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ORIGINAL ARTICLE

Sensitive and selective spectrophotometric assay of rizatriptan benzoate in pharmaceuticals using three sulphonphthalein dyes

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Abstract Three simple, rapid, selective and sensitive spectrophotometric methods are described for the determination of rizatriptan benzoate (RTB) in bulk drug and in tablets. The methods are based on the formation of intense yellow colored ion–pair complexes between RTB and sulphonphthalein acid dyes, namely, bromophenol blue (BPB), bromocresol purple (BCP), bromothymol blue (BTB) in chloroform medium. The colored products are measured at 425 nm (RTB–BPB complex, RTB–BCP complex) and 420 nm (RTB–BTB complex). The reactions were extremely rapid at room temperature and the absorbance values remained constant for 90 min (methods A and B) and over 12 h (method C). Beer's law was obeyed in the concentration ranges of 0.8–16.0, 1.0–20.0 and 1.2–24 μg ml^{-1} with molar absorptivity values of 1.76×10^4, 1.96×10^4 and 1.63×10^4 $l\,mol^{-1}\,cm^{-1}$ for BPB, BCP and BTB methods, respectively. The limits of quantification (LOQ) were 0.39, 0.34 and 0.27 μg ml^{-1} for BPB, BCP and BTB methods, respectively. Other method validation parameters, such as precision, accuracy, robustness, ruggedness and selectivity, were satisfactory. The composition of the ion–pair was found to be 1:1 by Job's method. The proposed methods were successfully applied to the determination of RTB in commercial tablets. No interference was observed from common tablet adjuvants. Statistical comparison of the results with the reference method showed excellent agreement and indicated no significant difference in accuracy and precision.

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1. Introduction

Rizatriptan benzoate (RTB) is chemically described as *N*,*N*-dimethyl-5-(1H-1,2,4-triazol-1-ylmethyl)-1H-indole-3-ethanamine monobenzoate (Fig. 1) and is a selective 5-hydroxytryptamine1B/1D (5-$HT_{1B/1D}$) receptor agonist. It has a weak affinity for other 5-HT receptor subtypes and was launched in 1998 for the acute treatment of migraine in adults (Goadsby, 1998). Migraine headache is recognized as a chronic disease with episodic occurrences, typically characterized by recurrent disabling attacks of severe headaches, autonomic nervous system

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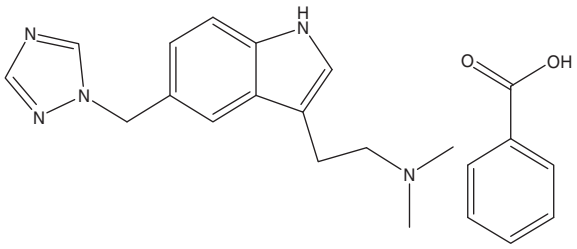

Figure 1 Structure of rizatriptan benzoate.

drug function and neurological aura symptoms. The effectiveness of triptans, which are serotonin 5-$HT_{1B/1D}$ receptor agonist drugs, in these conditions is due to their ability to block the stimulated secretion of neuropeptides from trigeminal nerves to break the nociceptive cycle of migraine. These actions also include constriction of meningeal and cerebral blood vessels (Gory et al., 2005; Oldman et al., 2002; Williamson et al., 1997).

Rizatriptan (RTB) is not official in any pharmacopoeia. A survey of literature reveals that RTB has been estimated in human plasma by liquid chromatography-electrospray tandem mass spectrometry, LC-MS/MS (Guo et al., 2006; Chen et al., 2006) and high performance liquid chromatography with fluorescence detection (Qin et al., 2006; Chen et al., 2004) and in human serum by LC-MS/MS (Vishwanathan et al., 2000). Development of a rapid, sensitive and selective method for the determination of RTB is essential for the analysis of drug in bulk, in drug delivery system and for release dissolution studies. A few methods are found in the literature for the determination of RTB in pharmaceuticals and include UV-spectrophotometry (Amol et al., 2009; Kumari et al., 2010; Vivek et al., 2010; Altinoz et al., 2002), spectrofluorimetry (Altinoz et al., 2002), HPLC when present alone (Zecevic et al., 2008; Jocic et al., 2007) or in combination with other anti-migraine drugs (Sagar et al., 2010). A micro-emulsion electro-kinetic chromatography (MEEKC) has also been developed for the determination of RTB and its degradation products (Mahuzier et al., 2001).

To the best of our knowledge, there are four reports on the use of visible spectrophotometry for the assay of RTB in pharmaceuticals. The first report (Shanmukha Kumar et al., 2010) is concerned with two methods based on either the formation of ion–pair complex between RTB and methyl orange which is extracted into chloroform or redox-complexation reaction in which iron(III) is reduced by RTB and the resulting iron(II) complexed with 2,2′-bipyridyl. The second report (Dannana Gowry and Marothu Vamsi, 2007) describes three methods. First method was based on the oxidative coupling reaction between RTB with 2,6-dichloroquinone-4-chlorimide (DCQC) and the color developed was measured at 610 nm. Second method measures the color produced when sulfonate group of 1,2-napthoquinone-4-sulfonic acid (NQS) replaces imino group of indole moiety of RTB at 530 nm. In third method oxidative coupling product of RTB with brucine in presence of sodium metaperiodate was measured at 530 nm. Third report (Shanmukha Kumar et al., 2011) consists of three methods. First method is based on oxidation followed by complex formation reaction of RTB with 1,10-phenanthroline, ferric chloride and ortho-phosphoric acid to form an orange red colored chromogen measured at 510 nm. In the second method the blue colored chromogen formed by reduction of FC-reagent in alkaline medium by RTB was measured at 610 nm. Third method was based on the measurement of color developed by extracted ion association complex between alizarin red and RTB at 425 nm. Fourth report (Ramzia et al., 2011) renders one method based on the formation of charge transfer complex between RTB and 7,7,8,8 tetracyanoquinodimethane (TCNQ) measured at 744 nm.

However, the reported methods, particularly those based on chromatography are complex, require expensive experimental setup and skilled personnel and inaccessible to many laboratories in developing and under developed nations. In contrast, visible spectrophotometry is considered as the most convenient analytical technique in most quality control and clinical laboratories. All the previously reported visible spectrophotometric methods are less sensitive and few methods require a rigid pH control and tedious liquid–liquid extraction steps, some methods have a relatively narrow linear range and involve heating step as cited in Table 1.

On the other hand, extraction-free spectrophotometry based on ion–pair reactions has, in recent years, received considerable attention for the quantitative determination of several pharmaceutical compounds (Al-Ghannam, 2006; Abdine et al., 2002; Manjunatha et al., 2008; Basavaiah et al., 2009 and Shahdousti et al., 2008) owing to its simplicity, speed, selectivity and sensitivity.

In the present communication, we report the development of three accurate and precise extraction-free spectrophotometric methods based on the chloroform soluble ion–pair complexes between RTB with sulphonphthalein dyes BPB, BCP and BTB. The absorbance measurements were made at 425 nm (BPB, BCP) or 420 nm with BTB without extraction. The methods were applied to the determination of RTB in tablets. No interference was observed from the tablet additives. The methods provide rapid and economic procedures, and more sensitive compared to the previously reported spectrophotometric methods (Shanmukha kumar et al., 2010, 2011; Dannana Gowry and Marothu Vamsi, 2007; Ramzia et al., 2011).

2. Experimental

2.1. Instrument

All the absorbance measurements were made using a Systronics model 106 digital spectrophotometer provided with 1 cm matched quartz cells.

2.2. Materials

Pharmaceutical grade rizatriptan benzoate (RTB) was received from Jubilant Life Sciences, Mysore, India, as a gift and used as received. The following formulations were obtained from commercial sources and subjected to analysis: Rizora-10 and Rizora-5 from Intas Pharmaceuticals Ltd., Ahmedabad, India.

2.3. Reagents and chemicals

All the reagents and solvents used were of analytical-reagent grade. Bromophenol blue (BPB), bromocresol purple (BCP) and bromothymol blue (BTB) (all from Loba Chemie Ltd.,

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