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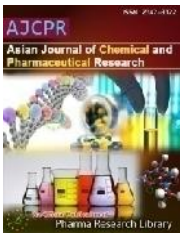

Research Article **Open Access**

Formulation Development and *In-Vitro* Evaluation of Mucoadhesive Buccal Tablets of Granisetron Hydrochloride

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A B S T R A C T

The objective of this study was to develop effective mucoadhesive buccal tablets comprising of drug containing bioadhesive layer. Granisetron hydrochloride was formulated as buccal tablets to improve its bioavailability by avoiding first pass metabolism. HPMC K15M, HPMC K100M and CARBOPOL 934 were selected as polymers various formulations were prepared by using these polymers. Ex-vivo permeation study of Granisetron hydrochloride drug solution through the Porcine buccal mucosa was performed using Franz diffusion cell and the flux value was found to be 424.735 µg hr-1cm-2. The pre-compression blend of Granisetron hydrochloride Buccal tablets were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio and all the results indicated that the blend was having good flow nature and better compression properties. The swelling studies were performed for the formulations which were shown desired drug release. The formulations prepared with Carbopal 934 in the concentration of 20mg (F8) were showing better result 92.09% drug release. The selected formulations F8 formulation was showing maximum flux value and permeability coefficient value i.e., 389.42 (µg hrs-1cm-2) and 0.111 (cm/h). From the release kinetics, data it was evident that the formulation was following zero order kinetics with regression value of 0.986 and it is following non-fickian diffusion mechanism.

Keywords: Granisetron Hydrochloride, Buccal Tablets, Carbopol

A R T I C L E I N F O

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1. Introduction

Buccoadhesive Drug Delivery

The potential route of buccal mucosal route of drug administration was first recognized by Walton and others reported in detail on the kinetics of buccal mucosal absorption. Buccoadhesion, or the attachment of a natural or synthetic polymer to a biological substrate, is a practical method of drug immobilization or localization and an important new aspect of controlled drug delivery. The unique environment of the oral (buccal) cavity offers its potential as a site for drug delivery. Because of the rich blood supply and direct access to systemic circulation. The Buccal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach or which are extensively metabolized in the liver (first pass effect).

Buccal route of administration:

The medicament is placed between the cheek and the gum. The barrier to drug absorption from this route is the epithelium of oral mucosa. Passive diffusion is the major mechanism for absorption of drugs. Drugs with short biological half-lives, requiring a sustained effect, poor permeability, sensitivity to enzymatic degradation and poor solubility may be successfully delivered via bioadhesive buccal delivery systems.

Advantages of Buccal route:

1. Rapid absorption and higher blood levels due to high vascularization of the region and therefore particularly useful for administration of anti-anginal drugs.
2. No first-pass hepatic metabolism.
3. No degradation of drugs such as that encountered in the GIT.
4. Presence of saliva facilitates both drug dissolution and its subsequent permeation by keeping the oral mucosa moist.
5. It is a safer method of drug administration, since drug absorption can be promptly terminated in cases of toxicity by removing the dosage form from the buccal cavity [4].

Disadvantages of buccal route:

1. Accidental swallowing of the formulation by the patient.
2. Difficulty in speaking and drinking.

Limitations:

1. Only limited amount of drug can be used in these systems (25-50 mg).
2. Drug must be non-irritant to the buccal mucosa.

Factors affecting systemic absorption of drugs through the buccal mucosa:

There are several factors affecting the absorption of drugs through the buccal mucosa.

Biological factors:

- Mucosal surface area
- Thickness of oral epithelium
- Structure of oral mucosa
- pH of environment
- Salivary secretion

Drug factors:

- Solubility
- Biological half life
- Drug stability
- Rate of absorption

Formulation factors:

- Size and shape
- Texture
- Properties of excipients
- Release characteristics
- Mobility of backing layer

2. Materials and Methods

Materials:

Granisetron Hydrochloride, Carbopol 934P, different grades of HPMC polymers, Magnesium stearate, Talc, Microcrystalline Cellulose.

Pre-formulation studies

Drug-excipient compatibility studies

Fourier Transform Infrared spectroscopic studies

A Fourier Transform – Infra Red spectrophotometer was used to study the non-thermal analysis of drug-excipients (binary mixture of drug: excipients 1:1 ratio) compatibility. The spectrum of each sample was recorded over the 450-4000 cm-1. Pure drug of Sumatriptan, Sumatriptan with physical mixture (excipients) compatibility studies were performed.

Preparation of standard graph in phosphate buffer pH 6.8: 100 mg of Pure Drug was dissolved in small amount of Methanol (5-10 ml) ,allowed to shake for few minutes and then the volume was made up to 100 ml with phosphate buffer pH 6.8, from this primary stock (1 mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer pH 6.8. From this secondary stock 1.0, 2.0, 3.0, 4.0, 5.0, ml was taken separately and made up to 10 ml with phosphate buffer pH 6.8 to produce 10, 20, 30, 40, 50 µg/ml respectively. The absorbance was measured at 272 nm using a UV spectrophotometer. The standard calibration curve of Sumatriptanin phosphate buffer pH 6.8 was shown in fig 6.

Solubility Studies

The solubility of Sumatriptanin phosphate buffer solution pH 6.8 was determined by phase equilibrium method. An excess amount of drug was taken into 20 ml vials containing 10 ml of phosphate buffers (pH 6.8). Vials were closed with rubber caps and constantly agitated at room temperature for 24 hr using rotary shaker. After 24 hr, the solution was filtered through 0.2 µm Whitman's filter paper. The amount of drug solubilized was then estimated by measuring the absorbance at 272 nm using a UV spectrophotometer. The standard curves for Sumatriptan were established in phosphate buffers (pH 6.8) and from the slope of the straight line the solubility of Sumatriptan was calculated. The studies were repeated in triplicate (n = 3), and mean was calculated.

Tissue permeation

Buccal tissue was taken from Pigs slaughter-house. It was collected within 10 minutes after slaughter of pig and tissue was kept in Krebs buffer solution. It was transported immediately to the laboratory and was mounted within 2hrs

of isolation of buccal tissue. The tissue was rinsed thoroughly using phosphate buffer saline to remove the adherent material. The buccal membrane from the tissue was isolated using surgical procedure. Buccal membrane was isolated and buccal epithelium was carefully separated from underlying connective tissue. Sufficient care was taken to prevent any damage to the epithelium.

Table 1: Composition of Tyrode solution (Krebs buffer)

Ingredients	Quantity(gm)
Sodium chloride	8.0
Potassium chloride	0.2
Calcium chloride dehydrate	0.134
Sodium bicarbonate	1.0
Sodium dihydrogen orthophosphate	0.05
Glucose monohydrate	1.0
Magnesium chloride	0.1
Distilled water up to	1.0Litre

Procedure for calibration curve of phenol red:

Various stock solutions of phenol red at concentrations ranging from 50 µg/mL to 1 µg/mL were prepared with phosphate buffer pH 6.6, 0.5 mL of Acetonitrile was added and vortexed. This was followed by addition of 2 mL of 0.2M NaOH, mixed well and volumes were made up to 10 mL with distilled water and were centrifuged. The resulting final concentration ranged from 2.5 µg/mL to 25 µg/mL. The absorbance was measured at 536 nm and standard graph was plotted.

Formulation and preparation of tablets

Buccal tablets were prepared by a direct compression method, before going to direct compression all the ingredients were screened through sieve no. 100. HPMCK4M, HPMCK15M, HPMCK100M and Carbopol 934P are the mucoadhesive and biodegradable polymers used in this preparation of buccal mucoadhesive drug delivery systems.

Sumatriptan was mixed manually with different ratios of HPMCK4M, HPMCK15M, HPMCK100M and carbopol 934P and Microcrystalline Cellulose as diluent for 10 min. In every formulation, constant amount of PVPK30 was added as binding agent. The blend was mixed with talc and magnesium stearate for 3-5 min.

Then the powder blend was compressed into tablets by the direct compression method using 6 mm flat faced punches. The tablets were compressed using a sixteen-station Cemach rotary tablet-punching machine. The weight of the tablets was determined using a digital balance and thickness with digital screw gauge.

Evaluation of Buccal Tablets

Physicochemical characterization of tablets

The prepared Sumatriptan buccal tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation: The weight variation test is done by taking 20 tablets randomly and weighed accurately. The composite weight divided by 20 provides an average weight of tablet. Not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than twice that percentage.

Tablet Thickness: The Thickness and diameter of the tablets from production run is carefully controlled. Thickness can vary with no change in weight due to difference in the density of granulation and the pressure applied to the tablets, as well as the speed of the tablet compression machine. Hence this parameter is essential for consumer acceptance, tablet uniformity and packaging. The thickness and diameter of the tablets was determined using a Digital Vernier caliper. Ten tablets from each formulation were used and average values were calculated. The average thickness for tablets is calculated and presented with standard deviation.

Tablet Hardness: Tablet hardness is defined as the force required to breaking a tablet in a diametric compression test. Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand the mechanical shocks during handling, manufacturing, packaging and shipping. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Six tablets were taken from each formulation and hardness was determined using Monsanto hardness tester and the average was calculated. It is expressed in Kg/cm^2.

Friability: Tablet hardness is not an absolute indicator of the strength because some formulations when compressed into very hard tablets lose their crown positions. Therefore another measure of the tablet strength, its friability, is often measured. Tablet strength is measured by using Roche friabilator. Test subjects to number of tablets to the combined effect of shock, abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm for 4 minutes, dropping the tablets to a distance of 6 inches in each revolution.

***In-vitro* release studies:**

The drug release rate from buccal tablets was studied using the USP type II dissolution test apparatus. Tablets were supposed to release the drug from one side only; therefore, an impermeable backing membrane was placed on the other side of the tablet. The tablet was further fixed to a 2x2 cm glass slide with a solution of cyanoacrylate adhesive. Then it was placed in the dissolution apparatus. The dissolution medium was 500 ml of pH 6.8 phosphate buffer at 50 rpm at a temperature of 37 ± 0.5 °C. Samples of 5 ml were collected at different time intervals up to 8 hrs and analyzed after appropriate dilution by using UV Spectrophotometer at 272 nm.

Release kinetics : Data of *in-vitro* release was fit into different equations to explain the release kinetics of candesartan release from buccal tablets. The kinetic equations used were zero – order and first order equations.

Zero – order release kinetics:

It defines a linear relationship between the fractions of drug released versus time

$$Q = kt$$

Where, Q is the fraction of drug released at time t

K is the zero order release rate constant

A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

First- order release kinetics:

Wagner assuming that the exposed surface area of a formulation decreased exponentially with time during dissolution process suggested that drug release from most slow release formulation could be described adequately by apparent first- order kinetics. The equation used to describe first- order release kinetics is

$$\ln (1-Q) = -kt$$

Where, Q is the fraction of drug released at time t and
K is the first order release rate constant.

Thus, a plot of the logarithm of the fraction of drug remained against time will be linear if the release obeys first order release kinetics.

Models of drug release mechanism [50]:

The release data of buccal tablets was fitted into different mechanism models like Higuchi model, Korsemeyer – Peppas model and Hixson- Crowel model to interpret the drug release mechanism from tablets.

Higuchi (Diffusion) equation:

It defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time.

$$Q = kt^{1/2}$$

Where, k is the release rate constant.

A plot of the fraction of drug released against square root of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law, square root time dependent.

Korsmeyer – Peppas kinetics:

A plot of the fraction of logarithm of % drug released against logarithm of time will be linear if the release obeys Korsmeyer–Peppas equation.

$$\log Q = \log k + n \log t$$

Where, k is the release rate constant.

Hixson- Crowel(Erosion) model:

This equation defines the drug release based on formulation erosion alone.

$$Q = 1-(1-kt)^3$$

Where, Q is the fraction of drug released at time t
K is the release rate constant

Thus a plot between $(1-Q)^{1/3}$ against time will be linear if the release obeys erosion equation.

Procedure:

Ex vivo permeation study of candesartan through the porcine buccal mucosa was performed using Franz diffusion cell and membrane assembly, at 37°C ± 0.2°C and 50 rpm. This temperature and rpm was maintained by magnetic stirrer. Porcine buccal mucosa was obtained from a local slaughter house and used within 2 hr of slaughter. The tissue was stored in Krebs buffer at 4°C upon collection. After the buccal membrane was equilibrated for 30 min with the buffer solution between both the chambers, the receiver chamber was filled with fresh buffer solution (pH 6.8), and the donor chamber was charged with 5 mL (1mg/mL) of drug solution. Aliquots (5 mL) were collected at predetermined time inter wells up to 8 hr and the amount of drug permeated through the buccal mucosa was then determined by measuring the absorbance at 272 nm using a UV spectrophotometer. The medium of the same volume (5 mL), which was pre-warmed at 37°C, was then replaced into the receiver chamber.

3. Results and discussion

Pre-formulation studies:

Standard Graph of Sumatriptan succinate at λ_{max} 272 nm: Standard stock solution of pure drug containing 100 mg of Granisetron hydrochloride/100 mL was prepared using buffer 6.8 pH phosphate buffer solution. The working standards were obtained by dilution of the stock solution in 6.8 pH phosphate buffer. The standard curve for Sumatriptan succinate was prepared in concentration range 10-50 µg/mL at the selected wavelength 272 nm. Their absorptivity values were used to determine the linearity. Solutions were scanned and beer lamberts law limit was obeyed in concentration range of 10, 20, 30, 40, 50 µg/mL. The same procedure is repeated by using pH 7.4 phosphate buffer.

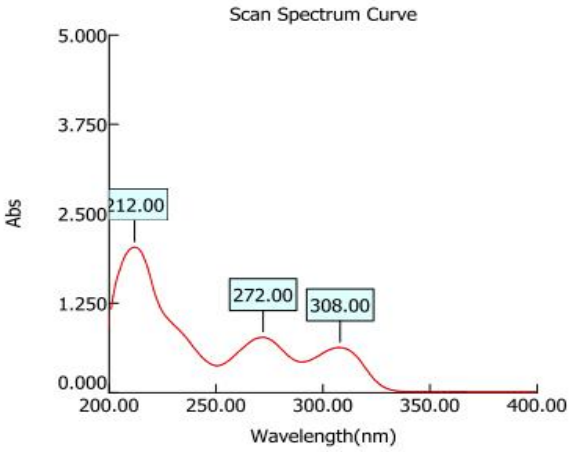

Figure: Spectrum showing Absorbance maxima value

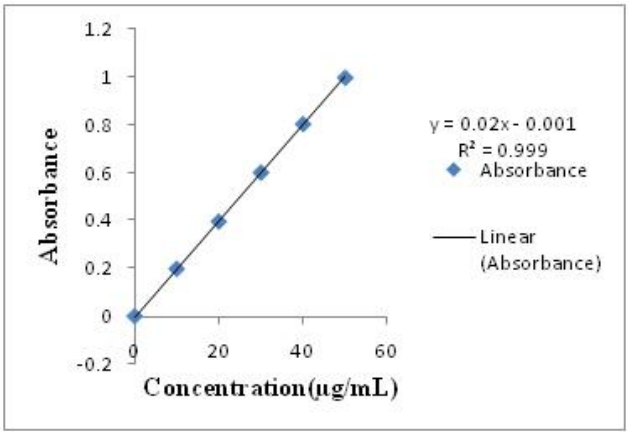

Figure 1: Standard graph of Sumatriptan succinate in 6.8 pH phosphate buffer

Table 2: Standard graph values of values of Sumatriptan succinate in 6.8 pH phosphate buffer

S. No	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.198
3	20	0.396
4	30	0.601
5	40	0.804
6	50	0.998

Table 3: Standard graph values of values of Sumatriptan succinate in 7.4 pH phosphate buffer

S. No	Concentration (µg/ml)	Absorbance
1	0	0
2	10	0.185
3	20	0.358
4	30	0.598
5	40	0.784
6	50	0.989

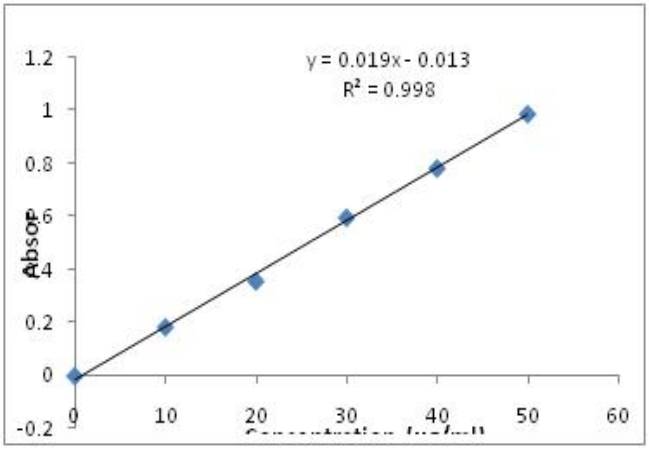

Figure 2: Standard graph of Sumatriptan succinate in 7.4 pH phosphate buffer

Calibration curve of phenol red:

Phenol red curve was plotted by taking the solution in the concentration ranges of 1 - 30 µg/ml. The following tabular column represents the corresponding values.

Table 4: Standard graph of Phenol red

S. No	Concentration (µg/ml)	Absorbance
1	0	0
2	1	0.09
3	5	0.143
4	7	0.198
5	10	0.543
6	20	0.654
7	25	0.792
8	30	0.881

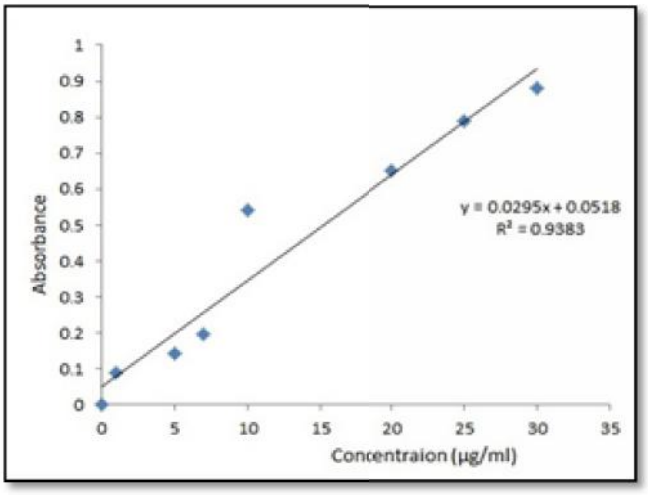

Figure 3: Standard graph of Phenol red

***Ex-vivo* permeation of drug solution through the Porcine buccal mucosa**

Ex-vivo permeation study of Sumatriptan succinate drug solution through the Porcine buccal mucosa was performed using Franz diffusion cell. The membrane assembly was kept at 37±0.2°C and 450 rpm. This rpm was maintained by magnetic stirrer. Phenol red was used as marker compound and is no expected to permeate through porcine membrane. Absence of phenol red in the receiver compartment indicates the intactness of the buccal membrane.

Table 5: Ex-vivo permeation of Sumatriptan succinate drug solution through the porcine buccal mucosa

Time (hrs)	Cumulative amount of Sumatriptan succinate permeated (%)
0	0
0.5	9.87±1.05
1	14.74±0.85
2	17.24±1.12
3	22.25±1.33
4	31.17±1.54
5	44.36±.98
6	52.69±1.15
7	77.75±0.74
8	89.91±0.75

Solubility Studies:

The solubility of Sumatriptan succinate in phosphate buffer solution pH 6.8 was determined by phase equilibrium method. An excess amount of drug was taken into 20 ml vials containing 10 ml of phosphate buffers (pH 6.8, pH 7.4 and water). Vials were closed with rubber caps and constantly agitated at room temperature for 24 hr using rotary shaker. After 24 hr, the solution was filtered through 0.2 µm Whatmann's filter paper. The amount of drug solubilized was then estimated by measuring the absorbance at 272 nm using a UV spectrophotometer

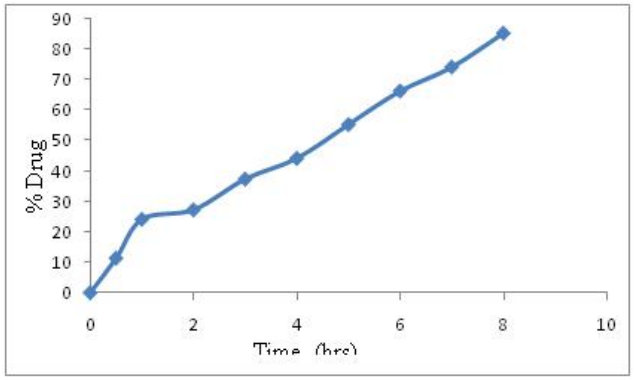

Figure 4: Ex-vivo permeation of Sumatriptan succinate drug solution through the porcine buccal mucosa

Table 6: Solubility studies

S.No	Medium	Concentration (µg/ml)
1	Phosphate 6.8 buffer	14.5
2	Phosphate 7.4 buffer	13.8
3	Water	12.4

Evaluation:

Characterization of Pre-compression Blend:

The pre-compression blend of Sumatriptan succinate Buccal tablets were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio**.** Angle of repose was less than 28^0, Carr's index values were less than 11 for the pre-compression blend of all the batches indicating good to fair flowability and compressibility. Hausner's ratio was less than 1.25 for all the batches indicating good flow properties.

Evaluation of Buccal Tablets:

Physical Evaluation of Sumatriptan succinate Buccal tablets:

The results of the weight variation, hardness, thickness, friability, and drug content of the tablets are given in table 16. All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limits. The hardness of the tablets ranged from 3.6 to 5 kg/cm^2 and the friability values were less than 0.561% indicating that the buccal tablets were compact and hard. The thickness of the tablets ranged from 2.71-2.91 cm. All the formulations satisfied the content of the drug as they contained 98-100% of Sumatriptan succinate and good uniformity in drug content was observed. Thus, all the physical attributes of the prepared tablets were found to be practically within control limits.

***In vitro* release studies:**

The drug release rate from buccal tablets was studied using the USP type II dissolution test apparatus. Tablets were supposed to release the drug from one side only therefore an impermeable backing membrane was placed on the other side of the tablet. The tablet was further fixed to a 2x2 cm glass slide with a solution of cyano-acrylate adhesive. Then it was placed in the dissolution apparatus. The dissolution medium was 500 ml of pH 6.8 phosphate buffer at 50 rpm at a temperature of 37 ± 0.5 °C. Samples of 5 ml were collected at different time intervals up to 8 hrs and analyzed after appropriate dilution by using UV Spectrophotometer at 272 nm.

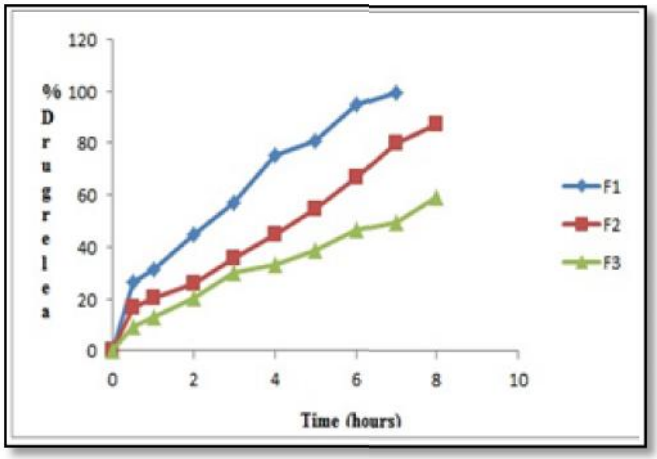

Figure 5: *In-vitro* dissolution data for formulations F1 - F3 by using HPMC K15M Polymer

From the above graphs, it was evident that HPMC K 15 M in the concentration of 20 mg (F2), is showing better result 87.7% drug release when compared with other two ratios.

Table 7: *In-vitro* dissolution data for formulations F4 - F6 by using HPMC K100M Polymer

Time(hrs)	% Drug release		
	F4	F5	F6
0	0	0	0
0.5	14.23	12.56	7.73
1	20.9	16.57	11.56
2	32.73	18.9	16.56
3	42.9	27.73	18.9
4	50.4	42.4	22.73
5	57.73	47.9	28.23
6	68.56	54.4	36.06
7	83.73	66.56	48.4
8	90.9	72.73	60.4

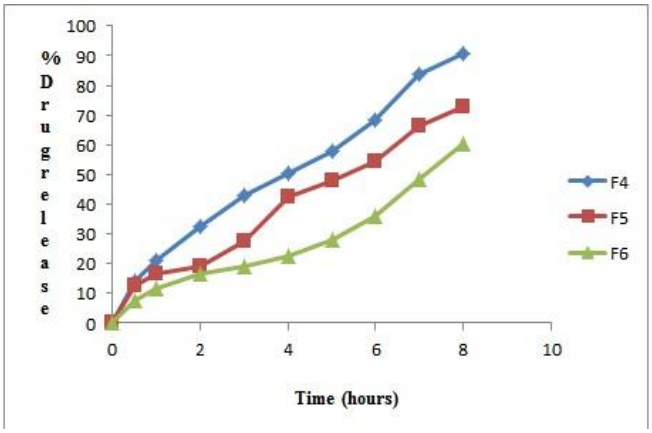

Figure 6: *In-vitro* dissolution data for formulations F4 - F6 by using HPMC K100 M Polymer

From the above graphs it was evident that HPMC K 100 M

in the concentration of 10 mg (F4), is showing better result 90.90% drug release when compared with other two ratios. As the concentration of polymer increases the retarding of drug release also increased. Hence they were not considered.

Table 8: *In-vitro* dissolution data for formulations F7 - F9 by using Carbopaol 934 Polymer

Time(hrs)	% Drug release		
	F7	F8	F9
0	0	0	0
0.5	24.4	16.56	11.06
1	35.56	26.23	16.73
2	49.9	35.56	21.06
3	61.06	44.23	34.4
4	70.73	50.56	41.06
5	81.73	66.56	46.56
6	93.73	78.23	52.4
7	98.4	89.4	60.73
8	98.23	92.06	70.4

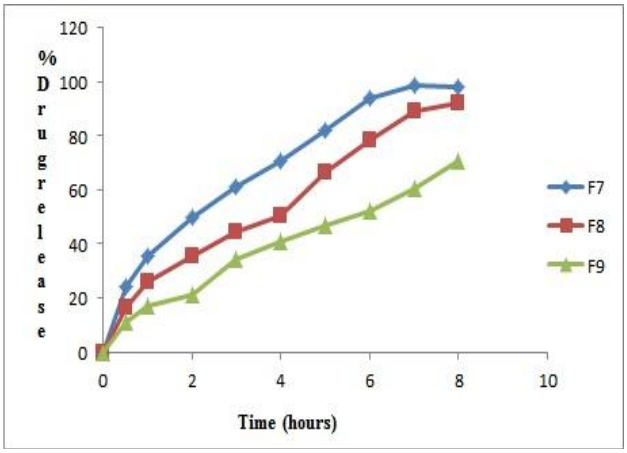

Figure 7: *In-vitro* dissolution data for formulations F10 - F12 by using Carbopaol 934 Polymer

From the above graphs it was evident that Carbopol 934 in the concentration of 20 mg (F8), is showing better result 92.06% drug release when compared with other two concentrations

Release kinetics:

Data of *in-vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Sumatriptan succinate release from buccal tablets. The data was fitted into various kinetic models such as zero, first order kinetics, Higuchi and Karsmeyer Peppas mechanisms and the results were shown in below table.

***Ex-vivo* residence time:**

It is one of the important physical parameter of buccal bioadhesive tablets. The ex-vivo residence time was determined by specially designed apparatus.

The moisture absorption:

This studies give important information of the relative moisture absorption capacities of polymers and it also give information regarding whether the formulations maintain the integrity or not.

The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible. The surface pH of the selected formulation (F8) was found to be 6.81±0.25.

Bioadhesion strength:

It was measured for the selected formulations**.** From this two parameters such as Peak detachment force (N) and work of adhesion were calculated and they were found to be good for the formulation F8.

Summary

- Sumatriptan succinate drug undergoes first-pass metabolism in the liver which is the reason for its lower bioavailability, so to improve its bioavailability it was formulated as buccal tablets.
- Bio adhesive polymers such as HPMC K15M, HPMC K100M and CARBOPOL 934 were selected as polymers, various formulations were prepared and studies for their characteristics by using these polymers alone and in different combinations.
- Analytical profile of drug was studied to determine their absorption maximum which was found to be 272 nm and to construct standard graph by using different standard concentrations of drug.
- All the formulations were prepared by direct compression method by using sixteen station rotary tablet punching machine with the utilization of 6 mm flat surfaced punch. In all the formulations, MCC was employed as diluent.
- Ex-vivo permeation study of Sumatriptan succinate drug solution through the Porcine buccal mucosa was performed using Franz diffusion cell and the flux value was found to be 391.690 µg.hr-1cm-2.
- The pre-compression blend of Sumatriptan succinate Buccal tablets were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio and all the results indicated that the blend was having good flow nature and better compression properties.
- The tables were prepared by taking the polymers in different concentrations alone and combinations. The prepared tablets were evaluated for various physical evaluation parameters of tablets such as weight variation, friability, hardness, thickness, diameter and assay. All the results were found to be within standard limits.
- The formulations prepared with Carbopal 934 in the concentration of 20 mg (F8) was showing better result 92.09% drug release.
- The swelling studies were performed for the formulations which were shown desired drug release and the value was found to be 68.5 % in 8 hours.Ex-vivo residence time, Moisture absorption, surface pH, Bioadhesion strength values for selected formulations were found to be good.
- The selected formulations F8 formulation was showing maximum flux value and permeability coefficient value i.e., 389.42 (µg.hrs-1cm-2) and 0.111 (cm/h).

Table 9: Composition of buccal tablets

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Drug	25	25	25	25	25	25	25	25	25
HPMCK15M	25	50	75	-	-	-	-	-	-
HPMCK100M	-	-	-	25	50	75	-	-	-
CARBOPAL 934	-	-	-	-	-	-	25	50	75
	5	5	5	5	5	5	5	5	5
MCC pH 102	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
Mg. Stearate	3	3	3	3	3	3	3	3	3
Aerosil	3	3	3	3	3	3	3	3	3
Total Weight (mg)	150	150	150	150	150	150	150	150	150

Table 10: Physical properties of precompression blend

Formulation Code	**Angle of repose (Θ)**	**Bulk density (gm/cm^3)**	**Tapped density (gm/cm^3)**	**Carr's Index (%)**	**Hausner's ratio**
F1	25.10°	0.53±0.01	0.59±0.01	9.43±0.12	1.09±0.02
F2	25.43°	0.54±0.03	0.60±0.02	9.40±0.13	1.10±0.01
F3	25.41°	0.54±0.02	0.58±0.03	10.01±0.19	1.13±0.06
F4	26.40°	0.51±0.01	0.61±0.06	10.11±0.02	1.16±0.01
F5	27.12°	0.58±0.03	0.63±0.03	10.34±0.13	1.17±0.03
F6	25.31°	0.59±0.03	0.64±0.04	10.12±0.34	1.11±0.06
F7	26.11°	0.56±0.01	0.63±0.01	9.93±0.11	1.13±0.03
F8	26.15°	0.53±0.03	0.58±0.03	10.13±0.02	1.12±0.01
F9	26.10°	0.54±0.01	0.61±0.03	10.20±0.13	1.13±0.03

All the values represent mean ± Standard deviation (SD), n=3

Table 11: Physical Evaluation of Sumatriptan succinate Buccal tablets

Formulation code	**Weight variation (mg)**	**Thickness (cm)**	**Diameter**	**Hardness (Kg/cm^2)**	**Friability (%)**	**Content uniformity (%)**
F1	103±1	2.76±0.01	6.12±0.01	4.5±0.7	0.420	99±0.12
F2	104±2	2.74±0.04	6.14±0.02	4.2±0.5	0.341	99±0.3
F3	101±1	2.71±0.01	6.01±0.01	3.6±0.6	0.363	100±0.1
F4	104±2	2.80±0.06	6.03±0.03	4.8±0.5	0.561	100±0.3
F5	105±3	2.81±0.04	6.04±0.04	3.8±0.4	0.482	99±0.6
F6	104±1	2.74±0.05	6.09±0.05	4.4±0.6	0.513	99±0.4
F7	99±1	2.76±0.03	6.11±0.03	5 ± 0.1	0.412	98±0.9
F8	100±2	2.71±0.04	6.09±0.06	4.6±0.2	0.432	99±0.1
F9	100±3	2.73±0.03	6.03±0.02	4.0±0.3	0.512	100±0.1

Table 12: *In-vitro* dissolution data for formulations F1 - F3 by using HPMC K15M Polymer

Time(hrs)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0	0	0	0	0	0	0	0	0	0
0.5	26.73	16.73	26.73	16.73	26.73	16.73	26.73	16.73	9.4
	31.06	20.4	31.06	20.4	31.06	20.4	31.06	20.4	13.23
2	44.9	25.9	44.9	25.9	44.9	25.9	44.9	25.9	20.4
3	57.06	35.56	57.06	35.56	57.06	35.56	57.06	35.56	29.9
4	75.56	44.9	75.56	44.9	75.56	44.9	75.56	44.9	33.23
5	81.06	54.4	81.06	54.4	81.06	54.4	81.06	54.4	38.73
6	94.9	66.56	94.9	66.56	94.9	66.56	94.9	66.56	46.56
7	99.56	79.9	99.56	79.9	99.56	79.9	99.56	79.9	49.9
8	-	87.73	-	87.73	-	87.73	-	87.73	59.56

Table 12

Formulation code	Mathematical models (Release Kinetics)				
	Zero order	First order	Higuchi	Korsmeyer-Peppas	
	R^2	R^2	R^2	R^2	n value
F8	0.986	0.9119	0.9348	0.9427	0.6177

From the above release kinetics data it was evident that the formulation was following zero order kinetics with regression value of 0.986 and it is following non fickian diffusion mechanism.

Table 13: *Ex-vivo* residence time, Moisture absorption, surface pH, Bioadhesion strength values of selected formulations

Formulation Code	EX-Vivo residence time (hr)	Moisture absorption	Surface pH	Bioadhesion strength	
				Peak detachment force (N)	Work of adhesion (mJ)
F8	6hr 33min	44±0.25	6.81±0.25	3.8±0.41	17.42±6.10

Each value represents the mean±SD (n=3)

4. Conclusion

Sumatriptan succinate was formulated as buccal tablets to improve its bioavailability by avoiding first pass metabolism. HPMC K15M, HPMC K100M and CARBOPOL 934 were selected as polymers various formulations were prepared by using these polymers. Ex-vivo permeation study of Sumatriptan succinate drug solution through the Porcine buccal mucosa was performed using Franz diffusion cell and the flux value was found to be 424.735 $\mu g.hr^{-1}cm^{-2}$. The pre-compression blend of Sumatriptan succinate Buccal tablets were characterized with respect to angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio and all the results indicated that the blend was having good flow nature and better compression properties. The swelling studies were performed for the formulations which were shown desired drug release. The formulations prepared with Carbopal 934 in the concentration of 20 mg (F8) was showing better result 92.09% drug release. The swelling studies were performed for the formulations which were shown desired drug release and the value was found to be 68.5 % in 8 hours. *Ex-vivo* residence time, Moisture absorption, surface pH, Bioadhesion strength values for selected formulations were found to be good. The selected formulations F8 formulation was showing maximum flux value and permeability coefficient value i.e., 389.42 (µg.hrs-1cm-2) and 0.111 (cm/h).

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