Available online at www.icjpir.com ISSN: 2349-5448

INTERCONTINENTAL JOURNAL OF PHARMACEUTICAL INVESTIGATIONS AND RESEARCH

ICJPIR |Volume 3 | Issue 1 | Jan – Mar- 2016

Research Article

Formulation and evaluation of sumatriptan oral thin films

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ABSTRACT

The main objective of the study was to formulate and evaluate oral thin film containing Sumatriptan succinate. The 4 and 5 % w/v HPMC, PVA, CMC films were prepared by solvent casting method. Compatibility of Sumatriptan with polymers was confirmed by FT-IR studies. Films were evaluated for weight variation and thickness showed satisfactory results. Tensile strength and folding endurance of the films were increased with increase in the concentration of polymer due to increase in the elasticity nature of the polymer. Mouth dissolving time and disintegration time of the films were increased with increase in the concentration of the polymer, as more fluid is required to wet the film in the mouth. The presence of disintegrant showed a considerable effect on the disintegration time of the films. Content uniformity study showed that the drug is uniformly distributed in the film. No differences were observed in *invitro* dissolution of drug from the film I - VI as the film instantly gets wet by dissolution medium. Present study reveals that all the formulated films showed satisfactory film parameters. It can be concluded that, Oral thin film-containing Sumatriptan can be prepared by solvent casting method. 4% w/v of HPMC (FV) film exhibited required tensile strength, folding endurance and disintegration time. The drug release was about 98.5 % in 300 seconds.

INTRODUCTION

Oral Thin Films

Fast dissolving oral films (FDOFs) or Oral wafers or Oral strips (OS) or sublingual strips or oral thin films (OTF) are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improve the efficacy of APIs by dissolving within minute in oral cavity after the contact with saliva without chewing and no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is 4-1000 times greater than that of skin [9]. FDOFs are useful in patients such as pediatric, geriatrics, bedridden, emetic patients, diarrhea, sudden episode of allergic attacks, or coughing for those who have an active life style. It is also useful

whether local action desired such as local anesthetic for toothaches, oral ulcers, cold sores or teething.

OTFs also have an established shelf life of 2-3years, depending on the API but are extremely sensitive to environmental moisture [10].

The OTFs place as an alternative in the market due to the consumer's preference for a fast-dissolving product over conventional tablets / capsules. The oral thin-film technology is still in the beginning stages and has bright future ahead because it fulfills all the need of patients. Eventually, film formulations having drug/s will be commercially launched using the OTF technology [11].

Oral thin films, a new drug delivery system for the oral delivery of the drugs, were developed based on the technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oro mucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. In contrast to other existing, rapid dissolving dosage forms, which consist of liophylisates, the rapid films can be produced with a manufacturing process that is competitive with the manufacturing costs of conventional tablets.

AIM AND OBJECTIVES OF THE STUDY

Aim

The aim of the present investigation is to design, formulate and evaluate the oral disintegrating films taking Sumatriptan as a model drug to improve the bioavailability and providing faster onset of action to relieve immediately acute migraine attack.

Objectives

- To carry out the pre formulation studies of Sumatriptan.
- To formulate mouth dissolving film containing Sumatriptan.
- To evaluate mouth-dissolving film, Weight variation, Thickness, Folding endurance, Disintegration time, Content uniformity and In vitro dissolution studies.
- To perform the stability studies for the optimized formulation.

METHODOLOGY

Analytical methods

Calibration curve of Sumatriptan in 6.8pH phosphate buffer

From the standard stock solution (1000 µg/ml), appropriate aliquot were transferred to series of 10 ml volumetric flasks and made up to 10 ml with buffer so as to get concentration of 2, 4, 6, 8, 10 µg/ml. the absorbance of the solution were measured at 282 nm. This procedure was performed in triplicate to validate calibration curve.

General method of formulation of oral thin films[3]

Following processes are generally used to manufacture the oral thin film: hot melt extrusion, solid dispersion extrusion, rolling, semisolid casting and solvent coating. The current preferred manufacturing process for making this film is solvent casting method. Water-soluble polymers are completely dissolved in a mixing tank to form a homogeneous viscous solution. Other ingredients, including active ingredient are dissolved in a small portion of aqueous solvent using a high shear processor. The active mixture is then added to the viscous colloidal solution to form a homogeneous viscous solution. This viscous solution is degassed under vacuum. The resulting bubble free solutions poured onto glass mould and were kept in oven. Dried film is then cut into the desired shape and size for the intended application.

Dose calculations

Diameter of the plate = 6 cm
Area of the plate = 28.6 cm2
No. of 2.25 cm^2 films present in whole plate = 28.6/2.25 = 12.7
Each film contains 25 mg of drug
12.7 no. of films contains mg of drug? = 12.7x5= 317.5 mg

The amount of drug added in each plate was approximately equal to 318 mg.

Preparation of Oral thin film

Film was prepared by using specified polymer by solvent casting method. The specified amount of polymer was weighed and dissolved in specified amount of water for overnight to get a uniform dispersion of 4 % and 5 % (w/v) solution respectively. Drug, cross carmellose sodium, aspartame, citric acid were dissolved in specific amount of water in a beaker. The drug solution was added to the polymer solution and mixed using magnetic stirrer for 1 hour. The resulting solution was degassed so as to remove any bubbles formed.

The bubble free solution was casted on to a petri dish of surface area 28.6 cm^2. It was dried for 24 hours at room temperature. The film was removed from the petri dish very carefully and observed for any imperfections. Film that was clear and bubble free was selected for further studies. Film of area 2.25 cm^2 (1.25 X 1.25) was cut and stored in a butter paper coved with aluminum foil and stored in a desiccator.

Table no 1: Composition of various oral thin film formulations

S no	Ingredients (mg/film)	F1	F2	F3	F4	F5	F6
1	Sumatriptan	25	25	25	25	25	25
2	CMC*	4	5	-	-	-	-
3	PVA*	-	-	4	5	-	-
4	HPMC* (15cps)	-	-	-	-	4	5
6	CCS	2	2	2	2	2	2
7	PG**	20	20	20	20	20	20
8	Aspartame	1	1	1	1	1	1
9	Sodium saccharine	1	1	1	1	1	1
10	Water	Qs	qs	qs	qs	qs	qs

* = Expressed as %w/v

** = Expressed as %w/w of the polymer

RESULTS AND DISCUSSION

Preformulation studies

The following preformulation studies were performed for Sumatriptan

Solubility

Slightly soluble in water.

Determination of pH

Sumatriptan 4% W/V solution in water showed pH around 7

Melting point

Melting point of the Sumatriptan was found to be 170.2^{0}C

Analytical methods

Standard Stock solution

100 mg of Sumatriptan was dissolved in 100 ml of 6.8 phosphate buffer (1000 µg/ml).

Calibration curve of Sumatriptan in 6.8 phosphate buffer

From the standard stock solution (1000 µg/ml), appropriate aliquot were transferred to series of 10 ml volumetric flasks and made upto 10 ml with buffer so as to get concentration of 2, 4, 6, 8, 10 µg/ml. the absorbance of the solution were measured at 282 nm. This procedure was performed in triplicate to validate calibration curve. A calibration curve was plotted.

Table no 2: calibration curve plot

S.No	Concentration in µg/ml	Absorbance
1	0	0
2	2	0.015
3	4	0.040
4	6	0.058
5	8	0.076
6	10	0.099

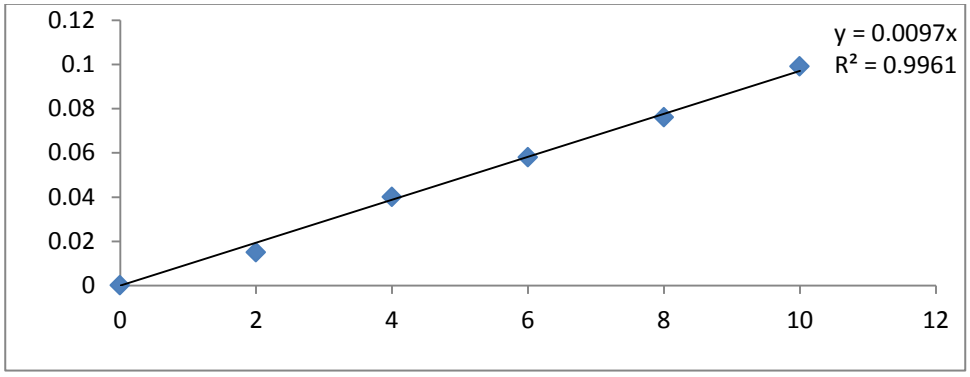

Fig No: 1 standard graph

Drug polymer compatibility studies

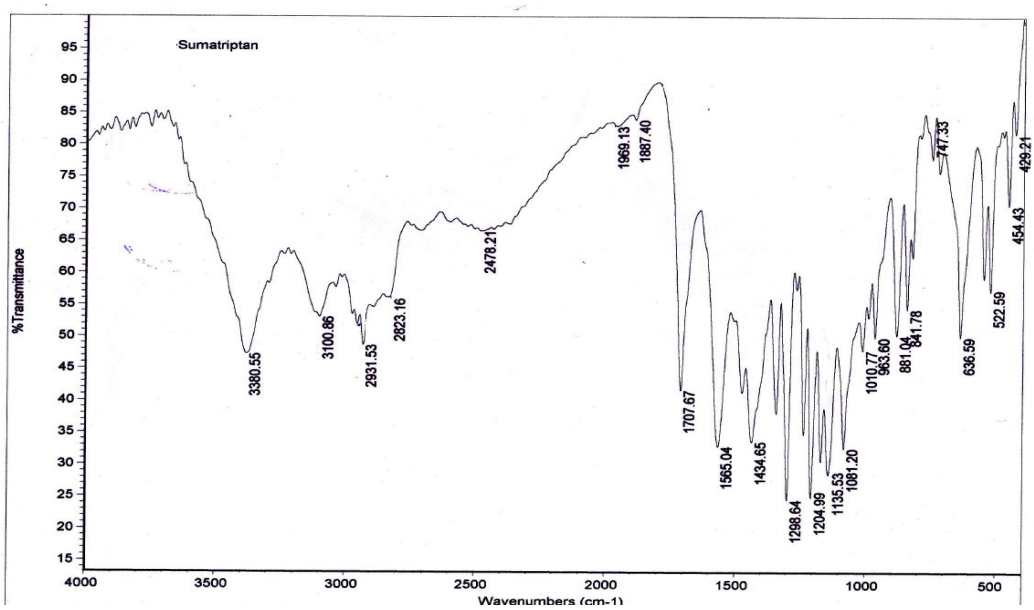

Fig No 2: FT-IR spectrum of sumatriptan

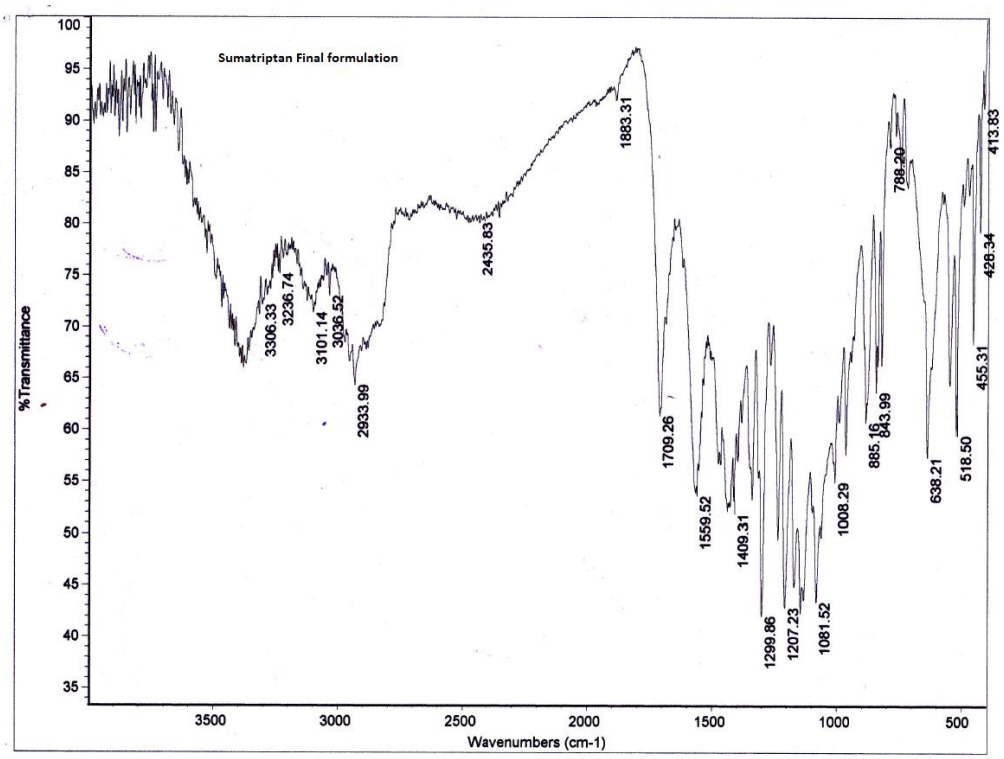

Fig No 3: FT-IR spectrum of final formulation using HPMC E 15 (FV)

Evaluation of oral thin films

Oral thin films were evaluated for the following parameters.

- Weight variation
- Thickness of film
- Folding endurance
- Disintegration time
- Mouth dissolving time
- Content uniformity
- *Invitro* dissolution studies

Weight variation of the films

Three Films each of 0.35 square inch were cut at three different places from casted films and weight variation was measured. Weight variation varies from 61.4 ± 0.51 to 76.16 ± 0.87. The results of weight variations are shown in the Table-3.

Table-3 Comparative evaluation of Weight variation of oral thin films

S.NO	Formulation code	Average weight of the 0.35 square inch film in mg			Mean ± SD*
		Trial 1	Trial 2	Trial 3	
1	I	62.6	61.58	62.0	62.06 ± 0.51
2	II	74.80	64	75.75	74.75 ± 0.56
3	III	63.8	63.2	64.4	63.8 ± 0.6
4	IV	76.4	75.2	76.9	76.16 ± 0.87
5	V	61	61.8	61.4	61.4 ± 0.43
6	VI	72.3	72.8	71.5	72.2 ± 0.65

***Standard deviation, n =3**

Thickness of the film

The thickness of the film was measured using digital Vernier Calliper with a least count of 0.01 mm at different spots of the film. The thickness was measured at three different spots of the film and average was taken and SD was calculated. It was observed that as the polymer concentration increases the thickness of the film also increases.

Table-4 Comparative evaluation of Thickness of oral thin films

S.NO	Formulation code	Average thickness in mm			Mean ± SD*
		Trial 1	Trial 2	Trial 3	
1	I	0.23	0.25	0.20	0.22 ± 0.025
2	II	0.28	0.30	0.30	0.29 ± 0.01
3	III	0.18	0.19	0.19	0.18 ± 0.00
4	IV	0.21	0.24	0.24	0.23 ± 0.01
5	V	0.08	0.10	0.12	0.1 ± 0.02
6	VI	0.15	0.18	0.15	0.16 ± 0.01

***Standard deviation, n =3**

Tensile strength of the films

Tensile strength measures the ability of the film to withstand rupture. The formulation FII shows the maximum value of tensile strength 4.32 ± 0.02 and folding endurance was 181 (no of folds) This might be due to the formation of strong hydrogen bonds between polymer and plasticizer there by imparting flexibility to withstand rupture. Tensile strength of the films was recorded in the Table-5

Table-5 Comparative evaluation of Tensile strength of oral thin films

S.NO	Formulation code	Tensile strength in MPa			Mean ± SD*
		Trial 1	Trial 2	Trial 3	
1	I	3.85	3.80	3.85	3.83 ± 0.02
2	II	4.35	4.30	4.35	4.32 ± 0.02
3	III	3.10	2.98	3.1	3.06 ± 0.06
4	IV	3.28	3.30	3.30	3.29 ± 0.01
5	V	1.80	1.82	1.80	1.80 ± 0.01
6	VI	2.10	2.15	2.12	2.12 ± 0.02

***Standard deviation, n =3**

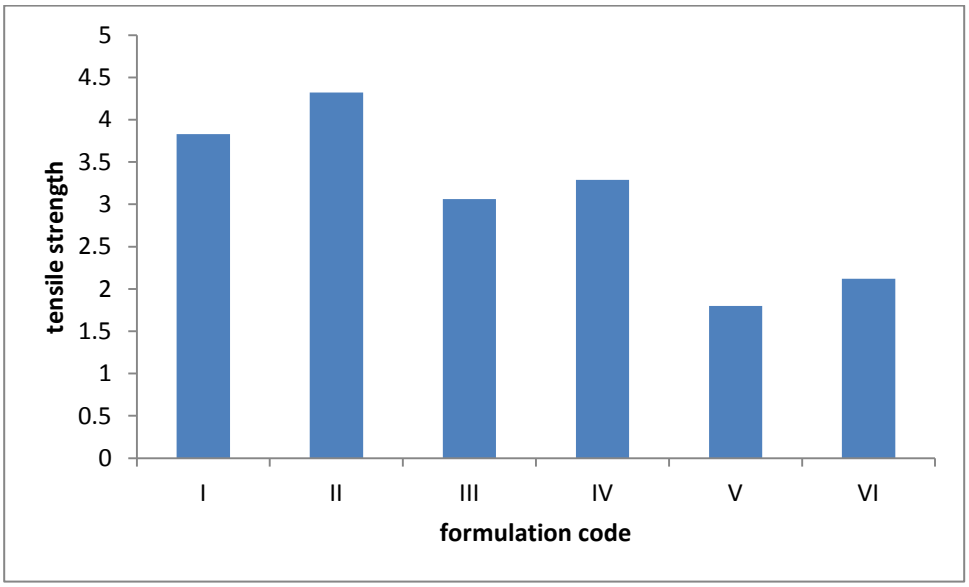

Fig No 4: Tensile strength of Oral thin formulations

Folding endurance of the films

The folding endurance was measured manually .A strip of film 4squre cm was cut and subjected for the folding endurance studies until it broke at the same place. Folding endurance increases with increase in polymer concentration. The no of times the film fold until it broke was reported in the Table-6

Table-6 Comparative evaluation of folding endurance of oral thin films

S.NO	Formulation code	Folding endurance (no of folds)			Mean±SD*
		Trial 1	Trial 2	Trial 3	
1	I	160	158	163	160 ± 2.15
2	II	178	185	180	181 ± 3.60
3	III	115	128	130	124 ± 8.14
4	IV	150	168	170	162 ± 11.01
5	V	90	93	102	95 ± 6.25
6	VI	110	105	117	110 ± 6.02

***Standard deviation, n =3**

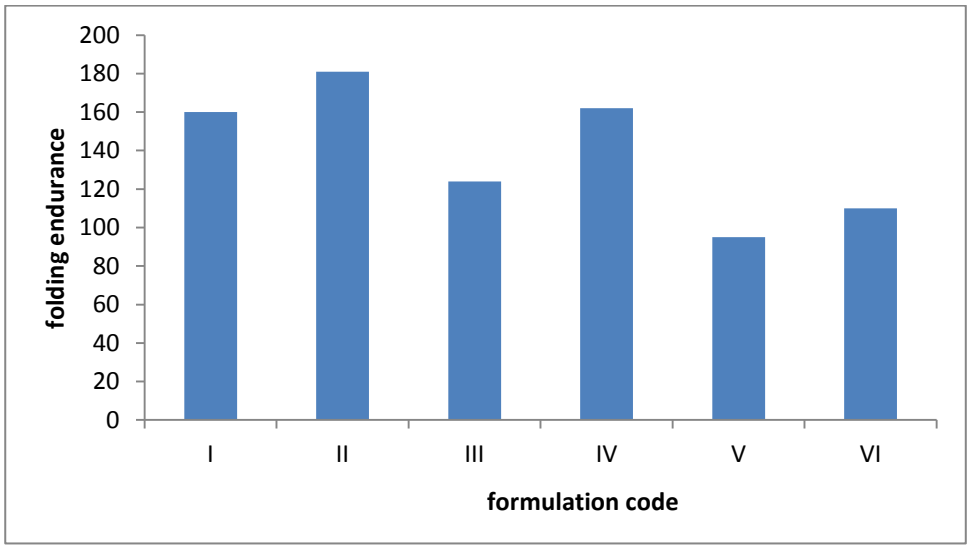

Fig No 5: Folding endurance of oral thin films

Disintegration time

The disintegration time of the film was done by using tablet disintegration test apparatus. Disintegration times of the films were found to be increased with increase in the concentration of the polymer. The formulation FV shows 33 Sec (disintegration time) as shown in the table 7.

Table-7 Comparative evaluation of Disintegration time of oral thin films

S.NO	Formulation code	Disintegration time in Sec			Mean ± SD*
		Trial 1	Trial 2	Trial 3	
1	I	46	44	48	46 ± 2
2	II	52	54	56	54 ± 2
3	III	41	43	42	42 ± 1
4	IV	44	46	46	45.33 ± 1.15
5	V	34	30	36	33.33 ± 3.05
6	VI	45	48	46	46.33 ± 1.52

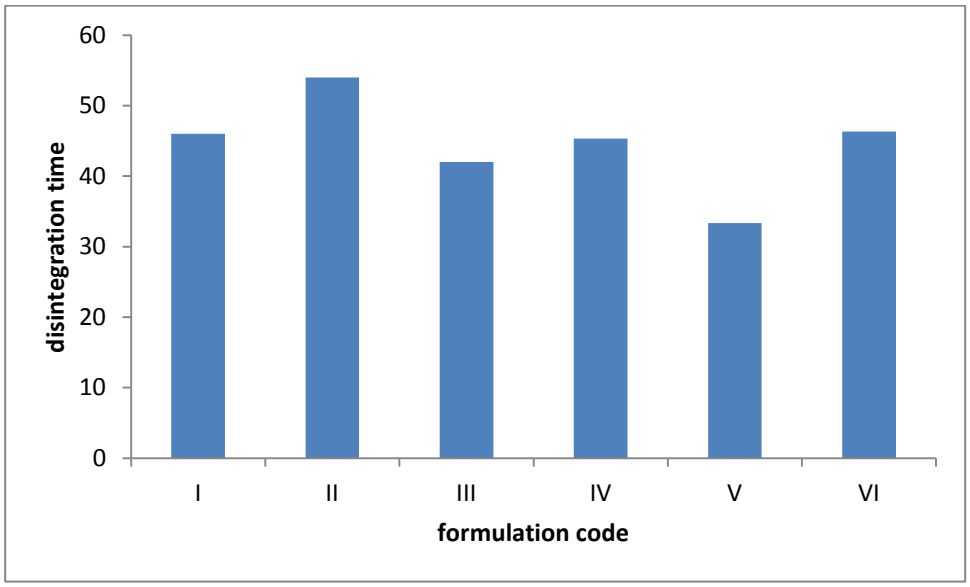

Fig no 6: Disintegration time of oral thin films

Mouth dissolving time

The mouth dissolving time was determined by using beaker containing 6.8-pH phosphate buffer. A size of 0.35 square inch film was subjected for this study. The mouth dissolving time of the film was reported in the Table-8.

Table-8 Comparative evaluation of Mouth dissolving time of oral thin films

S.NO	Formulation code	Mouth dissolving time in Sec			Mean ± SD*
		Trial 1	Trial 2	Trial 3	
1	I	54	55	52	53.6 ± 1.52
2	II	64	68	62	64.66 ± 3.05
3	III	47	49	45	47 ± 2
4	IV	52	58	56	55.33 ± 3.05
5	V	40	38	44	40.66 ± 3.04
6	VI	49	55	54	52.66 ± 3.21

***Standard deviation, n =3**

Drug content uniformity of films

The prepared film formulations were analyzed for drug content and it was observed that all the formulation found to contain almost uniform quantity of drug as per content uniformity studies indicating reproducible technique. The data is reported in the table-9.

Table-9 Results of drug content uniformity of oral film formulations

S.NO	Formulation code	Drug content in mg			Mean ± SD*	Drug content
		Trial 1	Trial 2	Trial 3		
1	I	24.85	24.96	25.1	24.97 ± 0.12	99.4 %
2	II	24.9	24.95	24.9	24.91 ± 0.02	98.2 %

3	III	24.8	24.75	24.8	24.78 ± 0.02	95.6 %
4	IV	24.8	24.82	24.79	24.79 ± 0.03	95.8 %
5	V	24.9	24.85	24.92	24.86 ± 0.02	97.2 %
6	VI	24.79	24.83	24.92	24.84 ± 0.06	96.8 %

*Standard deviation, n =3

Each film contain 25 mg / 0.35 inch^2

In-vitro dissolution

The dissolution study was carried out using USP Type I (Basket type) dissolution apparatus. The dissolution was carried out in 500 ml of pH 6.8 phosphate buffer maintained at 37 ± 0.5^{0}C at 50 rpm. 5 ml aliquots of samples were taken at various time intervals which were replaced with same volume of fresh pH 6.8 phosphate buffer maintained at 37 ± 0.5^{0}C. Sumatriptan in the samples was then determined spectrophotometrically at λmax of 282 nm. The results were expressed in table no 10.

Table-10 Comparative evaluation of *Invitro* dissolution profiles of oral thin Films

SNO	Time in min	Cumulative % of drug release					
		FI	FII	FIII	FIV	FV	FVI
1	2	26 %	22.6%	22%	21%	45%	41%
2	4	53.3%	45.9%	49.3%	39.8%	77.3%	69.3%
3	6	78.3%	71%	69%	56%	98.5%	90.9%
4	8	93.2%	85.3%	80%	81%	98.5%	96.8%
5	10	96.3%	92%	92.4%	92.4%	98.5%	96.8%
6	12	97.3%	93.9%	94.5%	96%	98.5%	96.8%
7	14	98.4%	94.9%	97%	97.3%	98.5%	96.8%
8	16	98.6%	96.1%	97%	98%	98.5%	96.8%
9	18	98.6%	97.2%	97%	98%	98.5%	96.8%
10	20	98.6%	98	97%	98%	98.5%	96.8%

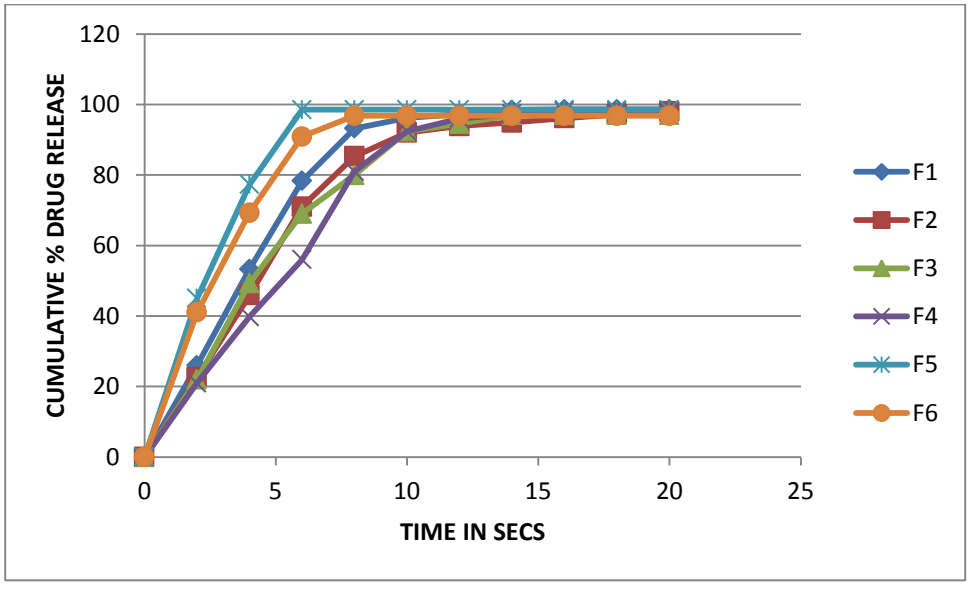

Fig no 7: Dissolution profile of Oral thin films

CONCLUSION

From the present investigation it can be concluded that oral thin film formulation can be a potential novel drug dosage form for pediatric, geriatric and also for general population.

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