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Effect of system variables involved in packed column SFC of nevirapine as model analyte using response surface methodology: Application to retention thermodynamics, solute transfer kinetic study and binary diffusion coefficient determination

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Abstract

A multifactor optimization technique is successfully applied to study the effect of simultaneously varying the system variables on feasibility of nevirapine analysis by packed column supercritical fluid chromatography (PC-SFC). The optimal conditions were determined with the aid of the response surface methodology using 3^3 factorial designs. The method is based on methanol-modified carbon dioxide as the mobile phase at flow rate of 3.0 ml/min with elution through a JASCO Finepak SIL-5, [C_{18} (5-micron, 25 cm × 4.6 mm, i.d.)] column using photodiode array detection. The method has been successfully used to analyze commercial solid dosage form to assess the chromatographic performance of SFC system. The present work briefs the thermodynamic applications of PC-SFC with an emphasis on the results of nevirapine. The foremost of such applications is the determination of solute diffusion coefficient in supercritical mobile phase by Taylor–Aris peak broadening technique.

Keywords: Nevirapine; Packed column Supercritical Fluid Chromatography (PC-SFC); Response surface methodology; Diode array detection; Thermodynamic applications; Diffusion coefficient; Taylor–Aris peak broadening technique

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1. Introduction

Supercritical Fluid Chromatography (SFC) is one of the most widely used methods for the separation of non-polar solutes [1–4]. Organic modifiers are used to increase the elution strength of the mobile phase [5,6]. Facility of on-line addition of modifier and controlling of backpressure has made routine SFC analysis of drugs more feasible [7–19]. The technique is faster, generates less disposable waste and offers more flexibility than LC for analysis [20–24].

The use of response surface methodology on PC-SFC variables interaction study using nevirapine as model analyte has been described. Nevirapine being partial non-polar in nature has been selected as a model analyte for this type of study. Results are presented for the three-factor study, where pressure, temperature and modifier concentration are chosen to give the optimal chromatographic performance. The effects of three factors were studied on different chromatographic parameters (dependent variables) like peak area, peak height, height equivalent to theoretical plate, asymmetrical factor, retention time and capacity factor. The best set of conditions was chosen for validation as per ICH guidelines [25,26] and its updated international convention [27].

Nevirapine (Fig. 1) chemically 11-cyclopropyl-5, 11-dihydro-4-methyl-6H-dipyrido [3, 2-b: 2′, 3′-e] [1,4] diazepin-6-one, a dipyridodiazepinone is a non-nucleoside reverse transcriptase inhibitor of human immunodeficiency virus type 1 (HIV-1) [28–31].

Literature survey reveals individual determination of nevirapine in biological fluids using GC [32], HPLC-UV methods [33–35], HPLC following SPE [36] and LC-MS-MS method [37] and HPTLC method [38]. Several HPLC methods [39–46] for the simultaneous quantitation of nevirapine along with other HIV suppressing drugs have been published.

Measurements of thermodynamic parameters by PC-SFC constitute an important, varied and intriguing application of this technique to produce chromatographic retention data. Using an octadecylsilica stationary phase over a temperature range from 313 to 333 K and an average pressure range from 15 to 35 Mpa, the thermodynamic and kinetic aspects of retention mechanism was examined. Thermodynamic behavior was characterized by the

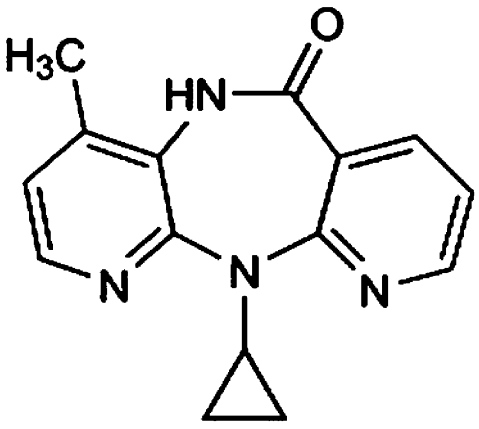

Fig. 1. Structure of nevirapine.