Simultaneous ultra-sensitive analysis of tamsulosin hydrochloride and tolterodine tartrate binary mixture in their dosage form via high-performance thin-layer chromatography with fluorimetric detection

M. Rizk1 · Zainab M. Mahmoud1 · Marwa M. Azab1

Received: 28 April 2022 / Accepted: 8 August 2022 / Published online: 24 September 2022
© The Author(s) 2022, corrected publication 2022

Abstract
A simple, sensitive, selective, and stability-indicating high-performance thin-layer chromatography method with fluorescence detection was developed for the analysis of a mixture of tamsulosin hydrochloride and tolterodine tartrate, used in the management of benign prostatic hyperplasia in their laboratory-prepared binary mixture and dosage form. The separation was employed on thin-layer chromatography silica gel 60 aluminum sheets. As developing system, ethyl acetate–n-hexane–diethylamine (9:3:1, V/V) was used. Tamsulosin and tolterodine had retention factors (Rf) of 0.40 ± 0.03 and 0.85 ± 0.03, respectively. A 225 nm excitation wavelength was used for the fluorescence detection. Linearity was in the range of 10.0–200.0 and 100.0–900.0 ng/band for tamsulosin and tolterodine, respectively. The method was validated successfully according to the International Council for Harmonisation guidelines. Our suggested method for determining tamsulosin and tolterodine in their dosage forms and in the presence of their degradation products could be conveniently applied in quality-control laboratories.

Keywords Benign prostatic hyperplasia · Tamsulosin hydrochloride · Tolterodine tartrate · High-performance thin-layer chromatography · Fluorescence

1 Introduction
Benign prostatic hyperplasia (BPH) is a prevalent disease in males over 50 years that causes bladder outlet obstruction and lower urinary tract symptoms (LUTS), which can be managed according to the symptoms only [1]. Combining alpha-blockers with muscarinic receptor blockers improves LUTS in men with BPH [2].

Tamsulosin hydrochloride (TAM) is chemically known as 5-][(2R)-2-][2-(2-ethoxyphenoxy)ethyl][amino][propyl][-2-methoxybenzenesulfonamide hydrochloride [3] (Fig. 1A). It is an official drug in the British Pharmacopoeia (BP) [3] and the United States Pharmacopoeia (USP) [4]. TAM is an α1A-adrenoceptor blocker used in BPH to relieve symptoms of urinary obstruction [5].

Tolterodine tartrate (TOL) is chemically known as 2-][(1R)-3-][bis(1-methylethyl)amino][phenylpropyl][-4-methylphenol (2R,3R)-2,3-dihydroxybutanedioate [3] (Fig. 1B). It is also an official drug in BP [3] and USP [4]. TOL is a tertiary anti-muscarinic drug, which has greater selectivity for the muscarinic receptors of the bladder, used in the management of urinary frequency, urgency, and incontinence in detrusor instability [5].

The combination of TAM and TOL is given orally in modified-release formulations in a usual dose of 0.4 and 4.0 mg once daily for TAM and TOL, respectively [6].

Many analytical methods have been reported for the determination of TAM in different matrices, either alone or in combination. Review article [7] mentioned various spectrophotometric, chromatographic, and electrochemical methods for TAM determination alone and in combinations in different matrices. Additionally, more recent spectrophotometry [8], spectrofluorimetry [9], high-performance liquid chromatography (HPLC) [10–15], and high-performance thin-layer chromatography (HPTLC) [16, 17] methods have been reported.
For TOL, spectrophotometry [18], spectrofluorimetry [19], HPLC [20], ultra-performance liquid chromatography (UPLC) [21], liquid chromatography–mass spectrometry (LC–MS) [22], and electrochemical [23, 24] recent methods of analysis are available.

For the analysis of TAM and TOL in combination, spectrophotometry [25], spectrofluorimetry [9], HPLC [26–28], UPLC [29], and only two HPTLC with ultraviolet (UV) detection [30, 31] methods were reported. No chromatographic method coupled with fluorescence detection has been reported for the determination of this mixture. This encouraged us to develop and validate a stability-indicating HPTLC method with fluorescence detection for the determination of TAM and TOL in their laboratory-prepared mixture and in the presence of their degradation products. The known advantages of HPTLC analysis with fluorescence detection are the high sensitivity, simplicity, selectivity, speed of analysis, and low sample and solvent consumption compared to HPLC.

2 Experimental

2.1 Instruments

For densitometric scanning, a TLC Scanner 4 densitometer, model S/N 230826 (CAMAG, Muttenz, Switzerland); CAMAG Linomat 5 auto-sampler with CAMAG microliter syringe (100 µL); 20 cm × 10 cm twin-trough glass chamber (CAMAG Automatic Developing Chamber 2) were used. Optical filter K 320 was used to measure the intensity of the emitted light after excitation at 280 nm by a mercury (Hg) lamp. CAMAG HPTLC software visionCATS Version 3 was used to analyze the peaks. Neutralization steps after stability studies and buffer preparations were done using a digital pH meter (Hanna HI 2211, Sigma Aldrich, St. Louis, MO, USA) equipped with a glass-calomel electrode combination. The dosage form solutions were sonicated using Powersonic 410 micro-process controlled bench-top ultrasonic cleaner (Hwashin, Yeongcheon, South Korea).

2.2 Materials and reagents

TAM reference standard (99.9% pure; batch number: 2122794) was gifted from Marcyrl Company (Cairo, Egypt). TOL reference standard (99.8% pure; batch number: 900111705006) was purchased from Bal Pharma Limited Company (Bengaluru, India). Roliflo-OD® cap contains 0.4 and 4 mg of TAM and TOL, respectively, per cap was purchased from Ranbaxy Laboratories Ltd. (Gurgaon, India). TLC silica gel 60 aluminum sheets, 20 × 20 cm, was from Merck (Darmstadt, Germany). Methanol (Fisher Scientific, Cambridge, UK) and ethyl acetate (Chem-Lab, Zedelgem, Belgium) were HPLC grade (99.9%). n-Hexane (Merck) and diethylamine (Loba Chemie, Mumbai India) were analytical reagent grade (99.5%). Hydrochloric acid and a 30% (V/V) solution of hydrogen peroxide (Piochem Company, Cairo, Egypt) were used.

2.3 TAM and TOL solutions

2.3.1 Standard stock solutions

Standard stock solutions of TAM (100.0 µg/mL) and TOL (1.0 mg/mL) were prepared separately by transferring 10.0 mg of TAM and 100.0 mg of TOL into 100-mL volumetric flasks, then dissolving and completing the volume to the mark with methanol. The volumetric flasks were protected from light by wrapping them with aluminum foil and stored in a refrigerator.

2.3.2 Standard working solution

By transferring 1 mL from each of the stock solutions into a 10-mL volumetric flask and filling to the mark with methanol, then wrapping with aluminum foil, a working standard solution of the binary mixture of TAM (10.0 µg/mL) and TOL (100.0 µg/mL) was prepared.
2.4 Procedures

2.4.1 Construction of the calibration curve

Using a CAMAG microliter syringe (100 μL), aliquots from the working stock solution were prepared as per the procedure described in Sect. 2.3.2, and spotted in triplicate as bands on TLC silica gel plates to yield a concentration range of 10.0–200.0 ng/band for TAM and 100–900 ng/band for TOL. Table 1 lists the optimal chromatographic conditions for developing and scanning the plates. To obtain the calibration curve and compute the regression equation, the average peak areas were plotted against the final concentrations in ng/band.

2.4.2 Procedure for capsule analysis

The contents of ten Roliflo-OD® caps were weighed and grinded to fine powder. Amounts equivalent to 2.5 mg and 25.0 mg of TAM and TOL, respectively, were transferred to a 25-mL volumetric flask, dissolved in methanol, and sonicated for 15 min, and diluted to the mark with methanol. The prepared solution (0.1/1.0 mg/mL) from TAM and TOL, respectively, was filtered using a disposable syringe filter (0.45 μm), then diluted with methanol to obtain a working stock solution of (10.0/100.0 µg/mL) from TAM and TOL, respectively. Aliquots from this solution were spotted in triplicate as bands on the silica gel plates to give concentration ranges of 30.0, 70.0, 90.0 ng/band of TAM and 300.0, 700.0, 900.0 ng/band of TOL. The plates were developed and scanned under the optimized chromatographic conditions (Table 1). The content of the capsules was then determined from the previously plotted calibration curve.

2.4.3 Procedures for stability-indicating assay

Forced degradation was performed on the Roliflo-OD® caps. A solution of 0.1/1.0 mg/mL from TAM and TOL, respectively, was prepared as per the procedure described in section Sect. 2.4.2. For each of these tests, 1 mL of this solution was transferred into a series of 10-mL volumetric flasks.

2.4.3.1 Alkaline and acidic degradation 1 mL of 1.0 M methanolic KOH and 1.0 M methanolic HCl were added to the prepared solution mixture of TAM and TOL. The volumetric flasks were wrapped with aluminum foil and left at room temperature for 1 h. After the required time, the solution was neutralized by 1.0 M methanolic HCl and 1.0 M methanolic KOH, respectively. The volume was then completed to the mark with methanol and filtered using a syringe filter (0.45 μm). Aliquots of 5 μL from each flask were spotted in triplicate on the plates and scanned as described under the chromatographic conditions in Table 1. The calibration curve was used to determine the nominal contents of the aliquots.

2.4.3.2 Oxidative degradation 1 mL of 10% (V/V) aqueous solution of H2O2 was added to the prepared solution mixture in two volumetric flasks, wrapped with aluminum foil, and left at room temperature for 2 h. After the required time, the solution was evaporated in front of a fan to get rid of H2O2, and the volume was then completed to the mark with methanol and filtered using a syringe filter (0.45 μm). The rest was proceeded as in Sect. 2.4.3.1.

2.4.3.3 Photolytic degradation One volumetric flask was exposed to sunlight for one day before being completed to the mark with methanol and filtered using a syringe filter (0.45 μm). The rest of the procedure was performed as described in Sect. 2.4.3.1.

Table 1 Summary of the optimized chromatographic conditions

| Parameters              | Chromatographic conditions                                      |
|-------------------------|-----------------------------------------------------------------|
| Stationary phase        | TLC silica gel 60 aluminum sheets                                |
| Mobile phase            | Ethyl acetate–n-hexane–diethylamine (9:3:1, V/V)                |
| Bandwidth               | 4 mm width                                                      |
| Slit dimensions         | 4 × 0.3 mm                                                      |
| Chamber saturation time | 15 min                                                          |
| Migration distance      | 80 mm                                                           |
| Scanning speed          | 20 mm/s                                                         |
| Wavelength              | 225 nm                                                          |
| Development time        | 18 min                                                          |
| Rf factors              | 0.40 ± 0.03 tamsulosin hydrochloride                             |
|                        | 0.85 ± 0.03 tolterodine tartrate                                |
| Temperature             | Room temperature                                                |
2.4.3.4 Wet-heat degradation Three volumetric flasks were heated for 1 h in a water bath at 90 °C, then completed to the mark with methanol and filtered using a syringe filter (0.45 µm). The rest was done in the same way as described in Sect. 2.4.3.1.

3 Results and discussion

An ultra-sensitive and stability-indicating analysis of TAM and TOL via HPTLC with fluorimetric detection method was developed and validated with various experimental parameters accurately tested and optimized as shown in Table 1. Fluorescence detection is a sensitive method for determining fluorescing compounds like TAM and TOL in planar chromatography. When compared to UV–visible absorption, fluorescence emission gives better selectivity and sensitivity.

3.1 Method development and optimization

Several chromatographic conditions were tried to get the highest sensitivity, greatest difference between the $R_f$ values of TAM and TOL, and the best resolution of the peaks over the reported HPTLC methods [30, 31].

3.1.1 Mobile phase system

Several solvent systems were tried to ensure sharp symmetric peaks, including different ratios of mixtures of methanol, ethyl acetate, and $n$-hexane. The medium was rendered alkaline by using ammonia, triethylamine, or diethylamine. The results provided that the best resolution, separation of the binary mixture, was provided by ethyl acetate–$n$-hexane–diethylamine system with a ratio of 9:3:1 (V/V).

3.1.2 Optimum wavelength selection

Several excitation wavelengths were tried, such as 200, 220, 225, and 280 nm, and it was found that 225 nm gave the highest fluorescence intensity, peak area, and sensitivity of the two drugs.

3.2 Validation of the method

The following parameters were evaluated for validation of the proposed method: linearity and range, limit of detection (LOD), limit of quantitation (LOQ), accuracy, precision, specificity, and robustness, according to the International Council for Harmonisation (ICH) guidelines Q2 (R1) [32].

3.2.1 Linearity and range

The linearity of the proposed method was estimated via constructing the calibration curve by plotting the peak areas against TAM and TOL concentrations in ng/band as shown in Fig. 2. The regression equations were computed,

![Fig. 2](image-url)
and the analytical data of the calibration curves are listed in Table 2. The linearity of the calibration curves was proved by the high value of correlation coefficients and the small value of residual standard deviations as shown in Table 2.

### 3.2.2 Limit of detection and limit of quantification

LOD and LOQ of TAM and TOL were calculated according to the ICH guidelines, as shown in Table 2, based on the equations:

\[
\text{LOD} = 3.3 \frac{\sigma}{S} \quad \text{and} \quad \text{LOQ} = 10 \frac{\sigma}{S},
\]

where \(\sigma\) is the residual standard deviation of the response and \(S\) is the slope of the curve.

### 3.2.3 Accuracy

As shown in Table 2, accuracy was calculated as percent relative error. Using the previously published enhanced spectrofluorimetric determination method of TAM and TOL [9], we were able to prove the accuracy of our proposed method. As shown in Table 3, a statistical comparison of the results obtained by our proposed method and those obtained by the reported method using mean recoveries, Student’s \(t\) test, and variance ratio \(F\) test revealed no significant difference between our proposed method and the reported one.

### 3.2.4 Precision

The precision of the method was determined in terms of intra- and inter-day precision by the replicate analysis of three different concentrations of the pure drugs (30.0, 70.0, 90.0 ng/band for TAM and 300.0, 700.0, 900.0 ng/band for TOL). The aliquots from the working stock solution were prepared as per the procedure described in Sect. 2.3.2 and spotted in triplicate. Each concentration was measured three successive times within one day to prove the intra-day precision and on three consecutive days to prove the inter-day precision. The same procedure was done for the capsules but aliquots were prepared as per the procedure described in Sect. 2.4.2. The results are summarized in Tables 4 and 5.

### 3.2.5 Selectivity

The specificity of the method was evaluated by peak purity of TAM and TOL spectrum in the calibration curve and forced degradation studies using the TLC scanner as shown

---

**Table 2** Regression parameters obtained from the calibration curves of tamsulosin hydrochloride and tolterodine tartrate

| Parameter                      | Tamsulosin hydrochloride | Tolterodine tartrate |
|--------------------------------|--------------------------|----------------------|
| Concentration range (ng/mL)    | 10.0–200.0               | 100.0–900.0          |
| Limit of detection (ng/mL)     | 2.6                      | 21.9                 |
| Limit of quantification (ng/mL)| 8.0                      | 66.5                 |
| Correlation coefficient        | 0.9999                   | 0.9996               |
| Slope                          | 13.813                   | 4.2928               |
| Intercept                      | 60.092                   | 15.182               |
| SD                             | 1.431                    | 1.054                |
| %RSD                           | 1.434                    | 1.052                |
| %E                             | 0.585                    | 0.429                |

**Table 3** Statistical analysis of the results of our proposed method of tamsulosin hydrochloride and tolterodine tartrate in pure form, compared with the reported spectrofluorimetric method

| Parameter | Our proposed HPTLC method | Compared spectrofluorimetric method [9] |
|-----------|---------------------------|----------------------------------------|
|           | Tamsulosin hydrochloride  | Tolterodine tartrate                   | Tamsulosin hydrochloride  | Tolterodine tartrate |
| Conc. (ng/band) % Recovery | Conc. (ng/band) % Recovery | Conc. (% recovery) | Conc. (% recovery) |
| 30.0       | 99.9                      | 300.0                                 | 100.0     | 101.4                       | 20.0       | 100.7     |
| 70.0       | 99.6                      | 700.0                                 | 99.6      | 100.2                       | 15.0       | 99.6      |
| 90.0       | 100.7                     | 900.0                                 | 99.9      | 100.4                       | 05.0       | 99.9      |
| Mean (X)   | 100.1                     | 99.8                                 | 100.7     | 100.1                       |
| ± SD       | 0.57                      | 0.21                                 | 0.64      | 0.57                        |
| No. of experiments | 3                        | 3                                    | 3         | 3                           |
| Variance   | 0.323333                  | 0.043333                            | 0.41      | 0.32                        |
| \(F\) test | 1.28 (19)\(^{a}\)         | 7.46 (19)\(^{a}\)                  |           |                             |
| Student’s \(t\) test | 1.21 (2.77)\(^{b}\)   | 0.67 (2.77)\(^{b}\)                |           |                             |

\(^{a,b}\)The numbers in parentheses are the tabulated \(F\) and \(t\) values, respectively, at \(p = 0.05\)
in Fig. 3. The 3D purity of the peak spectrum was assessed at three levels peak start, peak apex, and peak end. The correlation coefficient was 0.9996 for both drugs. The method was able to determine both drugs in their pure form, pharmaceutical preparations, and in the presence of their degradation products without interference from excipients or degradants.

3.2.6 Robustness

The robustness of the proposed method was assessed upon making minor deliberate changes in the method parameters, including room temperature ± 5 and changing the amounts of solvents in the mobile phase by ± 1 mL for ethyl acetate and ± 0.05 mL for other solvents, scanning wavelength ± 1 nm and saturation time ± 5 min. It was found that there was no significant difference regarding the response.

3.2.7 Application

Our proposed method was able to successfully determine the content of TAM and TOL in the prepared laboratory mixture from their dosage forms, as shown in Table 3. A standard addition technique was used to determine the matrix effect of the excipients, as shown in Tables 6 and 7, and it was found that there was no significant effect of the matrix.

3.3 Results of the stability-indicating assay

TAM and TOL were found to be liable to all tested degradation conditions, as shown in Table 8. The degradation of both drugs increased over time. There were no additional peaks for the degradation products as shown in Fig. 4C. It could be concluded that the degradation products have no fluorescence.

| Table 4 Repeatability and reproducibility of the proposed HPTLC method for the determination of tamsulosin hydrochloride in pure and dosage form |
|-----------------------------------------------|
| **Precision** | **Conc. (ng/band)** | **Pure form** | **Dosage form** |
|----------------|---------------------|---------------|-----------------|
| Intra-day precision | 30.0 | 99.9 ± 1.6 | 100.8 ± 0.8 |
| | 70.0 | 99.6 ± 0.8 | 101.3 ± 0.4 |
| | 90.0 | 100.7 ± 0.6 | 101.0 ± 0.5 |
| Inter-day precision | 30.0 | 99.9 ± 1.6 | 101.2 ± 1.2 |
| | 70.0 | 99.5 ± 1.4 | 100.9 ± 0.7 |
| | 90.0 | 100.6 ± 0.6 | 101.4 ± 0.5 |

| Table 5 Repeatability and reproducibility of the proposed HPTLC method for the determination of tolterodine tartrate in pure and dosage form |
|-----------------------------------------------|
| **Precision** | **Conc. (ng/band)** | **Pure form** | **Dosage form** |
|----------------|---------------------|---------------|-----------------|
| Intra-day precision | 300.0 | 100.0 ± 0.8 | 100.9 ± 0.8 |
| | 700.0 | 99.6 ± 0.5 | 100.8 ± 0.4 |
| | 900.0 | 99.9 ± 0.7 | 100.1 ± 0.6 |
| Inter-day precision | 300.0 | 100.2 ± 0.4 | 101.4 ± 0.8 |
| | 700.0 | 99.3 ± 0.4 | 101.0 ± 0.6 |
| | 900.0 | 99.6 ± 1.2 | 100.9 ± 0.8 |

Fig. 3 A Tamsulosin hydrochloride and B tolterodine tartrate overlaid UV spectra, recorded using the HPTLC scanner
4 Conclusion

A simple, sensitive, selective, and stability-indicating HPTLC method with fluorescence detection could be easily used in quality-control laboratories for the determination of TAM and TOL in their dosage forms and in the presence of their impurities or degradation products without the need of large amounts of sample or sample pre-treatment. The results also show the validity of our proposed method.
**Fig. 4** HPTLC densitograms of A tamsulosin hydrochloride and tolterodine tartrate reference standard; B tamsulosin hydrochloride and tolterodine tartrate dosage form, C alkaline degradation

**Funding** Open access funding provided by The Science, Technology & Innovation Funding Authority (STDF) in cooperation with The Egyptian Knowledge Bank (EKB).

**Declarations**

**Conflict of interest** The authors state that they have no known competing financial interests or personal relationships that would have influenced the work presented in this research.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

**References**

1. Foo KT (2019) What is a disease? What is the disease clinical benign prostatic hyperplasia (BPH)? World J Urol 37:1293–1296. https://doi.org/10.1007/S00345-019-02691-0
2. Cao Y, Wang Y, Guo L, Yang X, Chen T, Niu H (2016) A randomized, open-label, comparative study of efficacy and safety of tolterodine combined with tamsulosin or doxazosin in patients with benign prostatic hyperplasia. Med Sci Monit 22:1895
3. British Pharmacopoeia (2021) Vol. 1. Medicines and Healthcare Products Regulatory Agency, London
4. The United States Pharmacopeia and National Formulary (2020) The official compendia of standards, Asian Edition, USP 43-NF38. The United States Pharmacopeial Conversion Inc., Rockvill, MD
5. Martindale: The Complete Drug Reference (2017) 39th edition. The Stationery Office, London.
6. Mhamunkar S, Mhamunkar SM, Srinivasan G, Khan T, Bhoir SI (2013) Comparative dissolution studies of an extended release Formulation of Tolterodine Tartrate and Tamsulosin HCl. BioMedRx 1:333–338
7. Shrivastava A, Aggrawal P (2013) Various analytical methodologies for determination of selective α1A receptor blocker tamsulosin hydrochloride and its combinations in different matrices. World J Anal Chem 1(3):55006092
8. Giriraj P, Sivakkumar T (2017) Simultaneous estimation of dutasteride and tamsulosin hydrochloride in tablet dosage form
by vierordt’s method. Arab J Chem 10:S1862–S1867. https://doi.org/10.1016/J.ARABJC.2013.07.013
9. El-Kimary EI, Khamis EF, Belal SF, Abdel Moneim MM (2018) Enhanced spectrophotometric determination of two novel combination therapies for the treatment of benign prostatic hyperplasia containing tamsulosin hydrochloride. Luminescence 33:771–779. https://doi.org/10.1002/BIO.3475
10. Ganthi HKR, Park YJ, Bapatu HR, Park SJ, Cho WH (2016) Statistical indication HPLC method for quantification of solifenacin succinate & tamsulosin hydrochloride along with its impurities in tablet dosage form. Am J Anal Chem 7:840–862. https://doi.org/10.4236/AJAC.2016.711073
11. Pashaei Y, Ghorbani-Bidkorbeh F, Shekarchi M (2017) Superparamagnetic graphene oxide-based dispersive-solid phase extraction for preconcentration and determination of tamsulosin hydrochloride in human plasma by high-performance liquid chromatography—ultraviolet detection. J Chromatogr A 1499:21–29. https://doi.org/10.1016/j.chroma.2017.03.038
12. Walash MI, Belal F, Fathy M, Zayed S, Borg H (2019) Simultaneous HPLC determination of alfuzosin, tamsulosin and vardenafil in human plasma and pharmaceutical formulations using time programmed fluorescence detection. Ann Pharm Fr 77:28–37. https://doi.org/10.1016/j.pharma.2018.08.003
13. Boltia SA, Abdelkawy M, Taghreed AM, Mostafa NN (2021) Eco-friendly RP-HPLC and HPTLC methods for simultaneous determination of tamsulosin hydrochloride and deflazacort in the presence of 21-hydroxy deflazacort and testing the invito dissolution of the combined dosage form via RP-HPLC method. Chromatographia 84:285–295. https://doi.org/10.1007/s10337-021-04009-y
14. Monir HH, Refat RE, Abbas SS (2019) Chromatographic methods for determination of finasteride and tamsulosin hydrochloride and in presence of finasteride degradation product. Acta Chromatogr 32:95–101. https://doi.org/10.1556/1326.2019.00577
15. Monir HH, Ali AM, Refat RE, Abbas SS (2020) Chromatographic methods for determination of finasteride and tamsulosin hydrochloride and in presence of finasteride degradation product. Acta Chromatogr 32:95–101. https://doi.org/10.1556/1326.2019.00577
16. Tantawy MA, Weshahy SA, Wadie M, Rezk MR (2020) Novel HPTLC densitometric methods for determination of tamsulosin HCl and tadalafil in their newly formulated dosage form: comparative study and green profile assessment. Biomed Chromatogr 34:E4850. https://doi.org/10.1002/BMC.4850
17. Rezk MR, Abdel-Moety EM, Wadie M, Tantawy MA (2021) Stability assessment of tamsulosin and tadalafil co-formulated in capsules by two validated chromatographic methods. J Sep Sci 44:530–538. https://doi.org/10.1002/JSSC.202000975
18. Munjed I, Fraihat S (2015) Simple spectrophotometric methods for determination of tolterodine tartrate in pharmaceutical forms. Int F ChemTech Res 8:665–670
19. Tekkeli SE (2017) Spectrofluorimetric method for the determination of tolterodine in human plasma and pharmaceutical preparations by derivatization with dansyl chloride. Bezmialem Sci 5:50–55
20. Attaia AK, Frag EYZ, Mohamed GG, Ahmed HE (2016) Liquid chromatographic determination of solifenacin succinate, flavoxate hydrochloride and tolterodine tartrate in bulk drugs and their pharmaceutical dosage forms. J Chin Chem Soc 61:2772–2776. https://doi.org/10.4067/S0177-97072016000100005
21. Prakash L, Himaja M, Vasudev R (2015) Isolation, identification, and characterisation of degradation products and the development and validation of a stability-indicating method for the estimation of impurities in the tolterodine tartrate formulation. Sci Pharm 83:65–83. https://doi.org/10.3797/scipharm.1407-18
22. Kim YH, Byeon JY, Kim SH, Lee CM, Jung EH, Chae WK, Jang CG, Lee SY, Lee YJ (2017) Simultaneous determination of tolterodine and its two metabolites, 5-hydroxymethyltolterodine and N-dealkyltolterodine in human plasma using LC–MS/MS and its application to a pharmacokinetic study. Arch Pharm Res 40:1287–1295. https://doi.org/10.1007/s12272-017-0981-3
23. Attaia AK, Frag EYZ, Ahmed HE (2018) Validated electroanalytical determination of flavoxate hydrochloride and tolterodine tartrate drugs in bulk, dosage forms and urine using modified carbon paste electrodes. Arab J Chem 11:483–491. https://doi.org/10.1016/j.arabjc.2016.07.015
24. Langmaier J, Skopalová J, Navrátil T, Samec Z (2016) Development of antiuscarinic agents tolterodine and fesoterodine and their metabolite 5-hydroxymethyl tolterodine by ion transfer voltammetry at a polarized room-temperature ionic liquid membrane. Electrochim Acta 304:54–61. https://doi.org/10.1016/j.electacta.2019.02.086
25. Nanda KK, Gaikwad J, Prakash A (2009) Estimation of tamsulosin and tolterodine in its pharmaceutical dosage form by spectrophotometric method. Int J PharmTech Res 1:420–423
26. Gaikwad J, Ravindra NK, Prakash A, Nanda RK (2009) Simultaneous RP-HPLC estimation of tamsulosin and tolterodine in its pharmaceutical dosage form. J Pharm Res 2:1786–1788
27. Joshi HV, Shah UA, Patel JK, Patel TR (2019) Development and validation of stability indicating method for the simultaneous estimation of tamsulosin HCl and tolterodine tartrate in pharmaceutical dosage form. Asian J Pharm Anal 9:205–209. https://doi.org/10.5958/2231-5675.2019.00034.6
28. Mhamunkar SM, Vyavaharkar BY, Bhoir SI (2012) RP-HPLC method development and validation for the simultaneous estimation of tamsulosin HCL and tolterodine tartrate in pharmaceutical dosage form. Int J Pharm Pharm Sci 4:319–322
29. Sebaiy MM, El-Adl SM, Baraka M, Mohram MS, Ibrahim F (2019) Ultra sensitive UPLC method development and validation for the simultaneous estimation of tamsulosin hydrochloride and tolterodine tartrate in bulk and pharmaceutical dosage form. Acad J Chem 4:50–59
30. Patel M, Jbaliya HJ, Singh B (2015) Simultaneous estimation of Tolterodine tartrate and Tamsulosin HCL by validated HPTLC assay method from combination capsule form. J Chem Pharm Res 7:81–88
31. El-Kimary EI, Khamis EF, Belal SF, Abdel Moneim MM (2018) Novel validated HPTLC method for the analysis of two binary mixtures containing tamsulosin hydrochloride with antimuscarinic agents. J Chromatogr Sci 56:81–91. https://doi.org/10.1093/chromsci/bmx081
32. ICH (2014) Harmonised tripartite guideline, validation of analytical procedures: text and methodology Q2 (R1). In: International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use, Geneva