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ORIGINAL ARTICLE

Use of alizarin red S as a chromogenic agent for the colorimetric determination of dothiepin hydrochloride in pharmaceutical formulations

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Abstract The present study describes two simple, rapid, selective and cost-effective spectrophotometric methods for the determination of dothiepin hydrochloride (DOTH), an antidepressant drug, in bulk drug and pharmaceutical formulations. The first method (method A) is based on the formation of yellow colored ion-pair complex between DOTH and alizarin red S (ARS) in acid medium which was extracted into dichloromethane and the absorbance was measured at 445 nm. The second method (method B) is based on the breaking of the yellow DOTH–ARS ion-pair complex in alkaline medium followed by the measurement of the violet color free dye at 570 nm. Under the optimized conditions, Beer's law is obeyed over the concentration ranges of 2.50–55.0 and 1.00–35.0 μg ml^{-1} DOTH for method A and method B, respectively. The molar absorptivity, Sandell's sensitivity, detection and quantification limits are also calculated. The methods were validated for intra-day and inter-day accuracy and precision; selectivity and robustness and ruggedness. The proposed methods were applied successfully to the determination of DOTH in pure drug and commercial formulations. The accuracy and reliability of the proposed methods were further established by parallel determination by the official method and also by recovery studies via standard addition technique.

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1. Introduction

Dothiepin hydrochloride (DOTH) (dosulepin hydrochloride; 3-dibenzo[b,e]thiepin-11(6H)-ylidene-N,N-dimethyl-1-propanamine hydrochloride) is a tricyclic antidepressant drug (Merck Index, 2006). It is used to treat patients who experience difficulty in sleeping and a loss of appetite (Chen et al., 2008). The drug is official in the British Pharmacopoeia (BP, 2003) which describes a non-aqueous titration method for its determination with potentiometric end point detection. Several analytical methods have been published for the determination of DOTH in pharmaceuticals and include high-performance

liquid chromatography (HPLC) (Sane et al., 1989; Slais and Subert, 1980; Li and Irwin, 1979; Pawlak et al., 1990; Pawlak and Clark, 1989), capillary electrophoresis (Clark et al., 1992), voltammetry (Bishop and Hussein, 1984), ion-selective electrode potentiometry (Hosny, 2007), flow injection potentiometry (Abdel-Ghani et al., 2004a), conductometry (Youssef, 2005; Abdel-Ghani et al., 2004b), spectrofluorimetry (Abdellatef et al., 2006; Walash et al., 2010) and visible spectrophotometry (Abdellatef et al., 2006; Walash et al., 2010; Taha, 2003; Sane et al., 1988; Taha et al., 2002; Hassan, 2008).

To the best of our knowledge, six reports on the use of visible spectrophotometry were found in the literature for the determination of DOTH in pharmaceuticals. Abdellatef et al. (2006) have reported one method based on the condensation of the drug with the mixed anhydrides of malonic and acetic acids at 60 °C. An assay method based on the formation of a binary complex with eosin in acetate buffer has been reported by Walash et al. (2010). Taha (2003) has reported two methods for the assay of DOTH based on either kinetic oxidation reaction of the drug with alkaline potassium permanganate or reaction of the drug with 4-chloro-7-nitrobenzofurazan (NBD-Cl) in the presence of sodium bicarbonate. Few reports (Sane et al., 1988; Taha et al., 2002; Hassan, 2008) based on the formation of ion-pair complexes for the determination of DOTH by reacting of the drug with bromophenol blue (Sane et al., 1988; Taha et al., 2002), bromothymol blue and bromocresol purple (Sane et al., 1988), bromophenol red (Sane et al., 1988), thymol blue (Taha et al., 2002), methyl orange and orange G (Hassan, 2008) in acid medium were also found in the literature. Taha et al. (2002) have reported two methods based on charge-transfer complex formation between DOTH and 2,3-dichloro-5,6 dicyano-p-benzoquinone or p-chloranilic acid. A method based on ternary complex formation between cobalt thiocyanate and DOTH was reported by Hassan (2008). However, many of the previously reported methods suffered from one or the other disadvantage such as pH control, less stability of the measured species, narrow linear dynamic range, heating step, use of expensive chemical and/or complicated experimental setup.

Extractive spectrophotometric procedures have received considerable attention for quantitative determination of many organic compounds of pharmaceutical interest (Mostafa et al., 2002; Ashour et al., 2006; Harikrishna et al., 2008; Milano and Cardoso, 2005; Rajendraprasad et al., 2010). Also, alizarin red S (ARS) has been widely used as an ion-pairing reagent for quantitative analysis of many drugs in pharmaceutical formulations (Basavaiah et al., 1999; Farhadi and Maleki, 2002; Amin, 2002; Farhadia et al., 2003; Kamel et al., 2008). Therefore, the aim of this study was directed to develop two accurate, selective, precise and inexpensive procedures for the determination of DOTH in pharmaceuticals based on ion-pair complex formation using alizarin red S as a reagent.

2. Experimental

2.1. Instrument

A Systronics model 106 digital spectrophotometer (Systronics, Ahmedabad, Gujarat, India) equipped with 1 cm matched quartz cells was used for all absorbance measurements.

2.2. Materials

Pharmaceutical grade dothiepin hydrochloride (DOTH), certified to be 99.60% pure, was received from Abbott India Ltd., Mumbai, India. The following pharmaceutical preparations were purchased from commercial sources in the local market and subjected to analysis: Prothiaden 75 from Abbott India Ltd., Mumbai, India, and Dothip 50 from Micro Labs Ltd., Distt. solan, Himachal Pradesh, India.

2.3. Reagents and chemicals

All the reagents and solvents used were of analytical reagent grade and distilled water was used throughout the study.

1. Alizarin red S (S. d. Fine Chem., Mumbai, India): 0.05% (w/v) solution in water.
2. Hydrochloric acid (Merck, Mumbai, India, sp. gr. 1.18): 0.1 M in water.
3. Potassium hydroxide (Merck, Mumbai, India): 1.0% (w/v) in methanol.
4. Standard stock solution: A stock standard solution of 100 μg ml^{-1} of DOTH was prepared by dissolving accurately weighed 25 mg of pure drug in water and diluting to the mark with the same solvent in a 250 ml calibrated flask.

2.4. Recommended procedure

2.4.1. Method A (based on the measurement of ion-pair complex)

Different aliquots (0.25, 0.50–5.50 ml) of a standard DOTH (100 μg ml^{-1}) solution were accurately transferred into a series of 125 ml separating funnels and the total volume was adjusted to 6.0 ml by adding adequate quantity of water. To each funnel 5 ml of 0.1 M HCl was added, followed by 4 ml of 0.05% ARS solution. The content was mixed well and after 10 min, the formed ion-pair complex was extracted with 10 ml of dichloromethane after shaking for 1 min. The two phases were allowed to separate and the dichloromethane layer was dried over anhydrous sodium sulphate and the absorbance of the yellow DOTH–ARS ion-pair complex was measured at 445 nm against a reagent blank.

2.4.2. Method B (based on the measurement of the free form of ARS from the broken ion-pair)

Into a series of 125 ml separating funnels, 5.0 ml aliquots of a standard solution (100 μg ml^{-1} DOTH) were transferred separately and the total volume in each separating funnel was adjusted to 6.0 ml by adding 1 ml of water. To each funnel were added 5 ml of 0.1 M HCl and 4 ml of 0.05% ARS solution. The content was mixed thoroughly and after 10 min, the ion-pair complex was extracted with 10 ml of dichloromethane by shaking for 1 min. The two layers were allowed to separate and the organic layer of all separating funnels was passed over anhydrous sodium sulphate and then collected in a 50 ml dry standard flask. Varying aliquots (0.1–3.5 ml) of this organic layer, the ion-pair complex of DOTH–ARS (50 μg ml^{-1} in DOTH), were transferred into a series of 5 ml standard flasks and the total volume was adjusted to 3.5 ml by adding dichloromethane.