Journal of the Association of Arab Universities for Basic and Applied Sciences (2014) **15**, 53–60

University of Bahrain

Journal of the Association of Arab Universities for Basic and Applied Sciences

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ORIGINAL ARTICLE

Applications of simultaneous equation method and derivative method for the determination of rabeprazole sodium and levosulpiride in pharmaceutical dosage form and dissolution samples

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Received 2 September 2012; revised 18 May 2013; accepted 19 May 2013
Available online 17 June 2013

KEYWORDS

Rabeprazole sodium;
Levosulpiride;
Simultaneous equation method;
Derivative spectrophotometry;
Dissolution

Abstract Two simple, accurate, precise, economical procedures, entailing neither irksome sample treatment nor tedious extraction process have been developed for the simultaneous estimation of rabeprazole sodium and levosulpiride in combined tablet dosage form. The first method was based on employing simultaneous equation method for analysis of both drugs. Rabeprazole sodium and levosulpiride have shown absorbance maxima at 284 and 232 nm in methanol, respectively. The second method was based on derivative spectrophotometric method involving the determination of both the drugs at their respective zero crossing point (ZCP). The first order derivative spectrum was obtained in methanol and the determinations were made at 231.2 nm (ZCP of levosulpiride) for rabeprazole sodium and 246.2 nm (ZCP of rabeprazole sodium) for levosulpiride. The linearity was obeyed in the concentration range of 1-20 μg/ml for both drugs. The medium of dissolution was used 900 ml of phosphate buffer pH 7.4 using a USP type 2 apparatus at a stirring rate of 100 rpm. The drug release was evaluated by developed spectroscopic methods. The suitability of the developed method for quantitative determination of rabeprazole sodium and levosulpiride was proved by validation.

1. Introduction

Chemically, rabeprazole sodium (RAB) is 2-({[4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methanesulfinyl)-1H-benzimidazole sodium salt (Indian Pharmacopoeia, 2010; Merck Index, 2003) (Fig. 1) is a class of antisecretary compounds that selectively inhibits gastric acid secretion by inhibiting the H^+ and K^+ ATPase at secretary surface of the gastric parietal cell

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Peer review under responsibility of University of Bahrain.

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http://dx.doi.org/10.1016/j.jaubas.2013.05.005

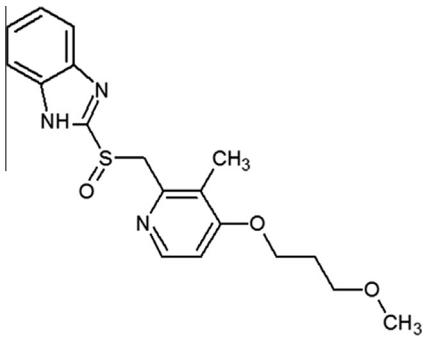

Figure 1 Structure of rabeprazole sodium.

(Tripathi, 2003). It has been shown to be effective for the treatment of gastric and duodenal ulcers and for gastro-esophageal reflux disease (GERD) (Swan et al., 1999).

Levosulpiride (LEV) is a levo-enantiomer of racemic sulpiride belonging to the substituted benzamide group. Chemically it is 5-(aminosulfonyl)-N-[(1-ethyl-2-pyrrolidinyl)methyl]-2-methoxybenzamide (Fig. 2) (Merck Index, 2003). It is a typical neuroleptic drug with sulpiride and inhibits dopaminergic D2 receptors at the trigger zone both in the central nervous system and in the gastrointestinal tract as stated (Barbeau, 2008).

Combination of rabeprazole sodium and levosulpiride is available in the market which is used to help to reduce such as the amount of acid produced by the stomach and improve gastrointestinal motility and to treat conditions such as heartburn, GERD and gastritis (Swan et al., 1999). Once rabeprazole has left the stomach, absorption occurs within 1 h of administration. The bioavailability is approximately 52%. Due to low solubility, oral formulations of levosulpiride suffer from low absorption in the gastrointestinal tract thus resulting to lower bioavailability. Orally administered levosulpiride is absorbed from upper portion of the small intestine (Barbeau, 2008).

Drug dissolution (or release) testing is an analytical technique used to assess release profiles of drugs in pharmaceutical products, generally solid oral products such as tablets and capsules (United States Pharmacopeia, 2009; Brown, 2005). This test gains its significance from the fact that if a drug from a product is to produce its effect; it must be released from the product and should generally be dissolved in the fluids of the gastrointestinal (GI) tract. Thus, a drug dissolution test may be considered as an indicator of potential drug release and absorption characteristics of a product in humans as well as

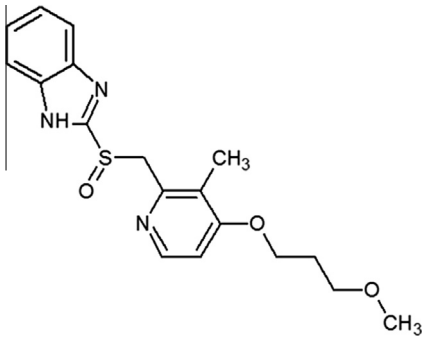

Figure 2 Structure of levosulpiride.

in animals. Therefore, a dissolution test is often considered a surrogate for the assessment of availability of drugs in the body, generally termed bioavailability (Siewert et al., 2003; Swartz, 2011).

RAB is official in Indian Pharmacopoeia which includes HPLC assay method. The literature reports many analytical methods like spectrophotometry (Gunji et al., 2012; Rahman et al., 2008), chromatography (Bharathi et al., 2009; Choudhary et al., 2009), Thin layer chromatography and High performance thin layer (Osman and Osman, 2009; Suganthi et al., 2008) and dissolution method (Garcia et al., 2006) for estimation of Rabeprazole sodium alone or in combination with other drugs. LEV is not official in any pharmacopoeia. Analytical methods like spectrophotometry (Manjunath et al., 2011), stability indicating HPLC and HPTLC (Naguib and Abdelkawy, 2010), and chromatography (Walash et al., 2012) for the determination of levosulpiride alone or in combination with other drugs have been reported.

Simultaneous estimation of RAB and LEV in combined dosage form by UV-spectrophotometric methods (Pekamwar et al., 2013; Bhalodia et al., 2012) and HPLC (Patel et al., 2012; Sirisha and Ravikumar, 2012; China Raju et al., 2012; Agarwal and Jagdigsh, 2012) has been reported in the literature. The reported UV method (Pekamwar et al., 2013) describes only direct simultaneous estimation of RAB and LEV at mentioned wavelengths.

The authors did not consider interference in quantitation of one drug due to absorption of other drugs at same wavelength. Another reported method (Bhalodia et al., 2012) was absorbance ratio method for simultaneous spectroscopic estimation of RAB and LEV.

In the present work, two simple UV spectrophotometric methods for simultaneous estimation of rabeprazole sodium and levosulpiride in combined dosage form and its application to determination of dissolution sample were reported. These methods were validated according to the ICH Q2 (R1) guidelines ICH (2005).

2. Experimental

2.1. Materials and reagents

Rabeprazole sodium and levosulpiride bulk drugs were obtained from Torrent Pharma. Pvt. Ltd, Gujarat, India, as gift samples. Methanol (AR Grade) was purchased from Merck (India) Ltd., Mumbai, India. AR grade chemicals and distilled water were used during experimentation. Commercial pharmaceutical preparation (Rabekind Plus®, Mankind Pharma, New Delhi) was procured from the local pharmacy shop, containing 20 mg of rabeprazole sodium and 75 mg of levosulpiride (extended release).

2.2. Instrumentation

A UV-Visible spectrophotometer (Shimadzu-1700, UV Probe 2.21 software) with a spectral bandwidth of 1 nm was employed for all spectroscopic measurements, using a pair of 1.0 cm matched quartz cells over the range of 200-400 nm. The USP dissolution apparatus Electrolab TDT-08L, was used for dissolution study. The Elico Li 614 pH analyzer was used to determine the pH of dissolution media, deaerated by