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Effect of Permeation Enhancer on the Diffusion of Carvedilol from the Buccal Adhesive Tablets

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ABSTRACT

Carvedilol is a non selective α and β receptor blocker which undergoes extensive hepatic first pass metabolism by liver and has poor oral bioavailability of 25% - 30%. In the present investigation Carvedilol was formulated as a bilayered buccal adhesive tablets in order to avoid the first-pass effect and decrease the drug loss using two different natural polymers and excipients. Six formulations were made using different concentrations (17%w/w, 35%w/w, 53%w/w) of Pectin and Guar gum. Formulation F5 was selected for further studies of permeability. Three concentrations of SLS (1%, 1.5% & 2%w/w) was used to study the effect of permeation enhancer and improve the permeability of drug. The formulations were tested for % weight variation, hardness, Friability, % Drug content, *in-vitro* drug release, surface pH, Swelling index and Mucoadhesive strength. Mucoadhesive strength was determined by the modified balance method in grams and was found to be between 23.75±0.332gm to 60.89±0.134gm and Surface pH was found to be 7. *In-vitro* release studies revealed that as polymer concentration increases from 17% to 53%w/w, rate of drug release was retarded and the data was fitted into pharmacokinetic models. Among all other formulations, formulations (F5) containing 35%w/w Guar gum were found to be best as the release was retarded upto 8 hours and they have good mucoadhesive strength and they follow zero order with non-fickian diffusion mechanism. Formulation F9 (2%w/w SLS) shows more permeability of drug (34%) compared to other formulations.

Keywords: Carvedilol, Pectin, Guar gum and Sodium lauryl sulphate(SLS).

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INTRODUCTION

Hypertension is a cardiac chronic medical condition in which the systemic arterial blood pressure is elevated. Dietary and life style changes can improve blood pressure control anddecrease risk of associated health complications although drug treatment proves necessary in some patients for whom lifestyle changes prove ineffective or insufficient. Carvedilol is a non-selective α1, β1, β2 -adrenergic antagonist used in the treatment of hypertension and stable angina pectoris. It also possesses antioxidant and antiproliferative effects, which may enhance its ability to combat the deleterious effects of sympathetic nervous system activation in heart failure. Carvedilol was selected as a model drug for the investigation because its oral dose is 6.25mg twice a day, having low molecular weight (406.48), short biological half-life(2-6hrs) and poor bioavailability(25-30%) due to extensive hepatic first pass metabolism when administered orally. To overcome these defeciencies mucoadhesive buccal tablets of Carvedilol were designed. Permeation enhancers were added to improve the permeation of drug and make drug 100% bioavailable[1].

MATERIALS AND METHODS

Carvedilol was obtained as a Gift sample from Aurobindo pharma ltd. Himachal Pradesh.,Guar gum, Pectin, Spray dried Lactose were purchased from S. D. Fine Chem. Ltd., Mumbai, Ethyl cellulose and Talc were purchased from Qualigens Fine Chemicals, Mumbai. All other chemicals were of analytical grade.

Preformulation studies

Drug-excipient compatibility studies[2]

Assessment of possible incompatibilities between an active drug substance and different excipients forms an important part of the pre-formulation stage during the development of solid dosage form. Therefore, the pure drug and the formulations mixed with polymers were subjected to infra-red (IR) studies.

The pure drug and formulations mixed with polymers were separately mixed with IR grade potassium bromide in a ratio (1:100) and pellets were prepared by applying 10 metric ton of pressure in hydraulic press. The pellets were then scanned over range of 4000-400cm^{-1} in FTIR instrument. IR spectra of drug and excipients were included as Figure 5, 6, 7 & 8.

In-vitro buccal permeation studies[3]:

In-vitro diffusion study of pure drug was carried out using fresh sheep buccal mucosa. It was studied using Franz diffusion cell. The donor compartment was filled with 6ml of 0.5%w/v sodium lauryl sulphate solution (SLS) containing 20% methanol. 6.25mg of drug was dissolved

in the above solution. The receptor compartment consists of 15ml of 0.5%w/v SLS solution to maintain sink conditions. The whole assembly was maintained at 37±1^{o} c Three ml of samples were withdrawn from the receptor compartment and replaced with same amount of fresh medium. The withdrawn samples were then diluted suitably and estimated for drug spectrophotometrically at 242.5nm and the % cumulative drug diffused was calculated.

Micromeritic properties [4]

Angle of repose*:*

The fixed funnel and free standing cone methods employ a funnel that is secured with its tip at a given height, h, which was kept 2cm above graph paper that is placed on a flat horizontal surface. With r being the radius, of base of conical pile, angle of repose can be determined by following equation: $\theta = \tan^{-1} (h/r)$

Where, θ is the angle of repose,

h is height of pile, r is radius of base of the pile

Bulk density and tapped density*:*

Both loose bulk density and tapped bulk density were determined. A quantity of 2gm of granules from each formula, previously light Shaken for the break of any agglomerates formed, was introduced into the 10ml of measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall down its own weight from the hard surface from a height of 2.5cm at 2 sec Intervals. The tapping was continued until no further change in the volume was noted

LBD and TBD were calculated using the following formulas:

LBD: Weight of the powder/volume of the packing.

TBD: Weight of the powder/Tapped volume of the packing.

Compressibility index*:* The compressibility index of the granules was determined by Carr's Compressibility index.

$$\text{Carr's index (\%)} = [(TBD-LBD) * 100] / TBD$$

Where,

LBD: Weight of the powder/volume of the packing.

TBD: Weight of the powder/Tapped volume of the packing.

Hausner's ratio*:* Hausner's ratio can be determined by the following equation,

$$\text{Hausner's ratio} = TBD / LBD$$

Where,

TBD -Tapped bulk densities & LBD- Loose bulk densities.

Formulation of mucoadhesive buccal tablets of carvedilol[5]

The composition of tablet formulations were shown in table 1. Required quantities of materials as per the formulae were weighed excluding EC and triturated in mortar. The blended powder was then slightly compressed and then EC was added to compact as backing layer and compressed into tablets employing direct compression technique using 16 station rotary tablet machine (Cadmach, India) with 9 mm round shaped flat punches.

Table 1: Formulation of Carvedilol Buccal Adhesive Tablets

S.No	Ingredients	Quantity per tablet in mg								
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	Carvedilol	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
2	Pectin	35.437	70.875	106.31	-	-	-			
3	Guar gum	-	-	-	35.437	70.875	106.31	70.875	70.875	70.875
4	SLS	-	-	-	-	-	-	2	3	4
5	Spray dried lactose	106.31	70.875	35.437	106.31	70.875	35.437	68.875	67.875	66.875
6	Talc	2	2	2	2	2	2	2	2	2
7	Ethyl cellulose	50	50	50	50	50	50	50	50	50
	Total weight (mg)	200	200	200	200	200	200	200	200	200

Evaluation of physical properties of tablet [4]

Hardness test*:* The hardness of the tablets were determined using Monsanto Hardness tester. It is expressed in kg/cm^2. Six tablets were randomly picked from each formulation and the mean and standard deviation values were calculated.

Friability: A friability test was conducted on the tablets using an roche friabilator. Twenty tablets were selected from each batch and any loose dust was removed with the help of a soft brush. The tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The drum was rotated at 25 rpm for 4 minutes after which the tablets were removed. Any loose dust was removed from the tablets as before and the tablets were weighed again (W_{final}).The percentage friability was then calculated by,

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} x100$$

% Friability of tablets less than 1% is considered acceptable.

Weight variation:

The weight variation test was conducted by weighing 20 randomly selected tablets individually, calculating the average weight and comparing the individual tablet weights to the average. The specification of weight variation is 10%.

% Drug Content[3]:

Three tablets were taken in separate 100 ml volumetric flaks containing 100 ml of 0.5%w/v SLS

and were kept for 24 hrs undisturbed. The solutions were taken in a mortar and pestle and triturated well. This is to be added The solutions were then filtered, diluted suitably and analyzed at 242.5 nm using UV- spectrophotometer. The average of three tablets was taken and %drug content was calculated.

Study the effect of permeation enhancers on drug permeation through sheep buccal mucosa[5]:

The second part of the present investigation was to study the effect of permeation enhancer Sodium lauryl sulfate (SLS) (1%, 1.5% and 2% w/w of total tablet weight) on drug diffusion through sheep buccal membrane and to report the optimum concentration of permeation enhancer in case of bilayered carvedilol buccal tablets.

Preparation of sheep buccal mucosa[5]:

The sheep buccal mucosa was obtained from the local slaughter house. The head of sheep was obtained and the buccal membrane was separated from the underlying connective tissues using surgical blades, scissors and forceps. Then the membrane was placed in buffer solution to maintain the integrity .The thickness of the membrane was measured using vernier calipers and the membrane of thickness 1mm was used for *ex vivo* permeation studies.

Calculation of flux[6]:

Flux can be calculated by measuring the permeability coefficient. The drug from the dosage form diffuses through the membrane by passive diffusion mechanism and this can be described by Fick's first law of diffusion. Thus the Flux can be calculated from the equation of fick's first law of diffusion.

$$\mathbf{J} = \frac{DKp}{h} C_D$$

J = flux of drug absorption i.e; the amount of drug moving across the oral mucosa per unit time and area.

D = diffusion coefficient of drug inside the oral mucosa

Kp = Partition coefficient between oral mucosa and the buffer solution

h = effective path length of oral mucosa across which the drug must traverse

CD = Drug concentration in donor chamber

The permeability coefficient (P) can be obtained from the above equation

$$P = \frac{DKp}{h}$$

Thus Flux is

$$J = PCD$$

$$= \frac{A}{St}$$

A = Amount of drug transported at time (t).

A = PSCDt

Therefore the total amount of drug on the donor side is(AT)

AT = VDCD

VD = volume of donor chamber

% of Drug transported (%T) can be known by equation

$$\%\mathbf{T} = \frac{A}{A_T}$$

$$= \frac{PS}{V_D} t$$

Thus permeability coffecient can be obtained from the slope of the graph plotted between % Drug transported (%T) and time(t).

Surface pH[3]:

The tablets were allowed to swell by keeping it in contact with 1 ml of distilled water (pH 6.5 ± 0.05) for 2hr at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablet and allowed it to equilibrate for 1min.

Swelling index[3]:

Tablets were weighed (W1) and placed separately in Petri dishes containing 20 ml of 0.5w/v SLS solution. At regular time intervals tablets were removed and the excess water on their surface was carefully removed using filter paper. The swollen tablets were reweighed (W2) and the index of swelling was calculated by the following formula and were reported in Table 2.

Swelling Index (S.I) = [(W2-W1)/W1] x 100

***In-vitro* mucoadhesive strength[3]:**

Adhesive properties of Carvedilol mucoadhesive buccal tablet formulations were carried out by using modified balance method described by Gupta et.al[9]. Sheep buccal mucosa were collected from the slaughter house and stored in 0.5%w/v SLS buffer solution. The sheep buccal mucosa was attached to the back of right pan of the balance by using cellophane tape. The balance was now balanced properly using sufficient weights. A tablet to be tested was attached to the base of a glass slide using cynoacrylate glue and the right pan was attached to it with mild force and weights were added slowly to the left pan and the weight in grams at which the tablet detaches form the sheep mucosal surface was noted. And reported in Table 2.

***In-Vitro* Release Studies[3]:**

In-vitro drug release studies of carvedilol buccal adhesive tablets were performed in 500 ml of 0.5%w/v SLS at 37±0.5°C using USP type II dissolution apparatus with a paddle speed of 50 rpm. The tablet was attached to a glass slide with instant adhesive and placed at the bottom of dissolution vessel. Aliquots (5ml each) were withdrawn at regular time intervals and replaced with fresh medium to maintain sink conditions. The samples were filtered, with appropriate dilutions with the above solution and were analysed spectrophotometrically at 242.5nm and correlation coeffecients, rate constant, T50, T90 were caluculated and reported in Table 3.

***In-vitro* Permeation studies[5]:**

In-vitro permeation studies were conducted by using Franz diffusion cell. The buccal epithelium of 1mm thickness was carefully mounted in between the two compartments of modified franz diffusion cell. Tablets were stuck to the mucosa by facing backing membrane to the donor side containing 6ml of phosphate buffer pH6.8 simulating saliva pH. Receptor compartment consists of 14ml of of pH 7.5 buffer and entire assembly was maintained at 37° ± 0.5 °c by placing it in water bath under gentle stirring. 3ml of aliquots were collected at regular intervals of time upto 12hrs. The volume was replenished with equal volume of buffer solution and the drug content was analysed by UV-Spectrophotometry at 242.5 nm and flux values, amount permeated, permeation coefficient were reported in Table 4.

RESULTS AND DISCUSSION:

Drug excipients interaction studies*:*

Spectra of the pure drug, excipient and physical mixture of drug and excipient were recorded (as shown in Table 2 and Figure. 1-5) in between 400-4000 wave number (cm^{-1}). The FTIR spectral analysis showed that there is no appearance or disappearance of any characteristic peaks of pure drug carvedilol and in the physical mixture which confirms the absence of chemical interaction between drug and polymers.

Table 2: Drug excipients interaction studies

Peak in pure drug and Functional group	Peak in physical mixture and Functional group
O-H and N-H (Stretching) 3341.24cm^{-1}	O-H and N-H (Stretching) 3341.24cm^{-1}
C-H (Stretching, vibration) 2921.08cm^{-1}	C-H (Stretching, vibration) 2921.08cm^{-1}
N-H bending - 1587.87cm^{-1}	N-H bending - 1587.87cm^{-1}
Skeletal vibrations of aromatic ring - 1501.93 and 1446.85cm^{-1}	Skeletal vibrations of aromatic ring - 1501.93 and 1446.85cm^{-1}

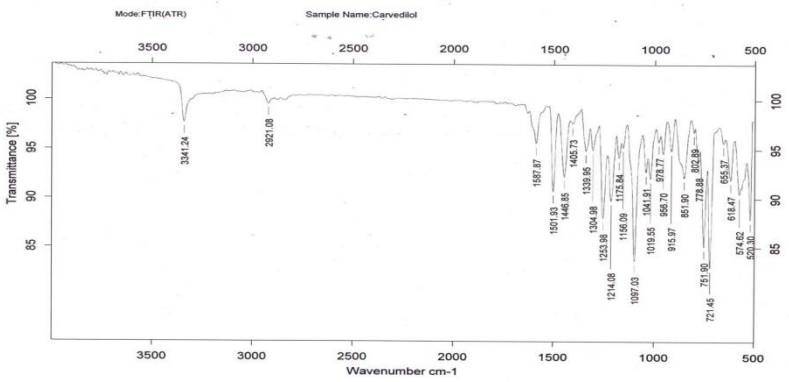

Figure 1: IR spectra of Carvedilol pure drug

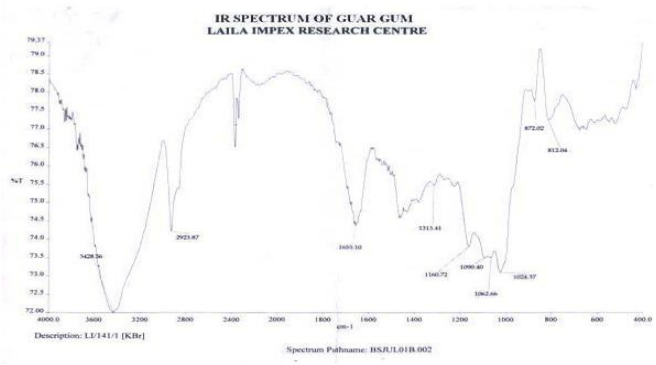

Figure2: IR spectra of Guargum:

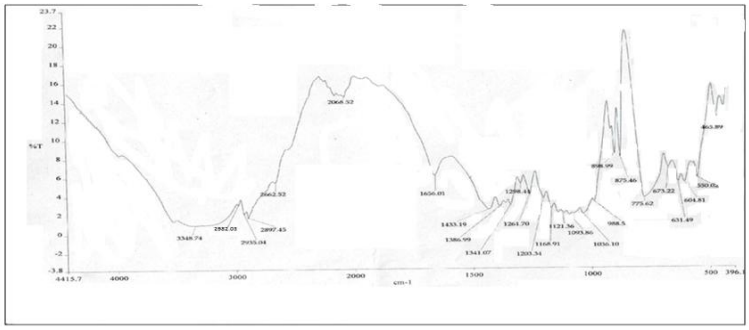

Figure 3: IR Spectrum Spray Dried Lactose:

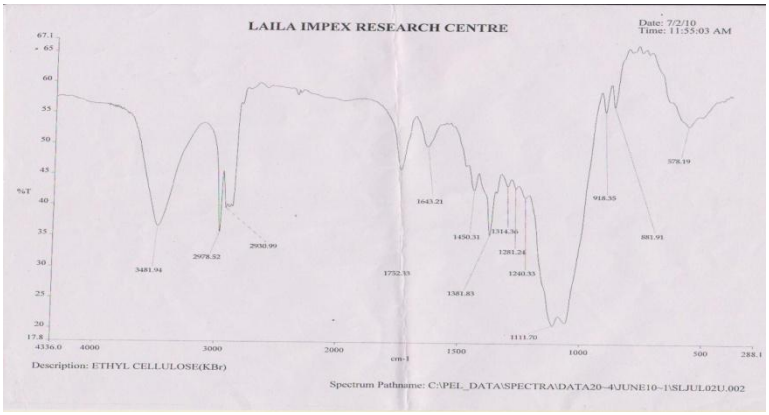

Figure 4: IR spectrum of Ethyl cellulose

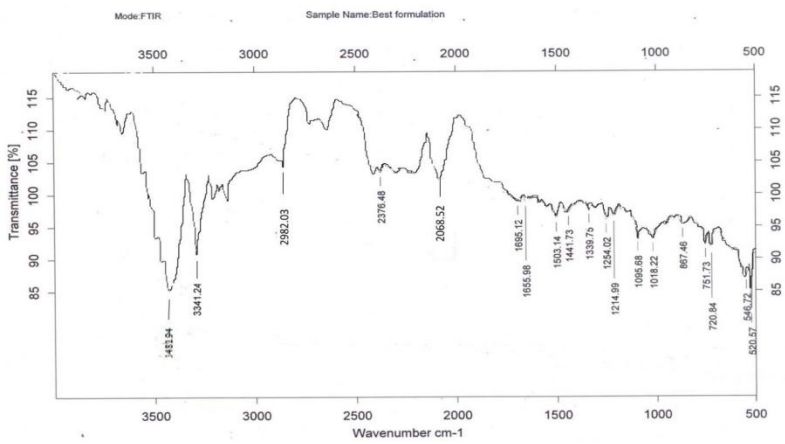

Figure 5: IR Spectrum of Best Formulation (F9)

Micromeritic properties:

Granules of all the formulations were subjected for various pre-compressional evaluations such as angle of repose, bulk and tapped density, compressibility index and Hausner's ratio. Results of all the pre-compressional parameters performed on granules for formulations shown in Table 3.

The angle of repose was found to be ranging from 17°.322"±0.036 to 20°.668"±0.076 for the granules of all the formulations. Compressibility index was found to be ranging from 13.33±0.156 to 16.987±0.146 % for the granules of all the formulations. The results of Hausner's ratio were found to be lesser than 1.25 which indicates better flow properties. The results of angle of repose (<30) indicates good flow properties of the powder. This was further supported by lower compressibility index values. Generally compressibility values up to 15% results in good to excellent flow properties.

Table 3: Results of physical evaluation of Pre-compression Blend

Formulations	Angle of repose (degree± SD)	Bulk Density (g/mL± SD)	Tapped Density (g/mL± SD)	Carr's Index (%± SD)	Hausner's ratio (%± SD)
F1	17.322°±0.036	0.386±0.078	0.457±0.064	15.33±0.342	1.18±0.055
F2	18.774°±0.028	0.392±0115	0.453±0.085	13.33±0.156	1.15±0.082
F3	20.636°±0.055	0.398±0.093	0.469±0.136	15.032±0.271	1.17±0.067
F4	18.267°±0.033	0.519±0.122	0.621±0.023	16.42±0.430	1.19±0.032
F5	19.735°±0.082	0.524±0.074	0.620±0.079	15.48±0.558	1.18±0.044
F6	20.668°±0.076	0.553±0.003	0.640±0.048	13.59±0.257	1.15±0.061
F7	18.565°±0.031	0.453±0.034	0.570±0.084	15.767±0.356	1.195±0.066
F8	20.645°±0.072	0.367±0.154	0.533±0.192	16.453±0.285	1.186±0.046
F9	19.483°±0.084	0.398±0.077	0.504±0.074	16.987±0.146	1.194±0.079

Evaluation of prepared tablets:

The results of physical evaluation of tablets were given in Table 4. The tablets of different batches were found uniform with respect to hardness within the range of 4.5±0.212 to 4.9±0.355

kg/cm^2. Another measure of a tablet's strength is friability. Conventional compressed tablets that lose less than 1% of their weight are generally considered acceptable. Results of friability test were also has been found within limit. In weight variation test, the pharmacopoeial limit for percentage deviation for tablets of more than 250 mg is ±5% and all the formulations were found to comply with the specifications given in I.P. for weight variation test. Good uniformity in drug content was found among the formulations, and percentage of drug content was more than 95%. All the tablet formulations showed acceptable pharmaco-technical properties.

Table 4: Evaluation of bilayered buccal adhesive tablets of carvedilol.

Formulation	%Weight Variation (mg)	Hardness (kg/cm^2)	%Friability	Surface pH	Drug Content (%)
F1	0.411±0.210	4.8±0.174	0.38±0.053	6.36±0.177	99.47±0.06
F2	0.456±0.304	4.6±0.355	0.47±0.039	6.31±0.0321	98.72±0.033
F3	0.407±0.158	4.9±0.197	0.55±0.062	6.24±0.035	100.11±0.55
F4	0.427±0.270	4.7±0.102	0.36±0.025	6.11±0.032	99.65±0.011
F5	0.435±0.166	4.5±0.212	0.53±0.023	6.25±0.242	100.82±0.043
F6	0.408±0.248	4.8±0.116	0.62±0.024	6.74±0.045	99.33±0.06
F7	0.432±0.034	4.8±0.177	0.46±0.055	6.5 ±0.114	99.57±0.026
F8	0.446±0.192	4.7±0.226	0.51±0.028	6.3±0.036	99.22±0.034
F9	0.318±0.333	4.9±0.209	0.62±0.036	6.6±0.217	100.37±0.25

Swelling index and Mucoadhesive strength:

The results of swelling index and mucoadhesive strength are given in Table 5. Swelling index is a property for uniform and prolonged release. Mucoadhesive property to remain the tablet in contact with buccal membrane for a long time. It was determined by modified balance method. The range of swelling index was found to be 19.04±0.321 to 200.05±0.255 and mucoadhesive strength ranges between 23.75±0.332 to 60.89±0.134g.

Table 5: Swelling index and Mucoadhesive strength of Formulations

S.No	Formulation	Swelling index	Mucoadhesive strength(g)
1	**F1**	25.76±0.321	23.75±0.332
2	**F2**	25.22±0.330	30.64±0.275
3	**F3**	19.04±0.321	38.11±0.163
4	**F4**	85.71±0.168	35.66±0.203
5	**F5**	175.41±0.217	55.36±0.175
6	**F6**	200.05±0.255	60.89±0.134
7	**F7**	173.24±0.211	50.75±0.234
8	**F8**	175.44±0.115	51.65±0.186
9	**F9**	174.58±0.305	52.43±0.099

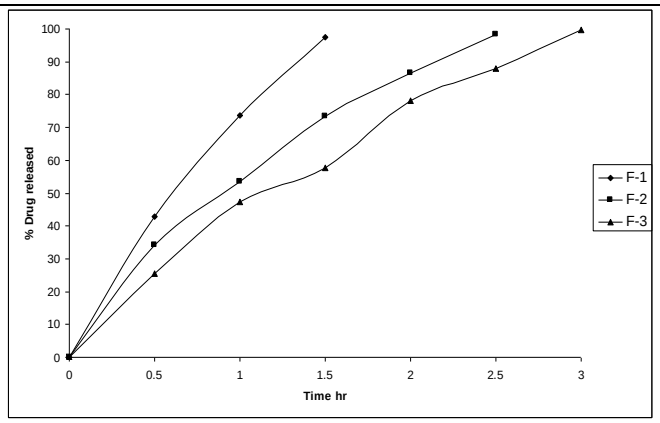

Figure 6: Comparative dissolution profile of Carvedilol buccal adhesive tablets formulated with Pectin

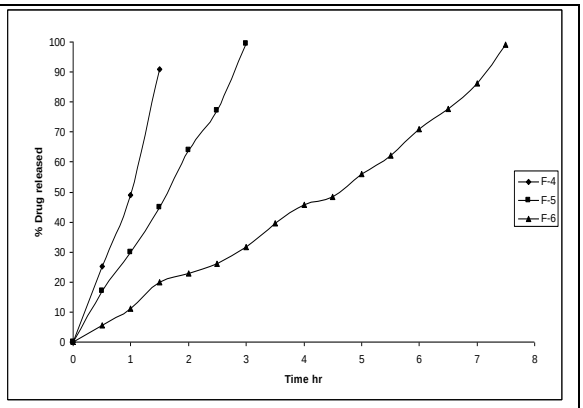

Figure 7: Comparative dissolution profile of Carvedilol buccal adhesive tablets formulated with Guar gum

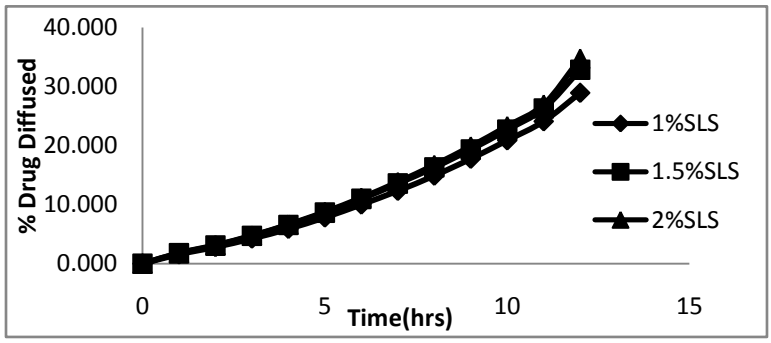

Figure 8: Comparative diffusion profile of buccal adhesive tablets of Carvedilol formulated with SLS as permeation enhancer

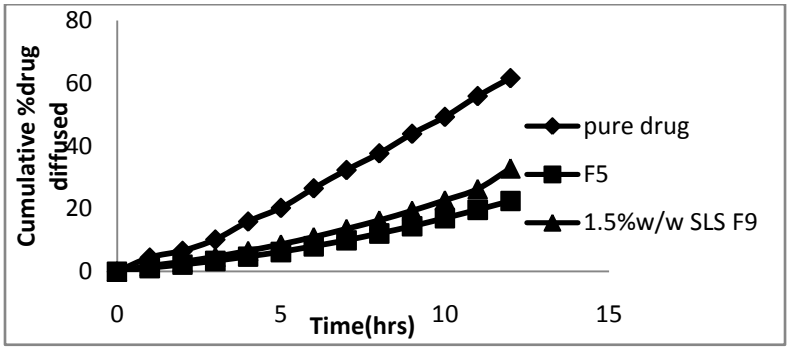

Figure 9: Comparative diffusion profile of pure drug, F_5 and F_9.

In - vitro drug release study:

The results of *in-vitro* drug release studies of individual polymers and permeation enhancer were depicted in Figure 9. The comparative *in-vitro* diffusion profile of pure drug, best formulation (F5) of guar gum and SLS was depicted in Fig 6-9. The percentage of drug released for the formulation F_5 was 99.296±0.82% at the end of 8.5 hrs. The % drug released was in the following order $F_4<F_5>F_6$. The % drug release from all the three formulations containing pectin

was found to be upto 98% within 2hrs which did not show a controlled release profile. Thus the formulation F5 containing 35% of guar gum was chosen as best formulation. The maximum %drug diffused was from the formulation F9 containing SLS as permeation enhancer which was found to be 34.743±0.13% for 12hrs.

Drug release study:

The drug release mechanisms were analyzed by *in-vitro* release data were fitted into various release equations and kinetic models as shown in Table 6. The drug release from the formulations containing guar gum followed zero order kinetics; the correlation coefficient revealed that the Peppas model was applicable to the release data as depicted in Figure 10. The drug release from the formulations containing pectin followed zero order kinetics; the correlation coefficient revealed that the Higuchian model was applicable to the release data indicating matrix type of drug release from the formulation as depicted in Figure 11. The values of release exponents 'n' for formulations F_1 to F6 are given in Table 6. The zero order release rate constant (k_o), t_{50} and T90 were also given in table 5. The R^2 value and 'n' value for best formulation F5 were found to be 0.9879 and 0.9848 respectively. The rate constant, t_{50} and T90 were found to be 1.5250 mg/hr, 3.9hr and 7.8hr. Thus by the above values it is indicated that the release is governed by non-Fickian anomalous transport for guar gum formulations and is Fickian diffusion for pectin formulations.

Table 6: *In-vitro* release kinetics of Carvedilol buccoadhesive tablets

S.No	Formulation	Correlation coefficient			Release Rate		
		Zero order	Peppas (n)	Higuchi	Ko(mg/hr)	T50(hr)	T90(hr)
1	**F1**	0.9741	1.000	0.9996	6.1287	0.2	0.8
2	**F2**	0.9286	0.9864	0.999	4.9233	0.3	1.2
3	**F3**	0.9051	0.9776	0.9903	4.4249	0.4	1.6
4	**F4**	0.9659	0.9817	0.9736	1.7936	2.8	5.7
5	**F5**	0.9879	0.9848	0.9677	1.5250	3.9	7.8
6	**F6**	0.9416	0.9257	0.9187	1.1735	6.9	12.2

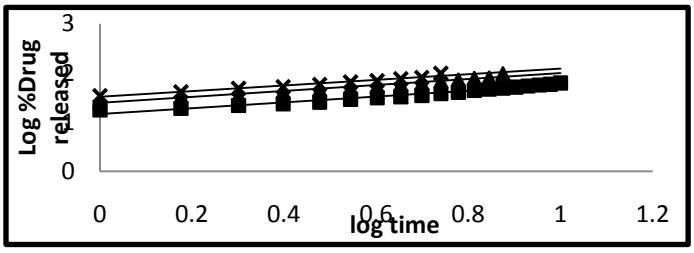

Figure 10:Comparative peppas plof for Carvedilol buccal Tablets formulated with Guargum

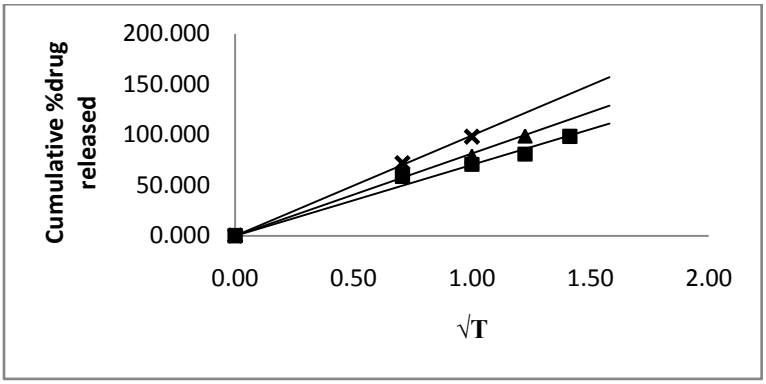

Figure 11: Comparative matrix plot for Carvedilol buccal adhesive tablets formulated with Pectin

Diffusion study:

In second part of the investigation, effect of permeation enhancer (SLS) was studied on drug release from the formulation F_5. F_5 was selected for further studies based on the results of Cumulative %drug released, Swelling index(S.I) and Mucoadhesive strength. Permeation studies on the formulation F_5 were conducted and the %cumulative drug diffused was 22.424±0.13%, Flux(J), Permeability coefficient and Amount of drug permeated were 8.903µg/cm$^{2/}$hr, 0.8586cm/hr and 1388.84µg respectively. Hence permeation enhancer was employed to increase the permeability of the drug through the membrane. The results of *in-vitro* permeation studies were reported in Table 7. The comparative *in-vitro* diffusion profile was depicted in Fig 9. The percentage of drug diffused for the formulations F_7, F_8 and F_9 was 28.066±0.13%, 32.825±0.13% and 34.743±0.13 % at the end of 12th hr. The % drug diffused was in the following order F_9>F_8>F_7.

The flux (J) for the formulations F_7, F_8 and F_9 was found to be 11.157 µg/cm^2/hr, 12.333 µg/cm^2/hr and 13.481 µg/cm^2/hr respectively. The permeability coefficient values were 1.0728cmhr^{-1}, 1.1859cmhr^{-1}, 1.2962cmhr^{-1} and the amount permeated in 12hrs was 1735.13 µg, 1918.03µg and 2096.56 µg reported in Table 7.

Table 7: Diffusion data of carvedilol tablets formulated with SLS

S. No	Formulation	Cumulative %drug diffused	Amount permeated in 12 hours (µg)	Flux (J) (µg/cm^2/hr)	Permeability coefficient (cm/hr)
1	**Pure drug**	61.591±0.13	3924	25.2315	2.4261
2	**F5**	22.424±0.13	1388.84	8.903	0.85865
3	**F7**	28.940±0.13	1735.13	11.157	1.0728
4	**F8**	32.825±0.13	1918.03	12.333	1.1859
5	**F9**	34.743±0.13	2096.56	13.481	1.3013

CONCLUSION:

Bilayer buccoadhesive tablets of Carvedilol were successfully developed with Guar gum and permeation enhancer (SLS) for controlled release. Among both the polymers employed at different concentrations of 17%w/w, 35%w/w and 53% w/w the formulations prepared with guar gum as polymer has shown more controlled release upto 8 hrs which is suitable for bucccal tablets. Further incorporation of permeation enhancer has also improved the diffusion of the drug from the tablet through the buccal membrane so that more amount of drug gets available to the body i.e the bioavailability of drug is increased. Thus the buccal adhesive tablets of Carvedilol have been successfully developed and has all the parameters within the qualifying limits.

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REFERENCES:

1. Tora-Tora Grabowski. "Principles of Anatomy & Physiology. 7th Edition, Edited by Gerard J. Toratora and Sandra Reynolds Grabouski". Harper Collins College Publishers; 770-774: 1992.
2. Mohd Abdul Hadi, Lokeswara Babu V, Narottam Pal, Srinivasa Rao A. Formulation and evaluation of Sustained release Matrix tablets of Montelukast Sodium. Int. J. of Pharm. 2012; 2(3): 574-582.
3. Soniya pandey, Aarti gupta, Jitendra singh Yadav and Shah DR. "Formulation and In-Vitro Evaluation of Bilayered Buccal Tablets of Carvedilol". Indian J. Pharm. Educ. Res. 44(3), June-Sep,2010.
4. Martin A, Swarbrick J, Cammarata A, editors. Physical Pharmacy, Physical chemical principles in the pharmaceutical sciences. 3 rd ed. Indian edition. Mumbai: Varghese Publishing house; 1991: 492-521
5. Vamshi vishnu Yamsani, Bhanoji Rao ME. Development and in-vitro evaluation of buccoadhesive Carvedilol tablets. Acta Pharm. 2007;57:185–197.
6. Jain NK. Controlled and Novel Drug Delivery. CBS Publishers, 1st Ed. New Delhi, 353-380, 2008.