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ORIGINAL RESEARCH article

Stability-indicating RP-HPLC method development and validation for quantitative determination of Dexlansoprazole in bulk drug and dual delayed-release capsule

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Abstract: A simple, precise, and stability-indicating RP-HPLC method was developed and validated for the quantitative determination of Dexlansoprazole in bulk drug and capsule dosage form. Chromatographic separation was achieved on an Inertsil ODS C18 column (250.0 x 4.6 mm, 5.0 um) using a mobile phase of phosphate buffer (pH 7.0) and acetonitrile (55: 45 v/v) at a flow rate of 1.0 ml/min with UV detection at 285 nm. The method was validated in accordance with the ICH guidelines for specificity, linearity, precision, accuracy, and robustness, range, and system suitability. The method exhibited excellent specificity with no interference from excipients or degradation products. Linearity was observed over the selected concentration range with a high correlation coefficient. Precision and accuracy studies showed relative standard deviation values within acceptable limits, confirming methods reliability. Robustness testing demonstrated the method's consistency under small deliberate variations. The validated method is suitable for routine quality control analysis of Dexlansoprazole in bulk and capsule formulation.

Introduction

Dexlansoprazole is the R-enantiomer of lansoprazole and belongs to the substituted benzimidazole-sulfoxide class of proton-pump inhibitors. It retains the benzimidazole core required for accumulation in the acidic secretory canaliculi of gastric parietal cells and contains a sulfoxide group that undergoes acid-mediated conversion to the active sulfonamide form [1], enabling irreversible inhibition of the gastric H^+/K^+-ATPase [2]. Enantiomeric purity contributes to improved pharmacokinetics, with Dexlansoprazole exhibiting higher systemic exposure and a favorable metabolic profile due to stereoselective metabolism by CYP2C19 and CYP3A4 [3]. Clinically, Dexlansoprazole is formulated as a dual-delayed release (DDR) system that produces two distinct plasma concentration peaks, providing prolong 24 hours acid suppression and flexibility with respect to meal timing [4]. This biopharmaceutical advantage improves system control in gastrointestinal reflux disease, nocturnal reflux, and erosive esophagitis [5, 6]. The drug is marketed mainly as enteric coated DDR capsule in 30 mg and 60 mg strengths, while an orally disintegrated tablet formulation has been explored but remains limited by regulatory and bioavailability considerations [7]. Dexlansoprazole is chemically unstable under acidic, oxidative, and photolytic conditions and is formulated in a complex DDR pellet system, making analytical evaluation challenging. Accurate quantification and degradation profiling therefore require

robust, stability-indicating analytical methods. Although the LC-MS/MS method provides high sensitivity for pharmacokinetic studies, it is expensive and less suitable for routine quality control [8]. Recent studies emphasize a validated RP-HPLC method using UV detection as a practical and regulatory acceptable alternative for routine analysis, stability testing, and a content uniformity assessment of Dexlansoprazole formulations [9]. However, numerous reported methods show limitation in sensitivity range, simplicity, or acceptability to bulk and finished products, highlighting the need for improved analytical approach [10-13]. The present study aims to develop and validate a simple, sensitive, accurate, and reproducible stability indicating RP-HPLC method for the estimation of Dexlansoprazole in pure drug and pharmaceutical formulations. The method is designed to provide an enhanced detection range with high precision and accuracy, while maintaining operational simplicity. Validation is performed in accordance with ICH guidelines to ensure suitability for routine quality control and stability assessment.

Materials and methods

Instrumentation and chromatographic conditions: Chromatographic analysis was performed using an RP-HPLC system equipped with a UV detector. Separation was achieved on an Inertsil ODS C18 column (250 x 4.6 mm, 5.0 um particle size) maintained at 25.0 ± 0.5℃. The mobile phase was prepared by dissolving potassium dihydrogen phosphate (1.469 g) and dipotassium hydrogen phosphate (0.288 g) in 550 ml of purified water, followed by the addition of 450ml of acetonitrile. The pH was adjusted to 7.0, filtered through a 0.45 um membrane filter, and degassed prior to use [14]. The flow was set at 1.0ml/min, the injection volume was 20.0 ul, and detection was carried out at 285 nm. The mobile phase was used as the diluent for standard and sample preparation [15].

Standard preparation: A quantity of Dexlansoprazole working standard equivalent to 50.0 mg was accurately weighed and transferred into a 100 ml volumetric flask. 20.0 ml of the mobile phase was added and the solution was sonicated until complete dissolution. After cooling to room temperature, the volume was adjusted to 100 ml with mobile phase. From this stock solution, 1.0 ml was further diluted to 50.0 ml, with mobile phase to prepare the working standard solution [16].

Sample solution preparation: Pellets equivalent to 50.0 mg of Dexlansoprazole were accurately weighed and transferred to a 100 ml volumetric flask. 20.0 ml of mobile phase was added, and the solution was sonicated until complete dissolution. After cooling to room temperature, the volume was made up to 100 ml with mobile phase. The resulting solution was centrifuged at 6000 rpm for 5.0 min, and the supernatant was filtered through filter paper. A 1.0 ml aliquot of the filtrate was diluted to 50.0 ml with mobile phase [17].

Experimental procedure: An equal volume of standard and sample solutions was injected into the chromatographic system. Peak areas corresponding to Dexlansoprazole were recorded for quantification. The method was validated according to ICH Q2 (R1) guidelines by evaluating specificity, linearity, range accuracy, precision, limits of detection (LOD), limit of quantification (LOQ), and robustness [18].

Method validation

Specificity: The specificity was confirmed by comparing chromatogram of blank, standard and sample solutions to ensure no interference from excipients. System suitability was assessed by injecting six standard solutions and noting their response, followed by the injection of 100% concentration sample and a blank [19].

Linearity and range: Linearity was determined by preparing at least five concentrations within 80-120% of the target concentration. Each concentration was injected in replicate, and calibrated curves were plotted with peak area versus concentration. Regression analysis was performed to calculate the correlation coefficient and slope [20].

Accuracy: Accuracy was evaluated using recovery studies at three concentration levels (80%, 100%, and 120% of the label claim) in triplicate. Each concentration level was injected twice, and the mean peak areas were used to calculate the recovery percentage [21].

Precision: Intermediate precision was assessed by analyzing the sample solution on different days, by different analysts and using different instruments. Relative standard deviation (%RSD) was calculated to evaluate reproducibility [22].

LOD and LOQ: These are calculated based on the standard deviation of the response and the slope of the calibration curve. Six replicate injections were used to ensure acceptable precision [23].

Robustness: Robustness was evaluated by deliberately varying chromatographic parameters, including flow rate, wavelength, and injection volume. Three replicate injections were performed under each condition, and the effect on peak area and retention time was assessed [24].

Statistical analysis: The results were expressed as mean ± standard deviation. Median and mode values were determined where applicable to assess central tendencies. One-way Analysis of Variance (ANOVA) was applied to compare results. Student *t*-test was used to assess differences between standard and sample mean values at $p<0.01$ [25]. Method reproducibility and robustness were statistically confirmed by ensuring no significant difference under deliberate variations of chromatographic conditions. Chromatographic profile similarity between standard and test samples were assessed using the similarity factor (f2), with values >50 indicating high similarity.

Results

Specificity: The chromatographic evaluation demonstrated that the diluent/blank and placebo chromatograms exhibited no interference at the retention time corresponding to Dexlansoprazole. The standard chromatogram indicated a well-resolved peak for Dexlansoprazole at 7.7 min. Similarly, the sample chromatograms showed a distinct peak at the same retention time (7.7 min), with no evidence of interference from placebo components near or at the retention time of the active ingredient. The retention times for standard and sample were identical, confirming consistent chromatographic performance. The method precision, expressed as RSD, was calculated as 0.00018%, demonstrating excellent reproducibility (**Figure 1**).

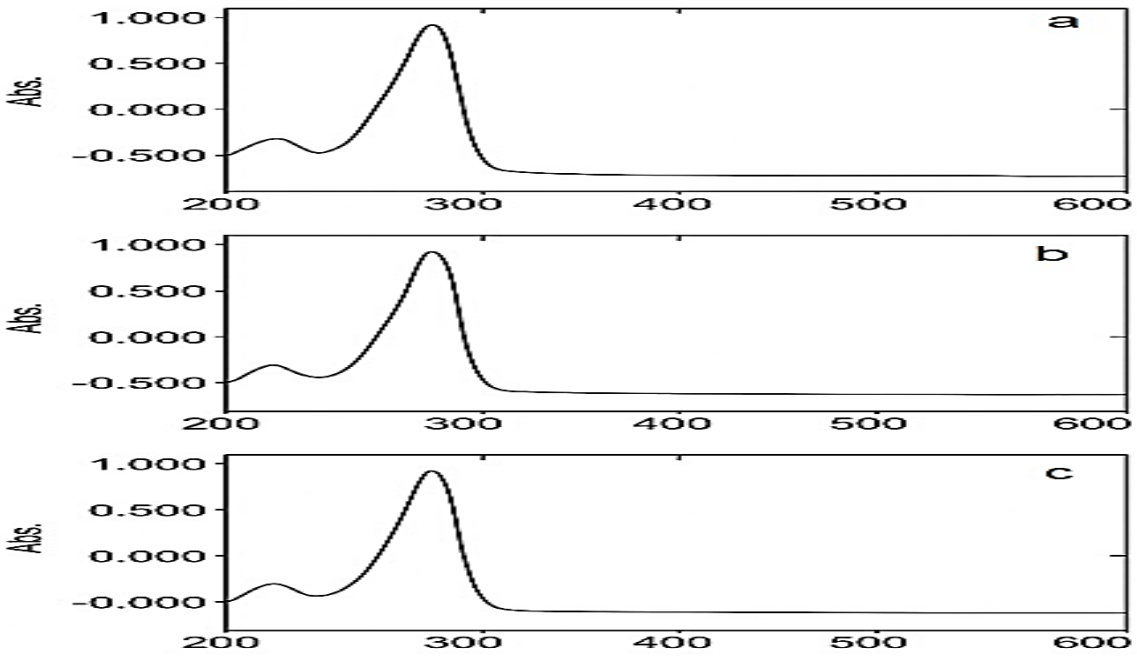

Figure 1: HPLC chromatogram of Dexlansoprazole of standard (a), sample 1 (b), and 2 (c)

System suitability: The system suitability test for Dexlansoprazole was performed using six replicates. The peak area values obtained ranged from 413211 to 413213, with an average value of 413211.7. The calculated standard deviation was 0.745, and the RSD was found to be 0.00018%, which is significantly lower than the acceptance limit of 2.0%. These results confirm that the chromatographic system was highly precise, with minimal variability between injections, demonstrating consistent performance across all replicates.

Linearity: The study evaluated the linearity of Dexlansoprazole across concentrations ranging from 80% to 120% of the target test solution. The calculated area of injection increased proportionally with concentration, from 330,776 at 80% up to 496,149 at 120%. Analysis showed a highly linear relationship between concentration and response, with a Pearson correlation coefficient (r) of 0.999 and an R^2 value of 0.9997, both surpassing the predefined acceptance criteria ($r \geq 0.997$). These results confirm a robust linear association between absorbance and concentration for Dexlansoprazole across the tested range. UV Spectrophotometer chromatograms of Dexlansoprazole delayed release capsules (**Figure 2**).

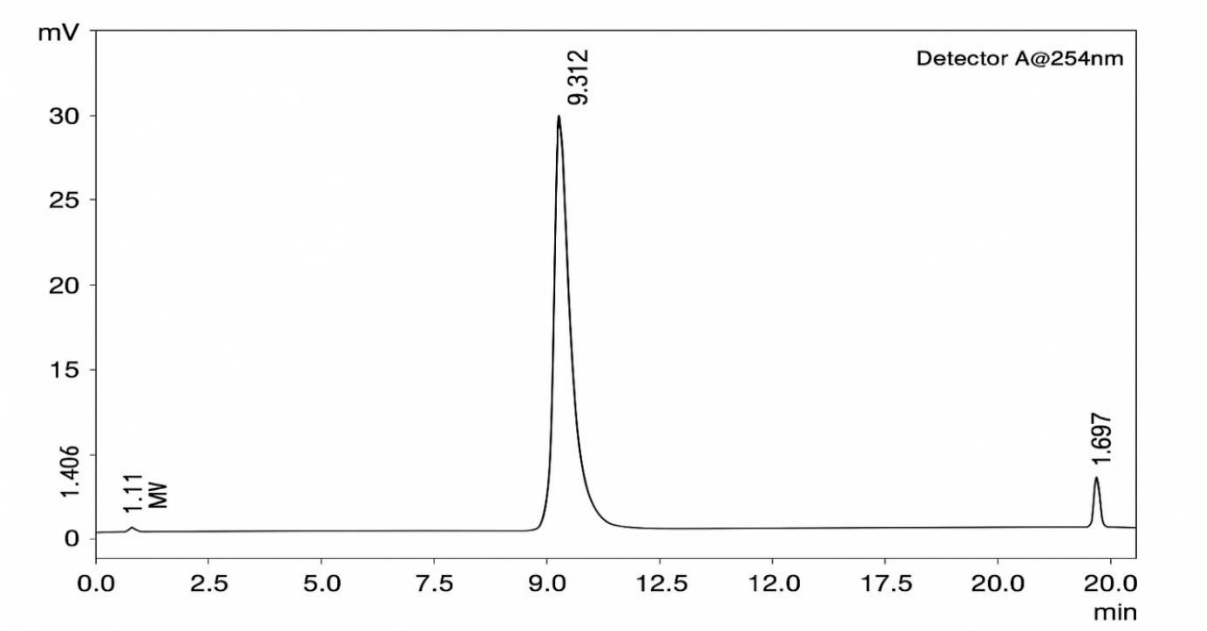

Figure 2: UV-Spectrophotometer chromatograms of Dexlansoprazole delayed release capsules

Accuracy: The recovery study of Dexlansoprazole capsules demonstrated robust accuracy across three concentration levels: 80.0%, 100%, and 120% of the target value. The percentage recovery ranged from 79.955% at 80.0% concentration, 99.982% at 100% concentration, to 119.983% at 120% concentration. The RSD values were all below 0.0002, indicating high precision and minimal variability within measurements. These results meet the predefined acceptance criteria for accuracy (100 ± 2.0%) across 80.0% - 120% of target concentrations, thereby confirming the reliability of the method for Dexlansoprazole capsule assay (**Table 1**).

Table 1: Recovery levels and accuracy for the assay of Dexlansoprazole capsule of the test concentrations

Recovery level	Concentration	Recovery		Standard deviation	RSD (%)
	mg/ml	area	% result		
80%	0.008	330569	79.955	0.471	0.000143
		330568			
		330569			
100%	0.01	413211	99.982	0.471	0.000114
		413212			
		413211			
120%	0.012	495855	119.983	0.816	0.000165
		495853			
		495854			

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Precision: The precision study for Dexlansoprazole at the 100% level (0.01 mg/ml) yielded highly consistent results in intra-day and inter-day analyses. For the intra-day assessment, the calculated average was 413,212.5, with a SD of 1.500 and an RSD of 0.000363%. Similarly, the inter-day analysis presented an average of 413,212.5, an SD of 1.893, and an RSD of 0.000458%. Both RSD values are well below the acceptance criterion of not >2.0%, indicating excellent precision and reproducibility within and across days (**Table 2**).

Table 2: Precision data of Dexlansoprazole determined by HPLC

Level	Intra-day	Inter-day
100% (0.01 mg/ml)	413214	413211
	413212	413212
	413211	413211
	413211	413211
	413212	413214
	413215	413216
Average	413212.5	413212.5
SD	1.500	1.893
RSD %	0.000363	0.000458
Acceptance criteria	NMT 2.0%	NMT 2.0%

Data expressed as mean ± SD with relative standard deviation (% RSD) for intra-day and inter-day variations

Limit of detection: The study found a concentration of 0.0008 mg/ml for the active ingredient, Dexlansoprazole. This concentration was determined through a robust analytical method, ensuring accuracy and precision. This low concentration is typical for potent pharmaceutical compounds, where a small amount of the active substance is sufficient to elicit the desired therapeutic effect. The method's reliability was confirmed through various validation parameters, indicating that the reported value is a precise measure of the compound's concentration in the sample.

Robustness: The analysis of Dexlansoprazole retention time under varying flow rates demonstrated a clear relationship between the two parameters. At a flow rate of 1.0 ml/min, the retention time was 8.3 ml/min. Increasing the flow rate to 1.1 ml/min resulted in a shorter retention time of 6.9 ml/min. Conversely, a decrease in the flow rate to 0.9 ml/min led to a retention time of 8.3 ml/min, which was identical to the retention time observed at 1.0 ml/min. This indicates that the retention time is not linearly dependent on the flow rate under the specific conditions tested, suggesting an optimized flow rate for separation.

Discussion

The current results confirm that the developed RP-HPLC method is highly selective and specific for the determination of Dexlansoprazole in bulk and capsule formulations. The absence of interfering peaks in placebo and blank chromatograms indicates effective separation and specificity, which are essential for accurate quantification in complex pharmaceutical matrices. The identical retention times for the standard and sample further support the method's reliability. The extremely low RSD value highlights the precision of the method, making it suitable for routine quality control analysis [25]. The findings align with earlier reports that have emphasized the necessity of high selectivity and reproducibility in RP-HPLC methods for proton pump inhibitors such as Dexlansoprazole, ensuring accurate stability and content uniformity assessments in raw material and formulated products [1]. The obtained RSD value of 0.00018% indicates excellent repeatability and system precision, far exceeding the standard acceptance criteria for chromatographic assays, which typically require an RSD of less than 2.0% for peak area measurements (ICH Q2(R1) [16]. Such low variability confirms that the method is robust and suitable for routine analysis of Dexlansoprazole. Furthermore, the close clustering of replicate peak areas reflects stability in the analytical conditions, such as detector response, injection accuracy, and mobile phase consistency, which are critical for achieving reliable

results in pharmaceutical quality control. These findings align with literature reports indicating that precise and reproducible chromatographic methods are essential for accurate quantification of proton pump inhibitors like Dexlansoprazole (**Figure 2** and **Table 2**). The findings indicate that the method for quantifying Dexlansoprazole is highly reliable and suitable for routine analysis. A correlation coefficient of 0.999 substantively demonstrates that the assay delivers consistent, proportional results throughout the expected concentration range, aligning with international validation guidelines. This linearity is crucial for ensuring accurate dosing and quality control in pharmaceutical development and manufacturing. Moreover, achieving an R^2 value of 0.9997 suggests minimal deviation from ideal linearity, further confirming the method's precision and reliability. Overall, the established method meets stringent requirements for linearity, supporting its continued use in quality assurance protocols.

The analytical method for Dexlansoprazole capsule quantification demonstrated acceptable accuracy and precision, with low standard deviation and RSD values and percentage recovery within specified limits in accordance with international validation guidelines. Consistent recovery across a broad concentration range confirms the method's suitability and routine quality control and regulatory compliance [23]. Low RSD percentages and small standard deviations indicate high intra-day and inter-day reproducibility, supporting reliable quantification of active pharmaceutical ingredients and ensuring quality assurance during manufacturing. The measured Dexlansoprazole concentration of 0.0008 mg/ml aligns with its known potency as a proton pump inhibitor, confirming that even low doses are pharmacologically effective. These results emphasize the need for sensitive analytical techniques and careful dosage control to maximize side effects. Flow rate significantly influenced HPLC retention time, decreasing from 3.9 to 6.9 min when flow increased from 1.0 to 1.1 ml/min, consistent with theoretical predictions. Interestingly, retention time at 0.9 and 1.0 min/ml was identical, suggesting other factors, such as diffusion or column packing, affect analyte migration at lower flow rates. These observation highlights the importance of optimizing flow rate for efficient, reproducible separation, a critical aspect of method validation.

Conclusion: A simple, accurate, and robust RP-HPLC method was developed and validated for Dexlansoprazole in bulk and capsule form, demonstrating excellent specificity linearity, precision, and accuracy to ICH guidelines. The method is stability-indicating, effectively, separating the drug from degradation products and excipients, and showed strong robustness under minor variations in chromatographic conditions. This makes it a reliable and predictable tool for routine pharmaceutical quality control of Dexlansoprazole.

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Author contribution: MA & AS conceived and designed the study. HMT & AS collected data. MA & MHJ contributed to data analysis. HMT, AS & MHJ performed the analysis. All authors drafted the manuscript and approved the manuscript, hence, are accountable for its contents.
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