

## Formulation, Development and Evaluation of Mucoadhesive Buccal Tablets of Aripiprazole Using Tamarind Cmc with B-Cyclodextrin

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**ABSTRACT:** Mucoadhesive buccal tablets of Aripiprazole were prepared with an objective to enhanced solubility and bioavailability. The solubility of Aripiprazole was increase by complexation with  $\beta$ -cyclodextrin. Various concentration of polymers such as Tamarind CMC and HPMC K4M was used. The preformulation study using FTIR spectroscopy revealed the compatibility of drug and polymer. The Aripiprazole: $\beta$ -cyclodextrin complex was prepared. The FTIR spectroscopy of prepared complex revealed that pyridine ring structure of Aripiprazole was involved in complex formation. The 1:2 complex shows the significant solubility in various solvent. The mucoadhesive buccal tablets are prepared by direct compression method using flat surface punch. The tablets were evaluated for Hardness, Thickness, Weight variation, Friability and Drug content result conclude that all these parameters were in acceptable range of pharmacopoeial specification. The tablets were studied for surface pH, swelling index and In-vitro drug release. The effect of tamarind CMC concentration on these parameters was studied. The surface pH of buccal tablets was from 6.99 to 7.10 pH which falls in the range of salivary pH. The buccal tablets showed good swelling of greater than 67% up to 8 hr maintaining the integrity of polymers. As the concentration of tamarind CMC increases the swelling index also increases. The in-vitro release of Aripiprazole was extended up to 8 hr, Tamarind CMC used in combination with HPMC K4M. In-vitro release obeyed zero order kinetics and follows super case-II transport. Hence, tamarind CMC and other polymer can be used to prepare mucoadhesive buccal tablets of Aripiprazole having prolonged therapeutic effect with enhanced bioavailability.

**Keywords:** Aripiprazole, Tamarind CMC, Swelling index, in-vitro drug release, mucoadhesion, simulated salivary fluid.

### I. INTRODUCTION

Amongst various routes of drug delivery oral route is perhaps the most preferred to the patient and the clinician. The conventional tablets seems to be popular because of its ease of transportation and comparatively low manufacturing cost. However the enzymes in the GI fluids, GIT-pH conditions, enzymes bound to GIT membranes, hand tremors, dysphagia in case of geriatric patients, underdeveloped muscular and nervous system in infant and non-co-operative patient and the problem of swallowing are a few factors responsible for the bioavailability problems.<sup>1</sup> But drug delivery via the buccal route using bioadhesive dosage forms offer such a novel route of drug administration and overcome all these disadvantages shown by other conventional dosage form.<sup>2</sup> It offers fast, accurate dosing in a safe, efficacious format that is convenient and portable, without need of water or measuring devices. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is greater than that of skin.<sup>3,4</sup>

Aripiprazole is an atypical III generation atypical antipsychotic and antidepressant used in the treatment of schizophrenia, bipolar disorder and clinical depression.<sup>5</sup> It was approved by USFDA for schizophrenia.<sup>6</sup> Aripiprazole exerts its effects through agonism of dopaminic and 5-HT<sub>1A</sub> receptors and antagonism of alpha adrenergic and 5-HT<sub>2A</sub> receptors.<sup>7</sup> The buccal tablets perfect fit to take dose of an antipsychotic easily.

## II. MATERIALS AND METHODS

### Materials:

Aripiprazole, Mecleods pharmaceutical, Mumbai India, Carboxymethyl Tamarind gum, Modern Science Pvt. Ltd, Nashik. HPMC K4M, Modern Science Pvt.Ltd, Nashik. B-cyclodextrin, Modern Science Pvt. Ltd. Nashik. Mannitol, Modern Science Pvt. Ltd. Nashik. Oleic acid Modern Science Pvt. Ltd. Nashik. Magnesium stearate Modern Science Pvt. Ltd. Nashik.

### Methods:

#### Preformulation study of the drug

##### 1. Organoleptic properties:

The Aripiprazole was studied for organoleptic properties such as appearance, color and odor. The results of this are shown in **Table 1**.

##### 2. Melting point:

The melting point of Aripiprazole was determined by melting point apparatus (KUMAR, Model-VMP-D) using Open capillary method. Drug was separately filled up to 5-6 mm in glass capillaries whose one end was sealed by flame. The capillary was dipped in liquid paraffin inside the M.P. apparatus equipped with magnetic stirring facility for uniform heat transfer. Melting point temperature range was noted when the drug just starts melting until it completely melts M.P. determination was repeated three times. The results are shown in the **Table 2**.

##### 3. Solubility study:

The solubility of Aripiprazole was determined in different solvents (Water, 0.1N HCl, Acetate buffer pH 4.6, Phosphate buffer pH (6.8) by adding drug in solvent and sonicate for 15 min. filtered the solution through whatmann filter paper, solubility was determined by using UV double beam spectrophotometer (Shimadzu 2600). The results of solubility are shown in **Table 3**.

##### 4. UV Spectroscopy:

The UV spectrum of Aripiprazole was scanned in methanol at 800-200 nm.

##### I. Determination of maximum absorbance ( $\lambda_{max}$ )

Stock solution (100  $\mu\text{g/ml}$ ) of Aripiprazole was prepared in methanol. This solution was appropriately diluted with the respective solvent to obtain a suitable concentration. The UV spectrum were recorded in the range 800-200 nm by using UV double beam spectrophotometer (Shimadzu 2600). The

wavelength of maximum absorption ( $\lambda_{max}$ ) was determined and is shown in **figure 1**.

##### II. Determination of Beers-Lambert's plot Calibration Curve of Aripiprazole in Methanol

Stock solution of 100  $\mu\text{g/ml}$  was prepared. Working standard solution of strengths 2, 4, 6, 8, 10 and 12  $\mu\text{g/ml}$  were made from the stock solution by appropriate dilutions. The above solutions were analysed by UV spectrophotometer at  $\lambda_{max}$  255 nm. Methanol was used as blank during spectrophotometric analysis. The standard calibration curve was obtained by plotting absorbance Vs. concentration. The concentration range over which the drug obeyed Beer-Lambert's law was chosen as analytical concentration range. Calibration curve is shown in **Graph 1 and Table 4**.

##### 5. Fourier Transform Infrared Spectroscopy (FT-IR):

The infrared spectrum of pure drug Aripiprazole was recorded by Shimadzu S 8400 FT-IR spectrometer. Drug was mixed with potassium bromide (KBr) in 1:9 proportion and spectrum was obtained in range of 4000-400  $\text{cm}^{-1}$ . Potassium bromide was used as a blank while running spectrum. The results are showed in **Figure 2 and Table 5**.

##### Compatibility studies:

To determine the compatibility of drug with excipients, drug-excipients compatibility study was carried out. Drug and excipient in 1:1% W/W was filled in the prewashed and dried amber colored glass vials and sealed with aluminium cap. These sealed vials were kept at  $40 \pm 2^\circ\text{C}$  for seven days in oven. At the end of seven days vials were removed from desiccator and compared with control samples which are kept at room temperature. The control and test samples were examined. They were examined for any color, odor, assay and FTIR values to ascertain any interaction that may occur between drug and excipients. The FTIR spectrum was shown in **Figure 3** and its FTIR interpretation shown in **Table 6**.

##### Complex Formation of Aripiprazole:

###### A) Solvent Evaporation Method:

The inclusion complexes of Aripiprazole with Beta-cyclodextrin were prepared in the 1:0.5, 1:1 and 1:2 molar ratio by solvent evaporation technique.

**Table 7: Molar Ratio Used for preparation of Inclusion Complex by Solvent Evaporation Method**

Carrier	Drug:Carrier Ratio (1:2 <sub>M/M</sub> )
Beta-Cyclodextrin	448:1134.98

**Characterization of Aripiprazole and Beta-Cyclodextrin Complex**

Complex of Aripiprazole and Beta- Cyclodextrin were characterized

1. Solubility studies
2. Drug content estimation
3. FT-IR spectral analysis

**Saturation solubility studies**

The solubility studies of prepared Aripiprazole:Beta-Cyclodextrin complexes are carried out in different media like water, 0.1 N HCl and Phosphate buffer of pH 6.8 and analyzed at 255 nm. The result were shown in **Table 8**.

**Drug content**

Aripiprazole-Beta cyclodextrin complex equivalent to 10 mg of Aripiprazole was weighed accurately and dissolved in 100 ml of methanol. Diluted suitably and drug content were analyzed at 255nm by UV spectrophotometer (SHIMADZU 2600). The results was show in **Table 9**.

**FT-IR Spectroscopy**

IR spectra of pure Aripiprazole, β-CD and with its complexes were obtained by a varian 640 IR spectrophotometer (SHIMADZU), using KBr

pellets method. The scanning range used for it was 4000-400 cm<sup>-1</sup>. The results was shown in **Figure 4**.

**Preparation and characterization of powder blend:**

The preparation of powder blend using following formula

Exactly 1819.8 mg of β-CD complex was taken in round bottom flask containing 100 ml of methanol. In a separate beaker 1350 mg of Tamarind CMC was taken in double distilled water. The aqueous solution of Tamarind CMC was sonicated for 15 minutes and then transfer into β-CD complex solution. The RBF was fitted to neck of rotary evaporator. Vacuum of 2 mm bar pressure was applied and the solution were evaporated out at 80 °C within 20 minutes. The dried powder was collected, pulverized through sieve no. 40 and it was used for preparation of tablet.

The formula for buccal tablet was shown in **Table 10**. The above tamarind CMC β-CD complex powder was mixed with HPMC K4M and oleic acid. The mannitol was mixed with the above mixture and lubricated with magnesium stearate. The powder blend was passed through sieve no.60. The precompression evaluation was performed. The buccal tablets was prepared using 6 mm round flat face punch.

**Table 10: Composition of formulations of Buccal Tablet of Aripiprazole**

Ingredients (mg/tablet)	Formulation Code				
	F1	F2	F3	F4	F5
Drug equivalent mg of Inclusion Complex	60.66	60.66	60.66	60.66	60.66
HPMC K4M	7.5	10.5	7.5	4.5	4.5
Tamarind Carboxymethyl Cellulose	45	45	60	52.5	60
Oleic acid	33.73	30.73	18.73	29.23	21.73
Mannitol	0.11	0.11	0.11	0.11	0.11

<b>Magnesium stearate</b>	3	3	3	3	3
<b>Total weight (mg/tablet)</b>	150	150	150	150	150

**Evaluation of precompression parameters:**

Drug, Polymer and Excipients are characterized for their physical properties like Angle of repose, Bulk density, Tapped density, Compressibility index and Hausner's ratio etc. The results are shown in **Table 11**.

**EVALUATION OF BUCCAL MUCOADHESIVE TABLET:**

**Characterization of prepared mucoadhesive tablets:**

Compressed tablets were characterized for their thickness, hardness, friability, weight variation and drug content parameters. The results are shown in **Table 12**.

**Thickness:**

Three tablets were taken from each formulation and their thickness was determined by using vernier calliper.

**Hardness:**

In this test crushing strength which cause the breaking of tablet is measured for that tablet is placed in between two anvils and then applies the force. Tablets were taken from each formulation and their hardness was determined by using Monsanto hardness tester.

**Friability:**

Ten pre-weighed tablets from each formulation were placed at each time in the Roche friabilator (Rimek, India) which was then operated for 100 revolutions at 25 rpm. The tablets were then dusted and reweighed. The friability was then calculated using following formula,  
**% friability = (initial weight – weight after 100 revolutions) / initial weight x 100**

**Weight variation:**

To study the weight variation, 20 tablets of each formulation were weighed using an electronic digital balance. The average weight of 20 tablets and standard deviation were calculated.

**Drug Content:**

Randomly selected 20 tablets were weighed and finely powdered. The quantity equivalent to 10 mg of Aripiprazole was weighed accurately and taken in 100 ml volumetric flask. Fifty milliliters of simulated salivary fluid (pH 6.75) was added, shaken for 5 min, made up to 100 ml with simulated salivary fluid of pH 6.75 and filtered. One ml of above solution was diluted to 10 ml in a volumetric flask and the drug concentration was determined at 255 nm by using UV spectrophotometer.

**Swelling study of formulations:**

Tablets were selected from each formulation. After weighing the initial weight (W1), the tablet was immersed separately in petri dishes containing 15 ml of simulated salivary fluid (pH 6.75) solution maintained at 37°C. After 8 hrs the tablets was removed from the petri dishes and excess surface water was removed carefully using the filter paper. The swollen tablets were then reweighed (W2). This experiment was performed in triplicate. The % swelling index was calculated as using following formula,

**Swelling Index =  $(W_2 - W_1) / W_1 \times 100$**

Where W1: initial weight of tablet.

W2: weight of tablet after time t.

The results are shown in **Graph 2** and **Table 13**.



Figure 5: Swelling Study

#### Surface pH study:

The surface pH of the buccal tablets is determined in order to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may cause irritation to buccal mucosa, we sought to keep the surface pH as close to neutral as possible. A combined glass electrode is used for pH determination. The tablet is allowed to swell by keeping it in contact with 1 ml of simulated salivary fluid of pH 6.75 for 2 hrs at room temperature. The pH is identified by bringing the electrode into contact with the tablet surface and allowing to equilibrate for 1 min. The result were shown in **Graph 3 and Table 14**.

#### In-vitro drug release:

To study the drug release from the tablet, the USP Type II (paddle) apparatus was employed. In this method, 900 ml of 6.75 simulated salivary fluid was used as the dissolution media and the paddle was rotated at 50 rpm speed. The temperature of the media was maintained at  $37 \pm 5^{\circ}\text{C}$ . Sample of 5 ml was removed at a time interval of 30 min for 8 hours and volume was replaced with the fresh medium. The samples were filtered and the concentration in each sample was determined by UV at 255 nm with a spectrophotometer and reported as average of three determinations. Cumulative percent drug release was calculated using an equation obtained from standard curve. Analysis was done using 'PCP Disso V-3' software, India. The results are shown in **Table 15**.

### III. RESULTS:

#### Preliminary study

#### Organoleptic Properties of Aripiprazole:

Table 1: Organoleptic properties of Aripiprazole

Sr. No.	Properties	Observation
1	Appearance	Solid powder
2	Color	White
3	Odor	Odorless

#### Melting point:

Table 2: Melting point of Aripiprazole

Drug	Theoretical range	Practically observed
Aripiprazole	$135^{\circ}\text{C}-139.5^{\circ}\text{C}$	$139^{\circ}\text{C}$

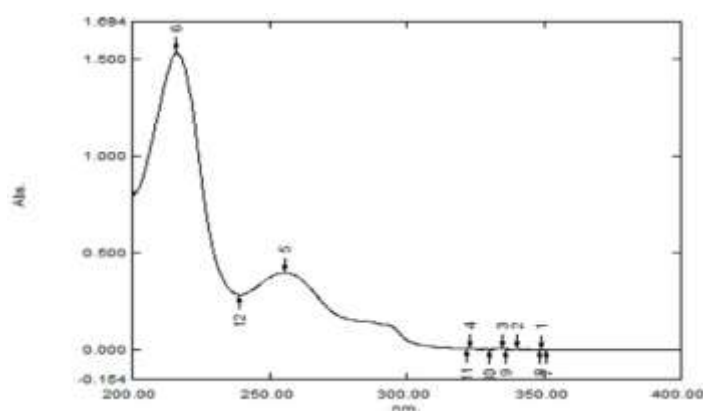
**Solubility study:**

**Table 3: Solubility of Aripiprazole**

Solvent	Solubility ( $\mu\text{g/ml}$ )
Water	$0.941 \pm 0.0282$
0.1 N HCl	$10.458 \pm 0.354$
Phosphate buffer 6.8 pH	$0.3 \pm 0.093$
Acetate buffer 4.6 pH	$2.325 \pm 0.2919$

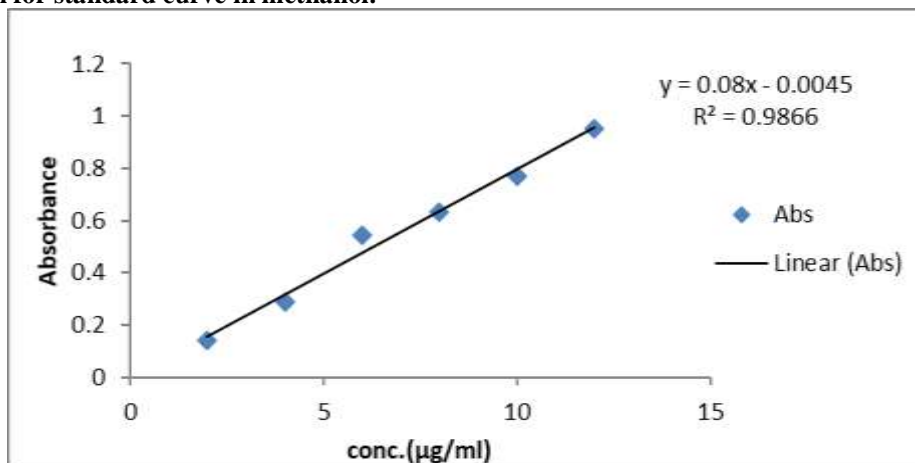
**Determination of  $\lambda$  max:**

**Preparation of calibration curve and spectrum of Aripiprazole:**



**Figure 1: UV spectrum of pure Drug Aripiprazole in Methanol**

**A] Equation for standard curve in methanol:**

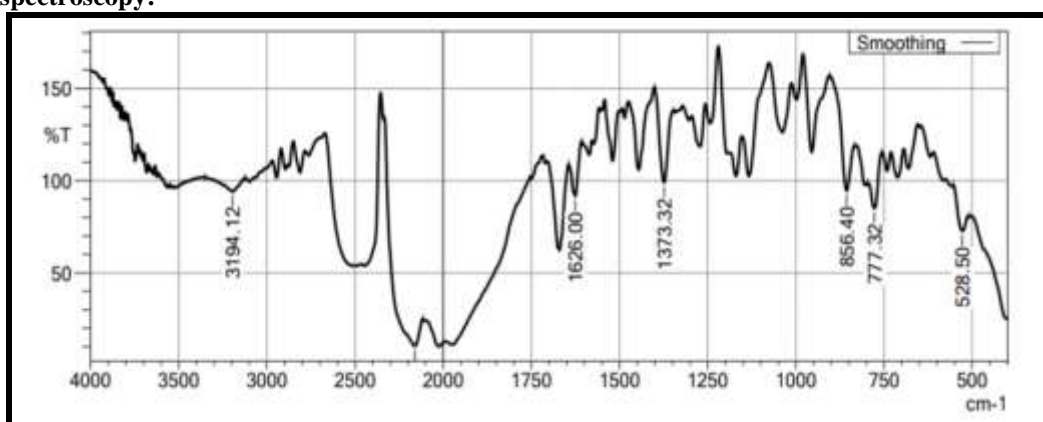


**Graph 1: Calibration curve of Aripiprazole in methanol**

**Table 4: Linearity ranges for Aripiprazole in Methanol at wavelength 255 nm**

Sr. No.	Concentration (µg/ml)	Absorbance
1	2	0.142
2	4	0.288
3	6	0.543
4	8	0.633
5	10	0.772
6	12	0.953

**FTIR spectroscopy:**

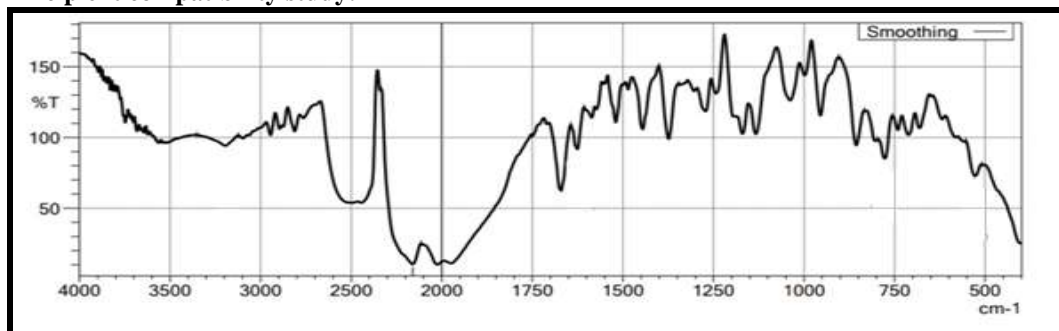


**Figure 2: FTIR spectrum of Aripiprazole**

**Table 5: Interpretation of FTIR spectrum of Aripiprazole**

Peak observed (cm <sup>-1</sup> )	Interpretation	Standard value
3194.12	N-H stretching	3500-3100
2949.16	Aliphatic -C-H stretching	3000-2850
1626.00	C=O stretching vibration in amide	1760-1680
1519.91	Aromatic compound C=C	1600-1475
1047.30 1265.10	C-N stretching in amines	1360-1180
1242.16	C-O stretching ether	1300-1050
856.40 777.32	C-H bending bonds of aromatics	900-690

**Drug- Excipient compatibility study:**



**Figure 3: FTIR spectrum of Aripiprazole and excipients**

**Table 6: FTIR Interpretation of Drug and Excipients**

Peak observed (cm <sup>-1</sup> )	Interpretation	Standard value
3194.18	N-H stretching	3500-3100
2951.09	Aliphatic –C-H stretching	3000-2850
1622.14	C=O stretching vibration in amide	1760-1680
1517.98	Aromatic compound C=C	1600-1475
1045.42 1188.15	C-N stretching in amines	1360-1180
1242.16	C-O stretching ether	1300-1050
810.11 785.03	C-H bending bonds of aromatics	900-690

**EVALUATION OF ARIPIPRAZOLE:BETA-CYCLODEXTRIN COMPLEX:**

**a) Saturation solubility study of Aripiprazole:β-cyclodextrin:**

**Table 8: Saturation solubility study of Aripiprazole:β-cyclodextrin**

Ratio of complex	Sample	Solubility in water (µg/ml)	Solubility in 0.1 N HCl (µg/ml)	Solubility in phosphate buffer of pH 6.8 (µg/ml)
Pure drug	Aripiprazole	35.62 ± 2.5	67.7 ± 6.8	58.12 ± 7.5
1:0.5	Aripiprazole B-CD complex	403.53 ± 46.45	406.63 ± 37.1	353.12 ± 19.31
1:1	Aripiprazole B-CD complex	421.87 ± 22.94	445.17 ± 57.99	381.45 ± 13.82
1:2	Aripiprazole B-CD complex	521.45 ± 10.02	538.53 ± 39.17	444.37 ± 3.42



b) Drug content of Aripiprazole:β-cyclodextrin:

Table 9: Drug content of Aripiprazole:β-cyclodextrin

Sr. No	Complex Ratio	% Drug content
1	1:0.5	87.13±2.120
2	1:1	93.9±2.569
3	1:2	97.3±1.14

c) FTIR spectroscopy of Aripiprazole:β-cyclodextrin:

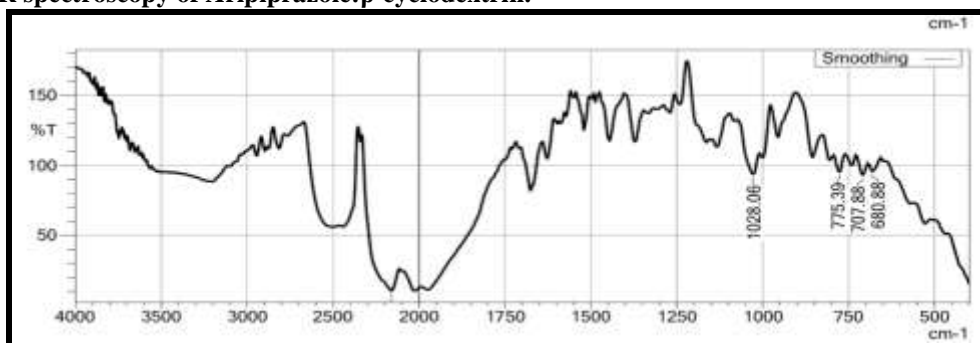


Figure 4: FTIR spectra of Aripiprazole-βCD complex (1:2) complex

EVALUATION OF PRECOMPRESSION PARAMETERS:

Table 11: Characteristics of Powder Blend

Formulation batch	Bulk density (gm/ml)	Tapped density (gm/ml)	% Compressibility Index	Hausner's Ratio	Angle of repose(°)
F1	0.5356	0.6511	17.73	1.2156	29.04
F2	0.5381	0.6458	16.67	1.2001	28.43
F3	0.5442	0.6422	15.26	1.18	28.81
F4	0.5412	0.6686	19.05	1.2354	30.83
F5	0.5349	0.6659	19.67	1.244	28.08

EVALUATION OF PREPARED BUCCOADHESIVE ARIPIPRAZOLE TABLETS:

Characterization of prepared buccoadhesive tablets:

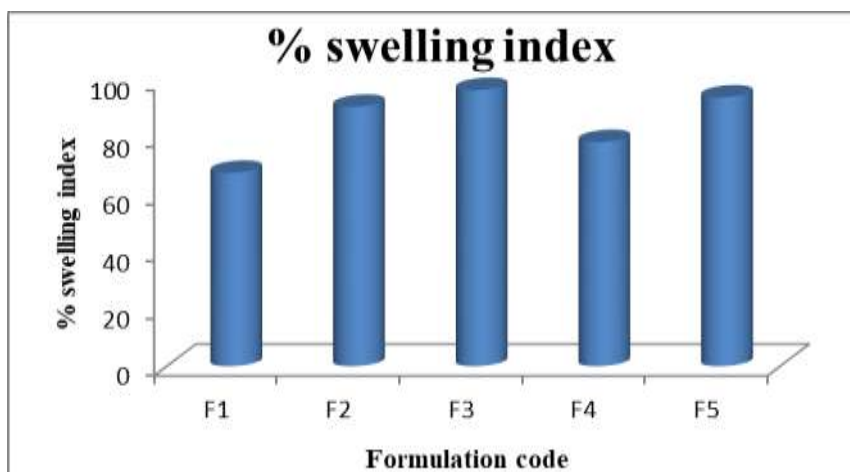
Table 12: Characteristics of prepared buccoadhesive tablets

Formulation Batches	Thickness (mm) ±SD (n=3)	Hardness (kg/cm <sup>2</sup> ) ±SD (n=3)	% Friability (%) ±SD (n=3)	Average weight (mg) ±SD (n=3)	Drug content (%)±SD (n=3)
F1	3.103 ±0.004	4.6 ±0.658	0.602 ±0.002	150.28 ±0.42	94.6 ±0.54
F2	3.11 ±0.001	4.44 ±0.091	0.528 ±0.0022	149.95 ±0.17	97.55 ±0.87
F3	3.116 ±0.005	4.96 ±0.231	0.455 ±0.003	150.01 ±0.18	100.1 ±0.64
F4	3.1 ±0.01	4.6 ±0.124	0.537 ±0.021	150.47 ±0.55	99.5 ±0.57
F5	3.116 ±0.014	4.68 ±0.412	0.463 ±0.0045	150.17 ±0.075	99.7 ±0.72

Swelling studies:

**Table 13: % swelling index of prepared buccoadhesive tablets**

Formulation Batch	% Swelling index
F1	67.62±0.1153
F2	90.7±0.1248
F3	96.66±0.02
F4	78.44±0.45
F5	94.0±0.10

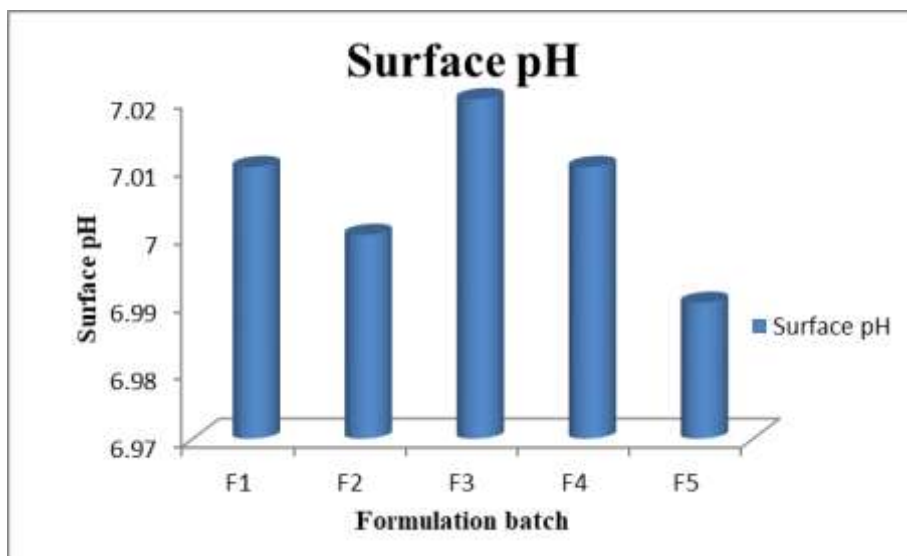


**Graph 2: % Swelling index of buccoadhesive formulation of Aripiprazole**

Surface pH studies:

**Table 14: Surface pH of prepared buccoadhesive tablets**

Formulation batch	Surface pH
F1	7.01±0.012
F2	7.00±0.10
F3	7.02±0.021
F4	7.01±0.011
F5	6.99±0.023

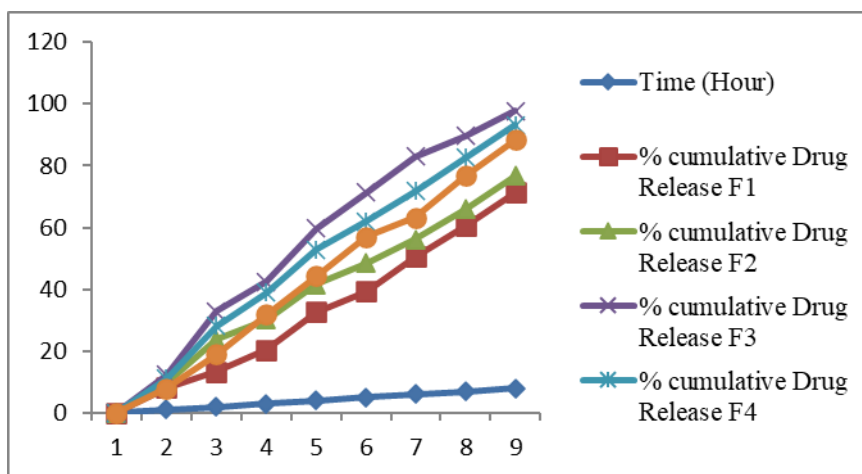


Graph 3: Surface pH of buccoadhesive formulations of Aripiprazole

In-vitro drug release

Table 15: Percent cumulative drug release from different formulation

Time (Hour)	% cumulative Drug Release				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	8.152	9.874	12.32	10.99	7.96
2	13.42	23.82	32.91	28.16	18.91
3	20.49	30.22	42.365	38.97	31.75
4	32.67	41.55	59.64	52.82	44.23
5	39.42	48.52	71.42	61.92	56.91
6	50.53	56.174	82.94	71.821	63.21
7	60.54	65.88	89.51	82.51	76.76
8	71.25	76.67	97.75	93.15	88.31

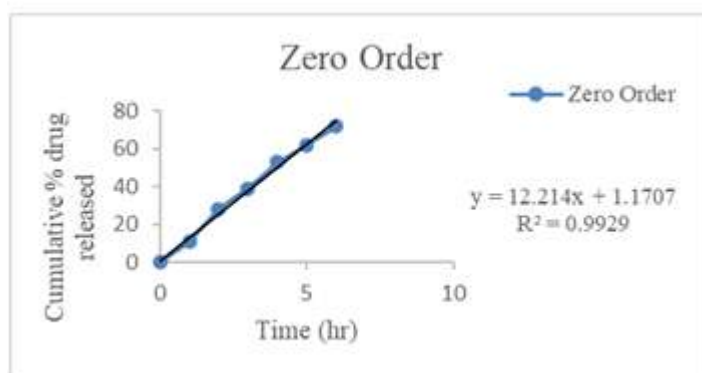


Graph 4: Cumulative drug release (F1 to F5 batch)

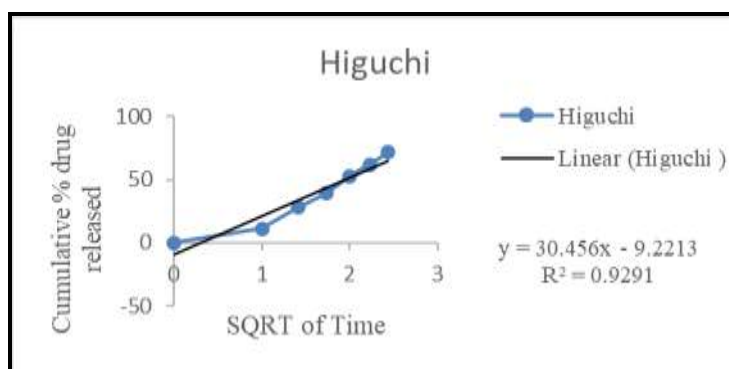
**Kinetic Data Treatment:**

**Table 16: kinetic data treatment**

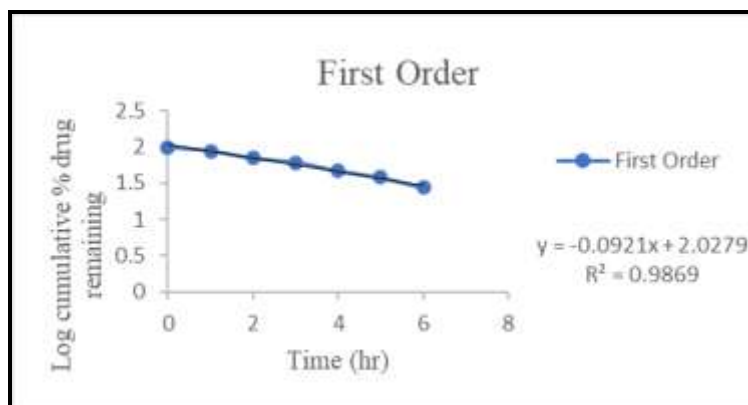
Formulation code	Zero order	First order	Higuchi model	Korsmeyer Peppes
	R <sup>2</sup>	R <sup>2</sup>	R <sup>2</sup>	R <sup>2</sup>
F3	0.9929	0.9869	0.9291	0.9767



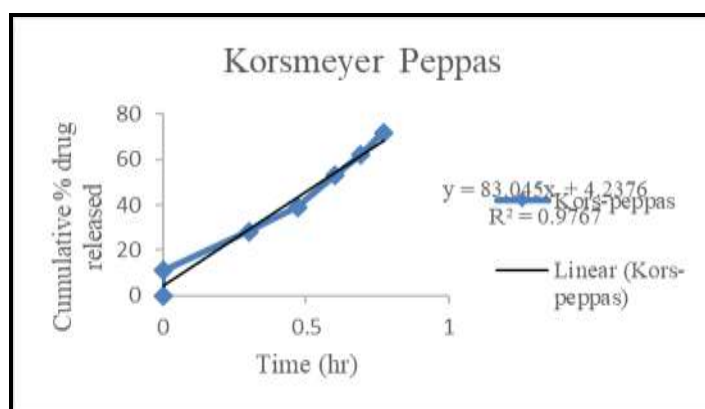
**Graph 5: Zero order Kinetic Representation of optimized batch (F3)**



**Graph 6: Higuchi Kinetic Representation of optimized batch (F3)**



**Graph 7: First Order Kinetic Representation of optimized batch (F3)**



Graph 8: Korsmeyer Peppas Kinetic Representation of optimized batch (F3)

#### IV. DISCUSSION:

The absorption maxima for Aripiprazole was found to be 255 nm in methanol. Regression coefficient ( $R^2$ ) was found to be 0.986. FTIR spectrum of Aripiprazole showed all the peaks corresponding to the functional groups present in the structure of Aripiprazole. From the Drug-excipient compatibility FTIR spectroscopy it was observed that major functional group peak of Aripiprazole was observed in the spectra which reveals that Aripiprazole was compatible with other excipients. The solubility study of Aripiprazole: $\beta$ -cyclodextrin complex reveals that complex of ratio 1:2 shows significant solubility 1:2 ratio was selected for formulation of buccal tablet of Aripiprazole. FTIR peak of Aripiprazole- $\beta$ -CD complex shows that peak corresponds to 1265.31  $\text{cm}^{-1}$  was absent which proves that pyridine ring structure of Aripiprazole is involved in complexation with  $\beta$ -CD. The Precompression parameters shows the significant flow properties and compressibility. Thickness of the tablets for all the formulations was found to be between 3.103 mm to 3.12 mm with the average 3.11 mm. The hardness of the tablets was found to be in the range 4.44  $\text{kg/cm}^2$  to 4.96  $\text{kg/cm}^2$  and it decrease with decreasing amount of tamarind CMC. The friability of the tablets for all the formulation was found in between 0.455 % to 0.602 % with the average of 0.517%. All the formulation batches pass the test for friability as per IP standard. The average weight of the tablets for all the formulation batches was found to be between 149.95 mg to 150.47 mg, maximum % deviation with the limit 7.5%. Hence, all the formulation passes the test for weight variation as per IP. Percent drug content for all the formulation was found in between 94.6% to 100.1%. Thus all tablets comply with the IP standards. The swelling indices of the tablets

containing tamarind CMC and HPMC K4M it was found that swelling was increase with the increasing amounts of Tamarind CMC. In-vitro drug release study of batches F1 to F5 was conducted. F3 and F4 batch shows 97.75 % and 93.15% drug release respectively. As F3 shows maximum drug release at 8 hr hence, It was considered to be optimized formulation batch. The optimized formulation (F3) batch follows the zero order and korsemeyer Peppas equation which follows the super case II transport drug release mechanism.

#### V. CONCLUSION

Amongst all formulation, the formulation F3 contains HPMC K4M 7.5 mg and Tamarind CMC 60 mg was the best one in all the aspects. The in vitro release kinetics studies reveals that all formulations its well with zero order kinetics followed by korsemeyer Peppas, the mechanism of drug release is super case II transport. Aripiprazole buccoadhesive tablets could be promising one as they, increase bioavailability, minimize the dose, reduces the side effects and improves the patient compliance hence, Aripiprazole might be a right candidate for oral sustained drug delivery via buccoadhesive tablets for the therapeutic use.

#### VI. AKOWLEDGEMENT:

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