International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 7(2): March-April 2017

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Research Paper……!!!**

Received: 26-01-2017; Revised: 28-02-2017; Accepted: 09-03-2017

STABILITY-INDICATING STUDY OF ACECLOFENAC AND PREGABALIN IN PHARMACEUTICAL TABLET DOSAGE FORM

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Keywords:

Hydrolysis, Oxidative, Aceclofenac, Pregabalin

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ABSTRACT

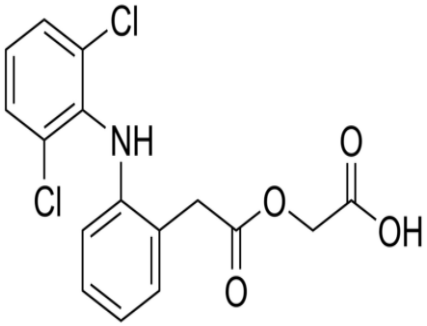
A stability-indicating high performance liquid chromatographic method was developed and validated for quantitative determination of Aceclofenac and Pregabalin in tablet dosage form. The separation was achieved by C_{18} - (250mm*4.6mm*5µ) (particle size) as stationary phase with mobile phase 0.02M potassium dihydrogen phosphate buffer and methanol (70:30%v/v) with flow rate of 1 ml/min retention time for Aceclofenac and Pregabalin were found to be 3.173min and 4.253min respectively. Aceclofenac and Pregabalin were exposed to acid/base hydrolytic, oxidative, thermal degradation and stressed sample were analysed by proposed method. There were other co-eluting, interfering peaks from excipients, impurities or degradation products due to variable stress conditions all graphs and percentage degradation is shown in result and discussion. The system suitability of the method shows that the performance of the chromatographic system is not significantly influenced by variations of the operational parameters inside an accepted domain.

INTRODUCTION

Aceclofenc is chemically known as [(2,6-dichlorophenyl)amino] phenylacetoxyacetic acid (figure: 1)[1]. It is a nonsteroidal anti-inflammatory drug (NSAIDs). Aceclofenc, a phenyl acetic acid derivative, has anti-inflammatory and analgesic properties. It is a potent inhibitor of cyclo-oxygenase which is involved in the production of prostaglandins which cause pain, swelling and inflammation[2-3]. It is official in British pharmacopeia (IP 2010)[4].

Pregabalin chemically known (*S*)-3-(aminomethyl)-5-methylhexanoic acid (Figure: 2)[5]. White to off-white, crystalline solid. Pregabalin is a structural derivative of inhibitory neurotransmitter gamma-amino butyric acid (GABA); it does not bind directly to GABA or benzodiazepine receptors. Pregabalin binds with high affinity to the alpha2-delta site of voltage-gated calcium channels in CNS tissues. In vitro, Pregabalin reduces the calcium-dependent release of several neurotransmitters, including glutamate, norepinephrine, and substance P, possibly by modulation of calcium channel function[2-3]. It is official in Indian Pharmacopeia (IP 2010)[6].

Literature survey reveals UV, HPLC and stability indicating HPLC methods have been reported for estimation of Aceclofenac and Pregabalin alone and in combination with other drug. Currently there is no stability indicating method has been reported for combination of Aceclofenac and Pregabalin till date. The combination of these two drugs is not official in any pharmacopoeia.



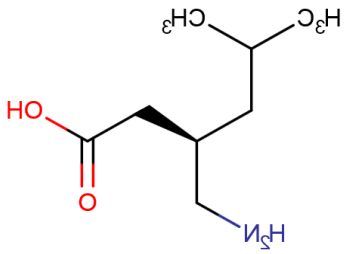


Figure: 1 Chemical structure of Aceclofenc **Figure: 2 Chemical structure of Pregabalin**

MATERIALS AND METHODS

Selection of analytical wavelength

10 µg/ml solutions of Aceclofenc and 10 µg/ml solutions Pregabalin were separately Prepared in mobile phase. Each solution was scanned between 200-400 nm in Double Beam UV-visible spectrophotometer (Shimadzu, model 1800). Wavelength was selected from the overlay spectra of Aceclofenc and Pregabalin. Both the components show reasonably good response at 210 nm. Overlain spectra of both the drug shown in figure no 3.

Selection of mobile phase

The mobile phase should be sufficiently transparent at the wavelength of detection 0.02 M potassium dihydrogen phosphate Buffer and methanol are the solvents which are tried for selecting solvent for mobile phase. In our studies various mobile phase with different ratio were used. The mobile phase consist of 0.02 M potassium dihydrogen phosphate Buffer and methanol (70: 30 %v/v) provided optimum polarity for proper migration, separation and resolution of Aceclofenc and Pregabalin.

Table 1: Optimized chromatographic condition

Parameters	Conditions
Mobile phase	Phosphate Buffer: Methanol (70: 30 %v/v).
Stationary Phase	ECO-C $_{18}$ (250mm*4.6mm*5µ) (particle size)
Flow rate	1ml/min
Run time	20min
Volume of injection	20µL
Detection wave length	290nm

System suitability parameters

Sample solution of Aceclofenc and Pregabalin were injected in triplicates as per the procedure. From the standard chromatogram system suitability parameters like theoretical plates, tailing factor, retention time, area and resolution are evaluated. The results are given in Table: 2.

Preparation of mobile phase

Buffer Solution: 2.72 g of Potassium dihydrogen phosphate was accurately weighed an dissolved in 1000 ml of HPLC water (0.02 M potassium dihydrogen phosphate) then pH 5.0 ± 0.1 was adjusted with 1% Ortho Phosphoric Acid.

Mobile Phase: Phosphate Buffer : Methanol (70 : 30% v/v).

Standard preparation of Aceclofenc and Pregabalin

An accurately weighed quantity of standard Aceclofenc (50 mg) and Pregabalin (37.5 mg) were transferred to 100 ml volumetric flasks and volumes were made up to mark with mobile phase to get 500 µg/ml of Aceclofenc and 375 µg/ml of Pregabalin. After that take 1 ml from above solution and diluted it to the 10 ml to get Aceclofenac (50 □g/ml) and Pregabalin (37.5 □g/ml). Graph shown in figure no: 4

Sample preparation

Twenty tablets were weighed accurately. Powder equivalent to 100 mg of Aceclofenc and 75 mg of Pregabalin was weighed and transferred in a 100 ml volumetric flask and mobile phase was

added. This solution was sonicated for 15 minutes and final volume was made to the mark with mobile phase. The solution was filtered through What man filter paper No. 41.The filtrate 1 ml was transferred in a 10 ml volumetric flask and diluted to the mark with mobile phase and then, Take 5 ml was transferred in a 10 ml volumetric flask and diluted to the mark with mobile phase to obtain Aceclofenc (50 □g/ml) and Pregabalin (37.5 □g/ml). Graph shown in figure no: 5

Preparation of Stock solution: (Aceclofenc 500 µg/ml and Pregabalin 375µg/ml)

An accurately weighed quantity of standard Aceclofenc (50 mg) and Pregabalin (37.5 mg) were transferred to 100 ml volumetric flasks and volumes were made up to mark with mobile phase to get 500 µg/ml of Aceclofenc and 375 µg/ml of Pregabalin.

Preparation of calibration curve

Take 0.50, 0.75, 1.0, 1.25, 1.5 ml of Aceclofenc and 0.50, 0.75, 1.0, 1.25, 1.5 ml of Pregabalin to the 10 ml volumetric flasks from both 500 µg/ml of Aceclofenc and 375 µg/ml of Pregabalin stock solution. Make up to mark with mobile phase to get final concentration of Aceclofenc (25, 37.5, 50, 62.5 and 75 µg/ml) and Pregabalin (18.75, 28.125, 37.5, 46.875 and 56.25 µg/ml). Plot the graph for area Vs time to get calibration curve. Calibration curve of Aceclofenc and Pregabalin shown in Figure No: 6 and 7.

Force degradation study

Procedure for acid, Base and Oxidative degradation

It is a process in which the natural degradation rate of a pharmaceutical formulation is increased by applying the additional stress. The prepared standard solutions (500 mg of Aceclofenc and 375 mg of Pregabalin) of Aceclofenc and Pregabalin was treated with 2 ml of 0.1 N HCl, 0.1 N NaOH, 3% H_2O_2, in 10 ml volumetric flask then solution was heated for 2 hr at 70^oC for acid, base and oxidative degradation. Then above mentioned degradation conditions, each degradation samples were neutralized with respective degradants. Mark with Mobile phase to get 500 µg/ml of Aceclofenc and 375 µg/ml Pregabalin and injected in to HPLC system. All graph shown in figure no: 8, 9 of acid degradation of both the drug individual figure no: 10 acid degradation of sample. Figure no: 11, 12 of base degradation of both the drug individual figure no: 13 base degradation of sample. Figure no: 14, 15 of oxidative degradation of both the drug individual figure no: 16 oxidative degradation of sample.

Procedure for Thermal Degradation.

Powder of Aceclofenc and Pregabalin was spread over petri dish and exposed to dry heat (80˚C) for 5hour in an oven then from that powder and accurately weighed quantity of Aceclofenc (50 mg) and Pregabalin (37.5 mg) was transferred to 100 ml separate volumetric flasks and 80 ml of

mobile phase was added. Flask was shaken, then volume was made up to mark with mobile phase to get 500□g/ml of Aceclofenc and 375 □g/ml of Pregabalin, then further dilution was carried out by diluting 1 ml of solution with 10 ml vol. flask with mobile phase to get 50□g/ml of Aceclofenc and 37.5 □g/ml of Pregabalin and injected in to HPLC system. Figure no: 17, 18 of thermal degradation of both the drug individual figure no: 19 thermal degradation of sample.

RESULTS AND DISCUSSION

Selection of analytical wavelength

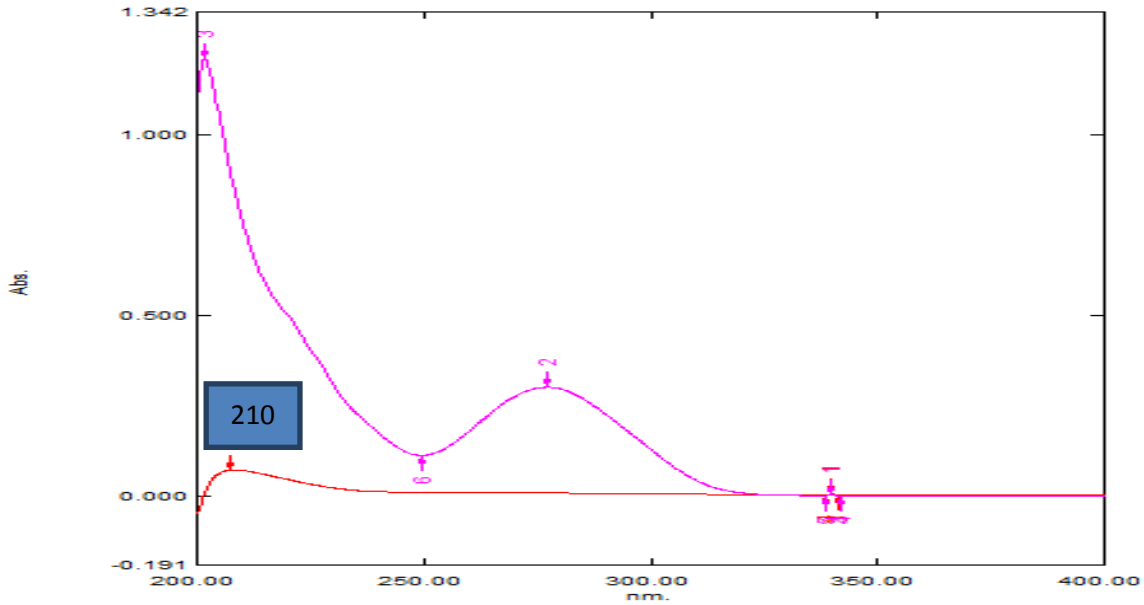


Figure no: 3 Overlain Spectra of Aceclofenac (10 □g/ml) and Pregabalin (10 □g/ml) for determination of wavelength for maximum absorbance

TABLE: 2 SYSTEM SUITABILITY PARAMETERS

System Suitability Parameters	Aceclofenac (n = 3)	Pregabalin (n = 3)
Retention Time (min)	3.173 ± 0.037	4.253 ± 0.027
Tailing factor	1.333 ± 0.019	1.407 ± 0.018
Theoretical plate	6887 ± 113.036	6960 ± 108.48
	5.827 ± 1.240	

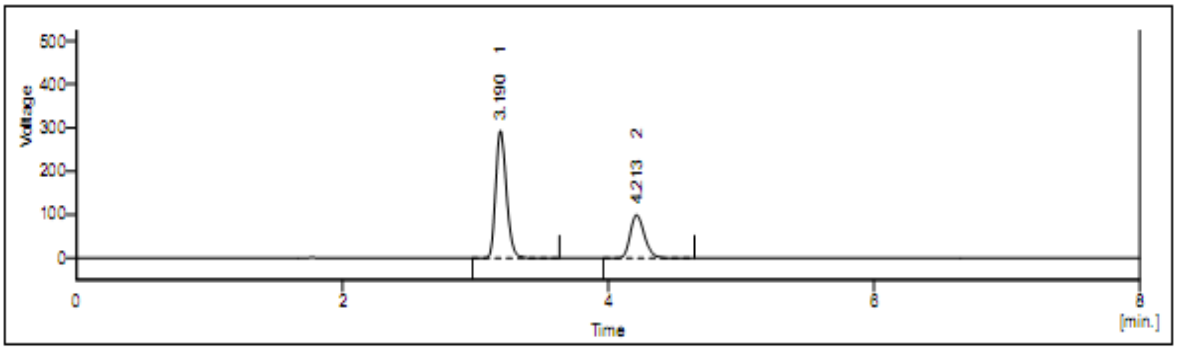


Figure no: 4 Chromatogram of Standard Aceclofenc (50 µg/ml) and Pregabalin (37.5µg/ml)

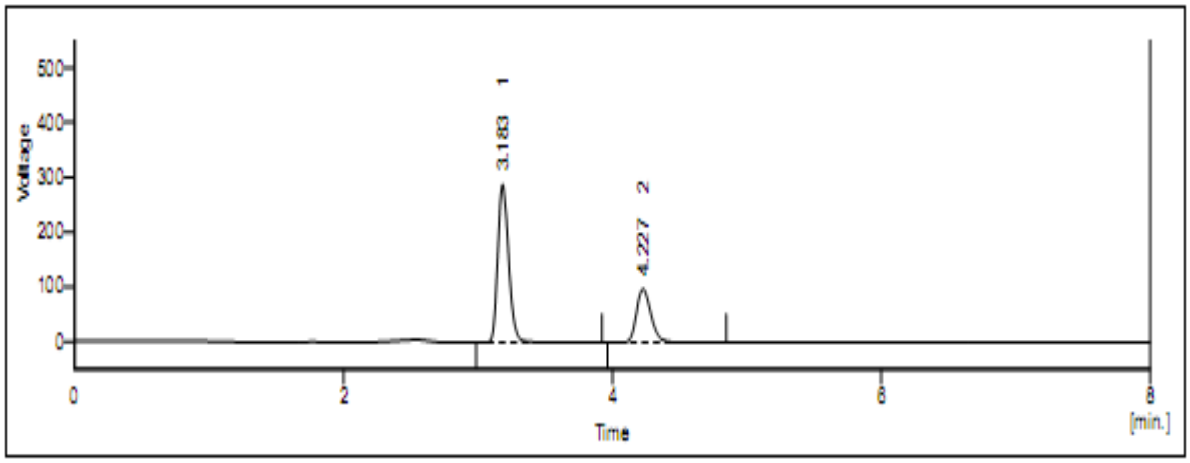


Figure no: 5 Chromatogram of Sample Aceclofenc (50 µg/ml) and Pregabalin (37.5 µg/ml)

DISCUSSION

From above chromatogram it is concluded that both the drug have good resolution with good pick shape and tailing factor is also with in the limit.

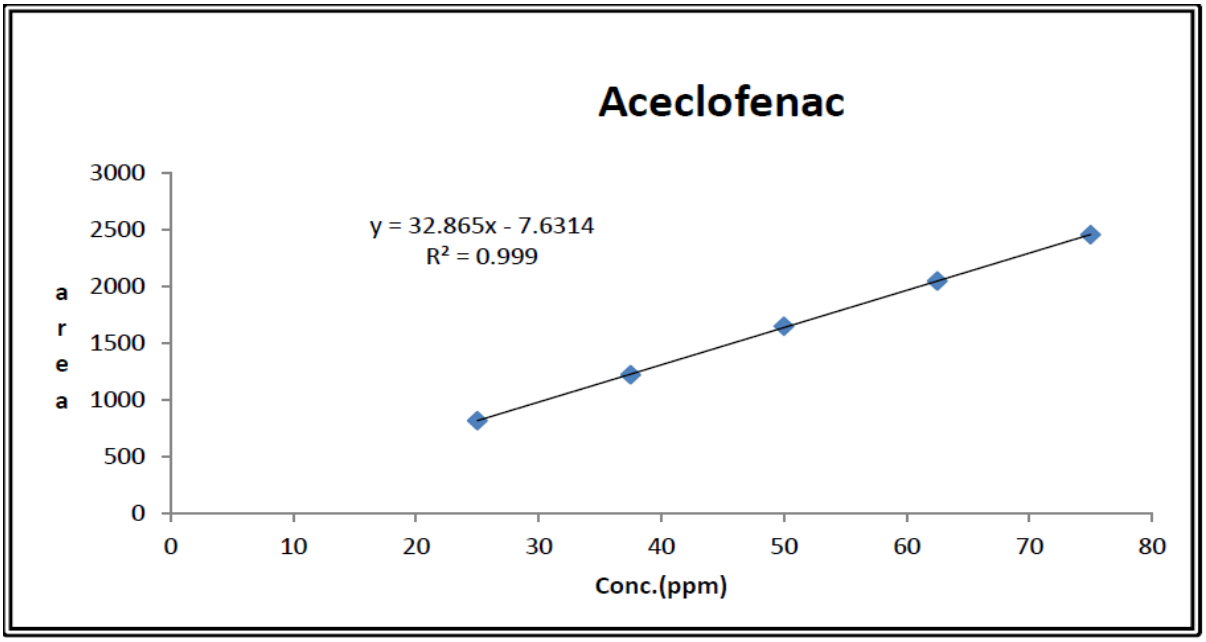


Figure:6 Calibration curve of Aceclofenac

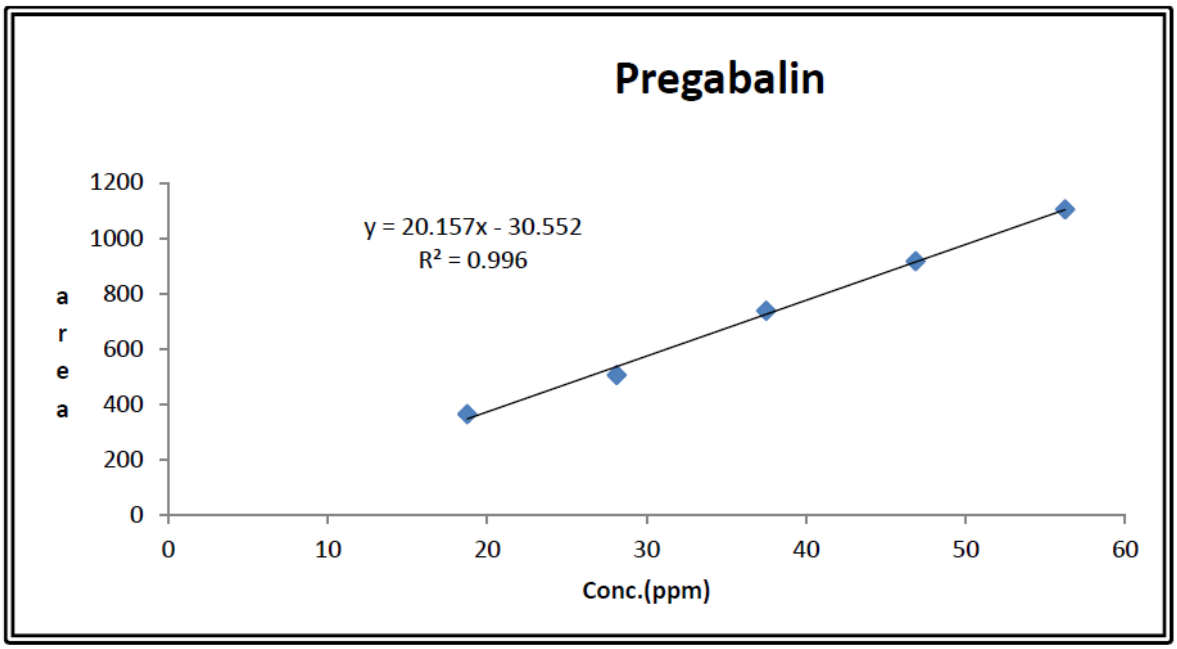


Figure: 7 Calibration curve of Pregabalin

Discussion :- From above chromatogram it is concluded that calibration curve of Aceclofenc and Pregabalin is linear and Regration value is also with in the limit 0.996 and 0.999.

Force degradation study

Acid degradation

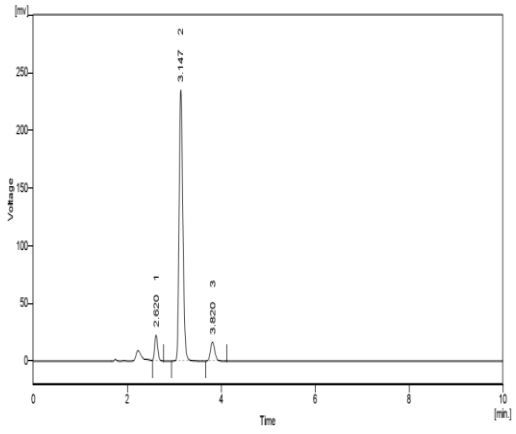


Figure no: 8 Aceclofenac

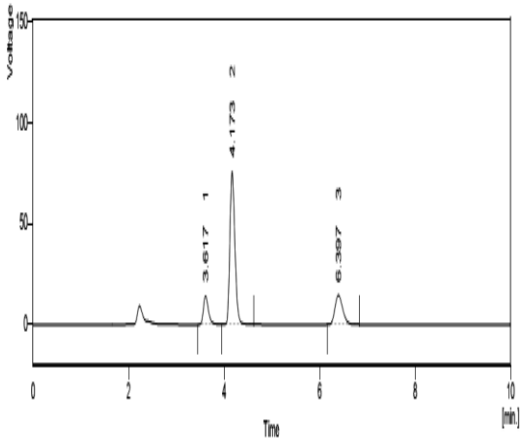
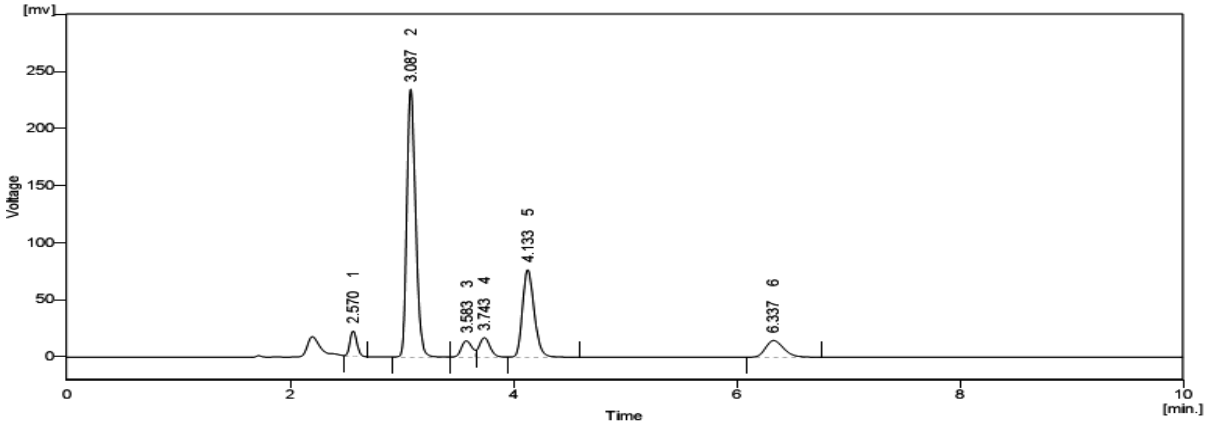


Figure no: 9 Pregabalin



Figuure no: 10 Mix standard of both the drug

Base Degradation

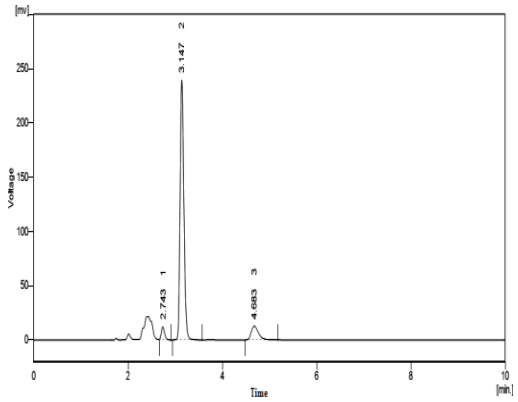


Figure no: 11 Aceclofenac

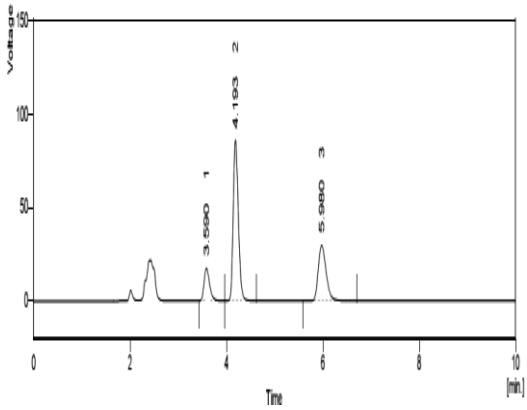


Figure no: 12 Pregabalin

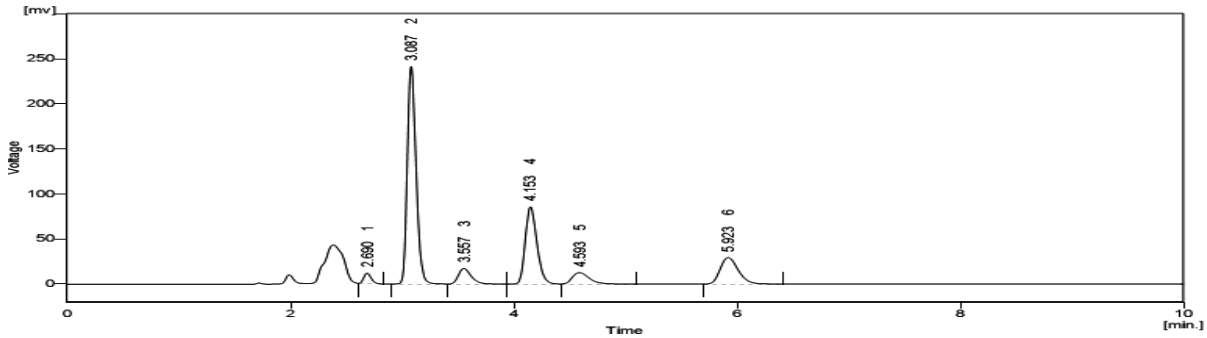


Figure no: 13 Combination pf both the drug

Oxidative degradation

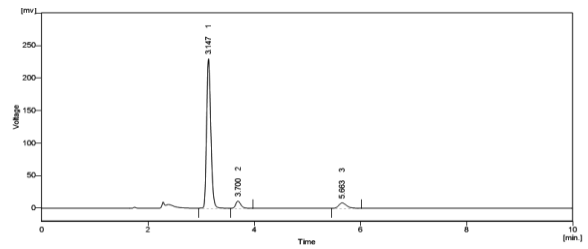


Figure no: 14 Aceclofenac

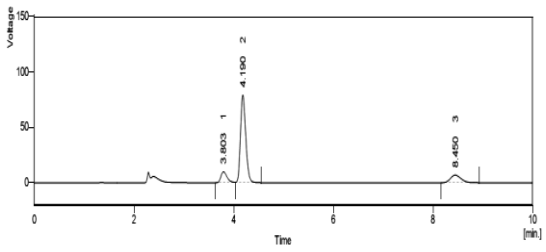


Figure no: 15 Pregabalin

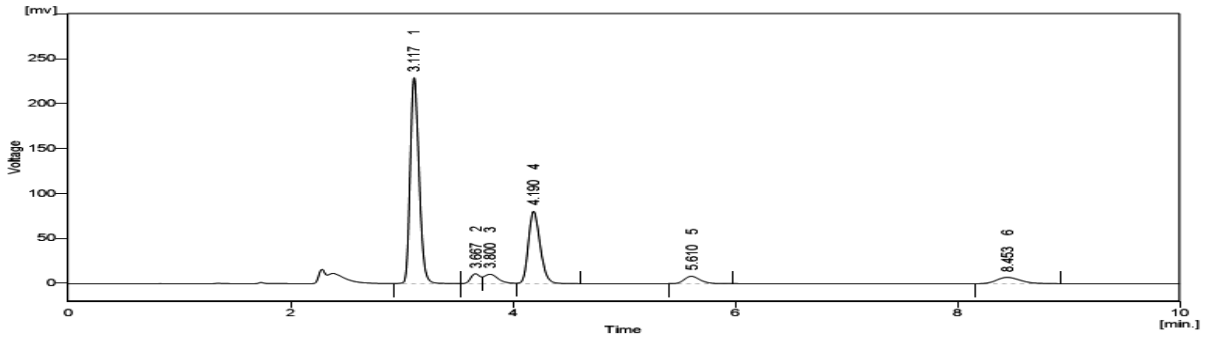


Figure no: 16 Combination of both the drug

Thermal Degradation

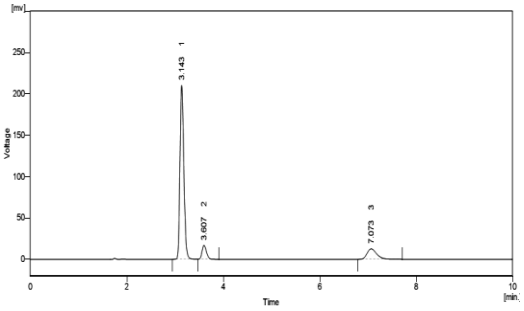


Figure no: 16 Aceclofenac

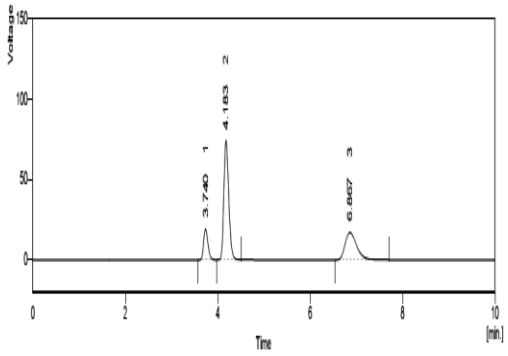


Figure no: 17 Pregabalin

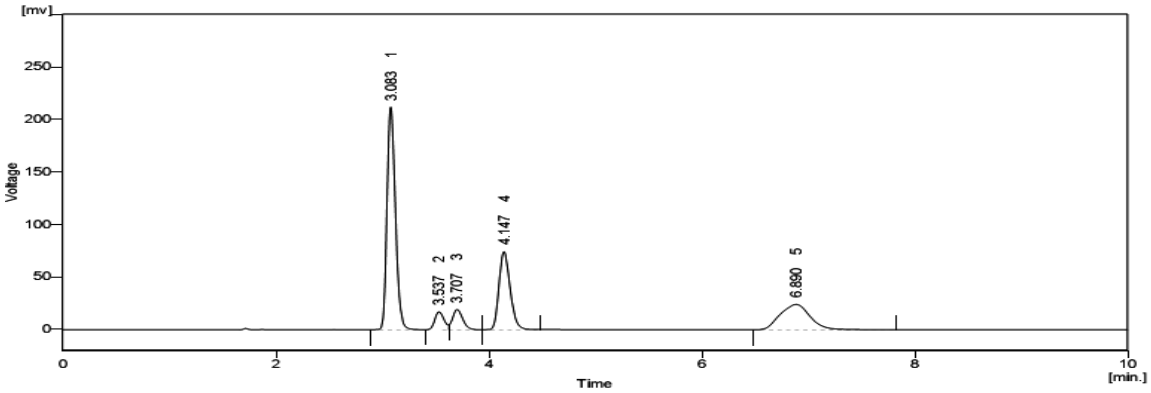


Figure no: 18 Combination of both the drug

TABLE NO: 3 RESULT OF STABILITY STUDY OF ACECLOFENAC & PREGABALIN (STANDARD)

Condition	% Degradation	
	Aceclofenac	Pregabalin
Acid	21.17	24.80
Base	19.75	14.41
Oxidative	23.03	21.35
Thermal	29.58	26.40

TABLE NO: 4 RESULT OF STABILITY STUDY OF ACECLOFENAC & PREGABALIN (SAMPLE)

Condition	% Degradation	
	Aceclofenac	Pregabalin
Acid	22.95	24.91
Base	20.41	15.36
Oxidative	23.90	19.80
Thermal	30.33	27.09

CONCLUSION

Degradation was found within limits for Aceclofenac and Pregabalin.

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