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FORMULATION AND EVALUATION OF MUCOADHESIVE BUCCALTABLETS OF SUMATRIPTAN SUCCINATE

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ABSTRACT

In recent years, the interest in novel routes of drug administration occurs from their ability to enhance the bioavailability of drugs. Drug delivery via the buccal route, using bioadhesive dosage forms offers such a novel route of drug administration. The present investigation is concerned with formulation and evaluation of Buccal tablets of Sumatriptan succinate by Direct compression technique using various Muccoadhesive polymers like Sodium CMC, Carbopol 974, HPMC K 15 and evaluated for various parameters like Weight variation, Hardness, Friability, swelling index, Mucoadhsive strength ,surface p^H , in vitro dissolution studies. The FTIR results showed no evidence of interaction between the drug and polymers. The *in vitro* release kinetics studies reveal that all formulations fits well with zero order kineticsfollowed by korsmeyerspeppas ,higuchi model and then first order and the mechanism of drug relese followed non-fickian diffusion with the peppas model .Optimized formulation containing Sodium CMC,Carbopol 974 showed significant mucoadhesive strength,*invitro* release profile and good swelling.

Key Words:- Buccal tablets, Sumatriptan succinate, Formulation, Evaluation.

INTRODUCTION

Among the various routes of drug delivery, the oral route is perhaps the one mostly preferred by patients and clinicians (Chinnareddy*et al*.,2011). Within the oral mucosal cavity, the buccal region offers an attractive route of administration for systemic drug delivery buccal mucosa has excellent accessibility, an expanse of smooth muscle and relatively immobile mucosa, hence suitable for administration of retentive dosage forms. Direct access to the systemic circulation through the internal jugular vein bypasses drugs from the hepatic first pass metabolism leading to high bioavailability (sudhakar*et al*.,2006).Buccal route for systemic drug delivery using mucoadhesive polymers to significantly improve the performance of many drugs has been of profound interest (kaul*et al*.,2011). Buccal tablets adhere to the mucosa, and are retained in position until dissolution and /or release is complete.

Sumatriptan is structurally similar to serotonin (5HT), and is a 5-HT(types 5-HT_{1D} and 5-HT_{1B}) agonist. It has the low oral bioavailability of 15% with a half life of 2.5 hrs.The clinical effectiveness of this medicine in treating migraine has been attributed to its ability to cause vasoconstriction of excessively dilated cranial blood vessels and to inhibit the release of neuropeptides from trigeminal sensory neurons preventing the development of neurogenic inflammation.Sumatriptan reduces the vascular inflammation associated with migraine Goodman and Gilmans,10theddition).

MATERIALS AND METHODS

Materials

Sumatriptan succinate was obtained as agift sample fromMatrix Labs,Hyderabad.Hydroxyl propyl

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methyl cellulose (K15M),Carbopol 974P,Sodium CMC,Aspartine,Mannitol,Sorbitol wasobtained from Sri Nihal Pharmachemicals.

Method of preparation of Mucoadhesivetablets

Direct compressionmethod was used to prepare buccaltablets of sumatriptansuccinate using carbopol,HPMC K15 and sodium CMC as polymers.All ingredients including drug andpolymer ,exicipientswere weighed accurately according to the batch formula.The drugandall the exipientsexcept the lubricants were taken on a butter paper with the help ofstainless steel spatula and the ingredients were mixed in the order of ascending weights andblended for 10 min.After uniform mixing of the ingredients lubricant was added again mixed for 2 min.The prepared blend of each formulation was compressed by using different punches (7mm and 8mm) according to their weight on a single stroke tablet punching machine(Fisher Scientific).

Drug –Exipientcompatability studies

FTIR studies are performed to ascertain the compatabilityof the Sumatriptan succinate with the selected polymers.The individual drug and drug with exipients werescanned separately.Pellets were prepared by using the sample with the KBr pellets in the ratio of 1:100 and corresponding pellets were prepared by applying 15000 lb of pressure in a hydraulic press. The pellets were scanned in an inert atmosphere over a wave number range of 4000-400 cm^{-1} in (Bruker 10066117) FTIR instrument.

Procedure: Potassium bromide was mixed with drug and polymer and the spectra were taken.FT-IR spectrum of sumatriptanSuccinate was compared with FT-IR spectra of Sumatriptansuccinate with polymer.Disappearanceof sumatriptanSuccinate peaks or shifting of peak in any of the graph was studied.

Determination of λmaxsumatriptan succinate in phosphate buffer pH 6.8

Weighed amountof sumatriptan Succinate dissolved in Phosphate buffer pH 6.8 to obtain 1000mcg/ml solution.This solution was subjected to scanning in UV-Spectrophotometer (Lab India)between 200-400nm and absorption maximum was determined.The effect of dilutiononabsorption maxima was studied by diluting the above solution to 10 mcg/ml and scannedfrom 200-400nm.From the spectra maximum absorbance found at 282 nm.

Construction of calibration curve of sumatriptan

Standard curveof sumatriptan was prepared in Phosphate buffer pH 6.8.

Preparation of stock solution: Sumatriptan (10 mg) was accurately weighed in a 100-mlvolumetric flask and dissolved in Phosphate buffer pH6.8, after which the flask was filled with same water up to the mark.

Preparation of dilutions: Different dilutions were made using the stock solution prepared. 1, 1.5, 2, 2.5,3.0 mlof stock solution was taken and diluted to 100ml of distilled water to get the concentrations of 10, 15, 20 ,25 and 30 µg/ml. The absorbance of above solutionswasmeasured in UV-spectrophotometer at 282nm wavelength. Graphwas plotted by taking the concentration (µg/ml) on x-axis and absorbance (nm) on y-axis as shownin figure1.

Evaluation of buccal tablets of sumatriptan succinate

Physical properties: The surface of the formulated tablets was evaluated to ensure that there was no capping, lamination, sticking or other defects during compression. The tablet surface should be smooth, and color should be white since no color is used in formulation and all ingredients were white in color. If color and odor of the tablet changes, it may be the indication of any chemical reaction that may effectthe properties of formulation.

Weight variation: weight variation test was performed according to USP. Average weight of twenty tablets was calculated and individual weight of each tablet was taken. % deviationwas calculated with respectto average weight. The maximum % deviation allowed is 7.5% as the tablet weight is between 130 -324 mg.The tablets meet the USP test if no more than two tablets are outside the% limit and if no tablet differs by more than two times the % limit.

Friability: Friability is related to tablets ability to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus(Electro lab). Compressed tablets that loose less than 0.5% to 1.0% in weight are generally considered acceptable. Ten tablets were weighed accurately and then initial weight was note down. There are introduced in the apparatus and subjected to 100 revolutions at a speed of 25 rpm for 4 min. When the drum stopped, tablets were taken and dedustedand final weight was taken. % Friability wascalculated by the formula.

$$\% \text{ Friability} = \frac{\text{Initial weight (gm)} - \text{Final weight (gm)}}{\text{Initial weight (gm)}} \times 100$$

Acceptance criteria: Thefriability value shouldbeless than 1.0%

Hardness: This test gives the indication for the tablets ability to with stand its integrity . It was determined by placing the tablet between the anvils only one of which is movable, driven by electricity. It presses the tablet at constant load till the tablet breaks. It wasrecorded in KP (1kP = 1 kg). Hardness of 10 tabletsdetermined and average hardness and rangewas calculated(Ansel's,Ninth Eddition)

Determination of Drug content

Five tablets from each formulation were taken, crushed and mixed and the powder equivalent to 75mg of drug was placed in a 100 ml conical flask.Phosphate buffer 6.8was added to volumetric flask and shaken well.Further the volumewas made up to the mark with phosphatebuffer 6.8.Thedrug content was determined by using U.V Spectrophotometer at 282 nm (Satyabrata*et al*.,2010).

Microenvironment pH

Themicroenvironment pH (surface pH) of the buccaltablets was determined in order toinvestigate the possibility of any side effects *in vivo*. As an acidic or alkaline pH maycause irritation to the buccalmucosa, it was determined to keep the surface pH as closeto neutral as possible. A combined glass electrode was used for this purpose. The tablet wasallowed to swell by keeping it in contact with 5 mL of distilled water (pH 6.8 ± 0.05) for 2 h at room temperature. The pH was measured bybringing the electrode in contact withthesurface of the tabletsand allowing it toequilibrate for 1 min(Agaiah*et al*.,2011).

Swelling Studies

Buccaltabletswere weighed individually (designated as W1) and placed separately in Petridishescontaining 15 mL of phosphate buffer (pH 6.8) solution. At regular intervals (1, 2, 3, 4, 5, 6, 7 , 8 and10 hr), thebuccal tablets were removed from thePetri dishes and excesssurfacewater was removedcarefully usingthefilterpaper. The swollen tablets werethenreweighed (W2**)**. This experiment wasperformed in triplicate(Ajit*et al*.,2012).The swellingindex (water uptake) calculatedaccordingto the following Eq**.**

Percentage hydration = [(W2-W1)/ W1] ×100

Bioadhesion studies

In evaluation of adhesion, it is important to use uniform surfaces that allow the formationof reproducible adhesive bonds. In present study, sheep buccalmucosa was used as amodel mucosal surface for bioadhesiontesting. Immediately after slaughter, the buccalmucosa was removed from the sheep and transported to laboratory in tyrodesolutionand kept it at 40ºC. The composition of tyrode solution (g/L)is sodium chloride 8g, potassium chloride 0.2g, calcium chloridedihydrate 0.134g, sodium bicarbonate 1.0g, sodiumdihydrogen phosphate 0.05g and glucose 1.0g and 1 litre Water.

Bioadhesivestrength of the tablets was measured on a modified physical balance. In order to find out the bioadhesionstrength first buccal tablet was stacked to the glassslidewith the help of mucoadhesivetape, which was situated at the base of left handpan. A preload of 5gm was placed on the pan for 5 minsto establish adhesive bondbetween the tablet and sheep buccalmucosa . The Sheepbuccalmucosa was placed overthe box. The left-hand sideof thebalance was exactly 5 g heavier than theright side.Nowfivegrams weight added to the rightpan toadjust the balance. Then the weights on theright-hand side were slowly added in increments of 0.1 g till the tablet just separatedfrom themembrane surface. The excess weight onthe right pan was taken as a measure ofthebioadhesive strength (Mahalaxmi*et al*.,2010).

In-Vitro Release Studies

The drug release rate from buccaltablets was studied using the USP (II) dissolution test apparatus (Electrolab) .The assembly is kept in a jacketed vessel of water maintained at 37 ± 5^0C. Buccal tablet was kept at the bottom of the flask. The beaker is filled with900 ml ofmixed phosphate buffer pH6.8. The vessel maintained at 50rpm under stirring conditions by means of paddle fabricated for purpose in dissolution apparatus. At various intervals oftime,samples were withdrawn. It is replaced immediatelywith equal amount of fresh buffer. Thesamples are thenanalyzed UV spectrophotometrically at 282 nm up to 10hours(Chaudhari*et al*.,2012).

Release kinetic modeling(Suvakanta*et al*.,2010)

Kineticmodels describe the overall release ofdrug from the dosage forms. Because qualitativeand quantitative changes in a formulation may alter drug release and in vivoperformance, developing tools that facilitate product development by reducing the necessity of bio-studies isalways desirable. In this regard, the use ofinvitrodrug dissolution data to predict in vivobio-performance can be considered as the rational development ofcontrolled release formulations. The methods of approach to investigate the kinetics ofdrug release from controlled release formulation can be classified into three categories:

1. Statistical methods (exploratory data analysis method, repeated measures design, multivariateapproach [MANOVA: multivariate analysis of variance].

2.Model dependent methods (zero order, firstorder, Higuchi, Korsmeyer-Peppas model, Hixson Crowell, Baker-Lonsdale model**,** Weibullmodel,etc.).

3.Model independent methods [difference factor(f1), similarity factor (f2)].

Model dependent methods

Model dependent methods are based on different mathematical functions, which describe the dissolution profile. Once a suitable function has been selected, the dissolution profiles are evaluated depending on the derived model parameters. In order to determine the suitable drug release kinetic model describing thedissolution profile. The model dependentapproaches included zero order, first order, Higuchi, Hixson-Crowell, Korsmeyer-Peppas, Baker-Lonsdale, Weibull, Hopfenberg, Gompertz and regression models.

Zero-order model

Drug dissolution from dosage forms that do not disaggregate and release the drug slowly can be represented by the equation.

$$Q0 - Qt = K0t$$

Qt is the amount of drug dissolved in time *t*, Q0 is the initial amount of drug in the solution (most times, Q0 = 0) and K0 is the zero order release constant expressed in units of concentration/time.To study the release kinetics, data obtained from in vitrodrug release studies were plotted as percent drug released versustime .

First order model

Thismodel hasalso been used to describeabsorption and/or elimination of some drugs.The release of the drug which followed first order kinetics can be expressed by the equation:

$\log C = \log C0\ n\ Kt / 2.303$

where *K* is first order rate constant expressed in units of time-1,C0 is the initial concentration of drug, k is the first order rate constant, and t is the time. The data obtained are plotted as log cumulative percentage of drug remaining vstime which would yield a straight line with a slope of -K/2.303.

Application: This relationship can be used to describe the drug dissolution in pharmaceutical dosage forms such as those containing water-soluble drugs in porous matrices.

Higuchi model

The first example of a mathematical model aimed to describe drug release from a matrix system was proposed by Huguchiin 1961. Initially conceived for planar systems, it was then extended to different geometrics and porous systems . This model is based on the hypotheses that (i) initial drug concentration in the matrix is much higher than drug solubility; (ii) drug diffusion takes place only in one dimension (edge effect must be negligible); (iii) drug particles are much smaller than system thickness; (iv) matrix swelling and dissolution are negligible; (v) drug diffusivity is constant; and (vi) perfect sink conditions are always attained in the release environment.

In a general way it is possible to simplify the Higuchi model as $f\ t = Q = KH\ \ t1/2$. where, KH is the Higuchi dissolution constant . The data obtained were plotted as cumulative percentage drug release versus square root of time.

Application: This relationship can be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms, asinthe case of some transdermal systems and matrix tablets with water soluble drugs.

Korsmeyer-Peppas model

Korsmeyer*et al*. (1983) derived a simple relationship which described drug release from a polymeric system equation .

$Mt / M\infty = Ktn$

where $Mt / M\infty$ is afraction of drug released at time t, k is the release rate constant and n is the release exponent. The n value is used to characterize different release for cylindrical shaped matrices. In this model, the value of *n* characterizes the release mechanism of drug as described in Table 1.

To find out the exponentof*n* the portion of the release curve, where $Mt / M\infty < 0.6$ should only be used. To study the release kinetics, data obtained from*in vitro* drug release studies were plotted as log cumulative percentage drug release*versus* log t

Table1.Interpretation of diffusional release mechanisms from polymeric films

Release exponent(n)	Drug transport mechanism	Rate as a function of time
0.5	Fickian diffusion	$t^{-0.5}$
$0.5 < n < 1.0$	Non -Fickian transport	t^{n-1}
1.0	Case II transport	Zero order release
Higher than 1.0	Super case II transport	t^{n-1}

Table 2.Formulation of Mucoadhesivebuccal tablets of Sumatriptan succinate

	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Sumatriptan	75	75	75	75	75	75	75	75	75	75	75	75
HPMC K15	35	35		75	35	35		35	75	50	50	
Carbopol 974		35	35				35	35			50	50
Sod CMC	35		35		35	35	35			50		50
Mannitol	35	35	35	30	50		50	50		45	45	45
Sobitol						50			70			
Aspartin	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Mg Stearate	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Total wt	183.25	183.25	183.25	183.25	198.25	198.25	198.25	198.25	223.25	223.25	223.25	223.25

RESULTS

Table3. Calibration data of sumatriptan inphosphate buffer pH 6.8

Concentration (µg/ml)	Absorbance
0	0
10	0.163
15	0.227
20	0.287
25	0.343
30	0.405

Table4.Post compression parameters.

Formulation Code	Friability (%)	Percent drug content*	Weight variation	Hardness	Surface pH
F1	0.62±0.03	98.85±0.72	Pass	3.8±0.04	5.7±0.64
F2	0.77±0.01	100.02±0.14	Pass	4±0.08	5.6±0.29
F3	0.68±0.01	99.45±0.62	Pass	4±0.08	5.6±0.16
F4	0.73±0.06	99.94±0.14	Pass	3±0.04	5.4±0.22
F5	0.96±0.08	99.84±0.48	Pass	4±0.08	5.7±0.22
F6	0.23±0.02	98.98±0.19	Pass	5±0.08	6.2±0.33
F7	0.43±0.03	99.32±0.64	Pass	5±0.08	5.6±0.29
F8	0.16±0.01	98.96±0.26	Pass	3.5±0.04	6.5±0.67
F9	0.75±0.03	99.12±0.31	Pass	5±0.08	6.1±0.36
F10	0.12±0.01	99.83±0.50	Pass	3.5±0.08	6.1±0.22
F11	0.21±0.03	99.41±0.29	Pass	5±0.04	6.1±0.21
F12	0.20±0.02	98.87±0.99	Pass	5±0.08	5.9±0.43

Table 5. Swelling index Studies

S.no	1hr	2hr	3hr	4hr	5hr	6hr	7hr	8hr	9hr	10hr
F1	61.74	142.62	161.74	188.52	204.91	210.92	222.95	225.13	227.86	227.89
F2	14.52	35.19	45.25	74.30	82.68	99.44	123.46	151.39	160.33	168.15
F3	34.60	74.42	140.04	146.21	149.57	157.43	170.89	179.30	196.13	200.61
F4	59.89	126.55	150.94	162.87	175.33	183.46	197.19	206.77	206.79	206.79
F5	41.24	88.33	114.43	161	176.35	179.42	188.12	192.3	199.89	203.4
F6	32.86	60.83	96.73	138.69	151.74	154.07	162.21	166.47	173.94	175.05
F7	12.64	22.88	88.42	115.56	118.63	123.24	132.97	142	157.04	169
F8	12.64	34.66	43.88	71.53	81.77	94.06	122.73	150.89	153.96	158.44
F9	61.69	92.41	128.08	152.03	161.06	171.03	174.16	175.06	180.03	181.84

F10	12.08	20.74	37.09	56.76	82.30	100.77	131.41	142.1	151.82	156.19
F11	12.41	29.57	42.35	51.24	72.91	91.42	97.74	124.37	133.86	141.08
F12	12.32	19.14	35.06	58.70	78.71	96.90	128.74	139.65	150.11	159.20

Table6.Bioadhesion studies

Formulation	Mucoadhesive strength	Force of adhesion
F1	19±0.82	0.186
F2	25±1.41	0.245
F3	35±0.82	0.343
F4	25±0.82	0.245
F5	17±0.82	0.166
F6	17±0.82	0.166
F7	32±1.41	0.313
F8	25±2.16	0.245
F9	25±1.63	0.245
F10	15±2.16	0.147
F11	20±0.82	0.196
F12	30±0.82	0.294

Table7. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing HPMC K 15 and sodium CMC

	In-vitro release			
Time(hrs)	F1	F5	F6	F10
1hr	26.49±1.64	23.49±0.41	24.69±0.56	15.89±0.26
2hr	47.54±1.42	37.82±0.96	36.8±1.02	23.38±0.46
3hr	61.06±2.28	51.80±0.60	52.49±0.75	31.09±1.15
4hr	70.53±2.10	63.68±1.60	64.08±0.84	38.87±1.13
5hr	80.68±2.44	70.85±1.34	71.04±0.90	46.61±0.47
6hr	87.84±1.11	78.99±0.14	78.88±0.99	54.45±0.52
7hr	96.97±1.66	83.03±0.26	83.23±0.34	62.50±0.67
8hr	98.62±0.88	88.35±0.38	87.35±1.03	70.94±1.15
9hr	100±0.17	94.68±0.88	92.67±0.71	77.89±0.67
10hr		97.42±0.26	94.60±0.71	86.73±0.93

Table 8. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing HPMC K 15 and carbopol 974

	In-vitro release		
Time(hrs)	F2	F8	F11
1hr	19.2±0.96	18.6±0.77	12.8±1.11
2hr	29.60±0.85	26.90±1.21	17.37±1.05
3hr	35.96±0.64	33.74±1.02	25.69±1.18
4hr	41.38±0.43	39.08±0.12	31.54±0.66
5hr	45.92±1.20	44.41±0.91	39.77±0.77
6hr	52.75±1.00	51.44±0.49	42.12±0.53
7hr	60.36±0.71	59.18±0.14	49.43±1.07
8hr	68.63±0.43	68.32±1.14	54.97±0.61
9hr	72.77±0.62	71.57±0.85	60.20±0.95
10hr	76±0.82	73.89±0.53	68.43±0.56

Table 9. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing carbopol 974 and Sodium CMC

Time(hrs)	In-vitro release		
	F3	F7	F12
1hr	18±0.82	14.73±0.98	14.58±1.00
2hr	33.59±0.99	28.88±1.23	19.38±1.62
3hr	39.78±1.18	39.06±0.79	32.40±0.63
4hr	47.82±0.91	46.01±0.84	45.67±1.43
5hr	52.86±0.44	51.95±0.79	56.67±1.59
6hr	60.59±0.64	59.18±0.77	64.34±0.40
7hr	67.33±1.73	65.21±0.72	71.23±0.43
8hr	75.26±0.70	74.06±0.71	78.59±0.36
9hr	83.70±0.84	82.19±0.54	82.23±0.90
10hr	92.15±1.35	92.15±0.49	88.9±0.55

Table 10. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing HPMC K 15

Time(hrs)	In-vitro release	
	F4	F9
1hr	29.89±1.10	32.7±0.83
2hr	49.12±0.53	42.37±0.38
3hr	62.22±0.57	56.73±0.96
4hr	70.84±0.51	66.91±0.84
5hr	81.99±1.52	74.66±1.02
6hr	90.09±1.41	81.8±0.84
7hr	97.19±0.24	85.24±0.44
8hr	100±0.99	87.56±0.44
9hr		91.47±0.82
10hr		93±0.71

Table 11.Regressional analysis of the in-vitro release data according to various release kinetic models

Formulation code	Zero order r^2	First order r^2	Higuchi r^2	Korsemeyer-peppas r^2	n
F1	0.925	0.914	0.980	0.979	0.601
F2	0.991	0.984	0.983	0.991	0.597
F3	0.991	0.907	0.983	0.990	0.667
F4	0.958	0.920	0.994	0.991	0.581
F5	0.947	0.945	0.991	0.988	0.620
F6	0.933	0.988	0.984	0.984	0.599
F7	0.989	0.897	0.989	0.991	0.749
F8	0.990	0.983	0.979	0.989	0.619
F9	0.917	0.997	0.974	0.982	0.510
F10	0.999	0.936	0.975	0.991	0.751
F11	0.99	0.981	0.978	0.988	0.746
F12	0.975	0.975	0.987	0.979	0.853

Figure1.FTIRspectrumofsumatriptansuccinate

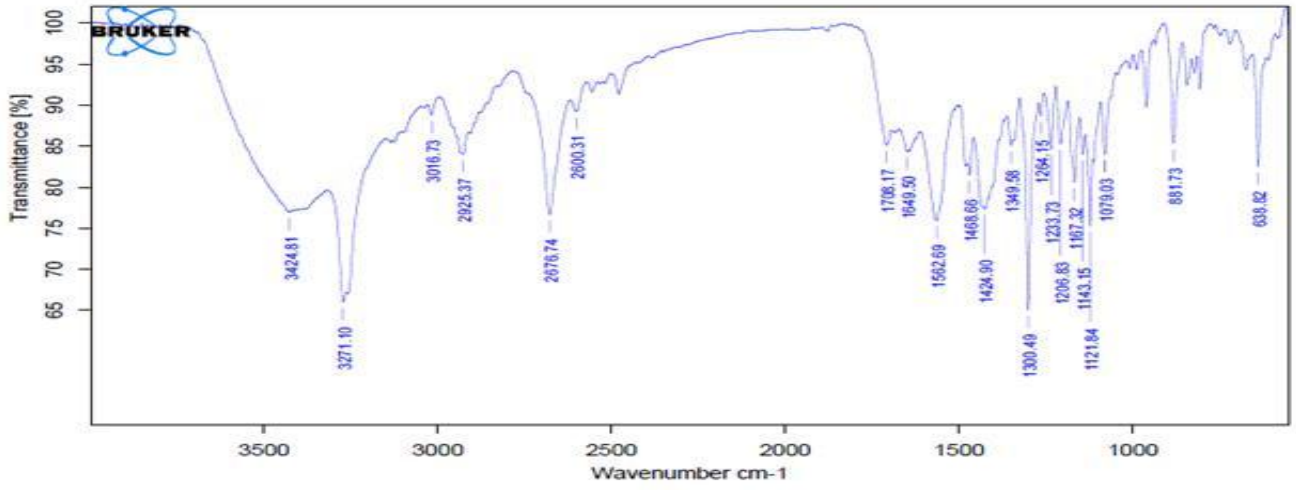


Figure2. FTIR Spectrum ofsumatriptansuccinate+HPMC k15

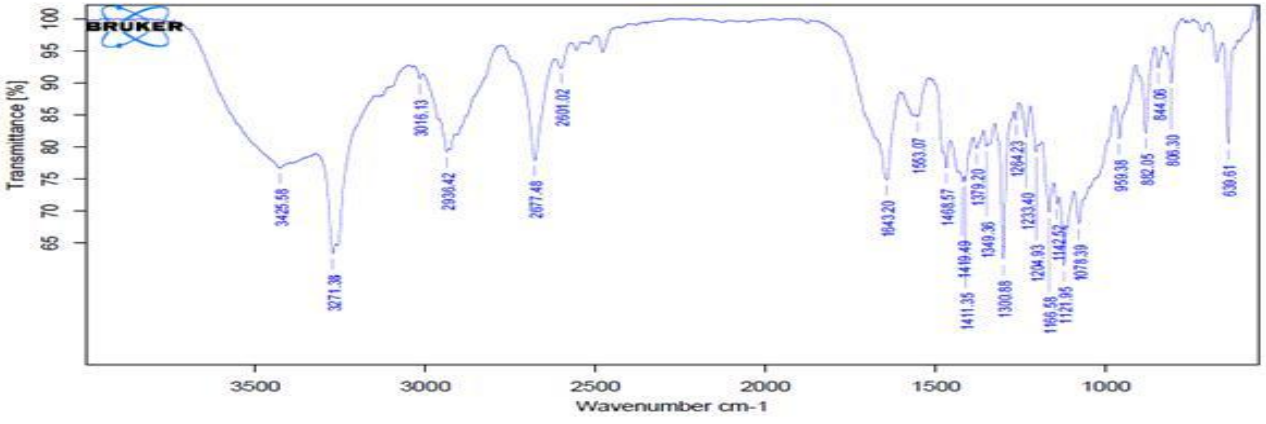


Figure3. FTIR Spectrum of sumatriptansuccinate+sodcmc

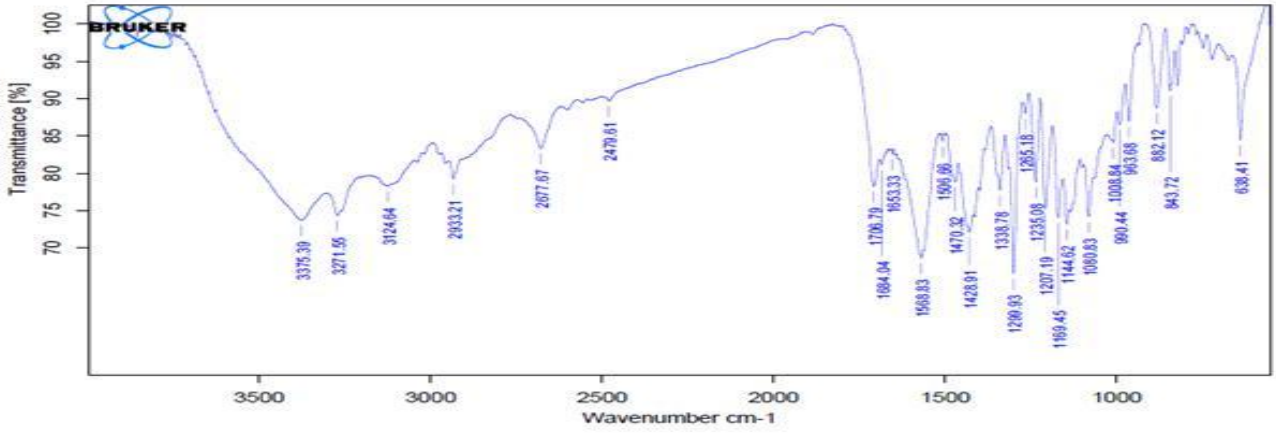


Figure4. FTIR Spectrum of sumtriptansuccinate+carbopol 974

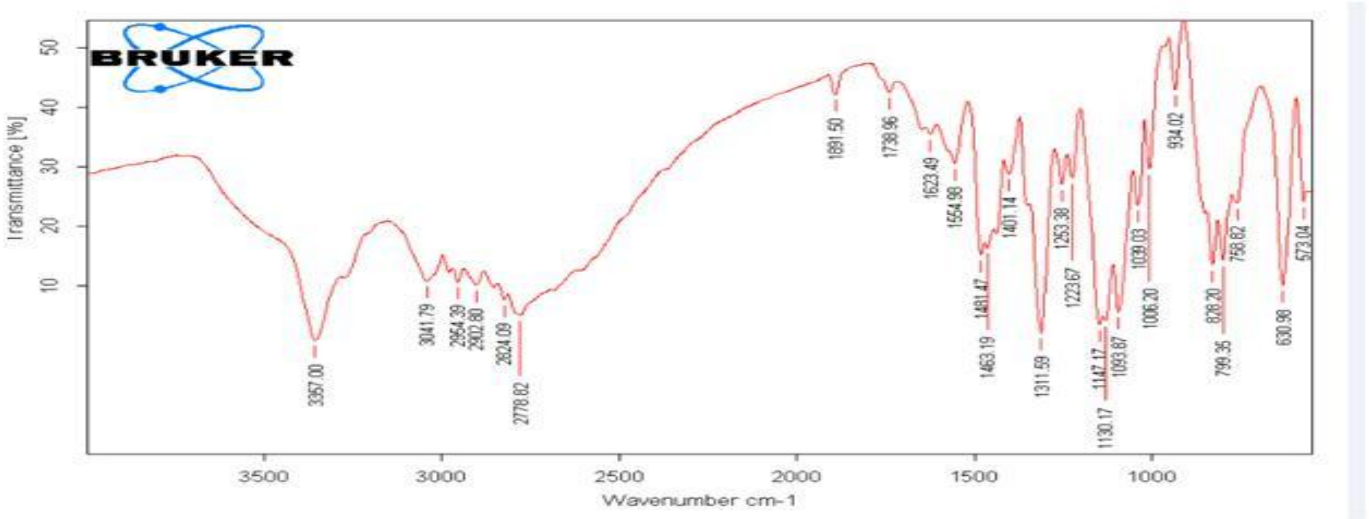


Figure 5. Calibration curve of sumatriptan in phosphate buffer pH 6.8(λmax=282nm)

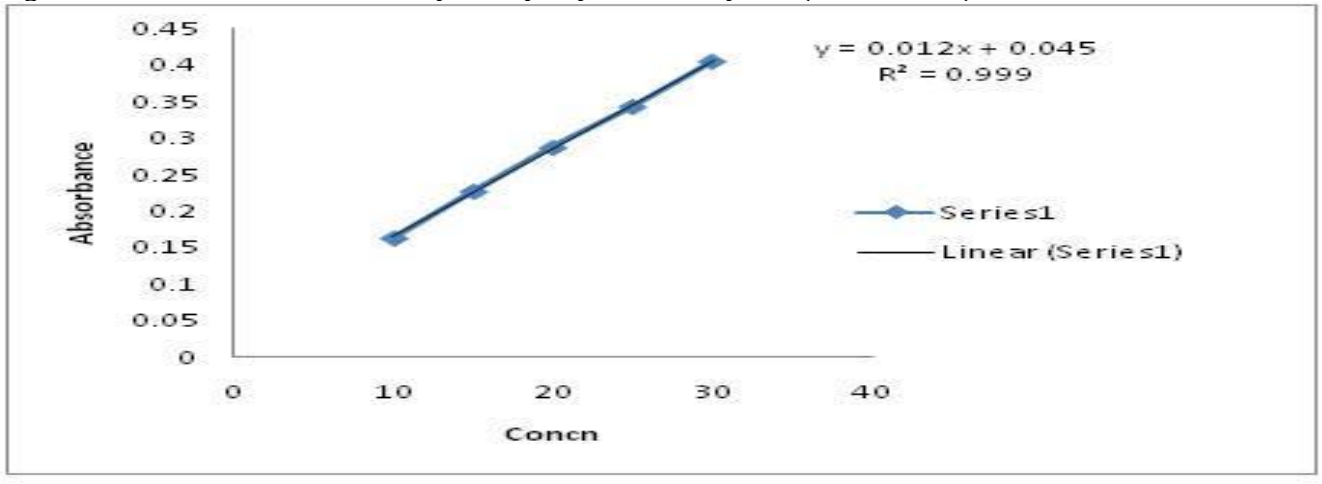


Figure6. Swelling studies

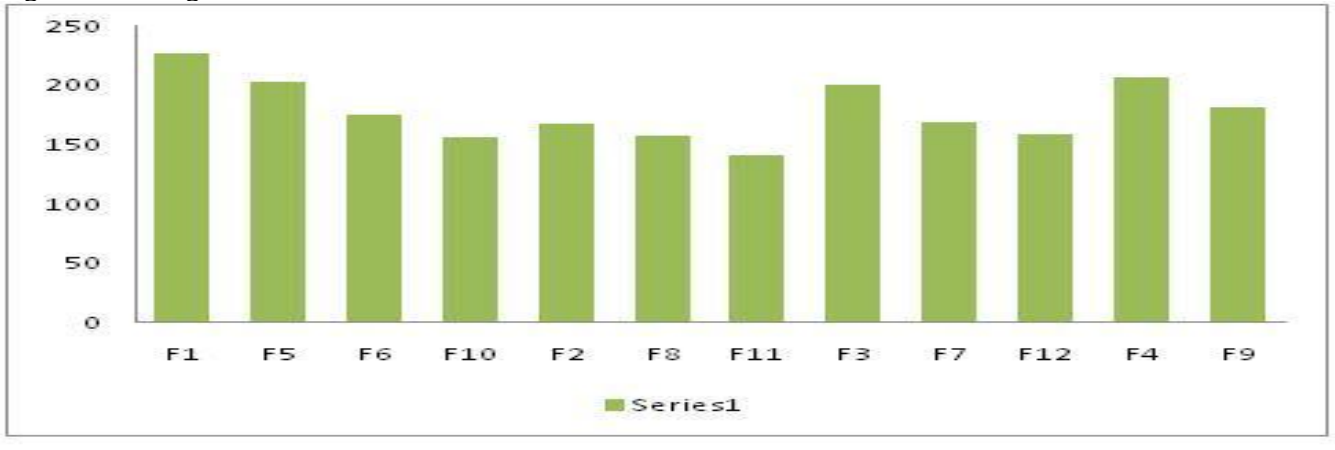


Figure7.Bioadhesion studies

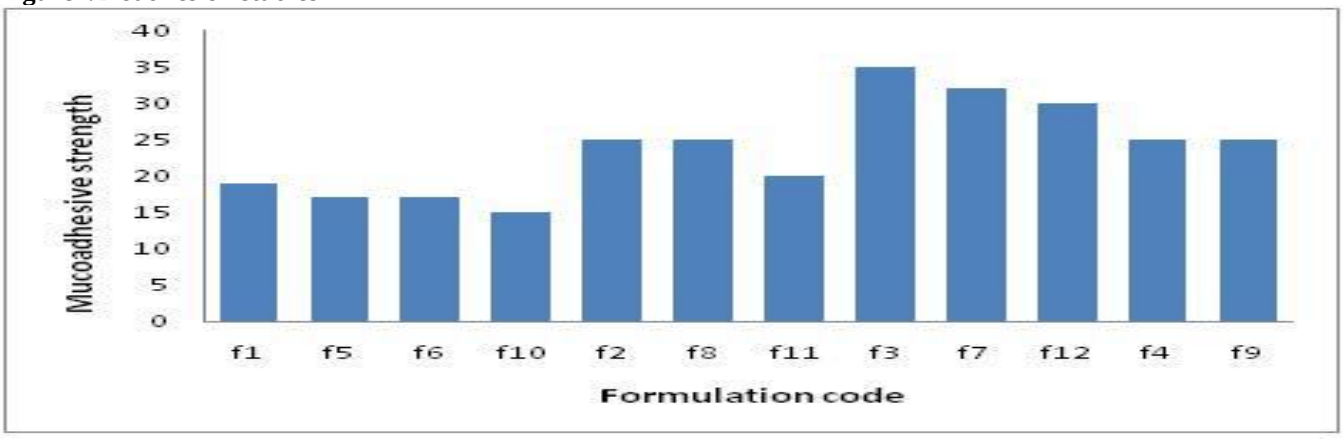


Figure 8. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing HPMC K 15 and sodium CMC

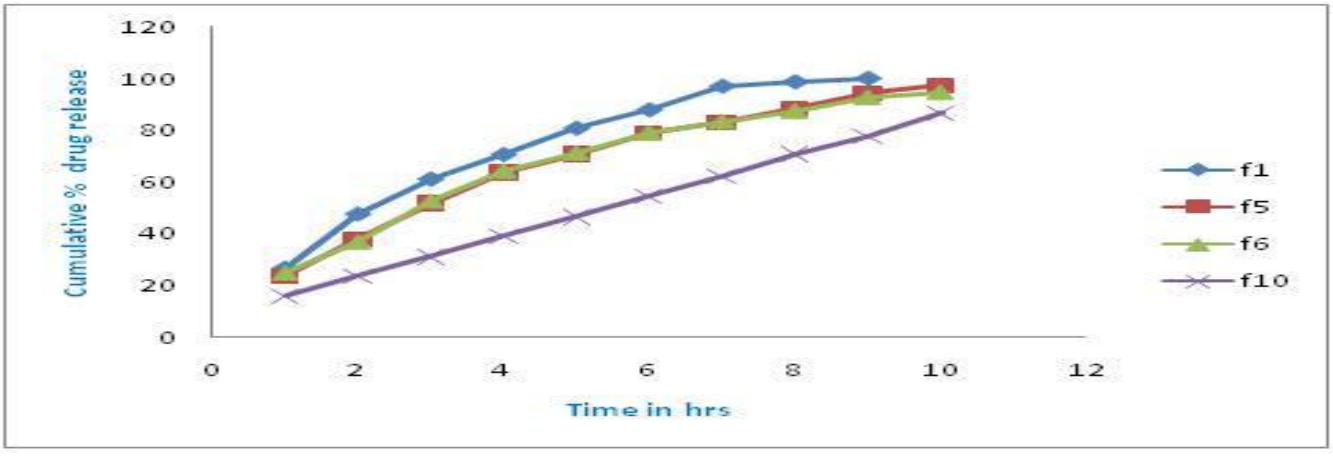


Figure 9. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing HPMC K 15 and carbopol 974

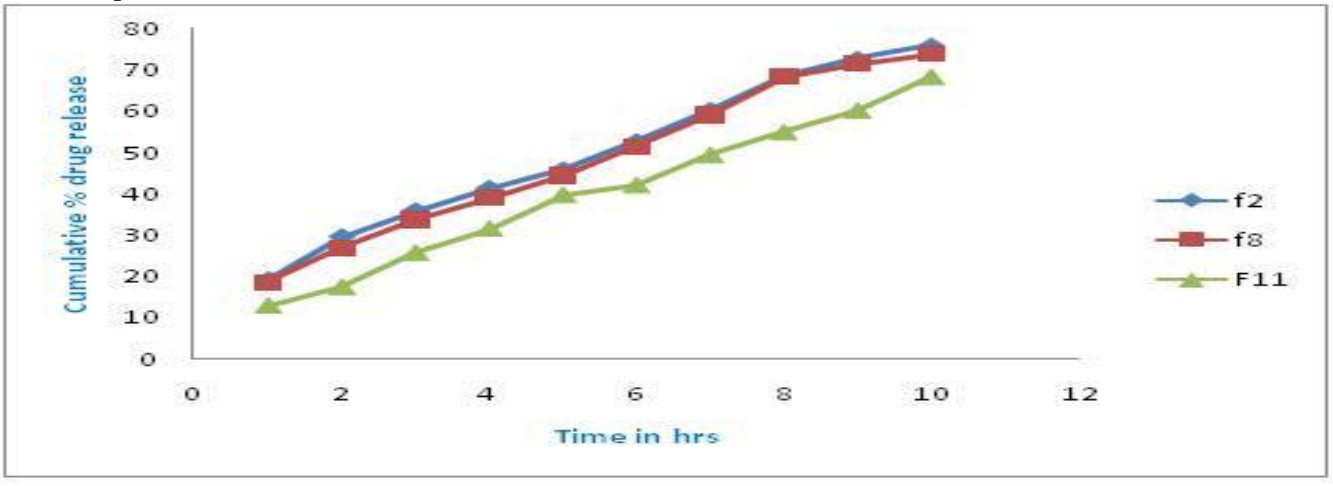


Figure 10. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing carbopol 974 and Sodium CMC

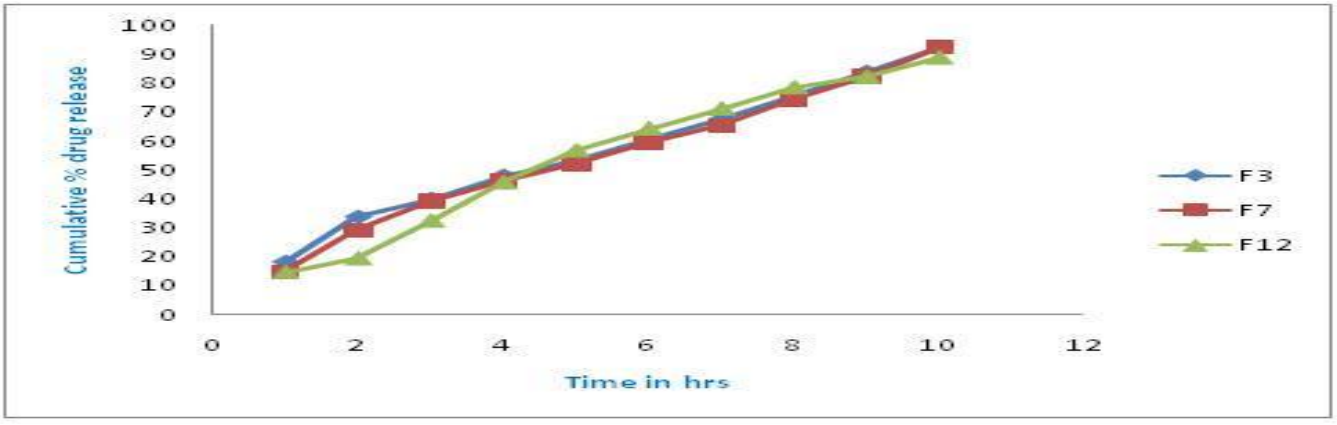
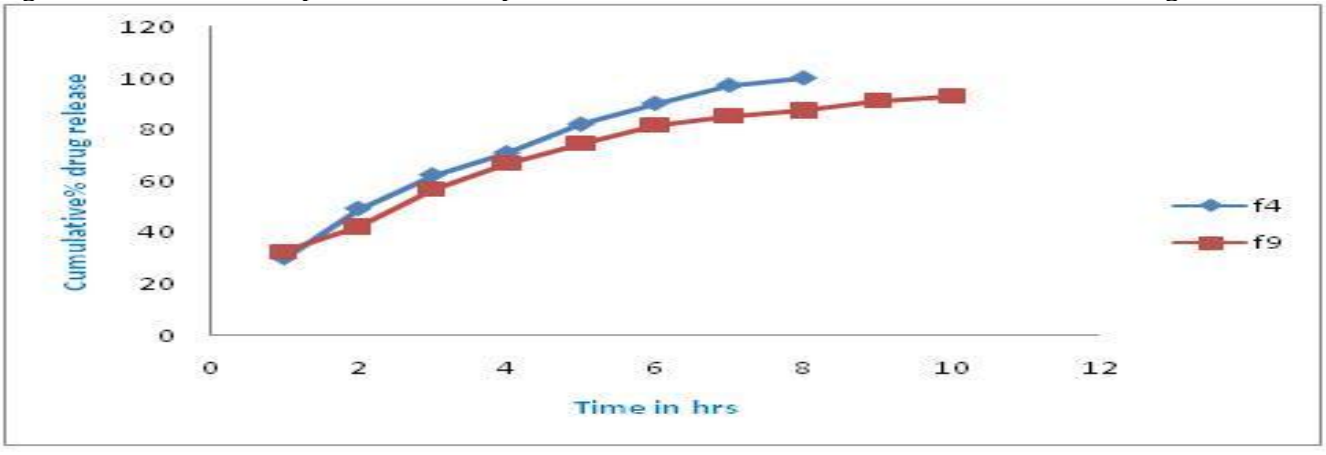


Figure11. In-vitro release profile of sumatriptan succinate from mucoadhesivebuccal tablets containing HPMC K 15.



DISCUSSION

Mucoadhesive tablets have the ability to increase the drug residence in the buccal cavity,control the rate of drug release as well as protect the drug from enzymatic degradation. Sumatriptan Succinate buccal tablets were prepared by direct compression method.The total weight obtained for tablets was 183.25-223.25 mg.

Drug –Exipientcompatability studies

The drug and polymer interaction was studied using FTIR spectroscopy for selected combination of drug with different polymers. The results indicated that the characteristic absorption peaks due to pure sumatriptan succinate have appeared in the formulations, with out any significant change in their position indicating no chemical interaction between pure sumatriptan succinate and polymers.

All the prepared mucoadhesivebuccal tablets of Sumatriptan Succinate were evaluated for hardness,weight variation,friability, uniformity of drug content,surface pH determination.The hardness of the prepared mucoadhesivebuccal tablets was from 3.5-5 kg/cm2.Hardness was increased due to increase in weight of polymers.All the prepared tablets complies Indian pharmacopeia standard for weight variation and friability.The drug content was from 98.85%-100.02% suggested uniform mixing of the drug.The surface pH of all the buccal tablets was from 5.4-6.1 .which was nearer to salivary pH so that it could'nt cause the mucosal irritation and discomfort.

Swelling studies

The swelling study of prepared buccaltablets was performed in pH 6.8 phosphate buffer.Swelling index increased as the weight gain by the tablets increased proportionally with the rate of hydration.The swelling behavior of a bioadhesive system is an important property for uniform and prolonged release of drug and

bioadhesion.The swelling behavior depends upon nature of polymer and the concentration of polymer.The maximum swelling was seen with the formulation f3 containing carbopol 974 and sodium CMC, increasing the carbopol 974 and sodium CMC concentration decreases the swelling index of f12.The formulation containing HPMC K15 and carbopol 974 was seen with the less swelling index compared with the formulation containing HPMC K15 and sodium CMC.Formulation f4 and f9 containg the HPMC K15 polymer alone was shown the similar swelling index values of f1, f5 and f6 which contains HPMC K 15 and Sodium CMC.

The in-vitro release studies

The in-vitro release studies of Sumatriptan Succinate were performed in pH 6.8 phosphate buffer and the percentage drug release was calculated.The *in vitro*relase of Sumatriptan Succinate was mainly affected by drug and polymer ratio,nature and amount of the polymer and the dissolution medium and also depends on swelling behavior of the polymers used. f1,f5,f6 formulations containing HPMC K15 and Sodium CMC release the drug 100%,94%,92% at the end of 9hrs and change of diluents for f1,f5,f6 shows no change in release profile and increase in the concentration of HPMC K15 and Sodium CMC f10 release 77% of drug with in 9 hrs.f2,f8, formulations containing HPMC K15 and Carbopol 974 shows the drug release of 76%,73% and by increase in the concentration of these polymers f11 shows 68% of drug release.f3 formulation was shown to release the 92% of drug at the end of 10hrs near complete rate and extent it contains Carbopol 974 and Sodium CMC with increase in concentration of this polymers the percentage of drug release of f12 was shown to decrease.The buccal formulation f4 containing HPMC K 15 alone showed rapid burst release of 90% with in 6hrs and due to the low viscosity of HPMC K 15 release is faster,with increased diluent concentration f9 found to decrease the drug release compared to f4 formulation.

The *In vitro* release data was subjected to Zero order,Firstorder,Higuchi,Korseymeyer-peppas in order to establish the drug release mechanism and kinetics of drug release from the buccal tablets.The regression analysis with correlation coefficient r^2 for different kinetic modelsis summarized in table 11. When the data was subjected to zero order,first order kinetic model,a linear relationship was observed with high ' $r^{2'}$ value for zero order model as compared to first order model suggested that the formulations were in zero order controlled release.korseymer -peppas model was applied which will define exact release mechanism when more than one type of release phenomenon was observed. Good linearity with high r^2 value was observed with korseymer –peppas model.The value of release exponent n calculated as a slope defines the release mechanism.The value of n obtained for all formulation was >0.5and<1.0 suggested that the drug release followed non –fickian diffusion due to higher affinity of hydrophilic polymers towards water.

Muoadhesion strength

Mucoadhesion strength was found to be increase with increasing amount of mucoadhesive polymer,the Mucoadhesive strength is affected by molecular weight of polymer and contact time with membrane and degree of swelling of the polymer. Bioadhesion strength was observed to be high for buccal tablets containing carbopol 974 followed by HPMCK 15 and sodium CMC as mucoadhesive polymers.The maximum mucoadhesive strength was observed with the formulation F3 containing Sodium CMC and carbopol 974.

CONCLUSION

The study performed on development and evaluation of mucoadhesivebuccal tablets of sumatriptan succinate by using the mucoadhesive polymers like HPMC K15,Sodium CMC,Carbopol 974. Release rate of sumatriptan succinate from tablets was significantly affected by the type and changes in the polymer mixing ratios and also the diluents.From the results it can be concluded that the formulation containing Sodium CMC,Carbopol 974 showed significant mucoadhesive strength,*in vitro* release profile and goodswelling.The *in vitro* release kinetics studies reveal that all formulations fits well with zero order kinetics followed by korsmeyerspeppas,higuchi model and then first order and the mechanism of drug release followed non-fickian diffusion. Hence the bioavailability of the drug can be improved by this buccoadhesive route by avoiding extensive first pass effect and increasing efficacy.Further work is recommended to support its efficacy and claims by long-term pharmacokinetic and pharmacodynamic studies in human beings.

REFERENCES

AgaiahGoud B, Kumara Swamy S, Praveen Kumar V. Formulation and evaluation of bioadhesivebuccal tablets of Simvastatin. *J Advanced Pharm Sci*, 1, 2011.

Ajit I, Senthil A, Rahul B, BirappaNarayanaswamy V. Formulation and Evaluation of Velnafaxine Hydrochloride MucoadhesiveBuccal tablets. *Int research J Pharm*, 3(1), 2012, 225-231.

Ansel's Pharmaceutical dosage forms and drug delivery systems, Ninth Eddition , 231-236.

ChaudhariAtul L, JagtapLeena S, MahajanAniruddha G, Swami Sima P, Mali Prabha R. Formulation and evaluation of buccal tablets of Salbutomolsulphate. *Intl research J Pharmacy*, 2(12), 2012, 238-242.

Chinna Reddy P, Chaitanya KSC, MadhusudanRao Y. A review on bioadhesivebuccal drug delivery systems: current status of formulation and evaluation methods.*DARU*, 19(6), 2011.

Goodman and Gilman's, The pharmacological basis of therapeutics, Tenth Edition, McGraw HillMedical publishing devision: 278-281.

Kaul M, Surender V, Aruna R Sapna S. An Overview OnBuccal Drug Delivery System. *Int J Pharm Sci Res*, 2(6), 2011, 1303-1321.

Mahalaxmi D, Senthil A, Prasad V, Sudhakar B, Mohideen S. Formulation and Evaluation of MucoadhesiveBuccal tablets of Glipizide.*Int Journal of Biopharmaceutics*, 1(2), 2010, 100-107.

Satyabrata B, Ellaiah P, Sujit Kumar M, PratitKanchan S, Sandip Prasad T, BibhutiBhusan P, Debajyoti D. Formulation and *in vitro* evaluation of mucoadhesivebuccal tablets of Timolol maleate. *Int J Pharm Biomed Res*, 1(4), 2010, 129-134.

Sudhakar Y, Kuotsu K, Bandyopadhyay AK. Buccalbioadhesive drug delivery - A promising option for orally less efficient drugs: A Review. *J of Controlled Release*, 114, 2006, 15-40.

Suvakanta D, Narasimha Murthy P, Lilikantanath, PrasantaC;Kinetic Modeling On Drug Release From Controlled Drug Delivery Systems. *ActaPoloniaePharmaceutica - Drug Research*, 67(3), 2010, 217-223.