International Journal of Research and Review
Vol.7; Issue: 5; May 2020
Website: www.ijrrjournal.com
Original Research Article *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Development and Evaluation of Buccal Film of Carvedilol Phosphate

Vishakha Dhananjay Jagtap

Department of Pharmaceutics, Lecturer at Seth Govind Raghunath Sable College of Pharmacy, Saswad, Maharashtra

ABSTRACT

The present study was undertaken to develop and evaluate buccal films of Carvedilol phosphate with an aim of improving patient compliance. Ease of administration with fast release of the drug was anticipated as the buccal films were prepared by using novel film forming agent obtained from natural source. Carvedilol phosphate buccal films were prepared by natural film former obtained from mucilage of Plantago ovata husk by solvent casting method. The films were evaluated for thickness uniformity, weight variation, surface pH, folding endurance, drug content uniformity, swelling index, disintegration time, tensile strength, in vitro drug dissolution study and ex-vivo drug permeation studies. *Ex vivo* permeation studies through goat buccal mucosa revealed optimum drug permeation within the span of 10 minutes. The factorial design was adopted to optimize the formulation. The optimized formulation of Carvedilol phosphate exhibited drug release upto 98.42 % at the end of 10 min. It was concluded that buccal film of Carvedilol phosphate can be formulated using Plantago ovata husk gel as a hydrophilic film forming material. The study suggested that Carvedilol phosphate can be conveniently administered orally in the form of buccal film to improve release, patient compliance and hence may show improved bioavailability.

Key Words- Buccal film, Carvedilol phosphate, natural film former, Plantago Ovata Husk, release, bioavailability

INTRODUCTION

Over the decades mucoadhesion has become popular for its potential to optimize localized drug delivery, by retaining a dosage form at the site of action (e.g. within the gastrointestinal tract) or systemic delivery by retaining the formulation in intimate contact with the absorption site (e.g. buccal cavity.)Well defined bioadhesion is the ability of a material (synthetic or biological) to adhere to a biological tissue for an extended period of time. The use of mucoadhesive polymers in buccal drug delivery has a greater application. Various mucoadhesive devices, including tablets, films, patches, disks, strips, ointments and gels, have recently been developed. However, buccal patch offer greater flexibility and comfort than the other devices. [1] Buccal patch is a non dissolving thin matrix modified release dosage form composed of one or more polymer films or layers containing the drug and/or other excipients. The patch may contain a mucoadhesive polymer layer which bonds to the oral mucosa, gingiva, or teeth for controlled release of the drug into the oral mucosa (unidirectional release), oral cavity (unidirectional release), or both (bidirectional release). The patch is removed from the mouth and disposed of after a specified time. [2] Buccal controlled drug delivery system has been developed since the environment of the oral cavity provides potential sites for drug delivery. The acid hydrolysis and first pass effects can be avoided. The release of drug can be affected by continuous secretion of saliva. The pH of buccal cavity ranges between 5-7, and does not cause any problem to the drug with the right dosage form design and formulation; the permeability and the local environment

of the mucosa can be controlled and manipulated in order to accommodate drug permeation. [3]

Mechanism of Buccoadhesion

Buccoadhesion is the attachment of the drug along with a suitable carrier to the mucous membrane. Buccoadhesion is a complex phenomenon which involves wetting, adsorption and interpenetration of polymer chains. Buccoadhesion has the following mechanism-

1. Intimate contact between a bioadhesive and a membrane (wetting or swelling phenomenon)
2. Penetration of the bioadhesive into the tissue or into the surface of the mucous membrane (interpenetration). [4]

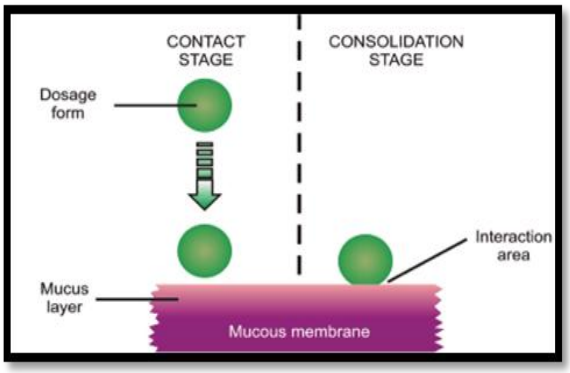


Figure1: Buccoadhesion Process [24]

Buccal Routes Drug Absorption

The cell membranes are relatively lipophilic and may create a barrier to polar hydrophilic permeants, and therefore, hydrophilic molecules perhaps permeate the buccal mucosa via the paracellular route. Though tight junctions are rare in oral mucosa and their existence between intestinal epithelial cells is the key barrier to paracellular drug transport through the intestine consequentially, passage of drugs through the intercellular domain of the buccal epithelium is more favorable than intestine. [5-6]

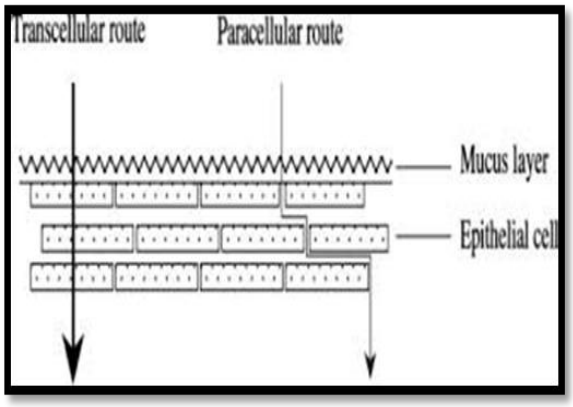


Figure2: Buccal route Absorption Mechanism [5]

MATERIAL AND METHODS

A gift sample of Carvedilol phosphate is provided by Alkem Laboratories (Mumbai) India. Plantago ovate Husk is isolated in laboratory. Sodium Starch glycolate is gifted by Ranbaxy Lab, Punjab. Sucrose, Polyethylene glycol 400, citric acid, orange flavor is provided by Research lab fine chem. Industries (Mumbai). Iconavit Red is provided by Colorcon Asia Pvt. Ltd (Goa).

METHODOLOGY

The Buccal films were prepared by solvent casting technique. Natural film former obtained from Plantago Ovata Husk is used as a film forming polymer. Film forming polymer was dissolved in distilled water and Carvedilol phosphate was added in to it. Mixture was stirred continuous by adding PEG400 (plasticizer) and other excipients mentioned in table1. Pour the solution in to petri plate and dried at 320mW for 10 min. Then the film was carefully removed and cut into suitable size i.e. 2cm x 1.5cm. The film was evaluated for folding endurance, thickness and % drug release.

Preparation and evaluation of factorial batches of Buccal film

A 2^2 factorial design was implemented for optimization of buccal film formulation of Carvedilol phosphate. According to the model it contained 2 independent variables at 2 levels, +1, -1. According to model total four formulations are possible, the

composition of different formulations are shown in Table 1. The different independent variables were addition of Sodium Starch Glycolate (X_1) and Plasticizer (X_2) and no addition of Sodium Starch Glycolate (X_1) and Plasticizer (X_2). Dependent factors included Disintegration time and folding endurance.

Table 1: Compositions of factorial batches

Formulation Contents in milligram (mg)	Formulation Code			
	F1	F2	F3	F4
Drug	25	25	25	25
Plantago ovate Husk gel	235	235	235	235
PEG 400 (%)	16	-	16	-
Superdisintegrant (%)	6	6	-	-
Citric Acid	9.9	9.9	9.9	9.9
Sucrose	8.8	8.8	8.8	8.8
Orange Flavor	q.s	q.s	q.s	q.s
Colour	q.s	q.s	q.s	q.s
Water (mL)	1	1	1	1

Table 2: Factorial Design for preparation of batches

Batches code	Variable Level In Coded Form	
	X_1	X_2
F_1	+1	+1
F_2	+1	-1
F_3	-1	+1
F_4	-1	-1

Table 3: Translation of Coded Value in Actual Unit

Variable level	(-1)	(+1)
X1=Amt.of Superdisintegrant [SSG] (%)	0	6%
X2= Plasticizer (%)	0	16%

The buccal films of factorial batches were evaluated for weight variation, thickness, tensile strength, Surface pH, folding endurance, Drug content uniformity, disintegration time, in vitro dissolution study, swelling index, ex-vivo diffusion study.

Evaluation parameters:

Weight of the film

All samples of 3cm^2 from each batch were randomly taken and weighed individually each film. Average weight is calculated and analyzed weight of film. [7]

Thickness

All the batches were evaluated for thickness using calibrated micrometer screw gauge. The thickness was measured at five different points of the each film and mean value was calculated. This was done to ascertain uniformity in the thickness of the film as it is directly related to the accuracy of dose in the film and supports the reproducibility of the method used for the formulation. [8]

Tensile strength

The tensile strength is the property of the film that requires a load to cause load deformation failure of film. Film strips in special dimension were held between two clamps positioned at a specific distance. Tensile strength was calculated by applying load at rupture as a mean of three measurements and cross sectional area of fractured film from following equation. [9]

Tensile strength (N/mm^2) = breaking force (N)/ cross sectional area of sample (mm^2)

Surface pH of the film

The films were allowed to swell by keeping them in contact with 1 ml of distilled water for 2 h at room temperature, and pH was noted down by bringing the electrode in contact with the surface of the film, allowing it to equilibrate for 1 min. [10]

Folding endurance

Folding endurance is to be determined by repeatedly folding the film at the same place, till it broke. The number of times, the film could be folded at the same place without breaking gives the value of folding endurance. [11]

Drug Content uniformity

Three films from each formulation batch were dissolved in 100 ml of pH 6.8 buffer separately and mixture was suitably diluted. The amount of drug in film was measured absorbance spectrophotometrically at 242 nm. The average drug content was calculated. [12]

In vitro disintegration time

It was determined visually in a petr iplate containing 2 ml distilled water with swirling every 10 seconds. The time at which film started to break or disintegrate was recorded as the in vitro disintegration time. It was performed in triplicate for all the batches. [13]

In vitro dissolution study

In vitro dissolution studies were carried out using USP type II apparatus. pH 6.8 buffer (50 mL) was used as a dissolution medium at 50 rpm speed and 37^{0}C temperature. At

periodic time intervals, 1 ml samples were withdrawn and replaced with the equal quantity of fresh dissolution medium. Samples were filtered through 0.45 µm Whatman filter paper, and analyzed spectrophotometrically at λmax of Carvedilol phosphate. The in vitro dissolution studies were performed in triplicate for all the batches. [14,15]

Dissolution kinetics study

It was done by determining the best fit mathematical model for formulations F1 to F2.

R and k values for different mathematical models were determined putting the dissolution data in respective mathematical models. The model for which the R value was the highest was considered the best fit model for the concerned formulation. The n value for the best fit model was recorded and it was used to determine the fickian or non-fickian diffusion pattern. [16]

Swelling index

The initial weight of the film was determined using a digital balance (W0). Then the films were allowed to swell on the surface of petri plate and kept in an incubator maintained at 37 °C. Weight of the swollen film was determined (Wt) at predetermined time intervals for 5 min. The percentage of swelling (% S) was calculated using the following equation. [17]

% S= (Wt-Wo)*100 /Wo

Where **Wt** is the weight of swollen patch after time t, $\mathbf{W_0}$ is the initial weight of patch at t=0.

Ex-vivo diffusion study

For in vitro release study, goat buccal mucosa membrane was used as a barrier membrane with Phosphate buffer (pH 6.8) as a medium. The films were evaluated for drug release using franz diffusion cells. Buccal mucosa membrane was mounted between the donor and receptors compartments. The film was placed on the mucosal membrane. The diffusion cell was placed in simulated saliva maintained at 37±2°C.The receptor compartment was filled with 50 mL phosphate buffer (pH 6.8) and hydrodynamics was maintained by stirring with a magnetic bead at 50 rpm. 1 mL sample was withdrawn and replaced with 1 mL fresh medium to maintain the sink condition. The samples were analyzed in U.V. spectrophotometer at 242 nm. [18, 19]

Stability study

Stability of a pharmaceutical product may be defined as the capability of a particular formulation, in a specific container / closure system, to remain within its physical, chemical, microbiological, therapeutic and toxicological specifications. The stability of all the formulations was carried out at different temperatures as per ICH guidelines. [20]

Stability study was carried out storage conditions; one was normal room conditions at 40^0C/75% RH for 3 months. Formulation F1 was packed in butter paper followed by aluminum foil. After 3 months, the films were evaluated for the DSC, FTIR, Folding endurance, disintegration time, drug content and in vitro drug release. [21]

RESULT AND DISCUSSION

The buccal films of factorial batches were evaluated for weight variation, thickness, tensile strength, Surface pH, folding endurance, Drug content uniformity, disintegration time, in vitro dissolution study, swelling index, ex-vivo diffusion study.

There was need to improve the release further. So it was decided to add Superdisintegrant to improve release of the drug from formulation further within 10 min. Sodium starch glycolate (SSG) has good hydrophilic property and highest swelling index as compared to other superdisintegrants like Croscarmellose sodium and Crosspovidone. Sodium starch glycolate is reported to improve release and bioavailability of poorly soluble drugs. [22] The usual concentration of SSG in formulation as a superdisintegrant is 2-8%.

[23] The addition of plasticizer also affects on the folding endurance of the film. Optimum folding endurance is essential as this parameter conveys suitability / processability of the buccal films for proper packaging.

Table 4: Data for Responses of Factorial formulations.

Response*	Disintegration Time (seconds)	Folding endurance
Formulation code		
F1	124±0.05	262±0.07
F2	126±0.69	244±1.19
F3	183±0.16	274±2.54
F4	248±0.18	230±1.15

*All values are expressed as Mean ± SD, (n = 3)

Regression analysis

The data obtained after evaluation of factorial batches was analyzed by using commercially available software Design Expert version 9.0.4.1. To describe the response surface curvature, the design was evaluated by quadratic model, which bears the form of equation -

$$Y = b_0 + b_1X_1 + b_2X_2 + b_3X_1X_2 + b_4X_1^2 + b_5X_2^2 \quad \text{.....Eq}^n\text{. 9.1}$$

Where Y is the response variable,

b_0 the constant, an arithmetic mean of all responses

b_1, b_2... the regression coefficients,

b_4, b_5... the regression coefficients show linearity

b_3... interaction coefficient show how response changes when two

Factors are simultaneously changed.

X_1 and X_2 stand for the main effect,

X_1X_2 are the interaction terms.

A.Effect of independent variables on Disintegration time (D.T.)

The polynomial equation obtained was:

$$Y \text{ (disintegration time)} = 181.58 - 57.42X_1 - 4.75X_2 + 4.25X_1X_2 \quad \text{.....Eq}^n\text{. 9.2}$$

Due addition of superdisintegrant disintegration time decreased as indicated by negative coefficient of X_1. Due to addition of plasticizer disintegration time decreased as indicated by negative coefficient of X_2. The interaction between the factor X_1 and X_2 was considerable and both were found to add the effect of each other. It was obvious by positive coefficient of X_1 X_2.

Table 5: ANOVA for selected factorial model (Response 1)

Response – 1 (Disintegration time) Analysis of variance						
Source	**Sum of square**	**Df**	**Mean square**	**F – value**	**P-value Prob>F**	
Model	40047.58	3	13349.19	2715.09	< 0.0001	Significant
A-Amt. of Gel	39560.08	1	39560.08	8046.12	< 0.0001	
B-concentration of PEG 400	270.75	1	270.75	55.07	< 0.0001	
AB	216.75	1	216.75	44.08	0.0002	

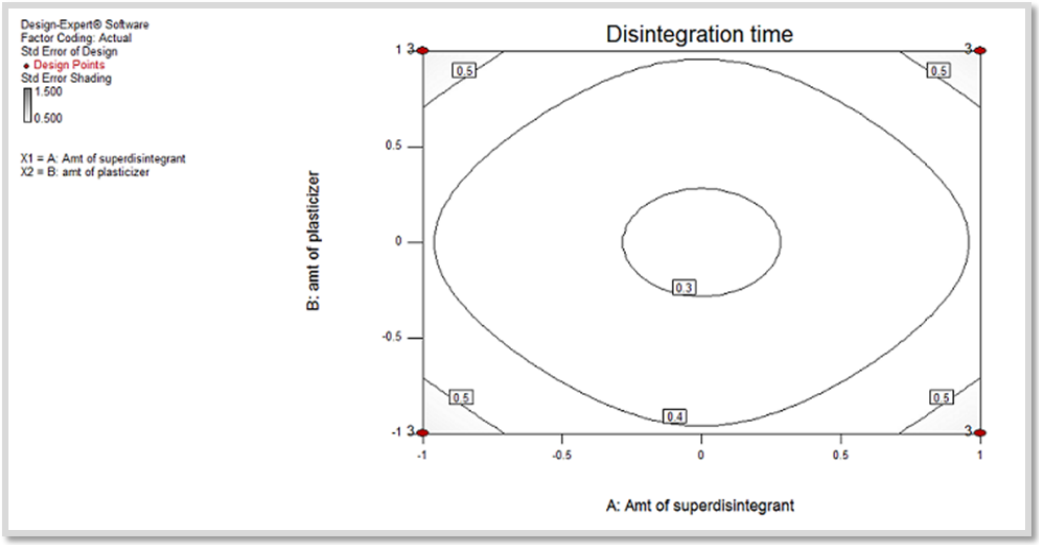


Figure3: Contour surface plot showing effect of formulation variables on disintegration time

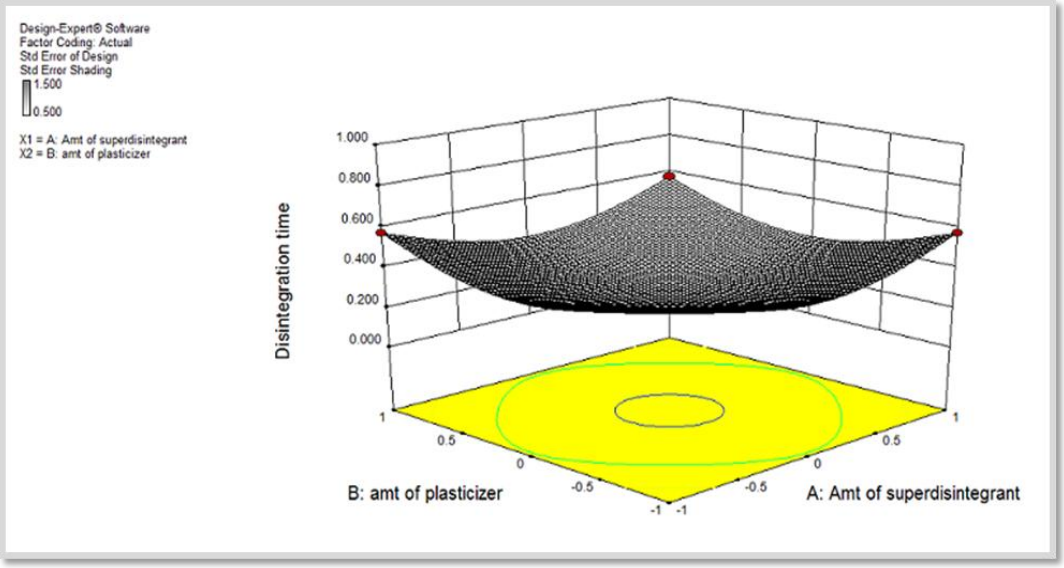


Figure4: Response surface plot showing effect of formulation variables on disintegration time

B.Effect of independent variables on Folding endurance

The polynomial equation obtained was:

Y (Folding endurance) = 247.83- 4.33X_1+ 11.50X_2- 9.67X_1 X_2…… Eq^n. 9.3

Due addition of superdisintegrant finding endurance slightly decreased as indicated by negative coefficient of X_1. Due to addition of plasticizer folding endurance increased as indicated by positive coefficient of X_2. The interaction between the factor X_1 and X_2 was considerable and both were found to negate the effect of each other. It was obvious by negative coefficient of X_1 X_2.

Table 6: ANOVA for selected factorial model (Response 2)

Response – 2 Folding Endurance) **Analysis of variance**						
Source	**Sum of square**	**Df**	**Mean square**	**F – value**	**P-value Prob>F**	
Model	2933.67	3	977.89	105.72	< 0.0001	Significant
A-Amt. of Gel	225.33	1	225.33	24.36	0.0011	
B-concentration of PEG 400	1587.00	1	1587.00	171.57	< 0.0001	
AB	1121.33	1	1121.33	121.23	< 0.0001	

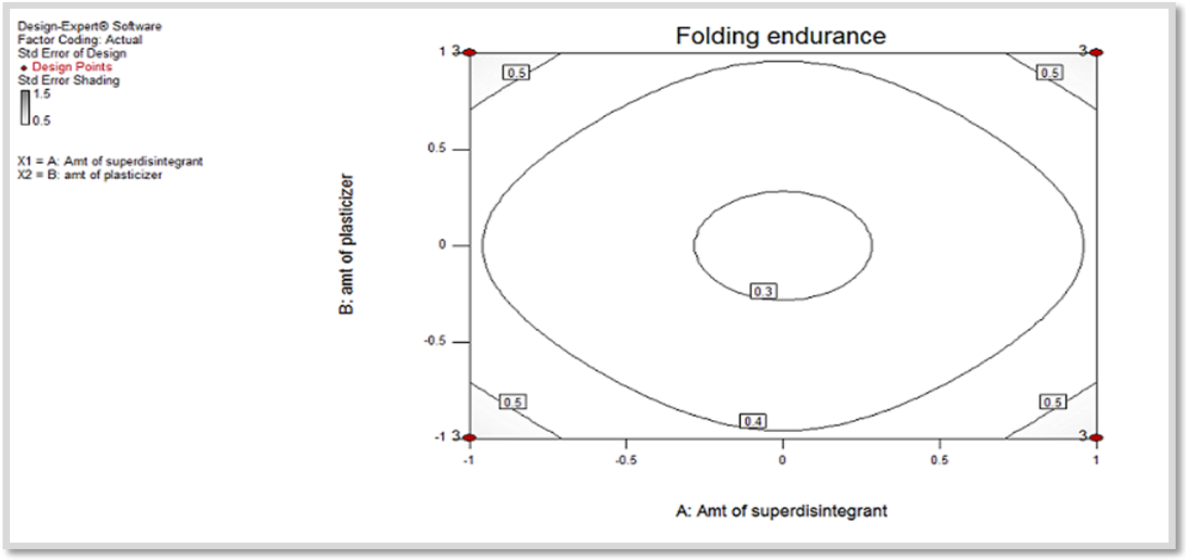
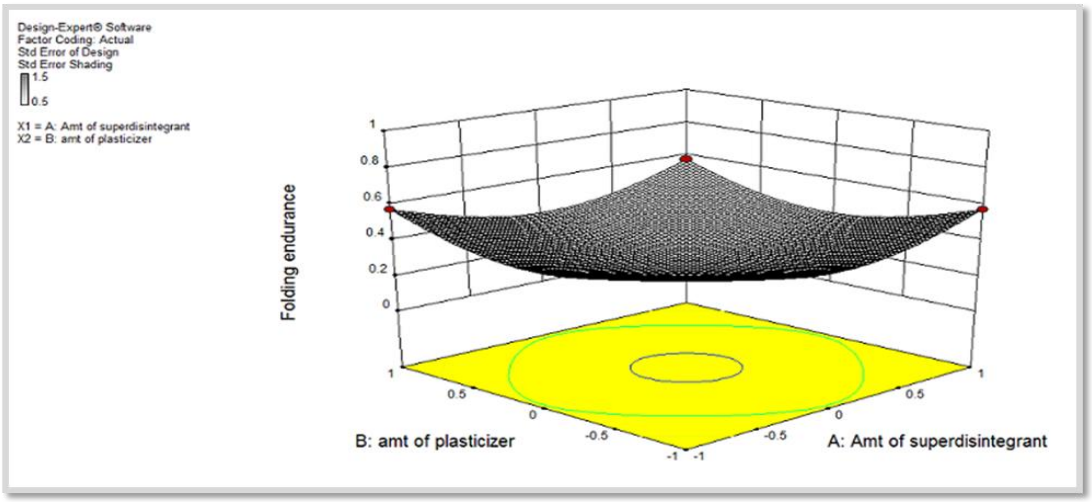


Figure5: Contour surface plot showing effect of formulation variables on Folding endurance



Figurre6: Response surface plot showing effect of formulation variables on folding endurance.

Evaluation of factorial Batches of buccal Films:

The results of evaluation parameters of factorial batches are reported in table no 7 to 13.

Weight of the film:

All the batches were evaluated for weight of the film. The weight of the films was found to be in range 56.38-54.50mg.

Thickness

The thicknesses of formulated films were found to be in range of 0.07 to 0.09 ± 0.01 mm. The values were almost uniform in all F1 to F4 formulations.

Tensile strength

The tensile strength of the formulation is given in the following table7. It shows that the mechanical properties of the all formulation were good.

Surface pH study

The surface pH values of the formulations are given in Table7. All the polymers resulted in the formulations that have neutral surface pH. The surface pH of the strips was ranging from 6.5 to 7. The neutral values of surface pH of films assured that there will be no irritation to the mucosal lining of the oral cavity.

Table 7: Physical evaluation parameters of all formulations

Formulation	Weight (mg)	Thickness (mm)	Tensile Strength (N/mm^2)	Surface pH
F1	56.38±0.06	0.08-0.09 ±0.05	2.45±0.04	6.78±0.04
F2	55.58±0.19	0.08-0.09±0.01	2.27±0.14	6.76±0.06
F3	54.5±0.01	0.07-0.08±0.08	2.18±0.03	6.75±0.03
F4	54.71±0.034	0.07-0.08±0.09	2.05±0.01	6.76±0.02

*****All values are expressed as Mean ± SD, (n = 3)

9.3.2.5 Folding endurance:

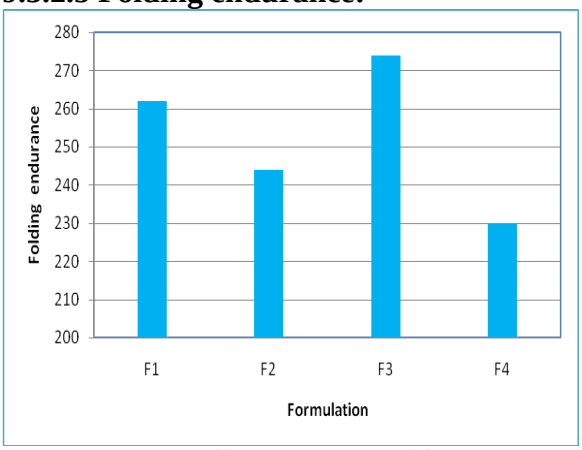


Figure 7: The results of folding endurance of factorial batches of buccal films

Drug content per sq. cm area:

The average content of Carvedilol phosphate per film (2cm x 1.5cm) was found to be 97.26%. The values were almost uniform in all F1-F4 formulations.

Disintegration time

The Disintegration time of films was in the range 124-248 seconds. It was observed that the addition of SSG in F1 and F2 formulation decreased disintegration time. The increase in disintegration time in formulation F3 and F4 formulation was but obvious as these bathes were prepared without addition of SSG.

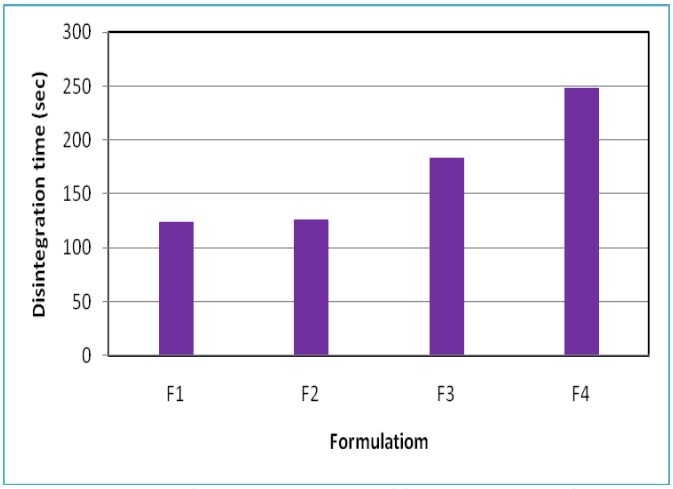


Figure 8: The results of disintegration time of factorial batches of Buccal Film

Table 8:Results of evaluation of Factorial Batches of Buccal Films

Sr. no.	Batch code	Folding Endurance	Drug content per film (2×1.5cm) %	Disintegration Time (sec)
1	F1	262±0.07	97.23%±0.05	124±0.05
2	F2	244±1.19	97.18%±0.17	126±0.69
3	F3	274±2.54	96.13%±0.04	183±0.16
4	F4	230±1.15	97.16%±0.05	248±0.18

*All values are expressed as Mean ± SD, (n = 3)

The films of factorial batches were found to be transparent, flexible and thin. Drug content was within the limit for all formulations. Folding endurance of film of different factorial formulation was found slightly different due to plasticizer addition. Disintegration time of film was found very less in formulation F1 and F2 as compared to Formulation F3 and F4 due to addition of Superdisintegrant.

In-Vitro Dissolution Studies

Table 9: Dissolution data of F1 to F4 formulations.

Time (min)	Cumulative Drug Release (%) of formulations F1 to F4 *			
	F1	**F2**	**F3**	**F4**
0	0	0	0	0
1	18.30±0.09	16.34±0.08	13.73±0.07	12.65±0.02
2	29.40±0.13	30.09±0.07	24.93±0.02	22.15±0.25
3	33.98±0.06	34.20±0.02	29.51±0.12	25.00±0.03
4	43.022±0.04	40.26±0.04	40.74±0.05	31.95±0.06
5	50.22±0.02	47.61±0.12	45.33±0.02	43.17±0.12
6	53.07±0.023	54.68±0.04	54.61±0.03	49.64±0.07
7	66.28±0.05	60.19±0.07	65.27±0.08	56.31±0.32
8	78.48±0.12	75.46±0.24	67.12±0.01	60.77±0.19
9	89.23±0.34	85.29±0.32	76.46±0.04	68.01±0.09
10	98.42±0.26	92.06±0.09	84.55±0.02	74.27±0.04

*All values are expressed as Mean ± SD, (n = 3)

The dissolution medium used was pH 6.8 buffer. The cumulative drug release (%) of F1 formulation was found to be maximum i.e. 98.42 % in pH 6.8 buffer in 10 min.

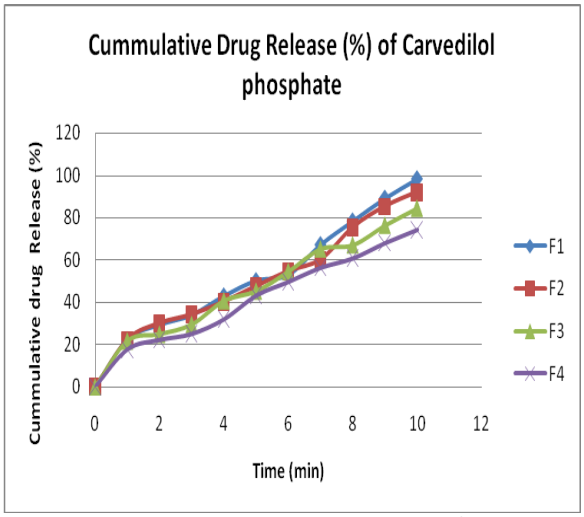
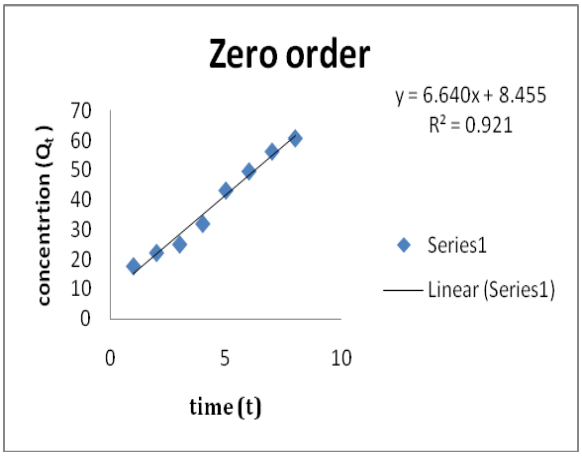


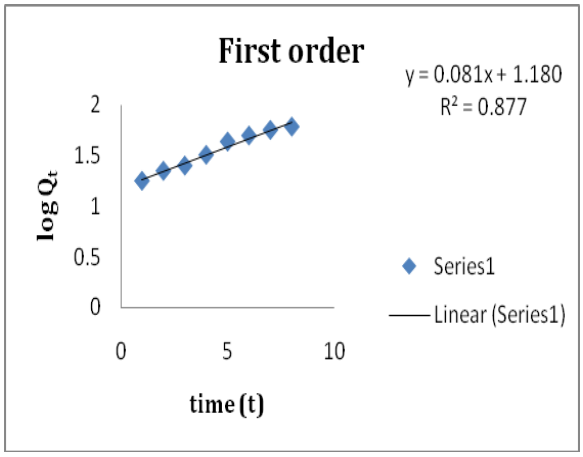
Figure 9. Cumulative drug Release (%) of Carvedilol phosphate buccal film

Dissolution Kinetic Study

Table 10: Dissolution kinetics of formulations F1 toF4

Models / Parameter	**R values for formulations F1 toF4**			
	F1	**F2**	**F3**	**F4**
Zero order	0.921	0.923	0.927	0.929
First order	0.877	0.854	0.848	0.886
Higuchi	0.944	0.932	0.927	0.914
Best Fit Model	Higuchi	Higuchi	Higuchi	Higuchi





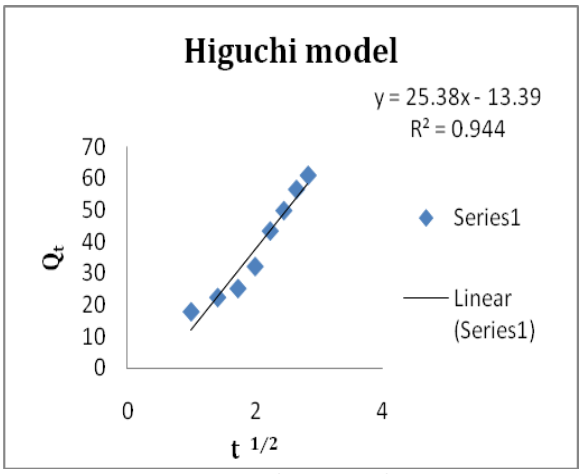


Figure 10: Models of optimized formulation

Higuchi model was found to be the best fit model for all formulations.

Swelling index

The swelling index of F1 to F4 formulation was found to be

Table11: Swelling index of Formulation F1 to F4

Sr. No	Formulation	Swelling Index
1	F1	34.82±0.08
2	F2	34.43±0.12
3	F3	22.61±0.01
4	F4	24.53±0.05

*All values are expressed as Mean ± SD, (n = 3)

Ex-vivo diffusion Study

Table12: Diffusion Study: Cumulative Drug Release (%) of Carvedilol phosphate through goat buccal mucosa

Time (min)	Cumulative drug Release (%) of formulations F1 to F4 *			
	F1	**F2**	**F3**	**F4**
0	0	0	0	0
1	9.719±0.09	8.8403±0.09	7.69±0.03	6.97±0.08
2	16.88±0.01	14.49±0.57	11.39±0.01	11.29±0.03
3	23.85±0.23	22.64±0.18	22.90±0.09	21.11±0.03
4	26.85±0.18	21.01±0.03	30.36±0.37	25.07±0.01
5	38.36±0.07	25.70±0.04	36.17±0.22	30.35±0.10
6	43.79±0.08	32.99±0.07	47.87±0.05	36.82±0..05
7	52.94±0.07	42.87±0.28	54.87±0.27	52.15±0.12
8	59.68±0.08	50.62±0.32	56.72±0.08	57.12±0.34
9	69.52±0.13	53.60±0.05	58.33±0.01	58.90±0.06
10	78.48±0.09	61.59±0.02	59.76±0.02	59.84±0.04

*All values are expressed as Mean ± SD, (n = 3)

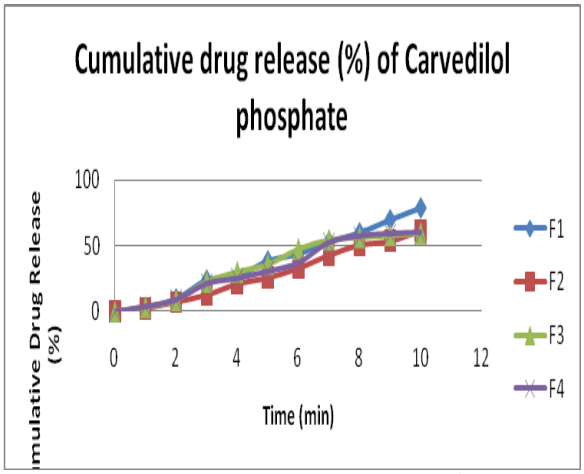


Figure11: Cumulative drug Release (%) of Carvedilol phosphate through goat buccal mucosa

Stability study

The optimized F1 formulation was selected for stability studies on the basis of high cumulative % drug release, highest diffusion, results of *in vitro* disintegration time and results of folding endurance. The formulation F1 was evaluated for above

mentioned parameters at the end of stability studies and the results are reported in Table 13. From these results it was concluded that, formulations F1 is stable and retained its original properties with minor differences. Additionally Formulation F1 was also evaluated for DSC and FTIR studies.

Table 13: Stability studies of optimized formulation

Parameters	Initial *	After 3 month stability studies *
Folding endurance	262±1.52	262±1.76
Drug content (%)	97.23±0.52	97.21±0.04
Disintegration time (sec)	124±2.08	122±2..64
Cummulative drug release (%)	98.42±0.03	98.40±0.02

*All values are expressed as Mean ± SD, (n = 3)

CONCLUSION

For the present study, Carvedilol phosphate was selected as a model drug candidate as no marketed film of Carvedilol phosphate is available in India. The present work was proposed to design and develop formulation which disintegrates in oral cavity in less than 4-5 minutes without the need of drinking water; and may results in improved patient compliance particularly for those who have difficulty in swallowing. A 2^2 factorial design was implemented for optimization of buccal film formulation of Carvedilol phosphate. According to the model it contained 2 independent variables at 2 levels, +1, -1. The different independent variables were addition of Sodium Starch Glycolate (X_1) and Plasticizer (X_2) and no addition of Sodium Starch Glycolate (X_1) and Plasticizer (X_2). Dependent factors included Disintegration time and folding endurance. Due addition of superdisintegrant disintegration time decreased and slightly decreased folding endurance. Due to addition of plasticizer disintegration time decreased and folding endurance increased. Both factors increase effect of each other. Formulation F1 was found best formulation which was taken for further stability study. The optimized formulation (F1) was found to be stable at the end of stability studies conducted as per ICH guidelines.

REFERENCES

1. Mishra S, Kumar G,Kothiyal P. Areview article: Recent advances in buccal patches.2012;1(7):78-86.www.thepharmajournal.com
2. Parmar HG, Jain JJ, Patel TK. Buccal patch: a technical note. Int. J of Pharmaceutical Sciences review and research.2010; 4(3):178-182
3. Tayal S, Jain N. Buccal control drug delivery system: a review. International journal of Pharmaceutical science and research.2011;2(1):13-24
4. Tangri P, Sateesh Madhav NV. Recent advances in oral mucoadhesive drug delivery system:review.2011;3(2):151-162
5. Dodla S, Velmurjan S.Buccal penetration enhancer-an overview. Asian J of Pharmaceutical and Clinical Research.2013;6(3):39-47
6. Naveen C, Kumar K,Venkteshwar Rao P. Chemical enhancer in buccal and sublingual delivery. Int.J of Pharmaceutical sciences and nanotechnology.2011:2(1):1307-1319
7. Nagich U, Choudhary V. Formulation and Development of Metoprolol Tartarate bucco adhesive films. The Pharma Research. 2009;(1):41-53
8. Lohani A, Prasad N, Arya R. Formulation and characterization of mucoadhesive buccal film of Ranitidine Hydrochloride. 2011:2(9):2457-2462
9. Mahajan A, Chhabra N, Aggarwal G. Formulation and characterization of fast dissolving buccal film.Scholars Research Library.2011;3(1):152-165
10. Kaur A, Kaur G. Mucoadhesive buccal patches of interpolymer complexes of chitosan pectin for delivery of carvedilol. Saudi Pharmaceutical Journal. 2012;(20): 21-27
11. Radha MB, Murthy VS. Buccal film drug delivery system-an innovative and emerging Technology. Molecular Pharmaceutics and Organic Process Research. 2013; 1(3):1-6
12. Verma N, Ghosh AK, Chattopadhyay P. Preparation and in vitro assessment of mucoadhesive buccal patches containing Carvedilol. Int. J of Pharmacy and Pharmaceutical Sciences.2011;3(3):218-220
13. Desu P, Sahu M. Formulation and evaluation of fast dissolving film of zolmitriptan. International Research J of Pharmacy. (2012);3(1):373-376

14. Shridhar I, Joshi A. Formulation and characterization of buccal patch of Ondanserton hydrochloride. Int. J of Pharmaceutical Research and development. 2013:5(8):84-94
15. Perioli L, Ambrogi V. Development of mucoadhesive patches for buccal administration of Ibuprofen. J of Controlled release. 2004;99:73-84
16. Costa P, Lobo J. Modeling and comparison of dissolution profiles. European J of Pharmaceutical sciences. 2001;(13):123-133
17. Govindsamy P, Keasavan BR. Formulation unidirectional release of buccal patch of carbamazepine and study of permeation through of porcine buccal mucosa. Asian Pacific J of tropical biomedicine. 2013;3(12):995-1002
18. John AS, Goli D. Development and evaluation buccoadhesive drug delivery system of Atovavastin calcium. J of Current Pharmaceutical Research. 2010;1:31-38
19. Kshirsagar N, Thamada N. Design and evaluation of chitosan containing muccoadhesive buccal patch of Fluoxtine HCL. 2012;2(6):1-5
20. Charyulu RN, Shripriya BS. Design and characterization mucoadhesive buccal patch containing antifungal agent for oral candidiasis. Int J of Pharmaceutical and Phytopharmacological Research. 2012:1-12
21. Bhyan B, Jangra S. Formulation and Evaluation of fast dissolving sublingual film of Rizatriptan Benzoate. Int J of Drug Development and Research. (2012);4(1): 133-144
22. Souto C, Rodriguez A. A comparative study of the utility of two superdisntegrant in microcrystalline cellulose pellets by extrusion and spheronization. European J of Pharmaceutics and Biopharmaceutics. 2011;91:94-99
23. Singh S, Gangwar S. Formulation and evaluation of rapid disintegrant film of Lecocetrizine Hydrochloride. Scholars Research Library. 2010;2(2):434-439
24. Gupta J, Mohiuddin M, Faisal S. A Comprehensive review on buccal drug delivery system. International Journal of Pharmaceutical Research and Development. 2012;3(11):67

How to cite this article: Jagtap VD. Development and evaluation of buccal film of carvedilol phosphate. International Journal of Research and Review. 2020; 7(5): 277-287.

******