}) Quinz in methanol solvent obtained against Quinz reagent blank solution prepared in the same solvent.

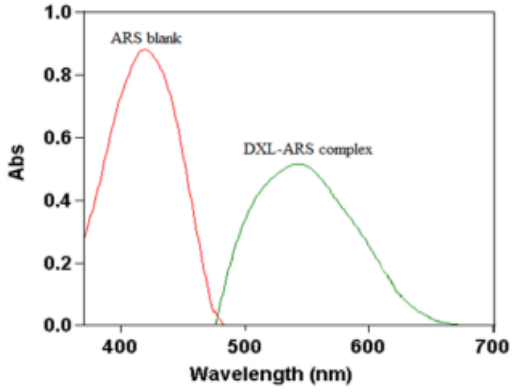

Figure 3: Absorption spectra of charge transfer complexes of 12 µg mL^{-1} DXL with (1.0 x 10^{-3} mol L^{-1}) ARS in methanol solvent obtained against ARS reagent blank solution prepared in the same solvent

El Sheikh Ragaa , Amin Alaa S , Gouda Ayman A, and Negeda Ola S have been developed two simple, sensitive, accurate, and precise spectrophotometric methods. The method was based on the formation of charge transfer complex between DXL and quinalizarin (Quinz) and alizarin red S (ARS) as chromogenic reagents in methanol which showed an absorption maximum at 558 and 542 nm using Quinz and ARS, respectively. The optimization of the reaction conditions such as the type of solvent, reagent concentration and reaction time were investigated. Under the optimum conditions, beer's law is obeyed in the concentration ranges 1.0-12 and 1.0-16 µg mL-1 using Quinz and ARS, respectively with good correlation coefficient ($r2 \geq 0.9994$) and with a relative standard deviation (RSD% ≤ 1.11). The molar absorptivity, Sandell sensitivity, detection and quantification limits are also calculated.(7)

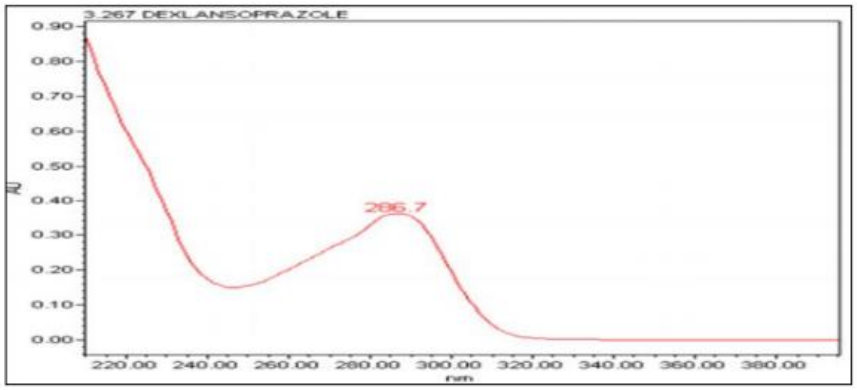

Fig 03 : UV Spectrum of Dexlansoprazole

2. Chromatographic Methods:

Reversed-Phase High-Performance Liquid Chromatography

The most common chromatographic method is reversed-phase chromatography, which is used to separate neutral compounds in solution according to how hydrophobic they are. Reversed-phase chromatography, also known as RP chromatography, is, as its name implies, the opposite of normal-phase chromatography in that it uses a non-polar stationary phase and a polar mobile phase. It makes sure that a drop in the mobile phase's polarity leads to a drop in solute retention. In reversed-phase chromatography (RPC), "where a functional group is bonded to the silica" often refers to the employment of chemically bonded stationary phases. The stationary phase is crucial to the retention process in the partitioning model of retention..(8)

Lakshmi Keerthi B, Deepthi R, Dr. Srinivasa Rao Y and Varaprasada Rao K. have been developed A simple, precise, specific, and accurate RP-HPLC method. and validated for the estimation of Dexlansoprazole in bulk and capsule dosage formulation. The separation was achieved by Enable C18column (250X 4.6mm, 5µm particle size) using a mobile phase consisting of methanol and water (95:5, v/v) at a flow rate of 1mL / min using detection wavelength at 247nm. The method was developed in isocratic mode. The retention time was around 2.914 minutes. The method showed linearity with correlation coefficient R 2 =0.997 over the range of 20-120µg/mL. The mean recoveries were found to be in the range of 99.3-99.7% for Dexlansoprazole.(2)

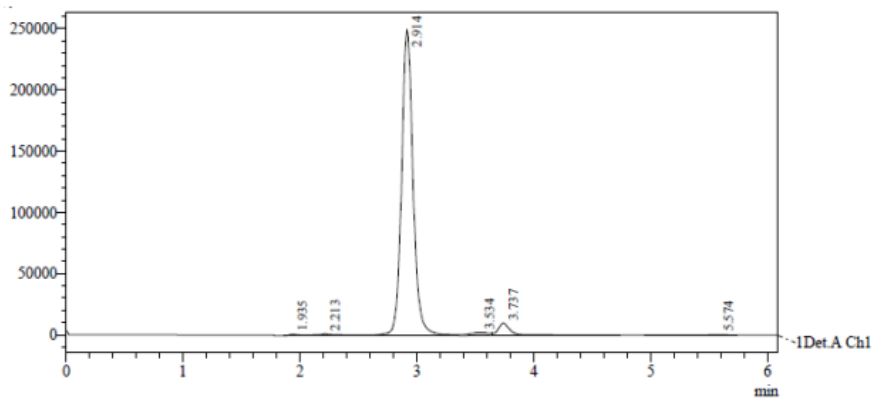

Fig 04 : Chromatograph of Dexlansoprazole

SANTHOSH KUMAR, MRS. AKKAMMA, Dr. C SRIDHAR, T SRINIVAS RAO have been developed a simple and accurate RP-HPLC method for the estimation of Dexlansoprazole, proposed method was validated according to an International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use (ICH) guidelines. : The column used for method development of Dexlansoprazole was Hypersil-BDS, C18, 250*4.6 mm, 5µ. Methanol and Acetonitrile were used in the ration of 60:40 for the method development and is used as mobile phase in gradient composition at a flow rate of 1.0 ml/min. UV detection was made at 283 nm. The developed method was validated for various parameters such as specificity, linearity, range, accuracy, precision, system suitability, robustness, ruggedness etc. The result obtained in this study demonstrated that the RP-HPLC method described is specific, accurate, precise, linear, ruggedness, robustness, stability, LOD and LOQ indicating for the determination of Dexlansoprazole.(9)

Column	Dimension (mm×mm×µ)	Mob phase	λmax (nm)	Linearity µg/ml	% Recovery	LOD, LOQ (µg/ml)	Detect or	r 2	Refer ence
C18column	250X 4.6mm, 5µm	methanol and water	247nm	20-120	99.43%	0.49µg/ml 1.65µg/ml	UV – Visible detector	0.997	2
C18	250x4.6mmx5 µ	methanol and acetonitrile	283nm	25-150	100.16	0.0929 0.282 µg/mL	PDA detector	0.999	9
X-Terra RP18column	(250×4.6mm, 5µ)	Orthophosphoric acid: Acetonitrile: TEA	285nm	50-150	97.77-103.94%	0.14 0.028	PDA detector	0.999	10
Chiralpak IC column	(250 mm x 4.6 mm, 5 µm)	Acetonitrile (ACN) and 10 mM dibasic potassium phosphate buffer of pH 7.20, adjusted with dilute ortho phosphoric acid	283 nm	0.25-1.50	93.8-102.5%	42 and 126 ng/ml	PDA detector	0.999	11

Table No 02 : RP-HPLC Validation Parameter of Dexlansoprazole

Santhosh Kumar Ettaboina, Komalatha Nakkala have been described the "Stability-indicating Method development and validation of Dexlansoprazole delayed release capsules using RP-HPLC" Isocratic separation was achieved by the use of X-Terra RP18column (250×4.6mm, 5µ), the mobile phase, consisting of a mixture of 10 mm dibasic potassium phosphate buffer, was prepared and the pH of the solution adjusted to 7.20 with dilute orthophospharic acid: acetonitrile: TEA at a ratio of 70:30:1 v/v/v was delivered at a flow rate of 1.2 ml/min and a wavelength detector of 285nm. The retention time for Dexlansoprazole was 6.8 min. The linearity range of Dexlansoprazole was 50µg/mL-150 µg/mL-1 with a regression coefficient (r2) of 0.999, accurate (recovery 97.77-103.94%). Precision (RSD ≤ 1.0 percent), sensitive, specific, simple, fast and robust.(10)

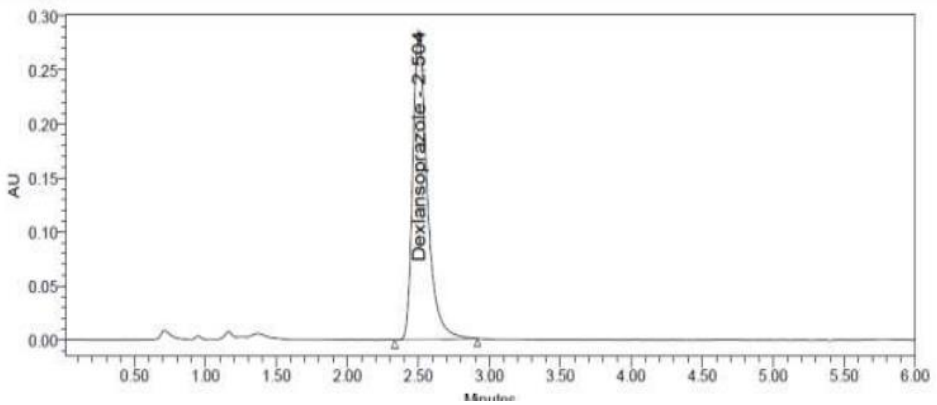

Fig 05 : Chromatograph of Dexlansoprazole

Santhosh Kumar Ettaboina, Komalatha Nakkala have been performed The forced degradation studies to demonstrate whether the analytical method was stability indicating and might unambiguously evaluate the analyte in the presence of impurities and degradation products. The solutions of a drug product and placebo were exposed to acid hydrolysis (1N HCl), base hydrolysis (1N NaOH), oxidation (30% H2O2), thermal (Heat_105°C) to form degradation products. The liberated degradation products evaluated in terms of co-elution with close eluting with any components in the chromatography and initiate to be selective and unambiguous.(10)

Stress Condition	% Assay of DEXP	% Total Impurities found	% Mass Balance	Dexlansoprazole	
				PA	PT
Control-Sample	99.0			0.127	0.304
1N HCl, refluxed at 80°C for 30min	88.3	10.2	98.6	0.188	0.353
1N NaOH, refluxed at 80°C for 30min	97.1	1.8	98.9	0.166	0.321
30% H_2O_2, refluxed at 80°C for 30min	90.0	8.5	98.5	0.541	0.625
Thermal 105° C for 1 hr	93.3	6.2	99.6	0.222	0.315
PA- Purity Angle, PT- Purity Threshold					

Table No 03 : Summary of forced degradation results

P. Balamurugan, K. Anver Basha, Jeenet Jayachandran, Manish Gangrade, P. Parthiban have developed a simple and accurate RP-HPLC method for simultaneous estimation of organic impurities, enantiomer and assay of Dexlansoprazole, proposed method was validated according to an International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use (ICH) guidelines.(11)

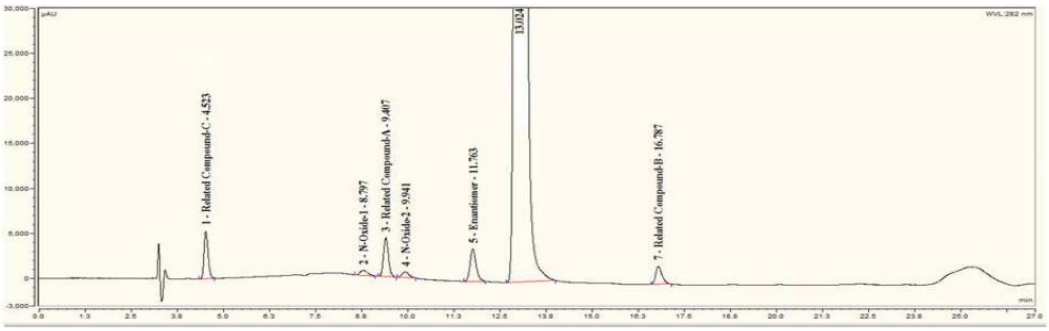

Fig 06 : Typical system suitability chromatogram of dexlansoprazole spiked with impurities

CONCLUSION:

In this paper, recent analytical methods employed for quantitative analysis of Dexlansoprazole in pharmaceutical formulations chiefly from 2009 to 2023 were reviewed. Several techniques like UV - Visible spectrophotometry including Area under curve, Chromatographic methods primarily (high - performance liquid - chromatography, high - performance thin - layer chromatography), Liquid chromatography is the major techniques that have been used, of which it is observed a development to use quicker techniques with cost savings and lessening in solvent consumption. From this work, it has been observed that High Performance Liquid Chromatography is extensively utilised for estimation of Dexlansoprazole in bulk material and pharmaceutical formulations. Further there has been always greater need to develop more sophisticated method to determine content of Dexlansoprazole in bulk and pharmaceutical dosage form.

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