Arabian Journal of Chemistry (2016) 9, 493–505

King Saud University

Arabian Journal of Chemistry

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

ORIGINAL ARTICLE

Forced degradation of mometasone furoate and development of two RP-HPLC methods for its determination with formoterol fumarate or salicylic acid

Ramzia I. El-Bagary [a], Marwa A. Fouad [a], Manal A. El-Shal [b], Enas H. Tolba [b,*]

[a] *Pharmaceutical Chemistry Department, Faculty of Pharmacy, Cairo University, Kasr El-Aini St., Cairo 11562, Egypt*
[b] *National Organization for Drug Control and Research (NODCAR), Giza 35521, Egypt*

Received 16 August 2013; accepted 7 May 2015
Available online 22 May 2015

KEYWORDS

Mometasone furoate;
Formoterol fumarate;
Salicylic acid;
Stability-indicating assay;
Forced degradation

Abstract Two simple, selective and precise stability-indicating reversed-phase liquid chromatographic methods were developed and validated for the determination of mometasone furoate in two binary mixtures, with formoterol fumarate (Mixture 1) and salicylic acid (Mixture 2). Also, a forced degradation study of mometasone furoate was carried out including acid and alkali hydrolysis, oxidation, thermal and photo-degradation. For mixture 1, the method was based on isocratic elution using a mobile phase consisting of (Acetonitrile: 3 mM Sodium lauryl sulfate) (60:40, v/v) at a flow rate of 1 ml min^{-1}. Quantitation was achieved applying dual wavelength detection where mometasone furoate and its degradation products were detected at 247 nm and formoterol fumarate and its degradation product were detected at 214 nm at 30 °C. For mixture 2 and for the forced degradation study, separation was based on isocratic elution of mometasone furoate, its degradation products and salicylic acid on a reversed phase C8 column using a mobile phase consisting of acetonitrile:water:methanol:glacial acetic acid (60:30:10:0.1, v/v) at a flow rate of 2 mL min^{-1}. Quantitation was achieved with UV detection at 240 nm. In addition, products from alkaline forced degradation of mometasone furoate were verified by LC–MS. Linearity, accuracy and precision were found to be acceptable over the concentration range of 10–800 μg mL^{-1} and 5–60 μg mL^{-1} for mometasone furoate and formoterol fumarate, respectively and over the concentration range of 5–320 μg mL^{-1} and 20–1280 μg mL^{-1} for mometasone furoate and salicylic acid,

* Corresponding author. Tel.: +20 1002768761.
E-mail address: nosso2@yahoo.com (E.H. Tolba).
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.arabjc.2015.05.005

respectively. The two proposed methods could be successfully applied for the routine analysis of the studied drugs in their pharmaceutical preparations without any preliminary separation step.

1. Introduction

Mometasone furoate (MF), 9α,21-dichloro-11β,17-dihydroxy-16α- methylpregna-1,4-diene-3,20-dione 17-(2-furoate), (Fig. 1a), is a topical corticosteroid. It has anti-infl ammatory, anti-pruritic, and vasoconstrictive properties. It is indicated for a number of conditions such as allergic reactions, eczema and psoriasis. Corticosteroids act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid (Shaikh et al., 2009).

Formoterol, ((*RR*)-(±)-*N*-[2-hydroxy-5-[1-hydroxy-2-[[2-(4- methoxyphenyl)-1 methylethyl]amino]ethyl]phenyl]forma mide), (Fig. 1b) is an adrenergic agent with high selectivity for the β_2 receptor (β_2-agonist) and has proven to be a very effective bronchodilating agent (Sardela et al., 2012). Hence, it is frequently applied therapeutically by means of metered dose inhalers for the treatment of asthma, bronchospasm and prophylaxis of exercise-induced bronchospasm.

Salicylic acid (SA), 2-hydroxybenzoic acid, (Fig. 1c) is widely used as a peeling or keratolytic agent to treat callus, keratosis or warts. Salicylic acid is further applied in the treatment of acne, psoriasis and photo ageing in various concentrations depending on the desired amount of keratolysis (Bashir et al., 2005). Salicylic compounds have also been synthesized for analgesics (acetylsalicylic acid or aspirin) and antipyretics.

Literature survey revealed the determination of mometasone furoate (MF) in plasma by LC-tandem mass spectrometry (Sahasranaman et al., 2005), and by HPLC with stability studies (Teng et al., 2001). Also, MF was determined in its dosage form by HPLC (Ourique et al., 2012). Kinetic study of MF in aqueous system (Teng et al., 2003) and supercritical fluid chromatographic impurity analysis (Wang et al., 2011) were also carried out. Moreover, determination of MF with fucidic acid, tazarotene using HPLC (Shaikh et al., 2009; Ankam et al., 2009) and with nadifloxacin using HPTLC (Kulkarni et al., 2010) was reported.

Besides, Several methods have been reported for the determination of formoterol fumarate (FF) by HPLC in mixtures (Assi et al., 2006; Sule et al., 2012; TRIVEDI et al., 2012; malik et al., 2011), by Chiral analysis (Samuel et al., 2009), and with its related substances (Samuel and Muhammad, 2003; Hassib et al., 2011). Several qualitative mass spectrometry based methods for the detection of formoterol in the field of doping analysis have been also described (Kang et al., 2007; Mazzarino and Botre, 2006; Thevis et al., 2003; Ventura et al., 2000; Peters et al., 2010; Kolmonen et al., 2009). For its quantitation, several non-mass spectrometric methods have been described in the frame of pharmacokinetic experiments (Nadarassan et al., 2007; Butter et al., 1996; Rosenborg et al., 1999). Quantitative detection methods applying mass spectrometric detection are limited to a GC–MS method (Kamimura et al., 1982), a UPLC-MS (Sardela et al., 2012), and two LC–MS/MS methods (Deventer et al., 2012; Marzo et al., 2000).

Also, several analytical methods have been reported for the determination of salicylic acid (SA) in mixtures using spectrophotometry (Salinas et al., 1990), colorimetry (Saha and Baksi, 1985), liquid chromatography (Aguiar et al., 2009; Akay et al., 2008), flow-through UV spectrophotometric sensor (Ruiz-Medina et al., 2001) and titrimetric method (Ruiz-Medina et al., 2001).

Mometasone furoate is incorporated in many pharmaceutical preparations, as inhaled corticosteroids for the treatment of bronchial asthma and as anti-inflammatory corticosteroids for the treatment of many skin disorders. The two pharmaceutical preparations analysed in this manuscript represent these binary usages of mometasone furoate.

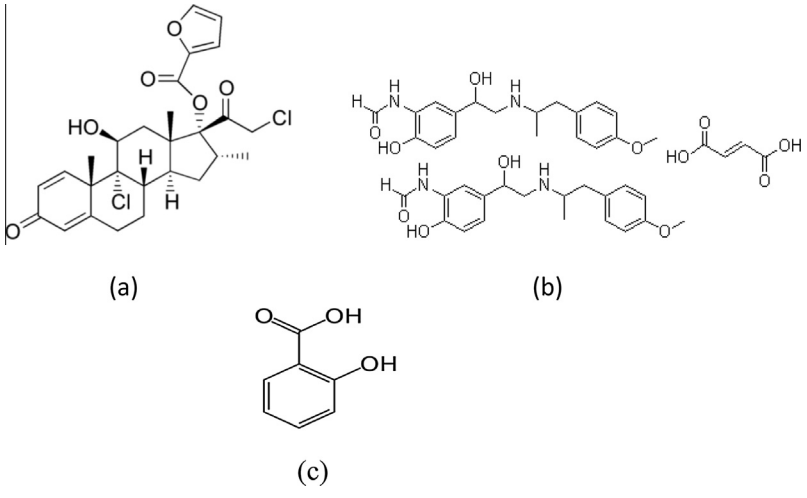

Figure 1 Chemical structure of (a) mometasone furoate, (b) formoterol fumarate and (c) salicylic acid.