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RESEARCH ARTICLE

# Spectrophotometric Studying for Some Organic Compounds as (Drugs) by using (FT.I.R.) Spectrum and High Performance Liquid Chromatographic Technic for Valsartan and Hydrochlorothiazide in Pharmaceutical Preparations Tablets

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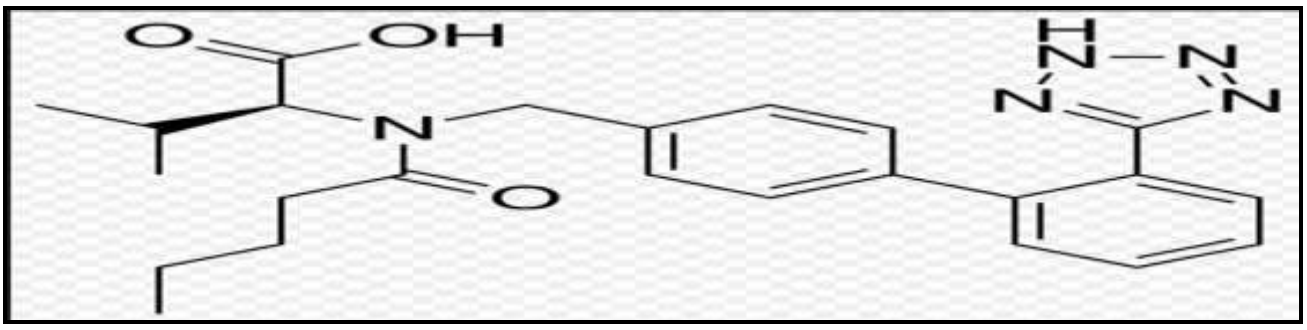
## Abstract

Used and complete organic analytical spectrum by using (FT.I.R.) spectrum to prove the chemical structures for some organic compounds as (drugs) of Valsartan and Hydrochlorothiazide (1) and supported by reverse phase high performance liquid chromatography (HPLC) method has been developed for the determination of valsartan and hydrochlorothiazide in pharmaceutical preparations tablets .Chromatography was carried out on supelco $L_7$ column (25cm×4.6m.m), 5µm. Using Buffer solution , methanol and acetonitrile at ratio 35 :25 :40 accurately as mobile phase. The flow rate was 1.0 $ml.min^{-1}$ with Uv-detection at 270 nm at 50C°. Separation was completed within 1.42 min and 5.74 min. Calibration curve was linear coefficient correlation 0.9948 and 0.9980 over a concentration range of (30-50µg.$ml^{-1}$) and (5-15µg.$ml^{-1}$). The relative standard deviation (RSD) was found <1%.The proposed method was successfully applied to the determination of valsartan and hydrochlorothiazide in pharmaceutical preparations.

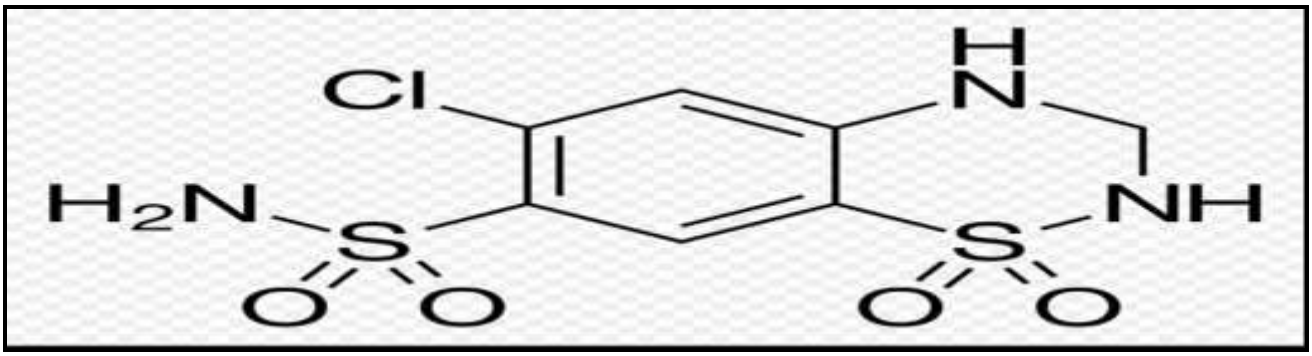
**Keywords:** *Valsartan, Hydrochlorothiazide, Linearity, FT.I.R., HPLC, Tablet form*

## Introduction

Introduction Valsartan is one of the most important drugs in medical applications. It acts as an active and inactive angiotensin receptor that acts as a subtype of the AT1 receptor. It also works to reduce pressure in blood vessels, treat heart failure and diabetes, and is chemically known as [1, 7].(2S)-3methyl-2-[N-({4-[2H-1234-tetrazol-5-yl) phenyl] phenyl} methyl) pentanamido] butanoic acid In reviewing the literature, we note the researchers' interest in this drug. It was appreciated in different ways, such as high performance liquid chromatography [8, 10].The mass spectrometry technique was used in its estimation [11], as well as spectrum derivative technique [12], and the chemical structure of the valsartan.



Hydrochlorothiazide is chemically called [13] 6-chloro-3, 4- dihydro- 2H-1, 2, 4- benzothiadiazine- 7-sulfonamide-1,1-dioxide This drug is used as a catalyst and is widely used in the treatment of high blood pressure Hind children, adolescents and pregnant women [14,15]. After reviewing the literature for investigating the methods of estimating the drug, many of them were found to be used in estimating such drugs as spectral methods [16, 18] and high-performance liquid chromatography [19], and electrolyte migration [20]. Figure 1, 2 shows the chemical composition of the drug.




## Experimental

### Apparatus

Chromatographic system consisted of a shimadzu HPLC model LC-20AT with UV detector model SPD-20A and $L_7$ supelco column (25cm ×4.6mm), 5 µm particle size HPLC condition are given in (Table 1).

**Table 1: some of physical properties for the organic compounds (drugs) as bellow**

| No | Name | Formula | Color | m.point C° | Solvent |
|---|---|---|---|---|---|
| 1 | Valsartan | $C_{24}H_{29}O_3N_5$ | white | 116-117 | methanol |
| 2 | Hydro. Thiaz. | $C_7H_8O_4S_2N_3$ | white | 523-526 | methanol |

**Table 2: HPLC conditions**

| Column | Supelco $L_7$ (25cm×4.6mm),5 µm |
|---|---|
| Wavelength | 270 nm |
| Mobile phase | Buffer : Methanol : Acetonitril |
| Retention time | 1.42 - 5.74 min |
| Flow rate | 1.0 ml.min$^{-1}$ |
| Temperature | 50C° |
| Injection volume | 20 µl |

### Reagents

All chemical used were of analytical or pharmaceutical grade and HPLC grade methanol was used throughout .A standard stock solution of Valsartan (40µg.ml$^{-1}$) and Hydrochlorothiazide (12.5µg.ml$^{-1}$) was prepared in mobile phase , Working standard solutions in a range of (30-50 µg.ml$^{-1}$) and (5-15 µg.ml$^{-1}$) were prepared by dilution from this stock solution.

### Determination of Val., Hyd. solution

A series of standard solution containing 30-50 µg.ml$^{-1}$ and 5-15 µg.ml$^{-1}$of valsartan and hydrochlorothiazide the sample solution of pharmaceutical preparation were applied respectively. A 20µl a aliquot of each solution was injected in to the column in a duplicate and the chromatograms were recorded. Calibration graph was constructed by plotting the mean peak area versus concentration of each drug the concentration of the unknown was read from the calibration graph or calculated from the regression equation derived from the concentration and peak area data.

### Procedures for Pharmaceutical Preparations

### Tablets

The content of 20 tablets was mixed and grinded with mortar. A liquots equivalent to 80mg of valsartan and 25mg hydro was transferred into 100ml volumetric flask and diluted 1ml of this solution to 20 ml with mobile phase to the volume. Calculate the percentage recovery using a calibration graph previously prepared.

### Procedure for Buffer Solution

Weight 0.5 gm of $NaH_2PO_4$ and dissolve in distilled water to 100 ml, and adjust the pH to 3.2 with $H_3PO_4$ or Noah solutions

## Results and Discussion

FT.I.R. spectrum for valsartan compound, the functional groups of it are. The carbonyl group of acid (-C=O) is observed at (1500 $cm^{-1}$) as double bands. The (-C=C-) of benzene rings are observed as strong band at (1600$cm^{-1}$) the carbonyl group of tertiary amide (lactam) (-C=O) is observed at (1720$cm^{-1}$) as single strong band . The three methyl groups (-CH3) are observed at the region in (2825-2925$cm^{-1}$) as triple bands. The hydroxyl group (-OH) of the carboxylic acid is observed at (3550$cm^{-1}$).

See the Figure (6).And FT.I.R. Spectrum for hydrochlorothiazide compound the functional groups of it are: The stretching band of (-S-C-) is observed at (1125-1175$cm^{-1}$) as strong trible bands. The double bands observed at (1300-1325cm-1) is due to stretching of the halogen in (-C=C-Cl) aromatic ring. The bands observed at (2825-2850 $cm^{-1}$) are due to the aliphatic (-CH).

The bands observed at the regions (3100,3250,3300,3550 $cm^{-1}$) are due to the stretching of the groups of (-N-H) this compounds [1] , see figure (7).The development of HPLC methods for the determination of drugs has received considerable attention in recent years because of their importance in the quality control of drugs and pharmaceutical products.

The aim of this study was to develop a rapid HPLC method for the determination of drugs in pure from, its pharmaceutical formulations using the most commonly employed RP L7 column with UV detection. The retention time (Rt) of valsartan was found to be 1.42 min and hydrochlorothiazide in 5.76 min. A typical chromatogram formulation of both drugs is shown in (Fig.3, 4).

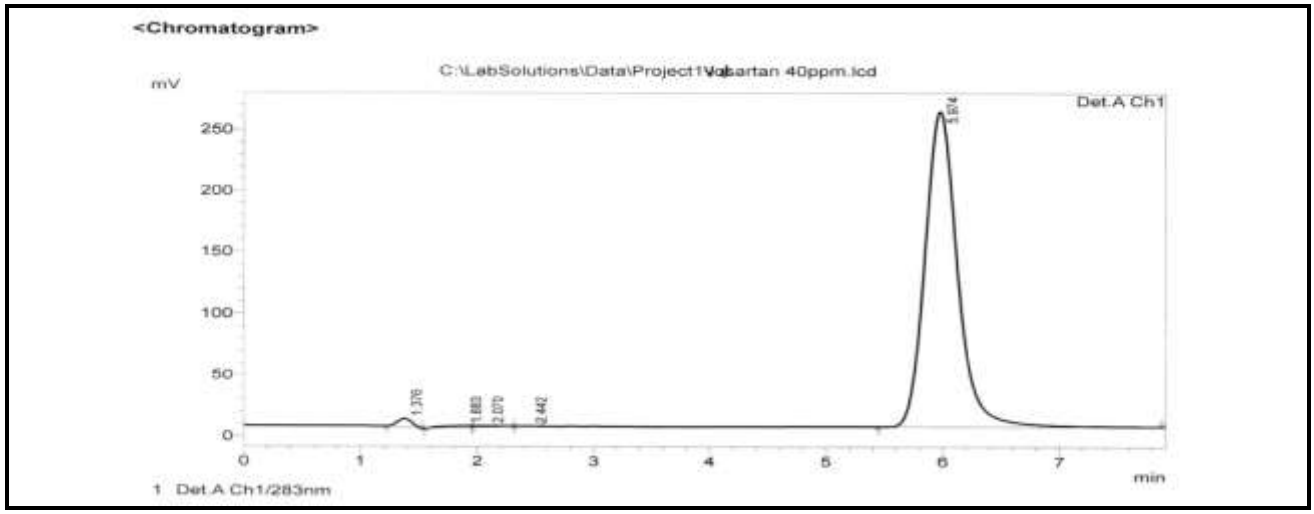



**Figure 3: Typical chromatogram (valsartan (40 µg/ ml)**

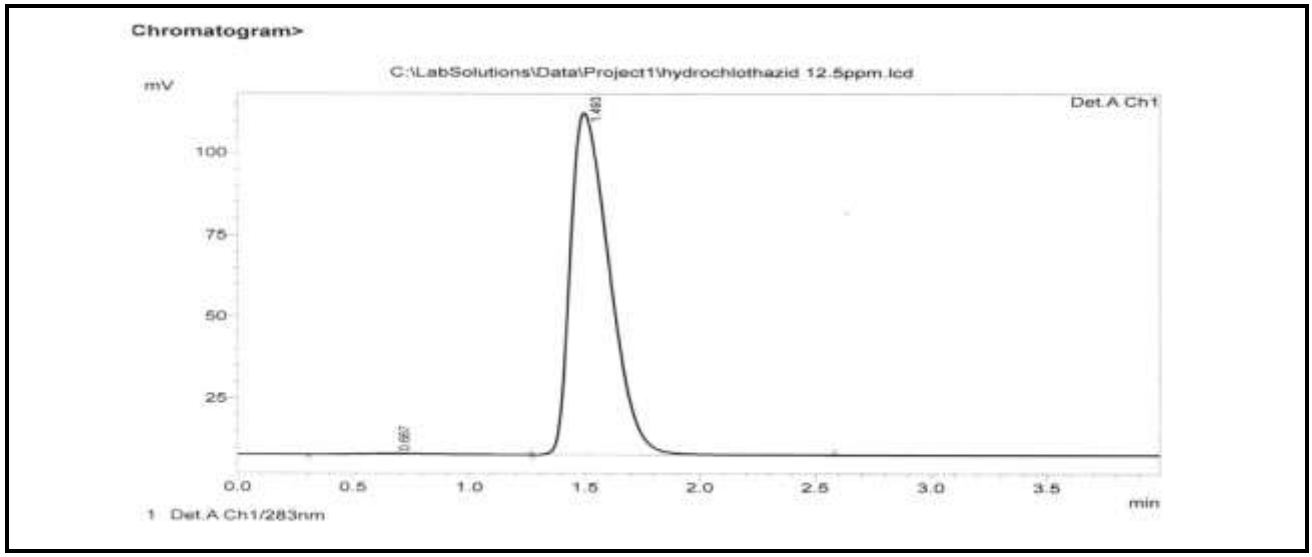
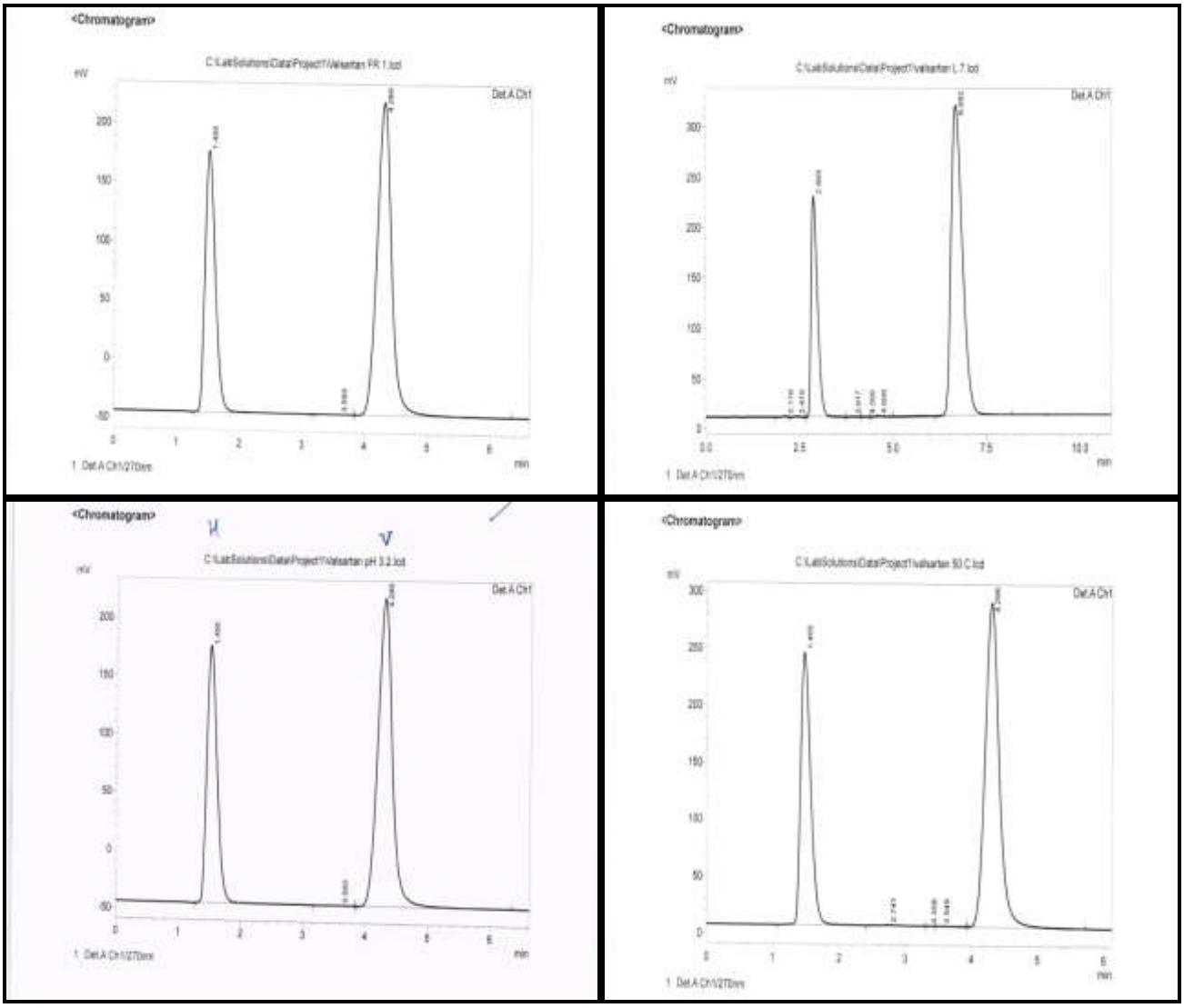
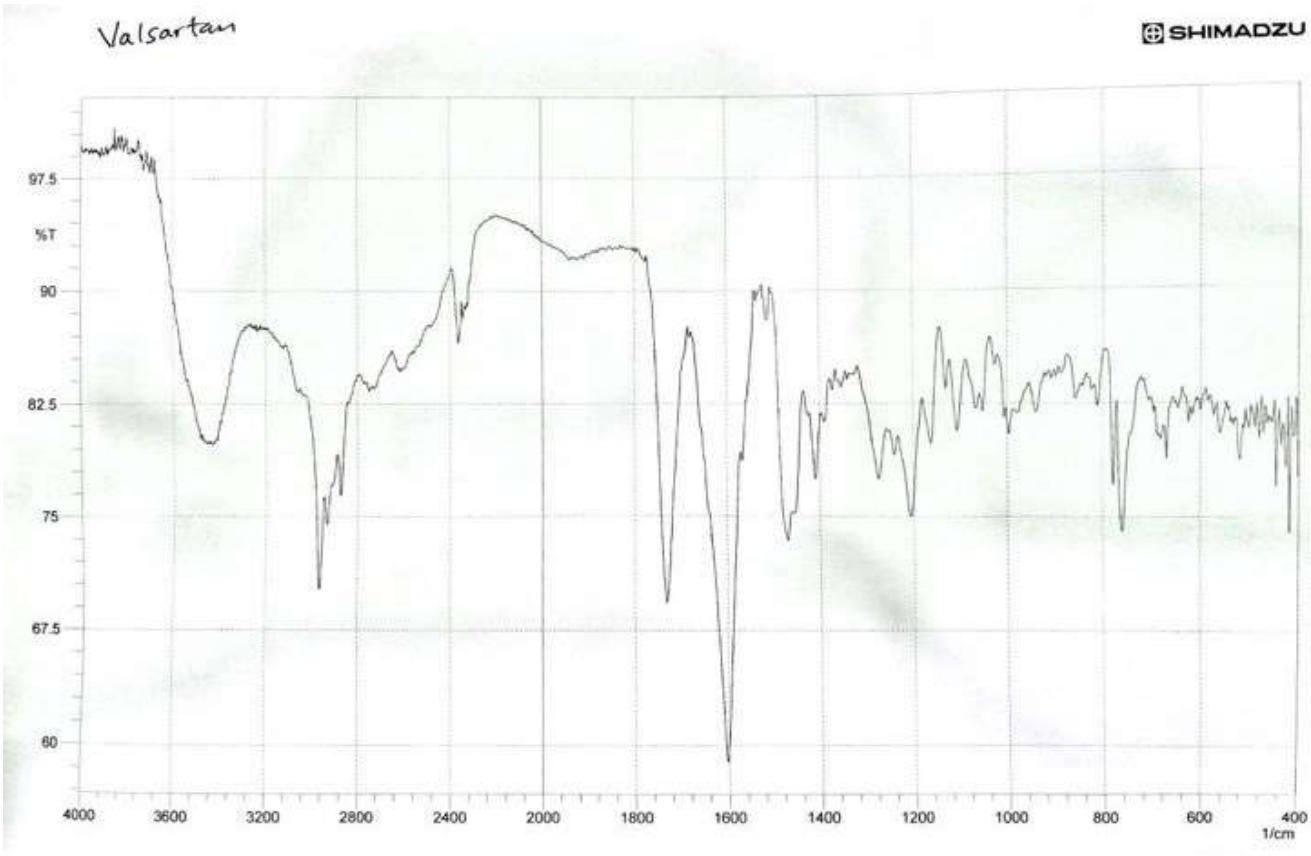



**Figure 4: Typical chromatogram (hydrochlorothiazide (12.5µg/ml)**

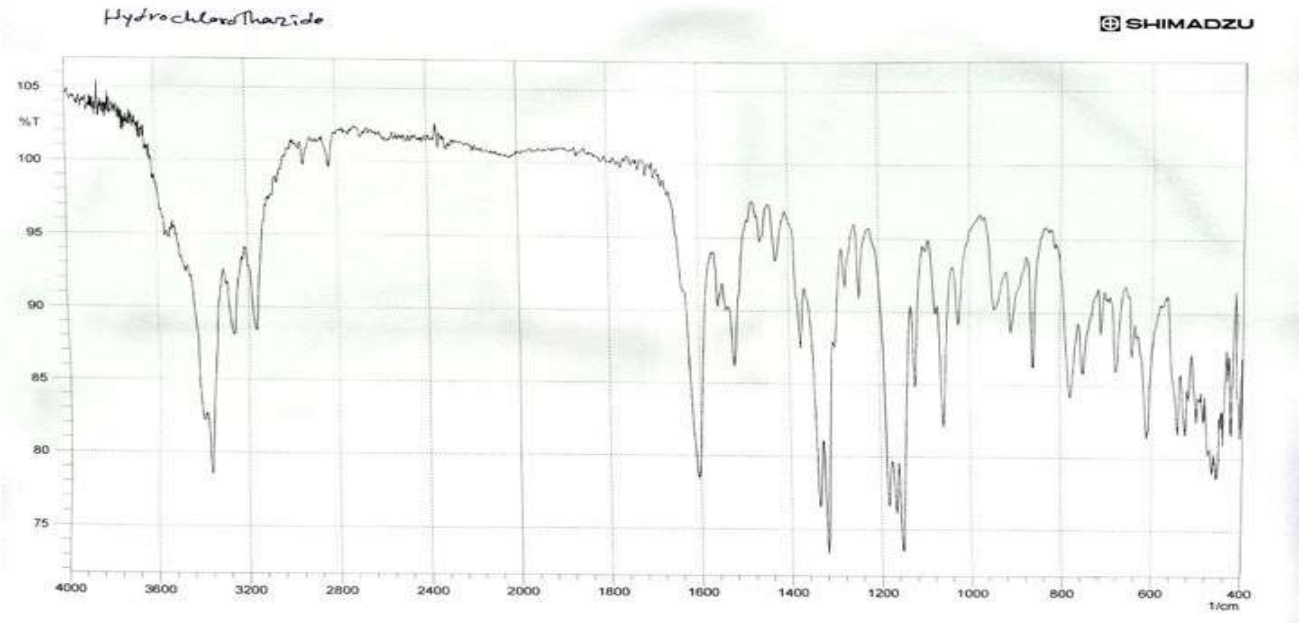



**Figures 5: Typical chromatograms ideal conditions**




**Figures 6: FT.I.R. Spectrum of valsartan**




**Figures 7: FT.I.R. Spectrum of hydrochlorothiazide**

Drug was constructed by plotting the peak area against concentration of drug .It was found to be linear with a correlation of 0.9948, the representative linear regression equation being Y=32443X+161473 and linear with a correlation of 0.9980, the representative linear regression equation being Y=19100X +26553 were Y is the mean peak area and X is the concentration in n=5 was expressed as relative standard deviation and rang between 0.17% and 0.95% (Table 3).

**Table 3: ideal conditions for drugs**

| Drug | SP | PE (mv) | PH (mv) | RT (min) | N | HETP |
|---|---|---|---|---|---|---|
| Valsartan | $L_7$ | 4670471 | 264067 | 5.745 | 643.55 | 0.33 |
| Hydroch. | $L_7$ | 1347468 | 109106 | 1.424 | 543.21 | 0.42 |

**Table 4: % Recovery of drug from synthetic mixture of each drug**

| Amount added Hydr. (conc.) | Amount found(conc.)* | % Recovery |
|---|---|---|
| 5 | 5.10 | 102.0 |
| 5 | 4.13 | 82.5 |
| 5 | 4.70 | 94.0 |
| 5 | 4.93 | 98.52 |
| 5 | 4.74 | 94.90 |
| **Mean value** | | **94.38** |

*Mean of five determinations

**Table 5: % Recovery of drug from synthetic mixture of each drug tablets**

| Amount added Vals. (conc.) | Amount found(conc.)* | %Recovery |
|---|---|---|
| 30 | 23.79 | 79.3 |
| 30 | 26.85 | 89.5 |
| 30 | 30.30 | 101.1 |
| 30 | 26.31 | 87.7 |
| 30 | 26.34 | 87.8 |
| **Mean value** | | **89.08** |

*Mean of five determinations

## Analytical Applicatio*n*

The proposed method was successfully applied to the assay of this drug. No interfering peaks were found in the chromatogram, indicating that the excipients did not interfere with the estimation of the drug by the proposed HPLC method. The results obtained are presented in tables [5].

## Application

A-Simultaneous High Performance Liquid Chromatography Determination of Tablets 80mg Valsartan and 25mg Hydrochlorothiazide and against with (U.S.P 2007 method) [21].Weigh 20 tablets 2mg/ Tablet, An accurately weighed quantity of the powder equivalent 80mg valsartan and 25mg hydrochlorothiazide and weight one tablet in

100 ml of volumetric flask with methanol and shacking, sonicate 20 minutes and this solution is filtered in filter paper 0.45 µm. And complet the volume with methanol up to the mark .Then pipette take 1ml of this solution and dilute to 20ml with the mobile phase. Using column type ($L_7$) and mobile phase consisting of buffer, methanol and acetonitril (35:25:40) were used, and flow rate 1.0 ml.min$^{-1}$ and wave length 270nm at 50 temperature .The result (peak height) is compared with standard curve with the same concentration. The recovery is found to be 101.1%. Buffer solutions prepare weight 0.5 gm of $NaH_2PO_4$ and dissolve in distilled water to 100 ml and adjust pH to 3.2 with $H_3PO_4$ or Noah.

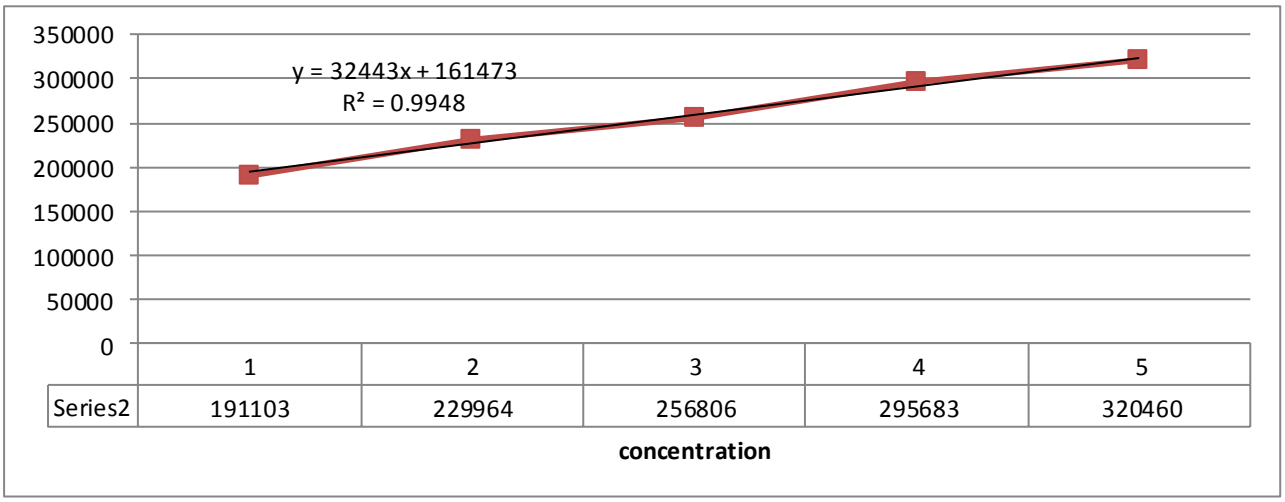



**Figure 8: Calibration curve for the determination of valsartan by the new developed method**

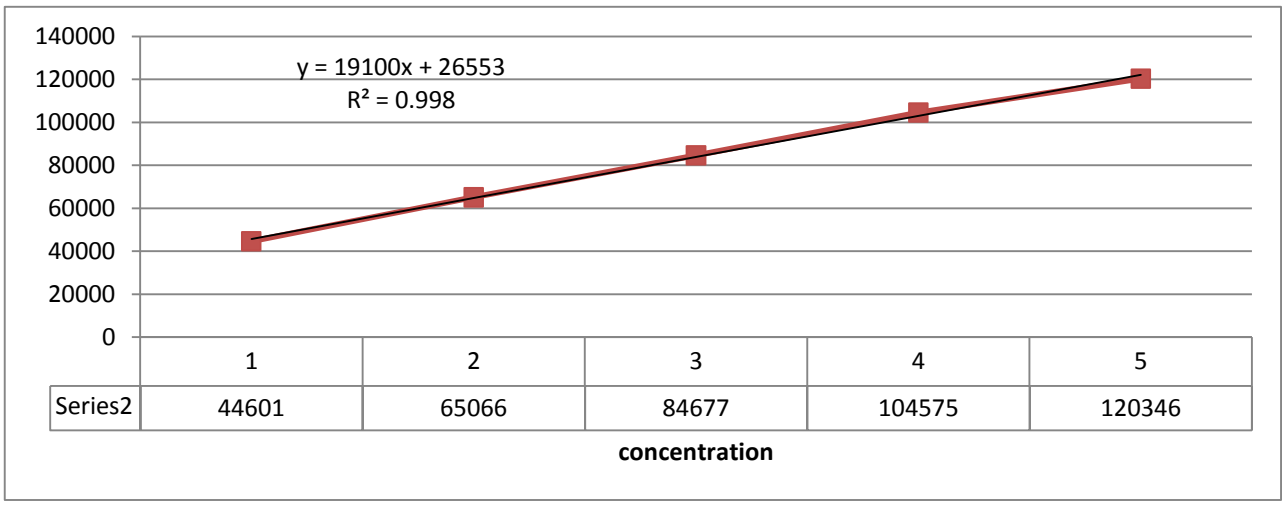



**Figure 9: Calibration curve for the determination of hydrochlorothiazide by the a new developed method**

**Table 6: The precision accuracy and the detection limit of valsartan drug was measured and detected**

| NO | Conc. Of drug (µg.ml$^{-1}$) | Peak height (mv) | Peak area (mv) | Calculated concentration | Recovery.% |
|---|---|---|---|---|---|
| 1 | 30 | 191103 | 3701413 | 23.79 | 79.3 |
| 2 | 30 | 244123 | 4182324 | 26.85 | 89.5 |
| 3 | 30 | 232003 | 4720123 | 30.30 | 101.1 |
| 4 | 30 | 244329 | 4095100 | 26.31 | 87.7 |
| 5 | 30 | 219872 | 4100098 | 26.34 | 87.8 |

**Table 7: The precision accuracy and the detection limit of Hydrochlorothiazide drug was measured and detected**

| NO | Conc. Of drug (µg.ml$^{-1}$) | Peak height (mv) | Peak area (mv) | Calculated concentration | Recovery.% |
|---|---|---|---|---|---|
| 1 | 5 | 44601 | 494544 | 5.10 | 102.0 |
| 2 | 5 | 40302 | 399926 | 4.13 | 82.5 |
| 3 | 5 | 39233 | 455871 | 4.70 | 94.0 |

| | | | | | |
|---|---|---|---|---|---|
| 4 | 5 | 44222 | 477551 | 4.93 | 98.5 |
| 5 | 5 | 37993 | 460021 | 4.74 | 94.9 |

## Conclusion

In this study, a simple, fast, efficient and reliable HPLC method was developed and validated for the determination valsartan and hydrochlorothiazide in pharmaceutical formulations tablets .The method presented in this study was selective enough using a conventional RP L7 analytical column and applicable to pharmaceutical preparation after simple extraction. Thus the developed method is recommended for control through out the entire manufacturing process of drugs as well as quality control of the finished product in view of its high recovery, precision and accuracy.

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