RESEARCH ARTICLE JPAR 2020

Journal of Pharmaceutical Advanced Research

(An International Multidisciplinary Peer Review Open Access monthly Journal)

Available online at: www.jparonline.com

Host-guest Inclusion complex of Hydroxyl propyl-β-cyclodextrin and Lisinopril and Its Analytical Applications

Hasna Ahmed Abdelhadi, Abdalla Ahmed Elbashir*

Chemistry Department, Faculty of Science, University of Khartoum, P.O. Box 321, Khartoum, Sudan.

Received: 04.05.2020 Revised: 18.05.2020 Accepted: 22.05.2020 Published: 30.05.2020

ABSTRACT: Background: Lisinopril is angiotensin-converting enzyme (ACE) inhibitor, used primarily in conventional treatment of hypertension (high blood pressure). **Aim:** The aim of this research is to investigate the inclusion complex of Lisinopril and Hydroxyl propyl-β-cyclodextrin and to develop analytical method for analysis of Lisinopril in Pharmaceutical formulation. **Methods:** The UV Spectrophotometric method was employed based on the remarkable enhancement of the absorption intensity. The inclusion complex was studied at pH 2.0 buffer solution with maximum absorption at wavelength of 206 nm and inclusion complex was characterized using FT-IR spectrometer. **Results:** The formation of the inclusion complex was properly interpreted by the change and shifts in FT-IR spectrum of the formed complex in comparison with pure reagent and drug spectra, especially the Hydroxyl propyl-β-cyclodextrin hydroxyl group peak from 3392 to 3319 cm^{-1}due to the formation of hydrogen bond after the guest (Lisinopril) has been entrapped into the host (Hydroxyl propyl-β-cyclodextrin) cavity. The stoichiometry was found to be 1:2. The proposed method is valid and obeying Beer`s law due to the linear relationship between the absorbance and the concentration of Lisinopril over the concentration range 5 to 30 mg/L with reasonable correlation coefficient 0.9997. Moreover, the limits of detection (LOD) and quantification (LOQ) thus obtained 0.2934 and 0.8862 µg/ml, respectively. The mean recoveries were found to be 101.90±0.15, 105.13±0.16 and 105.60±0.07. All the parameters have been calculated as per International Conference on Harmonization (ICH) guidelines. **Conclusion:** The established method is particularly applicable for the determination of Lisinopril in Pharmaceutical formulations.

Corresponding author*
Prof. Abdalla Ahmed Elbashir
Chemistry Department, Faculty of Science,
University of Khartoum, Khartoum, Sudan.
Tel: +24-9912989405
Mail ID: aaelbashir@uofk.edu

Keywords: Host-guest inclusion complex, Hydroxyl propyl-β-cyclodextrin, Lisinopril, FTIR, UV spectrophotometer.

INTRODUCTION:

Cyclodextrins (CDs) are a family of macrocyclic oligosaccharides, encompassed of several glucose units bonded together forming a ring structure. Various types of naturally occurring and industrially prepared CDs are obtained, but mainly the three forms alpha (-α), beta (-β), and gamma (-γ) CDs which composed of 6, 7, and 8 glycopyranose units respectively have been widely studied [1,2]. It is because of the hydroxyl groups on the

outer surface of the CDs molecules that enable them forming water soluble host-guest complexes with other molecules by hydrogen bonds also additional weak forces as Van der waals and hydrophobic dipole-dipole interactions. These molecules such like non-cyclic oligosaccharides and polysaccharides [3-6]. Likewise, these inclusion complexes can be formed as a result of either a complete or partial hosting of the molecules depending on the polarity, shape, hydrophobicity, and the size of the guest. The hydrophobic internal cavity and the hydrophilic external surface of the CDs dramatically affect the physiochemical properties of the guest molecules just as the solubility and reactivity [7-13]. Correspondingly, these effects have been extensively utilized in different scientific fields including the pharmaceutical industry resulting in the significant improvement of the pharmaceuticals stability and solubility [14-16]. On the other hand, formation of the inclusion complexes has an important benefit in progressive enhancement of the absorption intensity when using UV spectrophotometer, so analysts use this property in accurate determinations of different pharmaceutical drugs [17-19]. Many applications of CDs have been efficiently handled especially Hydroxylpropyl-β-CD (HPβCD) (Fig 1) due to its higher water solubility, greater biocompatibility possession, and the lowest toxicity compared to CDs [20,21].

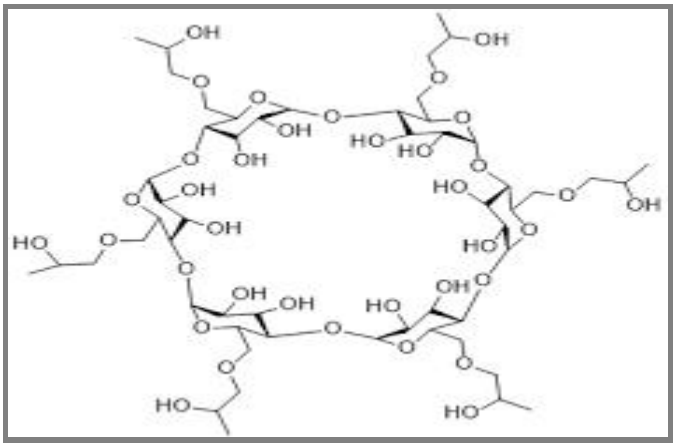

Fig 1. Chemical structure of Hydroxypropyl-β-cyclodextrin (HPβCD).

Lisinopril (LIS) is angiotensin-converting enzyme (ACE) inhibitor, used primarily in conventional treatment of hypertension (high blood pressure), congestive heart failure, and heart attack. Physically LIS is a white crystalline powder, highly soluble in water and sparingly soluble in alcohol. Furthermore, chemically LIS is {(S)-1-[N2-(1-carboxy-3-phenylpropyl)-l-proline} (Fig 2) [22-27]. A Number of analytical methods for the estimation of LIS starting from the official potentiometric titration and through the others LC-MS, HPLC, polarography, spectroflourimetry, and spectrophotometry have been reported [28-31]. However, some of these methods are time and chemical consuming, costly, and monotonous. Hence the reasonable demand for a rapid, simple, sensitive, and economical procedure is noticeable, especially for the routine analysis of pharmaceutical drugs that containing LIS. The objective of this study was to develop a rapid, selective, sensitive, and economical UV Spectrophotometric method for the determination of LIS in pharmaceutical dosage formulations.

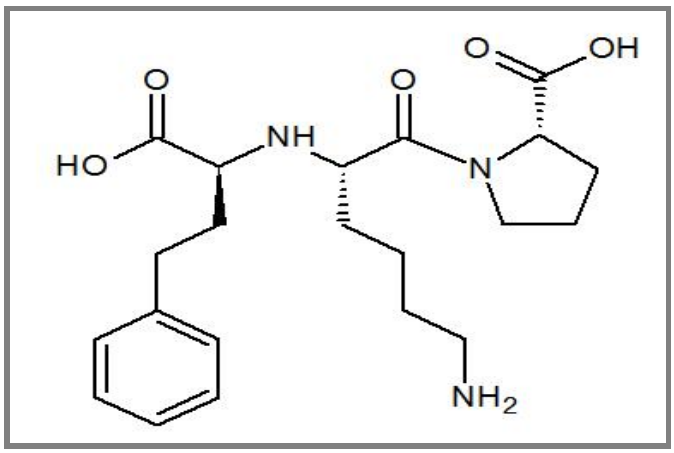

Fig 2. Chemical structure of Lisinopril (LIS).

MATERIALS AND METHODS:

Chemicals and reagents:

Hydroxylpropyl-β-cyclodextrin (HPβCD) was obtained from Sigma-Aldrich (ST. Louis, USA) and used without prior treatment. Lisinopril (LIS) was received from Azal pharmaceuticals company, Khartoum, Sudan. The two pharmaceutical formulations Zinopril and Linopril (10 mg/tablet) were purchased from the local market, which were manufactured by Jazeera pharmaceutical industries, Saudi Arabia and Pharma International Co. Amman, Jordan respectively. Doubled distilled water was used in all experiments. The whole reagents used were analytical grade.

Apparatus and instrumentation:

A PharmaSpec UV-1700 (Shimadzu, Japan) ultra violet spectrophotometer supplied with 1 cm quartz cell, Japan, has been used for all the quantitative measurement. pH meter model pH-3E for adjusting the pH. FT-IR data was carried out by Shimadzu FT-IR-8400S (Shimadzu, Japan) Fourier transform infrared spectrophotometer.

Preparations of standard and sample solutions:

***Preparation of HPβCD*:**

About 0.003 mol/l stock standards was prepared by dissolving 0.4126 g in 100 ml standard flask of doubled distilled water.

***Preparation of Lisinopril (LIS)*:**

About 100 mg/L stock solution was prepared by dissolving 0.01 g in 100 ml calibrated flask of doubled distilled water.

***Preparation of phosphate buffer solutions*:**

About 0.1 mol/l phosphate buffer solution was prepared by dissolving appropriate amounts of sodium dihydrogen phosphate (NaH_2PO_4) and disodium hydrogen phosphate (Na_2HPO_4) in doubled distilled water, the pH was adjusted from 1 to 6 using 0.1 mol/l hydrochloric acid (HCl) solution.

General recommended procedure:

About 1.5 ml of 100 mg/L LIS was transferred into a 10.00 ml volumetric flask, 1.5 ml of 0.1 mol/l phosphate buffer solution of pH 2.0, and 1.0 ml of 3.0×10^{-2} mol/l HPβCD were added sequentially, then it was diluted to the mark with doubled distilled water and mixed well. Only after the solution had equilibrated at 30 ˚C for 5 min, it was the absorbance measured at 206 nm against blank reagent prepared with the same reagents concentrations except the drug. The same method was applied to obtain the calibration graph by using aliquot volumes of LIS working solutions equivalent to 5 to 30 mg/L, then following the general procedure and plotting the absorbance versus the concentration of drug in mg/L.

Assay procedure for Lisinopril (LIS) tablets:

Twenty tablets were carefully weighed and finely powdered. An accurate weight equivalent to 10 mg of LIS was transferred into 100 ml conical flask and instantly dissolved and extracted in 60 ml distilled water. The residue was filtered through Whatmann filter paper no. 41 then transferred into 100 ml standard flask and diluted to the mark to obtain 100 mg/L stock solutions. Consequently, the prepared solutions were pursued the general recommended procedure.

Stoichiometric ratio of the inclusion reaction (Job`s method):

The stoichiometry determination of the inclusion complex was successfully performed using Job`s method of continuous variation [32,33]. Equimolar 1.0×10^{-4} mol/l aqueous solutions of LIS and HPβCD were prepared, then a series of 10.00 ml portions were made up constituting various complementary proportions (1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, and 9:1 ml). These solutions were properly treated as described in the general recommended procedure.

Characterization of LIS/HPβCD product:

The formed complex was investigated using Shimadzu FT-IR-8400S Fourier transform infrared spectrometer (FT-IR). The diffuse reflectance technique was carried out in the spectral region of 400 to 4000 cm^{-1}. The procedure consisting of placing the powdered dried sample which dispersed in KBr with 1:100 ratios respectively into a sampling cup, smoothing the powder into a disc, and compressing the powder using hand compressor. Having placed the sample into the light path, the spectrum was obtained. The FT-IR spectra of pure HPβCD, LIS, and LIS/HPβCD complex were also obtained following the same described procedure for comparison.

RESULTS AND DISCUSSION:

Absorption spectra:

The absorption spectra of LIS in the presence and absence of HPβCD was studied in the range of 200 to 400 nm. The obtainable results as shown in Fig 3 revealed that the λ_{max} of 15 mg/L LIS was found to be 206 nm. When 3.0×10^{-4} mol/l HPβCD was added to15 mg/L LIS in a buffer solution of pH 2.0, we clearly observed a significant increase of the absorbance without shift in wavelength. This experimentally confirmed the capability of LIS to form inclusion complex with HPβCD.

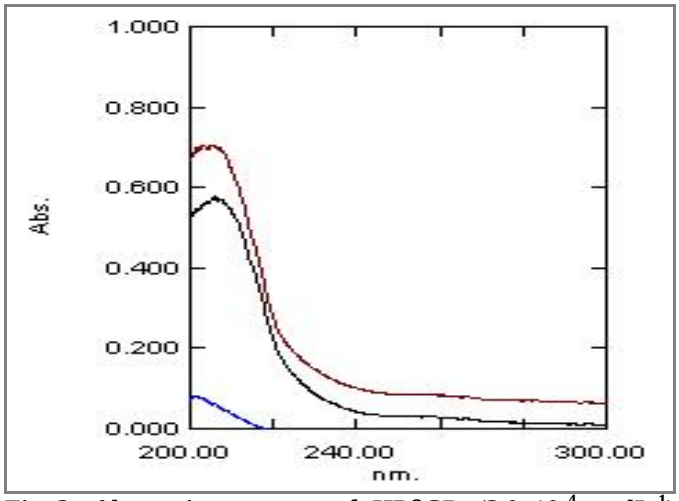

Fig 3. Absorption spectra of HPβCD (3.0×10^{-4} $molL^{-1}$) against water (▬), LIS (15 mg/L) against water (▬), and the reaction product of LIS (15 mg/L) with HPβCD (3.0×10^{-4} mol/l) against the reagent blank (▬).

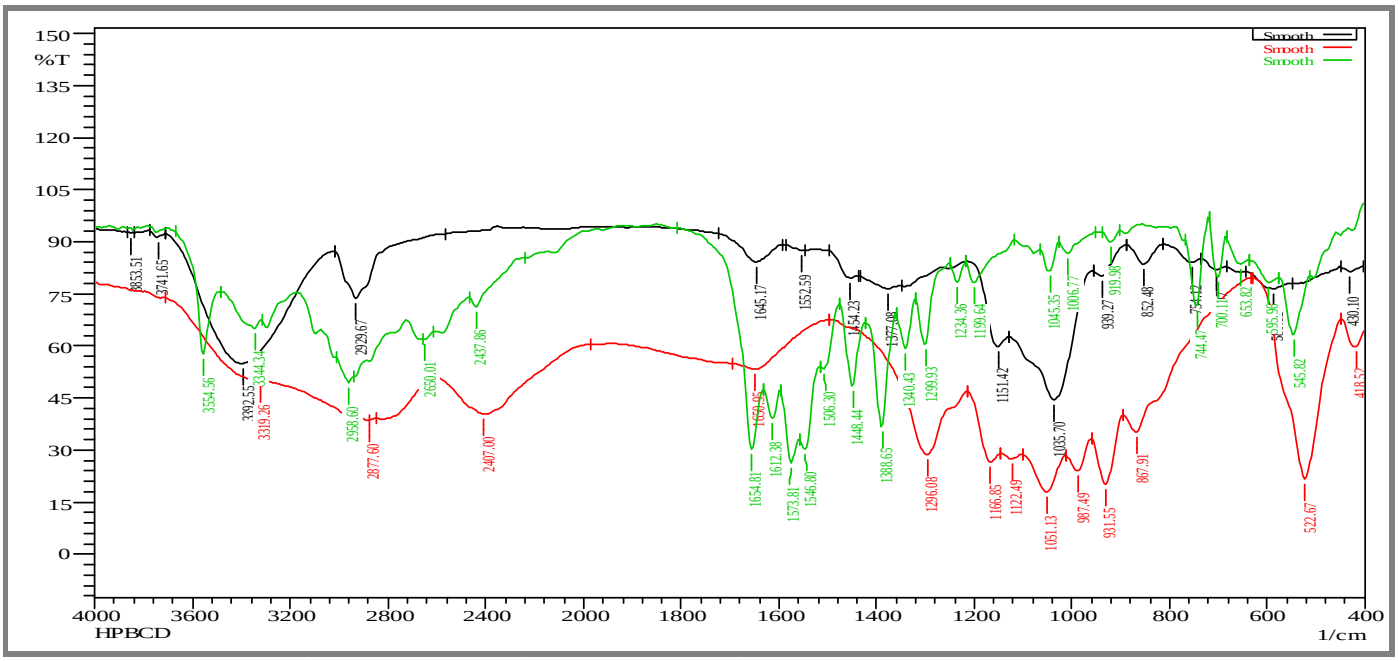

Fig 4. FT-IR spectra of (▬) Pure HPβCD, (▬) Pure LIS, and (▬) LIS- HPβCD complex.

FT-IR characterization of inclusion complex:

The IR spectrum of LIS/HPβCD product was conducted over the wave number from 400 to 4000 cm^{-1} using FT-IR spectrometer as described in Fig. 4. The IR spectrum of LIS was characterized by the presence of peaks for amine group, carboxyl group, and the aromatic structure of the pure drug. On the other hand, the presence of the strong stretching peak of hydroxyl group related to pure HPβCD reagent. In the spectrum, not only had the peaks shifted, but also they disappeared as noticed in LIS spectrum. Furthermore, the obvious shift and change can be explained as follows: in the spectral region 1400 to 1700 cm^{-1} of LIS we noticed the vibrations characteristic of the aromatic pure LIS at 1448, 1506 and 1546 cm^{-1}, amine group at 1537 cm^{-1}, and carboxyl groups at 1612 and 1654 cm^{-1} were shifted to 1650 cm^{-1} in the complex spectrum [34]. Additionally, in 2400 to 3600 cm^{-1} spectral region the presence of primary and secondary amine groups at 3344 and 3554 cm^{-1} respectively, hydroxyl groups at 2650 and 2958 cm^{-1}, we obviously noticed the disappearance of amine groups in the complex spectrum due to the intra-intermolecular hydrogen bonding because of the hydroxyl groups. The significant transformation and shift of the hydroxyl group peak in the pure HPβCD reagent from 3392 to 3319 cm^{-1} correctly interpret the formation of the LIS/HPβCD inclusion complex.

Optimization of the reaction conditions:

Numerous experimental parameters that affect the inclusion reaction of LIS and HPβCD were studied intensively and optimized. The main factors such as pH, volume of buffer, concentration of reagent, temperature, and reaction time were included.

Effect of pH:

The influence of pH on the absorbance of LIS/HPβCD complex was investigated over the range 1 to 6. The acidity of the solution was carefully adjusted by phosphate buffer solution. As shown in Fig 5, the maximum absorbance was noticed at pH 2.0 and started to gradually decrease until pH 6.0. Moreover, as pH value LIS is considered to be acidic due to the protonated amine functional groups [35] that is why pH 2.0 was reported as the optimum pH and properly chosen for the inclusion reaction with HPβCD.

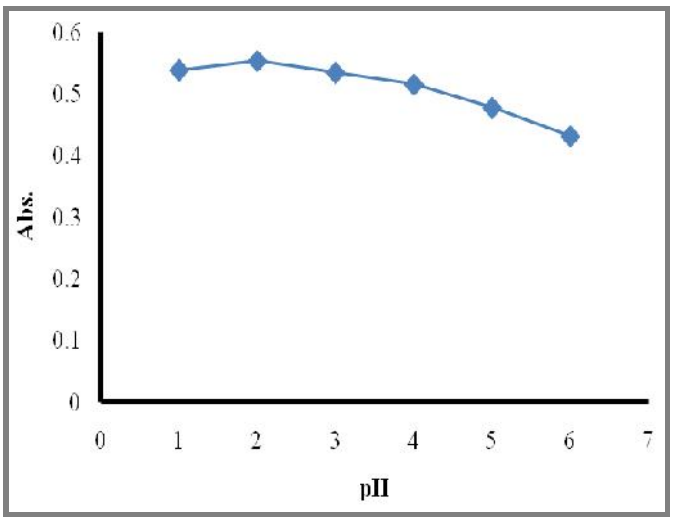

Fig 5. Effect of buffer pH on the reaction of LIS (15 mg/L) with HPβCD.

Effect of volume of buffer:

The influence of volume of phosphate buffer on the absorbance of the reaction product was studied using different volumes. It was found that the absorbance of LIS/HPβCD complex began to increase from 1.0 to 1.5 ml and then dramatically decreased as shown in Fig 6. Therefore, 1.5 ml of phosphate buffer of pH 2.0 had been selected as optimal volume.

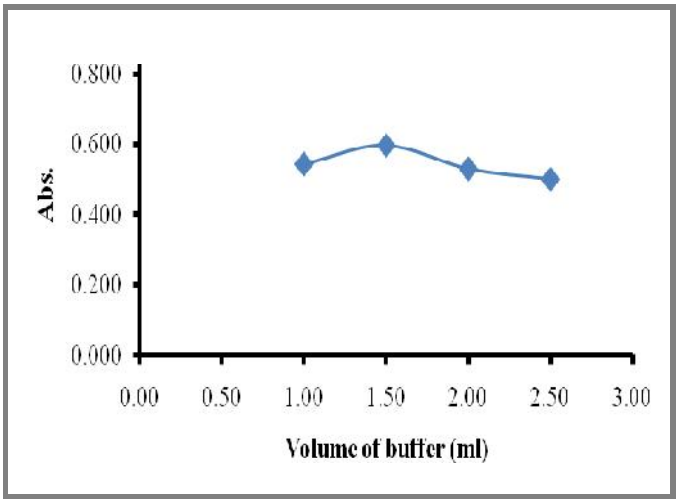

Fig 6. Effect of volume of buffer (pH 2.0) on the reaction of LIS (15 mg/L) with HPβCD.

Effect of concentration of HPβCD reagent:

The effect of HPβCD concentration was examined in intervals of 2.0 to 6.0×10^{-4} mol/L. It was observed that increasing in the concentration of HPβCD caused a noticeable increase in the product absorbance when reaching 3.0×10^{-4} mol/L as shown in Fig 7. Accordingly, 3×10^{-4} mol/L of HPβCD solution had been chosen as optimal concentration.

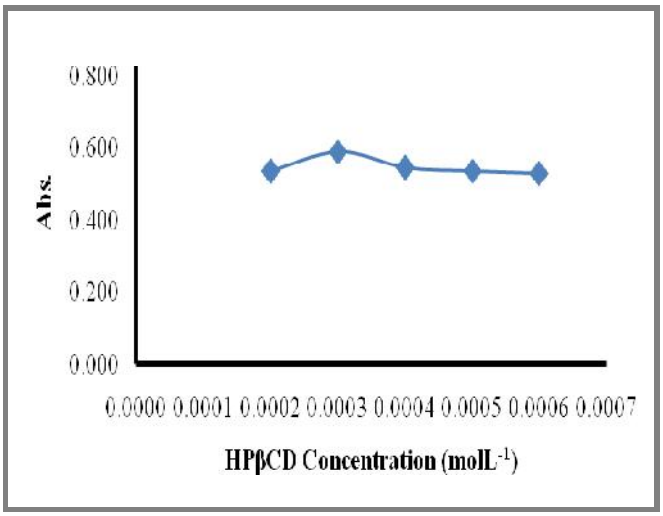

Fig 7. Effect of HPβCD reagent concentration on the reaction of LIS (15 mg/L) with HPβCD, buffer solution (pH 2.0): 1.5 ml.

Effect of temperature and reaction time:

The impact of temperature was evaluated in the range of 25 to 40 ˚C. The results as shown indicated that the absorbance of LIS/HPβCD complex subsequently increase when increasing the temperature up to 30 ˚C. Consequently, 30 ˚C had been appointed as the optimal temperature. On the other hand, the inclusion reaction was carried out in intervals of 5 to 20 min. It was recorded that the maximum absorbance of the reaction complex reached at 5 min and sharply decreased when increasing the time. Thus, 5 min had been designated as optimal time (data not shown).

Stoichiometry of the inclusion complex:

Following the optimum conditions of the reaction between HPβCD and LIS, the stoichiometry was well performed by Job`s method and it was found to be 1:2 respectively. The result is shown in Fig 8.

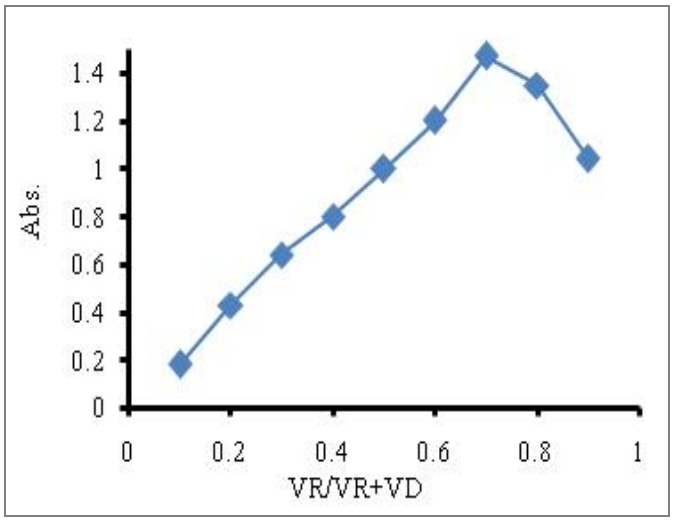

Fig 8. Determination of the product formation by continuous variation method.
V_R: HPβCD (1.0×10^{-4} mol/L); V_D: LIS (1.0×10^{-4} mol/L); V_R+V_D = 10 ml.

Method validation:

The validity of the proposed method was tested regarding to linearity, accuracy, precision, limits of detection (LOD) and quantification (LOQ), selectivity, and robustness according to ICH recommendations [36].

Linearity and sensitivity:

Under optimization conditions, the calibration graph was constructed by plotting the absorbance intensity of the inclusion reaction complex at 206 nm versus the concentration of LIS in mg/L. The obtainable calibration curve was linear over the range 5 to 30 mg/L. The regression equation had been reported from the data

analysis with correlation coefficient of 0.9997 which indicating good linearity due to its high value and conformity of Beer`s law.

The limit of detection (LOD) was determined by establishing the lowest concentration of LIS that can be readily detected and was measured according to ICH Q2(R1) recommendation, (LOD = 3.3 δ/S) where δ is the standard deviation of intercept of regression line of calibration curve and S is the slope. The limit of quantification (LOQ) was determined by evaluating the lowest concentration that can be calculated (LOQ = 10 δ/S). The recorded values of LOD and LOQ are summarized in Table 1. In addition to that, method sensitivity is numerically represented in terms of molar absorptivity (ε, l/mol cm) and Sandell's sensitivity which is well recognized by the following equation;

SS = (MW × N)/ MA ……. (1)

Where, SS is Sandell's Sensitivity, MW is molecular weight, N is the number of atoms in the element and MA is molar absorptivity and can be explicitly defined as the number of micrograms of elements which are in a column of solution having a cross section of 1 cm^2 showing absorbance of 0.001 and expressed as µg $ml^{-1}cm^{-2}$. The calculated values are abridged in Table 1.

Table 1. Parameters for the performance of the proposed method.

Parameter	Value
LIS λ_{max}, (nm)	206
LIS/HPβCD product λ_{max}, (nm)	206
Beer`s law limits, (mg/L)	5-30
Molar absorptivity, (L/mol cm)	1.4×10^4
Sandell sensitivity, (µg/cm^2)	0.0020
Limit of detection (LOD), (µg/ml)	0.2934
Limit of quantification (LOQ), (µg/ml)	0.8862
Regression Equation, Y*	
Intercept(a)	0.0371
Slope(b)	0.0352
Correlation coefficient(R^2)	0.9997
Standard deviation	0.0011
Relative Standard deviation** (%)	0.2469

***Y=a+bx, where Y is the absorbance, a the intercept, b the slope and x is the concentration in (mg/L).**
**** Calculated from three determinations.**

Accuracy and precision:

The accuracy of the developed method was practically confirmed by performing recovery studies by addition of known amount of the standard pure drug to pre-treated formulations at three different concentrations within the linear range and each one in triplicate. The experimental results have been described in Table 2. As a result of these values, being within the acceptable range and having a smaller relative error, it was obvious that the method is extremely accurate for quantitative estimation of LIS in tablet dosage formulations.

Table 2. Recovery studies for the determination of LIS by the proposed method.

LIS Taken	ASC (mg/L)	Found (mg/L)	Recovery (%±RSD)*	% RE
5	7	12.23	101.90 ±0.15	0.02
5	13	18.92	105.13 ± 0.16	0.05
5	17	23.23	105.60 ± 0.07	0.05

*** Calculated from three determinations. ASC – Added samples content. LIS taken in mg/L.**

The precision of the proposed method was carefully evaluated by analyzing three different concentrations of LIS working standards. For intra-day precision, three successive replicate determinations of each concentration were determined within the same day following the recommended procedure. The inter-day precision was carried out over three successive days with the same concentrations of LIS. The studied results are represented in Table 3 and the calculated relative standard deviations which were less than 2.0 and the smaller relative error indicating the good reproducibility of the established method. So this precision is adequately required for the routine analysis of LIS in quality control laboratories.

Table 3. Evaluation of intra-day and inter-day precision.

LIS Taken (mg/L)	Intra-day		
	Found (mg/L)	Recovery (%±RSD)*	% RE
12	12.12	101.03% ± 0.15	0.01
18	18.35	101.92% ± 0.09	0.02
22	22.23	101.04% ± 0.08	0.01
Inter-day			
12	12.75	104.74 ± 0.14	0.05
18	18.92	105.13 ± 0.16	0.05
22	22.58	102.63 ± 0.08	0.03

***Calculated from three determinations.**

Selectivity:

The selectivity of the proposed method had been examined by adding a minimal amount of known excipients used in the dosage forms to investigate the

interference. The analysis of these prepared samples following the recommended method revealed that the recovery values as shown in Table 4 had proved that there was no interference with the excipients.

Table 4. Investigation of LIS in the presence of the excipients.

Excipient	Recovery (%±RSD)*
Maize Starch	103.36±0.41
Magnesium Stearate	104.82±0.30
Sodium Starch Glycolate	101.22±1.71
Dibasic Calcium Phosphate	101.09±0.12
Micro-crystalline Cellulose	100.15±0.31
Lactose Monohydtare	100.33±0.12

***Calculated from three determinations.**

Robustness:

The robustness had been investigated by evaluating the major influence of the slight variation on its analytical performance. In the experiments, one parameter was changed while others were kept unchanged and the recovery percentage was calculated each time. It was reported that the tiny variation in method variables did not significantly affect the procedure. The recovery values as shown in Table 5 approved the reliability of the developed method during the routine analysis of LIS.

Table 5. Robustness of the proposed method.

Parameter	Modi-fication	Recovery (%±RSD)*
pH	1.95	95.03±0.12
	2.50	95.03±0.12
Volume of buffer (ml)	1.00	95.03±0.12
	2.00	96.42±0.21
HPβCD Concentration (mol/L)	0.0025	100.65±0.12
	0.0035	105.20±0.11
Temperature (˚C)	29.50	104.31±0.11
	30.50	105.01±0.11
Time(min)	4.50	96.29±0.12
	5.50	96.67±0.12

Application of method:

The proposed method was successfully applied to the accurately determination of LIS in some pharmaceutical formulations. The practical results as shown in Table 6 greatly indicated the high accuracy of the developed method and can be easily used for the analysis of LIS in quality control laboratories, since the recovery obtainable values were satisfactory.

Table 6. Results of assay of tablet formulations for the proposed method.

Tablet brand name	Label claim mg/tablet	Proposed method found (%±RSD)*
Linopril	10	101.41±0.12
Zinopril	10	99.58±0.12

***Calculated from three determinations.**

CONCLUSION:

The established method is rapid, simple, economical, selective, precise and highly sensitive. Moreover, it can be directly used in the routine analysis of LIS in pharmaceutical dosage formulations in quality control laboratories. Since the experimental results are reproducible regarding to the Spectrophotometric method.

REFERENCES:

1. Misiuk W, Jasiuk E. Study of the inclusion interaction of HP-γ-cyclodextrin with bupropion and its analytical application. J Mol Struct, 2014; 1060: 272-279.
2. Dsugi NFA, Elbashir AA, Suliman FO. Supramolecular interaction of gemifloxacin and hydroxyl propyl β-cyclodextrin spectroscopic characterization, molecular modeling and analytical application. Spectrochim Acta A, 2015; 151: 360-367.
3. Loftsson T, Duchene D. Cyclodextrins and their pharmaceutical applications. Int J Pharm, 2007; 329: 1-11.
4. Dani RMMA, Elbashir AA. Host-guest inclusion complex of β-cyclodextrin and cephalexin and its analytical application. Int J Pharm Chem Res, 2013; 2(1): 1-13.
5. Pena AMD, Ndou TT, Zung JB, Greene KL, Live DH, Warner IM. Alcohol size as a factor in the ternary complexes formed with pyrene and β-cyclodextrin. J Am Chem Soc, 1991; 113(5): 1572-1577.
6. Milewski M, Augustyniak W, Maciejewski A. Ternary complexes of 4H-1-benzopyran-4-thione with β-cyclodextrin and alcohols. J Phys Chem A, 1998; 102(38): 7427-7434.
7. Elbashir AA, Dsugi NFA, Aboul-Enein HY. Supramolecular study on the interaction between

ofloxacin and methyl β-cyclodextrin by fluorescence spectroscopy and its analytical application. J Fluoresc, 2014; 24: 355-361.
8. Linares M, De Bertorello MM, Longhi M. Preparation and characterization of solid complexes of naphtoquinone and hydroxypropyl-β-cyclodextrin. Molecules, 2000; 5(3): 342-344.
9. Macedo OFL, Andrade GRS, Conegero LS, Barreto LS, Costa NB, Gimenez IF, *et al*, Kubota, D. Physiochemical study and characterization of the trimethoprim/2-hydroxypropyl-γ-cyclodextrin inclusion complex. Spectrochim Acta A, 2012; 86: 101-106.
10. Misiuk W, Zalewska M. Spectroscopic investigations on the inclusion interaction between hydroxypropyl-β-cyclodextrin and bupropion. J Mol Liq, 2011; 159(3): 220-225.
11. Ge X, Huang Z, Tian S, Huang Y, Zeng C. Complexation of carbendazim with hydroxypropyl-β-cyclodextrin to improve solubility and fungicidal activity. Carbohydr Polym, 2012; 89(1): 208-212.
12. Misiuk W. Investigation of inclusion complex of HP-γ-cyclodextrin with ceftazidime. J Mol Liq A, 2016; 224: 387-392.
13. Fanali S. Enantioselective determination by capillary electrophoresis with cyclodextrins as chiral selectors. J Chromatogr A, 2000; 875: 89-122.
14. Radhouan M, Abderrahim R. Applications of cyclodextrins: formation of inclusion complexes and their characterization. Int J Adv Res, 2015; 3(2): 1030-1030.
15. Jullian C, Alfaro M, Zapata-Torres G, Olea-Azar C. Inclusion complexes of cyclodextrins with galangin: a thermodynamic and reactivity study. J Solution Chem, 2010; 39: 1168-1177.
16. Wang H, Wang S, Zhu H, Wang S, Xing J. Inclusion complexes of lycopene and β-cyclodextrin: preparation, characterization, stability and antioxidant activity. Antioxidants, 2019; 8(8): 314.
17. Elbashir AA, Dsugi NFA, Mohamed TOM, Aboul-Enein HY. Spectroflourometric analytical applications of cyclodextrins. Luminescence, 2014; 29: 1-7.
18. Dsugi NFA, Elbashir AA. Supramolecular interaction of moxifloxacin and β-cyclodextrin spectroscopic characterization and analytical application. Spectrochim Acta A, 2015; 137: 804-809.
19. Panda S, Nayak M. Taste masking of caffeine by inclusion complexation of β-cyclodextrin. J Pharm Adv Res, 2018; 1(4): 224-228.
20. Sapkal NP Kilor, VA Bhusari KP, Daud AS. Evaluation of some methods for preparing gliclazide-β-cyclodextrin inclusion complexes. Trop J Pharm Res, 2007; 6(4): 833-840.
21. Patel HH, Trivedi M, Maniar M, Ren C, Dave RH. Effect of β-cyclodextrin and hydroxypropyl β-cyclodextrin on aqueous stability, solubility and dissolution of novel anti-cancer drug rigosertib. J Pharm Res Int, 2018; 21(3): 1-20.
22. Preetham DN, Sujana K, Sankar PD. Development and validation of UV- spectrophotometric method for the estimation of lisinopril in bulk and pharmaceutical formulation. Int J Pharm Sci Rev Res, 2014; 25(1): 257-259.
23. Ahmed AA, Elbashir A. Spectrophotometric determination of lisinopril dehydrate in pharmaceutical formulations using sodium 1,2-naphthoquinone-4-sulfonic. ISESCO J Sci Technol, 2012; 8(13): 30-36.
24. Chavan V, Phasate P. Development and validation of a UV-spectrophotometric method for the determination of lisinopril both in bulk and marketed dosage formulations. Int J Pharm Sci Res, 2015; 6: 394-397.
25. El-adl SM, El-sadik ME, Saeed NM. Spectroflourometric determination of lisinopril dehydrate and methyl-dopa in bulk and pharmaceutical formulation by using dansyl chloride. J Pharm Pharmacol, 2018; 2(1): 1-14.
26. Raza A, Ansari TM, Rehman A. Spectrophotometric determination of lisinopril in pure and pharmaceutical formulations. J Chin Chem Soc, 2005; 52: 1055-1059.
27. Gul W, Augustine Z, Khan S, Saeed K, Raees H. Methods of analysis of lisinopril: a review. J Bioequiv Availab, 2017; 9: 331-335.
28. Rajendraprasad N, Basavaiah K. Development of membrane electrodes for selective determination of lisinopril in pharmaceuticals. J Anal Sci Technol, 2019; 10(37): 1-14.
29. Dawud ER, Shakya AK. HPLC-PDA analysis of ACE-inhibitore, hydrochlorothiazide and indapamide utilizing design of experiments. Arab J Chem, 2019; 12: 718-728.

30. Digambar MA, Santosh J, Ashpak T, Vijay K. Development and validation of UV-spectrophotometric estimation of lisinopril dehydrate in bulk and tablet dosage form using area under curve method. World J Pharmacy Pharm Sci, 2014; 4(2): 589-596.
31. El-gindy A, Ashour A, Abdel-Fattah L, Shabana MM. Spectrophotometric, spectroflourometric and LC determination of lisinopril. J Pharmaceut Biomed, 2001; 25(5-6): 913-922.
32. Bosque-Sendra JM, Almansa-Lopez E, Garcia-Campana AM, Cuadros-Rodriguez L. Data analysis in the determination of stoichiometries and stability constants of complexes. Anal Sci, 2003; 19(10): 1431-1439.
33. Upadhyay SK, Kumar G. NMR and molecular modeling studies on the interaction of fluconazole with β-cyclodextrin. Chem Cent J, 2009; 3: 1-9.
34. Olaru A, Borodi Gh, Kacso I, Vasilescu M, Bratu I, Cozar O. Spectroscopic studies of the inclusion compound of lisinopril with β-cyclodextrin. Spectrosc, 2009; 23: 191-199.
35. Novak KT, Deak K, Beni S, Volgyi G. Physico-chemical profiling of the ACE-inhibitor lisinopril: acid-base properties. ADMET & DMPK, 2013; 1(2): 6-16.
36. Validation of analytical procedures, text and methodology (ICH Q2(R1), complementary guideline on methodology, 2005.

Conflict of Interest: None
Source of Funding: Nil
Paper Citation: Abdelhadi HA, Elbashir AA*. Host-guest Inclusion complex of Hydroxyl propyl-β-cyclodextrin and Lisinopril and Its Analytical Applications. J Pharm Adv Res, 2020; 3(5): 881-889.