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Development and in vitro Evaluation of Floating Mucoadhesive Tablet of Acebutolol Hydrochloride

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Abstract

In this study, it was intended to formulate floating Mucoadhesive tablets containing Acebutolol hydrochloride, an antihypertensive agent, to release the drug for a prolonged period of time in the upper part of the gastrointestinal tract in order to first-pass metabolism for improvement in bioavailability, to decrease the frequency of dosing, and to improve patient compliance. The effects of several polymers, including HPMC K4M and Carbopol 934, on the Mucoadhesive strength and release kinetics of floating Mucoadhesive tablets of Acebutolol hydrochloride were studied. The pre-compression blend of Acebutolol hydrochloride mucoadhesive tablets were characterized with respect to angle of repose, bulk density, tapped density, carr's index and Hausner's ratio and all the results indicated that the blend was having good flow property and hence better compression properties. The swelling studies were performed for the formulations and the results depicted that all the formulations have a good swelling index. The drug release studies depicted that the formulations release the drug in first order. So based on the results, formulation F3 was found to be an optimized formulation.

Keywords: Mucoadhesive, Acebutolol hydrochloride, gastrointestinal, metabolism

Introduction

Oral route is considered to be the most safest and convenient route of drug delivery. 90% of the drug available is designed to be given through the oral route due to patient acceptance. In conventional oral drug delivery, the drug resides for a shorter period time in absorption window, so bioavailability is less. Oral controlled drug delivery systems represent the most popular form of controlled drug delivery. This type of drug delivery systems releases the drug with constant or variable release rates to meet the drug regime.[1]The most preferable approach of oral controlled drug delivery is gastroretensive drug delivery systems (GRDDS), in which the dosage form retains in stomach for prolonged period increasing the Gastric residence time (GRT). GRDDS can be defined as a system which retains in the stomach for a sufficient period of time and releasing the active moiety in a controlled manner.[2] Over the last two decades, numbers of GRDDS have been designed to prolong GRT. The main aim of preparing GRDDS is to minimize the problem associated with existing oral sustained release dosage form and to develop patient benefited drug delivery.[3] A floating dose unit is beneficial for drugs that operate locally in the

proximal gastrointestinal system. Drugs that are insoluble or unstable in digestive fluids can also benefit from these systems. Floating system examples include floating pills and floating capsules[4]. The majority of drugs are effectively absorbed from all parts of the gastrointestinal tract, while some are only absorbed from a particular area. This is primarily because of the drugs' low permeability or solubility in the intestinal tract, their chemical instability, their binding to the contents of the gut, and their degradation by the microorganisms found in the colon[5]. Acebutolol is a cardio selective beta-1 blocker and has intrinsic sympathetic activity. It is most commonly used for the treatment of hypertension, arrhythmias, angina pectoris and acute myocardial infarction in high-risk patients. It is 2- acetyl-4-(butanoyl amino) phenyl ether, slightly soluble in water, methanol and highly permeable. It is characterized as a biopharmaceutical classification system (BCS) class III drug.[6-7]It is low protein-bound (26%) and possesses a short biological half-life of 3 to 4 h. The usual dose of Acebutolol is 400 mg per day. The conventional dosage form of Acebutolol leads to a lot of inconvenience and fluctuations in therapy, with some adverse effects like gastrointestinal disturbances, hypotension, bradycardia, heart failure and hepatotoxicity. Thus, devising sustained-release medication is a good alternative for reducing its dosing frequency, for prolonged effect with improved bioavailability, while also improving safety and efficacy of the medication.[8]

Materials and Methods

Materials

Acebutolol HCL was obtained as gift sample from Gift Sample from Cipla Laboratories Ltd Goa, HPMC K4M, Carbopol 940 was obtaied from Blue Cross Laboratory, Ltd, Nashik. Sodium bicarbonate, Citric acid was purchased from S.D Fine Chemicals. Talc, Magnesium stearate ect was purchased from Research-Lab Fine Chem. Industry, Mumbai. All chemicals used were analytical grade.

Methods

Preformulation Study of Drug

Organoleptic Properties:

The sample of Acebutolol was studied for Organoleptic characteristics such as color, odor and appearance.

Melting Point:

Melting point of Acebutolol was determined by taking a small amount of sample in a capillary tube closed at one end and placed in melting point apparatus. The melting point was noted in triplicate and average value was noted.

Determination of solubility

Solubility of Acebutolol was determined in distilled water, ethanol and 0.1 N HCL. All solutions were prepared and 10 mg of Acebutolol HCl was added to 10 ml of each solution placed in the 10 ml volumetric flask and kept aside for 24 hr. After 24 h of shaking, 1 ml of aliquot was taken out from each sample and filtered through Whatman filter paper. After suitable dilutions, absorbance was measured at 233 nm and calculations for solubility were done.

Partition coefficient

The partition coefficient of the drug was determined by taking equal volumes of n-octanol and aqueous phases in a separating funnel. 20 mg of drug was added to n-octanol:

water (20:20) and was taken in a separating funnel and shaken for 10 minutes and allowed to stand for 2 h. The aqueous phase was separated from organic phase. The aqueous phase was assayed using UV Spectrophotometer at 233 nm and amount of drug in organic phase was determined using difference to get partition coefficient.

Loss on drying

Weighed a glass Stoppard shallow weighing bottle that has been drying under same conditions that has been employed in the determination.1gm of the sample was transferred to the bottle. Covered it and accurately weighed the bottle and the contents. Distributed the sample evenly by gentle sidewise shaking of the bottle. Dried the substance in the hot air oven at 105^0 C for 2 h and after allowed it to cool. Weighed the contents and the bottle. Calculated the difference in the initial and final weight of the substance.

Preparation of calibration curve in 0.1 N HCl

The above made solution was further diluted to obtain concentration ranging from 2-10 µg/ml. The absorbance of the resulting solutions was recorded at 233 nm using UV-visible spectrophotometer. 0.1 N HCL was taken as a blank. Calibration plots were constructed and the linearity was established. Calibration curve was performed in triplicate.

Compatibility Study

Infra- Red Spectroscopy

Composition of Formulation Floating Mucoadhesive tablets of Acebutolol

Compatibility study was carried out by using Fourier Transform Infrared Spectrophotometer (BRUCKER). Physical mixture of drug and excipients were prepared and samples kept for 1 month at 40^0C. The infrared absorption spectrum of Acebutolol HCL and physical mixture of drug and excipient was recorded using diamond disc.

Differential Scanning Calorimetry

The powdered sample (3 mg) was hermetically sealed in aluminum pans and heated at a constant rate 10^0C/min, over a temperature range of 30-300^0C with nitrogen flow rate of 30ml/min. Thermograms of the samples were obtained using differential scanning Calorimetry (DSC-60, Shimadzu, Japan). Thermal analysis data were recorded with Shimadzu software programs. Indian standard was to calibrate the DSC temperature and enthalpy scale.

Development of Floating Mucoadhesive Tablets of Acebutolol HCL

Preparation of Floating Mucoadhesive Acebutolol HCL tablet by direct compression

Direct compression has been used to produce floating Mucoadhesive tablets. The pre-compression characteristics of the blended powder were evaluated before it was compressed on a 10-station pilot press with 10 mm flat faced punches. The machine was set to make a 300 mg tablet with an approximate weight.

Table No.1: Composition of Floating Mucoadhesive tablet formulations

(All values are expressed in mg)

Ingredients	Formulation code								
Quantity (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Acebutolol HCL	100	100	100	100	100	100	100	100	100
HPMC K4M	50	50	50	60	60	60	70	70	70
Carbopol 934	10	15	20	10	15	20	10	15	20
Sodium Bicarbonate	30	30	30	30	30	30	30	30	30
Citric acid	10	10	10	10	10	10	10	10	10
Talc	3	3	3	3	3	3	3	3	3
Mg Stearate	3	3	3	3	3	3	3	3	3
Spray dried Lactose	94	89	84	84	79	74	74	69	64
Total Weight	300	300	300	3000	300	300	300	300	300

Evaluation of floating Mucoadhesive tablets of Acebutolol

Precompression Characteristics

Precompression evaluation includes measurement of Bulk Density, Tapped Density, Hausner's Ratio, and Compressibility Index of prepared formulations.

Bulk Density (BD)

An accurately weighed powder blend from each formula was lightly shaken to break any agglomerates formed and it was introduced in to a measuring cylinder. The volume occupied by the powder was measured which gave bulk volume. Bulk density (BD) of powder blends was determined.

Tapped density (TD)

An accurately weighed powder blend from each formula was lightly shaken to break any agglomerates formed and it was introduced into a measuring cylinder. The measuring cylinder was tapped until no further change in volume was noted which gave the tapped volume. The tapped densities (TD) of powder blends were determined

Compressibility Index

The compressibility indices of the powder blends were determined

Hausner's Ratio

The Hausner's ratio is an indication of the compressibility of a powder. It is calculated by the formula. Hausner's Ratio = Tapped Density/ Bulk Density

Angle of repose (θ)

The angle of repose (θ) for powder was determined by placing the powder in a funnel. The tip of the orifice of the funnel was fixed from the ground horizontal surface at a height of 1cm and the powder were allowed to flow only under the force of gravity.

Evaluation of compressional characteristics floating tablets

Hardness test

The hardness of the tablets here was measured using Monsanto hardness tester (Cadmech). In this, was tablet is placed between the plungers, and was tightened from one end, and pressure required to break tablet diametrically was measured. The hardness was measured in terms of kg/cm^2.

Uniformity of Thickness

The uniformity of thickness was measured using Digital Vernier caliper (Absolute Digimatic, Mitutoyo Corp., Japan). The average diameter and thickness of the tablet was calculated.

Friability Test

In this test 20 tablets were weighed and placed in a Roche Friabilator test apparatus, and then the tablets were subjected to rolling ad replaced shocks, resulting from free falls within the apparatus from the height of 6 inches. After 100 revolutions the tablets were removed, de-dusted and weighed again. The friability was determined as the percentage loss in weight of the tablets.

Drug Content

Floating tablets were selected at random and drug content was determined as specified in monograph. The tablet preparation complies with the test, only if each individual content lies between 85 to 115% of the average content.

Swelling Index

The swelling properties of matrices containing drug were determined by placing tablet matrices in the dissolution test apparatus in 900 ml 0.1 N HCl at 37 ± 0.5^0C. The tablets were removed periodically from the dissolution medium and, after removing free water, the weight gain was measured. The swelling characteristics were expressed in terms of the percentage water uptake (WU %) according to the equation.

$$\% \text{ Swelling Index} = [W_2 - W_1] / W_1 \times 100$$

Where W_1 is the initial weight of the tablet and W_2 is the weight of the tablet after the particular swelling time interval.

***In-Vitro* buoyancy studies**

Three individual tablets from each formulation were put in an individual flask containing 400 ml of 0.1 N HCl solutions. Then note time in minutes for each tablet to go from the bottom to the top of the flask (floating lag time) and the time for which tablets constantly float on the water surface (duration of floating) were measured.

Mucoadhesive Strength

Force of Mucoadhesion

Bioadhesive Strength = (Bioadhesive Strength/1000) × 9.81

Bond Strength (N/m2) = Force of adhesion (N)/ Surface area of disk (m^2)

i) Measurement of adhesion force

The goat mucosa was removed from refrigerator and allowed to attain equilibrium with ambient conditions in the laboratory. The goat mucosa was carefully excised, without removing connective and adipose tissue and washed with simulated buffer solution. The tissue was stored in fresh simulated buffer solution. Immediately afterwards the membrane was placed over the surface of lower teflon cylinder (B) and secured. This

assembly was placed into beaker containing simulated buffer solution pH 6.8 at 37±2^{0}C. From each batch, some quantity of formulation (tablet) was taken an applied on the lower surface of the upper teflon cylinder. The beaker containing mucosal tissue secured upon lower cylinder (B) was manipulated over the base of the balance so that, the mucosal tissue is exactly below the upper cylinder (A). The exposed part of the formulation (tablet) was simulated buffer solution, and then a weight of 10 gms was placed above the expanded cap, left for 10 minutes. After which the formulation binds with mucin. The weight was removed. Then slowly and gradually weights were added on the right-side pan till the formulation separates from the mucosal surface/ membrane. The weight required for complete detachment is noted (W1) (W1-5025G) gives force required for detachment expressed in weight in grams. Procedure was repeated for two more times. Average was computed and recorded.

ii) Calibration of test equipment

Initially, a formulation from the same batch was taken ten times and individual force required for complete detachment was noted and S.D.was calculated.

iii) Force of adhesion (N) = (Bioadhesive Strength/1000) × 9.81

Bond strength (N/m^2) = force of adhesion (N)/surface area of disk (m^2)

***In-Vitro* Drug Release Studies**

The samples were withdrawn at predetermined time points, diluted 10 times and were analyzed spectrophotometrically at 233 nm. *In-Vitro* drug release was performed for all prepared batches (F1-F9) and % cumulative drug release was computed.

Drug release kinetic study

In order to investigate the mode of release from the tablets the release data were analyzed with the mathematical models

Stability study

Stability studies were conducted to test the physical and chemical stability of the tablet at different stability conditions. The optimized formulation was subjected to stability study. These tablets were subjected for a period of three months as per ICH guideline at the 40^{0}C temperature and relative humidity 75% RH. The samples were withdrawn at, 1, 2, and 3 months for given temperature condition. The formulations were evaluated mainly for drug content and % drug release at the predetermined intervals.

Results and discussion

Preformulation study- Organoleptic Properties

Table No.2: Organoleptic Properties of Acebutolol

Identification test	Result of sample obtained	Reported standards
Colour	White	White
Odour	Odourless	Odourless
Melting point	141-143°C	142-143°C
Partition coefficient	1.53	1.49
Loss on drying	0.01 % w/v	NMT 0.5 % w/v

Solubility

Table No. 3: Solubility in different solvents

Sr. No	Solvent	Observation
1	Water	197.12 mg/mL
2	Ethanol	72.85 mg/mL
3	0.1 N HCl	68.36 mg/mL

Ultraviolet - Visible Spectroscopy Study

Calibration curve of Acebutolol HCL in 0.1 N HCl

The prepared stock solution of drug was subsequently diluted with 0.1 N HCl to get 2 µg, 4 µg, 6 µg, 8 µg and 10 µg of drug per ml. Then the absorbance of these dilute solutions was measured at λ_{max} of 233 nm by U.V. spectrophotometer against a blank of 0.1 N HCl. The calibration curve was found to be linear in the concentration range of 2-10 µg/ml having coefficient of regression value $R^2 = 0.9998$ and Slope y = 0.0808.

Table No.4: Absorbance of Acebutolol in 0.1 N HCl at 233 nm

Sr. No.	Concentration (ppm)	Absorbance
1	2	0.160
2	4	0.324
3	6	0.489
4	8	0.638
5	10	0.812

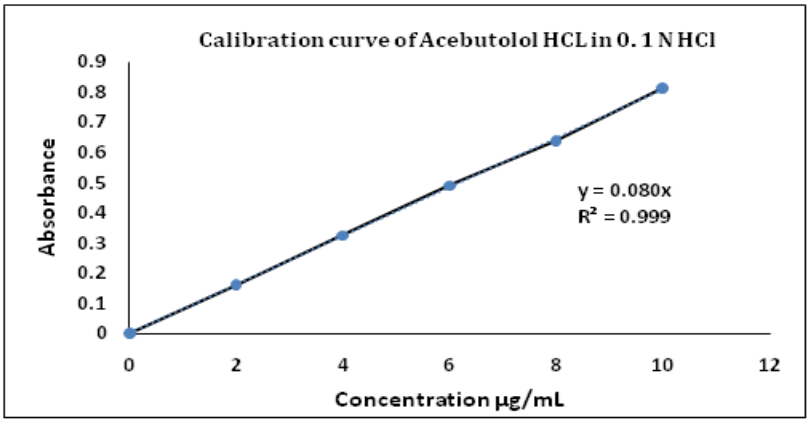

Figure No.2: Calibration curve of Acebutolol HCL in 0.1 N HCl

Infra-Red Spectrum of Acebutolol HCL

The Infra-Red spectrum of Acebutolol HCL is shown in figure

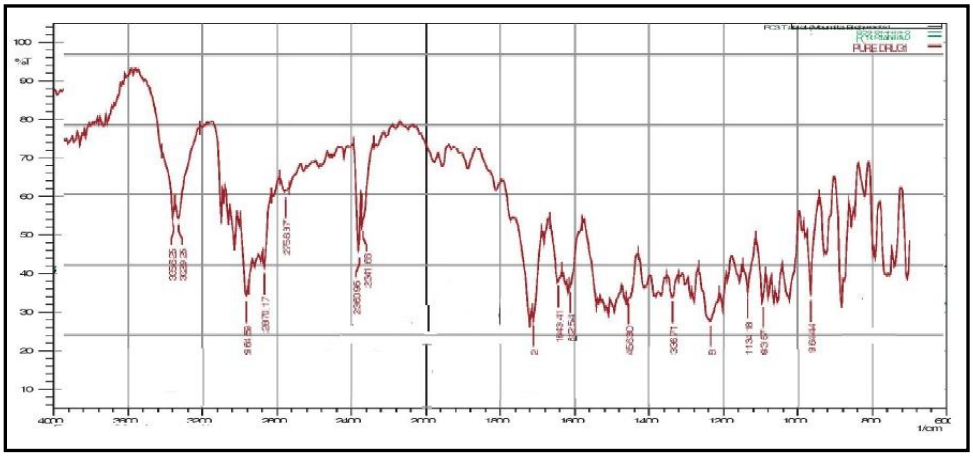

Figure No.3: FTIR Spectrum of Acebutolol HCL

The FTIR spectra of pure Acebutolol HCL showed the peaks at wave numbers (cm^{-1}) which correspond to the functional groups present in the structure of the drug and confirms the identity of pure drug.

Differential Scanning Calorimetry

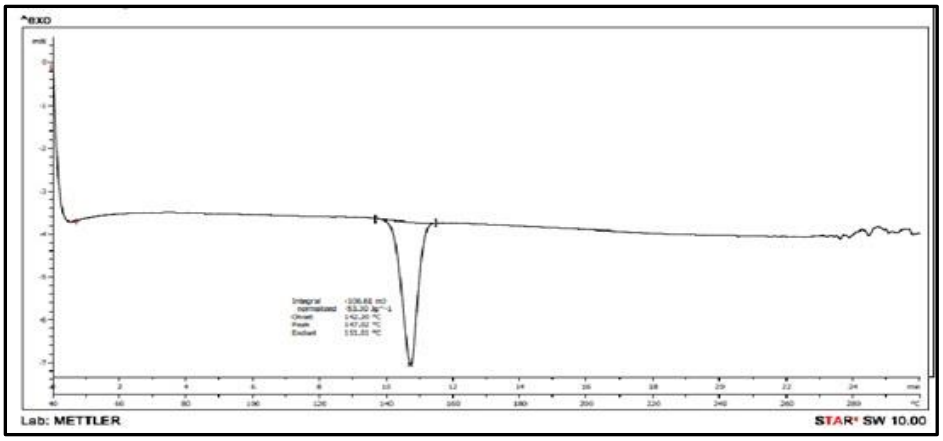

Figure No.4: DSC Thermogram of Acebutolol HCL

Table No.6: DSC Thermogram of Acebutolol HCL was interpreted

DSC Analysis	
Reported Standard in literature	**Observed**
141-143^{0}C	141^{0}C

The DSC curve of Acebutolol HCL showed a sharp endothermic peak at 141^{0}C corresponding to its melting, which confirm that purity of the drug. The drug did not decomposed followed by its melting.

Compatibility study

Fourier Transform Infrared Spectroscopy

The characteristic absorption peaks of drug Acebutolol HCl was remained unchanged in drug-polymer admixture which indicates that there is no prominent chemical reaction between drug and polymer mixture, proving compatibility of drugs with selected excipients for the study.

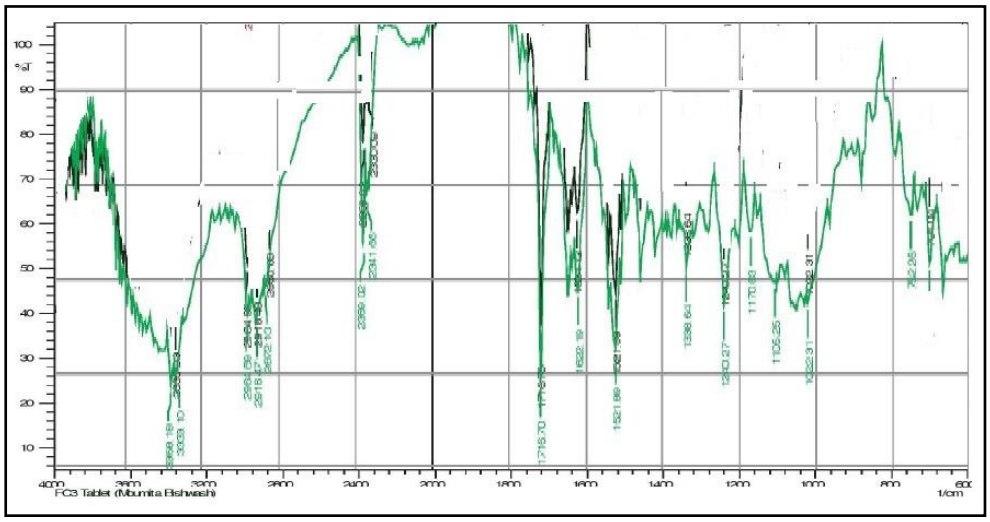

Figure No.5: IR Spectrum of Physical mixture of drug and excipients

Table No.7: Interpretation of IR spectra physical mixture of Acebutolol HCL and excipients

Functional group	Peaks	
	Pure drug	Physical mixture
C=O stretching	Yes	Yes
C-H stretching	Yes	Yes
C-N stretching	Yes	Yes
C-O stretching	Yes	Yes
C-H stretching	Yes	Yes
C-H stretching	Yes	Yes

Differential Scanning Calorimetry

The thermal behavior of drug and physical mixture of drug and polymer was studied by using DSC Thermogram. DSC thermogram of drug exhibited characteristic peak at 141^0C and physical mixture exhibited characteristic peak at 139.42^0C. DSC analysis was performed for pure acebutolol HCl and physical mixture of drug with various excipients. For physical mixtures, in all the cases melting endotherm of drug was well preserved with little or no change in enthalpy value of drug indicating compatibility of both drugs with selected excipients in the study shown in fig. The polymers HPMC K4M and carbopol 934 have been reported to be compatible with a number of drugs.

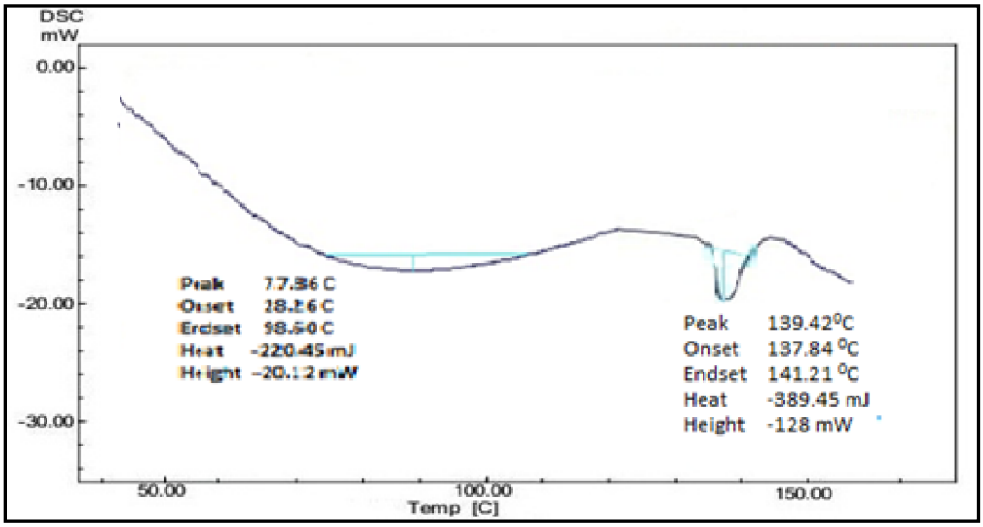

Figure No.6: DSC Thermogram of physical mixture of drug and excipients

Evaluation of floating tablet formulations of Acebutolol HCl

Evaluation of pre-compressional parameters

Before compression powder bed of all formulations were studied for various rheological characteristics bulk density, true density, compressibility index and Hausner's ratio shown in table. The results of the studies indicated that the powder bed is easily compressible and hence can be compressed into a compact mass of tablets. The uniformly blend of powder was then compressed in a 10-station tablet punching machine using 12 mm flat faced punches.

Table No.8: Evaluation of pre-compressional characteristics of floating tablets

Formulation code	Bulk density (gm/ml ±S.D.)	Tapped density (gm/ml ±S.D.)	Angle of Repose (θ±S.D.)	Compressibility index (%±S.D.))	Hausner's ratio (n=3)
F1	0.352±0.0040	0.416±0.0043	29.27±0.63	15.27±0.11	1.18±0.015
F2	0.365±0.0035	0.425±0.0042	28.62±0.57	14.01±0.10	1.16±0.005
F3	0.374±0.0032	0.412±0.0098	28.63±0.50	9.23±0.69	1.10±0.008
F4	0.387±0.0037	0.435±0.0026	26.57±0.56	11.02±0.55	1.12±0.006
F5	0.383±0.0032	0.442±0.0026	27.82±0.61	13.38±0.72	1.15±0.009
F6	0.361±0.0015	0.410±0.0025	27.64±0.54	12.03±0.24	1.13±0.003
F7	0.380±0.0036	0.459±0.0064	27.29±0.37	17.13±0.46	1.20±0.006
F8	0.376±0.0035	0.442±0.0060	29.35±0.52	14.80±0.16	1.17±0.024
F9	0.379±0.0021	0.441±0.0049	29.53±0.42	13.91±0.13	1.16±0.018

Evaluation of compressional characteristics of floating tablets

The results of thickness, hardness, drug content, % friability and swelling index for all tablet formulations are summarized in the table.

Table No.9: Evaluation of compressional characteristics of floating tablets

Formulation code	Hardness (kg/cm^2)± S.D.	% Drug content ± S.D.	Friability (%± S.D.)	% Swelling index	Thickness (mm)	Weight Variation mg
F1	3.42±0.058	88.35±0.040	0.166±0.033	34.07±0.67	3.76 ±0.26	298.13± 1.7
F2	3.51±0.074	89.00±0.027	0.219±0.047	40.73±0.74	3.87±0.15	299.81±0.01
F3	3.54±0.077	98.42±0.018	0.296±0.081	51.55±0.89	3.98±0.21	300.07±0.01
F4	3.32±0.055	91.69±0.029	0.341±0.181	42.22±0.89	3.91±0.41	298.3±0.023
F5	3.53±0.050	90.61±0.010	0.368±0.041	43.70±0.67	3.99±0.68	299.19±1.69
F6	3.58±0.079	95.53±0.017	0.372±0.028	44.88±0.44	3.90±0.12	298.12±0.16
F7	3.56±0.085	93.22±0.023	0.511±0.026	46.07±0.67	3.90±0.49	300.8±0.018
F8	3.57±0.05	92.65±0.030	0.534±0.33	47.25±2.10	3.91±0.16	299 ± 0.018
F9	3.77±0.011	95.14±0.025	0.610±0.23	47.40±0.68	3.93±0.08	300.35±0.15

In-Vitro buoyancy studies

The tablets were placed in 400 ml 0.1 M HCl in a beaker and the time required to rise to the surface and float (floating lag time) and the duration of time floating on the dissolution medium (total floating time) were determined. Floating lag time of all formulations was within the range 33-100seconds. All formulations floated in the 0.1 M HCl for more than 11 h showing good matrix integrity during this extended period of time. The results showed that as the concentration of HPMC K4M (X1) release retardant increased, the floating lag time increased. The floating lag time was decreased as the concentration of hydrophilic polymer carbopol 934 was increased due to the increasing hydrophilic nature of the polymer allowing penetration of liquid through pores formed on the Surface of the tablet, and the total floating time increased due to swelling of the tablet which keep it intact for a longer period of time. It was also found that the total floating time increased and the floating lag time decreased with increase in the HPMC K4M concentration. Sodium bicarbonate is necessary in formulations to make them float. It does this through reaction with acid to liberate CO_2, which gets trapped within the gel formed by hydration of polymer thus decreasing the tablet density to below $1g/cm^3$.

Table No.10: Floating duration time and Floating lag time

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Total Floating time (h)	11	12	12	13	14	14	14	14	15
Floating lag time (sec)	45	55	33	78	69	85	100	95	97

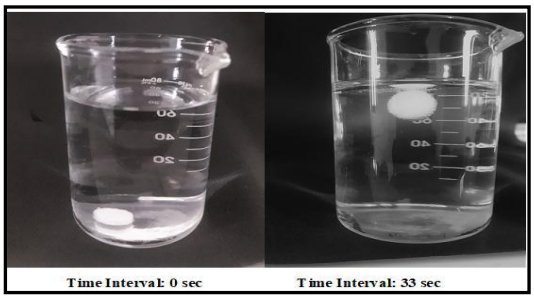

Figure No.7: Floating lag time of optimized tablet formulation F3

Mucoadhesive Strength

Table No.11: Mucoadhesive Strength and force of tablet

Formulation code	Mucoadhesive Strength (gm)	Mucoadhesive force (dyne) N
F1	10.15 ± 0.56	0.5657
F2	11.03 ± 0.02	0.6147
F3	20.05 ± 0.01	1. 1175
F4	12.50 ± 0.02	0.6967
F5	16.21 ± 0.07	0. 9035
F6	13.18 ± 0.01	0. 7346
F7	18.17 ± 0.05	1. 0127
F8	17.17 ± 0.01	0.9569
F9	16.85 ± 0.01	0.9391

In vitro drug release studies

The drug release shows that as the concentration of polymer goes on increasing the drug release also goes on decreasing and as well as time for drug release will be more sustained or release time will also goes on increasing, but we want more and optimize release at 12 h., it was shown by F3 batch 98.35 ±2.08. Hence, F3 batch was taken as optimize formulation due to highest drug release up to 12 h.

Table No.12: Percent % drug release of different Formulations (F1-F9)

Time (hr.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	6.36 ±1.98	6.64 ±5.95	7.57 ±2.15	9.12 ±2.42	7.78 ±2.06	8.84 ±1.90	8.06 ±2.02	4.90 ±2.10	5.70 ±1.53
2	17.29 ±2.38	21.68 ±1.93	19.27 ±2.25	15.79 ±1.74	16.43 ±2.83	16.67 ±2.32	15.58 ±4.11	10.15 ±2.04	10.57 ±2.08
3	25.42 ±2.06	27.57 ±1.83	25.14 ±2.05	25.34 ±2.31	19.06 ±1.99	23.18 ±2.50 1	17.46 ±2.05	19.25 ±2.07	12.86 ±2.84
4	35.88 ±2.52	31.58 ±2.54	32.99 ±2.21	31.70 ±1.58	21.81 ±2.61	29.81 ±2.49	18.03 ±2.56	24.45 ±2.83	23.46 ±2.01
5	39.84 ±1.87	39.84 ±2.22	40.14 ±1.94	42.31 ±2.41	25.34 ±1.91	36.72 ±1.92	22.24 ±1.93	30.41 ±1.95	30.41 ±1.90
6	46.40 ±2.02	48.55 ±2.39	48.55 ±2.11	47.24 ±2.15	28.29 ±2.15	38.05 ±1.9	33.08 ±2.07	37.90 ±1.90	39.25 ±1.89
7	55.16 ±2.10	57.31 ±2.62	57.39 ±1.99	53.01 ±1.94	31.84 ±1.95	45.69 ±2.34	36.87 ±2.00	45.43 ±1.43	47.58 ±4.95
8	61.10 ±2.04	65.66 ±2.19	68.37 ±2.04	62.00 ±2.17	43.97 ±2.06	49.72 ±2.06	45.22 ±2.15	53.01 ±2.11	50.86 ±2.47
9	64.98 ±2.07	73.26 ±2.04	75.24 ±2.54	69.41 ±2.00	54.99 ±2.00	65.32 ±1.98	53.29 ±2.01	62.43 ±1.92	55.16 ±1.81
10	71.44 ±2.64	80.21 ±2.03	82.71 ±2.36	76.94 ±1.86	64.87 ±1.63	76.74 ±2.45	65.36 ±2.56	70.44 ±1.36	59.30 ±1.56
11	76.73 ±2.42	79.53 ±2.69	86.63 ±1.96	79.53 ±2.62	82.36 ±1.25	83.18 ±2.48	70.61 ±2.00	75.90 ±2.33	65.37 ±2.06
12	84.53 ±2.48	84.48 ±2.09	98.35 ±2.08	82.72 ±2.08	89.63 ±1.98	90.82 ±2.63	86.43 ±2.53	79.87 ±1.88	72.97 ±1.32

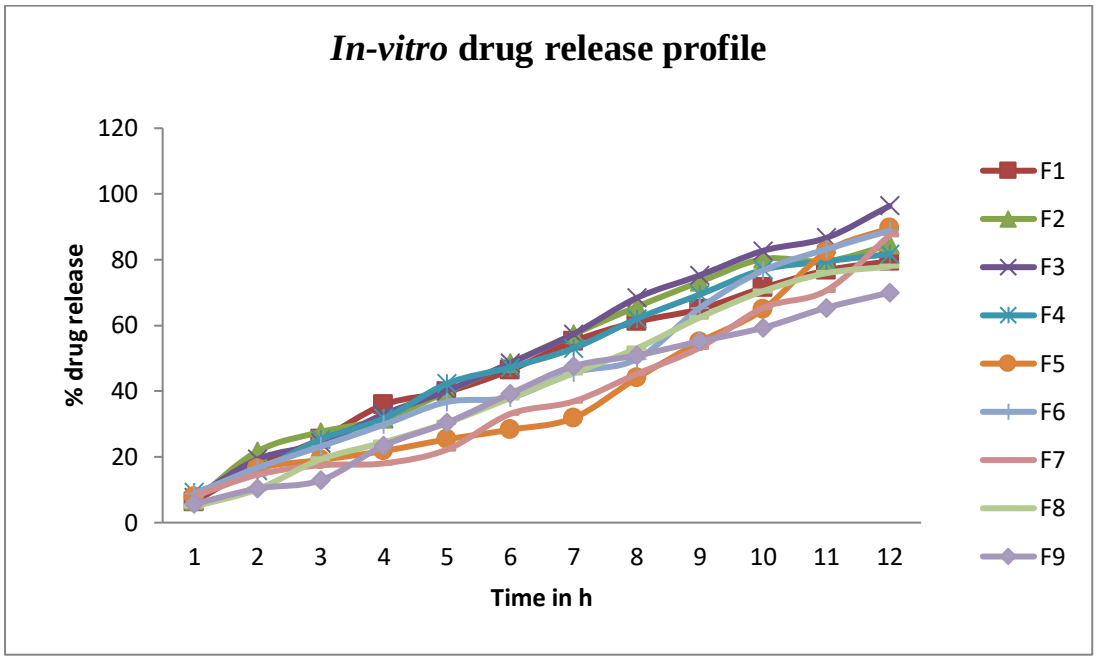

Figure No.8: Dissolution Profile of Formulation Batches (F1-F9)

F3 formulation and Marketed Formulation

Table No.13: Percent cumulative drug release of F3 and Marketed Formulation.

Time (hrs.)	% drug release	
	F3 Batch	Marketed formulation
1	7.57	5.56
2	19.27	13.63
3	25.14	21.69
4	32.99	28.96
5	40.14	37.42
6	48.55	50.56
7	57.39	46.31
8	68.37	55.23
9	75.24	66.41
10	82.71	77.13
11	86.63	82.29
12	96.15	84.66

Stability Studies

The stability study for optimized formulation F3 was conducted at 40^0 C, 75% RH as per ICH guideline. The formulation F3 were evaluated for the drug content and *in-vitro* % drug release after 8 days, 15 days, 1, 2 and 3 months. It was also observed that there was no significant variation in the physical appearance, average weight, hardness and loss of drying after placing the tablets at various temperature and humidity conditions for a period of 3 months.

Table No.18: Stability study for optimized formulation F3 at 40±2ºC+75% RH

Frequency of testing	Drug content (% ± S.D.)	Mucoadhesive strength (gm± S.D.)	% Drug release at 12 h (% ± S.D.)
	Formulation F3		
0	98.68±0.26	20.61±1.02	99.10±1.75
8 days	98.42±0.10	20.12±1.23	98.20±0.99
15 days	99.52±0.25	20.10±1.12	99.74±1.74
1 month	98.25±0.10	20.00±0.98	98.45±1.35
2 months	98.16±0.56	21.10±1.04	99.12±2.15
3 months	98.02±0.45	21.31±1.12	97.46±1.14

Conclusion

The absorbance, melting point, and solubility in water and other solvents of Acebutolol HCl were investigated. The effects of several polymers, including HPMC K4M and Carbopol 934, on the Mucoadhesive strength and release kinetics of floating Mucoadhesive tablets of Acebutolol HCL have been studied through experiments. Studies on in-vitro dissolution were carried out in apparatus II (using a paddle) for 12 hours at 50 rpm. It was shown by F3 batch 98.35 ±2.08. Hence, F3 batch was taken as optimize formulation due to highest drug release up to 12 h. The formulation F3 were evaluated for the drug content and *in-vitro* % drug release after 8 days, 15 days, 1, 2 and 3 months. It was also observed that there was no significant variation in the physical appearance, average weight, hardness and loss of drying after placing the tablets at various temperature and humidity conditions for a period of 3 months.

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