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FORMULATION AND EVALUATION OF FAST DISSOLVING ORAL FILMS CONTAINING BACLOFEN

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ABSTRACT

Fast dissolving oral films (FDOFs) are the most advanced form of oral solid dosage form due to more flexibility and comfort. Baclofen is a muscle relaxant used for the symptomatic relief of severe chronic spasticity associated with a variety of conditions. The present study was undertaken with the objective of formulating fast dissolving oral films of Baclofen to enhance the convenience and compliance by the patients specifically elderly and paediatric. The films were formulated by solvent casting method with different concentrations of Hydroxy propyl cellulose and hydroxyl ethyl cellulose as film forming polymers. Propylene glycol is used as plasticizer and croscarmellose sodium is used as superdisintegrant. The compatibility of the drug in the formulation was confirmed by FTIR studies. Fifteen formulations were prepared and evaluated for physico-chemical parameters such as weight uniformity, thickness uniformity, folding endurance, drug content, surface pH, tensile strength, percentage elongation, swelling index, water absorption ratio, *In-vitro* disintegration time, *In-vitro* dissolution studies and *In-vitro* permeation studies. The formulations having polymers at low concentrations showed better results. All formulated films showed the good physico-mechanical properties. The formulation containing 2.5%w/v of HEC and 8%w/w of croscarmellose sodium has a disintegration time of 34 seconds, folding endurance of 272 and %CDR of 95.32% at the end of 14 minutes.

Keywords: Fast dissolving oral films, Baclofen, Croscarmellose, Solvent casting method, Hydroxy propyl cellulose, Hydroxyl ethyl cellulose.

INTRODUCTION

Among the drug delivery routes, oral route is one of the most convenient, cost effective and preferred routes of drug administration. But some patients, especially paediatrics and geriatrics have difficulties in swallowing or chewing the oral solid dosage forms like tablets and hard gelatin capsules. In order to overcome these problems fast dissolving drug delivery systems came into existence[1].

Fast dissolving films, a type of oral drug delivery system were developed based on the technology of transdermal patch. This delivery system consists of a thin film, which is simply placed on patient's tongue or mucosal tissue, instantly wet by saliva; the film rapidly disintegrates and dissolves to release the medication for gastrointestinal or mucosal absorption. Fast dissolving films are most advanced form of

solid dosage form due to its flexibility. It improves efficacy of active pharmaceutical ingredient (API) by dissolving in a short duration in the oral cavity after the contact with less amount of saliva as compared to fast dissolving tablet.[2]

Baclofen is structural analogue of gamma amino butyric acid is a centrally acting skeletal muscle relaxant, which is widely used in the treatment of spasticity resulting from muscle sclerosis, muscle spasms, muscular rigidity and spinal cord injuries, where pain persist predominantly, in such cases the quick onset of action is of prime importance.[3]

The present study was aimed towards formulation and evaluation of fast dissolving oral films containing baclofen using Hydroxy propyl cellulose and hydroxyl ethyl cellulose as film forming polymers by solvent casting method which offers a suitable and practical approach of faster disintegration and dissolution characteristics.[2]

MATERIALS AND METHODS

Baclofen pure drug, Hydroxyl propyl cellulose and Hydroxyl ethyl cellulose was received from Yarrow Chem Products, Mumbai. All other excipients and solvents used were of the analytical pharmaceutical grade.

Compatibility Studies using FTIR Spectroscopy:

FTIR absorption spectra of pure drug and physical mixture were recorded in the range of 400 to 4000 cm^{-1} by using FTIR spectrophotometer. FTIR study was carried out individually for drug polymer, other excipients and physical mixture of drug with polymer. FTIR spectra of physical mixture of drug with all polymers were compared with FTIR spectra of pure drug and polymers and and peak matching was done to detect any appearance or disappearance of peaks.[4]

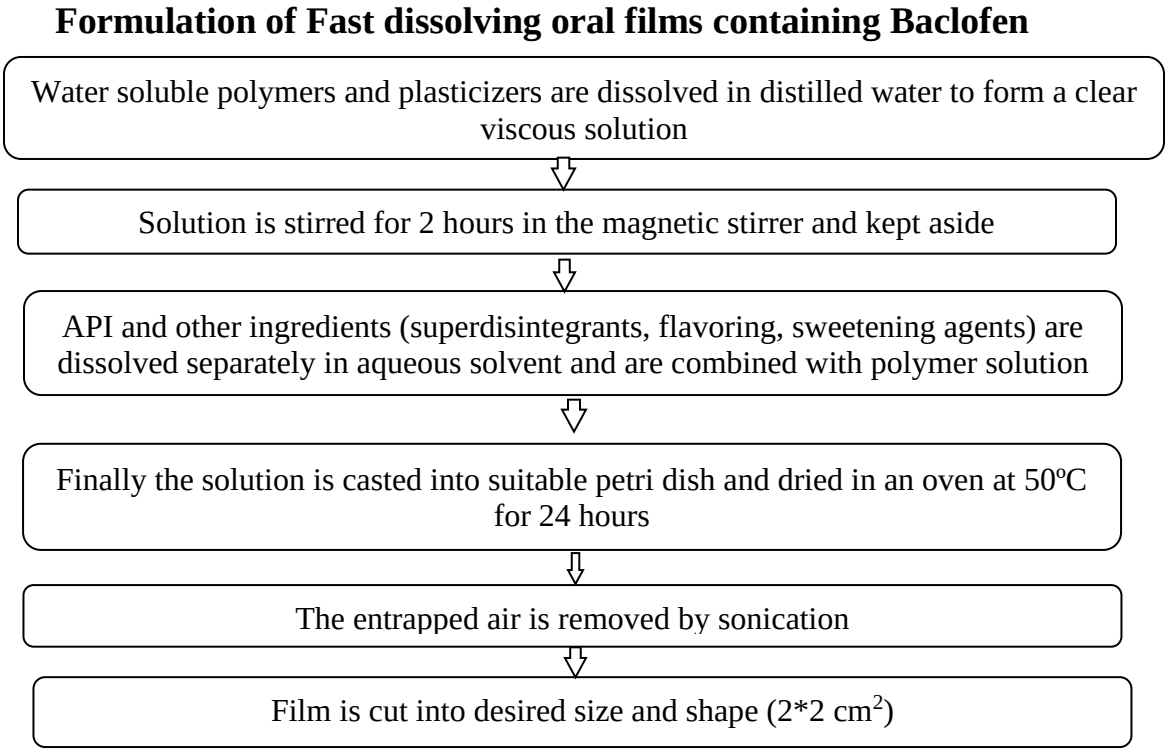

Figure 1: Solvent casting method to prepare oral films

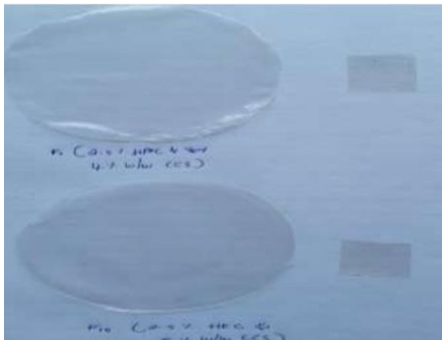

Figure 2: Prepared Baclofen fast dissolving oral film

Table 1: Composition of Baclofen oral film

Formulation Code	Baclofen (mg)	HPC (mg)	HEC (mg)	CCS (mg)	Citric acid (mg)	Sucrose (mg)	PG (%w/w)	Menthol (mg)	Water (ml)
F1	159	500	_	20	100	150	20	10	20
F2	159	750	_	30	100	150	20	10	20
F3	159	1000	_	40	100	150	20	10	20
F4	1 59	_	500	20	100	150	20	10	20
F5	159	_	750	30	100	150	20	10	20
F6	159	_	1000	40	100	150	20	10	20
F7	159	500	_	40	100	150	20	10	20
F8	159	750	_	60	100	150	20	10	20
F9	159	1000	_	80	100	150	20	10	20
F10	159	_	500	40	100	150	20	10	20
F11	159	_	750	60	100	150	20	10	20
F12	159	_	1000	80	100	150	20	10	20
F13	159	250	750	80	100	150	20	10	20
F14	159	500	500	80	100	150	20	10	20
F15	159	750	250	80	100	150	20	10	20

Calculation of the amount of drug for one cast film: -

- Internal diameter of the petridish = 9.0cm
- Radius of the petri dish = 4.5cm
- Internal surface area of petridish = πr^2
  = 22/7 x $(4.5)^2$
  = 3.142 x (20.25)
  = 63.585cm^2
- Surface area of strip = 2 x 2cm = 4cm^2
- 4cm^2 contains 10mg
- (63.585) cm^2 contains = 158.96mg of Baclofen

EVALUATION STUDIES OF FAST DISSOLVING ORAL FILMS:

Weight variation:

Three individual batches of fast dissolving film of size 2*2 cm^2 is cut and weighed on electronic balance for weight variation test.[10]

Thickness:

For evaluation of film thickness three films (2*2 cm^2 contains 10 mg) of each formulation were taken and the film thickness is measured using micrometer screw gauge at three different places and the mean thickness of films were calculated.[11]

Folding endurance:

It is determined by repeatedly folding a small strip of the film (2*2 cm^2) at the same place till it broke. The number of times a film can be folded at the same place without breaking gave the value of folding endurance.[12]

Surface pH:

The film to be tested was placed in a Petri dish and was moistened with 0.5 ml of distilled water and kept for 30 s. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min. The average of three determinations for each formulation was done.[13]

Tensile strength:

The tensile strength of the FDOF is measured using Asian tensile strength apparatus. The samples of FDOF at dimension of 5*2 cm^2 were held vertically between two clamps. The force at which the film starts to break was noted. The tensile strength was defined as the maximum load force to break the film and calculated by dividing the applied load at rupture with the cross-sectional area of the film.[14]

Tensile strength = force at break (kg) / initial cross-sectional area of the sample (cm^2).

Figure 3: Tensile strength apparatus

Swelling index:

The film sample (2*2cm$^{2)}$ is weighed and placed in a pre-weighed cover slip. The cover slip containing the film sample is submerged into 20ml of phosphate buffer pH 6.8 solution in a beaker. At definite time intervals, the cover slip is removed, excess moisture removed by carefully wiping with absorbent tissue and reweighed. Increase in weight of the film is determined at each time interval until a constant weight is observed. The degree of swelling is calculated using the formula: [15]

SI = $(Wt-Wo)/Wo$
SI = swelling index
Wt = weight of the film at time=t
Wo = weight of the film at time t=0.

Water absorption ratio:

A piece of tissue paper folded twice is placed in a small petridish containing 6 ml of water. A film (2*2cm^2) is placed on the paper and time required for complete wetting is recorded. The wetted film is then weighed. Water absorption ratio(R) is determined using following equation[16]

$$(Wa-Wb)/Wb \text{ X}100$$

Wb= weight of film before water absorption
Wa= weight of film after water absorption

Drug content:

The oral film of 2*2cm^2 is dissolved in 100 ml of phosphate buffer pH 6.8. Resulting solution is sonicated for 15 min and filtered. The filtrate is appropriately diluted and analyzed at λmax in UV spectrophotometer. The concentration of drug is calculated using standard calibration curve.[4]

In vitro Disintegration time:

The disintegration time is determined visually by dipping a film (2*2cm^2) in a petri dish containing 10 ml of phosphate buffer pH 6.8 at 37ºC. Petri dish is swirled at every 10 seconds and time is noted when the film starts to breaks or disintegrates.[4]

In vitro dissolution study:

The dissolution study is carried out using USP I basket apparatus at 37˚C±0.5˚C using 250ml of phosphate buffer pH 6.8 as dissolution medium. The drug loaded film (2*2cm²) is placed in medium. The basket is set at 50 rpm. 5ml samples were withdrawn at 2, 4,6,8,10,12,14-,16-,18- and 20-minute times and replaced with fresh dissolution medium. The samples were filtered through whatman filter paper and analyzed spectrophotometrically at λmax. [14]

In vitro permeation studies:

In vitro permeation studies through cellophane membrane is carried out using the Franz diffusion cell of internal diameter 2.5 cm. The cellophane membrane is mounted between the donor and receptor compartments. The receptor compartment is filled with phosphate buffer pH 7.4 which is maintained at 37±0.2˚C and hydrodynamics were maintained using magnetic stirrer. One film of dimension 2*2 cm² is previously moistened with few drops of phosphate buffer pH 6.8 and placed in donor compartment. The

donor compartment is filled with 1 ml of phosphate buffer pH 6.8. 1 ml samples from receptor compartment were withdrawn at suitable time intervals which is then replaced with 1 ml of phosphate buffer pH 7.4. The percentage of Baclofen permeated was determined by measuring the absorbance in UV spectrophotometer at λmax.[17, 18]

Stability studies:

The formulation was subjected to stability studies as per ICH guidelines. The formulated fast dissolving film was packed in an aluminum foil and stored in stability chamber controlled at accelerated testing condition at 40± 2˚C and 75% RH for 3 months. The samples were withdrawn after 3 month and analyzed for drug content, *in vitro* disintegration time and % drug release.[4, 19, 20]

RESULTS AND DISCUSSION

Compatibility Studies using FTIR Spectroscopy

Compatibility studies of Baclofen with different polymers were carried out prior to formulation of oral film.

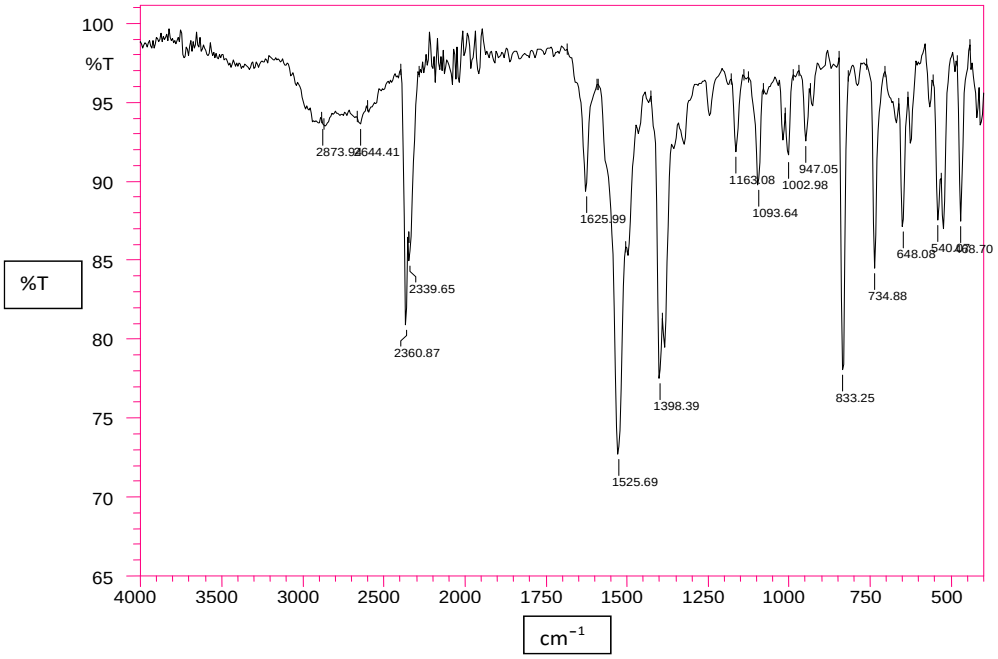

Figure 4: FTIR spectra of pure drug Baclofen

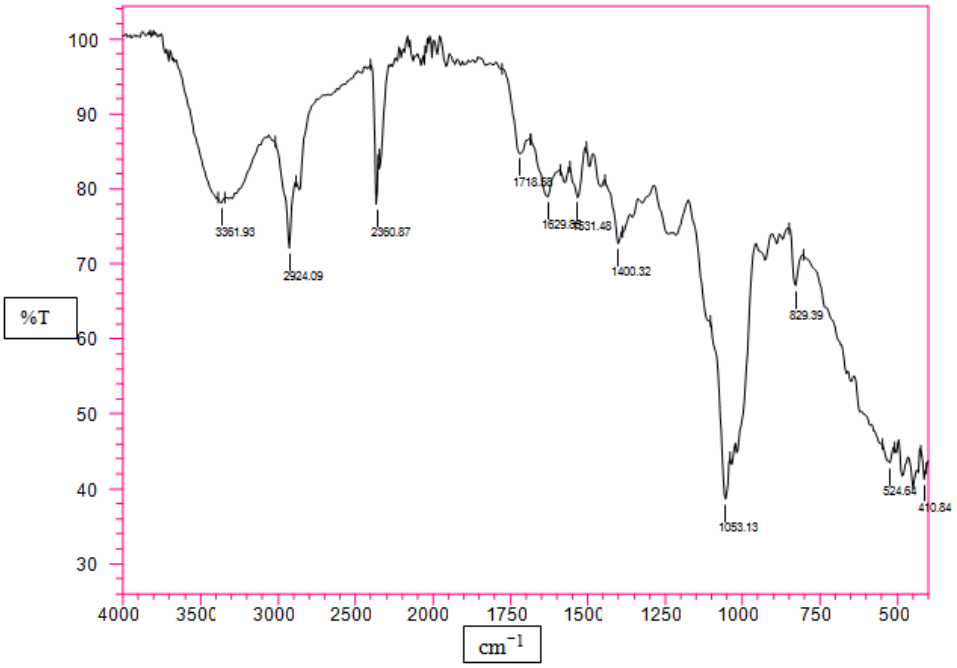

Figure 5: FTIR spectra of Baclofen+Hydroxy ethyl cellulose

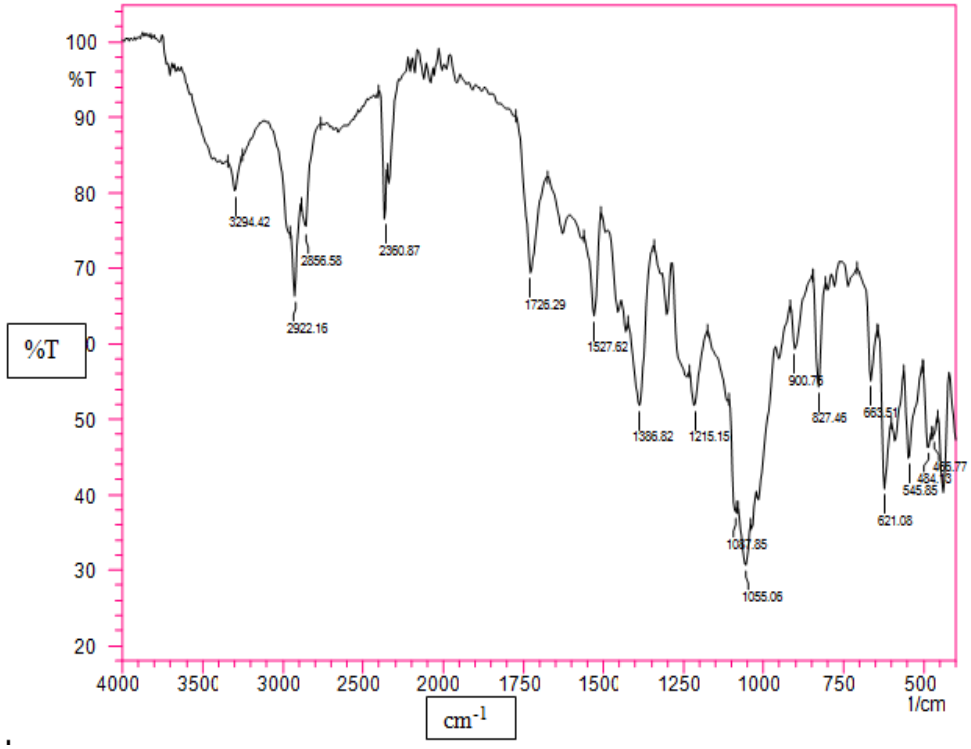

Figure 6: FTIR spectra of Baclofen+Hydroxy propyl cellulose

Table 2: Interpretation of FTIR spectra

Functional grp	Reported frequency	Baclofen	Baclofen+HEC	Baclofen+HPC
C=C stretch	1600-1400	1525.69	1531	1527.29
C-Cl stretch	1400-1200	1398.39	1400	1386.82
C=0 stretch	1820-1600	1625	1629	1726
NH_2stretch	2400-2200	2360.87	2360.87	2360.87

Compatibility studies were performed using FTIR spectrophotometer. The peaks obtained in the spectra of each physical mixture correlates with the peaks of drug spectrum. The FTIR of pure drug is characterized by C=C stretching at 1525.69 cm^{-1}, C-Cl stretching at 1398.39cm^{-1}, C=O stretching at 1625 cm^{-1}, and N-H stretching at 2360.87cm^{-1} respectively.

All the characteristic IR peaks related to pure drug, Baclofen also appeared in the FTIR spectrum of mixture of drug with polymers, so there was no chemical incompatibility between the drug and polymer.

EVALUATION STUDIES OF FAST DISSOLVING ORAL FILMS:

Table 3 : Evaluation studies of fast dissolving films containing Baclofen

Formulation code	Average weight (mg±SD*)	Thickness (mm±SD*)	Drug content (%±SD*)	Surface pH (*)
F1	51.33±0.47	0.21±0.012	89.6±1.96	6.50±0.08
F2	70.00±0.81	0.24±0.017	91.8±1.02	6.66±0.09
F3	89.66±0.47	0.26±0.016	93.3±1.69	6.80±0.08
F4	51.66±1.24	0.19±0.012	92.0±1.63	6.63±0.12
F5	65.00±0.81	0.22±0.020	95.0±0.81	6.56±0.16
F6	92.66±0.94	0.24±0.017	91.3±0.94	6.70±0.08
F7	52.00±1.41	0.25±0.028	90.3±1.24	6.60±0.08
F8	72.33±1.69	0.28±0.016	92.1±1.43	6.86±0.04
F9	90.00±1.63	0.29±0.030	89.0±0.81	6.70±0.14
F10	52.66±2.05	0.21±0.021	87.0±0.81	6.76±0.12
F11	64.66±2.05	0.23±0.017	91.6±1.24	6.70±0.08
F12	90.33±1.24	0.23±0.024	90.6±1.24	6.36±0.12
F13	88.33±0.47	0.20±0.017	90.3±0.47	6.50±0.08
F14	91.00±0.81	0.23±0.012	91.5±1.47	6.83±0.04
F15	92.00±1.63	0.22±0.016	93.6±1.24	6.66±0.04

All values represented are mean of 3 readings (n = 3)

The Average weight, thickness, drug content and surface pH of the prepared oral films are shown in Table 3.

Weight variation: The weight of prepared films was found to be in the range of 51.33±0.47mg to 92.66±0.94mg. Formulation F1 showed lowest weight of 51.33±0.47mg

Film thickness: Thickness of all fast dissolving film was measured with micrometer screw gauge. The thickness of the fast dissolving films F1 to F15varies from 0.19±0.012 mm to 0.29±0.030 mm with low standard deviation values. Formulation F4 showed lowest thickness of 0.19±0.012 mm and formulation F9 showed highest thickness of 0.29±0.030 mm.

Drug content uniformity: The content uniformity for all the formulations prepared by using different concentration of HPC and HEC was found to be in the range 87.0±0.81% to 95.0±0.81% which showed that there was uniform distribution of the drug in films of all formulations.

Surface pH: The surface pH of all the films were uniform and within the range 6.36±0.12 to 6.86±0.04.

Table 4 : Evaluation studies of fast dissolving films containing Baclofen

Formulation code	Folding endurance (*)	Swelling index (*)	Water absorption ratio (*)	*In vitro* Disintegration time (sec±SD*)
F1	250±2.05	3.52±0.01	278.7±5.09	37.6±1.24
F2	261±2.94	2.76±0.05	215.2±3.65	44.0±0.81
F3	262±3.85	1.91±0.06	165.6±1.88	47.6±1.24
F4	273±3.39	3.64±0.06	290.5±4.38	39.3±1.24
F5	268±3.74	2.81±0.08	238.3±2.17	44.0±1.63
F6	282±2.44	2.15±0.07	155.0±2.40	47.0±0.81
F7	256±4.92	3.78±0.03	292.6±2.93	36.0±0.81
F8	253±3.74	2.77±0.01	218.9±1.91	40.6±1.69
F9	262±5.31	2.43±0.04	162.9±4.0	41.0±1.41
F10	272±3.26	3.84±0.06	284.5±3.61	34.0±0.81
F11	271±1.24	2.82±0.06	220.7±4.72	36.0±0.81
F12	271±2.05	2.34±0.05	169.3±4.92	38.3±1.24
F13	265±2.62	2.19±0.07	176.7±3.10	41.3±1.69
F14	264±3.29	2.24±0.11	157.7±2.12	36.6±1.24
F15	265±3.26	1.97±0.10	165.0±2.85	39.6±1.24

*All values represented are mean of 3 readings (n = 3)

Folding endurance:

Folding endurance of the films F1 to F15 ranges from 250±2.05 to 282±2.44 as given in table 4(b). Formulation F1 had lower folding endurance of 250±2.05 since concentration of polymer was low (2.5% w/v of HPC). Formulation F6(5%w/v of HEC) showed highest folding endurance of 282±2.44. As the concentration of polymer increases, the

folding endurance also increases.

Swelling index:

The swelling index of the formulations F1 to F15 was found to be in the range of 1.91 ±0.06 to 3.84±0.06 respectively. Among these fifteen formulations F10 showed highest swelling index of 3.84±0.06 and F3 showed lowest swelling index of 1.91 ±0.06. As the concentration of superdisintegrant increases, the swelling index also increases due to the more water absorption.

Water absorption ratio:

The water absorption ratio of formulations F1 to F15 was found to be in the range of 155.0±2.40 to 292.6±2.93 respectively. Among these fifteen formulations, F7 showed highest water absorption ratio of 292.6±2.93 and F6 showed lowest water absorption ratio of 155.0±2.40.

***In vitro* disintegration time:**

All the films are disintegrating rapidly. The disintegration time of the films F1 to F15 was found to be in the range of 34.0±0.81 seconds to 47.6±1.24 seconds as shown in table 4(b). *In vitro* disintegration time of the formulation F10 containing 2.5%w/v of HEC showed lowest disintegration time of34.0±0.81seconds. Formulation F3 containing 5%w/v of HPC showed disintegration time 47.6±1.24 seconds. In vitro disintegration time of the films was found to decrease with increase in the amount of the superdisintegrant.

Tensile strength:

Tensile strength of the films F1 to F15 was ranging from 0.126±0.01 N/cm^2 to 0.250±0.02 N/cm^2 as shown in table 4(b). Formulation F7 containing 2.5% w/v of HPC showed minimum tensile strength of 0.126±0.01 N/cm^2 and formulation F6 containing 5% w/v of HEC showed maximum tensile strength of 0.250±0.02 N/cm^2. As the concentration of polymer increases, the tensile strength also increases.

In vitro drug release study of formulations:

Table 5: *In vitro* dissolution study of Baclofen fast dissolving film

Time (min)	%cumulative drug release					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
2	41.37	38.98	38.16	42.16	37.51	38.04
4	48.24	45.59	43.88	48.81	43.79	44.21
6	54.61	53.03	51.42	60.02	49.36	49.47
8	64.34	61.89	59.66	68.07	58.31	58.13
10	72.36	69.67	68.53	76.23	66.36	67.86
12	82.57	79.71	79.01	84.04	76.83	77.30
14	91.55	89.08	88.08	92.06	86.00	85.42

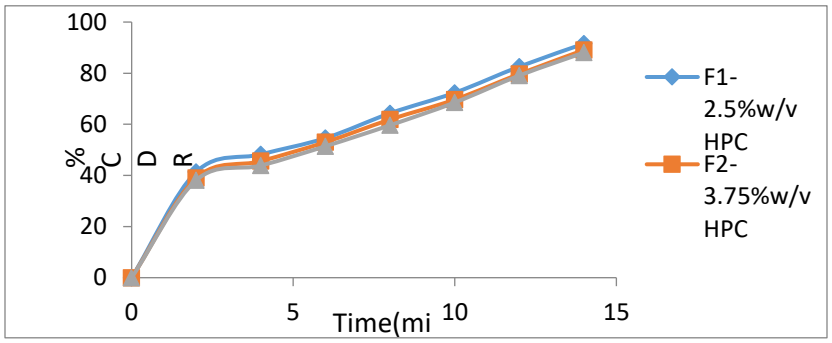

Figure 7: In vitro dissolution study of F1-F3 containing 4%w/w of CCS

The formulations F1,F2and F3 containing 2.5%, 3.75% and 5% w/v of hydroxyl propyl cellulose (4% w/w of croscarmellose sodium) showed percentage drug release of 91.55%, 89.08% and 88.08% respectively . In this, the formulation F1 showed a better drug release of 91.55% at the end of 14 minutes.

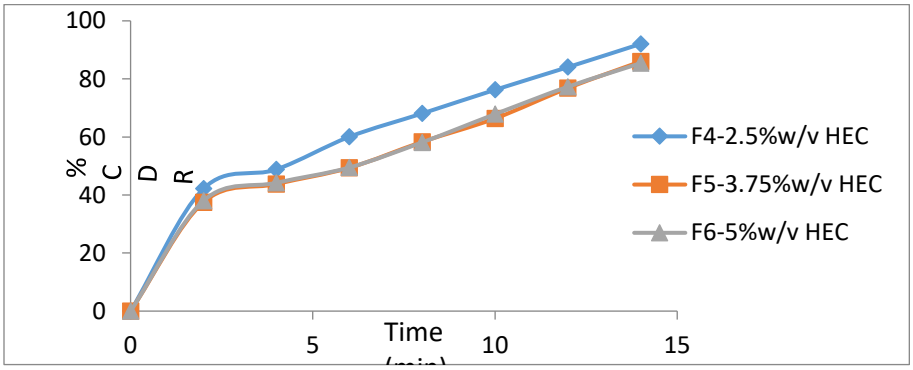

Figure 8: In vitro dissolution study of F4-F6 containing 4%w/w of CCS

The formulations F4, F5and F6 containing 2.5%, 3.75% and 5% w/v of hydroxyl ethyl cellulose (4% w/w of croscarmellose sodium) showed percentage drug release of 92.06%,86% and 85.42% respectively. Out of these three formulations, F4 showed a better drug release of 92.06% at the end of 14 minutes.

Table 6: *In vitro* dissolution study of Baclofen fast dissolving film

	%cumulative drug release					
Time (min)	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
0	0	0	0	0	0	0
2	43.15	42.18	41.72	44.17	41.44	40.25
4	49.79	48.16	48.73	53.90	48.96	46.75
6	56.72	55.39	56.23	62.63	60.01	57.28
8	64.42	61.96	62.92	72.63	68.40	65.97
10	73.47	71.59	72.77	81.7	75.45	73.91
12	82.66	79.09	80.15	87.82	82.86	80.50
14	92.07	89.12	87.08	95.32	90.79	88.52

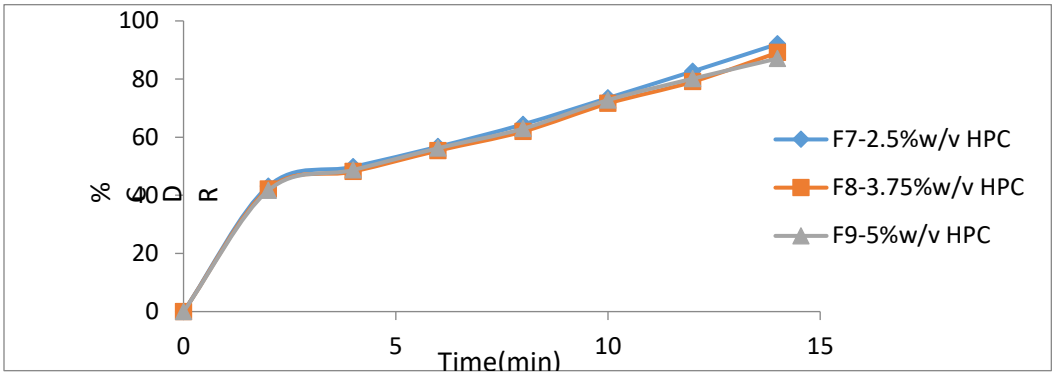

Figure 9: *In vitro* dissolution study of F7-F9 containing 8%w/w of CCS

The formulations F7, F8 and F9 containing 2.5%, 3.75% and 5% w/v of hydroxyl propyl cellulose (8% w/w of croscarmellose sodium) showed percentage drug release of 92.07%, 89.12% and 87.08% respectively. In this, the formulation F7 showed a better drug release of 92.07% at the end of 14 minutes.

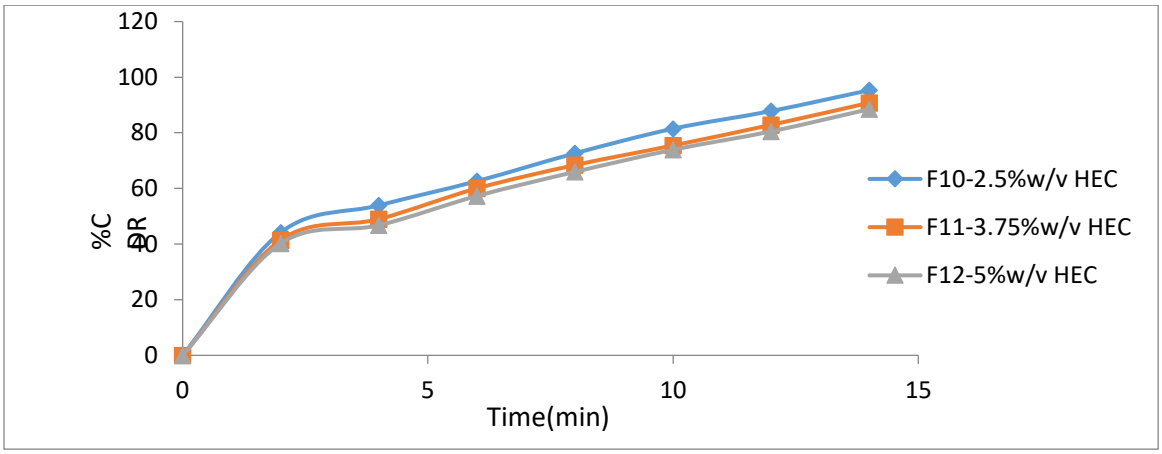

Figure 10: In vitro dissolution study of F10-F12 containing 8%w/w of CCS

Table 7: *In vitro* dissolution study of Baclofen fast dissolving film

Time(min)	%cumulative drug release		
	F13	F14	F15
0	0	0	0
2	40.99	42.29	37.77
4	48.27	47.93	44.88
6	57.32	55.86	52.24
8	64.62	64.57	60.71
10	72.38	72.40	69.50
12	80.28	80.49	78.01
14	89.03	90.19	88.81

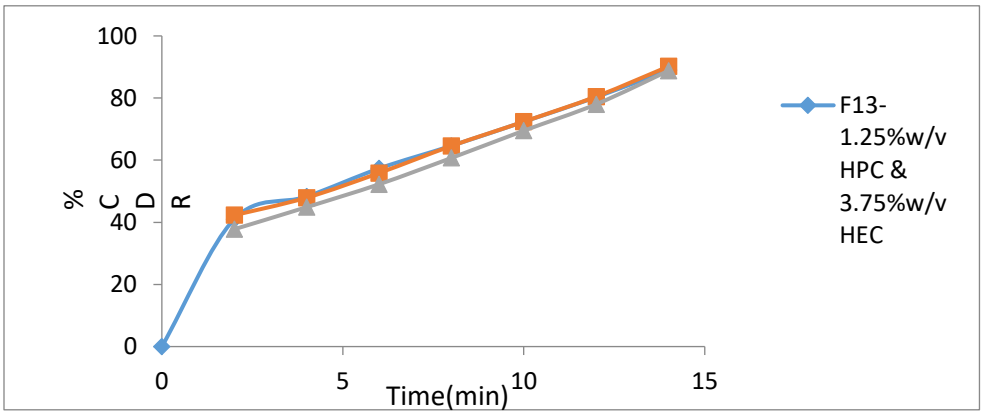

Figure 11: In vitro dissolution study of F13-F15 containing 8%w/w of CCS

Table 8: *In vitro* dissolution study of best Formulations

Time (min)	% cumulative drug release				
	F1	F4	F7	F10	F14
0	0	0	0	0	0
2	41.37	42.16	43.15	44.17	42.29
4	48.24	48.81	49.79	53.90	47.93
6	54.61	60.02	56.72	62.63	55.86
8	64.3	68.07	64.42	72.63	64.57
10	72.36	76.23	73.47	81.47	72.40
12	82.57	84.04	82.66	87.82	80.49
14	91.55	92.06	92.07	95.32	90.19

The formulations F13, F14 and F15 containing combination of two polymers also showed a better drug release. It released 90.19% of drug at the end of 14 minutes.

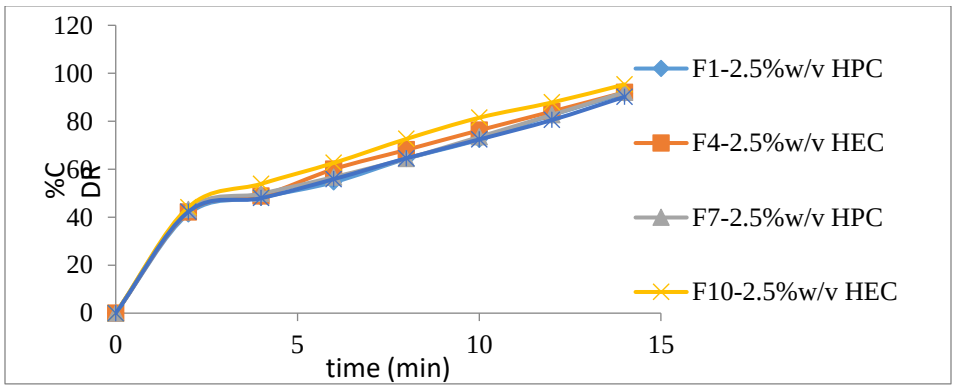

Figure 12: In vitro dissolution study of best formulations

Out of these three formulations, F14 containing 2.5%w/v of HPC and 2.5%w/v of HEC (8%w/w of croscarmellose sodium) showed a better drug release of 90.19 at the end of 14 minutes. Out of 5 best formulations F1, F4, F7, F10 and F14, the formulation F10 showed better drug release at the end of 14 minutes. Hence from the above results, it could be concluded that as the polymer concentration decreases, the percentage drug release increases.

In vitro permeation study:

Table 9: *In vitro* permeation study of Baclofen fast dissolving film

Time (min)	%cumulative drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	16.57	27.00	17.03	22.49	19.55	19.77
10	25.01	34.70	24.56	38.63	38.37	30.32
15	38.42	42.04	33.99	53.72	47.68	39.54
20	41.74	52.42	42.34	62.70	59.35	48.93
25	54.49	62.12	52.92	72.48	60.98	58.50
30	70.95	70.23	60.54	76.63	64.88	62.63
35	79.50	75.97	71.12	80.72	73.99	70.35
40	87.08	85.61	83.88	89.14	87.20	82.18

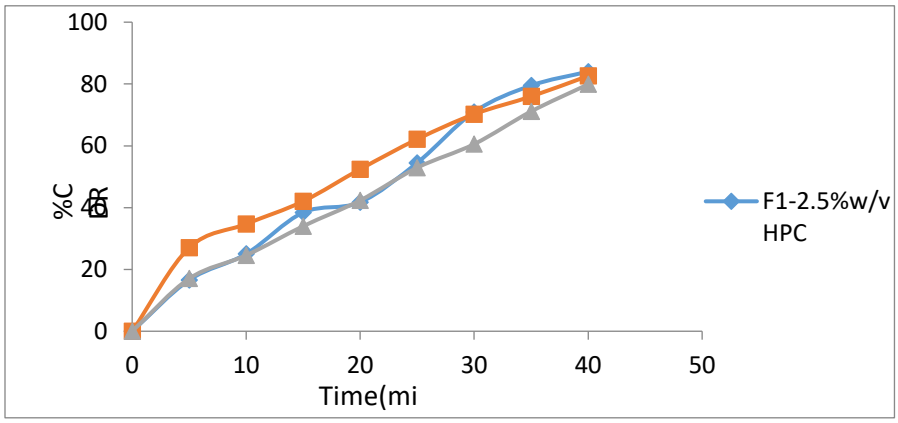

Figure 13: *In vitro* permeation study of F1-F3 containing 4%w/w CCS

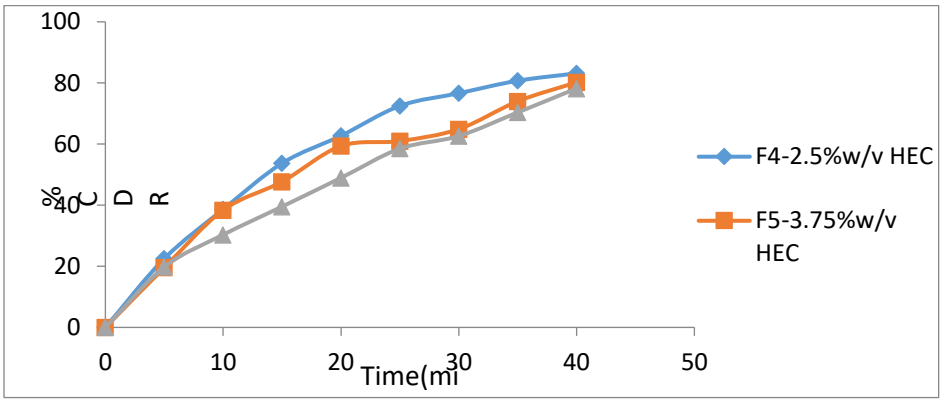

Figure14: *In vitro* permeation study of F4-F6 containing 8%w/w CCS

Table 10: *In vitro* permeation study of Baclofen fast dissolving film

Time (min)	%cumulative drug release					
	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
5	22.07	27.14	25.55	22.05	20.04	21.25
10	36.32	40.17	36.32	32.67	26.15	28.55
15	48.11	50.76	49.28	40.33	34.14	63.19
20	55.51	59.16	55.80	49.85	41.12	46.45
25	64.39	64.34	64.16	60.78	48.53	53.73
30	71.63	70.47	72.66	68.92	58.91	63.04
35	78.09	76.80	78.05	79.32	70.30	73.23
40	89.19	87.76	84.91	93.18	90.36	87.79

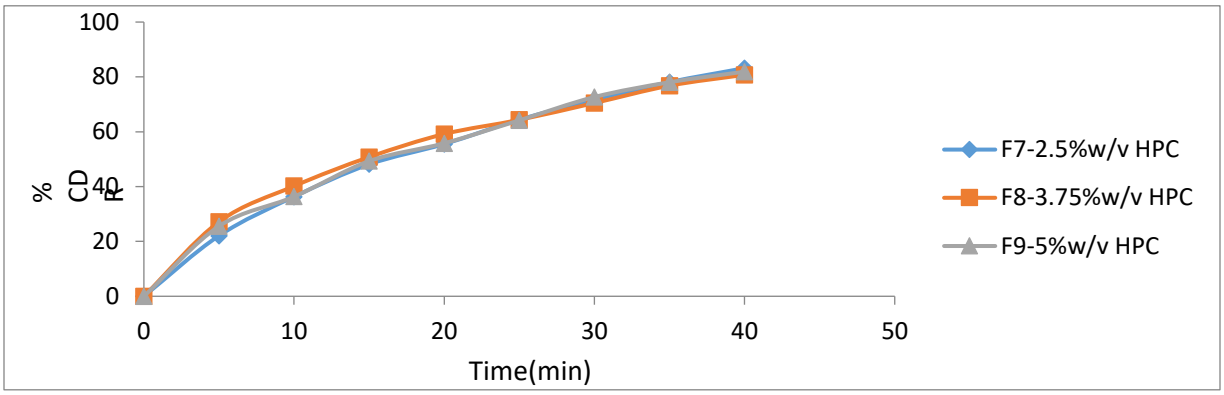

Figure15: In vitro permeation study of F7-F9 containing 8%w/w CCS

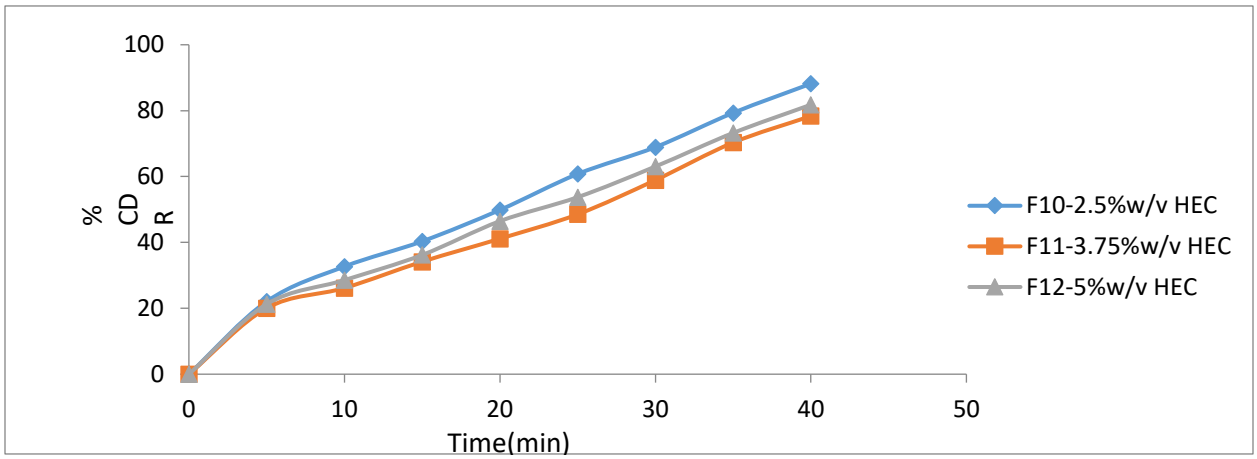

Figure 16: In vitro permeation study of F10-F12 containing 8%w/w CCS

Table 11: In vitro permeation study of Baclofen fast dissolving film

Time (min)	% cumulative drug release		
	F13	F14	F15
0	0	0	0
5	23.18	21.71	22.49
10	28.98	31.76	32.62
15	35.17	39.04	40.38
20	42.95	46.55	47.90
25	53.04	55.10	58.63
30	61.00	63.91	68.64
35	69.58	71.82	76.17
40	80.58	89.54	86.77

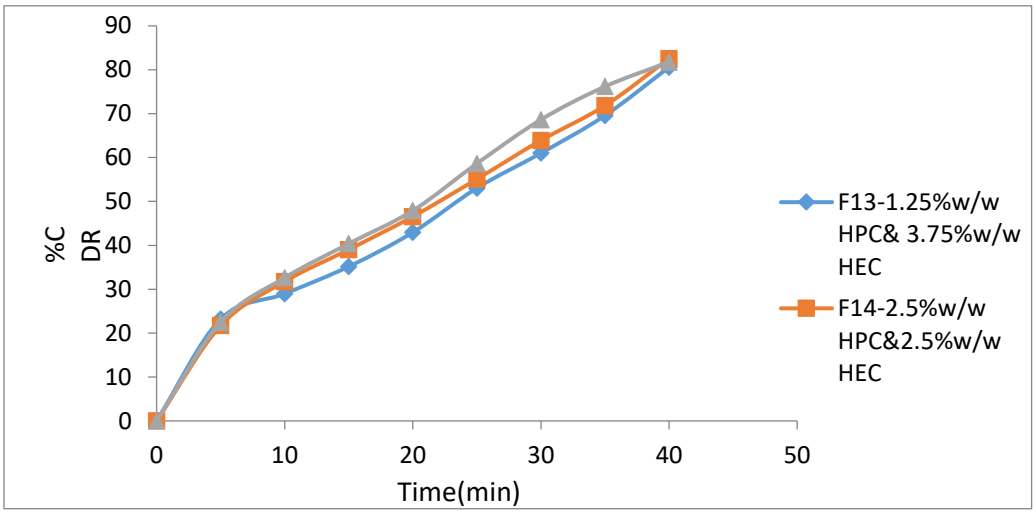

Figure 17: In vitro permeation study of F13-F15 containing 8%w/w of CCS

In vitro drug permeation studies:

The results obtained in the *in-vitro* permeation for the formulations F1 to F15 are tabulated in table 8(a), 8(b) and 8(c).From *in-vitro* drug permeation study, it was found that the formulation F10 containing 2.5%w/v of hydroxyl ethyl cellulose (8%w/w CCS) showed better drug permeation of 93.18% in 40 min. Formulation F1 containing 2.5%w/w hydroxyl propyl cellulose (4%w/w CCS) showed drug permeation of 87.08% in 40min. Formulation F4 containing 2.5%w/v of hydroxyl ethyl cellulose (4%w/w CCS) and formulation F7 containing 2.5%w/v of hydroxyl propyl cellulose (8% w/w CCS) showed drug permeation of 89.14% and 89.19% respectively at the end of 40 min. The result of *in-vitro* study showed that Baclofen from fast dissolving film was easily solubilised and absorbed from pregastric route, mouth, pharynx and oesophagus.

Stability studies of best formulations:

Stability study on F7 (2.5%w/v HPC& 8%w/w CCS)

Table 12: Stability study data of F7 (2.5%w/v HPC & 8%w/w of CCS)

Time (months)	Appearance*	In vitro disintegration time(sec) *	Drug content*
Zero	Transparent	36.0	90.3
First	Transparent	36.3	89.9
Second	Transparent	36.5	89.4
Third	Transparent	36.8	89.2

* 40±2°C and 75±5% RH

Table 13: Drug release under stability study of F7 (2.5%w/v HPC & 8%w/w of CCS)

Time (min)	%CDR			
	40±2°C and 75±5% RH			
	0 day	30 day	60 day	90 day
2	43.15	42.80	42.50	42.32
4	49.79	49.62	49.46	49.25
6	56.72	56.38	56.25	56.04
8	64.42	64.3	64.19	63.92
10	73.47	73.29	73.12	72.96
12	82.66	82.25	82.24	82.04
14	92.07	91.52	91.10	90.89

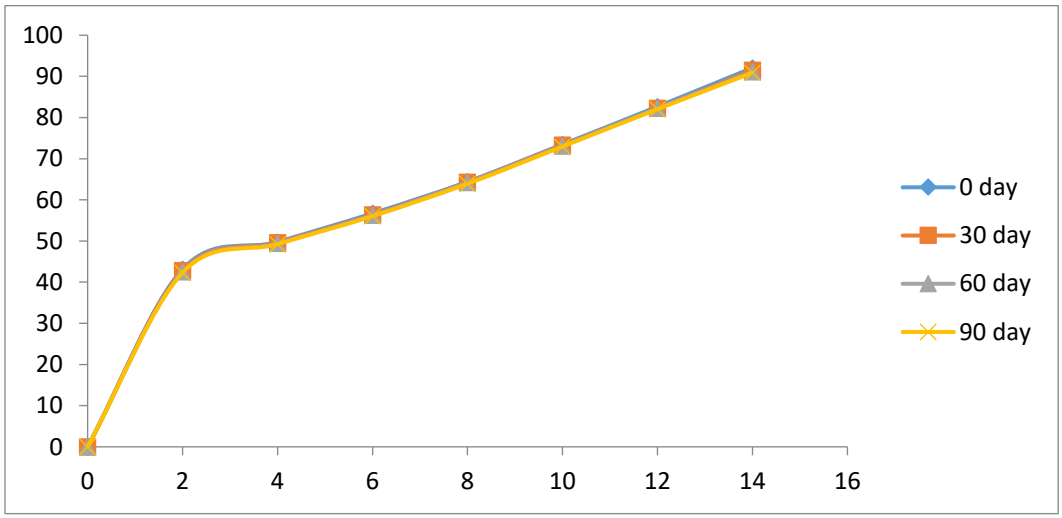

Figure 18: In vitro dissolution study of F10 under stability study (2.5%w/v HEC & 8%w/w of CCS)

F10 appeared to be transparent and showed disintegration time of 34.5, 34.8 and 35 sec in first, second and third month respectively. Drug content was found to be 91.52%, 91.21% and 91.05% in first, second and third month respectively. Drug release studies conducted on F10 showed that there was no significant change as it released 95.05%, 94.85% and 94.69% at the end of 14 min in first, second and third month respectively.

Stability study on F14 (2.5%w/v HPC, 2.5%w/v HEC& 8%w/w CCS):

Table 14: Stability study data of F14 (2.5%w/v HPC, 2.5%w/v HEC& 8%w/w CCS)

Time (months)	Appearance*	In vitro disintegration time(sec) *	Drug content*
Zero	Transparent	36.6	91.5
First	Transparent	36.8	91.18
Second	Transparent	37.2	90.92
Third	Transparent	37.7	90.79

* 40±2°C and 75±5% RH

Table 15: Drug release under stability study of F14 (2.5%w/v HPC, 2.5%w/v HEC& 8%w/w CCS)

	%CDR			
Time (min)	**0 day**	**30 day**	**60 day**	**90 day**
2	42.29	42.10	41.82	41.60
4	47.93	47.62	47.45	47.32
6	55.86	55.71	55.59	55.39
8	64.57	64.39	64.24	64.10
10	72.4	72.28	72.11	71.95
12	80.49	80.31	80.18	80.02
14	90.19	89.85	89.51	89.32

40±2°C and 75±5% RH

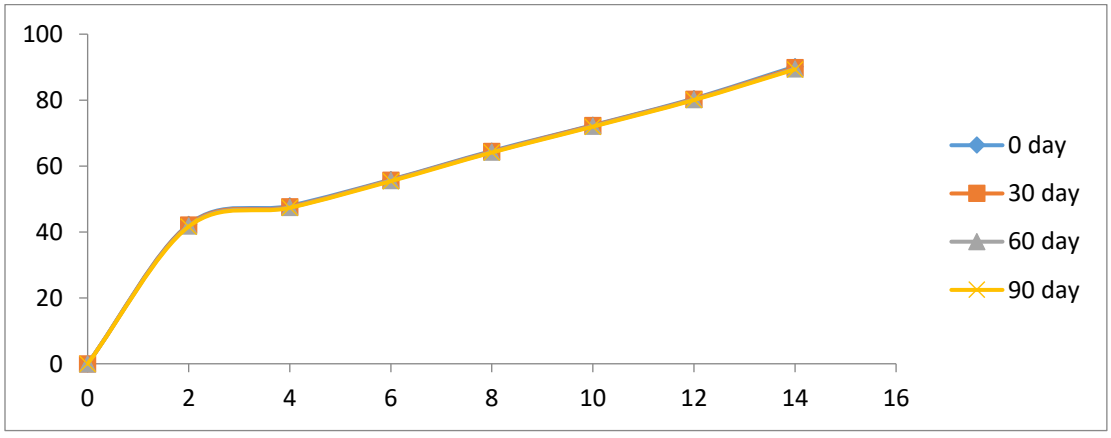

Figure 19: *In vitro* dissolution study of F14 under stability study (2.5%w/v HPC, 2.5%w/v HEC& 8%w/w CCS)

F14 appeared to be transparent and showed disintegration time of 36.8, 37.2and 37.7 sec in first, second and third month respectively. Drug content was found to be 91.18%, 90.92% and 90.79% in first, second and third month respectively. Drug release studies conducted on F14 showed that there was no significant change as it released 89.85%, 89.51% and 89.32% at the end of 14 min in first, second and third month respectively.

CONCLUSION

In the present study, an attempt was made to prepare fast dissolving oral films containing Baclofen, which were characterized for weight uniformity, thickness, folding endurance, drug content, surface pH, tensile strength, percentage elongation, swelling index, water absorption ratio, *In-vitro* disintegration time, *In-vitro* dissolution studies and *In-vitro* permeation studies. Among all the formulations F14 was selected as optimize formulation based on physico chemical studies, drug release studies and stability study data, and it is safe and effective for use.

REFERENCES

1. Julie MJ, Hari R, Fithal KJ and Saritha AS. Fast dissolving oral thin films: An effective dosage form for quick release. Int J Pharm Sci Rev Res. 2016; 38(1): 282-89.
2. Nishi T, Mayank B, Neha S, Ghanshyam Y and Pragati K. Overview-A novel approach of fast dissolving films and their patients. Adv Bio Res. 2013; 7(2): 50-58.
3. Tripati KD. Essentials of medical pharmacology. 6th ed. Jaypeebrothers publishers (P) Ltd. 2008; 349.
4. Abhijeet K, Vishaka D, Dhanik P, Simarpreetkaurr S, Sushma RS and Nilesh MK. Formulation and Evaluation of Dextromethorphan hydrobromide Fast Dissolving Film. IJIPSR 2015; 3(8):998-1008.
5. Bamiro OA, Bakre LG, Adeleye OA, Babalola CO and Femi-Oyewo MN. Formulation and evaluation of oral dissolving films of naproxen sodium from Terminalia randii gum. West African Journal of Pharmacy. 2020;31(1):97-110.
6. Deepthi A, Reddy BV and Navaneetha K. Formulation and evaluation of fast dissolving oral films of zolmitriptan. American journal of advanced drug delivery. 2014;2(2):153-63.
7. Ali MS, Vijendar C, Kumar SD and Krishnaveni J. Formulation and evaluation of fast dissolving oral films of diazepam. J Pharmacovigilance. 2016;4(3):210.
8. Raju PN, Kumar MS, Reddy CM and Ravishankar K. Formulation and evaluation of fast dissolving films of loratidine by solvent casting method. The pharma innovation. 2013;2(2).
9. Arya A, Chandra A, Sharma V and Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. Int J ChemTech Res. 2010;2(1):576-83.

10. Abhijeet K, Vishaka D, Dhanik P, Simarpreet kaurr S, Sushma RS and Nilesh MK. Formulation and Evaluation of Dextromethorphan hydrobromide Fast Dissolving Film. IJIPSR. 2015; 3(8):998-1008.
11. Brahmaiah B, Poornima G and Sreekanth N. Formulation and Evaluation of Fast Dissolving Films of Sumatriptan. Int J Adv Pharm. 2013; 3(2):118-21.
12. Anjum P, Mahesh KG, Neetesh KJ, Ankita D and Ankit A. Formulation and Evaluation of Fast Dissolving Oral Film of Promethazine hydrochloride using different surfactant. J Inn Pharm Bio Sci. 2016; 3(1):74-84.
13. Bhagyashri M, Viashali K, Suryakant J, Zamiruddin M and Vishvanath B. A Short Review on Fast Dissolving Oral Film. Wor J Pharm PharmSci. 2014; 3(3):463-75.
14. Priyanka P, Rikisha L, Mayur C and Ujjaval S. Development and Optimization of Fast Dissolving Orodispersible film of Baclofen using3^2 central composite design. IJPSR. 2014; 5(2):5539-47.
15. Mohammed AJ, Saleem MA, Rizwan HP, Imran K, Abdul M and Kamran A. Formulation and evaluation of oral fast dissolving film of Levocetrizine. Wor J Pharm PharmSci. 2014; 3(9):1310-23.
16. Hasan MR, Tabinda I, Mohammad S and Preeti J. Formulation design and evaluation of Baclofen Mouth Dissolving tablets. Eur J App Sci. 2012; 4(3):110-16.
17. Desai P and Basu B. Design and Evaluation of Fast Dissolving Film of Domperidone. Int Res J Pharm. 2012; 3(9):134-45.
18. Shweta K and Manoj KS. Preparation and evaluation of fast dissolving films of Losartan potassium. Asian J Pharm Life Sci. 2012; 2(4): 406-17.
19. Brahmaiah B, Poornima G and Sreekanth N. Preparation and evaluation of fast dissolving films of Sumatriptan. Int J Adv Biopharm. 2013; 3(2):118-21.
20. Poonam AP and Poonam PP. Formulation and evaluation of fast dissolving oral film of Bisoprololfumarate. Int J Pharm Sci Res. 2015; 6(1):135-42.