Nobel Med 2026; 22(1): 5-11

MEASUREMENT OF MONTELUKAST AND LEVOCETIRIZINE SERUM LEVELS IN ALLERGIC RHINITIS PATIENTS AND INVESTIGATION OF THEIR EFFECTS ON TREATMENT

Ümmügülsüm Can[1], Fatma Humeyra Yerlikaya Aydemir[2], Duygu Eryavuz Onmaz[3], Cengiz Burnik[4]

[1]*Konya City Hospital, Department of Biochemistry, Konya, Türkiye*
[2]*Selcuk University Faculty of Medicine, Department of Biochemistry, Konya, Türkiye*
[3]*Bandırma Onyedi Eylül University, Faculty of Medicine, Department of Biochemistry, Bandırma, Balıkesir, Türkiye*
[4]*Konya City Hospital, Department of Chest Diseases, Konya, Türkiye*

ABSTRACT

Objective: *To measure montelukast and levocetirizine levels in blood samples from allergic rhinitis (AR) patients using a validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) and to investigate the relationship between both drugs and various parameters such as hematological parameters.*

Material and Method: *Thirty-three AR patients were randomly assigned to receive montelukast (10 mg) and levocetirizine (5 mg) on admission and every evening for four weeks thereafter. Patients who were started on medication due to routine clinical necessity were included in the study.*

Results: *Serum montelukast and levocetirizine levels of AR patients receiving 10 mg of montelukast and 5 mg of levocetirizine daily were 273.0 (12.6-4330.0) ng/mL and 362.0 (11.8-2152.0) ng/mL, respectively. A negative correlation was observed between montelukast levels and WBC, MCV, MCH, NEU, and LYM ($p<0.05$). Similarly, levocetirizine levels showed negative correlations with WBC ($p<0.05$), NEU ($p<0.05$), and LYM ($p<0.005$). In contrast, montelukast levels were positively correlated with disease duration ($p<0.005$) and levocetirizine levels ($p<0.001$). Additionally, levocetirizine levels demonstrated a positive correlation with disease duration ($p<0.01$).*

Conclusion: *Montelukast and levocetirizine are clinically effective and have the capacity to improve the quality of life associated with rhinitis-asthma. The developed validated tandem mass spectrometric method has been successfully applied to measure serum montelukast and levocetirizine levels in AR patients.*

Keywords: *Allergic rhinitis, levocetirizine, montelukast.*

CORRESPONDING AUTHOR: **Ümmügülsüm Can** Konya City hospital, Department of Biochemistry, Akabe, Adana Çevre Yolu Cd. No:135/1, 42020 Karatay, Konya, Türkiye
cangulsum@yahoo.com

ÜC https://orcid.org/0000-0002-8967-2924 **FHYA** https://orcid.org/0000-0002-4107-5389 **DEO** https://orcid.org/0000-0001-8564-1824

CB https://orcid.org/0000-0001-5469-6021

DELIVERING DATE: 02 / 07 / 2025 • **ACCEPTED DATE:** 09 / 09 / 2025

ALERJİK RİNİT HASTALARINDA MONTELUKAST VE LEVOSETİRİZİN SERUM DÜZEYLERİNİN ÖLÇÜMÜ VE TEDAVİYE ETKİLERİNİN ARAŞTIRILMASI

ÖZET

Amaç: Alerjik rinitli (AR) hastaların kan örneklerinde montelukast ve levosetirizin düzeylerinin valide edilmiş sıvı kromatografisi-tandem kütle spektrometrisi (LC-MS/MS) kullanılarak ölçülmesi ve her iki ilaç ile hematolojik parametreler gibi çeşitli parametreler arasındaki ilişkinin araştırılması.

Materyal ve Metot: Otuz üç AR hastası, hastaneye yatış sırasında ve sonrasında dört hafta boyunca her akşam montelukast (10 mg) ve levosetirizin (5 mg) almak üzere rastgele seçildi.

Bulgular: Günlük 10 mg montelukast ve 5 mg levosetirizin alan AR hastalarının serum montelukast ve levosetirizin düzeyleri sırasıyla 273,0 (12,6-4330,0) ng/mL ve 362,0 (11,8-2152,0) ng/mL olarak bulundu. WBC (r=-0,373; p<0,05), MCV (r=-0,359; p<0,05), MCH (r=-0,361; p<0,05), NEU (r=-0,411; p<0,05) ve LYM (r=-0,433; p<0,05) ile montelukast düzeyleri arasında negatif korelasyon bulunurken; WBC (r=-0,413; p<0,05), NEU (r=-0,399; p<0,05) ve LYM (r=-0,545; p<0,005) ile levosetirizin düzeyleri arasında da negatif korelasyon mevcuttu. Montelukast, hastalık süresi (r= 0,526; p<0,005) ve levosetirizin düzeyleri (r=0,878; p<0,001) arasında pozitif bir korelasyon tespit edildi. Ek olarak, levosetirizin hastalık süresiyle pozitif bir korelasyon gösterdi (r=0,467; p<0,01).

Sonuçlar: Montelukast ve levosetirizin klinik olarak etkilidir ve rinit-astımla ilişkili yaşam kalitesini iyileştirme kapasitesine sahiptir. Geliştirilen valide edilmiş tandem kütle spektrometrik yöntem, AR hastalarında serum montelukast ve levosetirizin düzeylerini ölçmek için başarıyla uygulandı.

Anahtar kelimeler: Alerjik rinit, montelukast, levosetirizin.

INTRODUCTION

After being exposed to allergens, an IgE-mediated reaction causes allergic rhinitis (AR), an inflammatory disease of the nasal mucosa.[1] As stated in the new guidelines, AR is characterized by such typical clinical symptoms as, runny nose, itching, sneezing, and congestion, which can be intermittent or persistent.[2] Persistent AR is frequently related to comorbid asthma and is known as an important risk factor in terms of the development of asthma.[1]

Antihistamines are one of the first-line medications recommended at all stages of severe AR. As a recent-generation antihistamine, levocetirizine is effective in relieving seasonal and perennial rhinitis symptoms and improving the quality of life (QoL) of patients with rhinitis.[1]

Initially used to treat asthma, montelukast is an anti-inflammatory agent increasingly used to treat AR. Montelukast is an antagonist of type-1 cysteinyl-leukotriene receptors. Cysteinyl leukotrienes, important mediators of anaphylaxis and other allergic airway diseases, are arachidonic acid derivatives synthesized and released by immunocytes, mainly mast cells, in the respiratory mucosa in response to the presence of allergens.[3] Montelukast, a well-tolerated agent, has a favorable safety profile and is used extensively by providing an effective and well-tolerated oral treatment for allergic airway inflammation in AR patients. In a study, the treatment of montelukast was reported to provide a significant improvement in both AR patients and those with asthma.[3]

According to certain publications on montelukast detection techniques utilizing high-performance liquid chromatography (HPLC) or validated liquid chromatography-tandem mass spectrometry (LC-MS/MS), these techniques were stated to be used to detect plasma samples and describe the pharmacokinetic profile following oral administration by volunteers or model animals.[4,5]

However, verifications were not mentioned, and the specifics of the methods were not fully disclosed. To detect levocetirizine-montelukast in the serum of AR patients, this study set out to create and validate a straightforward, precise, highly sensitive, and selective LC-MS/MS method.

Accordingly, the present study aims to propose and validate an appropriate LC-MS/MS method for the simultaneous estimation of levocetirizine-montelukast binary mixture in human serum, investigate its potential effects in AR, and apply the established chromatographic procedure to obtain targeted drugs in human serum.

MATERIAL and METHOD

LC-MS/MS Analysis

Chemicals and Reagents

Methanol, donepezil, trichloroacetic acid, formic acid, and HPLC grade water were used, obtained from Sigma Aldrich (St. Louis, MO, USA), respectively.

Sample Preparation

Briefly, 100 µL internal standard (donepezil) and 500 µl precipitating agent (Trichloroacetic Acid (TCA) were added to the 200 µL sample and vortexed for 30 seconds. The mixture was centrifuged at 12 000 rpm for 10 minutes and 25 µL of supernatant was injected into the LC-MS/MS system.

LC-MS/MS

The Shimadzu HPLC system (Kyoto, Japan) and the Phenomenex C18 column (50 mm x 4.6 mm, 5µm, part no:00B-4041-E0) were used for the chromatographic analysis. An electrospray ionization API 3200 triple quadrupole mass spectrometer (Applied Biosystems/ MDS Sciex) was used to analyze for sensitive quantitative analyses of biomolecules. The mobile phase consisted of A: 0.1% formic acid/water (v/v%) and B: 0.1% formic acid/methanol (v/v%). The ion spray voltage of 4500 V, heater temperature of 400 °C, curtain pressure of 20 psi, and ion source pressures (GS1 and GS2) of 50 psi and 50 psi respectively were the mass spectrometric optimization parameters.

Under the Food and Drug Administration (FDA) and the Clinical and Laboratory Standards Institute (CLSI) C62-A: Liquid Chromatography-Mass Spectrometry Methods guidelines, this approach is stated to be a completely validated method.[5,6] For all analytes, the inter-assay accuracy values ranged from 90.8% to 114.8%, while the intra- and inter-assay imprecision values were less than 10%. All analytes had matrix effect values below 12% and extraction recoveries ranging from 88.2% to 114.5%.

Patients

Thirty-three AR patients admitted to the Outpatient Clinic of Department of Chest Disease in our hospital were included in the study. Patients who were started on medication due to routine clinical necessity were included in the study. The patients were administered 10 mg of montelukast and 5 mg of levocetirizine at admission and every evening for four weeks thereafter. AR was diagnosed on a clinical basis in line with the guidelines of the AR and its impact on Asthma (ARIA).[2] Informed voluntary consent form was obtained from all patients.

Exclusion criteria were composed of the following: Septal deviation, pregnancy, chronic asthma, long-term cancer treatment, systemic immunological conditions like diabetes mellitus, hypertension or other cardiovascular diseases, thyroid, liver, kidney dysfunction, and continuous specific immunotherapy are examples of anatomical abnormalities of the nose. The Local Ethics Committee of Selcuk University approved the study with the registration number: E-70632468-050.01.04-318011.

Within 12 hours of the last dose, whole blood samples were drawn into empty vacutainer tubes for LC-MS/MS drug level measurement. Serum samples were then stored at -80°C until the analyses.

The Beckman Coulter LH 780 analyzer (Beckman Coulter, Miami, FL, USA) was used to analyze the hemogram parameters, which included hemoglobin (HGB), mean corpuscular hemoglobin (MCH), red blood cell count (RBC), mean corpuscular volume (MCV), mean platelet volume (MPV), white blood cell count (WBC), neutrophil (NEU), monocyte (MONO), and lymphocyte (LYM) counts of the patients. Blood samples were collected in serum separator gel tubes and centrifuged at 2000xg for 15 minutes to measure such biochemistry parameters as creatinine (CRE), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). Additionally, commercially available kits, based on the standard procedures on the Architect C 8000 System (Abbott Laboratories, Abbott Park, Illinois, USA), were used to analyze the serum samples. An immunonephelometric technique using the IMMAGE 800 (Beckman Coulter, Brea, USA) immunochemistry system was used to measure the levels of serum C-reactive protein (CRP).

Data Analysis

Statistical analyses were carried out using the EP Evaluator Release, version 8 (Data Innovations, South Burlington, VT), the Statistical Package for Social Sciences for Windows version 21.0 (SPSS, IBM Corp., Armonk, NY. USA), and Excel (2010) programs. Data were analyzed through SCIEX Analyst® 1.6.2 Software. The One-Sample Kolmogorov-Smirnov test was used to examine the data distribution. The mean and standard deviation (SD) were used to represent parametric values, while the median and minimum-maximum

Table 1. Clinical, biological and demographic characteristics of the participants

Parameters	Allergic Rhinitis (n=33)
Age (years)	55.1 ± 12.3
Gender (M/F)	4/29
Disease duration (month)	4.0 (1.0-24.0)
Montelukast daily dosing	10 mg
Levocetirizine daily dosing	5 mg
Biological characteristics	
WBC (10^9/L)	8.5 ± 2.7
HGB (g/L)	13.6 ± 1.5
HCT(%)	41.6 ± 3.9
PLT (10^9/L)	276.5 ± 62.6
RBC (10^{12}/L)	4.9 ± 0.70
MCV (fL)	85.6 ± 5. 2
MCH (pg)	27.9 ± 2.1
RDW (%)	13.2 (12.4- 25.2)
PDW (%)	11.4 (8.80-22.2)
MPV (fL)	10.6 ± 1.2
NEU (10^9/L)	5.5 ± 2.3
LYM (10^9/L)	2.3 ± 0.6
MONO	6.7 (0.5-11.4)
EOS	1.3 (0.10-7.8)
BASO	0.3 (0.10-1.5)
ALT (U/L)	16 (6-50.7)
AST (U/L)	18 (9-91.5)
CREA (mmol/L)	0.70 (0.5- 6.03)
Estimated GFR, ml/minute	98.8 ± 23.9
CRP (mg/L)	3.2 (0. 6-35.2)
Montelukast (ng/mL)	273.0 (12.6-4330.0)
Levosetirizin (ng/mL)	362.0 (11.8-2152.0)

ALT: Alanine aminotransferase, **AST:** aspartate aminotransferase, **BASO:** basophils, **CRP:** C-reactive protein, **CREA:** creatinine, **EOS:** eosinophils, **GFR:** glomerular filtration rate, **HCT:** hematocrit, **HGB:** hemoglobin, **MCH:** mean corpuscular haemoglobin, **MCV:** mean corpuscular volume, **MPV:** mean platelet volume, **NEU:** neutrophil, **PLT:** platelet, **PDW:** platelet distribution width, **RBC:** red blood cells, **RDW:** red blood cell distribution width, **WBC:** white blood cell

were used to represent non-parametric values. Associations between serum drug concentrations and laboratory/clinical variables were initially evaluated using Spearman's rank correlation (reporting both r and exact *p* values). $p<0.05$ values were considered significant.

RESULTS

Serum montelukast levels of patients with AR using 10 mg of montelukast daily were 273.0 (12.6-4330.0) ng/mL and serum levocetirizine levels of patients with AR using 5 mg of levocetirizine daily were 362.0 (11.8-2152.0) ng/mL. No adverse events were observed in any of the patients. The characteristics of the patients are expressed in Table 1.

Given the Spearman's correlation analysis, a negative correlation was detected between WBC (r=-0.373; $p<0.05$), MCV (r=-0.359; $p<0.05$), MCH (r=-0.361; $p<0.05$), NEU (r=-0.411; $p<0.05$) ve LYM (r=-0.433; $p<0.05$) and montelukast levels, while a negative correlation was between WBC (r=-0.413; $p<0.05$), NEU (r=-0.399; $p<0.05$) ve LYM (r=-0.545; $p<0.005$) levels and the levocetirizine levels. Montelukast had a positive correlation with disease duration (r=0.526; $p<0.005$) and levocetirizine levels (r=0.878; $p<0.001$). Also, levocetirizine had a positive correlation with disease duration (r=0.467; $p<0.01$), and the findings are presented in Table 2. However, the results of the effects of levocetirizine and montelukast recovery and matrix are demonstrated in Table 3.

The stability of levocetirizine and montelukast stored at different temperatures is presented in Table 4, and the findings of levocetirizine and montelukast reproducibility are given in Table 5.

Linear range in two metabolites: 2.44-5000 ng/mL

Limit of detection (LOD) values: 1.22 ng/mL

Limit of quantification (LOQ) values: 2.5 ng/mL

DISCUSSION

The presented study aimed to measure the montelukast and levocetirizine levels in serum obtained from AR patients using a robust, straightforward, accurate, validated, highly sensitive, and selective LC-MS/MS. The study also sought to determine whether these levels were associated with the adverse effects. Among the patients completing the study, no side effects were observed, and all the values for accuracy and precision were within the acceptance range. This is the first comprehensive study to measure montelukast and levocetirizine levels in AR patients through the LC-MS/MS method.

In the study, the validated method was carried out to measure the levels of levocetirizine-montelukast in patients with AR. Montelukast used to treat chronic allergic bronchial asthma, rhinitis, and urticaria is a receptor antagonist of leukotrienes, which are responsible for many inflammatory processes.[7] To date, different techniques, such as spectroscopic, chromatographic, and electrophoretic procedures, have been initiated to quantify the drugs in the market in different formulations and biological matrices.[8-10]

Even so, the absence of reliable techniques to assess blood levels of levocetirizine-montelukast and the lack of a thorough analysis of the connections between the levocetirizine-montelukast levels, and clinical parameters and side effects are two

main shortcomings of these studies. A procedure for simultaneous evaluation of the levocetirizine-montelukast combination has yet to be established.

In a study evaluating globally the effects of levocetirizine in persistent AR and the association of asthma through a specific quality of life (QoL) questionnaire, eosinophils and neutrophils in nasal scraping were revealed to be significantly decreased in the levocetirizine group, and it was concluded that levocetirizine is clinically effective and capable of improving rhinitis asthma-related QoL.[1]

In a study performed by Wang et al., it was shown that LC-MS/MS method met all validation requirements of the bioanalytical method and was appropriate for assaying montelukast in an in vitro cell-based pulmonary pharmacokinetic system model.[11]

Levocetirizine in formulations, either alone or in combination with montelukast, or in plasma samples, is likely to be estimated by HPLC and LC-MS/MS techniques.[12,13] The combination of levocetirizine and montelukast is a newly marketed product. The findings demonstrated that the approach offered sufficient sensitivity, accuracy, precision, and reproducibility along with improved resolution for the simultaneous or individual analysis of levocetirizine in formulations.[14] Therefore, it can be asserted that the recommended approach can be applied to the routine analysis of pharmaceutical preparations, and these two medications in bulk without leading to any challenges. The evaluation of the clinical effectiveness of antihistamine and anti-leukotriene combinations has gained attention recently as a result of a better understanding of the distinct roles that histamine and leukotrienes play in allergic respiratory disorders.[15]

In a study by Cingi et al., the serum montelukast levels were reported as 337.65±150.63 ng/mL for 23 healthy volunteers receiving 10 mg/day.[15]

In a study, montelukast, levocetirizine, and their combination were found to be equally effective in controlling symptoms of allergic rhinitis.[16]

In another study, it was also stated that the administration of montelukast alone, levocetirizine alone, and/or the combinations of montelukast/antihistamine significantly ameliorated nasal symptoms during the first 24 hours and gradually rose during the six-week of treatment in those with persistent AR. In the study, the combination of montelukast and levocetirizine was concluded to be more effective than monotherapy of these agents for persistent AR.[17]

Table 2. The correlations between serum montelukast and levocetirizine levels and biological parameters

	Montelukast		Levocetirizine	
Parameters	r	*p*	r	*p*
WBC (10^9/L)	-0.373	<0.039	-0.413	<0.021
HGB (g/L)	-0.013	0.943	-0.033	0.859
HCT(%)	0.027	0.887	-0.032	0.862
PLT (10^9/L)	0.103	0.581	-0.261	0.157
RBC (10^{12}/L)	0.030	0.871	0.005	0.977
MCV (fL)	-0.359	<0.048	-0.254	0.168
MCH (pg)	-0.361	<0.046	-0.257	0.163
RDW (%)	0.101	0.588	0.006	0.976
PDW (%)	-0.241	0.191	-0.169	0.263
MPV (fL)	-0.216	0.242	-0.153	0.112
NEU (10^9/L)	-0.411	<0.021	-0.399	<0.026
LYM (10^9/L)	-0.433	<0.015	-0.545	<0.002
MONO	-0.025	0.896	0.005	0.977
EOS	-0.076	0.684	0.071	0.703
BASO	-0.187	0.314	-0.232	0.209
ALT (U/L)	0.139	0.488	0.144	0.475
AST (U/L)	0.069	0.744	0.140	0.503
CREA (mmol/L)	0.113	0.574	0.144	0.474
Estimated GFR, ml/minute	-0.130	0.517	-0.210	0.292
CDisease duration (months)	0.526	<0.002	0.467	<0.008

ALT: Alanine aminotransferase, **AST:** aspartate aminotransferase, **BASO:** basophils, **CRP:** C-reactive protein, **CREA:** creatinine, **EOS:** eosinophils, **GFR:** glomerular filtration rate, **HCT:** hematocrit, **HGB:** hemoglobin, **MCH:** mean corpuscular haemoglobin, **MCV:** mean corpuscular volume, **MPV:** mean platelet volume, **NEU:** neutrophil, **PLT:** platelet, **PDW:** platelet distribution width, **RBC:** red blood cells, **RDW:** red blood cell distribution width, **WBC:** white blood cell

Table 3. Levocetirizine and montelukast recovery and matrix effect results

Analyte	Concentration (ng/mL)	Recovery (%)	Matrix Effect (%)
Levocetirizine	2.5	111.8	8.1
	625	106.5	7.5
	5000	98.6	5.2
Montelukast	2.5	110.4	8,4
	625	105.7	6,5
	5000	99.6	4,8

Results were expressed as bias % values

The fixed-dose combination of montelukast and levocetirizine was also reported in another study to be more influential and safer in the treatment of perennial AR in patients with asthma than the use of montelukast alone.[18]

Another study, The LC-MS/MS validated method was successfully applied for drug level measurement in COVID19 patients receiving favipiravir. They suggested that the assay can be used for routine favipiravir therapeutic drug monitoring in clinical laboratories.[19]

Table 4. The stability of levocetirizine and montelukast stored at different temperatures

Analyte	Concentration (ng/mL)	Frozen -(20 °C) for 45 day			Freeze-thaw Stability		
		15. Day(%)	30. Day(%)	45. Day(%)	2.	3.	4.
Levosetirizin	10	2.12	4.87	7.58	3.66	4.98	6.59
	2500	-1.85	-4.22	-7.26	-1.48	-2.27	-4.95
Montelukast	10	3.82	4.63	5.99	4.44	5.96	8.24
	2500	-1.59	-3.68	-5.98	-1.68	-3.22	-5.04

Table 5. Levocetirizine and montelukast reproducibility study results

Analyte (ng/mL)	Concentration	Intra-assay			Inter-assay		
		Mean	SD	CV%	Mean	SD	CV%
Levosetirizin	2.5	3.0	0.243	8.1	2.8	0.21	7.5
	625	628.1	33.28	5.3	627.4	23.84	3.8
	5000	4998	209.9	4.2	5001	120.02	2.4
Montelukast	2.5	2.6	0.192	7.4	2.7	0.199	7.4
	625	624.3	38.08	6.1	624.2	26.21	4.2
	5000	5002	190.076	3.8	4999	144.97	2.9

SD: Standart deviation.

In the present study, we conducted the validated method to measure montelukast and levocetirizine levels in the sera of AR patients and found that our findings of montelukast and levocetirizine levels in AR patients were compatible with those reported in previous studies.

Therefore, by reducing inflammation, montelukast and levocetirizine are considered to be beneficial in regressing the activity of AR. The investigation of how different biological parameters are related to montelukast and levocetirizine levels was another crucial component of our research. Our literature scanning revealed that no research investigated the impact of levocetirizine and montelukast levels on hematological parameters.

Accordingly our findings, there was a negative correlation between WBC, MCV, MCH, NEU and LYM, and Montelukast levels (<0.05), while a negative correlation was between WBC (<0.05), NEU (<0.05), and LYM (<0.005) levels with levocetirizine levels. Montelukast had a positive correlation with disease duration (<0.005) and levocetirizine levels (<0.001). Also, levocetirizine had a positive correlation with disease duration (<0.01)

CONCLUSION

Serum levels of levocetirizine and montelukast in AR patients were successfully measured using the developed validated tandem mass spectrometric method, and the results were found to be consistent with the reported levels. Revealing an association between montelukast and levocetirizine levels on the limitation of inflammation and disease activity, our findings suggest that at therapeutic levels, montelukast and levocetirizine lead to no serious adverse effects in AR patients. The levels of serum montelukast and levocetirizine are linked to hematological parameters and inflammation.

Authors' Contributions

All authors contributed to the design of the study, interpretation of the results, writing, and validation.

*The authors declare that there are no conflicts of interest.

REFERENCES

1. Pasquali M, Baiardini I, Rogkakou A, et al. Levocetirizine in persistent allergic rhinitis and asthma: effects on symptoms, quality of life and inflammatory parameters. Clin Exp Allergy 2006; 36: 1161-1167.
2. Bousquet J and Van Cauwenberge P (eds). Allergic Rhinits its impact on Asthma. J Allergy Clin Immunol 2001; 108: 146-150.
3. Nayak A, Langdon RB. Montelukast in the treatment of allergic rhinitis: an evidence-based review. Drugs 2007; 67: 887-901.

4. Pasham M, Haridasyam SB, Boppy NVVDP, Venkatanarayana M, Palakurthi AK. Stability-indicating liquid chromatography method development and validation for impurity profiling of montelukast sodium in bulk drug and tablet dosage form. Biomed Chromatogr 2022; 36: 5330.
5. Wayne PA. CLSI document C62-A. Liquid Chromatography-Mass Spectrometry Methods; Approved Guidelines, Pennsylvania, USA, Clinical and Laboratory Standards Institute, 2014.
6. Guidance for Industry, Bionanalytical Method Validation, US Department of Health and Human Services/Food and Drug Administration Centre for Drug Evaluation and Research (CDER)/Centre for Veterinary Medicine (CVM), 2018.
7. Hosny NM, Badary DM, Hareedy MS. A feasible HPTLC method for concurrent quantitation of allopurinol-montelukast co-therapy in plasma and evaluation of their hepatic and renal effects in rats: Analytical, biochemical, and histopathological study. J Pharm Biomed Anal 2023; 5: 115439.
8. Magdy G, El Hamd MA, El-Maghrabey M, et al. A highly sensitive micelle-enhanced synchronous spectrofluorimetric determination of the recently approved co-formulated drugs, bilastine and montelukast in pharmaceuticals and human plasma at nanogram levels. Luminescence. 2023.
9. Revathi R, Ethiraj T, Thenmozhi P, Saravanan VS, Ganesan V. High performance liquid chromatographic method development for simultaneous analysis of doxofylline and montelukast sodium in a combined form. Pharm Methods 2011; 2: 223-228.
10. Flor S, Huala Juan M, Tripodi V, Lucangioli S. Development of an enantioselective capillary electrophoretic method for the simultaneous determination of montelukast enantiomeric and diastereoisomeric forms and its main degradation product. Electrophoresis 2016; 37: 2420-2428.
11. Wang S, Ni XJ, Wen YG, et al. A simple and sensitive HPLC-MS/MS assay for the quantitation of montelukast in cell-based systems in vitro pulmonary drug permeability study. J Pharm Biomed Anal 2021: 192: 113657.
12. Arayne MS, Sultana N, Nawaz M. Simultaneous quantification of cefpirome and cetirizine or Levocetirizine in pharmaceutical formulations and human plasma by RP-HPLC. J Anal Chem 2008; 63: 881-887.
13. Morita MR, Berton D, Boldin R, et al. Determination of Levocetirizine in human plasma by liquid chromatography-electrospray tandem mass spectrometry: Application to a bioequivalence study. J Chromatogr B 2008; 382: 132-139.
14. Reddy JM, Jeyaprakash MR, Madhuri K, Meyyanathan SN, Elango K. A sensitive RP-HPLC method for simultaneous estimation of diethylcarbamazine and levocetirizine in tablet formulation. Indian J Pharm Sci 2011; 73: 320-323.
15. Cingi C, Toros SZ, Ince I, et al. Does desloratadine alter the serum levels of montelukast when administered in a fixed-dose combination? Laryngoscope 2013; 123: 2610-2614.
16. Andhale S, Goel HC, Nayak S. Comparison of Effect of levocetirizine or montelukast alone and in combination on symptoms of allergic rhinitis. Indian J Chest Dis Allied Sci 2016; 58: 103-105.
17. Ciebiada M, Gorska-Ciebiada M, Barylski M, Kmiecik T, Gorski P. Use of montelukast alone or in combination with desloratadine or levocetirizine in patients with persistent allergic rhinitis. Am J Rhinol Allergy 2011; 25: 1-6.
18. Kim MK, Lee SY, Park HS, et al. A randomized, multicenter, double-blind, Phase III study to evaluate the efficacy on allergic rhinitis and safety of a combination therapy of montelukast and levocetirizine in patients with asthma and allergic rhinitis. Clin Ther 2018; 40: 1096-1107.
19. Onmaz DE, Abusoglu S, Onmaz M, Yerlikaya FH, Unlu A. Development and validation of a sensitive, fast and simple LC-MS / MS method for the quantitation of favipiravir in human serum. J Chromatogra B 2021; 1176: 122768.