معايرة لوزارتان بوتاسيوم بطريقة طيفية ضوئية بالتعقيد بانتقال الشحنة

جهاد دياب*

الملخص

هدف البحث عمل طريقة طيفية ضوئية بسيطة وحساسة ودقيقة بتقدير لوزارتان بوتاسيوم في المحاليل النقية والأقراص.

طرائق البحث: حيث تم تفاعل المركب مع 4،2 ثنائي الكلور-6- نيتروالفينول في وسط من الكحول الميثيلي حيث ينتج معقداً ملوناً له امتصاص ضوئي أعظمي عند طول موجة 462 نم، وبلغت قيمة عامل الامتصاص المولي نحو 4.40×10^4. تم دُرِسَت العوامل المؤثرة في لون المعقد مع تحديد أنسب الشروط. تبين أنه يمكن قياس العقار في هذه الطريقة بتراكيز تتراوح بين 25-75مكغ /مل مع حد كشف مرئي 1.0 مكغ/مل.بلغت قيمة عامل الارتباط 0.9994 والذي يشير إلى خطية جيدة. تم تعيين ستيوكيومترية التفاعل(نسبة المواد المتفاعلة) بين العقار والكاشف فكانت النسبة 1: 2 حسب طريقة جوب للتغير المستمر. وتتراوح درجة الدقة في هذه الطريقة بين 99.64 ± 0.72 في المحاليل النقية و 99.95 ± 0.65 في المستحضرات الصيدلية. اختبرت مصداقية الطريقة المقترحة بتطبيق طريقة الإضافية standard addition technique حيث بلغت الدقة 100.05± 0.87 والتي تشير إلى أنه لا يوجد تداخل من السواغات عند طول الموجة 462 نم.

الاستنتاج: أظهرت النتائج التي حصلنا عليها أنه لا يوجد فرق بين الطريقة المقترحة والطريقة الطيفية المشتقة المنشورة عند المقارنة بينهما بالنسبة إلى الدقة والضبط لدى التحليل الإحصائي للبيانات باستخدام كلٍّ من العامل F والاختبار t حيث كانت النتائج ذات دقة وضبط عاليين.

* مدرس– قسم الكيمياء التحليلية– كلية الصيدلة– جامعة دمشق.

Spectrophotometric Determination of Losartan Potassium by Charge Transfer Complexation

Jehad Mohammed Diab*

Abstract

Objective: Simple, sensitive and accurate spectrophotometric method for the determination of losartan potassium in pure sample and tablets is presented.

Methods: Charge transfer complexation of the drug with 2,4- dichloro-6-nitrophenol was carried out. The color formed due to the formation of charge transfer complex showed maximum absorbance at 462 nm, molar absorptivity was 4.40×10^3.The variables that affect development of color as reaction medium, color stability and reagent concentration were investigated and the conditions were optimized. The proposed procedure was applicable to determine 25-150 µg / ml of losartan potassium and the visual detection limit was 1.0 µg / ml.correlation coefficient was 0.9994 which indicate good linearty.The stoichiometry of losartan potassium – DCNP complex 1:2 as studied by Job's method of continuous variation. The mean percentage recoveries ± SD were found to be 99.64 ± 0.72 and 99.95 ± 0.65 in pure form and Hyposar® tablets respectively which indicate accurate and precise results. The validity of the method was checked by applying standard addition method, the mean percentage recovery was 100.05 ± 0.87 this means there is no interferences from excipients in tablets at 462 nm.

Conclusion: The obtained results showed no significant difference between the proposed method as compared to reported derivative spectrophotometric method with respect to precision and accuracy by statistical analysis of data using both *F* factor and *t* test.

Key words: Losartan potassium, charge transfer complexation spectrophotomety, pure samples, pharmaceutical preparations

* Dep. of chemistry- faculty of pharmacy, Damascus University.

Introduction:

Losartan potassium is an angiotensin II receptor (type AT l) antagonist. It is used in treatment of hypertension [1]. Losartan potassium is chemically described as 2-butyl-4-chloro-1- [p-(o-1H-tetrazol-5-ylphenyl) benzyl] imidazole -5- methanol mono potassium salt. Losartan potassium was previously determined by various analytical methods including spectrophotomety [2-5], high performance liquid chromatography [2, 6-10]. This paper describes the applicability of charge transfer complexation reaction for the spectrophotometric determination of losartan potassium in bulk drug and pharmaceutical preparations. Charge transfer complexation of drugs containing basic nitrogen atoms, which involve electron transfer from the nitrogen atoms to DCNP molecule, has been used as the basis for spectrophotometric determination [11].

Methods- Experimental

Apparatus:

All spectral and absorbance measurements were made on α1 Uvidec spectrophotometer, Jasco, Japan with 1 cm quarts cells.

Chemical and reagents:

All chemicals used were of analytical grade. Losortan potassium drug was obtained from the National Company for pharmaceutical Industry, Aleppo, Syria. Purity was 99.20 % (W/W). Hyposar® tablets a product of the above mentioned company; labeled to contain 25 mg of losartan potassium per tablet, Batch No.A007

Solutions:

2,4-Dichloro-6-nitrophenol solution (DCNP): 0.5% w/v was prepared freshly in methanol.

Standard drug solution, 1 mg / ml stock solution of the drug in methanol was used.

Procedures:

Determination of losartan potassium in bulk powder and pharmaceutical preparations.

Aliquots of the standard stock solution (1 mg / ml, 0.25-1.75 ml) were transferred into 10 ml volumetric flasks and one ml of DCNP solution 0.5% was added into each flask. The volume was made up to 10 ml with methanol. The absorbance was measured at 462 nm against a reagent blank prepared similarly without the drug solution within 30 minutes.

The above procedure was applied for the determination of the drug in tablet preparation; the contents of twenty tablets were weighed and powdered. An amount of the powder equivalent to 0.10 g of the drug was accurately weighed , transferred into 100 ml volumetric flask, added about 50 ml methanol and dissolved for 15 minute . The solution was diluted to volume with the same solution, mixed well and filtered. Portions of the filtrate (0.25-17.5 ml) were analyzed by the proposed method as mentioned above.

Determination of the composition of losartan potassium-DCNP complex by the continuous variation method [12].

Different volumes (0-5 ml) of 3×10^{-3}M methanolic solutions of losartan potassium were introduced into a series of 10 ml volumetric flasks and mixed with different volumes of 3×10^{-3}M methanolic solution of DCNP ranging from (5-0) ml and diluted to 10 ml with methanol. The absorbanes of these solutions were measured at 462 nm within 30 minutes against a reagent blank prepared similarly without the drug solution.

Results and Discussion:

Losartan potassium, being n-electron donor, interacts with the reagent DCNP in methanol which is electron acceptor giving charge transfer complex which may dissociate to radical ions. The reaction involves electron transfer from basic nitrogen atoms of the drug to DCNP molecule. Figure (1) shows the absorbance spectrum of colored product formed with the wavelength of maximum absorbance (λ max) at 462 nm.

Absorbance measurements were made at this wavelength to construct the calibration curve and subsequently for analysis. A plot of absorbance versus concentration was linear in the range 25-175 µg / ml. Regression analysis on the calibration curve gave the following equation:

$A=0.0015\ C + 0.1140, \quad r = 0.9994$

Where A stands for absorbance at 462 nm and C for concentration of losartan potassium in µg / ml and r for correlation coefficient which indicate good linearity. Several experiments were conducted to optimize the conditions for maximum color development in charge transfer complexation with DCNP

Among the various solvents used as the reaction medium, methanol gave satisfactory and more stable color and in addition

it is good for the DCNP reagent. Of the other solvents examined, dichloromethane is a possible substitute. One ml of reagent solution 0.5% (w/v) was required to get maximum color. The color remained stable for 30 minuet and intensity of the color decreased gradually thereafter. The stoichiometry of losartan potassium - DCNP complex was studied by employing Job's method of continuous variation which indicated a 1:2 drug: reagent, as shown in figure (2).

The accuracy and precision of the method was determined by analyzing standard solutions of the drug in different concentrations. The results were compared by derivative spectrophotmetric method [3]. The results given in table (1) shows that the recovery of losartan potassium was 99.64 ± 0.72 as calculated from the regression equation. The calculated *t* and *F* values were less than tabulated, so there is no significant difference between the two methods with respect to accuracy and precision. The applicability of the method for the assay of dosage forms was examined by analysis Hyposar®tablets. The results given in table (2) show that the recovery of the drug in tablets was: 99.95±0.65. The Validity of the method was assessed by applying the standard addition technique [13]. The mean percentage recovery was 100.05±0.87 which indicates that there is no interferences in tablets preparation at 462 nm.

Conclusion: the suggested method is simple, accurate and reproducible. Single step reaction and single solvent were required for the method. Losartan potassium has been determined by a variety of analytical techniques, but the spctrophotometric techniques may offer significant economic advantages over chromatographic methods and no expensive equipment is needed, so this method can be used as general method for the spectrophotometric determination of losartan potassium in bulk drug and dosage forms.

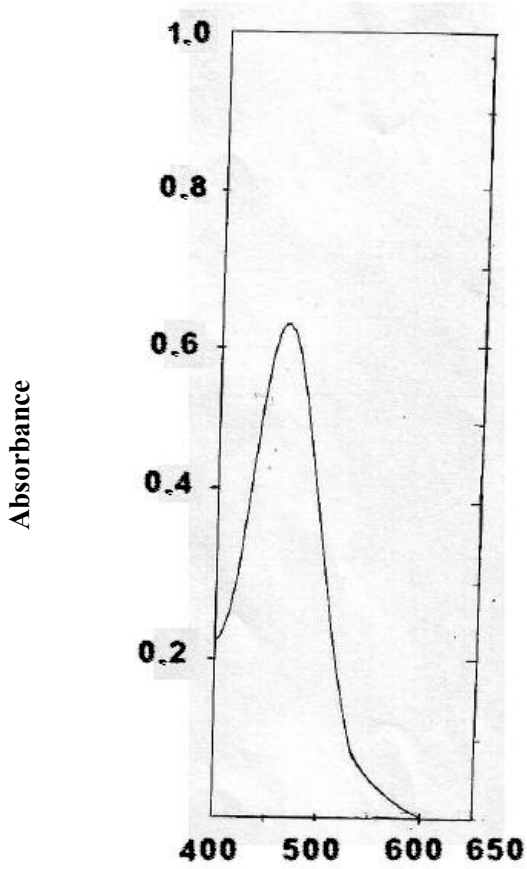

Figure (1): Absorbance spectrum of losartan potassium (100 µg/ml) – 2, 4- dichloro-6-nitrophenol complex in methanol

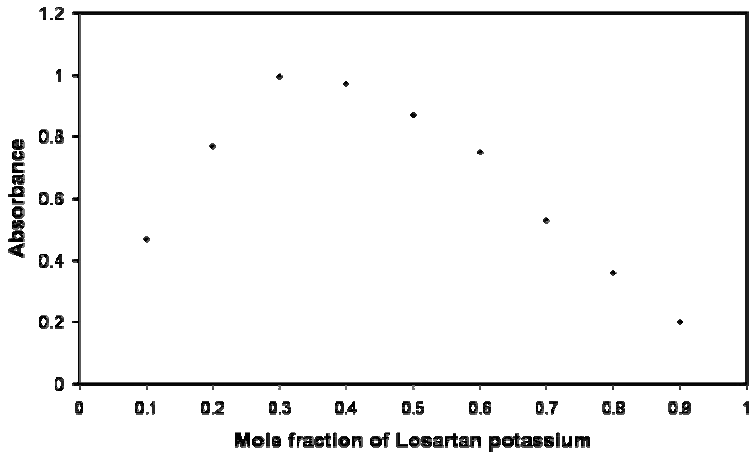

Figure (2): Determination of the stoichiometry of the reaction of losartan potassium and 2,4-dichloro-6-nitrophenol by the continuous variation method.

Table (1): Determination of losortan potassium in pure samples by spectrophotometric method

Taken µg/ ml	Found* µg/ ml	% Recovery	Reference method[3]
25	24.65	98.60	
50	49.60	99.20	
75	75.50	100.67	
100	99.00	99.00	
125	125.40	100.32	
150	150.36	100.24	
175	174.06	99.46	
Mean		99.64	100.55 ± 1.10
N		7	4
SD		0.72	1.10
variance		0.514	1.21
t		1.719(226)**	
F		2.35(4.76)**	

* Average of 3 determinations.
** Tabulated *t* and *F* values at the 95% confidence limit.

Tablet (2): Determination of losortan potassium in Hyposar® tablets by spectrophotometric method

Hyposar® tablets			Standard addition			
Claimed taken µg/ml	Found* µg/ml	% Recovery	Taken µg/ml	Pure added µg/ml	Pure found µg/ml	% Recovery
25	25.30	101.20	25	25	25.00	100.00
50	50.03	100.06	25	50	49.80	99.60
75	74.50	99.33	25	75	74.25	99.00
100	99.20	99.20	25	100	101.60	101.60
125	125.10	100.08	25	125	124.25	99.40
150	150.52	100.35	25	150	151.05	100.70
175	174.00	99.43				
Mean ± SD		99.95 ± 0.65				100.05 ± 0.87

* Average of 3 measurements.

References

1- Richard, D. Howland and Mary, J. Mycek "Pharmacology. Illustrated Reviews" 3rd ed., p.161, Lippincott Williams & Wilkins, USA (2006).
2- The Merck Index, 12th ed., Merck & Co. Inc., USA (1996).
3- Ansari. M, Kazemipour .M, Khosaravi . F and Baradaramn .M, A comparative study of first derivatives spectrophotomety and HPLC applied to the determination of losartan potassium in tablets;Chem. Pharm. Bull, 52(10), 1166-1170 (2004).
4- Lastra. O.C, Lemus. L.G, Sanchez. H.J and Perez. R.F: Development and validation of an UV derivative spctrophotometric determination of losartn potassium in tablets, J. pharm. Biomed. Anal. 33(2), 175-180 (2003).
5- Tatar. S and saglik. S: Comparison of UV and second derivative spectrophotometric and LC methods for the determination of valsartan in pharmaceutical formulations, J Pharm. Biomed. Anal, 30(2), 371-375 (2002).
6- Erk.N: Analysis of binary mixtures of losartan potassium and hydrochlorothiazide by using HPLC, ratio derivative spectrophotometric and compensation technique; J. Pharm. Biomed. Anal. , 24(4), 603-611(2001).
7- Polinko .M, Riffel .K, Song. H and Lo. M.W: Simultaneous determination of losartan and Exp 3174 in human plasma and urine utilizing LC, tandem mass spectrometry; J. Pharm. Biomed. Anal., 73(1), 73-84(2003).
8- Farthing. D, Sica. D, Fakhry. I, Pedro. A and Gher. T.W: Simple HPLC method for the determination of losartan and E- 3174 metabolite in human plasma, urine and dialysate; J. Chromatogr. B Biomed. SCi. Appl., 704 (1-2), 374-378 (1997).
9- Iwasa .T, Takano. T, Hara K and Kmei. T: Method for the simultaneous determination of losartan and its major metabolite, exp-3174 in human plasma by LC electrospray ionization tandem mass spectrometry; J. Chromatogr. B Biomed. SCi. Appl. 734(2), 325-330(1999).
10- Furtek. C. I and LO.M.W: simultaneous determination of novel angiotensin II receptor blocking agent. Losartan and its metabolite in human plasma and urine by HPLC; J. Chromatogr., 573(2), 295-301(1992).
11- Mulliken, R.S;'Molcular complexes' Wiley interscience, New York (1969).
12- Braun. R.D"Introduction to Instrumental Analysis" P. 291, Graw-Hill Book Company, New York (1987).
13- Robert.D.L"Principles of Quantitative Chemicals" p.440, the Mc Graw- Hill Companies, Inc.New York (1997).

تاريخ ورود البحث إلى مجلة جامعة دمشق: 2007/6/11.
تاريخ قبوله للنشر: 2008/5/20.