Arabian Journal of Chemistry (2015) **8**, 118–128

King Saud University

Arabian Journal of Chemistry

www.ksu.edu.sa
www.sciencedirect.com

ORIGINAL ARTICLE

Validated stability indicating RP-HPLC method for simultaneous determination and in vitro dissolution studies of thiocolchicoside and diclofenac potassium from tablet dosage form

Suraj D. Jadhav *, **S.R. Butle, Sachin D. Patil, P.K. Jagtap**

School of Pharmacy, Swami Ramanand Teerth Maharathwada University, Vishnupuri, Nanded 431 606, MS, India

Received 3 November 2010; accepted 16 January 2011
Available online 21 January 2011

KEYWORDS

Thiocolchicoside;
Diclofenac potassium;
Sink condition;
Photodiode array detector;
Dissolution

Abstract A simple, rapid, and robust stability indicating RP-HPLC method has been developed and validated to measure thiocolchicoside (TH) and diclofenac potassium (DP) at single wavelength (258 nm) in order to assess assay and in vitro drug release profile of drug from tablet formulation. A gradient elution of samples performed on Zorbax SB CN 250 mm × 4.6 mm, 5 μm column with buffered mobile phase consisting solvent A (5 mM sodium dihydrogen phosphate, pH 2.5) and solvent B (methanol) delivered at flow rate 1.0 mL/min. For dissolution study, the sink condition has been established from quantitative solubility of TH and DP API in different dissolution medium recommended by USP for immediate release formulation and the optimized dissolution condition was: pH 6.8 deaerated potassium dihydrogen phosphate buffers, paddle rotation speed 50 rpm and vessel volume 900 mL. Discriminating release of TH and DP achieved more than 96% of labeled amount over 45 min and drug dissolution was concluded after 60 min. The HPLC method and dissolution test condition were validated to meet requirement for regulatory filling and this validation inferred from specificity, precision, accuracy, linearity and robustness. In addition filter suitability, standard and sample solution stability was demonstrated.All results were acceptable and this confirmed that the method is suitable for its intended use in routine quality control and assay of drugs.

1. Introduction

Thiocolchicoside (TH) is (s)-N-[3-(BD-glucopyranoxyloxy)-5,6,7,9-tetrahydro-1,2-dimethoxy-10-(methylthio)9-oxobenzo-[a]heptalen-7yl]acetamide, sulfur derivative of cochicoside (Fig. 1a) and possesses non-sedating muscle relaxant action (Merck Index, 1998; Indian Pharmacopoeia, 2010), while diclofenac potassium (DP) is 2-[(2,6-dichlorophenyl)amino]

* Corresponding author. Tel.: +91 9096254036.
E-mail address: surajjadhav111@gmail.com (S.D. Jadhav).
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.arabjc.2011.01.018
1878-5352 © 2011 Production and hosting by Elsevier B.V. on behalf of King Saud University.

phenyl acetic acid (Fig. 1b) which possesses anti-inflammatory and analgesic properties (Indian Pharmacopoeia, 2010; British Pharmacopoeia, 2004; United State Pharmacopoeia, 2005). The combination of TH and DP have synergetic action and is prescribed for symptomatic relief of low back pain, post operative pain, and rheumatic arthritis osteoarthritis, musculoskeletal injuries and chronic pain associated with cancer (Janbroers, 1987).

Literature survey revealed that several analytical methods have been described for analysis of TH as single component or in combinations with other drugs, Viz-spectrophotometric methods (Sutherland et al., 2002; Lu et al., 2006), TLC (El-Ragehy et al., 2003), HPLC (Ondra et al., 1995; Rosso and Zuccaro, 1998; Tracqui et al., 1996) and radioimmunoassay (Sandouk et al., 1995). Similarly literature of DP revealed several spectrometric methods (Agatonovic-kustrin et al., 1997; Botello and Caballero, 1995; Matin et al., 2005; Sparidans et al., 2008) as well as chromatographic methods (Vora et al., 2007; Kaphalia et al., 2006; Lee et al., 2000; Klimes et al., 2001) for determination of DP as single drug or in combination with other drugs.

However, the exhaustive literature survey revealed that none of the most recognized pharmacopoeias or any journals includes these drugs in combination for the simultaneous determination of TH and DP and the information regarding the stability of the drugs is not available. So it is felt essential to develop a liquid chromatographic procedure which will serve a reliable, accurate and stability indicating HPLC method for the simultaneous estimation and in vitro dissolution studies of TH and DP in tablet dosage form.

The main purpose of an oral solid pharmaceutical dosage form is to make available a certain and defined amount of active substance to human body through the gastrointestinal system (Morrison and Campbell, 1965). The pharmaceutical industry and the regulatory agencies focus on the evaluation of the release kinetics from dosage forms, and this study is generally performed on official or nonofficial dissolution devices (Jashnani et al., 1993). The in vitro dissolution profiles obtained from dissolution rate studies have also been used in an attempt to characterize the in vivo behavior of drugs with little success (Rowe and Carless, 1981; Anchisi et al., 1998; Satiropoulus et al., 1981). The significance of stability testing is to provide evidence on how the quality of a
drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light, enables recommendation of storage conditions, retest periods, and shelf lives to be established.

The principal aspects of drug products that play an important role in shelf life determination of tablet formulation are assay and dissolution of active drug and degradants generated during the stability study. The assay of drug product in stability test sample needs to be determined using stability indicating method, as recommended by the International Conference on Harmonization (ICH) guidelines (ICH, 2000) and USP 29 (United State Pharmacopoeia, 2005).

The main purpose of this investigation is to develop and validate simple, precise, sensitive and accurate stability indicating reversed phase high-performance liquid chromatographic methods for assay and in vitro dissolution studies.

2. Experimental

2.1. Chemicals and reagents

All reagents and solvent were of analytical and HPLC grade and included hydrochloric acid, monobasic sodium phosphate, monobasic potassium phosphate, sodium acetate trihydrate, orthophosphoric acid and methanol were purchased from Merck Ltd., Mumbai, India. Wockhardt Ltd., Aurangabad, India, kindly supplies TH and DP API, tablet and placebo of tablet. High purity deionized water was obtained from Millipore, Milli-Q (Bedford, MA, USA) purification system. The 0.45-μm nylon filters were purchased from Advanced Micro Devices Pvt. Ltd., Chandigarh, India.

2.2. Instrumentations

HPLC system (Waters Milford, USA) equipped with in built auto-sampler and quaternary gradient pump with an on-line degasser was used. The column compartment having temperature control, photodiode array (PDA) detector (2996) and dual wavelength detector (2487) was employed throughout the analysis for detection. Chromatographic data was acquired using Empower software-2. All dissolution experiments were carried out using a dissolution instrument Electro lab TDT-08L (Electrolab, India) attached to auto-sampler.

2.3. Chromatographic condition

Zorbax SB CN 250 mm × 4.6 mm, 5 μm (Agilent technology, USA) column was used as stationary phase maintained at ambient temperature. Gradient elution with the mobile phase involved a variable composition of solvent A (5 mM sodium dihydrogen phosphate, pH 2.5) and solvent B (methanol). The mobile phase was pumped through the column with flow

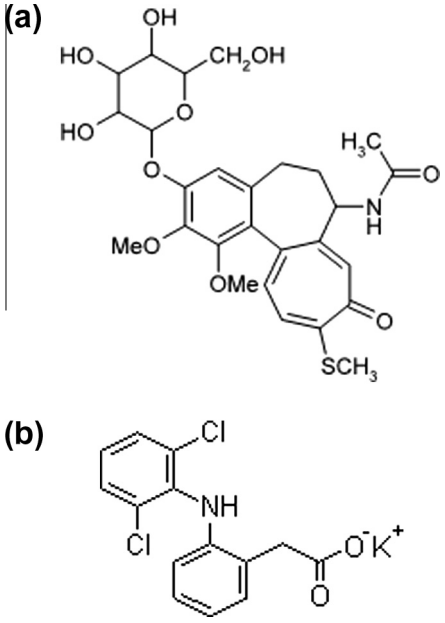

Figure 1 Chemical structure of (a) thiocolchicoside (TH) and (b) diclofenac potassium (DP).