

Simultaneous Estimation Of Rosuvastatin Calcium And Clopidogrel Bisulphate By UV Spectroscopy

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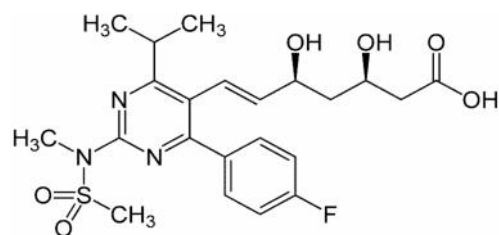
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Abstract: A rapid, precise, specific, accurate and simple UV spectrophotometric method using simultaneous equation method was developed for the simultaneous estimation of Rosuvastatin calcium and CLOPIDOGREL bisulphate in combined pharmaceutical dosage forms and laboratory prepared mixtures. The absorbance signals in simultaneous equation method were measured at a λ_{max} of 243 nm and 220 nm for ROSUVASTATIN and CLOPIDOGREL respectively. The linearity ranges for were found Rosuvastatin and CLOPIDOGREL to be 2-10 $\mu\text{g mL}^{-1}$ and 6-14 $\mu\text{g mL}^{-1}$ respectively. Concentrations of each of the drugs were obtained by using the absorptivity values calculated for both the drugs at these two wavelengths. The developed method was validated according to the ICH guidelines. The developed method was successfully applied to the commercial formulation and laboratory prepared mixtures.

KeyWords: Rosuvastatin Calcium, Clopidogrel bisulphate, Simultaneous Estimation, UV Spectroscopy.

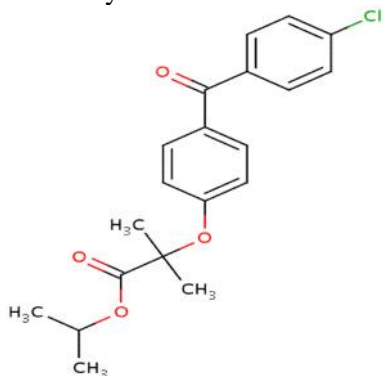
Introduction(1-4):

Rosuvastatin (RSV) is the calcium salt of (3R,5S,6E)-7-[4-(4-fluorophenyl)-2-(N-methylmethanesulfonamido)-6-(propan-2-yl)pyrimidin-5-yl]-3,5-dihydroxyhept-6-enoic acid. Rosuvastatin is a competitive inhibitor of the enzyme HMG-CoA reductase, having a mechanism of action similar to that of other statins. Its approximate elimination half life is 19 h and its time to peak plasma concentration is reached in 3–5 h following oral administration. Putative beneficial effects of rosuvastatin therapy on chronic heart failure may be negated by increases in collagen turnover markers as well as a reduction in plasma coenzyme Q10 levels in patients with chronic heart failure.



Clopidogrel (INN) is an oral, thienopyridine class antiplatelet agent used to inhibit blood clots in coronary artery disease, peripheral vascular disease, and cerebrovascular disease. Clopidogrel is a prodrug, the action of which may be related to an ADP receptor on platelet cell membranes. The drug specifically and irreversibly inhibits the P2Y₁₂ subtype of ADP receptor, which is important in activation of platelets and eventual cross-linking by the protein fibrin.^[1] The blockade of this receptor inhibits platelet aggregation by

blocking activation of the glycoprotein IIb/IIIa pathway. The IIb/IIIa complex functions as a receptor mainly for fibrinogen and vitronectin but also for fibronectin and von Willebrand factor. The literature survey reveals that there are no methods for this combination, so we do the simultaneous estimation of rosuvastatin calcium and clopidogrel formulation by UV method.



Materials And Methods

The bulk drugs of Rosuvastatin calcium and clopidogrel bisulphate were available in the college premises. All analytical grade chemicals and solvents were purchased from Merck, India.

Equipment

A Thermo scientific aquamate plus UV- Visible spectrophotometer with data processing system was used for all absorbance measurements. UV spectra of reference and sample solutions were recorded in 1 cm quartz cells at a scan speed 100nm per min.

Procedure

Preparation of standard stock solutions

Standard stock solutions of Rosuvastatin calcium and Clopidogrel bisulphate were prepared by dissolving 10mg each accurately weighed of standard RSV and CLOP in methanol and made the volume up to 50 ml with same solvent in 50ml volumetric flask. Working standard solutions were prepared by diluting aliquot portion of standard stock solution of each drug to give concentration 0.2µg/ml and 0.2µg/ml of RSV calcium and Clopidogrel bisulphate respectively.

Calibration curve

Each working standard solution was scanned between the range 200-400 nm. The calibration curves for RSV calcium and clopidogrel bisulphate were prepared in the concentration range of 2-10 µg/ml and 6-14 µg/ml respectively. The Linearity graphs of Rosuvastatin Calcium and Clopidogrel bisulphate.

Analysis of capsule formulation

Twenty capsules were weighed accurately and content were emptied. A quantity of powder equivalent to 10mg RSV Calcium and 75mg Clopidogrel bisulphate was weighed, transferred to 100ml volumetric flask, dissolved in 100ml methanol. The mixture was ultra sonicated for 20 min. The solution was filtered through whatmann filter paper no. 41 and suitably diluted with distilled water to have 4 µg/ml and 30µg/ml of Rosuvastatin and Clopidogrel respectively. Samples were analysed by the proposed methods.

Simultaneous equation method(9):

In quantitative determination of two drugs by these method two λ s that is 243nm as λ_{max} of RSV and 220nm as λ_{max} of Clop were selected at which both drugs have absorbance. A set of two simultaneous equations were formed using absorptivity coefficient at selected wavelengths.

The concentrations of two drugs in the mixture were calculated using set of two simultaneous equations:

$$C_{\text{rosuvastatin}} = \frac{A_2 \times a_{y1} - A_1 \times a_{y2}}{a_{x2} \times a_{y1} - a_{x1} \times a_{y2}} \quad (1)$$

$$C_{\text{clopidogrel}} = \frac{A_1 \times a_{x2} - A_2 \times a_{x1}}{a_{x2} \times a_{y1} - a_{x1} \times a_{y2}} \quad (2)$$

Where, a_{x1} and a_{x2} are absorptivities of RSV at (1) and (2) respectively.

a_{y1} and a_{y2} are absorptivities of clopidogrel at (1) and (2) respectively.

A_1 and A_2 are Absorbances of mixed standard at (1) and (2) respectively. The Results were given in the table no.1.

Validation(5-6):

Recovery studies

The accuracy of proposed methods was checked by recovery study by addition of standard drug solution to pre-analysed sample solution at three different concentration levels (50%, 100% and 150%) within the range of linearity for both the drugs. The basic concentration level of sample solution selected for spiking of the drugs standard solution was 4µg/ml of RSV and 30µg/ml of Clop for both the methods. The Values obtained were given in the table no.2.

Precision

Precision were investigated by analyzing six concentration of Rosuvastatin calcium and Clopidogrel bisulphate mixture in three independent replicates on the same day (Intra-day precision) and on three consecutive days (Inter-day precision). Intra-day and Inter-day relative standard deviation

was calculated. The optimal characteristics and their readings were given in the table no.3.

Sensitivity

High Molar absorptivity and low Sandell's sensitivity for the respective method reveals that all these methods are highly sensitive.

Assay Table No.1

Drug	Labelled amount (mg)	Amount present	% Assay
Rosuvastatin	10 mg	9.88147	98.8147
Clopidogrel	75 mg	74.23395	98.9786

Accuracy Table No.2

Recovery level	Recovery of	Simultaneous equation	%RSD
50	RSV Calcium	98.41	0.011
	CLO Bisulphate	98.60	0.023
100	RSV Calcium	99.14	0.017
	CLO Bisulphate	99.55	0.025
150	RSV Calcium	100.15	0.020
	CLO Bisulphate	100.41	0.030

Optimal Characteristics Table No.3

Parameters	ROSUVASTATIN CALCIUM	CLOPIDOGREL BISULPHATE
Linearity range	2-10 μ g/ml	6-14 μ g/ml
Slope	0.0791	0.0260
Intercept	0.0182	-0.0139
Correlation coefficient	0.998	0.998
Intraday Precision(%RSD)	0.29	0.30
Interday Precision(%RSD)	0.23	0.24

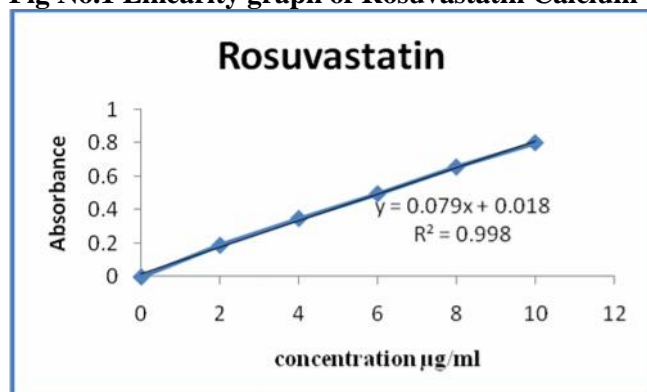
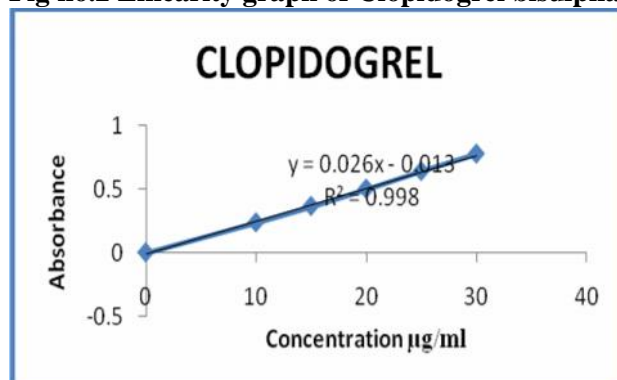
Fig No.1 Linearity graph of Rosuvastatin Calcium

Fig no.2 Linearity graph of Clopidogrel bisulphate**Result And Discussion(7-8):**

Literature survey reveals not a single method has been reported for simultaneous analysis of the Rosuvastatin calcium and Clopidogrel by UV spectrophotometric method. So, the proposed methods for simultaneous estimation of Rosuvastatin and Clopidogrel in combined dosage form were found to be new, simple, rapid, accurate and economic. For both the methods, linearity was

observed in the concentration range of 2-10 µg/ml and 6-14 µg/ml for RSV calcium and Clopidogrel bisulphate respectively. Marketed brand of capsule was analysed and amount of drug determined by proposed method ranges from 98 to 102% as shown in table no 1. The proposed method was validated as per ICH guidelines. The accuracy of method was determined at 50, 100 and 150% level. The percentage recovery ranges from 97.37 to 101.62% for both methods. Precision was calculated as interday and intraday variations (% RSD is minimum) for both drugs. The two methods can be successfully used for simultaneous estimation of RSV and CLOP in combined dosage form

Summary and conclusion:

The proposed methods have proved to be simple, rapid, precise, accurate sensitive and economical and are suitable for simultaneous quantification of RSV and CLOP in bulk and in pharmaceutical dosage form

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