Review Article

Analytical Methods for Quantitative Estimation of Montelukast Sodium: A Review

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Abstract:

Background: Montelukast sodium is a potent and selective orally active leukotriene receptor anatagonist. It is used for the treatment of asthma and allergic rhinitis in adults as well as children. It was first approved by FDA in 1998 under the trademark Singulair. This literature review summarizes the variety of analytical techniques that have been applied for the estimation of montelukast sodium.

Method: Various analytical techniques for the quantification of montelukast sodium for bulk, pharmaceutical formulations and biological samples have been reported. Assay methods include UV-spectroscopy, high performance liquid chromatography, high performance thin layer chromatography, capillary electrophoresis, spectrofluorimetry, super critical fluid chromatography.

Results: Literature review reveals that methanol is the most commonly used solvent for the analysis of montelukast sodium by spectroscopic technique. For estimation of montelukast sodium by high performance liquid chromatography, methanol and acetonitrile are the commonly used organic solvents in the mobile phase and phosphate buffer or trifluoroacetic acid is used to maintain the pH of the mobile phase. Protein precipitation technique is used widely for extraction of the montelukast from biological samples though liquid-liquid extraction and solid phase extraction has also been reported in fewer articles. The electroanalytical techniques reported for the analysis of the drug have provided methods with lower analysis time.

Conclusion:Amongst all the developed analytical methods, HPLC has been reported extensively for the quantification for montelukast sodium.

Keywords: montelukast sodium, analytical methods, HPLC

1. INTRODUCTION

Montelukast sodium (MON), chemically 1-[[[(1R)-1-[3-(1E)-2-(7-chloro-2-quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl]thio]-methyl] –cyclopropaneacetic acid, monosodium salt (Figure 1), is a potent and selective leukotriene receptor antagonist (1). It is used for the treatment of asthma and allergic rhinitis for adults as well as children (2-3).

MON was discovered in the Montreal labs of Merck and with the suffix-lukastthe generic name montelukastwas obtained.MON was approved by FDA in 1998 under the trademark Singulair(4). Singulair was covered by U.S. Patent No. 5,565,473(5)which expired on August 3, 2012 (6).Several generics of MON received approval by FDA after that. MON is available as solid oral dosage form as

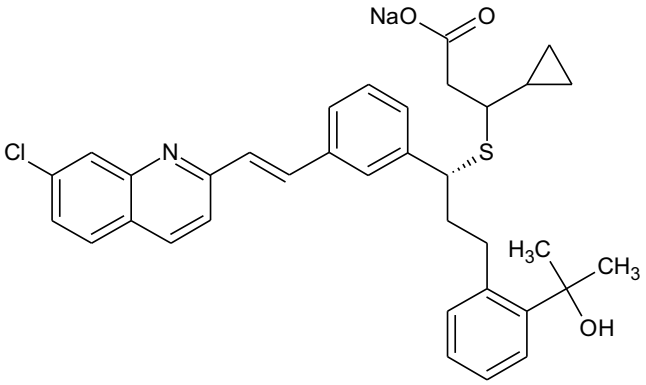

Figure 1 Chemical structure of Montelukast sodium

film coated tablets, chewable tablets and oral granules having strength 4mg, 5mg and 10mg (7). MON is available either individually or in combination with other APIs like levocetrizine, fexofenadine, bambuterolHCl, doxofylline, acebrophylline, desloratadine, ambroxol, etc are available in the market (8-9).

The drug is official in the Indian Pharmacopoeia 2014 (10), British Pharmacopeia 2016 (11),US Pharmacopoeia 2016 (12).The molecular weight of MON is 608.2 and it is a white to pale yellow(10). The drug is ahygroscopic powder and an optically active molecule. It is light sensitive and requires protective handling and storage. It is freely soluble in ethanol,methanol, and water while practically insoluble in acetonitrile (7). It is a lipophilic drug (logP=8.79) having a pka of 2.7 and 5.8 (13).

The present review of literature is based on the several reported analytical methods for estimation of MON in bulk, pharmaceutical formulations as well as biological samples. Methods like spectrophotometry, chromatography including HPLC, HPTLC, UPLC and LC-MS, electrochemical methods and capillary electrophoresis have been reported. HPLC methods have been extensively used (Figure 2).

2. SAMPLE PREPARATION

MON is unstable in the presence of light and moisture thus the monograph in the pharmacopoeia indicates special storage condition. As per the Indian Pharmacopoeia MON is required to be stored protected from light as well as moisture and at a temperature not exceeding 30°C(10). U.S. Pharmacopoeia indicates preserve the API in tight containers(12). Thus sample preparation is required to be done in amber glassware. It has been mentioned to use freshly prepared solvents always for the drug (10-11). Methanol has been used as a diluent for majority of the spectrophotometric methods of analysis for MON.Extraction of the drug from the biological sample includes sample preparation via protein precipitation, liquid liquid extraction and solid phase extraction (44-57). Acetonitrile has been reported extensively for the sample preparation by protein precipitation.

3. ANALYTICAL METHODS

3.1 SPECTROPHOTOMETRY

In the literature, different UV-spectrophotometric methods have been explored for the quantitative estimation of MON in combination with other drugs, including simultaneous equation method, Q-absorbance Ratio method and derivative method. Methanol is commonly used as a solvent for MON in the spectrophotometric methods.J.V. Shanmukhakumar et al.(14) and M. SaeedArayne et al. (15) have reported method for estimation of MON alone while other have reported simultaneous estimation with other API.Table 1 lists the spectrophotometric methods for analysis of MON.

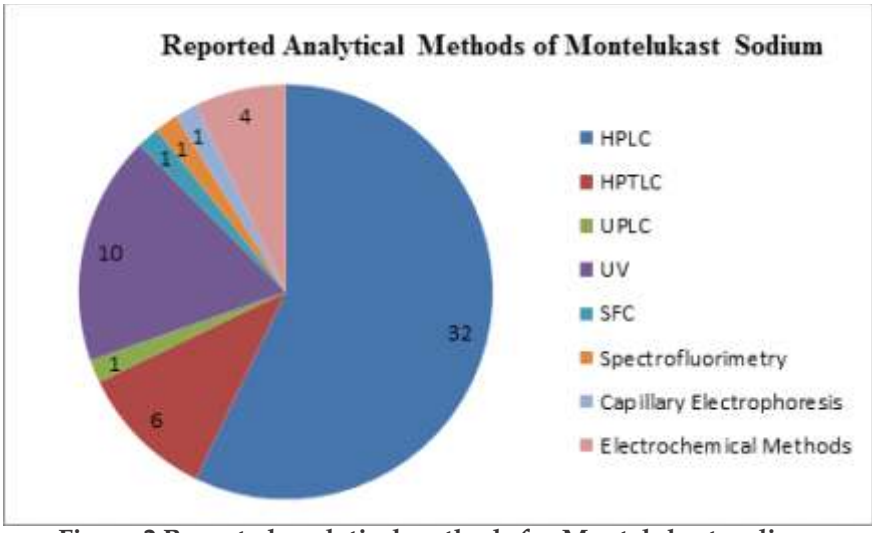

Figure 2 Reported analytical methods for Montelukast sodium

Table 1 Reported spectrophotometric methods for determination of Montelukast sodium individually or in combination with other drugs from the Pharmaceutical Dosage Forms.

API	Method	Solvent	Detection Wavelength (λ,nm)	Ref
Montelukast Sodium	A: Reduction of FE(III) to FE(II) by MTK B: MTK coupling with MBTH C: MTK reaction with 2, 2'-Bipyridyl	Ferric Chloride	A: 510 B: 610 C: 430	14
Montelukast	Spectrophotometric Method	Methanol	283	15
Montelukast Sodium and Theophylline	Simultaneous Equation and Q-Absorbance Ratio method	Water	287(MON) 271(THEO) 280 (isoabsorptive point)	16
Montelukast Sodium and Desloratadine	Q-Absorbance Ratio Method and Dual Wavelength Method	Methanol	283(MON) 263.6 (isoabsorptive point); 345 (MON) 265.6 and 294 (DESLO)	17
Montelukast Sodium and Desloratadine	RatioSpectra Derivative Spectrophotometric Method	Methanol	first derivative amplitudes: 218.6(MON), 262(DESLO)	18
Theophylline, Montelukast and Loratadine	Multivariate Spectrophotometric Calibration-partial least-squares, principal component regression and hybrid linear analysis.	Methanol	275 (THEO), 276(MKST), 251 (LORA)	19
Montelukast Sodium and LevocetirizineDihydrochloride	Derivative and Absorption Factor Spectrophotometric Method	Methanol	first derivative amplitudes: 340(MON), 331 (LEV); 232 (MON), 279 (LEV)	20
RupatadineFumarate and Montelukast Sodium	Q Analysis method	Methanol	260 (Isoabsorptivepoint) 244(RUPA)	21
Acebrophylline and Montelukast Sodium	Simultaneous Equation Method	Methanol	313 (ACBR) 344.5 (MTKT)	22
Rupatadine and Montelukast	First-order derivative UV spectroscopy	Methanol	first derivative amplitudes: 273.46 (MON) 297.27 (RUPA)	23

3.2 Chromatography

3.2.1 HPLC

Among the chromatographic methods employed for the analysis of pharmaceuticals, high performance liquid chromatography is the most widely used technique. Several assay procedures and analysis of related substances mentioned in the pharmacopoeias comprise the HPLC technique. More than twenty HPLC methods for the estimation of montelukast sodium have been summarized in table 2 and fourteen methods for estimation of the drug in biological samples have been summarized in table 3.

Analyte and Matrix	Mobile Phase	Stationary Phase	Detector	Detection Wavelength (nm)	Flow rate (mL/min)	Rt (min)	LOD (µg/ml)	Ref
Montelukast Sodium and its impurities from bulk	Gradient elution: solution A (0.1% OPA), solution B (water:acetonitrile, 5:95 v/v)	C18 column 250 x 4.6 mm i.d, 5 µm particle size	PDA	225	1.5	13.89	0.034	24
Montelukast Sodium from bulk and tablet	Acetonitrile: 1 mM sodium acetate buffer (pH 6.3 adjusted with acetic acid), 90:10v/v	C 18 column 250×4.6 mmi.d, 5 µm particle size	UV	285	1.5	3.4	1.31	25
Motelukast sodium and Theophylline in tablet	Methanol	C18 column 250 ×4.6mmi.d , 5 µm particle size	UV	210	1.0	4.17 (THEO) 2.91 (MON)	0.0073 (THEO), 0.0434 µg/ml (MN)	26
Montelukast Sodium and Doxofylline in tablet	Methanol:sodium phosphate buffer (pH 6.5 adjusted with orthophosphoric acid), 75:25 v/v	C8 column 250× 4.6 mm i.d, 5 µm particle size		230	1.0	3.4(DOXO), 5.5 (MON)	--	27
Montelukast and its degradation products in tablet	Acetonitrile: 0.01M potassium dihydrogen phosphate buffer (pH 4.0), 3:7 v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	SPD-M20A photodiode	355nm	1.0	--	5.51	28
Montelukast sodium in oral granules	0.05M Potassium dihydrogen phosphate buffer (pH 3.5) : acetonitrile, (30:70 v/v)	C18 column 50 × 4.6 mm i.d, 5 µm particle size	PDA	225	1.8	--	--	29

Analyte and Matrix	Mobile Phase	Stationary Phase	Detector	Detection Wavelength (nm)	Flow rate (mL/min)	Rt (min)	LOD (µg/ml)	Ref
Montelukast and Theophylline in tablet	0.3 % TFA in water (pH 2.5) : acetonitrile, 20:80 %v/v	C18 column 150 × 4.6 mm i.d, 5 µm particle size	UV	230	1.0	4.20 (THEO), 6.12 (MON)	0.521(THEO), 0.013 (MON)	30
Montelukast Sodium in tablet	Methanol: 0.02 M sodium phosphate buffer (pH 3.5 adjusted by 0.01 M Phosphoric acid), 15:85v/v	C8 column 250 × 4.6 mm i.d, 5 µm particle size	SPD-20 A VP	218	1.0	3.017	--	31
Montelukast Sodium in tablet	Methanol: TFA, 90:10 v/v.	C18 column 250 × 4.6 mm i.d, 5 µm particle size	UV	350	1.0	7.9	--	32
Montelukast Sodium and LevocetirizineDihydrochloride in bulk and tablet	0.02M Disodium hydrogen phosphate buffer : Methanol (7.0 pH adjusted ortho-phosphoric acid, 25:75 v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	UV/Vis	231	1.0	3.55(LEVO), 7.45 (MON)	--	33
Montelukast Sodium and Fexofenadinehydrochloride in tablet	50 mM Sodium acetate buffer:acetonitrile: methanol(8.2 pH adjusted with 5% o-phosphoric acid, 25:35:40 v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	UV/Vis detector	210	1.0	3.43 (MONT), 8.22(FEXO)	0.29 (MONT), 3.00 (FEXO)	34
Montelukast Sodium and BambuterolHydrochloride in tablet	Gradient elution: Solution A (0.025 M sodium phosphate buffer: methanol, 85:15v/v);Solution B (Acetonitrile:methanol85:15v/v)	C18 column 250 × 4.6 mm i.d, 5 µm particle size	UV/Vis detector	218	1.5	21.2 (MTK), 5.8 (BBL)	--	35
MontelukastSodium and Desloratadine in tablet	Orthophosphoric acid : water, 20:80v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	UV/Visible dual absorbance detector	280	1.0	2.92(MON), 4.43(DES)	0.176 (MON), 0.087 (DES)	36

Analyte and Matrix	Mobile Phase	Stationary Phase	Detector	Detection Wavelength (nm)	Flow rate (mL/min)	Rt (min)	LOD (µg/ml)	Ref
MontelukastSodium and Rupatadine fumarate in tablet	Methanol: Potassium dihydrogenphosphate buffer: Acetonitrile (3.0 pH adjustedwith 1% orthophosphoric acid), 50:30:20v/v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	PDA	226	1.0	2.48(RPM), 6.38 (MLT)	1.56 (RPM), 1.08 (MLT)	37
Montelukast Sodium and FexofenadineHydrochloride in tablet	0.1M potassium dihydrogen orthophosphate buffer (5.0 pH): methanol, 60:40 v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	UV-Visible detector	220	1.0	2.17 (MON), 6.24 (FEX)	0.1 (MON), 1.0 (FEX)	38
Montelukast Sodium in tablet	Water: acetonitrile (modified with 0.2% TFA), 50:50 v/v	Phenyl column 100×3.0 mm i.d, 5 µm particle size	variable wavelength UV detector	389	--	--	--	39
Montelukast and Ebastine in bulk and tablet	Methanol and water (3.0 pH adjusted by ortho phosphoric acid, 80: 20 v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	UV detector	268	1.0	6.58 (MTS), 2.98 (EBS)	1.05 (MTS), 1.13 (EBS)	40
Montelukast Sodium in tablet	Acetonitrile: 0.2% TFA, 50:50 v/v	Phenylcolumn 100 × 3.0 mm i.d, 5 µm particle size	UV detector	389	0.9	--	--	13
Montelukast and Loratadine in tablet	Sodium phosphate buffer (3.7 pH adjusted): Acetonitrile, 20:80 v/v	C18 column 250 × 4.6 mm i.d, 5 µm particle size	PDA	225	1.0	--	--	41
Montelukast Sodium in tablet	Acetonitrile:Methanol:Water (pH 3.8), 75:10:15 v/v/v	C18 column 150 × 4.6 mm i.d, 5 µm particle size	PDA	280	0.8	--	--	42

Analyte and Matrix	Mobile Phase	Stationary Phase	Detector	Detection Wavelength (nm)	Flow rate (mL/min)	Rt (min)	LOD (µg/ml)	Ref
MontelukastSodium in bulk and tablet	n-hexane: ethanol: 1,4-dioxane: TFA: diethylamine , 65:25:10:0.3:0.05 v/v	Cellulose tris (3,5-dimethylphenylcarbamate) coated on silica-gel column 25 × 4.6 mmi.d, 5 µm particle size	PDA	280	1.0	15	0.07	43

Table 3 Review of HPLC methods for estimation of Montelukast sodium in biological samples

Matrix	Internal Standard	Sample preparation	Mobile phase	Column	Detector and detection wavelength	Flow rate (ml/min)	Rt and LOD	Ref.
Human Plasma	Mefenamic acid	Protein Precipitation with Acetonitrile	Methanol: Acetonitrile:0.04M disodium hydrogen orthophosphate (4.9 pH), 22:22:56 v/v	C8 column 150mm×4.6mm i.d, 5µm particle size	fluorescence detector, em= 350nm ex=450nm	1.0	7.7 min; LLQC 5ng/ml	44
Human Plasma	Montelukast-*d*6	Protein Precipitation with Acetonitrile	10mM Ammonium formate (pH 4.0): Acetonitrile, 20:80 v/v	C18 column250 x 4.6 mmi.d,5µm particle size	ESI–MS/MS ;	0.8	2.8 ± 0.2; 0.20pg/ml LOD	45
human plasma	--	--	Gradient elution: Acetonitrile:0.1 MAmmonium acetate	C18 column 250×4.6 mm i.d	fluorescence detector, em= 350nm ex=400nm	1.0	1ng/ml LOQ	46
Human Plasma	--	Protein Precipitation with Acetonitrile	Acetonitrile: 0.02 M Ammonium phosphate (3.5 pH), 65:35 v/v	C18 column504.6 mm i.d,3µm particle size	fluorescence detector, em= 350nm ex=400nm	1.5	3.2min; 3ng/ml LLOQ	47
Human Plasma	Imipramine	Protein precipitation	Acetonitrile: Methanol: Water (containing 0.05% (v/v) formic acid),70:20:10 v/v/v	C8 column 50×4.6mm i.d, 5 µm particle size	LC-MS/MS-ESI	1.2	0.76min	48

Matrix	Internal Standard	Sample preparation	Mobile phase	Column	Detector and detection wavelength	Flow rate (ml/ min)	Rt and LOD	Ref.
Human Plasma	Quinine sulphate	Liquid Liquid Extraction	10 mMAmmonium acetate buffer (3.0 pH) : Acetonitrile, 35:65 v/v	C8 column 150 × 4.6 mmi.d, 5µm particle size	fluorescence detector, em=350nm ex=400nm	1.0	12 min; 5ng/ml LOD	49
Human Plasma	amlodipine	Liquid Liquid Extraction	10mM Ammonium acetate (6.4 pH): acetonitrile 15:85 v/v	C18 column 50 × 4.6 mmi.d, 5 µm particle size	MS (ESI)	0.5	2.77min; 0.25ng. ml LLOQ	50
Human Plasma	Zafirlukast	Protein Precipitation with Acetonitrile	Acetonitrile: 0.1% Formic acid, 84:16 v/v	C18 column 50 × 4.6 mm i.d, 1.8 µm particle size	MS	0.6	0.11ng/ ml LOQ	51
Human Plasma	montelukast-d6	Liquid Liquid extraction	20 mM Ammonium formate: Acetonitrile , 20:80 v/v	RP18e column 100× 4.6 mmi.d, 5 µm particle size	LC-MS/MS-ESI	1.2	2.5min	52
human plasma	montelukast d6	solid phase extraction	Acetonitrile: 5mM Ammonium acetate, 80:20 v/v	Phenyl column 75× 4.6 mmi.d, 3.5 µm particle size	LC-MS/MS-ESI	0.8	1.30min; 4.57 0.10 ng/ml LLOQ	53
Sheep plasma	montelukastd6	Protein Precipitation with Acetonitrile	mobile phase A (0.5% Formic acid: water) Mobile Phase B (0.5% Formic acid:Acetonitril)	RP18e column 25×4.6 mm i.d	LC-MS/MS-ESI	2.0	0.36 ng/mL LOQ	54
Human Plasma	--	Protein Precipitation with Acetonitrile	Acetonitrile : 0.05 M Ammonium phosphate buffer (pH 3.5), 62:38 v/v	C18 column 50 x4.6 mm i.d, 3µm particle size	fluorescence detector, em= 350nm ex=400nm	--	4.0min; 5ng/ml LOD	55
human plasma	--	Protein Precipitation with Acetonitrile	Solution 1: Methanol: 10mM Ammonium acetate (3.6 pH), 10:100 v/v Solution 2: Acetonitrile-10mM Ammonium acetate (5.8 pH), 32.5:100 v/v	Chiral AGP column 100× 4.0mmi.d, 5 µm particle size	fluorescence detector, em= 350nm ex=400nm	1.0	23min; 9.6ng/ ml	56

Matrix	Internal Standard	Sample preparation	Mobile phase	Column	Detector and detection wavelength	Flow rate (ml/ min)	Rt and LOD	Ref .
human plasma	Quinine bisulfate	Protein Precipitation with Acetonitrile	0.025 M Sodium acetate (4.0 pH): Acetonitrile, with 50 ml triethylamine (20:80% v/v)	C8 column 100 ×8 mm i.d, 4 µm particlesize	fluorescence detector, em= 350nm ex=400nm	1.0	1ng/ml LOD	57

3.2.2 HPTLC

High performance thin layer chromatographic technique has been widely accepted for drug analysis. It provides the advantages of ease of handling, short analysis time and flexibility to study a wide variety of compounds. About six HPTLC methods have been reported for quantitative analysis of montelukast sodium (Table 4). Mobile phase consisting of a combination of three or more solvents have been reported for montelukast sodium estimation(33, 58-62). The lowest detection limit reported is 1.536ng/spot (61). The detector involved in all the methods is UV detector.

Table 4 Reported HPTLC methods for determination of Montelukast sodium

Analyte and Matrix	Mobile Phase	Detector	Detection Wavelength (nm)	Rf	LOD (ng/spot)	Ref
Montelukast and Theophylline in bulk and tablet	Ethylacetate: Chloroform: Ethanol: Ammonia(6:4:3:1v/v/v/v)	UV	254	0.32 ± 0.01 (MONT) and 0.52 ±0.01 (THEO)	131.01 (MONT) and 597.82 (THEO)	58
Montelukast Sodium and LevocetirizineDihydrochloride in bulk and tablet	Toluene:EthylAcetate: Methanol:Ammonia (2.5: 7: 2.5: 1, v/v/v/v)	UV	231	0.31 (LEVO) 0.44 (MON)	90 (LEVO) 50 (MON)	33
Montelukast and Cetirizine in tablet	Ethyl Acetate : Methanol : Ammonia solution (25%) (14 : 3 : 2 v/v/v)	UV	230	0.30 ± 0.01 (CET) 0.52 ± 0.02 (MON)	3.94 (CET) 2.08 (MON)	59
Montelukast Sodium and Levocetirizine Dihydrochloride in tablet	ethyl Acetate: Methanol:Triethylamine (5:5:0.02 v/v/v)	UV	240	0.29±0.02 (MLS) 0.50±0.02 (LCD)	20.63 (MLS) 21.12 (LCD)	60
Montelukast Sodium and LevocetirizineDihydrochloride in tablet	Chloroform: Methanol: Toluene: Glacial acetic acid (10:5:3:0.5 v/v/v/v)	UV	269	0.89 (MON) 0.64 (LEVO)	1.536 (MON) 2.864 (LEVO)	61
Montelukast Sodium in bulk and tablet	Toluene:EthylAcetate: Glacial acetic acid (6.0:3.4:0.1 v/v/v)	UV	344	--	--	62

3.2.3 Ultra Performance Liquid Chromatography (UPLC)

Hanimi Reddy Bapatu*et al.* have developed a stability indicating UPLC method for montelukast impurities in montelukast sodium(MON) oral granules(63). The separation of the pure API and impurities were obtained on Acquity C18, 1.7µm (100 x 2.1 mm)column with a gradient elution of two solutions; mixture of buffer and acetonitrile (70:30 v/v) and mixture of buffer and acetonitrile in (30:70 v/v). The buffer composed 0.03M phosphate buffer and 1% of Sodium perchlorate and pH was adjusted to 4.9with ortho-phosphoric acid. Flow rate was 0.5mL/min, detection wavelength was 225nm and column temperature was maintained at 30°C. The method demonstrates quantitative determination of six montelukast impurities in pharmaceutical oral dosage forms in a run time of 45min. Specificity of the method has been evaluated by Forced degradation studies to generate the degradation products of the API and known impurities were spiked to the standard solution. Pure peak of MON is reported at 21.29min.

3.4 Electrochemical Analysis

Electrochemical methods of analysis posses the advantage of lesser analysis time and cost, higher sensitivity, wider linearrange, lower detection limits and portability in comparison to the other instrumental analytical techniques that require prior sample preparation, sophisticated instruments, reagents, precautions and experience (64).

N. Aslan*et al.* have for the first time published a potentiometric titration method for the estimation of montelukast sodium[MON] in a pharmaceutical preparation as well as its protonation constant (65). MON was titrated potentiometrically with hydrochloric acid as a titrant in 40% ethanol and 60% water (v/v) mixture. Potentiometric titration curve has been given and Gran's method was used for the determination of equivalence points from the potentiometric data. Authors have indicated that the similarity of the potentiometric titration curve of pure API and marketed formulations prove that the excipients added to the pharmaceutical formulation do not affect the titration curve.

I. Alsarra*et al.*reported the electrochemical property of montelukast sodium [MKST] and specifically its voltammetric behaviour(66) for the first time. Differential pulse polarographic analysis was performed on MKST in 0.1N HCl having 25% methanol as solubiliser. At pH values above 5, a decrease in diffusion current of MKST has been reported. The polarograms were generated at a scan rate 10mV/s with pulse amplitude of -50mV.The authors have demonstrated the cathodic reduction response of MKST and the involvement of reducible ethenyl group in conjugation with the quinoline nucleus and the phenyl group. The proposed method is free from interference of other API in combined pharmaceutical formulations.The limit of detection was found to be 3.41×10^{-7} M.

Ali F. Alghamdi et al. have published quantitative analysis of montelukast sodium by adsorptivestripping voltammetric method (67). The optimised experimental parameters for the voltammetric measurements were accumulation at -0.4V for 180secwith stirring at 3000rpm. The supporting electrolyte used was Britton-Robinson buffer at pH10. The applied potential was scanned at 650 mV/s, 130 Hz SW frequencyrate and 50 mV pulse amplitude. The detection limit for the proposed method was found to be 4×10^{-9} mol/L.

BernuColkesen*et al.*for the first time have reported investigation of montelukat sodium (MKST) using zinc oxide nanoparticles modified carbon paste electrode (ZnO-NP-CPE) (64).The use of mercury having toxic properties in the dropping mercury electrode has been avoided. The authors have explored the use of the ZnO nanoparticles having unique properties like fastelectron transfer kinetics and electrochemical activities. A square wave cathodicadsorptive stripping voltammeric method (SWCAdSV)was developed for estimation of MKST in pharmaceutical preparations as well as biological fluids. The LOD for the proposed method was found to be 7.7×10^{-9}mol/L.

3.5 Capillary Electrophoresis

YuliyaShakalisava et al. studied the separation of montelukast (MON) from its impurities by capillary electrophoresis and HPLC method (68). The authors found cyclodextrins had a positive effect on separation of compounds with structural similarity. Separation of MON from the impurities and it cis-isomer were obtained by using 20 mM borate buffer (pH 9.2) with 10 mM SDS and 10 mM (2-hydroxypropyl)-γ-CD (2HP-γ-CD). The results indicate that the analysis time for a single sample was 9min by the optimised CD-modified MEKC(Micellarelectrokinetic chromatography) method in comparison to the HPLC method having a run time of about 33min to resolve MON from its impurities. The Efficiency of the electrophoretic method (936859±34080 theoretical plates) was found to be higher in comparison to that of the HPLC method (3544±10 theoretical plates).

3.6 Spectrofluorometric

I. Alsarra et al. have developed a spectrofluorometric for estimation of montelukast (MKST) in dosage forms and human plasma (69). Methanol has been used as a solvent as MKST showed maximum fluorescence intensity in methanol compared to other solvents. The excitation and emission wavelengths were 340nm and 390nm respectively. Authors have reported the effects of different surfactants on the fluorescence intensity of MKST. Triton X 100 and β-cyclodextrin showed positive effect on fluorescence intensity of MKST while gelatine, CMC and sodium dodecyl sulphate showed negative effect. The authors have reported the effect of artificial daylight on the stability of MKST solution. Exposure to deuterium lamp did not affect the fluorescence intensity of the drug while the exposure to xenon lamp showed a decrease in fluorescence intensity by 50% in 25min. The LOD for the proposed method was found to be 0.02µg/ml for MKST. The proposed method was applied to paediatric tablets, chewable tablets and human plasma for assay of MKST.

4. CONCLUSION

This review is aimed at focussing on the thorough literature survey of the various analytical techniques reported for the assay of montelukast solid from different sample matrices. The literature review supports the fact that for estimation of montelukast sodium from biological samples where the concentration of the drug is in very small amount, the choice of detector becomes crucial. Reported methods show that only fluorescence detector (up to nanogram level) and mass spectrometer (up to picogram level) are effective for detection of the drug in the biological matrix. PDA detector has been reported for estimation of the drug in bulk and pharmaceutical dosage form only. The conventional UV spectroscopy has been used for assay of the drug individually or in combination with other API from bulk or a dosage form where the concentration of the analyte is higher in comparison to the biological sample. The presence of multiple drugs in a formulation causes a crucial challenge to the analyst during the selection of spectrophotometric methods of analysis. The review has summarised the simultaneous estimation methods developed for the assay of montelukast sodium in presence of multiple drugs in a formulation. For such cases, chemometric techniques for quantitative analysis can be considered (70-71, 19).The review also highlights the use of electroanaytical techniques for the assay of montelukast sodium. These techniques provide the advantage of analysis of multiple samples in a short duration with specific and lower detection limits.

5. CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

6. ACKNOWLEDGEMENT

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