Rajendraprasad and Basavaiah *Journal of Analytical Science and Technology* (2019) 10:37
https://doi.org/10.1186/s40543-019-0192-2

Journal of Analytical Science and Technology

RESEARCH ARTICLE Open Access

Development of membrane electrodes for selective determination of lisinopril in pharmaceuticals

Nagaraju Rajendraprasad[1*] and Kanakapura Basavaiah[2]

Abstract

Background: Lisinopril (LNP) is an angiotensin-converting enzyme inhibitor used as anti-hypertensive, cardiovascular, in anti-prophylactic and anti-diabetic nephropathy drug. Development of two new, simple, low cost, and selective membrane-based ion-selective electrodes has been proposed for the determination of LNP in pharmaceuticals.

Methods: The electrodes are based on poly(vinyl)chloride membrane doped with LNP-phosphotungstic acid (LNP-PTA) and LNP-phosphomolybdic acid (LNP-PMA) ion-pairs as molecular recognition materials.

Results: The developed LNP-PTA and LNP-PMA electrodes are applicable for the determination of LNP over the linear range of 5×10^{-5}–2.4×10^{-3} mol l^{-1}. The working pH ranges to measure potentials were 2.5 to 6.4 and 2.3 to 6.0 for LNP-PTA and LNP-PMA ISEs, respectively. The electrodes displayed the rapid Nernstian responses as revealed by the values of slopes 55.06 and 52.39 mV/decade, with limit of detection (LOD) values of 1.2×10^{-5} and 1.18×10^{-5} mol l^{-1} for LNP-PTA and LNP-PMA electrodes, respectively. The limits of quantitation (LOQ) values have also been calculated for both the electrodes. The developed electrodes have potential stability for up to 1 month and emerged as highly selective for the determination of LNP over other spiked ions and compounds.

Conclusions: The proposed electrodes have been validated and found that they are suitable for the determination of LNP in pharmaceuticals in pure form and in dosage forms. The results obtained in the analysis of LNP using proposed electrodes have been compared statistically with reference method's results to assess the accuracy and precision. Robustness and ruggedness of the developed electrodes have also been checked and found satisfactory. The recovery studies have been performed by standard addition procedure to assess the role of excipients in tablets containing LNP and the results obtained are satisfactory.

Keywords: Lisinopril, Cardiovascular drug, Ion-selective electrode, Pharmaceuticals

Background

Lisinopril (LNP) {1-[6-Amino-2-(1-carboxy-3-phenyl-propylamino)-hexanoyl]-pyrrolidine-2-carboxylic acid} (Fig. 1) is an angiotensin-converting enzyme inhibitor used in the treatment of hypertension and heart failure, in prophylactic treatment after myocardial infarction, and in diabetic nephropathy (Parfitt, 1999). Historically, LNP was the third ACE inhibitor, after captopril and enalapril, and was introduced into therapy in the early 1990s (Patchett et al. 1980).

The drug LNP is official in the British (BP) (The British Pharmacopoeia, 1998) and United States (US) pharmacopoeias (The US Pharmacopoeia, 2000). The British Pharmacopoeia (BP) describes a monograph of potentiometric titration of aqueous solution of the tablet containing LNP with 0.1 M NaOH and US Pharmacopoeia (USP) describes a chromatographic procedure for assay of LNP using C-8 (octylsilyl-silane) column at 50 °C and phosphate solution-acetronitrile (96:4 v/v) as mobile phase with UV detection at 215 nm.

* Correspondence: prasadtnpur@gmail.com
[1]PG Department of Chemistry, JSS College of Arts, Commerce and Science, Autonomous College of University of Mysore, B N Road, Mysuru, Karnataka 570 025, India
Full list of author information is available at the end of the article

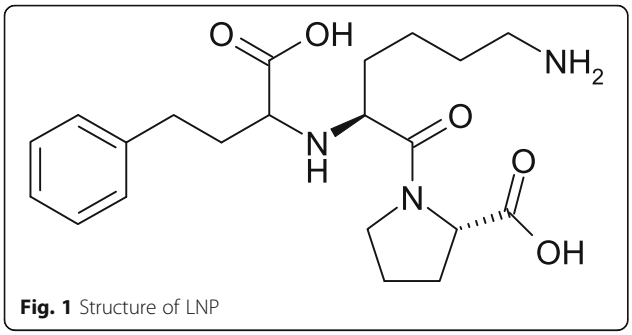


Fig. 1 Structure of LNP

Various analytical procedures were found in the literature for the determination of LNP using titrimetric (Basavaiah et al., 2010), visible spectrophotometric (Rahman et al., 2007; El-Yazbi et al., 1999; Rahman et al., 2005; El-Gindy et al., 2001; Paraskevas et al., 2002; Nafisur et al., 2005; Asad et al., 2005; Rajasekaran, and Udayavani, 2001; Basavaiah et al., 2009; Razak et al., 2003), derivative UV absorption spectrophotometric (El-Yazbi et al., 1999; Bonazzi et al., 1997a, b; Durisehvar and Hulya, 1999; Beata, 2005; Erk, 1998; Prasad et al., 1999; Jain and Agrawal, 2000; Mashru and Parikh, 2000), high-performance liquid chromatographic (HPLC) (The US Pharmacopoeia, 2000; Ivanoic et al., 2007; Nevin and Murat, 1999; Sane et al. 1992; Bonazzi et al., 1997a, b; El-Gindy et al., 2001; Christopher et al., 2004), high-performance thin layer chromatographic (HPTLC) (Pandya et al., 2017), gas chromatographic (Avadhanulu and Pantulu, 1993), capillary electrophoretic (Qin et al., 1993; Gotti et al. 2000), spectrofluorimetric (El-Gindy et al., 2001; Esra et al., 2003; Zacharis et al. 2004), and polarographic (Razak et al. 2003; El-Enany, Belal, and Al-Ghannam, 2003; Rajasekaran and Murugesan, 2001) techniques.

The performance characteristics of the reported and proposed analytical methods of LNP are presented in Table 1.

A report (Abdel-Fattah et al., 2010) describing preparation and uses of ion-selective electrode for study of plasma and plasma protein effect is found in the literature. The procedure describes the use of precipitate of LNP and bathophenanthroline-ferrous ion in polyvinyl chloride (PVC) and hydroxypropyl ß-cyclodextrin-based technique for the preparation of tecoflex-graphite sensors. These procedures are not applicable to determine LNP in pharmaceuticals.

Analytical methods with potentiometry and ion-selective electrodes are very popular for their simplicity, excellent applicability, robust and rugged working ability, and selectivity for the accurate and precise determination of analytes such as metal ions or molecular analytes directly. Researchers have reported (Vinod et al., 2011a, b; Vinod et al., 2013; Suresh et al., 1995a, b; Vinod et al., 2015; Vinod et al., 2014a, b; Suresh et al., 1996; Vinod et al., 2011c; Vinod et al., 2014a, b; Mehmet et al., 2014; Vinod et al., 2015a; Vinod et al., 2015b; Karimi-Maleh et al., 2015; Vinod and Pankaj, 1999; Ajay et al., 1995a, b) the use of variety of such electrochemical sensors for the determination of metals and pharmaceuticals in different real samples.

Since the drug LNP is a commonly used cardiovascular drug, a simple analytical method for its measurement is highly essential. Because of ever-increasing need for analytical methods with acceptable sample throughput, lower limit of detection, and low cost of maintenance, new methods are constantly being developed; therefore, it is imperative to develop a simple and suitable analytical method for the measurement of this drug in bulk and pharmaceutical preparations.

The reports being presented here are intended to propose two new ion-selective electrodes for the determination of LNP in pharmaceutical samples. The preparation of ion-selective membrane, fabrication of electrode, and its application to develop reliable, selective, accurate, precise, robust, and rugged analytical methods to determine LNP are proposed and presented in this report.

Methods

Apparatus

PICO digital dual channel potentiometer (Chennai, India) was used for measurement of potential. An Elico (Mumbai, India) conductivity meter with a cell of unit cell constant was used for conductometric titration. The double junction Ag/AgCl electrode (Metrohm) was used as reference electrode in conjunction with working ion-selective electrodes. An Elico pH meter (Mumbai, India) was used for measurement of pH. Silver and copper wires were used in all potential measurements.

Chemicals and reagents

All the chemicals and reagents used were of analytical grade. Distilled water was used throughout the work. The pure LNP (99.8%) was kindly provided by Cipla India Ltd. Listril tablets (10 mg LNP/tablet) (Torrent pharmaceuticals Ltd) were purchased from local commercial sources. Phosphotungstic acid (PTA), phosphomolybdic acid (PMA), tetrahydrofuran (THF), polyvinyl chloride (PVC), dioctyl phthalate (DOP), dibutyl sebacate (DBS), o-nitrophenyl octylether (NPOE), ammonia (NH_3), and concentrated sulphuric acid (H_2SO_4) (98% v/v, Sp. gr. 1.835) were supplied by S. D. Fine Chem Ltd, Mumbai, India.

The aqueous solutions of 0.01 mol l^{-1} of PTA and PMA were prepared by dissolving the required weights of the respective compound in distilled water and used in the preparation of ion-association complexes with LNP.

Table 1 Performance characteristics of existing methods of LNP

Sl. no.	Reagent(s)	Technique and methodology	Range	Remarks	Reference
1	NaOH	Potentiometric titration of LNP with 0.1 M NaOH	350 mg	Less sensitive method	British Pharmacopoeia, 1998
2	Mixture of phosphate: acetronitrile (96:4 v/v)	Chromatographic assay using C_8 (octylsilyl-silane) column at 50 °C with UV detection at 215 nm	-	Sophisticated instrument required	US Pharmacopoeia, 2000
3	NaOH, NaOMe, methanolic KOH, CH_3COOH, $HClO_4$	Titration of LNP with (a) $HClO_4$	2–20 mg	Large sample size (in milligramme levels) required	Basavaiah et al., 2010
		(b) NaOH	1–10 mg		
		(c) NaOMe and	2–20 mg		
		(d) KOH	5–15 mg		
4	N-Bromosuccinimide	Ultraviolet spectrophotometric determination by measuring absorbance at 353 nm	10–200 μg ml^{-1}	Less sensitive, use of organic solvents, measure at shorter wavelength	Rahman et al., 2007
	Chloranil	-	24–600 μg ml^{-1}		
5	Chloranil	Spectrometric detection of LNP at 346 nm	4–20 μg ml^{-1}	pH dependent, use of toxic reagents	El-Yazbi et al., 1999
	Dichlone	Measurement of absorbance of LNP-Dichlone at 580 nm	40–120 μg ml^{-1}		
	AcAc and HCHO	Spectrometric detection of LNP at (a) 356 nm	6–42 μg ml^{-1}		
		(b) 475 nm (fluorescence intensity)	0.03–0.27 μg ml^{-1}		
6	7,7,8,8-Tetracyanoquinodimethane	Spectrometric assay of LNP using TCQD by measuring absorbance at 743 nm	2–26 μg ml^{-1}	Expensive chemicals and organic solvent required	Rahman et al., 2005
	p-Chloranil	Spectrophotometric assay of LNP using p-chloranil by measurement of C-T complex at 525 nm	25–300 μg ml^{-1}		
7	(a) $NaClO_4$- phenyl hydrazine	Measurement of absorbance of condensation product of lisiniopril with $NaClO_{4-}$ phenyl hydrazine at 362 nm	40–200 μg ml^{-1}	Shorter wavelength employed for measurement of absorbance	El-Gindy, Ashour, Abdel-Fattah, and Shabana, 1991
	o-Phthalaldehyde	Spectrofluorimetric measurments at 340 and 455 nm of excitation and emission wavelengths	20–180 ng ml^{-1}	Less cost-effective technique	
	Mobile phase of methanol, water, and triethylamine in a ratio of 50:50:0.1 v/v and (pH 2.6)	HPLC analysis using 250 × 4.6 mm (i.d.) ILS Hypersil Silica (5 μm particle size) column and with UV detection at 210 nm	4–28 μg ml^{-1}	Sophisticated analytical technique required	
	o-Phthalaldehyde, 2-mercaptoethanol, borate buffer pH 9.5	The fluorescence of the reaction product measured upon excitation at a maximum of 340 nm with emission wavelength at 455 nm	20–180 ng ml^{-1}	Sophisticated analytical technique required	
8	1-Fluoro-2,4-dinitrobenzene (FDNB)	Measurement of absorbance at 356.5 and 405.5 nm	20–120 μg ml^{-1}	Less sensitive method	Paraskevas et al., 2002
9	(a). Ninhydrin i. Initial rate ii. Rate-constant	Measurement of absorbance of product at 595 nm	10–50 μg ml^{-1}	Kinetic studies; organic solvent used, rate is critically dependent on experimental variables	Nafisur et al., 2005
	(b) Ascorbic acid	Measurement of absorbance of product at 530 nm	5–50 μg ml^{-1}		
10	Ninhydrin	Measurement of absorbance at 600 nm	10–	Organic solvent required	Asad et al., 2005

Table 1 Performance characteristics of existing methods of LNP *(Continued)*

Sl. no.	Reagent(s)	Technique and methodology	Range	Remarks	Reference
			150 μg ml^{-1}		
11	Ninhydrin	Measurement of absorbance at 410 nm	10–40 μg ml^{-1}		Rajasekaran and Udayavani, 2001
12	Ninhydrin	Measurement of absorbance of LNP-ninhydrin reaction product at 420 nm	5–50 μg ml^{-1}	Less sensitive method	Basavaiah et al., 2009
13	Dimethylsulphoxide, methanol, and 2,4-dinitrofluorobenzene	Measurement of coloured product formed between lisinopril and 2,4-dinitrofluorobenzene in methanolic medium at 400 nm	4–24 μg ml^{-1}	Less sensitive and toxic solvents used	Razak et al. 2003
		The differential pulse polarographic measurement was performed with a − 50-mV pulse amplitude. The polarograms were recorded from − 500 to − 1200 mV vs Ag/AgCl reference electrode at a scan rate of 10 mV s^{-1}	4–14 μg ml^{-1}	Less cost-effective, less robust, and rugged method	
14	(a) 0.1 M Phosphate buffer (pH 2.8)–methanol (75:25 v/v)	Measurement of absorption by A. 1st derivative spectrometry at (a) 268 nm	0.604–2.402 mg ml^{-1}	Derivative spectrometry and less sensitive methods	Bonazzi et al., 1997a, b
		(b) 267.2 nm			
		B. 2nd derivative absorption spectrometry at (a) 270.4 and			
		(b) 271.6 nm			
	(b) Acetonitrile–20 mM sodium heptansulfonate (pH 2.5, 1:1 v/v)	HPLC analysis with UV detection at 215 nm using enalapril as internal standard	0.024–0.056 μg ml^{-1}	Sophisticated analytical technique required	
15	NaOH	Second derivative absorption spectrophotometric determination at 220 and 340 nm	30-2000 μg ml^{-1}	Less sensitive method	Durisehvar and Hulya, 1999
16	LNP in water	Measurement of drug by (a) UV spectrophotometry at 206 nm	3.2–35.2 μg ml^{-1}	Derivative spectrometric technique, less cost-effective method	Beata, 2005
		(b) first derivative spectrometry at 204 and 217 nm			
		(c) second derivative spectrometry at 209 and 221 nm			
		(d) third-order spectrometry at 211, 217, and 223 nm			
17	Methanol	First derivative spectrometric measurement of LNP and 269.6 nm	25.6–129.5 μg ml^{-1}	Derivative spectrometric technique, less sensitive, less cost-effective method	Erk, 1998
18	0.1 M HCl	Second derivative spectrometric measurement at 219.4 nm	5–15 μg ml^{-1}	Derivative spectrometric technique, less cost-effective method	Prasad et al., 1999
19	LNP solution	Derivative spectrometric measurements at 300, 271, 242, and 213 nm	5–30 μg ml^{-1}	Less cost-effective method	Jain and Agrawal, 2000
20	LNP solution	Derivative spectrometric measurement of LNP	-	Less cost-effective method	Mashru and Parikh, 2000
21	Mobile phase of 7:93 (v/v) Acetonitrile–25 mM potassium dihydrogen phosphate (pH 5)	HPLC analysis using a 4.6 mm × 20 mm, 3.5 μm particle size, C18 column, and UV detection at 215 nm	0.08–1 mg ml^{-1}	Sophisticated instrument, less cost-effective method	Ivanoic et al., 2007
22	Mobile phase of acetonitrile:water (20:80 v/v) (pH 3.8)	HPLC analysis using LiChrosorb RP -C_{18} column (5 μ, 20 cm × 4.6 mm) with UV detection at 213 nm	1.5–56 μg ml^{-1}	Sophisticated instrument, less cost-effective, and less sensitive method	Nevin and Murat, 1999
23	-	Reversed phase HPLC analysis	-	Sophisticated instrument,	Sane et al. 1992

Table 1 Performance characteristics of existing methods of LNP *(Continued)*

Sl. no.	Reagent(s)	Technique and methodology	Range	Remarks	Reference
				less cost-effective method	
24	Mobile phase of potassium phosphate buffer (pH 2.2, 30 mM):acetonitrile (91:9, v/v) flow rate 1.0 ml min^{-1}	HPLC analysis using platinum EPS C8 (250mm × 4.6 mm i.d.5 μm column, with UV detection at 215 nm	12.5–37.5 μg ml^{-1}	Sophisticated instrument, less cost-effective method	Christopher et al., 2004
25	Mobile phase: methanol–dichloromethane–glacial acetic acid (9.0:1.0:0.1, v/v/v)	HPTLC analysis with aluminium-backed layer of silica gel 60 F_{254}	400–2000 ng/band	Sophisticated instrument, less cost-effective method	Pandya et al., 2017
26	-	Gas chromatographic separation performance	-	Sophisticated instrument, less cost-effective method	Avadhanulu and Pantulu, 1993
27	Sodium cholate and 40 mM sodium dodecyl sulphate in 25 mM phosphate buffer (pH 9)	Capillary electrophoretic separation of lisinopril isomers	-	Applicable for separation of isomers	Qin et al., 1993
28	Borate buffer (50 mM) pH 8.5	Capillary electrophoretic separation with fused-silica 'bubble' capillary 58.5 cm (50 cm effective length) × 50 mm I.D.; applied voltage, 25 kV; detection 220 nm; temperature 50 °C; injection time 10 s.	-	Sophisticated instrument, less cost-effective method	Gotti et al. 2000
29	7-Chloro-4-nitrobenzofurazan and ethyl acetate	The fluorescence intensity of the lisinopril derivative with 7-chloro-4-nitrobenzofurazan in ethyl acetate measured at 528 nm with excitation at 465 nm	50–1000 ng ml^{-1}	Sophisticated instrument required	Esra et al., 2003
30	o-Phthalaldehyde, 2-mercaptoethanol borate buffer medium, pH = 10.6	Spectrofluorimetric measurement of reaction product of lisinopril with o-phthalaldehyde in the presence of 2-mercaptoethanol in borate buffer medium (pH = 10.6) at 455 nm with excitation at 346 nm	0.3–10.0 mg l^{-1}	Sophisticated instrument required	Zacharis et al. 2004
31	Sodium nitrite, ammonium sulphamate, hydrochloric acid sodium hydroxide, Britton-Robinson Buffers of pH range 1.0–8.0, dichloromethane	The polarographic analysis at potential scan rate of 10 mV/s using DME, Ag-AgCl, and a graphite rod as electrodes. The polarographic modes over the potential range − 0.2–1.6 V versus Ag-AgCl were by (a) Direct current polarographic method	2–24 μg ml^{-1}	Sophisticated instrument required	El-Enany, Belal, and Al-Ghannam, 2003
		(b) Direct potential polarographic method	1–20 μg ml^{-1}		
32	0.5 M Acetic acid and 10 mM copper sulphate	Polarographic analysis at potential range from +200 to − 1 V at scan rate of 100 mV s^{-1} using calomel reference electrode.	Up to 20 μg ml^{-1}	Sophisticated instrument required	Rajasekaran and Murugesan, 2001
33	Phosphotungstic acid (PTA), PVC, and THF Phosphomolybdic acid, PVC, and THF	Construction, validation, and use of ion-selective electrode for potentiometric determination of lisinopril	5×10^{-5}–2.4×10^{-3} mol l^{-1}	Wide linear range, cost-effective, and highly skilful operator not required	Present methods

A 1 mol l^{-1} solution of sodium acetate (NaOAc) and NH_3 was prepared in distilled water. Solutions of 1 mM each of sodium carbonate (Na_2CO_3), sodium hydrogen carbonate ($NaHCO_3$), sodium hydroxide (NaOH), acetic acid (CH_3COOH), potassium nitrate (KNO_3), potassium hydroxide (KOH), potassium dihydrogen orthophosphate (KH_2PO_4), orthophosphoric acid (H_3PO_4), manganous sulphate ($MnSO_4$), silver nitrate ($AgNO_3$), cadmium sulphate ($CdSO_4$), cupric sulphate ($CuSO_4$), calcium carbonate ($CaCO_3$), glycine, arginine, cysteine, talc, oxalic acid, urea, and glucose were prepared by dissolving required weight of the respective compound (all from S.D. Fine Chem Ltd., Mumbai, India) in distilled water. These solutions were used in the study of interferences and in determination of selectivity coefficients of ISEs.

Preparation standard LNP solution

A standard solution of 0.01 mol l^{-1} LNP was prepared by dissolving accurately weighed required quantity of pure drug in 100 ml of H_2O in a volumetric flask.

General procedures

Preparation of ion-associates

A 25 ml each of 0.01 mol l^{-1} solutions of LNP and PTA or PMA was transferred into a clean beaker and stirred

well for 20 min on a magnetic stirrer. The content was filtered through Whatman No. 41 filter paper and the obtained LNP-PTA or LNP-PMA ion-associate in the form of precipitate was dried overnight at room temperature and used for preparation of membrane ion-selective electrode.

Fabrication of the LNP-PMA/PTA ion-selective electrodes

A 40 mg of dried precipitate of LNP-PTA or LNP-PMA ion-associate was taken in a Petri Dish of 4 cm width, and a 0.1 g each of PVC and DOP was added and dissolved in 10 ml of THF. The content was allowed to evaporate under room temperature for 24 h. A 0.4-mm thick membrane was removed carefully and fused to one end of the Pyrex Glass tube by using THF. The tube was dried under room temperature for 24 h, filled by 3–5 ml internal solution of 5 mmol l^{-1} LNP ($[LNP]_{Int}$) and immersed into the drug solution of same concentration at least for 1.5 h for conditioning. A copper wire of 2.0-mm diameter and 0.16-m length was tightly insulated leaving 1.0 cm at the top and 0.5 cm below for connection. One terminal of the wire was inserted and the other terminal was connected to the potentiometer. The potential values were brought to stabilisation by soaking the electrode in analyte solution for 1.5 h.

Preparation of calibration curve

Varying aliquots of 0.01 mol l^{-1} LNP solution were transferred accurately into a series of 10.0-ml volumetric flasks with the help of a microburet. The pH of each solution in each flask was adjusted to the range 2.5 to 6.4 for LNP-PTA ISE or 2.3 to 6.0 for LNP-PMA ISE. The volume of each flask was adjusted to 10 ml with water. The LNP-PTA or LNP-PMA ISE and Ag/AgCl reference electrodes were immersed into each solution and the potentials were measured.

The calibration graphs of measured potentials versus log [LNP] were prepared separately for each ISE. The concentration of the unknown was found by using calibration graph or regression equation derived using potential and log [LNP] data.

Analysis of tablets

Twenty tablets were weighed and transferred into a mortar and powdered. A portion of the powdered tablet equivalent to 50 mg of LNP was transferred into a 50-ml volumetric flask and shaken with 30 ml of H_2O for 20 min. The content after diluting to the mark with water was mixed and filtered through Whatman No. 41 filter paper. A suitable aliquot was used for potential measurement by following the procedure as described under procedure for preparation of calibration curve using respective ISE. The concentration of LNP was calculated using the calibration curve or regression data.

Study of interferences

Into a series of 25-ml beakers each, a 4 ml of 0.01 mol l^{-1} standard drug solution was transferred and the volume of each beaker was adjusted to 8 ml with water. Then, added 2 ml of 1.0 mmol l^{-1} solutions of different interferents and mixed well. The potential of each was measured using the electrochemical cell as described above under preparation of calibration curve.

Determination of selectivity coefficient of ISEs

Into a series of 10-ml beakers, varying volumes (0.25 to 1.25 ml) of 0.01 mol l^{-1} solution of LNP were transferred, 2 ml of 1.0 mmol l^{-1} interferent was added to each beaker and the final volume was brought to 10 ml with water. The potential of each solution was measured. The procedure was repeated for each interferent separately.

The plot of measured potential versus log of the LNP's concentration was prepared. The point of intersection between two linear portions in the plot was located. At the point of intersection, the value of selectivity coefficient (K_{AI}) was calculated by using the formula (Harvey, 2000):

$$K_{AI} = \frac{[A]_E}{[I]_E^{Z_A/Z_I}} = \frac{[A]_{Int}}{[I]_{add}^{Z_A/Z_I}}$$

where Z_A and Z_I are the charges of the analyte and interferent, respectively, and $[A]_E$ and $[I]_E$ are the concentrations of analyte and interferent yielding identical cell potentials. $[A]_{int}$ is the LNP concentration in x-axis of the graph at the point of intersection and $[I]_{add}$ is the concentration of interferent added to the LNP solution.

Determination of stoichiometry of ion-pair complex

A 10 ml standard solution of 0.01 mol l^{-1} LNP was transferred into a clean beaker and it was placed on magnetic stirrer. The conductivity cell was immersed into the solution and the titration was carried out by adding 0.01 mol l^{-1} PTA or PMA. The conductance values were measured, the graphs of conductance against the molar ratio of titrant were plotted, and the stoichiometry for each ion-associate was determined.

Results and discussion

The structural formula of LNP with primary amine functional group hints to the formation of water insoluble ion-association complex between drug and PTA/PMA reagents in aqueous medium. This was prompted the authors to utilise the ion-associate to design two membrane sensors with PVC for the determination of LNP in pharmaceuticals employing highly cost-effective potentiometric technique. By this technique, it is possible for direct measurement of potential and thus the

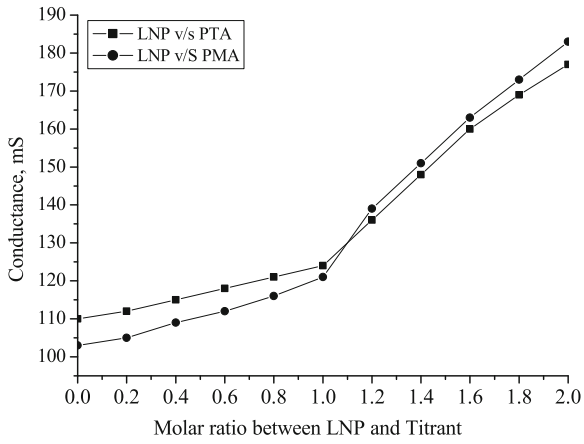


Fig. 2 Conductometric titration curves for titration of 10 ml of 0.01 mol l^{-1} LNP with 0.01 mol l^{-1} PTA or PMA

concentration of LNP in the solutions containing LNP can be determined.

The influence of the ion-associating reagent in the preparation of the complex, which is the major component of a membrane for an ISE, was investigated. PTA and PMA are two ion-associate reagents used to prepare ion-pair complex with drugs containing nitrogenous basic group (Ezzeldin et al., 2012; Issa and Khorshid, 2011; Hefnawy et al., 2014; Shawish et al., 2018; Al-Mohaimeed et al., 2012).

The initial experiments indicated that the LNP can react with either PTA or PMA forming water insoluble ion-associate or ion-pair complex. The stoichiometric ratio of the ion-pair was determined by conductometric titration of LNP with either PTA or PMA (Khalil et al., 2018). The titration curves (Fig. 2) revealed the stoichiometry of 1:1 with respect to LNP and ion-associate reagent. This was due to the reactivity and formation of ion-association complex between the protonated free primary amine ($-NH_3^+$) of LNP ($LNPH^+$) and anionic PTA (PTA^-) or PMA (PMA^-) (Scheme 1). This supported that the proposed electrodes have nearly Nernstian response while measuring the response. Slopes of 55.06 and 52.39 mV/decade, respectively, for LNP-PTA and LNP-PMA ISEs revealed the response in the expected manner. Therefore, in this study, the reagents, PTA and PMA, were tested as active materials for the development of LNP-selective electrodes for the determination of LNP and validated their functioning.

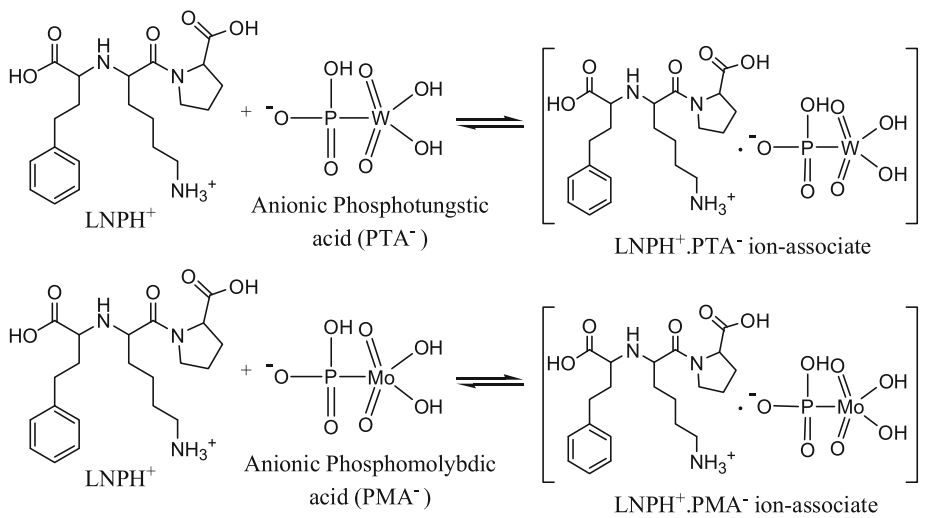
The resulted water insoluble ion-associate of $LNPH^+$, PTA^- or $LNPH^+$, and PMA^- is utilised to design a membrane electrode and thus electrochemical cell using Ag/AgCl reference electrode. The systematic representation of the electrochemical cell is depicted as follows:

Ag-AgCl Reference electrode ‖ LNP-PTA/PMA membrane | $(LNP\ solution)_{Int}$ | Cu

The above electrochemical cell for potentiometric determination of LNP obeys the Nernst equation (Harvey, 2000) and which can be written as follows:

$$E_{Cell} = K + 0.05916\ \log[LNP]_{Sample}$$

where K is a constant accounting for the potentials of the reference electrodes, any liquid junction potentials, the asymmetry potential, and the concentration of analyte in the internal solution. The equation given above is a clear route to show the linear relationship between E_{cell} and concentration of LNP in the sample solution. This linear relationship will be obeyed Nernstian response.



Scheme 1 Reaction pathway for the formation of ion-pair complex between LNP and PTA/PMA

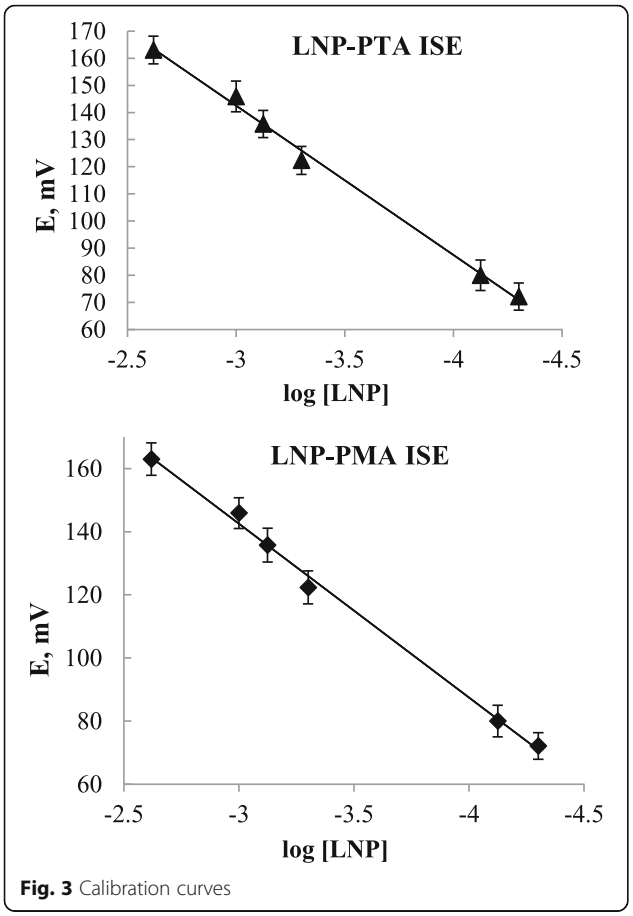


Fig. 3 Calibration curves

Optimisation of variables

Membrane composition

The influence of amounts of components used in the fabrication of membranes was studied by taking the different quantities of each. It was found from the preliminary experiments that when the weights of LNP-PTA or LNP-PMA ion-associates and PVC were 40 mg and 0.1 g, respectively, in 10 ml of THF volume yielded membranes of thickness 0.4 mm. The same membranes were used in the linearity studies to obtain the Nernstian responses. The Nernstian behaviour was not obviously observed from the membrane ISE constructed using other weights of ion-associates and PVC. The volumes of THF were also varied and 10 ml was found as optimum.

Choice of plasticiser

The membranes were developed separately by using dioctyl phthalate (DOP), dibutyl sebacate (DBS), and o-nitrophenyl octylether (NPOE) as plasticisers. The membrane fabricated using 40 mg of LNP-PTA or LNP-PMA ion-associate and 0.1 g of PVC with 0.1 g DOP as plasticiser was found to perform satisfactorily with respect to stable potential readings, conditioning, and response time. Therefore, DOP was used as plasticiser in fabricating the LNP-PTA and LNP-PMA ISEs.

Effect of concentration of internal solution

The effect of the concentration of internal LNP solution on the potential response of the ISEs was investigated. The concentrations of LNP were changed in the range from 1 to 7 mmol l^{-1} and the potential responses of the ISE were measured. It was found that the potential values were obtained in excellent linearity (Fig. 3) with the LNP internal solution concentration of 5 mmol l^{-1}. At the other LNP internal concentrations, the linearities and correlations between LNP concentrations and potential values were not in good agreement (Fig. 4). Therefore, 5 mmol l^{-1} LNP internal solution was used for performing analysis using the LNP-PTA or LNP-PMA ISEs.

Effect of soaking time

The surfaces of ISEs were effectively activated by soaking the fabricated membrane ISE in standard solution of analyte. The optimum soaking time to activate the ISE was fixed by measuring the potential at different times. From

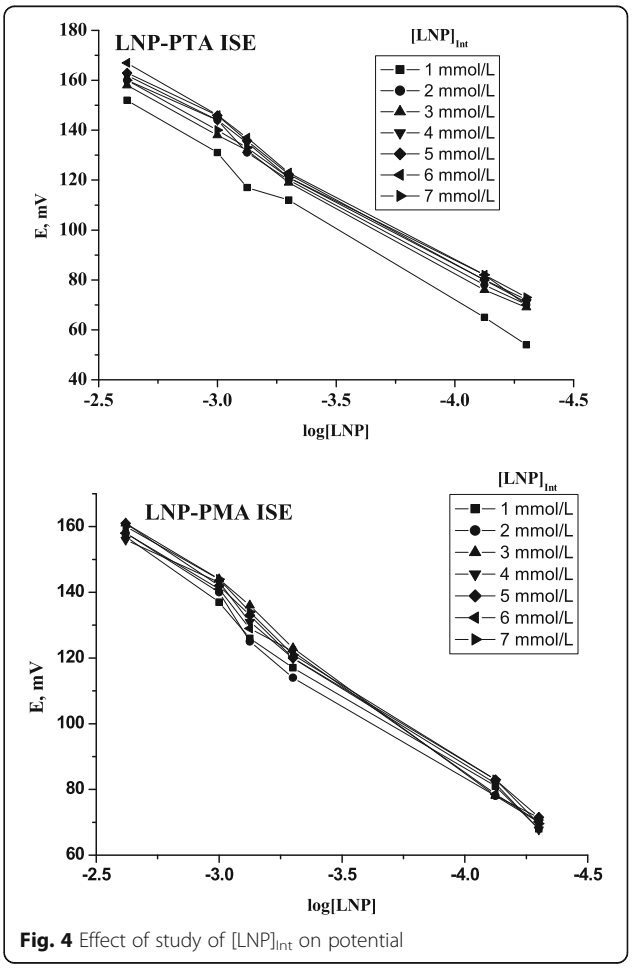


Fig. 4 Effect of study of $[LNP]_{Int}$ on potential

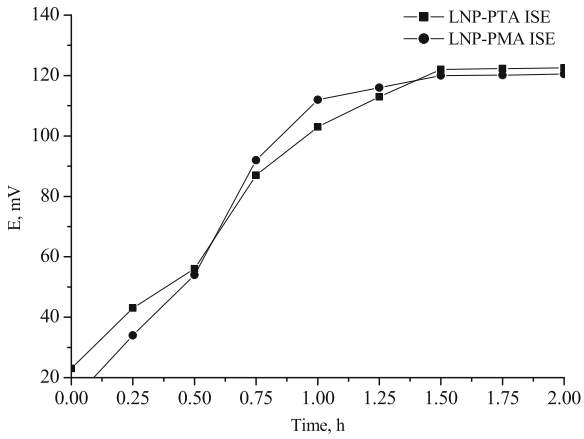


Fig. 5 Effect of soaking time on potential of 5.0×10^{-4} mmol l^{-1} LNP for LNP-PTA and LNP-PMA ISEs

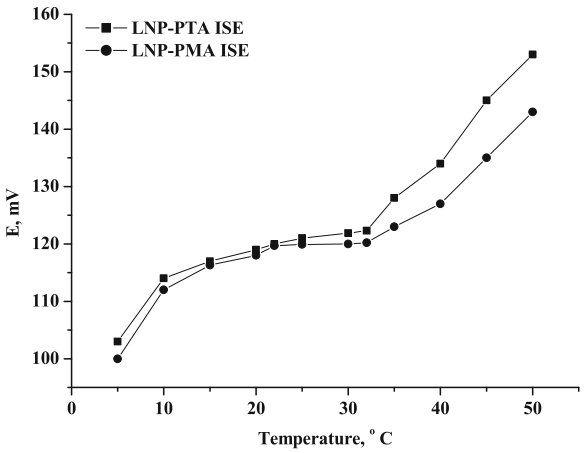


Fig. 7 Effect of temperature on potential of 5.0×10^{-4} mmol l^{-1} LNP for LNP-PTA and LNP-PMA ISEs

the obtained time to potential data, it was shown that the resulting potential values become constant in 1.5 h and thereafter, and thus the active surface of membrane was effective for its use in measuring the potential of LNP solutions of working concentration ranges, at 25 °C. The effect of soaking time on the potential for LNP-PTA and LMP-PMA ISEs is presented in Fig. 5. It was also revealed from the investigations and recommended that the electrodes may be kept dry and packed in an opaque closed vessel whenever they are not in use for longer time.

Effect of pH

Influence of pH on the potentiometric response of two ISEs in the pH range 1.0 to 10.0 was studied and the results obtained were used, plotted, and presented in Fig. 6. The pH of LNP solutions was varied by adding 1 M solutions of NaOAc or NH_3 before measuring the potential. It was confirmed from the results that the pH ranges of 2.5 to 6.4 and 2.3 to 6.0 were found as optimum in measuring the potentials, for LNP-PTA and LNP-PMA ISEs, respectively. Below and beyond these ranges of pH values, lower potential values were observed. Therefore, these ranges were fixed for LNP-PTA and LNP-PMA ISEs to measure the potentials during the analysis.

Effect of temperature on potentials

The effect of temperature on the fabricated LNP-PTA and LNP-PMA electrodes was studied. The potentials of the LNP test solutions of concentration between the working linear ranges were measured by varying the temperature from 5 to 50 °C. The resulted potentials were plotted as the function of varied temperatures (Fig. 7) and it was found from the investigation that the linear response of the electrodes was good for both electrodes in temperature between 22 and 32 °C and at other temperatures, there is decline in the potential from the

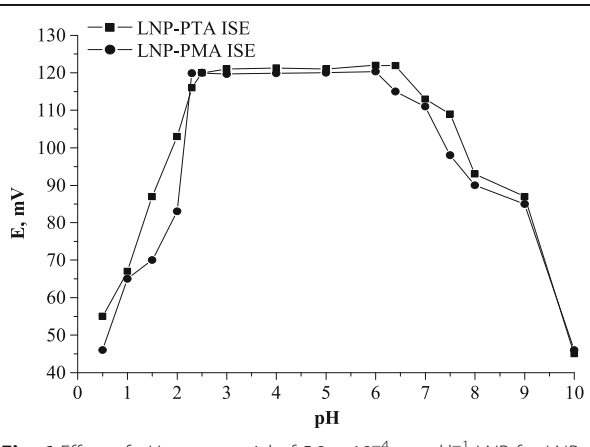


Fig. 6 Effect of pH on potential of 5.0×10^{-4} mmol l^{-1} LNP for LNP-PTA and LNP-PMA ISEs

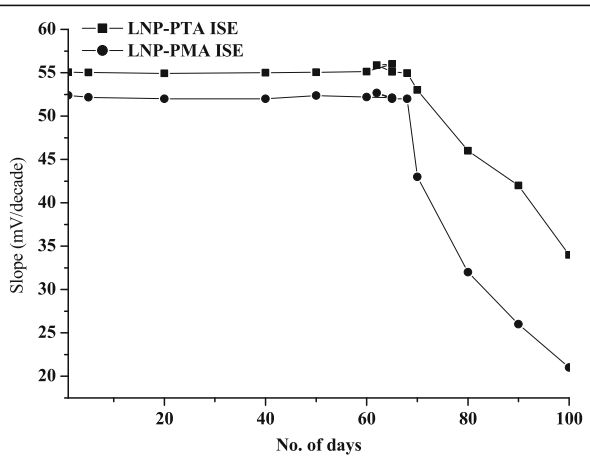


Fig. 8 Life time of LNP-PTA and LNP-PMA ISEs

Table 2 Results of interference study and determination of selectivity coefficients (K_{AI})

Interferent species	Selectivity coefficient, K_{AI}*	
	LNP-PTA ISE	LNP-PMA ISE
NaOH	0.0241	0.04
$NaNO_2$	0.0694	0.05776
$CdSO_4$	0.3978	0.4166
KNO_3	0.0421	1.45
HCl	0.0348	1.11
NaCl	1.21	0.035
$NaHCO_3$	1.34	0.05302
Oxalic acid	1.02	0.0943
Sucrose	1.12	0.4309

*Mean value of three determinations

expected values. Therefore, the optimum temperature ranges for these two electrodes were fixed as 22 to 32 °C.

Response time

The response time was checked to fix time to attain limiting potential by immersing the respective ISE into the solution of LNP. For both the ISEs at least 10 s of the average static time was required to attain stable potential readings. No change in the potentials observed up to 3 min. Therefore, the ISE was made to be static for a 10 s after its immersion into solution of LNP and then potentials measured before 3 min.

Life time

The life times of LNP-PTA and LNP-PMA ISEs were evaluated to assess their ability to maintain their performance for a certain period of time by performing the calibration of the electrochemical cells periodically with standard solutions of LNP and calculating the respective slopes. It was confirmed from the investigation that both the electrodes resulted Nernstian slopes without deviation from the actual optimum values for at least 68 days. This revealed that the ISEs could be used continuously up to 68 days. But after 68 days, their characteristics significantly drifted away from the Nernstian behaviour (Fig. 8). Therefore, the average life time for LNP-PTA and LNP-PMA ISEs was proposed as 68 days.

Selectivity coefficients of the electrodes

Selective functioning of the ISE is a characteristic parameter to assess the specificity in the determination of analyte of interest. Therefore, the selectivity coefficients (K_{AI}) of LNP-PTA and LNP-PMA ISE were investigated in the presence of inorganic and organic compounds as spikes. The values of K_{AI} of ISEs in the presence of various compounds have been determined experimentally by preparing a series of solutions, each of which contains the same concentration of interferent, $[I]_{add}$, but a different concentration of analyte and measuring the cell potential using respective ISE. A plot of cell potential versus the log of the analyte's concentration has two distinct linear regions (Harvey, 2000). When the analyte's concentration is significantly larger than $K_{A,I}[I]_{add}$, the potential is a linear function of log [A], in the presence and absence of interferents, as given by equations (Harvey, 2000):

$$E_{cell} = K + 0.05916 \log[LNP]_{sample}$$

$$E_{cell} = K + 0.05916 \log\left([LNP]_{sample} + K_{AI}[I]^{\frac{Z_A}{Z_I}}\right)$$

where $[LNP]_{sample}$ and [I] are the concentrations of LNP of charge Z_A and interferent of charge Z_I in the solutions.

If $K_{AI}[I]$ is significantly larger than the LNP's concentration, however, the cell potential remains constant. The concentration of analyte and interferent at the intersection of these two linear regions is used to calculate K_{AI} (Harvey, 2000).

The determined values of K_{AI} presented in Table 2 revealed that NaCl, $NaHCO_3$, oxalic acid, and sucrose

Table 3 Performance characteristics of LNP ISEs

Parameters	LNP-PTA ISE	LNP-PMA ISE
Linear range, mol l^{-1}	5×10^{-5}–2.4×10^{-3}	5×10^{-5}–2.4×10^{-3}
Limit of detection (LOD), mol l^{-1}	1.2×10^{-5}	1.18×10^{-5}
Limit of quantification (LOQ), mol l^{-1}	3.6×10^{-5}	3.7×10^{-5}
Slope (*m*), mV/decade	55.06 ± 1	52.39 ± 1
Intercept (*b*), mV	307.71	297.17
Correlation coefficient (*r*)	0.9980	0.9978
Response time, s	10	10
Working pH range	2.5–6.4	2.3–6.0
Temperature, °C	22–32	22–32
Life span of sensor, days	68	68

Table 4 Results of intra- and inter-day precision and accuracy

ISE	LNP taken, mmol l^{-1}	Intra-day variations			Inter-day variations		
		LNP found*, mmol l^{-1}	%RSD	%RE	LNP found$^{\$}$, mmol l^{-1}	%RSD	%RE
LNP-PTA	0.075	0.073	3.81	2.67	0.077	3.89	2.67
	0.500	0.509	4.89	1.80	0.511	4.11	2.20
	1.000	1.01	2.97	1.00	1.020	4.33	2.00
LNP-PMA	0.075	0.072	2.91	4.00	0.073	2.99	2.67
	0.500	0.494	4.19	1.20	0.516	3.15	3.20
	1.000	1.020	3.97	2.32	1.030	3.63	3.00

*Mean value of seven measurements; $^{\$}$Mean value of five measurements

were showed interference with LNP using LNP-PTA ISE, whereas for LNP-PMA ISE, KNO_3 and HCl were proved as interferents. However, the results presented below and values of K_{AI} of less than the unity proposed ISEs are suitable to determine LNP in the presence of other interferents.

Validation results

Linearity, analytical, and regression parameters

The performance of proposed LNP-PTA and LNP-PMA ISEs was evaluated for linearity according to IUPAC recommendations (IUPAC, 1994 and IUPAC Analytical Chemistry Division, 2000) using Ag-AgCl reference electrode. The data obtained are summarised in Table 3. The results showed that the ISEs provide rapid, stable, and linear response for the LNP concentration ranges presented in Table 3. The calibration graphs were linear and the regression equations were $y = 55.06x + 307.71$ and $y = 52.39x + 297.17$ for LNP-PTA and LNP-PMA ISEs, respectively, and the corresponding Nernstian slopes were 55.06 and 52.39 mV/decade. The regression parameters and the values of other performance characteristics are also presented in Table 3.

Intra- and inter-day precision and accuracy

The standard solutions of three different concentrations of LNP within the range of determination were prepared in seven replicates each. Intra-day variations were evaluated by measuring the potentials on same day and calculating the %RSD values for the amounts of LNP found. Inter-day precision was evaluated by analysing the pure LNP solutions at three different concentrations in five replicates during different days and by calculating the %RSD values for the found LNP amounts. The accuracy was evaluated by calculating the amount of LNP for respective potentials of drug solution. The relative error (RE), the metric for accuracy, is calculated for each concentration of LNP found. The obtained %RSD values ranged between 2.91 and 4.89% indicated the satisfactory precision of the results.

The percent relative error (%RE) which is an index of accuracy ranged from 1.00 to 4.0 indicated acceptable accuracy. The results of study of precision and accuracy are summarised in Table 4.

Robustness and ruggedness

The robustness of the proposed potentiometric ISEs was examined by deliberately slightly changing the working pH and temperatures. The solutions of 7500, 50, and 1 m mol l^{-1} LNP were used in this study. The %RSD values were calculated for the results of each variation. The pH was varied by 2 units at before and after the range of values for each sensor [2.5(± 2) to 6.4(± 2)] for LNP-PTA ISE and 2.3(± 2) to 6.0(± 2) for LNP-PTA ISE] and the calculated values of %RSD were ranged between 1.98 and 4.52. Besides, the robustness was also

Table 5 Results of robustness and ruggedness expressed as intermediate %RSD values

ISE	Concentration of LNP, mmol l^{-1}	%RSD values for varied parameters			
		Robustness		Ruggedness	
		pH	Temperature	Inter-potentiometric	Inter-analysts
LNP-PTA	0.075	2.56	3.52	2.23	3.43
	0.500	3.23	3.45	2.12	2.54
	1.000	2.21	2.98	2.22	3.56
LNP-PMA	0.075	1.98	2.14	2.14	2.18
	0.500	2.89	3.11	3.22	3.66
	1.000	1.99	2.11	2.14	4.00

Table 6 Results of analysis of tablets using proposed ISEs and statistical comparison of the results with the reference method

Brand name of tablet analysed	mg of LNP/ tablet	Found*		
		%Label claim ± SD		
		Reference method	ISE	
			LNP-PTA	LNP-PMA
Listril	10.00	98.72 ± 1.08	99.65 ± 1.21 t = 1.28 F = 1.25	98.38 ± 1.22 t = 0.47 F = 1.27

*Mean value of five determinations

been evaluated by varying the temperature by 1 °C during the measurement of potentials of LNP solutions of different concentrations. The temperatures of the LNP solutions were brought to 22 ± 1 and 32 ± 1 °C using LNP-PTA and LNP-PMA ISEs; potentials measured and calculated the RSD values. The values of RSD were in the range from 2.11 to 3.52 indicated the robust functioning ISEs.

The ruggedness was studied by the analyses with different potentiometers, on different days by different analysts. The inter-potentiometric and inter-analysts RSD values of < 4% showed the developed LNP-PTA and LNP-PMA ISEs are robust enough to function. The results of robustness and ruggedness expressed in %RSD are presented in Table 5.

Application of ISEs to tablet analysis

The extracts containing three different concentrations of active ingredient were prepared using LNP tablets. Five replicates of each of 7500, 50, and 1 m mmol l^{-1} in LNP were used to measure the potentials with proposed LNP-PTA and LNP-PMA ISEs by following the procedure described under 'procedure for tablets'. The mean of the measured potential of the tablet extract was obtained and found and percentage recovery values of LNP were calculated. These results were statistically compared with the results of reference method. (Ajay et al., 1995a, b) The method recommended the procedure of potentiometric titration of LNP tablet extract with 0.1 mol l^{-1} NaOH. The Student's t test and variance ratio F tests were performed on the results to evaluate the accuracy and precision, respectively. The calculated t and F values at 95% confidence level are tabulated in Table 6. The calculated t and F values are less than the tabulated values and hence, it was clear from the assessment that the proposed ISEs yielded accurate and precise results.

Recovery study

The accuracy of the proposed ISEs was further assessed by recovery studies by following the standard addition procedure. The aliquots of tablet extracts were prepared and spiked with pure drug solution at three different levels. The potential measured using the ISE. To a fixed amount of five replicates of LNP from tablet extract, pure LNP in amounts corresponds to 50, 100, and 150% to that of amount from tablets spiked, pH adjusted, and after diluting to 10 ml, the potential measured. For obtained potentials, the concentrations of LNP found were calculated using the derived regression equation. The percentage recovery of pure LNP was calculated. The percentage recovery of LNP ranged between 98.34 and 101.23 with standard deviation of less than 4% revealed good and acceptable recovery values from developed and proposed ISEs. These results are presented in Table 7.

Conclusions

For the very first time, development, validation, and application of two novel ion-selective electrodes (ISEs) using phosphotungstic and phosphomolybdic acids for the selective determination of lisinopril (LNP) in pharmaceuticals were described in this study. The proposed ISEs are highly selective, accurate, precise, robust and rugged, and applicable for the determination of LNP of amount in wide linear range with good Nernstian response and low detection limits. Working action of both ISEs is dependent on wide ranges of pH and temperature. These operative conditions of wide pH and temperature ranges hallmarked the advantageous features of the proposed ISEs. The statistical comparison of results of potentiometric determination of LNP using proposed ISEs with the official BP method [3] revealed selectivity and suitability of the electrodes for accurate and precise determination of LNP in real samples such as tablets or such other formulations. Furthermore, the results of recovery study were also indicated the inactive role of excipients in tablets in the determination of LNP

Table 7 Results of accuracy assessment by recovery test for listril tablets

ISE	LNP for tablet extract, mmol l^{-1}	Pure LNP added, mmol l^{-1}	Total LNP found, mmol l^{-1}	%LNP recovered*	SD
LNP-PTA	0.500	0.250	0.746	98.34	1.33
	0.500	0.500	0.996	99.23	0.96
	0.500	0.750	1.251	100.13	2.11
LNP-PMA	0.500	0.250	0.753	101.23	1.09
	0.500	0.500	0.993	98.56	2.12
	0.500	0.750	1.243	99.00	2.00

*Mean value of three measurements

in pharmaceuticals. Therefore, in contrast to many reported analytical methods, the proposed potentiometric method of determination of LNP using LNP-PTA and LNP-PMA ISEs found specific and relevant for their adoption as routine quality control analytical procedures in laboratories without any compromise with performance characteristics.

Abbreviations

LNP: Lisinopril; LNP-PTA: LNP-phosphotungstic acid; LNP-PMA: LNP-phosphomolybdic acid; LOD: Limit of detection; LOQ: Limits of quantitation; ISE: Ion-selective electrode; BP: British Pharmacopoeia; USP: United States Pharmacopoeia

Acknowledgements

Authors thank Cipla India Ltd., Mumbai, India, for gifting pure lisinopril sample. The first author gratefully acknowledges the UGC, SWRO, Bengaluru, India, for financial assistance (Award No. 1495-MRP/14-15/KAMY013/UGC-SWRO, dated 04-02-15) to pursue this research work. The same author is also grateful to the principal of the affiliating institute for providing the facilities to pursue this work.

Authors' contributions

NR developed the ISEs and validated, performed the data analysis, reviewed the literature, drafted, and revised the manuscript. KB supervised the experiment and given inputs in the method development. Both the authors read and approved the final manuscript.

Funding

UGC, SWRO, Bengaluru, India; Award No. 1495-MRP/14-15/KAMY013/UGC-SWRO, dated 04-02-15.

Availability of data and materials

Research data have been provided in the manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Author details

[1]PG Department of Chemistry, JSS College of Arts, Commerce and Science, Autonomous College of University of Mysore, B N Road, Mysuru, Karnataka 570 025, India. [2]Department Chemistry, University of Mysore, Manasagangothri, Mysuru 570 006, India.

Received: 27 July 2019 Accepted: 11 October 2019
Published online: 21 December 2019

References

Abdel-Fattah L, El-Kosasy A, Abdel-Aziz L, Gaied M. Novel ion selective electrodes for determination of lisinopril: a study of plasma and plasma proteins effect. J American Sci. 2010;6(10):1115–21.

Ajay KJ, Vinod KG, Binod BS, Lok PS. Copper(II)-selective electrodes based on macrocyclic compounds. Anal Proc Anal Comm. 1995a;32:99–101.

Ajay KJ, Vinod KG, Lok PS. Neutral carrier and organic resin based membranes as sensors for uranyl ions. Anal Proc Anal Comm. 1995b;32:263–5.

Al-Mohaimeed AM, Al-Tamimi SA, Alarfaj NA, Aly FA. New coated wire sensors for potentiometric determination of gemifloxacin in pure form, pharmaceutical formulations and biological fluids. Int J Electrochem Sci. 2012;7:12518–30.

Asad R, Tariq MA, Atta UR. Spectrophotometric determination of lisinopril in pure and pharmaceutical formulations. J Chin Chem Soc. 2005;52:1055–9.

Avadhanulu AB, Pantulu ARR. Gas liquid chromatographic estimation of lisinopril in its pharmaceutical dosage forms. Indian Drugs. 1993;30:646–9.

Basavaiah K, Tharpa K, Hiriyanna SG, Vinay KB. Spectrophotometric determination of lisinopril in pharmaceuticals using ninhydrin- a modified approach. J Food Drug Anal. 2009;17:93–9.

Basavaiah K, Tharpa K, Vinay KB. Titrimetric assay of lisinopril in aqueous and non-aqueous media. Ecletica Quimica. 2010;35(2):7–14.

Beata S. Estimation of the applicability of differential spectroscopic method for the determination of lisinopril in tablets and for its evaluation of its stability. Acta Pol Pharm. 2005;61:327–34.

Bonazzi D, Gotti R, Andrisano V, Cavrini V. Analysis of ACE inhibitors in pharmaceutical dosage forms by derivative UV spectroscopy and liquid chromatography. J Pharm Biomed Anal. 1997a;16:431–8.

Bonazzi D, Gotti R, Andrisano V, Cavrini V. Analysis of ACE inhibitors in pharmaceutical dosage forms by derivative UV spectroscopy and liquid chromatography. J Pharm Biomed Anal. 1997b;16:431–8.

Christopher AB, Jessica S, Zack Z, Robert AR. Development and validation of a stability indicating HPLC method for determination of lisinopril, lisinopril degradation product and parabens in the lisinopril extemporaneous formulation. J Pharm Biomed Anal. 2004;37:559–67.

Durisehvar O, Hulya S. Determination of lisinopril from pharmaceutical preparations by derivative UV spectrophotometry. J Pharm Biomed Anal. 1999;21:691–5.

El-Enany N, Belal F, Al-Ghannam S. Polarographic determination of lisinopril in pharmaceuticals and biological fluids through treatment with nitrous acid. Mikrochimica Acta. 2003;141:55–61.

El-Gindy A, Ashour A, Abdel-Fattah L, Shabana MM. Spectrophotometric, spectrofluorimetric and LC determination of lisinopril. J Pharm Biomed Anal. 2001;25:923–31.

El-Yazbi FA, Abdine HH, Shaalan RA. Spectrophotometric and spectrofluorometric methods for the assay of lisinopril in single and multicomponent pharmaceutical dosage forms. J Pharm Biomed Anal. 1999;19:819–27.

Erk N. Comparative study of the ratio-spectra derivative spectrophotometry, derivative spectrophotometry and Vierordt's method applied to the analysis of lisinopril and hydrochlorothiazide in tablets. Spectrosc Lett. 1998;31:633–45.

Esra SA, Lale E, Olcay S. A new spectrofluorimetric method for the determination of lisinopril in tablets. IL Farmaco. 2003;58:165–8.

Ezzeldin E, Hefnawy MM, Abounassif MA, Tammam MH, Mostafa GAE. PVC membrane sensors for potentiometric determination of bambuterol in pharmaceutical formulation. Int J Electrochem Sci. 2012;7:10570–81.

Gotti R, Andrisano V, Cavrini VC, Bertucci FS. Analysis of ACE-inhibitors by CE using alkylsulfonic additives. J Pharm Biomed Anal. 2000;22(3):423–31.

Harvey D, Text book of modern analytical chemistry, 1st Edition, DePAUW University, International Edition, McGraw-Hill Companies, pp 476-477, 2000.

Hefnawy MM, Homoda AM, Abounassif MA, Alanazi AM, Al-Majed A, Mostafa GA. Potentiometric determination of moxifloxacin in some pharmaceutical formulation using PVC membrane sensors. Chem Central J. 2014;8:59.

Issa YM, Khorshid AF. Using PVC ion-selective electrodes for the potentiometric flow injection analysis of distigmine in its pharmaceutical formulation and biological fluids. J Adv Res. 2011;2:25–34.

IUPAC Analytical Chemistry Division. Potentiometric selectivity coefficients of ion selective electrodes. Pure and Applied Chemistry. 2000;72:1851–2082.

IUPAC Analytical Chemistry Division. Recommendation for nomenclature of ion selective electrode. Pure and Applied Chemistry. 1994;66:2527–36.

Ivanoic D, Medenica M, Jancic B, Knezevic N. Validation of an analytical procedure for simultaneous determination of hydrochlorothiazide, lisinopril, and their impurities. Acta Chromatogr. 2007;18:143–56.

Jain HK, Agrawal RK. Spectrophotometric methods for simultaneous determination of amlodipine besylate and lisinopril in tablets. Indian Drugs. 2000;37:196–9.

Karimi-Maleh H, Tahernejad-Javazmi F, Necip A, Mehmet LY, Vinod KG, Ali AE. A novel dna biosensor based on a pencil graphite electrode modified with polypyrrole/functionalized multiwalled carbon nanotubes for determination of 6-mercaptopurine anticancer drug. Ind Eng Chem Res. 2015;54:3634–9.

Khalil MM, Abdel Moaty SA, Korany MA. Carbon nanotubes based potentiometric sensor for determination of bambuterol hydrochloride: electrochemical and morphology study. Sens Act B. Chem. 2018;273:429–38.

Mashru RC, Parikh PP. Development of a method for simultaneous determination of amlodipine besylate and lisinopril in their combined dosage forms. East Pharm. 2000;43:111–2.

Mehmet LY, Vinod KG, Tanju E, Arif EŞ, Necip A. A novel electro analytical nanosensor based on graphene oxide/silver nanoparticles for simultaneous determination of quercetin and morin. Electrochim Acta. 2014;120:204–11.

Nafisur R, Manisha S, Nasrul H. Optimized and validated spectrophotometric methods for the determination of lisinopril in pharmaceutical formulations using ninhydrin and ascorbic acid. J Braz Chem Soc. 2005;16:1001–9.
Nevin ERK, Murat K. Comparison of high-performance liquid chromatography and absorbance ratio methods for the determination of hydrochlorothiazide and lisinopril in pharmaceutical formulations. Anal Lett. 1999;32:1131–41.
Pandya JJ, Sanyal M, Shrivastav PS. Simultaneous densitometric analysis of amlodipine, hydrochlorothiazide, lisinopril, and valsartan by HPTLC in pharmaceutical formulations and human plasma. J Liq Chromatogr Rel Tech. 2017;40:467–78.
Paraskevas G, Atta-Politou J, Koupparis M. Spectrophotometric determination of lisinopril in tablets using 1-fluoro-2,4-dinitrobenzene reagent. J Pharm Biomed Anal. 2002;29:865–72.
Parfitt K. The complete drug reference. 32nd ed. Martindalle, MA: The Pharamaceutical Press; 1999. p. 898.
Patchett A, Harris E, Tristram E, Wyvratt M, Wu M, Taub D, Peterson E, Ikeler T, Broeke JT, Payne L, Ondeyka D, Thorsett E, Greenlee W, Lohr N, Hoffsommer R, Joshua H, Ruyle W, Rothrock J, Aster S, Maycock A, Robinson F, Hirschmann R, Sweet C, Ulm E, Gross D, Vassil T, Stone C. A new class of angiotensin-converting enzyme inhibitors. Nature. 1980;288:280–3.
Prasad CVN, Saha RN, Parimoo P. Simultaneous determination of amlodipine-enalapril maleate and amlodipine-lisinopril in combined tablet preparations by derivative spectrophotometry. Pharm Pharmacol Commun. 1999;5:383–8.
Qin XZ, Nguyen DST, Ip DP. Capillary electrophoresis of cardiovascular drugs. J Liq Chromatogr. 1993;16(17):3713–34.
Rahman N, Anwar N, Kashif M. Application of pi-acceptors to the spectrophotometric determination of lisinopril in commercial dosage forms. IL Farmaco. 2005;60:605–11.
Rahman N, Siddiqui MR, Azmi SNH. Spectrophotometric determination of lisinopril in commercial dosage forms using N-bromosuccinimide and chloranil. Chem Anal (Warsaw). 2007;52:465–80.
Rajasekaran A, Murugesan S. Polarographic studies of lisinopril. Asian J Chem. 2001;13:1245–6.
Rajasekaran A, Udayavani S. Spectrophotometric determination of lisinopril in pharmaceutical formulations. J Indian Chem Soc. 2001;78:485–6.
Razak OA, Belal SF, Bedair MM, Barakat NS, Haggag RS. Spectrophotometric and polarographic determination of enalapril and lisinopril using 2,4-dinitrofluorobenzene. J Pharm Biomed Anal. 2003;31:701–11.
Sane RT, Valiyare GR, Deshmukh UM, Singh SR, Sodhi R. Simultaneous HPLC determination of lisinopril and hydrochlorothiazide from its pharmaceutical preparations. Indian Drugs. 1992;29:558–60.
Shawish HA, Saadeh S, Tamous H, Tbaza A. Determination of atomoxetine hydrochloride in biological fluids using potentiometric carbon paste electrode modified by TiO2 nanoparticles. Acta Chim Slovenica. 2018;65(4):811–22.
Suresh KS, Vinod KG, Mithalesh KD, Suresh J. Caesium PVC–crown (dibenzo-24-crown-8) based membrane sensor. Anal Proc Anal Comm. 1995a;32:21–3.
Suresh KS, Vinod KG, Suresh J. Determination of lead using a poly(vinyl chloride)-based crown ether membrane. Analyst. 1995b;120:495–8.
Suresh KS, Vinod KG, Suresh J. PVC-based 2,2,2-cryptand sensor for zinc ions. Anal Chem. 1996;68:1272–5.
The British Pharmacopoeia, Her Majesty's Stationary Office, London, pp 799, 1998.
The US Pharmacopoeia, 24th revision, Asian Edition, United States Pharmacopoeial Convention, INC, Twinbrook Parkway, Rockville, MD, pp 979, 2149, 2000.
Vinod KG, Arunima N, Shilpi A, Barkha S. Recent advances on potentiometric membrane sensors for pharmaceutical analysis. Comb Chem High Thr Scr. 2011a;14:284–302.
Vinod KG, Ashok KS, Lokesh KK. Thiazole Schiff base turn-on fluorescent chemosensor for Al^{3+} ion. Sens Act B. 2014a;195:98–108.
Vinod KG, Ganjali MR, Norouzi P, Khani H, Arunima N, Shilpi A. Electrochemical analysis of some toxic metals by ion–selective electrodes. Crit Rev Anal Chem. 2011b;41:282–313.
Vinod KG, Karimi-Maleh H, Roya S. Simultaneous determination of hydroxylamine, phenol and sulfite in water and waste water samples using a voltammetric nanosensor. Int J Electrochem Sci. 2015;10:303–16.
Vinod KG, Kumar S, Singh R, Singh LP, Shoora SK, Sethi B. Cadmium (II) ion sensing through p-tert-butyl calix[6]arene based potentiometric sensor. J Mol Liq. 2014b;195:65–8.
Vinod KG, Naveen M, Lokesh KK, Ashok KS. A reversible fluorescence "off–on–off" sensor for sequential detection of aluminum and acetate/fluoride ions. Talanta. 2015b;144:80–9.
Vinod KG, Naveen M, Lokesh KK, Ashok KS. Selective naked-eye detection of magnesium (II) ions using a coumarin-derived fluorescent probe. Sens Act B Chem. 2015a;207:216–23.
Vinod KG, Pankaj K. Cadmium(II)-selective sensors based on dibenzo-24-crown-8 in PVC matrix. Analytica Chimica Acta. 1999;389:205–12.
Vinod KG, Sethi B, Sharma RA, Shilpi A, Arvind B. Mercury selective potentiometric sensor based on low rim functionalized thiacalix [4]-arene as a cationic receptor. J Mol Liq. 2013;177:114–8.
Vinod KG, Singh LP, Rakesh S, Upadhyay N, Kaur SP, Bhavana S. A novel copper (II) selective sensor based on Dimethyl 4, 4′ (o-phenylene) bis(3-thioallophanate) in PVC matrix. J Mol Liq. 2011c;174:11–6.
Zacharis C, Tzanavaras P, Themelis D, Theodoridis G, Economou A, Rigas P. Rapid spectrofluorimetric determination of lisinopril in pharmaceutical tablets using sequential injection analysis. Anal Bioanal Chem. 2004;379:759–63.

Publisher's Note