

FULL PAPER

New sensitive turbidimetric method for determination of losartan potassium in pharmaceutical formulations using flow injection combined with homemade turbidimeter

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This paper is describing a rapid and sensitive method for determination of Losartan potassium (LOS-K) in pure and drug forms. The method is based on the reaction of LOS-K with potassium hexacyanoferrate (III) in acidic medium to form a yellow precipitate. The precipitated product was monitoring and measurements using homemade (Ayah 6Sx1-T-2D solar cell) analyzer that combined with a continuous flow injection technique. Chemical and physical factors such as reagent concentration, acid medium, flow rate, sample volume, purge duration, and delay coil reaction were investigated and optimized. The linear dynamic range of LOS-K was 0.1-2 mmol/L with linearity percentage ($r^2\%$) 98.41%. Limit of detection (LOD) at a minimum concentration in the calibration graph was 5.8 $\mu\text{g}/\text{sample}$ and limit of quantitation was $\text{LOQ}=38.3 \mu\text{g}/\text{sample}$. A comparison of developed method with reference methods (UV-Spectrophotometry at $\lambda_{\text{max}}= 232$) was also made. These results indicate that the proposed method- which was successfully applied for determination of LOS-K in the pharmaceutical samples, can be used as an alternative for classical methods.

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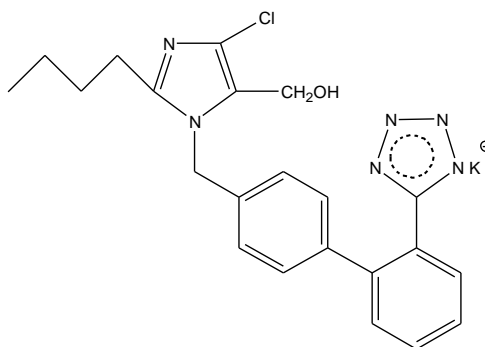
KEYWORDS

Losartan potassium; turbidity; continuous flow injection analysis; potassium hexacyanoferrate.

Introduction

Losartan potassium (LOS-K) is an oral drug which belongs to class of angiotensin receptor blockers⁽¹⁾. Losartan potassium has been

chemically described as 2-n butyl-4-chloro-5-hydroxymethyl-1((2-(1H tetrazol-5-yl)(biphenyl-4-4-yl)methyl) imidazole (Figure 1).

**FIGURE 1** Chemical structure of Losartan potassium

The anti-hypertensives drugs such as (LOS-K) have been frequently used for combat cardiovascular morbidity⁽²⁾. Losartan potassium is the first of a new class of drugs to be introduced for clinical use in hypertension. In general, the metabolite contributes substantially to its antihypertensive effect for patient that continues for 24 hours after the dose⁽³⁾. The dose of a 50-100 mg tablet daily can be taken for mild cases form high blood pressure, which a similar degree to atenolol, felodipine and enalapril⁽³⁾. In 1995, LOS-K became the first nonpeptide drug which is approved for the treatment of hypertension alone or in combination with other antihypertensive agent⁽⁴⁾. Also, LOS-K was used for the progression of renal disease to the terminal stage in diabetic patients, and LOS-K was applied to increase uric acid with excretion and combats proteinuria that could slow down the progress of diabetic nephropathy. LOS-K can be administered in combination with diuretics⁽⁵⁾. Losartan potassium (LOS-K) is white to off white powder, freely soluble in water ($pK_a = 4.9$), isopropyl alcohol and slightly soluble in acetonitrile in addition the melting point at range 183.5-184.5 °C with chemical formula $C_{22}H_{23}ClN_6O$ and average weight 462.01 g/Mol⁽⁶⁾. There are many methods for determination of LOS-K in pure form and pharmaceutical preparation, including: Spectrophotometric⁽⁷⁻⁸⁾, spectrophotometric and HPLC⁽⁹⁾, high performance liquid chromatography (HPLC)⁽¹⁰⁻¹¹⁾, conductometric⁽¹²⁾, spectrofluorimetric⁽¹³⁾ and electrochemical and photometric method⁽¹⁴⁾. In this research, the developed method was dependent on the on-line measurement of attenuation of incident light by homemade analyzer (Ayah 6Sx1-T-2D solar cell) for analysis the LOS-K in pharmaceutical preparation using potassium hexacyanoferrate (III) in acidic media as precipitating agent.

Materials and methods

Reagent and chemical

All chemicals used in this research were of analytical grade and distilled water was used in all dilution processes. A standard solution 10 mMol/L of LOS-K (molecular weight 462.01 g/mol) was prepared by dissolving 1.155 g in 250 mL; and 0.2 mol/L of Potassium hexacyanoferrate (III) (molecular weight 294.18 g/mol) was prepared by dissolved 14.709 g in 250 mL of distilled water.

Apparatus

A homemade Ayah 6Sxl-T-2D solar cell analyzer was used that contained a flow cell irradiated with six snow-white light emitting diode LEDs at 2 mm path length; and two solar cell used as detector for signals via sample travel for 60 mm length. The homemade Ayah 6Sxl-T-2D solar cell analyzer has been produced by Prof. Dr. Issam M.A. Shakir and Prof. Dr. Nagam S. Turkey⁽¹⁵⁾. Peristaltic pump that contain two-channel and variable speed (Ismatec, Switzerland) and six-port 2 directions injection valve with a different sample volume. The output response signals were obtained by x-t potentiometric recorder (Siemens Kompenco C-1032, Germany), while the comparison of the developed method was performed by determining the formed product using two references methods (UV-Vis Spectrophotometer (Shimadzu model UV-1800, Japan) and Turbidometry via Turbidity-meter, HANNA-Hungary).

Methodology

The design of the two-line manifold system (Figure 2) was used Ayah 6Sxl-T-2D solar cell analyzer for (LOS-K) determination of using potassium hexacyanoferrate (HCF) as precipitating agent. A preliminary experimental concentration (0.1 mMol/L) of precipitating agent that reacted with (2 mMol/L) LOS-K to form yellow precipitate as

an ion pair complex. The first line (carrier stream) is 10 mMol/L HCl at 1.6 mL/min flow rate, which leads to injection valve to carry LOS-K (2 mMol/L) from the sample volume 157 μ L and combine with the second line (1.4 mL/min) at Y-junction to form the precipitate

product. The measurements of responses were carried out by Ayah 6Sxl-T-2D solar cell; which was recorded *via* used x-t potentiometric recorder (Siemens Kompenso C-1032, Germany). The proposed mechanism of reaction is expressed in Scheme 1 [16].

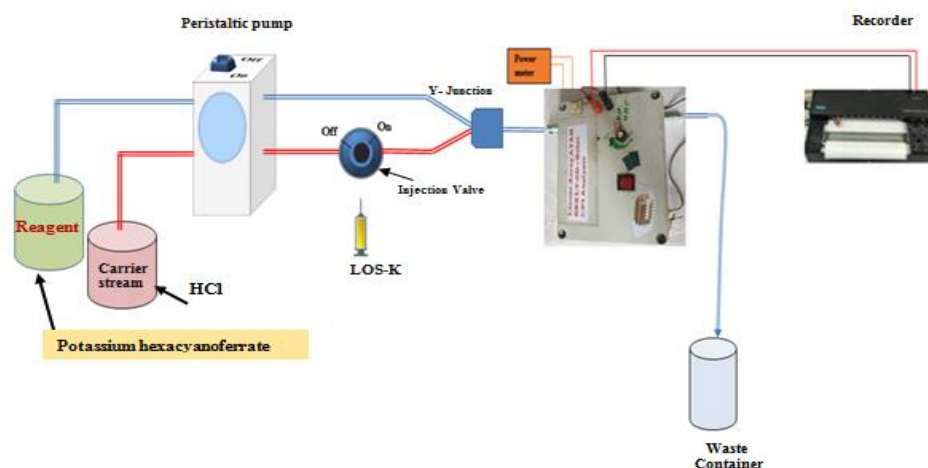
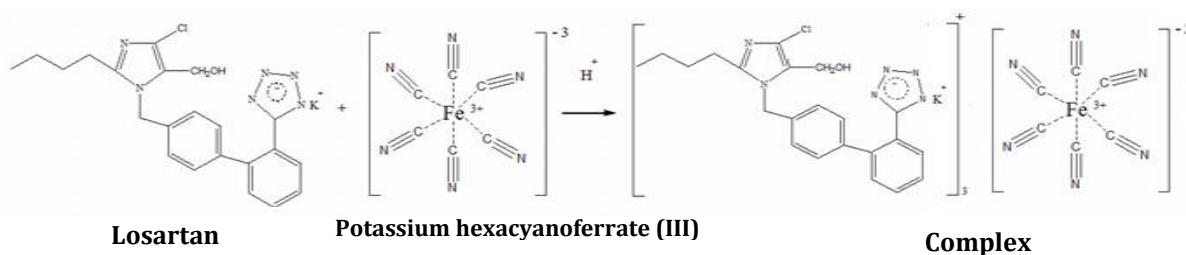


FIGURE 2 Two-line manifold system design for LOS-K determination using precipitation system [LOS-K]- $K_3[Fe(CN)_6]$ -HCl



SCHEME 1 Proposed mechanism of the reaction the Losartan potassium with potassium hexacyanoferrate (III)

Results and discussion

Optimization of reaction pattern parameters

A chemical as well as physical parameters that effect on the sensitivity of a clear profile of response were investigated. The chemical variables are the concentration of potassium hexacyanoferrate as reagents in presence of several kinds of acid and salts on sensitivity. In addition to studying the effect of acids type on the signal response, the physical variables involved: Flow rate, sample volume, purge time & coil length.

Chemical variables

Precipitating agent (potassium hexacyanoferrate III)

The study was carried out using a variable concentration of precipitating agent (potassium hexacyanoferrate (III)) ranging 0.05-7 mMol/L. The potassium hexacyanoferrate (III) reagents were prepared and transferred at 1.4 mL/min flow rate, while preliminary parameters such as a 1.6 mL/min flow rate for HCl as carrier stream, 157 μ L sample volume, open valve mode and 2 mMol/L concentration of LOS-K were used

in this study. The applied voltage to the LEDs was 2-volt DC. Figure 3 shows that the responses profile increase when the precipitate agent increases up to 0.3 mMol/L due to formation of precipitate particulate that might an increase the reflection of incident light and that refers to increase on incident light intensity. Each measurement was repeated for three times, while more than 0.3

mMol/L for potassium hexacyanoferrate (III) caused a decrease in the intensity of the light. It is possible due to formation of large agglomerate particles leading to form interstitial spaces that pass a larger amount of the focused light and thus reduces the response. Therefore, 0.3 mMol/L was selected as the optimum concentration.

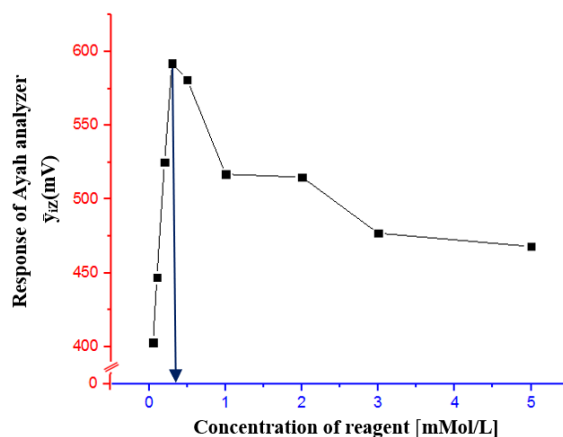


FIGURE 3 Variation of precipitating reagent (potassium hexacyanoferrate) (III) that effect on precipitation system for analysis LOS-K

Effect of reaction medium

A series of different medium solution at 10 mMol/L concentration H_2SO_4 , HCl, H_3PO_4 and CH_3COOH as acid media were prepared as carrier stream at 1.6 mL/min flow rate while reagent 1.4 mL/min flow rate, 2 mMol/L of LOS-K was used as the injected concentration and 157 μ L sample volume. It was found that during use of potassium hexacyanoferrate

(III) as a precipitating agent an increase of peak height and sharp response in presence of CH_3COOH as carrier stream. Most probably, the other medium (H_2SO_4 , HCl and H_3PO_4) causing dispersion of precipitate particulate into a smaller one that in turn were unable to reflect all light ⁽¹⁷⁾. Therefore CH_3COOH was the optimum choice to use for LOS-K-potassium hexacyanoferrate (III) system. All the obtained data are shown in Table 1.

TABLE 1 Effect of medium solution of carrier stream on potassium hexacyanoferrate to determination of LOS-K

Acid type [10 mMol/L]	Detector Response \bar{y}_{iz} (mV)	S.D.	RSD%	Confidence interval of the average at (95%) $\bar{y}_i \pm t_{(\alpha=0.05/2)} \frac{\sigma_{n-1}}{\sqrt{n}}$
potassium hexacyanoferrate				
H_2SO_4	278	1.305	0.469	278 ± 3.242
HCl	588	1.216	0.207	588 ± 3.021
H_3PO_4	273	1.210	0.441	273 ± 3.006
CH_3COOH	656	2.250	0.344	656 ± 5.589

Effect of CH_3COOH Concentration on diverged light for LOS-K - $\text{K}_3[\text{Fe}(\text{CN})_6]$ system

We used previously achieved experimental parameters: (2 mMol/L of LOS-K- 0.3 mMol/L $\text{K}_3[\text{Fe}(\text{CN})_6]$ system and 157 μL sample volume with open valve mode). A series of solution (CH_3COOH) was prepared (3,10,15 and 20 mMol/L) at 1.6 ,1.4 mL/min flow rate of carrier stream and reagent lines respectively. It was noticed that an increase in peak height with an increase of CH_3COOH concentration up to 10 mMol/L. This increase is due to the piling up of large precipitate particles and thus the reflection all light, while high concentration of CH_3COOH (i.e., over 10 mMol/L) led to decrease of peak response; it might be due to the dispersion of large precipitate particulate. Therefore, 10 mMol/L concentration of CH_3COOH was chosen as an optimum carrier stream that used for further experiments.

Physical parameters

Flow rate effect

We determined the preferred flow rate in the range of 0.4-4 mL/min for the carrier stream and 0.35-3 mL/min for the reagent and the 157 μL sample loop. Fixing all other variables constant (concentration) for LOS-K (2 mMol/L) - $\text{K}_3[\text{Fe}(\text{CN})_6]$ (0.3 mMol/L)- CH_3COOH (10 mMol/L) system, we was noticed the 3.1,2.7 mL/min flow rate for two lines respectively, the carrier stream and the reagent. There was an increase in peak base (Δt_B) that due to an increase diffusion and dispersion as shown in Figure 4. While at higher flow rate > 3.1 for carrier stream and more than 2.7 mL/min for and the precipitating reagent was a slightly decrease of response peak height due to departure of precipitate particulate from measuring cell at a short time⁽¹⁸⁾. Therefore, the optimum flow rate was chosen at 3.1, 2.7 mL/min flow rate for two lines; carrier stream and reagent, respectively.

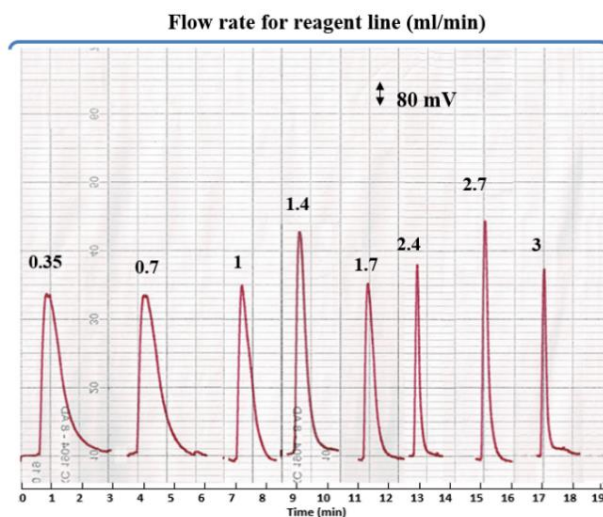


FIGURE 4 Peak profile for flow rate variation for system LOS-K- Potassium hexacyanoferrate (III)- CH_3COOH

Effect of variation of sample volume

The effect of variable sample volume (50-250) μL represented 20 cm up to 100 cm teflon tube of Φ (diameter) 1mm. It was noticed that an increase in sample volume led

to increase of peak response up to 157 μL , done by using precipitation system i.e., LOS-K(2 mMol/L)- $\text{K}_3[\text{Fe}(\text{CN})_6]$ (0.3 mMol/L)- CH_3COOH (10 mMol/L) system at 3.1 & 2.7 mL/min flow rate for carrier stream and reagent, respectively. But, using sample

volume more than 157 μL , the peak height decreased with increasing of base width (Δt_B) that caused by a decrease in the divergence of light. It was probably due to a slow movement of particles in front of flow cell, resulting from

the continuous relatively longer time duration of carrier stream to pass through injection valve⁽¹⁹⁾. Therefore, 157 μL was chosen as the optimum sample volume for carrying out the remainder of the studies (Figure 5).

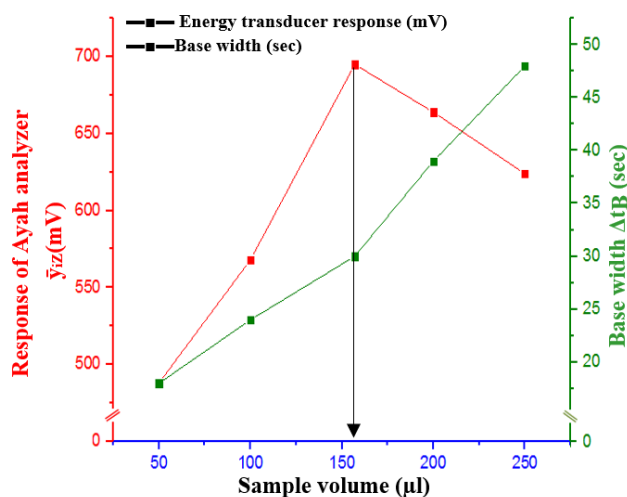


FIGURE 5 Effect of sample volume variation on precipitation system using 2mMol/L LOS-K concentration

Purge time

We determined the optimum duration of the injection time i.e., allowing permissible time for purging of the sample from the injection valve (157 μL sample loop). Different purge time was used for the segment at the range of 5-25 sec and an additional open valve. The peak height which increased with an increase of injection time up to open valve mode (25 Sec) for the precipitating system involved LOS-K(2 mMol/L)- $\text{K}_3[\text{Fe}(\text{CN})_6]$ (0.3 mMol/L)- CH_3COOH (10 mMol/L) system at 3.1 & 2.7 mL/min flow rate for the carrier stream and the reagent, respectively. Therefore, the continuous mode of valves (open valve) was selected as the optimum purge time.

Reaction coil

Variable coil reaction range (0-314) was added after the injection valve directly in flow

system (between Y-junction and measuring), which allowed mixing the precipitating agent potassium hexacyanoferrate (III) with LOS-K, and giving rearrangement of precipitated particulate. The study was achieved at an optimum all chemical and physical parameters (LOS-K(2 mMol/L)- $\text{K}_3[\text{Fe}(\text{CN})_6]$ (0.3 mMol/L)- CH_3COOH (10 mMol/L) system at 3.1 & 2.7 mL/min flow rate for carrier stream and reagent respectively. It was noticed the decrease in the peak high response with an increase coil reaction (reaction length) associated with increase of the base width (Δt_B). This was probably due to dilution and dispersion of the segment sample that led to an increase of dispersion regions, which reduced the reflected light [20]. Therefore, peak high and clearly response can be seen without coil reaction. Figure 6 shows the optimum choice of system.

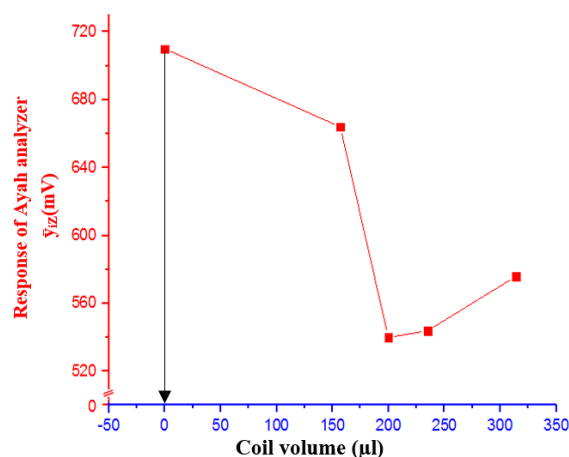
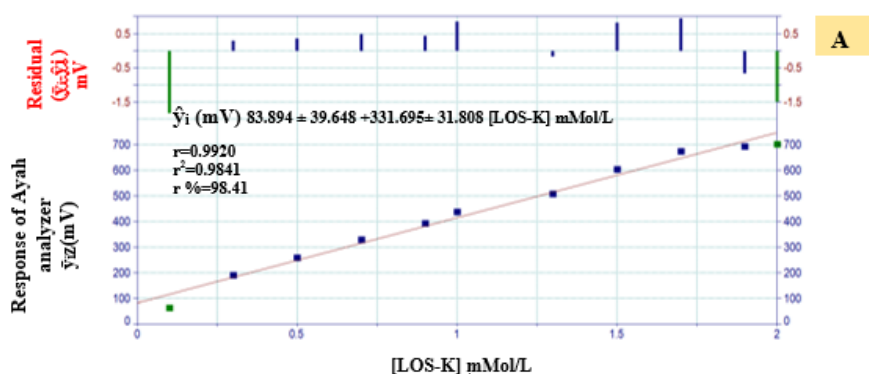


FIGURE 6 Effect of mixing coil length on developed method for analysis of LOS-K

Calibration Graph Study for Losartan potassium

The calibration curve of LOS-K was conducted by applying all of the optimum chemical and physical parameters for system. A set of LOS-K solution (0.08 – 2.3 mMol/L) was used with $K_3[Fe(CN)_6]$ (0.3 mMol/L)- CH_3COOH (10 mMol/L) system at 3.1 mL/min flow rate for reagent. Figure 7A shows linear calibration curve using a homemade Ayah 6Sxl-T-2D-solar cell analyzer at range (0.1-2 mMol/L) concentration of LOS-K. The method achieved in this research work was compared with the two classical methods, spectrophotometric and turbidometry methods. Figure 7B shows the calibration curve of classical method *via* the measurements of spectrum absorbance at

$\lambda_{max}=232$ nm [21]. In addition, measurements of the linearity calibration curve ranged from 0.01-0.4 mMol/L. Additional classical method, (turbidometry method) which was based on the reaction of $K_3[Fe(CN)_6]$ as a precipitating agent (optimum concentration of 0.5 mMol/L) with the LOS-K curve ranged from 0.01-0.7 mMol/L (Figure 7C). Table 2 illustrates all the results of determination of the LOS-K using a homemade Ayah 6Sxl-T-2D-solar cell analyzer and classical methods (spectrophotometric and turbidometry methods), including: measurements to estimate value of the response obtained from linear regression analysis, linearity percentage, correlation coefficient (r), coefficient of determination (r^2) and calculated t-value at 95% confidence level.



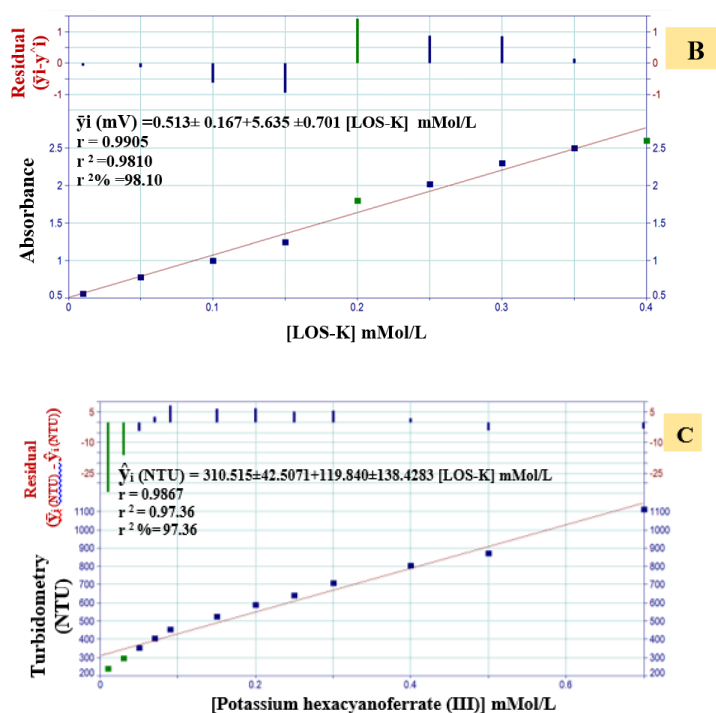


FIGURE 7 A. Linear calibration curve for determination LOS-K at range [0.1-2 mMol/L] n=11 by precipitation reaction of LOS-K- potassium hexacyanoferrate (III)(0.3 mMol/L)-CH₃COOH (10 mMol/L) system, B. Calibration curve for variation of LOS-K concentration using classical method (spectrophotometric method at λ_{\max} =232 nm), C. Calibration curve of turbidometric method (classical method) at range (0.01-0.7 mMol/L)

TABLE 2 A statistical Summary of Calibration curve results for the determination of LOS-K

Type of measurement	Linear dynamic range mMol/L	$\bar{y}_i = a \pm S_{a,t} + b \pm S_{b,t}$ [mMol/L] at confidence level at 95 %,n-2	r, r ² , r ² %	t _{tab} at 95%, n-2	Calculated t-value $\frac{t}{r/\sqrt{n-2}}$
Developed method	0.1-2 n=11	\bar{y}_i (mv)= 83.894 ± 39.648 + 331.695 ± 31.808 [LOS-K] mMol/L	0.9920, 0.9841, 98.41	2.262 << 23.587	
UV-Vis method at λ_{\max} =232nm	0.01 – 0.4 n=9	$\bar{y}_i = 0.513 \pm 0.167 + 5.635 \pm 0.701$ [LOS-K] mMol/L	0.9905, 0.9810, 98.10	2.365 << 19.013	
Turbidometry method	0.01 – 0.7 n=11	$\bar{y}_i = 310.515 \pm 42.5071 + 119.840 \pm 138.4283$ [LOS-K] mMol/L	0.9867, 0.9736, 97.36	2.228 << 19.231	

\hat{y} : estimated response (mV) for (n=3) expressed as average peak heights of linear equation of the form $\hat{y} = a + bx$, or without unit for spectrophotometric method or in NTU for turbidimetric method, volume of measuring cell 1 mL for UV-Sp. and 10 mL for turbidimetric. r: correlation coefficient. r²: coefficient of determination. r²%: linearity percentage

Limit of detection

The limit of detection was described as the lowest concentration of an analyte in sample

that can be detected; this description gives the accurate definition of the LOD. Based on three approaches, determining the L.O.D was achieved for LOS-K as shown in Table 3.

TABLE 3 Limit of detection for LOS-K using Ayah 6Sx1-T-2D- solar cell-CFI analysis at optimum parameters

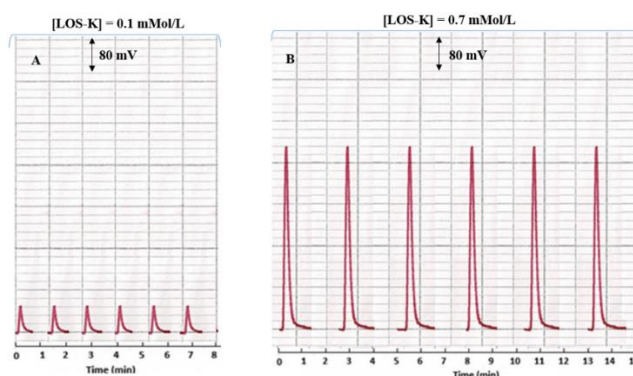
Minimum concentration n mMol/L	Practically based on the gradual dilution for the minimum concentration	Theoretical based on the volume of slope L.O.D = $3S_B / \text{slope}$	Theoretical based on the linear equation $\bar{Y} = Y_B + 3S_B$	LOQ $X = 10S_B / \text{slope}$
0.08 mMol/L	5.80 $\mu\text{g}/\text{sample}$	12.64 $\mu\text{g}/\text{sample}$	11.49 $\mu\text{g}/\text{sample}$	38.33 $\mu\text{g}/\text{sample}$

S_B = Standard deviation of intercept. Y_B = intercept value

Repeatability

The repeatability of the developed method was studied at concentration of LOS-K (0.1, 0.7

mMol/L). Figure 8 shows the repeated measurement of response-time profile in optimum parameters. The repeatability (% RSD) = 0.5% was found.

**FIGURE 8** Response profile for six successive repeatable measurements of LOS-K in different concentration: A-0.1 mMol/L and B- 0.7 mMol/L using LOS-K- $K_3[Fe(CN)_6]$ - CH_3COOH system

Application

The established method was used for the determination of LOS-K in two different companies of pharmaceutical drug (Iraq, 50mg- pioneer and India, 50 mg, Micro) use, i.e.; LOS-K- $K_3[Fe(CN)_6]$ (0.3 mMol/L)- CH_3COOH (10 mMol/L) system at 3.1, 2.7 mL/min flow rate for carrier stream and reagent respectively, using a homemade Ayah 6Sx1-T-2D-solar cell with CFI. The developed method was compared with two classical methods, including UV- spectrophotometric via the measurement of absorbance at $\lambda_{max} = 232$ nm by spectrophotometer [22], (uv-1800 Shimadzu) and turbidometry via Turbidimeter, HANNA (Hungary). A series of solution from each pharmaceutical drug was used via transferring 1 mL (0.5 mMol/L) of samples to six volumetric flasks (10 mL) of both system, followed by the addition of (0, 0.4, 0.6, 1, 1.2 and 1.5 mL) from 10 mMol/L of LOS-K standard solution to obtain (0, 0.4,

0.6, 1, 1.2 and 1.5 mMol/L), while in UV- Spectrophotometric method, transferring 0.04 mL from 5 mMol/L sample solution to each six volumetric flasks (10 mL) was carried out, followed by the addition (0, 0.03, 0.05, 0.07, 0.09 and 0.1 mL) from standard solution of LOS-K (10 mMol/L) to obtain (0, 0.03, 0.05, 0.07, 0.09 and 0.1 mMol/L); in addition to turbidometric method, a series of solutions was prepared by transferring 0.2 mL of 5 mMol/L concentration of two samples, followed by the addition of 0.3, 0.4, 0.5, 0.7 and 0.9 mL from standard solution of LOS-K (10 mMol/L) to obtain 0.3, 0.4, 0.5, 0.7 and 0.9 mMol/L. Results were mathematically treated for standard additions method and tabulated in Table 4 at confidence interval 95%. The paired t-test calculated for proposed method and classical methods are showed in Table 4.B. The result showed no significant difference between three methods at the calculated t-value.

TABLE 4A Summary of results from the devised method for determination of LOS-K in two medicines using standard additions

Commercial Name, Company Content Country	Confidence interval For the average Weight of table $\bar{w}_i \pm 1.96 \sigma_{n-1} / \sqrt{n}$ at 95% (g)	Weight of Sample equivalent to 0.115 gm (10 mmol/L) Of the active Ingredient W_i (gm)	Theoretical content for the active ingredient at 95% $W_i \pm 1.96 \sigma_{n-1} / \sqrt{n}$ (mg)	Method type	Equation of standard addition at 95% for n-2 $\hat{y}_i = a \pm s_a t + b \pm s_b t$	r r ² r ² %
Pioneer 50 mg Iraq	0.2072±0.0008	0.4786	50±0.1932	Developed method using Ayah 6Sx1-T-2D- solar cell-CFI analysis in mV	\hat{y}_i (mV)=223.8983±18.73 27+478.1360±20.8355	0.9995 0.9990 99.90
				UV-Spectrophotometric method at λ_{max} =232 nm	\hat{y}_i =-0.3390±0.1250+16.98 10±1.8790	0.9968 0.9937 99.37
				Turbidimetric method using Hanna Instrument	\hat{y}_i (NTU)=50.9459±41.4 529+510.4730±75.682 1	0.9943 0.9988 98.87
				Developed method using Ayah 6Sx1-T-2D- solar cell-CFI analysis in mV	\hat{y}_i (mV)=268.4689±34.3 469+537.1525±38.202 5	0.9987 0.9974 99.74
Micro 50 mg India	0.1746±0.0012	0.4030	50±0.3436	UV-Spectrophotometric method at λ_{max} =232 nm	\hat{y}_i =-0.3047±0.0677+15.79 91±1.0191	0.9989 0.9978 99.78
				Turbidimetric method using Hanna Instrument	\hat{y}_i (NTU)=57.3514±43.7 942+610.6757±79.957 1	0.9955 0.9911 99.11

TABLE 4B Summary of results for practical content and efficiency (Rec %) for determination of LOS-K-Potassium hexacyanoferrate (III) in two samples of drugs and t-test for comparison between three methods

Method type	Practical concentration (mMol/L) in 10 mL	Practical weight of LOS-K \bar{w}_i (g) $\pm 4.303 \sigma_{n-1} / \sqrt{n}$	Efficiency of determination Rec. %	Individual t-test for compared between quoted value & practical value $(\bar{w}_i - \mu) \sqrt{n} / \sigma_{n-1}$	Paired t-test Compared between two methods	
	Practical weight of LOS-K in (g)	Weight of LOS-K in tablet \bar{w}_i (mg) $\pm 4.303 \sigma_{n-1} / \sqrt{n}$			$t_{cal} = \bar{X}_d \sqrt{n} / \sigma_{n-1}$	t_{tab} at 95% confidence level
Developed method	0.4683	0.1082± 0.0217	93.69	/ - 1.4524 / << 4.303		
	4.6830	46.8429±9.3946				
	0.1082					
UV-Spectrophotometric method	0.01996	0.1153± 0.01675	99.83	/ - 0.0494 / << 4.303		
	4.9910	49.9168±7.2516				
	0.1153					
Turbidimetric method	0.0998	0.11527± 0.0109	99.81	/ - 0.0856 / << 4.303	$\bar{X}_d = / - 0.67065 /$ (UV-Sp.) $\sigma_{n-1} = 3.39871$ / - 0.2791 / < 12.706	
	4.9900	49.9044±4.8056				
	0.11527					
Developed method	0.4998	0.1155± 0.0189	100.08	0.0210 << 4.303	$\bar{X}_d = / - 0.0146 /$ (Tur.) $\sigma_{n-1} = 4.3090$ / - 0.0048 / < 12.706	
	4.9980	50.0400±8.1884				
	0.1155					
UV-Spectrophotometric method	0.0193	0.1115± 0.0183	96.61	/ - 0.3759 / << 4.303		
	4.8250	48.3074 ±7.9285				
	0.1115					
Turbidimetric method	0.0939	0.1085± 0.0281	94.01	/ - 1.0577 / << 4.303		
	4.6957	47.0077±12.1743				
	0.1085					

Conclusion

The proposed method for determination of LOS-K was characterized by speed, accuracy,

simple and sensitivity. The newly developed method was based on precipitation of LOS-K *via* using precipitate agent (potassium

hexacyanoferrate) to form yellow precipitate that irradiated by a six-snow white LED using Ayah 6Sxl-T-2D cell analyzer to combine with flow injection analysis. From the statistical results, it was observed that using three methods of analysis showed no significant difference between the developed method and references methods in analysis the losartan in pharmaceutical samples.

Acknowledgments

The authors extend sincere thanks and appreciation to Prof. Dr. Issam M.A. Shakir and Prof. Dr. Nagam S. Turkey, for their appreciable advice, provided the homemade Ayah 6Sxl-T-2D cell analyzer produced by them.

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How to cite this article: Firas T. Kareem, Mohammad K. Hammood*. New sensitive turbidimetric method for determination of losartan potassium in pharmaceutical formulations using flow injection combined with homemade turbidimeter. *Eurasian Chemical Communications*, 2021, 3(8), 572-583. **Link:** http://www.echemcom.com/article_134302.html