ANALYTICAL METHOD DEVELOPMENT AND VALIDATION OF FIMASARTAN BY USING UV-VISIBLE SPECTROPHOTOMETRIC METHOD

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Abstract:

For the determination of Fimasartan in pharmaceutical dosage forms, a straightforward, focused, accurate, and precise UV spectrophotometric approach was created and validated. The correlation was 0.9991, and the linearity was concentration range of 3-18 µg/ml. It was discovered that the regression equation was Y=0.0429x + 0.0034. Linearity, accuracy, precision, the limit of detection, the limit of quantitation, and the robustness of the method were all validated. The LOD and LOQ for estimation of Fimasartan were found to be 0.047 µg/ml and 0.144 µg/ml, respectively. Recovery of Fimasartan was found to be in the range of 98.37- 100.92 %. The challenges of this research work of UV method development for Fimasartan include the need for precise and accurate measurement of the drug's concentration and the potential interference from impurities or other substances in the sample. The contributions made in the research work of UV method development for Fimasartan include the establishment of a reliable and efficient method for determining the drug's concentration in various samples, which can aid in its formulation, quality control and pharmacokinetic studies. Additionally, this method can contribute to the development of new drug delivery systems and dosage forms for Fimasartan. The proposed method for quantifying Fimasartan in pharmaceutical dosage form was effectively used.

Keywords: Fimasartan, Method development, pharmaceutical dosage form, Precise, UV-Spectrophotometric method.

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INTRODUCTION

Fimasartan belongs to the class of non-peptide angiotensin II receptor antagonist. It is used for the treatment of anti-hypertensive and heart failure. Reversed-phase high performance liquid chromatography has been developed stability indication method determination of fimasartan in bulk and pharmaceutical dosage form.(Sruthi et al., 2020,Pandya and Rajput 2017) High performance thin layer chromatography has been developed for determination of fimasartan in bulk and pharmaceutical dosage form (Bedade et al.,2019). LC-MS method have been reported for the estimation of fimasartan in human plasma(Yoon et al., 2015). UV-Visible Spectroscopic has been developed for determination of Fimasartan in bulk and pharmaceutical dosage form.(Agrawal et al.,2019).

The study of how chemical substance molecules, ions, and atoms absorb electromagnetic radiation at specific and limited wavelength ranges is known as absorption spectroscopy (Kasture et al.,2007). Techniques most frequently used in the analytical sector include atomic absorption spectroscopy, visible light, infrared, and ultraviolet (Willard et al., 2004) . The wavelength range of UV radiation starts at the blue end of the visible light about (about 4000 A°) and ends at 2000 A°. Based on wavelength, the electromagnetic spectrum, which ranges from 100 to 780 nm, is classified into the following sections.(Dewan 2019, Kenkel 2009)

Basic Principles of UV spectroscopy: (Pavia et al.,2001, Jeffery et al.,1991)

Beer-Lamberts law: When beam of light is passed through a transparent cell containing a solution of an absorbing substance, reduction of the intensity of light may occur.

$$A = \frac{\log I_o}{I_t} = abc$$

Where,

A = Absorbance of the solution at particular wavelength of the light beam

I_o = Intensity of incident light beam

I_t = Intensity of transmitted light beam

a = Absorptivity of molecule at the wavelength of beam

b = Path length of cell in cm

c = Concentration of solution in gm/lit.

Fimasartan

2-butyl-5-dimethyl aminothiocarbonylmethyl-6-methyl-3[(2'-(1H-tetrazol-5-yl) biphenyl-4-yl] methyl] pyrimidine-4(3H)-one trihydrate of potassium Fimasartan (fig.1). Fimasartan belong to the antagonist receptor of non-peptide angiotensin II. Fimasartan is used for the prevention of heart failure and hypertension. Majority of it was discovered in the plasma and bile excretions in unmetabolized form. Less than 3% of the medication was excreted in the urine 24 hours after treatment, indicating that there is no renal excretion of the Fimasartan.(PubChem. ncbi.)

A literature survey has revealed that only two articles on UV spectrophotometric method of Fimasartan. A few methods in literature review include High Performance Thin Layer Chromatography (HPTLC) and Validation stability indicating RP-HPLC method.
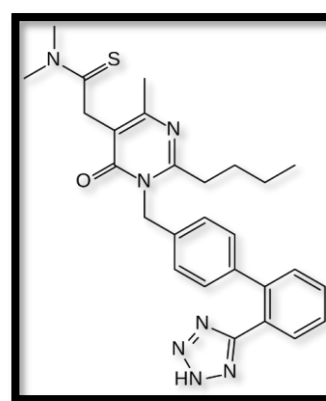
Fig. 1: Chemical structure of Fimasartan

Mechanism of action

Angiotensin II activates AR1, causing vasoconstriction and an increase in noradrenaline release, which acts on the 1-adrenergic receptor to cause even more vasoconstriction. Additionally, it promotes aldosterone secretion, which increases sodium and water absorption in the renal tubules. By binding to and inhibiting AR1, Fimasartan prevents vasoconstriction, lowers aldosterone secretion, and increases natriuresis, which decreases blood volume. These effects combine to have an antihypertensive effect. (Chi et al., 2013).

Pharmacology of Fimasartan

Seven days after treatment, Fimasartan is quickly absorbed and does not accumulate much in the body. The 9–16 hour half-life of Fimasartan makes it suitable for daily dosage. Fimasartan was found to be successful with a range of dose regimens, whether the patient was fasting or fed. The majority of the Fimasartan detected in the plasma and biliary excretion was unmetabolized. Less than 3% of the drug was excreted in the urine 24 hours after treatment, which indicates that Fimasartan does not go through renal excretion .(Lee et al., 2011).

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MATERIAL
Fimasartan pure drug was obtained as a gift sample by Ajanta Pharma Pvt. Ltd. India. Fimanta tablets containing 60 mg of Fimasartan was obtained from the market. Water was used as a solvent in the method development of UV-spectroscopy.

EXPERIMENTAL WORK
Selection of solvent
In order to select suitable solvent for determination of Fimasartan the solubility and stability was checked. It is found that Fimasartan was soluble in water. All the dilutions were prepared in the same solvent.

Preparation of standard stock solution
Standard stock solution of Fimasartan was prepared by accurately weighing 10 mg of Fimasartan to 100 ml volumetric flask with specific volume of water. The drug was sonicated for 5 min and volume was made up to mark with water to get the concentration of 100 µg/ml.

Selection of analytical wavelength
Standard stock solution 100 µg/ml, from that 1ml of solution was pipetted out separately transferred to 10 ml volumetric flask and made up the volume with water. Solution was scanned in the wavelength range of 200-400nm.

Analysis of Tablet formulation
Twenty tablets were weighed and finely powdered. Equivalent to 10 mg of Fimasartan was weighed and transferred to a 100 ml volumetric flask containing with specific amount of water and sonicated for 10 minutes. The solution was filtered through Whatmann filter 41 and volume was made up to mark with water and mixed to get 100µg/ml.

Method validation (ICH ,2005).
Linearity
The linearity of an analytical procedure is its ability to obtain test results which are directly proportional to the concentration of analyte in the sample. The linearity was accessed by plotting calibration curve of Fimasartan. For these, six different concentrations of Fimasartan ranging from 3-18 µg/mL were prepared and analyzed.

Precision
The precision study of an analytical method expresses the closeness of agreement obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Intraday precision was performed by taking three different concentrations (12, 15, 18 µg/ml) covering specified range in the triplicates and were analyzed three times within a day with same operator and with same equipment. Interday precision was determined by analyzing three different concentrations (12, 15, 18 µg/ml) in triplicates on three different days within same laboratory conditions.

Accuracy
Accuracy was determined by standard addition method. The study was determined by spiking known amount of standard stock to the test solution prepared from tablet formulation at three different spiking level 80%, 100%, 120% of the target concentration.

Limit Of Detection (LOD)
Limit of detection of an analytical procedure is the lowest concentration of an analyte in a sample which can be detected but not necessarily quantitated as an exact value. Limit of detection (LOD) was calculated using the following formula,
$$LOD = 3.3 \ \sigma/S$$

Limit of Quantitation (LOQ)
The limit of quantitation is ability of analytical procedure that the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy.
LOQ was calculated using the following formula,
$$LOQ = 10 \ \sigma/S$$

Robustness
The robustness of an analytical procedure is a measure a its reliability during normal usage. Changes in the environment's temperature, the solvent's strength, and the wavelength were used to test the robustness.

RESULTS AND DISCUSSION
UV spectrophotometric method was developed for estimation of Fimasartan in bulk and tablet dosage form. The wavelength maxima was found to be 261 nm and are shown in Fig. 2.
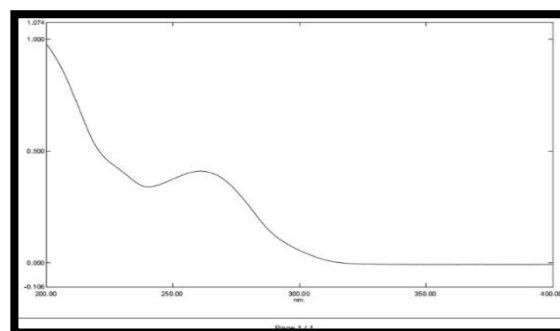

Fig. 2: Spectra of Fimasartan (10 ppm)

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Linearity

The method was found to be linear in concentration range of 3-18 µg/ml with correlation coefficient (r^2) 0.999. Results are shown in Table1 and calibration plot was shown in Fig. 3.

Table 1: Linearity study of Fimasartan

Sr. No.	Concentration (µg/ml)	Absorbance
1	3	0.140
2	6	0.260
3	9	0.378
4	12	0.520
5	15	0.643
6	18	0.783
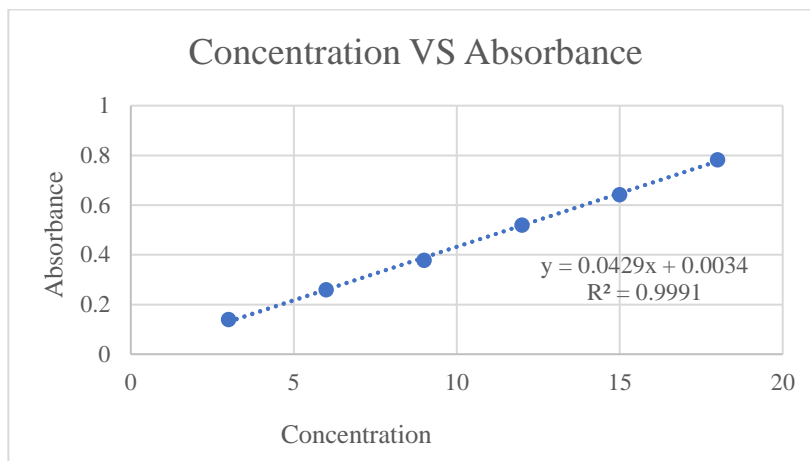
Fig. 3: Calibration curve for Fimasartan by UV spectrophotometric method

Analysis of tablet formulation:

Line equation obtained from calibration plot was used to calculate label claim of marketed formulation of Fimasartan. Results of Tablet analysis are shown in Table No.2.

Table 2: Analysis of Fimasartan Tablets (n=3)

Sr. no	Brand name	Concentration (µg/ml) (n=6)	Mean* Absorbance	Mean* % recovery	SD	% RSD
1	Fimanta	6	0.262	99.44	0.001	0.3

Accuracy

Accuracy was studied by standard addition method and % recovery found was within acceptable limit. Results of recovery study are shown in Table 3.

Table 3: Data for Recovery Study of Fimasartan

Sr.no	Concentration (µg/ml)	Mean* Absorbance	Mean* % recovery	SD	% RSD
1	80 %	0.471	100	0.0015	0.3
2	100 %	0.510	98.33	0.0055	1
3	120 %	0.558	99.26	0.0032	0.5

Precision

Intraday and Interday precision assures the repeatability of test results. The % RSD found was <2. Result of intraday and interday precision was shown in Table No.4 and Table No.5 respectively.

Table 4: Data for Intraday Precision of Fimasartan (n=3)

Sr.no	Concentration (µg/ml)	Mean* Absorbance	SD	% RSD
1	12	0.590	0.0017	0.29
2	15	0.634	0.0015	0.23
3	18	0.724	0.0017	0.2

Robustness

The prominent part of robustness is to develop methods that allow for predictable variations in the parameters. For method robustness, parameters such as variation in detector wavelength and solvents was carried out. The % RSD less than 2 which indicates that the method established is robust. There was no significant change in

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absorbance by changing the wavelength and solvent. Results are shown in Table No.7

Table 5: Data For Interday Precision of Fimasartan (n=3)

Sr.no	Concentration (µg/ml)	Mean* Absorbance	SD	% RSD
1	12	0.585	0.002	0.3
2	15	0.633	0.0015	0.23
3	18	0.750	0.0117	1.5

LOD & LOQ
Result of LOD and LOQ was show in Table 6.

Table6: Data For LOD and LOQ of Fimasartan

LOD (µg/ml)	LOQ (µg/ml)
0.047	0.144

TABLE 7: Data For Robustness Study Of Fimasartan Change In Wavelength (±2) n=3

Parameters	Change in wavelength (±2)					
	Wavelength (259nm)			Wavelength (263nm)		
	12	15	18	12	15	18
Mean (n=3)	0.528	0.602	0.725	0.527	0.602	0.720
SD	0.0063	0.00057	0.0046	0.0041	0.00230	0.0030
% RSD	0.29	0.23	1.5	0.7	0.3	0.4

CONCLUSION
In the UV-Visible Spectrophotometric method water was used as solvent and detection was done at 261nm. The % RSD for precision and robustness was found to be <2%. The % recovery was found to be 98.99-100%. LOD & LOQ value was found to be 0.047 µg/ml and 0.144 µg/ml. The result showed that the proposed method was suitable for the accurate, precise and rapid determination of Fimasartan in its bulk and tablet dosage form.

FUTURE SCOPE
The developed method can be used in pharmaceutical industry for quality control and manufacturing of fimasartan based medications such as dissolution, Assay of Pharmaceutical formulation .It can also be applied in clinical research and pharmacokinetic studies to ascertain the concentration of Fimasartan in biological samples.

Conflict of Interest: Authors have declared that no competing interests exist.

Author contributions:
Dr. Anuja P. Bhosale conceived and designed the analysis; Ms. Priyanka Sanap collected the data performed the analysis; Dr. Suvarna A. Katti anlaysed the data; Dr. Rupali A. Patil compiled the paper.

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