Available online at www.sciencedirect.com
SCIENCE DIRECT
Talanta 69 (2006) 239–242
Talanta
www.elsevier.com/locate/talanta

Flow-injection turbidimetric determination of homatropine methylbromide in pharmaceutical formulations using silicotungstic acid as precipitant reagent

Larissa S. Canaes, Oldair D. Leite, Orlando Fatibello-Filho *

Departamento de Química, Universidade Federal de São Carlos, P.O. Box 676, 13560-970 São Carlos, SP, Brazil

Received 30 July 2005; received in revised form 27 September 2005; accepted 27 September 2005
Available online 28 October 2005

Abstract

A flow-injection turbidimetric procedure exploiting merging zones is proposed for determining homatropine methylbromide (HMB) in pharmaceutical preparations. The determination is based on the precipitation reaction of homatropine methylbromide with silicotungstic acid in acidic medium to form a precipitate, which was measured at 410 nm. The analytical curve was linear in the HMB concentration range from 8.1×10^{-5} to 2.2×10^{-4} mol l^{-1}, with a detection limit of 5.0×10^{-6} mol l^{-1}. The recoveries ranged from 96 to 103%, the sampling frequency was 70 determinations per hour and relative standard deviations were less than 1.5% ($n = 10$). The results obtained for commercial formulations using the FIA procedure were in good agreement with those obtained by using a comparative method.

Keywords: Homatropine methylbromide; Flow injection; Turbidimetry; Pharmaceutical formulations

1. Introduction

Antimuscarinic compounds are drugs which play an important role in the central nervous system. The most widely used are atropine, scopolamine, homatropine and homatropine methylbromide (HMB). Atropine and scopolamine, also referred to as (±)-hyoscyamine and hyoscine, respectively, are extracted from plant species belonging to the Solanaceae family. Homatropine prepared synthetically by esterification of mandelic acid with 3α-tropine, is structurally related to atropine and scopolamine [1]. Its effects correspond to those of atropine but are 10 times less pronounced [2] and with the addition of a second methyl radical results in homatropine methylbromide. This compound is better than the atropine because it shows less toxicity in the central nervous system [3]. These drugs are utilized in several clinical situations such as in ophthalmic diagnosis as a mydriatic as well as anticholinergic, antispasmodic and preanesthetic agents [4]. Homatropine methylbromide and dimethicone are also used as antispasmodic and the dose recommended for adults is from 12 to 16 mg kg^{-1} per day and for children is 0.1 mg kg^{-1} per day. But in infants up to two months, daily use may cause episodes of transitory disturbances, like the typical symptoms of the basal ganglia dysfunction, characterized by repeated crises of short duration with tonic back-shift of the head (opisthotonos), deviation of the eyes upward with a looking-fixed and terrified expression and emission of crying and/or guttural sounds [3].

There are very few analytical methods for the determination of homatropine methylbromide in pharmaceutical products. Hanna et al. [5] developed a spectrophotometric method based on the formation of a picric acid–quaternary ammonium complex, which is adsorbed on acid-washed diatomaceous earth in alkaline medium followed by on-column chloroform extraction and spectrophotometric detection at 365 nm. An HPLC method [6] has been proposed in the literature. In this method, a Nucleosil 5 C_8 as stationary phase and acetonitrile plus 0.01 mol l^{-1} phosphate buffer solution at pH 5.0 and 2:3 (v/v) as mobile phase are employed. In the USP method [7], 700 mg of sample are dissolved in 50 ml of glacial acetic acid and 10 ml of 6.0×10^{-2} g ml^{-1} mercuric acetate. After the addition of one drop of crystal violet, the homatropine methylbromide is titrated with 0.1N perchloric acid to a blue-green endpoint. In the Brazilian Pharmacopoeia method [8], bromide anion of the drug is titrated with 0.1 mol l^{-1} silver nitrate solution. In this procedure a metallic silver indicator electrode and an Ag/AgCl

* Corresponding author. Tel.: +55 16 33518098; fax: +55 16 33518350.
E-mail address: bello@dq.ufscar.br (O. Fatibello-Filho).

0039-9140/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.talanta.2005.09.035

double junction reference electrode were used and each ml of the silver nitrate solution consumed corresponds to 37.028 mg of the homatropine methylbromide. Nevertheless, these methods are time-consuming, utilize very costly equipment and/or toxic reagents/organic solvents.

Krug et al. [9] were the first to report the use of turbidimetry in the flow-injection system for determining sulfate by monitoring the barium sulfate suspension. In spite of the routine use of flow-injection system with turbidimetric detection for the determination of inorganic species in plants and water [10], applications to pharmaceutical products are limited [11–13]. Recently, our group proposed a flow-injection turbidimetric method for determining tannin content in tea samples using copper(II) in acetate medium as the precipitant reagent [14].

This paper describes a fast, simple and accurate flow-injection turbidimetric procedure for the determination of homatropine methylbromide in pharmaceutical products. The proposed method is based on the precipitation of homatropine methylbromide with silicotungstic acid in acidic medium to form a precipitate in suspension that is determined turbidimetrically at 410 nm. Eq. (1) shows the reaction between homatropine methylbromide and silicotungstic acid.

$$4C_{16}H_{21}NO_3 \cdot CH_3Br_{(aq)} + H_4Si(W_3O_{10})_{4(aq)} \rightleftharpoons [C_{16}H_{21}NO_3 \cdot CH_3]_4[Si(W_3O_{10})_4]_{(s)} + 4HBr_{(aq)} \quad (1)$$

2. Experimental

2.1. Apparatus

A Hewlett-Packard (Boise, ID, USA) model 8452A UV–vis spectrophotometer with a quartz cell (optical path 1.0 cm) was used in the preliminary experiments.

A 12-channel Ismatec (Zurich, Switzerland) model 7618-50 peristaltic pump supplied with Tygon tubes was used for the propulsion of the solutions. The manifold was constructed with polyethylene tubes of 0.8 mm i.d. Sample and reference solutions were injected into the carrier streams using a laboratory-built three-piece manual injector-commutator made of Perspex®, with two sidebars and a sliding central bar. A Femto (São Paulo, Brazil) model 432 spectrophotometer equipped with a glass flow-cell (optical path of 1.0 cm) at 410 nm was used to monitor the absorbance signal of the insoluble ionic-pair ($[C_{16}H_{21}NO_3{\cdot}CH_3]_4[Si(W_3O_{10})_4]_{(s)}$) yield in the reaction shown in Eq. (1). Transient signals were recorded on a Cole Parmer (Chicago, IL, USA) model 1202-000 two-channels strip-chart recorder.

In the comparative method a metallic silver indicator electrode and an Ag/AgCl double junction reference electrode were used (Brazilian Pharmacopoeia) [8].

2.2. Reagents and solutions

The reagents and solutions were prepared with water from a Millipore (Bedford, MA, USA) Milli-Q system (model UV Plus Ultra–Low Organics Water), and all reagents were of analytical reagent grade.

A 0.05 mol l^{-1} HCl solution was prepared by dilution of 8.5 ml HCl (Merck) in 2000 ml and 25 ml of this solution was standardized with a 0.1 mol l^{-1} NaOH standard solution. A 500 mg l^{-1} homatropine methylbromide stock solution was prepared by dissolving 0.0215 g of homatropine methylbromide (Henrifarma, Brazil) in a 25 ml calibrated flask with 0.05 mol l^{-1} HCl solution. Reference solutions were prepared by proper dilution of the stock solution with 0.05 mol l^{-1} HCl solution.

A 1.0×10^{-3} mol l^{-1} silicotungstic acid stock solution was prepared by dissolving 71.950 mg of this acid (Sigma, USA) in a 25 ml calibrated flask with 0.05 mol l^{-1} HCl solution. Reagent solutions were prepared by proper dilution of the stock solution with the same HCl solution.

2.3. Sample preparations

Homatropine methylbromide was determined in liquid samples purchased from a local pharmacy. A suitable aliquot of each sample was transferred to a 10 ml calibrated flask and diluted to a volume with 0.05 mol l^{-1} HCl.

2.4. Flow diagram

Fig. 1 shows a schematic diagram of the flow-injection merging zones system used in this work. In the injection position, the reagent (L_1, 125 μl) and the sample or reference solution (L_2, 375 μl) were injected simultaneously as individual zones into the 0.05 mol l^{-1} HCl carrier streams (C_1 and C_2; flowing at 2.0 and 3.9 ml min^{-1}, respectively) and merged at the confluence point X. The precipitate formed in the reaction coil B (0.8 mm i.d., 50 cm) was transported to the flow-cell (D) and was monitored at 410 nm.

3. Results and discussion

3.1. Synchronicity and influence of manifold parameters studies

Preliminary studies were carried out to establish the best synchronicity between the sample or reference (S) and reagent solution (R). So, the flow system was evaluated using a colored compound (0.01%, m/m, potassium hexacyanoferrate(III)) as reagent solution (R) and 0.05 mol l^{-1} HCl instead of the sample solution (S) in the flow system diagram shown in Fig. 1. A systematic study was then made maintaining the flow rate of the sample solution in 3.9 ml min^{-1} and varying the flow rate of the reagent solution in the range from 1.5 to 4.7 ml min^{-1}. Afterwards, the flow rate of the reagent solution was fixed in 3.9 ml min^{-1} and the flow rate of sample solution (0.05 mol l^{-1} HCl solution) was changed in the range from 1.5 to 4.7 ml min^{-1}. Fig. 2 shows the best synchronicity obtained for a sample solution flow rate of 3.9 ml min^{-1} and reagent solution flow rate of 2.0 ml min^{-1}. Therefore those flow rates were selected for further studies.