

# METHOD DEVELOPMENT AND VALIDATION OF SIMULTANEOUS ESTIMATION OF PREGABALIN AND ETORICOXIB IN BULK AND PHARMACEUTICAL DOSAGE FORM BY UV-VISIBLE SPECTROSCOPY

## ABSTRACT

A simple, accurate, precise and economical method has been developed for the simultaneous estimation of pregabalin and etoricoxib in combined dosage form by using double point standardization method. Methanol is used as the solvent and chromogenic agent added was bromocresol green. Bromocresol green is only reactive with pregabalin form a green colour ion pair complex.  $\lambda_{max}$  of pregabalin and etoricoxib was at 618 nm and 235 nm, respectively. The method was found to be linear in the range of 6-22  $\mu\text{g mL}^{-1}$  for pregabalin and 4.8-17.6  $\mu\text{g mL}^{-1}$  for etoricoxib. Validation parameters was performed and method was found to be linear, accurate, precise, rugged and robust.

**Keywords:** Pregabalin, etoricoxib, double point standardization, validation

## INTRODUCTION<sup>1,2</sup>

Neuropathic pain is a type of ongoing agony that originates from the pathology of the sensory system, which is generally normal and is crippling, exorbitant, and hard to treat. It is the consequence of different pathways at the fringe, spinal and supra-spinal levels that trigger agonising conduction pathway changes. A bilayered uncoated FDC tablet containing pregabalin IP (75 mg) and etoricoxib (60 mg) has of late been authorized by Central Drugs Standard Control Organization (CDSCO) to consider synergistic consequences for the administration of ongoing back pain related with neuropathic segments. Pregabalin, anti-convulsant is a functioning (*S*)- enantiomer of 3-(aminomethyl)- 5-methylhexanoic acid and etoricoxib is a selective COX-2 inhibitor.

## MATERIALS AND METHODS

### Instruments

A UV-Visible double beam spectrophotometer Shimadzu 1800 Japan and 10mm quartz cells was used.

For weighing, Shimadzu balance model AY 220 was used.

### Materials

Pure drug samples of pregabalin and etoricoxib were gifted by Rubicon Pharma Ltd., Mumbai. Formulation used was Etoshine NP manufactured by Sun Pharmaceutical Industries Ltd., and obtained from a local pharamchy.

### Chemical and reagents

Methanol, bromocresol green (BCG)

### Methods<sup>3</sup>

#### Preparation of reagent solution

10 mg of BCG was added to 50 mL standard flask. Made up the volume using methanol. 200  $\mu\text{g mL}^{-1}$  concentration of BCG was obtained.

#### Selection of wavelength

10 mg of standard pregabalin and etoricoxib were weighed and transferred to 10 mL standard flask, made up the volume with methanol containing 100  $\mu\text{g mL}^{-1}$  concentrations of PGB and ETX.

1 mL of the solution mixed with 1 mL BCG solution and kept for 10 minutes. Then the volume was made up with methanol and scanned in the range of 200-800 nm and the absorption maxima was found at 235 nm and 618 nm for ETX and PGB respectively. Overlay spectra of both ETX and PGB were recorded.

#### Preparation of standard stock solution

10 mg of pregabalin and 8 mg of etoricoxib were weighed accurately and transferred to 50 mL standard flask. 10 mL methanol was added and sonicated for 3 minutes and then the volume made up with methanol. Stock solution contains 200  $\mu\text{g mL}^{-1}$  concentration of pregabalin and 160  $\mu\text{g mL}^{-1}$  of etoricoxib.

#### Analysis of formulation<sup>4</sup>

Weight equivalent to 38 mg was added to 50 mL flask, then 10 mL methanol mixture was sonicated for 10 minutes and the volume made up with methanol

**Table I: Analysis data parameter**

Sl. No.	Parameter	Pregabalin	Etoricoxib
1	Detection wavelength	618 nm	235nm
2	Linearity range	6-22 µg mL <sup>-1</sup>	4.8-17.6 µg mL <sup>-1</sup>
3	Regression equation	0.007x-0.006	0.099x-0.038
4	Correlation co-efficient(r <sup>2</sup> )	0.994	0.998
5	Slope	0.007	0.099
6	Intercept	-0.006	-0.038
7	LOD (µg mL <sup>-1</sup> )	2.31 µg mL <sup>-1</sup>	1.042 µg mL <sup>-1</sup>
8	LOQ (µg mL <sup>-1</sup> )	5.7 µg mL <sup>-1</sup>	3.159 µg mL <sup>-1</sup>
9	Quantification (% w/w content)	98.9	99.4
10	Accuracy (average % recovery)		
10.1	80	98.4	98.9
10.2	100	99.46	99
10.3	120	98.4	97.3
11	Precision (average % RSD)		
11.1	Intraday	0.93	0.61
11.2	Interday	0.41	0.25
12	Robustness (average % RSD)		
12.1	Reagent concentration (180 µg mL <sup>-1</sup> , 220 µg mL <sup>-1</sup> )	0.61	0.64
12.2	mL of reagent added (0.8, 1.2)	0.74	0.66
13	Ruggedness (average % RSD)	0.56	1.65

and filtered. The stock solution contained 200 µg mL<sup>-1</sup> of pregabalin and 160 µg mL<sup>-1</sup> of etoricoxib. 0.7 mL of stock solution was pipetted into 10 mL standard flask (14 µg mL<sup>-1</sup> of PGB and 11.2 µg mL<sup>-1</sup> of ETX) and 1 mL BCG solution added and kept for 10 minutes. Made up the volume with methanol and scanned in the range of 200-800 nm. The concentration of drugs in formulation was calculated by using double point standardization method. Concentration calculated using the equation

$$C_{\text{test}} = \frac{(A_{\text{test}} - A_{\text{std1}})(C_{\text{std1}} - C_{\text{std2}}) + C_{\text{std1}}(A_{\text{std1}} - A_{\text{std2}})}{A_{\text{std1}} - A_{\text{std2}}}$$

where

$A_{\text{test}}$  – Absorbance of test solution

$A_{\text{std1}}$  – Absorbance of standard 1

$A_{\text{std2}}$  – Absorbance of standard 2

$C_{\text{std1}}$  – Highest concentration than test solution

$C_{\text{std2}}$  – Lowest concentration than test solution

### Method validation<sup>5,6</sup>

The developed method was validated according to ICH guidelines by testing parameters like linearity, accuracy, precision, ruggedness, robustness, limit of detection and limit of quantification.

### Linearity

From the standard stock solution, 0.3 mL, 0.5 mL, 0.7 mL, 0.9 mL, 1.1 mL was pipetted and transferred to 10 mL standard flask and 1 mL BCG solution was added. Kept for 10 minutes and made up with methanol to give concentration of 6-22 µg mL<sup>-1</sup> of pregabalin and 4.8-17.6 µg mL<sup>-1</sup> of etoricoxib. Linearity was determined by regression analysis. Overlay spectrum is shown in Fig. 1.

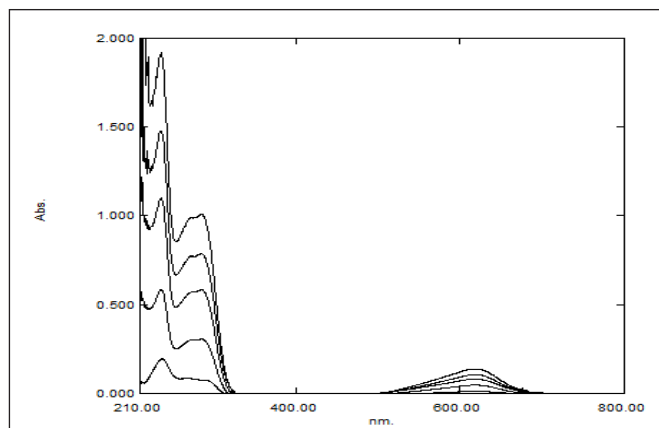


Fig. 1: Overlay spectrum of pregabalin and etoricoxib

### Accuracy

Accuracy of the developed method was determined using recovery studies. Known quantity of pure drug was added to formulation at 80%, 100% and 120% level. It was repeated thrice and percentage recovery and percentage relative standard deviation were calculated. Results are shown in Table I.

### Precision

From the formulation, concentration of  $14 \mu\text{g mL}^{-1}$  of PGB and  $11.2 \mu\text{g mL}^{-1}$  were prepared and analysed for three times in the same day (intraday) and on three consecutive days (interday). Then percentage relative standard deviation was calculated, as shown in Table I.

### Robustness

Robustness of the method was determined by changing reagent concentration and volume of BCG added. Results are as shown in Table I.

### Ruggedness

Ruggedness of the method was determined by performing the analysis of the formulation by three different analysts and are reported in Table I.

### LOD and LOQ

Limit of detection and limit of quantification were

determined using the formulae and calculated results are given in Table I.

$$\text{LOD} = 3.3 \frac{\sigma}{S} \quad \text{LOQ} = 10 \frac{\sigma}{S}$$

$\sigma$  – Standard deviation      S – Slope

### CONCLUSION

UV-Visible spectroscopic method was developed and validated for the simultaneous estimation of pregabalin and etoricoxib. The method was found to be simple, accurate, precise, robust, rugged and economical for the determination of pregabalin and etoricoxib in pharmaceutical dosage form. No other methods have been developed for the estimation of these drugs, so the method is novel. The excipients and additives present in the dosage form do not interfere in analysis of drug, hence the method can be used for the routine quality control of the drug in combined dosage form.

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