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ORIGINAL ARTICLE

Development and validation of new analytical methods for simultaneous estimation of Drotaverine hydrochloride in combination with Omeprazole in a pharmaceutical dosage form

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KEYWORDS

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Abstract A rapid and precise method (in accordance with ICH guidelines) is developed for the quantitative simultaneous determination of Drotaverine hydrochloride and Omeprazole in a combined pharmaceutical dosage form. Three methods are described for the simultaneous determination of Drotaverine hydrochloride and Omeprazole in a binary mixture. The first method was based on UV-Spectrophotometric determination of two drugs, using Vierordt's simultaneous equation method. It involves absorbance measurement at 226.8 nm (λ_{max} of Drotaverine hydrochloride) and 269.4 nm (λ_{max} of Omeprazole) in methanol; linearity was obtained in the range of 5–30 μg ml^{-1} for both the drugs. The second method was based on HPLC separation of the two drugs using potassium dihydrogen phosphate buffer pH 5.0: Acetonitrile: Triethylamine (60:40:0.5, v/v) as a mobile phase. Areas were recorded at 260 nm for both the drugs and retention time was found to be 2.71 min. and 3.87 min for Drotaverine hydrochloride and Omeprazole, respectively at 1.0 mL/min flow rate. The selected chromatographic conditions were found to determine Drotaverine hydrochloride and Omeprazole quantitatively in a combined dosage form without any physical separation. The method has been validated for linearity, accuracy and precision. Linearity was found over the range of 5–30 μg mL^{-1} for both drugs. The third method was based on HPTLC method for simultaneous quantification of these compounds in pharmaceutical dosage forms. Precoated silica

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gel 60 F_{254} plate was used as stationary phase. The separation was carried out using Glacial acetic acid:Cyclohexane:Methanol:(80:15:5 v/v/v) as mobile phase. The proposed method was found to be fast, accurate, precise, reproducible and rugged and can be used for a simultaneous analysis of these drugs in combined formulations.

1. Introduction

Drotaverine hydrochloride (DRO) chemically 1-[(3,4-[diethoxyphenyl) methylene]-6,7-diethoxy-1,2,3,4-tetrahydroisoquinolene (Fig. 1) is a *papaverine* analog mainly used as an antispasmodic and smooth-muscle relaxant in pain associated with gastrointestinal colic, biliary colic, and postsurgical spasms. It is an antispasmodic agent with smooth muscle relaxant properties. It exerts its action by inhibiting phosphodiesterase enzyme IV which is specific for smooth muscles (Sweetman, 2002; Oneil et al., 2001). Omeprazole (Fig. 2) is chemically known as 6-methoxy-2-[(4-methoxy-3,5-dimethylpyridin-2-yl)methylsulfinyl]-1H-benzimidazole. Omeprazole is a used as an antiulcer drug and against other acid-related diseases (Stenhoff et al., 1999). Omeprazole (OME) is the proton pump inhibitor. In the acidic conditions of the stomach, Omeprazole reacts with a cysteine group in H+/K+-ATPase, thereby destroying the ability of the parietal cells to produce gastric acid (Tripathi, 2008). Literature review reveals that methods have been reported for the analysis of Drotaverine hydrochloride by high-performance liquid chromatography (Bolaji et al., 1993; Lalla et al., 1993; Metwally et al., 2006; Panigrahi and Sharma, 2008; Patel et al., 2007; Topagi et al., 2010; Metwally, 2008), thin layer chromatography (Ayad et al., 2006; Metwally et al., 2006), spectrophotometry (Abdellatef et al., 2007; Dahivelkar et al., 2007; Kothapalli et al., 2010) and voltammetry (Ziyatdinova et al., 2007). Several analytical methods that have been reported for an estimation of Omeprazole are HPLC (Dubuc et al., 2001; El-Sherif et al., 2006; Murakami et al., 2007; Subramanian and Kumar,2007), LC–MS (Petsalo et al., 2008) and HPTLC (Raval et al., 2008). For Omeprazole methods reported are HPLC–MS and HPLC–UV in biological fluids (Kange et al., 2006; Yuch et al., 2001), capillary electrophoresis (Berzas and Castanda, 2005), HPLC employing electrochemical and coulometric detection (Gregory et al., 2001), TLC (Agbaba et al., 2004) and spectrophotometry (Lakshmi and Venkatesan, 2003).

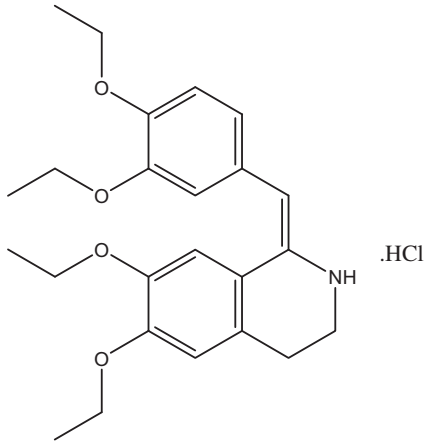

Figure 1 Structure of Drotaverine hydrochloride.

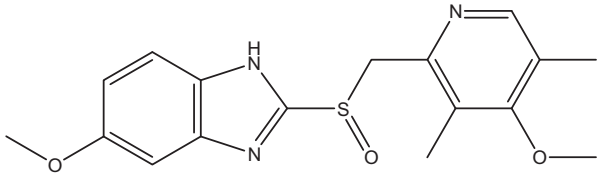

Figure 2 Structure of Omeprazole.

The purpose of this research was to establish and validate, in accordance with International Conference on Harmonization (ICH) guidelines, an accurate, economical, and reproducible procedure for quantitative analysis of Drotaverine hydrochloride and Omeprazole as the bulk drug and in tablet dosage forms. It was thought worthwhile to develop precise, accurate UV spectrophotometric, HPLC and HPTLC methods for simultaneous determination of Drotaverine hydrochloride and Omeprazole in tablets.

2. Materials and methods

2.1. Chemicals and reagents

Commercially available Ranispas-DV (Penta Biotech, India) drug containing 40 mg of Drotaverine hydrochloride and 10 mg of Omeprazole was used. HPLC grade acetonitrile and AR grade potassium dihydrogen phosphate was purchased from Merck, India and were used as received. All other reagents employed are of high purity analytical grade.

2.2. UV-spectrophotometry

SHIMADZU double beam UV/Visible recording spectrophotometer (Model:1700) with 2 nm spectral bandwidth was employed for all spectrophotometric measurements using 10 mm matched quartz cell and Borosil glass wares were used for the study. Calibrated electronic single pan balances Sartorius CP 225 D, pH Meter, Enertech Fast Clean Ultrasonicator were also used during the analysis. UV-Spectrophotometric determination of two drugs was done using Vierordt's simultaneous equation method (Davidson et al., 2001).

2.2.1. Standard stock solution

The standard stock solutions of Drotaverine hydrochloride and Omeprazole were prepared by dissolving accurately weighed 100 mg of drug in 100 ml of a mixture of methanol and double distilled water (50:50) in two separate 100 ml volumetric flasks to get a concentration of 1000 μg/ml. Both were appropriately diluted with a mixture of methanol and double distilled water (50:50) to get a concentration of 100 μg/ml and were kept as stock solutions.

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