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SIMULTANEOUS ESTIMATION OF CETRIZINE DIHYDROCHLORIDE AND AMBROXOL HYDROCHLORIDE IN PHARMACEUTICAL FORMULATION BY A NOVEL HPLC METHOD

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ABSTRACT

A rapid and sensitive high performance liquid chromatography method for determination of cetirizine dihydrochloride and ambroxol hydrochloride has been developed. The chromatography system used a reversed phase C-8 column with UV- Vis detection at 230 nm. Mobile phase consisted of acetonitrile – 0.1% triethlamine (50:50 v/v) (pH adjusted to 4.0 using 10% ortho phosphoric acid) at a flow rate of 1.5 ml/min using propranolol as internal standard (I.S.). The calibration curve was linear in the concentration range of 2-20 µg/ml for cetirize dihydrochloride, 24-240µg/ml for ambroxol hydrochloride. The lower limit of detection was found to be 0.06 µg and 0.02µg, for cetirizine dihydochloride and ambroxol hydrochloride respectively.

INTRODUCTION: Cetirizine dihydrochloride is non-sedating anti-histamine with potent anti-allergic action. It is used in the treatment of upper respiratory allergies and in seasonal asthma [1].

Ambroxol hydrochloride is an active metabolite of bromhexine which is a derivative of alkaloid vasicine. It is a potent mucolytic and mucokinetic capable of inducing thin copious bronchial secretion [2]. Paw B*. et al.,* developed and validated HPLC method for the determination of cetirizine dihydrochloride in Pharmaceutical Dosage Forms [3]. Vittorio Brizzi and Umberta Pasetti reported a HPLC method for determination of ambroxol hydrochloride in Pharmaceutical Dosage Forms [4, 5].

The objective of the present work was to develop and validate the rapid and sensitive high-performance liquid chromatography (HPLC) method for simultaneous determination of cetirizine dihydro-chloride and ambroxol hydrochloride in tablets.

MATERIALS AND METHODS:

Drugs: Cetirizine Dihydochloride and Ambroxol Hydrochloride.Trade drug product (Amcet)

Chemicals and Solvents: Triethylamine and orthophosphoric acid was purchased from S.D. Fine Chemicals Ltd., India. Acetonitrile of HPLC grade were purchased from Qualigens Fine Chemicals, India. The gift sample of the drug was received from Martine and Brown Pharmaceuticals (Hisar), India. Nylon syringe membrane filters (0.2 µm) were purchased from Sartoris, Germany.

HPLC System: The HPLC system consisted of a delivery pump (Water 600 pump controller), a reversed phase analytical column C-8 (250 × 4.6 mm) 5 µm (Kromasil), a Rheodyne sample injector with a 20 µl loop volume and a variable wavelength (UV-Vis) detector (waters 2487 Dual Absorbance Detector).

Chromatographic Conditions: Mobile phase consisted of acetonitrile – 0.1% triethlamine (50:50 v/v) (pH adjusted to 4.0 using 10% ortho phosphoric acid).

The solution was filtered through a 0.2 µm membrane filters. The eluent was monitored with a UV-Vis detector set at250 nm with a flow rate of 1.5 ml/min. Mobile phase was stirred on a magnetic stirrer during the HPLC run.

Standard solution and calibration curve: A standard stock solution of cetirizine dihydrochloride (500µg/ml), ambroxol hydrochloride (500µg/ml) and propanolol (1000 µg/ml, I.S.) were prepared in water for HPLC. Subsequent dilutions were made in mobile phase to give the concentrations 2, 4, 6, 10 and 20µg/ml for cetirizine dihydrochloride, 24, 48, 96, 120 and 240µg/ml for ambroxol hydrochloride. The calibration curve was obtained by plotting the ratio of peak area of drug/I.S. (20µg/ml) versus concentration.

Assay: Twenty tablets were weighed accurately and finely powdered. The powder equivalent to 5 mg of cetirizine dihydrochloride and 60 mg of ambroxol hydrochloride was weighed accurately and dissolved in 100 ml water for HPLC. The solution was filtered through 0.2 µm membrane filter paper. Five ml of the resulting solution was mixed with one ml of I.S. and was further diluted to get a solution having a concentration of 10µg/ml of cetirizine dihydrochloride, 120µg/ml of ambroxol hydrochloride and 20µg/ml of internal standard (I.S.). Twenty µl of this solution was injected in triplicate under the specified conditions. The peak area ratio (drug/I.S.) obtained were related to slops and intercepts from the calibration data to calculate concentration of the drugs (**Table 1**).

TABLE 1: RESULTS OF HPLC ASSAY

Cetirizine dihydrochloride		Ambroxol hydrochloride	
Amt. Claimed mg/tablet	Amt. found mg/tablet	Amt. Claimed mg/tablet	Amt. found mg/tablet
	5.02		60.01
5.0	4.98	60.0	59.09
	5.06		60.05
Mean	5.01		59.82
RSD	0.77		0.94

Validation of the assay: To study the accuracy, reproducibility and precision, recovery experiments were carried out. The recovery of the added standard was studied at three different levels. To an aliquot of the analyzed formulation a known concentration of standard solution was added. The content of cetirizine dihydrochloride and ambroxol hydrochloride was determined (**Table 2**). The linear of the standard curve was confirmed by plotting the peak area ratio of drug/I.S. versus concentration. Linear regression analysis was performed to calculate the slope, the intercept and the correlation coefficient (r) of the calibration curve (**Table 3**).

TABLE 2: RESULTS OF RECOVERY STUDIES

Cetirizine dihydrochloride			Ambroxol hydrochloride		
Amount added(mg)	Amount found(mg)	Percentage Recovery	Amount added(mg)	Amount found(mg)	Percentage Recovery
5	5.02	100.4	5	4.96	99.2
10	10.12	101.2	10	9.87	98.7
12	11.98	99.8	12	11.92	99.3
	Mean	100.46		Mean	99.06

TABLE 3: LINEAR REGRESSION DATA FOR CALIBRATION CURVE

Parameter	Cetirizine dihydrochloride	Ambroxol hydrochloride
Calibration Range(µg/ml)	2.20	24-240
Theoretical Plates	1698.62	1418.24
Tailing Factor	1.6	1.3
LOD(µg/ml)	0.06	0.02
LOQ(µg/ml)	0.18	0.4

RESULTS AND DISCUSSION: System suitability tests were carried out on freshly prepared standard stock solutions of drugs. The calibration curve was linear in the range of 2-20µg/ml for cetirizine dihydrochloride and 24-240µg/ml for ambroxol hydrochloride. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.06µg, 0.18µg/ml for cetirizine dihydrochloride and 0.02µg, 0.4µg/ml for ambroxol hydrochloride.

CONCLUSION: In conclusion, our method is rapid, sensitive, reproducible and well suited to the simultaneous determination of Cetirizine dihydrochloride and Ambroxol hydrochloride by internal standard method.

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