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DEVLOPMENT & CHARACTERIZATION OF FIMASARTAN TABLET USING UV SPECTROSCOPY

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ABSTRACT

Fimasartan is the non-peptide angiotensine II receptor antagonist which is utilized in hypertension. A simple accurate & cost-effective approach is established for the estimation of Fimasartan tablet employing uv spectrophotometer in the API & bulk dose form. The Fimasartan exhibits λmax at 261 nm using 10% methanol solution. Fimasartan fulfilled Beer-Lambert's law in the range of concentrations of 10-50µg/ml with pearson correlation (r2) of 0.999. The accuracy of the model was confirmed by percent recovery, by adding a known amount of the pure drug to the formulation and the percentage recovery was found to between 98.5 to 100.08% w/w, indicating that the developed method is accurate which indicates a good accuracy of the method and it shows that the method was free from the interference of excipients used in the formulation. The precision of the technique was provided in terms of the relative standard deviation, and it should be evaluated by utilizing a minimum of 6 determinations over 100 % concentration which reveals % RSD less than2 indicates that the procedure was exact. The limit of detection and quantification was determined to be 3 & 9.11, respectively. The percentage purity of the marketed formulation was found to be 97.18 % w/w. The suggested spectrophotometric approach was verified as per the ICH Q1A (R2) requirements.

KEYWORDS: Fimasartan, UV spectrophotometry, linearity, method development, Validation.

INTRODUCTION

UV Spectrophotometry: Quite possibly of the most frequently used procedure in drug examination is UV spectrophotometry. It contains deciding the amount UV or noticeable radiation a substance in arrangement retains. UV spectrophotometers are gear that action the proportion, or capability of proportion, of the power of two light emissions in the UV region. On the off chance that any recorded information is accessible, natural particles can be recognized involving a spectrophotometer in subjective information examination, and quantitative spectrophotometric examination is utilized to measure the amount of sub-atomic species retaining the radiation in quantitative examination. The specttrophotometric method is straightforward, fast, and moderately unambiguous, and evaluating minuscule amounts of substances might be utilized. The Beer-Lambert regulation is the principal regulation that controls quantitative spectrophotometric investigation.

Beers' regulation: It states that the force of a light emission monochromatic light falls dramatically with the quantity of retaining particles. At the end of the day, absorbance iscorresponding to the fixation.

Lambert's regulation: It declares that the power of a light emission monochromatic light decreases dramatically as it goes through a material of homogenous thickness. A blend of these two regulations gives the Beer-Lambert regulation.

BeerLambert regulation: When light emission is sent through a straightforward cell containing an answer of a retaining material, a decrease in the power of light might happen. Numerically, Beer-Lambert regulation is expressed as \sA=a b c.

Where, A=absorbance or optical density\s a=absorptivity or annihilation coefficient

b=path length of radiation through example (cm)\s c=concentration of solute in arrangement. Both b and an are steady hence an is precisely relative to the focus c When c is in gm/100 ml, then, at that point, the steady is signified \sA (1%, 1 cm) (1 percent, 1 cm) A = A (1 percent/1cm) bc Measurement of restorative material involving spectrophotometer may did by delivering\ssolution in clear dissolvable and estimating it's absorbance at OK frequency. The frequency by and large picked is frequency of greatest retention (λmax), where little mix-up in setting the frequency scale has negligible impact on noticed absorbance.

FIMASARTAN

Fimasartan is an angiotensin II receptor antagonist that is used to treat hypertension and heart failure. Fimasartan decreases the prohypertensive activity of angiotensin II, such as systemic vasoconstriction and water retention by the kidney, by blocking the angiotensin II receptor type 1 via oral administration. In clinical trials, concomitant administration of fimasartan and the diuretic hydrochlorothiazide was found to be safe. Fimasartan is marketed in India by Ajanta Pharma Ltd under the brand names Fimanta and Fimagen.

Description

IUPAC NAME: 2-[2-butyl-4-methyl-6-oxo-1-[[4-2-(2h-tetrazol5yl) phenyl] phenyl] Methyl]Pyrimidine5yl] N, N dimethylethanoethionamide.

Solubility: Easily solvable in methanol and dmso, weakly soluble in water, moderately soluble is acetone and acetonitrile.

Molar formula: $C_{27}H_{31}N_7OS$ Molarweight: 501.6 g/mol Melting point: 155°c.

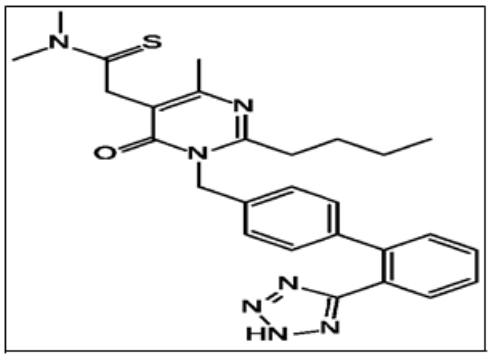

Figure 1: Structure of Fimasartan.

History

Fimasartan (Kanarb®), a pyrimidinone-related heterocyclic compound created by Boryung Pharm. Co., Ltd., is an angiotensin II receptor adversary with selectivity for the AT1 receptor subtype. Through in vitro and in vivo screening assessments, fimasartan was distinguished as an expected drug up-and-comer among a few combined substances. In a progression of nonclinical and clinical examinations, pharmacodynamic-pharmacokinetic elements and security profiles were found. Fimasartan is an original angiotensin receptor blocker that was approved by the Korean Food and Drug Administration in September 2010 for the treatment of fundamental hypertension. It is the main novel atomic element working on the cardiovascular framework. The technique of making mix treatment and it is currently in progress to enroll it in extra nations.

Mechanism of action

Fimasartan works by blocking the rennin-angiotensin system, which starts when the kidneys release renin, which causes angiotensinogen to be broken down into angiotensin I. The angiotensin-converting enzyme (ACE) then catalyses the reaction that produces angiotensin II, which binds to AT1 receptors in blood arteries, the heart, and the kidneys. The AT1 receptor on blood vessels is linked to an intracellular mechanism that promotes blood vessel constriction. Fimasartan decreases vasoconstriction by inhibiting the AT1 receptor, favouring vasodilation. Fimasartan and other ARBs have also been found to reduce the risk of stroke, myocardial infarction, and heart failure.

Pharmacology

Fimasartan is quickly assimilated and remains in the body negligibly seven days after treatment. Fimasartan has a half-existence of 9 to 16 hours, making it OK for routine use.

Fimasartan was shown to be powerful in a scope of portion regimens, whether fasting or took care of. Fimasartan was generally found in plasma and biliary discharges in its unmetabolized structure. The medication's pee disposal was insignificant, at under 3% 24 hours after treatment, showing that it isn't dispensed with by the kidneys.

3.1 MATERIAL AND METHOD

In the study we use Shimadzu UV-1800 double beam spectrophotometer, consisting two match quartz cell having 10mm light path for recording and measuring the spectra and absorbance ofthe Fimasartan.

Chemical and Reagents

Fimasartan pure drug was supplied as a gift sample by Pharmaffiliates Analytes and Synthetics Pvt. Ltd. The marketed formulation Fimagen tablets containing 60 mg of Fimasartan are purchased from local market. The analytical grade Methanol solvent was procured from E. Merck specialties private Ltd., Mumbai, India.

Selection of solvents

Many trials were performed for the selection of solvent for the dissolution of the drug. The solvent like acetonitrile, methanol, distilled water and dimethyl sulfoxide were tried depending upon the solubility of Fimasartan, Based on the solubility the methanol is selected throughout theexperiment.

Preparation of solutions

Preparation of standard solution

The standard Solution of Fimasartan was made by dissolving 50 mg of standard medicine in 25 ml of methanol in a 50 ml volumetric carafe. Blending till the whole disintegration of medication and making up the volume to 50 ml with methanol to arrive at the grouping of 1000 µg/ml.

Preparation of working standard solutions and construction of standard graph

The created stock solution was weakened with the 10% methanol in water to accomplish the standard arrangement of 100µg/ml of Fimasartan. From the

functioning standard arrangement, sequential \sdilutions 10µg/ml, 15µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, 50µg/ml using with a similar dissolvable. Then, at that point, the example was checked in UV-VIS Spectrophotometer in the reach 200 - 400 nm involving 10% methanol Solution as a clear and the Wavelength relating to greatest absorbance not set in stone to be 261 nm.

Calibration curve of Fimasartan

A calibration curve was plotted across a range of concentrations of 10-40 µg/ml for Fimasartan. Precise measurement known concentration of Fimasartan (10, 15, 20, 30, 40& 50) was changed to a series of 10 millilitre volumetric flasks and the capacity was filled up to 10 ml with 10 percent methanol solution. Calibration curve was produced putting the absorbance on Y-axis and concentration on the X-axis and its calibration curve is given in figure 2.

Procedure for assay of pharmaceutical formulation

Twenty Fimasartan (Fimagen) marketed tablets were carefully weighed, finely powdered and average weight of each tablet was estimated and the tablet fine powder corresponding to 50 mg of Fimasartan was placed into 100ml graduated flask and diluted in methanol to obtain 100µg/ml concentrations. The solution was then mixed till dissolution and filtered & additional dilutions were done with water to reach final concentration (10µg/ml) within the linearity range and measured λ max at 261 nm. Finally the medication content in each tablet and also bulk drug werefounded by using the usual graph.

Table 1: Assay of Pharmaceutical Formulation.

Absorbance	Concentration	%Purity
0.3224	9.717647059	97.1765

Label claim: 60 mg

3.2 METHOD VALIDATION

The presented approach has been verified as per ICH Q2 (R1) criteria by focusing on the following parameters.

Linearity

New solutions were produced using stock arrangements going between 10-50 µg/ml and the absorbance readings of each was estimated at 261 nm for this strategy involving a 10% Methanol arrangement as clear. The response was viewed as direct in the explored focus range.

Table 2: linearity data of Fimasartan.

S.no	Concentration (µg/ml)	Absorbance
1		s
2	10	0.324
3	15	0.523
4	20	0.684
5	30	1.036
6	40	1.395
	50	1.712

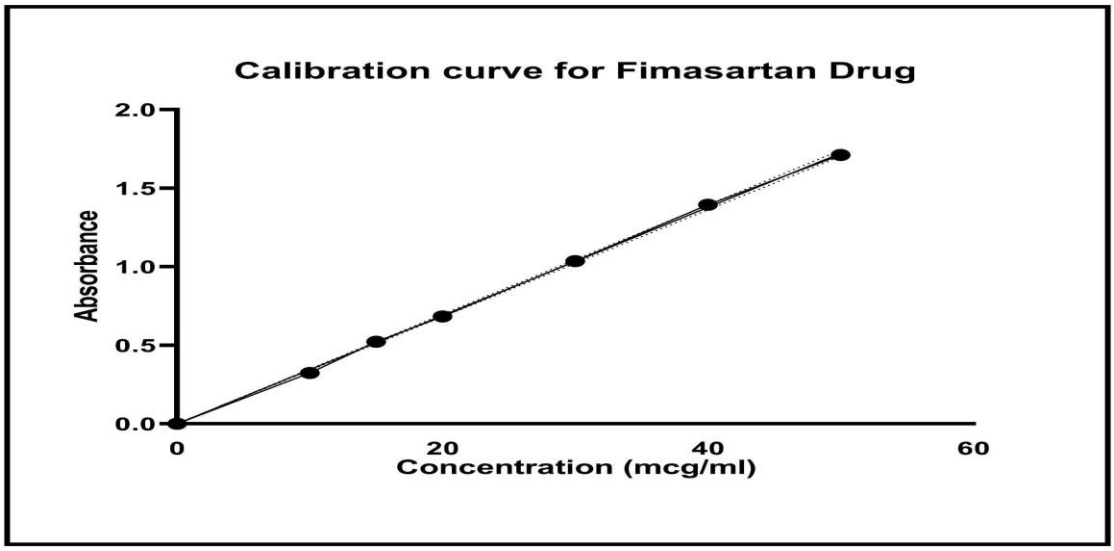

Figure 2: Calibration Curve of Fimasartan.

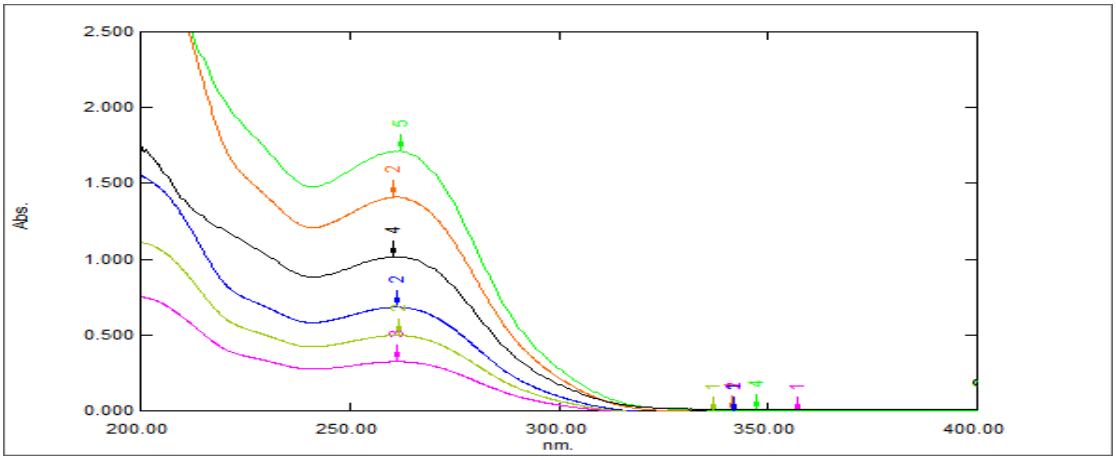

Figure 3: Overlay Spectrum Of Fimasartan.

Precision

Accuracy might be portrayed as "The level of relationship among individual test discoveries when the interaction is led more than once to a few samplings of a homogeneous example". The accuracy of the system was estimated by reproducibility (intraday) and middle person accuracy (between day) and given as percent RSD.

Table 3: Result for the intraday precision.

Concentration (µg/ml)	Absorbances	Mean	SD	%RSD
10	0.324	0.322	0.001247	0.386935
	0.321			
	0.322			
15	0.523	0.518333	0.003399	0.655822
	0.517			
	0.515			
20	0.684	0.680333	0.004497	0.660987
	0.674			
	0.683			

Table 4: Result for the inter day precision.

Concentration (µg/ml)	Absorbances	Mean	SD	%RSD
10	0.324	0.323667	0.001247	0.385341
	0.322			
	0.325			
15	0.523	0.522667	0.002055	0.393139
	0.520			
	0.525			
20	0.684	0.682333	0.0017	0.249097
	0.680			
	0.683			

Repeatability

Inside a short measure of time, repeatability is characterized as the level of understanding between commonly free test discoveries gathered involving a similar cycle on indistinguishable test material in a similar lab by a similar expert utilizing a similar gear.

Table 5: Result for the repeatability study.

Absorbance	Mean	SD	%RSD
0.324			
0.321			
0.324	0.3224	0.001356466	0.42074
0.321			
0.322			

Accuracy

Recuperation examinations were finished by utilizing the ordinary expansion strategy. To a known amount of the pre-examined drug test 80 percent, 100%, and 120 percent of standard medication material were added and satisfactorily weakened. The absorbances of the subsequent arrangements were estimated at 261 nm. The discoveries of the exactness examination are accounted for in Table 6.

Table 6: Accuracy studies of Fimasartan.

% Recovery	Absorbance	% Recovery	Mean	SD	%RSD
	0.616	98.52941176			
80	0.615	98.16176471	98.5294	0.36765	0.37313
	0.617	98.89705882			
	0.683	98.52941176			
100	0.69	100.5882353	99.8039	1.11351	1.1157
	0.689	100.2941176			
	0.755	99.75490196			
120	0.75	98.52941176	100.082	1.73887	1.73745
	0.764	101.9607843			

Limit of detection and quantification

Breaking point of discovery and evaluation was determined in view of the standard deviations of y captures of the regression line. The standard deviation of y blocks got from the six perceptions (n=6) was fill in for sigma in the identifying of condition 3.3 σ/S, and Quantitation of condition 10 σ/S, and S is the mean slant of the three alignment bends. The outcomes were given in table 7.

Table 7: LOD & LOQ of Fimasartan.

Standard	LOD	LOQ
Fimasartan	3.00	9.11

Optical Characteristics

The optical parameters such as Beer's laws limits, Molar absorptivity, Correlation coefficient, slope and intercept and percent Relative Standard Deviation (Precision) were calculatedand are described in Table 8.

Table 8: Optical Characteristics, regression data of method.

Parameter	Result
Detection wavelength (λmax)	261nm
Beer's law limits(µg/mL)	10-50µg/ml
Molar absorptivity (L. mole^{-1} cm^{-1})	162
Regression equation (Y = mx+ c)	0.034x-0.008
Intercept (a)	0.008
Slope (b)	0.034
Correlation coefficient (r^2)	0.999

RESULT AND DISCUSSION

The range absorbance readings of not set in stone at 261nm against Methanol as a vehicle clear in this suggested method.

In the scope of convergences of 10-50g/ml, Fimasartan submitted to Beer-regulation Lambert's with a relationship coefficient (r2) of 0.999.

The precision of the framework was approved by percent recuperation, which included adding a known measure of unadulterated medication to the plan and estimating the rate recuperation, which was viewed as somewhere in the range of 98.5 and 100.08 percent w/w, demonstrating that the created strategy is exact and liberated from obstruction from excipients utilized in the definition. The general standard deviation (RSD) of the procedure was provided, and it ought to be surveyed utilizing at least 6 conclusions over 100% focus, with a percent RSD under 2 showing that the cycle was precise.

The identification and quantitation limits were viewed as 3 and 9.11, correspondingly. The advertised definition's percent virtue was viewed as 97.18 percent w/w. The information were all decided to be inside as far as possible, showing that the recommended procedure is liberated from excipient impedance in the tablet dose structure.

DISCUSSION

The method for the determination of fimasartan in drug and in bulk dosage form is simple accurate and cost effective than the other past method. The method is verified according to the ICH guidelines and the precision and accuracy is with in the limit

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