WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 7, 1427-1442. Research Article ISSN 2277– 7105

FORMULATION AND OPTIMIZATION OF NOVEL EXTENDED RELEASE MUCOADHESIVE BUCCAL PATCHES OF CARVEDILOL

Chanda Bano*, Aditya Tiwari and Nitendra Sahu

Millinnium College of Pharmacy, Bhopal.

Article Received on
20 April 2022,

Revised on 10 May 2022,
Accepted on 30 May 2022

DOI: 10.20959/wjpr20227-24478

***Corresponding Author**
Dr. Chanda Bano
Millinnium College of Pharmacy, Bhopal.

ABSTRACT

The carvedilol characterized as white powder freely soluble in water, 0.1N NaOH, 0.1N HCl, 7.4pH buffer and insoluble in ethyl acetate, having melting point 122 ^{O}C and partition coefficient 0.868. UV spectrogram of carvedilol scanned from 200- 400 nm, λmax found at 220nm. Calibration Curve prepared in 7.4pH buffer and water with R^2 value 0.996 and 0.999 respective also calculated Linear equation. all the formulated transdermal patches are evaluated and found, all are flexible smooth and translucent, weight variation was under limits, average thickness was 0.15mm found, average tensile strength was 0.9 Kg/cm^2 found, drug content was 0.73 mg/cm^2 average, moisture content % and moisture uptake % also evaluated. The dissolution study of all formulation shows the percentage drug release were found to be F1-93.10%, F2 -95.25%,F3- 96.16%, F4- 93.95%, F5-96.91% and F6-88.25%, in 24 minutes. According to drug release studied F-3 and F-4 formulations shows excellent drug release profile in steady way. The data of drug release, it was found that all the formulations follow diffusion mechanism for the drug release. Cumulative amount of drug released Q (µg/cm^2) at different time intervals and steady state flux (Jss, µg/cm^2.hr) were obtained. Also permeability coefficient (Kp) are calculated and found F-3 and F-4 has steady diffusion per unit membrane surface area. Also it was observed that the flux and permeability of Carvedilol.

KEYWORDS: Carvedilol, Transdermal patches, Extended release, Mucoadhesive, Buccal patches.

INTRODUCTION

Mucoadhesivedrug delivery system through Buccal, sublingual, rectal and nasal mucosa can be faster and systemic mode of non-invasive drug administration to bypass first pass

metabolism.[1] Faster delivery and enhanced bio availability of drugs is observed through mucoadhesive administration.[2] Mucoadhesive preparations like Buccal patches, gels and chewing gums, may be used for the treatment of mouth ulcers, candidiasis, etc while the other dosage forms such as lozenges, mouthwashes, ointments, troches etc, are having the disadvantage of an initial burst of activity followed by a rapid decrease in concentration to below therapeutic levels and are incapable of maintaining the salivary concentration for a prolonged period.[3,4,5] Carvedilol reduces tachycardia through beta adrenergic antagonism and lowers blood pressure through alpha-1 adrenergic antagonism.[6] It has a long duration of action as it is generally taken once daily and has a broad therapeutic index.[7,8,9]

The aim of this project work is to development of novel Mucoadhesive formulation for buccal disorders which shows an intensive potential for site specific and sustained release drug delivery system. The distinctive advantage of these prepared formulations will be avoiding the initial burst activity, first pass metabolism and gastrointestinal degradation. This formulation will be useful for extended release drug delivery systems for oral cavity disorders.

MATERIALS AND METHODS

The standard drug: Carvedilol was obtained from Ranbaxy, Devas as gift. Chitosan, Poly vinyl pyrrolidone and Pectin were purchased from Rankem, Mumbai. All other used chemicals are belonging to laboratory grade.

Organoleptic properties: Are the aspects that can be experienced through one's senses like taste, smell, sight, and touch. It includes a recording of the color, odor, and taste of the drug.

Solubility: Solubility determine by drug dissolve in different solvent system like ethanol, methanol, chloroform, acetone, etc. and check according to solubility chart.

Partition Co-efficient: Partition coefficient is method to determine the lipophilicity and hydrophilicity of the drug. 10 mg drug dissolve in 25 ml water phase and 25 ml of Octanol in a separating funnel and mix well then allow standing for a time, so the two layers separate. One by one layer separate from funnel in separate beakers. Each layer diluted and takes absorbance to detect solubility, then partition coefficient calculated by following formulae

$$\text{Partition coefficient} = \frac{\text{concentration of drug in aqueous phase}}{\text{concentration of drug in oily phase}}$$

Melting point determination: Melting point of Carvedilol was determined by taking a small amount of drug in capillary tube sealed at one end using a Bunsen flame. The tube was put in melting point apparatus and temperature at which drug melts was noted by thermometer with it.

Determination of ultraviolet absorption maxima (λmax): Several methods are reported in the literature for the estimation of Carvedilol. In the present study, UV spectrophotometric method is selected for the estimation of Carvedilol. Ultraviolet absorption in the rage 200 to 400 nm of a 1000 µg/ml solution in 6.8 pH phosphate buffer was measured. The wavelength at maximum absorption (λmax) of Carvedilol in this solution was found to be 241 nm.

Preparation of calibration curve of carvedilol: Carvedilol (10 mg) was dissolved in 1ml 6.8 pH phosphate buffer and volume was made up to 10 ml volumetric flask using 6.8 pH phosphate buffers. Five micro liters of stock solution (1 mg/ml) was further diluted with 6.8 pH phosphate buffer, up to 10 ml. This solution (100µg/ml) was further diluted to 6.8pH phosphate buffer, to obtain solutions of 2 to 10µg/ml. Absorption of each solution was measured at 241nm using Systronics UV/Vis double beam spectrophotometer and 6.8pH phosphate buffer, as a reference standard.

Drug- excipient compatibility

- **Physical compatibility:** Color changes, dissolution, solubility, sedimentation rate, liquefaction, phase separation or immiscibility.
- **Chemical compatibility:** Undesirable reaction between drug and excipients to monitor if compounds undergo hydrolysis, oxidation, reduction, precipitation, decarboxylation, and racemization. FT-IR Spectroscopy method used for identification of chemical compatibility.

Method of preparation of mucoadhesive buccal patches

Buccoadhesive patches containing varying amounts of chitosan and pectin were prepared by solvent casting method with slight modification. Chitosan and drug were dissolved in 2% v/v glacial acetic acid solution and pectin was dissolved separately in distilled water. Chitosan solution containing drug was added to pectin solution with stirring. Glycerol 5% v/v was added as plasticizer under constant stirring. To improve patch performance and release characteristics, a water soluble hydrophilic additive, 1% w/v PVP K-30 was added. The resulting viscous solution was casted into petridish and dried in an oven at 50^{O}C for 48 hours.

The dried films were carefully removed and checked for any imperfection or air bubbles. The patches were packed in an aluminium foil and stored in an air tight glass container to maintain the integrity and elasticity of the patches. The compositions of different patches were described in Table.

Methods of evaluations of mucoadhesive buccal patches

Visual observation: Prepared patches were observed visually for transparency, bubble, trapped air, grittiness etc.

Physical stability of buccal patches: Patches were evaluated for it physical stability by storing them at elevated temperature and humidity using humidity chamber.

Mass uniformity and thickness: The assessment of weight and patch thickness was done in 10 different randomly selected patches from each batch. Patch thickness was measured using digital micrometer screw gauge at three different places and the mean value was calculated. For determination of mass, patches were directly weighed on a digital balance.

Tensile strength: The tensile strength of the patch was evaluated by using the Tensiometer. It consists of two load cell grips. The lower one was fixed and upper one was movable. Film strips with dimensions of 1x1cm were fixed between these cell grips, and force was gradually applied till the film broke. The tensile strength was taken directly from the dial reading in kg. The unit of tensile strength will be Kg/cm^2.

Folding endurance: Folding endurance of patches was determined by repeatedly folding one patch at the same place till it broke or folded up to 200 times without breaking.

Drug content: A specified area of patch ($1cm^2$) was dissolved in 100 ml ethanol and shaken continuously for 24 h. Then the whole solution was ultrasonicated for 15 min. After filtration, the drug was estimated spectrophotometrically at wavelength of 241nm and determined drug content.

Percentage moisture content: The prepared films were weighed individually and kept in a desiccator containing fused calcium chloride at room temperature for 24 h. After 24 h, the films were reweighed and determined the percentage moisture content from below mentioned formula:

$$\% \textbf{ moisture content } = \frac{(\text{initialweight} - \text{final weight})}{\text{final weight}} X\ 100$$

***In-vitro* swelling studies:** The weighed films were kept in a desiccator at room temperature for 24 h containing saturated solution of potassium chloride in order to maintain 84% RH. After 24 h, the films were reweighed and determine the percentage moisture uptake from the below mentioned formula:

$$\% \textbf{ moisture uptake } = \frac{(\text{final weight} - \text{initial weight})}{\text{initialweight}} X\ 100$$

Bioadhesion properties: Fresh sheep buccal mucosa was obtained from a local slaughterhouse and used within2 h of slaughter. The mucosal membrane was separated by removing the underlying fatand loose tissues. The membrane was washed with distilled water and then with isotonic phosphate buffer pH 6.8 at 37 °C. The bioadhesive strength was measured using a modified version of the apparatus previously applied. The device was mainly composed of a two-arm balance. Both the ends are tied to glass plate for keeping weight. The right and left pans were balanced by adding extra weight on the left hand. The piece of goat buccal mucosa was tied to the two glass slide separately. Buccal patch was placed between these two slides containing goat buccal mucosa, and extra weight from the left pan was removed to sandwich the two pieces of glass and some pressure was applied to remove the presence of air. The balance was kept in this position for 5 min. Weight was added slowly to the left hand pan until the two glass slides got detached from each other the weight require to detach the patch from buccal mucosa of goat gave the measure of bioadhesive strength.

Force of adhesion (N) = Bioadhesive strength X 9.81/1000

Bond strength (Nm-2) = Force of adhesion/Surface area

Mucoadhesion time: mucoadhesion time was evaluated (n= 3) after application of the patches onto freshly cut sheep buccal mucosa. The fresh sheep buccal mucosa was fixed in the inner side of the beaker, above 2.5 cm from the bottom, with cynoacrylate glue. One side of each patch was wetted with one drop of isotonic phosphate buffer pH 6.8 and pasted to the sheep buccal mucosa by applying a light force with a fingertip for 30 seconds. The beaker was filled with 500 mL of isotonic phosphate buffer pH 6.8 and was kept at 37±1 °C. After 2 minutes, a 50 rpm stirring rate was applied to simulate the buccal cavity environment, and patch adhesion was monitored up to 12 h. The time required for the patch to detach from the sheep buccal mucosa was recorded as the mucoadhesion time.

***In-vitro* drug release studies:** *In-vitro* drug release studies were carried out using the paddle over disc method. Dry films of known thickness were cut into circular shape, weighed, and fixed over a glass plate with an adhesive. The plate was then placed in a 900 ml phosphate buffer (pH 6.8) and the apparatus was equilibrated to 37°C ± 0.5°C. The paddle was then set at a distance of 2.5 cm from the glass plate and operated at a speed of 50rpm, and samples (5 ml aliquots) were withdrawn at appropriate time intervals up to 24 h and analyzed for drug content at 241nm using double beam UV -visible spectrophotometer. The experiment was performed in triplicate, and the mean value was calculated.

***In-vitro* buccal permeation study:** An *in-vitro* permeation study was carried out by using Franz diffusion cell. Freshly obtained sheep buccal mucosa was mounted between the donor and receptor compartments so that the smooth surface of the mucosa faced the donor compartment. The patch was placed on the mucosa and the compartments clamped together. Then the formulated patches were positioned over the membrane toward the donor compartment. The receptor compartment of the diffusion cell was filled with phosphate buffer (pH 6.8) and every 1 h, 5 ml of sample was taken and replaced the same with receptor fluid, and the sample was analyzed for drug content at 241nm using double beam UV -visible spectrophotometer.

Kinetic modeling of dissolution data: Drug release kinetics were analyzed by various mathematical models such as a zero-order and first-order kinetic models; Higuchi and Korsmeyer–Peppas models to ascertain the kinetics of drug release**.**

RESULT AND DISCUSSION

During the preformulation studies the carvedilol characterized as white powder freely soluble in water, 0.1N NaOH, 0.1N HCl, 7.4pH buffer and insoluble in ethyl acetate, having melting point 122 ^{O}C and partition coefficient 0.868. UV spectrogram of carvedilol scanned from 200- 400 nm, λmax found at 241nm**.** Calibration Curve prepared in 7.4pH buffer and water with R^2 value 0.996 and 0.999 respective also calculated Linear equation. FT-IR study indicated on the basis of peaks of both carvedilol (pure) and carvedilol + (HPMC + PVP +PEG), that there is no drug excipient interaction.

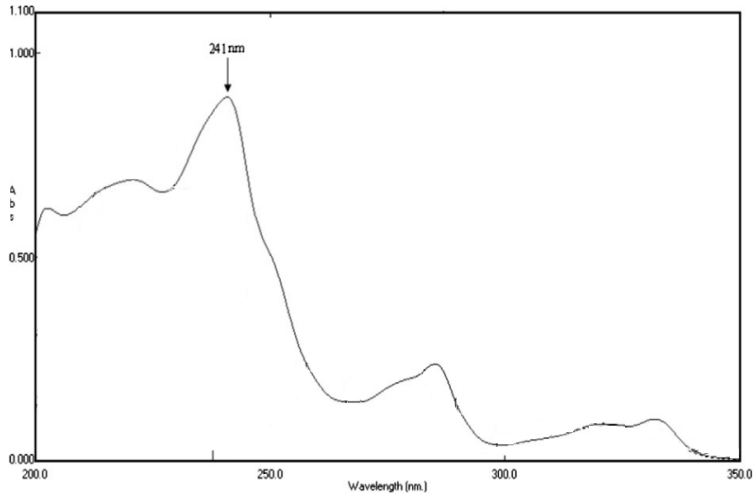

Figure no. 1: UV spectrogram of Carvedilol from 200- 400 nm.

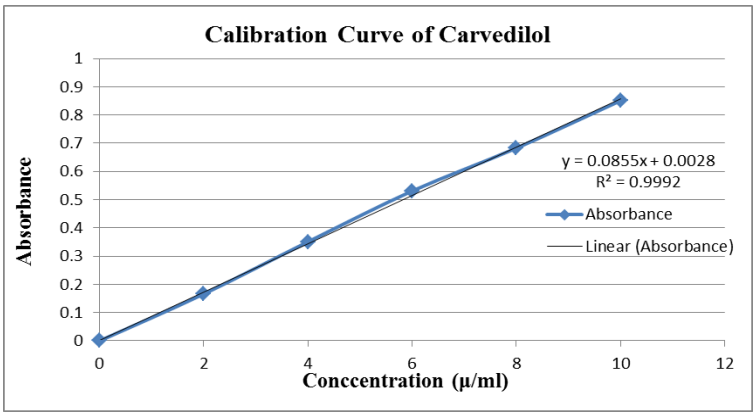

Figure no. 2: Calibration curve of carvedilol in phosphate buffer pH 6.8.

Drug excipient compatibility study: Performed by FTIR

Table no. 1: Important band frequencies in IR spectrum of Carvedilol.

S. No.	Reported frequency (cm^{-1})	Carvedilol peak (cm^{-1})	Optimized patch of carvedilol	Peak Assigned
1.	1275-1200	1249	1249	C-O str. ether
2.	1382-1266	1377	1377	C-N
3	3000-2840	2945, 2875	-	C-H str
4.	3200-3000	3126	3236	O-H str.
5.	3500-3000	3575	3577	N-H str.

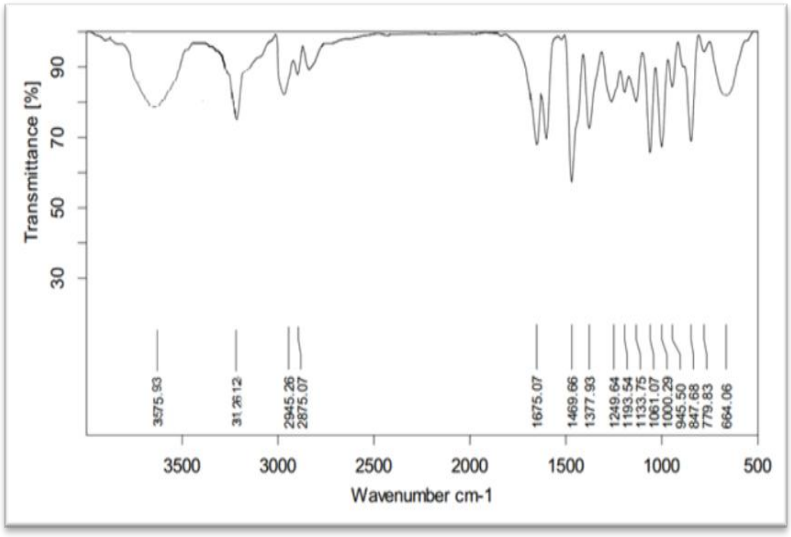

Fig. no. 3: FT-IR spectrogram of carvedilol.

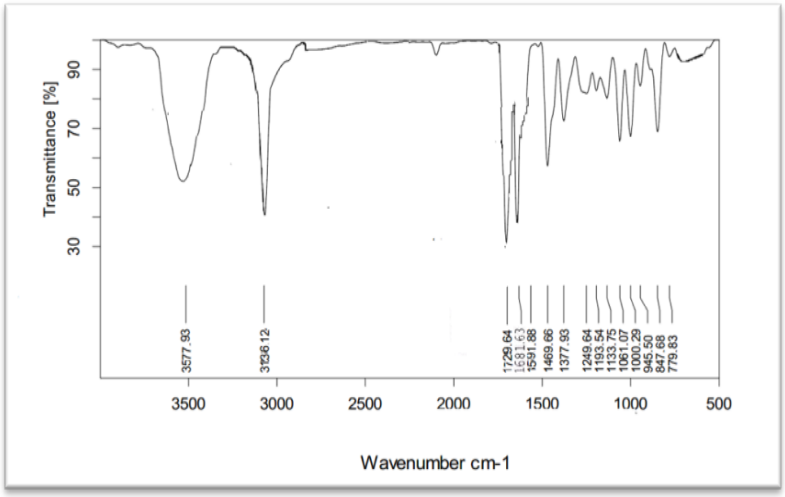

Fig. no. 4: FT-IR spectrogram of optimized patch of carvedilol.

Formulation of mucoadhesive buccal patches

Table no. 2: Formulation of mucoadhesive buccal patches.

Ingredients	F-1	F-2	F-3	F-4	F-5
Carvedilol (mg)	10	10	10	10	10
Chitosen (mg)	100	-	50	33	25
Pectin	-	100	50	66	75
Polyelectrolyte complex ration (Chitosen: Pectin)	-	-	1:1	1:2	1:3
Glycerol (5%)	5	5	5	5	5
PVP (1%)	1	1	1	1	1

Evaluations of mucoadhesive buccal patches

Table no. 3: Common parameters of evaluation of buccal patches of carvedilol.

Batch Code	Physical appearance	Weight variation (gms)	Thickness (mm)	Tensile strengths (Kg/cm^2)	Folding Endurance	Drug content (mg/cm^2)
F-1	Translucent flexible, smooth	0.550 ± 0.028	0.475 ± 0.009	0.846	179	0.734
F-2	Translucent flexible, smooth	0.562 ± 0.017	0.484 ± 0.013	0.922	183	0.713
F-3	Translucent flexible, smooth	0.521 ± 0.019	0.447 ± 0.003	0.932	192	0.724
F-4	Translucent flexible, smooth	0.516 ± 0.009	0.452 ± 0.008	0.955	185	0.734
F-5	Translucent flexible, smooth	0.498 ± 0.014	0.567 ± 0.015	0.934	188	0.741

Table no. 4: Evaluation of buccal patches of carvedilol.

Batch Code	Moisture content (%)	Moisture uptake (%)	Bioadhesive strength (g)	Force of Adhesion (N)	Bond strength (N/m^2)	Mucoadhesion Time (min)
F-1	3.31± 0.18	5.43 ± 0.01	9.6 ± 1.8	0.10	469	195 ± 6
F-2	2.77 ± 0.16	4.97 ± 0.04	12.6 ± 1.5	0.12	615	257 ± 7
F-3	2.09 ± 0.49	3.77 ± 0.09	11.4 ± 0.7	0.11	556	278 ± 8
F-4	2.59 ± 0.43	3.15 ± 0.01	10.1 ± 0.8	0.10	493	294 ± 4
F-5	1.24 ± 0.57	2.64 ± 0.02	13.5 ± 0.5	0.13	659	300 ± 7

***In-Vitro* drug release studies**

Table no. 5: *In-Vitro* release profile of mucoadhsive patch of carvedilol (F-1).

Time (hr.)	S.R.T.	Log T.	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	100	2
1	1	0	6.85	0.836	93.15	1.969
2	1.141	0.301	19.84	1.298	80.16	1.904
4	2	0.602	48.49	1.686	51.51	1.712
6	2.449	0.777	66.33	1.822	33.67	1.527
8	2.828	0.903	77.03	1.887	22.97	1.361
10	3.162	1.000	82.37	1.916	17.63	1.246
12	3.464	1.079	84.68	1.928	15.32	1.185
16	4	1.204	85.93	1.934	14.07	1.148
18	4.242	1.255	88.34	1.946	11.66	1.067
20	4.472	1.301	89.51	1.952	10.49	1.021
24	4.898	1.380	93.10	1.969	6.9	0.839

Table no. 6: *In-Vitro* release profile of mucoadhsive patch of carvedilol (F-2).

Time (hr.)	S.R.T.	Log T.	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	100	2
1	1	0	04.79	0.680	95.21	1.979
2	1.141	0.301	07.21	0.858	92.79	1.967
4	2	0.602	16.59	1.220	83.41	1.921
6	2.449	0.777	35.32	1.548	64.68	1.811
8	2.828	0.903	49.21	1.692	50.79	1.706
10	3.162	1.000	65.96	1.819	34.04	1.532
12	3.464	1.079	78.57	1.895	21.43	1.331
16	4	1.204	84.57	1.927	15.43	1.188
18	4.242	1.255	89.04	1.949	10.96	1.039
20	4.472	1.301	93.32	1.970	6.68	0.825
24	4.898	1.380	95.25	1.978	4.75	0.677

Table no. 7: *In-Vitro* release profile of mucoadhsive patch of carvedilol (F-3).

Time (hr.)	S.R.T.	Log T.	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	100	2
1	1	0	06.46	0.810	93.54	1.971
2	1.141	0.301	09.75	0.989	90.25	1.955
4	2	0.602	22.16	1.345	77.84	1.891
6	2.449	0.777	28.15	1.449	71.85	1.856
8	2.828	0.903	37.21	1.571	62.79	1.798
10	3.162	1.000	45.57	1.659	54.43	1.736
12	3.464	1.079	53.75	1.730	46.25	1.665
16	4	1.204	69.74	1.843	30.26	1.481
18	4.242	1.255	78.26	1.893	21.74	1.337
20	4.472	1.301	87.61	1.942	12.39	1.093
24	4.898	1.380	96.16	1.983	03.84	0.584

Table no. 8: *In-Vitro* release profile of mucoadhsive patch of carvedilol (F-4).

Time (hr.)	S.R.T.	Log T.	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	100	2
1	1	0	05.77	0.761	94.23	1.974
2	1.141	0.301	09.36	0.971	90.64	1.957
4	2	0.602	17.36	1.239	82.64	1.906
6	2.449	0.777	25.53	1.407	74.47	1.872
8	2.828	0.903	33.70	1.527	66.30	1.821
10	3.162	1.000	41.87	1.622	58.13	1.764
12	3.464	1.079	49.07	1.691	50.93	1.707
16	4	1.204	65.08	1.813	34.92	1.543
18	4.242	1.255	73.59	1.867	26.41	1.422
20	4.472	1.301	81.27	1.910	18.73	1.272
24	4.898	1.380	93.95	1.973	06.05	0.782

Table no. 9: *In-Vitro* release profile of mucoadhsive patch of carvedilol (F-5).

Time (hr.)	S.R.T.	Log T.	% C.R	Log % C.R	% Drug remaining	Log% drug remaining
0	0	0	0	0	100	2
1	1	0	05.87	0.768	94.13	1.973
2	1.141	0.301	08.27	0.917	91.73	1.962
4	2	0.602	17.36	1.239	82.64	1.917
6	2.449	0.777	30.03	1.477	69.97	1.845
8	2.828	0.903	38.76	1.588	61.24	1.787
10	3.162	1.000	50.06	1.699	49.94	1.698
12	3.464	1.079	63.01	1.799	36.99	1.568
16	4	1.204	76.44	1.883	23.56	1.372
18	4.242	1.255	87.32	1.941	12.68	1.103
20	4.472	1.301	94.40	1.975	05.60	0.748
24	4.898	1.380	96.91	1.986	03.09	0.490

Drug release kinetics models of mucoadhesive patches

A) Zero order kinetics

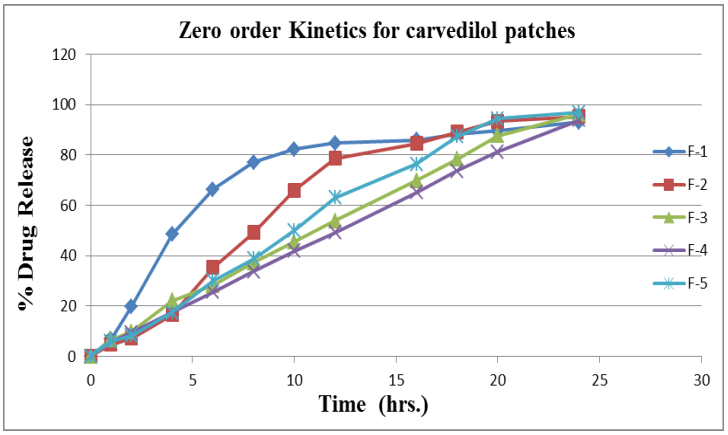

Fig. no. 5: Zero order plots of mucoadhesive patches.

B) First order kinetics

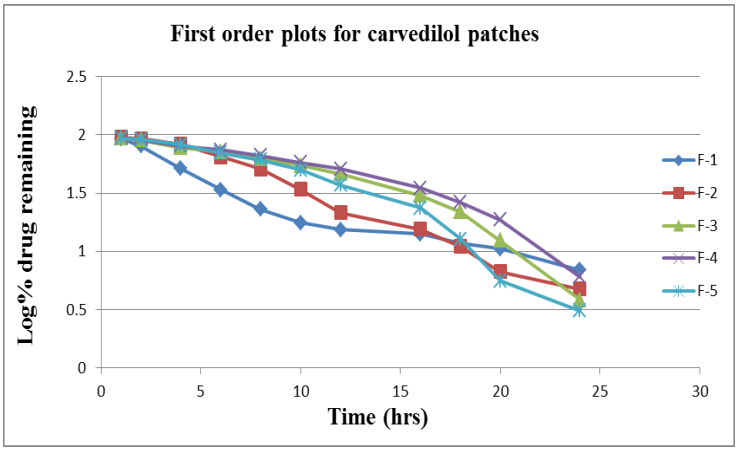

Fig. no. 6: First order plots of mucoadhesive patches.

C) Higuchi model of drug release kinetics

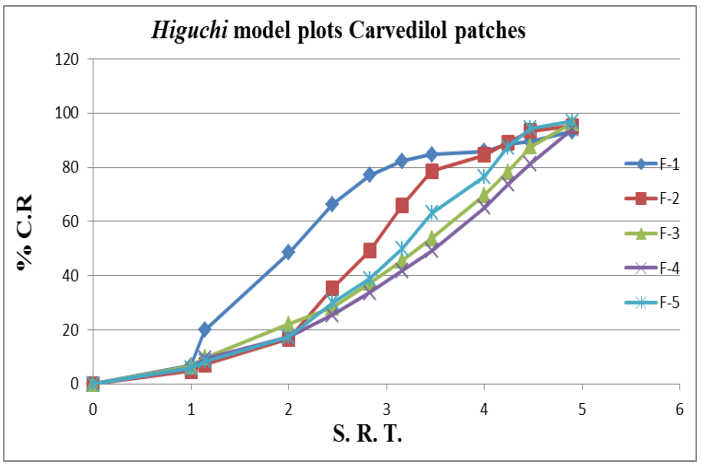

Fig. no. 7: *Higuchi* model plots of mucoadhesive patches.

D) Peppas model of drug release kinetics

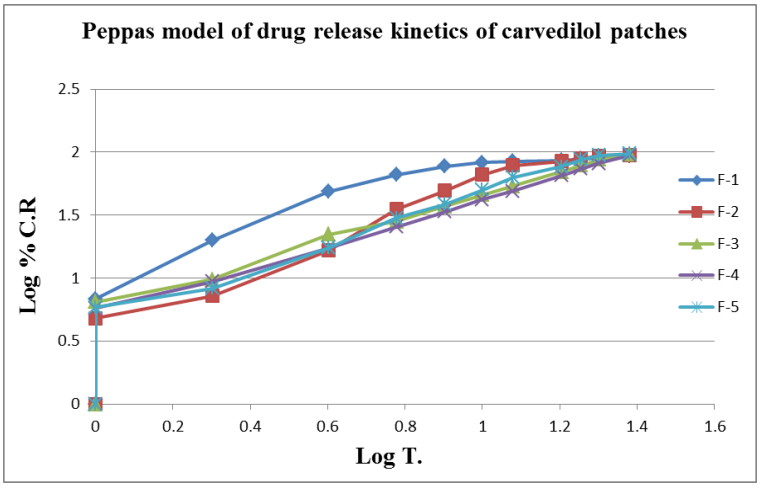

Fig. no. 8: *Peppas* model plots of mucoadhesive patches.

In-vitro permeation study of mucoadhesive buccal

Table 10: Cumulative amount of drug permeate Q (µg/cm^2) across mucous membrane.

Time (hr)	Q (µg/cm^2)				
	F-1	F-2	F-3	F-4	F-5
0	0	0	0	0	0
0.5	129.04	173.56	288.49	504.00	253.94
1	619..05	573.00	601.25	828.03	540.69
2	628.04	780.50	931.99	1251.04	777.79
4	801.00	871.13	1221.0	1577.02	929.70
6	1474.92	1395.01	1251.01	1579.45	1522.89

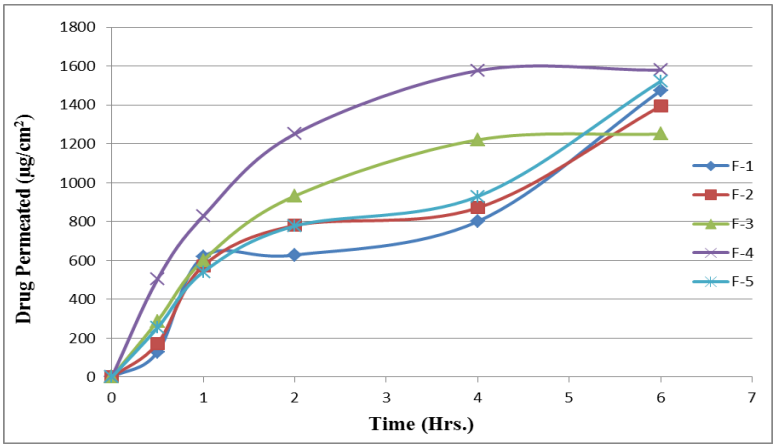

Figure 9: Plot for drug permeation across mucous membrane.

The permeation profiles were constructed by plotting the cumulative amount of Carvedilol diffused per unit membrane surface area (Q, µg/cm^2) versus time (hr). The steady state flux (Jss, µg/cm^2.hr) of Carvedilol was calculated from the slope of the plot using linear regression analysis.

Table 11: *In-vitro* permeation parameters across mucous membrane.

Formulation code	Q (µg/cm^2)	Jss (µg/cm^2.hr)	Kp (x 10^{-3})
F-1	1251.01	198.40	13.23
F-2	1395.01	202.00	13.47
F-3	1474.92	214.50	14.30
F-4	1522.89	225.10	15.01
F-5	1579.45	240.90	16.04

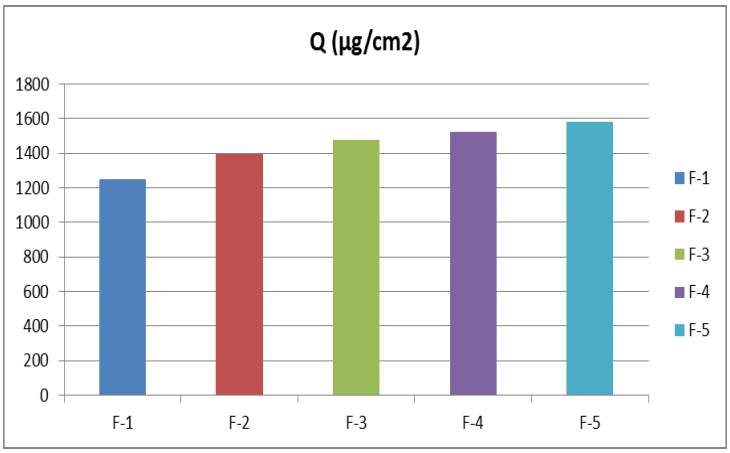

Figure 10: Carvedilol diffused per unit membrane surface area (Q, µg/cm^2) Vs time (hr).

DISCUSSION

Preformulation study: During the studies the carvedilol characterized as white powder freely soluble in water, 0.1N NaOH, 0.1N HCl , 7.4pH buffer and insoluble in ethyl acetate,

having melting point 122 ^{O}C and partition coefficient 0.868. UV spectrogram of carvedilol scanned from 200- 400 nm, λmax found at **241nm.** Calibration Curve prepared in 7.4pH buffer and water with R^2 value 0.996 and 0.999 respective also calculated Linear equation. FT-IR study indicated on the basis of peaks of both carvedilol (pure) and carvedilol + (HPMC + PVP +PEG), that there is no drug excipient interaction.

Evaluation of transdermal patches: All the formulated transdermal patches are evaluated and found, all are flexible smooth and translucent, weight variation was under limits, average thickness was 0.15mm found, average tensile strength was 0.9 Kg/cm^2 found, drug content was 0.73 mg/cm^2 average, moisture content % and moisture uptake % also evaluated.

***In-Vitro* Release Profile:** All the formulated transdermal patches were evaluated for their *In-Vitro* Release. The dissolution study of all formulation shows the percentage drug release were found to be F1-93.10%, F2 -95.25%,F3- 96.16%, F4- 93.95%, F5-96.91% and F6-88.25%, in 24 minutes. According to drug release studied **F-3** and **F-4** formulations shows excellent drug release profile in steady way.

Drug release kinetic: Kinetic modeling of release profile have done. From the data of drug release, it was found that all the formulations follow diffusion mechanism for the drug release**.**

***In-vitro* permeation study:** All formulations (F-1 to F-5) were subjected for diffusion study with mucosal membrane. Cumulative amount of drug released Q (µg/cm^2) at different time intervals and steady state flux (Jss, µg/cm^2.hr) were obtained. Also permeability coefficient (Kp) are calculated and found **F-3** and **F-4** has steady diffusion per unit membrane surface area. Also it was observed that the flux and permeability of Carvedilol.

CONCLUSION

Buccoadhesive patches containing varying amounts of chitosan and pectin were prepared by solvent casting method with slight modification. Glycerol 5% v/v was added as plasticizer under constant stirring, also 1% w/v PVP K-30 was added. Because Caredilol is insoluble in water so, the drug requires a novel drug delivery system which can provide enhanced solubility, an extended period of time and improve absorption via skin. Buccoadhesive patches were characterized for compatibility study, particle size and shape, % entrapment, *in-vitro* drug release. Due to their matrix character, these drug delivery systems showed good

enhanced solubility and sustained release, required for bioavailability and therapeutic activity. Carvedilol induced irritation on skin due to high dose can also be reduced by slow releaseof drug. Major advantages of this delivery system include ease of preparation, good enhanced solubility, high % encapsulation efficiency and sustained drug release. From this study, it was concluded that Buccoadhesive patches of Carvedilol were offers enhanced solubility and continuous release of the medicament and bioavailability of the drug and subsequent efficacy is improved.

Conflicts of interests

There are no conflicts of interests.

REFERENCES

1. Shin, S. C.; Lee, J. W.; Yang, K. H.; Lee, C. H. Preparation and evaluation of bioadhesive benzocainegels for enhanced local anesthetic effects. Int. J. harm, 2003; 260: 77-81.
2. Bindu MB, Zulkar NK. Mohammed, Ravinder NA, David Banji. Mucoadhesive drug delivery system: An overview. Journal of Advanced Pharmaceutical Technology & Research, 2010; 1(4): 381. http://dx.doi.org/10.4103/0110-5558.76436; PMid:22247877 PMCid:PMC3255397.
3. Gawas SM, Dev A, Deshmukh G, Rathod S. Current approaches in buccal drug delivery system. Pharm Biol Eval, 2016; 3(2): 165-77.
4. Khutoryanskiy VV. Advances in mucoadhesion and mucoadhesivepolymers. MacromolBiosci, 2011; 14-11(6): 748-64.
5. Roy S, Pal K, Anis A, Pramanik K, Prabhakar B. Polymers in MucoadhesiveDrug Delivery System. A Brief Note Designed monomers and polymers, 2009; 12(6): 483-95.
6. El-Sayed Khafagy, Amr S. Abu Lila, Nahed Mohamed Sallam, Rania Abdel-Basset Sanad, et al. Preparation and Characterization of a Novel Mucoadhesive Carvedilol Nanosponge: A Promising Platform for Buccal Anti-Hypertensive Delivery. Gels, 2022; 8: 235.
7. Vishakha Dhananjay Jagtap. Development and Evaluation of Buccal Film of Carvedilol Phosphate. International Journal of Research and Review, 2020; 7(5): 277-87.
8. Dhaval A. Chandarana, Keyur S. Patel, Samir C. Patel, Deepa R. Patel, Shailesh T. Prajapati. formulation and evaluation of mucoadhesive buccal tablets of carvedilol. Int J App Pharm, 2020; 12(4): 170-181.

9. Verma, Navneet, and Pronobesh Chattopadhyay. "Effect of novel mucoadhesive buccal patches of carvedilol on isoprenaline-induced tachycardia." Journal of advanced pharmaceutical technology & research, 2014; 5, 2: 96-103. doi:10.4103/2231-4040.133436.