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Spectrophotometric Determination Of Valsartan In Pure Form And In Its Pharmaceutical Preparations

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Spectrophotometric determination of Valsartan in pure form and in its pharmaceutical preparations

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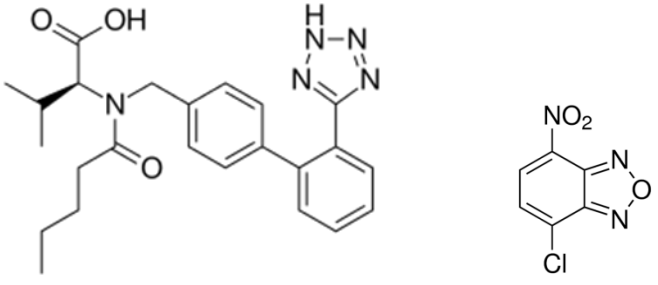
ABSTRACT

An easy, rapid and economical spectrophotometric method for determination of Valsartan (Val), by reaction with 4-chloro-7-nitrobenzofurazan (NBD-Cl) as reagent in an alkaline interemediate. This method is based on the forming of product between (Val) and the chromogenic reagent (NBD-Cl), to produce a brown color at (pH 11.9) and $\lambda_{max.}$ 470 nm. Beer's Law is obeyed at the concentrations range of (0.4-14.8 µg/ml), with molar absorptivity of (1.05×10^4 L/mol.cm) and correlation coefficient 0.9827, The limit of detection was 0.557 µg/ml. The suggested method was prosperity implement to the determination of (Val) in pure form and in its pharmaceutical formulations (tablets).

1. Introduction

Valsartan [Fig.1(a)], is a medication used to treat high blood pressure, heart failure, and diabetic kidney disease, It is a reasonable initial treatment for high blood pressure, It is taken by mouth [1], Valsartan is chemically described as *N*-(1-oxopentyl)-*N*-[[2′-(1*H*-tetrazol-5-yl) [1,1′-biphenyl]-4-yl]methyl]-L-valine. Its empirical formula is $C_{24}H_{29}N_5O_3$, its molecular weight is 435.5[5], Several methods have been reported for determination of this drug, such as HPLC [8,12], TLC [2,4], HPTLC [11], Voltammetry [6,10], UV-Vis. Spectrophotometry [15,3]. "4-Chloro-7-nitrobenzofurazan (NBD-Cl) is a highly sensitive chromogenic and fluorogenic reagent" [7].



(a) (b)

Fig. (1): Chemical Structures of (a) Valsartan (b) NBD-Cl reagent

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The research aims at finding a simple, fast and economical spectral methods for determination of (Val) by chromogenic reagent NBD-Cl in alkaline medium.

2- Experimental

2-1 Apparatus

T90 UV-VIS spectrophotometer double beam (PG Instruments Ltd) with 1 cm quartz cells, UV-VIS spectrophotometer single beam (Genesys UV 10), pH meter InoLab pH/INO735 (Jenway 3310), Balance Kern 770GS/GJ (Sartorius BL210S), Oven (Memmert), Schutzart DIN 40050-IP20.

2-2 Materials

Valsartan %99 (SDI Samarra-Iraq), "4-Chloro-7-nitrobenzofurazan (NBD-Cl)" %98 (Solarbio), Sodium hydroxide (NaOH) %98 (GCC), Ethanol %99.9 (Scharlau).

2-3 Solutions

- **Valsartan Stock solution (1000 µg/ml)**: An exactly (0.1000 gm) of (Val) were dissolved in (100 ml) ethanol.
- **NBD-Cl (1×10^{-2}M)**: was prepared by dissolving (0.1996 gm) of NBD-Cl in (100ml) ethanol.
- **NaOH (1M)**: was prepared by dissolving (4 gm) of NaOH in (100 ml) distilled water.

3- Procedures

Valsartan: A 0.5 ml from 100 µg/ml of (Val) standard was carried into 25ml volumetric flask, followed by adding 3.0 ml from10^{-2} M "NBD-Cl" and 1.0 ml of 1.0 M NaOH. After 15 min., the volume was supplemented to volume by distilled water, and was measured at 470 nm against reagent blank.

3-1 Procedures for stoichiometric ratio

The reaction of equivalence between this drug and the reagent have been estimated by carrying out molar ratio and continuous variation method. In these methods, equimolar concentrations of (0.5 ml) (Val) and NBD-Cl (8×10^{-3}M) was used. Varying aliquots of NBD-Cl was added to constant aliquots of drug solution, final volumes (25ml) and the absorbance was measured at 470 nm, opposite the reagent blank treated similarly. While in the latter method, a series of Val:NBD-Cl solutions was kept at (5ml) (0.5**:**4.5, 1**:**4, 1.5**:**4.5, 2**:**3, 2.5**:**2.5, …… 4.5**:**0.5).

3-2 Application of the proposed methods

We weighed ten tablets and took an average of their calculations, then grinded these tablets in the form of a fine powder, after which a carefully weighed quantity was transferred to a beaker and was shaken using 50 ml of distilled water and then filtered, washed and the washes were collected in a volumetric flask 100 ml. The final concentration of the resulting solution was 100 µg\ml and it was successful suggested methods of estimating (Val) in various commercial tablets.

4- Results and discussion

Absorption spectrum of Val-NBD-Cl against reagent blank in an alkaline medium at room temperature (25^{o}C) producing a brown colored product where absorbs maximally at 470 nm (Fig. 2), and reagent blank against ethanol (Fig. 3).

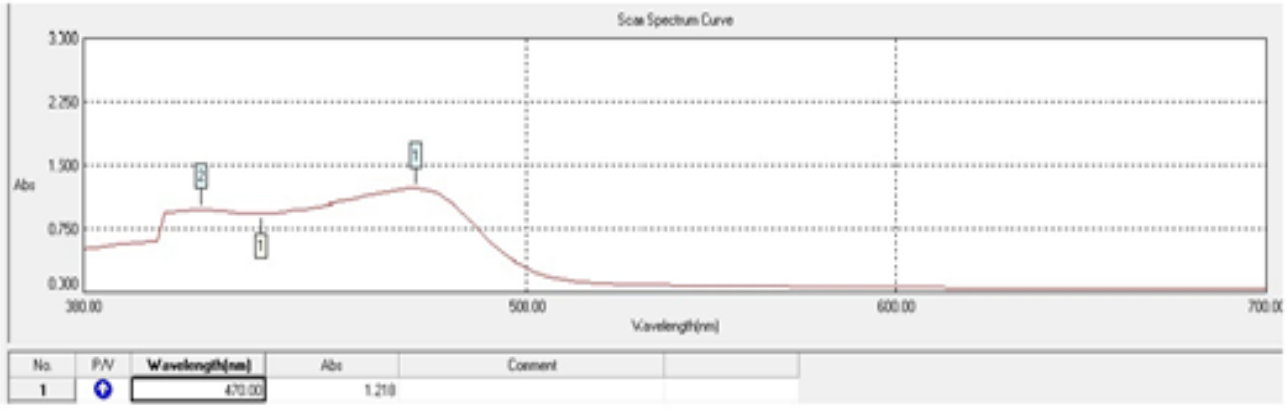


Figure 2: Absorption spectrum of Val-NBD-Cl against blank

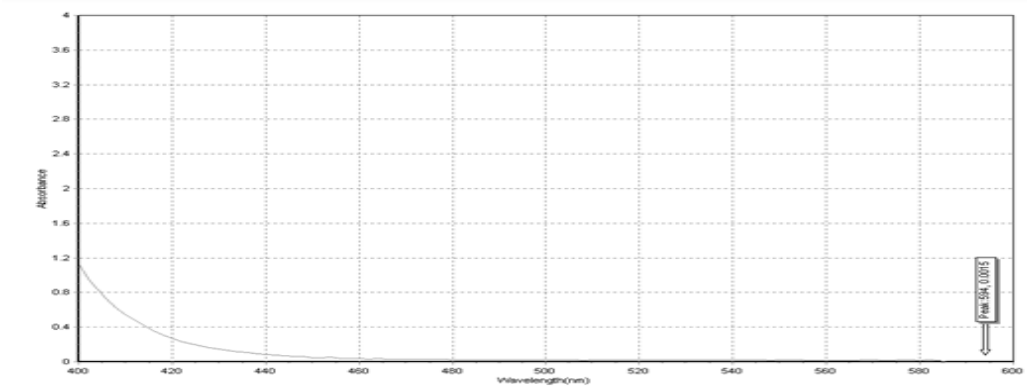


Figure 3: Absorption spectrum of reagent blank against ethanol

4-1 Optimum conditions

The optimum conditions, required to study the effect of colored product with maximum stability and sensitivity, the influence of volumes of NBD-Cl, addition of alkaline intermediate, reaction time and the stability of colored product were studied at "room temperature (25^{0}C)".

4-1-1 Effect of reagent volume

The effect of reagent concentration on the reactions was studied at room temperature. The reaction of (Val) with reagent was to rely on the concentrations of NBD-Cl. So, its concentrations were studied by

different volumes (0.3-4.7) ml of (0.01 M) NBD-Cl, while the (Val) concentration was constant at (2.0 µg/ml). The color intensity was found to increase with addition of NBD-Cl up to a particular concentration and then either decrease or remain steady, the highest absorption intensity were attained when the volumes of NBD-Cl were 3.0 ml of (0.01 M) NBD-Cl, Therefore, this volume was used in subsequence experiment, as shown in Fig. (4).

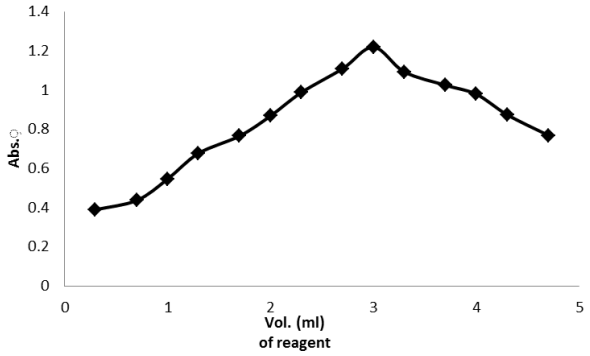


Figure 4: Effect of reagent volume on product

4-1-2 Effect of pH

An alkaline medium was required, because this drug does not reacts with "NBD-Cl" in acidic media, the result appeared that the absorbance at "pH < 8 was close to 0", in the acidity intermediate, this drug has hardness to react with "NBD-Cl". different concentrations from NaOH were tested; best results were at higher concentrations of NaOH (1.0 M), with pH 11.9, as illustrated in Fig. (5).

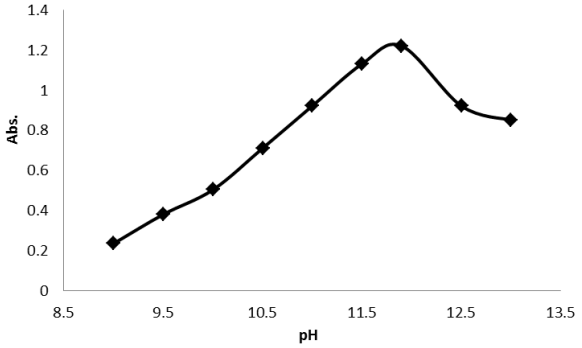


Figure 5: Effect of pH on Val-NBD-Cl product

4-1-3 Effect of Time

Under the optimum conditions, the effect of reaction time of (Val) with reagent in "alkaline medium" was constructed, and the product remained stable for 50 min., as illustrated in table (1).

Table 1: Effect of time on product

Time (min.)	Abs.
0.0	1.025
10	1.140
15	1.211
25	1.215
30	1.218
35	1.219
40	1.217
45	1.212
50	1.209
55	1.195
60	1.116
65	1.112

4-1-4 The stoichiometry of the product

Under the "optimum conditions", (cons. of NBD-Cl, pH, time) "the stoichiometry" of the reaction between (Val) and the reagent was studied by mole–ratio and continuous variation methods. The equivalence between reagent and this drug was 1:1 (Figs. 6, 7).

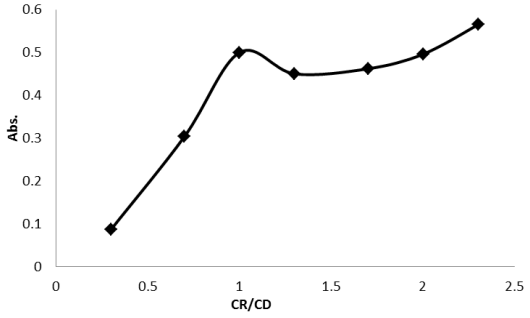


Figure 6: Mole-ratio method of Val-NBD-Cl product

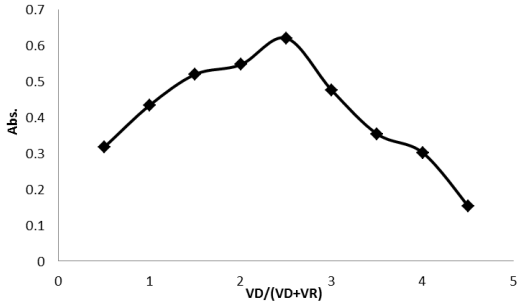
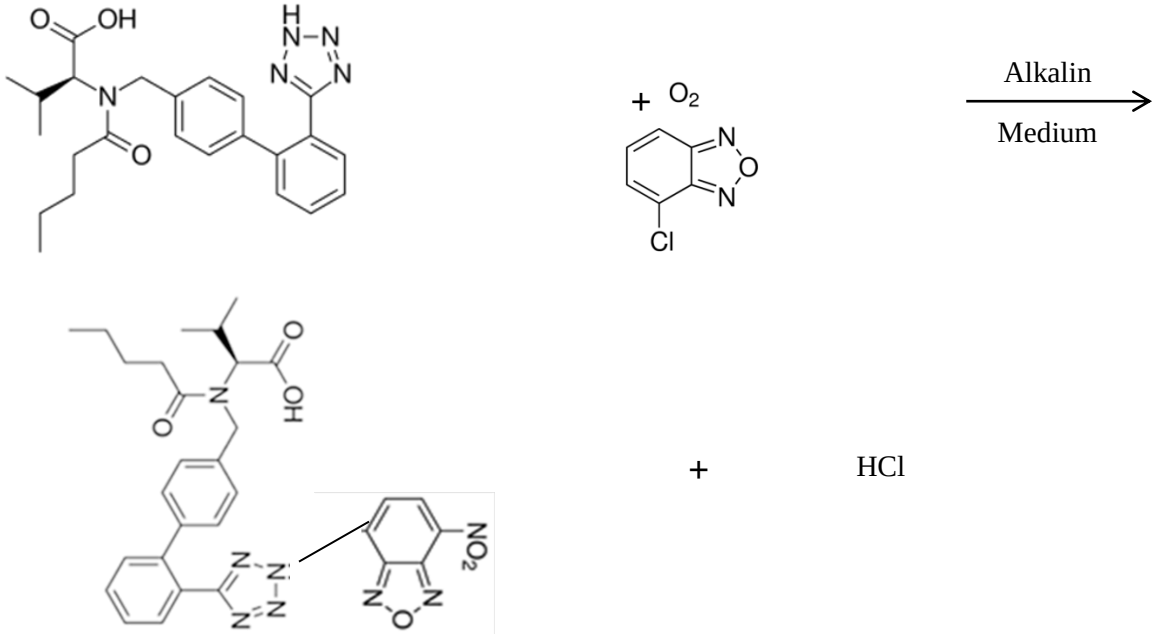


Figure 7: Continuous variation method of Val-NBD-Cl product

So the proposed interaction can be as in the following equation (in scheme 1): (the drug are associated with the reagent through the amine group) [13-15]:



Scheme 1: Suggested interaction

4-1-5 Calibration curve

The calibration curve for (Val) standard form with NBD-Cl showed the linearity at concentrations range of (0.4-14.8 µg/ml), as shown in Fig. (8).

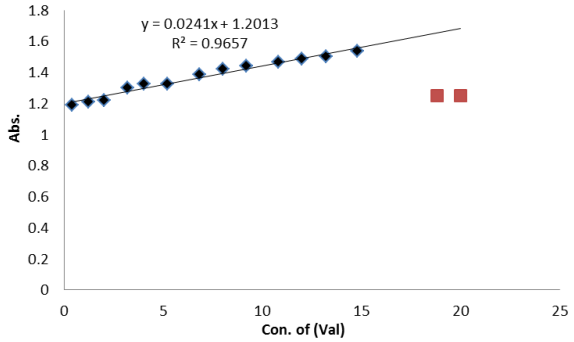


Figure 8: Calibration curve of Val - NBD-Cl product

4-1-6 Construction of calibration curve

Calibration curve was constructed according to the optimum conditions in table (2).

Table 2: Optical characteristics of the calibration curve for spectrophotometric determination of (Val) by NBD-Cl reagent

Parameter	(Val)
λ_{max}.(nm)	470
Beer`s law (µg/ml)	0.4-14.8
Molar absorptivity(L/mol.cm)	1.05×10^4
Correlation coefficient (r)	0.9827
Limit of Detection (µg/ml)	0.557
Slope	0.0241
Intercept	1.2013
%RSD	0.341

4-1-7 Effect of Additives

The effect of additives on the composition of the product between (MZ) with reagent was studied, and there is no effect of additives on absorption values, as shown in table (3).

Table 3: Effect of Additives

Additives	%Rec. of 2 (µg/ml) of Valsartan	
Amount	20 (µg/ml)	40 (µg/ml)
Starch	100.36	100.76
Lactose monohydrate	100.52	99.85
Sodium starch glycolate	98.26	100.06
Magnesium stearate	99.47	98.34

4-1-8 Application of the proposed methods

In table (4), the result of determination of (Val) in the pharmaceutical preparations (as tablets).

Table 4: Determination of (Val) in commercial tablets by spectrophotometric method

pharmaceutical preparations	Content (µg/ml) declared	Found (µg/ml) by proposed method	%Recovery
Novartis	1.2	1.23	102.5
	2	1.97	98.5
	4	4.05	101.3
Arbitan	1.2	1.18	98.3
	2	2.06	103
	4	4.08	102
Diovan	1.2	1.19	99.2
	2	1.92	96
	4	4.09	102.3

5- Conclusion

This method described with this study is simple, rapid, convenient and do not requires special working conditions unlike many other reported methods. The procedure showed shorter reaction time, stable colored species with inexpensive reagent. The determination can be performed at room temperature and do not require heating step. And the effect of additives on the colored product was studied, and not observed any effect. The proposed method can be applied to determination of (Val) in pharmaceutical preparations (Tablet).

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