

DETERMINATION OF CITALOPRAM AND ITS PRESERVATIVES IN ORAL SOLUTION BY USING RP-HPLC METHOD

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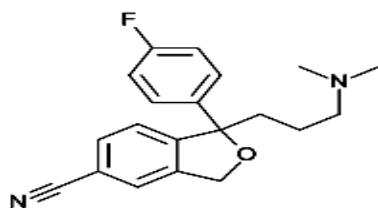
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ABSTRACT

The present work describes a RP-HPLC Method for simultaneous estimation of Citalopram in combination with Preservatives i.e., Methylparaben and Propylparaben in Oral solutions. Chromatography was Performed on Water Symmetry RP 18 (250 x 4.6mm i.d., Particle size 5µm) Column in isocratic mode with mobile phase containing pH 2.5 Buffer: Methonal: Acetonitrile in the ratio 57:18:25 %(v/v/v). The flow rate was 1.0ml/min and the eluent was monitored at 255nm. The selected chromatographic conditions were found to effectively separate Citalopram, Methylparaben and Propylparaben 13.47, 8.87 and 24.97 mins respectively. Linearity for Citalopram Methylparaben and Propylparaben was found in the range of 12.5-75.4 µg/ml. The method showed precision value (RSD %) at 0.57% for oral solutions. The Proposed method was statistically evaluated and can be applied for routine quality control analysis of Citalopram, Methylparaben and Propylparaben.

Key words: Citalopram HBr, Methylparaben, Propylparaben, RP-HPLC, Oral solutions.

INTRODUCTION:



Citalopram is an antidepressant used in treatment of Depression and generalized anxiety.

It is freely soluble in methanol and Dimethylsulfoxide (DMSO). Citalopram is

(*RS*)-1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile. However, to our knowledge, there is no method for the simultaneous determination of these drugs by RP-HPLC in the literature. The aim of this work is to develop an accurate, specific, repeatable and validated method for the simultaneous determination of Citalopram, Methylparaben and Propylparaben in oral solutions.

MATERIALS AND METHODS:

Citalopram, Methylparaben, Propylparaben and oral solution of Citalopram containing 10mg/5ml solution which was manufactured by Hetero Drugs Ltd, Hyderabad, India. potassium Di hydrogen phosphate, Sodium-1-octane sulphonate and Ortho phosphoric acid of AR grade and methanol and Acetonitrile of HPLC grade were obtained from Merck.

HPLC Method and Chromatographic Conditions:

The chromatography estimation was performed using the following conditions, Water symmetry RP₁₈(250x4.6mm i.d., Particle size 5µm) and mobile Phase containing

Buffer (Prepared by 2.72g of potassium Di Hydrogen Phosphate and 1g of Sodium-1-Octane dissolve in 1000ml of miliQ-water sonicate to dissolve adjust the P H to 2.5 ±0.5 with OrthoPhosphoric acid and filter through 0.45µm nylon membrane filter and Degas)Methanol and acetonitrile in the ratio of 57:18:25 %(v/v/v).The flow rate is monitored at 1.0ml/min. the column temperature is maintained at ambient temperature and detection was carried out at 255nm.

PROCEDURE:

PREPARATION OF STANDARD SOLUTIONS:

Citalopram Standard stock

Preparation:

Weigh and transfer accurately about 63.0mg of Citalopram Hbr Working Standard into a 100 ml clean dry volumetric flask, add about 60 ml of Diluent, sonicate for 5 minutes, and dilute to volume with Diluent.

Methyl paraben Standard stock

Preparation:

Weigh and transfer accurately about 45.0 mg of Methyl paraben Working Standard into a 200 ml clean dry volumetric flask, add about 120 ml of

diluent, sonicate for 5 minutes, and dilute to volume with Diluent.

Dilute 5ml of above solution to 25 ml with Diluent and mix

Propyl paraben Standard stock Preparation:

Weigh and transfer accurately about 25.0 mg of Propyl paraben Working Standard into a 100 ml clean dry volumetric flask, add about 60 ml of Diluent, sonicate for 5 minutes, and dilute to volume with Diluent. Dilute 5ml of above solution to 50ml with Diluent and mix

Preparation of Standard solution of Citalopram oral solution :

Pipette out 5 ml of the Citalopram standard stock solution, 5ml of Methyl paraben Standard stock solution and 5ml Propyl paraben Standard stock solution in a 25 ml Volumetric flask and add diluent and sonicate for 15mins and then dilute to 25 ml with diluent.

Preparation of Standard solution of Citalopram oral solution for assay:

Pipette out 5 ml of the Citalopram standard stock solution, 5ml of Methylparaben Standard stock solution and 5ml Propylparaben Standard stock solution in a 25 ml Volumetric flask and add diluent and sonicate for 15mins and then dilute to 25 ml with diluent. The

solution was filtered through 0.45 μ m, membrane filter and then 20 μ l of filtrate was injected each time into the column at flow rate of 1.0ml/min. Evaluation of the drug was performed with PDA detector at 255nm. Peak area was recorded for all peaks. A plot for peak area versus the respective concentration over the peak area was computed. The regression equation was used to estimate the amount of Citalopram in oral solution.

Assay method for Oral solution:

Accurately transfer a 5ml Citalopram oral solution in 100ml volumetric flask. Add about 60ml of diluent and sonicate for 15mins and then dilute with diluent. Filter a portion of the solution through 0.45 μ membrane filter. Separately inject 20 μ l of the blank, Standard (five injections) and sample solution in duplicate into the liquid chromatograph, record the chromatographs and measure the peak areas. Precision of the method is expressed in terms of % RSD.

RESULTS AND DISCUSSIONS:

The present study was carried out to develop a sensitive, precise and accurate HPLC method for the analysis of Citalopram in bulk samples and its pharmaceutical dosage form. The

retention time for Citalopram, Methylparaben and Propylparaben in its formulation 13.47, 8.87 and 24.97 mins respectively. Each of the samples was injected five times and the same retention times were observed in all cases. The peak area of different concentration set up as above was calculated. The peak area for the solution was reproducible as indicated by low coefficient of variation (0.54). A good linear relationship ($r = 0.9999$) was observed between the concentrations of Citalopram and respective peak areas. The calibration graph was found to be $Y = y = 10708x + 2.466$ where Y is the peak area and X is the concentration of

Citalopram in the range of 12.5-75.4 $\mu\text{g/ml}$ when we analyzed the proposed RP-HPLC method for finding out intra and inter-day variations, a low coefficient of variation was observed (Table 4).

This shows that the present HPLC method is highly precise. The drug content in the oral solution was quantized using the proposed analytical method. The mean content of Citalopram in oral suspensions is shown in (Table 3). The amount of Citalopram from the preanalyzed sample containing known amounts of the drug is shown in (Table-2).

TABLE: 1 CALIBRATION OF PROPOSED METHOD:

Concentration(ppm)	Average Area
12.55	1343950
25.10	2687900
37.65	4031850
50.20	5375837
62.75	6719750
75.30	8063700

Regression equation from 12.5 -75.4 $\mu\text{g/m}$: $y = 10708x + 2.466$ $R^2 = 0.999$

TABLE: 2 RESULTS OF THE RECOVERY STUDY:

Amt of drug	Recovery from suspension		Recovery from drug	
	n=3 Mean amt found	Mean % recovery	n=3 Mean amt found	Mean % recovery
25	25.066	100.2664	24.59333	98.372
50	50.083	100.166	49.33333	98.66
75	75.326	100.4267	73.91667	98.55467

TABLE: 3 ASSAY OF CITALOPRAM IN ORAL SOLUTION:

S.NO	LABEL amt of drug(mg)	Mean(\pm S.D) Amt(μ g)found by the proposed	Mean of% label amt(\pm S.D)
Suspension-I	2.0mg	1.986 \pm 0.020	99.33 \pm 1.040
Suspension-II	2.0mg	1.987 \pm 0.010	99.16 \pm 0.28

TABLE: 4 PRECISION OF THE PROPOSED METHOD

Conc. Of Citalopram μ g/ml	Observed conc. Of Citalopram (μ g/ml)			
	Intra day		Inter day	
	Mean	CV	Mean	CV
25	25.066	0.1151	24.593	0.706
50	50.083	0.2511	49.333	0.409
75	75.326	0.4334	73.916	0.612
100	100.99	0.5116	98.101	0.20

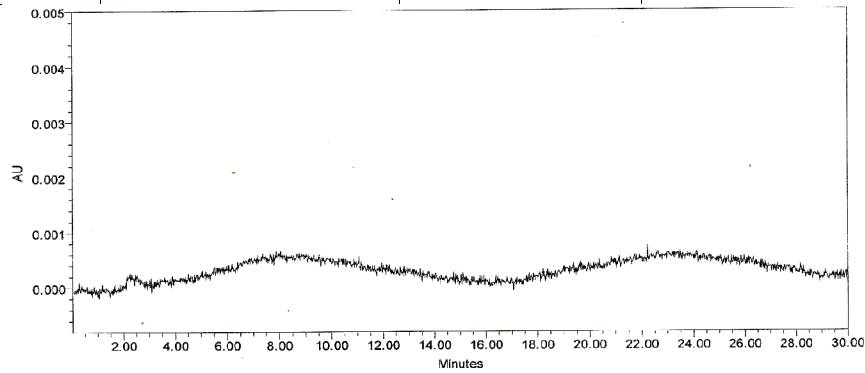


Fig: 1 Chromatogram of Citalopram, Methylparaben, and Propylparaben (Blank)

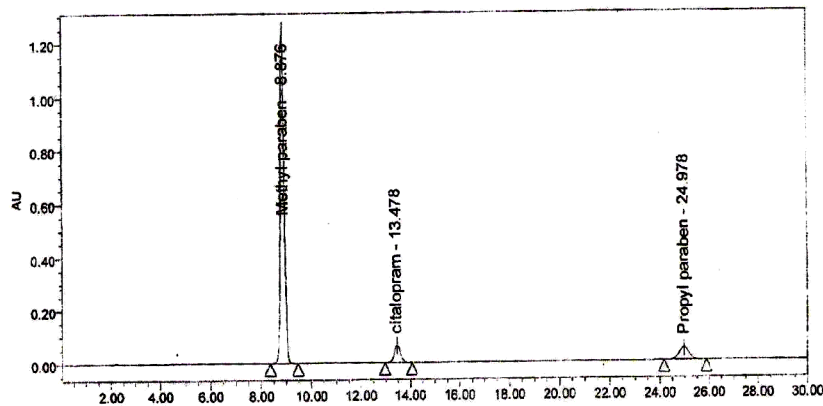


Fig:2 Chromatogram of Citalopram, Methylparaben, and Propylparaben (Standard)

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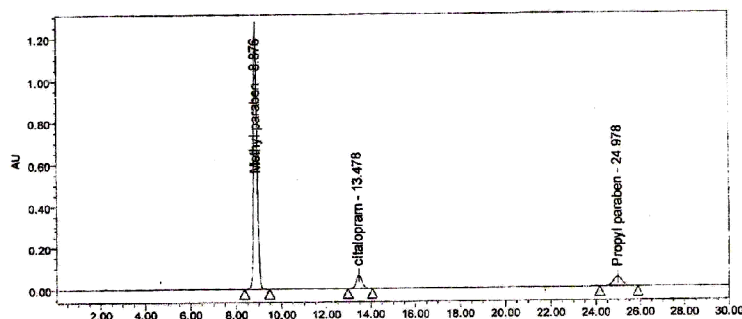


Fig: 3-Chromatogram of Citalopram, Methylparaben, and Propylparaben (Sample)

ACKNOWLEDGEMENT: We wish to express our gratitude to Dr. V. Girija Sastry, Associate Professor, A. U. College of Pharmacy, Visakhapatnam, Andhra Pradesh, India for her inspiration and constant support through-out the study.

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