Research Article

DETERMINATION OF MONTELUKAST SODIUM IN ORAL GRANULES DOSAGE FORMS BY A SIMPLE AND ACCURATE UV SPECTROPHOTOMETRIC METHODS

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ABSTRACT

This paper describes a simple, accurate, specific and validated method for quantitative determination of Montelukast Sodium in oral granules dosage form. Pharmacopeias have not yet provided any compendial or official method for its quantification. A study was carried out of all the parameters established as per ICH, to validate an analytical method for a solid oral granule, i.e. linearity, range, accuracy, precision and specificity. A wavelength maxima of Montelukast Sodium was selected at 285 nm as its characteristic property. Method was found to be linear in the range of 2.4 ppm to 24 ppm with a correlation coefficient (r) of 0.9998. This sensitive method was capable to recover accurately and precisely from 50 % level to 150 % level of target concentration. Bench top stability of the standard solution and test solution was also established. Method was successfully validated. In addition, this proposed method was simple, sensitive, easy to apply, does not use polluting reagents and requires relatively inexpensive instruments. The proposed method can be used for analysis in routine quality control tool and for quantitative determination of the Montelukast sodium in its oral granules dosage form in pharmaceutical industries.

Keywords: Montelukast Sodium, oral granules, UV method, Stability of Montelukast solution.

INTRODUCTION

Montelukast Sodium (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 is a white colored powder and it is freely soluble in ethanol, methanol, and water and practically insoluble in acetonitrile. Molecular weight of Montelukast Sodium is 608.2 g/mol and formula is $C_{35}H_{35}ClNO_3S.Na$. For structure refer Figure 1.[1-3]
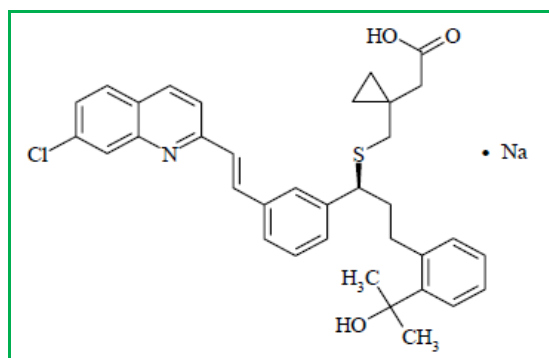

Figure 1: Structure of Montelukast Sodium

Montelukast (sodium salt) is potent, selective CysLT1 receptor anatagonist. It is indicated for the prophylaxis and chronic treatment of asthma in adults and pediatric patients. The drug is commercially available in various forms of once-daily oral dosage formulations including oral granules. In oral dosage form, each packet contains Montelukast Sodium equivalent to 4 mg of Montelukast.

Several analytical methods have been reported for determination of Montelukast including derivative spectroscopic[4], by colorimetry[5], by flouorimetry[6], by TLC[7], by HPTLC[8], by simultaneous UV determination in combination drug formulation[9], by voltametry[10], by high performance liquid chromatography (HPLC)[11] and by LCMS[12].

To our knowledge, there is no simple and accurate UV spectrophotometric method for quantitative determination of Montelukast Sodium in its oral granules dosage form. Pharmacopeias have not yet provided any compendial or official method for its quantification.

The objective of study to develop and validate a simple, eco-friendly UV spectrophotometric method for the determination of Montelukast in Montelukast Sodium oral granule dosage forms (strength is 4 mg as Montelukast). Also method should be capable and eco-friendly to apply in routine Quality control analysis.

MATERIALS AND METHODS

Instrument, Chemicals, Reagents and Samples

Analysis for determination were carried out on UV-Visible spectrograph (Shimadzu UV-2450) with 1 cm quartz cell (Hellma) QC working standard of Montelukast Sodium salt was used. Test sample used for development & validation study of Montelukast Sodium oral granules dosage form and its respective placebo were manufactured in-house ie. Generics Research and Development, Integrated Product Development, Dr. Reddy's Laboratories Ltd., Hyderabad, India.

Sodium Lauryl Sulfate (SLS) (AR grade, Merck), ethanol (AR grade, Standard) and de-ionized water were used for analysis.

Experimental Conditions

Standard preparation, test preparation and respective placebo preparation were scanned between 200-400 nm. Absorbance of the solution was measured at wavelength maxima of Montelukast at 285 nm.

Standard and Test Preparation

Standard solution was made from Montelukast Sodium Working standard and test solution was made from its oral dosage formulation. Both standard and test were prepared accordingly with a target concentration of 12 ppm as Montelukast in diluent (0.5 % w/v SLS in de-ionized water) and kept stored at bench top (room temperature), protected from light. Placebo was also made similarly as per test preparation to observe any placebo interference. Absorbances of the solutions were measured at 285 nm.

RESULTS AND DISCUSSION

Method Development and Optimization

To dissolve standard and test 0.5% w/v SLS in de-ionized water was found suitable and also taken for UV baseline correction. Standard solution and placebo solution were scanned from 200 nm to 400 nm. No placebo interference was found. So, to establish a simple determination method, wavelength maxima was extracted from zero order of Montelukast spectrum ie. 285 nm. Test target concentration was finalized to have absorbance about 0.5 AUFS so that during method validation absorbance of 50 % to 150 % of test target concentration should fall in absorbance range as per Beer Lambert's law (between 0.1 to 1.0 AUFS)

Method Validation

Validation of the developed method was carried out as per ICH guidelines. Parameters such as Method precision, Specificity, Linearity, Accuracy and Solution stability were taken up as tests for method validation.

Linearity

For quantitative analysis of Montelukast, the linearity curve was plotted. Linearity range of Montelukast was established in concentration range of 2.4 ppm to 24 ppm. The slope and intercept along with its correlation coefficient is given in Figure-2. % Bias of linear curve was also calculated [(intercept of linear curve / Response at 100% target concentration) x 100] and was found satisfactory (refer table-1).

Specificity

Method was found specific as no placebo interference was found (refer Figure-3).

Precision

The precision of the analytic methods are determined by repeatability. RSD for six data of absorbance for standard solution found satisfactory and six samples of oral dosage formulations are prepared and analyzed. Method was

found précised. Refer table 1. Refer spectrum for Standard solution (Figure-4) and for sample solution (Figure- 5).
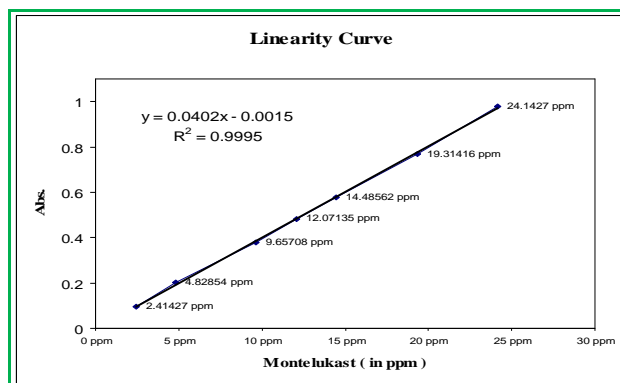

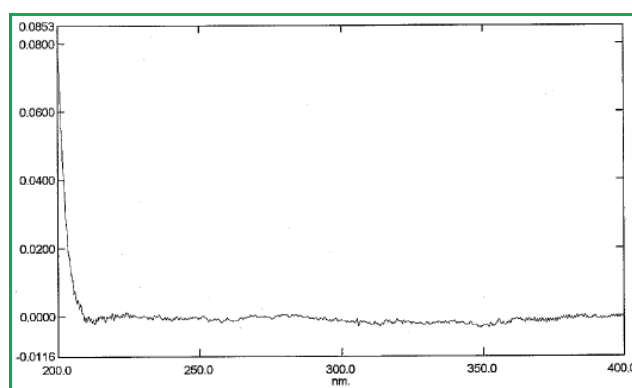**Figure 2:** Linearity plot of Montelukast
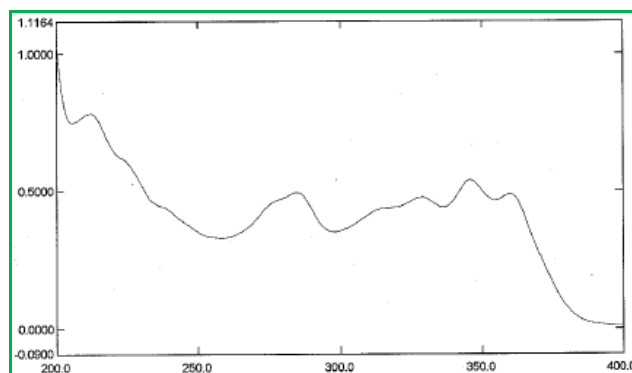

Figure 3: UV spectra of Placebo

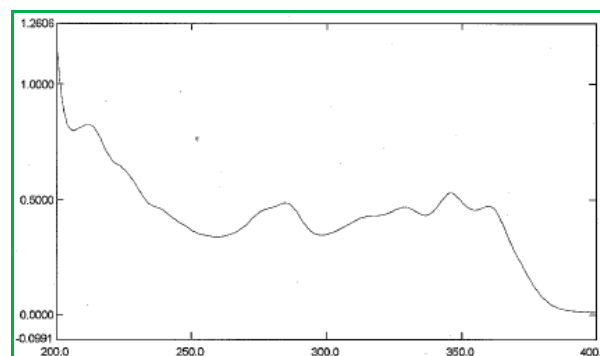**Figure 4:** UV spectra of Montelukast Standard

Figure 5: UV spectra of Montelukast Test

Accuracy / Recovery

To determine accuracy of the analytical method for Montelukast content in oral dosage formulations, the recovery was determined at six levels ie. 50%, 75%, 100%, 125% and 150% of target concentration (12 ppm of Montelukast). To ensure the precision at 50% level and at 150% level, at each level six samples of oral dosage formulations are prepared and analyzed. Results of are tabulated in table 1.

Stability

To evaluate the bench top stability up to one day for Montelukast in standard solution and test solution, solution were kept at room temperature.

For standard solution, similarity factor was calculated from initial to one day and was found within the acceptance criteria of 0.98 to 1.02. A formula for similarity factor is mentioned below.

Similarity factor = (Absorbance of initial standard solution / Absorbance of bench top stable standard solution)

Refrigerator stability was not required as it was found stable at room temperature.

For test solution, % assay of Montelukast test solution were estimated against freshly prepared standard solution. The difference in % assay of Test preparations from initial to one day was found to be within the limits (difference in % assay value from initial should be not more than 3.0 %).

Placebo solution was also kept along with standard and test solution to ensure no further enhancement in interference. No placebo interference is observed from bench top stable placebo solution. It is also found bench top stable up to 1 day.

The developed method was found to be precise, specific, linear and accurate during method validation. Bench top stability (up to 1 day) of standard and test preparation were established by keeping the preparation at room temperature and the preparations were found to be stable. The results are summarized in table 1.

Table 1: Table of results of method validation

Validation parameters	Montelukast
Method Precision	
(Mean % assay ± % RSD, n = 6)	99.6 ± 0.51
Linearity	
a) Correlation coefficient (2.41 ppm to 24.14 ppm)	0.9998
b) R^2 (RSQ)	0.9995
c) % Bias at 100 % response level	0.30%
Accuracy	
a) at 50% level (6.10 ppm) (n=6)	98.7 %
b) at 75% level (9.23 ppm)	100.5 %
c) at 100% level (12.25 ppm)	99.6 %
d) at 125% level (15.31 ppm)	100.1 %
e) at 150% level (18.38 ppm) (n=6)	101.4 %
Bench top stability (1 day)	
a) Standard solution stability (Similarity Factor)	1.01
b) Test solution stability (Assay value difference from initial)	0.24 %
c) Placebo solution stability	Yes

CONCLUSION

The proposed method is simple, sensitive, easy to apply, cost effective, does not use polluting reagents and rapid to analyze. This proposed method can be used as a routine quality control tool for estimation of Montelukast in Montelukast Sodium oral granule dosage forms as a unique active principle in pharmaceutical industries.

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