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## DEVELOPMENT AND OPTIMIZATION OF FAST DISSOLVING ORODISPERSIBLE FILM OF BACLOFEN USING $3^2$ CENTRAL COMPOSITE DESIGN

Patel Priyanka\*, Limbashiya Rikisha, Chavda Mayur and Shah Ujjaval

Bhagwan Mahavir College of Pharmacy, Surat, Gujrat, India

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### Correspondence to Author:

**Patel Priyanka**

(M. Pharm, Pharmaceutical  
Technology) Bhagwan Mahavir  
College of Pharmacy, Surat, Gujrat,  
India


**E-mail:** priyapatel3355@gmail.com

**ABSTRACT:** The aim of present research work to develop and optimize orodispersible film of baclofen to improve bioavailability and patient compliance. Orodispersible films of baclofen were prepared by solvent casting method using HPMC E5 LV as a film forming polymer and propylene glycol as a plasticizer, crospovidone as a superdisintegrant and sucralose was added as a sweetener. The physical mixture of drug and polymer characterized by FT-IR showed no incompatibility. A  $3^2$  central composite design was applied using two independent variables such as  $X_1$  (Polymer) and  $X_2$  (Propylene glycol) and folding endurance ( $Y_1$ ),  $T_{90\%}$  ( $Y_2$ ), *In-vitro* Disintegration time ( $Y_3$ ). The prepared films were evaluated for weight, thickness, folding endurance, disintegration time, *in vitro* drug release, drug content and their mechanical properties such as tensile strength and % elongation. From the result obtained optimized formulation was prepared with 2.58% w/v HPMC E5 LV and 2.02 % w/v of propylene glycol showed folding endurance of 68.59, disintegration time 53.4 seconds,  $T_{90\%}$  of 9.12 minutes. A stability study result reveals that there was no significant change after one month.

**INTRODUCTION:** The oral route of drug administration is the most common and convenient for patient use. Tablets and capsules represent the most commonly used solid oral dosage forms. However, many patients suffer from dysphagia or difficulty in swallowing, which can pose a compliance problem for such patients when medications are prescribed. It is estimated that 35% of the general population, 30–40% of elderly nursing home patients, and 25–50% of patients hospitalized for acute neuromuscular disorders and head injuries have dysphagia.<sup>1</sup>

FDSDS is easy to administer and provides better patient compliance in the elderly, pediatric, mentally retarded, nauseated and uncooperative patients.<sup>2</sup> This delivery system consists of the solid dosage forms that dissolve quickly i.e. within a matter of seconds in the oral cavity without the administration of water. The delivery system consists of a very thin oral strip which is simply placed on the patient's tongue or any other oral mucosal tissue and instantly gets wetted by saliva.<sup>3</sup>

The film rapidly hydrates onto the site of application. It then rapidly dissolves and disintegrates to release the medication for oromucosal absorption. Fast dissolving oral thin films are widely accepted by patients and also to the caregiver for their ease-of-delivery, portability and accurate dosing.<sup>4</sup> The robustness of the film depends upon the type and amount of polymer used and general dissolution time for orally dissolving film is 5–20 min. as per pharmacopoeia.<sup>5, 6</sup> They

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also provide quick onset of action within few seconds as the oro-mucosal absorption of drug occurs directly from the site of administration to the systemic circulation avoiding first pass metabolism to produce the desired effect.<sup>7</sup>

Fast-dissolving oral delivery systems include tablets, caplets, wafers, films, granules, and powders. There is a rising interest in the development of orodispersible films (ODFs) as an alternative to fast dissolving tablets<sup>8</sup>, which is attributed to their faster dissolution rate, higher durability, and better patient compliance. Recently, research work on the use of ODFs as promising carriers for multiple active pharmaceutical ingredients has emerged<sup>9, 10</sup>. Baclofen is structural analog of gamma aminobutyric acid is a centrally acting skeletal muscle relaxant, which is widely used in the treatment of spasticity resulting from multiple sclerosis, muscle spasms, muscular rigidity and spinal cord injuries, 3 where pain persist predominantly, in such cases the quick onset of action is of prime importance. Baclofen is moderately bitter in taste. Hence the present work was aimed to formulate the taste masked fast dissolving or dispersible film of baclofen.<sup>11</sup>

The dose of baclofen is either 10 or 25 mg given two or three times daily. Baclofen is an ideal drug candidate for an ODF application because of its special indication in patients with swallowing problems and its low-dose requirement. The formulation of Baclofen as a strip film to be placed on the patient's tongue for dose administration, without the need to swallow, would significantly facilitate dose administration, with subsequent improvement in patient compliance.<sup>12, 13</sup>

#### MATERIALS AND METHODS:

Baclofen was purchased from Triveni chemicals Vapi, HPMC E5 LV, Propylene glycol, PEG 400, Crospovidone and Glycerol were purchased from Astron chemicals Ahmadabad, HPMC E15 LV, PVA (poly vinyl alcohol), Sucralose, Xylitol, and Menthol were purchased from Chemdyes Corporation Ahmedabad.

#### FTIR study:

Fourier-transform infrared (FT-IR) spectra were obtained using an FT-IR spectrometer (Shimadzu

8400S, Japan). The Compatibility of baclofen with HPMC E5 LV and Propylene glycol individually and combine in physical mixture were previously ground and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:5 (Sample:KBr) ratio, respectively. The KBr discs were prepared by compressing the powders at a pressure of 5 tons for 5 min in a hydraulic press. Sixteen scans were obtained at a resolution of 4 cm<sup>-1</sup>, from 4000 to 400 cm<sup>-1</sup>.<sup>14</sup>

#### Taste evaluation:

The films were checked for various organoleptic characteristics such as appearance, size, taste etc. For evaluation of the taste, special controlled human taste panels are used.

**Part-1:** Tasting will be done by taking the Pure drug baclofen (up to 5mg) into the mouth, placing it on tongue for approximately 30 seconds without swallowing (the drug or saliva), and then spitting it out. Immediately after tasting each treatment, participants will score the treatments for taste as per following **Table 1**.

**TABLE 1: TASTE EVALUATION**

Numerical value	Scale
0	Tasteless or taste masked
1	Slightly bitter
2	Slight to moderate bitter
3	Moderate to strong bitter
4	Strong bitter

**Part-2:** Now after completing part-1, wash the mouth or gargles with drinking water 3 times. After that once again tasting will be done by taking the Baclofen sweetener complex(up to 5mg) into the mouth, placing it on tongue for approximately 30 seconds without swallowing (the drug or saliva), and then spitting it out. Immediately after tasting each treatment, participants will score the treatments for taste as per above table mentioned in part-1. Participants will be permitted to select score number from above table between the minimum score of 0 and the maximum score of 4. The higher the score, the greater the bitterness. If more than 50% patients feel no bitterness, the drug will be considered as taste masked.<sup>16</sup>

#### Preliminary trials:

**Selection of polymer:** Various polymers were selected and trails were done. HPMC E5 LV below

2% did not show good film (the film was not easily peelable) and above 3% concentration, the film was sticky in nature. Hence all the percentage between 2–3% was trailed of HPMC. A range of 2–3% was selected for the formulation of films.

### Selection of plasticizer:

Various plasticizers were selected and trails were done. Propylene glycol below 1.5% did not show good film properties as was tested by the folding endurance of the film. Hence, a range of plasticizer (propylene glycol) was used in the range of 1.5–2.5%.<sup>15</sup>

### Preparation of orodispersible films (ODF):

The required percentage of polymer solution was prepared by dispersing the polymer powder in distilled water with continuous stirring. After continuous stirring the solution was left undisturbed for three to four hours to remove all the air bubbles. Accurately weighed quantity of drug, plasticizer and all other excipients was separately dissolved in distilled water in another beaker.

**TABLE 3: FORMULA FOR EXPERIMENTAL DESIGN**

Ingredients	PF1	PF2	PF3	PF4	PF5*	PF6	PF7	PF8	PF9
Baclofen (mg)	159	159	159	159	159	159	159	159	159
HPMC E5 LV(% w/v)	450	450	450	600	600	600	750	750	750
Propylene Glycol (% w/v)	1.5	2.0	2.5	1.5	2.0	2.5	1.5	2.0	2.5
Sucralose (mg)	60	60	60	60	60	60	60	60	60
Crospovidone (mg)	90	90	90	90	90	90	90	90	90
Menthol (mg)	100	100	100	100	100	100	100	100	100
Xylitol (mg)	320	320	320	320	320	320	320	320	320
Ethanol (ml)	3	3	3	3	3	3	3	3	3
Distilled Water (up to)	20	20	20	20	20	20	20	20	20

\* Indicates that three replication of central level will be considered for number of runs in design expert software 9.0.2.0. i.e. there will be total 11 runs.

### Determination of evaluation parameters:

**Properties:** Colour, transparency and surface of the oral films were evaluated by visual inspection.

**In-vitro disintegration time:** The *in vitro* disintegration time of film strips was determined by the visual method. The film strip was placed in a glass Petri dish containing 25 ml of distilled water at 37°C, with swirling every 10 s. The *in-vitro* disintegration time was recorded as the time at which the film starts to break or disintegrate.<sup>19</sup>

**Folding endurance:** Folding endurance was determined by repeatedly folding the film at the same place till it break. The numbers of times the

After complete hydration of the polymer with water, drug-plasticizer and all other excipient solutions were added and mixed thoroughly, and the volume was made up ten milliliters with distilled water. The polymeric solutions were then poured on the mold, allowed to dry and stored in aluminum foil.<sup>15</sup>

The different formulations were prepared incorporating polymer (2.5–3.0% w/v), plasticizer (1.5–2.5% w/v), and water using 3<sup>2</sup> central composite design and optimized formulation was generated using statistical screening. The eleven runs of the experiment were evaluated for the percentage folding endurance (Y<sub>1</sub>), T<sub>90%</sub> (Y<sub>2</sub>, time required to release 90% of drug), disintegration time (Y<sub>3</sub>) are listed in **Table 3**. The composition of factorial design batches is shown in **Table 3**.

**TABLE 2: INDEPENDENT VARIABLES IN DESIGN**

Factor	Levels		
	-1 (Low)	0 (medium)	+1 (High)
X1(polymer)%W/V	2%	2.5%	3%
X2(plasticizer)%W/V	1.5%	2.0%	2.5%

film can be folded at the same place without breaking give the value of folding endurance.<sup>14</sup>

### Thickness:

The thickness of each sample was measured using vernier Calipers. Ten film samples (2cm×2cm) were taken and the mean thickness calculated.

### In-vitro dissolution study:

Five film units (2 cm× 2 cm) were cut from the four corners and the central part of the film. Each film unit was placed in 100 ml of distilled water. The solutions were filtered and analyzed at 219 nm using UV-Visible Spectrophotometer. The

dissolution study was carried out using USP paddle apparatus at  $37^{\circ}\text{C} \pm 0.5^{\circ}\text{C}$  using 250 ml of phosphate buffer (pH 6.8) as dissolution medium. The agitation rate of paddle was 50 rpm. The drug loaded film (2cm× 2cm) was placed in medium. Five ml samples were withdrawn at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10. Minute times and were filtered through whatman filter paper and analyzed spectrophotometrically at 219 nm. An equal volume of the fresh dissolution media, maintained at the same temperature, was added after withdrawing the sample to maintain the volume.<sup>19</sup>

**Surface pH:** Surface pH of the films was determined by placing the film in water and followed by placing pH paper on films. The change in the colour of pH paper was observed and reported.

**Mechanical Properties:** Mechanical Properties such as tensile strength and % elongation were measured as per given below:<sup>19</sup>

#### **Tensile Strength:**

The tensile strength of the ODF was measured using a texture analyser (TX-XT2 texture analyser, North America). The samples of ODF at dimension of 20×20 mm, were held vertically between two clamps of 1 cm apart. The ODF was pulled by the clamp at a rate of 100 mm/min and contact force of 0.05 N. The tensile strength was defined as the maximum load force to break the ODF and calculated by dividing the applied load at rupture with the cross-sectional area of the film.

Tensile Strength ( $\text{kg}/\text{cm}^2$ ) = Force at break (kg)/  
Initial cross sectional area of the sample ( $\text{cm}^2$ )

#### **% Elongation:**

When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases.

% Elongation = Increase in length ×100/Original length

#### **Short term accelerated stability study:**

The hygroscopic nature of ODF makes it unstable, which is a major disadvantage. Special packaging

is needed to protect the product, which increases the production cost. Development of a stable formulation would help to reduce the packaging cost. The optimized formulation of orodispersible film stored in stability chamber under these conditions given below:

#### **Storage conditions:**

Temperature at  $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ , and

Room temperature at  $75\% \text{RH} \pm 5\% \text{RH}$

Time period: 1 month

At the end of month, the films were usually examined for any physical changes, changes in drug content and *in vitro* disintegration time, cumulative drug release (% CDR).

#### **3<sup>2</sup> Central composite Design ( $\alpha=1$ , Face Centered):**

A 3<sup>2</sup> Central composite Design was used in the present study. In this design 2 factors are evaluated, each at 3 levels. The Concentration of polymer ( $X_1$ ) and Concentration of plasticizer ( $X_2$ ) was selected as independent variables. Folding endurance ( $Y_1$ ),  $T_{90\%}$  (Time required to release 90% of drug release in minutes,  $Y_2$ ), Disintegration time (sec)  $Y_3$  were selected as dependent variables.

For optimization, the effects of independent variables upon the responses were modelled using the following quadratic mathematical model generated by 3<sup>2</sup> factorial design<sup>20</sup>:

$$Y = b_0 + b_1X_1 + b_2X_2 + b_3X_1X_2 + b_4X_{21} + b_5X_{22}$$

Where, Y is the response,  $b_0$  is the intercept, and  $b_1$ ,  $b_2$ ,  $b_3$ ,  $b_4$ ,  $b_5$  are regression coefficients.  $X_1$  and  $X_2$  are individual effects;  $X_{21}$  and  $X_{22}$  are quadratic effects;  $X_1X_2$  is the interaction effect. One-way ANOVA was applied to estimate the significance ( $p < 0.05$ ) of the model and individual response parameters. The surface response plots and contour plots were analyzed to reveal the effect of independent factors on the measured responses.

#### **RESULT AND DISCUSSION:**

**FTIR study:** The pure drug baclofen showed **Figure 1** and **Figure 2** absorption peaks with a strong C=O of carboxylic group at  $1499.7 \text{ cm}^{-1}$ . C-H stretching shown absorption peak at  $2984.94 \text{ cm}^{-1}$

<sup>1</sup>. Structurally, baclofen consists of amine N-H bending which showed its absorption peak at  $1627.01\text{cm}^{-1}$ . C-Cl stretching shown absorption peak at  $1094.69\text{cm}^{-1}$ . It was found that all the prominent functional group peaks were observed in drug-polymer mixture and frequencies of drug and physical mixture are similar. Suggesting that it is the IR of mixtures but not of any reaction product and there was no interference in the functional groups as the principle peaks of the baclofen were found to be unaltered in the spectra of the drug-polymer physical mixture. This confirmed that there was no interaction between drug-excipient or incompatibility between drug and excipient.<sup>17, 18</sup>

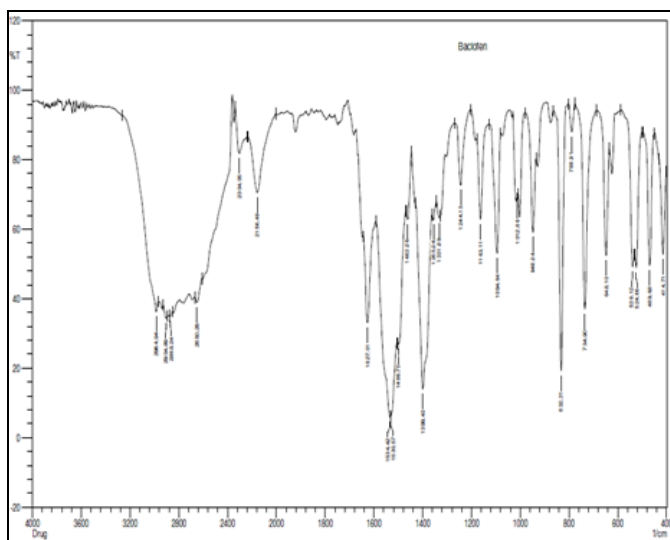


FIG. 1: FTIR SPECTRA OF PURE DRUG BACLOFEN

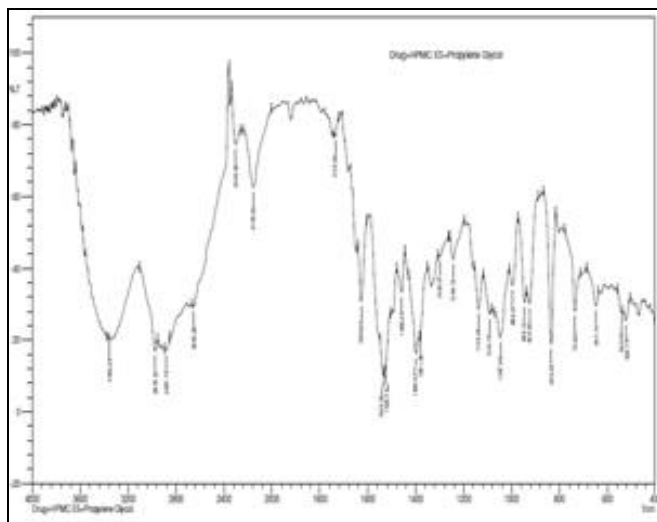


FIG. 2: FTIR SPECTRA OF PHYSICAL MIXTURE

#### Evaluation of taste:

Results for taste masking were shown in the **Table 4**. The developed formulations were tested for bitter taste by using sensory approach.<sup>16</sup>

TABLE 4: RESULTS FOR TASTE MASKING OF DEVELOPED FORMULATION

Formulation Code	Volunteer						Bitter Index
	1	2	3	4	5	6	
F1	0	0	0	0	0	0	0
F2	0	0	0	0	1	0	1
F3	0	0	0	0	0	0	0
F4	1	0	0	0	0	0	1
F5	0	0	0	0	0	0	0
F6	0	0	0	0	0	0	0
F7	0	0	0	0	0	0	0
F8	0	0	0	0	0	0	0
F9	0	0	0	0	0	0	0

As per methodology section **2.4.2**, more than 50 % of volunteers feels no bitter taste. The bitter index for all formulation was found to be zero and 1. Hence the bitter taste of drug was masked.

#### Optimization of independent variables:

HPMC in a range of 2.0-3.0 % was selected for the formulation of fast dissolving orodispersible films (ODF). It was found that on increasing the amount of polymer above 3% the percentage drug release and disintegration time kept on increasing; while at 2.5% the disintegration time kept on decreasing. Plasticizer was selected in the range of 1.5-2.5%. Since above 2.5% ODF became stickier and below 1.5% the film did not show good flexibility of ODF.

#### Characterization of fast dissolving film:

Baclofen orodispersible films prepared were transparent, colorless, thin, and soft, with no spot on the film surface. The prepared ODF was evaluated according to the following parameters: % drug content, thickness, weight variation, surface pH, folding endurance and percentage drug release, *in-vitro* disintegration time shown below in **Table 5**.

As shown in **Table 5**, folding endurance was increase from formulation F1 to F6, as the polymer concentration increases. But formulation F7, F8 and F9 showed decrease in folding endurance due to increase polymer concentration so, film becomes brittle. It was concluded that as the polymer concentration increases from F1 to F9 formulation, there was increase in *in-vitro* disintegration time. There is increase in tensile strength and increase in % elongation from F1 to F9 formulation due to increase in plasticizer concentration.

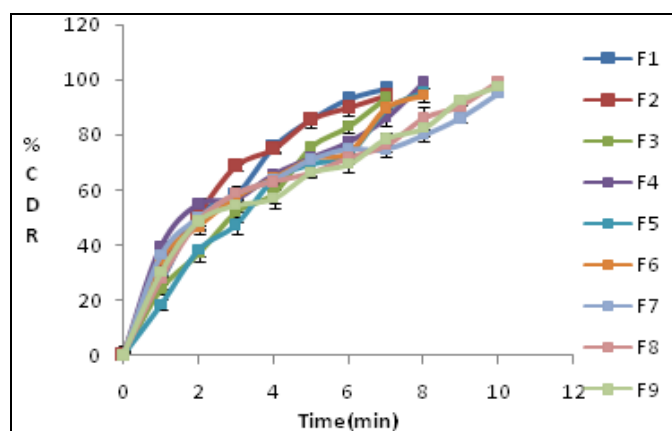
**TABLE 5: DATA OF EVALUATION PARAMETERS**

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Weight (mg) ± SD	88.67 ± 1.5	90.11 ± 1.1	90.16 ± 1.43	102.72 ± 1.52	107.77 ± 3.2	106.83 ± 2.08	119.3 ± 2.8	123.44 ± 1.82	124.5 ± 2.8
Thickness (mm) ± SD	0.19 ± 0.09	0.20 ± 0.02	0.17 ± 0.01	0.22 ± 0.04	0.31 ± 0.04	0.28 ± 0.01	0.33 ± 0.03	0.21 ± 0.02	0.23 ± 0.05
Folding Endurance (Average)	41.53	46.22	51.11	50.28	52.29	55.71	51.75	52.6	53.84
% Drug release	96.47 ± 3.11	94.07 ± 2.80	93.31 ± 1.11	99.07 ± 1.9	96.61 ± 2.1	97.48 ± 1.8	94.96 ± 3.0	99.04 ± 2.1	97.61 ± 2.22
<i>In-vitro</i> disintegration time (sec) ± SD	41.53 ± 2	46.2 ± 2	51.11 ± 4	50.28 ± 2	52.24 ± 3	55.71 ± 4	51.75 ± 3	52.6 ± 2	53.8 ± 2
Drug content (%)	99.62	98.28	99.11	98.30	99.2	98.7	97.08	98.66	97.96
pH	7.0	7.0	6.89	6.90	7.0	6.69	6.90	6.70	7.0
Tensile strength (Mpa)	3.29	3.86	4.13	3.09	3.95	4.08	2.25	3.99	4.9
% Elongation	10.5	12.7	19.48	25.93	40.38	43.61	24.71	30.52	19.53

(Mean ± S.D.), n=3

### %CDR of F1 to F9 batches:

By plotting various graphical models the *in vitro* drug release profile of the prepared orodispersible films were studied. The percentage cumulative drug release data from formulations F1 to F9 were mentioned in **Figure 3**. It indicates that cumulative percentage drug release of was decrease as polymer concentration increase.



**FIG. 3: %CDR OF F1 TO F9 BATCHES**

### Optimization:

For the  $3^2$  factorial design, a total of 9 experimental trial formulations were proposed by Design Expert® Version 9.0.2.0 software for two factors, concentration of polymer and concentration of plasticizer, which were varied at three different levels (high, medium and low). According to this experimental trial proposal, 9 formulations of film containing baclofen were prepared by solvent casting technique. The effects of independent variables (factors) upon Folding endurance,  $T_{90\%}$  (Time required to release 90% of drug release in minutes), Disintegration time (sec) were

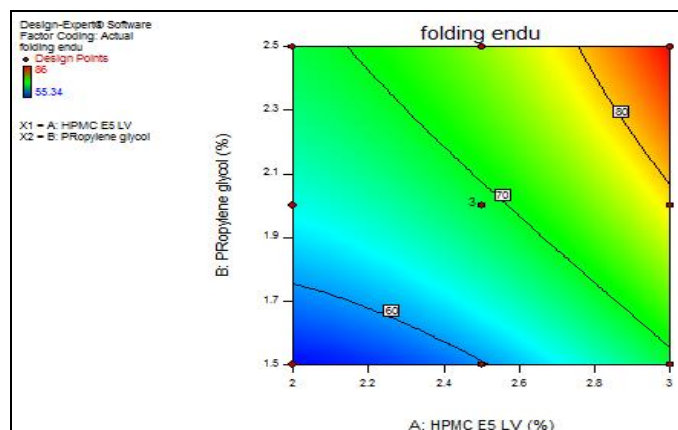
investigated as optimization response parameters in this study.

### Response 1 ( $Y_1$ ): Folding endurance:

The model proposes the following polynomial equation for Folding endurance

$$Y_1 = + 68.90 + 7.66 * A + 7.59 * B - 0.99 * AB + 2.36 * A^2 - 1.55 * B^2$$

where,  $Y_1$  is folding endurance,  $X_1$  is the polymer concentration, and  $X_2$  is the concentration of plasticizer. The Model F-value of **4633.74** implies the model is significant  $p < < 0.0001$ . The contour plots **Figure. 4** showed the effect of different independent variables on folding endurance ( $Y_1$ ).



**FIG. 4: CONTOUR PLOT SHOWING THE EFFECT OF POLYMER CONCENTRATION ( $X_1$ ) and plasticizer ( $X_2$ ) on response  $Y_1$**

The folding endurance of film was increases as the amount of propylene glycol and polymer increases. In above polynomial equation for  $Y_1$  response,  $b_1$  with positive value was obtained which described

increase in concentration of factor X<sub>1</sub> (HPMC E5 LV), there was increase in response Y<sub>1</sub> (Y<sub>1</sub>= Folding Endurance). Coefficient b<sub>2</sub> with positive value for Y<sub>1</sub> was obtained which also describe increase in concentration of factor X<sub>2</sub> (propylene glycol), there was increase in response Y<sub>1</sub> (Y<sub>1</sub>= Folding Endurance).

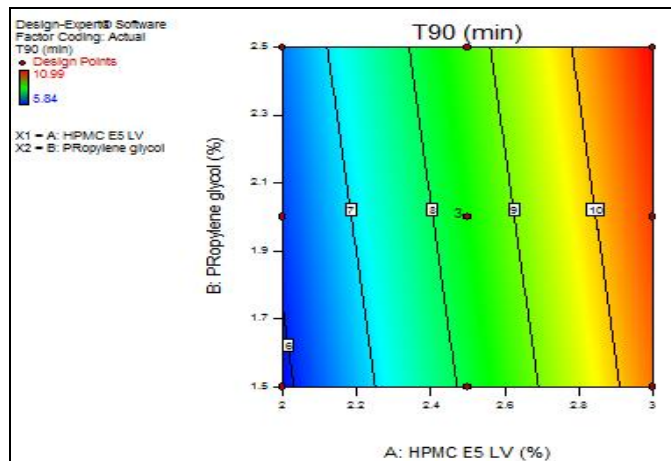
**Response 2 (Y<sub>2</sub>):**

**T<sub>90%</sub> (Time required to release 90 % of drug):**

$$Y_2 = + 8.43 + 2.27*A + 0.30*B$$

where, Y<sub>1</sub> is T<sub>90%</sub> (Time required to release 90 % of drug), X<sub>1</sub> is the polymer concentration, and X<sub>2</sub> is the concentration of plasticizer. The Model F-value of 29507.37 implies the model is significant p < 0.0001. The contour plots **Figure. 5** showed the effect of different independent variables on T<sub>90%</sub> (Time required to release 90 % of drug) (Y<sub>2</sub>). The T<sub>90%</sub> of film was increases as the amount of polymer and plasticizer increases.

In above polynomial equation for Y<sub>2</sub> response, b<sub>1</sub> with positive value was obtained which described increase in concentration of factor X<sub>1</sub> (HPMC E5 LV), there was increase in response Y<sub>2</sub> (Y<sub>2</sub>= T<sub>90%</sub>). Coefficient b<sub>2</sub> with positive value for Y<sub>2</sub> was obtained which also describe increase in concentration of factor X<sub>2</sub> (propylene glycol), there was increase in response Y<sub>2</sub>.



**FIG. 5: CONTOUR PLOT SHOWING THE EFFECT OF POLYMER CONCENTRATION**

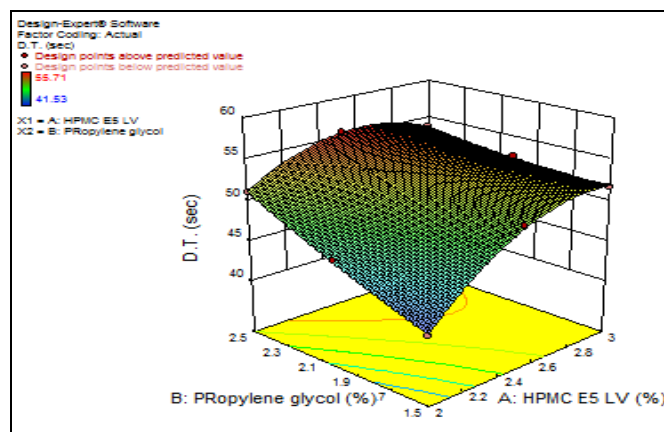
**(X<sub>1</sub>) and plasticizer (X<sub>2</sub>) on response Y<sub>2</sub>**

**Response 3 (Y<sub>3</sub>): (In-vitro disintegration time)**

$$Y_3 = + 52.34 + 3.22*A + 2.85*B - 1.87 *AB - 3.13*A^2 + 0.45*B^2$$

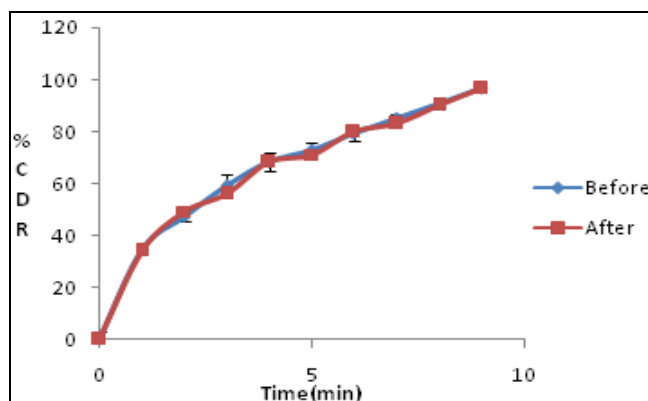
where, Y<sub>3</sub> is *in-vitro* disintegration time, X<sub>1</sub> is the polymer concentration, and X<sub>2</sub> is the concentration of plasticizer. The Model F-value of **430.45** implies the model is significant p < 0.0001. The contour plots **Figure. 6** showed the effect of different independent variables on *In-vitro* disintegration time (Y<sub>3</sub>). The *In-vitro* disintegration time of film was increases as the amount of polymer and plasticizer increases, but after excessive amount of polymer increase the film became brittle so there was slight decrease in *in-vitro* disintegration time.

In above polynomial equation for Y<sub>3</sub> response, b<sub>1</sub> with positive value was obtained which described increase in concentration of factor X<sub>1</sub> (HPMC E5 LV), there was increase in response Y<sub>3</sub> (Y<sub>3</sub>= *In-vitro* disintegration time). Coefficient b<sub>2</sub> with positive value for Y<sub>3</sub> was obtained which also describe increase in concentration of factor X<sub>2</sub> (propylene glycol), there was increase in response Y<sub>3</sub> (Y<sub>3</sub>= *In-vitro* disintegration time).



**FIG. 6: CONTOUR PLOT SHOWING THE EFFECT OF POLYMER CONCENTRATION (X<sub>1</sub>) and plasticizer (X<sub>2</sub>) on response Y<sub>3</sub>**

**%CDR of optimized batch before and after stability study:**



**Short term Accelerated stability testing of optimized batch:**

From the **Table 6**, The stability studies indicate no physical change in appearance except a slight

increase in *in-vitro* disintegration time, % cumulative drug release and slight decrease in drug content.

**FORMULATION AND EVALUATION OF OPTIMIZED CHECKPOINT BATCH:****TABLE 6: FORMULATION OF OPTIMIZED FORMULATION (OF)**

Ingredients	Baclofen (mg)	HPMC E5 LV (%w/v)	Propylene glycol (% w/v)	Sucralose (mg)	Crospovidone (mg)	Menthol (mg)	Xylitol (mg)
Optimized formulation(OF)	159	2.58	2.02	60	3	100	320

Optimized formulation contains Ethanol 3 ml and Distilled water 20 ml.

**TABLE 7: EVALUATION OF OPTIMIZED BATCH**

Parameters	Weight (mg) $\pm$ SD	Thickness (mm) $\pm$ SD	Folding endurance	% Drug release	T <sub>90%</sub> in minutes
Optimized formulation(OF)	110.55 $\pm$ 2.97	0.38 $\pm$ 1.63	68.59	96.52	9.12

(Mean  $\pm$  S.D.), n=3

**TABLE 8: EVALUATION OF OPTIMIZED BATCH**

Parameters	<i>In-vitro</i> disintegration time (sec)	Drug content (%)	Taste	Tensile strength (Mpa)	% Elongation
Optimized formulation(OF)	53.4 $\pm$ 1.4	99.83	Sweet	3.69	32.07

(Mean  $\pm$  S.D.), n=3

**TABLE 9: COMPARISON OF EXPERIMENTAL AND PREDICTED RESULT**

Parameters	Optimized formulation (experimental response)	Predicted response
Folding endurance	70.64	68.59
T <sub>90%</sub> (min)	8.84	9.12
<i>In-vitro</i> disintegration time (sec)	52.91 $\pm$ 1.4	53.4 $\pm$ 2.1

(Mean  $\pm$  S.D.), n=3

**CONCLUSION:** The main aim of the present study was develop taste masked orodispersible film of baclofen for the treatment of muscle spasm resulting from multiple sclerosis. Orodispersible film preped by HPMC E5 LV as a film forming polymer, Propylene glycol as a plasticizer, sucralose as sweetener, menthol as Flavoring agent, Xylitol sweet taste that imparts a cooling sensation. Optimization was done by using 3<sup>2</sup> central composite design.

The optimized batch was prepared by using HPMC E5 LV (2.58% w/v) and propylene glycol (2.02 % w/v).It gave folding endurance value 68.59, T<sub>90%</sub> (Time required to release 90% drug release) was 9.12 minutes and disintegration time of 53.4 sec. Developed orodispersible film was stable after one month of storage at 40°C / 75% RH. From the above research work it is concluded that

orodispersible film of baclofen was successfully designed and developed by solvent casting method and it is suitable for quick onset of action, improved bioavailability and patient compliance.

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