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RESEARCH ARTICLE

HPLC Method Development for Estimation of Dissolution of Antipsychotic Drug as Sublingual Film Dosage Form

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Abstract: A simple, accurate, precise and specific reversed phase high performance liquid chromatography method was developed for the quantitative determination of antipsychotic drug Asenapine maleate in a novel dosage sublingual film form. A phenomenex C_{18}, 5 µm column having 250×4.6 mm (internal diameter) in isocratic mode, with mobile phase containing water : methanol (60:40, v/v) was used. The flow rate was 1.0 mL min^{-1} and effluents were monitored at 231 nm. The retention time of asenapine was 4.54 min. The developed method was checked for assay of Asenapine sublingual film using different composition of dosage form. The method was successfully applied to the estimation of Asenapine in sublingual film dosage form.

Keywords: Asenapine dimaleate, High performance liquid chromatography, Novel dosage form, Sublingual film, Dissolution

Introduction

Asenapine maleate (Figure 1) is a novel dibenzoxepinopyrrole [*rel*-(3a*R*,12b*R*)-5-chloro-2-methyl-2,3,3a,12b-tetrahydro-1*H*-dibenzo[2,3:6,7]oxepino[4,5-*c*]pyrrole (2*Z*)-but-2-enedioate] with unique receptor pharmacology and is available as a fast-dissolving tablet for sublingual administration. It has potent dopaminergic (D_1-D_4), serotonergic (5-HT_{2A}, 5-HT_{2C}, 5-HT_6 and 5-HT_7), adrenergic (α_1 and α_2) and histaminergic (H_1) activity, but it lacks significant anti-muscarinic activity[1]. ASP is an atypical antipsychotic drug approved in the USA in adults for the treatment of schizophrenia and for the acute treatment, as monotherapy or adjunctive therapy to lithium or valproate, of manic or mixed episodes associated with bipolar I disorder[2]. In the European Union Asenapine is associated with the treatment of moderate to severe manic episodes associated with bipolar I disorder in adults[3]. In short-term trials, asenapine has demonstrated superiority over placebo in the treatment of schizophrenia[4,5] and acute manic episodes associated with bipolar I disorder[6,8]. The proposed metabolism of asenapine and the excretion profiles were published.

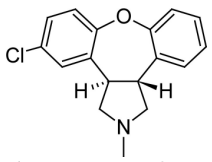

Figure 1. Structure of Asenapine

Experimental

Instrumentation

The liquid chromatographic system of waters (Calcutta, India) containing 515 HPLC isocratic pump, variable wavelength programmable 2998 photodiode array detector and rheodyne injector with 20 µL fixed loop was used. A phenomenex C_{18} column with 250×4.6 mm *i.d*. and 5 µm particle size was used as stationary phase. Electrolab disolution apparatus with six bowl used.

Chemicals and reagents

Asenapine pure drug was obtained as a gift sample. Sublingual film of asenapine was developed for better patient compliance. Composition of Sublingual film contains various excipients like polymer, plasticizer, flavouring agent and sweatner. All the chemicals used were of analytic al grade. Analytically pure Asenapine maleate was procured as from API supplier. Methanol, water (E. Merck, Mumbai, India) was of LC grade, were of analytical grade and used for the preparation of mobile phase. Asenapine Sublingual film contains labeled amount of 10 mg of asenapinie. Acetate buffer was prepared using sodium acetate and acetic acid.

Mobile phase was prepared by taking water : methanol (60:40 V/V). The solution was filtered with Whatman filter paper No. 42 (0.45 µm). The solution was sonicated for 15 min for degassing prior to use.

Stock solutions were prepared by accurately weighing 14.06 mg of asenapine maleate equivalent to asenapine 10 mg and transferring to 10 mL volumetric flasks containing 3 mL of methanol. The flasks were sonicated for 10 min to dissolve the solids. Volumes were made up to the mark with methanol, which gave 1000 µg/mL.

Preparation of sample solution

Sample solutions were prepared by dissolving asenapine maleate film in 500 mL acetate buffer 4.5. Dissolution sample 5 mL of asenapine maleate equivalent to asenapine (20 µg/mL) was taken and transferring to 10 mL volumetric flasks containing 3 mL of methanol. The flasks were sonicated for 10 min to dissolve the solids. Volumes were made up to the mark with methanol, which gave 10 µg/mL.

Preparation of blank

Blank solution was prepared by taking mobile phase water : methanol (60:40 V/V). The solution was filtered with Whatman filter paper No. 42 (0.45 µm). The solution was sonicated for 15 min for degassing prior to use.

Preparation of placebo

Placebo was prepared by taking placebo sample in 1000 µg/mL and dissolved in mobile phase water : methanol (60:40 V/V). The solution was filtered with Whatman filter paper No. 42 (0.45 µm). The solution was sonicated for 15 min for degassing prior to use.

Chromatographic conditions

A reversed phase C18 column equilibrated with mobile phase comprising of water : methanol (60:40 V/V) was used. Mobile phase flow rate was maintained at 1 mL/ min and effluent was monitored at 231 nm. A 10 µL of sample was injected using a fixed loop and the total run time was 8 min. All the chromatographic separations were carried out at controlled room temperature (25±2 °C).

Results and Discussion

Quantification in dissolution sample

To analyse the concentration of drug in dissolution sample, sample of ASP (antipsychotic drug) sublingual film dissolution sample was diluted with mobile phase. Sample of 5 mL was accurately taken and diluted to a 100 mL volumetric flask, dissolved in methanol, sonicated. The solution was centrifuged for the excipients to settle down and the resulting solution was filtered using 0.2 mm nylon filter. The solution was suitably diluted so as to obtain a concentration in the linearity range and injected in chromatographic condition and response was measured. The results of analysis are shown in below. Quantification in sublingual film was measured and presented in below graph (Figure 2-4).

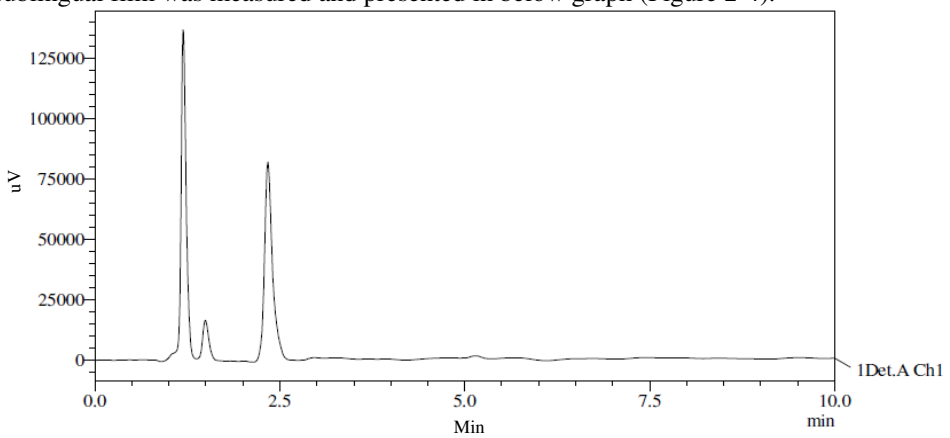

Figure 2. Chromatograph of blank and placebo

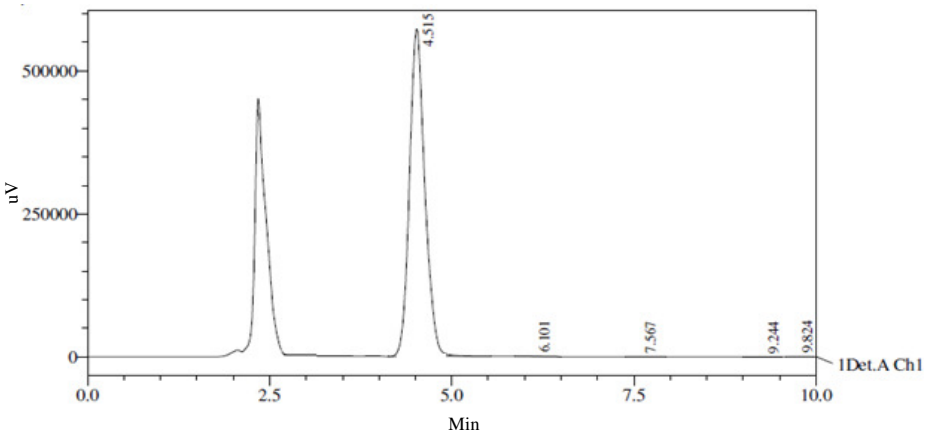

Figure 3. Chromatograph of asenapine maleate

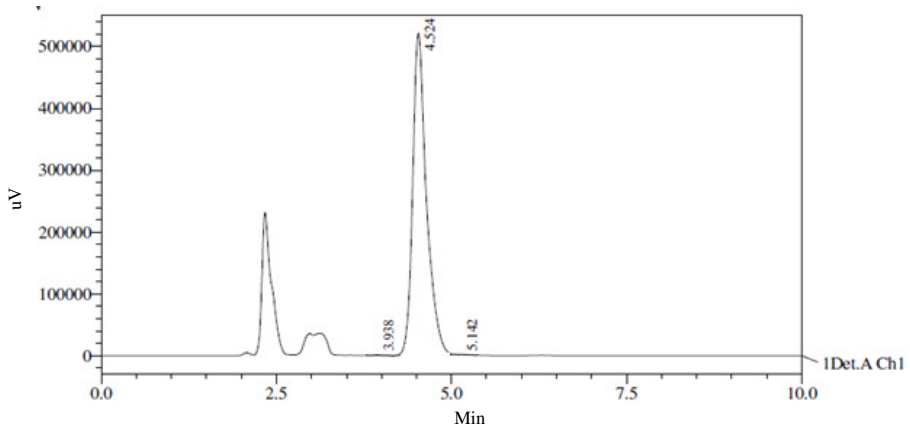

Figure 4. Chromatograph of asenapine maleate dissolution sample

Conclusion

The developed method can be concluded to be reliable for analysis of proposed asenapine sublingual 10 mg dissolution sample. The proposed method is specific without and interference of excipients and hence can be used for the routine analysis of asenapine in asenapine sublingual film dissolution study.

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