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"FORMULATION DEVELOPMENT AND EVALUATION MOUTH DISSOLVING FILM OF SAFINAMIDE"

[1]Shubhangi S. Mulane [2] Snehal M. Kankate [3] Dr.Ramdas T.Dolas

Pharmaceutics Department

Pravara rural Education Society college of pharmacy (for Women) Chicholi Tal. Sinnar, Nashik.

FORMULATION DEVELOPMENT AND EVALUATION MOUTH DISSOLVING FILM OF SAFINAMIDE

Abstract

The Aim of this study is to formulate and evaluate Safinamide immediate mouth dissolving oral film using solvent casting method. To prepare Safinamide oral dissolution membranes using different concentrations of membranes. Molding polymers and plasticizers. Develop and evaluate formulas for pre-compression parameters (such as solubility, melting point, heavy metal content, FT-IR research) and post-compression parameters (such as weight change, thickness, bending resistance, tensile strength, elongation percentage), and drug content , Content, disintegration time, dissolution test and SEM analysis . Improve patient compliance and obtain rapid onset to relieve symptoms of
Parkison.

Keyword

Oral dissolving film,safinamide, solvent casting metod, in vitro dissolution

Introduction

Due to ease of ingestion, avoidance of pain, versatility (to adapt to various types of drug candidates), and most importantly patient compliance and a strong drug delivery system, oral administration is the most popular route without sterility Conditions, so it is cheaper to produce. Recently, several new technologies for oral administration can be used to solve the physicochemical and pharmacokinetic characteristics of drugs while improving patient compliance. Electrostatic drug deposition and coating and computer-aided 3D printing (3DP) tableting are also available recently. The rapid dissolving drug delivery system was first developed in the late 1970s as an alternative to tablets, capsules and syrups for pediatric and elderly patients. Difficulty in swallowing traditional oral solid dosage forms.

The new technology for fast-dispersing dosage forms is called fast-dissolving, fast-dissolving, fast-melting and fast-disintegrating tablets. However, the functions and concepts of all these dosage forms are similar. According to the definition, a solid dosage form dissolves or disintegrates rapidly in the oral cavity to form a solution or suspension without the need to administer water. It is called a fast-dispersing oral dosage form. Dysphagia (dysphagia) is common in all age groups, especially the elderly, and can also occur when swallowing regular tablets and capsules. Dysphagia is associated with many diseases, including stroke, Parkinson's disease, AIDS, thyroidectomy, head and neck thyroid therapy, and other neurological diseases, including cerebral palsy. The most common complaint is the size of the tablet, followed by the surface, shape and taste. The problem of swallowing tablets is most pronounced in elderly and pediatric patients, as well as those who travel frequently and and do not have easy access to water.

FAST DISSOLVING FILMS[2]

Oral film is the latest technology in the production of oral disintegrating dosage forms. They are thin and elegant films of edible water-soluble polymers of various sizes and shapes (such as square, rectangular or disc). The stripes can be flexible or brittle, opaque or transparent. They are designed to break down quickly on the tongue without the need for water. Fast disintegrating membrane (FDF) has a large disintegration surface area. These films alleviate the danger/fear of suffocation, they are easy to handle and administer, and they keep a simple and traditional container to manufacture, thus overcoming the short-lived failure of fast disintegrating oral tablets. The main limitations of these dosage forms are low drug loading and limited taste masking options. The fast-disintegrating film is a thin film with a thickness of 1-10mm and an area of any geometric shape with an area of 1-20cm2. The drug can be incorporated into a single dose of up to about 15 mg. The immediate dissolution in saliva is due to the special matrix made of water-soluble polymers, which usually has low viscosity and is easy to handle and apply. However, through wetting, the wet tack and mucoadhesive properties of the system are designed to hold the film at the application site. The flexibility and strength of the film are selected to facilitate the manufacturing process and processes such as rewinding, die cutting, and packaging. The rapidly disintegrating film is placed on the patient& tongue and mucous tissue, and it is immediately wetted by saliva. The film quickly hydrates and adheres to the application site. It then quickly disintegrates and dissolves to release the drug for absorption from the oral mucosa or for stomach absorption when swallowed.

Table 1: comparison between oral fast dissolving films and oral disintegrating tablets

Oral dissolving films	Oral disintegrating tablets
It is a film	It is a tablet
Greater dissolution due to large surface area	Lesser dissolution due to less surface area
Better durable than oral disintegrating tablets	Less durable as compared with oral films
More patient compliance	Less patient compliance than films
Low dose can only be incorporated	High dose can be incorporated
No risk of chocking	It has a fear of chocking

PROPERTIES OF THE ORAL FILMS[4]

Table 2: Properties of the oral films

PROPERTY	FLASH RELEASE	MUCOADHESIVE MELT RELEASE	MUCOADHESIVE SUSTAINED RELEASE
Area (cm2)	2-8	2-7	2-4
Thickness (μm)	20-70	50-500	50-250
Structure	Film single layer	Single or multilayer system	Multilayer system
Excipients	Soluble, highly hydrophilic polymer	Soluble, hydrophilic polymer	Low/non soluble polymer
Drug phase	Solid solution	Solid solution/suspends drug particle	Suspension or solid solution
Application	Tongue (upper plate)	Gingival or buccal region	Gingival (or other region of oral cavity)
Dissolution	Maximum sixty second	Disintegration in few minutes, forming gel	Maximum 8-10 hours
Site of action	Systemic or local	Systemic or local	Systemic or local

Safinamide

Chemical Name : (2S)-2-[({4-[(3-fluorophenyl)methoxy]phenyl}methyl)amino]propanamide; methanesulfonic acid
Chemical Formula : C18H23FN2O5S
Molecular Weight: 398.45 g/mol
Melting point: 210-212 oC
Solubility: Safinamide is **sparingly soluble in ethanol** and is practically insoluble in ethyl acetate. In aqueous buffers that span a pH range of 1.2 to 7.5, safinamide mesylate is highly soluble at pH 1.2 and 4.5, but shows low solubility (<0.4 mg/mL) at pH 6.8 and 7.5.
Bioavailability: 95 %
Category: Used in the Treatment of Parkinson disease
BCS Class: II
Half life: 20-30 hours
Dose: 50 mg twice a day
pKa: 15.76
Log P: 2.48

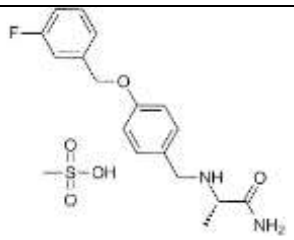

Fig. Structure of Safinamide

Mode of action: Safinamide is a unique molecule with multiple mechanisms of action and a very high therapeutic index. It combines potent, selective, and reversible inhibition of MAO-B with blockade of voltage-dependent Na+ and Ca2+ channels and inhibition of glutamate release. Safinamide has neuroprotective and neurorescuing effects in MPTP-treated mice, in the rat kainic acid, and in the gerbil ischemia model.

Materials and Equipments

MATERIALS AND METHODS

Table 3: List of materials

Material	Manufacturer
Safinamide	PharmaTech Solutions
HPMC E15	Accent microcell industries
HPMC E5	Symonds pvt ltd
PEG 400	BASF
Propylene glycol	Spectrum chemicals
Sodium saccharin	Aptuit laurus ltd
Phosphate Buffer 6.8	-

Table 4 :List of equipment

Name of Instrument	Model and Manufacturer
Digital balance	Mettler Toledo PR203
Hot air oven	Thermolab
UV Spectrometer	Lab india UV 3000
Dissolution test Apparatus	Lab india D5 8000
Micrometer screw gauge	Mitutoyo, china
Disintegration test apparatus USP	Electro Lab
pH meter	Electro Lab
Stability chamber	Thermo lab Pvt ltd

FORMULATION DEVELOPMENT OF SAFINAMIDE ORAL FILM[34]

Table 5: Formulation trials

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Safinamide (gm)	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
HPMC E15 (g)	1.0	1.25	1.5	-	-	-	1.25	-	1.25
HPMC E5 (g)	-	-	-	1.0	1.25	1.5	-	1.25	1.25
PEG 400 (g)	1.5	1.25	1.0	-	-	-	-	1.25	-
Propylene glycol (ml)	-	-	-	1.5	1.25	1.0	1.25	-	-
Citric acid (g)	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Sodium Saccharin (g)	0.125	0.125	0.125	0.125	0.125	0.125	0.125	0.125	0.125
Flavor (g)	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Distilled water (ml)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs

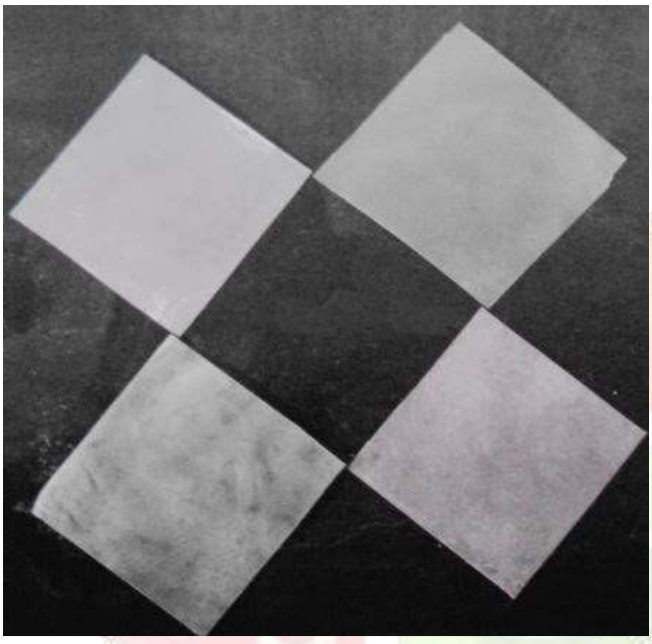

Fig : Fast Dissolving Films

PROCEDURE[37-40]

The water-soluble polymer and plasticizer are dissolved in distilled water. Stir the solution on a magnetic stirrer for 2 hours and set aside to remove all trapped air bubbles. At the same time, dissolve the excipients and drugs and fully stir for 30 minutes. After the stirring is completed, mix the two solutions. Finally, the solution is poured on a suitable petrochemical plate to form a thin film. The plate was kept in a hot air oven at 60°C for 1 hour. The dried film is gently peeled from the glass plate and cut to the required size.

Dose calculations

Inner radius of glass plate = 5.65 cm.
Inner Area of the plate (πr^2) = 3.14 x 5.65 x 5.65 = 100 cm2.
No. of 4 cm2 films present whole plate =100/4 =25 films.
Each films contains 50 mg of drug.
25 films contain 1250 mg drug (25×50). Labelled claim= 50 mg

EVALUATION OF ORAL FILM[44]

1.Thickness45

Use a micrometer thread gauge to measure the thickness of the film. In order to obtain the uniformity of the film, the thickness was measured at 5 different places. The thickness of the film must be less than 5%.

2.Folding endurance47

To determine the bending resistance, the film was cut and quickly folded in the same position until it broke. The number of times the film can be bent at the same position without breaking gives the value of the bending strength.

3.Percentage elongation48

It was calculated by

Percentage elongation = Increase in length of strip × 100

Initial length of strip

4.Tensile strength49

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the formula

Tensile strength = Load at failure × 100

Strip thickness × strip width

5.In-vitro disintegration50, 51

Disintegrating time is defined as the time (sec) at which a film breaks when brought in contact with water or saliva.

6.Petri dish method

Put 2ml of distilled water into a petri dish, add a film on the water surface, and measure the time for the oral film to completely dissolve.

7.In-vitro dissolution52

Use 900 ml Phosphate buffer 6.8 as the medium and keep it at 37±0.5°C while setting the basket to 100 rpm. Cut 4 cm2 (2 x 2 cm) film sample and place five films in the basket. Take 5 ml samples every 30 sec and replace the same amount of samples with fresh Phosphate buffer 6.8. The extracted samples were filtered and analyzed using an ultraviolet spectrometer at a wavelength of 228 nm.

8.Drug content53

The test is performed by dissolving a 4 cm2 area film in 50 ml Phosphate buffer 6.8 under stirring. Filter the solution using Whatman filter paper and dilute the filtrate to 100 ml with the same buffer in a volumetric flask. The solution was analyzed using an ultraviolet spectrometer.

9.Assay

The test is performed by dissolving a 4 cm area film in 50 ml of pH 6.8 phosphate buffer under stirring. Filter the solution using Whatman filter paper and dilute the filtrate to 100 ml with the same buffer in a volumetric flask. The solution was analyzed using an ultraviolet spectrophotometer.

10. Stability studies54

Stability studies are conducted according to ICH to evaluate the stability of pharmaceutical preparations. The optimized formula of F3 is sealed in polyethylene laminated aluminium packaging. The samples were kept at 40 degrees Celsius and 75% RH for 3 months. At the end of the study period, changes in the physical appearance, color, drug content and drug release characteristics of the preparation were observed.

11. SEM analysis56

The morphological study of the oral adhesive strips is carried out by scanning electron microscopy (SEM) at a prescribed magnification. The research involves the difference between the upper and lower surfaces of the film. It also helps determine API distribution.

RESULTS AND DISCUSSION

PREFORMULATION STUDIES

1 Solubility

Solubility is expressed in terms of parts per million of solvent in which 1g of solid is soluble. Solubility of the powder in different solvents like water, ethanol etc was determined at 20°c.

2 Heavy metal content

The part of Lead per million parts of powder was examined by comparing sample solution with 10 ppm lead standard solution for 2 gm material.

3 Melting point

The melting point was carried out by using capillary tube method.

Table no 5: API characterization – Safinamide

S.No	Test	Specification	Result
1	Description	White powder	White powder
2	Solubility	Soluble in water, Methanol, DMSO	Complies
3	Taste	Tasteless	Complies
4	Odor	Odorless	Complies
5	Heavy metals (ppm)	Should not be more than 20 ppm	Less
6	Melting point	Range :209-213° c	211 °c

CALIBRATION CURVE OF SAFINAMIDE

The stock solution was prepared with 10 mg Safinamide in 10 ml water. Extract 10 ml from this stock solution and dilute to 100 ml with water. Prepare the calibration curve by appropriately diluting the stock solution and using different concentrations (5 µg/ml-25 µg/ml). The absorbance is measured at 228 nm. The absorbance of various concentrations measured at 228 nm is shown in Table 10 below. Standard curve of Safinamide is shown in figure 13

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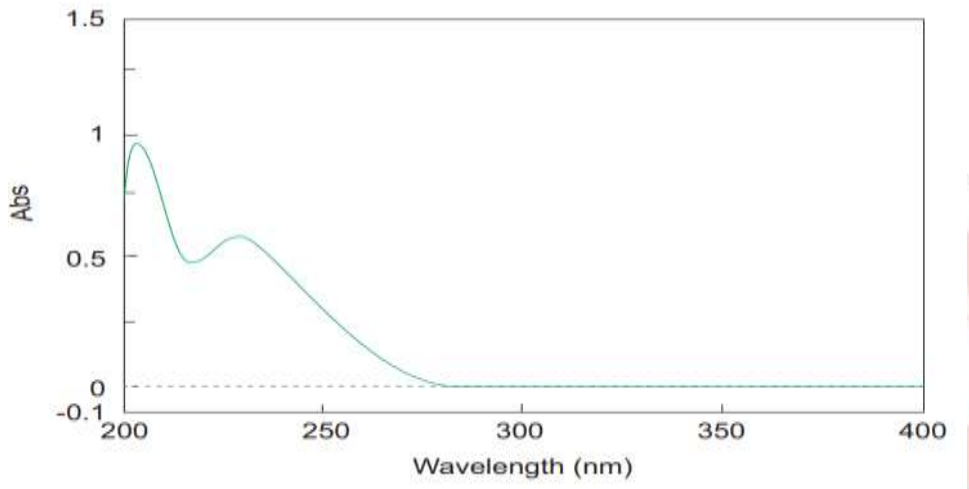


Fig 12: UV spectrum of Safinamide

Table no 10: Standard graph of Safinamide

S. No	Concentration µg/ml	Absorbance (228 nm)
1	5	0.1634
2	10	0.3317
3	15	0.4918
4	20	0.6778
5	25	0.8549

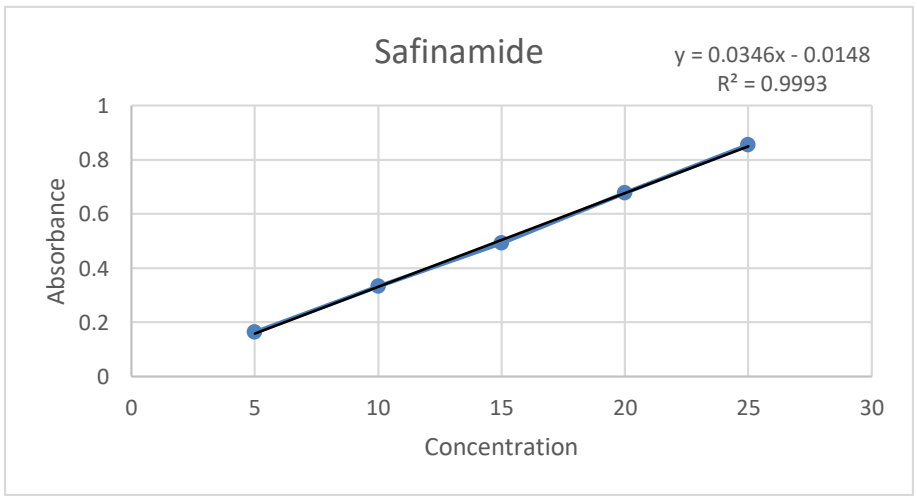


Fig 13: Standard graph of Safinamide

From the calibration curve the regression equation was found to be y = 0.0346x - 0.0148 and r^2= 0.9993 which will helpful in drug content and % CDR determination on UV spectrophotometer.

3. FT-IR Studies

An FTIR study was conducted to check the compatibility of the drug with the polymer. The infrared spectrum of Safinamide was measured on a Fourier transform infrared spectrophotometer using the KBr scattering method. Use dry potassium bromide for baseline correlation. Then use the FTIR spectrophotometer to analyze the spectrum of the dry mixture of the drug and potassium bromide with various polymers, and then the drug. The maximum absorption in the spectrum obtained with the test substance corresponds to the maximum absorption of the reference spectrum in position and intensity.

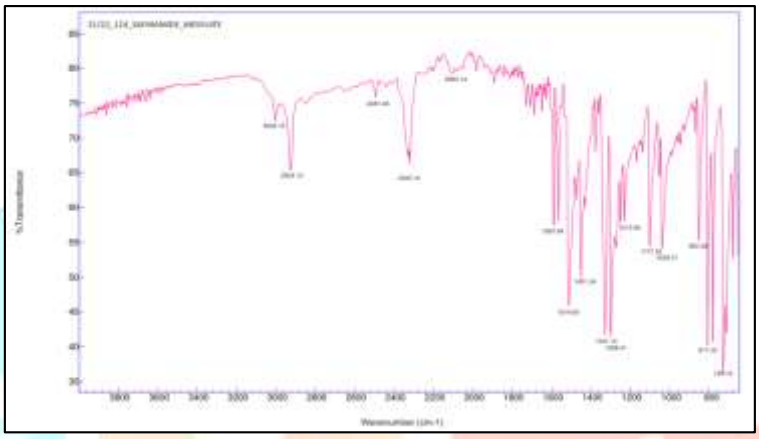


Fig 14:IR Spectra of Safinamide

Table 11: Principal peak and functional group present FTIR spectra of Safinamide

Functional Group	Reported Peak(cm-1)	Observed Peak (cm-1)
N-H Stretch	2900-2945	2924.12
C-N Stretch	2235-2255	2345.14
C=C Stretching	1510-1538	1514.65
C-H bending	1300-1340	1327.14
C-H bending (Aromatic)	1425-1470	1451.34
C-F stretch	1300-1250	1288.41

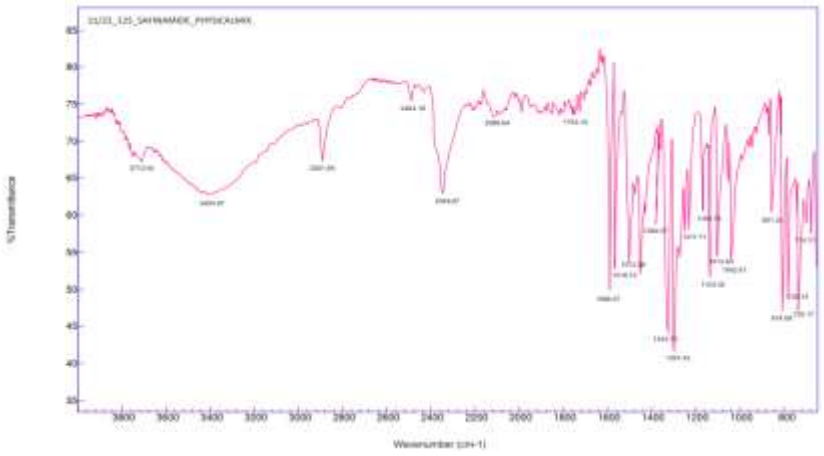


Fig 15: IR Spectra of Physical Mixture

Table 12: Interpretation of FTIR Spectrum of physical mixture

Functional Group	Peaks	
Pure Drug	**Physical Mixture**	
N-H Stretch	Yes	Yes
C-N Stretch	Yes	Yes
C=C Stretching	Yes	Yes
C-H bending	Yes	Yes
C-H bending (Aromatic)	Yes	Yes
C-F stretch	Yes	Yes

From the Infrared spectrometer it was found that all the principal peaks in Safinamide is represent in FTIR of physical mixture; Hence it is concluded that no significant interaction was found in drug and excipients.

EVALUATION PARAMETERS

9.4.1 Thickness

Use a micrometer thread gauge to measure the thickness of the film. In order to obtain the uniformity of the film, the thickness was measured at 5 different places. The thickness of the film must be less than 5%.

From the evaluation of thickness of F1 to F9 batches was found in between 0.52 mm - 0.56 mm. Table 13 and Figure 16 show the thickness of the fast-dissolving film for all formulations.

9.4.2 Folding endurance

To determine the bending resistance, the film was cut and quickly bent at the same location until it broke. The number of times the film can be bent at the same position without breaking gives the value of the bending strength.

From the evaluation of Folding endurance of F1 to F9 batches was found in between 8 to 144. The folding resistance of the fast-dissolving film of all the formulations shown in Table 13 and Figure 16.

9.4.3 Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the formula.

$$\text{Tensilestrength} = \frac{\text{Loadat failure} \times 100}{\text{Strip thickness} \times \text{strip width}}$$

From the evaluations of tensile strength of F1 to F9 batches was found in between 47.86 to 59.36 gm/cm^2. The tensile strength of fast dissolving films of all formulations given in table 13 and figure 16.

9.4.4 Percentage elongation

It was calculated by

$$\text{Percentage elongation} = \frac{\text{Increasein length of strip} \times 100}{\text{Initial length of strip}}$$

From the evaluation of % elongation of F1 to F9 batches was found in between 8 to 12. The percentage elongation of fast dissolving films of all formulations given in table 13 and figure 16.

9.4.5 In-vitro disintegration

Petri dish method

Put 2ml of distilled water into a petri dish, add a film on the water surface, and measure the time for the oral film to completely dissolve.

From the evaluations of in-vitro evaluation of F1 to F9 batches was found in between 23 to 33 sec. The in vitro disintegration time of the fast-dissolving film of all formulations given in Table 13 and Figure 16.

Formulations	Thickness (mm)	Folding endurance	Tensile strength (g/cm2)	% elongation	In-vitro disintegration time(sec)
F1	0.53	11	51.34	9	26
F2	0.55	9	49.28	11	26
F3	0.53	14	54.15	12	24
F4	0.56	12	55.36	10	26
F5	0.53	9	58.30	11	31
F6	0.55	10	51.40	8	23
F7	0.54	12	59.36	10	24
F8	0.56	11	50.36	12	31
F9	0.52	8	47.86	11	33

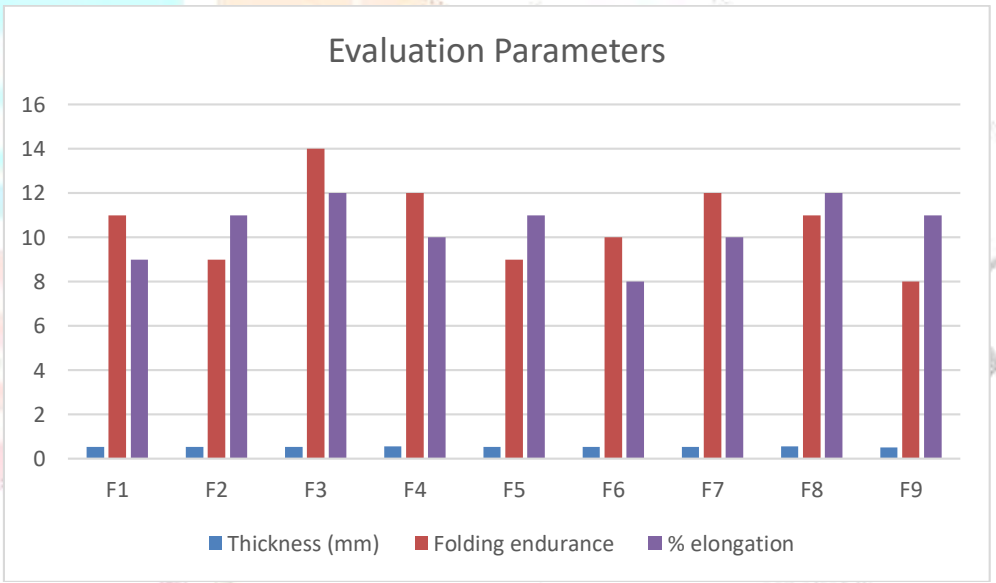


Fig 16: Barchart of evaluation parameters

5. WEIGHT VARIATION

9.5.1 Weight variation

Ten films are randomly selected and their average weight is weighed. Weigh a single film and compare it with the average deviation weight. From the evaluations of weight variation of F1 to F9 batches was found in between 161.2 to 167.4 mg. The weight change of the instant film of all the formulations shown in Table 14 and Figure 17.

Table no 14: Weight Variation

Formulations	Weight variation (mg)
F	164.2
F	163.8
F	164.8
F	166.7
F	162.1
F	163
F	164.9
F	167.4
F	161.2

Fig 17:Barchart of weight variation

6. DRUG CONTENT AND ASSAY

6.1 Drug content

The test is performed by dissolving a 4 cm2 area film in 50 ml of Phosphate buffer 6.8 under stirring. Filter the solution using Whatman filter paper and dilute the filtrate to 100 ml with the same buffer in a volumetric flask. The solution was analyzed using an ultraviolet spectrometer. From the evaluations of Drug content of F1 to F9 batches was found in between 48.36 to 50.72 mg. The results of the drug content of all formulations shown in Table 15 and the values shown graphically in Figure 18.

6.2 ASSAY

The test is performed by dissolving a 4 cm2 area film in 50 ml pH 6.8 phosphate buffer under stirring. Filter the solution using Whatman filter paper and dilute the filtrate to 100 ml with the same buffer in a volumetric flask. The solution was analyzed using an ultraviolet spectrophotometer. From the % assay

evaluations of F1 to F9 batches was found in between 96.6 to 101.42 %. The test results of all formulas are shown in Table 15, and the values are shown graphically in Figure 18.

Table no 15:Drug content and Assay

Formulations	Drug content (mg)	Assay (%)
F1	50.12	100.24
F2	48.3	96.6
F3	49.81	99.62
F4	48.5	97
F5	50.71	101.42
F6	49.76	99.52
F7	48.36	96.72
F8	50.02	100.04
F9	48.64	97.28

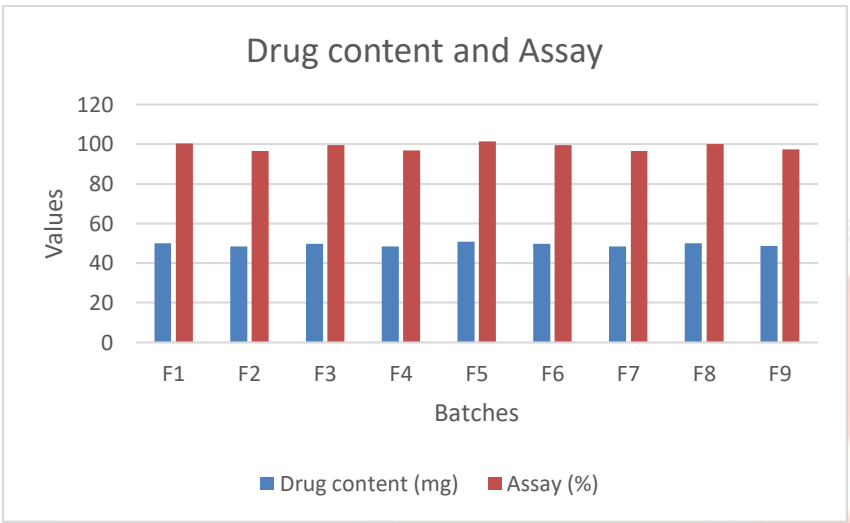


Fig.18: Barchart of drug content and assay

9.7 IN-VITRO DISSOLUTION

In-vitro dissolution

Use 900 ml Phosphate buffer 6.8 as the medium and keep it at 37±0.5°C while setting the basket to 100 rpm. Cut 4 cm2 (2 x 2 cm) film sample and place five films in the basket. Take 5 ml samples every 30 seconds and replace the same amount of samples with fresh Phosphate buffer 6.8. The extracted samples were filtered and analyzed using an ultraviolet spectrometer at a wavelength of 228 nm. The in vitro dissolution profile data of all preparations are given in Table 16-24 and Figure 19-27. The cumulative drug release percentage of F1-F9 is shown in Table 25 & Figure 28. The in vitro dissolution profile data of the marketed formulations shown in Table 26 and Figure 29. The comparison of the in vitro release data of the commercial formulations and formulation 3 shown in the table 27 and Figure 30.

Table 16: In-vitro dissolution ofF1

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0454	0.0454	19.91
1	0.0752	0.0752	32.98
1.5	0.1247	0.1247	54.69
2	0.1631	0.1631	71.54
2.5	0.1959	0.1959	85.92
3	0.2182	0.2182	95.70

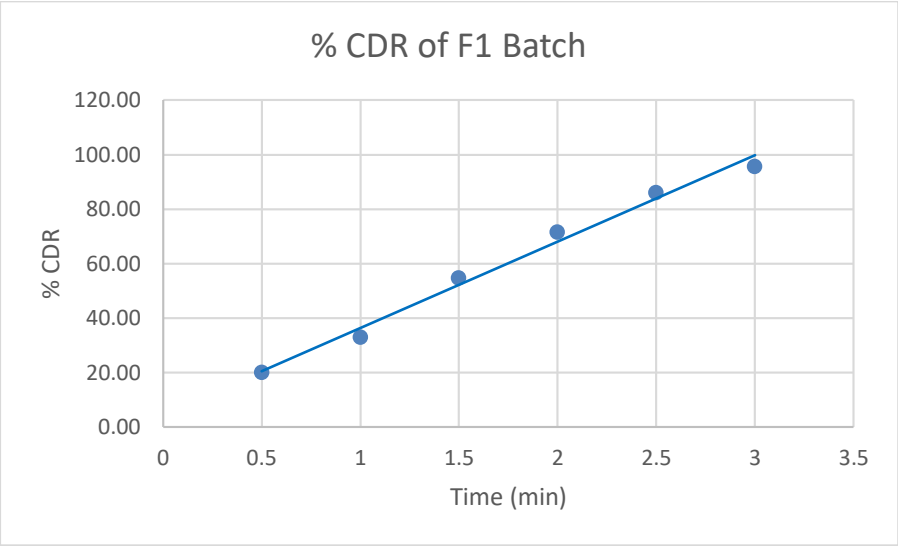


Fig 19:In-vitro dissolution ofF1

Table 17:In-vitro dissolution ofF2

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0464	4.07	20.35
1	0.088	7.72	38.60
1.5	0.1367	11.99	59.96
2	0.1622	14.23	71.14
2.5	0.2138	18.75	93.77
3	0.2228	19.40	97.02

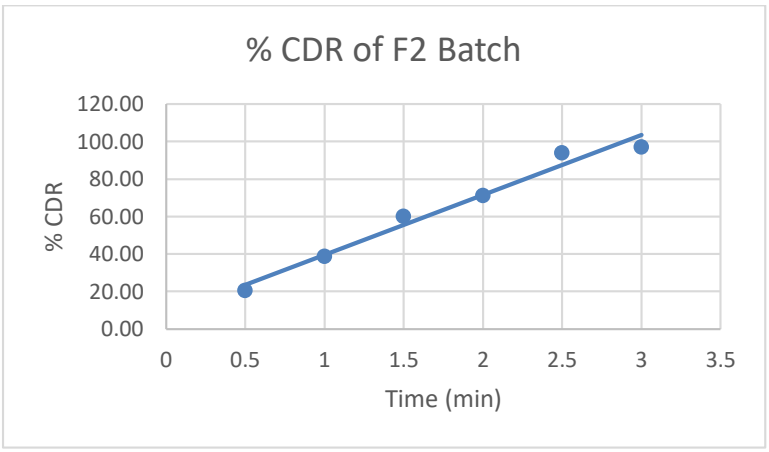


Fig 20: In-vitro dissolutionofF2

Table 18: In-vitro dissolution ofF3

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0526	4.61	23.07
1	0.0948	8.32	41.58
1.5	0.1455	12.76	63.82
2	0.1719	15.08	75.39
2.5	0.2034	17.84	89.21
3	0.2253	19.76	98.82

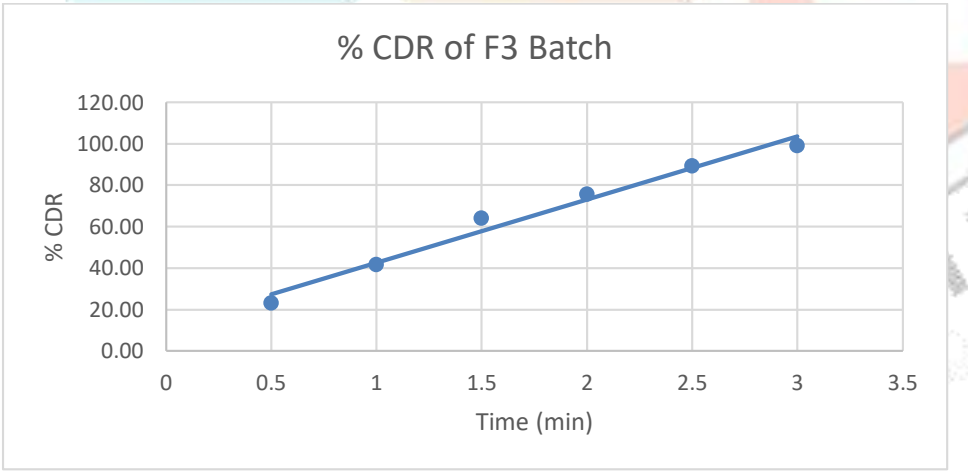


Fig 21: In-vitro dissolutionofF3

Table 19: In-vitro dissolution ofF4

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0573	5.03	25.13
1	0.0948	8.32	41.58
1.5	0.1341	11.76	58.82
2	0.1619	14.20	71.01
2.5	0.1892	16.60	82.98
3	0.2228	19.54	97.72

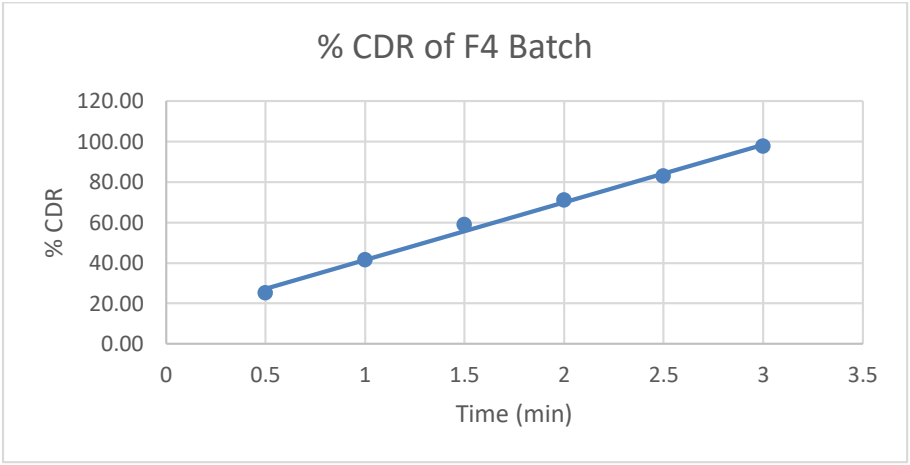


Fig 22: In-vitro dissolutionofF4

Table 20: In-vitro dissolution ofF5

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0513	4.50	22.50
1	0.0919	8.06	40.31
1.5	0.1229	10.78	53.90
2	0.1621	14.22	71.10
2.5	0.1865	16.36	81.80
3	0.2193	19.24	96.18

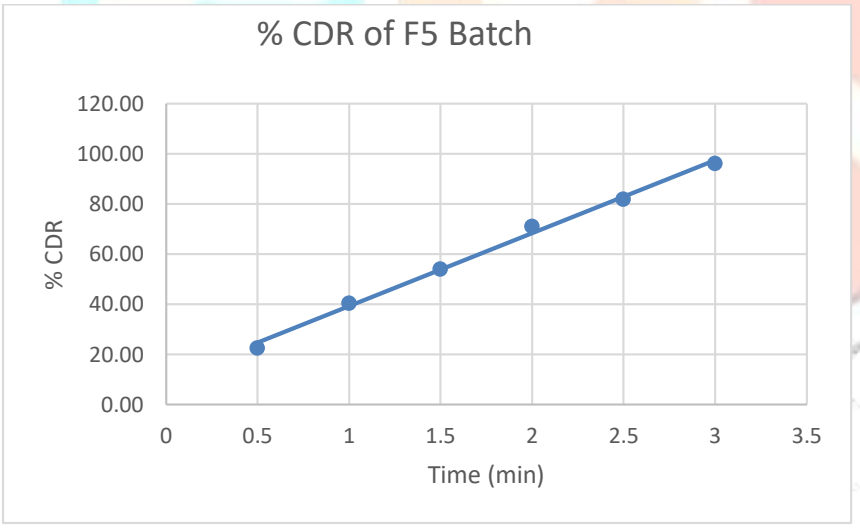


Fig 23: In-vitro dissolution F5

Table 21: In-vitro dissolution ofF6

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0435	3.82	19.08
1	0.0913	8.01	40.04
1.5	0.1332	11.68	58.42
2	0.1618	14.19	70.96
2.5	0.1935	16.97	84.87
3	0.2285	18.64	93.20

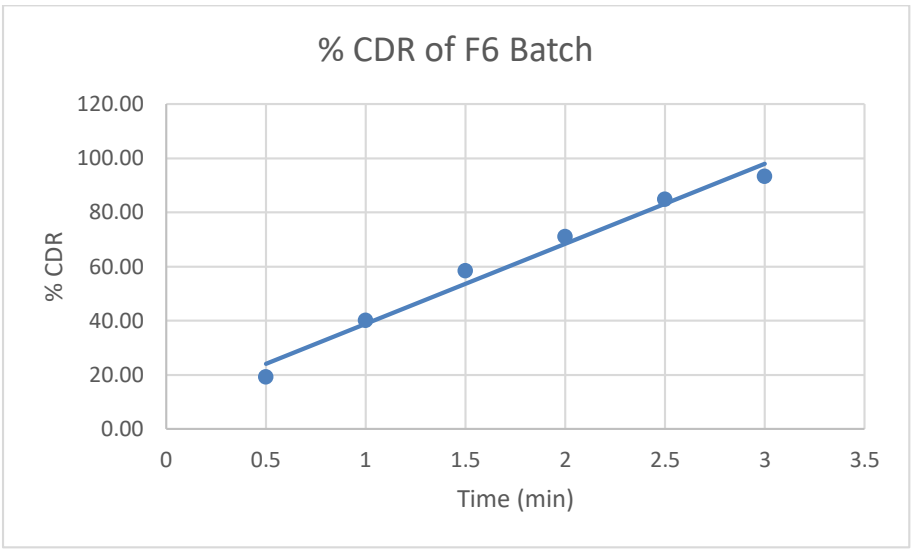


Fig 24: In-vitro dissolutionofF6

Table 22: In-vitro dissolution ofF7

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0513	4.50	22.50
1	0.089	7.81	39.04
1.5	0.1274	11.18	55.88
2	0.1653	14.50	72.50
2.5	0.1924	16.88	84.39
3	0.2228	19.40	97.02

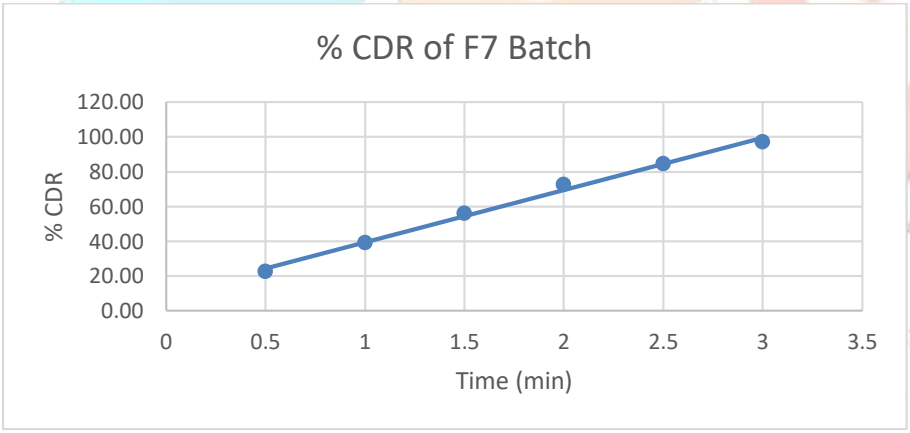


Fig 25: In-vitro dissolutionofF7

Table 23: In-vitro dissolution ofF8

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.0413	3.62	18.11
1	0.0782	6.86	34.30
1.5	0.136	11.93	59.65
2	0.1672	14.67	73.33
2.5	0.1942	17.04	85.18
3	0.2204	19.33	96.67

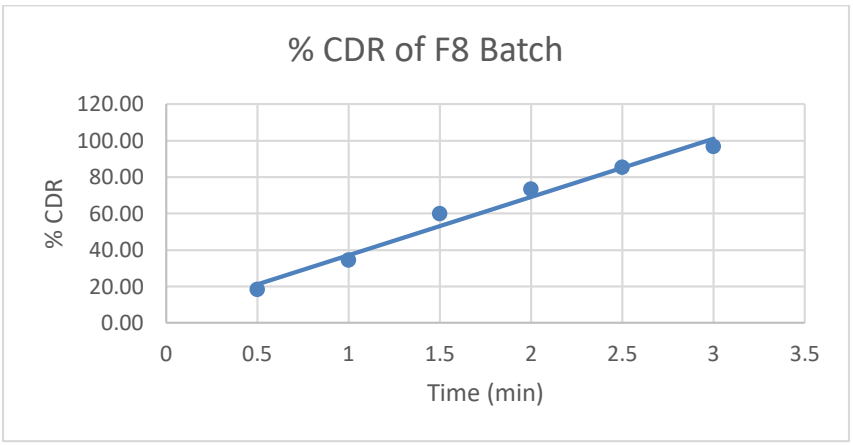


Fig 26: In-vitro dissolutionofF8

Table 24: In-vitro dissolution ofF9

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
0.5	0.044	3.86	19.30
1	0.0882	7.74	38.68
1.5	0.1424	12.49	62.46
2	0.1639	14.38	71.89
2.5	0.1842	16.16	80.79
3	0.2175	19.08	95.39

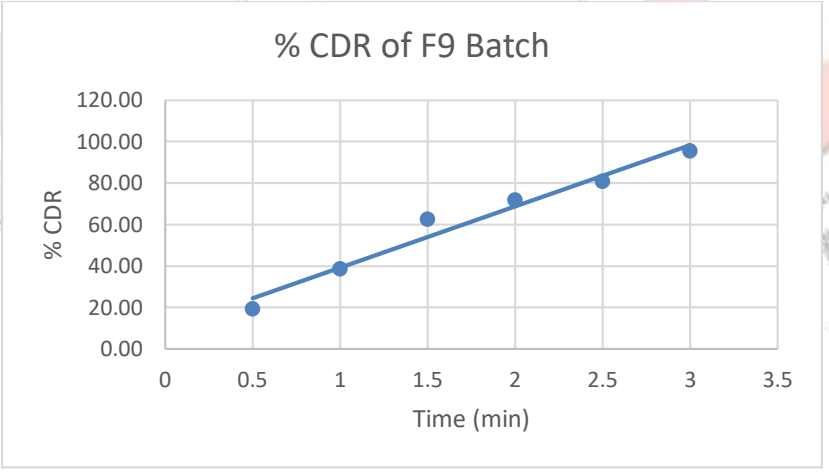


Fig 27: In-vitro dissolutionofF9

Table no 25:*In-vitro* dissolution ofF1-F9

Percentage drug released									
Time (min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0.5	19.91	20.35	23.07	25.13	22.5	19.08	22.5	18.11	19.3
1	32.98	38.6	41.58	41.58	40.31	40.04	39.04	34.3	38.68

1.5	54.69	59.96	63.82	58.82	53.9	58.42	55.88	59.65	62.46
2	71.54	71.14	75.39	71.01	71.1	70.96	72.5	73.33	71.89
2.5	85.92	93.77	89.21	82.98	81.8	84.87	84.39	85.18	80.79
3	95.7	97.02	98.82	97.72	96.18	93.2	97.02	96.67	95.39

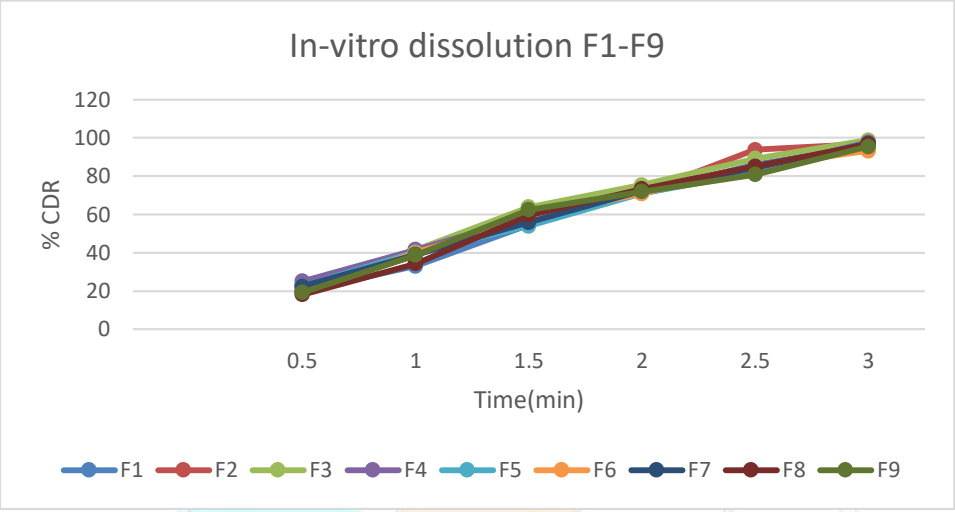


Fig 28:*In-vitro* dissolution ofF1-F9

8.8 In-vitro drug releaseprofiledata ofmarketed formulation

Table no 26: *in-vitro* drug release profile data of marketed Tablet formulation (Xafinact 50mg)

Time (min)	Absorbance (228 nm)	Concentration (µg/ml)	Cumulative Percentage Release
10	0.0412	5.02	18.07
20	0.0869	10.59	38.11
30	0.1413	17.22	61.97
40	0.1673	20.38	73.38
50	0.1963	23.92	86.10
60	0.2241	27.30	98.29

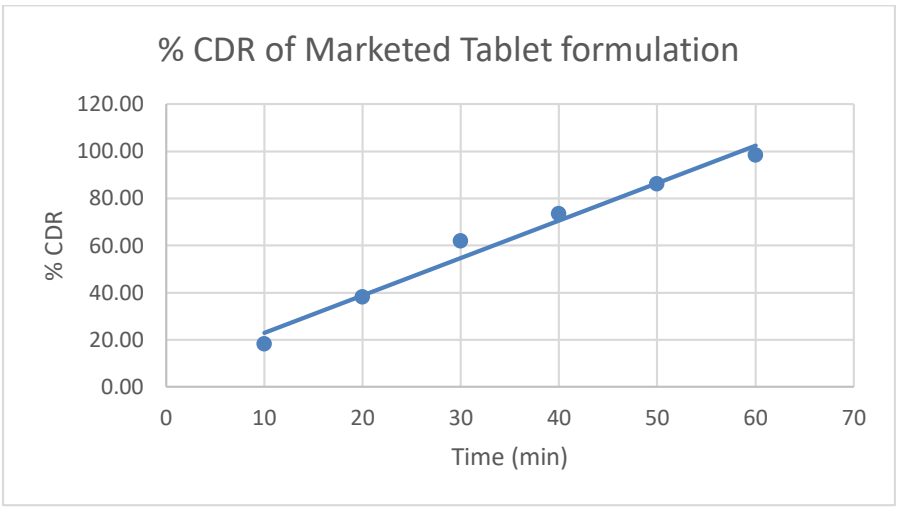


Fig 29:*in-vitro* drug release profile data of marketed Tablet formulation

9.9 Comparison of in-vitro drug release data of marketed formulation and formulation 3

Table no 27: Comparison of in-vitro drug release data of marketed Tablet formulation and formulation 3

Time (mins)	% CDR Marketed Formulation	% CDR F3
0.5	0	23.07
1	0	41.58
1.5	0	63.82
2	0	75.39
2.5	0	89.21
3	0	98.82
10	18.07	
20	38.11	
30	61.97	
40	73.38	
50	86.10	
60	98.29	

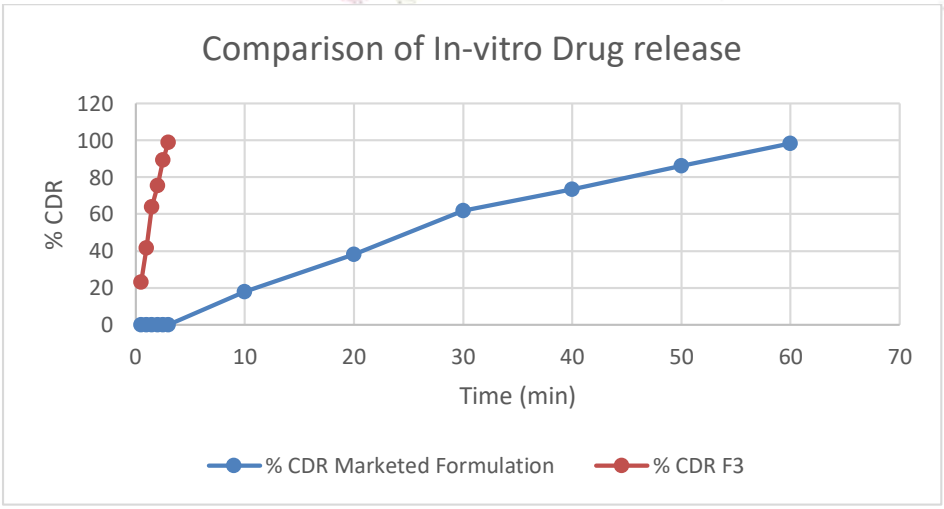


Fig 30: Comparison of in-vitro drug release data of Marketed Tablet formulation and formulation 3

9.10 STABILITY STUDIES (F3)

Stability studies are conducted according to ICH to evaluate the stability of pharmaceutical preparations. The optimized formula of F3 is sealed in polyethylene laminated aluminum packaging. The samples were kept at 40 degrees Celsius and 75% RH for 3 months. At the end of the study period, changes in the physical appearance, color, drug content, and drug release characteristics of the preparation were observed.

Table no28:Stability studies of F3 Batch [Condition(40°C/75%RH)]

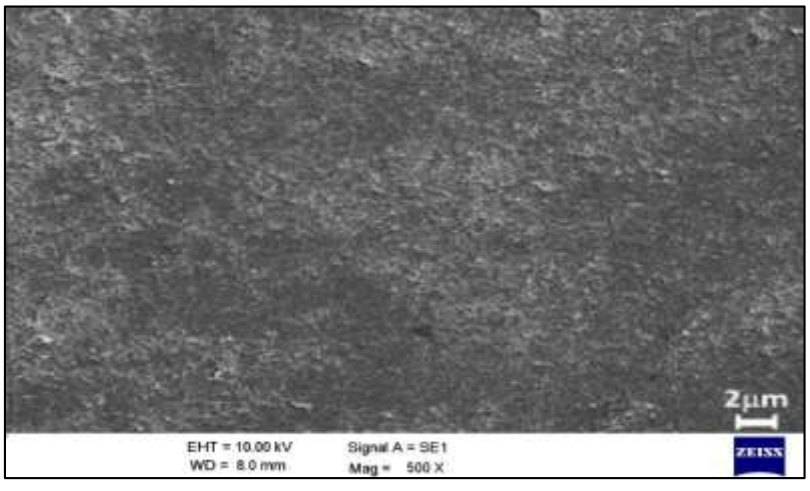
Parameters	Initial	1 month	3 months
Thickness (mm)	0.53	0.52	0.52
Folding endurance	14	12	12
Tensilestrength (gm/cm^2)	54.15	54.11	53.27
in-vitro disintegration time (sec)	24	23	21
in-vitro dissolution (%)	98.82	97.56	96.45

Test frequency: Initial & 3 months

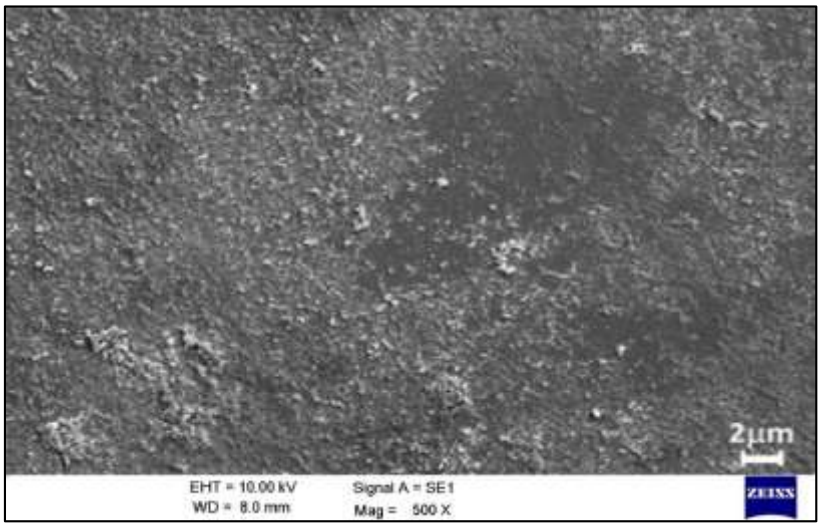
- It is found to be all the physical and chemical parameters are satisfactory based on initial stability data.
- Photo stability studies have shown that the medicinal product is non-light sensitive

9.11 SEM ANALYSIS

The morphological study of the oral adhesive strips is carried out by scanning electron microscopy (SEM) at a prescribed magnification. The research involves the difference between the upper and lower surfaces of the film. It also helps determine API distribution.



(a)



(b)

Fig 31: SEMimages of F3 Batch

The morphological study (SEM) of F3 shows more porous. The surface is without any scratches and striations which indicate Safinamide is uniformly distributed in the films and no crystals of drug were observed on the surface of mouth dissolving films. Therefore rapid drug release was achieved for the immediate onset of action. The surface photographs by SEM study is shown in fig. 31.

9.12DISCUSSION

The present investigation was undertaken to formulate Safinamide oral films for the treatment of Parkinson.

F1-F3 were carried out with HPMC E15 cps, PEG 400, sodium saccharin, citric acid and flavor. The films were clear and transparent. The thickness also uniform. The flexibility also good. The films shown good mechanical properties. According to the assay result the drug was properly loaded in the film.

F4-F6 were carried out with HPMC E5, propylene glycol, sodium saccharin, citric acid and flavor. The films shows good appearance. The thickness also not uniform. The flexibility of the film was not good. The percentage drug release was found to be.

F7 was formulated with HPMC E15, propylene glycol, sodium saccharin, citric acid and flavor. The appearance of the film was also good but the thickness and disintegration time was more.

F8 was formulated with HPMC E5, PEG 400, sodium saccharin, citric acid and flavor. F9 was formulated with HPMC E15 & E5 without the addition of plasticizers. The formulated films were more brittleness.

Among all the formulations F3 shown good mechanical properties and less disintegration time of 24 seconds. All the parameters of film were found to be satisfactory. And the dissolution profile was found to be desirable and reproducible. The morphological study (SEM) of F3 shows more porous. Therefore rapid drug release was achieved for the immediate onset of action.

The stability studies were performed for about 1 month and 3 months. No significant changes were observed in the thickness, tensile strength, in-vitro disintegration and in-vitro drug release.

The film (F3) samples evaluated gave maximum release within 3 minutes indicating the rapid drug release profile which entails in faster onset of action for the medicament. Therefore the oral films have considerable advantage over the conventional dosage forms.

Conclusion

The primary objective of this work was to develop a mouth dissolving film with Safinamide, along with basic ingredients like polymers, plasticizers, sweetener, saliva stimulating agent and flavor.

The films were prepared by solvent casting method.

HPMC E5 cps, which was not able to impart thickness to the film. HPMC E15 shown good flexibility.

The plasticizer propylene glycol which was not able to impart flexibility and folding endurance to the film. PEG 400 produced good folding endurance, tensile strength and percent elongation.

The optimized formulation (F3) was shown good mouth feel, folding endurance, instant drug release as well as good mechanical properties.

The F3, shown less disintegration time of 24 seconds and 98% drug released within 3 minutes while the marketed formulation took 1 hour.

Therefore rapid drug release was achieved for immediate onset of action which is beneficial when compared to conventional dosage form.

Acknowledgement

I would like to submit the manuscript entitled " **FORMULATION DEVELOPMENT AND EVALUATION MOUTH DISSOLVING FILM OF SAFINAMIDE**" for peer review and consideration for publication as a research article in the ijcrt

To prepare Safinamide oral dissolution membranes using different concentrations of membranes. Molding polymers and plasticizers.

Develop and evaluate formulas for pre-compression parameters (such as solubility, melting point, heavy metal content, FT-IR research) and post-compression parameters (such as weight change, thickness, bending resistance, tensile strength, elongation percentage), and drug content , Content, disintegration time, dissolution test and SEM analysis. Improve patient compliance and obtain rapid onset to relieve symptoms of Parkinson.

We affirm that this manuscript is original, it has not been published

elsewhere, nor is it currently under consideration by the author journal or any other publisher. As the corresponding author, I can confirm that the submission has been approved by all authors.

We look forward to your response following the peer review of our manuscript

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