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Formulation and Evaluation of Lignocaine Hydrochloride Buccal Tablets

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ABSTRACT

Lignocaine Hydrochloride (LH) is a local anesthetic agent used in the treatment of periodontal and various other dental diseases. It undergoes extensive first pass metabolism with a consequent low bioavailability. Keeping this into account the research work was focused to formulate buccal tablets of LH in an effort to achieve prolonged relief from pain. Buccal tablets were prepared by direct compression method using different bio-adhesive polymers such as chitosan with methocel K15, sodium alginate and methocel K4. Ethyl cellulose (EC) was used as an impermeable backing layer. The optimized formula (F9) was evaluated for in vitro drug release (99.51%±0.59) in phosphate buffer for 6 hrs and bio adhesion strength was found to be 22 gr. The amount of drug permeated through the buccal membrane was found to be 85.03 ±0.21.Stability studies of the F9 indicated no significant changes with respect to drug content, *in-vitro* release and *ex-vivo* permeation.

Key Words: Lignocaine hydrochloride, Buccal drug delivery system, First pass hepatic metabolism, *Ex vivo* permeation studies.

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INTRODUCTION:

Over the last few decades pharmaceutical scientists throughout the world are exploring the potential of buccal mucosal route for the delivery of drugs as an alternative to parenteral administration of drugs and delivery systems. Moreover, buccal drug delivery is also a promising alternative to the conventional oral therapy especially for drugs that undergo extensive first pass metabolism or drugs that undergo degradation in the gastrointestinal tract due to acidic environment in the stomach resulting in poor bioavailability[1].

Within the oral mucosal cavity, the buccal region offers an attractive route of administration for the systemic delivery of drugs due to its rich vascularization and ease of accessibility. In the recent past, drug delivery systems based on bioadhesion have received considerable attention as absorption promoters due to their ability to adhere to the mucin/epithelial cell surface and thereby anchoring the dosage form at the site for optimum drug absorption and consequent increase in bioavailability. Buccal drug delivery systems utilizes the property of bioadhesion of certain water soluble or swellable polymers which become adhesive on hydration and hence can be used for targeting a drug to particular regions of the body where mucus or receptive epithelial cells are present e.g. nasal, buccal, gastrointestinal tract and vagina.

These drug delivery systems are classified into three categories: (a) sublingual delivery, which is a systemic delivery of drugs through the mucosal membranes lining the floor of the mouth (b) buccal delivery, which is drug administration through the mucosal membranes lining the cheeks (buccal mucosa), and (c) local delivery, which is drug delivery into the oral cavity. The buccal mucosa offers several advantages for controlled drug delivery for extended periods of time as it has a rich supply of blood and lymphatic drainage. These drug delivery systems also avoids first-pass metabolism in the liver and pre-systemic elimination in the gastrointestinal tract[2].

Lignocaine Hydrochloride is a local anesthetic used in management of periodontal infection, toothache, and dental stomatitis. The drug is highly water soluble and it undergoes extensive hepatic first-pass metabolism with bioavailability of 35%.Its biological half-life ranges from 1.5-2 hrs. It has a low molecular weight of 234.34 grams/mol making it a suitable candidate for administration by the buccal route[3].

MATERIALS AND METHODS

Materials:

Lignocaine HCl was obtained as a gift from AR-ECH pharmaceuticals**.** Hyderabad, India. Chitosan, Spray dried lactose, aspartame were obtained from Dr Reddy's laboratories,

Hyderabad, India. Hydroxy propyl methyl cellulose K15M, Hydroxy propyl methyl cellulose K4M, Magnesium stearate, microcrystalline cellulose, Ethyl cellulose, were procured from Vilin Biomed Ltd, Roorkee, India.

Solubility Studies:

The solubility of Lignocaine HCl was determined in phosphate buffer solution by phase equilibrium method. An excess amount of drug was taken into Conical Flasks containing 20 mL of phosphate buffer (pH 6.6), closed with aluminum foil and constantly agitated at room temperature for 24 hrs in a rotary shaker. After 24 hr, the solution was filtered through filter paper and the amount of drug solution was then estimated by measuring the absorbance at 215 nm using a UV spectrophotometer [4].

Preparation of bilayered buccal tablets:

Bilayered buccal tablets were prepared by direct compression method. All the ingredients were screened through sieve no.100. After sufficient mixing, lubricant was added and again mixed for 2-3 min. Preparation of buccal tablets involved two steps, first the mixture was compressed using 7 mm flat faced punch on a 16 station rotary tablet compression machine. Then, the upper punch was raised and the backing layer of ethyl cellulose was placed on the compact and then the two layers were compressed again to obtain bilayered buccal tablet[5]. Composition of the compressed bioadhesive buccal tablet formulations, ratios of the polymers were presented in Table.1.

Table 1 Composition of formulations containing Spray dried lactose as Diluent

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Polymer ratios	1:1	1:2	1:3	1:1	1:2	1:3	1:1	1:2	1:3
Lignocaine HCl (mg)	15	15	15	15	15	15	15	15	15
Chitosan (mg)	30	20	15	30	20	15	30	20	15
HPMCK15M (mg)	30	40	45	-	-	-	-	-	-
Sodium alginate (mg)	-	-	-	30	40	45	-	-	-
HPMCK4M (mg)	-	-	-	-	-	-	30	40	45
Spray dried lactose (mg)	23	23	23	23	23	23	23	23	23
Aspartame (mg)	1	1	1	1	1	1	1	1	1
Mg stearate (mg)	1	1	1	1	1	1	1	1	1
EC(BACKING)	50	50	50	50	50	50	50	50	50
Total weight(mg)	150	150	150	150	150	150	150	150	150

HCl =Hydrochloride; HPMCK15M = Hydroxy Propyl Methyl CelluloseK15M; HPMCK4M = Hydroxy Propyl Methyl CelluloseK4M; Mg = Magnesium; EC =Ethyl Cellulose

Evaluation of buccal tablets

Thickness: The thickness of ten individual buccal tablets from each batch was determined using digital micrometer and the results were averaged.

Weight variation test: Weight variation was performed by taking 10 tablets from each batch using an electronic balance and average values were calculated.

Hardness: Hardness was measured by taking 3 tablets from each batch using Monsanto hardness tester and average values were calculated.

Drug content uniformity: Ten tablets were weighed and grounded in a mortar with pestle to get fine powder; powder equivalent to the mass of one tablet was dissolved in phosphate buffer by sonication for 30 min and filtered through filter paper. The drug content was analyzed spectrophotometrically at 215 nm.

Bioadhesion strength: Bioadhesive strength of the tablets was measured on a modified physical balance[6].The apparatus consisted of a modified double beam physical balance in which the lighter pan was replaced the right pan and the left pan had been replaced by a glass slide (4 cm length and 2.5 cm width) with plastic hang suspended by Teflon rings and copper wire. The left-hand side of the balance was exactly 5 g heavier than the right side .The height of the total set up was adjusted to accommodate a glass container of 6.6 cm height were shown in Figure 1. In order to find out the bioadhesion strength, first buccal tablet (n=3) was stacked to the glass slide with the help of knob, which was situated at the base of physical balance. Five grams weight from the right pan was then removed. This lowered the glass slide along with the tablet over the membrane with a weight of 5.0 g.

Entire setup was kept undisturbed for 5 min and then the weights on the right-hand side were slowly added in increments of 0.1 g till the tablet was just separated from the membrane surface. The excess weight on the right pan, i.e. total weight minus 5g was taken as a measure of the bioadhesion strength [7].

***Ex vivo* residence time:** The *ex vivo* residence time was determined using a locally modified USP disintegration apparatus, based on the apparatus applied by Nakamura et al., 1996 shown in Figure.1[8] The disintegration medium was composed of 800 mL of phosphate buffer maintained at 37°C. The porcine buccal tissue was glued to the surface of a glass slab, vertically attached to the apparatus. The buccal tablet was hydrated from one surface using 0.5 mL of pH 6.6 phosphate buffer and then the hydrated surface was brought into contact with the mucosal membrane. The glass slab was vertically fixed to the apparatus and allowed to run in such a way that the tablet was completely immersed in the buffer solution at the lowest point and wash out at the highest point. The time necessary for complete erosion of the tablet from the mucosal surface was recorded. The experiments were performed in triplicate (n=3) and mean of triplicate was determined[9].

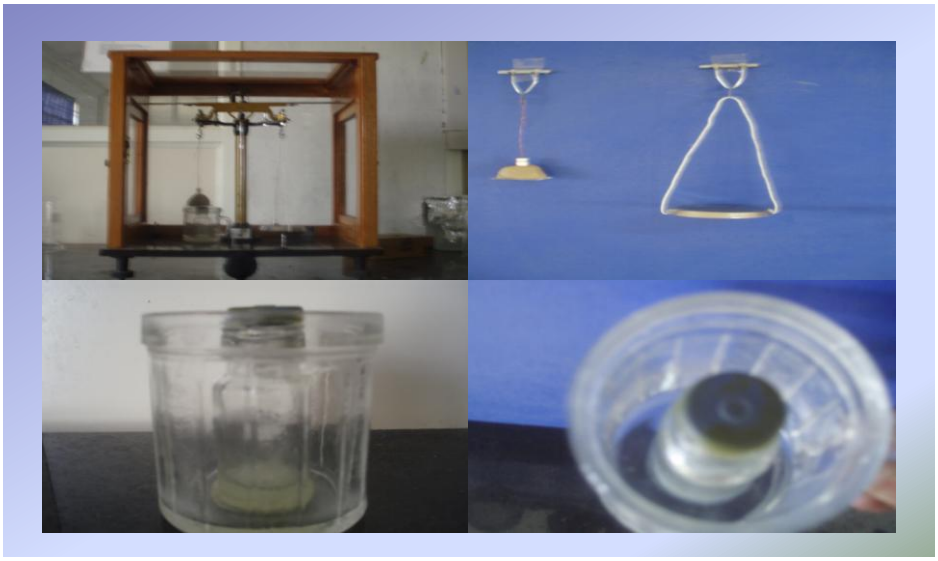

Figure 1. Bioadhesion strength apparatus.

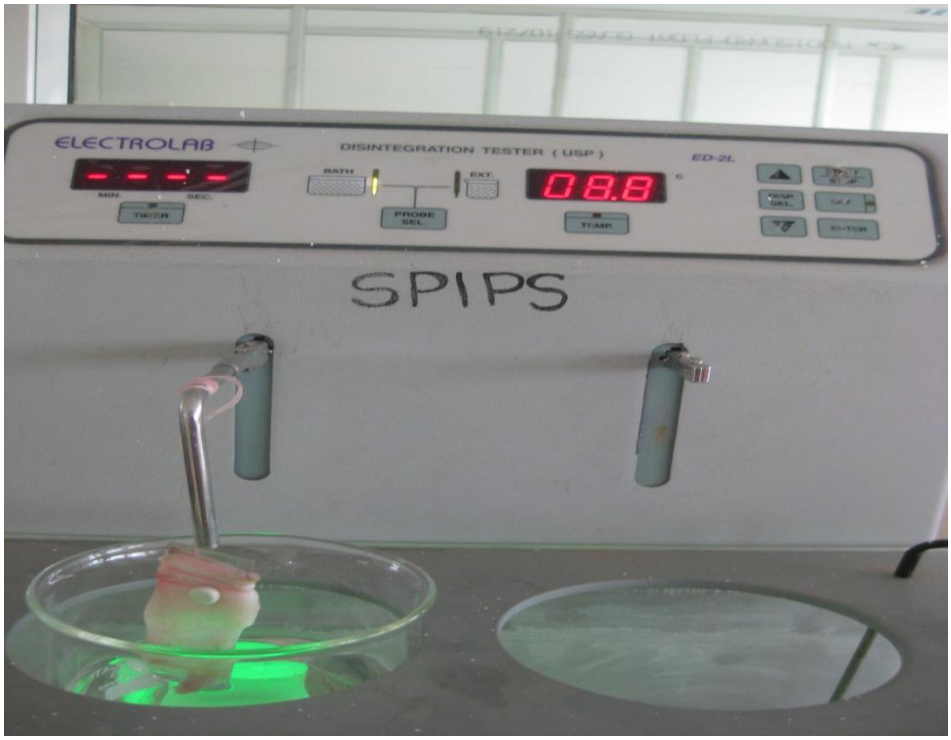

Figure 2. *Ex vivo* residence time measurement apparatus.

Swelling Studies: Buccal tablets were weighed individually (designated as W_1) and placed separately in petri dishes containing 15 mL of phosphate buffer solution. At regular intervals (1, 2, 3, 4, 5 and 6 hr), the buccal tablets were removed from the petri dishes and excess surface water was removed carefully using the filter paper. The swollen tablets were then reweighed (W_2)[10]. This experiment was performed in triplicate. The swelling index (water uptake) was calculated according to the following Eq.

$$\text{Swelling index} = (W_2 - W_1)/W_1$$

Surface pH Study: The bioadhesive tablet was allowed to swell by keeping it in contact with 1 mL of distilled water for 2 hr at room temperature. The pH was measured by bringing the pH-meter electrode, in contact with the surface of the tablet and allowing it to equilibrate for 1 min[11].

***In vitro* drug release:** The United States Pharmacopeia (USP) XXIV rotating paddle method was used to study the drug release from the buccal tablets. The dissolution medium was consisted of 200 mL of phosphate buffer. The release studies were performed at 37^{o}C ± 0.5^{o}C, with a rotation speed of 50 rpm. The backing layer of buccal tablet was attached to the glass slide with instant adhesive (cyanoacrylate adhesive). The slide was placed in to the bottom of the dissolution vessel and samples (5 mL) were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through filter paper and analyzed after appropriate dilution by UV spectrophotometer at 215 nm[7].

***Ex vivo* permeation of buccal tablets:** *Ex vivo* permeation studies were performed using porcine buccal mucosa in Franz diffusion cell at 37°C ± 0.2°C and 50rpm on a magnetic stirrer. Porcine buccal mucosa was obtained from a local slaughter house and used within 2 hrs of procurment. The tissue was stored in Kreb's buffer at 4°C upon collection. The epithelium was separated from underlying connective tissue with surgical scissors. Fresh buccal mucosa was mounted between the donor and receptor compartments. The buccal tablet was placed in donor chamber and 1mL of buffer solution was added. The receptor compartment was filled with phosphate buffer pH 7.4. Aliquots of 1ml sample were collected at predetermined time intervals 1, 2, 3, 4, 5, 6 hrs and analyzed for drug content by spectrophotometrically at 215 nm using phosphate buffer pH 7.4 as blank .The experiments were conducted in triplicate (n = 3) and mean value was used to calculate the flux, permeability coefficient[7].

Stability of buccal tablets:

Stability studies were performed in normal human saliva for the optimized formulation (F9). The human saliva was collected from humans and filtered through filter paper. Buccal tablets were placed in separate petri dishes containing 5 mL of human saliva and placed in a temperature-controlled oven for 6 hr at 37°C ± 0.2°C. At regular time intervals (0, 1, 2, 3, 4, 5, and 6 hr), the formulation was examined for any change in color, surface area and integrity. The experiments were repeated in triplicate (n = 3).

Fourier transform infrared spectroscopic studies: FTIR spectroscopic studies were conducted for Chitosan, optimized formulation and Lignocaine Hydrochloride pure drug.

Ex vivo permeation of drug solution: *Ex vivo* permeation study of Lignocaine Hydrochloride through the porcine buccal mucosa was performed using dissolution cell and membrane

assembly , at 37°C ± 0.2°C and 50 rpm on magnetic stirrer. Fresh buccal mucosa was mounted between the donor and receptor compartments. The donor compartment was filled with 5ml of phosphate buffer pH 6.6 containing drug solution. The receptor compartment was filled with phosphate buffer (pH 7.4). 1 ml of sample was collected at predetermined time intervals 1, 2, 3, 4, 5, 6 hrs and analyzed for drug content by spectrophotometrically at 215 nm using phosphate buffer (pH 7.4) as blank.

The experiments were performed in triplicate (n = 3) and mean values were used to calculate flux (J) and permeability coefficient (P).

$$J = (dQ/dt) / A$$

$$P = \underline{(dQ/dt)} /\Delta CA$$

Where J is Flux ($mg.hrs^{-1}cm^{-2}$); P is permeability coefficient (cm/h); dQ/dt is the slope obtained from the steady state portion of the curve; ΔC, the concentration difference across the mucosa and A the area of diffusion (cm^2)[12].

RESULTS AND DISCUSSION

The solubility study was conducted in phosphate buffer pH 6.6 as it represents the average pH value of oral cavity and blood respectively. Solubility of Lignocaine Hydrochloride was found to be 13±1.95 mg/mL. The flux and permeability coefficient of drug solution was found to be 0.453 $mg.hrs^{-1}cm^{-2}$ and 0.302cm/h respectively. The values of weight variation and friability were found to be within the prescribed limits. Thickness of the tablets varied from 1.5±0.04 mm to1.9±0.09 mm. Hardness of the tablets was found to be increased with the increasing concentration of chitosan and ranged from 3.02 Kg/cm^2 to 4.55Kg/cm^2. The assay values were also within the limits of 97.0%-101%.

Measurement of bioadhesion strength: Bioadhesion strength depends on molecular weight and swelling behavior of the polymers, contact time with mucus. Test was conducted for all formulations, and it was found that there was a gradual decrease in bioadhesion strength from F1 to F3. F1 exhibited maximum bioadhesion strength of 43.0 gm while F6 has shown bioadhesion strength of 20.0 gms. Formulations containing higher proportion of chitosan have shown good bioadhesion strength at 5 min of contact time probably due to ionization of Chitosan at salivary pH, leading to the formation of secondary bioadhesion bonds with mucin and interpenetration of the polymer chains in the interfacial region, while other polymers undergo superficial bioadhesion [13]. The optimized tablet (F9) showed 22.0±0.29 g of bioadhesion strength.

Bioadhesion strength values of all the formulations were represented in Table 3 and the comparison of bioadhesion strength of all formulations was shown in Figure 3.

Table 2. Physico-chemical parameters of formulations

Formulation Code	Thickness (mm)	%Weight variation	Hardness (Kg/cm2)	% Friability	%Drug content
F1	1.7±0.08	0.93±0.21	4.12±0.11	0.09±0.01	99.1±0.5
F2	1.6±0.05	0.81±0.20	3.97±0.17	0.07±0.03	99.4±0.6
F3	1.5±0.04	0.91±0.19	3.82±0.22	0.04±0.01	98.2±0.4
F4	1.7±0.05	0.79±0.17	4.08±0.12	0.41±0.06	100.2±0.5
F5	1.7±0.06	0.86±0.12	3.80±0.23	0.21±0.03	98.3±0.7
F6	1.6±0.06	0.84±0.16	3.58±0.51	0.43±0.02	99.4±0.6
F7	1.8±0.05	0.76±0.18	4.55±0.26	0.71±0.01	100.2±0.3
F8	1.7±0.06	0.87±0.19	4.19±0.47	0.47±0.03	99.1±0.2
F9	1.7±0.05	0.79±0.21	3.81±0.97	0.89±0.04	98.4±0.4

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

Table 3.Bioadhesive strength, *ex vivo* residence time and surface pH values of formulation

Formulation code	Bio adhesion Strength (gm)	*Ex vivo* residence time(hr)	Surface pH
F1	42±0.21	13±0.14	6.13±0.03
F2	37±0.11	9±0.21	6.27±0.01
F3	21±0.56	8±0.77	6.39±0.02
F4	39±0.44	10±0.11	6.42±0.05
F5	35±0.19	8±0.44	6.11±0.02
F6	20±0.72	7±0.13	5.99±0.06
F7	43±0.66	14±0.76	5.81±0.02
F8	38±0.41	10±0.41	6.36±0.07
F9	22±0.29	7±0.47	6.33±0.03

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

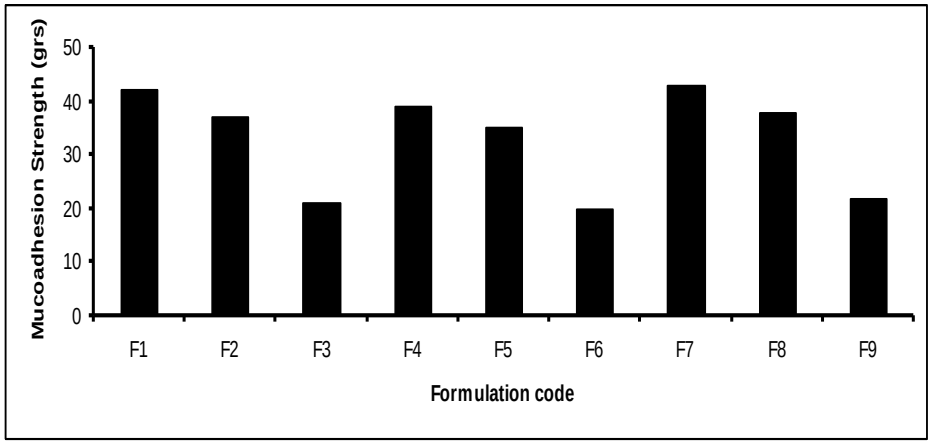

Figure 3 Bioadhesion strength profile of formulations

***Ex vivo* residence time:** *Ex vivo* residence time for all the formulations varied from 7 to 14 hours. The optimized formulation (F9) showed 7.00±0.47 hours. The mucoadhesion time was

found to be increased. *Ex vivo* residence time values were given in Table 3. The maximum *ex vivo* residence time (14.0 hr) was observed with formulation F7, and low *ex vivo* residence time was observed with formulations F6, F15 (7.0 hr).

Swelling Studies of buccal tablets: Buccal tablets should possess adequate swellable behavior for uniform and prolonged release of drug and proper mucoadhesion[14]. The formulations containing Sodium alginate (F6) showed a swelling index of 1.3. Among the formulations containing HPMC K15M, F3 showed high swelling index of 1.5, whereas among the formulations containing HPMC K4M F9 exhibited maximum swelling index of 2.4. Hence it was selected as optimized formulation and furtherer studies were conducted on these formulation. The optimized formulation contains spray dried lactose employed as directly compressible vehicle and showed higher swelling index values compared to MCC, because of its hydrophilic nature.

Table 4 Swelling Index profile of formulation

Time (hrs)	0	1	2	3	4	5	6
F1	0	0.31	0.34	0.47	0.67	0.92	1.07
F2	0	0.54	0.68	0.94	1.01	1.18	1.41
F3	0	0.59	0.79	1.01	1.12	1.23	1.56
F4	0	0.24	0.27	0.38	0.46	0.89	1.02
F5	0	0.27	0.44	0.72	1.07	1.08	1.21
F6	0	0.41	0.52	0.70	1.14	1.17	1.32
F7	0	0.39	0.61	0.94	1.08	1.37	1.69
F8	0	0.45	0.88	1.02	1.31	1.46	1.93
F9	0	0.59	0.98	1.16	1.54	1.71	2.40

Surface pH Study of buccal tablets: The surface pH of the optimized formulation F9 was found to be 6.33. This pH is near to the neutral, so the formulation does not cause any irritation on the mucosa. The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects *in vivo*. 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 .Surface pH values for all the formulations shown in Table 3.

***In vitro* drug release of buccal tablets:** *In vitro* drug release studies revealed that the release of Lignocaine Hydrochloride from different formulations varies with the characteristics and composition of matrix forming polymers. The release rate of Lignocaine Hydrochloride was increased with increasing concentration 1:3 ratios of HPMC K15M, Sodium alginate and HPMC K4M in F3 (79.7±0.7%),F6 (72.9±0.4%)and F9(99.5±0.5%) respectively. These findings are in compliance with the ability of these cellulose derivatives to form complex matrix network which

leads to delay in the release of drug from the device. Formulations with spray dried lactose showed higher percentage drug release values compared to MCC, this is because of the water soluble diluents (spray dried lactose) can absorb more water and swell and then release the drug rapidly compared to that of water insoluble diluent (MCC) that retards the release. The maximum cumulative percent release of Lignocaine Hydrochloride is identified with formulation F9 found to be 99.5±0.5%.

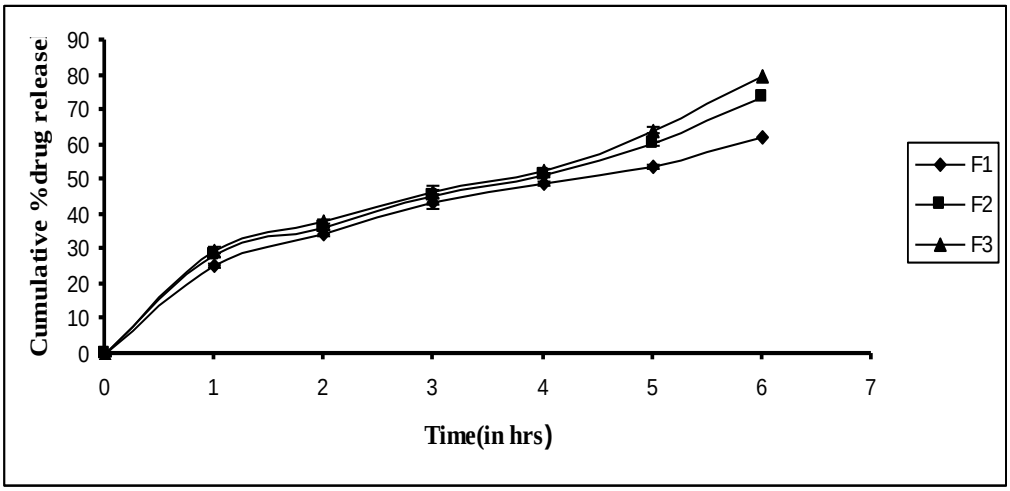

Figure 4 *In vitro* cumulative percentage drug release profile of formulation containing Chitosan: HPMC K15M with Spray dried lactose as diluent.

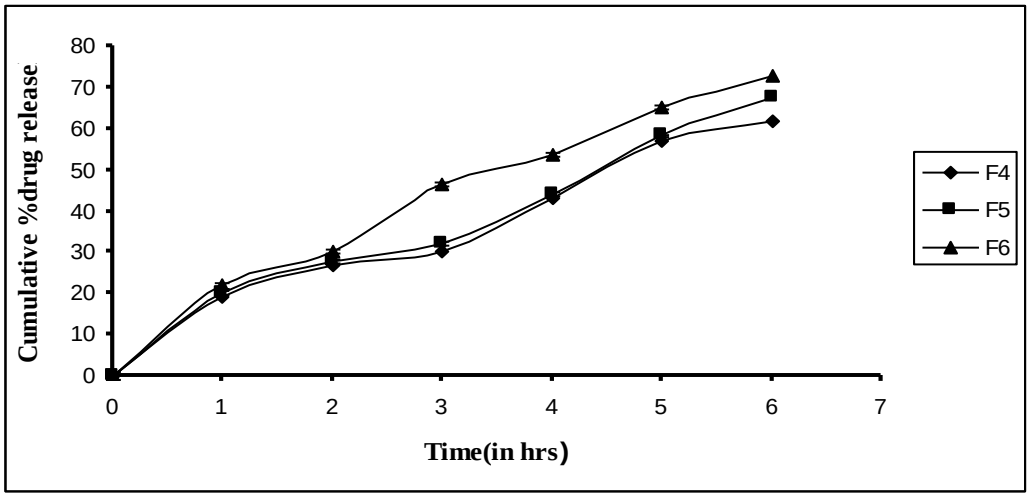

Figure 5 *In vitro* cumulative percentage drug release profile of formulation containing Chitosan: Sodium alginate with Spray dried lactose as diluent.

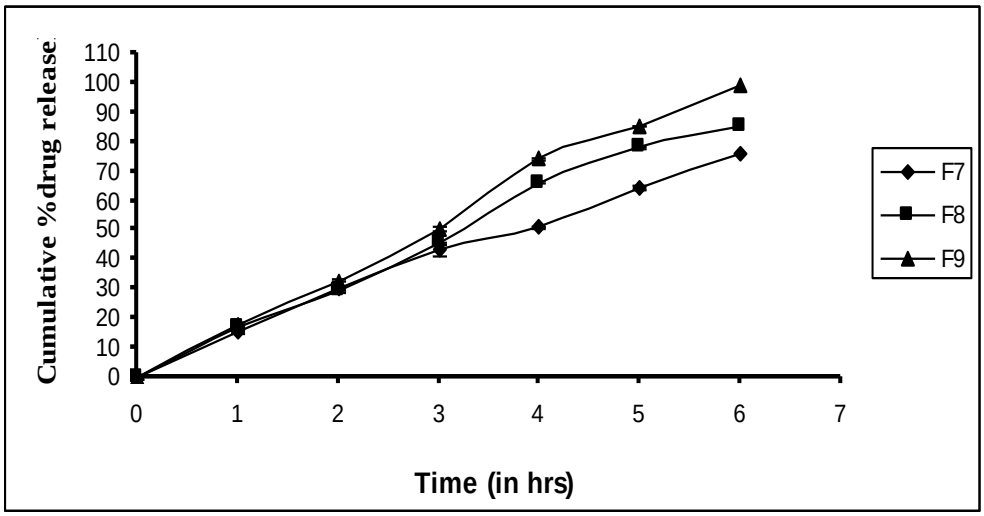

Figure 6 *In vitro* cumulative percentage drug release profile of formulations containing Chitosan: HPMC K4M with Spray dried lactose as diluent.

Release kinetics and mechanism: The release mechanism and kinetics of Lignocaine Hydrochlorides, optimized formulation was attempted to fit in to mathematical models and n, r^2 values for zero order, First order, Higuchi and Peppas models were represented in Table 5.

For non-fickian release, the value of n falls between 0.5 and 1.0; while in case of fickian diffusion, n = 0.5; for zero-order release (case II transport), n = 1; and for supercase II transport, n > 1[3]. The values of Release kinetics and mechanism of optimized formulation were given in Table 11.Observation of all the r^2 values indicated that the highest r^2 (0.9946) value was found for Zero order release. According to 'n' value it is one, so it follows non-fickian diffusion with zero order release (case II transport).

Table 5 Release kinetics and mechanism of optimized formulation

Formulation code	Mathematical models (Kinetics)				
	Zero order	First order	Higuchi	Peppas model	
9	r^2	r^2	r^2	n	r^2
	0.9946	0.9186	0.9147	1.1021	0.9954

***Ex vivo* permeation of drug solution:** The flux, permeation coefficient and cumulative percent drug permeated from formulation F9 were found to be 0.6029 $mg.hrs^{-1}cm^{-2}$, 0.0753cm/h and 58.4% respectively. The flux, permeability coefficient and cumulative percent drug permeated values were found to be 0.8519 $mg.hrs^{-1}cm^{-2}$, 0.1064cm/h and 85.6% respectively. This results in enhancing the passive diffusivity of the drug via transcellular (crossing the cell membranes and entering the cell) and Para cellular routes. All these effects may contribute to the enhancing the permeation of the drug. The values of cumulative amount of drug permeated and cumulative

percent drug permeated, the values o flux, permeability coefficient, and *Ex vivo* drug permeation of drug solution drug permeated from drug solution.

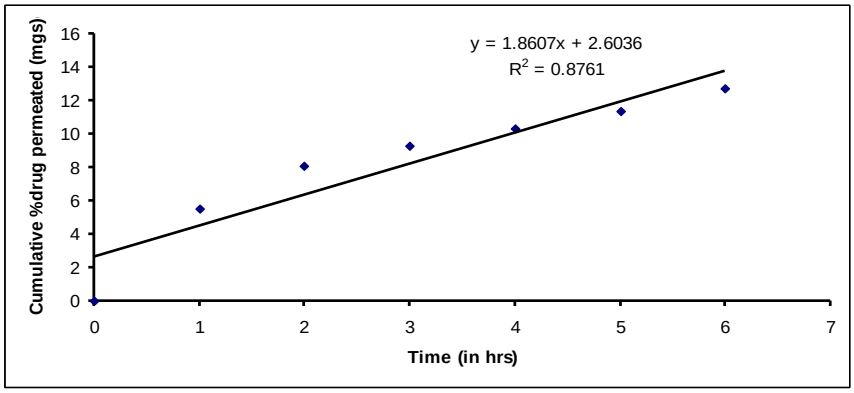

Figure 7 *ex vivo* drug permeation of drug solution

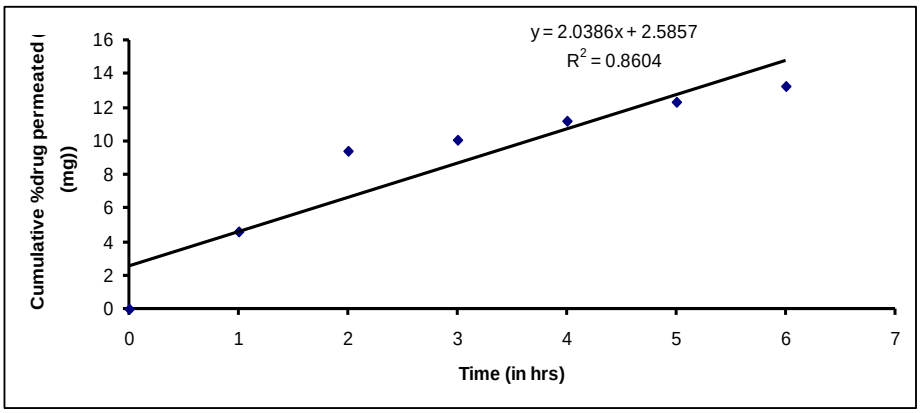

Figure 8 *ex vivo* drug permeation of optimized formulation

Table 6 *ex vivo* drug permeation profiles of drug solution and optimized formulation

Time (hr)	Drug solution		Optimized formulation	
	Cumulative amount drug permeated (mg)	Cumulative % drug permeated	Cumulative amount drug permeated (mg)	Cumulative % drug permeated
0	0	0	0	0
1	5.51±0.1	36.74±0.3	4.61±0.3	30.74±04
2	8.10±0.4	54.66±0.2	9.40±0.4	62..67±0.7
3	9.30±0.6	62.17±0.1	10.11±0.6	64.47±0.3
4	10.35±0.7	69.25±0.9	11.21±0.8	74.73±0.9
5	11.40±0.1	76.37±0.4	12.32±0.1	82.12±0.9
6	12.75±0.8	85.08±0.5	13.32±0.8	88.80±0.3

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

Table 7 Flux and Permeability coefficient values of drug solution

	Flux(mg.hrs^{-1}cm^{-2})	permeability coefficient(cm/h)
Drug solution	0.453	0.302
Optimized Formulation (F9)	0.497	0.331

The drug release rate of formulations prepared with HPMC K15M (Max79.7±0.6%), Sodium alginate (max72.9±0.4) was retarded due to the high viscosity of the polymer and formation of complex matrix network when compared to the low viscosity polymers HPMC K4M (max. 99.5±0.5%). The rate of drug release of the formulations prepared with MCC as a diluent was less due to its water insoluble nature compared to water soluble diluents like spray dried lactose. Bioadhesion strength value were found for formulations prepared with Chitosan: HPMC K15M (42±0.21g), Chitosan: Sodium alginate (39±0.44g) and Chitosan: HPMC K4M (43±0.66g). The physico-chemical properties of all the formulations prepared with different polymers like HPMC K15M, Sodium alginate and HPMC K4M were shown to be within the limits [15].

Stability of buccal tablets: Stability study was conducted only for optimized formulation (F9). There was no change in the colour and integrity of the tablets. From the stability results it was known that formulation F9 has stability in human saliva, if it is unstable color would change. Physical properties Lignocaine Hydrochloride of the buccal tablets such as thickness and diameter slightly changed owing to swelling of the system in human saliva. Buccal tablets maintained their integrity in the human saliva throughout the study, conforming the sufficient strength of the system[16-18].

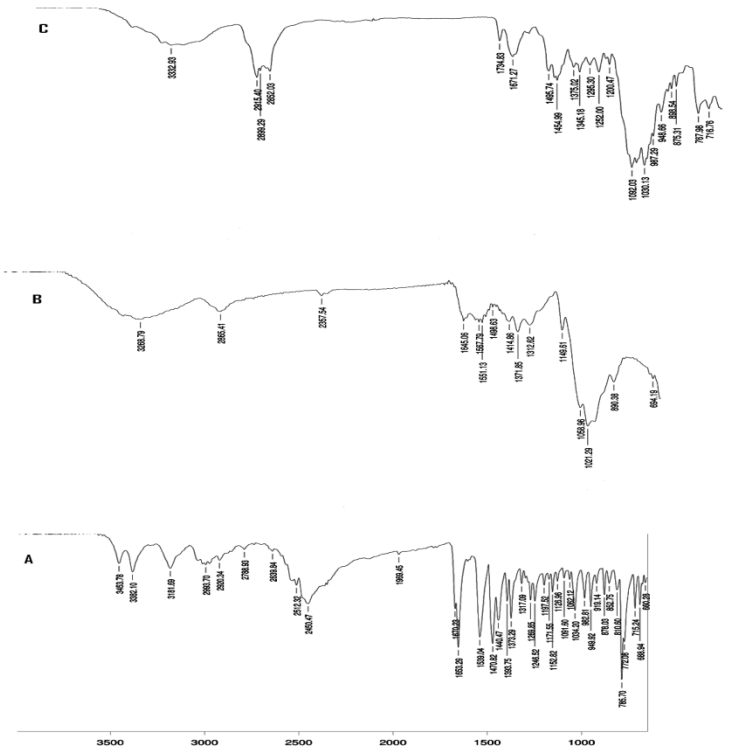

Figure 9 FTIR spectra for A) Lignocaine Hydrochloride pure drug B) optimized formulation C) Chitosan

Table 8 Stability profile of optimized formulation in human saliva

Sampling interval (hrs)	Change in colour	Change in surface area(cm2)	Change in integrity
0	NO	NO	NO
1	NO	0.4	NO
2	NO	1.00	NO
3	NO	1.50	NO
6	NO	3.00	NO

Fourier transform infrared spectroscopic studies (FTIR):

Characteristics peaks of Lignocaine hydrochloride, chitosan, Optimized formulatoion shown in FTIR spectra Figure 9. Prominent drug peaks, 1670, 1653, 1393, 1197, 1091.Chitosan peaks 1498, 1414, 1371, 1058, were obseverved in optimized formulation.

CONCLUSION

The present study conclude that buccal tablets of LH can be a good way to bypass the extensive hepatic first- pass effect metabolism and to improve the bioavailability to significant extent. A combination of Chitosan and hydroxyl propyl methyl cellulose (HPMC K4M) at the ratio of 1:3 is with complementary physical parameters. From the results, it was concluded that the *in vitro* drug release, bioadhesion strength, *ex vivo* residence time of the optimized formulation is suitable for buccal delivery. Bioadhesion strength values were found for formulations prepared with Chitosan: HPMC K15M (42±0.21 g), Chitosan: Sodium alginate (39±0.44g) and Chitosan: HPMC K4M (43±0.66g). The release pattern followed non-fickian diffusion with Zero order release. FTIR studies concluded that there was no interaction between drug and excipients.

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