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Validated HPTLC method for the simultaneous determination of alfuzosin, terazosin, prazosin, doxazosin and finasteride in pharmaceutical formulations

Tarek S. Belal [a,*], Mohamed S. Mahrous [b], Magdi M. Abdel-Khalek [b], Hoda G. Daabees [c], Mona M. Khamis [b,d]

[a] Pharmaceutical Analytical Chemistry Department, Faculty of Pharmacy, University of Alexandria, Elmessalah 21521, Alexandria, Egypt
[b] Pharmaceutical Chemistry Department, Faculty of Pharmacy, University of Alexandria, Elmessalah 21521, Alexandria, Egypt
[c] Pharmaceutical Chemistry Department, Faculty of Pharmacy, Damanhour University, Damanhour, Egypt
[d] College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK, Canada

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ABSTRACT

Benign prostatic hyperplasia (BPH) is one of the most common chronic diseases affecting men and it increases in both incidence and prevalence with age. This work presents a simple, sensitive and fast generic high performance thin layer chromatographic (HPTLC) method for the simultaneous determination of five drugs prescribed for the treatment of BPH. These drugs include the α_1-adrenergic blockers; alfuzosin hydrochloride (ALF), terazosin hydrochloride (TER), prazosin hydrochloride (PRZ) and doxazosin mesylate (DOX) in addition to the 5α-reductase inhibitor; finasteride (FIN). The cited drugs were separated on TLC-silica plates using a mobile phase composed of methylene chloride:*n*-hexane:methanol (8.8:0.3:0.9, by volume). Densitometric analysis was carried out at 254 nm for the α-blockers while FIN was measured at 220 nm. The five drugs were detected at R_f values of 0.26, 0.36, 0.45, 0.59 and 0.69 for ALF, TER, PRZ, DOX and FIN, respectively. The developed method was validated according to the International Conference on Harmonization (ICH) guidelines regarding; linearity, ranges, accuracy, precision, selectivity, robustness and limits of detection and quantification. The proposed method showed good linearity ($r > 0.9990$) in the ranges; 30–350, 30–350, 20–200, 30–350, 200–2000 ng/spot for the cited drugs, respectively. The applicability of the proposed method was verified through the analysis of laboratory-prepared mixtures and percentage recoveries between 98.27% and 101.97% were obtained. Commercial tablets were also analyzed by the developed methodology with no interference detected from the co-formulated excipients. The high sensitivity, simplicity and selectivity of the proposed method suggest its applicability for routine quality-control analysis purposes of any of the titled drugs in their pharmaceutical preparations.

1. Introduction

Benign prostatic hyperplasia (BPH) is a common disorder of the male urogenital tract and it is the main cause of lower urinary tract symptoms (LUTS) in older men. It affects almost 50–90% of the men aging from 50 to 85 years [1]. Compared to surgery, pharmacological intervention results in significant improvement of the symptoms with fewer, less serious and reversible side effects. Two main pharmacological classes of drugs are available; the selective α_1-adrenoreceptor blockers and the 5α-reductase inhibitors. The first acts by the selective blockade of the α_1-adrenoreceptors that are widely distributed in the prostatic tissues, thus inhibiting the sympathetic stimulation of the prostatic smooth muscles and relieving the urinary obstruction [1]. The alternative treatment strategy is the 5α-reductase inhibitors that exert their action by interrupting the conversion of testosterone into 5α-dihydrotestosterone and therefore reducing the prostate volume [2]. In addition to monotherapy, several studies have proven the beneficial use of these drugs in combination for treating men at higher risk of BPH progression [1–3]. The α_1-adrenoreceptor blocker family includes, but not exclusive to; alfuzosin hydrochloride (ALF), doxazosin mesylate (DOX), prazosin hydrochloride (PRZ) and terazosin hydrochloride (TER) [1,3]. All four members share a similar nucleus, namely; the 4-amino-6,7-dimethoxyquinazoline (Fig. 1). On the other hand, finasteride (FIN) is a 5α-reductase inhibitor, and it is chemically known as N-tert-butyl-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide (Fig. 1) [3].

* Corresponding author. Tel.: +20 3 4871351; fax: +20 3 4873273.
E-mail address: tbelaleg@yahoo.com (T.S. Belal).

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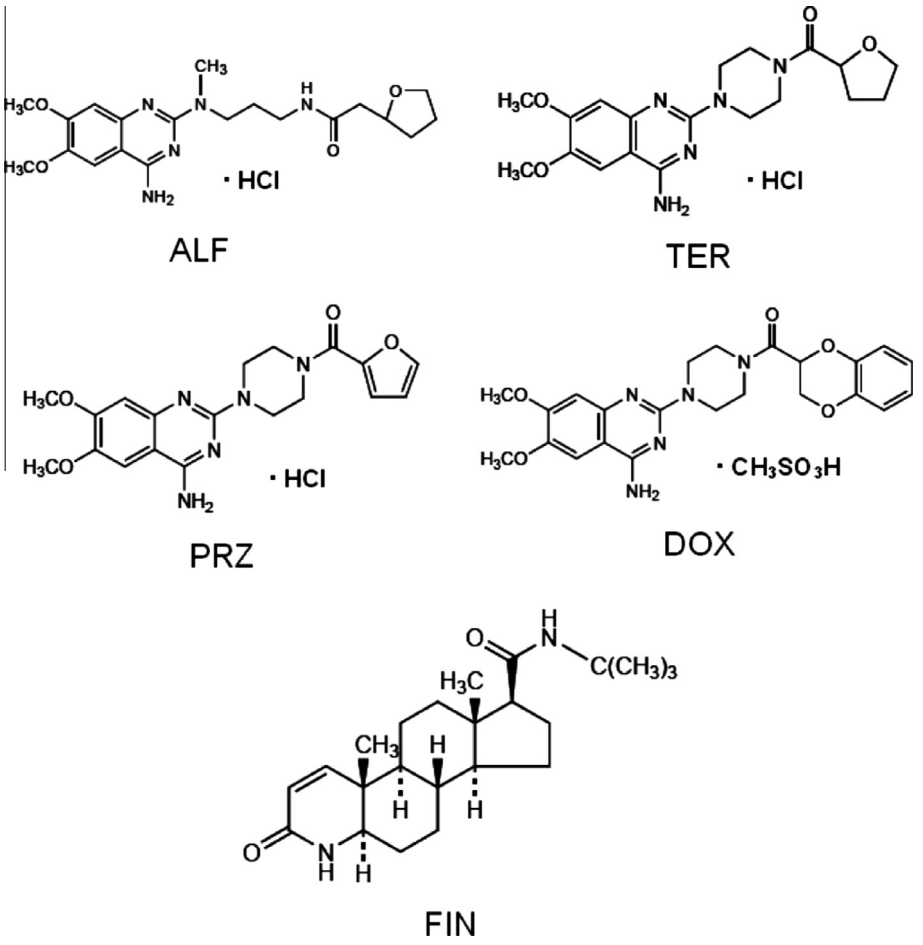

Fig. 1. Chemical structures of ALF, TER, PRZ, DOX and FIN.

Literature review reveals the presence of numerous methods for the determination of these five drugs in different matrices. A couple of review articles were published where they provided information about the various analytical methods available for these drugs [4,5]. In this work, special emphasis will be given to analytical reports involving the use of HPTLC. Such technique was used for the quantification of ALF in plasma [6] as well as in tablets either alone [7] or in the presence of its forced degradation products [8]. DOX was also assayed in tablets using HPTLC [9,10]. In addition, HPTLC methods were reported for the simultaneous determination of the binary mixtures; ALF/solifenacin [11], DOX/celecoxib [12] and FIN/tamsulosin [13]. Furthermore, TLC methods were applied for detection of 29 different pharmaceutical compounds including DOX, PRZ and TER in adulterated herbal remedies [14].

On the other hand, several reports investigated the simultaneous quantification of either of the selected drugs with one another or with other pharmacologically related compounds using several chromatographic methods. The use of a monolithic weak cation-exchange column was described in the HPLC concomitant determination of ALF, DOX, PRZ and TER in human plasma [15]. DOX, PRZ and TER were also simultaneously assayed using a stability-indicating HPLC-UV method [16]. In addition, PRZ and TER were concurrently determined via HPLC methods in tablets [17] and in biological fluids [18]. Moreover, HPLC with UV detection methods were presented for the specific determination of DOX, PRZ and TER in presence of their degradation products [19]. On the other hand, FIN was simultaneously determined with tamsulosin in combined dosage forms using several HPLC methods [13,20,21]. Finally, flow injection analysis with fluorescence detection method was recently reported for determination of the four α_1-blockers in pharmaceutical formulations [22].

To the best of our knowledge, we could not find any articles in the literature describing the simultaneous determination of the five selected drugs by any analytical methodology. Moreover, no reports could be found for the simultaneous determination of the four structurally related α_1-blockers using HPTLC. This encouraged us to investigate the development of a generic, simple and selective HPTLC procedure applicable for the routine quality control analysis of any of the designated drugs in their pure or tablets dosage forms.

2. Experimental

2.1. Materials and reagents

ALF was kindly provided by Amriya Pharmaceutical Industries (Alexandria, Egypt), while, DOX was a gratuity from the Egyptian International Pharmaceutical Industries Co., EIPICO (10th of Ramadan City, Egypt). PRZ and TER were supplied by Pfizer Egypt S.A.E. (Cairo, Egypt) and European Egyptian Pharmaceutical Industries (Alexandria, Egypt), respectively. FIN was generously donated by Adwia Co. S.A.E. (10th of Ramadan City, Egypt). HPLC grade methanol was purchased from Lab-Scan Analytical Sciences (Gliwice, Poland). Methylene chloride (CDH, India), HPLC grade *n*-hexane (Carlo Erba, France), absolute ethanol (BDH Laboratory Suppliers, Poole, England) and ethyl acetate (Chemajet Chemical Company,