*Original Research Article*

# FORMULATION AND EVALUATION OF ARIPIPRAZOLE ORAL DISINTEGRATING TABLETS


## ABSTRACT

**Aim:** This work aims to develop oral disintegrating tablets from solid dispersion of aripiprazole that are capable of enhancing solubility.

**Methodology:** Aripiprazole an antipsychotic is a BCS class IV drug with Oral bioavailability of 87%. To enhance the solubility of this drug the solid dispersions were prepared by using a combination of β-Cyclodextrin and PVP K30 in 1:1, 1:2 by using a physical mixture and solvent evaporation method. The prepared solid dispersions were analyzed for all the physical parameters and drug excipient interactions. The solid dispersion was optimized for the preparation of oral disintegrating tablets by direct compression technique using different concentrations of various natural super disintegrants namely Tapioca starch, Amorphophallus campanulactus, and synthetic super disintegrants namely Sodium starch glycolate, crospovidone.

**Results:** FTIR showed that the drug and excipients are compatible with each other. Among all the solid dispersion formulations SCD6 (Drug: β-cyclodextrin) shows a high percentage of drug release i.e., 98.58±0.28% for 45 min, and solubility was found to be 0.954±0.32mg/ml. Percentage practical yield was found to be 98.36±0.14% and drug content was found to be 97.31±0.04%. SCD6 formulation was optimized for the preparation of oral disintegrating tablets. The post-compression parameters of all the prepared tablets were within the limits. Among all, F3 formulations containing tapioca starch, 7.5% were found to possess a better disintegration time (28±1.52sec) and in-vitro dissolution (98.64±0.29% for 45min).

**Conclusion:** It can be concluded that solid dispersions of Aripiprazole incorporated in oral disintegrating tablets are a very useful approach for better release of Aripiprazole in an efficient manner.

**Keywords:** *Aripiprazole, Oral disintegrating tablets, Solid dispersion, Solubility enhancement, Super-disintegrants.*

## 1. INTRODUCTION

"The simplest and easiest way of administering drugs is through the oral route. Over other types of dosage forms, oral dosage forms have many advantages like accurate dosage, less bulk, greater stability and easy production is possible. The drugs with poor water solubility often show poor oral bioavailability due to the low absorption levels. As a result, a medicine with poor water solubility often exhibits dissolution rate-limited absorption, while a drug with poor membrane permeability typically exhibits permeation rate-limited absorption. The oral bioavailability of active agents includes (i) enhancing the solubility and dissolution rate of poorly water-soluble drugs and (ii) enhancing the permeability of poorly permeable drugs. One of the best methods for enhancing the drug release of poorly soluble medicines is the use of solid dispersions. Sekiguchi and Obi were the first to describe solid dispersions in 1961. Solid dispersion is one of the important strategies to tackle dissolution rate-limited oral absorption of poorly soluble compounds" [1]. "Formulation of poorly soluble compounds as solid dispersions might lead to particle size reduction, and improved wetting" [2]. "Oral drug delivery is currently regarded as the safest, most convenient and most economical method of drug delivery with the highest patient complaints. The Oral route is the most preferred route of administration, tablets and capsules are the most preferred dosage forms. Orally disintegrating tablets have been developed and new orally disintegrating tablets (ODTs) technologies compensate for many pharmaceuticals and patients' needs, ranging from convenient dosing for paediatric, geriatric, and psychiatric patients with dysphasia. Over the decades, ODTs have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance" [3]. "ODTs aren't meant to be ingested whole like regular tablets; they're meant to dissolve on the tongue. ODTs dissolve in saliva within three minutes or less when no water is consumed. In recent years, there is a growing demand for good ODT formulations with new disintegrants and convenient preparation methods. The bioavailability of drugs may be increased due to absorption of the drugs in the oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach.

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Moreover, the amount of drug subjected to first-pass metabolism is reduced compared to standard tablets" [4].

## 2.MATERIALS

Aripiprazole was purchased from Anwitha drugs & chemicals, Patancheru. Crospovidone was Purchased from Corel pharma chemical Ltd. Polyvinylpyrrolidone PVP K30, Amorphophallus campanulatus and Microcrystalline cellulose were purchased from Yarrow chemical products, Mumbai. β -Cyclodextrin was from Gangwal chemicals Ltd, Mumbai. Sodium starch glycolate was from Sigma Aldrich, Bangalore. Tapioca Starch was from Angel Starch & Food Pvt Ltd. Emcosoy was from JRS pharma. Aspartame, Magnesium stearate (Mg stearate), Talc, Methanol, and Hydrochloric acid (HCl) were purchased from S.D. Fine Chemicals Ltd.

## 3.METHODOLOGY

### 3.1 Drug-Excipient compatibility studies:

#### 3.1.1 Fourier transform infrared spectroscopy:

The spectrum analysis of pure drugs and different excipients, which are used for the preparation of solid dispersion, were studied by FTIR. FTIR spectra were recorded by preparing potassium bromide (KBr) disks using a Shimadzu (Kyoto, Japan) facility (model-8400S). Potassium bromide (KBr) disks were prepared by mixing a few mg of drug with potassium bromide and then by compacting the mixture in a hydraulic press under vacuum by application of 6-8 tons of pressure. The obtained disc was placed in a suitable holder in an IR spectrophotometer and the IR spectrum was recorded from 4000$cm^{-1}$ to 500 $cm^{-1}$ in a scan time of 12 minutes. To check for any spectra alterations, the final spectrum was compared. They were observed for the presence of characteristic peaks for the respective function [5].

### 3.2 Preparation of Solid dispersion

Solubility enhancement of Aripiprazole by solid dispersion technique:

#### 3.2.1 Preparation of physical mixture solid dispersion:

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From this method powders of Aripiprazole and water-soluble carriers like β-cyclodextrin and PVP k30, were weighed accurately and mixed in the required proportion in mortar and pestle by simple blending for 30 min and passed through a 60 # sieve (250µm). The mixture was prepared in a 1:1, 1:2 ratio of drug: carrier respectively.

**3.2.2 Preparation of Solvent evaporation solid dispersion:**

Aripiprazole and each water-soluble carrier such as PVP K30 and β-cyclodextrin were added into methanol in a mortar with constant stirring. Subsequently, methanol was evaporated in a hotplate at 50$^{o}$C and resulting in solid dispersion was stored at room temperature for 24 hrs. The dried powder was triturated in a mortar and passed through a 60# sieve (250µm). The mixture was prepared in a 1:1, 1:2 ratio of drug: carrier respectively as given in table 1.

**Table 1. Formulation of Aripiprazole solid dispersions**

| Formulation code | Drug: carrier ratio | Method of preparation |
|---|---|---|
| PCD1 | 1:1 | Physical mixture |
| PCD2 | 1:2 | Physical mixture |
| PVP3 | 1:1 | Physical mixture |
| PVP4 | 1:2 | Physical mixture |
| SCD5 | 1:1 | Solvent evaporation |
| SCD6 | 1:2 | Solvent evaporation |
| SPV7 | 1:1 | Solvent evaporation |
| SPV8 | 1:2 | Solvent evaporation |

## 3.3 Evaluation of Solid dispersions:

**3.3.1 Physical appearance:**

All the batches of Aripiprazole solid dispersions were evaluated for colour and appearance.

**3.3.2 Percent practical yield:**

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Percentage practical yield was calculated to know about per cent yield or efficiency of any method; thus, it helps in the selection of the appropriate method of production. Solid dispersion was collected and weighed to determine practical yield (PY) from the following equation [6].

PY (%) = practical mass (solid dispersion) / Theoretical mass x100

**3.3.3 Drug content:**

Solid dispersions equivalent to 10mg of Aripiprazole were weighed accurately and dissolved in the 10 ml of methanol. The solution was filtered with Whatman filter paper and and diluted suitably and drug content was analysed at 218nm by UV spectrophotometer(Lab India Analytical UV 3200). The actual drug content was calculated by using the following equation [7].

% Drug content = Actual drug content in the weighed quantity of Solid dispersion Drug **/** Theoretical amount of drug present in solid dispersion.

**3.3.4 In-vitro dissolution study:**

The dissolution studies of solid dispersion were performed using the USP II paddle dissolution test apparatus (Dissolution apparatus: ElectroLab TDT-08L USP disso tester). The Volume of dissolution media was 900ml with a stirring speed of 50 rpm and the temperature of the medium was maintained at 37±0.5$^0$C. All dissolution studies were conducted under these conditions. The drug release study was carried out in 0.1N HCl for 45min. Samples of 5ml were withdrawn at specified time intervals and analysed spectrophotometrically at 218nm using a UV spectrophotometer. The samples withdrawn were replaced by fresh medium, and each preparation was tested in triplicate. Then the per cent of drug release was calculated [8].

## 3.4 Preparation of Aripiprazole oral disintegrating tablets

**3.4.1 Preparation of Aripiprazole oral disintegrating tablets by direct compression method:**

Solid dispersion of Aripiprazole was prepared by a solvent evaporation method. An accurate amount of Aripiprazole: β-cyclodextrin (1:2) was taken and dissolved in methanol with continuous stirring. The solvent was removed at 60$^o$C. The obtained mass dried, pulverized, passed through a 60 #sieve, and was stored in a desiccator. Oral disintegrating tablets of Aripiprazole and an optimized batch of selected method of solid dispersion of Aripiprazole were formulated by direct compression method

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using various proportions of of Sodium starch glycolate (SSG), crospovidone, tapioca starch, Amorphophallus campanulactus as super disintegrants shown in table 2. All the ingredients were triturated individually in a mortar and passed through a 60 #sieve. Then required quantity of all ingredients was weighed for a batch size of 50 tablets and mixed uniformly in a mortar except talc and magnesium stearate. Finally, magnesium stearate and talc were added as a lubricant. This uniformly mixed blend was compressed into tablets containing 15mg of drug using 4mm flat face surface punches on a Rimek-1 rotary tablet machine by the direct compression method. The total weight of the tablet was kept at 50mg.

**Table 2. Formulation of Aripiprazole oral disintegrating tablets using natural super disintegrants.**

| **Ingredients** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** |
|---|---|---|---|---|---|---|---|---|
| Aripiprazole (mg) | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| Tapioca starch (mg) | 1.25 | 2.5 | 3.75 | 5 | - | - | - | - |
| Amorphophallus Campanulactus (mg) | - | - | - | - | 1.25 | 2.5 | 3.75 | 5 |
| PVP K30 (mg) | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| MCC (mg) | 29.9 | 28.65 | 27.4 | 26.15 | 29.9 | 28.64 | 27.4 | 26.15 |
| Aspartame (mg) | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0..1 | 0.1 | 0.1 |
| Mg stearate (mg) | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Talc (mg) | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 |
| Total weight (mg) | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg |

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**Table 3. Formulation of Aripiprazole oral disintegrating tablets using synthetic super disintegrants.**

| Ingredients | F9 | F10 | F11 | F12 | F13 | F14 |
|---|---|---|---|---|---|---|
| Aripiprazole (mg) | 15 | 15 | 15 | 15 | 15 | 15 |
| Sodium starch glycolate (mg) | 1.25 | 2.5 | 3.75 | - | - | - |
| Crospovidone (mg) | - | - | - | 1.25 | 2.5 | 3.75 |
| PVP K30 (mg) | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| MCC (mg) | 29.9 | 28.65 | 27.4 | 29.9 | 28.65 | 27.4 |
| Aspartame (mg) | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| Mg stearate (mg) | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Talc (mg) | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 |
| Total weight (mg) | 50mg | 50mg | 50mg | 50mg | 50mg | 50mg |

## 3.5 Evaluation of aripiprazole oral disintegrating tablets

### 3.5.1 Evaluation of pre-compression parameters:

#### *3.5.1.1 The angle of repose:*

The frictional forces in powder can be measured by the angle of repose. The angle of repose of the prepared powder was evaluated by using the fixed funnel method. A specified quantity of the powder was taken and poured into the funnel, which automatically forms the heap. The formed heap's diameter and height were measured. Then the angle of repose of the powder was measured by using the below-mentioned formula.

$$\text{Tan } \theta = h/r;\ \theta = \tan^{-1} h/r$$

Where, θ = angle of repose, h = height of the heap (in cm), and r = radius of the base (in cm)

#### *3.5.1.2 Bulk density:*

Bulk density, ρb, is defined as the mass of the powder divided by the bulk volume.

$$\rho b = \text{weight in gms} / Vb \text{ (bulk volume)}$$

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***3.5.1.3 Tapped density:***

Tapped density, ρt, is defined as the mass of the powder divided by the tapped volume.

$$\rho t = \text{weight in gms} / Vt \text{ (tapped volume)}$$

***3.5.1.4 Compressibility index:***

Carr's index was calculated from the following equation using the values of bulk density (ρt) and tapped density (ρt) obtained in the earlier experiments.

$$C = (\rho t - \rho b / \rho t) \times 100$$

***3.5.1.5 Hausner's ratio:***

Hausner's ratio is an indirect measure of the ease with which powder flows. It is calculated by the following formula.[9]

$$\text{Hausner's ratio} = \rho t / \rho b$$

Where ρt is tapped density and ρb is bulk density. Lower Hausner's ratio (<1.25) indicated better flow properties than higher ones.

**3.5.2 Evaluation of Post-compression parameters**

***3.5.2.1 Weight variation:***

"Twenty tablets were selected at random, individually weighed in a single pan electronic balance (Contech CAH-123) and the average weight was calculated. The uniformity of weight was determined according to Indian Pharmacopeia (I.P.) Specifications. As per I.P not more than two of individual weights should deviate from the average weight by more than 5% and none deviate more than twice that percentage" [10].

***3.5.2.2 Thickness:***

The thickness and diameter of the tablets were measured using a vernier calliper. Ten tablets were selected from each batch and the results were expressed as mean values ±SD.

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***3.5.2.3 Hardness:***

Tablet requires a certain amount of strength or hardness and resistance of friability to withstand mechanical shocks of handling during manufacture, packing and shipping. The Monsanto hardness tester was used for the measurement of the hardness of the prepared ODT. Three tablets were selected from each batch for testing and the results were expressed in $Kg/cm^2$.

***3.5.2.4 Friability test:***

"It was done in a Roche friability apparatus where the tablets were subjected to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of six inches with each revolution. Pre-weighed samples of 20 tablets were placed in the friabilator, which was operated for 100 revolutions. The tablets were reweighed. Conventional compressed tablets less than 0.5 to 1.0% of their weight which is generally considered acceptable" [11].

$$F\ \% = (1\text{-}W0\ /W) \times 100$$

Where W0 is the weight of the tablets before the test and W is the weight of the tablets after the test.

***3.5.2.5 Drug content uniformity:***

"Twenty tablets were individually weighed and crushed using mortar and pestle. A quantity equivalent to the mass of 25mg of the drug is weighed and extracted with 100 ml of 0.1 N HCl. The solution was filtered through wattmans filter paper. The drug content was determined by UV visible-spectroscopy (Shimadzu Corporation, Tokyo, Japan) at a wavelength of 218 nm after suitable dilution with 0.1 N HCl. The amount of drug was calculated using a standard graph" [12].

***3.5.2.6 Wetting time:***

Five circular tissue papers of 10 cm diameter were placed in a petri dish with a 10-cm diameter. 10 ml of water at 37ºC+0.5ºC containing eosin, a water-soluble dye, was added to the petri dish. A tablet was carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablets was noted as the wetting time. Six tablets from each formulation batch were tested randomly and the average reading was noted [13].

***3.5.2.7 Water absorption ratio:***

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A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio R was determined using the following equation.

$$R = Wa - Wb / Wb \times 100$$

Wa = weight of the tablet after absorption

Wb = weight of the tablet before absorption.

***3.5.2.8 In-vitro disintegration time:***

Disintegration time was measured using a modified disintegration method. For this purpose, a petri dish was filled with 10 ml of water at 37ºC±0.5ºC. The tablet was carefully put in the centre of the petri dish and the time for the tablet to completely disintegrate into fine particles was noted [14].

***3.5.2.9 In-vitro dissolution test:***

Dissolution studies of prepared ODT were performed in triplicate, in a USP dissolution test apparatus, type-II (paddle method) at 37±0.5°C. The paddles rotated at a rate of 50 revolutions per minute. The tablets were placed in 900 ml of 0.1 N HCl solution. Aliquots of 5 ml were withdrawn at regular time intervals from the dissolution medium and filtered through Whatman's filter paper. The drug content was determined spectrophotometrically at a wavelength of 218 nm, as mentioned before. After each withdrawal, 5ml of fresh medium was replaced into the dissolution vessel. The cumulative percentage of drug release was calculated using an equation obtained from the standard graph [15].

***3.5.2.10 Stability studies:***

Stability studies for optimized oral disintegrating tablets of aripiprazole was carried out as per ICH guidelines. The optimized formulation was kept at 40 ± 2°C with 75 ± 5% RH for a period of 3 months. Tablets were tested for physical appearance, Drug content, Disintegration time, and Drug dissolution studies.[16]

## 4.RESULTS AND DISCUSSIONS

### 4.1 Analytical Method Development for Aripiprazole:

#### 4.1.1 Determination of Absorption maxima (λ max) of Aripiprazole in 0.1N HCl:

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The analytical method development of Aripiprazole was performed for the determination of absorption maxima using 12µg/ml of standard solution by using a double beam spectrophotometer against 0.1N HCl as the blank.

**4.1.2 Construction of standard graph of Aripiprazole in 0.1N HCl**:

The media was prepared and the standard graph was constructed according to the procedure given in the experimental methodology. Standard solutions in the range of 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml, 10µg/ml, and 12µg/ml were prepared and absorption values for the above solutions were recorded at 218nm against 0.1N HCl as the blank by using UV spectrophotometer. The calibration curve of Aripiprazole was constructed by plotting absorbance on the Y-axis against concentrations (µg/ml) on X-axis. Standard graph of Aripiprazole was represented in figure 1.

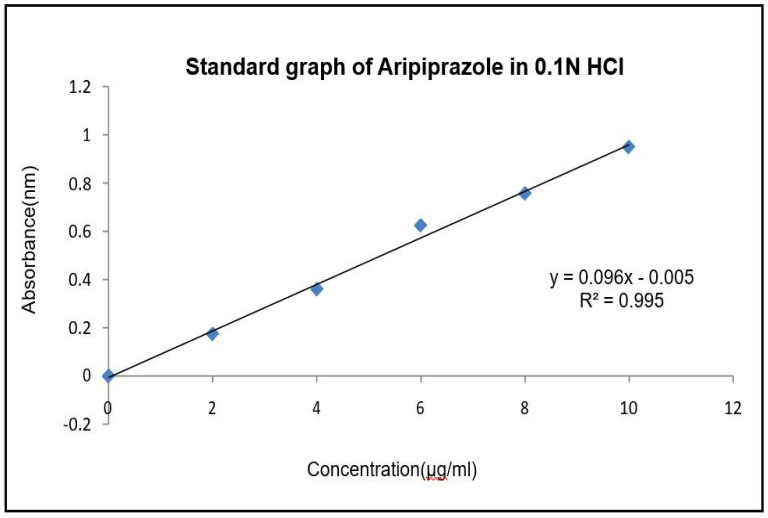


**Figure 1. Standard graph of Aripiprazole in 0.1 N HCl**

## 4.2 Drug excipient compatibility studies by Fourier Transform Infrared Spectroscopy:

The FTIR spectra of both pure drug and excipients individually and optimized formulation are shown in Figures no 2,3 and 4.

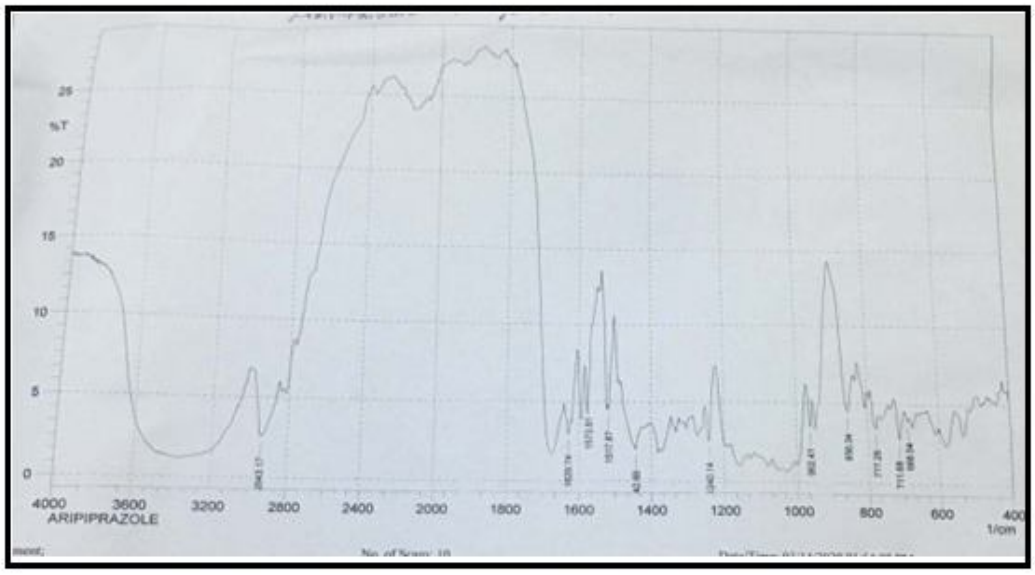


**Figure 2. FTIR spectra of pure Aripiprazole**

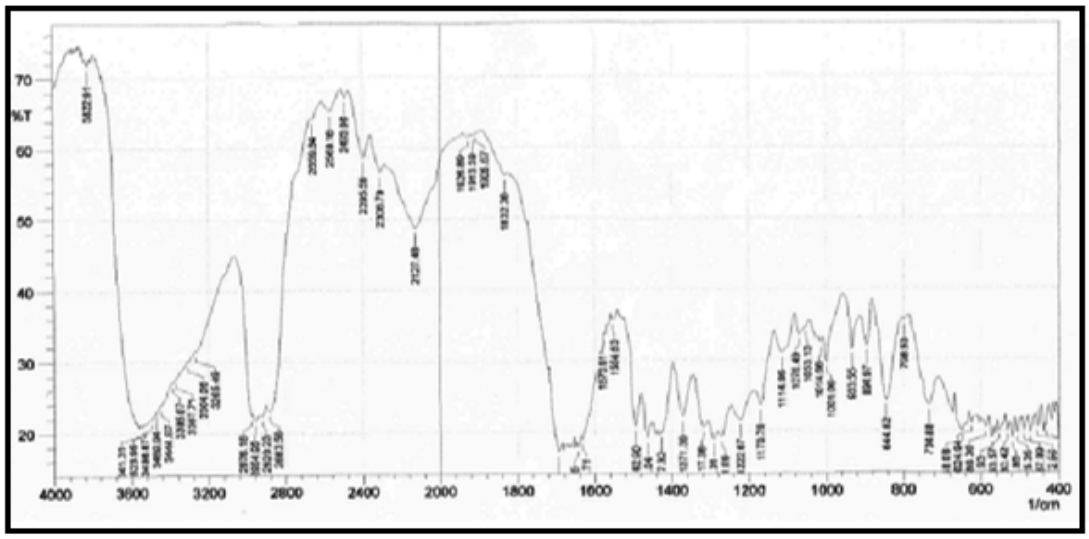


**Figure 3. FTIR spectra of Tapioca starch**

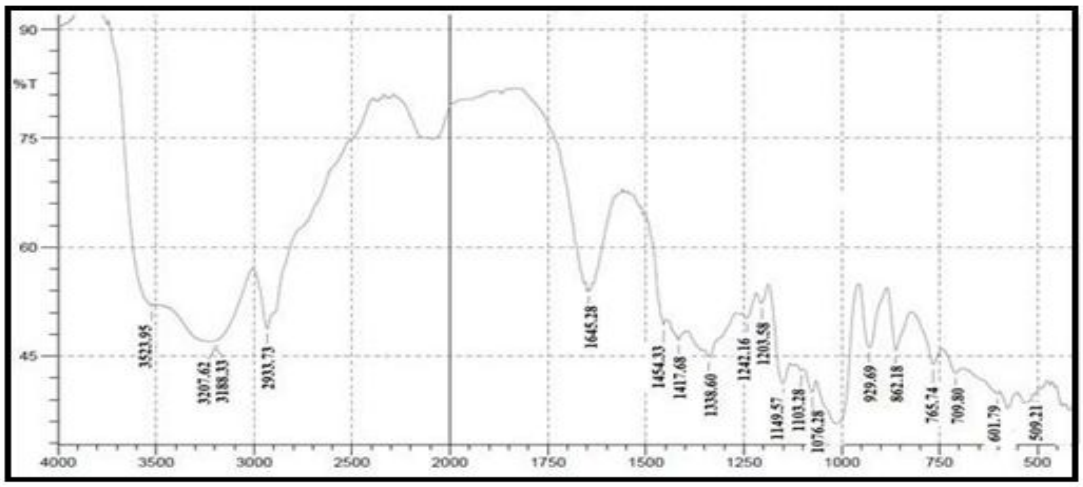


**Figure.4 FTIR spectra of mixture of pure Aripiprazole and Tapioca starch**

From the above FTIR spectra, the peaks representing the pure drugs were similar to that of the combination of the drug and tapioca starch and suggesting that there are no interactions.

## 4.3 Evaluation of solid dispersions:

### *4.3.1 The physical appearance of Aripiprazole solid dispersion:*

These studies were conducted manually by visual inspection. This study showed that all formulations were made of PVP K30 and β-cyclodextrin showed a good physical appearance. The physical appearance of all formulation codes from SCD1 to SVP8 is shown in table 4.

### 4.3.2 Percentage practical yield:

The formulation SCD6 was found to have the highest per cent practical yield 98.36 ± 0.14% respectively when compared with other formulations. The results are given in table 4.

### 4.3.3 Drug content:

Drug content was performed according to the procedure given in the experimental methodology. Drug content of all prepared solid dispersions was found to be in the range of 89.37±0.60% to 97.31±0.045 respectively. The maximum drug content was found to be 97.31±0.04% in the SCD6 (1:2) formulation, indicating the uniform distribution of drug content in the formulation. The results are given in table 4.

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**4.3.4 Solubility studies:**

Solubility studies were carried out according to the procedure given in the experimental methodology. The maximum solubility was found to be 0.954 ± 0.32mg/ml in the SCD6 (1:2) formulation. The results are given in table 4.

**4.3.5 In-vitro dissolution studies:** In-vitro dissolution studies were carried out according to the procedure given in the experimental methodology. The maximum drug release was found to be 99.58 ± 0.24% in 45mins. The results are represented in figures no 5 and 6.

**Table 4. Evaluation of Aripiprazole solid dispersion**

| Formulation code | Physical appearance | | Percentage Practical yield (%) | Drug content (%) | Solubility (mg/ml) |
|---|---|---|---|---|---|
| | Colour | Appearance | | | |
| PCD1 | White | Fine powder | 89.20±0.11 | 91.24±0.69 | 0.523 ± 0.48 |
| PCD2 | White | Fine powder | 91.98±2.6 | 93.69±0.77 | 0.678 ± 0.07 |
| PVP3 | Light yellow | Powder (granular) | 92.89±1.44 | 89.37±0.60 | 0.624 ± 0.11 |
| PVP4 | Light yellow | Powder (granular) | 91.32±1.8 | 93.06±0.99 | 0.593 ± 0.25 |
| SCD5 | White | Fine powder | 93.97±0.69 | 94.07±0.57 | 0.897 ± 0.64 |
| SCD6 | White | Fine powder | 98.36±0.14 | 97.31±0.04 | 0.954 ± 0.32 |
| SPV7 | Light yellow | Powder (granular) | 94.05±0.82 | 93.32±0.34 | 0.794 ± 0.17 |
| SPV8 | Light yellow | Powder (granular) | 97.33±0.17 | 91.27±0.13 | 0.828 ± 0.19 |

**Note:** values are expressed as mean SD±n=3

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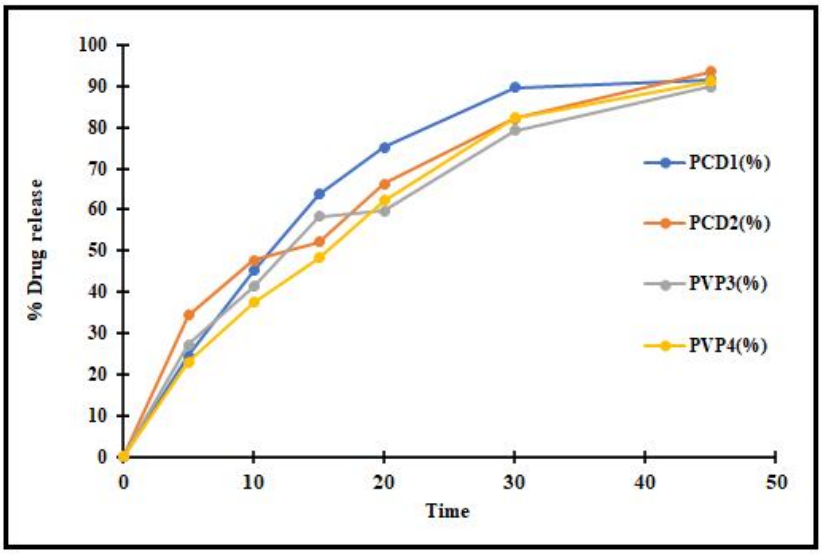


**Figure 5. Dissolution profile of solid dispersion from PCD1 to PVP4**

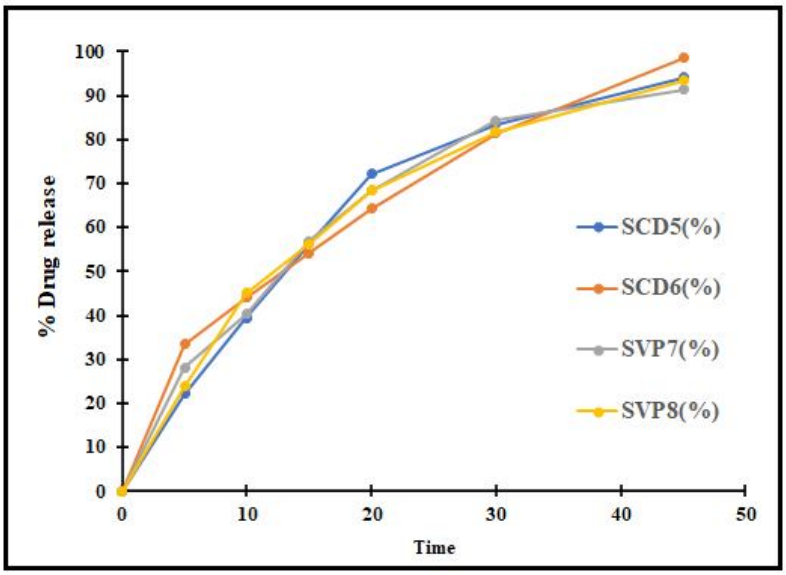


**Figure 6. Dissolution profile of Solid dispersions from SCD5 to SVP8**

## 4.4 Evaluation of aripiprazole oral disintegrating tablets

### 4.4.1 Evaluation of pre-compression parameters:

The flow properties like bulk density, tapped density, carr's index, Hausner's ratio and angle of repose of Aripiprazole formulations are determined.

***4.4.1.1 Carr's index:***

Most of the formulations showed carr's index within the range of 09.13±0.82 to 14.4±0.18 indicating that they have good flow properties.

***4.4.1.2 Hausner's ratio:***

Most of the formulations showed Hausner's ratio within the range of 1.10±0.04 to1.14±0.09 indicating that they have good flow properties.

***4.4.1.3 The angle of repose:***

All the formulations showed an angle of repose within the range of $15.80\pm0.29^0$ to $24.09\pm0.23^0$. The results of all pre- compression parameters are given in table no 5.

**4.4.2 Evaluation of post-compression parameters:**

The prepared tablets were evaluated for hardness, thickness, friability, and weight variation.

***4.4.2.1 Weight variation:***

20 tablets were selected for the determination of weight variation and the test was performed as per the procedure in the experimental methodology. The range for weight variation was 48±0.53 to 51±0.24mg.

***4.4.2.2 Hardness and Thickness:***

The hardness and Thickness of the tablet were evaluated as per the procedure. The results are shown in Table 6. The hardness was found to be in the range of 2.4±0.17 to 3.3±0.15 kg/cm2 and the thickness was found to be in the range of 1.9±0.18 to 2.7±0.37mm.

***4.4.2.3 Friability:***

20 tablets were randomly selected for the friability test. The test was performed as per the procedure given in the experimental methodology.

The results of post compression parameters are shown in table 6.

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**Table 5. Evaluation of pre-compression parameters**

| Formulation | Bulk density (gm/ml) | Tapped density (gm/ml) | Carrs index % | Hausner's ratio | Angle of repose ($^0$) |
|---|---|---|---|---|---|
| **F1** | 0.465±0.18 | 0.480±0.18 | 12.1 ± 0.15 | 1.12 ± 0.15 | 16.80±0.25 |
| **F2** | 0.486±0.24 | 0.525±0.22 | 14.4 ± 0.18 | 1.12± 0.16 | 17.70±0.19 |
| **F3** | 0.445±0.20 | 0.480±0.19 | 12.1 ± 0.15 | 1.12 ± 0.14 | 15.80±0.29 |
| **F4** | 0.52±0.15 | 0.51±0.56 | 09.41±0.49 | 1.13±0.03 | 22.56±0.27 |
| **F5** | 0.59±0.97 | 0.59±0.33 | 11.42±0.86 | 1.13±0.06 | 21.67±0.33 |
| **F6** | 0.50±0.57 | 0.60±0.32 | 09.31±0.22 | 1.14±0.09 | 23.05±0.25 |
| **F7** | 0.54±0.34 | 0.50±0.28 | 11.48±0.24 | 1.13±0.05 | 23.30±0.17 |
| **F8** | 0.59±0.95 | 0.69±0.56 | 11.03±0.45 | 1.13±0.03 | 21.09±0.32 |
| **F9** | 0.52±0.52 | 0.67±0.31 | 10.11±0.54 | 1.11±0.03 | 22.45±0.43 |
| **F10** | 0.54±0.18 | 0.67±0.49 | 11.34±0.63 | 1.12±0.09 | 23.42±0.32 |
| **F11** | 0.57±0.11 | 0.63±0.41 | 11.29±0.82 | 1.11±0.04 | 22.99±0.52 |
| **F12** | 0.54±0.47 | 0.66±0.19 | 09.13±0.82 | 1.10±0.04 | 22.78±0.46 |
| **F13** | 0.52±0.41 | 0.64±0.37 | 10.39±1.07 | 1.12±0.06 | 24.09±0.23 |
| **F14** | 0.57±0.11 | 0.57±0.45 | 11.29±0.82 | 1.11±0.04 | 22.99±0.52 |

**Note: Values are expressed as mean SD±n=3**

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***4.4.2.4 Wetting time:***

The Wetting time of the tablet was evaluated as per the procedure given in the experimental methodology and the results are shown in Table 4. The wetting time was found to be in the range of 34±1.24 to 72±1. 25sec.migration time was found to be in the range of 28±1.52 to 72±1.76 sec.

***4.4.2.5 Water absorption ratio:***

The water absorption ratio of the tablet was evaluated as per the procedure given in the experimental methodology and the results are shown in Table 7. water absorption ratio was found to be in the range of 56±1.45 to 98.9±0.17

***4.4.2.6 Drug content uniformity:***

Drug content uniformity studies were carried out as per the procedure given in the experimental methodology and the results are shown in Table 7.

***4.4.2.7 In-vitro disintegration studies:***

The in-vitro disintegration studies were carried out as per the procedure given in the experimental methodology. The results are shown in figures 7& 8.

***4.4.2.8 In-vitro dissolution studies:***

In- vitro release studies of tablets were carried out in USP type II apparatus (paddle) at 37o ± 1oC and 50 rpm in 0.1N HCl for 45 mins. The samples were analysed by UV spectrophotometer as discussed in the experimental methodology. The results of the in-vitro studies are even in figure 9,10 and 11.

***4.4.2.9 Stability studies:***

Stability studies data revealed that there is no significant change in physical appearance, drug content, Disintegration time and drug dissolution studies. Results are shown in the Table.8

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**Table 6. Evaluation of post-compression parameters**

| Formulation code | Weight variation(mg) | Hardness ($Kg/cm^2$) | Thickness(mm) | Friability (%) |
|---|---|---|---|---|
| **F1** | 49±0.98 | 2.4±0.17 | 1.9±0.18 | 0.23±0.16 |
| **F2** | 48±1.84 | 3.2±0.24 | 2.5±0.29 | 0.25±0.21 |
| **F3** | 51±0.89 | 3.3±0.15 | 2.7±0.28 | 0.27±0.19 |
| **F4** | 49±1.26 | 2.7±0.13 | 2.7±0.16 | 0.31±0.13 |
| **F5** | 48±0.53 | 2.9±0.26 | 2.4±0.23 | 0.34±0.17 |
| **F6** | 49±1.98 | 2.7±0.21 | 2.3±0.56 | 0.31±0.43 |
| **F7** | 49±1.26 | 2.8±0.12 | 2.1±0.45 | 0.29±0.24 |
| **F8** | 50±0.42 | 2.3±0.35 | 2.5±0.51 | 0.33±0.14 |
| **F9** | 51±0.24 | 2.6±0.23 | 2.3±0.53 | 0.36±0.67 |
| **F10** | 49±1.72 | 3.0±0.64 | 2.1±0.32 | 0.29±0.23 |
| **F11** | 50±1.84 | 2.7±0,16 | 2.2±0.74 | 0.34±0.19 |
| **F12** | 48±1.37 | 3.2±0.24 | 2.0±0.26 | 0.32±0.33 |
| **F13** | 50±1.14 | 3.1±0.45 | 2.5±0.51 | 0.28±0.43 |
| **F14** | 50±1.37 | 2.9±0.43 | 2.7±0.37 | 0.31±0.21 |

**Note:** values are expressed as mean SD±n=3

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**Table 7. Evaluation of Post compression parameters**

| Formulationcode | Wetting time (Sec) | Water absorption ratio | Drug content Uniformity (%) |
|---|---|---|---|
| **F1** | 37±1.32 | 77±0.89 | 99.24±0.24 |
| **F2** | 39±1.57 | 63±0.43 | 99.45±0.52 |
| **F3** | 34±1.24 | 98.9±0.17 | 99.85±0.76 |
| **F4** | 43±1.21 | 81.41±0.96 | 99.62±0.42 |
| **F5** | 51±0.67 | 56±1.45 | 99.13±0.15 |
| **F6** | 37±0.45 | 78±1.56 | 99.21±0.56 |
| **F7** | 48±1.46 | 67±1.72 | 99.34±0.72 |
| **F8** | 57±1.32 | 86±1.41 | 99.19±0.34 |
| **F9** | 36±1.29 | 75±1.34 | 99.29±0.19 |
| **F10** | 59±0.78 | 93±0.78 | 99.56±0.56 |
| **F11** | 67±0.54 | 95±1.37 | 99.47±0.37 |
| **F12** | 72±1.25 | 73±0.12 | 99.72±0.29 |
| **F13** | 53±1.67 | 67±1.76 | 99.43±0.31 |
| **F14** | 49±0.79 | 83±1.45 | 99.54±0.34 |

**Note:** Values expressed as Mean SD±n=3

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In the present study, it is observed that the disintegration time of the tablets decreased (P<0.05) with increase in concentration of Tapioca starch; as the concentration of Amorphophallus Campanulactus increases the disintegration time also increases while there is no significant difference (P>0.05) with change in concentration of Sodium Starch Glycolate and Crospovidone. Wetting time of the tablets showed significant decrease (P<0.05) with an increase in the level of Tapioca starch while it increased (P<0.05) with increase in the level of Amorphophallus Campanulactus. These results are inconsistent with disintegration test results.

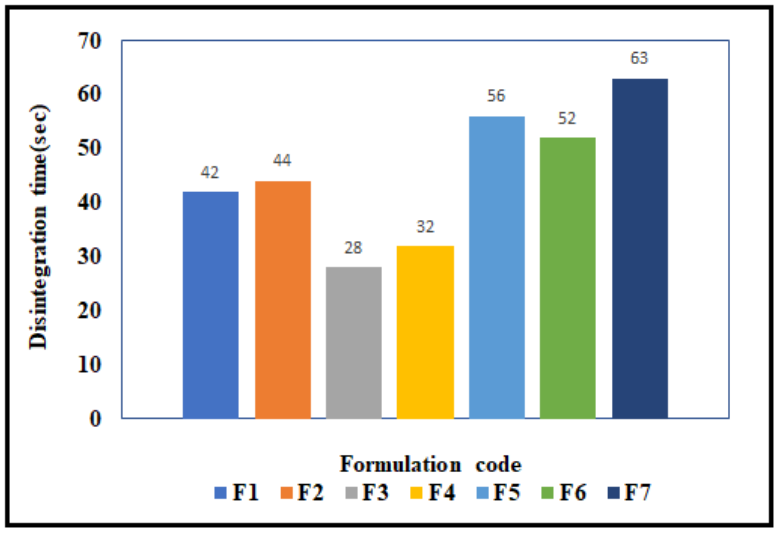


**Figure 7. Disintegration time of Aripiprazole oral disintegrating tablets from F1 to F7**

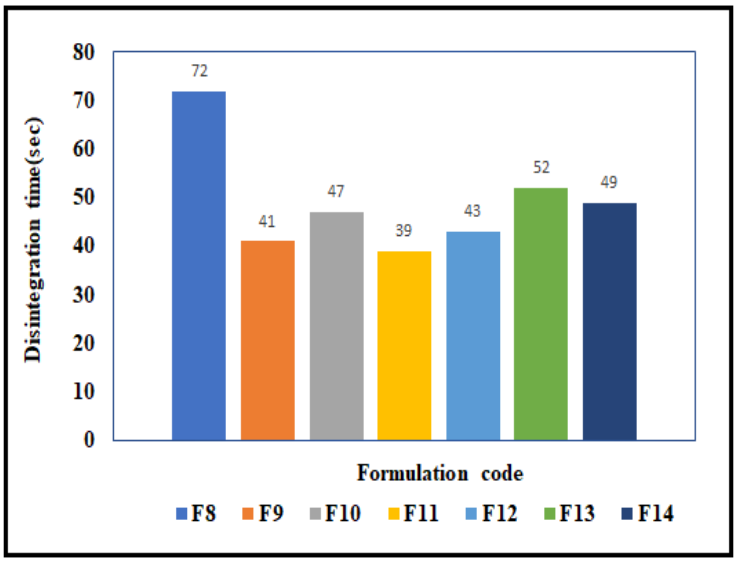


**Figure 8. Disintegration time of Aripiprazole oral disintegrating tablets from F8 to F14**

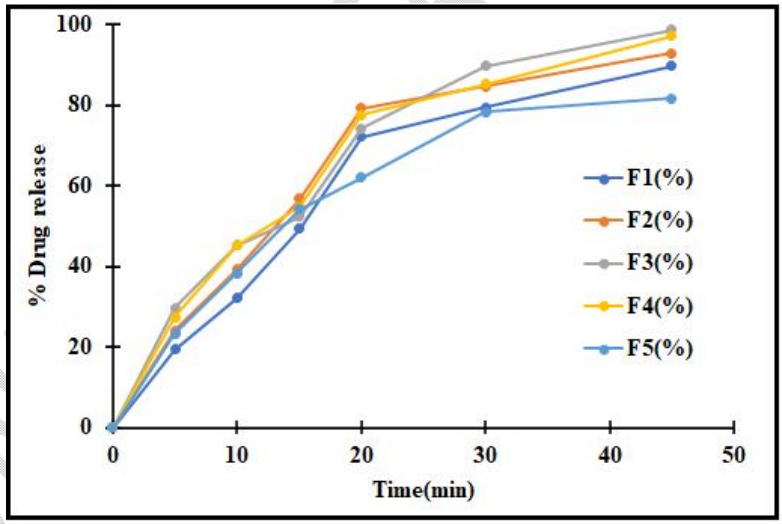


**Figure 9. Dissolution profile of Aripiprazole oral disintegrating tablets from F1 to F5**

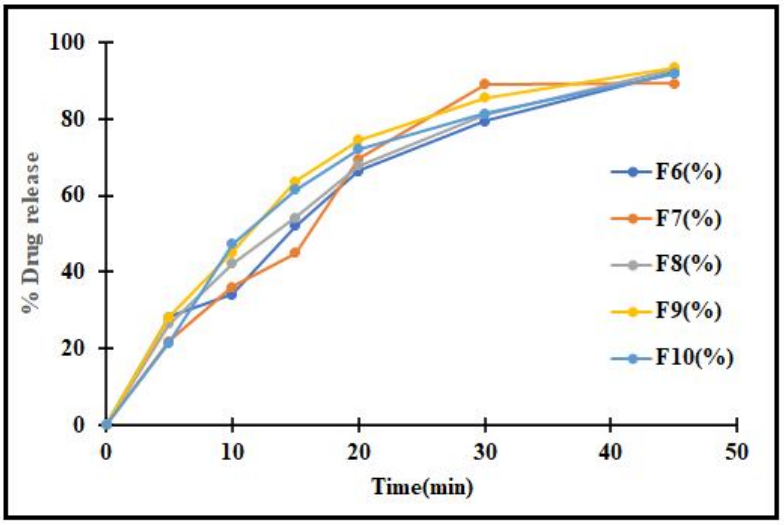


**Figure 10. Dissolution profile of Aripiprazole oral disintegrating tablets from F6 to F10**

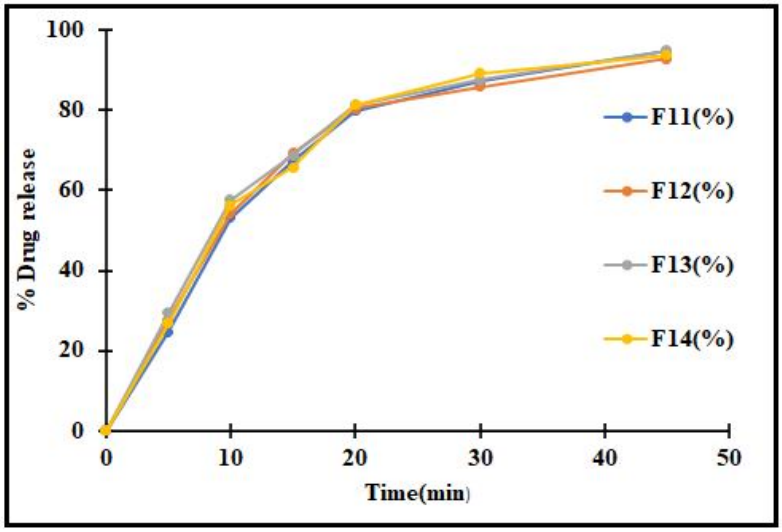


**Figure 11. Dissolution profile of Aripiprazole oral disintegrating tablets from F11 to F14**

**Table 8. Stability studies of optimised ODTs tablets**

| Test | Initial | 1st month | 2nd month | 3rd month |
|---|---|---|---|---|
| **Physical appearance** | White colour | White colour | White colour | White colour |
| **Drug content uniformity** | 99.85±0.76 | 99.80±0.32 | 98.65±0.24 | 98.53±0.12 |
| **Disintegration time(sec)** | 28±1.52 | 28±0.69 | 27±0.24 | 27±0.20 |
| **In- vitro Dissolution (45min)** | 98.64±0.29 | 98.52±0.34 | 98.34±0.36 | 98.33±0.38 |

## 5. CONCLUSION:

Aripiprazole solid dispersions were prepared using PVP K30 and β-cyclodextrin in 1:1 and 1:2 ratios by physical mixture and solvent evaporation methods. The evaluation of solid dispersions was performed. Based on the in-vitro dissolution studies SCD6 showed a high percentage of drug release 98.58±0.28% in 45 min. SCD6 is selected as an optimized formulation for the preparation of oral disintegrating tablets of Aripiprazole with natural and synthetic super disintegrants. The pre-compression evaluation was performed and all the formulations exhibited good flow properties. The evaluation of post compressional parameters of ODT tablets was performed. From the in-vitro release studies, it was seen that the F3 formulation containing tapioca starch (7.5%) was optimized which showed a disintegration time of 28±1.52 sec, drug release of 98.64±0.29% in 45mins, wetting time 34±1.24sec and water absorption ratio 98.9 and found to be better when compared to other synthetic super disintegrants such as sodium starch glycolate and crospovidone having disintegration time of 39±1.43 and 43±0.42 respectively. Based on the in-vitro dissolution studies a natural super disintegrant, Tapioca starch showed better drug release than the most widely used synthetic super disintegrants like sodium starch glycolate, and crospovidone. Hence it concluded that solid

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dispersions incorporated in oral disintegrating tablets are a very useful approach for better release of Aripiprazole in an efficient manner.

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