Original Article

Formulation and Evaluation of Mucoadhesive Buccal Films of Propafenone HCl

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Abstract

Buccal drug delivery is the most suited route for local as well as systemic delivery of drugs. Conventional tablet (150mg) Propafenone HCl (PP) is available in market is used three times a day for effective treatment of supraventricular tachyarrhythmiasis. The oral absorption of Propafenone HCl is dose highly variable, with short biological half life 1.0 hr and has high first-pass metabolism leading to low bioavailability. Decrease in frequency of high dose drug via buccal drug release. There is a need to formulate mucoadhesive buccal film of PP that promotes systemic delivery, bypass of hepatic first pass metabolism and improved bioavailability and reduce the repeated administration. PP buccal films were prepared by a solvent-casting technique using various concentrations of mucoadhesive-polymers such as Hydroxyl propyl methyl cellulose (HPMC) K4M, K15M and K100M as film forming as well as rate retarding polymer with different combinations of mucoadhesive polymers like Sodium CMC, Hydroxy Propyl Cellulose (HPC), propylene glycol (PG) was selected as plasticizer and ethyl-cellulose as backing-layer, which acts like a patch providing unidirectional drug release. Prepared films were evaluated for their weight variation, thickness, surface-pH, swelling-index, and drug content uniformity, in vitro residence time, folding endurance, tensile strength and *in vitro* release and permeability studies. The Fourier Transform Infra-Red (FTIR) spectra and DSC thermogram showed no interaction, and Physico-chemical characteristics were found within the limit. All the developed buccal films exhibited optimal physico mechanical and pharmaceutical characteristics. From the *in vitro* drug release studies, this study concluded that the buccal film was successfully formulated by using a combination of HPMC K100M and HPC with the potential drug retardant characteristics compared with the polymers HPMCK4M and HPMCK15M by increasing its contact time and controlling the release. The optimized formulation followed zero order kinetics. The formulation of PP mucoadhesive buccal film was found to be satisfactory and reasonable. The *in vivo* pharmacokinetic study was conducted in healthy rabbits and it was observed from the results that the oral bioavailability of optimized formulation (PP18) was increased significantly when compared to the marketed formulations. Relative bioavailability with respect to marketed formulation (Rythmol) was found to be 124.9. The increased bioavailability may be due to the mucoadhesive mechanism of dosage form in buccal area for longer duration.

Keywords: Buccal film, Mucoadhesive Polymers, Propafenone HCl, Solvent-casting method

INTRODUCTION

Muco-adhesive buccal films may be preferred over adhesive tablets in terms of flexibility and comfort and they do not get easily washed away or removed by saliva as may in case of oral gels (1).

The rich vascularization of the oral mucosa and its permeability too many drugs makes this route an attractive alternative to oral or parenteral route for systemic drug delivery (2)

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Over the last two decades the term mucoadhesion attracted the researchers for its potential to optimize localized drug delivery, by retaining a dosage form at the site of action or systemic delivery, by retaining a formulation in intimate contact with absorption site (in the buccal cavity) (3). The oral Trans mucosal drug delivery bypasses liver and avoids pre-systemic elimination in the gastro intestinal tract and liver. These factors make the oral mucosa a very attractive and feasible site for systemic drug delivery (4). Buccal film is a non-dissolving thin matrix modified release dosage form composed of one or more polymer films or layers containing the drug and/or other excipients (5). Buccal drug delivery is a highly effective way to increase bioavailability. This is because the buccal mucosa has a rich in blood supply which facilitates the direct entry of the drug into the systemic circulation. In addition, buccal dosage forms allow drug absorption to be rapidly terminated in case of an adverse reaction. Formulations of buccal dosage forms include- tablets, gels and patches of which patches are preferable in terms of flexibility and comfort (6). In addition they can circumvent the relatively short residence time of oral gels on the mucosa, which are easily washed away and removed by saliva (7).

Propafenone HCl (PP) is a Class 1C antiarrhythmic drug which is having direct stabilizing action on myocardial membrane as well as a local anaesthetic effect. It is mainly used in the treatment of supraventricular Tachyarrhythmiasis. PP has a short half-life i.e. about 2-10 hrs and low bioavailability. It is also having a narrow absorption window. Because of this the drug has to be taken frequently. The usual dose is 150 mg to taken three times a day or 300 mg twice a day. Moreover absorption site of PP is a GI tract. In the treatment of cardiac arrhythmias, angina and hypertension, a loading as well as maintenance dose is required (8, 9). The present research work is aimed at formulating and evaluating mucoadhesive buccal films to act as transmucosal drug delivery systems containing the drug PP in order to improve oral biological half life and oral bioavailability.

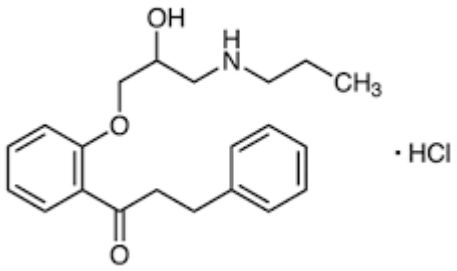

Figure 1: Structure of Propafenone HCl

Materials And Methods

Propafenone Hydrochloride (PP) obtained from Mylan laboratories Hyderabad, HPMC K4M, HPMC K15M, HPMC K100M and Ethyl cellulose, Sodium CMC, HPC were gift samples from Colorcon Pvt. Ltd. Verna, Goa. All other chemicals and reagents were analytical and pharmacopeial grade.

Methods

Drug-excipient compatibility study

Fourier Transforms Infra Red (FTIR) spectroscopy

Compatibility studies were carried out to know the possible interactions between Propafenone HCl and excipients used in the formulation.

Differential Scanning Calorimetry (DSC)

The physicochemical compatibilities of the drug and the excipients were tested by differential scanning calorimetric (DSC) analysis. DSC thermograms of the drug alone and optimized formulation were derived from DSC (DSC 4000, Perkin-Elmer, New York, NY) (10).

Determination of Absorption maximum (λ_{max}) of Propafenone HCl

From the UV spectrophotometric analysis it was conclude that the drug, Propafenone HCl showed a λ_{max} at 303 nm. Therefore the observed λ_{max} was used for further work to analyze the test samples.

Calibration curve

The calibration curves for Propafenone HCl in pH 6.8 was developed spectrophotometrically at 303 nm and further developed in 0.1 N HCl, phosphate buffer pH 6.8, pH 7.5 (11).

Preliminary Solubility studies Propafenone HCl

The solubility of Propafenone was determined by adding excess amount of drug in the solvent and equilibrium solubility was determined by taking the supernatant and

analyzing it spectro-photo metrically with water, 0.1N HCl, Methanol, 6.8 pH buffer, chloroform and Alcohol by using the following formula:

% solubility=sample absorbance/ standard absorbance *dilution factor*100

Preparation of Mucoadhesive buccal films of Propafenone HCl

The films containing Propafenone HCl were prepared by solvent casting technique. Different formulations were developed using HPC and Sodium CMC as mucoadhesive release rate retarding polymers and HPMCK4M, HPMCK15M and HPMCK100M as film forming as well as release rate retarding polymers (12). Propylene glycol was used as plasticizer. Different formulations of mucoadhesive films were shown in tables 1, 2 and 3. The backing membrane was prepared by dissolving Ethyl cellulose (5%) in mixture of Acetone and Isopropyl alcohol (65:35), and 20 % dry weight of polymer of Dibutyl phthalte as plasticizer. The plasticized Ethyl cellulose solution was poured in to a petri dish on level surface and solvent was allowed to evaporate at controlled rate by covering the mould with inverted glass funnel, to avoid blistering effect on dried films. The calculated quantities of polymers were dispersed in Ethanol and water. An accurately weighed drug was incorporated in polymeric solutions after levigation with propylene glycol (PG) which served the purpose of plasticizer as well as permeation enhancer. The Drug polymer solution was subjected to sonication in a bath sonicater to remove the air bubbles. The plasticized polymeric solution was poured in to mould containing a backing membrane and was dried in vacuum oven at 50ºC for 24 h. The dried bilayer films were cut into square pieces of sides 2 cm containing 150 mg of drug per film, and then were packed in aluminum foil and stored in desiccator and used for further studies.

Table 1: Composition of various Propafenone HCl mucoadhesive buccal film formulations with HPMCK4M

Formulation Code	*Propafenone HCl (mg)*	*HPMC K4M (mg)*	*Sodium CMC (mg)*	*HPC (mg)*	*Ethanol (ml)*	*Water (ml)*	*PG (ml)*
PP1	150	200	100	-	6	3.5	0.5
PP2	150	200	200	-	6	3.5	0.5
PP3	150	200	300	-	6	3.5	0.5
PP4	150	200	-	100	6	3.5	0.5
PP5	150	200	-	200	6	3.5	0.5
PP6	150	200	-	300	6	3.5	0.5

Table 2: Composition of various Propafenone HCl mucoadhesive buccal film formulations with HPMCK15M

Formulation Code	*Propafenone HCl (mg)*	*HPMC K15M (mg)*	*Sodium CMC (mg)*	*HPC (mg)*	*Ethanol (ml)*	*Water (ml)*	*PG (ml)*
PP7	150	200	100	-	6	3.5	0.5
PP8	150	200	200	-	6	3.5	0.5
PP9	150	200	300	-	6	3.5	0.5
PP10	150	200	-	100	6	3.5	0.5
PP11	150	200	-	200	6	3.5	0.5
PP12	150	200	-	300	6	3.5	0.5

Table 3: Composition of various Propafenone HCl mucoadhesive buccal film formulations with HPMCK100M

Formulation Code	*Propafenone HCl (mg)*	*HPMC K100M (mg)*	*Sodium CMC (mg)*	*HPC (mg)*	*Ethanol (ml)*	*Water (ml)*	*PG (ml)*
PP13	150	200	100	-	6	3.5	0.5
PP14	150	200	200	-	6	3.5	0.5
PP15	150	200	300	-	6	3.5	0.5
PP16	150	200	-	100	6	3.5	0.5
PP17	150	200	-	200	6	3.5	0.5
PP18	150	200	-	300	6	3.5	0.5

Characterization of Buccal Films

Evaluation of Propafenone HCl mucoadhesive buccal film

Appearance

Visual inspection of mucoadhesive buccal films was assessed for their appearance of visible imperfections and surface texture of films was analyzed by feel or contact (13).

Weight variation

Three films of every 9 films of 2×2 cm^2 for each formulation were weighed individually and calculated. A calibrated electronic weighing balance is used for weighing mucoadhesive buccal film. The mean weight of all films is calculated (14).

Thickness

A calibrated digital micrometer screw gauge is used to determine the thickness of the mucoadhesive buccal film. The thickness of films was measured at five different points (four on the corners and one in the center) (15).

Folding endurance

Folding endurance of the films was determined by repeatedly folding the small strip of size (2×2 cm^2) at the same place till it breaks. The numbers of times the film can be folded at the similar place without breaking give the value of folding endurance (16).

Tensile strength

Mucoadhesive buccal film of size 2×2 cm^2 was placed between the clamp of the stand & clip through which the weighing pan was attached above the ground level in the air. Measurement of tensile strength of the film the weights were added to the pan till the film breaks (17). Calculated by the following equation:

Tensile strength = Force at breakage (kg)/ Film thickness (mm) × film width (mm)

Unit Kg/cm^2, Multiply Kg/cm^2 by 0.098 (acceleration due to gravity) to get N/mm^2.

Mucoadhesive strength

The mucoadhesive strength is determined by a modified analytical balance. Mucoadhesive buccal film is placed on the glass slide by placing a drop of water on slide on the one side of analytical balance another end weighing pan was attached. Weight was slowly added to the pan until glass slide get detached from film. Weight required to detach the film from the glass slide is measured as mucoadhesive strength (18).

Surface pH

For determining the surface pH of mucoadhesive buccal film, three buccal films of each formulation were allowed to swell for 15 min at room temperature in the contact of 1 ml distilled water (pH 6.8±0.5), and the pH was determined by bringing the electrode in contact of buccal film surface and allowing equilibrate for 1 min (19).

Drug content uniformity

Film of dimension 2×2 cm^2 was added in 100 ml of phosphate buffer pH 6.8, stirred continuously in bench top orbital shaker for 24h. Additionally, this solution was filtered, suitably dilution, and analyzed at 303 nm (20).

Swelling index

Swelling index was determined by positioning the buccal film of size 2×2 cm^2 pre-weighed on wire mesh placed into a clean petri plate filled with 15 ml of pH 6.8 PBS. Buccal film weight was measured at the regular interval till it remained constant. Calculated by using the following formula (21).

$$\text{Swelling index (SI)} = \{(W-Wo) / Wo\} \times 100$$

Where; SI = Swelling index (%), Wo = Initial weight of film, W = Final weight of film

Percentage moisture Absorption

In order to evaluate the films of dimension 2×2 cm^2 were weighed and accurately placed in the desiccator at room temperature for 3 days with saturated ammonium chloride solution and maintained 79.5% Relative Humidity. The films were taken out and weighed after 3 days (22). Calculated using the following formula.

Moisture absorption (%) = Final weight-Initial weightx100/Initial weigh

Percentage moisture loss test

In an evaluation of percent moisture loss, the accurately weighed film was placed in the desiccator containing calcium chloride (fused anhydrous) for 3 d. After 3 d the film was reweighed, percentage moisture loss was calculated by the following formula (23).

Moisture loss (%) = Initial weight - Final weightx100/Initial weight

Residence time

Residence time of film was obtained on goat mucosal surface. A film of dimension 2×2 cm^2 was placed on outer layer of mucosa, and both the layer were put into the petri

plate filled with 5 ml of PBS pH 6.8. After that the petri plate was placed in bench top orbital shaker at 50 rpm at 37ºC.

Determined by the time at which buccal film disintegrates on buccal mucosa (24).

In vitro drug release

For *in vitro* drug release study IP type II apparatus (Basket type) dissolution test apparatus containing 250 ml of PBS of pH 6.8 as a dissolution medium at 37±0.5^{O}C temperature and speed at 50 rpm. 5 ml of sample solution was withdrawn at time intervals of 30 min, 1h, 1.5h, 2h, 3 h, 4h, 5h, 6h, 7h and 8h then equilibrated with a new or fresh dissolution medium to maintain sink state. Drug release was analyzed spectrophotometrically at a λ_{max} of 303 nm (25).

Ex vivo permeation studies

The *ex-vivo* permeation studies were carried out using a modified Franz diffusion cell. The mucoadhesive buccal film of Propafenone HCl through an excised layer of goat buccal mucosa (washed in isotonic phosphate buffer (pH 6.8) after excised and trimming from the sides) was obtained from local slaughterhouse. The receptor compartment of Franz diffusion cell containing phosphate buffer of pH 6.8 (20 ml) medium and mini magnetic bead was placed in receptor compartment. A mucoadhesive buccal film of the dimension of 2×2 cm² optimized batch was placed over the goat buccal mucosal membrane fitted between the donor and receptor compartment. The whole assembly was placed on a magnetic stirrer; the temperature was maintained at 37±0.5ºC at 50 rpm. 0.5 ml of the sample was withdrawn from the receptor compartment side chain and replace with fresh medium at a regular time interval of 30 min, 1h, 1.5h, 2h, 3 h, 4h, 5h, 6h, 7h and 8h. Suitable dilution was carried out and was spectroscopically analyzed at a λ_{max} of 303 nm and to determine the amount of drug permeated (26).

In vitro drug release kinetics

Kinetic models are used to describe the drug release from immediate and modified release dosage forms. In order to determine the kinetics and mechanism of drug release from prepared patches of different drug and polymer ratios the release data were examined using various models such as Zero order kinetic, First order kinetic, Higuchi kinetic and Korsmeyer-Peppas model. n = diffusional release exponent indicative of release mechanism. The 'n' value could be used to characterize different release mechanisms as follows n = 0.5 means Fickian diffusion, 0.5 < n <1.0 non-Fickian diffusion, and n = 1.0 case II diffusion (27).

Stability studies

A stability study of optimized formulation was executed as per ICH guidelines. The single film of dimension 2×2 cm² was wrapped individually in butter paper followed by packing in aluminum foil and maintained at room temperature 25±2ºC and 60±5% RH and placed in accelerated stability condition at 40±2ºC and 75±5% RH for the period of 3 months. Changes in appearance, folding endurance, tensile strength, Swelling index, Residence time, drug content, pH, % drug release of the stored mucoadhesive buccal film were analyzed at a regular interval for 3 months (28).

In Vivo Studies

In vivo experiments were performed after approval of the protocol from Institutional Animals Ethics Committee (Registration No. IAEC12/ASPEN/2019). It follows the systematic procedure (29).

Bioanalytical method development of Propafenone hydrochloride

i. Chromatographic conditions

The reverse phase HPLC (RP-HPLC) analysis was carried out using Elico double beam SL 210 UV-visible spectrophotometer having Deuterium lamp at λmax 303 nm. HPLC analysis was performed with Agilent 1260 infinity DAD detector using Eclipse XDB C18 column with 5 µm particle size having dimensions 4.6 X 250 mm column, 1260 infinity quaternary pump using Ezchrome software at a flow rate of 1 ml/min and a run time pressure of 2140 psi. The mobile phase used was 0.01mmono basic Potassium phosphate buffer: Acetonitrile (40:60) and the effluents were analyzed at 303 nm at a flow rate of 0.7 ml per minute. This RP-HPLC method was used for the determination of PP (internal standard) in rabbit plasma. The Injection volume was 20 µL. The running time was 10 min for each sample. Ambient temperature was maintained throughout the running time.

ii. Standard solutions

Sample was prepared by adding 400 µL of acetonitrile solution to 100 µL of freshly withdrawn serum. After vortex for 1min and then centrifuged at 4500 x g for 30 min, the clear supernatant liquid was transferred to another microtube and evaporated to dryness. The residue was reconstituted with 100 µL of mobile phase, and 20 µL of this solution was subjected to HPLC analysis.

iii. Extraction

Rabbit blood containing heparin as an anticoagulant was used for the preparation of calibration standard. Calibration standard solution samples were freshly prepared in rabbits plasma by adding to 0.5 mL of plasma appropriate aliquots

of working standard solutions to yield concentration of 25, 50, 100, 150 and 200 µg / mL. After 2 min of agitation, samples were mixed with 5 mL of 0.1M-bis-(2 ethyl hexyl) phosphate in Chloroform centrifuged at room temperature at 2000 rpm for 10 min. About 2.5 mL of the supernatant liquid was then transferred into a second tube and 1 mL of 0.5N HCl was added to it. After 5 min of centrifuge, the aqueous layer was separated and 20 µL was injected to HPLC. The chromatogram was recorded and response of major peaks was measured.

Amount of drug in % =
AS/AT×WS/100×5/50×100/WT×50/5×P/100×AV×100

Where, AS = average area of drug peak for standard, AT = average area of drug peak for test sample, WS = weight of drug taken for standard (in gm), WT = weight of drug taken for test sample (in gm), P = percentage purity of standard, AV = average weight in gm.

Procedure: i. Animal model

The bioavailability and pharmacokinetic parameters of Propafenone hydrochloride optimized formulation AS18 and was assessed using white rabbits as an animal model. Rabbits were used because its buccal membrane closely resembles the human buccal membrane in structure and permeability. For this study, white rabbits weighing 2.5 to 3 kg were used. The study was performed with respect to the guidelines provided 97 by the Institutional Animal Ethical Committee and under the supervision of a registered veterinarian. Animals were kept in standard cages in light controlled room at 25 ± 2ºC and 50 ± 5% RH. For the experiment, rabbits were issued and acclimatized ten days before the experimentation. Animals were kept on standard pellet diet and water ab libitum during period of acclimatization. Animals were kept on fasting 6 h prior to the actual start of the experimentation.

ii. Dosing

The animals were divided at random into two groups (six animals each), and under random study design, first group animals received aqueous solutions of Propafenone hydrochloride. And second group received mucoadhesive buccal film formulations AS18 corresponding to a dose of 16 mg and 40 mg. Prior to experimentation, rabbits were anaesthetized by an intramuscular (I.m.) injection of 1:5 mixture of Xylazine (1.5 mg/kg) and Ketamine (9.0 mg/kg). The light plane of anesthesia was maintained by administering one third of initial dose of Xyalzine and Ketamine intramuscularly as needed. After 10 minutes of initiation of the anesthesia, the rabbit mouth was opened using specially designed mouth restrainer. The buccal films containing the drug were moistened with 30 µl of simulated saliva of pH 6.8 and applied to the buccal section of the oral cavity with the film side and held firmly in place with a finger over the lip for 30 seconds to ensure adhesion. To the second group, 5 ml aqueous solution containing the same amount of drug as the films was administered orally through an infant feeding tube. The placebo films were used as the control group.

iii. Blood sample collection and processing

Blood sampling was continued at intervals for up to 10 h. The drug bioavailability of the formulated film was compared with that of the aqueous drug solution containing same amount of the drug as in the optimized film formulation in phosphate buffer administered to the rabbits. In each study, 1 ml blood sample was withdrawn from the marginal ear vein of the animals at 0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 8.0 hr post dosing using a 21 G needle. Blood sample was also collected prior to dosing from all the rabbits. The blood was collected in 2 ml centrifuge tubes containing 100 µl of EDTA solution (1.0 mg/ml) and centrifuged at 4000 rpm for 4 min at 4ºC. The plasma supernatant obtained was collected and stored at -20ºC till further processing for analysis.

iv. Sample analysis

Frozen plasma samples were thawed by keeping the sealed tubes at room temperature (25 ± 2ºC) for at least 60 min. The protein present in the plasma samples was precipitated with Acetonitrile. For this, 300 µl of plasma samples were taken and 1.5 ml of Acetonitrile was added to it and vortex mixed. The mixture was then centrifuged for 20 min at 13000 rpm at 4ºC. The supernatant was carefully taken and evaporated to dryness using vacuum evaporator. The dried residue was further reconstituted with a solvent system containing 1:4 (% v/v) of Methanol and Phosphate buffer (pH 6.8). Finally, the samples were analyzed using RPHPLC analytical method. The plasma drug concentration at various time points of the study was thus measured. Estimation of drug concentration was carried out by interpolating the peak area of the best formulation on calibration curve spiked the blank plasma over the range assayed.

v. Pharmacokinetic Analysis

Various pharmacokinetic parameters like C_{max}, T_{max}, Elimination rate constant (K_{el}), Area under the curve (AUC), Area under the momentum curve (AUMC), Mean and Biological Half-Life ($t_{1/2}$) were calculated. The maximum plasma concentration (C_{max}) and time to reach maximum plasma concentration (T_{max}) were obtained directly from the plasma concentration-time data. The area under the plasma concentration time curve up to the last time (t) showing a measurable concentration (C_t) of the analyte (AUC_{0-t}) was determined by applying the linear trapezoidal rule. The apparent elimination rate constant (K_{el}) was calculated by log-linear regression of the data point describing a terminal log-liner decaying phase. The $AUC_{0-\infty}$ values were determined by adding the quotient of $*C_t$ and the appropriate K_{el} to the corresponding AUC_{0-t}.

$$AUC_{0-\infty} = AUC_{0-t} + *Ct / K_{el}$$

Where $*C_t$ is the last detectable plasma drug concentration.

The apparent elimination half -life ($t_{1/2}$) of drug in plasma was calculated by using the following equation,

$$t_{1/2} = (\ln^2)/K_{el}$$

All values are expressed as the mean ± standard deviation (SD). The pharmacokinetic parameters obtained by following a single dose administration of the reference standard and the film formulations to normal rabbits were compared using paired t test, considering a probability of $P<0.05$ to be significant. Bioavailability test is performed by using, PK function (Microsoft Excel add In) programme and The Modern Version 6 software. Statistical analysis was performed using Microsoft Excel (Analysis Tool Pak add in). The plasma drug concentration data for PP was presented in tables. Comparative plasma drug concentration profile of PP and PP18 buccal film formulation was shown in figure.

Results And Discussion

Evaluation of prepared mucoadhesive buccal films of Propafenone HCl

Drug excipient compatibility studies

The drug excipient compatibility was studied by FTIR studies and DSC Analysis.

FTIR Studies

The possible interaction between drug and excipient used in the formulation development of mucoadhesive buccal films of Propafenone HCl was studied by FTIR spectroscopy.

Inference

It can be seen that well-defined absorbance spectra were obtained between 4000 and 500 cm-1. The spectrum of PP showed characteristic bands, at wave number 1662 cm-1 corresponding to the carbonyl group (-C=O), 3421 cm_1 corresponding to the tertiary amine group (-N-H), 3312 cm cm-1 corresponding to the hydroxyl group (-O-H) and another peak at 2940 cm cm-1 refer to methyl group. From the FTIR spectra, it was found that all the characteristic peaks of PP were also found in the spectrum of formulations. The results suggest that the drug is intact in the formulations and there is no interaction found between the drug and the contents. It was observed that main peaks of Propafenone were present in mixture of drug and polymer, and no change in main peaks of the drug IR spectra in a mixture of drug and polymers was found.

Differential Scanning Calorimetry (DSC)

The physicochemical compatibilities of the drug and the excipients were tested by differential scanning calorimetric (DSC) analysis. Thermogram of Propafenone HCl exhibits a sharp endothermic peak at 173ºC, which corresponds to its melting point. It was found that there are no new peaks appeared in the thermogram of the drug and excipients. Thus, there is no interaction between the drug and the tablet excipients, was observed.

Determination of absorption maximum (λ_{max}) of Propafenone HCl

From the UV spectrophotometric analysis it was conclude that the drug, Propafenone HCl showed a λ_{max} at 303 nm. Therefore the observed λmax was used for further work to analyze the test samples.

Calibration curve

The calibration curves for Propafenone HCl in 0.1 N HCl (pH 1.2), phosphate buffer pH 6.8, pH 7.5 was developed spectrophotometrically.

Solubility studies

The solubility of Propafenone HCl was determined in various pH ranges. The solubility of Propafenone HCl was found to be 260 mg/ ml (pH 1.2). 870 mg/ml in phosphate buffer pH 6.8 and 940 mg/ml in phosphate buffer pH 7.5.

Appearance

The physical appearance and flexibility were noted visually, for all the films from PP1 to PP18 were cream yellow in color, smooth, and homogeneity and elegant in appearance.

Weight variation

The weight of mucoadhesive buccal film was determined using digital weighing balance and the average weight of all film (PP1 to PP18) was found to be in the range of 93.73±0.63 to 96.56±0.51 mg. From the result, it was observed that the weight of films increases with the increased in the polymer concentration ratio. The drug-loaded buccal films were found to be uniform.

Thickness of films

The average thickness of all the films ranges from 0.120±0.002 mm to 0.158±0.002 mm. PP1 shows the lowest thickness and PP18 shows the highest thickness value. The measured thickness of PP1-PP18 films was approximately less than 1 mm which implies their usefulness for buccal application with least discomfort to the patients.

Folding endurance

The average folding endurance value of all the mucoadhesive buccal films ranges from 118.26±2.08 to

136.15±2.08. The values were optimum to reveal good buccal film properties. Formulation PP1 shows the highest folding endurance value and PP18 shows the lowest folding endurance value due to high viscosity of polymer.

Mucoadhesive strength

The mucoadhesive strength values ranged from 5.10±0.5 to 7.2±0.1. Formulation PP1 shows the lowest mucoadhesive strength value and PP18 shows the highest mucoadhesive strength value. The present of hydrophilic group in polymer bind to mucin through hydrogen bond; leading to increase in mucoadhesive strength interaction. The Formulation PP1 and PP2 have lowest polymer concentration of HMPCK4M; thus, have lowest mucoadhesion. The formulation PP18 shows highest mucoadhesive strength.

Surface-pH

The surface-pH was noted by pH meter and all films were found to be in the range of 6.80±0.01 to 6.85±0.01 pH (n=3). All the formulation batches show pH in neutral range, which indicates for the absences of buccal irritation.

Drug content

The percent of drug content for all the formulations PP1 to PP18 was obtained in the range of 95.50±0.31 to 98.67±0.52. The results indicate that the drug is distributed uniformly in all film formulations and will deliver the dose of drug accurately.

Table 4: Evaluation of mucoadhesive buccal film of Propafenone HCl

Formulation code	*Weight variation (mg)*	*Thickness (mm)*	*Folding endurance (Folds)*	*Mucoadhesive Strength (dyne/cm2)*	*Surface pH*	*Drug content (%)*
PP1	93.73±0.63	0.120±0.002	118.26±2.08	5.10±0.5	6.80±0.01	95.50±0.31
PP2	94.61±0.54	0.120±0.001	119.42±2.08	5.20±0.09	6.85±0.02	98.26±0.45
PP3	96.28±0.57	0.122±0.001	120.32±1.02	5.41±0.57	6.82±0.01	97.62±1.62
PP4	94.2±0.88	0.133±0.001	122.31±2.01	5.8±0.26	6.82±0.01	95.26±0.43
PP5	95.61±0.60	0.138±0.001	125.52±1.02	6.0±0.2	6.83±0.01	96.55±1.61
PP6	96.70±0.51	0.149±0.001	129.25±2.08	6.91±0.1	6.81±0.01	96.89±0.56

All data are given in Mean±SD

Table 5: Evaluation of mucoadhesive buccal film of Propafenone HCl

Formulation code	*Weight Variation (mg)*	*Thickness (mm)*	*Folding endurance (folds)*	*Mucoadhesive Strength (dyne/cm2)*	*Surface pH*	*Drug content (%)*
PP7	94.73±0.63	0.125±0.002	119.11±2.06	5.15±0.5	6.81±0.01	94.25±0.13
PP8	95.81±0.54	0.129±0.001	119.12±2.05	5.20±0.09	6.83±0.02	96.16±0.42
PP9	95.56±0.57	0.130±0.001	120.26±1.02	5.73±0.57	6.81±0.01	97.24±1.61
PP10	94.82±0.88	0.135±0.001	125.26±2.01	6.0±0.26	6.82±0.01	96.46±0.58
PP11	95.61±0.60	0.147±0.001	128.17±1.02	6.2±0.2	6.83±0.01	97.85±1.37
PP12	96.86±0.51	0.150±0.001	130.22±2.08	7.0±0.1	6.84±0.01	98.92±0.68

All data are given in Mean±SD

Table 6: Evaluation of mucoadhesive buccal film of Propafenone HCl

Formulation code	*Weight variation (mg)*	*Thickness (mm)*	*Folding endurance (folds)*	*Mucoadhesive Strength (dyne/cm2)*	*Surface pH*	*Drug content (%)*
PP13	95.73±0.63	0.130±0.002	120.16±2.08	5.5±0.5	6.81±0.01	94.64±0.53
PP14	95.61±0.54	0.132±0.004	120.24±2.08	5.80±0.09	6.82±0.02	96.39±0.41
PP15	96.66±0.57	0.135±0.002	125.22±1.52	5.53±0.57	6.81±0.01	96.28±1.56
PP16	95.2±0.88	0.145±0.003	128.18±2.51	6.2±0.26	6.83±0.01	98.28±0.81
PP17	94.61±0.60	0.149±0.003	130.39±1.52	6.8±0.2	6.84±0.01	97.52±1.36
PP18	96.56±0.51	0.158±0.002	136.15±2.08	7.2±0.1	6.85±0.01	98.67±0.52

All data are given in Mean±SD

Percent moisture absorption

The percent moisture absorption of all formulations from PP1 to PP18 was estimated. The average % moisture absorption was found in the range of 1.46±0.29 % to 3.17±0.15 %. All formulation shows moisture absorption within limits that is evidence for the physical stability of the film in humid conditions.

Percent moisture loss

The percent moisture loss of all formulations from PP1 to PP18 was estimated. The average % moisture loss was found in the range of 1.26±0.05 % to 2.42±0.22 %. All formulation shows moisture loss within limits that is evidence for the stability of the film against microbial growth.

Tensile strength

Tensile strength of prepared buccal film varies from 2.06±0.12 to 16.26±0.61 kg/cm² revealing that the films had good mechanical strength and flexibility. Tensile strength of buccal film increases with the increase in the polymeric concentration. Formulation PP1 showed the lowest tensile strength, whereas formulation PP18 showed the highest tensile strength.

Swelling index

The swelling index values of the film ranges from 18.75±1.04 to 46.64±1.44. The formulation PP1 showed the lowest swelling index & formulation PP18 showed the highest swelling index. Swelling increases with the increase in HPMCK100M concentration due to the presence of more hydroxyl group & in combination of HPC.

In vitro residence time

The *in vitro*-residence time of all formulations from PP1 to PP18 was evaluated of film ranges from 3.98±0.03 to 8.83±0.04. The *in vitro* residence time of all the films were found to be optimum and therefore, films exhibited good swelling and drug release properties.

Table 7: Evaluation of mucoadhesive buccal film of Propafenone HCl

Formulation code	*Moisture Absorption (%)*	*Percent moisture Loss (%)*	*Tensile strength (kg/cm2)*	*Swelling Index (%)*	*In vitro residence time (h)*
PP1	1.46±0.29	1.26±0.05	2.06±0.12	18.75±1.04	3.98±0.03
PP2	2.52±0.06	2.02±0.02	3.09±0.27	20.89±0.79	4.27±0.04
PP3	3.62±0.25	2.36±0.12	5.08±0.40	26.20±0.33	6.96±0.06
PP4	2.43±0.31	1.64±0.02	3.09±0.41	32.72±0.38	3.64±0.05
PP5	2.46±0.42	1.76±0.01	6.68±0.39	34.56±0.03	4.85±0.02
PP6	2.51±0.61	1.82±0.08	8.05±0.61	36.84±1.44	5.68±0.04

All data are given in Mean±SD

Table 8: Evaluation of mucoadhesive buccal film of Propafenone HCl

Formulation code	*Percent moisture Absorption (%)*	*Percent moisture loss (%)*	*Tensile strength (kg/cm2)*	*Swelling Index (%)*	*In vitro residence time (h)*
PP7	2.68±0.11	1.89±0.22	3.08±0.12	20.87±1.04	3.95±0.03
PP8	3.24±0.04	2.13±0.02	6.09±0.17	24.84±0.79	5.86±0.04
PP9	3.27±0.15	2.22±0.12	9.06±0.40	29.60±0.33	6.90±0.06
PP10	2.21±0.31	1.68±0.02	4.68±0.41	32.72±0.38	4.24±0.05
PP11	1.53±0.42	1.73±0.01	10.43±0.39	37.49±0.03	5.68±0.02
PP12	1.92±0.61	1.89±0.08	14.82±0.61	38.86±1.44	6.46±0.04

All data are given in Mean±SD

Table 9: Evaluation of mucoadhesive buccal film of Propafenone HCl

Formulation code	*Percent moisture Absorption (%)*	*Percent moisture loss (%)*	*Tensile strength (kg/cm2)*	*Swelling Index (%)*	*Residence time (h)*
PP13	2.65±0.11	2.31±0.22	6.09±0.12	20.87±1.04	3.95±0.03
PP14	2.42±0.14	2.12±0.02	8.06±0.17	24.63±0.79	4.64±0.04
PP15	3.61±0.18	2.64±0.12	10.08±0.40	29.84±0.33	6.92±0.06
PP16	3.18±0.31	1.52±0.02	8.39±0.41	31.76±0.38	3.26±0.05
PP17	2.69±0.42	1.61±0.01	14.22±0.39	35.82±0.03	5.63±0.02
PP18	3.17±0.15	2.42±0.22	16.26±0.61	46.64±1.44	8.83±0.04

All data are given in Mean±SD

In vitro drug release

Table 10: *In vitro* drug release of Propafenone HCl mucoadhesive buccal film

Time	*PP1*	*PP2*	*PP3*	*PP4*	*PP5*	*PP6*
0	0	0	0	0	0	0
30 min	22.39 ±0.76	20.14 ±0.74	18.89 ±1.07	35.33 ±1.5	30.9 ±0.21	18.72 ±0.22
1 hr	53.69 ±0.05	43.14 ±0.96	25.74 ±0.59	80.05 ±1.08	48.38 ±0.31	39.88 ±0.64
1.5 hr	78.86 ±0.43	59.82 ±0.89	48.33 ±0.72	92.41 ±1.45	62.62 ±0.84	59.89 ±0.79
2 hr	89.41 ±0.96	69.15 ±0.71	63.33 ±1.42	96.53 ±1.21	79.62 ±1.28	78.05 ±0.27
3 hr	98.18 ±0.29	86.1 ±1.12	83.78 ±0.73	99.12 ±1.01	84.53 ±0.59	94.24 ±1.17
4 hr	-	98.86 ±1.26	96.59 ±0.29	-	98.84 ±0.59	96.18 ±0.83
5 hr	-	-	99.53 ±0.25	-	-	98.46 ±0.83

All data are given in Mean±SD

Table 11: *In vitro* drug release of Propafenone HCl mucoadhesive buccal film

Time	*PP7*	*PP8*	*PP9*	*PP10*	*PP11*	*PP12*
0	0	0	0	0	0	0
30 min	20.16 ±0.51	18.38 ±0.15	16.68 ±0.9	20.46 ±0.14	16.64 ±0.54	14.92 ±0.13
1 hr	42.82 ±0.59	30.65 ±1.44	27.89 ±1.29	46.28 ±0.04	30.78 ±0.06	27.89 ±0.78
1.5 hr	58.38 ±0.68	49.16 ±1.35	45.64 ±1.26	70.43 ±0.94	47.96 ±0.57	36.62 ±1.42
2 hr	79.95 ±1.13	60.32 ±0.85	56.42 ±1.49	82.86 ±1.3	70.85 ±1.49	49.57 ±0.25
3 hr	97.59 ±0.93	84.64 ±0.49	69.18 ±0.82	89.41 ±1.22	78.68 ±1.41	72.69 ±0.26
4 hr	-	96.15 ±0.22	76.36 ±0.18	97.89 ±0.27	86.24 ±0.89	83.61 ±0.8
5 hr	-	98.26 ±0.29	84.12 ±0.55	-	97.89 ±0.5	96.24 ±0.78
6 hr	-	-	98.64 ±0.61	-	-	99.86 ±0.12

All data are given in Mean±SD

Table 12: *In vitro* drug release of Propafenone HCl mucoadhesive buccal film

Time	*PP13*	*PP14*	*PP15*	*PP16*	*PP17*	*PP18*
0	0	0	0	0	0	0
30 min	20.36 ±1.1	19.23 ±1.3	12.65 ±1.5	18.47 ±1.5	16.99 ±0.8	12.48 ±1.2
1 hr	25.87 ±0.2	23.54 ±0.9	20.84 ±0.8	30.64 ±0.7	26.90 ±0.7	24.54 ±1.1
1.5 hr	40.75 ±1.2	38.67 ±0.7	30.58 ±0.7	64.68 ±1.2	54.67 ±1.1	36.78 ±1.1
2 hr	68.89 ±0.7	62.49 ±0.3	42.67 ±0.7	82.79 ±1.3	68.89 ±1	49.89 ±0.6
3 hr	98.52± 0.53	94.58 ±1.1	66.89 ±1.4	99.69 ±1.3	96.68 ±1.1	79.62 ±1.1
4 hr	-	98.69 ±1.4	76.87 ±0.6	-	98.54 ±1.1	86.69 ±1.1
5 hr	-	-	86.53 ±0.8	-	99.61 ±1.1	94.47 ±0.8
6 hr	-	-	98.89 ±1.4	-	-	96.53 ±0.8
7 hr	-	-	-	-	-	98.14 ±0.12
8 hr	-	-	-	-	-	99.78 ±0.21

All data are given in Mean±SD

In vitro dissolution of Propafenone HCl mucoadhesive buccal film investigation was carried out in pH 6.8 PBS. Drug release from PP1 to PP18 was found to be ranges of 98.18±0.29 % per 3hr to 99.78±0.21 % per 8 hrs respectively. It was observed that the drug release slower with increasing polymer concentration. Replacement of Sodium CMC with HPC showed slower drug release rates. This can be attributed to the lower solubility of HPC relative to Sodium CMC. Also, increasing the amount of HPC produced the water-swollen gel like state that could substantially reduce the penetration of the dissolution medium into the films and so the drug release was retarded. Addition of non-ionic polymer HPC to Sodium CMC has been shown to provide significant decrease in dissolution rate when compared to Sodium CMC. It has been reported that the addition of HPC to Sodium CMC matrices caused further retardation to the release profiles. This retardation has been attributed to a stronger gel layer of the resultant matrix, reducing the diffusion and erosion rate characteristics of the gel layer. The formulation PP18 was selected as an optimized formulation (Combination of KPMC K100M + HPC) based on these in vitro release

studies which showed satisfactory drug release rate

99.78±0.21 % in 8 h. The selected optimized formulation PP18 was used further for the evaluation of *ex-vivo*

permeation studies through goat buccal mucosa. Based on the results obtained from the *in vitro* drug release studies and mucoadhesion strength the formulation PP18 was selected as best formulations containing the mucoadhesive material HPMC and HPC.

Ex vivo permeation studies

Table 13: *Ex vivo* permeation studies of optimized formulation PP18

Time (hrs)	*0.5*	*1*	*1.5*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
Cumulative % drug release	8.79 ±0.2	14.44 ±0.32	19.68 ±0.13	27.6 ±0.43	45.61 ±1.04	69.8 ±1.3	82.41 ±0.41	88.15 ±0.62	96.34 ±0.83	98.68 ±0.47

The oral mucosa shows intermediate permeability characteristics between skin epidermis and the gut. It acts as a barrier to drug permeation. Hence to get idea of total buccal barrier and effectiveness of buccal absorption for drug PP in PP18 formulation in the form of buccal films is determined by *ex- vivo* permeation studies. The percentage of the permeated drug through the buccal mucosa at the end of 8 hrs was found to 98.68±0.47% for PP18 formulation.

Mechanism of release kinetics

The mechanism of release was determined by fitting the release data to the various kinetic equations such as zero order, first-order, Higuchi, Korsmeyer–Peppas. r^2 values were determined by regression formed by the index of linearity. Finally it follows zero order kinetics based on Regression coefficient (r^2) value.

Table 14: Regression Coefficient of PP18

Formulation	*Regression coefficient (r^2) values*			
Propafenone HCl buccal film	Zero order	First Order	Higuchi Model	Korsmeyer - peppas
	0.9998	0.9755	0.8623	0.8541

Stability studies

Based on the above result, stability studies were conducted only for optimized formulation PP18. Form the stability studies, it was known that optimized formulation PP18 had stability in human saliva; there was no change in the color and integrity of the buccal film. The optimized formulation PP18 was selected for short term stability studies at temperature 25±2ºC and 60±5% RH and accelerated stability studies were carried out at 40±2ºC and 75±5% RH for the period of 3 months. The buccal films were analyzed for folding endurance, tensile strength, drug content and in vitro drug release. There was a minor decrease in all the parameters. Hence the formulation PP18 was indicated stable. `

Table 15: Short term and accelerated stability studies of optimized batch PP18

	25 ±2°C/60% RH±5% RH				*40±2°C/75% RH±5% RH*			
Time (days)	*Physical appearance*	*Folding endurance*	*Tensile strength*	*Swelling index*	*Physical appearance*	*Folding endurance*	*Tensile strength*	*Swelling index*
0	No change	136.15 ±2.08	16.26 ±0.61	46.64 ±1.44	No change	136.15 ±2.08	16.26 ±0.61	46.64 ±1.44
30	No change	136.15 ±2.08	16.26 ±0.75	46.53 ±1.12	No change	136.15 ±2.08	16.26 ±0.75	46.53 ±1.12
60	No change	135.24 ±1.06	15.89 ±0.23	46.43 ±1.64	No change	135.24 ±1.06	15.89 ±0.23	46.43 ±1.64
90	No change	135.35 ±2.06	15.86 ±0.54	45.64 ±1.31	No change	135.35 ±2.06	15.86 ±0.54	45.64 ±1.31

All data are given in Mean±SD

Table 16: Short term and accelerated stability studies of optimized batch PP18

	25 ±2°C/60% RH±5% RH				*40±2°C/75% RH±5% RH*			
Time (days)	*Residence time*	*pH*	*Drug content*	*In vitro drug release*	*Residence time*	*pH*	*Drug content*	*In vitro drug release*
0	8.83±0.04	6.85 ±0.01	98.67 ±0.52	99.78 ±0.21	8.83±0.04	6.85 ±0.01	98.67 ±0.52	99.78 ±0.21
30	8.83±0.05	6.85 ±0.03	98.67 ±0.41	99.65 ±0.21	8.83±0.05	6.85 ±0.03	98.67 ±0.41	99.65 ±0.21
60	8.76±0.02	6.83 ±0.01	98.62 ±0.34	99.49 ±0.21	8.76±0.02	6.83 ±0.01	98.62 ±0.34	99.49 ±0.21
90	8.60±0.03	6.82 ±0.01	98.50 ±0.52	99.40 ±0.21	8.60±0.03	6.82 ±0.01	98.50 ±0.52	99.40 ±0.21

All data are given in Mean±SD

In vivo pharmacokinetic results

Table 17: Plasma concentration of Propafenone HCl conventional tablets (Rythmol) in rabbits (n=6) at different time intervals (Reference formulation)

	Plasma concentration (ng/mL)							
Time (hrs)	*Animal 1*	*Animal 2*	*Animal 3*	*Animal 4*	*Animal 5*	*Animal 6*	*Average*	*SD*
0	0	0	0	0	0	0	0	0
0.5	112.5	120.8	104.5	121.8	105.6	103.2	111.40	8.32
1	220.6	215.6	224.5	205.6	212.3	204.3	213.82	8.05
1.5	212.3	221.3	218.5	215.9	221.3	219.7	218.17	3.51
2	200.2	221.3	178.5	189.6	210.2	205.6	200.90	15.20
2.5	185.4	179.8	181.5	189.6	191.5	192.6	186.73	5.34
3	161.2	188.6	129.6	157.8	161.3	163.2	160.28	18.76
4	132.5	133.6	158.5	106.5	134.5	128.5	132.35	16.57
6	124.5	125.6	144.6	110.2	120.1	118.5	123.92	11.52
8	95.6	100.2	90.5	92.6	93.4	98.7	95.17	3.73
12	74.5	80.5	70.6	68.9	75.6	71.4	73.58	4.20
24	34.6	40.1	42.5	32.6	33.5	35.4	36.45	3.95

In vivo Pharmacokinetic study of Propafenone HCl

Various pharmacokinetic parameters were estimated such as C_{max}, t_{max}, AUC and relative bioavailability were given in Table 19.

Table 18: Plasma concentration of Propafenone HCl optimized buccal film (PP18) in rabbits (n=6) at different time intervals (Test Formulation)

Time (hrs)	*Plasma concentration (ng/mL)*							
	Animal 1	*Animal 2*	*Animal 3*	*Animal 4*	*Animal 5*	*Animal 6*	*Average*	*SD*
0	0	0	0	0	0	0	0	0
0.5	41.6	55.6	46.5	41.2	42.5	43.5	45.15	5.46
1	64.2	66.5	71.2	60.2	62.5	63.5	64.68	3.80
1.5	85.7	90.2	87.5	80.2	82.5	83.6	84.95	3.61
2	101.2	130.2	85.6	102.9	105.3	104.6	104.97	14.36
2.5	122.7	125.9	151.2	112.5	132.5	125.2	128.33	12.95
3	145.8	186.5	147.8	148.9	120.2	151.4	150.10	21.19
4	192.5	185.9	178.9	199.6	189.7	193.7	190.05	7.10
6	235.6	240.2	222.4	225.6	255.6	217.5	232.82	13.98
8	185.6	220.5	155.9	184.3	181.2	178.5	184.33	20.79
12	109.8	141.2	110.2	82.5	105.6	104.6	108.98	18.83
24	45.6	51.6	47.8	55.6	54.3	48.9	50.63	3.88

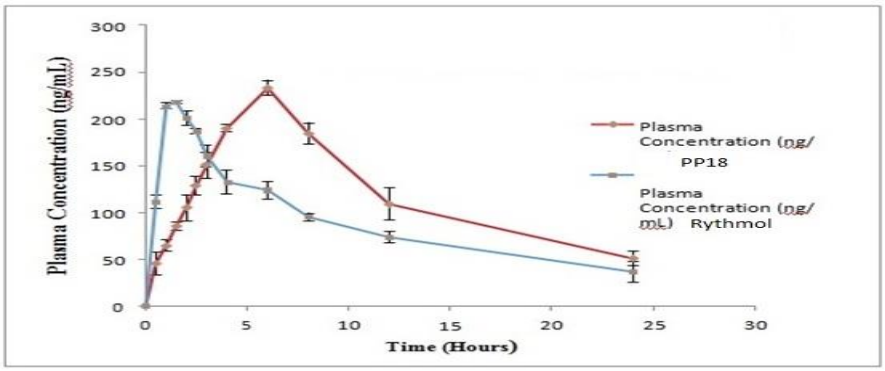

Figure 2: Mean Plasma concentration time Profile of Propafenone HCl test (PP18) and reference (Rythmol) formulations

Table 19: Mean pharmacokinetic parameters of Propafenone HCl as Reference and test tablets in Rabbits

Pharmacokinetic parameter	*Unit*	*Reference*	*Test*
C_{max}	ng/mL	218.66	232.82
t_{max}	H	1.5	6
AUC_{0-t}	ng/mL×h	2124.948	2805.96
$AUC_{0-\alpha}$	ng/mL×h	2736.03	3418.66
$t_{1/2}$	h	8.38	11.62

The mean area under plasma time curve AUC_{0-t} and $AUC_{0-total}$ of reference formulation was 2124.948 ng/ml×h and 2736.03 ng/ml×h and while AUC_{0-t} and $AUC_{0-total}$ of test formulation was 2805.9608 ng/ml×h and 3418.66 ng/ml×h, This indicates that the overall absorption of PP was more in the test formulation with respect to the reference product at the same dose. It was observed from the results that the oral bioavailability of optimized formulation (PP18) was increased significantly when compared to marketed formulation. Relative bioavailability with respect to marketed formulation was found to be 124.9 which are due to prolonged gastric residence time of PP buccal films.

Conclusion

The following conclusion could be drawn from the various experiments. FTIR and DSC studies revealed that there is no incompatibility or interaction between PP and excipients. The mucoadhesive buccal film containing backing layer, which acts like a patch providing unidirectional drug release of PP, could be prepared by the solvent casting technique with mucoadhesive polymers like Hydroxyl propyl methyl cellulose (HPMC) K4M, K15M and K100M as film forming as well as rate retarding polymer with different combinations of mucoadhesive polymers like Sodium CMC, Hydroxy Propyl Cellulose, propylene glycol (PG) was selected as plasticizer. Formulated buccal films give satisfactory film characteristics. From the study, it can be

concluded that the combination of HPMC K100M and HPC could obtain good film characteristics with a controlled release over 8 hours. The combination also improved residence time and mucoadhesive strength for sufficient contact time to the mucosa. The overall results show the potential combination of HPMC and HPC to increase bioavailability and half-life of Propafenone HCl. The optimized formulation followed zero order kinetics. Short term stability studies of optimized formulation as per ICH guidelines indicated that there is no significant change in physical appearance, drug content determination and *in vitro* drug release. So finally it can be concluded that buccal films of PP could provide Controlled release over 8 hrs. Hence, present study concludes that the Propafenone HCl could be delivered through the buccal route. The *in vivo* pharmacokinetic study was conducted in healthy albino rabbits and it was observed from the results that the oral bioavailability of optimized formulation (PP18) was increased significantly when compared to the marketed formulations. Relative bioavailability with respect to marketed formulation (Rythmol) was found to be 124.9. The increased bioavailability may be due to the mucoadhesion mechanism of dosage form in buccal area for longer duration.

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