ISSN:2249-1236

INTERNATIONAL JOURNAL OF RESEARCH AND REVIEWS IN PHARMACY AND APPLIED SCIENCES

Research Article

Received: 16-09-2011 *Accepted: 03-10-2011* *Published: 29-11-2011*

APPLICATION OF MBTH/FECL$_3$: A RELIABLE AND COAST EFFECTIVE ANALYTICAL METHODOLOGY FOR ROUTINE PHARMACEUTICAL DETERMINATION OF CHLORPROMAZINE HYDROCHLORIDE

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ABSTRACT

The present work reports a new spectrophotometric method for chlorpromazine hydrochloride (CPZ) assay. This is based on the oxidative coupling ability of 3-Methylbenzthiazolinone-2-hydrzone (MBTH) with the drug in presence of $FeCl_3$ under acidic condition. The resultant water soluble colored chromogen showed maximum absorbance at 720nm.The reaction system obeyed Beer's law in the range of 2-10µg/ml. The proposed method has been successfully applied for routine pharmaceutical analysis of the sited drug.

Key words: Chlorpromazine hydrochloride, 3 -Methylbenzthiazolinone-2-hydrzone, Beer's law..

INTRODUCTION

Chlorpromazine (10-[3-dimethylaminopro-pyl] phenothiazine) belongs to the primary chemical group of antipsychotic agents known as the phenothiazines. It has an aliphatic side chain and is referred to as a typical phenothiazine with a low to moderate-potency antipsychotic action. Apart from its antipsychotic activity where it is used as a tranquilizer and maintenance therapy to prevent acute relapse in chronic schizophrenic patients, chlorpromazine is also used for the treatment of vomiting and vertigo because of its sedative and extra pyramidal effects[1, 2]. Although chlorpromazine has been replaced by newer generation of antipsychotic agents which have improved action and side effect profile, it is still used in the management of acute and chronic psychosis including schizophrenia and the manic phase of manic depression as well as amphetamine induced psychosis, other serious psychiatric illnesses marked with agitation, and impaired reasoning. Chlorpromazine is highly lipophilic, membrane- bound, and protein-bound (especially albumin protein) and accumulate in the brain, lungs, and other tissues with a high blood supply[3]. The peak plasma concentration of chlorpromazine and other phenothiazines are attained within 2 – 4 hours and intramuscular administration helps to avoid much of the first-pass metabolism in the liver leading to increased bioavailability[4]. Chlorpromazine is mainly metabolized by oxidative processes mediated largely by the hepatic cytochrome oxidase and by conjugation processes[5]. Presently, there is an increase in the number of generic drug products from multiple sources and this has placed the pharmacists and other health practitioners in a position of having to select one among several seemingly equivalent products.

There are few spectrophotometric methods for CPZ estimation in pharmaceutical dosage forms and in biological fluids blood, urine, and other tissues [6] are available till date .The estimation of CPZ extractive ion pair complex formation was carried out with chlorophenol red[7] , determination of CPZ was performed by ternary complex formation with o-Sulfophenylfluorone-Molybdenum(VI) [8] CPZ analysis in its binary mixture was done by use of the kinetic wavelength pair-method[9]and by multivariate calibration methods and derivative spectrophotometry[10], color reaction of CPZ with palladium (II) and o- hydroxylhydro-quinonephthalein has been utilized for the determination of CPZ[11], Sensitive titrimetric assay was developed for chlorpromazine with bromate-bromide mixture[12] thin layer chromatography[13], gas liquid chromatography[14], gas chromatography/mass spectrometry[15], radioimmunoassay[16,17], voltammetry[18] , chemiluminescence method [19], electron spin resonance spectroscopy[20] , nuclear magnetic resonance (nmr) spectroscopy[21] ,Other analytical procedures for CPZ has been done by flow-injection analysis [22], HPLC and fluorescence detection [23].

To the best of our knowledge, there is no work in the literature reported about the analysis of CPZ using MBTH and $FeCl_3$ in either biological fluids or pharmaceutical formulations. Hence the author has made an attempt to develop simple and rapid methods for the estimation of CPZ in bulk drugs and in pharmaceutical formulations. In the present work the determination of CPZ was done by using MBTH as reagent. An oxidative coupling reaction occurs between MBTH and selected drug in acidic medium. The literature survey on the analytical applications of

MBTH indicates that this compound has not been earlier reported as reagent for the spectrophotometric determination of CPZ with $FeCl_3$ mediated oxidative coupling reaction.

Some specific advantage that the proposed method posses are as follows,

1. Other active compounds present in the formulations may not interfere if they are resisting the reaction conditions established for the proposed method.
2. High water solubility of the resulting dye.
3. And the resulting dye was stable in an aqueous medium.

EXPERIMENTAL

Apparatus:

Elico UV – Visible double beam spectrophotometer model SL-159.

Materials and Reagents:

All the chemicals used were of analytical grade. All the solutions were freshly prepared in distilled water.

Reagents:

1. 0.2% MBTH
2. 0.7% Fecl3 in 0.5% Hcl

Analytical procedure for the determination of Chlorpromazine:

Aliquots of standard drug solution containing 0.2-1.0µg of chlorpromazine were transferred into a series of graduated tubes. To each tube 1.5ml MBTH and 2 ml $FeCl_3$ were added shake well and kept for 10 minutes. Transfer the contents of each tube in to a series of 10 ml volumetric flasks and made up the volume up to the mark with distilled water. The green color developed was measured at 720nm against reagent blank and the calibration curve was prepared.

RESULTS AND DISCUSSION

MBTH was synthesized by Besthorn, and become an analytical tool of considerable versatility. MBTH can be used for the determination of polyhydroxy compounds, aromatic amines, aliphatic and salicylic amines. Azodyes, stilbenes and Schiff bases as well as pyrrole derivatives also react with MBTH under oxidative conditions [24]. MBTH in combination with oxidant like Ferric chloride has been mostly used for the determination of aromatic and heterocyclic amines in acidic conditions[25]. The drug reacts with MBTH in presence of $FeCl_3$ in acidic medium to give green colored product. Actually, this is an iron catalyzed oxidative coupling reaction of MBTH with the drug. Under reaction conditions, on oxidation, MBTH losses two electrons and one proton forming an electrophilic intermediate, which is the active coupling species. The intermediate undergoes electrophilic substitution with the drug to form the colored product. The proposed reaction mechanism was shown in reaction scheme I. The optimum conditions affecting the formation of colored complex were studied and maintained throughout the experiment to determine the quantity of sited drugs in bulk and formulations. The results indicate that the

maximum absorbance was found with 1.5 ml MBTH and 2ml $FeCl_3$ at room temperature after 10 minutes of incubation time.

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity for these methods are presented in Table-1.The regression analysis using the method of least squares was made for the slope (a) and intercept (b) obtained from different concentrations are summarized in Table-1. The precision and accuracy were found by analyzing six replicate samples containing known amounts of the drug and the results are summarized in Table-1

TABLE – 1: Optical Characteristics, Precision and Accuracy of Proposed Method

Parameters	Method A
λ_{max} (nm)	720
Beer's law limit (µg / mL)	2-10
Sandell's Sensitivity (µg/cm^2/0.001 abs. unit)	0.0281
Molar absorptivity(Litre.mole^{-1}.cm^{-1})	$1.261X10^4$
Stability of Color (hours)	24
Regression equation (Y)*	
Intercept (a)	0.0102
Slope(b)	0.0034
% RSD$	1.408
% Range of errors (95% confidence limits):	
0.05 significance level	1.177
0.01 significance level	1.741

* Y = a + bx, where Y is the absorbance and x is the concentration of chlorpromazine hydrochloride in µg/ mL $ For six replicates

TABLE – 2: Assay and Recovery of chlorpromazine hydrochloride in Pharmaceutical Formulations

Formulations	Labeled amount(mg)	Recovery by reference method*(%)	Recovery by proposed method (%) **
			Method A
Chlorpromazine	50	98.95	99.89
Clozine	50	99.90	99.94

* Reference method was UV method developed in the laboratory. ** Recovery amount was the average of six determinants

CONCLUSION

It could be concluded that the developed method for chlorpromazine assay is simple, sensitive, relatively precise, and accurate and can be satisfactorily applied to the analysis of chlorpromazine in bulk and pharmaceutical formulations. The proposed method was used for the routine analysis of the drug in the quality control.

ACKNOWLEDGEMENTS

The authors are grateful to the Centre for Biotechnology, Acharya Nagarjuna University, and Guntur for providing their continuous support throughout the work.

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