



## Research Article

### DRUG CHARACTERIZATION STUDY OF ARIPIRAZOLE FOR FORMULATION AND DEVELOPMENT OF NEWER ANTIPSYCHOTIC FORMULATION

Poonguzhali Sathish Kumar <sup>1\*</sup>, Subal Chandra Basak <sup>1</sup>, Sitty Manohar Babu <sup>2</sup>

<sup>1</sup>Department of Pharmacy, Annamalai University, Chidambaram, Tamil Nadu, India

<sup>2</sup>Department of Pharmacology, SIMS College of Pharmacy, Guntur, Andhra Pradesh, India

\*Corresponding Author Email: poongi2007@gmail.com

Article Received on: 13/01/17 Approved for publication: 23/02/17

DOI: 10.7897/2230-8407.080333

#### 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<sup>1,2,3</sup>. It is used to treat the symptoms of psychotic conditions such as schizophrenia and bipolar disorder (manic depression)<sup>4,5</sup>.

Aripiprazole possess a different mechanism of action which is different from other FDA - approved atypical antipsychotics approved by Food and Drug Administration<sup>6,7,8</sup>. Instead of acting as an antagonist at D<sub>2</sub> receptor it acts as a partial agonist at the D<sub>2</sub> receptor<sup>9,10</sup>. It also acts as the partial agonist at the 5-HT<sub>1A</sub> receptor but exhibits the role of the antagonist at 5-HT<sub>2A</sub> receptor similar to that of the other atypical antipsychotics<sup>11</sup>. Aripiprazole also possess high affinity towards 5-HT<sub>7</sub> receptor (acts as antagonist) and 5-HT<sub>2C</sub> receptor (acts as a partial agonist)<sup>12,13</sup>. Its action on the 5-HT<sub>7</sub> receptor and 5-HT<sub>2C</sub> receptor is found to be the main cause of weight gain of the patient during the treatment period<sup>14</sup>. Aripiprazole also possess moderate affinity for histaminergic,  $\alpha$ -adrenergic, dopaminergic receptors and serotonin transporter<sup>15</sup>. It has a very less affinity for muscarinic acetyl choline receptors<sup>16</sup>. 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<sup>17,18</sup>:

##### 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.

$$q = \tan^{-1} (h/r)$$

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,

$$\text{Bulk Density: Mass / Bulk Volume}$$

$$\text{Tap Density: Mass / Tap Volume}$$

$$\text{Hausner Ratio: Tap Density / Bulk Density}$$

$$\text{Carr's Index: } \left\{ \frac{\text{Tap density} - \text{Bulk Density}}{\text{Tap Density}} \right\} \times 100$$

**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:

$$\text{Wt. of blend in each sieve} = \text{Wt. of blend and sieve} - \text{Wt. of empty sieve}$$

$$\% \text{ retained} = \frac{\text{Wt. of blend in each sieve}}{\text{Initial wt. of the blend}} \times 100$$

**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,

$$\% \text{ MC} = \frac{W1 - W2}{W1} \times 100$$

Where, W1 = Final wt. of petri dishes,

W2 = Initial wt. of petri dishes

**Table 1: Relative humidity of different saturated salt solutions**

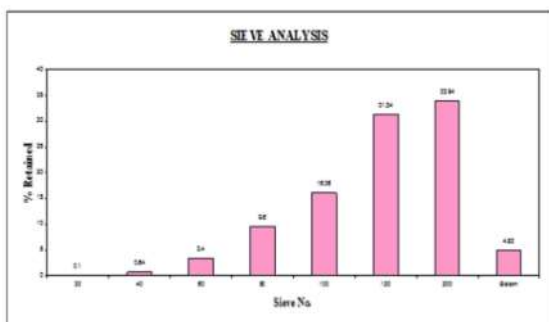
Salt	Relative Humidity (%)
Potassium Chloride	43
Magnesium Nitrate	52
Sodium Chloride	75
Potassium Nitrate	92

**Table 2: Flow property of the API**

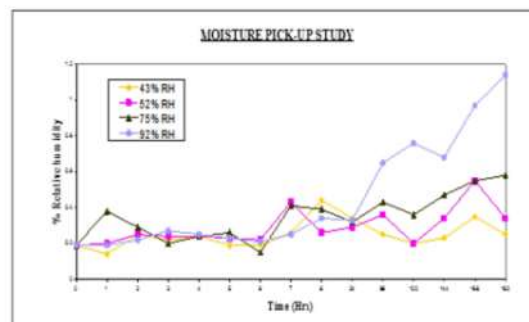
S.NO.	'h' in cm	'r' in cm	$\theta = \tan^{-1}(h/r)$
1	2	1.89	46.61
2	2	1.88	46.77
3	2	1.88	46.77

**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 46° 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 8<sup>th</sup> hour, with 0.2% increase in moisture compare to initial value.
- In 52% RH, API reaches saturation level at the end of 24<sup>th</sup> 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 8<sup>th</sup> 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.

## ACKNOWLEDGEMENTS

The authors are thankful to management of SIMS College of Pharmacy, Guntur, Andhra Pradesh for providing the drug and other facilities required to carry out this research work.

## REFERENCES

1. Baldessarini RJ, Tarazi FI. Drugs and the treatment of psychiatric disorders. In: Brunton LL, Lazo JS, Parker KL, editors. Goodman and Gilman's the pharmacological basis of therapeutics. 11th McGraw-Hill; New York: 2005. pp. 429–500.
2. Keith S. Advances in psychotropic formulations. Progress in Neuro-Psychopharmacology and Biological Psychiatry 2006; 30(6):996-1008.
3. Keck Jr PE, Calabrese JR, McIntyre RS, McQuade RD, Carson WH, Eudicone JM et al. Aripiprazole monotherapy for maintenance therapy in bipolar I disorder: a 100-week, double-blind study versus placebo. The Journal of Clinical Psychiatry 2007; 68(10):1480-91.
4. Rabin C, Liang Y, Ehrlichman RS, Budhian A, Metzger KL, Majewski-Tiedeken C, Winey KI, Siegel SJ. In vitro and in vivo demonstration of risperidone implants in mice. Schizophrenia Research 2008; 98(1):66-78.
5. Wolf J, Janssen F, Lublin H, Salokangas RK, Allain H, Smeraldi E et al. A prospective, multicentre, open-label study of aripiprazole in the management of patients with schizophrenia in psychiatric practice in Europe: broad effectiveness trial with aripiprazole in Europe (EU-BETA). Current Medical Research and Opinion 2007;23(10):2313-23.
6. Masanori KU, Toshiko KO, Maune H, Fukuda T, Azuma J. Pharmacokinetics of aripiprazole, a new antipsychotic, following oral dosing in healthy adult Japanese volunteers: influence of CYP2D6 polymorphism. Drug Metabolism and Pharmacokinetics 2007;22(5):358-66.
7. Buchanan RW, Freedman R, Javitt DC, Abi-Dargham A, Lieberman JA. Recent advances in the development of novel pharmacological agents for the treatment of cognitive impairments in schizophrenia. Schizophrenia Bulletin 2007;33(5):1120-30.
8. Huang HC, Liu CH, Lan TH, Hu TM, Chiu HJ, Wu YC et al. Detection and quantification of aripiprazole and its metabolite, dehydroaripiprazole, by gas chromatography-mass spectrometry in blood samples of psychiatric patients. Journal of Chromatography B 2007;856(1):57-61.
9. Biederman J, Mick E, Spencer T, Doyle R, Joshi G, Hammerness P et al. An open-label trial of aripiprazole

- monotherapy in children and adolescents with bipolar disorder. *CNS Spectrums* 2007; 12(09):683-9.
10. Howland RH. Paliperidone extended-release tablets: a new atypical antipsychotic. *J Psychosoc Nurs Ment Health Serv* 2007;45(5):15-8.
  11. Obradovic M, Mrhar A, Kos M. Cost-effectiveness of antipsychotics for outpatients with chronic schizophrenia. *International Journal of Clinical Practice* 2007;61(12):1979-88.
  12. Sachs G, Sanchez R, Marcus R, Stock E, McQuade R, Carson W, et al. Aripiprazole in the treatment of acute manic or mixed episodes in patients with bipolar I disorder: a 3-week placebo-controlled study. *Journal of Psychopharmacology* 2006; 20(4):536-46.
  13. Bond DJ, Pratoomri W, Yatham LN. Depot antipsychotic medications in bipolar disorder: a review of the literature. *Acta Psychiatrica Scandinavica* 2007;116:3-16.
  14. Nyilas M, Carson W, Forbes R, Ashfaque S, McQuade R, Owen R, et al. 36-Long-term efficacy and safety of aripiprazole in pediatric patients with bipolar I disorder. *Schizophrenia Research* 2008;98:48.
  15. Yokoi F, Gründer G, Biziere K, Stephane M, Dogan AS, Dannals RF, et al. Dopamine D2 and D3 receptor occupancy in normal humans treated with the antipsychotic drug aripiprazole (OPC 14597): a study using positron emission tomography and [<sup>11</sup>C] raclopride. *Neuropsychopharmacology* 2002 ;27(2):248-59.
  16. Leite JV, Guimarães FS, Moreira FA. Aripiprazole, an atypical antipsychotic, prevents the motor hyperactivity induced by psychotomimetics and psychostimulants in mice. *European Journal of Pharmacology* 2008 ;578(2):222-7.
  17. Das Arun Kumar, Bhanja Satyabrata, Hardel Danendra Kumar, N.Sri Lakshmi, Pandit Pranali. Formulation design and invitro evaluation of anti-psychotic drug Quetapine fumarate. *Int.J.Res.Ayurveda.Pharm* 2013;4(2):266-71.
  18. Shivaramakrishna Baddam, Sreedhar Bhandari, G.B.Chaitanya. Formulation and evaluation of fast dissolving tablets of ofloxacin by direct compression method. *Int.Res.J.Pharm* 2013; 4(11):79-86.

**Cite this article as:**

Poonguzhali Sathish Kumar et al. Drug characterization study of aripiprazole for formulation and development of newer antipsychotic formulation. *Int. Res. J. Pharm.* 2017;8(3):35-38  
<http://dx.doi.org/10.7897/2230-8407.080333>

Source of support: Nil, Conflict of interest: None Declared

Disclaimer: IRJP is solely owned by Moksha Publishing House - A non-profit publishing house, dedicated to publish quality research, while every effort has been taken to verify the accuracy of the content published in our Journal. IRJP cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of IRJP editor or editorial board members.