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SIMULTANEOUS ESTIMATION OF PARACETAMOL AND ETODOLAC BY HPLC METHOD IN PURE AND COMBINATION FORMULATION

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ABSTRACT

Paracetamol and Etodolac are non- steroidal anti-inflammatory drugs with analgesic and antipyretic properties, was determined by a new RP-HPLC method. The method was developed on aphenomenex C18 (4.6 x 250mm, 5µ i.d) column, aided by a mobile phase mixture ofmethanol and phosphate buffer of pH 6.8, in the ratio 80:20%, v/vat a flow rate of 1.0 mL/min and monitored at 231nm. Retention time of about 4.89min and 3.79min was observed for paracetamol and etodolac, respectively. Linearity showed good correlation close to 1 for both the drugs in a range of 200-700 µg/ml for paracetamol and 0.5-3mg/ml for etodolac.The LOD and LOQ values were found to be 19.14 and 58 µg/mL for paracetamol and 3.089 and 9.3 µg/mL for etodolac, respectively. The proposed method was demonstrated to be most accurate, precise, specific, and robust which was found to be useful for routine analysis.

Keywords: Paracetamol, Etodolac, HPLC and binary mixture.

INTRODUCTION

Paracetamol[1] is chemically N-(4-hydroxyphenyl) acetamide and Etodolac[2,3] is chemically 1, 8 diethyl-1,3,4,9-tetrahydropyrano[3, 4-b] indole-1-acetic acid. Both these drugs belong to class of non-steroidal anti-inflammatory drugs (NSAIDs). Literature survey revealed that only few LC, spectrophotometric methods for the estimation of paracetamol and etodolac[4-8]in tablet dosage forms are available. In this present study RP-HPLC method was developed for the simultaneous estimation and validation of paracetamol and etodolac in pure and combination formulation.

EXPERIMENTAL

Equipment

SHIMADZU LC 20AD system with SPD-20A UV/VIS detector equipped with Spinchrom software was used for method development, double-beam Perkin Elmer (LAMBDA 25) UV-VIS spectrophotometer was used for spectral measurements and ELICO pH meter for pH measurements.

Reagents and pharmaceutical preparations

Gift samples of Paracetamol and Etodolac presented by Aurobindopharma Ltd, Hyd, were used as standards without further purification. Water, methanol (HPLC grade, Rankem), potassium dihydrogenortho phosphate, sodium hydroxide (A.R grade, Rankem) were used in the analysis.

Preparation of Buffer (pH-6.8)

125 ml of 0.2 M KH_2PO_4 was taken in a 500 ml volumetric flask, 56 ml of 0.2 M NaOH was added and finally made upto the volume with HPLC grade water.

Methanol and phosphate buffer pH 6.8 (20:80%v/v) were filtered through 0.45µm membrane filter and degassed for further use.

Chromatographic conditions

The method was developed with a mobile phase of methanol:buffer of pH 6.8 in the ratio of 80:20 v/v and at a flow rate of 1 ml/min. The detection was monitored at 231 nm and at ambient temperatures.

METHOD OPTIMIZATION

The separation was achieved on a Phenomenex C_{18}(250 mm x 4.6 mm, 5 µ) column based on the polarity of the drug. Mobile phase was selected after several trials with acetonitrile, methanol and buffers of various pH of 6, 6.8, 7 and 7.2. Phosphate buffer with pH-6.8 and methanol were showing lower retention time and good peak shape without tailing. Composition of mobile phase mixture, flow rate and the detection was monitored at 231 nm. Results were depicted in table-1.

METHOD VALIDATION

The method was validated for accuracy, precision, linearity, LOD, LOQ, ruggedness and robustness and the results were found to be satisfactory. Regression parameters were presented in table 1.

Linearity and range

Linearity was assessed by performing single measurement at several analyte concentrations of paracetamol and etodolac injected at an interval of 10min and showed good correlation between concentration range of 200-700µg/ml for paracetamol and 0.5-3mg/ml for etodolac. The results were produced in table 2 and table 3 and pictured in fig 1 and fig 2.

Accuracy

The recovery studies yielded the mean results within 98-102% of true concentration of each drug indicating that the test method has an acceptable level of accuracy and the results were presented in table 4.

Precision

Five replicate injections of working standard solutions have been studied for system precision and method precision and the results were presented in table-5 indicating reproducibility of the method.

Robustness

Robustness was checked by altering the optimized parameters and the %RSD was found to be <2 i.e within acceptable limit. And the results were given in table 1.

Ruggedness

System to system/ analyst to analyst/ column to column variability study was conducted on different HPLC systems, different columns and different analysts under similar conditions at different times and the results were shown in table 1.

Limit of detection (LOD) and limit of quantification (LOQ)

LOD AND LOQ were determined by analyzing progressively lower concentrations of the standard solutions using optimized chromatographic conditions and the results were found to be satisfactory and were presented in table 1.

CONCLUSION

The proposed RP-HPLC method for estimation of paracetamol and etodolac in tablet dosage method was more accurate, simple, efficient and the results were found to be satisfactory with retention time <7min, so the method is not time consuming and can easily applied for routine laboratory analysis.

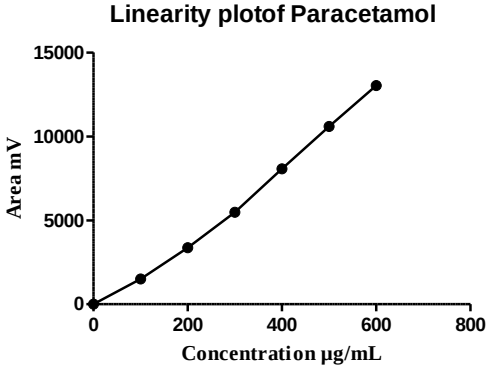

Fig. 1: Linearity plot of Paracetamol

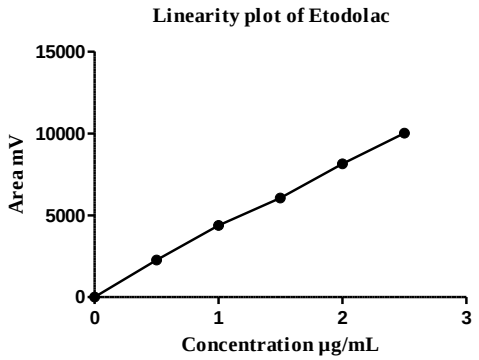

Fig. 2: Linearity plot of Etodolac

Table 1: Optical and regression parameters

PARAMETER	PARACETAMOL	ETODOLAC
Theoretical plates	11842.22	11769.12
Retention time, min	4.897	3.797
Correlation coefficient	0.9996	0.998
%RSD	0.22	0.79
LOD, mcg/ml	19.14	3.089
LOQ, mcg/ml	58	9.3
Tailing factor	0.08	0.06
Linearity range	200-700µg/ml	0.5-3mg/ml

Table 2: Linearity of Paracetamol

Conc., µg/mL	Area, Mv
100	1502.0
200	3372.5
300	5487.0
400	8073.0
500	10589.0
600	13032.0

Table 3: Linearity of Etodolac

Conc., µg/mL	Area, mv
0.5	2263.9
1.0	4382.1
1.5	6052.5
2.0	8137.6
2.5	10012.7

Table 4: Recovery studies of Paracetamol and Etodolac

Concentration added, %		Percentage recovered*		% RSD*	
PCM	ETD	PCM	ETD	PCM	ETD
50	80	99.17	98.3	0.7	0.9
100	100	99.85	99.9	0.7	0.7
150	120	99.78	99.6	0.6	0.7

*Mean of three replicates

Table 5: Precision studies of Paraceamol and Etodolac

Parameter	Conc, %	Mean Peak area		SD		%, RSD	
		PCM	ETD	PCM	ETD	PCM	ETD
System Pression*	100	10374	7459.2	6.63325	7.628	0.063	0.10
Method Pression*	100	99.3	99.1	0.7	0.8	0.765	0.80

*Mean of six replicates

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