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Research Article

A STABILITY INDICATING MICELLAR LIQUID CHROMATOGRAPHIC METHOD FOR THE DETERMINATION OF DEFERASIROX IN SOLUBILIZED SYSTEM

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ABSTRACT

A simple, isocratic and stability indicating micellar liquid chromatographic (MLC) method containing a surfactant solution above its critical micellar concentration (CMC) was developed and validated for determination of Deferasirox (BTBA) content in active pharmaceutical ingredient and its pharmaceutical formulations. The analysis was performed in on isocratic mode at 40^0C temperature through Thermo Hypersil ODS 100mm×4.6mm, 3 µm particle size columns. The UV detection wavelength was set at 250 nm in the mobile phase containing 0.1 M Cetyl trimethyl ammonium bromide (CTAB) buffer (pH – 2.5) and 10% 1-butanol. The method was successfully validated following as per the requirements of ICH guidelines. The proposed method was successfully applied as stability indicating method for determination of BTBA under different stressed conditions. The method allows accurate and reliable determination of BTBA for drug stability assay in pharmaceutical investigations.

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INTRODUCTION:

Deferasirox [4-[3,5-bis (2-hydroxyphenyl)-1H-1,2,4-triazol-1-yl] benzoic acid (BTBA)] (Figure 1) is an oral iron chelator and well known antidote. BTBA is an orally active chelator that is selective for iron (as Fe3+). It is a tridentate, oral, iron-chelating agent used in the management of chronic iron overload secondary to various RBC transfusions, i.e., transfusional iron overload such as β-thalassemia sickle cell disease, other unusual anemias, and myeloproliferative disorders4. It is an initial oral medication prescribes for such patients in the USA. The affinity and selectivity of the molecule is very high towards iron with high affinity in a 2:1 ratio. BTBA can be efficiently processed as chronic iron toxicity such chelation therapy. BTBA is the first FDA approved oral drug for chronic iron overload[1].

A comprehensive survey of the literature for BTBA analysis reveals that only a few systematic methods are available in favor of BTBA, By Liquid Chromatography Mass Spectrophotometry (LC–MS)[2]. Terbium - sensitized fluorescence method, LC method for pharmaceutical formulation, a stability representative LC method for bulk drug and pharmaceutical dosage forms, comparative bioavailability, dispersion and dispersed in various drinks, Pharmacokinetics, allocation, metabolism, and emission and its iron complex, were reported. In this present study an attempt was made to develop a rapid and economical micellar liquid chromatographic method for assessment of BTBA in bulk and pharmaceutical formulation with improved sensitivity, precision and accuracy using Cetyl trimethyl ammonium bromide (CTAB) as surfactant above its critical micellar concentration. Micellar liquid chromatography is successfully used in the analysis of variety of compounds in several types of samples[3-4].

MATERIAL AND METHODS:

Chemicals and reagents

BTBA standard was obtained as a gift samples from Medilux Laboratories Pvt. Ltd and it's formulate table "Desirox-250 mg" (Cipla pharmaceutical Ltd) were procure from a viable source. All Reagents were of analytical grade and solvents were of HPLC grade.

Instrumentation

An analytical balance, pH, vortex shaker were used to prepare the standard and sample solution. Chromatographic separations were performed in an Agilent and Waters Separation HPLC. The photo stability chamber utilized during forced degradation

studies was controlled by a temperature controller. All measurements were carried out at 25±20C temperature.

Micellar liquid chromatographic conditions

Mobile phase was prepared by mixing of 0.1 M CTAB buffer solution at pH 2.50 and n-butanol in ratio of 90:10 v/v and filtered through 0.22 mm nylon filter paper. The stationary phase was Thermo Hypersil ODS column 100mm X 4.6mm, 3µm. Mobile phase flow rate was 1.0 mL/minute and column temperature 400C temperature as well as detection wavelength of 250nm. The total run time was set as 15 minute and injection volume was 10 µl. Under these optimized analytical conditions, BTBA was eluted at about 3.6 minute as shown in Figure 2[5].

RESULTS AND DISCUSSION:

Selection of appropriate detection wavelength

Analysis of reference and test solutions were performed and peak purity spectra were obtained over a wavelength range 200-400 nm. It was found that 250 nm is the optimum detection wavelength to maximize the sensitivity of the BTBA. A typical UV-Vis absorption spectrum obtained with the present method is depicted in Figure 3.

Surfactant concentration

Various types of surfactants were used to optimize the surfactant selection. Each individual surfactant exhibited different type of selectivity for BTBA. The increased selectivity is achieved in CTAB surfactant media. The effect of Cetyl trimethyl ammonium bromide (CTAB) buffer concentration on asymmetry, retention time and efficiency of BTBA was studied. After optimization of these variables, best shape and lowest peak tailing were achieved with well-defined peaks and good sensitivity within a reasonable analytical run time.

Effect of the pH variation

To study the effect of pH on Peak response, Retention time, Peak tailing, Peak area, Peak height and Theoretical number of plate, Injections (each time) were made using 0.1 M CTAB buffered solution between pH 4.8 to pH 2.0. It was observed that 0.1 M CTAB buffer pH 2.50 gave good combination between peak symmetry and analysis time.

Method Validation

The validation of the proposed method was performed according to ICH guidelines17 pertaining to the Specificity (Identification and force degradation), system suitability solution, linearity, range, LOD, LOQ, accuracy (recovery), precision, sample solution stability and robustness18. All the measurements for validation were performed using BTBA standard solution in mobile phase.

Specificity

Specificity of proposed method was determined by injecting sample and standard solutions. It was checked that no interference was created by blank and placebo at the retention time of BTBA peak. Peak purity of stressed samples was checked and confirmed the spectral purity of BTBA. The obtained results indicated that the proposed method is selective and able to determine BTBA and its degradation impurities.

Instrumental precision

The instrumental precision was checked by injecting six replicates of standard solution containing BTBA (0.1 mg mL-1) and % RSD, Peak asymmetry and Number of theoretical plate counts were determined. %RSD was found 0.37%, Peak asymmetry-1.34 and Theoretical plate – 1916, respectively.

Linearity and range

Linearity of assay test method was carried out progressively diluting BTBA standard stock solution. A calibration curve was obtained by plotting area response against concentration in ppm and calculate residual sum of the squares (r2), slope and y-intercept using the plot.

Accuracy

The accuracy of the method was ascertained by calculating recoveries of BTBA by the standard addition method. Known amount of standard of BTBA was spiked in three different levels (80%, 100% and 120%) and prepared three spiked samples at each level (Total 9, determinations are as per ICH guideline). These spiked samples were analyzed against working standard and recovery of BTBA in three different levels was calculated. The obtained recovery found in ranged between 99.28% - 99.63%.

Precision study (repeatability and reproducibility) the method precision of the proposed method was determined by preparing six different sample solutions of same batch and analyzed against working standard solutions. Assay values of these all six samples were calculated. % RSD of assay values were found 0.21%.

The low % RSD values indicate that the proposed method is precise and repeatable. Intermediate precision study was performed by same concentrations as prepared in method precision and analyzed against working standard solutions on different days. % RSD of assay values of 12 samples (Method and Instrument precision sample) were found to be 0.30%. The closeness of assay results and % RSD values indicate that the proposed method is reproducible.

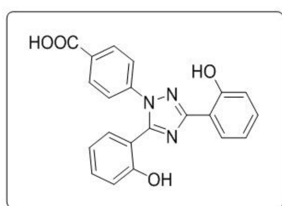

Figure 1: Structure of Deferasirox (BTBA)

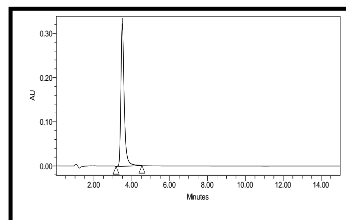

Figure 2 : Typical chromatogram of BTBA after Optimized chromatographic condition

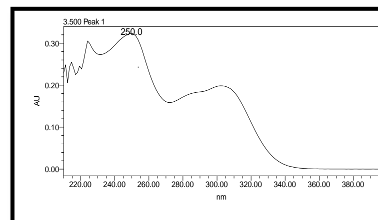

Figure 3 : Absorption spectrum of BTBA

CONCLUSIONS:

Micellar liquid chromatography described the optimization strategy used to select the best mobile phase for the resolution and determination of compounds in pharmaceutical preparations, serum, urine, and food samples. The projected method was found accurate, simple, precise, rapid and economical. Method validation parameters meet the specifications laid down in ICH guidelines with satisfactory results in the linearity, selectivity, precision, accuracy (recovery) and robustness. It is worth to mention that proposed methodology meets the fundamentals of the "green chemistry" exploring the use of environment-friendly reagents. Also the strategy is relatively inexpensive compared to other methods, thus making it more attractive and highly useful for many pharmaceutical analysis studies.

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