Celecoxibin Bulk Drug And Its Tablet Formulation Subjected To Forced Degradation Study

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Abstract:
The Celecoxib drug were subjected to forced degradation conditions and the formed degradation products were well separated and resolved from the drug and excipients on SunFire C18 column (250 × 4.6 mm, 5 µ) using blend of Acetonitrile: Water (80: 20 v/v) pH 7.0 in isocratic mode at a flow rate of 1.0mL/min at an ambient temperature of 28 °C with the detection wavelength at 251nm. The retention time of Celecoxib was found 4.32 min. The linearity was performed in the concentration range of 20-100 ppm with correlation factor of 0.999 for Celecoxib. The percentage purity of Celecoxib tablet was found 99.98%.The drug was found to degrade under acid, alkali condition but found stable under photolytic conditions.

Keywords: Celecoxib, RP-HPLC, Method Development, Method Validation, Stability, Tablet (CELACT-MD).

1. Introduction:

Celecoxib is a selective noncompetitive inhibitor of cyclooxygenase-2 (COX-2) enzyme. The inhibition of this enzyme reduces the synthesis of metabolites that include (PGE2), prostacyclin PGI2, TXA2, PGD2and PGF2. Resultant inhibition of these mediators leads to the lessening of pain and swelling [10-12]. Literature survey on the analytical methods for Celecoxib revealed that quit number of analytical methods were development for Celecoxib by using Spectrophotometry, HPLC and HPTLC [1-11] but it was seen that economically method need to be developed so we were developed simple as well as economic method for Celecoxib will be used for routine analysis.

2. Material and Methods:

Pharmaceutical grade Celecoxib was kindly supplied as gift sample from Mylan Laboratories Ltd.

3. Experimental work:

The procured reference standard of Celecoxib was found to melt in the range of temperature 156 - 158 °C.The drug was found to be freely soluble in Acetonitrile, Acetone and Methanol

The UV Absorption spectrum of Celecoxib showed a λmax at 251nm in methanol when scanned in the range of 400-200nm.

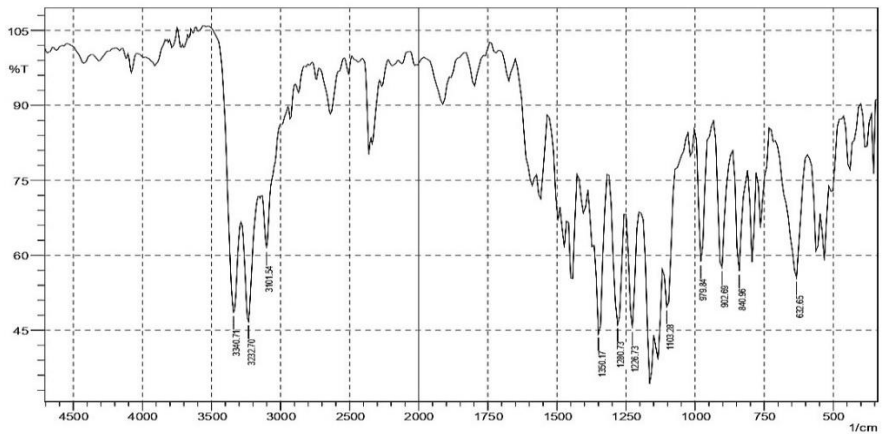

Figure No:01 Infrared Spectrum of Celecoxib

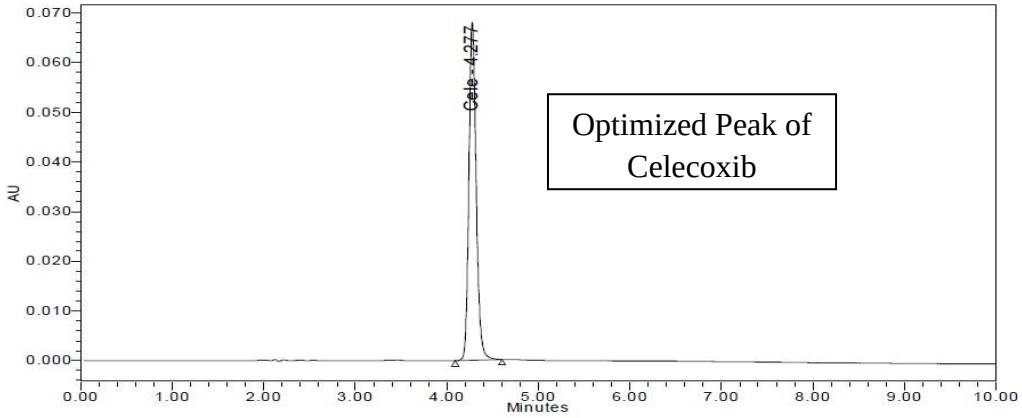

Figure No: 02 Representative Chromatogram of Celecoxib in Acetonitrile: Water (80: 20 v/v) pH 7.0, 1mL/min

4. Result and Discussion:

4.1.1 System Suitability

Table No: 01 System Suitability Parameters

Celecoxib (20PPM)	Retention Time (min)	Area	Tailing Factor
Standard 1	4.279	310075	1.1621
Standard 2	4.278	310289	1.1550
Standard 3	4.278	310164	1.1648
Standard 4	4.279	310265	1.1706
Standard 5	4.280	310284	1.1662
	Mean	**310215.4**	
	SD	**93.4574**	
	%RSD	**0.03012**	

4.2. Experiment Calibration.

Calibration standard in the range of 20-100µg/mL was analysed and regression analysis was carried out from plot of peak area v/s concentration. The representative linear equation was Y = 15454x + 1000 where x is the concentration and Y is are of peak.

Table No:02 Calibration Curve of Celecoxib

Sr. No	Concentration	Area
1	20	310075
2	40	620150
3	60	930225
4	80	1230300
5	100	1550375
	Slope	**15467**
	Intercept	**1000**
	Correlation	

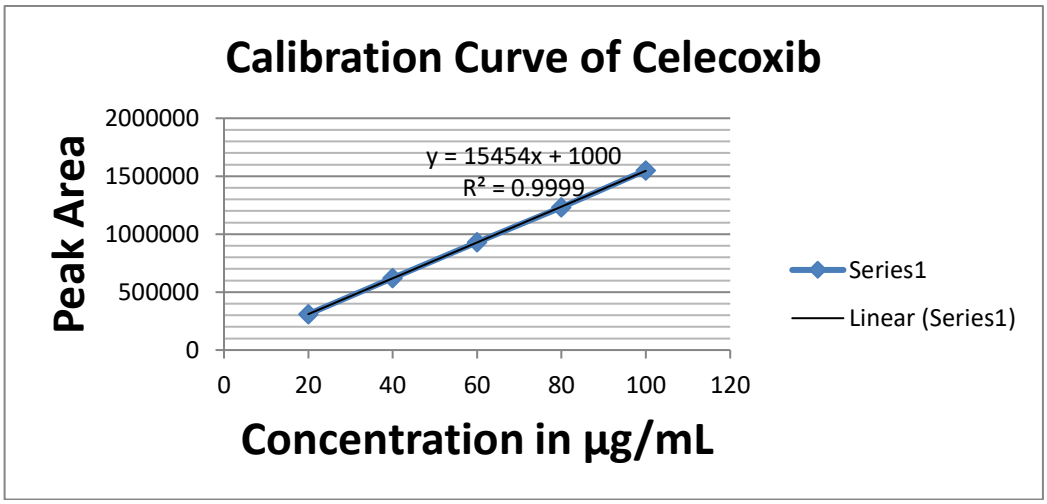

Fig. No: 3 Calibration Curve of Celecoxib

4.2.1 Specificity

The HPLC chromatogram recorded for the Blank, Placebo, Standard and Sample solution showed that Celecoxib peak was not affected by diluent and placebo.

Chromatograms for Specificity:

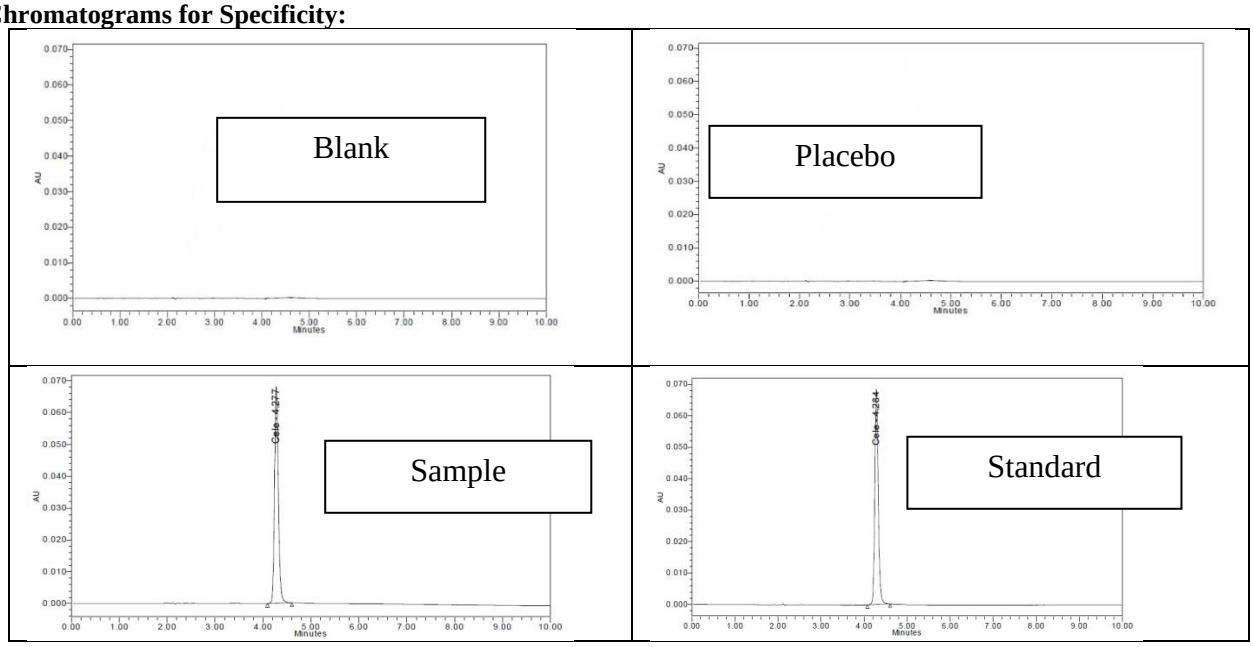

Fig. No: 4 chromatogram recorded for the Blank, Placebo, Standard and Sample solution of Celecoxib

4.2.3 Accuracy

The data obtained from precision and accuracy experiments are summarized in **Table No:03**

Table No:03 Accuracy Results

Sr. No	Conc. Level	Conc. (µg/mL) Sample Solution Taken	Conc. (µg/mL) Std. Stock Solution Added	Area	Avg. Peak Area	Conc. Found (µg/mL)	% Recovery	SD	% RSD
1	80%	20	16	556089	**556188**	**35.89**	**99.69**	**99.50**	**0.0178**
		20	16	556288					
		20	16	556188					
2	100%	20	20	617986	**617485**	**39.85**	**99.62**	**501**	**0.0811**
		20	20	616984					
		20	20	617485					
3	120%	20	24	679250	**679539**	**43.87**	**99.70**	**289**	**0.0425**
		20	24	679828					
		20	24	679539					

Table No: 04 Precision Results

Sr. No.	Conc. in (µg/mL)	Conc. in %	Peak Area	Average	Standard Deviation	% RSD
1	20	100%	310075	**309941**	**657.1212**	**0.2120**
2	20	100%	310289			
3	20	100%	310164			
4	20	100%	308634			
5	20	100%	310041			
6	20	100%	310443			

4.3. Calculation of LOD

The LOD of the method was found to be 0.916µg/mL

4.4. Calculation of LOQ

The LOQ of the method was found to be 2.778µg/mL

4.5 Forced Degradation of Celecoxib

4.5.1 Acid Degradation

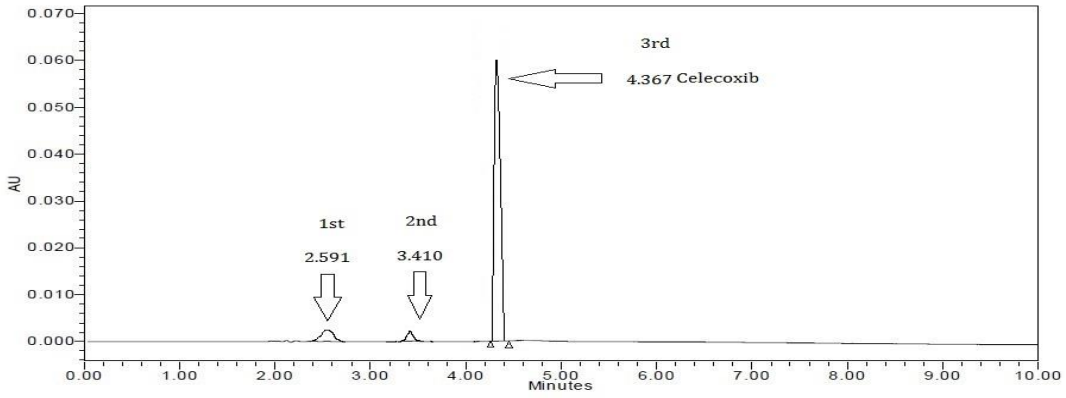

Figure No:05 Acid Treated chromatogram of Celecoxib (1 N HCl for 1 h reflux)

When stressed sample was analysed showed two addition peaks at the retention time of 2.591 & 3.410 Comparison of the peak area of Celecoxib in stress condition with that of the zero-time samples revealed 11.22% Degradation.

Table No: 05 Forced Degradation Results

Sr. No	Stress Condition	Drug peak area at zero-time sample	Drug peak area of stressed sample	Retention time of degradation product (min)	% Degradation
1	Acid Hydrolysis (1 N HCl of 1Hr)	310064	275275	4.367	11.22%
2	Alkali Hydrolysis (1 N NaOH of 24 Hrs)	310064	286437	4.354	7.62%
3	Oxidative (3% v/v H_2O_2) in direct room temperature	-	-	-	-
4	Photolytic (exposed to direct sunlight for 1 Month)	310068	301293	No Degradation Peak	2.81%
5	Dry Heat 80 °C (Kept in oven for 8 Hrs)	-	-	-	-

5. Summary and Conclusion:

Stress testing of Celecoxib was carried out under Acidic, alkaline, oxidative, photolytic and dry heat conditions.The HPLC analysis of Celecoxib was carried out using SunFire C18 Column (250×4.6mm, 5µ) during the stress studies Celecoxib was found to degrade under acidic, alkaline, oxidative condition but stable at to dry heat and photolytic condition. The degradation products and tablet excipients were well resolved from the drug using mobile phase of Acetonitrile: Water (80:20 v/v). The detection wavelength was 251nm.

The developed method was validated as per ICH Guidelines. The method was found to be accurate, precise, robust and linear in the range of 20-100µg/mL.

The LOD and LOQ were found to be 0.916µg/mL and 2.778µg/mL respectively. It can be concluded that the HPLC method developed for Celecoxib is capable of discriminating between the drug and degradation products. The method has the necessary accuracy and precision in the range tested can be used in routine quality control and stability studies for the assay of Celecoxib from tablet formulations.

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