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Original Article

A simple and reproducible estimation of tolterodine tartrate by ion-pair extractive colorimetric method using methyl orange as chromogen

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ABSTRACT

Aim: To develop a simple and validated extractive colorimetric method for the estimation of tolterodine tartrate (TL).

Methods: Extractive colorimetric estimation of tolterodine tartrate (TL) in bulk and pharmaceutical formulation using acidic dye methyl orange (MO) as ion-pairing agent was developed. The yellow ion-pair complex was extracted with chloroform and estimated spectrophotometrically at 420 nm.

Results: Ion-pair complex of TL and MO obeys Beer's law in the range of 2.5–20 μg/mL of TL with a correlation coefficient and Sandal's sensitivity of 0.998 and 0.0494 respectively. The LOD and LOQ of the method were found to be 0.06 and 1.5 μg mL^{-1} respectively. The accuracy and precision of the method was also good in agreement with the recommended % RSD.

Conclusion: The method portrayed here is accurate, precise, rugged, robust and reproducible. The developed method is sensitive and specific for the intended purpose of estimating TL in formulation.

1. Introduction

The antimuscarinic drug tolterodine tartarate (TL) is chemically (R)-N,N-diisopropyl-3-(2-hydroxy-5-methylphenyl)-3-phenylpropanamine L-hydrogen tartarate (Fig. 1), is used to treat urinary incontinence.[1] TL having a high binding affinity for the cholinergic muscarinic receptors that mediates contraction there by in controls the hyperactive the urinary bladder and prevent the frequent urinations.[2] TL does not caused any side effects such as dry mouth, constipation and urine retention like other muscarinics.[3]

We found following methods were reported for the estimation TL either in biological matrix or in pharmaceutical formulation both individual and combined are UV and visible spectrophotometric methods,[4–8] HPLC,[9] HPLC–mass spectrometry,[10,11] capillary chromatography,[12,13] chiral HPLC,[14]

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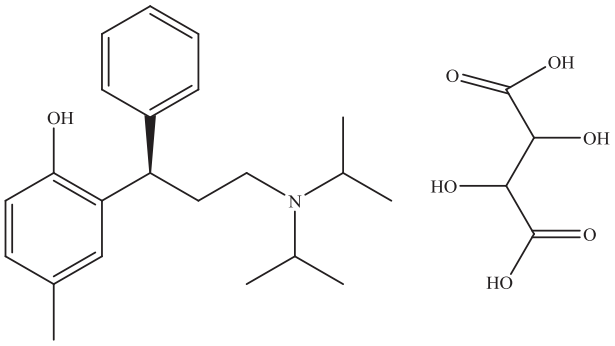

Fig. 1 – Structure of tolterodine tartrate.

HPTLC,[15] UPLC[16] and potentiometric determinations using ion selective electrodes[17] for the estimation of TL and its metabolite. Even though the regular sophisticated methods and such as HPLC and LC–MS/MS are more accurate to estimate the drug in nano gram level, they need complex sample treatment and expensive solvents and reagents for analysis. Hence, the spectrophotometric methods still keep their credential role in drug analysis. UV methods are very simpler than any other methods but they too lack in specificity, they easily affected even by a small amount of UV sensitive solvents or excipients used in formulations but the specificity of visible methods are found to be more than UV by the use of specific reagents suitable to produce chromogen with target analyte because. Among the colorimetric methods of estimation the extractive colorimetric methods are more easy handle and needs less reagents, solution, solvents and non hazardous. In pharmaceuticals many extractive colorimetric methods were reported as in the name of ion-association and ion-pair complex.[18–22]

To the best of our knowledge none of the researchers were reported the estimation of TL using ion-pair complex formation using methyl orange. Hence, in the present study a quantitative ion-pair extractive colorimetric analysis of TL using MO was commenced. The main aim of the present report was to accomplish a simple, accurate, precise and validated extractive colorimetric method for the determination of TL and its checks suitability for assaying the TL content in formulations according to the requirements of United States Pharmacopeia (USP) and International Conference on Harmonization (ICH) guidelines for method validation.[23,24]

2. Experimental

2.1. Chemicals

All chemicals were of analytical reagent grade purchased from Daejung Chemicals & Metals, Gyeonggi-do, South Korea. Doubly distilled water was used to prepare all solutions. Freshly prepared solutions were used for method development and validation. Standard tolterodine tartarate was obtained from Sigma Aldrich and tablets containing 4 mg TL were purchased from a retail pharmacy.

2.2. Instrumentation

A Shimadzu UV mini-1240 UV-visible spectrophotometer with 1 cm quartz cells was used for all spectral measurements with Shimadzu UV Probe system software (version 2.1) and SCINCO, Neosys-2000 DRS-UV provided with liquid sample handling accessories. pH measurements were carried out using a calibrated digital pH meter (Neomet pH-200 L, South Korea).

2.3. Preparation of phosphate buffer

Phosphate buffer of pH4 was prepared by regular procedure.

2.4. Preparation of MO

Require quantity of MO reagent for different concentration (0.01, 0.03, 0.05, 0.05, 0.07, 0.09 wt%) was taken in a100 mL volumetric flask then add 10 mL of 95% alcohol then the remaining volume using water.

2.5. Preparation standard drug solution

A stock solution of 1 mg mL^{-1} was prepared by dissolving a accurate quantity of TL in 10 mL alcohol (99%) and further diluted with water. Working standards were prepared by suitably diluting the above standard stock solution.

2.6. Sample preparation

From the 100 μg mL^{-1} working standard solution, various quantities were transferred in to a series of 100 mL separating funnels then add 2 mL of buffer (pH 4) and 1 mL of 0.1% w/v MO shaken well for 5 min for to complete the complexation. Then 10 mL of chloroform was added. The contents were shaken well and kept aside for few minutes. The organic layer was separated and passed through anhydrous sodium sulphate (previously dried) to remove the water in the organic layer.

2.7. Determination of maximum absorbance λ_{max} and linearity

Full scan absorption spectrum of the yellow TL–MO ion-pair complex thus formed was obtained by scanning the chromogen extracted from 400 to 600 nm using a colorless blank solution prepared in the same way to that of sample solution.

2.8. Validation of the method

For the routine use of the method, optimization was carried out for rapid and quantitative formation of colored ion-pair complexes by a number of preliminary experiments. USP[23] and ICH[24] guidelines were followed for method validation.

2.9. LOD and LOQ

The limit of detection (LOD) is the lowest possible quantity of drug can detectable by the method, and limit of quantitation