تقدير زافيرلوكاست بالطريقة الطيفية المباشرة

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الملخص

تم في هذا البحث استنباط طريقة طيفية لتقدير زافيرلوكاست في الصورة النقية والمستحضرات الصيدلية، وذلك بالقياس المباشر للامتصاص الطيفي في المنطقة فوق البنفسجية للعقار عند طول موجة الامتصاص الأعظمي 208 نم، حيث كان عامل الامتصاص المولي 1.770×10^4 ليتراً سم$^{-1}$ مول$^{-1}$. تبين أنه يمكن قياس المركب المذكورفي هذه الطريقة بتراكيز تتراوح بين 5-30 مكغ/مل ووصل حد الكشف المرئي إلى 0.30 مكغ/مل، وكان عامل الارتباط يساوي 0.9999 والذي يشير إلى خطية جيدة. وتتراوح درجة الدقة في هذه الطريقة بين 99.75 ± 0.57 في المحاليل النقية و 99.35 ± 0.71 في المستحضرات الصيدلية.أُكدت مصداقية الطريقة بتطبيق طريقة الإضافة القياسية standard addition technique حيث بلغت الدقة 99.73 ± 0.56، والتي تشير إلى أنه لا يوجد تداخل في مستحضرات الأقراص من السواغات عند طول الموجة 208 نم.أجري تحليل إحصائي للنتائج في الطريقة المقترحة باستخدام العامل F و الاختبار t وذلك بمقارنتها بالطريقة المرجعية الطيفية المشتقة بالنسبة إلى الدقة والضبط فكانت النتائج ذات دقة وضبط عاليين.

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Direct Spectrophotometric Determination of Zafirlukast

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Abstract

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

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Introduction:

Zafirlukast is used for clinical management of asthma by blocking the interaction of leukotriene with its receptor [1]. Its IUPAC chemical name is 4-5(-cyclopentyl-oxy-carbonylamino-1-methyl-indole-3-ylmethyl)-3-methoxy-n-o- tolylsulfonylbenzamide[2]. Chromatographic methods have been appeared in literature. K.H.Bui et al. reported a normal phase HPLC method for the determination of Zafirlukast in human plasma using fluorescence detection [3]. Ficarra et al. described an LC method for the analysis zafirlukast in pharmaceutical formulations [4]. T.Radakrishna et al described stability indicating LC and derivative spectrophotometric methods for the determination of zafirlukast [5]. Voltametric method was developed for the determination of zafirlukast in pharmaceutical formulation [6]. This paper describes the applicability of direct spectrophotometric determination of zafirlukast in pure samples and tablets preparation.

Experimental

Apparatus:

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

Chemicals and Reagents:

All chemicals used were of analytical grade. Sample of Zafirlukast bulk drug was obtained from Zeneca limited, England. The purity was found to be 100.00 %(w/w). Accolate® tablets manufactured by Zeneca limited were purchased from local Saudi Arabia market; each tablet is labeled to contain 20 mg of zafirlukast, Batch No. UA 976. Hydrochloric acid solution (0.1 N) was prepared in distilled water.

A 200 µg/ml stock solution of zafirlukast in 0.1 N Hydrochloric acid was used as standard solution.

Procedure:

Preparation of standard solution of zafirlukast:

Aliquots of the drug solution in 0.1 N HCl (200 µg/ml, 0.25-1.5ml) were transferred into 10ml volumetric flasks. The volume was made up to 10 ml with 0.1 N HCl. The absorbance was measured at 208 nm against a reagent blank prepared similarly without drug solution.

Preparation of zafirlukast samples from Accolate® tablets:

About 20 tablets of Accolate®, (each containing 20 mg of zafirlukast were ground to fine powder. The amount of powder equivalent to 50 mg

of the active compound was transferred to 50 ml volumetric flask. The volume was made up to 50 ml with 0.1 N HCl. the solution was then extracted for 15 minutes, and then filtered. Aliquot, 10 ml of the filtrate was transferred into 50 ml volumetric flask then diluted to the volume with 0.1 N HC to obtain a sample stock solution of 200 µg/ml. The procedure was continued as above.

Results and Discussion

Of all solvents attempted to dissolve zafirlukast, 0.1 N HCl solution was very suitable where the substance dissolved freely in it. Zafirlukast was found to yield a maximum absorption at 208 nm as shown in figure (1). Absorbance measurements were

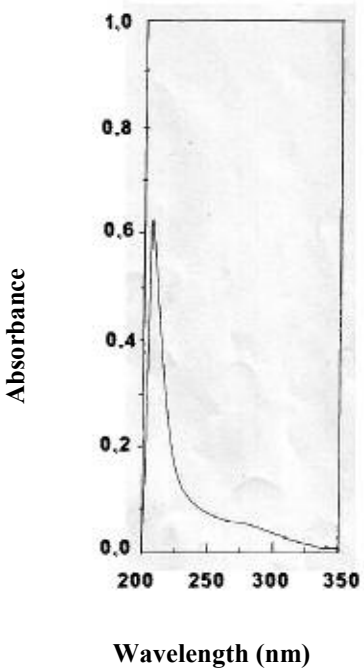

Figure (1): Absorbance spectrum of zafirlukast (20 µg/ml) in 0.1 N HCl solution.

made at this wavelength to construct calibration curve and subsequently for analysis. A plot of Absorbance versus concentration was linear in the range 5-30 µg/ml. Regression analysis on the calibration curve gave the following equation:

$$A = 0.0305\ C + 0.0022\ , \qquad r = 0.9999$$

Where A stands for the absorbance at 208 nm and C for
Concentration of zafirlukast in µg/ml and r for correlation coefficient which indicates good linearity. The accuracy and precision of the method was checked by analysis of different concentration of pure zafirlukast. The results were compared with derivative spectrophotometric method [5]. The mean percentage recovery in pure sample was 99.75±0.57, as calculated from the regression equation, table (1). The calculated *t* and *F* values were less than tabulated, so there is no significant difference between the proposed method and derivative method with respect to accuracy and precision.

The proposed spectrophotometric method was applied to the assay of zafirlukast in Accolate® tablets and the validity of the method was assessed by applying the standard addition technique, table (2). The accuracy of the method when applied to Accolate tablets was found to be 99.35±0.71 and the mean percentage recovery by applying the standard addition technique was 99.73±0.56 which indicate that there is no interferences in tablets preparation at 208 nm.

The proposed method is simple, accurate and sensitive where it can be used for the routine determination of zafirlukast in bulk drug and pharmaceutical preparations.

Table (1): Determination of zafirlukast in bulk drug by the direct spectrophtometric method.

Taken µg/ml	Found* µg/ml	% Recovery	Reference method [5]
5	4.94	98.80	
10	10.03	100.30	
15	14.97	99.80	
20	20.01	100.05	
25	24.80	99.20	
30	30.10	100.33	
Mean		99.75	99.75
N		6	5
SD		0.570	0.780
Variance		0.323	0.608
t		0.398 (2.26)**	
F		1.861 (5.19)**	

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

Table (2): Determination at zafirlukast in Accolate® tablets by direct spectrophotometric method.

Accolate® tablets			Standard addition			
Claimed mg/tablet	Found*	% Recovery	Taken µg/ml	Pure added µg/ml	Pure found**	% recovery
20	19.87	99.35±0.71	5	5	4.95	99.00
			5	10	10.03	100.30
			5	15	15.07	100.47
			5	20	19.90	99.50
			5	25	24.85	99.40
Mean ± SD						99.73 ± 0.56

* Average of 6 measurements.
** Average 3 determinations.

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