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A COMPARATIVE REVIEW ON EVALUATING THE GREENNESS OF UV SPECTROPHOTOMETRIC AND RP-HPLC METHODS FOR FEXOFENADINE AND MONTELUKAST ANALYSIS

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ABSTRACT

Fexofenadine hydrochloride (FEX) and montelukast sodium (MON) are often prescribed together for allergic rhinitis and airway disorders because they work well together. FEX is a second-generation H_1-receptor antagonist. It offers non-sedative antihistaminic effects along with some anti-inflammatory benefits. MON is a cysteinyl leukotriene receptor antagonist, which helps reduce inflammation and bronchoconstriction caused by leukotrienes. Using both medications together provides better symptom control, especially for nasal congestion, compared to taking either one alone.

Effective methods for estimating FEX and MON at the same time are important for ensuring quality in pharmaceuticals and monitoring therapy. Several methods have been reported, including UV spectrophotometry, stability-indicating assays, and reversed-phase high-performance liquid chromatography (RP-HPLC). UV methods are straightforward and environmentally friendly, but they often lack selectivity. On the other hand, RP-HPLC methods offer accuracy and reliability for stability studies, although they usually require toxic solvents and more resources.

This review looks closely at the existing methods for analyzing FEX and MON together, focusing on sustainability. Green metrics like Analytical GREEnness (AGREE) and Green Analytical Procedure Index (GAPI) were used to evaluate eco-friendliness. The results show a trade-off between sensitivity and environmental impact, highlighting the need for greener yet reliable options.

Keywords: Fexofenadine, Montelukast, UV spectrophotometry, HPLC, Green analytical tools, AGREE, GAPI

INTRODUCTION:

In clinical practice, fexofenadine hydrochloride and montelukast sodium are commonly used combined as oral medicines to treat allergic airway and nasal illness because they work on distinct inflammatory pathways. Transporters (P-gp, OATP) have a greater impact on the pharmacokinetics of fexofenadine than does substantial CYP metabolism. Fexofenadine is a second-generation, peripherally selective H_1-receptor antagonist with a positive safety and non-sedative profile as well as additional anti-inflammatory properties **[1, 2]**.

Montelukast is used to treat and prevent all ergic rhinitis, a condition in which leukotrienes cause inflammation and congestion.

It is a selective antagonist of the cysteinyl l eukotriene receptor ($CysLT_1$), which prevents mucus secretion, vascular permeability, and bronchoconstriction caused by leukotrienes **[3]**.

Fexofenadine is chemically 2-[4-[1-hydroxy-4-[4-hydroxy (diphenyl) methyl] piperi din-1-yl] butyl] phenyl]-2-methylpropanoic acid and it has molecular formula of $C_{32}H_{39}NO_4$ **[4]**.

Montelukast is chemically 2-[1-[[(1R)-1-[3-[(E)-2-(7-chloroquinolin-2-yl) ethenyl] phenyl]-3-[2-(2-hydroxypropan-2yl) phenyl] propyl] sulfanyl methyl] cyclopropyl] acetic acid and it has molecular formula of $C_{35}H_{36}ClNo_3S$ **[5]**. **Figure 1 and 2** represents chemical structure of Fexofenadine and Montelukast.

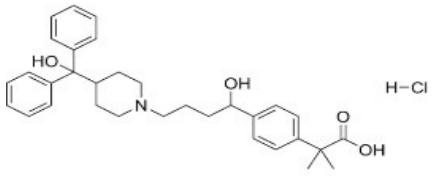


Figure 1: Represents chemical structure of Fexofenadine hydrochloride

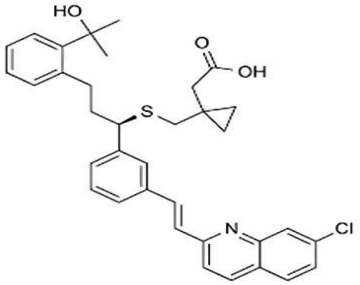


Figure 2: Represents chemical structure of Montelukast sodium

Combining a H_1-antagonist with a leukotriene receptor antagonist produces additive symptom control since histamine and cysteinyl leukotrienes influence complimentary components of the allergic reaction. This is particularly true for nasal congestion and symptoms that antihistamines alone are unable to completely alleviate. Improved symptom scores with such combinations are also supported by post-marketing and randomized studies **[6]**.

Safety considerations, especially the boxed warning for montelukast regarding uncommon but severe neuropsychiatric side effects, should be considered when considering dual therapy and therapeutic monitoring **[7]**.

In this review, we are evaluating the green metrics including AGREE and GAPI for the different analytical methods for the simultaneous estimation of Fexofenadine and Montelukast.

ANALYTICAL METHODS FOR SIMULTANEOUS ESTIMATION OF FEXOFENADINE AND MONTELUKAST:

Various UV spectrophotometric methods have been proposed for concurrently estimating Fexofenadine and Montelukast.

The estimation of Fexofenadine hydrochloride and Montelukast sodium in bulk and tablets has been accomplished by Sowjanya *et al*. using a straightforward simultaneous equation method by UV spectrophotometry. The maximum absorbance for Fexofenadine hydrochloride and Montelukast sodium in 0.1N NaOH was measured at 259 nm and 344.5 nm, respectively **[8]**.

Kothapalli *et al*., have developed an accurate and simple spectrophotometric methods with selected wavelength of 259.0 nm and 282.0 nm for the estimation of FEX and MON **[9]**. Patle *et al*., have introduced a simple method using wavelength of 259.60nm for FEX and 283 nm for MON using methanol as a solvent **[10]**.

Onur *et al*., have developed three new spectrophotometric methods, original UV spectrophotometry, first and second order derivative UV spectrophotometry with wavelength of 258.7 nm, 270.4 nm, and 252.84 nm respectively **[11]**.

A novel, accurate RP-HPLC technique for the simultaneous measurement of FEX and MON has been devised by Swarnalatha *et al*. Hypersil BDS C18 was used for the experiment. Acetonitrile and a mixture of phosphate buffer pH-3 (20:80% v/v) made up the mobile phase, which had a flow rate of 1 mL/min **[12]**.

With a mobile phase consisting of ortho phosphoric acid (pH 6.2): methanol (40:60) and a flow rate of 1.0 mL/min, Vasanth *et al*. developed a novel technique on an ACE C8 column. The column temperature was

28±2ºC, and the wavelength was 290 nm **[13]**.

Rajeev kumar *et al*., developed a stability indicating RP-HPLC method using c_{18} column as stationary phase and Methanol: 0.1% Orthophosphoric acid (90:1) as mobile phase at pH 6.8 with flow rate of 1mL/min **[14]**. Pankhaniya *et al*., introduced a new stability indicating RP-HPLC method using Zorbax aglient column and Phosphate buffer with pH 4.0 and acetonitrile (60:40). The detecting wavelength was 248nm and the flow rate was fixed as 1ml/min **[15]**.

Priyanka *et al*., developed a RP-HPLC method employing Phenomenex C18 column (250 4.6mm, 5m) and mobile phase of 0.5%orthophsophoric acid pH adjust to 6 by triethylamine with the flow rate of 1.0ml/min. the detecting wavelength was 240nm **[16]**. Tamilselvi *et al*., originated a new method using C18 column with 0.5% Orthophosphoric acid pH adjusted to 6 (tri ethyl amine): Acetonitrile (40:60 v/v) at a flow rate of 1Ml/min, with column temperature of 25°C and UV detection at 240 nm **[17]**.

In a novel procedure, Uthirapathy *et al*., used water symmetry C8 as the stationary phase and 0.05 m potassium di hydrogen ortho phosphate: acetonitrile as the mobile phase. The ratio was 35:65, and triethylamine was used to adjust the pH to 6. The wavelength chosen for the quantization was 226 nm, and the flow rate was 1.0 ml/min **[18]**. Tukaram *et al*., performed a HPLC separation utilizing hypersil ODS-C18 and methanol: acetonitrile: 1% trifluoroacetic acid (80:10:10 v/v/v) as mobile phase solvent at a flow rate of 1.0 mL/min. UV detection was performed at 210 nm **[19]**.

Vekaria *et al*., devised an RP-HPLC method employing X-bridge C18 column with a mobile phase composed of 50 mM Sodium acetate buffer: acetonitrile: methanol (25:35:40) modify pH 8.2 with 5% o-phosphoric acid at a flow rate of 1.0 mL/min. The column temperature of 40±2 C and UV detection measured at 210 nm **[20]**.

Chabukswar *et al*., introduced a method for separation using Kromasil C18 and mobile phase composed of sol-A: Water, sol-B: Acetonitrile and Methanol (50:50) was used at the flow rate 1ml/min. The column temperature is 50°C and detector wavelength is 241 nm **[21]**. Godavarthi *et al*., developed a method employing agilent T.C – C18 column and acetonitrile: tri ethyl amine (PH 6) (80:20v/v) as mobile phase. The flowrate was 1mL/min and detection wavelength was 220nm **[22]**.

Green Analytical Chemistry and Greenness Assessment Tools

The principles of Green Analytical Chemistry (GAC) focus on reducing the environmental and health impacts of analytical practices while maintaining reliability, accuracy, and compliance with

regulations. In pharmaceutical analysis, this means lowering the use of solvents and reagents, avoiding toxic chemicals, cutting down on energy use, and encouraging waste management strategies.

To objectively measure the environmental sustainability of analytical methods, specific greenness assessment tools have been created. Among these, the Analytical GREEnness (AGREE) and the Green Analytical Procedure Index (GAPI) are the most common.

The AGREE tool is based on the twelve principles of GAC and offers a complete assessment. It features a clock-like pictogram with color coding (green, yellow, red) to show how well each parameter meets the standards. This results in a score between 0 (poor greenness) and 1 (excellent greenness). It provides a quick visual comparison of analytical methods and highlights areas that need improvement **[23]**.

The GAPI tool examines the entire analytical workflow, from sample collection to final determination. It looks at factors like sample preparation, solvent and reagent use, instrumentation, and energy consumption. Its pictogram, which has colored sections, allows for a step-by-step analysis of green strengths and weaknesses, offering a process-oriented perspective **[24]**.

RESULTS:

This review applies both AGREE and GAPI to the methods reported for simultaneously estimating fexofenadine (FEX) and montelukast (MON). The findings show that while UV spectrophotometric methods achieve higher greenness scores due to low solvent use, RP-HPLC methods are often penalized for their high consumption of acetonitrile, methanol, and buffer salts, even though they are robust and sensitive. This highlights the need for greener alternatives, like bio-based solvents, smaller chromatographic systems, and solvent-free techniques. Combined, AGREE and GAPI provide a solid framework for assessing sustainability, ensuring that pharmaceutical analysis moves toward methods that are environmentally friendly and scientifically valid. A summary of the greenness evaluations is presented in the following **Table 1**.

Table 1: UV Spectrophotometric methods for the analysis of FEX and MON simultaneously from dosage forms

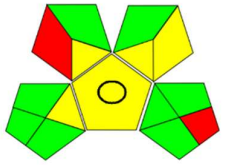
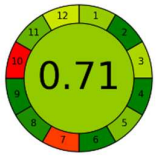
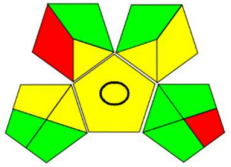
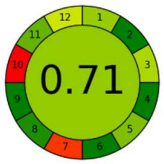
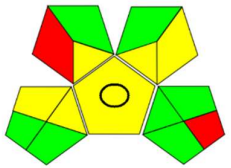
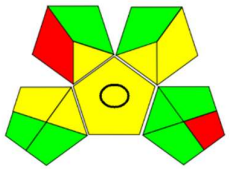
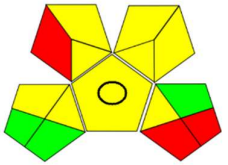
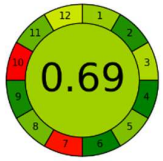
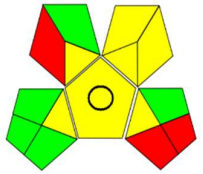
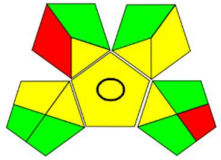
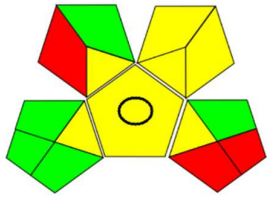
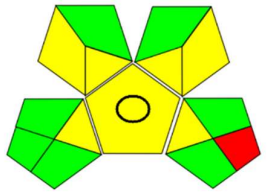
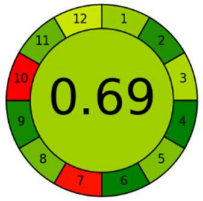
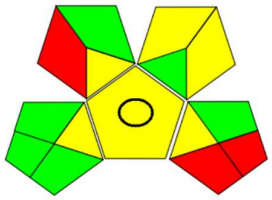
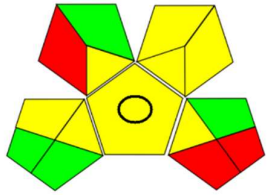
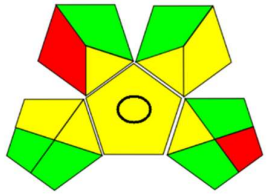
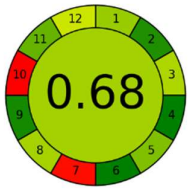
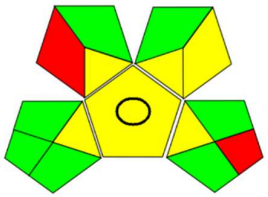
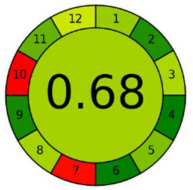
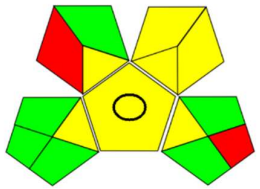
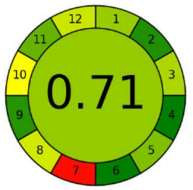
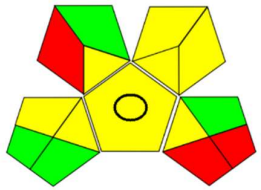
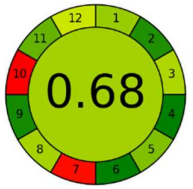
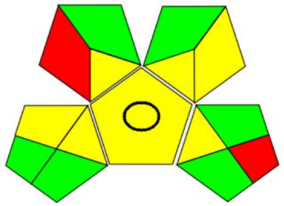
ANALTYE	WAVELENGTH (nm)	SOVENT / REAGENT	LINEARITY RANGE	AGREE	GAPI	REFERENCE
FEX; MON	259nm; 344.5nm	0.1NNaOH	50-180µg/mL and1-35µg/mL			40
FEX; MON	259nm; 282nm	0.1NHCl	24-144 µg/mL and2-12 µg/mL			41
FEX; MON	259.6nm; 283nm	Methanol	30-120 µg/mL and 6-20 µg/mL			42
FEX; MON	258.7nm; 270nm; 252.84nm	Methanol and water (1:1)	100 -1000 µg/mL			44

Table 2: Reported stability indicating RP-HPLC methods and simultaneous method for determination of FEX and MON combination

STUDY AIM	MOBILE PHASE	COLUMN	WAVE LENGTH	FLOWRATE	LINEARITY RANGE	AGREE	GAPI	REFERENCE
Stability indicating method (MON and FEX)	ortho phosphoric acid (pH 6.2): methanol (40:60)	ACE C8 column (250 mm x 4.6 mm, 4µ particle size)	290nm	1.0 mL/min	2-6µg/mL and 24-72µg/mL			66
	acetonitrile: 10 mM potassium dihydrogen phosphate solutions: methanol of pH 4.5 (50:30:20) v/v/v	X bridge C18, 250 x 4.6 mm	248nm	1.5 ml/ min	0.020-0.100 µg/mL and 0.016-0.064 µg/mL			67
	methanol:0.1% o-phosphoric acid (90:10 v/v), pH 6.8	Lichrospher® 100, RP-18e	226 nm	1.0 mL/min	2-10 µg/ mL and 24-120 µg/mL			68

STUDY AIM	MOBILE PHASE	COLUMN	WAVE LENGTH	FLOWRATE	LINEARITY RANGE	AGREE	GAPI	REFERENCE
Simultaneous estimation method for FEX and MON	phosphate buffer pH-3 and Acetonitrile (20:80% v/v)	Hypersil BDS C18 (250 mm length x 4.6 mm ID, 5µm)	240nm	1 mL/min	0.4-2.4 µg/ mL and 4.8-28.8 µg/mL			46
	water and methanol (70:30)	Hypersil-BDS C18 column (250mm × 4.6mm,5µ)	259nm	1 mL/min	10-80 µg/mL			80
	0.5% Orthophosphoric acid: Acetonitrile(40:60 v/v)	phenomenex C18 column (150mm x 4.6 mm, 5 µm)	240 nm	1 mL/min	72-120 µg/mL and 6-10 µg/mL			81

	0.05 m potassium di hydrogen ortho phosphate: acetonitrile (35:65)	**Water symmetry C8 (150X4.6mm 5µm)**	**226 nm**	**1 mL/min**	**4.8 - 28.8 µg/mL and 0.4 – 2.4 µg/mL**			**83**
	methanol: acetonitrile: 1% trifluoroacetic acid (80:10:10 v/v/v)	**hypersil ODS-C18 (5 µ, 250 mm x 4.6 mm)**	**210 nm**	**1 mL/min**	**2.5-15 µg/mL and 30-180 µg/mL**			**84**
	phosphate buffer (pH 6.0) and methanol (25: 75, v/v)	**Thermo BDS HYPERSIL C18 column (250mm × 4.6 mm)**	**220nm**	**1 mL/min**	**84–156 µg/mL and 7-13 µg/mL**			**85**
	50 mM Sodium acetate buffer: acetonitrile: methanol (25:35:40)	**X-bridge C18 column (250 mm 4.6 mm, 5 mm)**	**210nm**	**1 mL/min**	**12.5-37.5 µg/mL and 150- 450 µg/mL**			**86**

	sol-A: Water, sol-B: Acetonitrile and Methanol (50:50)	**Kromasil C18 (250 × 4.6 mm)**	**241nm**	**1 mL/min**	**0.05-10µg/mL and 0.6-120 µg/mL**			**87**
	acetonitrile: Triethylamine (pH 6) (80:20v/v)	**agilent T.C – C18 column (4.6×250mm)**	**220nm**	**1 mL/min**	**12-144µg/ml and 1-12 µg/mL**			**89**

CONCLUSION

The simultaneous estimation of fexofenadine hydrochloride (FEX) and montelukast sodium (MON) is crucial for pharmaceutical quality assurance. These drugs are commonly used together for allergic rhinitis and related respiratory disorders. Over the years, various analytical methods have been developed to meet this need. These include UV spectrophotometry, stability-indicating assays, and RP-HPLC techniques. UV methods are simple, allow for rapid analysis, and align well with green chemistry principles. However, their usefulness is often limited by selectivity and sensitivity issues. On the other hand, RP-HPLC methods offer high precision, durability, and are suitable for stability studies. Yet, they often require toxic solvents, longer analysis times, and more resources.

The use of green analytical chemistry tools like AGREE and GAPI on the methods discussed shows a clear balance between analytical performance and environmental sustainability. Most traditional HPLC methods score poorly on green metrics due to their use of acetonitrile, methanol, and phosphate buffers. In contrast, UV spectrophotometric methods are more eco-friendly but do not provide the analytical depth needed for regulatory approval.

Future studies should focus on incorporating greener options into chromatographic workflows. This includes using bio-based solvents, smaller techniques, and connected methods that maintain sensitivity while promoting sustainability. By developing reliable and environmentally friendly methods, the pharmaceutical industry can better align routine quality control with green chemistry principles, ensuring therapeutic safety and environmental care.

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REFERENCES:

[1] Naclerio RM, Ansotegui IJ, Canonica GW, Rouadi P, Zhang L, Murrieta-Aguttes M. Twenty-five years: The fexofenadine clinical experience. World Allergy Organ J. 2024;17:100950. doi:10.1016/j.waojou.2024.100950.

[2] Batool M, Zamir A, Alqahtani F, Ahmad T, Saeed H, Rasool MF. Clinical pharmacokinetics of fexofenadine: a systematic review. Pharmaceutics. 2024;16(12):1619. doi:10.3390/pharmaceutics16121619.

[3] Kordjazy N, Amini S. A review of the therapeutic potential of the cysteinyl leukotriene antagonist

montelukast in the treatment of bronchiolitis obliterans syndrome following lung and hematopoietic-stem cell transplantation and its possible mechanisms. Ther Adv Respir Dis. 2024;18:17534666241232284. doi:10.1177/17534666241232284.

[4] Montvale N. J.; Thomson P. D. R. (60th Eds). The Physicians' Desk Reference; Florence, 2006, pp 2857–5858.

[5] Martindale: The Complete Drug Reference, 36th ed.; Pharma Press: London, 2009, pp 1126–1127.

[6] Mahatme MS, Dakhale GN, Tadke K, Hiware SK, Dudhgaonkar SD, Wankhede S. Comparison of efficacy, safety, and cost-effectiveness of montelukast-levocetirizine and montelukast-fexofenadine in patients of allergic rhinitis: a randomized, double-blind clinical trial. Indian J Pharmacol. 2016 Nov-Dec;48(6):649–653. doi:10.4103/0253-7613.194854.

[7] U.S. Food and Drug Administration. FDA requires boxed warning about serious mental health side effects for asthma and allergy drug montelukast (Singulair); advises restricting use for allergic rhinitis. 2020. (FDA Drug Safety Communication).

[8] Sowjanya, G.; Trideva Sastri, K. UV Spectrophotometric Method Development and Validation for Simultaneous Determination of Fexofenadine Hydrochloride and Montelukast Sodium i Tablets.World J. Pharm. Pharm. Sci. 2017,6,780–789.

[9] LataKothapalli, P.; AtulMahajan, G. B.; AshaThomas, B.; Rabindra Nanda, K.; Narnaware, S. Simultaneous Spectrophotometric Estimation of Fexofenadine Hydrochloride and Montelukast Sodium in Pharmaceutical Dosage Form. Int. J. InstitutionPharm.LifeSci.2012,2,72–80.

[10] PatleD.;Nagar, S.UV Visible Spectrophotometric Method for Estimation of Montelukast and Fexofenadine by Simultaneous Equation Method in Bulk and Combined Dosage Form. Curr. TrendsBiotech.Pharm.2017,11,382–388.

[11] Kozan, I.; Murat Palabiyik, I.; Karacan, E.; Onur, F. Spectrophotometric and High Performance Liquid Chromatographic Determination of Fexofenadine Hydrochloride in Pharmaceutical Formulations.

Turk. J. Pharm. Sci. 2008, 5, 175–189.

[12] Swarnalath,G.; Vijayakumar,B.; Jothieswari,D.; Poojitha,M.; Ravi Chandrakumar, A.; Gobala Krishnan, P. RP-HPLC Method Development and Validation for Simultaneous Estimation of Montelukast Sodium and Fexofenadine HCl in a Pharmaceutical Dosage Form. Int. J.Med. Chem.Anal. 2016, 6,44–51.

[13] Rameezuddin, M. D.; Vasanth, P. M.; Ramesh, T.; Ramesh, M. Method Development and Stability Indicating RP-HPLC Method for the Estimation of Montelukast and Fexofenadine for Bulk and Pharmaceutical Dosage Form. Int. J. Chem. Tech. Res. 2013, 5, 2821–2829.

[14] Rajeev Kumar, P.; Kumar, R. R. Validated Stability-Indicating Isocratic RP-HPLC Method of Estimation of Montelukast Sodium and Fexofenadine Hydrochloride in Bulk and in Solid Dosage by Vierodt's Method. J. Chem. Pharm. Res. 2017, 9, 297–243.

[15] Pankhaniya, M.; Patel, P.; Shah, J. S. Stability-Indicating HPLC Method for Simultaneous Determination of Montelukast and Fexofenadine Hydrochloride. Indian J. Pharm. Sci. 2013, 75, 284–290. DOI: 10.4103/0250-474X.117426.

[16] Priyanka, S.,D.; Akiful Haque, M.; Harshini, S.; Baskshi, V. Method Development and Validation of Fexofenadine Hydrochloride and Montelukast Sodium in a Combined Dosage Form by RP-HPLC Method. Int. J. Med. Nanotechnol. 2014, 1, 174–178.

[17] Tamilselvi, N.; Sruthi, K. Development of Validated HPLC Method for Simultaneous Estimation of Fexofenadine Hydrochloride and Montelukast Sodium in Tablet Dosage Form. Int. J. Pharm. Sci. Res. 2012, 3, 4876–4881.

[18] Ravisankar, M.; Uthirapathy, S.; Thangadurai, A.; Munusamy, J.; Dhanapal, K. Simultaneous Estimation of Fexofendine Hydrochloride and Montelukast Sodium in Bulk and Marketed Formulation by RP-HPLC Method. Int. Res. J. Pharm. 2014, 3, 356–359.

[19] Kalyankar Tukaram, M.; Wale Risha, R.; Kakde Rajendra, B. Development and Validation of RP-HPLC Method for Estimation of Montelukast Sodium and Fexofenadine Hydrochloride in

Pharmaceutical Preparations. Chem. Sci. Trans. 2013, 2, 889–899. DOI: 10.7598/cst2013.361.

[20] Tushar Kakade, C.; Atul Rathore, S.; Lqhidasan, S.; Kakasaheb Mahadik, R. Separation and Determination of Fexofenadine Hydrochloride and Montelukast Sodium in Tablet Dosage 14 C. N. NALINI AND V. KUMAR Form Using RP-HPLC. Anveshana Int. J. Res. Pharm. Life Sci. 2016, 1,54–65.

[21] Vekaria, H.; Limbasiya, V.; Patel, P. Development and Validation of RP-HPLC Method for Simultaneous Estimation of Montelukast Sodium and Fexofenadine Hydrochloride in Combined Dosage Form. J. Pharm. Res. 2013, 6, 134–139. DOI: 10.1016/j.jopr.2012.11.028.

[22] Chabukswar Anirudha, R.; Choudhari Vishnu, P.; Jagdale Swati, C.; Sharma Shialesh, N.; Bari Nilesh, A. Pagare Bharat D. Simultaneous Estimation of Montelukast Sodium and Fexofenadine HCl in Pharmaceutical Formulation by RP-LC PDA. Int. J. Pharm. Sci. Res. 2012, 3, 241–248.

[23] Godavarthi, M.; Sujana, K.; Pramila Rani, A. Method Development and Validation for the Simultaneous Determination of Fexofenadine Hydrochloride and Montelukast Sodium Using RP-HPLC. ISRN Anal. Chem. 2012, 2,41–48. DOI: 10.9790/3013-25404148.

[24] Pena-Pereira F, Wojnowski W, Tobiszewski M. AGREE—Analytical GREEnness Metric Approach and Software. *Anal Chem*. 2020;92(14):10076–10082. doi:10.1021/acs.analchem.0c01887

[25] Płotka-Wasylka J. A new tool for the evaluation of the analytical procedure: Green Analytical Procedure Index. *Talanta*. 2018;181:204–209. doi:10.1016/j.talanta.2018.01.013