Validation of RP-HPLC Method for Simultaneous Estimation of Cefixime Trihydrate and Clavulanate Potassium in Tablets

S.S. Zade*, V.B. Bhatpalliwar, N.S. Mendhule, M.V. Murkhekar, R.N. Alaspure, and N.J. Durugkar
Sharad Pawar College of Pharmacy, Wanadongri, Nagpur 441 110, Maharashtra, India.
Received September 6, 2012; accepted March 17, 2013

ABSTRACT
A simple, accurate, precise, rapid and economic HPLC method has been developed and validated for the simultaneous estimation of cefixime trihydrate and clavulanate potassium in tablet dosage forms. The chromatographic separation was achieved on a Hypersil C18 column (4.6 x 250 mm, 5 μm particle size). For HPLC method development, a mobile phase consisting of methanol: 30 mM potassium dihydrogen phosphate buffer pH 3.0 adjusted with orthophosphoric acid (30:70 v/v) was used at flow rate of 1.0 ml/min. The optimum wavelength selected was 278 nm. Under these chromatographic conditions, cefixime trihydrate and clavulanate potassium peaks were well resolved, with retention times of cefixime trihydrate and clavulanate potassium being 5.8266 and 3.2633 min, respectively. The proposed method was found to have excellent linearity in the concentration range 20-100 μg/ml with correlation coefficients r2 = 0.9946 and 0.9926, respectively. The method was validated for linearity, precision, LOD, LOQ and robustness. The proposed method was optimized and validated as per the ICH guidelines.

KEYWORDS: Cefixime trihydrate, Clavulanate potassium, RP-HPLC, Validation.

Introduction
High performance liquid chromatography offers advantages of speed, resolution and sensitivity. Reverse phase high pressure liquid chromatography (RP-HPLC) is particularly useful for separating polar compounds such as drugs and their metabolites, peptides, and vitamins (Chatwal, 2002). Cefixime in anhydrous trihydrate in tablet form (200 mg) in combination with clavulanate potassium (125 mg) is introduced by Cipla, FDC and Piramal under brand names CLACENT, ZiFiCV200 and OMNATAX-CV, respectively. Cefixime trihydrate is an orally active, third generation cephalosporin antibiotic that acts by inhibiting cell wall synthesis and clavulanate potassium, which is an irreversible inhibitor of bacterial beta-lactamase enzymes from streptomycetes clavuligerus. Chemically, CEF is (6R,7R)-7-[(2-oxo-4-thiazolyl)glyoxylamido]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-carboxylic acid, 7-[(Z)-O-(carboxymethyl)oxime]trihydrate, a white to light yellow crystalline powder soluble in methanol (IP, 1996) and CLAVP is 4-Oxa-1-azabicyclo[3.2.0]heptanes-2-carboxylic acid, 3-(2-hydroxyethylidene)-7-oxo-monopotassium salt, 2R-(2a,3Z,6a)-, a white light yellowish white, crystalline powder soluble in water and methanol (IP, 1996).

Literature surveys reveal that several methods were reported for cefixime trihydrate and clavulanate potassium individually and with other combinations (Khandagle, 2011; Rathinavel, 2008; Raj et al.2010; Dragica, 2003; Kathiresan, 2009; Neto et al., 2005; Aghazadeh, 2001; Kim, 2009; Shah, 2006;2010; Krzysztof, 2001; Malathi, 2009; Dhoka, 2010; Khaja, 2010; Deshpande et al., 2010; Nanda, 2009). However, there are few reports of methods for simultaneous estimation of cefixime trihydrate and clavulanate potassium in a single dosage form.