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**Research Article**

# STABILITY INDICATING RP-HPLC ASSAY METHOD FOR THE DETERMINATION OF DEXLANSOPRAXOLE IN BULK AND CAPSULEDOSAGE FORMS

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**A B S T R A C T**

In this study, dexlansopraxole was determined by stability indicating RP-HPLC analysis. The mobile phase was eluted with a Phenomenex C18 column (150 × 4.6 mm, 5 µm). 0.1M $NaH_2PO_4$: methanol (55:45) was used as mobile phase. The flow rate was 1.0 ml/min and eluents were detected at 270 nm at column temperature of 30 °C. Dexlansopraxole was subjected to stress conditions like acid, base, oxidative, thermal and photolytic. The degradants produced were well resolved from dexlansopraxole with different retention time values. The method linearity ($R^2$ = 0.9998) is in the range of 25 - 200 µg/ml. The precision (relative standard deviation values are less than 0.5%) and accuracy (percent recovery values are nearer to 100%) results were satisfactory. The proposed method has high throughput as short run time (5 min) was short. The proposed method was successfully applied for the determination of dexlansopraxole in capsule dosage forms with acceptable results.



## INTRODUCTION

Dexlansoprazole, an acid/proton pump inhibitor/gastric antisecretory agent, is used in the interim treatment of all grades of erosive esophagitis (Skrzydło and Radwan, 2015). Dexlansoprazole is also used to manage the symptoms in patients with gastroesophageal reflux but without erosive esophagitis (Goh *et al*., 2016; Fass and Frazier, 2017). Hydrogen-potassium ATPase, an acid pump, of gastric parietal cells is inactivated by dexlansoprazole through binding. This blocks the secretion of HCl in the last step which results in long-lasting gastric acid secretion inhibition (Shin and Kim, 2013). Dexlansoprazole is lansoprazole's R-enantiomeric form. Dexlansoprazole was approved by the U.S. Food and Drug Administration approved dexlansoprazole in 2009 (FDA Approves Kapidex, 2009). Chemically dexlansoprazole is described as (R)-(+)2-([3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl]methylsulfinyl)-1H-benzimidazole (Figure 1).

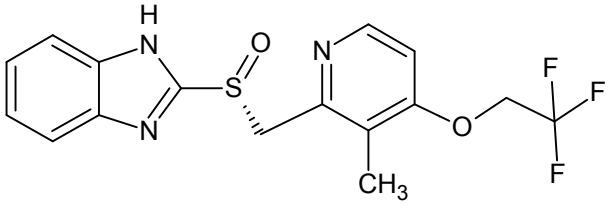

**Figure 1** Dexlansaprazole chemical structure

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Few analytical methods using spectrophotometry (Sekharan *et al*., 2015a,b; El Sheikh *et al*., 2018) and LC-MS/MS (Kishore *et al*., 2012) exist for the quantification of dexlansoprazole in bulk (Sekharan *et al*., 2015a,b; El Sheikh *et al*., 2018), human plasma (Sekharan *et al*., 2015a,b; Kishore *et al*., 2012) and pharmaceutical formulation (El Sheikh *et al*., 2018). None of the methods are stability indicating. The stability-indicating RP-HPLC assay method is rapid, reliable and accurate. This assay method involves simultaneous analysis of many samples with small volume of mobile phase. This minimizes the time of analysis per sample and cost per analysis. Stress testing gives data on the variation in the drug substance quality with time under the influence of various environmental (temperature, light, humidity, etc.) and chemical (acid, base and hydrogen peroxide) factors. The stress testing also provides information about the shelf life of the drug and storage conditions recommended for the drug.

To the best of our literature review knowledge, one stability indicating RP-HPLC method was reported (Geetharam *et al*., 2013). In the reported method, the chromatography was performed on a Hypersil BDS C18 column with a mobile phase consisting of $KH_2PO_4$ (0.01M, pH 7.0): acetonitrile (60:40 v/v) and UV detection at 283 nm. Mobile phase flow rate was set at 1.2 ml/min. the linearity was 25–150 µg/ml with mean recovery in the range of 99.8–100.16%. Realising the necessity for a stability indicating RP-HPLC method, the present work describes the development and validation of a simple, rapid, precise, accurate and specific method for dexlansoprazole assay in bulk and capsules. The developed

stability indicating method offered a less run time for analysis (5 min run time), less flow rate of mobile phase (1.0 ml/min) and broad range of linearity for dexlansoprazole (25-200 µg/ml), and utilized only 10 µl of sample for analysis.

***Experimental***

***Instrumentation***

Chromatography separation and analysis of dexlansoprazole was performed on a Waters HPLC system using a Phenomenex column (C18 150 mm, 4.6 mm, and 5 µm) equipped with binary solvent delivery pump (model 2695), autosampler, vacuum degasser and photodiode array (model 2998) detector.

***Chromatographic conditions and optimized parameters***

The column oven temperature is set at 30°C. Ambient temperature is maintained at autosampler. Throughout the chromatographic run, isocratic mobile phase flow was performed. Total run time was 5 min with a flow rate of 1.0 ml/min and an injection volume of 10 µl. The effluents were monitored at 270 nm and processed by Empower 2 software.
The mobile phase was prepared by mixing 550 ml portion of 0.01 M, pH 7.0, $NaH_2PO_4$ (analytical reagent grade, Sd. Fine Chemicals Ltd., Mumbai, India) with 450 ml of methanol (HPLC grade, Merck India Ltd., Mumbai, India) and shaken well. The prepared mobile phase was filtered using 0.45 µm membrane filter. The same solvent mixture was also used as diluent for preparations of the standard and capsule sample.

***Standard solutions***

The reference standard dexlansoprazole was procured from Rainbow pharma labs, Hyderabad, India. The standard stock solution (1 mg/ml) of dexlansoprazole was prepared by accurately dissolving a weighed 100 mg of dexlansoprazole in 100 ml mobile phase in a 100 ml volumetric flask. The working standard solutions with concentrations 25 µg/ml, 50 µg/ml, 75 µg/ml, 100 µg/ml, 125 µg/ml, 150 µg/ml and 200 µg/ml of dexlansoprazole were obtained by exactly diluting the standard stock solution with mobile phase.

***Analytical procedure***

***Preparation of calibration curve***

Aliquots (10 µl) of working standard solution in the concentration range of 25-200 µg/ml were injected into the HPLC system and eluted with mobile phase under the described chromatography conditions. The dexlansoprazole peak area vs dexlansoprazole concentration in µg/ml was plotted. Then again, regression equation was derived using peak area and concentration data. The concentration of the unknown drug was computed from the regression equation or from calibration curve.

***Preparation of capsule sample and assay procedure***

Dexlansoprazole capsules, Dexilant (Takeda Pharmaceuticals America, Inc. Deerfield), labeled to contain 30 mg and 60 mg, were obtained from local pharmacy store. The average weight content of 10 capsules containing 100 mg of dexlansoprazole was calculated. The powder was then homogenized. Amount of powder equivalent to 100 mg of dexlansoprazole was transferred to a volumetric flask (100 ml). This is followed by the addition of 50 ml of mobile phase. The contents of flask were sonicated for 20 min. The flask was filled to 100 ml mark with mobile phase. The solution was filtered by 0.45 µm membrane filter. The prepared stock standard capsule solution (1 mg/ml) was diluted appropriately with mobile phase to yield a concentration of 100 µg/ml dexlansoprazole. The capsule extract was injected to the HPLC column and eluted with mobile phase under the described chromatography conditions. The content of dexlansoprazole in capsule was computed from the regression equation or from calibration curve.

***Stress Study***

The stress study was performed following ICH guidelines (International Conference on Harmonization, 2003) with capsule solution at a dexlansoprazole concentration of 100 µg/ml. Acid hydrolysis was performed in 0.1N HCl (Sd. Fine Chemicals Ltd, Mumbai, India) with sonication for 30 min at room temperature. The hydrolysis in alkaline condition was carried out in 0.1N NaOH (Sd. Fine Chemicals Ltd, Mumbai, India) with 30 min sonication at room temperature. Oxidative degradation was carried at room temperature with 30 min sonication in 30% hydrogen peroxide (Sd. Fine Chemicals Ltd, Mumbai, India). For photolytic and thermal degradation, capsule powder in solid state was exposed to sun light for 24 hr and exposed to 105°C for 30 min in oven, respectively. Samples were withdrawn at suitable time, cooled, and neutralized by adding base (in acid hydrolysis) or acid (in alkaline hydrolysis) and subjected to analysis with the developed method after appropriate dilution.

## RESULTS AND DISCUSSION

***Method development***

In order to get well defined symmetrical peak with good sensitivity, several experimental trials were performed. Two different columns, Inertsil C8 (250 mm × 4.0 mm, 5.0 µm particle size) and Phenomenex C18 (150 mm × 4.0 mm, 5.0 µm particle size), were used for investigation of chromatography performance. Phenomenex C18 (150 mm × 4.0 mm, 5.0 µm particle size) was found suitable with respect to sensitivity. The photodiode array detector response of dexlansoprazole solution in mobile phase was investigated. The detection wavelength was fixed at 270 nm, as drug showed maximum response at 270 nm. Several alterations in the mobile phase compositions were tried to get improved performance characteristics. These alterations included, ratio of the organic modifier (methanol), pH and flow rate. A well defined peak, reasonable retention time and good sensitivity was achieved with 0.01 M $NaH_2PO_4$ (pH 7.0) and methanol in ratio 55:45 (v/v) with 1.0 ml/min flow rate (Figure 2).

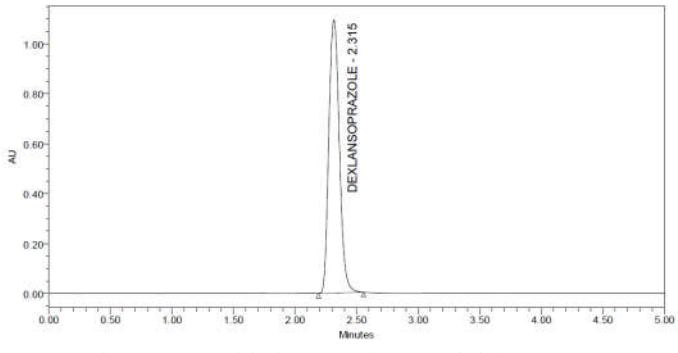


**Figure 2** Chromatogram of dexlansoprazole (100 µg/ml) in 0.01 M $NaH_2PO_4$ (pH 7.0) and methanol in the ratio of 55:45 (v/v) as mobile phase with 1.0 ml/min flow rate

***Method validation*** (International Conference on Harmonization, 2005, The United States Pharmacopoeia, 2004)

***System suitability***

System suitability was demonstrated from five replicate injections of dexlansoprazole solution containing 100 µg/ml. The percent relative standard deviation of dexlansoprazole peak area and dexlansoprazole retention time was calculated. Other parameters like column plate number and peak tailing factor was also determined. The developed method met these requirements within the United States Pharmacopoeia accepted limits (Table 1) (The United States Pharmacopoeia, 2004).

**Table 1** Separation characteristics of dexlansoprazole using optimized conditions

| Sample No. | RT | Peak area | Plate count | Tailing factor |
|---|---|---|---|---|
| 1 | 2.317 | 7243434 | 3623 | 1.16 |
| 2 | 2.314 | 7296705 | 3674 | 1.16 |
| 3 | 2.31 | 7260523 | 3714 | 1.16 |
| 4 | 2.308 | 7273762 | 3670 | 1.15 |
| 5 | 2.304 | 7242770 | 3667 | 1.16 |
| **Mean** | 2.311 | 7263438.800 | 3669.600 | 1.158 |
| **RSD (%)** | 0.220 | 0.312 | 0.880 | 0.386 |

***Selectivity***

The establishment of method's selectivity was carried out by investigating the interference of the excipients commonly used in the pharmaceutical formulation and components of the mobile phase. For this purpose, chromatograms of pure dexlansoprazole solution (100 µg/ml), blank mobile phase (without drug), blank placebo solution (contains common excipients) and capsule sample solution (100 µg/ml) were compared. The selectivity study results are depicted in Figure 3. The retention time of dexlansoprazole in capsule sample and in pure dexlansoprazole solution was similar (Figures 3.3 and 3.4). Figure 3.4 indicated that no interferences are found at the retention time of dexlansoprazole due to the excipients in capsule formulation. No peaks were observed in blank mobile phase and blank placebo (Figures 3.1 and 3.2). As a result, the developed method was considered to be selective and is appropriate to quantify dexlansoprazole in capsule dosage forms.

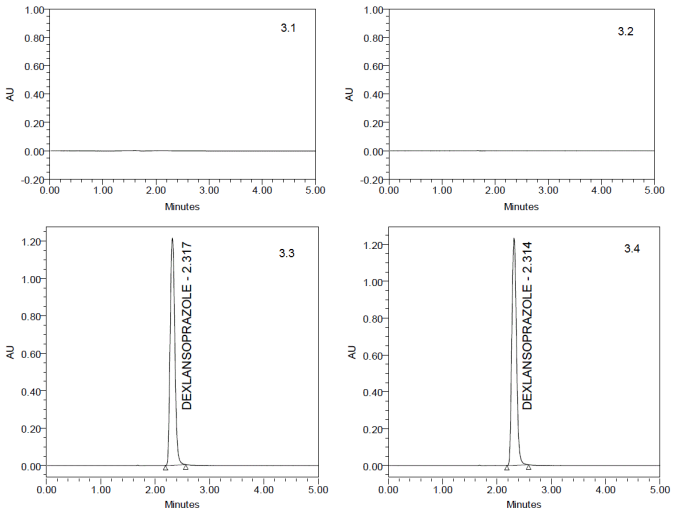


**Figure 3** Chromatogram of [3.1] Blank mobile phase [3.2] Blank placebo [3.3] Pure dexlansoprazole solution [3.4] Capsule sample solution

***Linearity and sensitivity***

The linearity of method was evaluated by increasing concentration of dexlansoprazole solution from 25 to 200 µg/ml. The calibration curve was obtained by plotting the dexlansoprazole peak areas against its concentration. The method was linear in the concentration range of 25–200 µg/ml that demonstrated good linearity of proposed method. The correlation coefficient of calibration curve was 0.9998. The regression equation was y = 72623 x - 151.1, where 'y' is peak area and 'x' is concentration drug.

Assessment of sensitivity of the assay method was performed by estimating the limits of detection (*LOD*) and quantitation (*LOQ*) following ICH recommendations. The LOD and LOQ were 0.189µg/ml and 0.631 µg/ml, respectively. Values demonstrated the adequate sensitivity of the method.

***Precision***

The method's intra-day repeatability was investigated by analyzing dexlansoprazole at three different concentrations (25µg/ml, 100 µg/ml, 200 µg/ml). The relative standard deviations of peak area response were less than 0.2% (Table 2). The low values of relative standard deviations indicated that the proposed method can be applied in the quantification of dexlansoprazole with satisfactory precision.

**Table 2** Proposed method repeatability

| Concentration (µg/ml) | Peak area (mAU) | Concentration (µg/ml) | Peak area (mAU) | Concentration (µg/ml) | Peak area (mAU) |
|---|---|---|---|---|---|
| 25 | 1819794 | 100 | 7268296 | 200 | 14533508 |
| 25 | 1815612 | 100 | 7264735 | 200 | 14551016 |
| 25 | 1816094 | 100 | 7260961 | 200 | 14543462 |
| 25 | 1817589 | 100 | 7260641 | 200 | 14542011 |
| 25 | 1811172 | 100 | 7260402 | 200 | 14570813 |
| 25 | 1813684 | 100 | 7265020 | 200 | 14589945 |
| **Mean** | 1815658 | **Mean** | 7263343 | **Mean** | 14555126 |
| **RSD (%)** | 0.165 | **RSD (%)** | 0.044 | **RSD (%)** | 0.146 |

***Accuracy***

The method's accuracy was established through analyzing dexlansoprazole at three different concentrations (25 µg/ml, 100 µg/ml, 200 µg/ml). The recent recoveries of dexlansoprazole were good (Table 3). The values of good recoveries indicated that the method has satisfactory accuracy for the quantification of dexlansoprazole.

**Table 3** Proposed method accuracy

| Concentration (µg/ml) | Recovery (%) | Concentration (µg/ml) | Recovery (%) | Concentration (µg/ml) | Recovery (%) |
|---|---|---|---|---|---|
| 25 | 99.82 | 100 | 99.67 | 200 | 99.65 |
| 25 | 99.59 | 100 | 99.62 | 200 | 99.77 |
| 25 | 99.61 | 100 | 99.57 | 200 | 99.71 |
| 25 | 99.69 | 100 | 99.56 | 200 | 99.70 |
| 25 | 99.34 | 100 | 99.56 | 200 | 99.90 |
| 25 | 99.48 | 100 | 99.62 | 200 | 100.03 |
| **Mean** | 99.59 | **Mean** | 99.60 | **Mean** | 99.79 |
| **RSD (%)** | 0.167 | **RSD (%)** | 0.046 | **RSD (%)** | 0.145 |

***Recovery study***

Recovery study was carried out for dexlansoprazole by spiking preanalyzed capsule sample solution with known amounts of pure dexlansoprazole at three concentration levels (50%, 100% and 150%). Recovery of dexlansoprazole at each concentration level was determined using the proposed method. Satisfactory recoveries ranging from 99.58 to 99.68% showed that the proposed method could be used to quantify accurately

dexlansoprazole accurately in capsule forms without interference from excipients.

**Table 4** Recovery results of proposed method

| Level (%) | Spiked (µg/ml) | Found (µg/ml) | Assay (%) | Mean recovery (%) |
|---|---|---|---|---|
| 50 | 50.00 | 49.82 | 99.63 | |
| 50 | 50.00 | 49.81 | 99.61 | 99.68 |
| 50 | 50.00 | 49.90 | 99.80 | |
| 100 | 100.00 | 99.59 | 99.59 | |
| 100 | 100.00 | 99.60 | 99.60 | 99.59 |
| 100 | 100.00 | 99.59 | 99.59 | |
| 150 | 150.00 | 149.35 | 99.57 | |
| 150 | 150.00 | 149.41 | 99.61 | 99.58 |
| 150 | 150.00 | 149.33 | 99.55 | |

***Specificity***

The stress conditions applied were adequate to degrade dexlansoprazole. Dexlansoprazole was degraded up to 5.28%, 5.04% when 0.1N HCl and 0.1N NaOH, respectively. Dexlansoprazole was degraded up to 4.38% under oxidative stress using 30% hydrogen peroxide. Dexlansoprazole was degraded up to 4.25% under thermal stress (105°C) and 4.79% under photolytic stress. Using stress study results it was concluded that Dexlansoprazole were not stable in acidic, basic, acidic, oxidative, photo and thermal conditions applied. The results of stress study are shown in Table 5.

Number of degradation products were produced under acidic (1 degradation peaks with retention time 1.818 min), basic (2 degradation peaks with retention times 1.875min and 9.514 min), oxidative (2 degradation peaks with retention times 1.821 min and 12.794 min), thermal stress (2 degradation peaks with retention times 1.358 min and 1.818 min) and photolytic stress (3 degradation peaks with retention times 1.872 min, 3.991 min and 5.204 min). The developed method separated the degradants from dexlansoprazole peak effectively (Figure 4.1-4.5). The peak purity and peak threshold values of dexlansoprazole indicted that the peak of dexlansaprazole is pure in all the degradation conditions applied. Thus, the developed method was considered specific for intended use and demonstrated its stability indicating nature.

**Table 5** Summary of dexlansoprazole degradation under different stress condtions

| Type of degradation | Peak area | Recovered (%) | Degraded (%) | Purity Angle | Purity Threshold |
|---|---|---|---|---|---|
| Undegraded | 7263438 | 100 | - | - | - |
| Acid | 6907433 | 94.72 | 5.28 | 0.836 | 1.291 |
| Base | 6924915 | 94.96 | 5.04 | 0.875 | 1.352 |
| Peroxide | 6973362 | 95.62 | 4.38 | 0.997 | 1.5 |
| Heat | 6982504 | 95.75 | 4.25 | 0.874 | 1.418 |
| Sunlight | 6942971 | 95.21 | 4.79 | 0.949 | 1.435 |

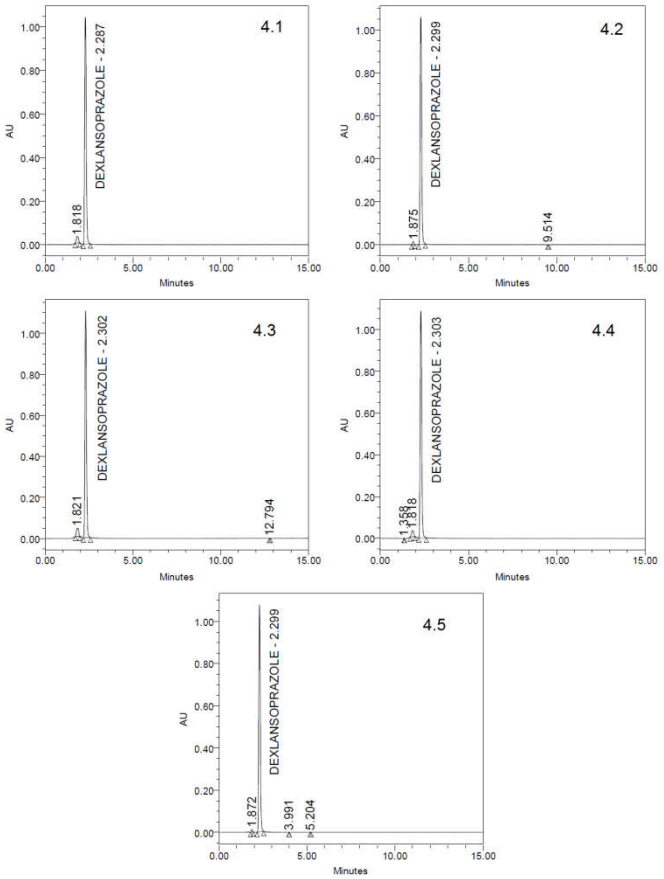


**Figure 4** Chromatogram of dexlansopraxole capsule sample after [4.1] Acid degradation [4.2] Base degradation [4.3] Oxidative degradation [4.4] Thermal degradation [4.5] Photo degradation

***Robustness***

Dexlansoprazole standard solution (100 µg/ml) were prepared and analyzed by variation of following chromatographic parameters: mobile phase flow rate (± 0.1 ml) and column temperature (± 2°C). System suitability parameters were determined for each condition and the obtained data were within the acceptable limits (Table 6). Hence, the proposed method is robust.

**Table 6** robustness results of the proposed method

| Chromatographic condition | Retention time (min) | Peak area | Plate count | Tailing factor |
|---|---|---|---|---|
| Flow rate 1.1 ml/min | 2.980 | 9388542 | 4167 | 1.13 |
| Flow rate 0.9 ml/min | 2.883 | 9437451 | 3633 | 1.27 |
| Column temperature 28°C | 2.285 | 7290138 | 3176 | 1.23 |
| Column temperature 32°C | 2.299 | 7246212 | 3554 | 1.20 |

## CONCLUSION

A stability indicating RP-HPLC method for the quantification of dexlansoprazole in bulk and capsule formulations was developed, optimized and validated. Dexlansoprazole linearity was demonstrated by proposed method over the range of 25–200 µg/ml. Method validation data demonstrate that developed method provides a sensitive, selective, accurate, precise and robust analytical approach allowing quantitative determination of dexlansoprazole. Good assay of dexlansopraxole was shown under different stress conditions using the developed method. the proposed method could be applied in quality control laboratories.

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