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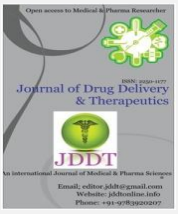

Open Access Research Article

DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR THE ESTIMATION OF OLANZAPINE IN MARKETED FORMULATION

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ABSTRACT

A simple, accurate, precise and rapid stability indicating RP-HPLC method was developed and validated for the analysis of Olanzapine in marketed formulation. Analysis was performed on a C-18 (250mm x 4.60mm, 5 µm) column as stationary phase and using mobile phase which was Potassium di-hydrogen phosphate Buffer (pH 6): Acetonitrile (60:40) (v/v) at a flow rate of 1ml/min with UV detection at 258 nm at constant room temperature. The injection volume was 20 µl and the chromatographic runtime of 5 min was used. Proposed method was found to be linear in the range of 5-25 µg/ml with the correlation coefficient 0.998. The validation and the reliability of proposed method were assessed by recovery study. The recovery of added standards (80%, 100% 120%) was ranging from 99.58% - 100.50%. The robustness of developed method was checked by changing temperature, flow rate and mobile phase ratio.

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INTRODUCTION:

The quantitative estimation of the active constituents is an integral part of developing and manufacturing process of pharmaceutical dosage forms. There is a need for development of better and reliable methods for the estimation of pharmaceutical dosage form. The official methods for the analysis of active ingredients of formulations are few and the most of the methods available for the analysis of active ingredients are applicable only after prior separation that involves tedious and time-consuming procedures.

Literature survey reveals that lesser method development of RP-HPLC method for the determination of Olanzapine in bulk forms or other pharmaceutical dosage form has been reported. Literature survey also indicates that LCID/ MS,[1] TLC-spectrodensitometric method[2], Ultra Performance Liquid Chromatography (RP-UPLC) technique[3] were also been developed for the determination of Olanzapine.

Therefore in this study an attempt is made to develop RP-HPLC methods for the method development of the drug in pharmaceutical formulations. Hence, the proposed method is simple, fast, accurate, precise and reproducible and can be applied for routine quality control analysis of drugs in bulk or in pharmaceutical formulations.

MATERIALS AND METHODS:

Olanzapine was made available from Bioplus, Bangalore (Purity 99.8%). Methanol (AR Grade) was purchased from Merck Ltd., India were used for sample preparation. Acetonitrile (HPLC), Methanol (HPLC) and Water (HPLC) were purchased from Merck Ltd., India used for the preparation of mobile phase. Potassium di-hydrogen phosphate, Ortho Phosphoric acid and Triethyl amine used for the preparation of buffer. Olanzapine marketed formulation (Oleanz-10 containing 10mg of Olanzapine which was manufactured by Sun Pharma, Mumbai, India) was procured from a local pharmacy. Chromatographic separation was performed on Waters HPLC system. The output signal was monitored and processed using empowers software. The chromatographic column used was C-18 (250mm x 4.60mm, 5µm).

Analytical Method Development by RP-HPLC: Mobile Phase selection was done by selecting numbers of mobile phase in different ratio. Taking into consideration of the system suitability parameter, the mobile phase found to be most suitable for analysis was Buffer (1.75 gm KH_2PO_4 in 1000 ml water add 1 ml of TEA adjust the pH 6 with OPA): Acetonitrile (60:40). Solubility and FTIR of standard Olanzapine drug was performed.

Selection of wavelength was done by making a solution of 10µg/ml of standard Olanzapine drug and scanned over UV range (200-400nm). Selection of separation

variable was done by preparing Olanzapine solution in different mobile phase and chromatograph was recorded by using different column at different chromatographic condition like different flow rate and temperature. Considering the theoretical facts and after several trials separation variables were selected which were constant during whole experiment. Separation variables were set and mobile phase was allowed to saturate the column at 1.0 ml/min. After complete saturation of column, three replicates of working standard of Olanzapine 10 µg/ml was injected separately. Peak report and column performance report were recorded for all chromatogram checking the system suitability parameters. Different working standard solutions were made of concentrations 5, 10, 15, 20, 25 µg/ ml using the diluents Water: ACN (50:50 v/v)**.** Standard drug solutions were injected 3 times and the mean peak area of drug was calculated and plotted against the concentration of the drug. The regression equation was found out by using this calibration curve. A solution was made containing 10 µg/ml of Olanzapine from marketed formulation and the amounts of Olanzapine in tablet formulation were calculated by extrapolating the value of area from the calibration curve. Analysis procedure was repeated three times with tablet formulation.

Validation: Linearity was observed by plotting the calibration curve after analysis of five different (from 5 to 25 µg/ ml) concentrations and areas for each concentration were recorded three times, and mean area was calculated. The regression equation and correlation coefficient of curve were noted and the response ratio (response factor) was found.

Recovery studies were performed to validate the accuracy of developed method. To preanalysed sample solution, a definite concentration of standard drug (80%, 100%, and 120%) was added and then its recovery was analyzed.

Precision was observed by repeatability and intermediate precision (Intra-day Precision, Inter-day Precision Analyst to Analyst). Standard dilutions were prepared and three replicates of each dilution were analyzed in different days and by different analysts. Robustness was performed by altering the pH, temperature and concentration of the mobile phase.

RESULTS AND DISCUSSION:

Olanzapine was yellow powder with melting point 195 ^{o}C. Solubility study shows that Olanzapine was freely soluble in acetonitrile, 0.1 N HCl, benzene, methanol, slightly soluble in ethyl alcohol and insoluble in water, 0.1 N NaOH, phosphate buffer pH 7.4. The interpretation by FTIR shows that the drug was Olanzapine; the peaks were at 3565.69 cm^{-1}, 2171.25 cm^{-1}, 1964.27 cm^{-1}, 1889.97 cm^{-1}, 1771.24 cm^{-1}, 1646.19 cm^{-1}, 1515.62 cm^{-1}, 1540.45 cm^{-1} and 1139.06 cm^{-1}. Maximum absorbance was found at λmax 258.00 nm. Taking into consideration the system suitability parameter the mobile phase found to be most suitable for analysis was Buffer (1.75 gm KH_2PO_4 in 1000 ml water add 1 ml of TEA adjust the pH 6 with OPA): Acetonitrile (60:40). The separation variables were set at flow rate 1ml/min, wavelength at 258 nm, the injection volume was 20 µl and the chromatographic runtime of 5 min was used at room temperature. The system suitability parameters study was done in three replicates and the mean was calculated; retention time 3.476 min, theoretical plate 3077.333 and tailing factor 1.176667. An assay of marketed formulation was performed and mean reading of three batch of formulation was 10.076 mg. The validation and the reliability of proposed method were assessed by recovery study. The recovery of added standards 80%, 100% 120% was ranging from 99.56%, 100.10% and 90.75% respectively. By the Repeatability study the amount of Olanzapine in marketed formulation was found 9.95mg i.e. 99.50%. By Intra-day Precision after 6 hr the amount of Olanzapine in marketed formulation was found to be 98.97%, by Inter-day Precision the amount of Olanzapine in marketed formulation was found to be 97.10% and by Analyst to Analyst precision the amount of Olanzapine in marketed formulation was found to be 99.84%. The robustness of developed method by altering the pH, temperature and concentration of the mobile phase were made and the method capacity remains unaffected.

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