CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.6787705

Available online at: http://www.iajps.com *Research Article*

ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR THE SIMULTANEOUS ESTIMATION OF MIRABEGRON AND SOLIFENACIN IN BULK AND PHARMACEUTICAL DOSAGE FORM BY RP-HPLC

Running title: Simultaneous HPLC quantification of Mirabegron and Solifenacin in bulk and pharmaceutical dosage forms

K. V. L. D. Spandana, N. J. P. Subhashini*

Department of Pharmacy, University College of Technology, Osmania University, Hyderabad, India
Email: njsubhashini@yahoo.co.in

Article Received: May 2022 **Accepted:** May2022 **Published:** June 2022

Abstract:

A rapid stability-indicating RP-HPLC was developed and validated for the estimation of Mirabegron and Solifenacin combination in bulk and tablet dosage form using Thermo C18 column (250 x 4.6 mm,5m) as a stationary phase and a mixture solution of 0.1 percent Diazanium sulphate buffer: Acetonitrile (60:40v/v) as the mobile phase at a flow rate of 1 ml/min. A photodiode array detector was used for detection at 246 nm. The linearity, sensitivity, selectivity, robustness, specificity, precision, and accuracy were all determined.

The peak area response-concentration curve was rectilinear over the concentration ranges of 25-75 g/ml (Mirabegron) and 2.5-7.5 g/ml (Solifenacin), with quantitation limits of 0.793 g/ml (Mirabegron) and 0.307 g/ml (Solifenacin). The proposed method was validated for the simultaneous determination of mifepristone and misoprostol in combined tablet dosage form. In comparison to previously reported RP-HPLC methods, the performance of the proposed method was found to be rapid and cost-effective. The developed and validated stability-indicating RP-HPLC method was suitable for quality control and drug analysis.

Key words: *RP-HPLC, stability-indicating, tablet dosage form*

Corresponding author:

Dr. N.J.P. Subhashini,
Department of Pharmacy,
University College of Technology,
Osmania University, Hyderabad, India
Email: njsubhashini@yahoo.co.in

QR code

Please cite this article in press Konduru Spandana et al, ***Analytical Method Development And Validation For The Simultaneous Estimation Of Mirabegron And Solifenacin In Bulk And Pharmaceutical Dosage Form By RP-HPLC.,*** *Indo Am. J. P. Sci, 2022; 09(6).*

INTRODUCTION:

Overactive bladder syndrome (OAB) is a chronic medical condition that has a significant negative impact on quality of life. Mirabegron is a first-in-class, orally active beta-3 agonist that has received clinical approval for the treatment of overactive bladder. It is also used to treat neurogenic detrusor overactivity (NDO), a bladder disorder caused by neurological disability (1). Activation of the beta-3 receptor relaxes the detrusor smooth muscle during the storage phase of the urinary bladder fill-void cycle, increasing bladder storage capacity and decreasing feelings of urgency and frequency (2). Solifenacin is a new once-daily competitive M3 receptor antagonist that is both effective and well-tolerated in patients with overactive bladder (3,4). The combination of Beta-3 adrenoreceptor agonist and muscarinic receptor antagonist is more likely to result in successful treatment of OAB symptoms than monotherapy (5,6). Numerous clinical trials have shown that fixed dose combinations of solifenacin and mirabegron are highly effective in treating patients with overactive bladder disorder (OAB) (7). Mirago S®, a new combination therapy consisting of Solifenacin and Mirabegron, was approved for the treatment of OAB in 2018. (8).

Several HPLC, HPTLC, and UV methods have been reported in the literature for the determination of Solifenacin [9-22] and Mirabegron [23-30] alone or in combination with other drugs in bulk, as well as in pharmaceutical formulations. To date, no HPLC method for determining Solifenacin and Mirabegron in pharmaceutical dosage form has been reported. The current study describes a simple, selective, and sensitive method for simultaneous quantitation of Solifenacin and Mirabegron using greener solvents and photo diode array detection..

MATERIALS AND METHODS:

Materials

Acetonitrile, HPLC grade (LichrosolR, Merck Lifesciences Pvt. Ltd., Mumbai, India), HPLC grade water (Thermo Fischer Scientific Pvt Ltd., Mumbai, India), and triethylamine (S D Fine –Chem. Ltd., Mumbai, India) were used in the study. Glenmark and Cipla Pharmaceuticals Ltd., India, generously provided the working standards for mirabegron and solifenacin succinate. Mirago S® tablet containing 50mg of mirabegron and 5mg of solifenacin succinate was purchased from the local market.

Methods

Instrumentation

Chromatographic separation was accomplished using an HPLC waters alliance system outfitted with an autosampler and PDA detector. Empower 2 software was used to process the eluted components. For thermal degradation, a hot air oven was used, and for photolytic degradation, a UV crossinker with a series of 23400 model UV chambers equipped with a UV fluorescence lamp with a wavelength range of 200 – 300nm was chosen. The study employed an ultrasonic bath (Unichrome), a digital PH metre (Eutech), and a UV/VIS spectrophotometer (Labindia UV 3000).

a) Operating conditions of HPLC

Analytes were separated using a Thermo C18 column (250 x 4.6 mm, 5m) at room temperature. At a flow rate of 1 ml/min and injection volume of 10 µl, the samples were eluted using phosphate buffer: acetonitrile (60:40v/v) as the mobile phase. The mobile phase and samples were ultrasonically degassed for 20 minutes before being filtered through a 0.45m Nylon (N66) 47mm membrane filter. The eluted compounds were monitored at 246nm, and all determinations were performed at the ambient column temperature (25°C). The chromatograms of mirabegron and solifenacin standard stock solutions were recorded under optimised chromatographic conditions.

b) Solutions Preparation

Preparation of 0.1% Diazanium sulphate buffer : Weigh 13.214g $(NH_4)_2SO_4$ into a 1000ml beaker and dissolve it in water that has been filtered through a 0.45-micron membrane filter and sonicated for 10 minutes**.**

Preparation of mobile phase: 600 ml (60%) of Diazanium sulphate buffer and 400 ml of Acetonitrile (40%) were mixed and degassed in an ultrasonic water bath for 15 minutes and then filtered through 0.45 µ filter under vacuum filtration.

Preparation of Standard Solutions

A primary stock solution was made by dissolving 50mg of mirabegron reference standard and 5mg of solifenacin reference standard in diluent to achieve 50 µg/mL and 5 µg/mL of mirabegron and solifenacin, respectively.

Preparation of sample solution

Using a mortar and pestle, 10 tablets were finely crushed, weighed a quantity equivalent to 50mg of mirabegron and 5mg of solifenacin, and transferred to a 100mL volumetric flask. Added 140mL diluent and sonicated for 30 minutes with intermediate shaking to disperse the content before diluting to volume with diluent to yield a solution containing 50 µg/mL mirabegron and 5 µg/mL solifenacin. This solution was filtered through a PVDF syringe filter with a pore size of 0.45 µm.

Validation of Method Developed

According to the ICH guidelines, the proposed method was validated for system suitability, specificity, recovery, precision, linearity, robustness, limit of detection (LOD), and limit of quantification (LOQ).

System suitability test

The chromatographic conditions were used to optimise the HPLC system. In the chromatographic system, 10µl of drug standard solutions were injected in triplicate. The parameters retention time, theoretical plates, and tailing factor were calculated to determine the system's suitability for the proposed method.

Specificity

The method's specificity was evaluated to check if there was any interference from impurities in the retention time of analyte peaks. The specificity was tested by injecting blank, placebo, and standard drug solutions.

Linearity

Mirabegron and solifenacin standard stock solutions were diluted with mobile phase to yield a series of solutions containing 25,37.50,50,62.5, and 75 µg/mL of mirabegron and 2.5,3.75,5,6.25, and 7.5µg/mL of solifenacin, respectively. The linearity was determined by calculating a regression line from a plot of the drug's peak area ratio and IS versus concentration. The method was evaluated using the ICH guidelines for determining the correlation coefficient and intercept values.

Precision

Precision is defined as the degree of agreement between a series of measurements obtained from multiple samplings of the same homogeneous sample. Six replicate injections of mirabegron (50 µg/mL) and solifenacin (5 µg/mL) were analysed on the same day by injecting them into an HPLC column. The intermediate precision was calculated by injecting samples prepared at the same concentrations on three different days by different operators. The peak area ratios of all injections were measured, and the standard deviation, percent relative standard deviation (RSD), was calculated.

Accuracy

Accuracy is tested by the standard addition method at different levels : 50, 100 and 150%. A known amount of the standard drug was added to the blank sample at each level. The mean recovery of mirabegron and solifenacin were calculated.

Limit of Detection and Limit of Quantification

The calibration curve method was used to determine the limit of detection (LOD) and limit of quantification (LOQ) of mirabegron and solifenacin. Mirabegron and solifenacin solutions were prepared in the linearity range and injected in triplicate. The concentration was plotted against the average peak area of three analytes. LOD and LOQ were calculated by using the following equations:

$LOD = 3.3\ \sigma / S$

$LOQ = 10\ \sigma / S$

Where σ = the standard deviation of the blank measurements

S = the slope of the calibration curve

Robustness

To assess the robustness of the analytical method, the HPLC conditions were slightly modified. The flow rate, column temperature, and mobile phase composition were altered (31).

To assess the robustness of the analytical method, the HPLC conditions were slightly modified. The flow rate, column temperature, and acetonitrile proportion in the mobile phase were modified.

Forced Degradation Study

Alkaline, acidic, oxidative stress, thermal, water and direct exposure to UV were carried out (32).

Alkali Hydrolysis: To 10 ml of mirabegron and solifenacin stock solution, 4 ml of 1N sodium hydroxide was added, and the mixture was refluxed at 60°C for 30 minutes. The solution was cooled to room temperature, neutralised with 1N HCL, and then made up to the target concentration with deionized water.

Acid Hydrolysis: To 10 ml of stock solution of mirabegron and solifenacin, 4 ml of 1M hydrochloric acid was added, followed by 30 minutes of refluxing at 60°C degrees Celsius. After cooling to room temperature, the solution was neutralised with 1N NaOH before being made up to the target concentration with deionized water.

Oxidative Stress: To 10 ml of stock solution of mirabegron and solifenacin, 1 ml of 20% hydrogen peroxide (H2O2) was added, and the solutions were maintained at 60°C for 30 minutes. The solution was cooled to room temperature before being diluted with deionized water to the desired concentration.

Thermal Degradation:

To study dry heat degradation, 10ml of standard stock solution of drugs was transferred to a 100ml

volumetric flask and placed in an oven at 800C for 6 hours. The solution was then cooled and completed to mark with deionized water to reach target concentration.

Hydrolytic Degradation:
10ml of standard stock solution of drugs was transferred to 100ml volumetric flask, 10ml of deionized water was added and heated on water bath for 1hr. Finally solution was cooled and made up to target concentration with deionized water.

RESULTS AND DISCUSSION:

The HPLC method developed involves separation of mirabegron and solifenacin on Thermo C18 column (250 x 4.6 mm, 5 µm) at an ambient column temperature. The optimized mobile phase consists of 0.1% Diazanium sulphate buffer: Acetonitrile (60:40 v/v) with a flow rate of 1ml/min and UV detection at 246nm. Retention time was 3.05min for mirabegron and 4.21 min for solifenacin.

Validation of Method Developed
The proposed method was validated according to the ICH guidelines for system suitability, specificity, recovery, precision, linearity, robustness, limit of detection (LOD) and limit of quantification (LOQ) (33).

System suitability
Under optimal conditions, the mirabegron and solifenacin retention times were 3.05 minutes and 4.21 minutes, respectively. For two of them, peak symmetries were 1.5, theoretical plate numbers were >2000, and the percent RSD of six standard injection areas was less than 2. These values fall within the range permitted by ICH guidelines. The results are given in **Table 1.**

Table 1. System suitability results

Parameter	Mirabegron	Solifenacin
Peak area	4348892	1237980
Theoretical plates	9139	6660
Retention time	3.05min	4.21 min
Tailing factor	1.16	1.15

Specificity:
To evaluate the method's specificity, interference from excipients in the placebo solution-formulated pharmaceutical dosage form was assessed. (Fig. 1) depicts a mirabegron and solifenacin chromatogram that has been optimised. The chromatogram clearly demonstrates the method's capacity to determine the concentration of the analyte in the presence of other excipients.

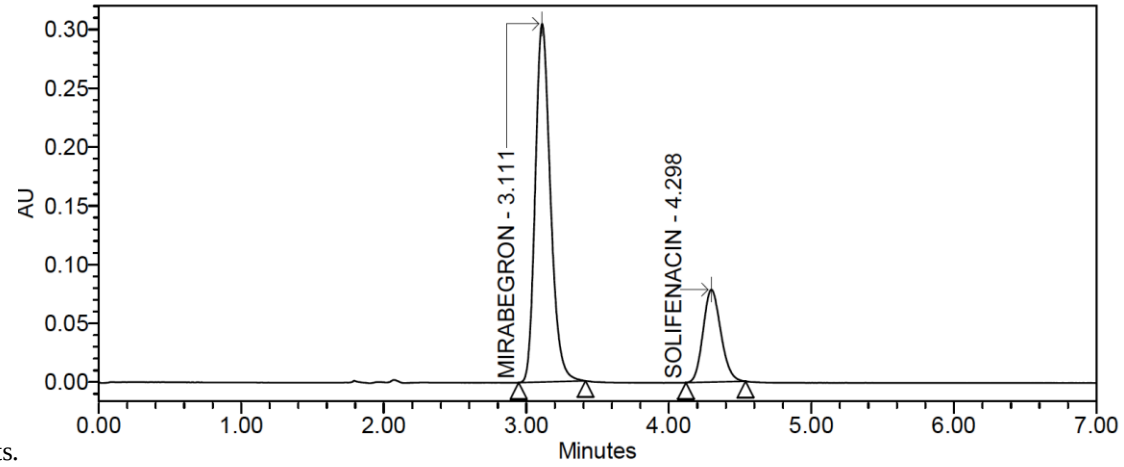

Fig. 1. Optimized chromatogram of Mirabegron and Solifenacin

Linearity and Range:
At concentration ranges of 25-75 µg/ml for mirabegron and 2.5-7.5 µg/ml for solifenacin, linearity was evaluated. **Table 2** displays the concentration of drugs and the corresponding area for the construction of calibration curves. **Figures 3 and 4** depict the relationships between concentrations and peak area ratios. In each case, a strong linear

relationship was observed between concentration and peak area. The relationship is described by the linear equations y = 43633x - 18350 for mirabegron and y = 12255x + 6446,4 for solifenacin. Where X represents the drug concentration and Y the peak area. In every instance, the regression coefficient (R2) was 0.999. The R2 value conformed to ICH recommendations.

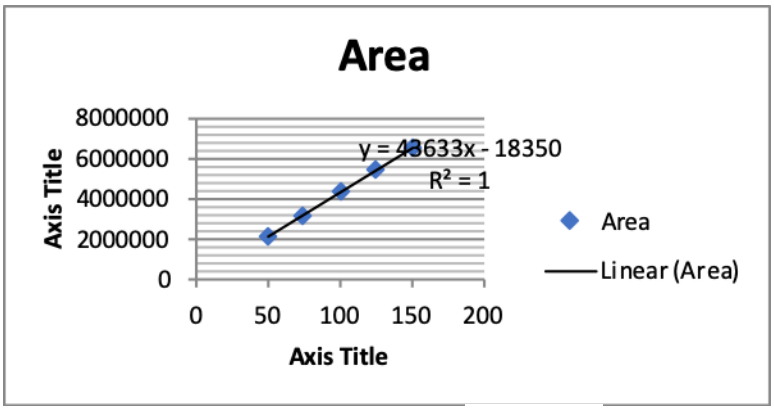

Fig. 3. Linearity graph of Mirabegron

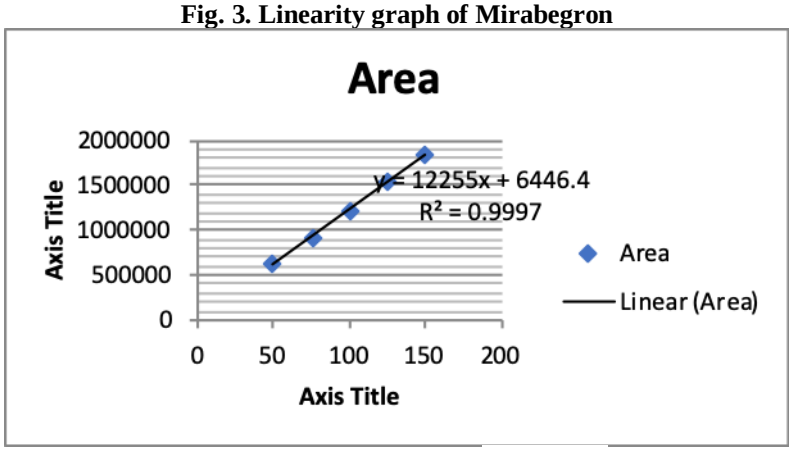

Fig. 4. Linearity graph of Solifenacin

Table 2 : Linearity data

Conc. of Mirabegron (µg/ml)	Peak area	Conc. of Solifenacin (µg/ml)	Peak area
25	2164011	2.5	621628
37.50	3254872	3.75	931849
50.00	4340736	5	1220976
62.5	5438849	6.25	1532021
75	6526103	7.50	1853470

Precision

System Precision:

One dilution containing 50 ppm of Mirabegron and 5 ppm of Solifenacin in six replicates was injected into the HPLC system and the results were within the acceptance limits (RSD<2), as shown in **Table 3**.

Table 3. System Precision data

S.No	Mirabegron		Solifenacin	
	Conc. (ppm)	Peak area	Conc. (ppm)	Peak area
1	50	4345274	5	1225044
2	50	4340448	5	1222257
3	50	4358624	5	1212768
4	50	4349004	5	1232716
5	50	4354277	5	1229487
6	50	4345242	5	1212820
Avg		4348812		1222515
SD		6654.3		8344.2
%RSD		0.2		0.7

Method Precision (Repeatability):
Six injections of a sample preparation with a known concentration of 50 ppm Mirabegron and 5 ppm Solifenacin were analysed on the same day by injecting them into an HPLC column. The calculated percent RSD was found to be within the acceptable range. The results of precision are given in **Table 4**.

Table 4. Method Precision data

S.No	Mirabegron		Solifenacin	
	Conc. (ppm)	Peak area	Conc. (ppm)	Peak area
1	50	4345184	5	1225820
2	50	4340183	5	1222392
3	50	4358183	5	1212601
4	50	4349185	5	1232204
5	50	4354803	5	1229307
6	50	4345720	5	1212290
Avg		4348876		1222436
SD		6648.4		8411.3
%RSD		0.2		0.7

Accuracy:
A known amount of the standard drug was added to the blank sample at each level. Good recovery of the spiked drugs was obtained at each added concentration, and the mean percentage recovery of mirabegron and solifenacin was achieved between 100-101% and 100-102 %. The results are given in **Tables 5,6**.

Table 5. Recovery data of Mirabegron

Sample name	Amount added(µg/ml)	Amount found(µg/ml)	% Recovery
S1:50%	24.750	24.84	100
S1:50%	24.750	24.81	100
S1:50%	24.750	24.73	100
S1:100%	49.500	49.70	100
S1:100%	49.500	49.81	101
S1:100%	49.500	49.65	100
S1:150%	74.250	74.57	100
S1:150%	74.250	74.51	100
S1:150%	74.250	74.66	101

Table 6. Recovery data of Solifenacin

Sample name	Amount added(µg/ml)	Amount found(µg/ml)	% Recovery
S1:50%	2.450	2.49	102
S1:50%	2.450	2.48	101
S1:50%	2.450	2.48	101
S1:100%	4.900	4.95	101
S1:100%	4.900	4.89	100
S1:100%	4.900	4.89	100
S1:150%	7.350	7.41	101
S1:150%	7.350	7.45	101
S1:150%	7.350	7.41	101

Limit of Detection (LOD) and Limit of Quantitation (LOQ):

Limits of detection and quantification were determined by serial dilutions of analyte stock solution to achieve a signal-to-noise ratio of 3:1 for LOD and 10:1 for LOQ, respectively. The LOD values for mirabegron and solifenacin were determined to be 0.238 µg/mL and 0.0092 µg/mL, and the LOQ values were calculated to be 0.793 µg/mL and 0.307 µg/mL respectively.

Robustness:

Robustness evaluation was performed by varying flow rate, column temperature, and acetonitrile proportion in the mobile phase. The results were found to be in the range of 98.4-101.23% for both drugs.

Forced degradation studies:

Developing a stability-indicating method requires a study of forced degradation to demonstrate specificity. A stability-indicating method is one that accurately quantifies the active ingredient in the absence of interference from degradation products, excipients, and other potential impurities. Stress degradation studies were conducted for acid hydrolysis (1M HCl heated at 60°C for 30 minutes), alkali hydrolysis (1 N NaOH heated at 60°C for 30 minutes), oxidative degradation (20% H2O2 heated at 60°C for 30 minutes), and thermal degradation (samples placed in an oven at 80°C for 6 hours). For hydrolytic degradation, samples were placed in a bath of hot water for one hour. Results are shown in **Tables 7.8.**

Table 7. Forced Degradation studies of Mirabegron

Sample Name	Recovery (%)	Degradation (%)	Purity Angle	Purity Threshold
Water Degradation	89.65	10.35	0.211	0.653
Acid Degradation	92.09	7.91	0.259	0.855
Alkali Degradation	93.56	6.44	0.290	0.753
Peroxide Degradation	90.71	9.29	0.341	0.645
Thermal Stress Sample	95.08	4.92	0.288	0.607
Photo Stress Sample	99.11	0.89	0.341	0.645

Table 8. Forced Degradation studies of Solifenacin

Sample Name	Recovery (%)	Degradation (%)	Purity Angle	Purity Threshold
Water Degradation	90.10	9.9	0.310	0.584
Acid Degradation	94.84	5.16	0.323	0.785
Alkali Degradation	89.28	10.72	0.460	0.685
Peroxide Degradation	92.25	7.75	0.294	0.785
Thermal Stress Sample	98.45	1.55	0.307	0.808
Photo Stress Sample	91.76	8.24	0.294	0.785

CONCLUSION:

According to ICH guidelines, an RP-HPLC method for the simultaneous estimation of mirabegron and solifenacin in tablet dosage form was developed and validated. With correlation coefficients (r2 = 0.998), linearity was established in the ranges of 25-75 µg/ml for mirabegron and 2.5-7.5 µg/ml for solifenacin. The percentages of mirabegron and solifenacin recovered were between 100 and 102 percent, which met the acceptance criteria. The RSD percentage was NMT 2%, proving that the developed method was accurate. The developed method is simple, sensitive, rapid, linear, rugged, precise, robust, and specific.

Disclosure Statement

The authors report no conflicts of interest. The authors alone are responsible for content and writing of this article.

REFERENCES:

1) Sacco E, Pinto F, Bassi P. Emerging pharmacological targets in overactive bladder therapy: experimental and clinical evidences. International Urogynecology Journal. 2008 Apr;19(4):583-98.
2) Takasu T, Ukai M, Sato S, Matsui T, Nagase I, Maruyama T, Sasamata M, Miyata K, Uchida H, Yamaguchi O. Effect of (R)-2-(2-aminothiazol-4-yl)-4′-{2-[(2-hydroxy-2-phenylethyl) amino] ethyl} acetanilide (YM178), a novel selective β3-adrenoceptor agonist, on bladder function. Journal of Pharmacology and Experimental Therapeutics. 2007 May 1;321(2):642-7.
3) Dawood O, El-Zawahry A. Mirabegron. InStatPearls [Internet] 2020 Jul 15. StatPearls Publishing.
4) Kreder KJ. Solifenacin. Urologic Clinics. 2006 Nov 1;33(4):483-90.
5) Abrams P, Kelleher C, Staskin D, Rechberger T, Kay R, Martina R, Newgreen D, Paireddy A, van Maanen R, Ridder A. Combination treatment with mirabegron and solifenacin in patients with overactive bladder: efficacy and safety results from a randomised, double-blind, dose-ranging, phase 2 study (Symphony). European urology. 2015 Mar 1;67(3):577-88.
6) Gratzke C, van Maanen R, Chapple C, Abrams P, Herschorn S, Robinson D, Ridder A, Stoelzel M, Paireddy A, Yoon SJ, Al-Shukri S. Long-term safety and efficacy of mirabegron and solifenacin in combination compared with monotherapy in patients with overactive bladder: a randomised, multicentre phase 3 study (SYNERGY II). European urology. 2018 Oct 1;74(4):501-9.
7) Gratzke C, van Maanen R, Chapple C, Abrams P, Herschorn S, Robinson D, Ridder A, Stoelzel M, Paireddy A, Yoon SJ, Al-Shukri S. Long-term safety and efficacy of mirabegron and solifenacin in combination compared with monotherapy in patients with overactive bladder: a randomised, multicentre phase 3 study (SYNERGY II). European urology. 2018 Oct 1;74(4):501-9.
8) Krauwinkel WJ, Kerbusch VM, Meijer J, Tretter R, Strabach G, Van Gelderen EM. Evaluation of the pharmacokinetic interaction between the β3-adrenoceptor agonist mirabegron and the muscarinic receptor antagonist solifenacin in healthy subjects. Clinical Pharmacology in Drug Development. 2013 Jul;2(3):255-63.
9) Desai N, Hussen SS, Vasanthraju SG, Karthik A, Udupa N. Development & validation of stability indicating HPLC method for determination of solifenacin in bulk formulations. International Journal of Pharmacy and pharmaceutical sciences. 2011;3(1):70-4.
10) Shaik RP, Puttagunta SB, Kothapalli Bannoth C, Challa BS. Analytical method development and validation of solifenacin in pharmaceutical dosage forms by RP-HPLC. International Scholarly Research Notices. 2014;2014.
11) Wadie M, Abdel-Moety EM, Rezk MR, Tantawy MA. Eco-friendly chiral HPLC method for determination of alfuzosin enantiomers and solifenacin in their newly pharmaceutical combination: Method optimization via central composite design. Microchemical Journal. 2021 Jun 1;165:106095.

12) Tantawy MA, Weshahy SA, Wadie M, Rezk MR. A novel HPLC-DAD method for simultaneous determination of alfuzosin and solifenacin along with their official impurities induced via a stress stability study; investigation of their degradation kinetics. Analytical Methods. 2020;12(26):3368-75.
13) Desai D, Patel G, Shukla N, Rajput S. Development and validation of stability-indicating HPLC method for solifenacin succinate: isolation and identification of major base degradation product. Acta Chromatographica. 2012 Sep 1;24(3):399-418.
14) Israel DS, Krishnachaitanya K, Gowrisankar D. RP-HPLC method for the estimation of tamsulosin and solifenacin in bulk and its dosage forms. International Journal of Pharmaceutical Sciences and Research. 2013 Nov 1;4(11):4343.
15) Reddy BV, Reddy BS, Raman NV, Reddy KS, Rambabu C. Development and validation of a specific stability indicating high performance liquid chromatographic methods for related compounds and assay of solifenacin succinate. Journal of chemistry. 2012;2013.
16) Bhavana V, Kumar HT, Rao SY, Rao VP. RP-HPLC method for estimation of solifenacin succinate in API and tablet dosage form. Asian Journal of Pharmaceutical Analysis. 2019;9(3):118-22.
17) El-Henawee MM, Abd El-Hay SS, Attala K, Eissa MS. Smart UV spectrophotometric methods based on simple mathematical filtration and classical methods for the simultaneous determination of tamsulosin and solifenacin: A comparative study of efficacy and spectral resolution. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2021 Feb 15;247:119151.
18) Alia Afra S, Rameeja S, Madhavi R, Venkataramanamma C, Divya G, Srilakshmi Y, Gobinath M, Saravanan D. A new spectrophotometric method for the determination of Solifenacin in pure form and in pharmaceutical formulations. Int. J. Res. Pharm. Sci. 2013;4:221-5.
19) Teja GD, Dasu CD, Srinivasa BP, Ravisankar P. Quantitative analysis of solifenacin succinate in pharmaceutical dosage form using UV absorption spectroscopy. J Chem Pharm Sci. 2013;6:195-8.
20) Papanna RK, Kanakapura B, Gowda SB, Basavaraju M, Puttegowda VK. Determination of Solifenacin Succinate in Pure and Pharmaceutical Dosage forms by Spectrophotometry. Journal of Analytical Chemistry. 2021 Nov;76(11):1262-70.
21) Tantawy MA, Weshahy SA, Wadie M, Rezk MR. Stability-indicating HPTLC method for the simultaneous detection and quantification of alfuzosin hydrochloride, solifenacin succinate along with four of their official impurities. Microchemical Journal. 2020 Sep 1;157:104905.
22) Shah DA, Tahilramani PJ, Patel VB, Chhalotiya U. High-Performance Thin-Layer Chromatographic Method for the Estimation of Mirabegron and Solifenacin Succinate Used in the Treatment of Overactive Bladder Syndrome. JPC–Journal of Planar Chromatography–Modern TLC. 2019 Aug;32(4):323-7.
23) Ravisankar P, Vidya VS, Nithya PD, Babu PS. Validated UV spectrophotometric method for quantitative determination of Mirabegron in bulk and Pharmaceutical dosage form. Der Pharmacia Lettre. 2016;8(14):96-103.
24) Spandana R, Rao RN, Reddy LS. Analytical method development and validation for the estimation of mirabegron in bulk and pharmaceutical dosage form by RP-HPLC. IAJPR. 2016;6(11):6880-7.
25) Suresh BK, Anusha N, Sravani AB. Analytical method development and validation for the estimation of Mirabegron in pure and its solid dosage form by UV spectrophotometric method. International Journal of Research in Pharmaceutical Sciences and Technology. 2020 Jul 20;1(4):146-50.
26) Roopa KP, Basavaiah K, Shankara BS, Mahesh B. Development and Validation of Spectrophotometric Methods for the Assay of Mirabegron in Bulk and Pharmaceutical Formulations. Journal of Applied Spectroscopy. 2021 Jan;87(6):1171-8.
27) Papanna RK, Gowda JB, Nagaraja P. An experimental design approach for optimization of spectrophotometric estimation of mirabegron in bulk and Pharmaceutical formulations. Journal of Analytical Chemistry. 2018 Sep;73(9):884-93.
28) Rao RN, Madhuri D, Reddy LS, Rani K, Tejaswini P, Gandla KS. Development and validation of derivative spectrophotometric method for estimation of Mirabegron in bulk and tablet dosage form. World Journal of Pharmaceutical Research. 2017 Sep 2;6(14):760-7.
29) Ramazani A, Rezaei M. RP-HPLC method development and validation for the quantitative estimation of mirabegron in extended-release tablets. Journal of Medicinal and Chemical Sciences. 2018;1(2):36-40.
30) Yehia AM, Sami I, Riad SA, El-Saharty YS. Comparison of Two Stability-Indicating Chromatographic Methods for the Determination

of Mirabegron in Presence of Its Degradation Product. Chromatographia. 2017 Jan;80(1):99-107.
31) Kommineni V, Chowdary KP, Prasad SV. Development of a new stability indicating RP-HPLC method for simultaneous estimation of saxagliptine and dapagliflozin and its validation as per ICH guidelines. Int J Pharm Sci Res. 2017 Sep 1; 9:2920-32.
32) Kommineni V, Chowdary KP, Prasad SV. Development of a new stability indicating RP-HPLC method for simultaneous estimation of Metformin hydrochloride and Teneligliptin hydrobromide and its validation as per ich guidelines. Indo American Journal of Pharmaceutical Sciences. 2017 May 1;4(5):1109-19.
33) Guideline IH. Validation of analytical procedures: text and methodology. Q2 (R1). 2005 Nov;1(20):05.