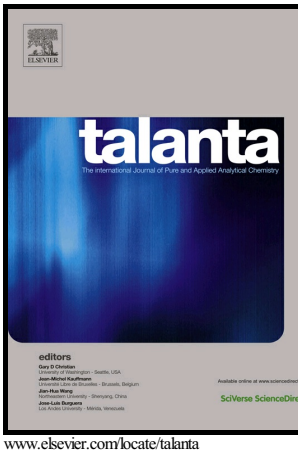

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Novel liquid chromatographic methods for the determination of varenicline tartrate

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Abstract

Two simple, sensitive, rapid, and stability- indicating liquid chromatographic (LC) methods have been developed for the determination of varenicline tartrate. They comprised the determination of varenicline (VRC) in the presence of its oxidative degradates and related impurity (*N*-formyl varenicline) (NFV). The first method was a LC with diode array detection (DAD) at 235 nm using Ristek –Ultra® C_{18} column (100 mm x 2.1 mm, 5 µm). Isocratic elution of VRC was employed using a mobile phase consisting of buffer mixture (1.2% potassium dihydrogen phosphate and 0.08% octane sulphonic acid): acetonitrile (86: 14, v/v), pH (5.0). In the second method; a fluorimetric detection technique was developed, based on precolumn derivatization of VRC using 7-chloro-4-nitrobenzo-2-oxa-1, 3-diazole (NBD- Cl). The fluorescence detector (FLD) was operated at 474 nm for excitation and 539 nm for emission. Isocratic elution was applied with a mobile phase consisting of methanol - distilled water (70: 30, v/v). Separation was achieved using Symmetry® Waters C_{18} column (150 mm x 4.6 mm, 5µm). Linearity, accuracy and precision were found to be acceptable over the concentration ranges of 0.5–20.0 µg mL^{-1} and 0.2 –20.0 µg mL^{-1} with the first and the second method, respectively. The optimized methods were validated and proved to be specific, simple, and accurate for the quality control of the drug in its pharmaceutical preparation.

Keywords: Varenicline tartrate; Diode array detector; Fluorescence detector; NBD- Cl.

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1. Introduction

Varenicline tartarate, [7, 8, 9, 10-Tetrahydro-6, 10-methano-6*H* pyrazino [2, 3-*h*] [3] benzazepine (2*R*, 3*R*) -2,3dihydroxybutanedioate] (Fig.1a) is a novel drug used in the treatment of smoking cessation [1]. VRC is a partial agonist on $\alpha_4\beta_2$ nicotinic acetylcholine receptor. It acts by decreasing the degree of cravings and withdrawal symptoms during the period of smoking cessation [2].

In *vivo*, studies revealed that in the presence of nicotine, VRC acts as a partial agonist by stimulating the release of dopamine and simultaneously blocking the nicotine receptors [3, 4]. VRC is considered the most efficient option for smoking cessation when compared to other pharmacotherapies (e.g., nicotine replacement therapy and bupropion) [5].

Few methods have been described for the determination of VRC in its pharmaceutical preparation using spectrophotometry [6], HPLC [7-9] and LC/MS/MS in