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# Method Development and Validation of Forced Degradation Studies of Montelukast Sodium by Using UV Spectroscopy

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## ABSTRACT

A new, rapid, precise, selective and sensitive validative forced degradative UV spectroscopy method was developed for estimation of Montelukast sodium in bulk and pharmaceutical formulation in the developed method, the absorbance was measured at 272.19nm.the drugs obeyed the Beer's law in the concentration range of 30-150µg/mL. Accuracy studies of the method were determined by recovery studies and were found to be 99.9 for Montelukast sodium. It can be used for routine analysis of drug in bulk and in pharmaceutical formulation.

**Keywords:** forced degradation studies, Montelukast sodium,validation.

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## INTRODUCTION

Montelukast sodium[1] is 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. Selectively antagonist leukotriene D4(LTD4), at thecysteinyl leukotriene receptor, cys LT1 ,in the human airway montelukast inhibit action of LTD4at the cyst1 receptor, preventing airway edema, smooth muscle contraction and enhance secretion of thick viscous mucous. Literature survey revealed that there are several methods for analysis of Montelukast sodium using spectroflurometric method, visible spectropphotometric methods,. Forced degradation studies method has not been reported for estimation of montekuast sodium.In this study a simple, precise, accurate and validated method is described for estimation of montelukast sodium in bulk and pharmaceutical formulation.

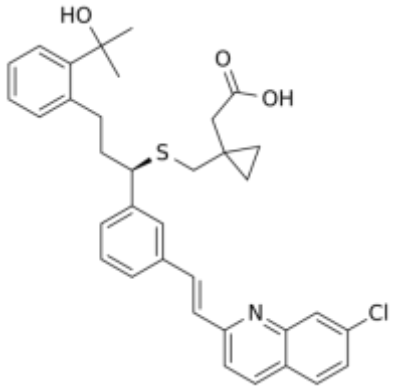


**Figure 1: Structure of Montelukast**

## MATERIALS AND METHODS

### Apparatus

Shimadzu UV -1800 double beam spectrophotometer with 1cm path length supported by shimadzu UV-probe software ,version 2.21 was used for spectral measurements with 10mm matched quartz cells . Shimadzu balance (BL-220H) was used for weighing.

### Chemicals and solvents used

Hydrochloric acid (AR Grade) , Sodium hydroxide(AR Grade) , Hydrogen peroxide(AR Grade) was purchased from Merck fine chemicals(Mumbai, India), double distilled water was used.

### Drug samples

Montelukast sodium (working standard 99.7) was obtained as gift sample from sun pharmaceuticals, India. Commercial tablets of Montelukast sodium (ROMILAST) was purchased from local pharmacy.

**Preparation of standard solution:** Accurately weighed 10mg of MKT working standard in 10mL. volumetric flask containing 5mL. of water shaken for 5min then remaining volume made up to the mark with distilled water. The final concentration obtained was 1000µg/mL. It was further diluted to get concentration 100µg/mL.was prepared with distilled water .From this a series of aliquots were prepared to get concentration ranging from 30-150µg/mL.in 10mL. vol. flasks using distilled water.

**Calibration curve of standard solution**

The wavelength was selected by preparing a solution of concentration 30µg/mL by diluting the standard solution with distilled water. The solution was scanned in the wave length range of 200-400nm using distilled water as blank. The UV spectrum of MONTELUKAST SODIUM showed $\lambda_{max}$ at 272 nm .The calibration curves was prepared in concentration range of 30-150µg/mL.. Absorbance of each concentration plotted by taking absorbance on y-axis and concentration on x-axis. The regression equation was calculated and the results were shown in the table.The regression equation was used to estimate the drug content in tablet dosage form.

**Preparation of sample solution**

For the estimation of Montelukast sodiumin the commercial formulations, 20 tablets(ROMILAST) each containing 10mg of Montelukast sodiumwere weighed and the average weight was calculated. The tablets were crushed and powdered in glass mortar. For the analysis of drug, quantity of powder equivalent 10 mg of Montelukast sodium was transferred to 10 mL. volumetric flask and dissolved in sufficient quantity of distilled water and volume made up to the mark with distilled water to obtain conc. of 1000 µg/mL.. ofMontelukast sodium .Then the solution was filtered through whattman filter paper no.41.Further dilutions of the solution were made in distilled water to get required concentration of 30 µg/mL. The assay procedure was repeated for six times (n= 6).

**Validation of the Method**

Validation of the respective method for the following parameter'swas carried as per the ICH guidelines

**Linearity**

The linearity of the proposed UV spectroscopic method was evaluated by analyzing different concentrations of standard solutions of Montelukast sodium and by plotting absorbances of analyte against concentrations of the analyte. Beer's law was obeyed in the range of 30-150 µg/mL.. A good linear relationship ($R^2$ =0.996) was observed between the concentrations of Montelukast sodium and the corresponding absorbance. The regression analysis was made for slope, intercept

and correlation coefficient values. The slope, intercept and the correlation coefficient of the drug were shown in the table.

**Accuracy**

Accuracy is express as degree of closeness of experimental value to the true value. To study the accuracy of the proposed method and to check the interferences from excipients used in the dosage forms, recovery experiments were carried out by standard addition method. This parameter is evaluated by percent recovery studies at concentration levels of 50,100 and 150 % which includes addition of known amounts of Montelukast sodium working standard to a prequantified sample solution. Each of the dilution was observed six times. The samples were reanalyzed by proposed methods. The amount of Montelukast sodium was estimated by applying obtained values to regression equation. The percentage recovery of the drug was calculated. The results were shown in the Table No

**Precision**

Precision is the level of repeatability of results as reported between samples analyzed on the same day (Intra – day) and samples run on three different days (Inter – day). To check the intra – day and inter – day variation of the methods, solutions containing 30,60 and 90µg/mL.concentrations of Montelukast sodium were subjected to the proposed spectrophotometric method of analysis and the recoveries obtained were noted. The precision of the proposed method i.e. the intra and inter day variations in the absorbance of the drug solutions was calculated in terms of % RSD. The values were shown in table.

**Stability Studies**

**Acid degradation**

Transfer 1mL. (1000ug/mL. MKT) of above stock solution to10mL. volumetric flask and add 1mL. of 1N HCL and finally make up the volume with distilled water and kept aside for 24hrs at room temperature. From this transfer 0.6mL. drug solution into 10mL. volumetric flask and neutralize with 1mL. of 1N NaOH, the final volume made up to with distilled water to get the concentration of 60µg/mL.. The absorbance was measured using above developed methods against blank contain 0.5mL. of 1NHCl and 0.5mL. of 1NNaOH in 10mL. volumetric flask the final volume made up to the mark with distilled water.

**Basic degradation**

Transfer 1mL. (1000ug/mL. MKT) of above stock solution to10mL. volumetric flask and add 1mL. of 1N NaOH and finally make up the volume with distilled water and kept aside for 24hrs at room temperature. From this transfer 0.6mL. drug solution into 10mL. volumetric flask and

neutralize with 1mL. of 1N HCl, the final volume made upto the mark with distilled water to get the concentration of 60µg/mL. The absorbance was measured using above developed methods against blank contain 0.5mL. of 1NHCl and 0.5mL. of 1NNaOH in 10mL. volumetric flask the final volume made up to the mark with distilled water.

**Peroxide condition**

Transfer 1mL (1000ug/mL. of MKT) of above stock solution to10mL volumetric flask and add 1mL of 3%v/v $H_2O_2$ and finally make up the volume with distilled water and kept aside for 24 hrs at room temperature from this transfer 0.6mL of above solution in to 10mL. volumetric flask and final volume made up to the mark with distilled water to get the concentration of 60µg/mL. The absorbance was measured using above developed methods against blank contain above solution without drug in 10mL. volumetric flask the final volume made upto the mark with distilled water.

## RESULTS AND DISCUSSIONS

The proposed method for estimation of Montelukast sodium were found to be simple, precise, accurate and economical , the absorption maxima was found to be 272.19 nm, The calibration curve was linear in the concentration range 30-150 µg/mL. (table no.8.5). The % assay by the three methods was found to be in the range 99-103% for montelukast. No interference was observed from the pharmaceutical excipients. The recovery studies showed that this method is accurate and reproducible. The results revealed that any change in the drug concentration could be accurately determined by the this method. Accuracy and reproducibility of the proposed methods were further confirmed by percent recovery values, as shown in the table. Intermediate precision studies for the method % RSD is not more than 2.0 indicate good intermediate precision which were shown in table Hence, the proposed methods were validated in terms of linearity, precision and accuracy. Characteristic parameters and summary of validation parameters for all the three methods were given in table. By observing the validation parameters, the method were found to be simple, accuracy and precise. Hence these methods can be employed for the routine analysis of Montelukast sodium in tablet formulations.

**Degradation studies**

Results are tabulated in table no.9.6

**Acid hydrolysis (figure 9.3.1)**

Upon performance of acid degradation studies 5% ofMontelukast sodium was degraded for 24hrs,

**Base hydrolysis (figure.9.4.1)**

Upon performance of base degradation studies 1% ofMontelukast sodium was degraded for 24hrs,

**Peroxide hydrolysis (figure.9.5.3)**

Upon performance of peroxide degradation studies 3% of Montelukast sodium was degraded for 24hrs,

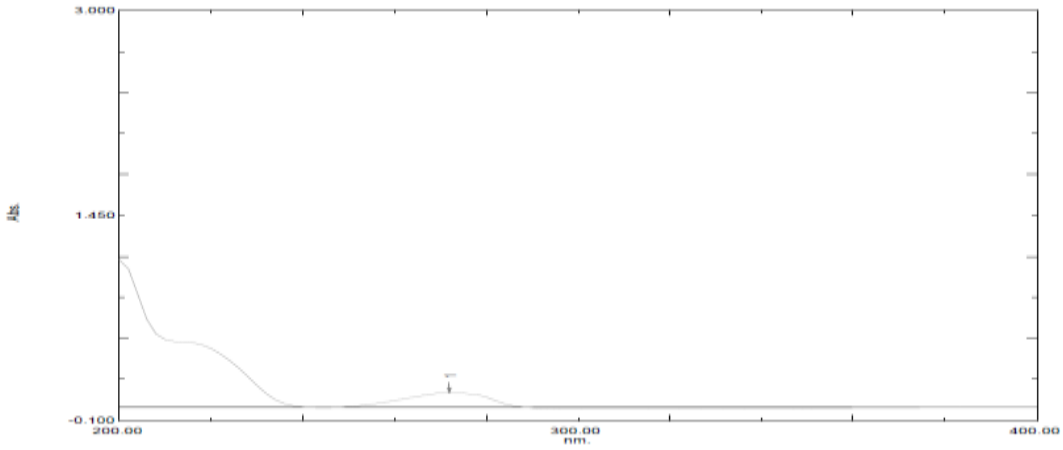


**Figure 2: λMax spectrum of Montelukast sodium**

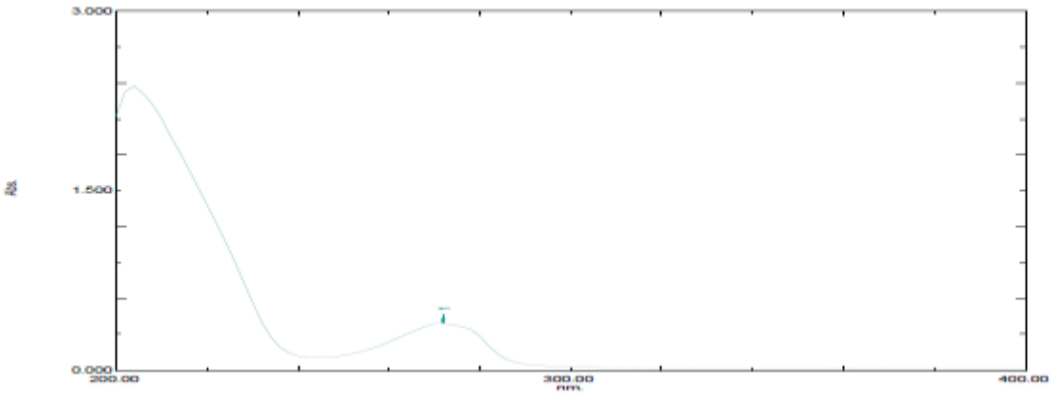


**Figure 3: 1N HCL 60µg/mL.**

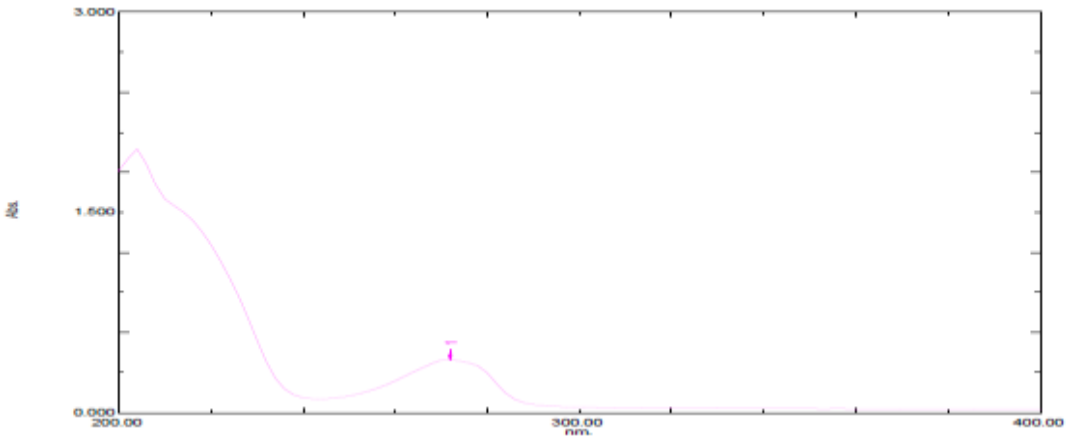


**Figure 4: 1N NAOH 60µg/mL**

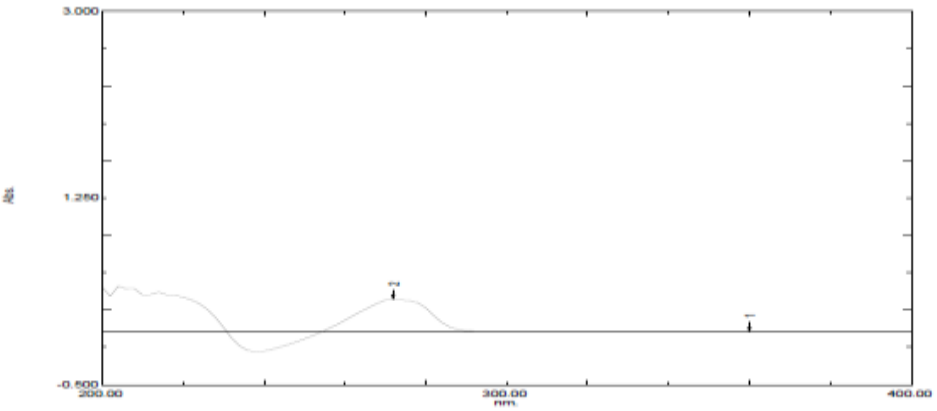


**Figure 5: 3%$H_2O_2$ 60µg/mL.**

**Table 1: Optical characteristics of proposed UV method**

| Parameter | Method |
|---|---|
| Max | 272.19 |
| Beer's limit (µg/mL..) | 30-90 |
| Molar extinction coefficient (L/Mol.cm) | 0.006 |
| Correlation coefficient ($r^2$) | 0.996 |
| Slope (a) | 0.006 |
| Intercept (b) | 0.003 |

**Table 2: Recovery studies of proposed UV method**

| Conc. taken (µg/mL) | Recovery level (%) | Amount added (µg/mL.) | Amount found (µg/mL.) (n = 6) | % Recovery |
|---|---|---|---|---|
| 30 | 50 | 15 | 44.685 | 98.33 |
| 30 | 100 | 30 | 59.25 | 98.75 |
| 30 | 150 | 45 | 74.25 | 99.00 |

**Table 3: Precssion studies of the proposed method**

| Concentration taken (µg/mL) | Intra day precision | | Inter day precision | |
|---|---|---|---|---|
| | %Recovery±SD; (n=3) | % RSD | %Recovery±SD; (n=3) | % RSD |
| 30 | 99.66±0.173 | 0.86 | 99.92± 0.28 | 0.94 |
| 60 | 99.99±0.753 | 0.93 | 98.70± 0.980 | 0.98 |
| 90 | 98.92 ±1.38 | 1.25 | 97.97 ±1.53 | 1.58 |

**Table 4: Stability studies of Montelukast sodium**

| Stress Condition | Concentration Taken | $\lambda_{max}$ | Normal absorbance | Absorbance (24hrs) | %degradation |
|---|---|---|---|---|---|
| Acidic/0.1N HCl/24hr at room temperature | 60 | 272.19 | 0.401 | 0.380 | 5% |
| Basic/0.1N NaOH/24hr at room temperature | 60 | 272.19 | 0.401 | 0.400 | 1% |
| Oxidising 3%v/v $H_2O_2$ 24hr at room temperature | 60 | 272.9 | 0.401 | 0.388 | 3% |

**Table 5: Summary of validation parameters of Montelukast sodium**

| Parameter | Method |
|---|---|
| $\lambda_{max}$ | 272 nm |
| Beer's limit (µg/mL) | 30-150µ |
| Linearity indicated by correlation coefficient | 0.996 |
| LOD(µg/mL.) | 1.33 |
| LOQ(µg/mL.) | 3.99 |
| Precision indicated by % RSD | 0.86 |
| Accuracy indicated by % recovery | 98.33 |

## CONCLUSION

The proposed method is simple, sensitive, and reproducible and hence can be used in routine analysis for determination of Montelukast sodium in bulk as well as in pharmaceutical preparations.statistical analysis of the results has been carried out revelin high accuracy and good precission.

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## REFERENCES

1. Shanmukhakumar.j.v, et al spectrophotometric determination of montelukast sodium in bulk and pharmaceutical formulation scholars research library 2012, 4(2); 720-724
2. K. pallaviet al validated UV spectroscopic method for estimation of montelukastsodium from bulk and tablet formulations international journal of advances in pharmacy and bilogy volume.1 (4) oct-dec , 2012.
3. G.srihari, et al a simple spectrophotometric assay of montelukastsodium in pharmaceutical formulations J.chem.pharma .Res , 2011, 3(6);23-27.
4. Alsarra,Net al spectrofluorometric determination of montelukast sodium in pharmaceutical dosage forms and spiked human plasma pharmazie 60;823-826 (2005).
5. PatelNilam.K et al spectrophotometric determination of montelukast sodium and levocitrizine in tablet dosage form by AUC method Der pharma chemical 2011,3,(5) ;135-140.
6. S.R.B hagade et al spectrophotometric determination of montelukast sodium in bulk and pharmaceutical formulation IJPSR , 2013 vol.4 (11) ;4432-4434.
7. R IMA m .Banker et al simultaneous estimation of montelukast sodium and desloratadine by ratio spectra derivative spectrophotometry method in combined dosage forms journal of

chemical and pharmaceutical research, 2013, 5(1); 193-199.

8. Mineketansahoo et al method development and validation of montelukast sodium in bulk and pharmaceutical formulation by RP–HPLC journal of biomedical and pharmaceutical research 1(2) 2012, 18-26.
9. A Laxmanaraoet al method development and validation ofmontelukast sodium in bulk and pharmaceutical formulation by RP – HPLC IJPCBS 2011, 1(1),12-16
10. J Roman et al stability indicating method for montelukastsodium in bulk and pharmaceutical formulation by micellarelectrokinetic capillary chromatography Pharmazie 65(2010) 644-647.