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ORIGINAL RESEARCH ARTICLE

Method Development and Validation of Sumatriptan In Bulk and Pharmaceutical Dosage Forms By UV Spectrophotometric Method.

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ABSTRACT

This paper describes the analytical method suitable for validation of Sumatriptan by UV Spectrophotometric method. The method utilized UV spectroscopy (Shimadzu, model 1700).The solvent system was consists of Methanol at wave length (λ_{max}) 282 nm. Validation experiments were performed to demonstrate System suitability, Specificity, Precision, Linearity, Accuracy Interday assay, intraday assay, robustness, ruggedness, LOD, &LOQ. The method was linear over the concentration range of 10-70 µg/ml. The method was showed good recoveries (99.28- 100.37%) and the recovery studies were carried out by adding different amounts (80%, 100% & 120%) of bulk samples of Sumatriptan. The Proposed method was simple, sensitive &reliable with good Precise, Accurate, and Reproducible and rapid for the determination of Sumatriptan. While estimating the commercial formulation without interference of excipients & other additives .hence this method can be used for routine determination of Sumatriptan in bulk and their pharmaceutical dosage forms.

Key Words: UV Spectroscopy, Sumatriptan, Analytical Method, Validation, Shimadzu.

INTRODUCTION

Simvastatin (SIM) butanoic acid, 2, 2- dimethyl-, 1,2, 3, 7, 8, 8a-hexahydro-3, 7-dimethyl-8-[2(tetrahydro-4-hydroxy- 6-oxo-2H-pyran-2-yl)-ethyl]-1-naphthalenyl ester, is a lipid-lowering agent that is derived synthetically from fermentation products of Aspergillus terreus[1]. After oral ingestion SIM, this is an inactive lactone, is hydrolyzed to corresponding ortho-hydroxy acid leading to the inhibition of 3-hydroxy 3-methyl glutaryl – coenzyme A. (HMG-CoA) reductase, responsible for catalyzing the conversion of HMG CoA to mevalonate [2], which is an early and rate limiting step in cholesterol biosynthesis. Literature review reveals that few methods have been published for analysis of Sumatriptan succinate in the bulk form and in pharmaceutical preparations. Available methods including European Pharmacopoeia, United Pharmacopoeia, and which suggest chromatographic method for Sumatriptan succinate, simultaneous RP HPLC[3], simultaneous spectrophotometric[4], HPTLC[5], LC−MS fully automated solid phase extraction[6], HPLC with fluorescence detection in plasma [7], HPLC in plasma[8], HPLC for transdermal diffusion study[9] , single spectrophotometric[10], LC/Electro spray tandem mass spectrometry in human serum[11], HPLC with electrochemical detection[12], and densitometric TLC[13]. The disadvantages of other HPLC methods include low sensitivity, long analysis time, and mostly in plasma and tissue. The objective of this work was to develop and validate an isocratic HPLC-UV method for quantitative analysis of Sumatriptan succinate in a tablet dosage form. The validated method was also used for analysis of Sumatriptan succinate in commercially available tablets.

MATERIALS AND METHODS

Chemicals and reagents:

Methanol used was of extra pure and were purchased from Merck. The formulation of brand Imitrex, purchased from GSK, each tablet containing 25 mg of Sumatriptan, and procured from local market and used for analysis of marketed formulation.

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Apparatus:

Digital balance, Ultrasonicator, a double-beam UV-Visible spectrophotometer, 1700 pharmaspec with spectral band width of 2nm, wavelength accuracy ± 0.5nm and a pair of 1-cm matched quartz cells was used to measure absorbance of the resulting solutions.

Solvent used:

Methanol was used as a solvent system.

Preparation of Stock Solutions:

Standard stock solution of Sumatriptan was prepared by dissolving 10 mg of each drug in 100ml of Methanol. Shake it properly to dissolve the drug and then adjusted the volume with methanol to get 100 µg/ml.

Preparation of working Standard Solutions:

The Prepared stock solution was further diluted with methanol to get working standard solution of 10ppm to 70ppm to construct Beer's law plot for Sumatriptan. The absorbance of each solution was measured at 282 nm against methanol as blank. The standard graph for Sumatriptan was plotted by taking concentration of drug on X-axis and absorbance on Y-axis

Scanning and determination of maximum wavelength (λ_{max}):

In order to ascertain the wavelength of maximum absorbance (λ_{max}) of the pharmacodynamic agents solutions of particular concentrations of drugs 100 mg/ml and 10 mg/ml in methanol were scanned within the wavelength range of 200-400nm against a corresponding reagent blank. The resulting spectra were shown in (**Fig 1**).The absorption curves showed characteristic absorption maxima at 282 nm for Sumatriptan.

Preparation Calibration Curve:

The calibration curve was plotted by taking concentration of drug on x-axis and absorbance on y-axis and was shown in (**Fig 2**) the drug has obeyed Beer's law in the concentration range of 5-60 µg/ml, and it was found to be linear with R^2= 0.999.

Linearity:

The linear fit of the system was illustrated graphically. Least square regression analysis was carried out for the slope, intercept and correlation coefficient. The linearity range was found to be in between 10-70 µg/ml. The linearity range and linearity graphs were shown in (**Table 1**) and the optical characteristics on (**Table 2**).

Accuracy:

To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (80%, 100%, and 120%) of bulk samples of Sumatriptan along with internal standard (I.S) within the linearity range were taken and added to the pre-analyzed formulation of concentration 10 µg/ml. From that percentage recovery values were calculated. The results were shown in (**Table 3**).

Precision:

The precision of the proposed method was ascertained by actual determination of eight replicates of fixed concentration (10 µg/ml) of the drug within the beer's range and finding out the absorbance's by the proposed method. From this absorbance's mean, Standard deviation, %R.S.D was calculated and presented in the (**Table 4**).

The precision of the assay was also determined in terms of intra-and inter-day variation in the absorbance for a set of drug solutions on three different days. The intra-and inter-day variation in the absorbance of the standard drug solution was calculated in terms of % RSD and the results were shown in (**Table 4**).i, 4.ii.

Analysis of formulations:

For analysis of commercial formulations, 2 tablets were weighed and powdered and powder equivalent to 10mg of Sumatriptan were transferred into 100ml volumetric flasks and dissolved in methanol to get 100 µg/ml solutions. Then the solution was sonicated for 15 min and filtered and further dilutions were made with methanol to get the concentrations within the linearity range of respective drugs and measured the absorbance at 282 nm for solution against methanol. Here 2ml was taken and made up to 10ml. The drug content in each tablet was estimated by using the standard graph and the percentage recoveries are shown in (**Table 5**).

Ruggedness (Intermediate Precision):

To determine the ruggedness the same procedure was carried by another analyst and the results was compared with the same previous procedure and the results were shown in (**Table 6**).

Robustness:

This procedure was carried out by changing the solvent system composition in different ratio (90:10, 95: 05). Then results were compared. And the results were shown in (**Table 7**).

Limit of detection and Limit of Quantification:

Limit of detection (LOD) and Limit of quantification (LOQ) of Sumatriptan was calculated by using equation given in the ICH guidelines. The result of the same is shown in the (**Table 8**).

RESULTS

Fig-1: A Typical UV Chromatogram Showing Sumatriptan at 282nm

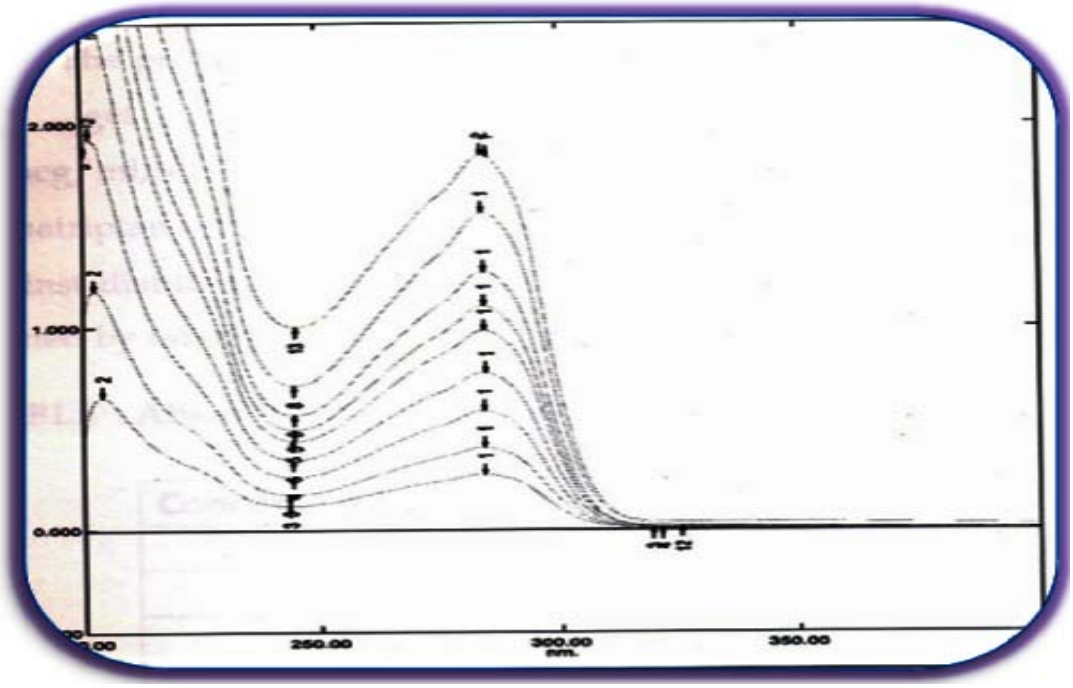

Table-1: Linearity Table of Sumatriptan

S. No	Concentration (µg/ml)	Mean Absorbance (n=6)
1	10	0.48
2	20	0.899
3	30	1.404
4	40	1.86
5	50	2.30
6	60	2.78
7	70	3.22

Fig-2: Linearity Graph of Sumatriptan

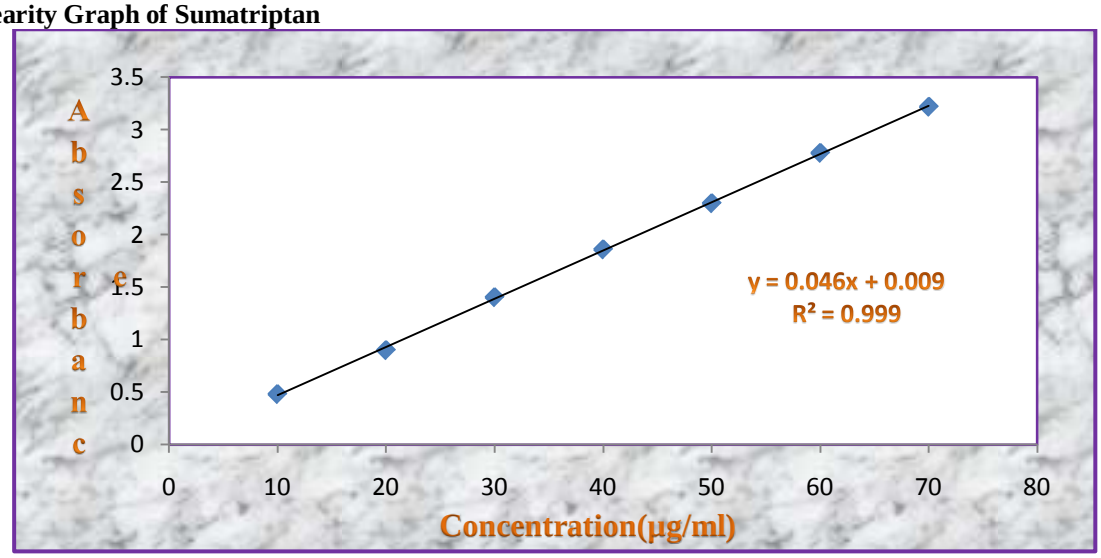

Table-2: Optical Characteristics of Sumatriptan

S.No	Characteristics	Values
1	Absorbance Maxima	282nm
2	Beer's Limit	10-70 µg/ml
3	% R.S.D	0.409663
4	Regression equation (Y*)	0.046x+0.009
5	Slope (a)	0.046
6	Intercept (b)	0.009
7	Correlation Coefficient (R^2)	0.999

Table-3: Accuracy Reading Of Sumatriptan

	No. of preparations			Statistical Analysis		
	Formulation	Pure Drug	% Recovery	Mean	SD	%RSD
S1 : 80 %	10	8	100.2			
S2 : 80 %	10	8	99.07	99.32	0.78143	0.78678
S3 : 80 %	10	8	98.7			
S4 : 100 %	10	10	100.08			
S5 : 100 %	10	10	101.3	100.37	0.820325	0.817301
S6 : 100 %	10	10	99.74			
S7 : 120 %	10	12	100.04			
S8 : 120 %	10	12	99.2	99.28	0.713956	0.719134
S9 : 120 %	10	12	98.62			

Table-4: Precision Results Showing Repeatability of Sumatriptan

Concentrations (µg/ml)	Absorbance	Calculated Amount	Statistical Analysis	
10	0.47	10.0217		
10	0.472	10.0652	Mean	10.04706
10	0.475	10.1304	SD	0.085245
10	0.468	9.9782	%RSD	0.848452
10	0.476	10.15217		
10	0.466	9.9347		

Table-4(i): Intra Day Assay of Sumatriptan

Conc.(mcg/ml)	Absorbance1	Absorbance 2	Absorbance 3	Statistical Analysis
10	0.479	0.472	0.469	
10	0.473	0.48	0.477	
10	0.476	0.478	0.479	Mean=10.12077
10	0.468	0.473	0.471	St Dev=0.017123
10	0.474	0.479	0.477	
10	0.472	0.469	0.476	%RSD=0.169182
Mean	0.473667	0.475167	0.474833	
Calc.Amt.	10.10145	10.13406	10.12681	

Table- 4(ii): Inter Day Assay of Sumatriptan

Conc.(µg/ml)	Day 1	Day 2	Day 3	Statistical Analysis
10	0.477	0.479	0.469	
10	0.471	0.481	0.476	
10	0.47	0.48	0.471	
10	0.478	0.472	0.48	Mean=10.13889
10	0.474	0.476	0.472	St Dev=0.03519
10	0.48	0.475	0.476	
Mean	0.475	0.477167	0.474	%RSD=0.347083
Calcd. Amt.	10.13043	10.17754	10.1087	

Table-5: Test for Specificity showing no effect of excipient (Test for Specificity)

S.No	Excipient Conc.(%)	Sumatriptan Input (mg)	Sumatriptan Recovered (mg)	Sumatriptan Recovered (%)	Mean Recovered (%)	S.D.	%RSD
1	100	20	19.98	99.90			
2	50	20	19.95	99.75	99.916	0.1755	0.00175
3	150	20	20.02	100.10			

Table-6: Results Showing Ruggedness of Sumatriptan

Analyst-1				Analyst-2			
Conc. (mcg/ml)	Abs.	Calcd. Amt.	Statistical Analysis	Conc. (mcg/ml)	Abs.	Calcd. Amt.	Statistical Analysis
10	0.475	10.13043		10	0.473	10.08696	
10	0.472	10.06522		10	0.478	10.19565	
10	0.474	10.1087	Mean=10.14855	10	0.472	10.06522	Mean=0.474
10	0.48	10.23913	St Dev=0.062125	10	0.471	10.04348	St Dev=0.00260
10	0.476	10.15217	%RSD=0.612154	10	0.474	10.1087	%RSD=0.55014
10	0.478	10.19565		10	0.476	10.15217	

Room Temperature				At 20^{0}C Temperature			
Conc. (mcg/ml)	Abs.	Calcd. Amt.	Statistical Analysis	Conc. (mcg/ml)	Abs.	Calcd. Amt.	Statistical Analysis
10	0.475	10.13043	Mean=10.148 S.D=0.0794 %RSD=0.0078	10	0.473	10.08696	Mean=10.14493 S.D.=0.07977 %RSD=0.0078
10	0.470	10.02174		10	0.481	10.26087	
10	0.476	10.15217		10	0.476	10.15217	
10	0.481	10.26087		10	0.479	10.21739	
10	0.475	10.13043		10	0.472	10.06522	
10	0.478	10.19565		10	0.473	10.08696	

Table-7: Results Showing Robustness of Sumatriptan at Different Solvent Composition

(90:10)				(95:05)			
Conc. (mcg/ml)	Abs.	Calcd. Amt.	Statistical Analysis	Conc. (mcg/ml)	Abs.	Calcd. Amt.	Statistical Analysis
10	0.473	10.08696	Mean=10.1	10	0.47	10.02174	Mean=10.0913
10	0.475	10.13043	SD=0.04237	10	0.473	10.08696	SD=0.067706
10	0.471	10.04348		10	0.478	10.19565	
10	0.476	10.15217	%RSD=0.41957	10	0.471	10.04348	%RSD=0.67093
10	0.473	10.08696		10	0.474	10.1087	

Table 8: Limit of detection & limit of quantification calculation

S.No	Parameters	S.D*	b**	Formula	Calculation
1	LOD	0.004617	0.046	$3.3(S.D/b)$	0.335063
2	LOQ	0.004617	0.046	$10(S.D/b)$	1.015342

DISCUSSION

In the proposed method, the λ_{max} of Sumatriptan was found to be 282 nm.Quantification was linear in the concentration range of 10-70 µg/ml. The regression equation of the linearity plot of concentration of Sumatriptan over its Absorbance was found to be y = 0.046x+0.009 (R^2=0.999), where X is the concentration of Sumatriptan (µg/ml) and Y is the corresponding Absorbance. The accuracy of the method at 80%,100% and 120% level performed and shows the result of mean in the range 99.28-100.37,%RSD=0.817301.The repeatability of results (Precision) shows mean=10.04 and %RSD=0.0841. The Robustness performed by taking the different solvent composition, it also show the mean=10.0913 and %RSD=0.6703. The limit of detection and limit of quantification were found to be 0.33506 µg/ml and 1.0153 µg/ml respectively, which indicate the sensitivity of the method. The use of Methanol as solvent gives good linear range. The Mean Recovery from the formulation was 99.16%.

CONCLUSION

The proposed method was simple, sensitive and reliable with good precision and accuracy. The proposed method is specific while estimating the commercial formulation without interference of excipient and the other additives. Hence, this method can be used for routine determination of Sumatriptan in bulk sample and pharmaceutical formulation.

The proposed UV-Spectrophotometric method was evaluated over the linearity, accuracy, precision, specificity, LOD and LOQ and proved to be convenient and effective for the quality control and stability studies of Sumatriptan.

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