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DESIGN AND EVALUATION OF BUCCAL TABLETS OF SIMVASTATIN

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Abstract:
In present study mucoadhesive buccal tablet of simvastatin was prepared and evaluated. The different formulations of buccal tablets of simvastatin containing the polymers in various combinations were prepared by direct compression method and characterized for swelling studies, surface pH, mucoadhesive properties and in vitro release studies. All the formulations showed the satisfactory results bioadhesive performance. The swelling index was proportional to carbopol content & another bio-adhesive polymer. The surface pH of all tablets was found to be satisfactory, close to neutral pH; hence, buccal cavity irritation should not occur with these tablets. Drug release and drug diffusion from the tablets were depended on the ratio and type of the polymer used in the formulation. The formulation (F10) containing carbopol and guargum (1:3 ratio) the maximum percentage of in-vitro drug release for 8h. The formulation F10 was optimized based on good bioadhesive strength and in vitro drug release (88.05 % for 8h).

Key words: Bioadhesive, simvastatin, carbopol and guargum

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1. INTRODUCTION:

Drug delivery via the buccal route using bioadhesive dosage forms offers such a novel route of drug administration. Extensive first-pass metabolism and drug degradation in the harsh gastrointestinal environment can be circumvented by administering the drug via buccal route [(1)]. Buccal delivery involves administration of desired drug through the buccal mucosal membrane lining of oral cavity. The mucosal lining of oral cavity offers some distinct advantages. Drug absorption through buccal mucosa is mainly by passive diffusion into the lipoidal membrane. After absorption the drug is transported through facial vein which then drains into the general circulation via jugular vein bypassing the liver and there by sparing the drug from first-pass metabolism. Buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins oligonucleotides and polysaccharides as well as conventional small drug molecules [(2)].

Drug absorption through buccal mucosa is mainly by passive diffusion into the lipoidal membrane. After absorption the drug is transported through facial vein which then drains into the general circulation via jugular vein bypassing the liver and there by sparing the drug from first-pass metabolism. Buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins oligonucleotides and polysaccharides as well as conventional small drug molecules [(3)].

2. MATERIALS AND METHODS:

2.1. Materials

Simvastatin (SIM) was obtained as a gift sample from Euro Labs, Hyderabad. Carbopol934P, SCMC, HPMC, Ethyl cellulose and Guargum were purchased from Signet Chemical Corporation, Mumbai. Magnesium stearate and MCC were purchased from S.D. fine chemicals, Mumbai.

2.2 Methods

2.2.1. Preformulation studies

It is one of the important pre-requisites in development of any drug delivery system. Pre-formulation studies were performed on the drug, which included melting point determination, pH, solubility studies and Infrared (IR) absorption spectroscopy [(4)].

2.2.2. Pre-compression parameters

2.2.2.1. Angle of Repose

The angle of repose was determined by the funnel method suggested by Newman. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

$$\mathbf{Tan\ \theta = h/r,\quad \theta = tan\text{-}1\ h/r}$$

Where; θ = angle of repose, h = height of the cone**,** r = radius of the cone base

2.2.2.2. Bulk Density

Specific bulk volume or reciprocal of bulk density is called bulkiness or bulk. Bulkiness increases with a decrease in particle. The bulkiness can be calculated by the following formula [(5)],

Bulkiness= 1/ Db

Where, Db = Bulk Density.

Bulk density is defined as the mass of the powder divided by the bulk volume and is expressed as gm/ cm3.

$$Db=M/Vb$$

Where; Db =bulk density, M = weight of sample in gm, Vb = bulk volume (untapped volume)

2.2.2.3. Tapped Density

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. It is expressed in g/ml and is given by:

$$\mathbf{Dt = M / Vt}$$

Where; M = mass of powder, Vt = tapped volume of the powder.

2.2.2.4. Void Volume

The volume of the spaces is known as the void volume "v" and is given by the Formula,

$$\mathbf{V=Vb-Vt}$$

2.2.2.5. Porosity

The porosity € of powder is defined as the ratio of void volume to the bulk volume of the packaging. The porosity of the powder is given by

$$\mathbf{€= Vb - Vt/ Vb =1- Vt/Vb}$$

Porosity is frequently expressed in percentage and is given as; **%€ = (1 - Vt/ Vb) X 100.**

2.2.2.6. Carr's index

It indicates powder flow properties. It is expressed in percentage and is give

I = Dt-Db/Dt X 100

2.2.2.7. Hausner's ratio:

A similar index to indicate the flow properties can be defined by Hausner's ratio. Hausner's ratio can be calculated by using following formula:

Hausner ratio = Dt/Db

Where; Dt = tapped density, Db = bulk density.

2.2.3. Spectral analysis of simvastatin:

2.2.3.1. Determination of λmax

100 mg of simvastatin was dissolved in 100ml of methanol giving 1mg/1ml solution. Suitable dilutions were made in phosphate buffer pH 6.8 and finally scanned for maximum absorbance using UV spectrophotometer in the range from 200-800nm [(7)].

2.2.3.2. Construction of standard graph of simvastatin

An accurately weighed 100mg of simvastatin was dissolved in 100ml of methanol and volume was made up to mark using methanol, to make (1mg/ml) standard stock solution. Then 10ml stock solution was taken in another 100ml volumetric flask and further dilution up to 100 ml with methanol to give 100µg/ml standard stock solution. Final concentrations were prepared 2, 4, 6, 8, 10, 12 and 14µg/ml. the absorbance of standard solution was determined UV-VIS spectrophotometer at 239nm. Linearity of standard curve was accessed from the square of correlation coefficient (r^2) which determined by least-square linear regression analysis [(8)].

2.2.4. Formulation development of buccal tablets of simvastatin

Preparation of buccal tablets:

Buccoadhesive buccal tablets were prepared by a direct compression method. Various batches of buccal tablets were prepared by varying the concentration of CP, HPMC K100, sodium CMC and guar gum. The drug and mucoadhesive polymer mixture (core layer) were prepared by homogeneously mixing the drug with CP, HPMC K4M, sodium CMC and guar gum, microcrystalline cellulose and magnesium stearate in a glass mortar for 15 m. The composition of formulation development is shown in table no 1.

The mixture was then compressed using indigenously developed and standardized stainless-steel punches and die. The upper punch was raised and the backing layer of EC granules (50 mg) was placed on first layer; the 2 layers were then compressed to form buccoadhesive bilayer tablet. Each tablet weighed around 300 mg with a thickness around 8 mm [(9)].

Table 1: Composition of buccal tablets of simvastatin

Ingredients used in formulations (mg)	Formulations codes									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Simvastatin	20	20	20	20	20	20	20	20	20	20
Carbopol 934	150	_	_	_	75	50	75	75	50	50
HPMC K100	_	150	_	_	75	100	_	_	_	_
Sodium CMC	_	_	150	_	_	_	75	_	100	_
Guargum	_	_	_	150	_	_	_	75	_	100
Microcrystalline cellulose	100	100	100	100	100	100	100	100	100	100
Ethyl cellulose	20	20	20	20	20	20	20	20	20	20
Magnesium stearate	10	10	10	10	10	10	10	10	10	10

Total weight	300	300	300	300	300	300	300	300	300	300

2.2.5. Post compression parameters

2.2.5.1. Hardness

The hardness of the tablet was determined using hardness tester, for each batch three tablets were tested,it is expressed in kg/cm^2 [(10)].

2.2.5.2. Thickness

Twenty tablets were randomly selected from each batch and their thickness was measured by using vernier calipers, it is expressed in millimeter [(11)].

2.2.5.3. Friability

Twenty tablets were weighed and placed in the roche friabilator. The apparatus was rotated at 25 rpm for 4 min. After revolutions the tablets were dedusted and weighed again. The percentage friability was measured using the formula [(12)].

2.2.5.4. Uniformity of weight

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets were calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviate from the average weight by more than the percentage [(13)].

2.2.5.5. Percentage Drug content

Ten tablets were taken and powdered; powder equivalent to one tablet was weighed accurately and allowed to dissolve in 10 ml ethanol and make up to 100 ml with distilled water on a rotary shaker overnight. After filtration through whatmann filter paper and sufficient dilution with distilled water, samples were analyzed spectrophotometrically at 239 nm. This procedure was repeated thrice. Amount of drug present was determined from the standard curve of simvastatin [(14)].

2.2.5.6. Surface pH determination

The surface pH of the buccal tablets was determined to investigate the chances of any side effects. As an acidic or alkaline pH may irritate the buccal mucosa, the surface pH should be close to neutral. The method used to determine surface pH of the formulation was according the reported method. In briefly, a combined glass electrode was used to measure the surface pH. The tablet was allowed to swell by keeping them in contact with 1 ml of distilled water (pH 6.8 ± 0.05) for 2 h and pH was noted by bringing the electrode in contact with the surface of the formulation and allowing it to equilibrate for 1 min [(15)].

2.2.5.7. Swelling studies:

The swelling property of buccal tablets was evaluated by determining percentage hydration. Each tablet was weighted (W1) and placed in phosphate buffer pH 6.8 for predetermined time intervals. After immersion for a specified time, tablets were wiped out to remove excess of surface water by using filter paper and again weighted (W2). Percent hydration was calculated by using following formula [(16)].

$$\% \text{ hydration} = \frac{W2-W1}{W1} \times 100$$

Where; W1 - initial weight of the tabet, W_2- weight of the tablet after swelling.

2.2.5.8. Mucoadhesive strength:

Mucoadhesive strength of the buccal tablets was measured on the modified physical balance method. The method used goat buccal membrane as the model mucosal membrane. The fresh goat buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. A piece of mucosa was tied to the glass slide which was moistened with phosphate buffer pH6.8. The tablet was stuck to the lower side of another glass slide with glue. The both pans were balanced by adding an appropriate weight on the left hand pan. The glass slide with mucosa was placed with appropriate support, so that the tablet touches the mucosa. Previously weighed beaker was placed on the right hand pan and water was added slowly to it until the tablet detach from the mucosal surface gave the bioadhesive strength. The experiment was performed in triplicate and average values were calculated [(17)].

2.2.5.9. In vitro drug release studies:

To study the drug release from the buccal tablets, the USP type II apparatus paddle method was used. The dissolution medium used consisted of 900 ml of phosphate buffer (pH 6.8) of saline. The release was performed at 37^0c ± 0.5^0c, with a rotation speed of 50 rpm. The backing layer of buccal tablet was attached to the glass slide with cyanoacrylate adhesive. The glass slide was placed to the bottom of the dissolution vessel. At a predetermined time intervals, samples (5 ml) were withdrawn and replaced with fresh medium. The samples were filtered through whatman filter paper and after appropriate dilution analyzed by UV spectrophotometer at 239 nm [(18)].

2.2.6. Drug release kinetics

2.2.6.1. Zero-order release kinetics

$$Q(t)=k_o t$$

Where Q (t) is percent of drug dissolved as function of time't' min and k_o is dissolution rate constant for zero order release. A plot of %drug released versus time will be linear if release obeys zero order kinetics.

2.2.6.2. First-order release kinetics

$$\mathbf{logQ_{t=}\ logQ_o+k_1t/2.303}$$

The first order equation describes the release from systems where release rate is concentration dependent. Where Q_o is the initial amount of the drug't' is in min. and k_1 describes the dissolution rate constant for first order release kinetics.

2.2.6.3. The simplified Higuchi model

$$\mathbf{Q(t)=K_Ht^{1/2}}$$

Where, Q(t) is the percent of drug dissolved, time 't' in min, K_H is a dissolution rate constant for square root of time kinetics in percent dissolved $min^{1/2}$.

2.2.6.4. The Korsemeyer – peppas kinetics

A plot of the fraction of the logarithm of % drug released against logarithm of time will be linear if the release obeys Korsemeyer – peppas equation [19].

$$\mathbf{Log\ Q = log\ k + n\ log\ t}$$

Where, k is the release rate constant.

3. RESULTS AND DISCUSSION:

3.1. Standard graph of simvastatin

The concentrations are ranged between (2 to 14µg/ml). The absorbance of standard solution was determined UV-VIS spectrophotometer at 239nm. Linearity of standard curve was accessed from the square of correlation coefficient was found to be R^2 0.998. The results are shown in figure 1.

Table 2: Precompression parameters of powder blend

Formulation code	Bulk density	Tapped density	Compressibility index	Hausner Ratio	Angle of repose
F1	0.88±0.05	0.87±0.08	11.04±0.05	1.03±0.01	32.69±0.15
F2	0.89±0.02	0.86±0.02	8.36±0.01	1.07±0.02	24.96±0.15
F3	0.86±0.015	0.84±0.03	8.75±0.02	1.01±0.01	27.56±0.11
F4	0.85±0.02	0.89±0.024	7.4±0.02	1.04±0.015	29.23±0.3
F5	0.87±0.06	0.87±0.05	6.89±0.015	1.01±0.01	28.21±0.2
F6	0.82±0.09	0.83±0.014	8.12±0.02	1.06±0.04	23.4±0.17
F7	0.84±0.010	0.91±0.06	7.54±0.02	1.01±0.03	24.56±0.35
F8	0.87±0.024	0.92±0.041	7.43±0.02	1.05±0.015	28.4±0.3
F9	0.89±0.05	0.89±0.05	6.5±0.02	1.02±0.01	21.4±0.36
F10	0.86±0.02	0.97±0.06	7.42±0.025	1.10±0.015	24.3±0.26

Table 3: Post compression parameters

Formulation codes	Thickness (mm) ±S.D.	Weight variation (mg) ± S.D.	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	3.46±0.80	300±0.53	6.90±0.05	0.16	98.52±0.323
F2	3.41±1.05	299±0.20	6.8±0.06	0.24	98.64±0.224
F3	3.40±1.26	298±0.13	6.3±0.12	0.13	98.32±0.384
F4	3.43±1.09	299.5±0.36	6.65±0.09	0.33	98.20±0.655
F5	3.42±1.35	297±0.46	7.05±0.14	0.28	98.42±0.123
F6	3.45±0.80	298.6±0.06	6.68±0.22	0.20	101.42±0.224
F7	3.45±1.25	300±0.53	6.20±0.26	0.32	99.16±0.673
F8	3.41±1.12	298.6±0.06	6.20±0.34	0.30	99.40±0.577
F9	3.49±1.43	300±0.53	6.26±0.42	0.13	99.53±0.619
F10	3.46±1.5	300±0.53	6.96±0.54	0.25	98.07±0.383

Table 4: Surface pH, swelling index & mucoadhesive strength of formulations

Formulation	Surface pH	Swelling index	Mucoadhesive strength(g)
F1	5.8±0.31	47.53±0.553	30.00±0.65
F2	6.0±0.25	38.32±1.432	26.52±0.42
F3	6.8±0.19	38.19±1.037	22.30±0.33
F4	6.6±0.23	33.24±1.06	18.65±0.42
F5	6.8±0.32	36.33±0.281	24.22±0.66
F6	6.3±0.22	37.07±0.89	23.86±0.51
F7	6.5±0.24	37.28±0.62	20.20±0.35
F8	6.4±0.20	36.85±0.575	18.50±0.60
F9	6.6±0.30	38.22±0.471	18.68±0.68
F10	6.2±0.20	36.42±0.682	28.20±0.45

5: Release kinetics of simvastatin

Batch Code	Zero Order	First Order	Higuchi release	Peppas release	
	r^2	r^2	r^2	r^2	n
F1	0.897	0.110	0.949	0.897	**0.103**
F2	0.894	0.057	0.959	0.894	**0.108**
F3	0.953	-0.87	0.952	-0.22	**0.091**
F4	0.897	0.083	0.954	0.897	**0.106**
F5	0.899	0.029	0.966	0.899	**0.110**
F6	0.850	-0.03	0.964	0.850	**0.110**
F7	0.976	-0.84	0.944	-0.18	**0.088**
F8	0.925	0.009	0.950	0.925	**0.119**
F9	0.916	0.036	0.949	0.897	**0.124**
F10	0.931	-0.04	0.963	0.931	**0.123**

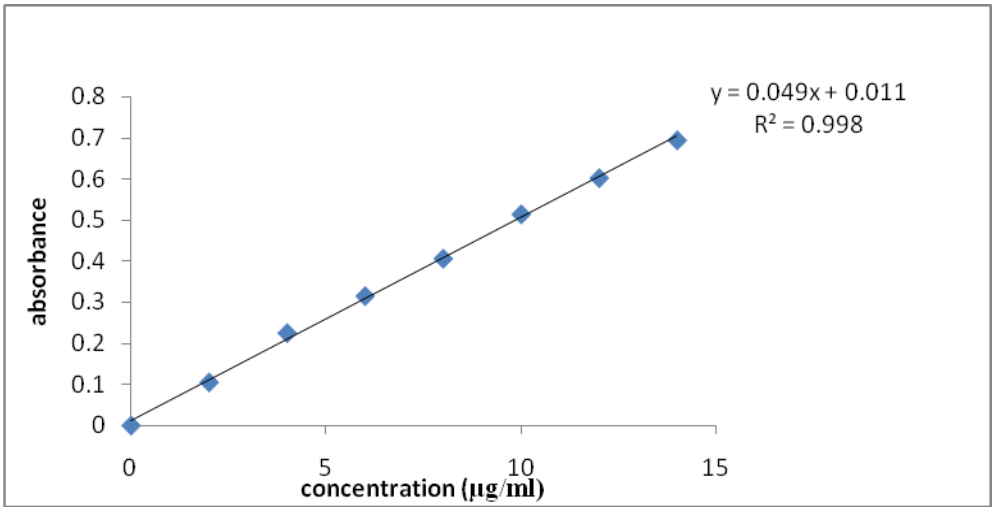

Figure 1: Calibration curve data of simvastatin

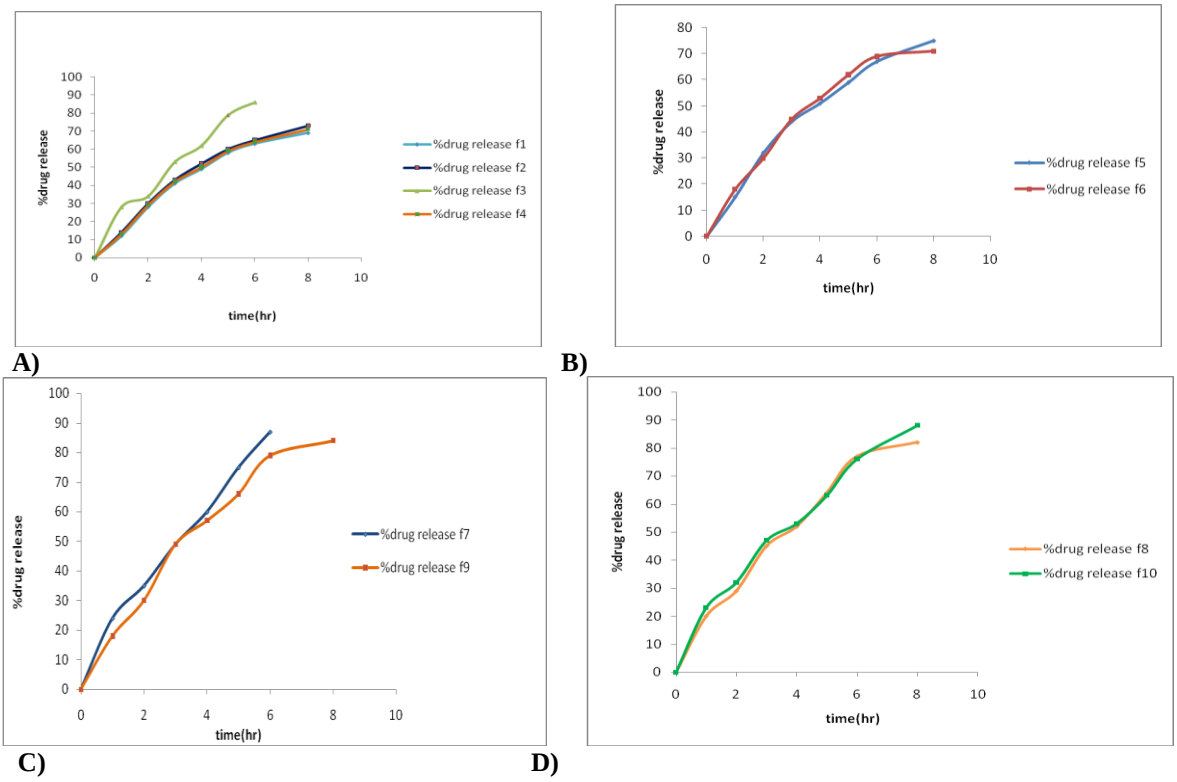

Figure 2: *In-vitro* drug release of formulations A) F1 to F4, B) F5 and F6, C) F7 and F9, D) F8 and F10.

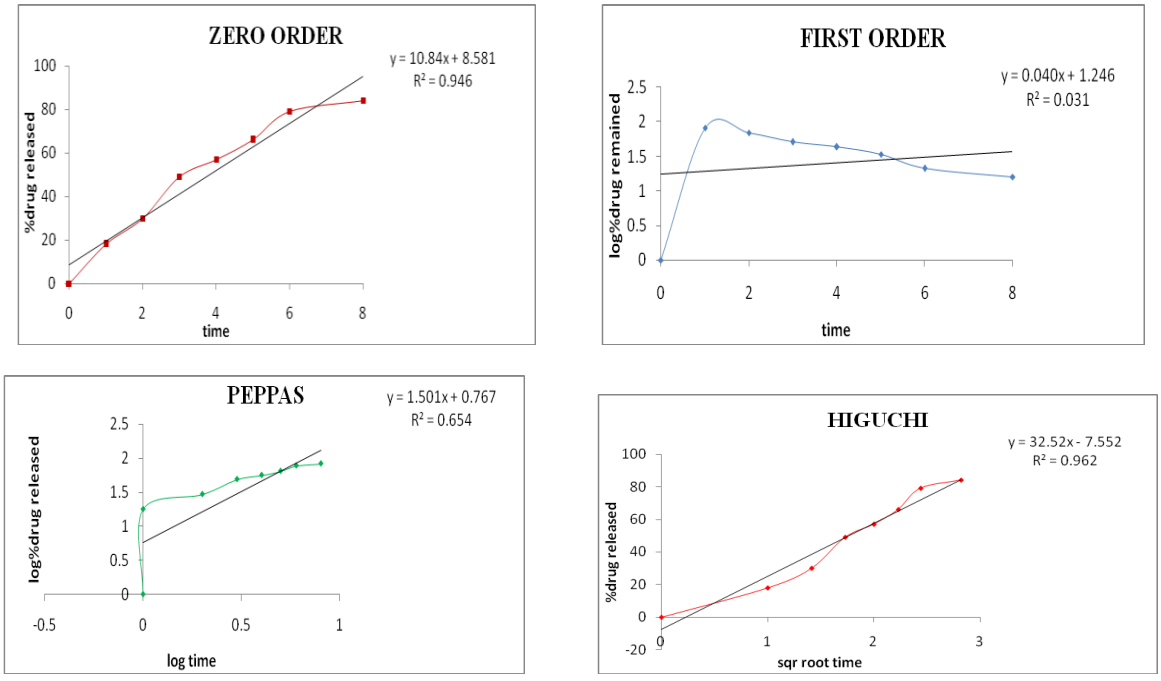

Figure 3: Release kinetics data for optimized formulation F10

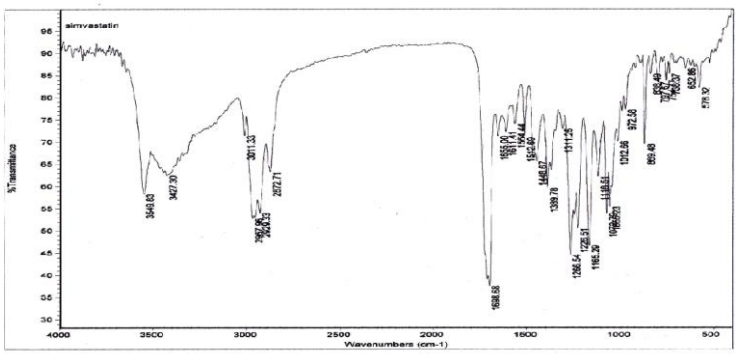

Figure 4: FT-IR spectra of pure drug

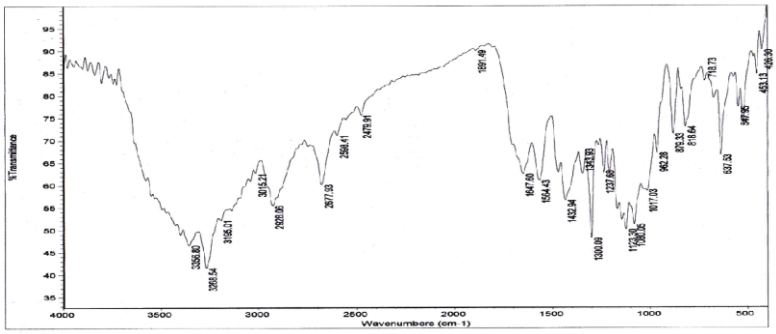

Figure 5: FTIR Spectra of drug & guar gum

3.2. Pre-compression parameters

All the formulations showing free flowing properties and results are found within the limits. The formulations F1 and F4 showing passable flow, remaining all formulations shows good flow properties. Bulk density, tapped density and hausner's ratio were found within the limits [20]. The results are represented in table 2.

3.3. Post compression parameters

All the prepared formulations were tested for physical parameters like hardness, thickness, weight variation and friability found to be within the Pharmacopoeia limits. The results of the tests were tabulated. The drug content of all the formulations was determined and was found to be within the permissible limit. The results are shown in table 3.

The thickness of the tablet was measured by using vernier calipers. The range of thickness between 3.40 to 3.45mm, within the limits. The weight variation is carried by weighing of 20 tablets individually. The weight variation of the all the tablets within the limits, i.e. 297 to 300mg.

The results of hardness, friability and assay of the 20 tablets were found to be within the limits of conventional oral tablets stated in the Indian Pharmacopoeia (IP, 1996). Hardness of the tablets was in the range 6.2 to 7.05 kg/cm^2 the friability ranged from 0.13 to 0.32% and the drug content ranged from 98.07 to 101.42%. The hardness, friability and drug content of all compressed tablets were within the limits as per USP [21].

3.4. Surface pH, swelling index and mucoadhesive strength

The surface pH of all formulations was within a range of 5.8 to 6.8 close to neutral pH. These results reveal that all the formulations provide an acceptable pH in the range of salivary pH (6.6 to 7.0). They did not produce any local irritation to the mucosal route [22]. The results of all the above-mentioned tests are shown in table 4.

Swelling index increased as the weight gain by the tablets increased proportionally with the rate of hydration. In swelling study, it was found that the amount of carbopol plays an important role in swelling of the matrix and leads to the drug diffusion. The fastest hydration rate was obtained from F1 and F5 that hydrated above 44 % within 6 hr. It was observed that swelling rate increased with an increase in carbopol polymer content of the prepared tablets. Carbopol having poor mucoadhesive strength while guargum having high adhesive strength. The amount of sodium CMC increases adhesion force decreased.

3.5. *In-vitro* drug release studies

Buccal tablets of simvastatin all are prepared were subjected to *in vitro* drug release studies for about 8 hr period and drug release profile showed in figure 2.

The formulations F1, F2, F3, and F4 were prepared using individual polymers as carbopol 934, HPMC K100, Sodium CMC, guargum, drug released 69±0.054, 73±0.066, 71±0.050 and F3 showed maximum release 86± 0.056 at 6hr due to failed in bioadhesion.

The formulations F5 and F6 were prepared using carbopol and HPMC in 1:1 &1:3 ratios; drug released was 75±0.055 and 71±0.055.

The formulations F7 and F9 were prepared using carbopol and sodium CMC in 1:1&1:3 ratios, drug released was maximum 87± 0.055 at 6hr for F7 formulation due to failed in bioadhesion and 84±0.052 for F9 formulation.
The formulations F8 and F10 were prepared using carbopol and guargum in 1:1&1:3 ratios; drug released was 82±0.044 and 88±0.049.

3.6. Drug release kinetic studies of simvastatin

The release mechanism and kinetics of simvastatin, the release data was fitted into mathematical models and n, r^2 values for zero order, first order, higuchi and peppas models were represented in table 5& figure 3 [(23)].

To ascertain the drug release mechanism, the optimized formulation was plotted as zero order, first order, peppas and higuchi plots. The higher r^2 values for zero order and higuchi suggest that the drug release follows zero order kinetics with diffusion mechanism. The release exponent "n" values were less than 0.5, which indicates that the drug release from all the batches followed fickian mechanism.

3.7. FTIR studies

FTIR has been used to assess the interaction between drug and polymers. Important peaks detected in the spectrum of drug, polymers and formulations are described as follows, the spectrum of pure simvastatin in presented characteristic peaks at 3448.54 cm^{-1}(alcoholic O-H stretching vibration), 2934.74 cm^{-1} (methyl and methylene C-H asymmetric and symmetric stretching vibration), 1713.94 cm^{-1} (lactone C=O and ester C=O stretching),1462.43,1411.99 cm^{-1} (methyl and methylene C-H bending vibration) and 1123.27,1074.23 cm^{-1} (lactone and ester C-O-C bending vibration) respectively.

IR analysis revealed that there was no chemical interaction occurred between the drug with polymers and other ingredients used in buccal tablets. The results of FTIR spectra and polymer (guar gum) showed in figures 4 and 5.

4. CONCLUSION:

Buccoadhesive tablets were prepared by direct compression method of simvastatin and different polymers like carbopol, HPMC K100, Na CMC and guargum in different ratios and ethyl cellulose as backing layer in order to release the drug in unidirectional.

The prepared tablets were evaluated for various parameters such as compatibility studies, drug content, weight variation, hardness thickness, friability, swelling studies, microenvironment pH. *In vitro* drug release studies and release rate kinetics.

From the above results formulation F10 was found to be best formulation for the buccoadhesive buccal drug delivery of simvastatin that complied with all the parameters, however, *in-vivo* experiments need to be carried out to know the absorption pattern and bioavailability of drug from the buccoadhesive buccal tablets and thus enabling us to establish *in vitro- in vivo* correlation.

5. REFERENCES:

1. Vyas SP, Khar RK. Controlled drug delivery–concepts and advances. 1st ed. Newdelhi; Vallabh Prakashan; 2002.
2. Swarbrick James. Bioadhesive drug delivery systems. 1sted. Newyork: Marcel Dekker Inc;1999:541-562.
3. Martin L, Wilson CG, Koosha F, Uchegbu IF. Sustained buccal delivery of the hydrophobic drug denbufylline using physically cross-linked palmitoyl glycol chitosan hydrogels.Eur J Pharm Biopharm. 2003;55:35-45.
4. Sellappan Velmurugan and Kiran kumar. Raghavarapu, Formulation and In-vitro evaluation of Glipizide mucoadhesive buccal tablets, Int J of Pharma and Biosciences,2013Apr;4(2):P 594-607.
5. Erukulla Durgaprasad, S.Indira, M.Kirankumar and M.Divya, Formulation and evaluation of buccoadhesive bi-layered tablet of Atomoxetine hydrochloride, Int J of Research in Pharmacy and Chemistry, 2012, 2(3).
6. B. Agaiah Goud, Kumara Swamy.S and Praveen kumar,V, Formulation and evaluation of bioadhesive buccal tablets of Simvastatin, J of Adv Pharma Sci,2011 ,vol 1, issue 1.

7. A.Ankarao, P.Jitendrakumar,CH.Babu rao, N.Devanna and B.Venkata phani Deepthi, Formulation and evaluation of buccoadhesive bilayered tablets of Carvedilol, Int J of Pharmaceutical, chemical and biological sciences,2011,1(1),6-11.
8. S.Velmurugan, K.Nagaraju, B.Deepika, Sundar Vinushitha, Formulation and In-vitro evaluation of buccal tablet of Metaprolol Tartarate, Int J of Pharmacy and Pharmaceutical Sciences,2011,vol 3,issue 2,P239-246.
9. M.A.Saleem, Sudhir S.Pange, Shaikh Ahnaf Umair, Vishal Kumar Singh, Formulation And Evaluation of mucoadhesive buccal tablet of Sumatriptan Succinate, Int J of Novel drug delivery tech,2011,vol 1,issue 2:105-113.
10. A.R.Shabaraya, K.Aiswarya and Mohd.Azharuddin, Formulation and evaluation of mucoadhesive bilayered buccal tablets of Labetalol Hcl using natural polymers, Int J of Adv in Pharmacy, Biology and Chemistry,2012,vol 1(3).
11. Asha S.John,Sathesh B.P.R, Goli Divakar, Manoj .K, Jangid and Kapil K.Purohit,Development and evaluation of buccoadhesive drug delivery system for Atorvastatin Ca, J of Current Pharmaceutical Research,2010,01;31-38.
12. J.G.Hiremath, MD.Sarfaraz, D.Hiremath, Sasarudkar, Preparation and physicochemical characterization of Simvastatin loaded mucoadhesive bilayered tablet, Indian J of Novel drug delivery 1(1),2009,P 18-24.
13. V.M Vaidya, J.V.Manwar, N.M.Mahajan and D.M.Sakarkar, Design and In-vitro evaluation of mucoadhesive buccal tablets of Terbutaline sulphate, Int J of Pharma tech Research, 2009,vol 1, no.3, P588-597.
14. R.Manivannan, A.Balasubramaniam, D.C.Prem bAnand, G.Sandeep and N.Rajkumar, Formulation and In-vitro evaluation of mucoadhesive buccal tablets of Diltiazem Hcl, Research J. Pharm and Tech, 1(4),2008.
15. Narendrachary.T, Burle Sivakumar, S.Venkata Ramanachary,B.Satyavathi, Studies on Formulation Development and In-vitro Release kinetics of mucoadhesive buccal tablets of Secnidazole, Int J of Pharma World Research,2012,vol 3,issue 1.
16. Prasanth Vasantha Viswanadhan, Anand Padole, Abin Abraham and Sam thomarayil Mathew,Buccal tablets of Lisinopril by Direct compression method for buccal drug delivery, Int Research J of Pharmaceuticals,2012,vol 2,(P 30-38).
17. G.Manasaveena, K.V.Subramanyam, Formulation and evaluation of mucoadhesive buccal tablets of Alfuzosine Hcl, Int J of Pharma World Research, 2012,vol 3, issue 3.
18. A.R.Shabaraya, K.Aiswarya and Mohd.Azharuddin, Formulation and evaluation of mucoadhesive bilayered buccal tablets of Labetalol Hcl using natural polymers, Int J of Adv in Pharmacy, Biology and Chemistry,2012,vol 1(3).
19. M.A.saleem, sudhir s.pange, shaikh ahnaf umair, vishal kumar singh, formulation and evaluation of mucoadhesive buccal tablet of sumatriptan succinate, int j of novel drug delivery tech, 2011,vol 1,issue 2:105-113.
20. S.Velmurugan, K.Nagaraju,B.Deepika,Sundar Vinushitha, Formulation and In-vitro evaluation of buccal tablet of Metaprolol Tartarate, Int J of Pharmacy and Pharmaceutical Sciences,2011,vol 3,issue 2,P239-246.
21. AmishV.Panchal,MarkanandMehta,ViralH.Shah, UmeshUpadhyay,Formulation and In-vitro evaluation of Mucoadhesive bi layered buccal tablets of Rosuvastatin Calcium, Int J of Pharm Sci and Research,2012,vol(3), issue 08;2733-2740.
22. Erukulla Durgaprasad, S.Indira, M.Kirankumar and M.Divya, Formulation and evaluation of buccoadhesive bi-layered tablet of Atomoxetine hydrochloride, Int J of Research in Pharmacy and Chemistry, 2012,2(3).
23. AmishV.Panchal,MarkanandMehta,ViralH.Shah, UmeshUpadhyay,Formulation and In-vitro evaluation of Mucoadhesive bi layered buccal tablets of Rosuvastatin Calcium, Int J of Pharm Sci and Research,2012,vol(3), issue 08;2733-2740.