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RESEARCH ARTICLE

Determination of S-(−)-lansoprazole in dexlansoprazole preparation by capillary zone electrophoresis

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Abstract Capillary zone electrophoresis was successfully applied to the enantiomeric purity determination of dexlansoprazole using sulfobutyl ether-β-cyclodextrin and methyl-β-cyclodextrin as chiral selectors. Separations were carried out in a 50 μm, 64/56 cm fused-silica capillary. The optimized conditions included 90 mM phosphate buffer, pH 6.0, containing 30 mM sulfobutyl ether-β-cyclodextrin, 20 mM methyl-β-cyclodextrin as background electrolyte, an applied voltage of 25 kV and a temperature of 16 °C, detection was at 280 nm. The assay was validated for the S-(−)-lansoprazole in the range of 0.2–1.0%. The limit of detection was 0.07%, the limit of quantitation was 0.20%, relative to a total concentration of 4.0 mg mL^{-1}. Intra-day precision varied between 1.72 and 2.07%. Relative standard deviations of inter-day precision ranged between 1.62 and 1.96% for peak area ratio. The assay was applied for the determination of the chiral purity of dexlansoprazole capsules. Recovery in capsules was ranged between 101.7 and 103.1%.

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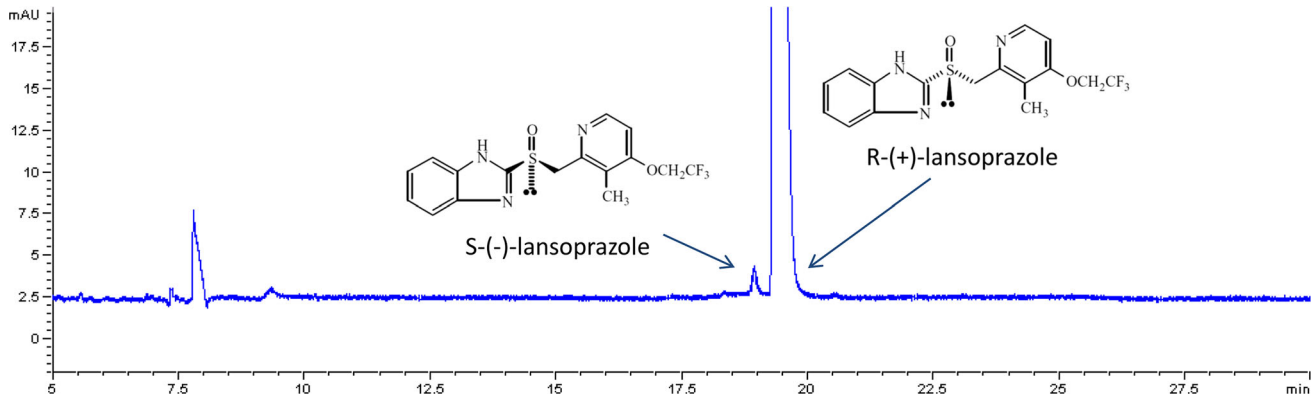
Graphical Abstract



Keywords Capillary electrophoresis · S-(−)-Lansoprazole · Enantiomeric impurity · Cyclodextrin derivatives · Dexlansoprazole preparation

Introduction

Lansoprazole 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl] methyl]-sulphinyl]-1H-benzimidazole (Fig. 1) is a proton pump inhibitor (PPI) that suppresses gastric acid secretion through interaction with (H^+/K^+)-ATPase in gastric parietal cells and has proved effective in the treatment of duodenal and gastric disorders (Barradell et al. 1992). This drug, which contains an asymmetric sulfur atom in its chemical structure, is clinically administered as a racemic mixture of R-(+)-lansoprazole and S-(−)-lansoprazole (Nevado et al. 2009).

In recent years, there has been a growing interest for pharmaceutical companies to develop enantiomerically pure gastric acid secretion inhibitors in a relation of the chiral switch to single enantiomer. Omeprazole has been developed and marketed as a single enantiomer (esomeprazole) under the trade name Nexium™. The S-(−) form of pantoprazole has been developed by Emcure Pharmaceuticals Ltd. in 2006 and it is known as Pantopure®. Studies on the extent of enantioselective binding of lansoprazole to human serum proteins estimated by ultrafiltration techniques showed that R-(+)-lansoprazole is greater bound than S-(−)-lansoprazole to human serum proteins ($P < 0.05$). Consequently, the R-(+)- enantiomer may be poorly distributed and slowly eliminated, resulting in a higher serum concentration than those of the S-(−)-lansoprazole. Therefore, the use of R-(+)-lansoprazole would be highly desirable for clinical application. It would be useful and imperative to develop a simple and suitable method for the measurement of S-(−)-lansoprazole in R-(+)-lansoprazole to be adapted for routine and in-process quality control analysis or similar studies (Cirilli et al. 2009).

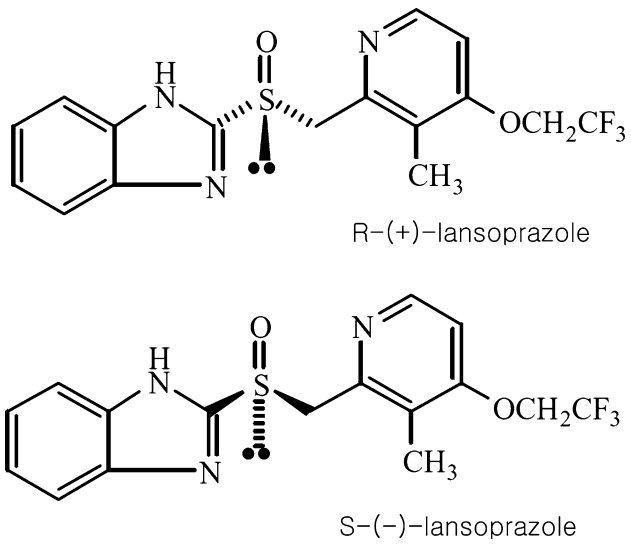


Fig. 1 Chemical structure of R-(+)-lansoprazole and S-(−)-lansoprazole

It is well known that pharmaceutical and clinical analyses depend mainly on high performance liquid chromatography (HPLC). Several HPLC methods have been used for enantioseparation of lansoprazole (Borner et al. 1998; Katsuki et al. 2001; Miura et al. 2004; Sun et al. 2015; Wang et al. 2015). On the other hand, capillary electrophoresis (CE) was introduced as an alternative technique for HPLC. Comparing with chromatographic techniques, capillary electromigration techniques require smaller amounts of chiral selectors and solvent and smaller sample volumes. These techniques also have many other advantages, such as high efficiency, high resolving capacity and various separation modes, as well as high flexibility in choosing and changing types of solvents and selectors (Lee et al. 2015). In future years, CE will influence many new research areas in academic and industrial laboratories because it complements well and successfully competes with the established instrumental techniques in chiral

analysis. In the words of one of the pioneers of modern CE, Professor J.W. Jorgenson "The high theoretical plate counts (100,000–200,000 plates in a typical capillary) make CE particularly amenable to separating chiral molecules" (Chankvetadze 1997).

In order to perform chiral discrimination, one or more chiral selectors are added into background electrolytes. The enantioseparation is based on the different binding constants of the enantiomers with the chiral selector and/or the different mobilities of the diastereomeric associates. Due to their good solubility in aqueous solvents, low toxicity, low UV absorbance and widespread application range, cyclodextrins have been extensively used for chiral separation in CE (Stavrou et al. 2015).

Nevado et al. reported a CE method for the determination of lansoprazole enantiomers in pharmaceuticals using β–CD as a chiral selector (Nevado et al. 2009). In this study, less effective enantiomer, S-(−)-lansoprazole appeared later in the chromatogram. This migration order may be a limitation for determination of enantiomeric impurity of R-(+)-lansoprazole because the small peak of S-(−)-lansoprazole may be easily overlapped by tailing region of R-(+)-lansoprazole's peak. Also, the concentration range validated in the study was 2–25 μg mL^{-1} which is not sufficient enough for enantiomeric impurity detection.

To the best of our knowledge, no validated CE method for enantiomeric purity determination of R-(+)-lansoprazole in bulk drug and commercial products has been published. In this study, we developed a CE method for determination of S-(−)-lansoprazole in R-(+)-lansoprazole material and pharmaceutical capsules using a dual chiral selector system consisted of sulfobutyl ether-β-cyclodextrin and methyl-β-cyclodextrin. The influences of buffer, cyclodextrin derivatives, capillary temperature and applied voltage were systemically investigated. Method validation was conducted according to ICH guideline Q2 (R1) (ICH: International Conference on Harmonisation 2005).

Materials and methods

Material

R-(+)-lansoprazole was purchased from Carbosynth (Berkshire, UK). Racemic lansoprazole was gifted by Daewoong Pharmaceutical Co., Ltd. (Seoul, Korea). β-cyclodextrin (β-CD), acetyl-β-cyclodextrin (A-β-CD), sulfated-β-cyclodextrin (S-β-CD), hydroxypropyl-β-cyclodextrin (HP-β-CD) and heptakis(2,6-di-O-acetyl-6-O-sulfo)-β-cyclodextrin (HEP-β-CD) were obtained from Sigma-Aldrich (St. Louis, MO, USA). Sulfobutyl ethers-β-cyclodextrin sodium salts (SBE-β-CD) was obtained from Cydex (La Jolla, CA, USA). Carboxymethyl-β-cyclodextrin (CM-β-CD) was obtained from Wacker (Munich, Germany) and methyl-β-cyclodextrin (M-β-CD), γ-cyclodextrin (γ-CD) was obtained from TCI (Tokyo, Japan). Other chemicals and reagents used in this study were of analytical grade and were purchased from Sigma-Aldrich unless otherwise indicated. The commercially available drug containing 60 mg of dexlansoprazole was purchased from Takeda Pharmaceutical Co. Ltd (Osaka, Japan). Deionized water was prepared in our laboratory using Aqua Max water purification system from Young Lin Instrument Co., Ltd. (Anyang, Korea).

Apparatus

All experiments were performed on an HP^{3D} CE system (Hewlett-Packard, Waldbronn, Germany) equipped with an on-column diode array detector (DAD). Instrument control and data acquisition was performed with the HP^{3D} CE ChemStation software. The capillary (Agilent Technologies, Waldbronn, Germany) was uncoated fused-silica capillaries of 50 μm ID. Capillaries had a total length of 64.5 and 56 cm to the detector. The capillary was thermostated at 16–30 °C. Buffer solution pH was determined with a SevenEasy pH meter (Mettler Toledo, Columbus, OH, USA).

Electrophoretic conditions

A new capillary was treated with 1 M sodium hydroxide (NaOH) for 10 min, 0.1 M NaOH for 20 min, 0.1 M phosphoric acid and water for 10 min each. At the beginning of the day, the capillary was rinsed with water, 0.1 M NaOH and 0.1 M phosphoric acid for 5 min each followed by flushing with water for 10 min. Prior to the injections, the capillary was washed subsequently with 0.1 M NaOH and water for 2 min each followed by a rinse with the background electrolyte for 5 min. At the end of the day, the capillary was flushed with water for 2 min, 0.1 M NaOH for 10 min, water for 1 min, 0.1 M phosphoric acid for 5 min and water for 10 min. Samples were introduced by hydrodynamic injection at 50 mbar for 7 s.

Preparation of standard solutions

All stock solutions were prepared weekly. 200 mg of R-(+)-lansoprazole was dissolved in 20 mL of 0.1 M NaOH to produce a concentration of 10.0 mg mL^{-1}. 10 mg of racemic lansoprazole was dissolved in 10 mL of 0.1 M NaOH to produce a concentration of 1.0 mg mL^{-1}. All stock solutions were stored at 4 °C. Working solutions of lansoprazole, its R-(+)-enantiomer was prepared daily in 0.1 M NaOH.

Calibration curves were prepared by taking appropriate aliquots of racemic lansoprazole, R-(+)-lansoprazole standard stock solutions and diluting with 0.1 M NaOH to obtain final concentrations of 0.2, 0.3, 0.4, 0.6, 0.8 and 1.0% for S-(−)-lansoprazole, relative to a total concentration of 4.0 mg mL^{-1}. All solutions (buffers, standards, and samples) were filtered through 0.45 μm pore size membrane and sonicated before use.

Preparation of pharmaceutical samples

Available commercial brand of capsules containing 60 mg of dexlansoprazole (R-(+)-lansoprazole) were chosen for testing the suitability of the proposed method. The contents of 10 capsules (equivalent to about 600 mg of R-(+)-lansoprazole) were transferred to a 100 mL volumetric flask containing 20 mL of 0.1 M NaOH and sonicated until completely disintegrate. After adding 3 mL of acetonitrile, the flask was vortex mixed for 5 min to ensure complete dissolution of the drug. Then 0.1 M NaOH was added to make 100 mL of approximately 6.0 mg mL^{-1} of dexlansoprazole. The resultant solution was pre-filtered through filter paper to remove large particles before diluting with 0.1 M NaOH to produce 4.0 mg mL^{-1} of R-(+)-lansoprazole. This solution was filtered through 0.45 μm pore size membrane to completely remove excipients and introduced to capillary. The amount of S-(−)-lansoprazole was calculated from the corresponding regression equation.

Method validation

The assay was validated for concentrations that referred to a range of 0.2–1.0%. Method validation was conducted according to ICH guideline Q2 (R1) (ICH: International Conference on Harmonisation 2005) with regard to linearity, limit of detection (LOD) and limit of quantitation (LOQ), precision and accuracy and robustness of the method.

Linearity was constructed with six different S-(−)-lansoprazole percentages: 0.2, 0.3, 0.4, 0.6, 0.8 and 1.0% relative to a total concentration of 4.0 mg mL^{-1}. Detection and quantification limits were based on signal-to-noise ratio, 3:1 and 10:1, respectively.

The intraday precision was calculated from five replicate injections of three concentrations in the same day. The interday precision and accuracy were based on three replicate injections of three concentrations on three consecutive days.

Accuracy was determined by recovery test which was performed by adding known amounts of the standard at low (80% of the known amount), medium (same as the known amount) and high (120% of the known amount) levels. The spiked samples were then extracted, processed, and quantified in accordance with the methods mentioned above. Three replicates were performed for the test.

Results

Selection of chiral selector system

The selectivity of enantiomeric separation for a given analyte will obviously depend on the nature of the cyclodextrin added to the background electrolyte (Fillet et al. 1998). To find the suitable condition for enantiomeric impurity determination of dexlansoprazole, preliminary experiments were conducted at different pH and buffers with different compositions. In the preliminary analysis, we used 100 mM phosphate buffer (pH 2.5 and pH 6.0) and 100 mM borate buffer (pH 7.0) as background electrolytes (BGE), buffer pH was modified by the addition of 0.1 M acid phosphoric, 0.1 M NaOH and 1.0 M acid boric solution. Various types of cyclodextrins were investigated: native CDs (β-CD, γ-CD), neutral CDs (M-β-CD, A-β-CD, HP-β-CD) and negatively charged CDs (CM-β-CD, HEP-β-CD, S-β-CD, SBE-β-CD). Lansoprazole is a weak base (Cirilli et al. 2009). It was pointed out by Stavrou et al. (2015) that the negatively charged CDs are more widely used than the positively charged CDs because a broad spectrum of analytes chiral compounds are pharmaceuticals, which are mostly basic and positively charged. Thus, positively charged CDs were not included in this study. As can be seen from Table 1, the use of single chiral selector did not successfully resolve the two enantiomers, so we conducted further investigations using dual chiral selector systems. Because the charged CD derivatives possess a self-electrophoretic mobility which is absent in native and neutral CD (Chankvetadze 1997), the combination of two neutral CDs, two native CDs, neutral and native CD were not tested to reduce the number of experiments. Additionally, among the natively charged CDs, SBE–β-CD was considered high potential for chiral CE separation (Chankvetadze 1997). Therefore, SBE-β-CD was paired with other CDs to form dual systems. When combination SBE-β-CD (hepta-substituted preparation), and M-β-CD (mixture of several methylated, mean degree of substitution: 10.5–14.7), in phosphate buffer pH 6.0 was used, lansoprazole enantiomers (at a concentration of 500 μg mL^{-1} each) were resolved with the resolution of 3.36 (Table 1).

Optimization of the electrophoretic conditions

CE is usually used for the analysis of charged compounds and therefore the role of pH of the medium where the separation take place is important. The effective charge

Table 1 Effect of chiral selectors on the enantioseparation of lansoprazole enantiomers

Chiral selector	Concentration of chiral selector (mM)	Buffer pH	R_s
β-CD	20	2.5	1.43
		7.0	–
γ-CD	20	2.5	0.98
		7.0	0.47
M-β-CD	20	2.5	1.52
		7.0	0.71
A-β-CD	20	2.5	–
		7.0	–
HP-β-CD	20	2.5	1.00
		7.0	–
CM-β-CD	20	2.5	–
		7.0	0.17
HEP-β-CD	20	2.5	–
		7.0	0.47
S-β-CD	20	2.5	–
		7.0	–
SBE-β-CD	20	2.5	–
		7.0	0.90
SBE-β-CD	30	7.0	1.68
γ-CD	20		
SBE-β-CD	30	6.0	2.51
γ-CD	20		
SBE-β-CD	30	6.0	3.36
M-β-CD	20		

"-" not separated

Concentration of each enantiomer: 500 μg mL^{-1}

Experiment condition: fused-silica capillary 64.5 cm, 50 μm I.D. (effective length 56 cm), hydrodynamic injection (7 s at 50 mbar), 15–30 kV, 16 °C and detection at 280 nm

and, consequently, the mobility of an analyte directly depend on the pH. Additionally, the EOF in a bare silica capillary, the self mobility of charged chiral selectors and the chiral recognition ability are also pH dependent (Chankvetadze 1997).

Lansoprazole is unstable in acid media, which facilitate its oxidation by air. Under especially unfavorable conditions, the compound can be degraded within only a few hours (Nevado et al. 2009). Thus, the effect of buffer pH on the resolution of lansoprazole enantiomers was studied using pH values at 5.5, 6.0, 6.5 and 7.0 with 90 mM phosphate buffer and containing 20 mM SBE-β-CD and 20 mM M-β-CD as BGE with applied voltage at 25 kV and capillary temperature of 16 °C. As shown in Fig. 2a, with an increased pH value, EOF increased, thus migration time decreased. However, higher resolution between the two isomers was only obtained when pH values were decreased. To compromise between good separation and acceptable analysis time, pH 6.0 was chosen.

At optimized pH, the effect of the buffer concentration was studied in the range of 50–130 mM, maintaining 20 mM SBE-β-CD and 20 mM M-β-CD as BGE with applied voltage at 25 kV and capillary temperature 16 °C in all prepared electrolytes. A 90 mM buffer concentration was selected to obtain good peak shape and low current in order to minimize the noise and baseline aberrations (Fig. 2b).

The effect of M-β-CD concentration was studied in the range of 10–25 mM for the enantioseparation of lansoprazole. As shown in Fig. 2C, with increased concentration of M-β-CD from 10–20 mM, the migration time decreased while resolution of lansoprazole enantiomers increased. But at the concentration of 25 mM, the migration time continued to decreased but resolution of lansoprazole enantiomers decreased. It is predicted theoretically by Chankvetadze (1997) that an optimum concentration of the chiral selector for the mobility difference should exist for each particular enantiomeric pair, many experimental studies (Shibukawa et al. 1993; Penn et al. 1993; Guttman and Cooke 1994) also indicated that a further increase in the concentration of the chiral selector over the optimum concentration may lead to a decrease in the resolution. As a consequence, 20 mM M-β-CD was selected as optimum for the enantioseparation of lansoprazole.

At optimized condition of pH, buffer concentration and M-β-CD concentration, the influence of SBE-β-CD concentration was investigated in the range of 10–35 mM. As shown in Fig. 2d, when SBE-β-CD concentration increased, both migration time and resolution increased. At 35 mM, best resolution was observed but two enantiomers were retained more than 40 min. As a consequence, SBE-β-CD concentration of 30 mM was selected as optimum for the enantioseparation of lansoprazole.

The effect of applied voltage on the enantioseparation was studied in the range 10–30 kV by steps of 5 kV. Raising the voltage led to shorter migration time and sharper peaks. However, increasing voltage also resulted in high current, increased Joule heating and degraded compound. A significant decrease in peak areas was observed when 30 kV voltage was applied. Hence, 25 kV was chosen as the applied voltage (Fig. 3a).

Controlling the capillary temperature in CE is important in order to avoid unwanted changes in EOF, efficiency, viscosity, electrophoresis mobility and migration time. The effect of temperature was investigated in the range of 16–30 °C. Increasing the capillary temperature resulted in decreased migration time and also in poorer resolution (Fig. 3b), probably by effect of restricted solute–CD interaction. As a consequence, the experiments were all

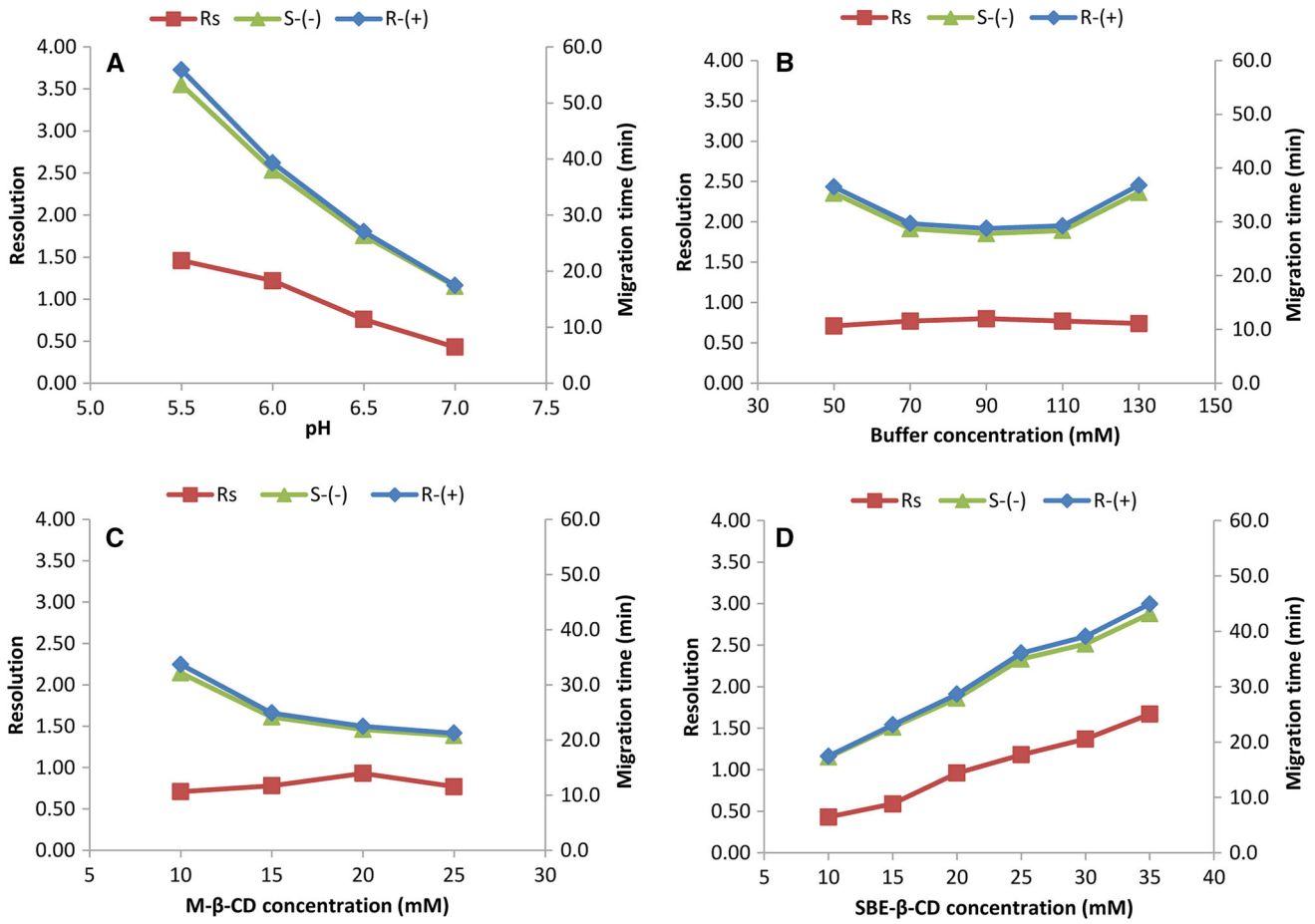


Fig. 2 Effects of pH (**a**), buffer concentration (**b**), M-β-CD concentration (**c**) and SBE-β-CD concentration (**d**) on migration time and resolution of lansoprazole enantiomers

done at 16 °C of the temperature providing the best compromise between resolution and runtime.

The selected electrophoretic conditions were a buffer consisted of 90 mM phosphate adjusted to pH 6.0, 30 mM sulfobutyl ether-β-CD, 20 mM methyl-β-CD, 25 kV of applied voltage and 16 °C of capillary temperature. From this optimized method, it can be ascertained that the selected electrophoretic procedure provided a good separation of lansoprazole enantiomers.

Determination of impurity in R-(+)-lansoprazole standard

The content of impurity in R-(+)-lansoprazole was investigated by injecting six replicates each of three concentrations 2.0, 4.0 and 6.0 mg mL^{-1}. At the concentration of 2.0 mg mL^{-1}, no other peaks near R-(+)-lansoprazole were observed. However, when the concentration increased to 4.0, 6.0 mg mL^{-1} a small peak appeared near R-(+)-lansoprazole with increased area relative to concentrations which demonstrated presence of S-(−)-lansoprazole. An estimation of 0.076% of S-(−)-lansoprazole (relative to the R-(+)-lansoprazole concentration of 6.0 mg mL^{-1}) was calculated from peak area ratios. Figure 4a, b showed the electropherograms of 0.1 M NaOH (blank) and 4.0 mg mL^{-1} R-(+)-lansoprazole standard, respectively.

Stability of solutions

The stability of racemic lansoprazole and R-(+)-lansoprazole in sodium hydroxide solutions was studied by keeping the samples in tightly capped volumetric flasks both at 4 °C and at room temperature. The samples were analysed every 12 h and peak areas compared.

Lansoprazole enantiomers were found to be stable in sodium hydroxide solution for at least 10 days when stored at 4 °C and 2 days when stored at room temperature with RSD value under 2%. No degradation products were detected.

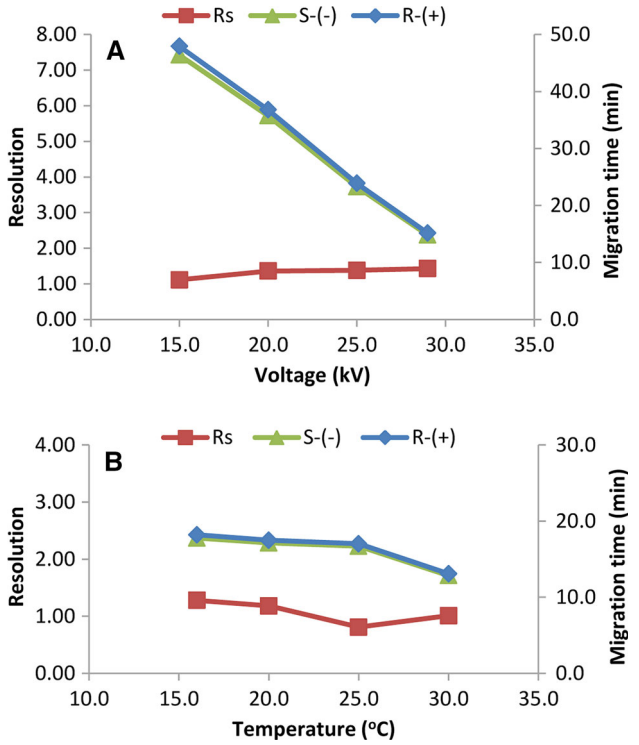


Fig. 3 Effects of applied voltage (**a**) and capillary temperature (**b**) on migration time and resolution of lansoprazole enantiomers

Method validation

Specificity

In this study, we validated the purity of the peaks for S-(−)-lansoprazole and R-(+)-lansoprazole by comparing the absorbance ratios of two enantiomers at four different wavelengths: 214; 280; 292 and 306 nm. The absorbance ratios of two enantiomers (at a concentration of 500 μg mL^{-1} each) were remained 0.97 at four wavelengths, showed the peaks for S-(−)-lansoprazole and R-(+)-lansoprazole to be highly pure.

System suitability

System suitability was tested by performing six replicate injections and determining migration time and peak area ratios, theoretical plate number (N), resolution (Rs), and symmetry factor (As) for the analyte of interest. The relative standard deviations (RSD) of these properties were used as indicators of system suitability. The migration time of S-(−)-lansoprazole was 19.71 min, that of R-(+)-lansoprazole was 19.95 min (Fig. 4c). RSD of migration time of S-(−)-lansoprazole and R-(+)-lansoprazole were 2.00 and 1.39%, respectively. The mean value of N for S-(−)-lansoprazole, R-(+)-lansoprazole were 385,354 and 37,363 respectively. Similarly, as value were 0.72; 0.14. The band broadening problem probably because of high concentration of SBE-β-CD resulted in electrodispersion of the peaks due to the conductivity mismatch between the solute–selector complexes and the BGE, so-called (Chankvetadze 1997). However, as can be seen from Fig. 4c, S-(−)-lansoprazole and R-(+)-lansoprazole were baseline separated. RSD of the peak area ratio of S-(−)-lansoprazole and R-(+)-lansoprazole was 1.46%.

Linearity

For the purpose of calibration, a long series of mixed standard solution, including R-(+)-lansoprazole spiked with its S-(−)-enantiomer in different concentrations, was examined under the optimized conditions. The peak area ratios on the concentration of S-(−)-enantiomer in R-(+)-lansoprazole were studied over the range of 0.2–1.0%, relative to a total concentration of 4.0 mg mL^{-1}. The linearity was expressed as r^2, which was 0.9992 for S-(−)-lansoprazole, y-intercept and slope of the regression line were shown in Table 2. The LOD and LOQ concentration were estimated to be 0.07 and 0.20% for the S-(−)-enantiomer, when signal-to-noise ratios of 3 and 10 were used as the criteria.

Precision

The precision of method were evaluated using intra- and inter-day variations of three concentrations: 0.2, 0.4 and 0.6% S-(−)-lansoprazole. The results of precision were reported in Table 3. Intra-day precision (RSD) ranged from 1.72 to 2.07% with the recovery from 99.5 to 100.6%. Inter-day precision (RSD) ranged from 1.62 to 1.96% with the recovery from 99.6 to 100.4%.

Accuracy (recovery)

Table 4 showed a summary of recovery in capsules sample. The developed method had good accuracy with overall recovery of 101.7–103.1% with RSD <1.5% for the analyte. Considering the results of the recovery test, the method was deemed to be accurate.

Robustness

The robustness of an analytical procedure refers to its capability to remain unaffected by small and deliberate variations in method parameters without changes in quantitation. For the determination of the method's robustness, three factors (parameters) were selected from the analytical procedure to be examined in the robustness testing:

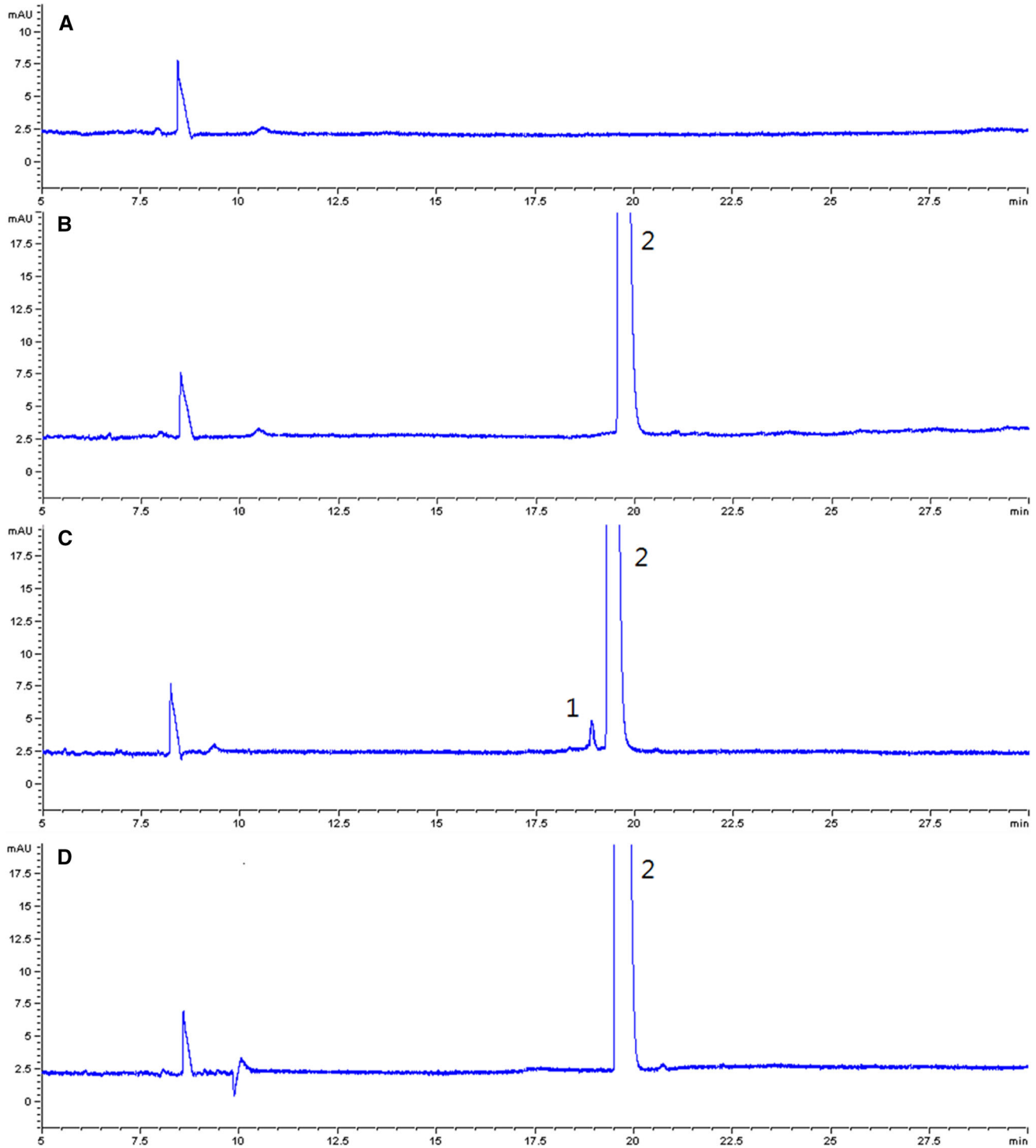


Fig. 4 Typical electropherograms of S-(−)-lansoprazole, R-(+)-lansoprazole. Operating condition: BGE solution: phosphate buffer (pH 6.0, 90 mM) containing 30 mM using SBE-β-CD and 20 mM M-β-CD; fused-silica capillary 64.5 cm, 50 μm I.D; hydrodynamic injection (7.0 s at 50 mbar); applied voltage from 25 kV and capillary temperature from 16 °C, detection at 280 nm. **a** blank, **b** R-(+)-lansoprazole standard, **c** R-(+)-lansoprazole spiked with S-(−)-lansoprazole, **d** sample prepared from dexlansoprazole capsules. Peak *1*: S-(−)-lansoprazole (16 μg mL^{-1}). Peak *2*: R-(+)-lansoprazole (4.0 mg mL^{-1})

Concentration of SBE-β-CD 30 ± 2 mM; applied voltage 25 ± 2 kV; temperature 16 ± 2 °C. Relative standard deviations of peak ratios were not more than 2.16% indicated that these minor changes from the optimized conditions barely affected the peak area ratio of the studied lansoprazole enantiomers.

Table 2 Regression curve and sensitivity data of the proposed method

Parameter	S-(−)-lansoprazole
Slope ± SD	0.0103 ± 0.0003
Intercept ± SD	0.0001 ± 9.9933E − 05
Correlation coefficient (r^2)	0.9992
Number of data points	6
Linearity range (%)	0.20–1.00
Detection limit (%)	0.07
Quantification limit (%)	0.20

Table 3 Intra- and inter-day precision of the proposed method

Con. (%)	Intra-day (n = 5)		Inter-day (n = 11)	
	RSD (%)	Recovery (%)	RSD (%)	Recovery (%)
0.20	1.93	100.6	1.96	99.6
0.40	1.72	99.6	1.62	99.7
0.60	2.07	100.7	1.82	100.4

Table 4 Recoveries for the assay of S-(−)-lansoprazole in dexlansoprazole capsules

Sample	Concentration (%)			Recovery (%)	RSD (%)
	Original	Added	Found		
A	ND	0.32	0.33	103.1	1.41
B	ND	0.40	0.41	102.1	1.28
C	ND	0.48	0.49	101.7	1.16

Recovery (%) = [(found − original)/added] × 100

ND not detected (under LOD), *A* the samples added known amounts of standards at low level, *B* the samples added known amounts of standards at medium level, *C* The samples added known amounts of standards at high level

Application to capsules sample

The method was applied to determine S-(−)-enantiomer in commercial dexlansoprazole capsules (60 mg). An electropherogram of sample from dexlansoprazole is shown in Fig. 4D. The amounts of S-(−)-lansoprazole in dexlansoprazole capsules could be calculated using calibration curve method. However, S-(−)-lansoprazole was not detected in six capsules samples analysed, probably because the amount of S-(−)-lansoprazole in capsules was less than method's LOD which was 0.07%. Recoveries in capsules were ranged between 101.7 and 103.1% with RSD <1.5% (Table 4).

Discussion

In conclusion, this paper described the development, optimization, validation and application of a CE method for the quantitative analysis of S-(−)-lansoprazole in R-(+)-lansoprazole material and commercial capsules. The use of single enantiomer standard with the simple preparation made the present method more promised for quality control and similar studies of dexlansoprazole. This method is satisfactory in terms of accuracy, precision, sensitivity, and robustness. It has been successfully applied to commercial capsules without any interference from the excipients.

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Compliance with ethical standards

Conflict of interest All authors declared no conflict of interest.

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