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Spectrophotometric determination of chlorodiazepoxide in pharmaceutical preparations by ion pair formation

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Abstract : Simple, rapid and sensitive spectrophotometric methods were developed for the determination of chlorodiazepoxide drugs in pharmaceutical dosage forms. This method is based on ion pair and charge transfer complexation reactions. The method is based on the reaction of the chlorodiazepoxide drug with Mo(V)–thiocyanate in hydrochloric acid medium followed by an extraction of the coloured ion-pair with 1,2-dichloroethane and the absorbance of the ion pair was measured at 470 nm. All the optimum conditions are established. The calibration graphs are rectilinear in the concentration ranges 5-35 mg L^{-1} for chlorodiazepoxide. The limit of detection (LOD) and relative standard deviation are 0.52 mg L^{-1} and 2.3% respectively.
Keywords: Liquid-liquid extraction,Chlordiazepoxide,1,2 dichloroethane , Spectrophotometry.

1. Introduction

Chlordiazepoxide (7-chloro-N-methyl-5-phenyl-3H-1, 4-benzodiazepine-2-amina-4-oxide) is used as an anxiolytic, sedative, hypnotic, anticonvulsant, and/or skeletal muscle relaxant. The drug may inhibit monosynaptic and polysynaptic reflexes by acting as an inhibitory neuronal transmitter or by blocking excitatory synaptic transmission. The drug may also directly depress motor nerve and muscle function [1, 2]. Clidinium bromide (3-[(hydroxy-diphenylacetyl)-oxy]- 1-methyl-1-azoniabicylo-[2.2.2] octane bromide is an anticholinergic drug which may help symptoms of cramping and abdominal stomach pain by decreasing stomach acid and slowing the intestines. It is commonly prescribed in combination with chlordiazepoxide by the name of clidinium-c [3]. Few methods for the determination of clidinium bromide and chlordiazepoxide in combined dosage forms including HPLC [4], derivative spectrophotometry [5], spectrophotometry using multivariate calibration techniques [6], and capillary SFC [7] have been reported. Literature survey revealed that some analytical methods have been used for the individual estimation of clidinium bromide and chlordiazepoxide. Capillary electrophoresis [8] and kinetic spectrophotometric [9] methods for clidinium bromide have been described. Chlordiazepoxide has been determined either alone or with other compounds in pharmaceutical formulations using high-performance liquid chromatography [10], first-derivative spectrophotometry [11], spectrophotometry [12], HPTLC [13], voltammetry [14]. There are many papers which related determination and some specification of many drugs and components [15-24].

The proposed methods are applied successfully to the determination of chlordiazepoxide and osapride citrate either in pure or in dosage forms, with good accuracy and precision.

2. Experimental

2.1 Instrumentation

A Shimadzu 2100 UV–visible spectrophotometer (Shimadzu, Japan), A Jenway model 3510 pH meter was used for pH measurements. An electronic analytical balance (220LA, ADAM) was used for weight the materials.

2.2. Materials

All solutions were prepared with ultra pure water (obtained from HAMILTON, England) Laboratory glass was kept overnight in a 10% (V/V) HNO3 solution and then rinsed with deionized water. All reagents were made from Merck.

Stock (1 mg mL_1) solutions of chlordiazepoxide (CDZ) was prepared by dissolving the accurate weighed amount in a definite volume of methanol, to get the required concentration. Dilute solutions were prepared by accurate dilution from the stock solution to get the desired concentrations.

10% (w/v) Solutions of each of ascorbic acid and ammonium thiocyanate were prepared by dissolving the accurate weight (10 g) of each substance in 100 mL bidistilled water. 0.02% (w/v) ammonium molybdate solution was prepared by dissolving the accurately weighed (0.02 g) of ammonium molybdate in bidistilled water.

Universal buffer solutions of different pH values ranging from 2 to 6 were prepared by adjusting 100 mL solution of the acid mixture to the desired pH value using 0.1 N NaOH solutions. Borax and acetate buffer solutions were prepared using the recommended method by Britton and Robinson concentrations.

2.3. Procedure

1 mL of 0.02% (w/v) of Mo(VI) solution, 1 mL of 4M HCl, 1 mL of 10% (w/v) ascorbic acid and 1 mL of 10% (w/v) ammonium thiocyanate solution were placed in a 100 mL capacity separating funnel. The mixture was left for 15 min at 40 _C. Different volumes (0.1–3.5 mL) of chlorodiazepoxide (1 mg mL^{-1}) were added and diluted with bidistilled water up to 10 mL. After another 10 min, 10 mL of dichloroethane was added twice with 5 mL portions and the solution mixture was shaken vigorously for 1 min. The solution was allowed to be separated into two phases. The organic layer was collected in a 10 mL measuring flask. The absorbance of the formed ion pair was measured at 470 nm, against a blank solution.

3. Results and discussion

3.1. Determination of chlorodiazepoxide using Mo(V)–thiocyanate reagent

This work is undertaken from the view that an ion-pair is formed between the chlorodiazepoxide and Mo(V)–thiocyanate binary complex. The ion-pair formed is soluble in 1,2-dichlo-roethane, while Mo(V)–thiocyanate binary complex is insoluble. The absorption spectrum of the ion-pair shows a maximum at 470 nm against a blank reagent. It is found that, the reduction probability of Mo(VI) to Mo(V) may occur by ascorbic acid or by SCN^- in acidic medium. The sensitivity and stability of Mo(V)–thiocyanate binary complex are enhanced considerably by using ascorbic acid. Ascorbic acid gives reproducible value and masks many interfering ions. It is found that 0.5 %W/V of 10% ascorbic acid is sufficient for a complete conversion of 0.01 mg mL^{-1} of 0.02% (w/v) Mo(VI) to Mo(V) (Fig. 1). Also, it is found that 5 mg mL^{-1} of 10% ammonium thiocyanate is required for maximum absorbance in a final volume of 10 mL aqueous solution (Fig. 2). The maximum absorbance of the formed ion-pair is obtained using 1 mL of 4M hydrochloric acid. represents the reaction of Mo(VI) with ammonium thiocyanate in 1 mL 4 M HCl and in the presence of ascorbic acid. In this method, the complete formation of the ion-pair needs 10 min before extraction with 1,2-dichloroethane at 40°C . The absorbance of Mo(V)–thiocyanate binary complex is stable after 15 min while the ion-pair needs another 10.0 min for its complete formation.

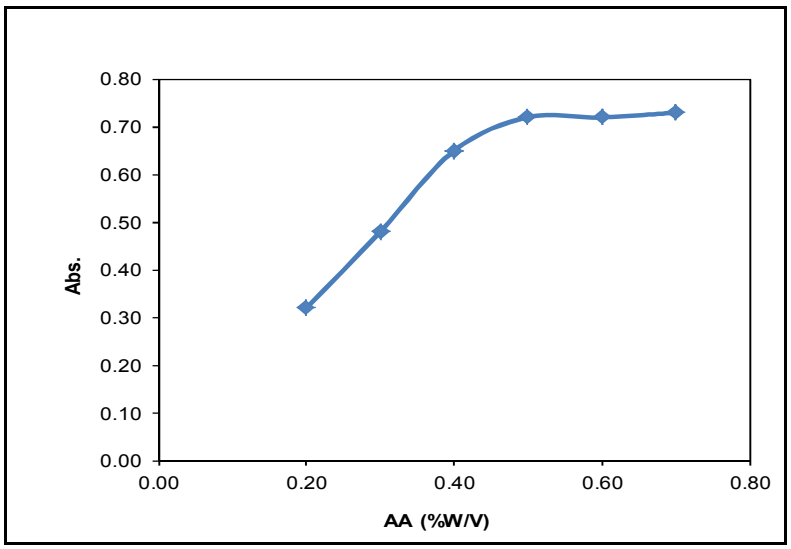

Figure 1. Effect of ascorbic acid concentration on the determination of CDZ using Mo(V)–thiocyanate-drug ion pair at λmax = 470 nm.

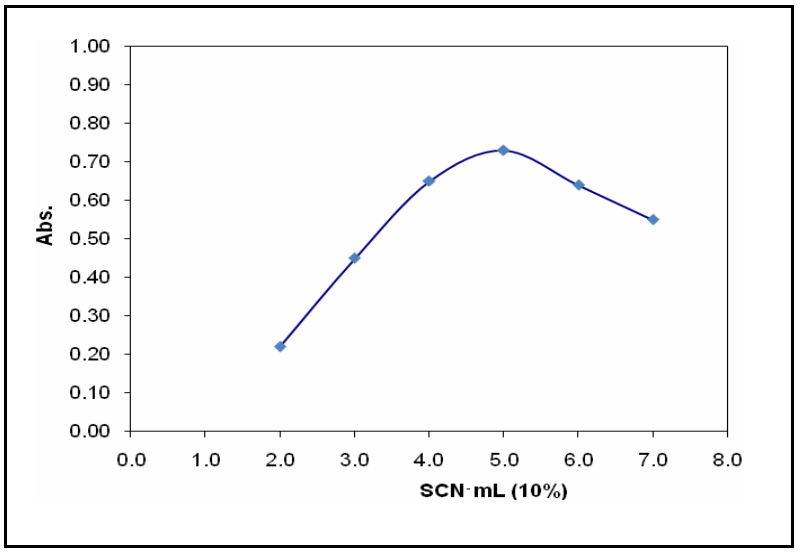

Figure 2. Effect of thiocyanate ion concentration on the determination of CDZ using Mo(V)–thiocyanate-drug ion pair at λmax = 470 nm.

3.5. Analytical figures of merit

Under the optimum conditions, a linear calibration curve over the range of 5-35 mg mL^{-1} was constructed for CDZ. The equation for the line was y= 0.0238X + 0.0314 with regression coefficient (R^2) of 0.9995. Detection limit based on three times standard deviation of the blank (3Sb) was 0.52 mg mL^{-1} and the relative standard deviation (R.S.D) was 2.3 %.

3.6. Determination of CDZ in real sample

In order to test the reliability of the proposed methodology suitable for the assaying of CDZ in pure and pharmaceutical preparations sample. For this 10 tablet of each drug company were prepared and used it to prepare a sample solution with a concentration of appropriate amount of CDZ. After extraction with 3 ml solvent, was called absorption compared to the control solution. The experiment was repeated 3 times for each concentration. The result in Table 1 has been reported.

Table1. Determination of CTAB in anti-Dandruff shampoo

% Recovery	CDZ found (mg L^{-1})	CDZ added (mg L^{-1})	Sample
-	550.0	0.0	Drug from company 1
99	554.0	5.0	
-	535.0	0.0	Drug from company 2
98	540	7.0	
-	545.0	0.0	Drug from company 3
100	555.0	10.0	

4. Conclusion

The data given above reveal that the proposed methods are simple, accurate and sensitive with good precision and accuracy. Also, the reagents utilized in the proposed methods are cheaper, readily available and the procedures do not involve any critical reaction conditions or tedious sample preparation. Thus, this proposed spectrophotometric method can be successfully applied for the determination of chlorodiazepoxid in in pharmaceutical preparations.

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