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New Validated Spectroscopic Method for the Simultaneous Estimation of Simvastatin and Sitagliptin.

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Research Article

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ABSTRACT

A new, simple, sensitive, rapid, economic, UV Spectroscopic method was developed for the estimation of Simvastatin-Sitagliptin in Pure and Tablet dosage forms. The differences in solubilities of drugs were used for the estimation by extracting them into individual solvents. The linearity for Simvastatin was found between 6-20 µg/ml and between 10-50 µg/ml for Sitagliptin. Simvastatin showed the maximum absorbance at 232nm & Sitagliptin at 246nm and Validation parameters like Precision, Accuracy, and System suitability parameters were determined and examined by applying validated parameters.

INTRODUCTION

The present study is unique and has not been attempted to analyse these dosage forms in the method explained in later part of the work. It is relatively simple than any other method reported for this dosage form. The information required to obtain the percentage purity is minimum and doesn't involve any complicated mathematical formulas and calculations.

Sitagliptin is (3R) -3-amino-1-[3-(trifluoromethyl)-6,8-dihydro-5h- [1,2,4] triazolo [3,4-c] pyrazin-7-yl]-4-(2,4,5-trifluorophenyl) butan-1-one, an oral hypoglycemic agent that blocks the dipeptidyl peptidase 4 (DPP-4) enzyme activity[1, 2]. This enzyme inhibition will leads to increased amount of active incretins, glucagon like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP), which significantly increases insulin secretion. And in turn decreases blood glucose level [3].

Simvastatin , a methylated analog of lovastatin, is -(+)-{1S,3R,7S,8S,8aR)-1, 2, 3, 7, 8, 8a-hexahydro-3,7-dimethyl-8-[2-(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]- naphthyl-2,2-dimethyl butanoate. It acts by inhibiting HMG CoA reductase and is used for the treatment of hypercholesterolemia. After oral administration, this prodrug is converted into ß hydroxy acid of Simvastatin, which is a potent inhibitor of HMG CoA reductase, a key enzyme required for the synthesis of cholesterol in liver [2].

The literature review suggested that there were methods available for the estimation of Sitagliptin[4,5,6,7,8,9,10] and Simvastatin[11,12] individually with the help of instruments like UV-Spectrophotometer and HPLC. An attempt was made to develop a UV-Spectroscopic method which is precise, accurate, simple, and most economic method so far for their simultaneous determination.

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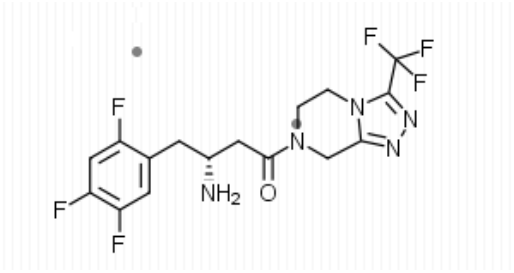

Figure 1: Structure of sitagliptin

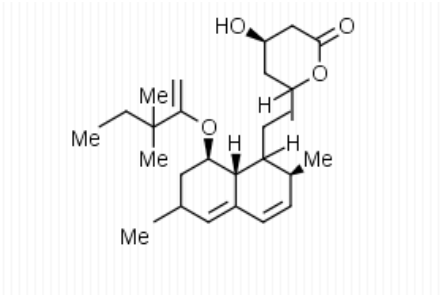

Figure 2: Structure of Simvastatin

METHOD

Sitagliptin is soluble completely in 0.1N HCl where as Simvastatin is insoluble. The combination tablet dosage form is powdered and extracted initially with 0.1N HCl. The residue is then solubilised in Methanol : Water :: 40 : 60 for the estimation of Simvastatin.

Calibration Curve Method

The standard solutions of Simvastatin and Sitagliptin were taken and scanned individually in the range of 200-400nm for their maximum absorbances. Simvastatin showed maximum absorbance at 232nm & Sitagliptin at 266nm.Calibration curves were constructed at their linearity ranges. The linearity range for Simvastatin was found to be in between 6-20µg/ml and Sitagliptin it is between 10-50µg/ml. The line equations were determined for both the linear curves. The concentration of samples were calculated by using the formula-

$$Y = mX + C$$

Where, 'Y' is the absorbance of sample, 'm' is the slope, 'X' is the concentration of sample and 'C' is the intercept of 'Y'.

EXPERIMENTAL

Preparation of Standard Solutions

100mg portions of Simvastatin and Sitagliptin were separately dissolved in 100ml volumetric flasks and make up the volume with 0.1N HCl for Sitagliptin and Methanol: Water (40:60) for Simvastatin respectively. From this above stock solutions a series of concentration such as 10, 20, 30, 40, 50 µg/ml for Sitagliptin and 6, 8, 10, 12, 14, 16, 18, 20 µg/ml for Simvastatin were prepared with Methanol: Water (40:60) and 0.1N HCl respectively.

Preparation of Sample Solution

The marketed formulation of combined drugs was obtained from local pharmacy which contains 50 mg of Sitagliptin and 20mg of Simvastatin as labeled claim. 20 tablets were weighed and powered finely. A weight of tablet powder equivalent to 100 mg of Sitagliptin (which also contain a tablet powder equivalent to 40 mg of Simvastatin). The tablet powder was extracted with three portions of 25ml of 0.1N HCl and filtered. All the three filtrates were combined and the final volume was made up to 100ml with 0.1N HCl. The residue after filtration contains Simvastatin and it is dissolved in 40: 60 portions of Methanol and Water and made the volume up to 100ml with same solvent. The final concentration of Sitagliptin was made up to 50 µg/ml with 0.1N HCl and concentration of Simvastatin was made up to 20 µg/ml with Methanol: Water. Finally the absorbances were measured at their corresponding absorption maxima.

RESULTS

An attempt was made to develop a UV Spectroscopic method which is new economic, accurate, precise and sensitive for the determination of Simvastatin-Sitagliptin in combined dosage form. The spectroscopic conditions were optimized. Simvastatin was found linear between the concentrations 6 to 20 µg/ml and 10 to 50 µg/ml for Sitagliptin. Their correlation coefficients were found from the linear graph as 0.9995 and 0.9999 for Simvastatin and Sitagliptin respectively. Limit of Detection and Limit of Quantification (Table-1) were calculated from the regression lines using their standard deviation and slope. LOQ is 3.3s/S & LOD is 10s/S. All the optimized conditions were mentioned (Table-1). The precision (Table-2) of the method was determined from one lot of combined dosage forms by considering intraday & inter day measurements. The Recovery (Table-3) of the method was checked by performing recovery studies.

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The recovery was determined at three levels Viz- 80, 100 and 120% of the selected concentrations. Three samples were prepared for each recovery level. The assay (Table-4) was made for the combination tablets by preparing the solutions of concentrations from tablet powder which falls between the linear ranges of standard solution. All the validated parameters were checked by applying statistical formulas such as standard and relative standard deviation. The results were found to fall within the prescribed limits.

Table 1: Optimized Conditions

Parameters	Sitagliptin	Simvastatin
Calibration range(µg/ml)	10-50	6-20
Maximum absorbance(λmax)	246	232
Regression equation	Y= 0.01x+0.006	Y= 0.035x+0.0037
Slope	0.01	0.035
Intercept	0.006	0.0037
Correlation coefficient(r^2)	0.9999	0.9995
LOD(µg/ml)	1.716	1.308
LOQ(µg/ml)	5.2	3.96

Table 2: Precision studies for Sitagliptin and Simvastatin

	Intra day (Amt)	Standard deviation	%RSD	Inter day (Amt)	Standard deviation	%RSD
Sitagliptin	49.5	0.416	0.832	50.2	0.25	0.499
	50.3			50.3		
	50.1			49.8		
Simvastatin	19.9	0.1509	0.793	20.4	0.305	0.151
	20.2			19.8		
	20.02			20.2		

Table 3: Recovery studies for Sitagliptin and Simvastatin

S.NO	Preanalysed Sample Con.(µg/ml)	Recovery Level (%)	Amount Added (µg/ml)	*Total amount found(µg/ml) Mean±SD	%Recovery	%RSD
1	SIT-50	80	40	90±0.015	100.01	0.016
		100	50	100.14±0.152	100.29	0.151
		120	60	110.04±0.221	100.21	0.2
2	SIM-20	80	16	36.07±0.153	100.19	0.424
		100	20	40.43±0.503	101.07	1.24
		120	24	44.33±0.115	100.75	0.25

*Mean of three values

Table.4: Assay Data for Sitagliptin and Simvastatin

Drug	Amount found	% Assay	Mean Assay	SD	%RSD
Sitagliptin	49.5	99	99.9	0.56568	0.566
	50.3	100.6			
	50.1	100.2			
	50	100			
	49.8	99.5			
	50.2	100.1			
Simvastatin	19.9	99.8	100.06	0.1505	0.1504
	20	100			
	20.02	100.1			
	20.05	100.2			
	20.1	100.1			
	20.06	100.2			

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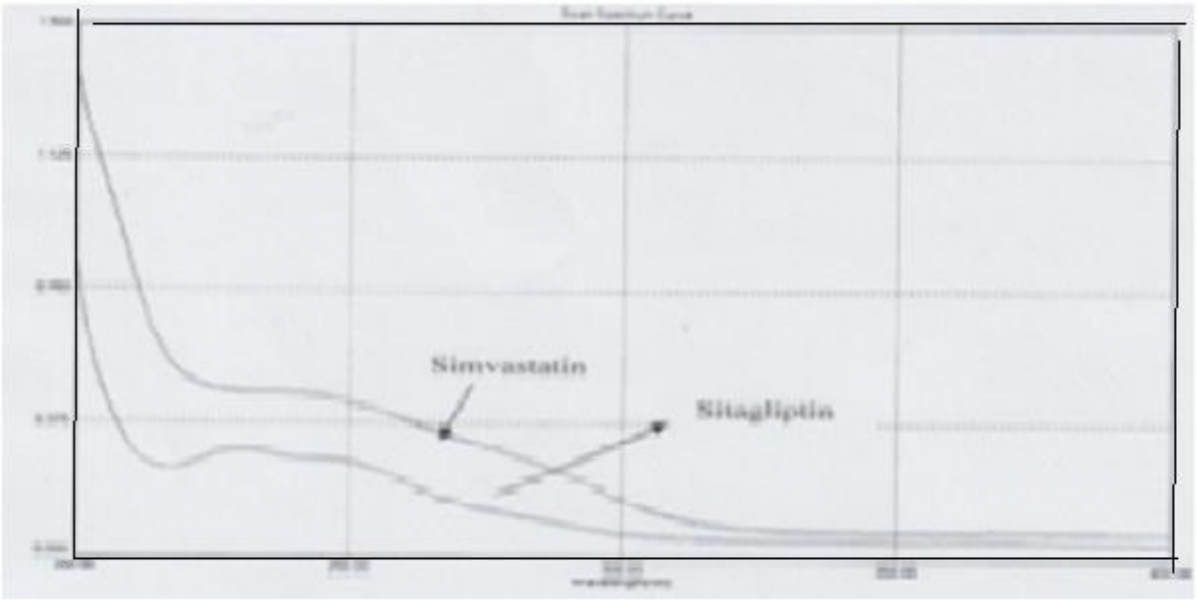
Figure 3: UV Overlain spectrum of Sitagliptin & Simvastatin



DISCUSSION

The present combination Simvastatin and Sitagliptin is marketed as one formulation (Juvisync 50 mg/20mg).

Simvastatin – 50 mg/tablet
Sitagliptin – 20 mg/tablet

The fixed dose combination tablet Sitagliptin and Simvastatin was subjected to simultaneous estimation by UV Spectroscopic method. The proposed method was validated by evaluation of the validation parameters. Assay was performed within a short analysis time.

Highly reliable and cost efficient UV method was developed for the quantitative estimation of Sitagliptin and Simvastatin in combined tablet dosage form. The results obtained were reproducible and reliable. The validity and precision of the methods were evident from the statistical and analytical parameters obtained.

CONCLUSION

From the forgoing it is concluded that the methods developed are simple, rapid, selective and precise hence suitable for application in routine analysis of pharmaceutical preparations.

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