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Research Article

Formulation and Evaluation of Mucoadhesive Bi-layer Buccal Tablets of Labetalol Hydrochloride Using Natural Polymers

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ABSTRACT

Labetalol hydrochloride is a lipophilic anti hypertensive drug having poor bioavailability(25%) and shorter biological half life ($t_{1/2}$-4-6hr) Buccoadhesive tablets of Labetalol hydrochloride were developed to prolong its release and improve the bioavailability by avoiding hepatic first pass metabolism during the treatment . In present investigation an attempt was made to develop and evaluate buccoadhesive tablets of Labetalol hydrochloride using natural polymers. Different formulations were developed with varying concentrations of polymers like Sodium alginate and Guar gum. Ethyl cellulose is used as a backing layer. Based on the preformulation studies, formulations were prepared by direct compression method. Prepared tablets were comparatively evaluated for their physicochemical parameters like weight variation, hardness, thickness, and friability test. The surface pH, swelling index, bio-adhesive strength are also carried out which has been important aspect for success of mucoadhesive buccal tablets. *In-vitro* drug release rate of Labetalol hydrochloride was studied in phosphate buffer 6.8 containing 0.2% sodium lauryl sulphates at 37±0.5^{0}C. The data obtained from dissolution studies followed non fickian diffusion.

Keywords: Labetalol hydrochloride, Sodium alginate, *In-vitro* drug release, on fickian diffusion.

INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms[1]. There are four potential regions for drug delivery in the oral cavity, namely buccal, sublingual, palatal, and gingival (the epithelial permeability rank order is sublingual >buccal>palatal>gingival). Buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotides and polysaccharides as well as conventional small molecules[2]. In general, rapid absorption from buccal route is observed because of the thin mucus membrane and rich blood supply. After absorption, drug is transported through the deep lingual vein or facial vein which then drains into the general circulation via the jugular vein, bypassing the liver and thereby sparing the drug from first- pass metabolism[3].

Labetalol hydrochloride is an anti-hypertensive belongs to the class of alpha and beta blocking agents which is used to treat high blood pressure. It is slightly soluble in water and is well absorbed from the GIT. Labetalol hydrochloride is rapidly absorbed following an oral dose but undergoes extensive first pass metabolism, resulting in only 25% oral bioavailability. The drug is eliminated rapidly, so repeated daily administration are required to maintain the effective plasma levels. The half-life of Labetalol hydrochloride is approximately 4-6 hours[4]. Thus an attempt has been made to develop a buccal drug delivery system of Labetalol hydrochloride for improving and enhancing the bioavailability.

The main objective of the study of the study were to formulate and evaluate buccoadhesive bi-layered tablets containing Labetalol hydrochloride using natural polymers for releasing the drug unidirectionally in the buccal cavity in order to bypass the first pass metabolism for improving the oral bioavailability thus can decrease the dose, dosing frequency and maintain prolonged therapeutic levels of the drug.

MATERIALS AND METHODS

Labetalol hydrochloride was obtained from Yarrow chemicals, Mumbai. Ethyl cellulose was obtained from Hi-media lab chemicals, Mumbai. Sodium alginate, Guar gum, Mannitol, Aerosil, PEG 6000, Magnesium stearate was procured from the college laboratory. All the chemicals and materials used were of analytical grade. Single punch tablet compression machine was used to punch tablets. In addition an electronic balance, tablet dissolution tester (Electrolab), UV Spectrophotometer (Shimadzu, model1700), IR Spectrophotometer (Jasco model FT/IR 4100) was used in this study.

Construction of calibration curve

A stock solution of Labetalol was prepared by dissolving 100mg in 100ml of phosphate buffer pH 6.8. From this stock solution, suitable dilutions were prepared using the same solvent in the range of 10-100µg/ml. The λmax of the drug was determined by scanning one of the dilutions between 400 and 200nm using a UV-visible spectrophotometer. At this wavelength, the absorbance of all the other solutions was measured against a blank which was phosphate buffer pH 6.8. Standard curve between concentration and absorbance was plotted and intercept (B) and slope (K) values were noted.

Preformulation studies

Identification of drug sample

Labetalol hydrochloride was scanned in UV range from 400-200 nm in phosphate buffer pH 6.8 using UV spectrophotometer.

Solubility study

The solubility of the Labetalol was determined in various solvents by adding an excess amount of drug to 10 ml of solvent in conical flasks. The flasks were kept at 25± 0.5^{0}C in isothermal shaker for 72 hours to reach equilibrium. The equilibrated samples were removed from the shaker and centrifuged at 4000 rpm for 15 minutes. The supernatant was taken and filtered through whatmann filter paper. The concentration Labetalol was determined in supernatant a suitable dilution by using UV-visible spectrophotometer at 302nm.

Bulk Density

It is the ratio of total mass of powder to the bulk volume of powder.

It is expressed in g/ml and is given by

$$\text{Density} = \text{Mass} / \text{Volume}$$

Tapped density

The tapped density was determined by using the following formula

$$\text{Tapped density} = \frac{\text{Weight of powder taken}}{\text{Tapped volume}}$$

Carr's index (or) % compressibility

It indicates powder flow properties. It is expressed in percentage and is given by

$$\text{Carr's index} = \frac{\text{Tapped density - Bulk density}}{\text{Tapped density}} \text{ X } 100$$

Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Angle of Repose (θ)

It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\text{Angle of repose } (\theta) = \tan^{-1} (h/r)$$

Drug excipient Compatibility study

I.R spectroscopy can be used to investigate and predict any physiochemical interaction between different excipients. A physical mixture of drug, polymer and other excipients were prepared and mixed with suitable quantity of potassium bromide. This mixture was compressed to form a transparent pellet using a hydraulic press at 15 tons pressure. It was scanned from 4000 to 400 cm-1 in a FTIR spectrophotometer (FTIR 4100, Jasco). The IR spectrum of the physical mixture was compared with those of pure drug and polymer and peak matching was done to detect any appearance or disappearance of peaks.

Preparation of mucoadhesive buccal tablets of Labetalol hydrochloride

Unidirectional, bi-layered muco-adhesive tablets of Labetalol hydrochloride were prepared by direct compression technique using a flat-faced 13 mm hydraulic press involving two consecutive steps. Initially, a backing layer was made using ethyl cellulose, onto which the drug containing layer were placed and recompressed to get a bilayered tablet. In the formulation of bilayered tablets, labetalol was the drug, sodium alginate and guar gum were used as muco-adhesive polymers, magnesium stearate was used as a lubricant and mannitol was used as diluent. The backing layer was prepared using ethyl cellulose to make the release unidirectional from the tablet. Poly ethylene glycol 6000 was used as permeation enhancer in the formulation

Evaluation of bi-layered tablets of Labetalol hydrochloride

Weight variation

Twenty tablets were randomly selected from each batch weighed individually. The average weight and standard deviation was calculated**.**

Thickness

3 tablets from each batch of formulation were collected and the thicknesses of the tablets were measured with the help of vernier caliper. The average thickness was calculated.

Hardness

Hardness or tablet crushing strength (f_c) is the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. The hardness of five tablets in each batch was measured and the average hardness was calculated.

Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. The friability (F) was given by the formula.

$$F = (1- W_0 / W) \times 100$$

Where, W_0 is the weight of the tablets before the test and W is the weight of the tablet after the test.

Drug content

For determination of drug content at least five tablets from each formulation were weighed individually, crushed and diluted to 100 ml with sufficient amount of phosphate buffer of pH 6.8 in a volumetric flask. Then aliquot of the filtrate was diluted suitably and analyzed spectrophotometrically at 302 nm against blank. Drug content was calculated using standard curve.

***In-vitro* swelling studies**

Eight buccal tablets were weighed (W_1) and placed separately in petri dishes with 5ml of phosphate buffer of pH 6.8. At the time interval of 1,2,3,4,5,6,7 and 8 hrs, tablets were removed from the petri dish and excess water was removed carefully using filter paper. The swollen tablet were then reweighed (W_2) and the percentage hydration was calculated using the following formula

$$\text{Percentage hydration} = [(W_2-W_1)/W_1] \text{ X100.}$$

Surface pH

A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping them in contact with 2 ml of phosphate buffer pH 6.8 in a test tube for 2 hrs. The pH was then noted by bringing the electrode in contact with the surface of the formulation pH and allowing it to equilibrate for 1 min.

***In-vitro* mucoadhesion studies**

Mucoadhesive strength of the buccal tablets was measured on the "Modified Physical Balance method" which is shown in figure 1. The method used porcine buccal membrane as the model mucosal membrane. The fresh porcine buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. The both pans were balanced by adding an appropriate weight on the left- hand pan. A piece of mucosa was tied to the surface of the beaker and placed below the left pan which was moistened with phosphate buffer pH 6.8. The tablet was stuck to the lower side of left pan with glue. Previously weighed beaker was placed on the right hand pan and water (equivalent to weight) was added slowly to it until the tablet detach from the mucosal surface. The both pans were balanced by adding an appropriate weight on the left- hand pan. The weight required to detach the tablet from the mucosal surface gave the bioadhesive strength. The experiment was performed in triplicate and average value was calculated.

Force of adhesion =
(mucoadhesive strength/100) ×9.81.

***In-vitro* release studies**

The drug release rate from buccal tab paddle method at 37 ± 0.5^0C layer were attached to the glass slide with any glue and the glass slide is dropped into 900 ml of phosphate buffer pH 6.8 containing 0.2% of sodium lauryl sulphate. Samples were withdrawn at 0.25, 0.5, 0.75, 1, 2, 3, 4, 5, 6, 7 and 8 hrs and replaced with fresh dissolution medium. The amount of Labetalol released was determined spectrophotometrically at 302 nm. The % drug release was calculated using the calibration curve of the drug in phosphate buffer pH 6.8.

Release kinetics

Several theories/kinetic models describe drug dissolution from immediate and modified release dosage forms. In order to analyze the release mechanism, several release models were tested such as:

$$\text{Zero order} \quad Q_t = Qo + Kot \quad \text{----------1}$$

Where Q_t is the amount of drug released at time *t*, Ko is the apparent dissolution rate constant or zero order release constant and Qo is the initial concentration of the drug in the solution resulting from a burst effect; in this case the drug release runs as a constant rate.

First order $\ln Q_t = \ln Qo + K_1 t$ ----------2

Where K_1 is the first order release constant; in this case the drug released at each time is proportional to the residual drug inside the dosage form.

Higuchi $Q_t = K_H \sqrt{t}$ ----------3

Where Q_t is the amount of drug released at time *t* and K_H is the higuchi release rate constant; this is the most widely used model to describe drug release from pharmaceutical matrices.

Korsmeyer-Peppas $Q_t/Q_\infty = K_k t^n$ ----------4

Where K_k is a constant incorporating structural and geometric characteristic of the drug dosage form and n is the release exponent, indicative of the drug release mechanism.

The value of n for a tablet, n = 0.45 for Fickian (Case I) release, >0.45 but <0.89 for non-Fickian (Anomalous) release and 0.89 for Case II (Zero order) release and >0.89 for super case II type of release. Case II transport generally refers to the dissolution of the polymeric matrix due to the relaxation of the polymer chain and anomalous transport (Non Fickian) refers to the summation of both diffusion and dissolution controlled release.

Stability study

Selected formulations were subjected to stability studies as per I.C.H. Guidelines.

Following condition was used for stability study

*40°C/75 % RH analyzed at a time interval of 15 days till a period of 60 days

RESULTS AND DISCUSSION

λ max was found to be 302nm. Linearity was observed between the range 10-100µg/ml. The saturation solubility of Labetalol was determined in different solvents. The results are given in table.no.2. The spectra obtained from IR studies at wavelength 4000cm^{-1} to 400cm^{-1} are shown in fig.no.2-4. FT-IR reveals that there was no interaction between drug and selected polymers. In the formulations drug has maintained its identity and has not shown any interaction with the polymers.

Plain Labetalol hydrochloride exhibited angle of repose value of 39.71 ± 0.69^o indicating poor flow property. It was further supported by high Carr's index (28.89 ± 0.111) and Hausner's ratio (1.40 ± 0.0022). Table.No.3 shows the micromeritic property of precompression mixture. It exhibited the angle of repose value of 21.32 – 29.10^0. It was further supported by good Carr's index value of 15.47 - 19.85% and Hausner's ratio of 1.19 - 1.24 for all precompressional mixtures. Hence powder mixture was found suitable for direct compression method.

The results of physico-chemical evaluation of bilayer matrix tablets are given in Table.No.4. The tablets of different batches of sodium alginate and guar gum alone and in combination were found uniform with respect to thickness (3.62 to 3.77 mm). Hardness (3.0 to 4.5 kg/cm^2) and friability (0.27 to 0.35 %) were also found uniform indicating good handling property of the prepared bilayer matrix tablets. The % drug content of all formulation was found to be in the range of 97.46% to 99.29%. Thus all the physical parameters of the tablets were within control.

Swelling index or water uptake test is of great significance, as variation in the water content causes significant variation in the mechanical properties of the formulations. On comparing the swelling index, it was observed that guar gum tablets swelled more than that of sodium alginate. Table.No.5 and Fig.No.5 depicts the swelling behavior of different matrix tablets.

The observed surface pH of the different batches of tablets has been given in the table no.6 and fig.no.6. The results reveal that all the formulation provide an acceptable pH in the range of 6.01 to 6.62. Hence may not produce any local irritation to the mucosa.

The bioadhesive strength (in grams) observed for the different tablets is shown in the table No.7 and Fig.No.7. The bioadhesive strength of the tablets was found to be a function of concentration of polymer. Among the formulations, composition containing sodium alginate with guar gum exihibited maximum bioadhesive strength. As none of the tablets were dislodged before the end of the study period i.e. 8 hours, the bioadhesive strength exihibited by all the tablets can be considered satisfactory for maintaining them in the oral cavity for 8 hours.

Dissolution studies of prepared mucoadhesive buccal tablets were carried using 900ml of phosphate buffer of pH 6.8 containing 0.2% of sodium lauryl sulphate at 50rpm at 37^0 C±0.5^0 C in USP Type II apparatus. The samples were analyzed spectrophotometrically at 302 nm.

Formulation L1, L2 and L3 showed percentage drug release of about 97.70, 98.49 and 90.39% at the end of 7.5, 8 and 8 hrs respectively. The study indicates that the release rate was influenced by the polymer concentration. The rate of drug release from the tablets was found to decrease with increase in the concentration of sodium alginate. The reason attribute to this fact is slow erosion gelled layer from the tablet containing amount of sodium alginate.

The formulation L4 released 99.89% drug in 6 hrs, L5 released 99.12 % drug in 8 hrs and L6 released 89.42% drug in 8 hrs. This clearly indicates that release rate was influenced by polymer level. This retardation of drug release might be due to increase in the gum level tends to decrease drug release

because of formation of a thick gel structure that delays drug release from the matrix, where hydration of the individual guar gum particles results in a extensive swelling and increase in diffusion path length. The formulation L7 released 99.69% drug in 8 hrs.

Ethyl cellulose is an excellent backing layer because of low water permeability, hydrophobicity and moderate flexibility. The double layered structure design was expected to provide drug delivery in a unidirectional fashion to the mucosa and to avoid loss of drug to wash out by saliva, release drug immediately to provide a prompt pharmacological action and remain in oral cavity and provide a sustained release of enough drug over an extended period of time. The results are given in Table.No.8 & Fig.No.8.

To study the release mechanism of mucoadhesive buccal tablets, various dissolution models were applied to the *in-vitro* release profiles of different formulations. Kinetic results revealed that, all the formulations followed zero order kinetics as correlation coefficient (r^2) values (0.9738-0.9921) are higher than that of first order release kinetics. The prepared mucoadhesive buccal tablets showed non-fickian (anomalous) release, as the values of release exponent (n) lies between 0.5594-0.8662 with their correlation coefficient (r^2) values between 0.9778-0.9985, indicating that coupled diffusion, polymer swelling and relaxation were involved in the release process.

The stability studies were carried out for the selected formulations at 40±2°C/ 75±%5 RH for one month. Table.No.10 shows the values of post-compressional parameters after stability studies at different temperature and humidity conditions. The results indicated that the tablets did not show any physical changes (hardness and friability) during the study period and the drug content was found above 98% at the end of one month. This indicates that tablets are fairly stable at storage condition

CONCLUSION

The overall studies indicated that the polymers Sodium alginate and Guar gum in the ratio of 6:1.5 showed satisfactory mucoadhesive properties. Formulation L7 using these polymers in the above ratio with drug exhibited significant swelling properties with optimum release profile. Hence formulation (L7) will be useful for buccal administration for the treatment of hypertension.

ACKNOWLEDGEMENT

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Table 1: Composition of Mucoadhesive Buccal Tablets of Labetalol Hydrochloride

Ingredients (mg)	Formulation code						
	L1	L2	L3	L4	L5	L6	L7
Core layer containing drug							
Labetalol hydrochloride	50	50	50	50	50	50	50
Sodium alginate	30	37.51	45	-	-	-	30
Guar gum	-	-	-	7.5	15	22.5	7.5
PEG 6000	2.25	2.25	2.25	2.25	2.25	2.25	2.25
Mannitol	61.75	54.25	46.75	84.25	76.75	69.25	54.25
Aerosil	4.5	4.5	4.5	4.5	4.5	4.5	4.5
Mg.Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Backing layer							
Ethyl cellulose	50	50	50	50	50	50	50
Total weight	200	200	200	200	200	200	200

Table 2: Preformulation Studies of Labetalol Hydrochloride

Studies	Identification (UV)	Melting point (°C)	Solubility (gm/ml)		
			Phosphate buffer pH 6.8 containing 0.2% sodium lauryl sulphate	pH 6.8 (phosphate buffer)	pH 7.0 (Water)
Result	302.0	180	107 ±0.57mg/ml	81 ± 0.57µg/ml	20 mg/ml
Reported	302.0	180~184	---------	----------	20mg/ml

Table 3: Micromeritic Properties of Precompressional Powder Blend

Formulation code	Angle of repose (θ)	Carr's index (%)	Hausner's ratio
LH	39.71±0.69	28.89±0.111	1.40±0.0022
L1	26.04±0.95	18.34±1.170	1.22±0.018
L2	27.13±0.98	19.85±0.414	1.24±0.005
L3	29.31±2.41	15.47±0.596	1.18±0.009
L4	21.32±0.41	17.74±0.828	1.22±0.012
L5	23.13±0.83	16.69±0.178	1.20±0.0023
L6	25.07±0.22	16.36±0.145	1.19±0.002
L7	29.10±0.62	19.33±0.108	1.24±0.005

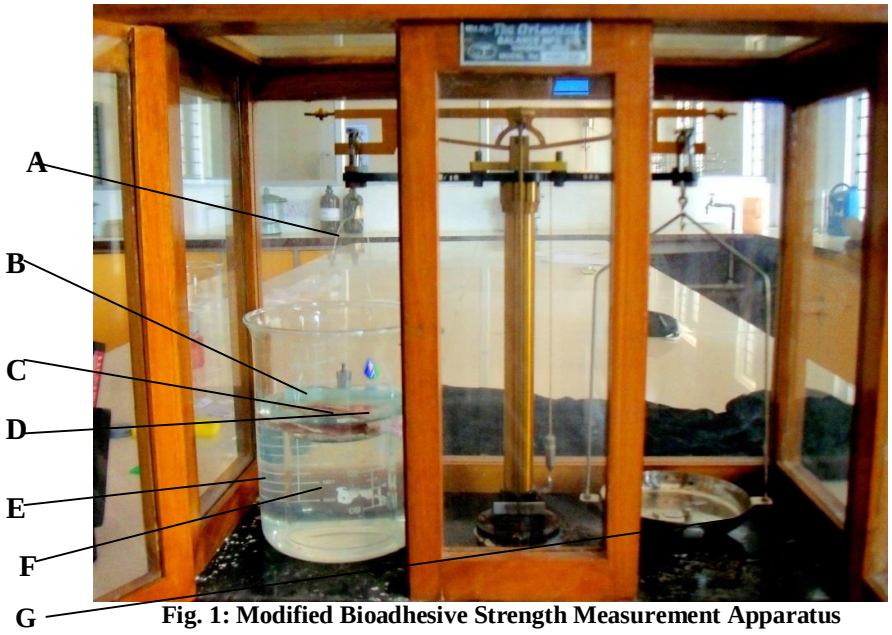

Fig. 1: Modified Bioadhesive Strength Measurement Apparatus

A – Plastic string
B – Bunch of glass slide
C – Tablet stacked to glass slide
D – Bovine cheek pouch
E – Glass container with phosphate buffer
F – Inverted glass beaker to which bovine pouch is adhered
G – Right hand pan in which weights are added.

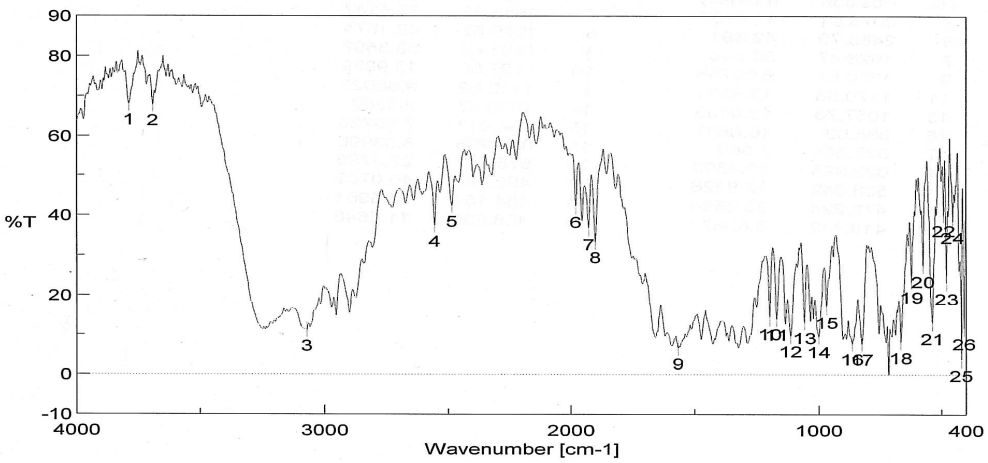

Fig. 2: FT-IR spectrum of pure drug (Labetalol hydrochloride)

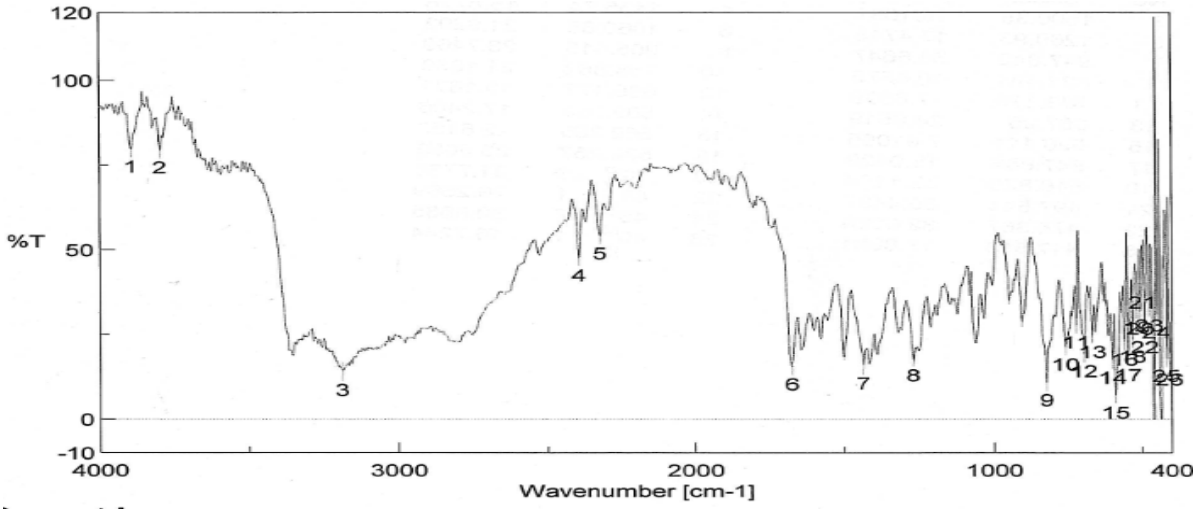

Fig. 3: FT-IR spectrum of pure drug+sodium alginate+all excipients

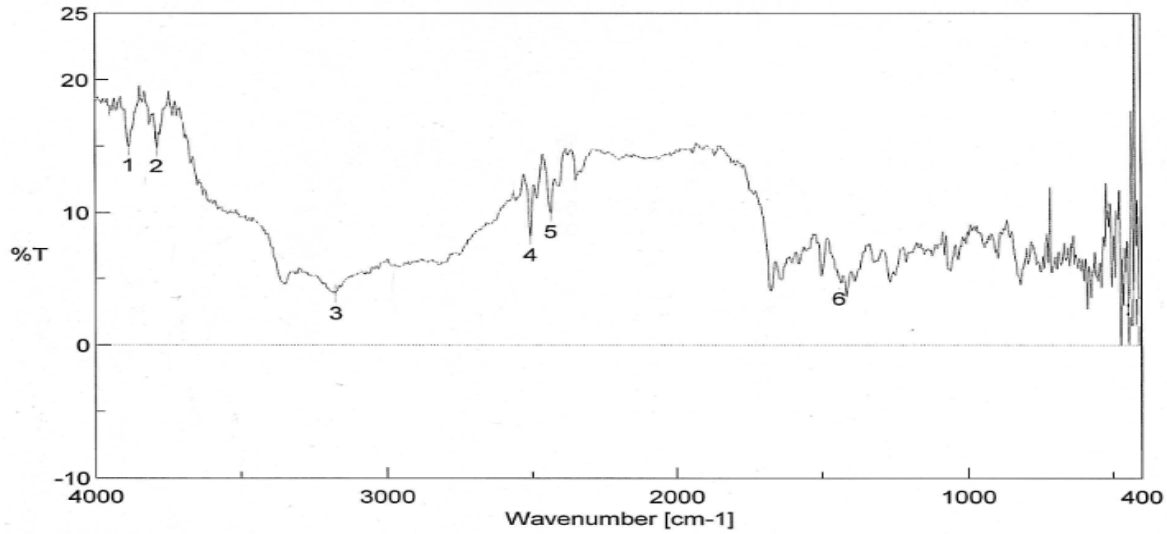

Fig. 4: FT-IR spectrum of formulation pure drug+guar gum+all excipients

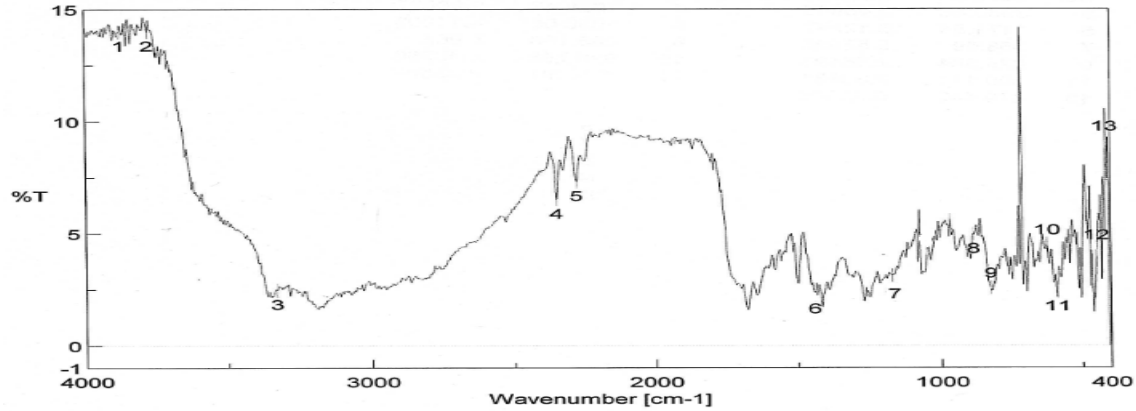

Fig. 5: FT-IR spectrum of pure drug+sodium alginate+guar gum+all excipients

Table 4: Evaluation of Different Mucoadhesive Buccal Tablets of Labetalol Hydrochloride

Formulation code	Hardness^{+} (kg/cm^2)	Friability† (%)	Thickness† (mm)	Drug content (%)	Weight variation*
L1	4.0±0.24	0.32±0.06	3.65±0.05	97.46	199.8±0.65
L2	4.23±0.34	0.28±0.13	3.77±0.07	99.02	201.4±0.34
L3	3.98±0.32	0.35±0.14	3.65±0.04	98.67	200.5±0.52
L4	4.0±0.35	0.33±0.05	3.62±0.10	99.29	200.8±0.51
L5	4.5±0.17	0.31±0.09	3.66±0.05	97.91	201.6±0.31
L6	3.0±0.14	0.27±0.08	3.70±0.02	97.78	200.6±0.52
L7	4.5±0.23	0.35±0.08	3.74±0.12	98.49	201.0±0.47

Table 5: Swelling Study of Different Mucoadhesive Buccal Tablets of Labetalol Hydrochloride

Time (hrs)	% Swelling Index						
	L1	L2	L3	L4	L5	L6	L7
0	0	0	0	0	0	0	0
1	22.61	29.35	33.67	36.18	38.89	41.41	37.56
2	32.66	38.27	40.91	43.15	43.43	45.18	44.39
3	39.89	48.48	49.75	51.27	53.27	54.04	47.47
4	47.45	55.10	57.58	58.59	60.61	64.29	56.06
5	51.52	60.71	62.76	64.49	65.48	67.51	65.66
6	57.07	62.76	64.79	66.49	66.67	68.69	70.71
7	64.82	65.66	66.67	68.02	70.20	72.73	75.63
8	69.52	70.01	71.78	72.46	75.63	77.82	80.47

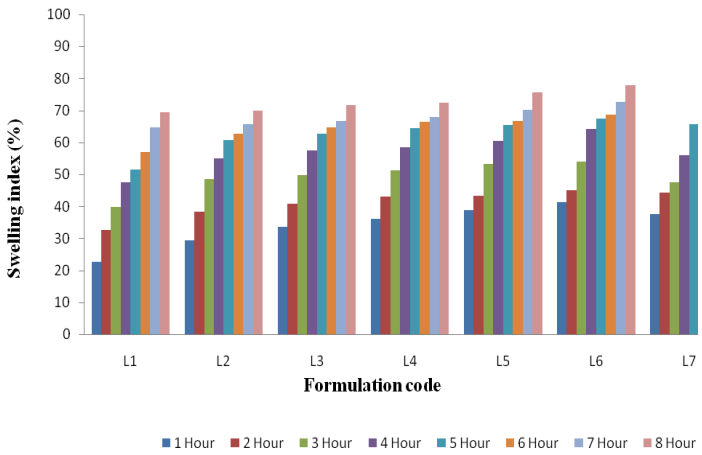

Fig. 5: Percentage Swelling of Developed Mucoadhesive Buccal Tablets of Labetalol Hydrochloride

Table 6: Surface pH of Various Buccal Tablets of Labetalol Hydrochloride

Formulation code	Buccal pH
L1	6.30
L2	6.20
L3	6.38
L4	6.20
L5	6.49
L6	6.01
L7	6.62

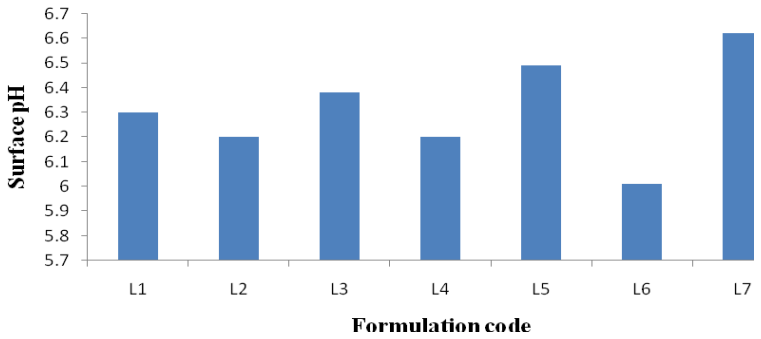

Fig. 6: Surface pH profile of Labetalol hydrochloride

Table 7: Bioadhesive Strength of Various Buccal Tablets of Labetalol Hydrochloride

Formulation code	Bioadhesive strength (gm)*
L1	22.30
L2	26.80
L3	28.40
L4	24.30
L5	27.23
L6	30.23
L7	34.50

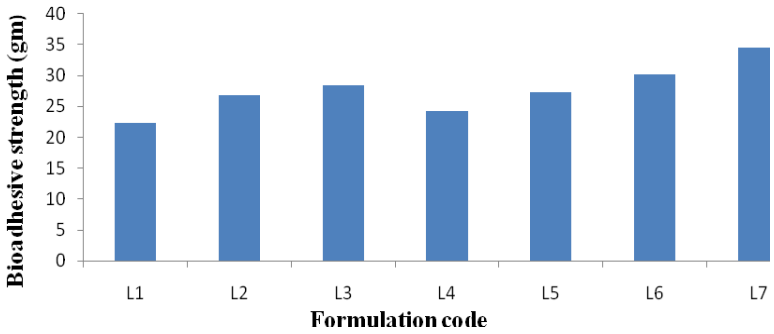

Fig. 7: Bioadhesive Strength Profile of Various Buccal Tablets of Labetalol Hydrochloride

Table 8: *In-Vitro* Drug Release Parameters

Time (hrs)	Cumulative % drug release						
	L1	L2	L3	L4	L5	L6	L7
1	40.23	27.43	12.54	45.64	25.34	19.53	24.37
2	55.92	39.28	25.14	59.23	36.37	26.89	33.27
3	66	52.82	38.11	72.18	45.86	35.02	42.77
4	73.75	62.32	47.99	83.04	55.74	42.19	53.79
5	81.10	70.65	59.41	93.11	66.19	52.44	65.03
6	91.75	81.48	71.60	99.51	77.03	64.25	79.54
7	97.57	89.62	80.52	----	91.16	77.61	91.17
7.5	99.70	94.46	84.59	----	96.59	84.57	95.24
8	--------	98.49	90.39	----	98.12	89.42	99.69

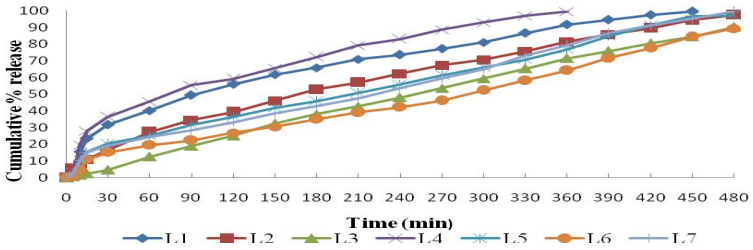

Fig. 8: *In-vitro* release profile of sodium alginate, guar gum bilayer buccal tablets of Labetalol hydrochloride (alone and combination)

Table 9: Drug Release Kinetics of the Formulated Products of Labetalol Hydrochloride

Formulation code	Zero order	First order	Highuchi	Korsmeyer-peppas	
	R^2	R^2	R^2	N	R^2
L1	0.9801	0.8436	0.9467	0.7342	0.9935
L2	0.9924	0.9346	0.9639	0.6401	0.9978
L3	0.9912	0.9126	0.9648	0.6245	0.9989
L4	0.9891	0.8478	0.9613	0.6733	0.9924
L5	0.9902	0.8303	0.9684	0.6352	0.9957
L6	0.9916	0.8627	0.9733	0.7212	0.9964
L7	0.9925	0.8666	0.9558	0.6485	0.9984

Table 10: Physico-Chemical Data of Selected Mucoadhesive Buccal Tablets of Labetalol Hydrochloride Before and After Stability Study

Formulation code	Hardness test* (kg/cm^2)		Friability** (%)		Weight variation***		Thickness** (mm)		Drug content* (%)	
	Before	After	Before	After	Before	After	Before	After	Before	After
L2	4.5± 0.17	4.23±0.34	0.28 ± 0.13	0.29 ± 0.03	201.7±0.37	200.8±0.51	3.80 ± 0.06	3.77 ± 0.08	98.49	97.61
L5	4.0± 0.24	3.98±0.32	0.32± 0.06	0.33± 0.05	200.6±0.52	199.8±0.65	3.77± 0.07	3.74± 0.12	98.89	97.91
L7	3.5± 0.23	3.0± 0.14	0.28± 0.08	0.29± 0.04	202.0±0.22	201.6±0.31	3.67± 0.15	3.66± 0.05	99.02	98.31

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