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METHOD DEVELOPMENT FOR ANALYSIS OF LOSARTAN POTASSIUM IN PHARMACEUTICAL SAMPLES USING TURBIDITY FLOW INJECTION

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ABSTRACT

Determination of Losartan Potassium in its pure form and pharmaceutical preparations in a new method, accurate, rapid, sensitive, and low cost. The process was based on the formation of a white precipitate by the reaction of LOS with cadmium chloride in an acidic solution. Use a homemade flow injection technique for precipitate measurement and a continuous flow injection approach. Reagent concentration, acidic medium, flow rate, sample volume, and purge time are chemical and physical parameters that can be improved. The linear dynamic range of the LOS was 0.1-1.5 mmol/L with a linearity ratio (r^2%) 93.42%. The lowest concentration of the calibration graph (L.O.D) of 6.3 µg/sample and (LOQ) was 39.1 µg/sample. The developed method and the classical methods were compared. The proposed method is effectively used to determine LOS in pharmaceutical samples and its alternative method.

KEYWORDS: Losartan potassium (LOS), flow injection analysis, Turbidity, cadmium chloride.

INTRODUCTION

This drug is an oral angiotensin receptor blocker for the treatment of high blood pressure.[1] Losartan potassium chemically description 2-n-butyl-4-chloro-5-hydroxymethyl-1((2-(1H-tetrazol-5-yl) methyl) imidazole) (diphenyl-4-4-yl)imidazole (Figure 1).

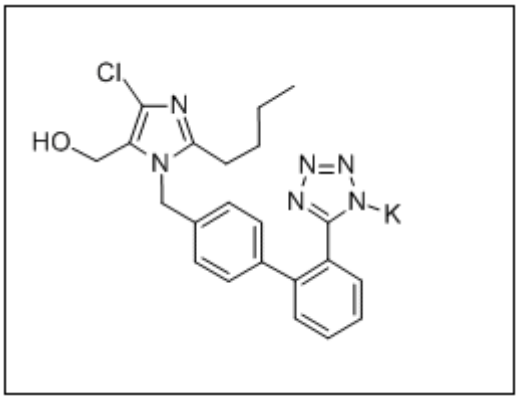


Fig. 1: The chemical structure of losartan potassium.

One of the most commonly used as antihypertensive medications for treating cardiovascular problems is losartan potassium. The losartan potassium (LOS) is white powder free soluble in water (pKa = 4.9) isopropyl alcohol and slightly soluble in acetonitrile in addition to the melting point at range 183.5-184.5°C.[2] There are many techniques for determine LOS in pharmaceuticals, including high-performance liquid chromatography (HPLC)[3], spectrophotometry[4], conductivity measurement[5], electrochemical and photometric approaches.[6] In this study, a method for LOS analysis in pharmaceuticals use cadmium chloride as a precipitating agent is developed. It is based on the direct measurement of incident light attenuation using a solar cell analyzer.

MATERIALS AND METHODS

Reagent and Chemical

In this research, distilled water was used in all dilution steps and all chemicals were of analytical grade. 1.149 g of losartan, which has a molecular weight of 462.01 g/mol, was dissolved in 250 ml to create a standard solution, and 14.72 g of cadmium chloride has molecular mass of 183.32 g/mol, was dissolved in 250 ml of distilled water to create a standard solution of 0.2 mol/l for the reagent.

Apparatus

We used a homemade analyzer, and detector used two solar cells via sample travel for 60mm length. Six-port 2 directions injection valve with different sample sizes and a four-channel variable speed peristaltic pump Ismatec. The x-t voltage potentiometric recorder used for the described method plotted the output response signals. Turbidometry via Turbidity-meter and spectrophotometer UV-Vis Shimadzu was used as a reference method.

METHODOLOGY

Losartan potassium (LOS) was measured using a solar cell analyzer with cadmium chloride as a precipitating agent. The initial concentration of the precipitating agent was 0.11 mmol/L which reacted with LOS at a concentration of 2 mmol/L to produce a white precipitate that was an ion pair compound. The first line (carrier stream) is 10 mmol/L HCl at a flow rate of 1.7 mL/min. The LOS injection valve (2 mmol/L) transports a sample volume of 157 µL and collects it with the second line (1.5 mL/min) at the Y junction to form a precipitate. The solar cell analyzer was used to measure the responses.

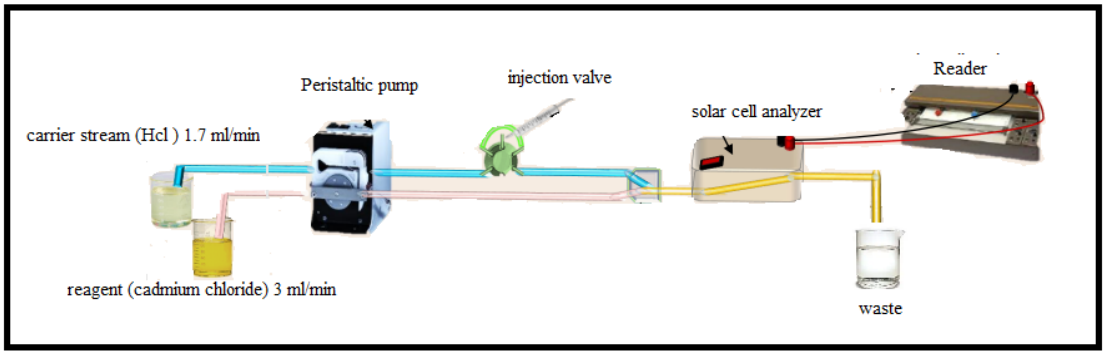


Fig. 2: Two-line manifold system design using precipitation system [LOS]-$CdCl_2$-HCl for LOS determination.

RESULTS AND DISCUSSION

Optimization of Reaction Parameters

A response profile has been achieved using a number of chemical and physical variables that affect sensitivity to drug concentrations. Chemical variables include the concentration of cadmium chloride used as a reagent in the presence of various acids and salts when the reactions occur. In addition to study how different types of acids affect the signal response. Flow rate, sample size, purge time, and coil length are examples of physical variables.

Chemical Variables

precipitating agent (Cadmium chloride)

Cadmium chloride has been used in various concentrations ranging from 0.05 to 7 mmol/L. Choose a flow rate of 1.5 mL/min while using a carrier stream of 1.7 mL/min of HCl, a sample volume of 157 µL using the open valve mode, and a concentration of 2 mmol/L of LOS. It was discovered that the profile of responses increases when the precipitation agent increases to 0.3 mmol/L due to the formation of precipitated particles that may increase the reflection of the incident light, which may indicate an increase when cadmium chloride is used, the light intensity decrease at concentrations greater than 0.3 mmol/L. interstitial spaces are responsible for the formation of larger agglomerate particles, allowing more light to pass through while reducing interaction. As a result, 0.3 mmol/L was determined to be the ideal concentration.

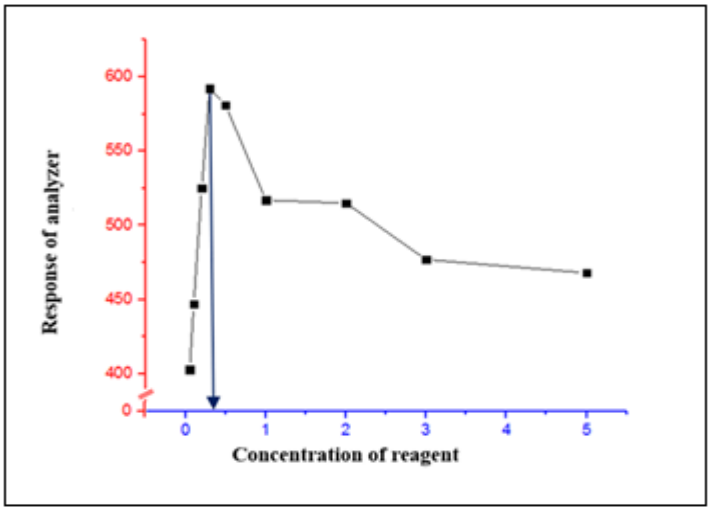


Fig. 3: different concentration of reagent (cadmium chloride).

Effect of reaction medium

Different concentrations of different solutions were prepared as acidic media with a concentration of 9 mmol/L H_3PO_4, HCl, H_2SO_4 and CH_3COOH as a carrier stream with a flow rate of 1.7 ml/min, while the flow rate of the reagent is 1.5 ml/min, 2 mmol/L of LOS was used as an injected concentration, and a sample volume of 157 µl was used. The CH3COOH best choose of as a carrier current resulted in an increase in peak height and acute reaction.

Table 1: Effect of medium solution of carrier stream on cadmium chloride to determination of LOS-K.

Acid type [10 mmol/L]	Response of analyzer (mV)	S.D.	RSD%	Confidence interval of the average at (95%) $\bar{y}_i \pm t_{(\alpha=0.05/2)}$
H_3PO_4	**275**	**1.305**	**0.471**	**275 ±3.193**
HCl	**586**	**1.198**	**0.211**	**586 ±3.105**
H_2SO_4	**272**	**1.210**	**0.441**	**272 ±3.186**
CH_3COOH	**655**	**2.199**	**0.367**	**655 ±5.498**

Effect of CH3COOH Concentration on diverged light for LOS – $CdCl_2$ system

To choose the best concentration, a series of CH3COOH solutions were made with different concentrations (4, 10, 15, 25 mmol/L). It was shown that up to 10 mmol/L of CH_3COOH concentration leads to increased peak height. This is due to the increased formation of large precipitate, which leads to the final reflection of all light, while the concentration of CH3COOH (greater than 10 mmol/L) causes a decrease in the peak response, which may be due to the scattering of large precipitate.

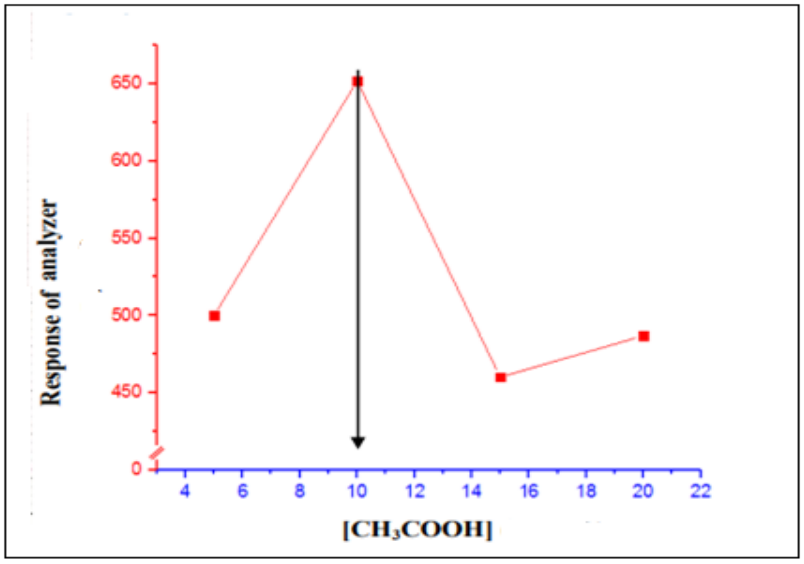


Fig. 4: Effect of different Concentration of CH_3COOH.

Physical parameters

Flow rate effect

0.25-4 mL/min for the carrier current and 0.25-4 mL/min for the reagent and the 157 µl sample loop were chosen as the ideal flow rates. The LOS system's optimal conditions (concentration) (2 mmol/L) were used. 0.3 mmol/L of $CdCl_2$ and 10 mmol/L of CH3COOH. The carrier and reagent currents on two lines, respectively, were seen to flow at a rate of 3-1.7 ml/min. The diffusion and dispersion led to an increase in peak width (Δt_B). This led to the selection of 3 and 1.7 ml/min as the ideal flow rates for the carrier and current reagent, respectively.

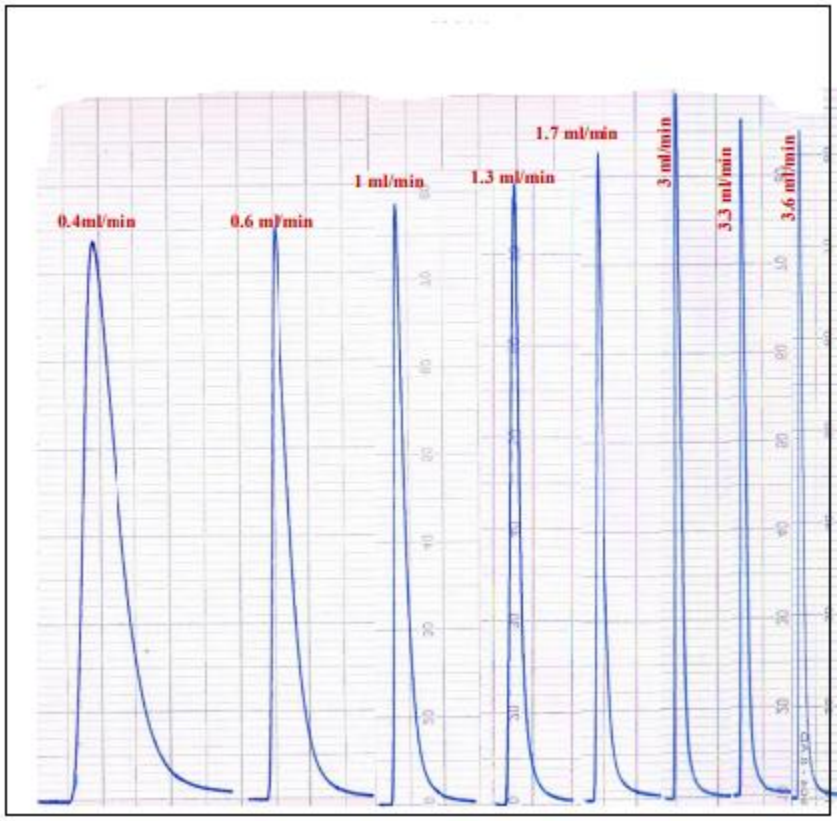


Figure 5: Peak profile for flow rate different for system LOS-cadmium chloride.

Effect of different of sample volume

With a Teflon tube of 15 cm to 100 cm and a diameter of 1 mm, a variable sample volume (40–250 µL) was With a Teflon tube of 15 cm to 100 cm and a diameter of 1 mm, a variable sample volume (40–250 µL) was use with a with a 2 mMol/L LOS concentration. The peak height was shown to decrease with increasing base width (Δt_B) by lowering the light contrast when the sample volume was more than 157µl. As a result, the ideal sample volume was determined to be 157µl.

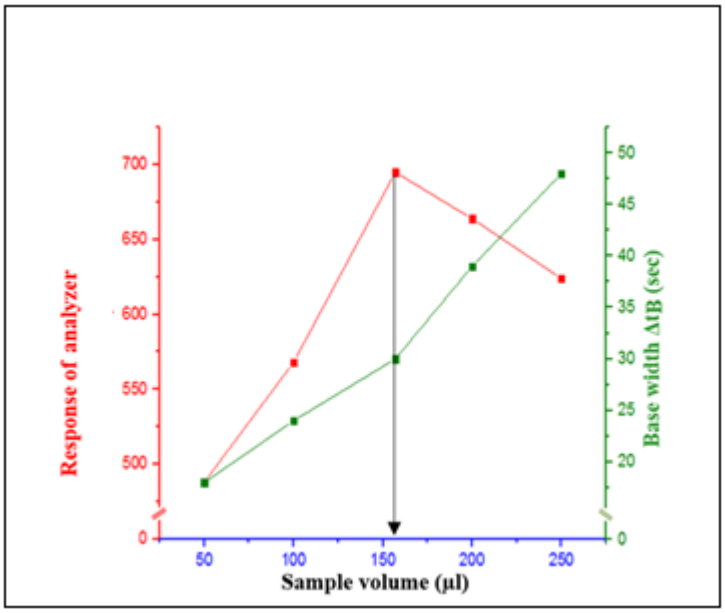


Figure 6: Effect of sample volume variation

Purge time

The ideal injection time was calculated to be 157 µl from the sample loop, which is the time allowed to flush the sample from the injection valve. There were different purging times for the pieces ranging from 5 to 25 seconds and an extra valve open. All responses had

variable peak height that increased with increasing injection time until valve position opened (25 s), the best purge time was determined using continuous valve position.

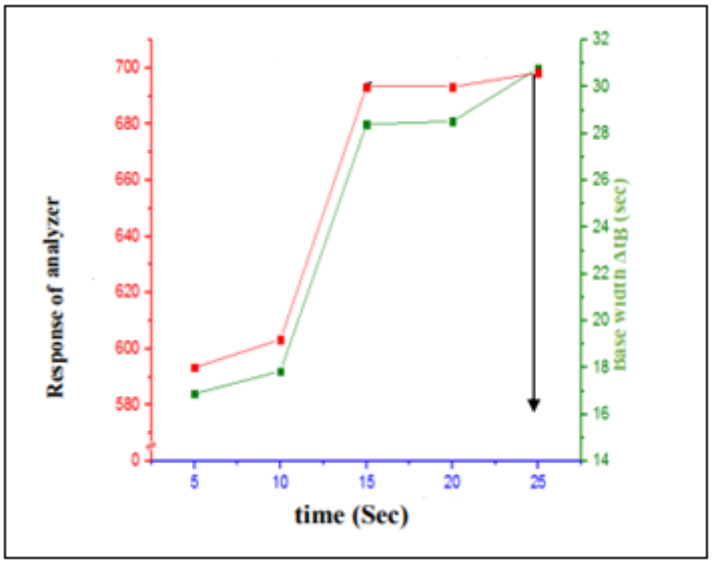


Figure 7: Response profile over time using the purge time variable.

Reaction coil

Various reaction forms (0-314) µl were used. After injection, the valve is placed directly into the flow system (between the Y-junction and the metering unit), allowing the cadmium chloride to be mixed with LOS to complete the mixing process and reorganize the precipitated particles. Figure 6 shows a decrease in the high response peak along with an increase in coil reaction (reaction length) associated with an increase in base width (Δt_B) as a result of sample dilution and dispersion, resulting in increased dispersion.

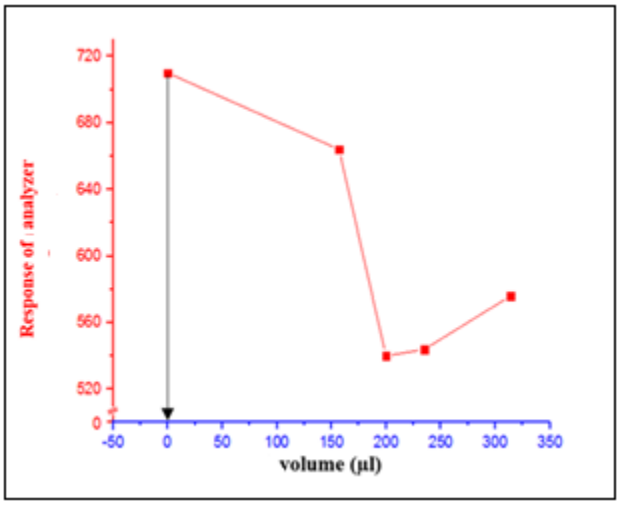
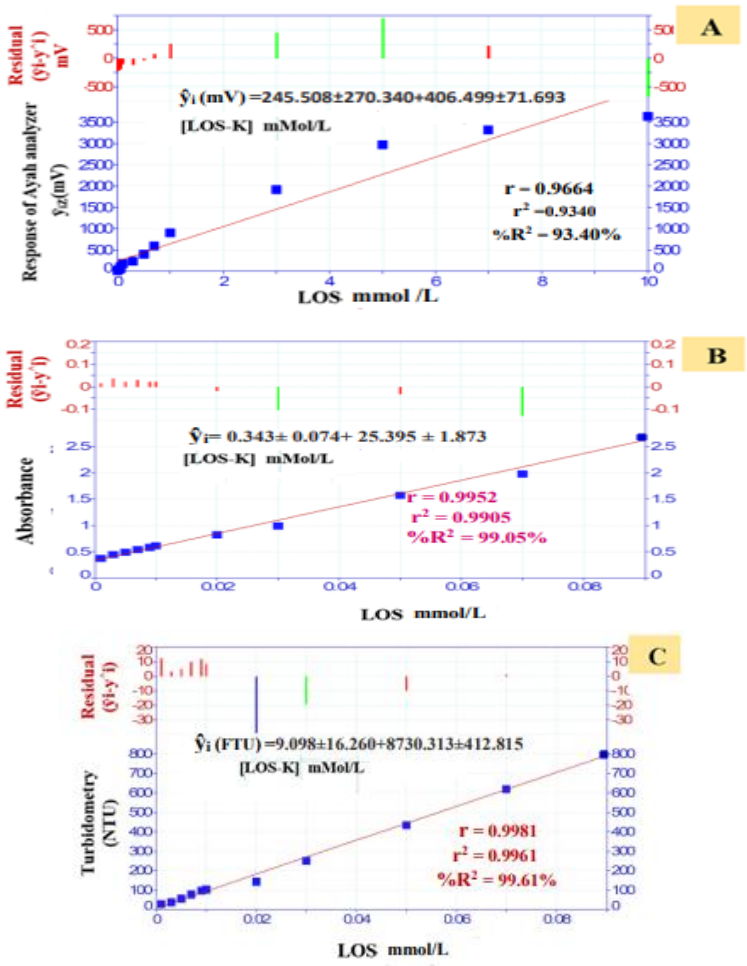


Fig. 8: Effect of mixing coil length on the new method for analysis of LOS.

Calibration Graph Study for LOS-K

Using the best chemical and physical parameters, the LOS calibration curve was generated. With a $CdCl_2$ (0.3 mmol/L)-CH3COOH (10 mmol/L) system and a flow rate of 3 mL/min for the reagent, LOS-K solution. When the LOS concentration is between 0.01-10 mmol/L, a linear calibration curve is made using a homemade technique. The calibration curve for classical methods ranged from 0.001-0.09 mmol/L. like that Calibration curve (turbidimetry method) based on the reaction of $CdCl_2$ as a precipitating agent (ideal concentration 0.5 mmol/L) with LOS ranging from 0.001-0.09mmol/l.



A: calibration curve for the determination of LOS in the range (0.01-10 mol/L) by new method **B**: calibration curve for changing the LOS concentration using the spectrophotometric method (classical method) in the range (0.001-0.09mmol/L).**C**: calibration curve for the turbidity measurement method (classical method) in the range (0.001-0.09mmol/L).

Limit of detection

The lowest concentration of an losartan potassium can be detected.

Table 2: L.O.D for losartan potassium using develop method at optimum parameters.

Minimum concentration mMol/L	Practically based on the gradual dilution for the minimum concentration	Theoretical based on the volume of slope L.O.D =$3S_B$/ slope	Theoretical based on the linear equation $\bar{Y}=Y_B+3S_B$	LOQ $X=10S_B$/ slope
0.01 mmol/L	**5.82 µg/sample**	**11.98 µg/sample**	**11.51 µg/sample**	39.1 **µg/sample**

SB= Standard deviation of intercept. YB = intercept value

Application

Using the LOS-$CdCl_2$ (0.3 mmol/L)-CH3COOH (10 mmol/L) system and flow rates of 3 and 1.7 mL/min for carrier and reagent flows, respectively, the developed method has been used to estimate LOS in pharmaceutical company (Taj, India 50 mg). The developed method was compared with two conventional methods, by measuring UV spectrophotometer at maximum absorbance = 232 nm by spectrophotometer and measuring turbidity using turbidimeter A 95% confidence interval was used in the mathematical treatment of the results. The calculated paired t-test results for the developed method and the conventional methods are presented in Table 4. The statistical results showed that, at the calculated t-value, there is no significant difference between the three methods.

Table 3. A: 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 Wi (gm)	Theoretical content for the active ingredient at 95% (mg) $Wi \pm 1.96\ \sigma_{n-1}/\sqrt{n}$	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%
Taj 50 mg India	0.1687±0.0015	0.4021	50±0.3461	develop method	$\hat{y}_i$ (mV)= 245.508±270.340+406.499±71.693	0.9651 0.9342 93.42
				Spectrophotometric method	$\hat{y}_i$ = 0.343± 0.074+ 25.395 ± 1.873	0.9954 0.9904 99.04
				Turbidimetric method	$\hat{y}_i$ (NTU)= 9.098±16.260+8730.313±412.815	0.9985 0.9963 99.63

Table 4. B: Results summary for practical content and effectiveness (Rec percent) for LOS-Cadmium chloride determination in one drug samples and t-test for comparison of three techniques.

Method type	Practical concentration (mMol/L) in 10 ml in 50 ml Practical weight of LOS-K in (g)	Practical weight of LOS-K $\bar{w}i(g) \pm 4.303\ \sigma_{n-1}/\sqrt{n}$ Weight of LOS-K in tablet $\bar{w}i(mg) \pm 4.303\ \sigma_{n-1}/\sqrt{n}$	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 $t_{cal} = \bar{X}d\sqrt{n}/\sigma_{n-1}$	Paired t –test Compared between two methods t_{tab} at 95% confidence level
Developed method	0.4897 49.4423 0.1136	0.1201± 0.02001 49.4220±8.6956	98.85	/ - 0.2721 / << 4.313	$\bar{X}d$ = / - 1.7937 / (UV-Sp.) σ_{n-1}= 1.8905 /-1.3635/ < 12.714 $\bar{X}d$ = /- 0.0138/ (Tur.) σ_{n-1}= 4.3081 / -0.0047/ < 12.714	
UV-Spectrophotometric method	0.01989 4.9878 0.1168	0.1247± 0.01768 49.9213±7.2516	99.84	/ - 0.0489 / << 4.313		
Turbidimetric method	0.0989 4.9901 0.11626	0.11611± 0.0108 49.9132±4.8103	99.82	/ - 0.0848/ << 4.313		

CONCLUSION

The new LOS analysis method is rapid, accurate, low coast, and reduces contamination. LOS determine by using a precipitating agent (cadmium chloride) to form a white precipitate. The results showed through three methods of analysis that there is no difference between the develop method and the classical method for the determination of losartan in pure form and pharmaceutical samples.

REFERENCES

1. Sleight P, Yusuf S, Pogue J. Blood-pressure reduction and cardiovascular risk in the HOPE study. Lancet, 2001; 358: 2130-1.
2. Wright JT Jr, Bakris G, Greene T. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: Results from the AASK trial. J Am Med Assn, 2002; 288: 2421-31.
3. M. A. Hinge, V. M. Bhanusali, and R. J. Mahida, "Spectrophotometric and High Performance Liquid Chromatographic Determination of Chlorthalidone and Losartan Potassium in Combined Dosage Form," Anal. Chem. Lett., 2016; 6(4): 408–420.
4. L. Latheeshjlal, P. Parthiban, V. Alagarsamy, M. Sunil, J. V. Mahul, and T. R. Mohan, "Spectrophotometric determination of lorsartan potassium and its dosage form by bromothymol blue and phosphate buffer," J. Chem., 2010; 7(1): 320–324.
5. de Oliveira Rossini, Pamela, Fabiana S. Felix, and Lúcio Angnes. "A simple and precise conductometric method for the determination of losartan in pharmaceutical products." Central European Journal of Chemistry, 2012; 10(6): 1842-1849.
6. Ghanbari, Khadijeh, and Ashraf Sivandi. "Development of a Novel Nanocomposite Based on

Reduced Graphene Oxide/Chitosan/Au/ZnO and Electrochemical Sensor for Determination of Losartan." Current Analytical Chemistry, 2020; 16(80): 996-1009.
7. Issam, M. A. and Nagam, S., T., 2014, Ayah 6SX1-ST-2D solar cell CFI Analyzer, Patent, Present to central organization for standardization and quality control- Baghdad-Iraq, GO1N21/00.
8. N. S. T. Al-Awadi and R. A. K. Aldeen, "CFIA-Turbidimetric and Photometric Determination of Vitamin B9 (Folic acid) Using LEDs as a Source of Irradiation and Two Solar Cells as an Energy Transducer," Baghdad Sci. J., 2017; 14: 4.
9. Skoog, D.A., 2007. Principle of instrumental analysis. 6th Ed. Thomson, Canada.
10. rtz, J. S., M. Dahle, and R. B. Robinson., 2008, Concentration-durationfrequency curves for stream turbidity: possibilities for assessing biological impairment. Journal of the American Water Resources Association, 44: 879-886.
11. Carter, M. W., D. E. Shoup, J. M. Dettmers, and D. H. Wahl., 2010, Effects of turbidity and cover on prey selectivity of adult smallmouth bass. Transaction of the American Fisheries Society, 139: 353-361.
12. Marcos F.S. T. 2005. Flow injection turbidimetric determination of dipyrone using a solid –phase reactor containing silver chloride immobilized in a polyester resin. Quim. Nova, 28(5): 783-787.
13. Nagam S.T. Al-Awadie, and Khichari A.F., 2014. Determination of bismuth (III) ion by continuous flow injection analysis via turbidimetric (T180°) and scattered light effected two opposite position (2N90°) using Ayah 4SW-3D-T180-2N90-Solar – CFI Analyser. Journal of Kerbala university, 12(2): 182- 198.
14. Suarez W.T., Vieira H.J., and Fatibello F. O., 2007. Flow injection turbidometric determination of acetyl cysteine in pharmaceutical formulations using silver nitrate as precipitant reagent. Journal of the Brazilian chemical society, 18(5): 1028-1033.
15. March J.G., Simonet B.M., and Grases F., 2000. Kinetic –turbidimetric determination of phytic acid by sequential injection analysis, Analytica Chimica Acta., 409: 9-16.
16. Nagam S.T. Al-Awadie and Khudhair A.F., 2013. Determination of ciprofloxacin –HCl in pharmaceutical formulations by continuous flow injection analysis via turbidometric (T180°) and scattered light effected two opposite position (2N90°) using Ayah 4SW3D-T180-2N90-Solar – CFI Analyser. Journal of Kerbala University, 11(4): 153-196.
17. Li-Qun, W., Yang-Jun, O. & Xia-Ling, L. 2001. A study on Turbidimetric determination of potassium in tea by flow injection analysis. Food Science, 22(11): 82-84.
18. Mir, A.F., and Sepideh, N. 2002. Anew simple and accurate turbidometric method for determination of ascorbic acid in pharmaceutical and fruits. Journal of the Chinese chemical society, 49: 949-956.