Trade Science Inc.

January 2008 Volume 7 Issue 2

Analytical CHEMISTRY

An Indian Journal

Full Paper

ACAIJ, 7(2) 2008 [59-61]

Simultaneous determination of cetrizine and ambroxol in formulation by RP-HPLC

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Received: 11th August, 2007 ; Accepted: 16th August, 2007

ABSTRACT

A simple, precise and rapid reversed phase HPLC method was developed for the simultaneous estimation of cetrizine(CT) and ambroxol(AM) in combined formulation. The method was carried out on a Hypersil BDS C18 column using a mixture of water: methanol (pH adjusted to 3.5 with ortho-phosphoric acid): tetrahydrofuran(60:37:3 v/v/v) and detection was carried out at 230 nm. The drug CT showed linearity in the range of 4-32mcg/ml and AM in the range of 48-384mcg/ml. Limits of quantification was found to be 20 and 4ng/ml for CT and AM respectively.

KEYWORDS

Cetrizine;
Ambroxol;
Simultaneous estimation.

INTRODUCTION

Cetrizine, (CT) chemically known as 2-[4(4-chlorobenzhydryl) piperazin-1-yl] ethoxy acetic acid and is used as histamine H_1 receptor antagonist[1]. Ambroxol,(AM) chemically known as N-(trans-p-hydroxy cyclohexyl)-(2-amino-3,5-dibromo benzyl) amine which is used as mucolytic drug[2]. A combination of 5mg of CT and 60mg of AM is commercially available in tablet form.

Estimation of CT from human plasma and urine was reported by Moncrieff et al.[3]and Rosseel et al.[4]. These methods were carried out using ODS columns and by UV and diode array detection. HPLC methods for the estimation of CT from pharmaceutical dosage form were reported by Suryanarayana et al. [5] and Walily et al.[6]. Determination of AM from human plasma and urine by HPLC method[7] was developed by Rotter holm et al. A validated HPLC method[8]was developed for the estimation of AM in formulation. The reported methods are applicable for the estimation of either for CT or AM individually from pharmaceutical dosage forms or biological fluids. No method was reported for the estimation in combined dosage form. The present work describes the development of a validated RP-HPLC method, which can quantify these components simultaneously from a combined dosage form.

EXPERIMENTAL

Reagents and chemicals

CT and AM were received as gift samples from Sai Mirra Innopharm Pharmaceuticals Limited, Chennai. HPLC grade solvents were purchased from S.D. Fine Chemicals Limited, Mumbai. Analytical grade chemicals were obtained from Qualigens Fine Chemicals.

Apparatus

HPLC was carried out using a model LC-10A system(Shimadzu, Japan) equipped with an SPD10A UV-Visible detector. The column used was Hypersil BDS C18,(250/ 4.6 mm I.D. 5μm).

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HPLC conditions

A mixture of methanol: water(pH adjusted to 3.5 by orthophosphoric acid): tetrahydrofuran(60:37:3 v/v/v) was used as mobile phase at a flow rate of 1 ml/min with an operating pressure of 3000 psi. A Rheodyne® 7725i injector with a 20µl loop was used for the injection of samples. Detection was done at 230 nm, with a sensitivity of 0.001 AUFS. The mobile phase was filtered through 0.2µ membrane filter and degassed. The separation was carried out at room temperature, 25±1^{0}C.

Preparation of standard solutions

The stock solutions of CT and AM each of 1mg/ml concentration in mobile phase were prepared and used. The working standards of CT and AM were prepared by dilution of standard solution with mobile phase.

Analysis of formulation

Twenty tablets, each containing 5mg of CT and 60mg of AM were weighed and finely powdered. A quantity of powder equivalent to 10 mg of CT and 120mg of AM was weighed accurately and transferred to a 50ml volumetric flask and the volume was made up with the mobile phase and it was filtered using 0.45µ membrane filter. From the above prepared solution, 1ml was taken and diluted to 10ml with the mobile phase. The 20µ l of the above solution was injected in to the column and chromatogram was recorded.

Recovery studies

Recovery studies were carried out by adding 10mg of standards of CT and AM to an equivalent quantity of the formulation in a 25ml volumetric flask. The volume was made up with mobile phase. Further dilutions were made and the contents of CT and AM were once again determined by the proposed method by recording the chromatograms. The concentration of CT and AM added, amount found after recovery study, the % R.S.D. and % accuracy are shown in TABLE 1. From the amount of the drug present, percentage recovery was calculated and shown in TABLE 2.

RESULTS AND DISCUSSION

Chromatograms of mixed standard solutions, which contained CT and AM, were recorded and shown in figure 1. The retention times of AM and CT were 4.8 and 8.4 min, respectively. The system suitability parameters are shown in TABLE 1.

TABLE 1: System suitability parameters

Parameters	CT	AM
Retention Time(min)	4.8	8.4
Linearity range(mcg/ml)	4-32	48-384
Correlation coefficient(r)	0.9999	0.9992
Slope	0.0278	0.0001
Intercept	0.2474	0.0566
Coefficient of variation(%)	1.16	1.54

TABLE 2: Analysis of formulations and recovery studies

Drug	Amount(mg/tablet)		% Label claim[a]	% recovery[a]
	Labelled	Found[a]		
Cetrizine	5	4.99±1.31	99.8±0.97	99.27±0.65
Ambroxol	60	59.6±1.52	99.3±1.33	99.53±0.72

[a]Mean±S.D of six observations

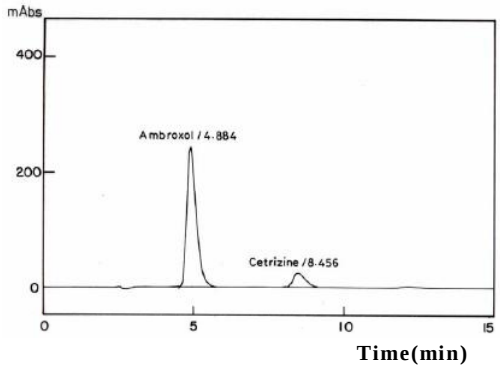

Figure 1 : Chromatogram of cetirizine and ambroxol sample

From the marketed formulation, sample solutions were made and the response factor was used to calculate the concentration of each drug. From the concentration, the amounts of each drug present in tablets were calculated(TABLE 2). Precision of the method was studied by making repeated injections of the mixture of drugs.

The stability of analytes(CT and AM) during analysis was observed in room temperature and under refrigeration. This was carried out by injecting the stored samples and by comparing the peak areas of CT and AM with the peak areas of freshly prepared solutions of CT and AM. They were stable up to 6h under room temperature and for 4 days under refrigeration.

The percentage label claim obtained by proposed method was in good agreement for both the drugs individually and also in combination. There was no interference found due to excipients was supported by the

%R.S.D. values of recovery studies. Further this method eliminates complicated extraction of individual drugs for quantitation. Both the drugs are estimated within 15min. Hence the present method is cost effective and faster analytical method.

CONCLUSION

The application of suggested procedure was successfully applied to the detection of these drugs in pharmaceutical preparation with high % recovery, good accuracy and precision. Hence this method is simple, sensitive and readily adaptable to routine determination of CT and AM in combined formulation.

ACKNOWLEDGMENTS

The authors are thankful to Sai Mirra Innopharm Pharmaceuticals Limited, India for providing facilities for research work.

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