Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfda-online.com

Original Article

An ecofriendly green liquid chromatographic method for simultaneous determination of nicotinamide and clindamycin phosphate in pharmaceutical gel for acne treatment

Fawzia Ibrahim [a], *Asmaa Kamal El-Deen* [a,b], *Samah Abo El Abass* [a], *Kuniyoshi Shimizu* [b,*]

[a] *Department of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Mansoura University, Mansoura 35516, Egypt*

[b] *Department of Agro-Environmental Sciences, Graduate School of Bioresource and Bioenviromental Sciences, Kyushu University, Fukuoka 812-8581, Japan*

ARTICLE INFO

Article history:
Received 5 July 2016
Received in revised form
30 August 2016
Accepted 19 September 2016
Available online 1 December 2016

Keywords:
clindamycin phosphate
gel formulation
micellar liquid chromatography
nicotinamide

ABSTRACT

A new green micellar liquid chromatographic method was developed and validated for the quantitative estimation of nicotinamide (NICO) and clindamycin phosphate (CLD) in bulk and pharmaceutical gel formulation. The analytes are well resolved in less than 6.0 minutes using micellar mobile phase consisting of 0.10M sodium dodecyl sulfate (SDS), 0.3% triethylamine, and 10% 2-propanol in 0.02M orthophosphoric acid at pH 3.0, running through an Eclipse XDB-C_8 column (150 mm × 4.6 mm, 5 μm particle size) with flow rate 1.0 mL/min. The effluent was monitored with diode array detection at 210 nm. The retention times of NICO and CLD were 3.8 minutes and 5.6 minutes, respectively. The method was validated according to the International Conference on Harmonisation (ICH) guidelines in terms of linearity, limit of detection, limit of quantification, accuracy, precision, robustness, and specificity to prove its reliability. Linear correlation was achieved by plotting the peak area of each drug against its concentration. It was found to be rectilinear in the ranges of 1.0–40.0 μg/mL and 0.5–15.0 μg/mL with limits of detection of 0.06 μg/mL and 0.03 μg/mL and limits of quantification of 0.19 μg/mL and 0.09 μg/mL for NICO and CLD, respectively. The method was successfully implemented for the simultaneous determination of the analytes in their bulk powder and combined gel formulation with high % recoveries. The ease of sample treatment facilitates and greatly expedites the treatment with reduced cost and improved accuracy of the procedure.

* *Corresponding author*. Department of Agro-Environmental Sciences, Graduate School of Bioresource and Bioenvironmental Sciences, Kyushu University, 6-10-1 Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan.
E-mail address: shimizu@agr.kyushu-u.ac.jp (K. Shimizu).

http://dx.doi.org/10.1016/j.jfda.2016.09.009

1. Introduction

Acne vulgaris is one of the most common skin disorders which mainly affect adolescents, although it may present at any age. Definitely, acne is a multifactorial chronic inflammatory disease of pilosebaceous units [1]. Recently, new therapeutic modalities and various combinations have been designed for acne treatment including benzoyl peroxide, antibiotics, retinoids, etc., as the mainstay of treatment in topical formulations [2]. Among the different available drugs for the treatment of acne, nicotinamide (NICO) and clindamycin phosphate (CLD) have been recently combined in a topical dosage form at a pharmaceutical ratio 4:1, respectively, for the treatment of mild to moderate inflammatory acne [3].

NICO (Figure 1A) [3] is chemically defined as pyridine-3-carboxamide. It is also known as nicotinic acid amide, nicotylamide, and niacinamide (vitamin B3). It is a water-soluble vitamin. Topical NICO is used in the treatment of mild to moderate inflammatory acne. CLD (Figure 1B) [3], methyl 6-amino-7-chloro-6,7,8-trideoxy-*N*-[(2*S*,4*R*)-1-methyl-4-propylprolyl]-1-thio-L-threo-D-galacto octopyranoside-2-(dihydrogen phosphate), is a lincosamide antibacterial with a primarily bacteriostatic action against Gram-positive aerobes and a wide range of anaerobic bacteria. CLD was found to have an activity against *Propionibacterium acnes* when used topically. Both NICO and CLD are official drugs in the United States Pharmacopoeia [4] which recommends a high performance liquid chromatography (HPLC) method for the determination of both drugs in their pure form, separately. Also, the British Pharmacopoeia [5] determined CLD by a HPLC method and NICO by a titrimetric method, both in their pure form. In addition, several methods were reported for the determination of CLD in pharmaceutical preparations, either alone or in combination with other drugs, including spectrophotometry [6–9] and HPLC [10–16]. For NICO, spectrophotometry [17,18], HPLC [19] and high performance thin layer chromatography (HPTLC) [20] were reported for its analysis in pharmaceutical preparations either alone or in combination with other drugs.

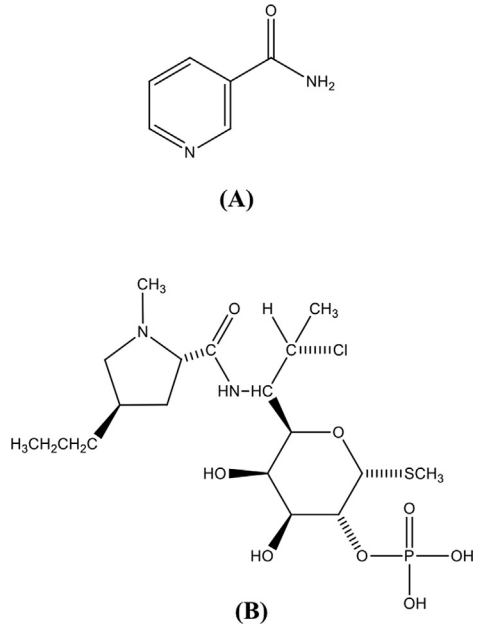

Figure 1 – Structural formulas of (A) nicotinamide and (B) clindamycin phosphate.

To the best of our knowledge, there is only one reported HPLC method for the simultaneous determination of NICO and CLD in coformulated preparation [21]. This method is of narrow linearity range, low column efficiency, and of lower sensitivity. Additionally, the tedious, multistep, and lengthy procedure for extraction of both drugs from their pharmaceutical formulation is one of its drawbacks. This method also consumes large quantities of organic solvents which are toxic to the analyst and the environment. So, this promoted us to develop a new rapid, inexpensive, environmentally friendly, and reliable analytical method to overcome all of these drawbacks.

Micellar liquid chromatography (MLC) has recently gained interest as an efficient alternative to conventional liquid chromatography, aiming to reduce the amount of organic solvent consumed and thus decrease the generated waste without affecting the chromatographic performance. MLC has many merits over conventional HPLC, like low environmental impact, low cost, safety, easy sample treatment, and direct on-column injection of physiological fluids [22]. Thus, MLC is exploited to allow direct injection of the sample and resolve the analytes in a short chromatographic run time.

The present study overcame the problems faced in the reported method for the simultaneous determination of NICO and CLD, since it showed excellent sensitivity with good linearity. Additionally, it is less hazardous, nontoxic, time saving, and cost-effective.

Previous trials in our laboratory were made to establish a simple and selective derivative spectrophotometric method to resolve the highly overlapping spectra of NICO and CLD, but it failed to give positive results due to the low molar absorptivity of CLD compared to NICO and also due to its lower ratio in its mixture with NICO (1:4). This added more advantages to the use of MLC method for a sensitive and selective determination of the studied drugs in their combined gel formulation.

2. Methods

2.1. Instrumentation

An Agilent 1220 Infinity LC system (G4294B configuration; Agilent Technologies, Santa Clara, CA, USA), which consisted of a dual solvent deliver system, an auto sampler, and a diode array detector (DAD), was used. An ultrasonic bath (S 100 H, Elmasonic, Singen, Germany) and a Docu pH-meter (Sartorius, Bohemia, NY, USA) were used.

2.2. Chemicals and reagents

All the used chemicals were of analytical reagent grade, and the solvents were of HPLC grade. NICO, CLD, SDS (90%), triethylamine (TEA), orthophosphoric acid (85%), methanol, 2-propanol, and acetonitrile (HPLC grade) were obtained from Wako Pure Chemical Industries, Ltd. (Osaka, Japan).