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FORMULATION AND EVALUATION OF MUCOADHESIVE BUCCAL TABLETS CONTAINING IVABRADINE HYDROCHLORIDE BY USING NATURAL POLYMERS

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ABSTRACT:
The buccal mucosa is moderately permeable, strong when match up with the other mucosal tissues and is more tolerant to potential allergens which have a compact affinity to unalterable irritation or harm. Mucoadhesive buccal drug delivery system offers a control release system; it entails the administration of required drug through the buccal mucosal membrane lining of the oral cavity. The Bioadhesive was resulting from the need to limit drugs at a definite site in the body. Significantly at the absorption site, enhance the degree of drug absorption is restricted by the residence time of the drug. The API, blend of excipients and drug were prepared at the ratio of 1:1, filled in closed vials and kept in accelerated environmental conditions (40°C/75% RH) for a period of 1 month. Excipients were employed here to assess the compatibility issue with the active ingredient. The possible drug and polymer interaction studies were assessed by using FTIR. Calibration curve of ivabradine HCl was constructed by dissolving pure drug of ivabradine HCl (100 mg) in 100 mL of phosphate buffer (pH 6.8) to give 1mg/mL concentration and designed as stock solution-1. The angle of repose was determined by fixed funnel method. The prepared mucoadhesive buccal tablets were estimated for post compression factors such as thickness, friability, drug content and hardness. The surface pH study was conducted on ivabradine HCl mucoadhesive buccal tablets, carried out to predict the comfort of the buccal formulation into the possibility of any side effects in buccal mucosa environment. F1 and F5 possessed the best results among all the formulations in terms of *in vitro* release of drug. However, F2 formulation shows highest mucoadhesive and swelling index than other formulation. Therefore, from the data, it may be concluded that F2 formulation might be considered as promising mucoadhesive buccal tablet formulation for a suitable sustained drug delivery system for ivabradine.
Keywords: Ivabradine Hydrochloride, Buccal tablet, Mucoadhesive, Natural Polymers.

1. INTRODUCTION:

The oral administration of pharmaceutical compound has been several troubles such as irregular and variable absorption, GI intolerance, decreased bioavailability; pre-systemic exclusion has provoked the consideration of other possible route for administration. For example, it is complicated to continue the medicament at the preferred site so that it can be absorbed, distributed and metabolized effortlessly. This restriction leads to the enhancement of other routes of administration[1].

1.1 Necessitate of Mucoadhesive DDS:

Buccal mucosa is soft and comparatively stationary surface and is appropriate for the assignment of controlled-release system. The buccal mucosa is moderately permeable, strong when match up with the other mucosal tissues and is more tolerant to potential allergens which have a compact affinity to unalterable irritation or harm.

1.2 Mucoadhesive Buccal Drug Delivery System

Mucoadhesive buccal drug delivery system offers a control release system; it entails the administration of required drug through the buccal mucosal membrane lining of the oral cavity. It is very helpful for transmucosal (systemic effect) and mucosal (local effect) drug administration. In the foremost case, involves drug absorption through the mucosal barrier, to attain the systemic circulation whereas the second cases to attain a site-specific release of the drug on the mucosa[9].

1.3 Routes of Drug Transport across the buccal mucosa

The two major mechanisms concerned for the penetration of different substances include passive transmission intra cellular or Trans cellular (crossing through the cell membranes with a lipid domain and a polar) whereas the passive diffusion intercellular or para cellular (passing around between the cells) carrier intervened transport and pinocytosis[12].

1.4 Classification of permeation enhancers

- **Chelators:** Methoxy salicylates, EDTA, sodium salicylate, citric acid[15].
- **Surfactants:** Polyoxythylene-20-cetylether, polyoxyethylene. sodium lauryl sulphate, Benzalkoniumchloride, Polyoxyethylene-9-laurylether,
- **Bile salts:** sodium tauro cholate, sodium glycocholate, sodium tauro deoxycholate, sodium deoxy cholate.
- **Fatty acids:** oleic acid, lauric acid, capric acid, phosphatidylcholine, methyl oleate, propylene glycol.
- **Inclusion complexes:** cyclodextrins.
- **Others:** azone aprotinin, sulfoxides, polysorbate 80, dextran sulfate, cyclodextrin, various alkyl glycosides and menthol.
- **Thiolated polymers:** chitosan–cysteine, chitosan-4-thioglycholic acid, chitosan-4-thiobutylamide.

1.5 Use of Buccal Adhesive Preparations

The Bioadhesive was resulting from the need to limit drugs at a definite site in the body. Significantly at the absorption site, enhance the degree of drug absorption is restricted by the residence time of the drug. The mucus layer, which covers the epithelial surface, has various roles.

- Protective role
- Barrier role
- Adhesion role
- Lubrication Role
- Marketed products of Mucoadhesive Buccal Dosage Forms

Table 1: Mucoadhesive buccal dosage forms (Market available)

Drug Name	Manufacturers Name/Brand name
Nitro-glycerine	Glenmark (nitrogard)
Miconazole	BioAlliancePharmaSA (loramyc)
Methyl testosterone	Bayer Schering Pharma (Oreton methyl)
Hydrocortisone	Auden Mckenzie (corlan pellets)
Fentanyl	Cephalon (fentora CII)
Insulin buccal delivery	Shreyalife sciences (Oral Recosulin)
Omeprazole	Astrazeneca (Prilosec)
Vitamin-C	Zhongnuo (CSPC)
Clotrimazole	Lotrimin, Mycelex
Testosterone	Actient pharmaceuticals (Striant) [72]

2. EXPRIMENTAL WORK

Table 2: Equipments were used for this present work

Equipment	Model	Manufacturers	Manufacturer Location
Franz diffusion cells apparatus	EDC-07	Electro lab	Mumbai, India
Tablet pilot press 10 stations	PP-1	Karnavathi	Ahmadabad,India
UV-visible Spectrophotometer	2602	Shimadzu	Mumbai, India
pH Meter	L1127	Elico Ltd	Hyderabad, India
Friabilitor	EF-2,double drum	Electro lab	Mumbai, India
FT-IR Spectroscopy	8400S(Shimadzu)	Shimadzu	Japan
Digital balance	CA224	LWL Precision instrument	Mumbai, India
Hardness tester	Monsanto	Kshitij International	Haryana, India
Hot air oven	i-therm	Jainson	Mumbai, India

Table 3: Materials used in this present work

Material	Source
Ivabradine HCl	The Madras Pharmaceuticals Pvt. Ltd- Chennai
Guar gum	ASES Chemical Works ,Jodhpur
Pectin	CDH Laboratory, New Delhi
Chitosan	Cochin foods, Cochin Kerala
Ethyl cellulose	CDH Laboratory, New Delhi
Magnesium stearate	CDH Laboratory, New Delhi
Potassium dihydrogen phosphate	New India chemical Enterprises,Mumbai
Disodium hydrogen phosphate	New India chemical Enterprises,Mumbai
Lactose anhydrous	Qulaligens Fine Chemicals,Mumbai

2.1 Preformulation studies:

2.1.1 Drug-polymer compatibility studies by physical examination

The API, blend of excipients and drug were prepared at the ratio of 1:1, filled in closed vials and kept in accelerated environmental conditions (40°C/75% RH) for a period of 1 month.

2.1.2 Drug-polymer interaction studies by FTIR

Excipients were employed here to assess the compatibility issue with the active ingredient. The possible drug and polymer interaction studies were assessed by using FTIR (Fourier transform infrared spectroscopy).

2.1.3 Construction of calibration curve for Ivabradine HCl

Calibration curve of ivabradine HCl was constructed by dissolving pure drug of ivabradine HCl (100 mg) in 100 mL of phosphate buffer (pH 6.8) to give 1mg/mL concentration and designed as stock solution-1

2.1.4 Evaluation of pre-compression parameters of sustained release mucoadhesive buccal tablet blends of ivabradine HCl

Precompression evaluation parameters furnish the data's necessary to describe the character of the drug material and offer a outline for the drug grouping with pharmaceutical excipients in the manufacture of a dosage form.

2.1.5 Measurement of powder flow characteristics

The angle of repose was determined by fixed funnel method[19]. The funnel kept at a altitude of 2.5 cm from the surface. Samples were poured onto the centre of the dish from a funnel that can be elevated perpendicularly; till it formed a heap is obtained. The radius was calculated and the angle of repose was planned by means of the formula mentioned below. The identical process was repeated for three times and the average value was taken.

$\tan \theta = h/r$ (or) $\theta = \tan^{-1}(h/r)$

2.1.6 Measurement of powder density (g/cc)

Bulk density refers to a measure used to describe a packing of particles or granules. An precisely weighed amount of a powder (W) which was formerly accepted through sieve number 22 was cautiously poured into a graduated cylinder and the volume (Vo) occupied was calculated[21].

2.1.7 Measurement of powder compressibility

Compressibility is a significant measure that can be attained from tapped and bulk densities[104]. The fewer compressible a substance the more flow proficient it is. Compressibility index calculated by means of the following formula and expressed in terms of %.

$I = 100(D_t - D_b)/ D_t$

3. EXPERIMENTAL DESIGN

Formulation design was created to determine and optimize the effect of the three polymers concentration variables.

Table 4: Composition variables of Ivabradine Hydrochloride buccal tablets

Drug Reservoir (mg)						**Drug Free Backing Layer (mg)**	
Formula code	Drug	Guar gum	Chitosan	pectin	Lactose	EC	Mg. Stearate
F1	5	35	25	20	65	20	10
F2	5	60	25	20	40	20	10
F3	5	35	40	20	50	20	10
F4	5	60	40	20	25	20	10
F5	5	35	25	40	45	20	10

F6	5	60	25	40	20	20	10
F7	5	35	40	40	10	20	10
F8	5	60	40	40	5	20	10

Each tablet weight is 180 mg

3.1 Evaluation of Post compression parameters of mucoadhesive buccal tablets of Ivabradine HCl:

The prepared mucoadhesive buccal tablets were estimated for post compression factors[26]such as thickness, friability, drug content and hardness.

3.1.1 Thickness

The thickness of randomly selected average of the five buccal tablets was used from each formulation, resoluted by using screw guage and results were articulated in millimeter.

3.1.2 Hardness

Tablets have need of a definite sum of resistance and hardness or strength to resist involuntary shocks of managing in packaging, shipping and manufacture. The rigidity of five tablets randomly selected from each formulation, calculated by means of monsanto hardness tester apparatus and results were and expressed in Kg/cm^2.

3.1.3 Friability

Friability test is assessing the strength of the granules; friability test was done by using Roche friability test apparatus was used to conclude the friability of the prepared buccal tablets. Twenty pre-weighed buccal tablets was located in the friabilator apparatus and activated for 100 revolutions (25 rpm) in four minutes and the buccal tablets freed from dust and reweighed. The prescribed limit for loss on friability is not more than 1% w/w. The percentage friability was evaluated according to the following formula.[27]

$$\% \text{ Friability} = \frac{\text{Pre weight-Final Weight}}{\text{Pre weight}} \times 100$$

3.1.4 Drug content

Ten prepared buccal tablets were selected randomly from each formulation were delicately powdered and equalivalent weight of 5 mg of ivabradine HCl powder was exactly weighed and place in to 100 ml volumetric flasks having 50 ml of phosphate buffer pH 6.8. The volumetric flasks were shaken to mix the stuffings carefully. The amount was made up to the mark with phosphate buffer pH 6.8 and filtered. 1 ml of the filtrate with appropriate dilution was calculated for ivabradine HCl content at 285 nm by means of a double beam UV-visible spectrophotometer.

3.1.5 Surface pH study

The surface pH study[28]was conducted on ivabradine HCl mucoadhesive buccal tablets, carried out to predict the comfort of the buccal formulation into the possibility of any side effects in buccal mucosa environment. The prepared buccal tablet were permissible to distend by maintaining it make contact with 5ml of phosphate buffer containing 2% w/v agar medium (pH 6.8 ± 0.01) at room temperature for 2 hrs. The surface pH was deliberate by keeping the electrode in make contact with the surface of the buccal tablet and permiting it to equilibrate for 1 minute. The mean of three reading was recorded.

3.2 Swelling index characteristics for buccal tablets

The swelling index performance study was carried out on ivabradine HCl buccal tablets. The degree of swelling index was on purpose in terms of % weight gain[29]by the mucoadhesive buccal tablets. The swelling index velocity of the bioadhesive buccal tablet was estimated by means of 1% agar gel plate. The initial weight of the buccal tablet was deliberate (W1). The buccal tablet from each formulation was located on gel surface in a petridish

incubator at 37 ± 5°C. The buccal tablets were detached at dissimilar time intervals (1, 2, 3, 4, 5 and 6 h) and wiped with filter paper and weighed again (W2). The swelling index performance was estimated by the formula.

S.I = [(W2-W1)/ W1] X 100

Where S.I= Swelling Index W1- Initial weight of buccal tablet, W2- weight of swollen buccal tablet at time (t).

3.3 Measurement of *invitro* buccoadhesive strength

Measurement of mucoadhesive strength[24] required breaking the adhesive bond between a buccal membrane and buccal tablets was carried by modifying balance method. Fresh Sheep buccal mucosa was employed as model membrane. Fresh sheep buccal mucosa were acquired from a local slaughter-house and utilized for the study within 2 h of slaughter.

3.4 *Ex-vivo* Drug Permeation through sheep buccal mucosa

An *ex-vivo* buccal permeation study[19]Ivabradine HCl tablet was carried through the sheep buccal mucosal membrane. The buccal tablet was positioned in such a way that it fixed on the mucous membrane and the compartments clamped together. The receptor compartment was packed with isotonic phosphate buffer pH 6.8. The assembly was sustained temperature at 37 ± 5°C and stirred with a magnetic bead at 50 rpm. Samples were withdrawn and filtered through whatman filter paper; at regular time intervals analyzed by means of UV Spectrophotometer at 285 nm.

3.5 *In-vitro* kinetics studies

The *in-vitro* release data was fit into kinetic models to explain the release kinetics[26] of ivabradine HCl from the buccal tablets. The kinetic models used were a zero-order equation, First order kinetics, higuchi's and Korsemeyer- Peppa's models.

3.6 Stability Studies

Short term stability study [30] was carried out on the optimized ivabradine HCl buccal tablets. Adequate number of buccal tablets were filled in amber colored rubber Stoppard bottles and reserve in stability compartment maintained at temperature at 40 ± 2°C / 75 ± 5% RH for three months were analysed regularly, for their swelling index, physical appearance, buccoadhesive strength, drug content, and *in-vitro* drug release. All the datas collected were analysed by using Prism software 5.

4. RESULT AND DISCUSSION:

4.1 Drug-polymer compatibility studies by physical examination

Table 5: Compatibility data for Ivabradine HCl and excipients

API and Excipients	Ratio	1St Week	2nd Week	3rd Week	4th Week
		40°C/ 75% RH	40°C/ 75% RH	40°C/ 75% RH	40°C/ 75% RH
Ivabradine HCl	..	√	√	√	√
Ivabradine HCl + Guar gum	1:1	√	√	√	√
Ivabradine HCl + chitosan	1:1	√	√	√	√
Ivabradine HCl + Pectin	1:1	√	√	√	√
Ivabradine HCl + ethylcellulose	1:1	√	√	√	√
Ivabradine HCl + Magnesium stearate	1:1	√	√	√	√
√ = No change					

The physical observation of drug and mixtures shows no change in their physical properties. This is revealed that there is no significant interaction between the drug and polymers. The results were present in the Table 5

4.2 Drug-polymer interaction studies by FTIR

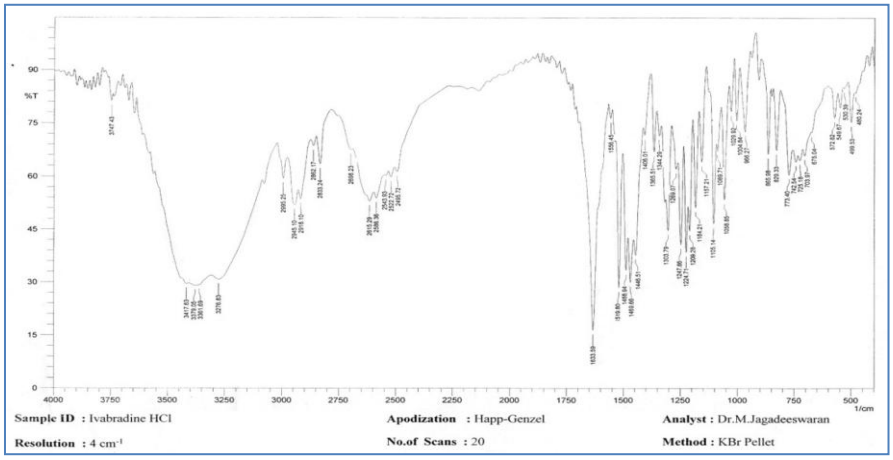
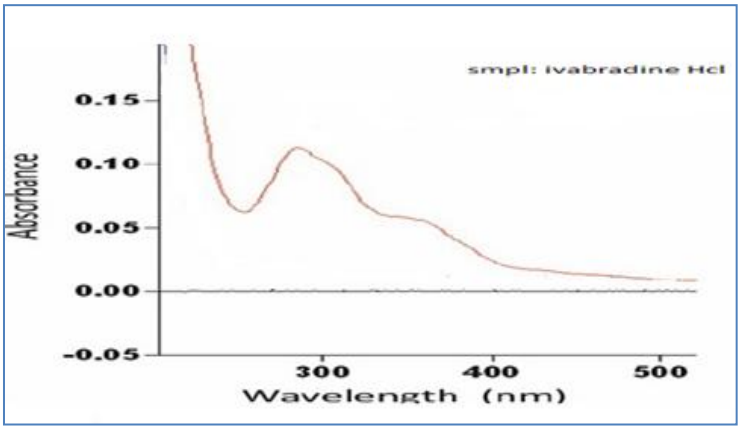


Figure 1: Fourier transform infrared spectroscopy spectrum of Ivabradine Hydrochloride

4.3 Construction of calibration curve for Ivabradine HCl



Determination of the lambda maximum

Figure 2: UV spectra Lambda maximum of Ivabradine HCl

Table 6: Calibration Curve of ivabradine HCl

Concentration (µg/ml)	Absorbance at 285 nm
0	0
5	0.082
10	0.164
20	0.328
30	0.492
40	0.656
50	0.812

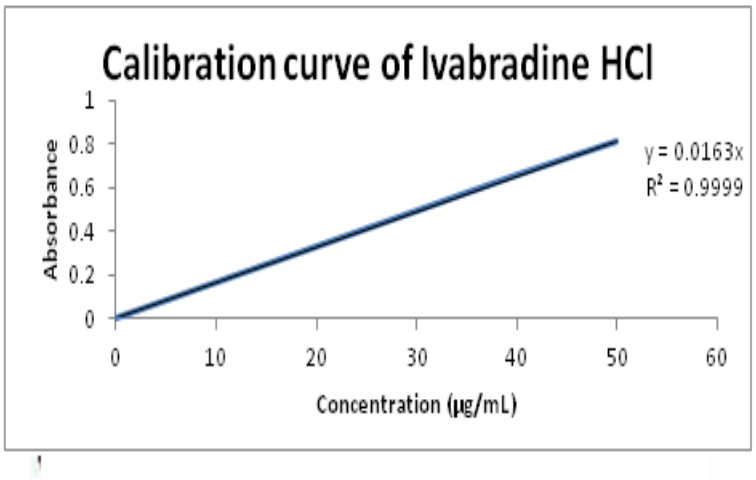


Figure 3: Calibration Curve for ivabradine HCl

4.3.2 Evaluation of pre-compression parameters of sustained release mucoadhesive buccal tablet blends of ivabradine HCl

Table 7: Micrometric properties of Ivabradine HCl tablet blends

Formulation Code	Derived properties Mean± SD (n=3)		Flow properties Mean± SD (n=3)		
	Bulk Density (g/cc)	Tapped Density (g/cc)	Angle of repose (^{o})	Carr's index (%)	Hausner's ratio (%)
F1	0.32±0.02	0.356±0.01	27.13±0.32	09.34±0.10	1.18±0.07
F2	0.34±0.01	0.350±0.01	28.36±0.15	02.82±0.05	1.15±0.14
F3	0.30±0.01	0.346±0.01	27.53±0.55	13.44±0.01	1.13±0.01
F4	0.32±0.01	0.326±0.02	30.13±0.95	02.12±0.09	1.02±0.05
F5	0.32±0.01	0.343±0.02	28.13±0.25	06.78±0.01	1.25±0.30
F6	0.33±0.01	0.350±0.01	27.66±0.68	03.79±0.01	1.13±0.09
F7	0.32±0.02	0.360±0.01	27.83±0.20	11.40±0.57	1.15±0.04
F8	0.32±0.05	0.340±0.01	28.46±0.40	04.12±0.32	1.14±0.09

4.3.3 Post compression evaluations of ivabradine HCl buccal tablets

Table 8:

Formulation code	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)	Surface pH
F1	5.83±0.57	3.2±0.73	0.89±0.75	94.42±0.55	6.53±0.18
F2	6.13±1.52	3.5±0.75	0.99±0.15	96.75±1.07	6.71±0.48
F3	6.21±0.70	3.8±0.51	0.31±0.40	98.82±0.98	6.62±0.41
F4	5.85±0.60	3.9±0.40	0.28±0.94	90.86±0.99	6.49±0.47
F5	5.86±0.56	4.1±1.05	0.58±0.52	92.59±0.34	6.79±0.68
F6	6.03±0.70	4.0±0.75	0.23±0.80	94.89±0.22	6.44±0.85
F7	6.02±0.40	3.2±0.50	0.82±0.92	94.76±0.33	6.76±2.14
F8	6.23±0.17	3.8±0.86	0.71±0. 79	99.98±0.16	6.78±0.91
Mean±SD (n=3)					

4.3.4 Swelling performance of mucoadhesive buccal tablets

Table 9:

Formulation code	Swelling index (Mean± SD)				
	Time in hrs				
	1	2	3	4	5
F1	17.41±0.32	21.41±0.59	23.43±0.53	26.14±0.67	27.18±0.69
F2	31.08±1.10	32.88±0.29	35.03±1.72	35.03±1.06	36.36±0.75
F3	17.82±0.62	21.87±0.40	25.43±0.62	28.63±0.49	29.46±0.36
F4	25.62±0.53	27.92±0.37	29.56±0.40	32.11±0.36	32.71±0.70
F5	19.63±0.44	20.12±0.66	24.14±0.86	26.92±0.33	27.46±0.29
F6	15.82±0.37	18.03±0.70	23.76±0.34	24.38±0.41	26.66±0.25
F7	16.42±0.44	19.40±0.37	24.64±0.36	24.79±025	30.43±054
F8	15.19±0.17	16.32±0.17	22.43±0.35	24.29±0.27	27.39±0.21

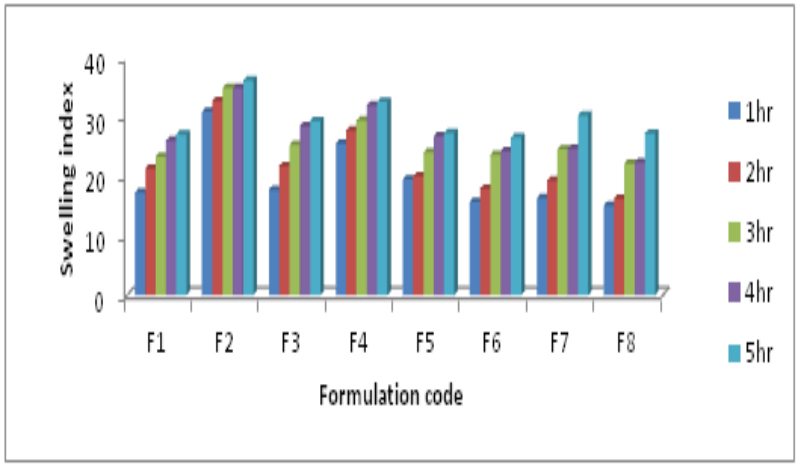


Figure 5: displays the diagram of swelling index of formulations with respect to time

Effect of formulation variables on mucoadhesive strength

Table 10: Mucoadhesive strength of buccal tablets

Formulation Code	Mucoadhesive Strength(g) (Mean± SD)
F1	37.43±0.40
F2	50.27±0.25
F3	40.33±0.35
F4	40.53±0.25
F5	45.33±0.35
F6	40.43±0.40
F7	35.43±0.45
F8	35.26±0.30

4.3.5 *In vitro* permeation studies of sheep buccal mucosa

The Modified Franz diffusion apparatus was used for the *in vitro* permeation studies. Excised sheep buccal mucosa was employed for the permeation studies. The quantity of drug that permeates through the sheep buccal mucosa at distinct intervals in a phase of 4 hours was determined spectrophotometrically at 285nm.

Table 11: shows cumulative percentage of ivabradine HCl from different formulations (±SD)

Time (min)	Formulation code							
	F1	**F2**	**F3.**	**F4**	**F5**	**F6**	**F7**	**F8**
0 0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
30	4.25±0.21	5.06±0.90	6.06±022	5.68±0.98	7.00±045	9.87±0.98	14.50±0.34	4.62±035
60	10.06±0.23	12.31±1.20	12.50±1.02	12.31±1.43	14.37±0.98	20.18±1.23	35.18±1.54	12.06±098
90	17.31±1.20	20.37±2.30	23.87±1.22	20.18±1.90	22.062±1.23	31.18±1.09	57.50±1.23	17.56±1.32
120	30.62±1.02	30.25±1.50	37.18±1.23	29.00±0.80	30.25±0.92	43.43±1.98	81.31±1.02	28.43±20.12
150	44.25±2.40	40.37±1.30	51.06±0.34	36.87±0.87	38.68±0.78	5 5.06±0.87	94.50±0.99	41.81±1.67
180	60.62±1.50	50.81±1.40	64.50±0.89	47.37±0.51	47.93±1.22	66.37±0.76	-	56.25±1.32
240	80.06±1.50	65.43±0.21	78.87±1.43	60.62±0.45	58.37±1.23	82.31±0.23	-	68.93±1.87

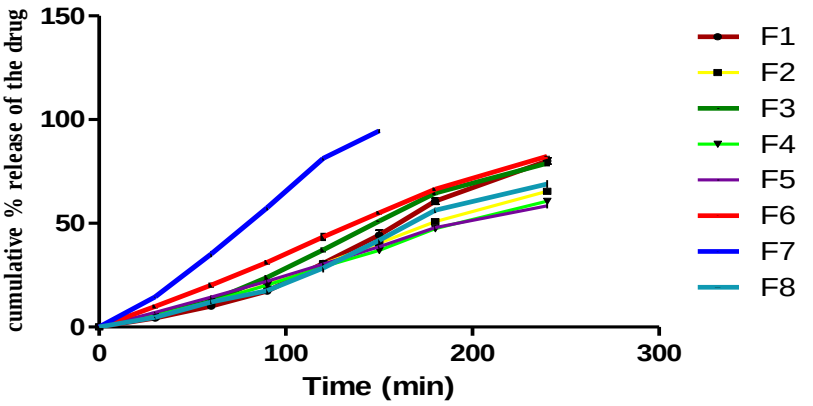


Figure 7: depicts *in vitro* cumulative percentage drug release of all formulations

Table 12: Release kinetics behavior of different formulations of ivabradine HCl buccal tablet

Formulation code	Zero-Order [r] (Mt vs t) (±SD)	First-Order [r] $\log(M_0-M_t)$vs t (±SD)	Higuchi-Matrix[r] (M vs $t^{0.5}$) (±SD)	Korsmeyer Peppas Log(Mt) vs log(t)	
				[r]	N
F1	0.945±0.033	0.893±0.020	0.712±0.014	0.879±0.002	0.70
F2	0.986±0.064	0.963±0.038	0.798±0.006	0.929±0.10	0.70
F3	0.976±0.040	0.944±0.015	0.783±0.046	0.93±0.12	0.70
F4	0.992±0.048	0.972±0.045	0.816±0.027	0.946±0.22	0.69
F5	0.995±0.154	0.987±0.031	0.858±0.028	0.971±0.01	0.70
F6	0.996±0.006	0.956±0.013	0.862±0.016	0.984±0.003	0.70
F7	0.992±0.045	0.885±0.037	0.862±0.034	0.989±0.43	0.88
F8	0.963±0.047	0.939±0.007	0.754±0.007	0.908±0.65	0.69

All values are expressed as Mean±SD

4.3.6 Stability studies of best formulation(F2)

Table 13:

Parametrers	After 30 days	After 60 days	After 90 days
Physical appearance	No changes	No changes	No changes
Swelling index (at end 5^{th} hr)	37.3±0.15	38.63±1.32	37.22±0.25
Buccoadhesive strength	49.92±0.34	51.72±0.35	51.01±1.33
Hardness	3.7±0.55	3.8±0.23	3.2±0.12

Short term stability study of the optimized ivabradine HCl buccal tablets, the obtained results reflect that there is no significant change such as physical appearance, and their mucoadhesive strength, swelling index and *in-vitro* drug release, suggesting the satisfactory stability of the buccal tablets.

5. SUMMARY AND CONCLUSION:

An antianginal drug ivabradine HCl which has poor oral bio-availability and lesser biological plasma half life, hence an attempt was made to prepare mucoadhesive buccal tablets of ivabradine HCl in order to enhance the bioavailability and sustain its release by utilizing natural biodegradable polymers like guar gum pectin and chitosan incorporated in

the formulations to attain a buccal sustained release of the ivabradine HCl.

Physiochemical properties studies like precompression, UV analysis and compatibility study of ivabradine HCl was complied with standard.

The following parameters were selected during evaluation:

All the prepared formulations were subjected for evaluations like post compression studies, surface pH of tablets, mucoadhesive strength, and *ex-vivo* drug permeation through sheep buccal mucosa, release kinetics, and stability study have shown satisfactory results.

The FTIR spectra shown that, there was no chemical interaction between polymers and ivabradine HCl.

In-vitro drug release of the formulation of ivabradine HCl tablet which was prepared with guar gum, pectin and chitosan (F2) with high level concentration guar gum and least level concentration of pectin and chitosan was showed maximum sustained release (10 hr), depicted in figures no 7.5.

The drug release kinetic study indicated that the release data was best fitted with zero order, and Kormeyer peppas model shown in figure no 7. Which explains the anomalous diffusion mechanism or non-Fickian of drug release through buccal tablets.

The short term stability study result confirms that no appreciable changes in physical appearance, swelling index, drug content, bucco-adhesive strength and *in-vitro* drug release profile obtained. Hence formulations were found to be stable under the conditions used for the stability studies.

6. CONCLUSION

Mucoadhesive buccal tablet of ivabradine HCl were successfully prepared by direct compression method presented herein based on the natural polymers blend hold promise for oral administration of ivabradine HCl and also found to be simple and reproducible.

The polymers guar gum, pectin and chitosan are used as carrier and also easily available and biocompatibility.

F1 and F5 possessed the best results among all the formulations in terms of *in vitro* release of drug. However, F2 formulation shows highest mucoadhesive and swelling index than other formulation. Therefore, from the data, it may be concluded that F2 formulation might be considered as promising mucoadhesive buccal tablet formulation for a suitable sustained drug delivery system for ivabradine.

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