

# Newly Simple Quantitative Determination of Montelukast Sodium by Ultraviolet-Spectrophotometry



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## ABSTRACT

Montelukast sodium is well known pharmaceutically for its action as leukotriene antagonist and relieving symptoms associated with asthma is available in the market as tablet, chewable tablet, and powder. The aim of this study was to develop newly simple selective ultraviolet spectrophotometry (UV) method for daily routine analysis of quality control department. The UV method was developed with wavelength at 287.0 nm. This newly developed method was effectively applied to tablet dosage form of the motelukast sodium follow the Beer's Lamberts at range 2.5–50 µg/mL. The validated parameters were carryout such as linearity, accuracy, precision, and specificity. The result of validation statistically studied and found to be satisfactory.

**Index Terms:** Ultraviolet, Montelukast, Determination, Validation, Quantitative, Method

## 1. INTRODUCTION

Montelukast sodium (MTK) which has the following chemical structure (Fig. 1) is considered as a good alternative to corticosteroid inhaler in treating asthma and rhinitis since it has fewer side effects [1]. MTK mechanism of action is by blocking the action of CysLT receptor Type 1 in respiratory system that results in relaxing smooth muscle and decreasing inflammation. MKT hydrophobic acidic drug that has water solubility about 0.2–0.5 µg/mL at room temperature; therefore, it is considered as Class II compound according to biopharmaceutic category system [2].

Montelukast base solubility enhanced through salt formation as sodium salt of montelukast MTK. MTK possess acidic

lipophilic property with a PKa between 2.7 and 5.8 and logP 8.79 which make it soluble in higher pH media [2]. MTK is available as a tablet dosage form under the brand name of Singulair for both adult and children from age 6 months and older with no detected adverse effect [3].

Different methods have been studied to determine amount of MTK in its dosage form such as capillary electrophoresis [4], cyclic voltammetry [5], high performance liquid chromatography (HPLC) with florescence detection [6], and HPLC with ultraviolet (UV) detection [7], this study develop simple, specific, accurate, and precise method by UV-spectrophotometry and validate it according to International Council for Harmonisation (ICH) guideline, and evaluate this new method with previously published method that has the same way of determination.

## 2. MATERIALS AND METHODS

### 2.1. Instrumentation

For determination UV double beam (Spekol 2000, analytikjena, Canada) with two identical 1 cm quartzes cell

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was used, all materials were weighed by electronic sensitive balance (Sartorius, Germany), water bath sonicator (Starsonic, Italy) used to aid dissolving solute in solvent during solution preparation.

## 2.2. Materials

Pure MTK, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and croscarmellose sodium were kindly provided by PiONEER for pharmaceutical industry, Iraq. Ethanol 96% was purchased from Merck, Germany.

## 2.3. Standard Stock Solution and Calibration Curve Solution Preparation

Stock solution of  $100 \mu\text{g mL}^{-1}$  of active pharmaceutical ingredient (API) was prepared by dissolving 25 mg of API into 250 mL of diluent (Water: Ethanol) (1:1 V/V)

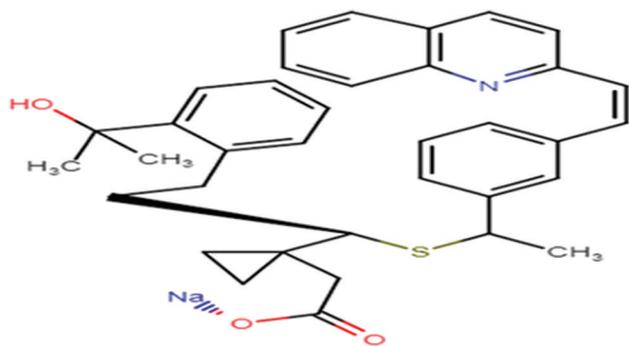


Fig. 1. Chemical structure of montelukast sodium.

sonicated for few minutes. Series solutions of the following concentration were prepared from stock solution in same the diluent (2.5, 5, 10, 15, 25, and 50  $\mu\text{g/mL}$ ). Each solution was read triplicate and average of each sample was put into linear graph.

## 2.4. Method Development

Different media for dissolving MTK were evaluated to choose best solvent for API depending on solubility of MTK, stability, cost, selectivity, and toxicity. First water used as solvent then ethanol was added gradually till found that ethanol with water by 1:1 (V/V) will give clear solution. The prepared standard solution scanned and found that best absorption would be at 287.0 nm.

## 2.5. Stability

Stability of MTK solution of calibration was determined at room temperature in day light condition for a period of 24 h by observing change in absorbance at the same wavelength.

## 2.6. Analytical Validation

ICH (Q2) R guideline of validation of analytical procedure was applied for validating developed method as the following:

### 2.6.1. Precision

Both interday and intraday of precision were analyzed with median concentration of API. Intraday precision was completed by evaluating the median concentration of the MTK at the

TABLE 1: Different concentration of MTK solution at different level with corresponding absorption

Linearity sample 2 zero time					
level	Conce ug/mL	abs	avearge Area		
50%	2.50	0.1136	0.113866667	slope	0.04699946417
		0.114		intercept	0.01064293369
		0.114		r	0.9996766948
				r2	0.9994
75%	5.00	0.2447	0.2449		
		0.245			
		0.245			
100%	10.00	0.4784	0.4784		
		0.4784			
		0.4784			
125%	15.00	0.7093	0.7093		
		0.7093			
		0.7093			
150%	25.00	1.225	1.226533333		
		1.2273			
		1.2273			
200%	50.00	2.3433	2.3433		
		2.3433			
		2.3433			

same day while interday precision was studied over consecutive days for the same concentration repeated 6 times. Evaluating precision of an analytical procedure provide statistics data on the unsystematic error. It states agreement between numbers of measurements achieved from several sampling of the same identical sample under approved conditions. The percentage of relative standard deviation (% RSD) values were studied and the low value of % RSD indicated the precisely of the analytical procedure. The value % RSD for the precision study according to ICH guideline should be <2% (interday precision) this to confirms good precision of the method.

### 2.6.2. Recovery

Recovery was completed using the method where identified quantity of standard MTK equivalent to 75, 100, and 125% of linear concentration had been added to placebo. The samples were read 3 times and percentage amount of API was calculated at each level.

### 2.6.3. Linearity

Calibration curve for standard MTK solution was obtained in range from  $2.5 \mu\text{g mL}^{-1}$  to  $50 \mu\text{g mL}^{-1}$  for MTK. Peak absorbance for each concentration must plot against respective concentrations and linear regression analysis should obtain the correlation coefficient higher than 0.999 to confirm that there is an excellent relationship between the absorbance and concentration of the samples and method have linear in response.

### 2.7. Statistical Analysis

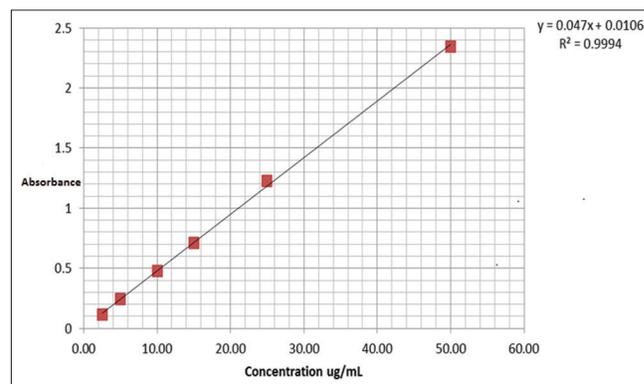
Basic statistical analysis was applied such as mean, standard deviation, average, and RSD% using Microsoft Excel.

## 3. RESULTS AND DISCUSSION

This rapid technique for determination of the MTK is useful in drug analysis especially in pharmaceutical industry when time costs especially using HPLC for determination of MTK is time consuming and requires effort and high cost. Choosing the best solvent for preparing solution of MTK is a bit challenging in this study. Different solvents have been tried and found that equal volume of (water: ethanol) give clear solution, its cheap, available in almost every laboratory, and easy to use. This diluent makes this study different from other previously studies in which in most of them, Methanol 100% [8]-[10], Methanol 50% [11], [12], methanol with 0.1N NaOH [13], chloroform [14], or 7.4 pH phosphate buffer with 0.5% sodium lauryl sulfate [15] were used during solution preparation of MTK.

**TABLE 2: Precision of the method (n=6).**

Parameter	Amount obtained by the proposed method in (mg)	
	Interday	Intraday
Mean	10.13	10.44
SD	0.00923	0.0105
RSD%	0.91%	1.01%



**Fig. 2.** Calibration curve of MTK at different concentration.

Different wavelengths have been suggested for reading MTK standard solution in different articles such as 344.4 [11], 359 [8], 344.3 [10], 283 [9], 287.3 [15], 286.5 [13], and 280 nm [12] but in the present research when standard solution of MTK in equal mixed volume of (ethanol: water) scanned by UV absorbance to find characteristic peak at wavelength between 400 and 200 nm by 0.2 nm interval, it was found that best absorbance is at 287.0 nm at nominal concentration of 10–15  $\mu\text{g/mL}$ . The suggested method was validated regarding to ICH guideline in the following aspects.

### 3.1. Specificity and Selectivity

MTK solution of concentration 10  $\mu\text{g/mL}$  in diluent was prepared in both alone and mixed with common excipient such as (lactose monohydrate, magnesium stearate, microcrystalline cellulose, and croscarmellose sodium) separately to know the interference of these excipients with API. Both solutions were scanned at wavelength between 400 and 200 nm. Method was specific and selective and there was no interference in reading between API and excipients.

### 3.2. Linearity

For linearity, six different concentrations were prepared from lower concentration 2.5  $\mu\text{g/mL}$  to higher concentration 50.0  $\mu\text{g/mL}$ . Each concentration was read 3 times as shown in the Table 1. Linear relationship was observed between

**TABLE 3: Accuracy of MTK**

Standard Data						
Weight	dil. Factor	Conc. µg/mL	Area	Average Area	SD	RSD%
		10.000	0.47840 0.47840 0.47840	0.4784	0.00	0.0%
Accuracy - recovery of MTK						
Level	Quantity spiked µg/mL	Area	Quantity recovered µg/mL	% recovery	Average Recovery (%)	%RSD
75	5.00	0.2395	5.01	100.13	100.25	0.11
		0.2400	5.02	100.33		
		0.2399	5.01	100.29		
100	10.00	0.4760	9.95	99.50	99.45	0.04
		0.4757	9.94	99.44		
		0.4756	9.94	99.41		
125	15.00	0.7105	14.85	99.01	99.04	0.04
		0.7110	14.86	99.08		
		0.7107	14.86	99.04		
Average					99.58	

concentrations of MTK besides mean reading of absorbance at each point as it is clear in Fig. 2 the determination correlation coefficient ( $r^2$ ) equal to 0.999.

### 3.3. Precision

The method was evaluated to confirm precise in repeatability of analyzing six samples. The samples were prepared and the percentage of label claim of API of each sample was statistically evaluated. Results are shown in Table 2. The results were accepted according to acceptance criteria for assay value obtained from single analyst %RSD should be <2.0% while %RSD of two analyst performing the same samples that terminated in both days should not be more than 3.0%.

### 3.4. Recovery

Accuracy and recovery of assay for the method was demonstrated by analyzing data achieved from standard addition into placebo solution at three levels. The amount of recovery of each sample was determined in percentage at each level and % RSD was calculated that was <2.0% shows a good accuracy of method. As it is clear in Table 3, according to ICH guidelines, good recovery of API should lie within the range of 98–102% which means the percentage recovery of API added to placebo should be in range of  $100 \pm 2.0\%$  for average of three weight samples at each level.

### 3.5. Stability

The prepared solutions were stored at room temperature 25°C, analyzed after 24 h and it was found that MTK is stable for this period of analysis in diluent.

## 4. CONCLUSION

The validated UV method for MTK determination indicated that the method is linear, accurate, rapid, and specific. The simplicity of method allows it to be used in laboratories that have simple equipment and lack HPLC, liquid chromatography mass spectrometry, or ultra-performance liquid chromatography especially for repetitive analysis of MTK in pharmaceutical dosage form or during development of new dosage form of MTK. The current method is also useful for quantitative determination of MTK in quality control department in pharmaceutical industry.

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