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Research Article

Quantitative Estimation of Clobazam in Bulk drug and tablets

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ABSTRACT

A sensitive and rapid extractive spectrophotometer method has been developed for the assay of clobazam in bulk drug and tablets. The method is based on the formation of a chloroform soluble ion-pair complex between clobazam and bromophenol blue in an acidic medium. The complex shows maximum absorbance at 413 nm. Beer's law was obeyed in the concentration range of 5-25 µg /ml. Results of analysis were validated statistically and by recovery studies. The proposed method is now simple, new, reproducible, and accurate and successfully employed in routine analysis of clobazam bulk drug and tablet dosage forms.

Keywords: Clobazam, bromophenol blue, chloroform, methanol, spectrophotometer

INTRODUCTION

Clobazam is chemically 7-chloro-1,5-dihydro-1-methyl-5-phenyl-1,5-benzodiazepine-2,4(3H)-dione[1].It is slightly soluble in water[2] clobazam is official in European and Indian pharmacopoeia2007[3][4]. Clobazam is a long-acting 1,5-benzodiazepine with uses similar to those of diazepam as 1,4-benzodiazepine. It is used in the treatment of epilepsy in association with other antiepileptics. It is also used in the short-term treatment of acute anxiety.UV spectrophotometric method is mentioned in IP-07. An alternative colorimetry method is developed in the present investigation. The method is based on the formation of a chloroform soluble ion-pair complex between clobazam and bromophenol blue in an acidic solution [5]. The amino groups bind the proton more strongly than water molecules and that is the main driving force for the extraction. Different acids show very different degrees of extraction under similar conditions and hence extraction also depends upon the anion[6].

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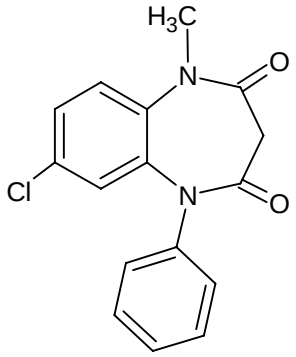
Literature survey revealed that several methods such as spectrophotometry [6],[7],[8], voltammeter[9] and HPLC[10] in biological samples for the drug have been reported. A new sensitive extractive spectrophotometric method was developed for the estimation of clobazam in pharmaceutical dosage forms. The proposed investigation is undertaken with the aim of developing Visible Spectrophotometric technique for the analysis of slightly water soluble drug from single component formulations.

Figure: 1 structure of clobazam



7-chloro-1-methyl-5-phenyl-1*H*-1,5-benzodiazepine-2,4(3*H*,5*H*)-dione

EXPERIMENTAL

All spectral measurements were made on a Systronic UV-Visible recording double beam spectrophotometer (model 2101) with a 1 cm matching quartz cell. Clobazam drug sample was supplied as gift sample by Sun Pharma Labs. Ltd., Jammu. Commercial tablets of etoricoxib were procured from the market (CLOBATOR-5 mg from M/s Torrent Pharma. Ltd., CLODUS-10 mg from M/s Zydus Cadila Healthcare Ltd., FRISIUM 20 mg from M/s Sanofi Aventis Pharma. Ltd.).All chemicals used were of analytical reagent grade.

Standard solution of clobazam was prepared by dissolving 5 mg of pure drug in methanol and diluting to 100 ml with methanol. A 20 ml aliquot of this solution was diluted to 50 ml with distilled water.

Twenty tablets of formulation-I (CLOBATOR) were weighed and powdered. An amount of the powder equivalent to 5 mg of the drug was weighed, transferred into a 50 ml volumetric flask, dissolved and diluted to 50 ml with methanol. It was sonicated for ten minutes and filtered through Whatman filter paper No. 42. A 20 ml aliquot of the filtrate was pipetted out and diluted to 50 ml with water.

An aliquot of 10 ml each of the standard and sample preparation was transferred to 125 ml separating funnel followed by 2 ml 0.1 N HCl, 3 ml of bromophenol blue solution and rest water to make the volume to 25 ml. The solution was extracted three times successively with 10, 5, 5 ml portions of chloroform and filtered through anhydrous sodium sulphate into 25 ml volumetric flask and diluted to 25 ml with chloroform. A reagent blank was prepared in a similar manner without adding the drug. The absorbance of yellow coloured chromogen was measured at 413 nm against the reagent blank. Similar procedures were adopted in cases of formulation-II (CLODUS) and formulation-III (FRISIUM). The drug content of the formulations were conducted. The results of such studies are presented in [Table 1]. Clobazam reacts with Bromophenol blue in acidic solution to give chloroform soluble yellow coloured ion-association complex, which exhibits an absorption maximum at 413 nm. The optimum reaction conditions for the quantitative determination of the ion-pair complex were established through a number of preliminary experiments.

Table-I: Results of analysis of commercial tablets of Clobazam

Tablet formulation	Label claim (mg)	% Label claim estimated* (Mean ± S.D.)	% Coff. of variation	Standard error
I(CLOBATOR)	5	98.236 ± 0.918	0.934	0.411
II (CLODUS)	10	101.064 ± 0.782	0.773	0.350
III (FRISIUM)	20	98.152 ±1.069	1.089	0.479

*Average of six determinations

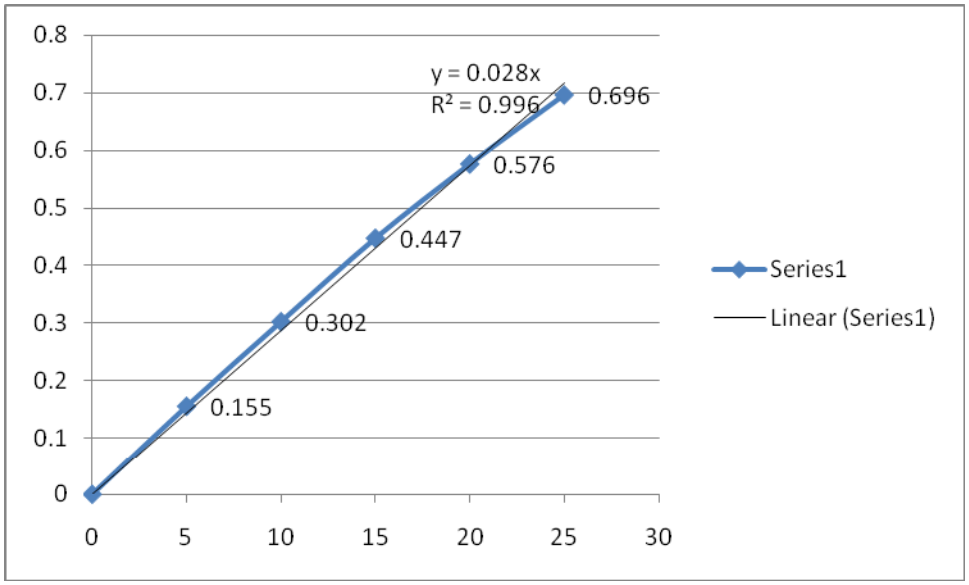
Table-II: Recovery studies of commercial tablets of Clobazam

Tablet Formulation	Label claim (mg)	Drug added (mg)	% Label claim estimated* (Mean ± S.D.)	% Coff. of variation	Standard error
I (CLOBATOR)	5	2	99.560 ± 1.595	1.601	0.718
II (CLODUS)	10	4	100.404 ± 1.124	1.239	0.504
III (FRISIUM)	20	8	98.696 ±0.750	0.760	0.336

*Average of six determinations

The optimum concentration of the reagent was studied. It was observed that 3 ml of 0.05% bromophenol blue solution was sufficient for maximum colour development of the complex. The effect of pH was studied by extracting the coloured complex in presence of various acid solutions and buffers. The maximum and constant colour intensity was observed when 0.1 N HCl was used. Several organic solvents such as methylene dichloride, chloroform and carbon tetrachloride were tried for extraction of the coloured complex from the aqueous phase. However, chloroform was found to be the most suitable solvent. The absorbance of the complex was found to be stable for more than 12 h. The proposed method of determination of clobazam shows molar absorptivity of 1.8×10^4. Linear regression of absorbance with concentration gave a correlation coefficient of 0.9995 and RSD was found to be less than two. The method developed in the present work was found to be sensitive, accurate, precise and reproducible and can be used for routine determination of carvedilol in bulk and in dosage forms.

Curve:1 Standard curve for clobazam at 413 nm



For recovery studies, tablet powder of formulation I ((CLOBATOR) equivalent to 5 mg drug was taken in a 50 ml volumetric flask. In this flask 2 mg of pure drug (corresponding spiked drug) was transferred and 20 ml of methanol was added and the flask was shaken for about 10 min. Then volume was made upto the mark with methanol and filtered through Whatman filter paper No. 42. An aliquot of 10 ml each of the standard and sample preparation was transferred to 125 ml separating funnel followed by 2 ml 0.1 N HCl, 3 ml of bromophenol blue solution and rest water to make the volume to 25 ml. The solution was extracted three times successively with 10, 5, 5 ml portions of chloroform and filtered through anhydrous

sodium sulphate into 25 ml volumetric flask and diluted to 25 ml with chloroform. The absorbance of yellow coloured chromogen was measured at 413 nm against the reagent blank. Similar procedures were adopted for formulation II (CLODUS) and formulation III (FRISIUM). The results of analysis of recovery studies are presented in (Table 2).

RESULTS AND DISCUSSION

From Table 1, it is evident that there is good agreement between the amounts of clobazam estimated and those claimed by the manufacturers. Percent label claims are very close to 100 with low values of standard deviation, % coefficient of variation and standard error. Accuracy, reproducibility and precision of the proposed methods were further confirmed by percent recovery values, which were close to 100 with low values of standard deviation, percent coefficient of variation and standard error (Table 2).

It is thus concluded that the proposed method is new, simple, cost effective, accurate, safe, free from pollution and precise and can be successfully employed in the routine analysis of these drugs in pharmaceutical dosage forms. The proposed method shall prove equally effective to analyze clobazam in the corresponding drug sample and may prove to be of great importance in pharmaceutical analysis.

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