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Research Article

DRUG CHARACTERIZATION STUDY OF ARIPIPRAZOLE FOR FORMULATION AND DEVELOPMENT OF NEWER ANTIPSYCHOTIC FORMULATION

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ABSTRACT

Aripiprazole is an antipsychotic medication, works by changing the actions of chemicals in the brain. It is used to treat the symptoms of psychotic conditions such as schizophrenia and bipolar disorder (manic depression). In order to formulate a newer aripiprazole immediate release of strength 30mg we performed the drug characterization study for the active pharmaceutical ingredient. Morphological characteristics, melting point, angle of repose, bulk density, tapped density, carr's index, hausner ratio, sieve analysis, water content and moisture pick up were determined. The results obtained were satisfactory and within the specified limits. The drug characterization study was found to be useful for formulation and development of aripiprazole immediate release tablet.

Keywords: Aripiprazole, antipsychotics, schizophrenia, drug characterization, immediate release tablets.

INTRODUCTION

Aripiprazole is an antipsychotic medication, works by changing the actions of chemicals in the brain[1,2,3]. It is used to treat the symptoms of psychotic conditions such as schizophrenia and bipolar disorder (manic depression)[4,5].

Aripiprazole possess a different mechanism of action which is different from other FDA - approved atypical antipsychotics approved by Food and Drug Administration[6,7,8]. Instead of acting as an antagonist at D_2 receptor it acts as a partial agonist at the D2 receptor[9,10]. It also acts as the partial agonist at the 5-HT_1A receptor but exhibits the role of the antagonist at 5-HT_2A receptor similar to that of the other atypical anti-pshycotics[11]. Aripiprazole also possess high affinity towards 5-HT_7 receptor (acts as antagonist) and 5-HT_2C receptor (acts as a partial agonist)[12,13]. Its action on the 5-HT_7 receptor and 5-HT_2C receptor is found to be the main cause of weight gain of the patient during the treatment period[14]. Aripiprazole also possess moderate affinity for histaminergic, α-adrenergic, dopaminergic receptors and serotonin transporter[15]. It has a very less affinity for muscarinic acetyl choline receptors[16]. The main aim and objective of this work is to perform the drug characterization study to formulate a stable and robust formulation of aripiprazole immediate release tablet 30mg, which is used in the treatment of schizophrenia and bipolar disorders.

MATERIALS AND METHODS

Drug characterization study

In order to perform the drug characterization study for the selected anti-psychotic drug the following studies were carried out[17,18]:

Morphology

Morphological characteristics of the selected anti-psychotic drug such as color, form, odour, taste etc was studied.

Melting Point

The melting range of the selected anti-psychotic drug was studied using melting point apparatus.

Angle of Repose

The angle of repose was determined by fixed funnel height method. Angle of repose was determined by fixed funnel method, drug was passed through a funnel kept at a height of 2cm from the surface. The powder was passed, till it formed a heap that touches the tip of the funnel. The radius was measured and the angle of repose was calculated using the formula mentioned below.

$$q = \text{Tan-1 } (h/r)$$

Where, q - Angle of repose; h – Height of the heap formed from the surface (which was fixed as 2 cm); r – Radius of the heap in cm.

Bulk density, Tapped density, Carr's Index and Hausner ratio

For determining the BD, a weight of the powder constituting 50-100ml in a 100ml cylinder is taken in a tarred measuring cylinder. The weight and volume are noted and BD was determined. For determining the TD, a mechanical tapped density tester is used. USP Method II was used where the blend is subjected to 500 and 750 tapings; at 300 drops/min and 14±2mm drop length. Volume is determined after 500 and 750

tapings and if the difference in volume is less than 2%, volume after 750 taps is taken as final volume, and TD is determined. Bulk density, Tap density, Hausner ratio and Carr's index were calculated by using the below mentioned formula,

Bulk Density: Mass /Bulk Volume

Tap Density: Mass / Tap Volume

Hausner Ratio: Tap Density / Bulk Density

Carr's Index: {(Tap density – Bulk Density) / (Tap Density)} x 100

Sieve analysis

Particle size distribution was determined by sieve analysis. This was carried out by arranging the sieves in ascending order as 30,40,60,80,100,120,200 and fine collector. A weighed quantity of the powder was transferred onto the top of the sieve set up. The whole set up was fitted in the mechanical sieve shaker with amplitude of 60, interval on for 10 minutes. The percentage of the powder retained on each sieve was then calculated by using the formula:

Wt. of blend in each sieve = Wt. of blend and sieve – Wt. of empty sieve

% retained = Wt. of blend in each sieve / Initial wt. of the blend x 100

Water content

Karl Fischer reagent (Sulfur dioxide and iodine are dissolved in pyridine and methanol) is used to determine the water content. The determination of water is based upon the quantitative reaction of water with an anhydrous solution of sulfur dioxide and iodine in the presence of a buffer that reacts with hydrogen ions.

Moisture pick-up studies

Moisture pick up study of API was carried out at different relative humidity conditions (43%, 52%, 75% & 92%) at 25°C ± 2°C in desiccators by preparing the following saturated salt solutions (Table 1)

Saturated solutions were placed in desiccators for equilibration, once they reached the required value, the study was started. Moisture absorption at different humidity conditions was determined by weight method. Clean and dry the petri dishes were taken and neatly labeled as per requirements. Empty weights of the petri dishes were taken and in each, dried samples were added. They were then placed inside the desiccators and at different time intervals (1hr, 2 hr, 3hr, 4hr, 5hr, 6hr, 7hr, 8hr, 24hr, 96hr, 120hr, 144hr, 168hr and 192hr) the petri dishes were reweighed. When the weights reached an almost constant value, which took around a week, the study was stopped.
% Moisture content was determined using the formula,

% MC = W1 –W2 /W1 x 100

Where, W1 = Final wt. of petri dishes,

W2 = Initial wt. of petri dishes

Table 1: Relative humidity of different saturated salt solutions

Salt	Relative Humidity (%)
Potassium Chloride	43
Magnesium Nitrate	52
Sodium Chloride	75
Potassium Nitrate	92

Table 2: Flow property of the API

S.NO.	'h' in cm	'r' in cm	$\theta=\tan^{-1}$ (h/r)
1	2	1.89	46.61
2	2	1.88	46.77
3	2	1.88	46.77

Table 3: Compressibility index parameters of the API

Bulk Density in gm/ml	0.252
Tap Density in gm/ml	0.455
Hausner Ratio	1.805
Carr's Index in %	44.615

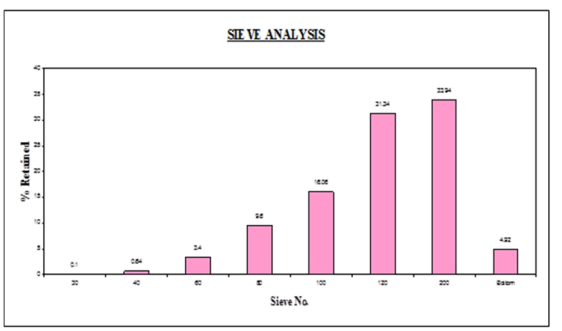

Figure 1: Particle size of the selected API

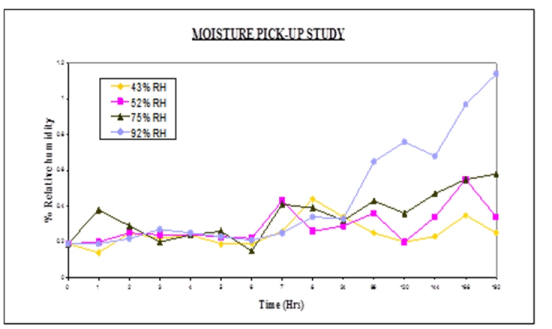

Figure 2: % relative humidity of API

RESULTS

Morphology
From the morphology study of the selected anti-psychotic drug the following characteristics was inferred: a) Color: Off - white, b) Form: Crystalline powder, c) Odour, Characteristic, d) Taste: Bitter.

Melting Point
The melting point of the selected anti-psychotic formulation lies in the range between 139°C – 139.5 °C.

Flow property study (Angle of Repose)
The flow property of the active pharmaceutical ingredient was determined by the determination of angle of repose (Table 2).

Bulk Density, Tapped Density, Carr's Index and Hausner Ratio
The compressibility index parameters values are presented in the table 3.

Sieve analysis
The results particle size determination carried out by sieve analysis is presented in the Figure 1.

Water Content
The moisture content of API by Karl Fischer method was found to be 0.29%.

Moisture pick up studies
The weight and the percentage of the water absorbed by API in different relative humidity conditions (43%, 52%, 75% and 92%) at different time intervals is provided graphically below in Figure 2.

DISCUSSION

The morphological characteristics and the melting point data of the tested active pharmaceutical ingredient was satisfactory and found to be within prescribed limits.

From the study of flow property data (Table 2) it is evidenced that since the angle of repose is 46º indicating poor flow property of the API. Therefore, the flow property of the active pharmaceutical ingredient needs to be improved using suitable excipient.

From the Table 3 it is inferred that compressibility index of API with 44.615, indicates very poor flow property, which should be improved to get a desired dosage form.

From the sieve analysis data it is obvious that majority of the particles lie between the size range of 75µm and 125µm, indicates that particle size of API was very fine.

The moisture content of the active pharmaceutical ingredient was found to be within the limits.

From the figure the weight and percentage of the water absorbed by API in different relative humidity conditions (43%, 52%, 75% and 92%) at different time intervals revealed the following:

- In 43% RH, API attains equilibrium at the end of 8th hour, with 0.2% increase in moisture compare to initial value.
- In 52% RH, API reaches saturation level at the end of 24th hours with 0.7% increase in moisture content compare to initial value.
- In 75% RH, API reaches gradually raises until 192 hours to an extend of 0.4% increase in moisture content.
- In 92% RH, API raises gradually until 8th day with a 1% increases compare to the initial value.

Therefore, from the moisture pick up study it was inferred that the moisture absorbed by the API was very less in the above condition, therefore it was non-hygroscopic.

CONCLUSION

The active pharmaceutical ingredient (aripiprazole) was evaluated for its morphological, physical characteristics and stability. The results obtained were satisfactory and within the specified limits. The results of the study were found to be useful in the formulation development of newer aripiprazole immediate release tablet of 30mg.

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