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ORIGINAL ARTICLE

Extractive-spectrophotometric methods for determination of anti-Parkinsonian drug in pharmaceutical formulations and in biological samples using sulphonphthalein acid dyes

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Abstract A simple, accurate and highly sensitive spectrophotometric methods are proposed for the rapid and accurate determination of amantadine HCl (AMD) using bromocressol green (BCG), bromophenol blue (BPB) and bromothymol blue (BTB). The developed methods involve formation of stable yellow colored chloroform extractable ion-associate complexes of the amino derivative (basic nitrogen) of the AMD with three sulphonphthalein acid dyes, namely; BCG, BPB and BTB, in acidic medium. The ion-associates exhibit absorption maxima at 415, 412 and 414 nm for BCG, BPB and BTB, respectively. AMD can be determined up to 1.5–16.5, 1.4–14.0 and 1.6–17 μg mL^{-1}, respectively. The effect of optimum conditions via acidity, reagent concentration, time, and solvent was studied. The stoichiometry of the reaction was found to be 1:1 in all cases. The low relative standard deviation values indicate good precision and high recovery values. These methods have been successfully applied for the assay of AMD in pharmaceutical formulations. Statistical comparison of the results with the reference method shows excellent agreement and indicates no significant difference in accuracy and precision.

1. Introduction

Amantadine (Scheme 1), an aliphatic tricyclic primary amine (pK_a = 10.1), is excreted predominantly unchanged into the urine and undergoes limited metabolism in man (Aoki and Sitar, 1988). Amantadine HCl (AMD) chemically, 1-adamantanamine hydrochloride, or known formally as 1-aminoadamantane hydrochloride. The molecule consists of adamantane backbone that is substituted at one of the four methyne positions with an amino group. This compound is sold under the name "Symmetrel" for use both as an antiviral and an anti-Parkinsonian drug, against Asian influenza and eventually received

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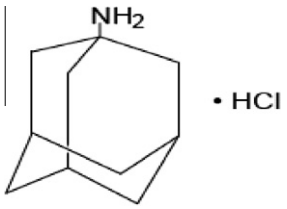

Scheme 1 The chemical structure of amantadine HCl.

approval for the treatment of influenza virus A (Moiseev et al., 1976; Maugh, 1979) in adults, issued an alert to doctors not to prescribe amantadine any more for the season. Among some Asian countries, A/H3N2 and A/H1N1 resistance has reached 100% (Varough et al., 2007). Amantadine HCl is an antiviral agent used against infection with influenza type A virus and to ameliorate symptoms when administered during the early stages of infection as well as in the management of herpes zoster (Prud'homme et al., 1997). It has mild anti-Parkinsonism activity and thus it has been used in the management of Parkinsonism, mainly in the early disease stage and when the symptoms are mild. AMD is usually given by mouth as the hydrochloride salt (Martindale, 2002).

The analytical methods reported for AMD, included high-performance liquid chromatography (Suckow et al., 1999; Fujino et al., 1993), liquid chromatography–mass spectrometry (Wang et al., 2009), liquid chromatography–tandem mass spectrometry (Arndt et al., 2005), Crystal structure and mass spectrometry (Sotolarova et al., 2009), gas chromatography (Leis et al., 2002), capillary electrophoresis (Reichova and Pazourek, 2002), potentiometry (Abdel-Ghani et al., 2002), and fluorimetry (Darwish et al., 2005), Resonance Raman spectroscopy (Stanic et al., 2001), NIR-spectroscopy (Dou et al., 2005), Due to the absence of chromophores and/or auxochromes in the amantadine molecule, it shows no distinct absorption in the UV region above 200 nm. Therefore direct UV spectrophotometry is not useful for its determination. Few spectrophotometric methods (Omara and Amin, in press; Darwish et al., 2005; Stanic et al., 2001; Dou et al., 2005; Sultan, 2004; Rizk and Sultan, 2003; Darwish et al., 2006; Mahmoud et al., 2009) have been reported for its determination. These methods were sophisticated to perform and/or time consuming.

Spectrophotometry is considered as the most convenient analytical technique in pharmaceutical analysis because of its inherent simplicity and availability in most quality control and clinical laboratories (Amin et al., 2009a,b,c; Amin et al., 2008; Gouda et al., 2008). However, AMD does not possess any chromophore in its molecule, which is the essential requirement for the direct or indirect spectrophotometric analysis.

Bromocressol green (BCG), bromophenol blue (BPB) and bromothymol blue (BTB) are known to yield an ion-pair complex, which are applied in the determination of many pharmaceutical compounds (Nafisur et al., 2004; Nafisur and Syed, 2000; Amin et al., 2007; Sevgi, 2007; Gowda et al., 2001; Al-Ghannam, 2006; Incilay and Ayla, 2002; Gouda et al., 2008; Safwan and Raghad, 2005; Abdine et al., 2002; Faten et al., 2006; Parvin et al., 2008; Hérida and Elfrides, 2001; Armağan, 2009; Hisham, 2007).

The present work aims to present a simple, rapid and sensitive method for the determination of AMD in pure form and in their pharmaceutical preparations and can be used for the quality control and assurance of these drugs in industry. The methods are based on the formation of ion-associate between the cited drug and BCG, BPB or BTB. These methods are very simple in applications and less expensive in comparison to the above-mentioned techniques, whereas at the same time offering a high degree of accuracy and precision when compared to the pharmacopoeia method and could be used simply to determine the shelve stability time of the drug.

2. Experimental

2.1. Apparatus

All the spectral measurements were made using either Perkin Elmer Lambda 12 or Perkin Elmer 73B spectrophotometers, with scanning speed 400 nm/min and band width 2.0 nm, equipped with 10 mm matched quartz cells. A centrifuge Model 90-1 with speed 50,000 rpm (USA) was used to carry out for the spiked plasma samples.

2.2. Reagents and materials

All chemicals used were of analytical or pharmacopoeia grade purity and doubly distilled water used. Standard amantadine HCl was obtained from Egyptian Organization for Control and Pharmaceutical Research, Cairo, Egypt.

The acid dye reagents BCG, BPB and BTB were obtained from E. Merck Darmstdt F.R., Germany.

Standard solution 100 μg mL^{-1} of amantadine HCl was prepared by dissolving 10 mg of pure drug (pharmaceutical grade) in the least amount of bidistilled water and made up to 100 mL in measuring flask with bidistilled water. The solution remained stable for 1 month when kept refrigerated.

Stock solution of bromocressol green (BCG), bromophenol blue (BPB) and bromothymol blue (BTB) (1.0×10^{-3} M), were prepared by dissolving 0.0698, 0.0670 and 0.0624 g, respectively, in 100 mL acetone. The acid dye reagents were stable for several weeks.

A 1.0 M solution of HCl was prepared by diluting appropriate volume of AnalaR stock solution to 100 mL measuring

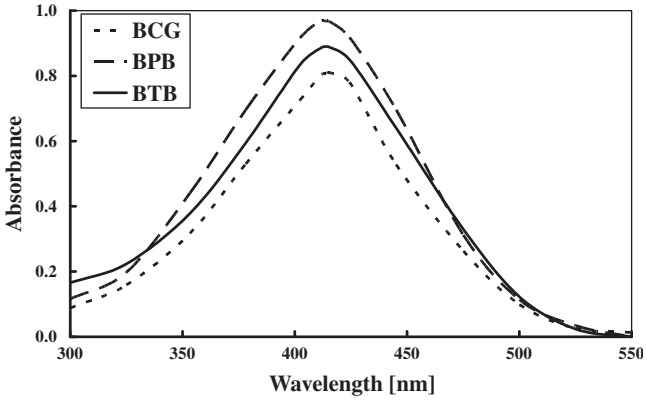

Figure 1 Absorption spectrum of ion-associate complexes of AMD (10 μg mL^{-1}) with (1×10^{-3} M) BCG, BPB and BTB against reagent blank.