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Research Article

Development and *In-vitro* Evaluation of Zolmitriptan Mucoadhesive Buccal Tablets

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ABSTRACT

In this study, an attempt was made to develop and evaluate mucoadhesive buccal tablets of Zolmitriptan. Following direct compression method mucoadhesive buccal tablets of zolmitriptan were prepared to increase bioavailability and prolonged therapeutic efficacy using the bioadhesive polymers being HPMC K-15, Guar Gum and Xanthan Gum at various concentrations and chitosan as permeation enhancer. The physical properties of the prepared tablets were essentially within prescribed limits and showed good flow qualities of the mixture when all batch formulations were assessed for various parameters for pre and post compression. The *FT-IR* spectroscopy revealed the drug compatibility and showed no drug-polymer and drug-excipient interactions. The tablets' hardness, thickness, weight variance, friability, and drug content were all assessed, & it was determined that all of these parameters fell within the pharmacopoeial specification's acceptable range. All formulation tablets were also evaluated for surface pH, swelling behaviour, *in- vitro* drug release, mucoadhesive strength and *ex-vivo* diffusion study. The tablet's surface pH ranged from 6.29 to 7.25, which is within the range of salivary pH. The buccal tablets maintained the integrity of the polymers with good swelling of >69% up to 8 hours. When compared to other formulations, the formulation F5 exhibits an excellent drug release of 96.84% by 6 hours according to *in-vitro* testing of zolmitriptan. All the tablets showed mucoadhesive strength 5.87 to 8.86 g and are enhanced by concentration of polymers. The *ex-vivo* drug permeation showed the drug being permeated up to 6 h. The formulation F5 containing Zolmitriptan and Guar Gum as mucoadhesive polymer is the ideal optimized formulation. The kinetic release study reveals that it followed zero order release and was best fitted in Korsmeyer- Peppas model suggesting the mechanism of drug release to be diffusion and non-Fickian release.

Keywords: Mucoadhesive buccal tablet, Zolmitriptan, HPMCK100, Guar Gum, Xanthan Gum, direct compression method.

INTRODUCTION

Buccal administration is a topical route of administration by which drugs held or applied in the buccal area (in the cheek) diffuse through the oral mucosa and enter directly into the bloodstream. Buccal delivery refers to drug release which can occur when a dosage form is placed in the outer vestibule between the buccal mucosa and gingiva. Buccal tablets soften & adhere to the buccal mucosa and are retained in position until dissolution and/or release is complete. Buccal administration may provide better bioavailability of some drugs and a more rapid onset of action compared to oral administration because the medication does not have to pass through the GIT and thereby avoids first pass metabolism[1].

Anti-migraine medications are used to treat severe headaches caused by migraine. Zolmitriptan was patented in 1990 and came into medical use in 1997. Zolmitriptan is available as a generic medication. Zolmitriptan is selected as a model drug for the present study. Zolmitriptan belongs to the class of medication called triptans under abortive medication for the treatment of severe headaches caused by acute migraine. The drug acts by constricting blood vessels in brain and also inhibiting release of pro-inflammatory neuropeptides from trigeminal perivascular nerve endings, preventing transmission of pain signals to the brain, and inhibiting release of certain natural substances that trigger pain[2].

The purpose of this research study was to develop and *in-vitro* evaluation of Zolmitriptan mucoadhesive buccal tablets using mucoadhesive polymers such as HPMC K15, Guar Gum & Xanthan Gum and chitosan as permeation enhancer by direct compression method with an objective to improve the bioavailability of drug and to avoid hepatic first pass metabolism, predictable and prolonged duration of action, minimizing undesired side effect increase residence time of drug in the body most importantly, and also providing patient compliance as the drug delivery is painless.

MATERIALS AND METHODS

Material

Zolmitriptan was purchased from Carbanio chemicals Pvt. Ltd. HPMC K-15, Guar Gum, Xanthan Gum and Chitosan was obtained from S.D. Fine Chemicals Pvt. Ltd. Mumbai, India. All other chemicals and solvents used were of standard analytical grades.

Methods

Pre formulation Studies

Solubility The solubility of the chosen drug was carried in distilled water, 0.1 M HCl, phosphate buffer pH 6.8, methanol and acetone following standard method.[3]

Melting Point Glass capillary tube filled with the drug, sealed from one end was tied to a thermometer with a thin thread and immersed in Thiele tube containing liquid paraffin in such a way that the lower tip of capillary tube barely the liquid paraffin. The tube was heated where the temperature was noted as the drug starts to melt and thus melting point was determined.[4]

Estimation of Zolmitriptan for absorption maxima

Zolmitriptan's stock solution I was prepared by dissolving 100 mg of drug with 100 ml of phosphate buffer pH 6.8 (1 µg/ml) and then serially diluted with phosphate buffer pH 6.8 in 100 ml volumetric flask and stock solution II was obtained (100 µg/ml). Aliquot was withdrawn from stock II and diluted with phosphate buffer pH 6.8 to obtain 5 µg/ml and scanned over the wavelength range of 200-400 nm using UV spectrophotometer against blank.[5]

Determination of Calibration Curve of Zolmitriptan

A stock solution I of 1mg/ml of Zolmitriptan was prepared and serially diluted to obtain stock solution II of 100 µg/ml. From the stock solution II, pipette out 2, 4, 6, 8 and 10 ml of solution in 10 ml volumetric flask and diluted with phosphate buffer pH 6.8 to produce 2, 4, 6, 8 and 10 µg/ml concentration. The absorbance of these solutions was measured at 222.6 nm against blank.

Compatibility Studies using *FT-IR*

Fourier Transform Infrared Spectrophotometer (FT-IR) was done to understand the compatibility between the drug and excipients by potassium bromide pellet method. The sample disc was prepared by triturating approximately 1-2 mg of sample substance with around 10-20 mg KBr and then compressing by hydraulic press to form a thin disc of around 10-15 mm diameter. The disc was scanned in the range of 4000-400 cm^{-1} in a FT-IR spectrophotometer in order to get a spectrum by placing in sample holder. The obtained spectra of the drug and the excipients were compared and it was interpreted for the functional group peaks in order to check for any interactions.[6]

Preparation of mucoadhesive buccal tablets

The mucoadhesive buccal tablets were prepared by direct compression method using HPMC K15, Guar Gum and Xanthan Gum as mucoadhesive polymers. According to the batch formula, the drug, polymers and all excipients were weighed accurately. Except lubricant and glidant, all other ingredients were mixed in ascending order and triturated in a glass mortar for 15 minutes. After mixing of ingredients, lubricant and glidant were added and mixed again for 3 minutes. Final mixed powder blend was then compressed in to tablets according to their weight using 8 mm round flat punches.[7]

EVALUATION PARAMETERS

Evaluation of Buccal Tablets

The formulated tablets were evaluated for the following tests.

Weight Variation Test The 20 tablets were chosen randomly and weighed individually and average weight was determined. The individual weights were compared to the average weight to determine the weight variance.[8]

Hardness The resistance of tablets to shipping or breakage under the conditions of storage, transportation and handling before use relies on strength or hardness of tablet. Pfizer hardness tester was used for measurement of ten randomly selected buccal tablets that measures the pressure required to break tablets by applying pressure with coiled spring and expressed in Kg/cm^2.

Friability Friabilator apparatus (Roche Friabilator) was used to check the friability and 10 tablets were selected randomly from each formulation which revolves at 25 revolution per minute for 4 minutes dropping tablets from a distance of 6 inches with each revolution. After 100 revolution tablets were dedusted, reweighed and percentage loss was determined. [9]

% Friability = (Initial weight of tablets – Final weight of tablet) / Initial weight of tablets) X 100

% Percentage friability of tablets less than 1% was considered as acceptable.

Thickness and Diameter The thickness and diameter of formulated tablets were determined by digital Vernier's caliper. For this, 10 tablets from each representative formulation were taken and the thickness and diameter were measured for each of them and the mean of these readings were taken as the mean tablet thickness and mean tablet diameter.

Drug Content

Ten tablets from each formulation were triturated in mortar & pestle and powder equivalent to one tablet mass was extracted in suitable quantity of phosphate buffer pH 6.8 and filtered through a Whatman's filter paper. Phosphate buffer pH 6.8 was used to dilute the filtrate and analysed for drug content by measuring the absorbance at λmax 222.6 nm in UV spectrophotometer using the reference to the standard calibration curve of Zolmitriptan.

Drug Content = Absorbance / Slope × Dilution factor / 1000

The % drug content for the tablet should be within the range of 85% - 115%.

Surface pH

The surface pH of the manufactured tablets was measured in order to identify any potential buccal mucosa discomfort. It is important to maintain the surface pH as close to neutral as feasible or within the salivary pH range as an acidic or alkaline pH may irritate the buccal mucosa. For this, combined glass electrode is employed. The tablets were kept in contact with 1 ml of phosphate buffer pH 6.8 for 2 hours at room temperature in order to allow the tablets to swell. The electrode was placed in contact with enlarged tablet to test the pH after one minute of equilibration.

Swelling Index Study

In phosphate buffer pH 6.8, the buccal tablet's swelling index study was assessed. Each tablet's initial weight (W_1) was calculated, and the tablet was then kept in a petri dish with 5 ml of phosphate buffer pH 6.8 and incubated at 37°C. The tablets were taken at various intervals (1, 2, 3, 5, 6, 7, and 8 hours), wiped with filter paper, and reweighed (W_2).[10] The swelling index was determined by;

Swelling Index = 100 × (W_2 – W_1) / W_1

In-vitro Drug Release Studies

The in-vitro release of drug from the tablet was investigated using the USP type-II rotating paddle method. The phosphate buffer pH 6.8 in 900 ml served as the dissolving media. At a rotational speed of 50 rpm and a temperature of 37.5°C, the release study was conducted. The disc was put in the dissolution vessel's bottom. To maintain sink conditions, aliquots were taken out at regular intervals and replaced with fresh buffer. Using Whatman filter paper, the samples were filtered, and 1 ml of the filtrate was taken out and diluted to 10 ml of phosphate buffer pH 6.8. The diluted samples were calibrated at 222.6 nm for absorbance, and the % cumulative drug release was calculated using Zolmitriptan calibration curve.[11]

Mucoadhesive Strength

The mucoadhesive strength of each formulation is determined by measuring the force required to detach tablet from sheep buccal mucosal tissue using modified balance. Fresh buccal mucosa of sheep was obtained from a local slaughter house and within 3 hours of slaughtering was used. The mucosal membrane was washed properly with distilled water followed by rinsing with phosphate buffer pH 6.8. A double bean physical balance was used and a thick thread was strung from the left arm of the balance and a glass stopper with a uniform surface was connected to the bottom side of thread. The buccal mucosa was tightly fastened with mucosal side facing up using thread over base of an inverted 50 ml glass beaker that was placed in a 500 ml beaker filled with phosphate buffer pH 6.8 preserved at 37 °C

so that buffer reaches surface of mucosal membrane keeping it wet.

Prior to study, the balance's two sides were made equal by maintaining weight on right-hand pan. The right pan was opened and 5 g of weight was taken out which was used to descend the glass stopper and the tablet over the mucosal membrane. The balance was held in this position for three minutes. Then the weight on the right pan were raised until the tablet just parted from mucosal membrane. So, mucoadhesive strength would be that excessive weight on right pan i.e. total weight minus 5 g. Three trials were done to determine mean value taken for each set of formulations. The tissue was gently and thoroughly rinsed with phosphate buffer after each measurement and left for 5 min before placing a new tablet in order to get appropriate results for formulation. After calculating mucoadhesive strength, the force of adhesion was also calculated from following equations as,

Force of Adhesion (N) = Mucoadhesive Strength × 9.8 / 1000

In vitro drug release kinetics

In-vitro release data were plotted in different kinetic models to analyse in-vitro drug release kinetics: Zero-order as % drug released Vs time, First order as log % cumulative drug released Vs time, Higuchi as % cumulative drug released Vs time, Korsmeyer-Peppas as log % drug released Vs log time are some examples. The best-fit model was chosen by contrasting the r2-values that were obtained.

Ex-vivo Drug Permeation Study

Using Franz Diffusion cells adjusted to 37.5^{O}C, the transmucosal permeation flow of the drug from the chosen formulation and the control (solution) will be measured. Between the donor and recipient chambers, a goat's buccal mucosal membrane was held. Tablets containing medication was applied to the mucosal surface. The phosphate buffer (pH 6.8) was added to the lower receiver chamber and agitated at 50 rpm. Aliquots from the receiver fluid was withdrawn and replaced with the fresh buffer to maintain sink condition. The withdrawn samples were diluted and then analysed by UV spectrophotometer for absorbance. The amount of drug released was calculated by measuring the individual permeation data.[13]

Stability Studies

As per ICH guidelines, accelerated stability study was conducted on the promising buccal zolmitriptan tablets for three months (90 days) at a temperature of 40 ± 2^{O}C and 75 ± 5% RH. A sufficient number of pills (10) were placed in an amber coloured screw cap bottle and individually wrapped in aluminium foil before being maintained in a stability chamber for three months. Each month, samples were evaluated for appearance, hardness, friability, surface pH, drug content, and in-vitro drug release studies.[14]

RESULTS AND DISCUSSION

Zolmitriptan was found to be very soluble in 0.1M HCl, freely soluble in methanol, and soluble in phosphate buffer pH 6.8. The drug was found to be slightly or very slightly soluble in water. The melting point of Zolmitriptan was determined by Theile tube method and found to be 138^{O}C. The compatibility study was carried by *FT-IR* spectroscopy and studied for interaction through following *FT-IR* spectra peaks. By using *FT-IR* Spectroscopy, drug-polymer compatibility studies were conducted to determine any potential interactions between excipients and the drug in the formulation. For compatibility study, the *FT-IR* spectrum of drug alone and in combination with excipients was determined. The physical mixture of the drug and polymers as well as the pure drug Zolmitriptan's *FT-IR* spectra were provided in given table. The primary absorption peaks for the pure drug were found to be at 2759.70 cm^{-1} (N-CH_3), 2889.37 cm^{-1} (C-H), 3411.55 cm^{-1} (N-H), and 1746.64 cm^{-1} (C=O), respectively. The spectra of the physical mixture, which contains the drug and excipients, showed vibrations as well. Since it displays the distinctive peak of drug and excipients, the *FT-IR* study demonstrated that there is no significant drug excipients interactions.

All tablets composing of different concentration of polymers were within the weight variance

range as per IP limit. The maximum weight was 199 mg and the minimum observed was 197 mg. The thickness and diameter of all the compressed tablets of all formulations were within the limits as per USP. The thickness and diameter of all formulations were found to be within the acceptable range of 2.24 to 2.31 mm and 7.88 to 7.92 mm respectively. For all formulations the average percentage friability was in the range of 0.276% to 0.511% and have an average hardness in between 4.8 to 6.4 kg/cm^2 which was considered to be acceptable.

The percent drug content was found to be in the range of 85.12 % to 95.60 % which ensures that all formulations contain stated or labelled amount of Zolmitriptan in the prepared tablets. The surface pH was determined in range of 6.25 to 7.25 for different batches of formulations i.e. within the range of buccal mucosa. Hence it will not produce any local irritation to the mucosa. The swelling index study was carried by using phosphate buffer pH 6.8.

Ingredients (mg)	**Formulation codes**											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Zolmitriptan	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
HPMC K-15	2	4	6	8	-	-	-	-	-	-	-	-
Guar Gum	-	-	-	-	2	4	6	8	-	-	-	-
Xanthan Gum	-	-	-	-	-	-	-	-	2	4	6	8
Mannitol	124.5	122.5	120.5	118.5	124.5	122.5	120.5	118.5	124.5	122.5	120.5	118.5
Chitosan	8	8	8	8	8	8	8	8	8	8	8	8
Na CMC	10	10	10	10	10	10	10	10	10	10	10	10
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2	2	2
Talc	1	1	1	1	1	1	1	1	1	1	1	1
Ethyl Cellulose	50	50	50	50	50	50	50	50	50	50	50	50
Total	200	200	200	200	200	200	200	200	200	200	200	200

Table 1: Formulation of Single Mucoadhesive Buccal Tablets Containing Zolmitriptans

Fig 1: Modified balance for muco-adhesion

Formulation Codes	Evaluation Parameters						
	Thickness (mm)	**Weight Variation (mg)**	**Diameter (mm)**	**Friability (%)**	**Hardness (Kg/cm^2)**	**Drug Content (%)**	**Surface pH**
F1	2.31	199	7.89	0.276	5.9	94.8	7.10
F2	2.24	198	7.91	0.334	6.8	88.3	6.66
F3	2.27	198	7.89	0.329	6.1	91.2	6.72
F4	2.24	198	7.92	0.452	6.4	88.2	6.45
F5	2.26	199	7.88	0.281	4.8	95.60	6.75
F6	2.27	198	7.90	0.511	5.6	85.4	6.32
F7	2.28	199	7.89	0.367	6.0	86.0	6.29
F8	2.28	197	7.91	0.410	6.0	95.60	6.80
F9	2.29	197	7.90	0.388	5.6	87.6	6.25
F10	2.26	198	7.89	0.459	5.8	86.4	6.85
F11	2.28	197	7.88	0.505	5.8	85.12	7.25
F12	2.27	198	7.89	0.510	5.6	92.6	6.84

Table 2: Post compression parameters results for formulation F1-F12

Time (h)	Percentage Weight Change											
	F1 (%)	**F2 (%)**	**F3 (%)**	**F4 (%)**	**F5 (%)**	**F6 (%)**	**F7 (%)**	**F8 (%)**	**F9 (%)**	**F10 (%)**	**F11 (%)**	**F12 (%)**
1	20.27	22.97	22.14	25.67	18.79	20.27	15.54	34.87	14.14	16.92	17.76	18.18
2	29.72	36.48	35.57	33.78	46.30	35.13	23.64	40.00	20.07	21.02	26.39	24.24
3	37.16	47.29	47.65	40.54	58.30	50.00	47.29	43.58	24.10	24.25	28.42	36.36
4	40.54	50.67	50.33	43.91	60.40	57.43	59.45	45.64	25.12	29.29	31.47	40.90
5	44.65	53.65	52.16	49.78	62.56	58.13	60.81	48.71	28.90	31.81	36.82	42.39
6	46.76	55.70	55.93	56.32	64.76	59.40	61.48	49.74	32.60	34.82	42	46.50
7	49.12	58.63	57.12	59.28	66.18	61.82	62.96	51.31	34.82	36.32	44.19	48.20
8	51.31	60.08	60.18	60.80	67.49	62.38	63.41	52.08	35.16	37.18	47.12	50.16

Table 3: Swelling Index Data of Formulations F1 - F12.

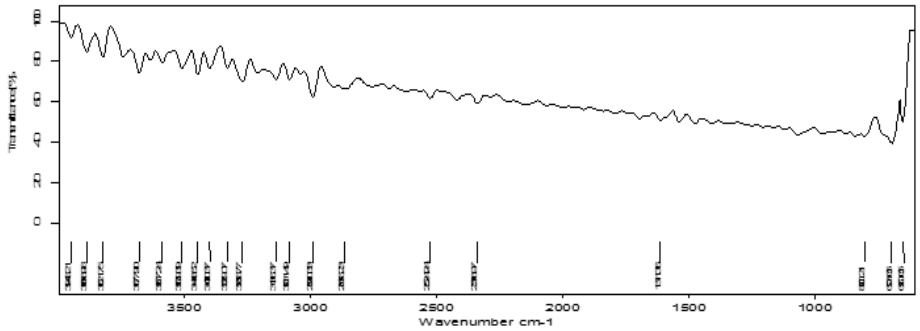

Fig 2: FT-IR Spectrum of Pure Drug Zolmitriptan

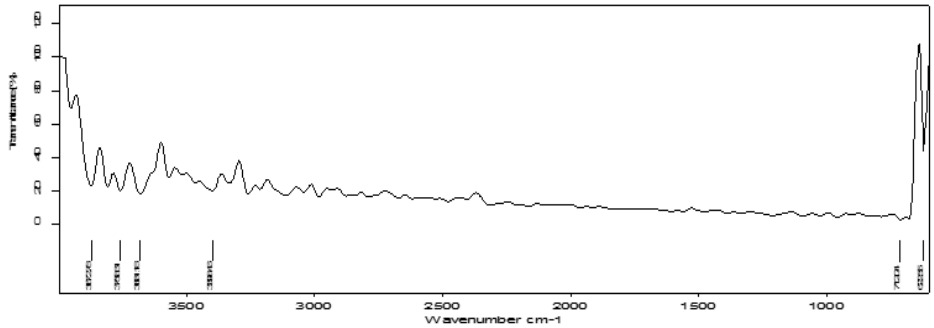

Fig 3: FT-IR spectrum of Zolmitriptan + HPMC K-15

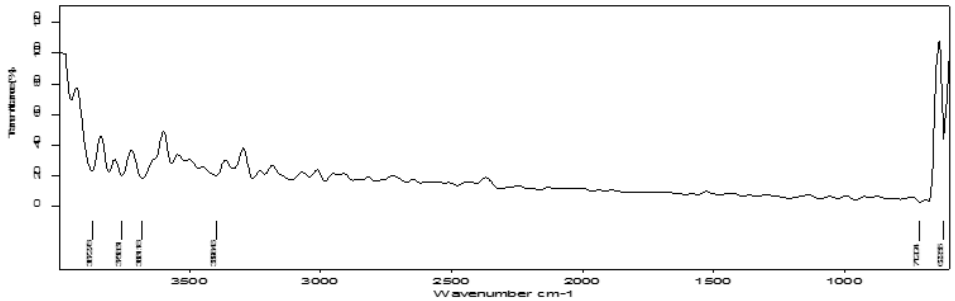

Fig 4: FT-IR spectrum of Zolmitriptan + Guar Gum

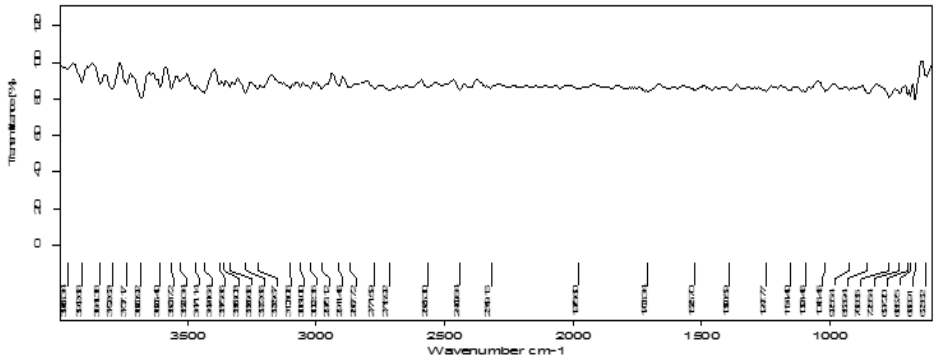

Fig 5: FT-IR spectrum of Zolmitriptan + Xanthan Gum

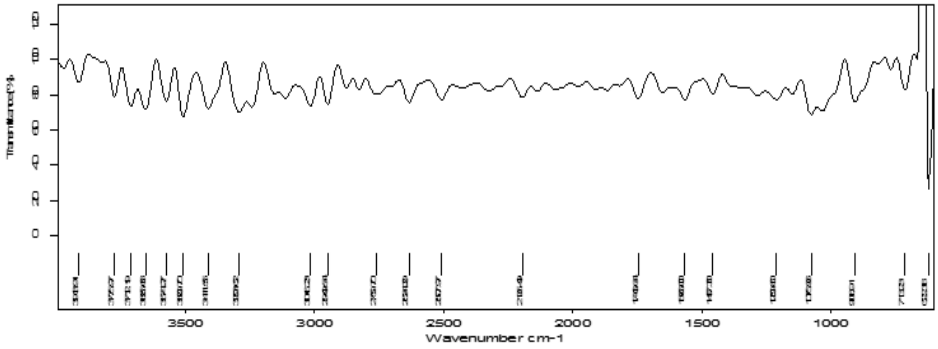

Fig 6: FT-IR spectrum of Zolmitriptan + Chitosan

Time (Hr)	Formulation codes											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0.5	12.73	12.18	8.25	7.53	12.68	10.88	8.39	6.95	11.42	9.26	8.25	7.82
1	17.22	14.14	12.0	11.47	18.79	17.34	15.39	11.79	19.68	17.85	12.08	12.69
1.5	28.30	21.47	17.06	16.04	28.47	28.46	23.45	20.92	30.45	21.00	19.64	16.42
2	40.50	34.39	26.49	19.46	37.98	39.59	35.47	35.47	40.86	34.55	30.40	21.15
3	51.46	49.82	34.60	29.10	50.38	52.86	45.53	43.29	50.02	48.96	44.28	30.66
4	62.04	58.45	42.62	38.36	69.39	62.40	53.98	51.48	57.76	60.64	54.49	47.51
5	79.12	74.09	57.19	51.60	84.41	75.01	62.58	58.86	71.44	69.71	66.19	54.51
6	89.95	79.00	71.53	64.26	96.84	83.85	78.26	71.46	81.01	76.66	71.67	62.61

Table 4: *In-vitro* Drug Release Study Results

Formulation Codes	Muco-adhesive strength (g)	Force of Adhesion (N)
F1	7.83	0.768
F2	6.50	0.637
F3	7.45	0.730
F4	8.05	0.789
F5	8.86	0.869
F6	8.56	0.839
F7	8.19	0.803
F8	7.78	0.763
F9	5.87	0.575
F10	6.53	0.640
F11	6.76	0.663
F12	5.87	0.575

Table 5: Mucoadhesive Strength Results

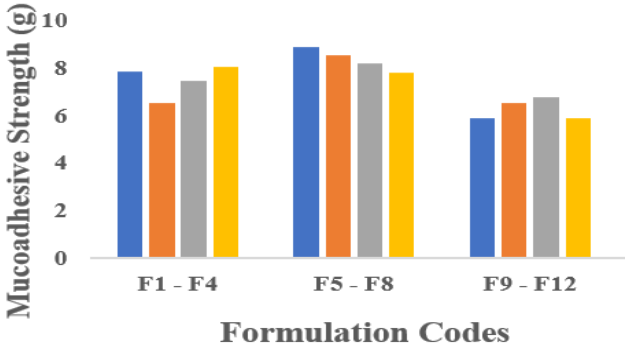

Figure 7: Mucoadhesive Strength Results

Time (Hr)	Formulation codes											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0.5	17.12	8.24	7.48	3.21	12.74	11.56	9.64	8.76	8.60	7.86	7.84	6.84
1	26.98	13.11	10.79	8.87	18.44	16.45	14.76	12.75	17.48	14.48	11.95	9.74
1.5	33.47	21.52	15.55	12.80	27.36	26.27	24.33	21.36	27.79	20.50	16.04	12.42
2	38.86	32.68	20.06	18.16	42.67	31.23	31.44	28.72	39.87	27.11	21.51	16.59
3	45.40	45.40	31.45	27.02	56.22	47.09	44.13	38.13	5.22	39.34	32.63	24.70
4	55.12	55.03	39.08	32.79	70.63	59.36	50.14	43.59	51.18	4.24	37.31	33.96
5	71.87	60.58	44.82	40.90	81.74	68.15	57.84	50.71	60.00	50.19	43.48	44.58
6	82.63	68.53	58.77	51.91	92.77	80.11	69.85	61.60	66.36	60.39	51.99	48.59

Table 6: *Ex-Vivo* Drug Permeation Results

Formulation	Kinetic Drug Release	Mechanism of Release			
	Zero order	First order	Higuchi	Korsemeyer peppas	
	Correlation coefficient (r^2)	Correlation coefficient (r^2)	Correlation coefficient (r^2)	Correlation coefficient (r^2)	Slope 'n' value
F5	0.9958	0.9162	0.980	0.9935	0.85

Table 7: Regressional analysis of the *in vitro* release model of optimized formulation F5

Days count	Friability (%)	Hardness (kg/cm^2)	Drug Content (%)	Surface pH	Swelling Index (%)	% CDR
0	0.281	4.8	95.60	6.75	67.49	96.84
30	0.276	4.7	95.25	6.75	66.88	96.31
60	0.274	4.7	94.78	6.70	66.10	95.80
90	0.274	4.6	94.55	6.63	65.25	95.05

Table 8: Stability Study Results

A bioadhesive system's swelling behaviour is an important characteristic for consistent and extended drug release and bioadhesion. The composition of the polymer, its concentration, and the medium's pH all affect how the polymer swells. As time proceeds, all of the tablets' swelling increases because the polymer's hydrophilicity causes it to gradually absorb water. From the data it is obvious that, swelling index was increased as time and concentration of polymers increases since weight gained by tablet was increased proportionally with rate of hydration. From the results given in above table it was evident that Guar Gum as mucoadhesive polymer in the concentration of 2 mg (F5) showed better drug release by 6 hours when compared to other formulations.

The degree of swelling of the polymers, contact time with buccal membrane, and molecular weight of the polymer all have an impact on the mucoadhesive strength. The formulation employing guar gum as the polymer produced the highest mucoadhesive strength of 8.86 g, followed by HPMC K-15 at 8.05 and xanthan gum at 6.76. Due to these polymers' noticeable swelling after being hydrated, they exhibited the highest mucoadhesive strength. Due to its minimal swelling propensity and quick detachment after hydration, Xanthan Gum formulations had the lowest mucoadhesive strength 5.87.

Comparing to other formulations, F5 showed greater and better drug permeation release by 6 hours. The results also showed the chitosan as a permeation enhancer plays a major role to increase the drug permeation through the buccal

mucosa directly to blood stream. Thus, permeation enhancers can be used to improvise the higher permeability of the low permeable drug via mucoadhesive dosage formulations.

In vitro drug release followed zero-order kinetic and release data was best fit with Korsemeyer's peppas kinetics since the value of r^2 was greater for this model. The slope 'n' value was found to be 0.85 for best formulation F5 indicating that the drug release mechanism to be diffusion dependent and non-Fickian release.

According to ICH criteria, a stability study for the optimal formulation over three months was conducted. After Formulation F5's organoleptic characteristics were examined, several post-compression studies showed that there had been no change in its outward appearance. The analysis of the friability, hardness, drug content, surface pH, swelling index, and percentage of drug release showed that no clear change was seen that would support drug breakdown.

CONCLUSION

In order to increase patient compliance for treatment of headache caused by severe acute migraine, this proposed study was carried out to create and assess muco-adhesive buccal tablets of Zolmitriptan with a prolonged release feature. F5 demonstrated prolonged and efficient drug release, swelling index, and mucoadhesive strength among the 12 distinct formulations. Additionally, all of the formulations' physiochemical characteristics met pharmacopoeial requirements and were within acceptable bounds. The results also showed that chitosan as permeation enhancer has a major role to improve the release and permeation of low permeable drug via buccal mucosa and thus increased bioavailability could be achieved. Higher concentrations of polymers could result in abrupt release of the drug. *In vitro* drug release followed zero-order kinetic and release data was best fit with Korsemeyer's peppas kinetics since the value of r^2 was greater for this model. The slope 'n' value was found to be 0.85 for best formulation F5 indicating that the drug release mechanism to be diffusion dependent and non-Fickian release. Additionally, Zolmitriptan mucoadhesive buccal tablets' formulation may be a highly effective way to minimise first pass metabolism, resulting in increased bioavailability and sustained therapeutic benefits for the better treatment of migraines.

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