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RESEARCH ARTICLE……!!!

SIMULTANEOUS ESTIMATION OF CELECOXIB AND AMLODIPINE BESYLATE IN BULK AND COMBINED TABLET DOSAGE FORM BY UV SPECTROMETRIC METHOD

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KEYWORDS:

Celecoxib, Amlodipine Besylate, Zero order method, ICH guidelines.

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ABSTRACT

Simple, precise and accurate spectrophotometric method have been developed and validated for simultaneous estimation of Celecoxib and Amlodipine Besylate in bulk and pharmaceutical formulations. Zero order derivative spectrophotometry, which involved measuring the absorbance values at 253 nm and 361 nm of zero derivative spectrum, without mutual interference with a linearity range of 5-25 µg/ml and 12-60 µg/ml for the estimation of Celecoxib and Amlodipine Besylate for the zero order method. The method is validated according to ICH guidelines. The % RSD of all validation parameters found to be less than 2% indicating high degree of accuracy and precision of the proposed zero order derivative method. Results of analysis were statistically reported and were found to be satisfactory.

INTRODUCTION:

Celecoxib is chemically known as 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1 yl] benzenesulfonamide. A highly selective reversible inhibitors of the cox-2 isoform of cyclooxygenase. Celecoxib inhibits the transformation of arachidonic acid to prostaglandin precursors. Therefore, it has antipyretic, analgesic and anti-inflammatory properties. Non selective NSAIDs (aspirin, ibuprofen) inhibit both COX-1 and COX-2. Celecoxib is approximately 10-20 times more selective for COX-2 inhibition over COX-1. It binds with its polar sulfanamide side chain to a hydrophilic side pocket region close to the active COX-2 binding site. This selectivity allows Celecoxib to reduce inflammation while minimizing gastrointestinal adverse drug reactions that are common with non selective NSAIDs[1-3].

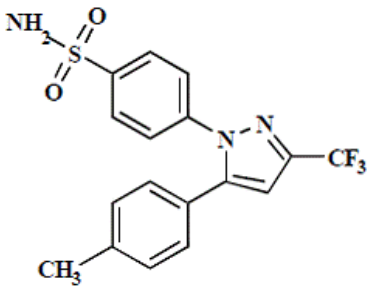

Fig 1: Structure of Celecoxib

Amlodipine Besylate is chemically known as 3-ethyl 5-methyl 2-[(2-aminoethoxy) methyl]-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5 dicarboxylate benzenesulfonate. Amlodipine Besylate is an angioselective calcium channel blocker and inhibits the movement of calcium ions into vascular muscle cells and cardiac muscle cells which inhibits the contraction of cardiac muscles and vascular smooth muscle. Amlodipine Besylate inhibits calcium ion influx across cell membranes with greater effect on vascular smooth muscle cells. This causes vasodilation and a reduction in peripheral vascular resistance thus lowering the blood pressure. Its effect on cardiac muscle also prevents excessive constriction in the coronary arteries[4-6].

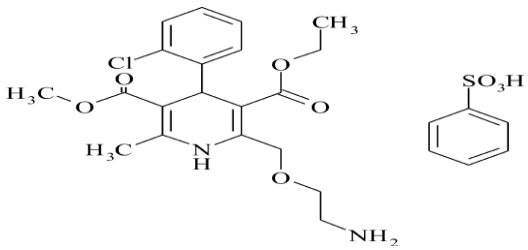

Fig 2: Structure of Amlodipine Besylate

On literature survey, it was found that no method has been reported for the simultaneous estimation of Celecoxib and Amlodipine Besylate in combined dosage forms and no method is available in the pharmacopoeias. Few analytical methods have been developed for the determination of Celecoxib and Amlodipine Besylate individually[7,8] and in combination with the other drugs[9,10]. The present UV-Spectrophotometric method was validated according to ICH guidelines[11,12].

EXPERIMENTAL

Instrument and materials

For the zero order derivative methods, Shimadzu-1800 UV-Vis spectrophotometer was used with 1cm match quartz cell of 10mm optical path length, spectral band width of 1±0.2nm, and wavelength accuracy of ±0.3nm. The working standards of celecoxib and Amlodipine were gifted from Shyam Sundar Brawn labs Ltd Haryana and micro labs Ltd, Bangalore.

Preparation of standard solutions

100mg each of Celecoxib and Amlodipine Besylate were weighed separately and transferred in two different 100ml volumetric flasks. Both the drugs were dissolved in 50ml of ethanol by ultrasonication and then volume was made upto the mark with ethanol to obtain the concentration of 1000µg/ml of each component (stock A and A' solution). From the above stock A and A' 10ml of aliquot was pipetted out into a 100ml volumetric flask and volume was made up to the mark with ethanol to obtain the final concentration of 100µg/ml of each component (stock B and B').

Analysis of tablet formulation

Twenty tablets of Celecoxib and Amlodipine in combination were weighed and their average weight is determined. The tablets were crushed to fine powder, tablet powder equivalent to 100 mg of Celecoxib was weighed which also contains 5 mg of Amlodipine and transferred to 100 ml volumetric flask. And dissolved in 100ml of the ethanol. The solutions was filtered through whatmann filter paper No. 41, finally the volume was made up to the mark with the solvent to get a concentration of 1000 µg/ml of Celecoxib and 50 µg/ml Amlodipine and these solutions were used as stock A solutions.

From the above stock A solutions, a required volume of the solution was pipette and transferred to a 100 ml volumetric flask. To that add 23.5ml (235µg/ml) of standard Amlodipine Besylate (from stock B) to bring the Amlodipine concentration within the range. Then volume was made up to the mark with the solvent to obtain solutions with a desired concentration range of Celecoxib and Amlodipine (Stock B).

Appropriate aliquots were prepared from the above sample stock B solution to get a concentration of 5, 10, 15, 20, 25 µg/ml of Celecoxib and 12, 24, 36, 48, 60 µg/ml of Amlodipine. Six such solution

mixtures were prepared as above and analysed at the selected analytical wavelengths, 253 and 361nm and their results were statically validated.

Validation of the methods

Accuracy

The method was validated according to ICH guidelines by carrying out analysis of six replicate samples of tablet formulation. Recovery studies were carried out at three different levels i.e. 80%, 100% and 120% by adding the pure drug to previously analysed tablet formulation sample. From the amount of drug found, percentage recovery was calculated. The results were given in the table 1

Precision

It is the procedure which express closeness of agreement between a series of measurement obtained from multiple sampling of the same homogenous sample under the prescribed condition.

Procedure for determination of Intraday Precision

In intraday precision CEL and AML was analysed six times at different time interval in the same day at their selected analytical wavelength at 253 and 361nm. The variation of the results within the same day was analysed and statistically validated.

Procedure for determination of Inter day Precision

In inter day precision CEL and AML were prepared and analysed six times at same time on three different days of a week at their selected analytical wavelength at 253 and 361 nm. The variation of the results on different days was analysed and statistically validated. The mean, standard deviation and % RSD for the absorbance of Celecoxib and Amlodipine Besylate from sample solutions were calculated. The results were given in the table 2.

Table 1: Results of accuracy

Level of (%) Recovery	Mean*		Standard deviation*		% Coefficient of Variation*		Standard Error*	
	CEL	AML	CEL	AML	CEL	AML	CEL	AML
80%	99.62	99.61	0.192	0.173	0.193	0.174	0.018	0.004
100%	99.18	99.80	0.404	0.107	0.407	0.107	0.014	0.004
120%	99.76	99.73	0.183	0.126	0.184	0.127	0.019	0.005

*n=6

Table 2: Intraday Precision

Component	Mean*	Standard deviation*	%Coefficient variation*	Standard Error*
CEL	99.17	0.599	0.604	0.059
AML	99.47	0.601	0.605	0.017

*n=3

Table 3:Interday Precision

Component	Mean*	Standard deviation*	%Coefficient variation*	Standard Error*
CEL	99.10	0.556	0.561	0.079
AML	99.29	0.319	0.321	0037

*n=3

RESULTS AND DISCUSSION

The estimation of Celecoxib and Amlodipine in Tablet formulation was found to be accurate and reproducible with a linearity of 5-25 µg/ml and 12-60 µg/ml respectively for the method and the correlation coefficient 0.999 and 0.999 for the zero order method. The optical characteristics such as linearity range, percentage relative standard deviation of recovery studies and precision was calculated and the results were reported in Table-3. Also the regression characteristics like slope (m), intercept (c) and correlation coefficient (r^2) were calculated and presented in Table-3. The accuracy was found by recovery studies at three different levels i.e. 80%, 100% and 120%. The values of standard deviation were satisfactory and the recovery studies were close to 100%. The % RSD value was less than 2%, an indicative of the accuracy of the methods. The results of formulation were reported in Table-4. The absorption spectra of Celecoxib, Amlodipine Besylate and formulation by Zero order derivative method are reported (Fig 3, 4 and 5) and calibration curve was plotted (Fig 6 and 7).

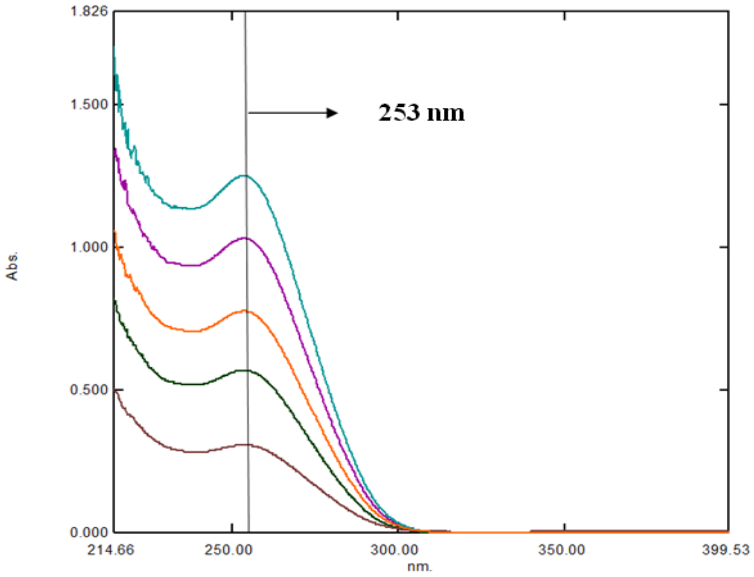

Fig 3: The overlay spectrum of CFL at 253 nm

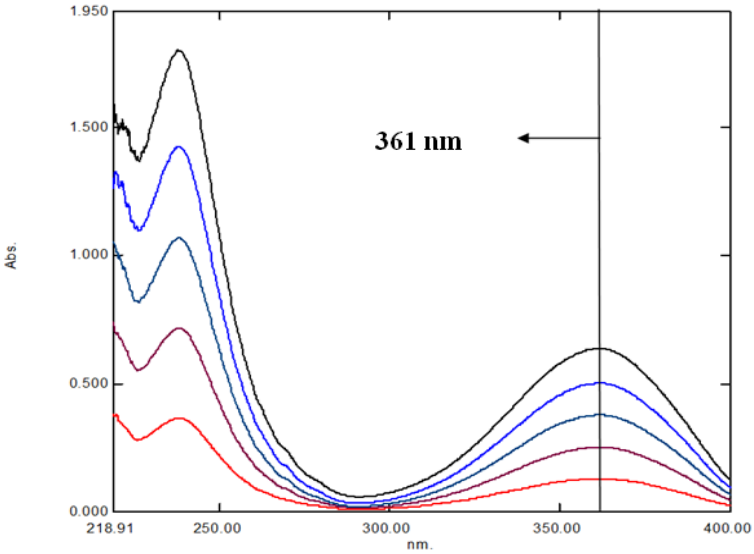

Fig 4: The overlay spectrum of AML at 361 nm

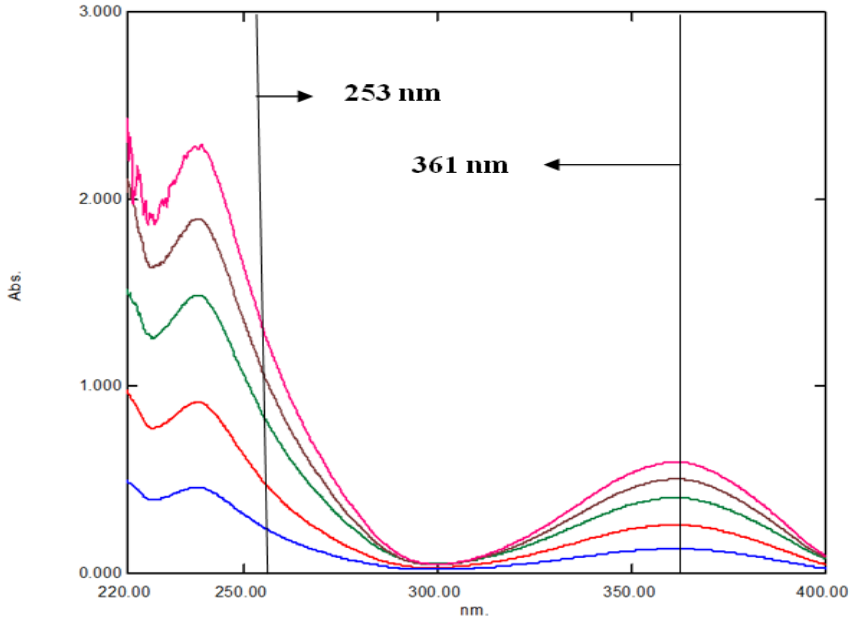

Fig 5: Overlay spectrum of formulation

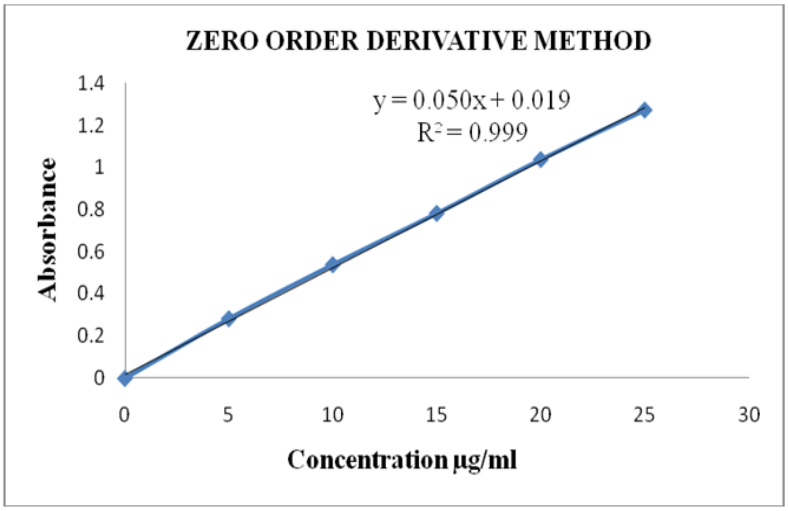

Fig 6: Calibration curve for celecoxib at 253 nm

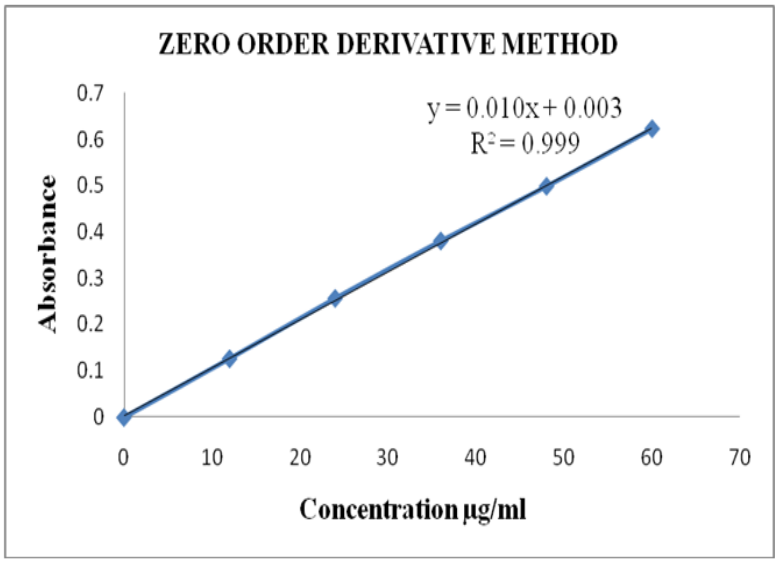

Fig 7: Calibration curve for AML at 361 nm

Table 4: Optical characteristics and other parameters for zero order derivative method

Parameters		CEL	AML
Linear range (µg/ml)		5-25 µg/ml	12-60 µg/ml
Wavelength (µg/ml)		253 nm	361 nm
Coefficient of correlation		0.999	0.999
Slope* (m)		0.050	0.010
Intercept* (c)		0.019	0.003
Accuracy (%RSD)	**80%**	0.193	0.174
	100%	0.407	0.107
	120%	0.184	0.127
Precision (%RSD)	**Intra day**	0.604	0.605
	Inter day	0.561	0.321
Limit of Detection (µg/ml)		0.303	0.594
Limit of Quantification (µg/ml)		0.920	1.800

Table 5: Result of Formulation

Brand name	Label Claim(mg)		% Recovery*		% RSD*		Standard Error*	
	CEL	AML	CEL	AML	CEL	AML	CEL	AML
Consensi	100	10	98.97	99.86	0.654	0.641	0.047	0.003

*n=6

CONCLUSION

The developed method was validated for various parameters as per ICH guidelines like linearity, accuracy, precision, LOD and LOQ. The results obtained were within the acceptance criteria for the parameters. The value of standard deviation and % RSD were found to be < 2%, indicates high precision of the method. High % recovery and low % RSD suggest that the above method can be applicable for routine analysis of CEL and AML in formulations. The proposed method was applied for simultaneous estimation of Celecoxib and Amlodipine Besylate in marked formulation. Hence the proposed method was found to be satisfactory and could be used for the routine analysis of Celecoxib and Amlodipine Besylate in bulk drug and pharmaceutical formulations.

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