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Method Development and Validation for the Simultaneous Estimation of Montelukast Sodium and Levocetirizine Hydrochloride Tablet using RP-HPLC

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Abstract:

A simple, accurate and sensitive isocratic reverse phase high performance liquid chromatography method was developed for simultaneous determination of montelukast sodium and levocetirizine hydrochloride in tablets. The effective separation was achieved on Hypersil C18, 100 x 4.6 mm, 3 µm. The mixture of buffer and acetonitrile in the ratio 90: 10v/v used as a mobile phase. The buffer is prepare as 2.8g of disodium hydrogen orthophosphate in 1000 ml of purified water and adjust with diluted ortho-phosphoric acid upto pH 7.0. The flow rate of the mobile phase was 1.0mL/min and the total elution time was 15 minutes. The UV detection wavelength was carried out at 230 nm and experiments were done at 25°C. The developed method were validated in terms of system suitability, selectivity, linearity, precision, accuracy, limits of detection and quantification for the impurities following the ICH guidelines and successfully applied for the determination of investigated drugs in tablets.

Keywords:levocetirizine, method development, montelukast, validation

INTRODUCTION

Montelukast sodium is the active ingredient in SINGULAIR, it is selective and orally active leukotrienereceptor antagonist that inhibits the cysteinyl leukotriene CysLT1 receptor. Montelukast sodium is described chemically as [R-(E)]-1-[[[1-[3-[2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropaneacetic acid, monosodium salt (Fig 1) [1-5].

Montelukast sodium is a hygroscopic, optically active, white to off-white powder. Montelukast sodium is freely soluble in ethanol, methanol, and water and practically insoluble in acetonitrile [6-8].

Cetrizine is chemically (±)-[2-[4-[(4-chlorophenyl)phenylmethyl]-1- piperazinyl]ethoxy] acetic acid (Fig 2). It is a second generation antihistamine, is a major metabolite of hydroxyzine, and selective peripheral histamine H1 receptor antagonist used in the treatment of allergies, hay fever, angioedema, and urticaria. It is most commonly used in reducing the severity of common cold. Levocetirizine (as levocetirizinedihydrochloride) is a third-generation non-sedative antihistamine, developed from Cetirizine. Chemically, levocetirizine is the active enantiomer of cetirizine. It is the R-enantiomer of the Cetirizine which is a racemate. Levocetirizine works by blocking histamine receptors. It does not prevent the histamine release from mast cells, but prevents the binding to its receptors. This increased blood supply to the area and prevents the release of other allergy chemicals, and provides relief from the typical symptoms of hay fever [9-17*]*

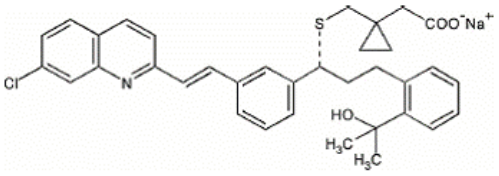

Fig 1.Structure of Montelucast

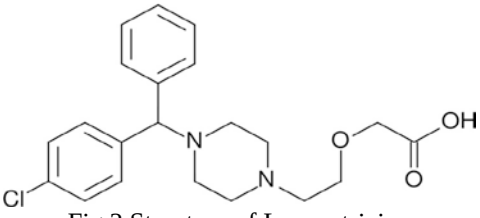

Fig 2.Structure of Levocetrizine

MATERIAL AND METHOS

Instrumentation and software

A high performance liquid chromatography system were manufactured by Agilent which consist of VWD detector, Quaternary solvent manager, Sample manager, column heating compartment was used for determination of montelukast sodium and levocetirizine hydrochloride assay. In HPLC instrument Chromeleon software is used. A Hypersil BDS C8, 250 x 4.6 mm, column with particle size of 5µm was used as stationary phase for chromatographic separation. For weighing Sartorius semi micro analytical balance was used, and for adjustment of pH Labindia pH meter was used, and Bandelinsonicator used to dissolve the standard, sample and were centrifuged by using Hermle centrifuge machine.

Chemicals and Reagent

All the reagents used of analytical reagent grade unless stated otherwise. Distilled and de-ionized HPLC-grade water, HPLC grade methanol, Disodium Hydrogen Orthophosphate and orthophosphoric acid was purchased from Merck, Mumbai.

Preparation of Mobile Phase

Make the mixture of buffer solution and methanol in the ratio 25: 75% (v/v) was used as mobile phase. Take 2.8 g of Disodium Hydrogen Orthophosphate in 1000 mL of water and adjusts the pH of the solution to 7.00 with orthophosphoric acid.

Preparation of Montelukast Solution:
Weighed accurately about 25mg of montelukast sodium working standard and transfer into a 50 mL volumetric flask then add 30ml of methanol, sonicate the solution to dissolve and make up with methanol upto the mark.

Preparation of Levocetrizine Standard Solution:
Weighed accurately about 31mg of montelukast sodium working standard and transferred into a 50 mL volumetric flask then add 30ml of methanol, sonicate the solution to dissolve and make up with methanol upto the mark.

Preparation of Final Standard Solution:
Transferred 5 mL of montelukast standard solution then add 2 mL of levocetirizine standard solution into a 50 mLvolumetric flask and make up the volume with mobile phase as diluent.

Preparation of Sample Solution:
Transferred 5 tablets into a 100 mL volumetric flask, add 5 mL of water, sonicate to dissolve for 5 min then add 60 mL of methanol, sonicate to dissolve for 5 min and dilute to the volume with methanol. Filter the solution through 0.45 µm Nylon filter. Further diluted 5 mL of this solution to 50 mL with diluent.

Method Validation Parameter:
The system suitability was conducted by using standard preparation and evaluated by injecting the injections in five replicate. Specificity is the ability of analytical method to assess certainly the analyte in the presence of component that may be expected to be present. Specificity parameter method was performed by injecting diluent, placebo into the chromatographic system and evaluated by show any peak at theretention time of analyte. Performed the linearity with montelukast sodium and levocetirizinehydrochloride in the range of 25 to 150% of specification limit. The area response was recorded for each level and calculated slope, intercept & correlation coefficient. The precision of an analytical method is the degree of agreement among individual test results when an analytical method is applied repeatedly to multiple sampling of a homogeneous sample. The precision of analytical method is usually expressed as the standard deviation or relative standard deviation for statistically number of measurements. The system precision was conducted using montelukast sodium and levocetirizine dihydrochloride and evaluated by making six replicate injections. The accuracy of the method by recoveries of montelukast sodium and levocetirizine hydrochloride sample solutions at different concentration levels ranging from 25 to 150%.The robustness of an analytical method is a measure of its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

RESULTS AND DISCUSSION

Calibration curves were plotted and method was found to be linear in concentration range of 1-10 µg/mL with correlation coefficient r^2 value of 0.999 formontelukast sodium and levocetirizine hydrochloride.The estimation of other parameters like specificity, accuracy, precision ,linearity , robustness, limit of detection (LOD) and limit of quantitation (LOQ) . Placebo solution and process impurity should not interfere at the same retention time of any of the known (degradation) impurity and levocetirizine peak. All the known impurity peaks should be well resolved from each other.

Accuracy all individual recoveries should be between 80.0% to 120.0%. recovery of LOQ level 105.0 % to 110.0%. recovery of 50% level 94.9% to 115 7%. %. recovery of 100% level 109.4% to 113.6%.%. recovery of 150% level 92.1% to 101.1%.%. recovery of 250% level 91.9% to 107.1%. precision repeatibility the methodology section on six sample preparatiions the % impurity was calculated. The relative standard deviation (%RSD) of assay results obtained from six sample preparations is 2.20. and the intermediate precision (% RSD)mean is 1.00. (the %RSD for method precision and intermediate precision should not more then 15.0% . Robustness the absulute difference in the results obtained in robustness study and mean repeatability study should not be more then 15% of specification limit. Linearity and range correlation coeficient for each impurity and main drug standard should not less then 0.99, the % Y- intercept should be within +-10.0. for the range relative standard deviation should not be more then 10.0% for six replicate injection. Range for RSD at LOQ 2.40%. and RSD at 250% 0.09%. Precision repeatability relatiuve standard of individual and total impurity results obtained in six sample preprations should not be more then 15.0%. Intermediate precision realtive.

CONCLUSION:

The proposed RP-HPLC method was validated as per ICH guidlines and can be applied for the determination of montelukast sodium and levocetrizine hydrochloride in pharmaceutical dosage form. The method was found to be system suitability, specificity, accuracy, recovery, robustness, linearity, and limit of detection and limit of quantification. . The recovery studies of montelukast sodium was found to be 97.66% and linearity method was investigated and observed in the range of 5- 30 ug/ml for the montelukast sodium and the method was found to be precise as indicated by the repeattability analysis showing NMT % RSD 2.0%.

The accuracy of all individuals recoveries of levocetrizine should be between 80.0% to 120.0%. The %RSD for the method precision and intermediate percision should not more then 15.0%.the linearity and range correlations coefficeint foe each impurity and main drug standard should not less then 0.99. the % Y-intercept should with in ±10.0. The proposed method could be useful for the national quality control laboratories in developing countries.

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