IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
November 2020 Vol.:19, Issue:4

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

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Priyanka Jadhav*[1], Varsha Tambe[2], Ambadas Rote[3], Ritesh Karmarkar[4]

*[1]*Department of Pharmaceutical Quality Assurance, MGV'S Pharmacy college, Panchavati, Nashik 422003 India.* [2]*Department of Pharmaceutical Quality Assurance, MGV'S Pharmacy college, Panchavati, Nashik 422003 India.* [3]*Department of Pharmaceutical chemistry, MGV'S Pharmacy college, Panchavati, Nashik 422003 India.* [4]*Department of Pharmaceutics, MGV'S Pharmacy college, Panchavati, Nashik 422003 India.*

Submission: 20 October 2020
Accepted: 27 October 2020
Published: 30 November 2020


www.ijppr.humanjournals.com

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

ABSTRACT

Mucoadhesive buccal tablets of Aripiprazole were prepared with an objective to enhanced solubility and bioavailability. The Aripiprazoles solubility increase by complexation with β-cyclodextrin. Various concentration of polymers like Tamarind CMC and HPMC K4M was used. The preformulation study using FTIR spectroscopy revealed the compatibility of drug and polymer. The Aripiprazole:β-cyclodextrin complex was prepared. The FTIR spectroscopy of prepare complex revealed that pyridine ring structure of Aripiprazole was involved in complex formation. The 1:2 complex show 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 the 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 to7.10 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 polymers can be used to prepare mucoadhesive buccal tablets of Aripiprazole having a prolonged therapeutic effect with enhanced bioavailability.

INTRODUCTION

Amongst various routes of drug delivery oral route is perhaps the most preferred to the patient and the clinician. The conventional tablets seem to be popular because of its ease of transportation and comparatively low manufacturing cost. 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[1]. 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 forms[2]. It offers fast, accurate dosing in a safe, efficacious format that is convenient and portable, without the 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[3,4].

Aripiprazole is an atypical III generation atypical antipsychotic and antidepressant used in the treatment of schizophrenia, bipolar disorder and clinical depression[5]. It was approved by USFDA for schizophrenia[6]. Aripiprazole exerts its effects through agonism of dopaminic and 5-HT1A receptors and antagonism of alpha-adrenergic and 5-HT2A receptors[7]. The buccal tablets perfect fit to take a dose of an antipsychotic easily.

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 the Open capillary method. The 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 a 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 **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 insolvent and sonicate for 15 min. filtered the solution through Whatman filter paper, solubility was determined by using UV double beam spectrophotometer (Shimadzu 2600). The results of the 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 (λ max)

Stock solution (100 µg/ml) of Aripiprazole was prepared in methanol. This solution was appropriately diluted with the respective solvent to obtain a suitable concentration. The UV spectrum was recorded in the range 800-200 nm by using a UV double beam spectrophotometer (Shimadzu 2600). The wavelength of maximum absorption (λ max) was determined and is shown in **figure 1.**

II. Determination of Beers-Lambert's plot

Calibration Curve of Aripiprazole in Methanol

A stock solution of 100 µg/ml was prepared. Working standard solution of strengths 2, 4, 6, 8, 10, and 12 µg/ml were made from the stock solution by appropriate dilutions. The above solutions were analyze by UV spectrophotometer at λmax 255 nm. Methanol was used as a 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 the analytical concentration range. The 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. The drug was mixed with potassium bromide (KBr) in 1:9 proportion and the spectrum was obtained in the range of 4000-400 cm^{-1}. Potassium bromide was used as a blank while running spectrum. The results was shown in **Figure 2 and Table 5.**

Compatibility studies:

To determine the compatibility of the drug with excipients, a drug-excipients compatibility study was carried out. Drug and excipient in 1:1% W/W were filled in the prewashed and dried ambar colored glass vials and sealed with aluminum cap. These sealed vials were kept at 40 ± 2^0C for seven days in the oven. At the end of seven days, vials were removed from the 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 No.7: Molar Ratio Used for preparation of Inclusion Complex by Solvent Evaporation Method

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

Characterization of Aripiprazole and beta-cyclodextrin Complex

The 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 are shown in **Table 8.**

Drug content

Aripiprazole-Beta cyclodextrin complex equivalent to10 mg of Aripiprazole was weighed accurately and dissolved in 100 ml of methanol. Diluted suitably and drug content analyzed at 255nm by UV spectrophotometer (SHIMADZU 2600). The results are shown in **Table 9.**

FT-IR Spectroscopy

IR spectra of pure Aripiprazole, β-CD, and its complexes were obtained by a variant 640 IR spectrophotometer (SHIMADZU), using the KBr pellets method. The scanning range used for it was 4000-400 cm^{-1}. The results are shown in **Figure 4.**

Preparation and characterization of powder blend:

The preparation of powder blend using the following formula.

The β-CD complex was taken in a round bottom flask containing 100 ml of methanol. In a separate Tamarind CMC was taken in distillled water. The aqueous solution of Tamarind

CMC was sonicated for 15 minutes and then transfer into the β-CD complex solution. The RBF was fitted to the neck of the rotary evaporator. Vaccum of 2 mm bar pressure was applied and the solution evaporated out at 80 ^{0}C within 20 minutes. The dried powder was collected, pulverized through sieve no. 40 and it was used for the preparation of the tablets.

The formula for the 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 are prepared using a 6 mm round flat face punch.

Table No.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
Magnesium stearate	3	3	3	3	3
Total weight (mg/tablet)	150	150	150	150	150

Evaluation of pre-compression parameters:

The drug, Polymers and Excipients are characterized for their physical properties like Angle of repose, Bulk density, Tapped density, Compressibility index, and Hausner's ratio. 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 a vernier caliper.

Hardness: 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 the 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 a simulated salivary fluid of pH 6.75 and filtered. One ml of the above solution was diluted to 10 ml in a volumetric flask and the drug concentration was determined at 255 nm by using a 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 37^0C. After 8 hrs the tablets are 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 using the 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 **Table 13.**

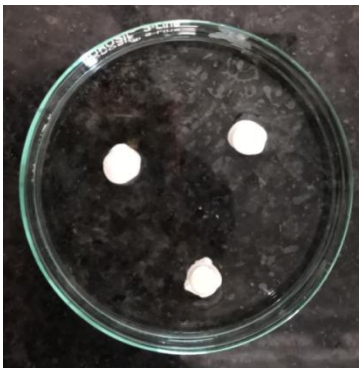


Figure No. 5: Swelling Study

Surface pH study:

The surface pH of the buccal tablets is determined to investigate the possibility of any side effects *in vivo*. As an acidic or alkaline pH may irritate 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 it to equilibrate for 1 min[8]. The result are shown in **Table 13.**

***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 ± 5^0C. A 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 an average of three determinations. Cumulative percent drug release was calculated using an equation obtained from the standard curve. The analysis was done using 'PCP Disso V-3' software, India. The results are shown in **Table 14.**

RESULTS AND DISCUSSION

RESULTS

Preliminary study

Organoleptic Properties of Aripiprazole:

Table No.1: Organoleptic properties of Aripiprazole

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

Melting point:

Table No.2: Melting point of Aripiprazole

Drug	Theoretical range	Practically observed
Aripiprazole	135^0C-139.5^0C	139^0C

Solubility study:

Table No.3: Solubility of Aripiprazole

Solvent	Solubility (µg/ml)
Water	0.941±0.0282
0.1 N HCl	10.458±0.354
Phosphate buffer 6.8 pH	0.3±0.093
Acetate buffer 4.6 pH	2.325±0.2919

Determination of λ max:

Preparation of calibration curve and spectrum of Aripiprazole:

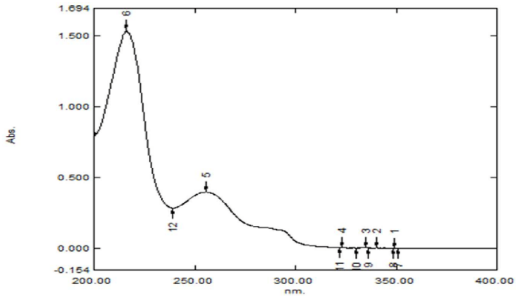
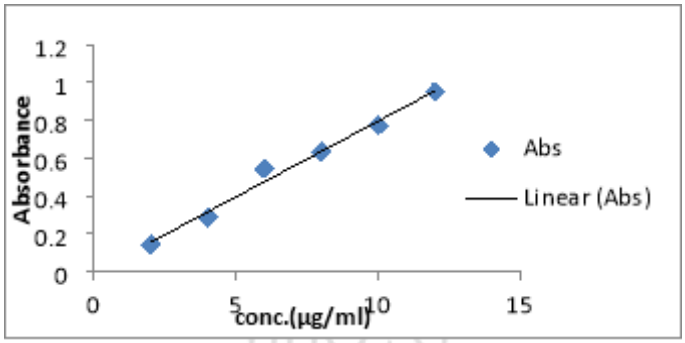


Figure No. 1: UV spectrum of pure Drug Aripiprazole in Methanol

A] Equation for standard curve in methanol:



Graph 1: Calibration curve of Aripiprazole in methanol

Table No.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:

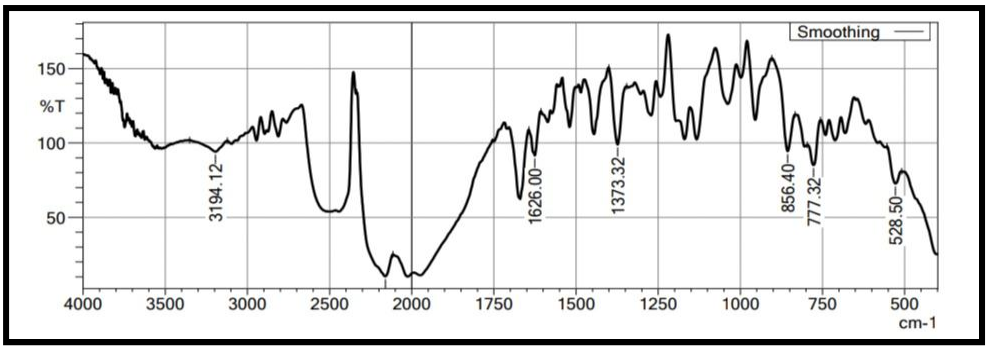


Figure No. 2: FTIR spectrum of Aripiprazole

Table No.5: Interpretation of FTIR spectrum of Aripiprazole

Peak observed (cm^{-1})	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:

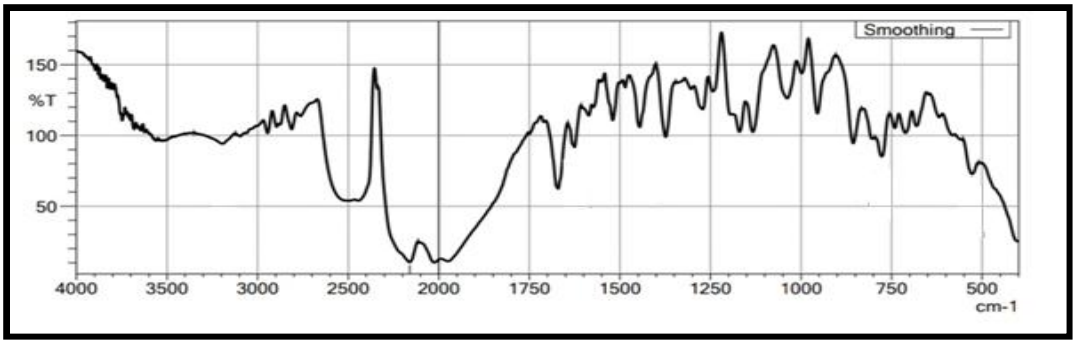


Figure No. 3: FTIR spectrum of Aripiprazole and excipients

Table No.6: FTIR Interpretation of Drug and Excipients

Peak observed (cm^{-1})	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 No.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 No. 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:

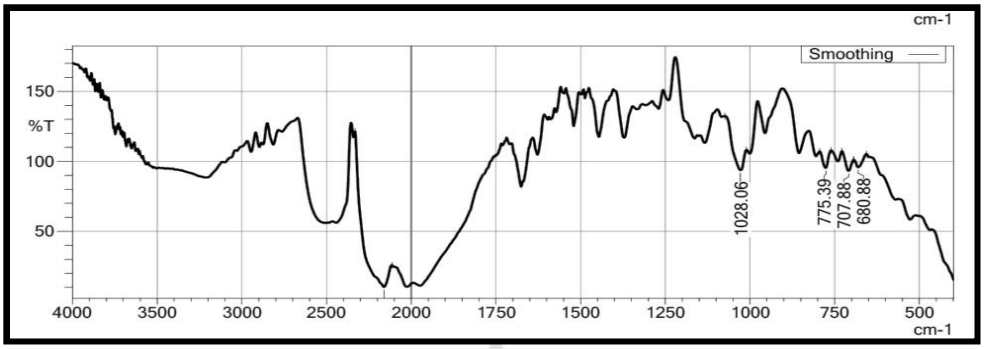


Figure No. 4: FTIR spectra of Aripiprazole-βCD complex (1:2) complex

EVALUATION OF PRECOMPRESSION PARAMETERS:

Table No. 11: Characteristics of Powder Blend

Formulation batch	Bulk density (gm/ml)	Tapped density (gm/ml)	% Compressibility Index	Hausner's Ratio	Angle of repose(^{0})
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 No. 12: Characteristics of prepared buccoadhesive tablets

Formulation Batches	Thickness (mm) ±SD (n=3)	Hardness kg/cm^2) ±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:

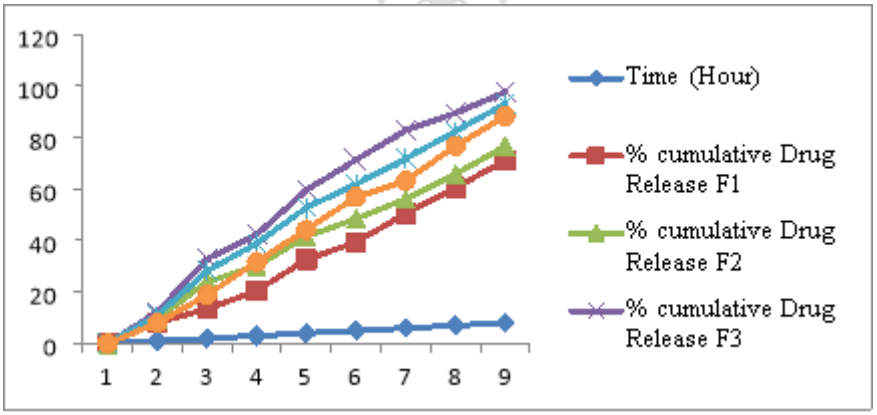
Table No. 13: swelling index and Surface pH of prepared buccoadhesive tablets

Formulation Batch	% Swelling index	Surface pH
F1	67.62±0.1153	7.01±0.012
F2	90.7±0.1248	7.00±0.10
F3	96.66±0.02	7.02±0.021
F4	78.44±0.45	7.01±0.011
F5	94.0±0.10	6.99±0.023

***In–vitro* drug release:**

Table No. 14: 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

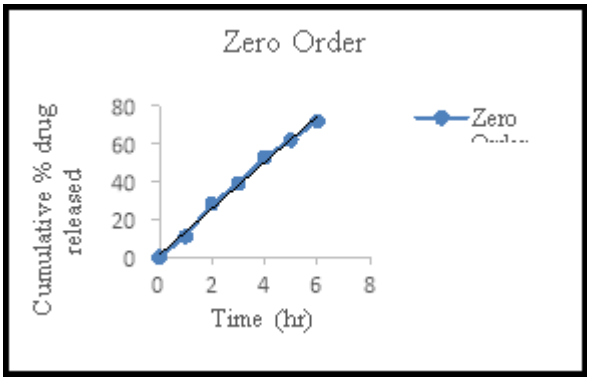


Graph 2: Cumulative drug release (F1 to F5 batch)

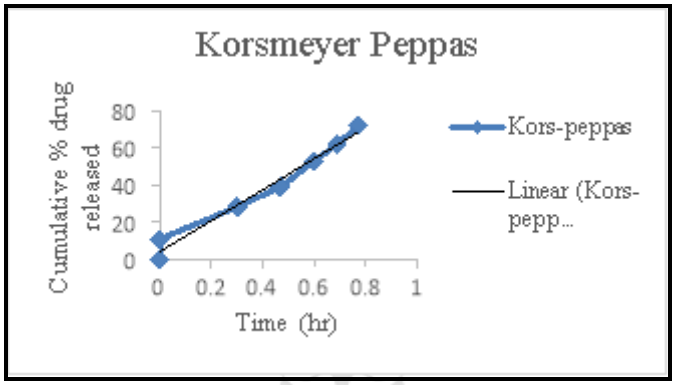
Kinetic Data Treatment:

Table No.15: Kinetic data treatment

Formulation code	Zero order	Korsmeyer Peppes
	R^2	R^2
F3	0.9929	0.9767



Graph 3: Zero-order Kinetic Representation of optimized batch (F3)



Graph 4: Korsmeyer Peppas Kinetic Representation of optimized batch (F3)

DISCUSSION

The absorption maxima for Aripiprazole was found to be 255 nm in methanol. The 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 a 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:β-cyclodextrin complex reveals that complex of ratio 1:2 shows significant solubility 1:2 ratio was selected for the formulation of the buccal tablet of Aripiprazole. FTIR peak of Aripiprazole-β-CD complex shows that peak corresponds to 1265.31 cm^{-1} was absent which proves that the pyridine ring structure of Aripiprazole is involved in complexation with β-CD. The Precompression parameters show significant flow properties and compressibility. The thickness of the tablets for all the formulations was found to be between 3.103 mm to 3.12 mm with an average of 3.11 mm. The hardness of the tablets was found to be in the range 4.44 kg/cm^2 to 4.96 kg/cm^2 and it decreases with decreasing amount of tamarind CMC.

The friability of the tablets for all the formulation was found between 0.455 % to 0.602 % with an 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 between 149.95 mg to 150.47 mg. maximum % deviation with the limit of 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 increased 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 an optimized formulation batch. The optimized formulation (F3) batch follows the zero-order and Korsmeyer peppas equation which follows the super case II transport drug release mechanism.

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-vitr*o release kinetics studies revels that all formulations its well with zero-order kinetics followed by Korsmeyer peppas the mechanism of drug release is super case II transport. Aripiprazole buccoadhesive tablets could be promising as they, increase bioavailability, minimize the dose, reduces the side of oral sustained drug delivery via buccoadhesive tablets for therapeutic use.

ACKNOWLEDGMENT

The authors are sincerely thankful to the Principal and research guide of MGV's Pharmacy College, Panchavati, Nashik for providing the needful facilities and moral support to carry out this research work. I sincerely express my gratitude to Mecleods pharmaceutical, Mumbai India for providing Aripiprazole as a gift sample.

REFERENCES

[1] Jain NK. Controlled and novel drug delivery. 1st ed. New Delhi: CBS Publishers and Distributors; 1997: 52-81.
[2] Patel VM, Prajapati BG, Patel MM. Formulation, evaluation, and comparison of bilayered and multilayered mucoadhesive buccal devices of propranolol hydrochloride, AAPS Pharm Sci Tech 2007; 8(1): 1-8.
[3] Shojaei HA. Buccal mucosa as a route for systemic drug delivery: A Review. J Pharm Sci 1998; 1(1):15-30.

[4] David H, Robinson JR. Buccal drug delivery via the mucous membranes of the oral cavity. J Pharm Sci 1992; 81(1):1-9.
[5] Indian Pharmacopoeia (2014) vol. 1, A publication of the I.P. Commission, Ministry of Health & Family Welfare Government of India, Published by I.P. commission. 2014; 1081-1082.
[6] https://psychopharmacologyinstitute.com/publication/aripiprazole-indications-fda-approved-and-off-label-uses-2120.
[7] https://go.drugbank.com/drugs/DB01238
[8] Kuipers ME, Heegsma J, Bakker HI, Meijer DK, Swart PJ, Frijlink EW, Eissens AC, Vries-Hospers HG, Berg J. Design and fungicidal activity of mucoadhesive lactoferrin tablets for the treatment of oropharyngeal candidosis. Drug Deliv. 2002; 9: 31-38.

Image *Author -1*	***Author Name – Corresponding Author*** :Priyanka Jadhav *Author Affiliation:* Department of Pharmaceutical Quality Assurance, MGV'S Pharmacy college, Panchavati, Nashik 422003 *Author Address/Institute Address:* MGV'S Pharmacy college, Panchavati, Nashik 422003
Image *Author -2*	***Author Name:*** Varsha Tambe *Author Affiliation:* Department of Pharmaceutical Quality Assurance, MGV'S Pharmacy college, Panchavati, Nashik 422003 *Author Address/Institute Address:* MGV'S Pharmacy college, Panchavati, Nashik 422003
Image *Author -3*	***Author Name:*** Ambadas Rote *Author Affiliation:* Department of Pharmaceutical chemistry, MGV'S Pharmacy college, Panchavati, Nashik 422003 *Author Address/Institute Address:* MGV'S Pharmacy college, Panchavati, Nashik 422003
Image *Author -4*	***Author Name:*** Ritesh Karmarkar *Author Affiliation:* Department of Pharmaceutics, MGV'S Pharmacy college, Panchavati, Nashik 422003 *Author Address/Institute Address:* MGV'S Pharmacy college, Panchavati, Nashik 422003