METHOD DEVELOPMENT AND PARTIAL VALIDATION FOR ANTIPSYCHOTIC DRUG OLANZAPINE
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Abstract

Psychotic illness is considered to be caused by disturbances in the activity of neurotransmitters (mainly dopamine) in the brain. Schizophrenia is known to be associated with an over activity of dopamine in the brain, and this may be associated with the delusions and hallucinations that are a feature of this disease.

Keywords: Dopamine, Olanzapine, Antipsychotic, Agranulocytosis.

Introduction

A typical antipsychotic not only have incremental pharmacological actions beyond SDA actions, they also have additional favorable and unfavorable clinical properties beyond the limited clinical definition of reduced EPS and positive symptoms of schizophrenia.

Examples of the favorable properties of atypical tipsychotics are the ability to improve negative symptoms, cause little or no evation of prolactin levels, improve mood and reduce suicide and ability to act on patients who have resistant to conventional antipsychotic. However, problems like weight gaining, sedation, seizures or agranulocytosis are still a major put down to atypical antipsychotic as the mode of actions of how the drugs cause the above problems are still beyond understanding and therefore, unavoidable. There are many types of antipsychotic drugs available in the market now-a-days.

Our present paper is related to olanzapine, which is an atypical antipsychotic drug, was launched in October 1996. The initial impression is of a useful antipsychotic with few EPS and with a potential to reduce positive and negative symptoms to a better degrees than some conventional antipsychotic and some other 'atypical' antipsychotic.
There is good tolerability in humans. Olanzapine appears to be effective and safe for patients with psychotic depression. Further prospective studies ascertain that olanzapine's unique pharmacological profile is useful for the treatment of psychotic depression either alone or in combination with antidepressants.

**Material and Methods**

**I. Deciding the wave length for HPLC Method:**

First, the Olanzapine solution in methanol (20mcg/ml) has been prepared and scanned the UV spectrum in the range of 200 to 400nm. This has been performed to know the maxima of Olanzapine, so that the same wave number can be utilized in HPLC - UV Detector for estimating the Olanzapine. While scanning the Olanzapine solution, we observed three maxima namely at 204 nm, 228 nm and 260 nm. The UV Spectrum has been recorded on Shimadzu make UV- VIS Spectrophotometer.

**II. HPLC Method Development:**

After doing all the hit and trials we have arrived to a suitable method of analysis for Olanzapine and details of the procedure is as explained below.

**III. Mobile Phase Preparation:**

In 1000ml of chilled methanol (approx 15 °C), 1.5 ml of concentrate Ammonium Hydroxide solution (NH₄OH) was added and properly mixed. Once the homogeneous solution is achieved, the pH of the solution was brought to 6.5 by the help of Ortho-phosphoric acid. Bring the temperature of the mobile phase to Room Temperature (25°C) use it for the analysis. Filter the mobile phase using 0.45 micron filter (Millipore) and sonicate for 5 min (degassing) before using the mobile phase.

**IV. Sample Preparation:**

20mg of Olanzapine was transferred into 20ml volumetric flask containing about 5 ml Methanol, dissolved and make up to volume with Methanol. Sample was injected in HPLC by using above method and a very nicely resolved peak has been obtained at a Retention Time of about 2 min.

**V. Method Validation:** Though the product is very nicely resolved but to strengthen the method of analysis we need to validate the method by following some of the major ICH Guideline parameters. We have chosen following
parameters to validate the analytical method of Olanzapine. By validating the method for these parameters, if it complies with the Acceptance criteria, one can conclude that the method is suitable for intended use.

VI. Specificity:

This parameter is performed to identify the retention time of the product. To perform this, 20mg of Olanzapine was transferred into a 20ml volumetric flask containing about 5 ml Methanol, dissolved and made up to volume with Methanol. And injected 20 micro liter of the solution by following the above method.

VII. System Precision / System Suitability:

To perform this parameter, 20mg of Olanzapine was transferred into a 20ml volumetric flask containing about 5 ml Methanol, dissolved and made up to volume with Methanol. 20 micro liter of the solution was injected in HPLC by following the above method in five replicates. Acceptance Criteria: Relative Standard Deviation (RSD) for areas should not be more than 5.0 % and RSD for Retention Times should not be more than 1.0%.

VIII. Linearity:

For performing this test Olanzapine Solution was prepared in three concentrations namely, 75%, 100% and 125%. 1mg/ml shall be treated as 100 % solution. Details of solution preparation are as follows:

- Sample preparation for linearity 75%: Taken 15mg of sample into a 20ml volumetric flask. Dissolved and made up to volume with Methanol.
- Sample preparation for linearity 100%: Taken 20mg of sample into a 20ml volumetric flask. Dissolved and made up to volume with Methanol.
- Sample preparation for linearity 125%: Taken 25mg of sample into a 20ml volumetric flask. Dissolved and made up to volume with Methanol.

Results and discussion:

This parameter was performed to demonstrate and verify that the System Suitability parameters of the chromatographic system are adequate for the subjected analysis. After injecting 20 micro litre of the solution in HPLC in five replicates, data was statistically evaluated for the % RSD of Area and Retention Time. Data is recorded in the following table:
It is evident from the above table that % RSD of Area and Retention Time is 0.2 % and 0.06 %, respectively. Where as the limit for % RSD of Area & Retention Time is 5 % and 2 %, respectively. The results show the reproducibility and precision in the estimation of Olanzapine Drug, hence the method can be defined as suitable for analyzing the drug by this method.

**Linearity:**

Linearity parameter was performed to demonstrate that the analytical method is capable to obtain test results, which are directly proportional to the content of Olanzapine. For performing this test Olanzapine Solution was prepared in three concentrations namely, 75%, 100% and 125%. All the three concentrations have been injected in the HPLC by adopting the above recommended method and recorded the chromatograms. For each concentration, the area obtained is presented in the following table:

<table>
<thead>
<tr>
<th>CONCENTRATION</th>
<th>AREA</th>
</tr>
</thead>
<tbody>
<tr>
<td>75 %</td>
<td>22481250</td>
</tr>
<tr>
<td>100 %</td>
<td>25667593</td>
</tr>
<tr>
<td>125 %</td>
<td>28504321</td>
</tr>
</tbody>
</table>

Coefficient of Correlation 0.999439
Coefficient of correlation was calculated for it and has been found to be 0.999 against the requirement of Not Less Than 0.98. On the basis of this result, it can be assumed that this method is linear over the entire selected range.

**Conclusion**

It is evident from the above study that the method developed by us meets the acceptance of selected ICH parameters in the process of analytical method validation. Apart from this the developed HPLC method has been adopted to quantify the content of Olanzapine in the market sample with the name of Oleanz, manufactured by sun Pharmaceuticals and it has been observed that the drug content 9.90 mg has been obtained against the label claim of 10 mg per tablet.

**References**


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