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Development, Optimization and In Vitro Evaluation of Buccal Tablet of Posaconazole

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Abstract

Buccal route of administration has many advantages such as improving patient compliance, bypassing the GIT and hepatic first pass effect. The objectives are to formulate Mucoadhesive buccal tablet using Posaconazole and compatible excipients, and to evaluate the product using quality control tests and in vitro tests. In the development of buccal tablet of antifungal drug Posaconazole to treat oral thrush locally and to improve the solubility and bioavailability of drug, simultaneously enhances the erosion rate of tablet Mucoadhesive dosage forms have long been employed to improve the bioavailability of drugs undergoing significant hepatic first-pass metabolism and control the release of drugs from hydrophilic matrices. Therefore, it is needed to develop suitable controlled release Mucoadhesive buccal tablets containing an antifungal agent, Posaconazole. The present study has been planned to formulate the Mucoadhesive buccal tablets of posaconazole by using xanthan gum and carbopol 940. This formulation used for the treatment of oral candidiasis. *In vitro* drug release results of all the formulations were conducted for 12 h which indicated that, tablet formulations, F1- F9 were found to be following non-fickian diffusion. The formulation F5 was taken as an optimized batch. Stability studies were conducted at 40^0C and 75 % RH as per ICH guidelines.

Keywords: Posaconazole, Buccal, bioavailability, Mucoadhesive, ICH guidelines.

Introduction

Buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotide, and polysaccharides as well as conventional small drug molecule. The oral cavity can be used for local and systemic therapy. Examples of local therapy would be the treatment of oral infections, dental caries, mouth ulcers and stomatitis. The buccal route is of particular interest with regard to systemic delivery of small molecule that are subjected to first pass metabolism of protein and peptides.[1] Over the last two decades mucoadhesion has become of interest for its systemic delivery by retaining formulation intimate contact with buccal cavity. The term bioadhesion has been used to define the attachment of synthetic natural molecule to biological tissue for an extended period of time.[2]

Posaconazole tablets, oral suspension are used to prevent certain fungus (yeast) infections (eg, invasive Aspergillus or Candida infections) in patients who have a

weakened immune system (e.g., hematopoietic stem cell transplant or HSCT recipients, or patients with blood cancers). Posaconazole tablets are also used to treat invasive aspergillosis. Posaconazole oral Tablets is also used to treat a fungus infection of the mouth or throat called oral thrush (candidiasis).[3]**Mucoadhesive Tablets**

Oral mucosa is richly supplied with blood vessels which prove to be ideal site of administration to treat oral candidiasis locally. Moreover this route provides additional advantage over oral route to overcome the demerits of drug inactivation by first pass effect and gastrointestinal.[4] The buccal route of administration improves the bioavailability of drug and its action locally. Oral candidiasis of very common infection that occurs commonly in immune compromised pateints.[5]

Mucoadhesive drug delivery system

Sublingual delivery administration of drug via the sublingual mucosa to the systemic circulation.

Buccal delivery is the administration of drug via buccal mucosa (the lining of the cheek) to the systemic circulation; and Local delivery for the treatment of conditions of the oral cavity principally apthous ulcers, fungal conditions and periodontal diseases by application of the bioadhesive system either to the palate, the gingiva or the cheek. [(8)]These oral mucosal sites differ greatly from one another in terms of anatomy, permeability of an applied drug and their ability to retain a delivery system for a desired period of time. From the viewpoint of permeability, the non-keratinized buccal and sublingual region appears to be more attractive site. However other factors such as blood flow should also be taken into account. [6]

Materials and Methods

Materials

Posoconazole was obtained as gift sample from Gift Sample from Cipla Ltd, Nashik Xanthan gum; Carbopol 940 was obtaied from Blue Cross Laboratory, Ltd, Nashik. Talc, Magnesium stearate, Mannitol, ect was purchased from Research-Lab Fine Chem. Industry, Mumbai. All chemicals used were analytical grade.

Methods

Preformulation studies of drug

Organoleptic properties

The drug Posoconazole was studied for Organoleptic characteristics such as color, odor and appearance.

Melting point

The melting point of the drug was determined by placing a little amount of the drug in a capillary tube with one end closed and placing it in Thiele's melting point apparatus and recording the temperature at which the drug melts.

Determination of solubility

An excess amount of the drug was taken and dissolved in a measured amount of distilled water in a volumetric flask to get a saturated solution. The solution was shaken intermittently to assist the attainment of equilibrium with the un- dissolved drug particles. Then measured quantity of the filtered drug solution was withdrawn after 24 h and successively diluted with distilled water suitably and the concentration was measured in a UV spectrophotometer at their respective absorbance maxima. Similarly, the solubility of drug determined in water, methanol, ethanol, and phosphate buffer of 0.01M pH 6.8.

Partition coefficient

The partition coefficient of the drugs was determined by taking equal volumes of n-octanol and aqueous phases in a separating funnel. A drug solution of 1mg/ml was prepared and 1ml of the solution was added to n- Octanol: water (50:50) was taken in a separating funnel and shaken for 10 minutes and allowed to stand for 2 h. the aqueous phase was separated, centrifuged for 10 min at 2000 rpm.

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 side wise shaking of the bottle. Dried the substance in the hot air oven at 105˚ 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.

Calibration curve of Posoconazole

The stock solution of drug was subsequently diluted with 0.01M Phosphate buffer (pH 6.8) to get 5µg/ml- 50 µg/ml. Then the absorbance of these dilute solutions was measured at a λ_{max} of 262 nm Calibration curve was performed in triplicate.

Compatibility Study of drug and excipients

Fourier Transform Infrared Spectroscopy

Compatibility study was carried out by using Fourier transform infrared spectrophotometer (BRUKER OPUS 7.5). FTIR study was carried on pure drug and physical mixture of drug and polymers.

Differential scanning calorimetric studies

The sample of pure drug, physical mixture of drug and polymer were weighed and heated at a scanning rate of 10°C/min between 40 and 200°C and 40 ml/min of nitrogen flow. The differential scanning colorimetric analysis gives an idea about the interaction of various materials at different temperatures. It is also allowing us to study the possible degradation of the material.

Development of buccal tablets of Posoconazole

All the ingredients as mention in table were accurately weighed and passed through sieve no.120 and blended thoroughly to obtain uniform mixing.

Method of preparation of Posaconazole tablets

Buccal tablets were prepared by direct compression method. The blended powder was evaluated for its pre-compression characteristics and then compressed on 10 station pilot press using 13 mm flat faced punches. The machine was adjusted to produce an approximate weight of 300 mg tablet.

Evaluation of precompression characteristics of powder blend

Bulk density

Bulk density was determined by placing the powder blend in a measuring cylinder and the total volume was noted.

Tapped density

The tapped density was obtained by dividing the mass of powder by the tapped volume in cm^3.

Compressibility index

Compressibility index was determined by placing the powder in a measuring cylinder and the volume (V0) was noted before tapping. After 100 tapings again volume (V) was noticed.

Hausner's ratio

Table No. 1: Composition of buccal tablet formulations

Formulation Code → / Ingredients ↓	F1	F2	F3	F4	F5	F6	F7	F8	F9
Posaconazole	100	100	100	100	100	100	100	100	100
Xanthan gum	30	45	60	30	45	60	30	45	60
Carbopol 940	30	30	30	45	45	45	60	60	60
Magnesium stearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Mannitol	30	30	30	30	30	30	30	30	30
Spray dried Lactose	104	89	74	89	74	59	74	59	44
Total	300	300	300	300	300	300	300	300	300

It is the ratio of tapped density to bulk density. Hausner's ratio is an ease of powder flow; calculated

Angle of repose (°θ)

Angle of repose was determined by measuring the height and radius of the heap of the powder bed.

Evaluation of compressional characteristics of the buccal tablets

Weight uniformity

Twenty tablets were taken and weighed individually. Average weight was calculated standard deviation was computed.

Thickness test

The tablets were evaluated for their thickness using vernier calipers. Average of three readings were taken and the results were tabulated (n = 3)

Hardness test

The tablets were evaluated for their hardness using Pfizer hardness tester. Average of three reading were taken and tabulated (n = 3).

Surface pH

Three tablets were allowed to swell for 04 h in simulated saliva fluid of pH 6.75. pH was found out by placing the electrode of pH meter just in contact with the surface of the tablets. Average of three readings was computed.

Drug content uniformity

Powder equivalent to 100 mg of drug was transferred into 100 ml volumetric flask containing 10 ml of mixture of 0.1M HCl: methanol (1:9) and volume was made up to 100 ml with 0.01M phosphate buffer pH 6.8 and stirred constantly for 24 h to extract the

total drug present in the tablet. Then the solution was filtered and the volume was made with 0.01 M pH 6.8 phosphate buffer and analyzed for drug content at λ max of 262 nm against drug devoid phosphate buffer as blank. Averages of triplicate readings were taken. The content of drug was calculated using standard graph.

Swelling studies

Preparation of simulated saliva solution

Weigh accurately 2.38g of Na2HPO4, 0.19 g KH2PO4, 8.00g NaCl and dissolve in 1000 ml of distilled water to produce simulated saliva solution; finally adjusted the pH with phosphoric acid to 6.75.

% Swelling Index

Three tablets were weighed individually (W1) and immersed in a petridishes containing simulated saliva fluid (pH 6.75) for predetermined times (1, 2, up to 12 h). After immersion tablets were wiped off by the excess surface water by the use of filter paper and weighed (W2). T

Determination of *in-vitro* Mucoadhesion strength of different tablet formulations

In vitro bioadhesion studies were conducted using modified bioadhesion test.

Measurement of adhesion force

Goat cheek pouch was obtained commercially; the cheek pouch was collected into a sterile container containing sterile buffer solution of pH 6.75. The cheek pouch brought was stored in a refrigerator until use. The cheek pouch was removed from refrigerator and allowed to attain equilibrium with ambient conditions in the laboratory. The goat cheek pouch was carefully excised, without removing connective and adipose tissue and washed with simulated saliva solution. The tissue was stored in fresh simulated saliva solution pH 6.75. Immediately afterwards the membrane was placed over the surface of lower Teflon cylinder (B) and secured. This assembly was placed into beaker containing simulated saliva solution pH 6.75 at 37 ± 2°C. From each batch, one tablet at a time was taken and stuck to the lower surface of teflon cylinder with a standard cyanoacrylate adhesive. 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 tablet was wetted with a drop of simulated saliva solution, and then a weight of 20 gm was placed above the expanded cap, left for 10 minutes. After which the tablet binds with mucin. The weight was removed. Then slowly and gradually weights were added on the right-side pan till the tablet separates from the mucosal surface/ membrane. The weight required for complete detachment is noted (W1) (W1-5.25 gm) gives force required for detachment expressed in weight in grams. Procedure was repeated for two more tablets. Average was computed and recorded. (n=3).

Calibration of test equipment

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

In-vitro dissolution studies [66]

In-vitro release method for Posoconazole tablets

The drug release profile was studied using USP 24 dissolution testing apparatus method

II using a paddle at 100 rpm. 500ml dissolution fluid, simulated saliva solution pH 6.75, was used and a temperature of 37° ±0.5°C was maintained. 1ml aliquots at 0.25, 0.5, 1h, 2h, 3h, 4h, 5h, 6h, 7h, 8h, 9h, 10h, 11h, 12 h respectively were pipette out and the same volume was replaced with simulated saliva solution pH 6.75. A drug free tablet was taken as blank. Absorbance was measured at λ max 262 nm and from which percentage of posoconazole was calculated using calibration curve.

Kinetics of drug release from buccal tablet containing posoconazole

To examine the drug release kinetics and mechanism from the tablets, release data was assessed using the zero-order model, first order model, Higuchi model, and Korsmeyer-Peppas model. The drug release from buccal tablets created followed zero order kinetics, according to analysis using zero order and first order kinetic models.

Stability Study

The sample was removed from the oven at the end of specified time intervals and analyzed for drug content for 90 days. Stability study of optimized formulation was conducted to investigate the influence of temperature and relative humidity on the drug content, Mucoadhesive strength and % drug release. The formulation was exposed to temperature of 40^0C/75% RH in a hot air oven for a period of 3 months as per ICH guidelines. The samples were withdrawn and tested at 1, 2, and 3 months for given temperature and humidity condition.

Results and Discussions

Preformulation study of drug

Physical parameters

The drug sample was subjected to preformulation studies like melting point, solubility, partition coefficient and Organoleptic properties.

Table No.2: Preformulation data for drug sample

Preformulation parameter	Posaconazole	
	Observed value	Reported value
Color	White	--
Appearance	Crystalline	--
Melting point	170-172^{0}C	172^{0}C
Solubility in water	0.47 µg/mL	0.49µg/mL
Solubility in ethanol	9.25 mg/mL	10 mg/mL
Solubility in methanol	10.29 mg/mL	10-12 mg/mL
Solubility in pH 6.8 phosphate buffer	0.195 µg/mL	0.200 µg/mL
Partition coefficient (pKa)	Log P 4.6	≥ 4.0
Loss on drying	0.01 % W/V	NMT 0.5%W/V

The solubility of Posaconazole was determined at 37 ± 2^{0}C in distilled water, ethanol, methanol and pH 6.8 phosphate buffer. The equilibrium partition coefficient of Posaconazole were determined in n-octanol/ pH 6.8 phosphate buffer system by

shake flask method. Partition coefficient (Log P) of the drug was found to be 4.6. The loss on drying was carried out in hot air oven at 105^0C for 2 h. The values were putted in the formula and it was found that the loss on drying for drug sample was 0.01% w/w.

Determination of λ_{max} of Posaconazole in 0.01M pH 6.8 phosphate buffer

Solutions of Posaconazole prepared in 0.01 M pH 6.8 phosphate buffer and scanned between 200-400 nm using UV Spectrometer which showed peak at 262 nm.

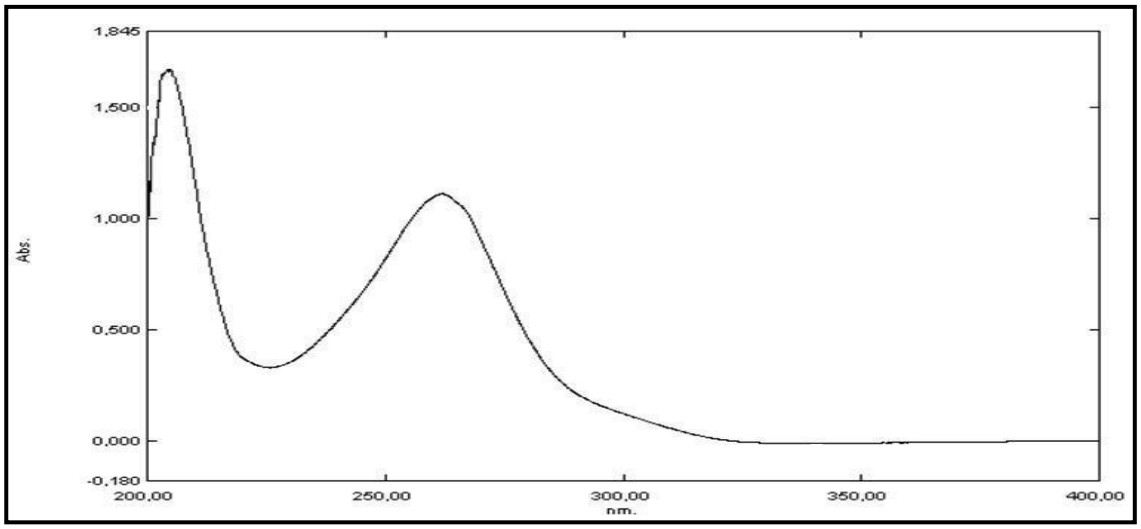

Figure No. 1: UV-visible spectrum of Posaconazole in pH 6.8 phosphate buffer

Calibration curve of Posaconazole 0.01 M pH 6.8 phosphate buffer

Calibration curve was found to be linear in the concentration range of 5-50 µg/ml having coefficient of regression value R^2 = 0.999 and Slope y = 0.0038x.

Table No.3: Spectrophotometric data for the estimation of Posaconazole at 262 nm

Sr. No	Concentration (µg/ml)	Absorbance
1	0. 00	0. 00
2	5.00	0.019
3	10. 00	0. 037
4	15. 00	0. 056
5	20.00	0. 074
6	25.00	0. 096
7	30.00	0.115
8	35.00	0.132
9	40.00	0.153
10	45.00	0.170
11	50.00	0.192

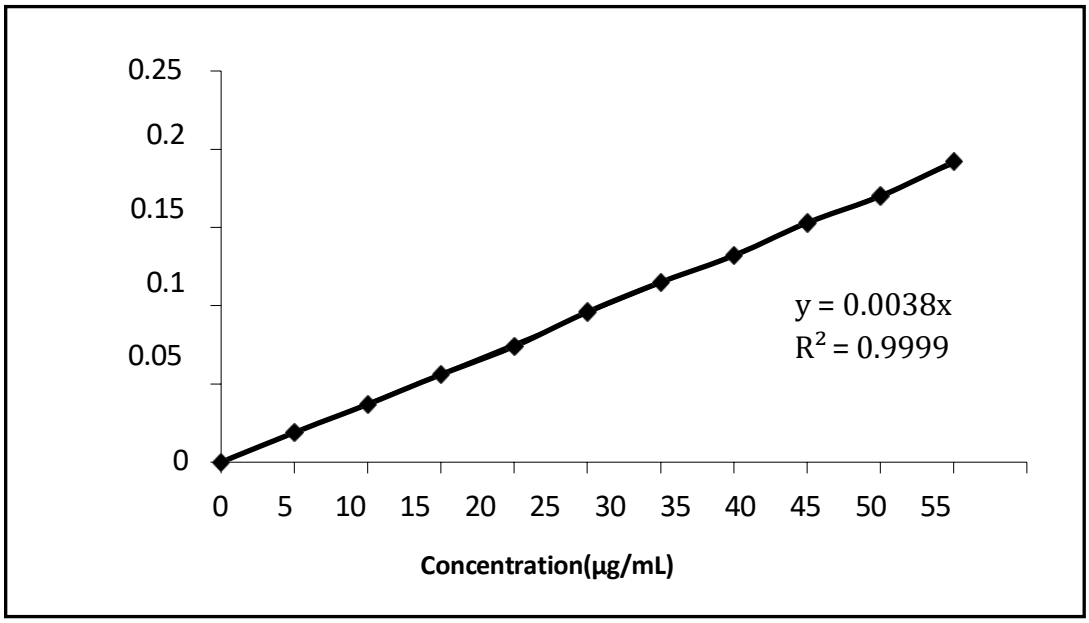

Figure No. 2: Calibration curve of Posaconazole in 0.01 M pH 6.8 phosphate buffer

Table No.3: Accuracy and precision studies

Drug	Formulation	Amount drug added (mg/ml)	Amount Drug recovered (mg/ml)	Accuracy	Precision
Posaconazole tablets	**F 1**	100	99.14	99.14	0.36
	F 2	100	97.28	97.28	0.42
	F 3	100	95.87	95.87	0.32
	F 4	100	96.54	96.54	0.29
	F 5	100	97.68	97.68	0.23
	F 6	100	98.06	98.06	0.20
	F 7	100	97.21	97.21	0.66
	F 8	100	98.70	98.70	0.15
	F 9	100	99.00	99.00	0.29

Compatibility Study of drug and excipients by FTIR

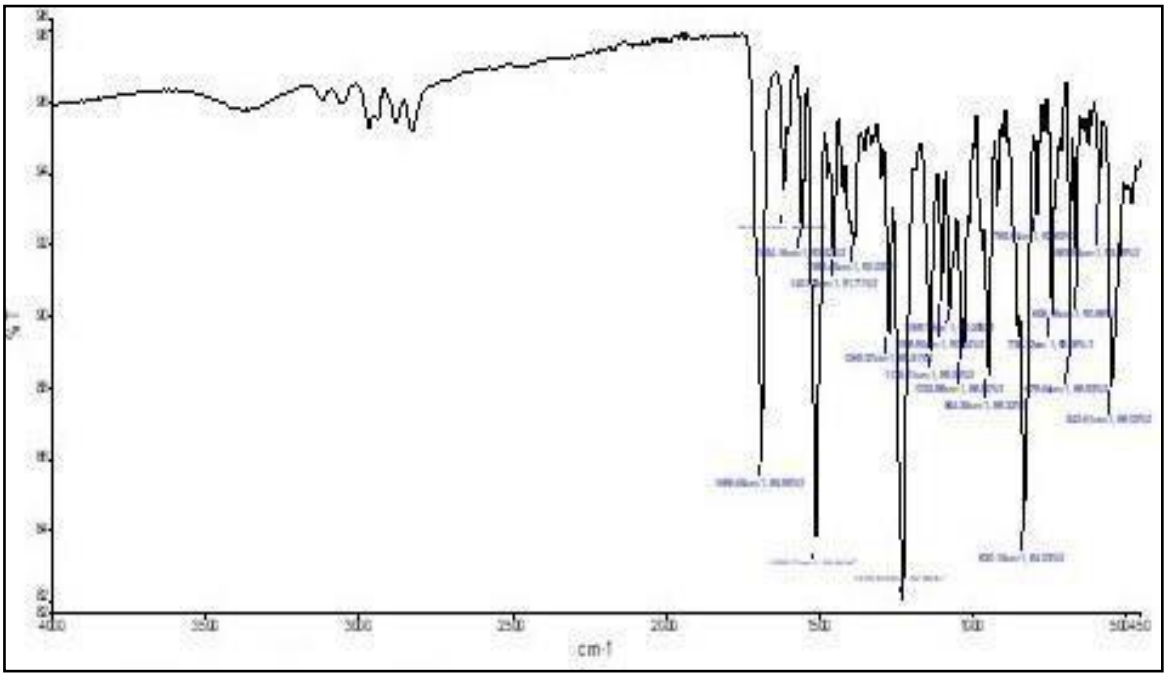

Figure No.3: IR Spectra of drug Posaconazole

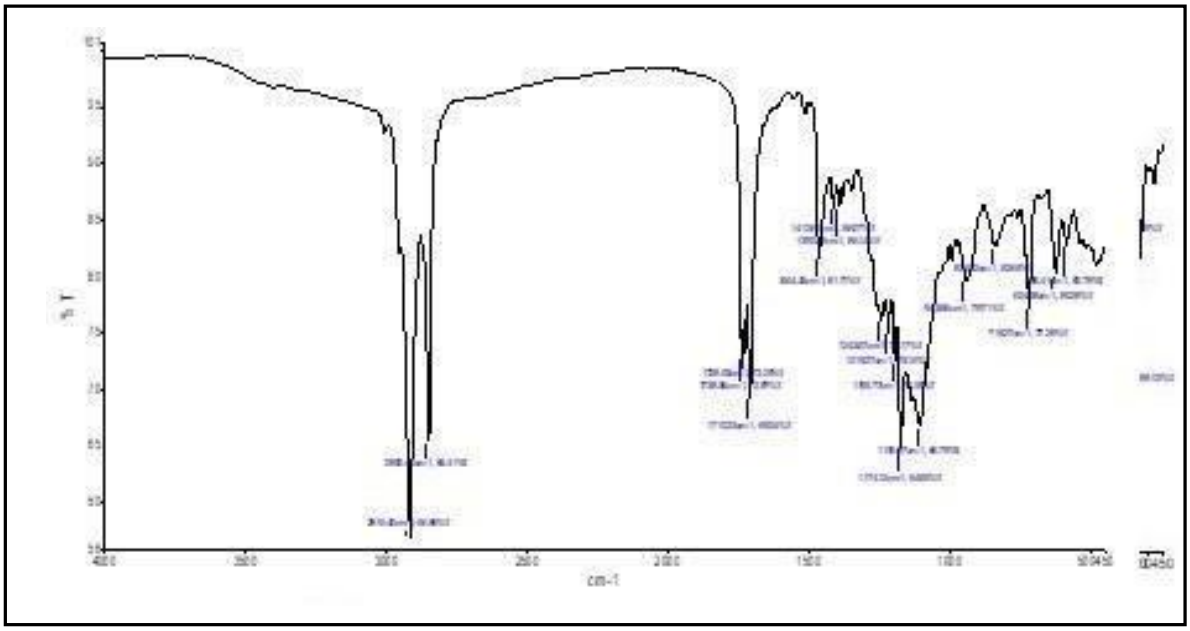

Figure No.4: IR Spectra of Physical mixture of drug and polymers

The characteristic absorption peaks of drug posaconazole 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.

The DSC Thermo gram of posaconazole exhibited an endothermic peak at 170.6 ^{0}C confirms the identity and purity of the sample

Differential scanning Calorimetry

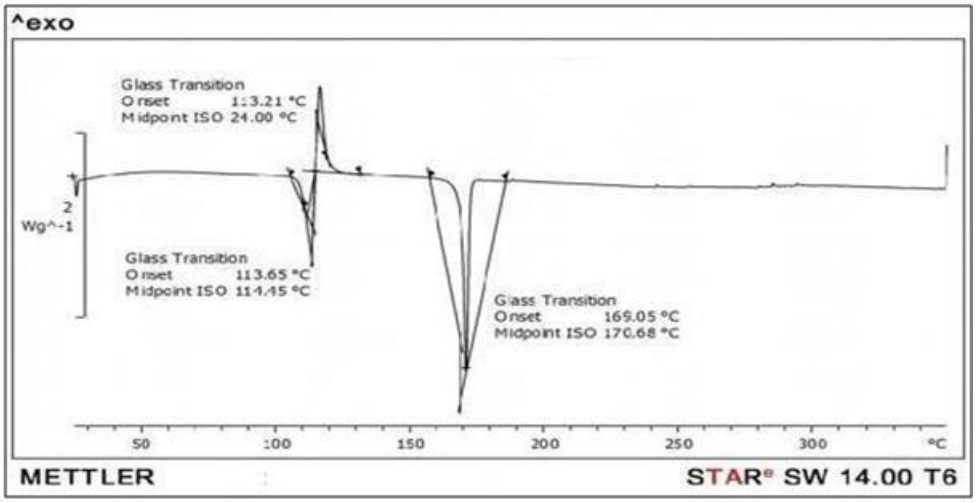

Figure No.5: DSC Thermo gram of posaconazole

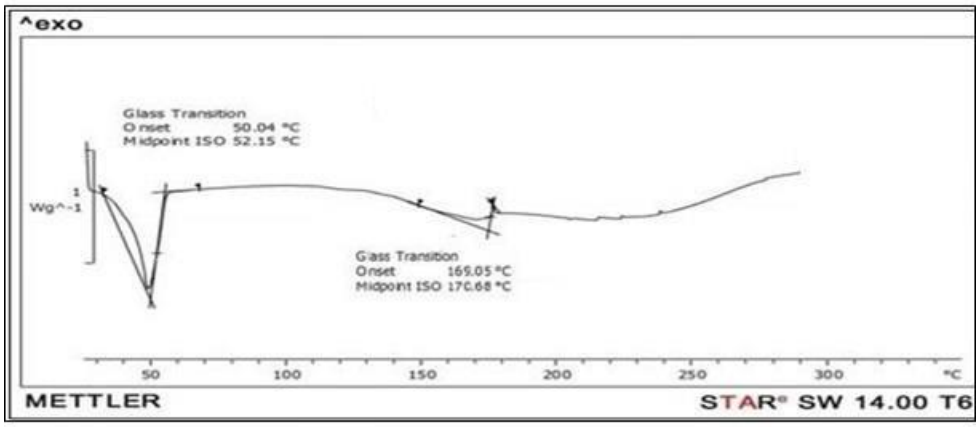

Figure No.6: DSC Thermo grams of physical mixture of posaconazole and polymers

DSC thermo gram of drug exhibited characteristic peak at 170^{0}C and physical mixture exhibited characteristic peak at 171.20^{0}C.

Evaluation of Precompression characteristics of Mucoadhesive tablet formulation Precompression study

The results of the studies indicated that the powder bed is easily compressible, and hence can be compressed into a compact mass of tablet. The angle of repose is an indicative parameter of powder Flow ability from hopper to die cavity. A repose angle between 25^0 to 30^0 indicates excellent Flow ability of powder bed. In this work, the angle of repose was found to be varying between 27.43º and 29.32º when glidant were

incorporated. These studies indicated that, the powder beds of all formulations are easily flow able.

Table No.4: Precompression characteristics of all tablet formulations

Formulation code	Angle of repose(θ) Mean± S.D.	Bulk density (gm/cm^3) Mean± S.D.	Tapped density (gm/cm^3) Mean± S.D.	Compressibility index (%) Mean± S.D.	Hausner's ratio Mean± S.D.
F1	29.93±0.668	0.3560±0.0023	0.4160±0.002	14.67±0.50	1.169±0.003
F2	30.52±0.652	0.3654±0.0027	0.4237±0.002	13.74±0.371	1.159±0.01
F3	29.17±0.454	0.3721±0.0016	0.4086±0.009	8.702±0.30	1.096±0.004
F4	25.76±0.538	0.3866±0.0025	0.4366±0.001	11.44±0.163	1.129±0.002
F5	27.95±0.647	0.3810±0.0031	0.4440±0.003	14.11±0.794	1.163±0.001
F6	26.80±0.527	0.3650±0.0072	0.4322±0.004	12.19±0.633	1.184±0.031
F7	28.12±0.728	0.3790±0.0054	0.4601±0.005	14.20±0.85	1.20±0.010
F8	26.28±0.713	0.3754±0.0021	0.4048±0.003	7.250±0.178	1.058±0.003
F9	28.07±0.731	0.3820±0.0030	0.449±0.005	15.0±0.508	1.178±0.006

Evaluation of compressional characteristics of all Mucoadhesive formulations

Table No.5: Evaluation of compressional characteristics of posaconazole tablets

Formulation code	Hardness (kg/cm^2)	Thickness (mm)	Weight variation (mg)	%Drug content	Surface pH
F1	4.13±0.01	2.80±0.01	298.6±1.1	94.84±0.49	6.3±0.2
F2	4.30±0.02	2.72±0.02	297±1.5	97.66±0.5	6.5±0.40
F3	4.11±0.01	2.75±0.08	296±1.0	96.95±0.60	6.8±0.15
F4	4.12±0.02	2.73±0.02	295±1.3	95.06±0.70	6.6±0.14
F5	4.69±0.01	2.72±0.01	294±1.5	91.89±0.50	6.6±0.15
F6	4.68±0.01	2.79±0.04	298±1.2	94.48±0.61	6.5±0.011
F7	4.51±0.01	2.79±0.02	297±1.5	92.19±0.70	6.7±0.058
F8	4.21±0.02	2.82±0.04	296±1.5	93.42±0.61	6.8±0.057
F9	3.94±0.02	2.81±0.02	298±1.7	95.88±0.60	6.7±0.057

Hardness of the tablets varied between 3.94 ± 0.02 Kg/cm^2 and 4.69 ± 0.01 Kg/cm^2 indicating good binding and satisfactory strength of tablets to withstand stress during transportation and also may offer good adhesion to mucosa. %. The drug content of the formulations F1 to F9 were found to be in between 91.89% and 97.66%. The surface pH of all the Mucoadhesive tablet formulations was found to be uniform, consistent between 6.3 to 6.8 indicating that all the formulations provide an acceptable pH in the range of salivary pH (5.5 to 7.0).

Table No.6: Evaluation of compressional characteristics of posaconazole tablets

Formulation code	Hardness (kg/cm^2)	Thickness (mm)	Weight variation (mg)	%Drug content	Surface pH
F1	4.13±0.01	2.80±0.01	298.6±1.1	94.84±0.49	6.3±0.2
F2	4.30±0.02	2.72±0.02	297±1.5	97.66±0.5	6.5±0.40
F3	4.11±0.01	2.75±0.08	296±1.0	96.95±0.60	6.8±0.15
F4	4.12±0.02	2.73±0.02	295±1.3	95.06±0.70	6.6±0.14
F5	4.69±0.01	2.72±0.01	294±1.5	91.89±0.50	6.6±0.15
F6	4.68±0.01	2.79±0.04	298±1.2	94.48±0.61	6.5±0.011
F7	4.51±0.01	2.79±0.02	297±1.5	92.19±0.70	6.7±0.058
F8	4.21±0.02	2.82±0.04	296±1.5	93.42±0.61	6.8±0.057
F9	3.94±0.02	2.81±0.02	298±1.7	95.88±0.60	6.7±0.057

Swelling study

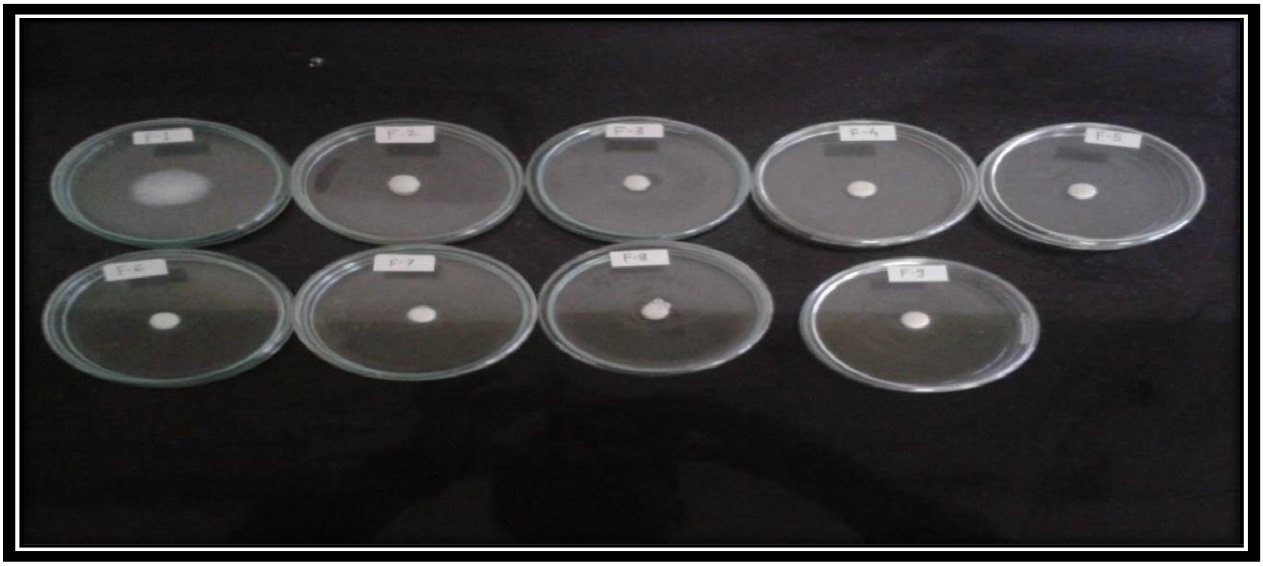

Figure No.7: Swelling study of Mucoadhesive tablet formulations F1 to F9 at 12 h

Table No.7: % swelling studies of buccal tablets Posoconazole

Formulation code / Time in h	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.25	18.65	16.65	17.88	18.84	17.45	18.05	15.36	16.36	17.59
0.5	27.62	29.62	28.56	27.96	31.37	30.12	28.87	27.87	30.27
1	32.99	43.99	44.26	38.27	36.77	35.17	32.92	30.92	36.37
2	49.87	58.87	57.6	50.43	50.16	49.48	44.32	43.32	49.05
4	60.41	63.41	65.17	62.99	63.84	65.87	55.84	53.84	62.05
8	70.36	72.36	74.47	76.34	78.34	80.04	68.05	65.05	69.24
12	82.56	83.56	84.89	85.25	89.25	92.85	81.96	84.96	87.23

Mucoadhesive strength

It was found that, all the tablet formulations possess adequate bioadhesion. Xanthan gum and carbopol influences the bioadhesion strength irrespective of the polymer used. Also, bioadhesion is found to be increasing with increase in concentration of polymers used.

Table No.8: Mucoadhesive strength of tablet formulations

Sr. No.	Formulation code	Mucoadhesive strength (N)
1	F1	0.0673±0.03
2	F2	0.1011±0.010
3	F3	0.1268±0.070
4	F4	0.0699±0.025
5	F5	0.1555±0.020
6	F6	0.1420±0.010
7	F7	0.1188±0.015
8	F8	0.11\312±0.025
9	F9	0.1680±0.01

In-vitro drug release study

Table No.9: In-vitro Drug released study of posaconazole buccal tablet F1 to F9

Time in h	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.25	24.17	12.37	10.37	10.37	12.37	4.02	2.42	2.02	2.42
0.5	44.67	16.82	14.82	14.82	17.82	6.02	4.75	4.02	4.75
1	47.20	21.18	18.18	18.18	22.18	7.01	6.01	7.01	6.01
2	55.78	28.02	21.02	21.02	29.02	9.5	8.63	8.15	8.5
3	64.86	34.75	27.75	27.75	38.75	11.25	10.25	11.25	10.25
4	72.73	42.66	32.66	32.66	50.66	16.14	21.14	14.14	14
5	79.13	45.89	36.89	36.89	54.89	21.72	31.72	21.72	19.72
6	84.19	52.38	48.38	48.38	57.38	33.56	37.56	28.56	25.56
7	92.23	55.99	54.99	54.99	64.99	39.06	43.06	36.06	38.06
8	97.82	64.26	62.26	62.26	68.26	45.07	46.07	48.07	46.07
9	99.90	72.82	70.82	70.82	76.82	51.82	49.82	52.82	49.82
10		79.3	74.3	74.3	84.3	57.56	58.56	56.46	54.56
11		86.7	80.87	80.87	94.76	61.79	62.79	61.79	60.79
12		87.68	84.68	83.68	99.96	67.46	77.46	66.46	64.46

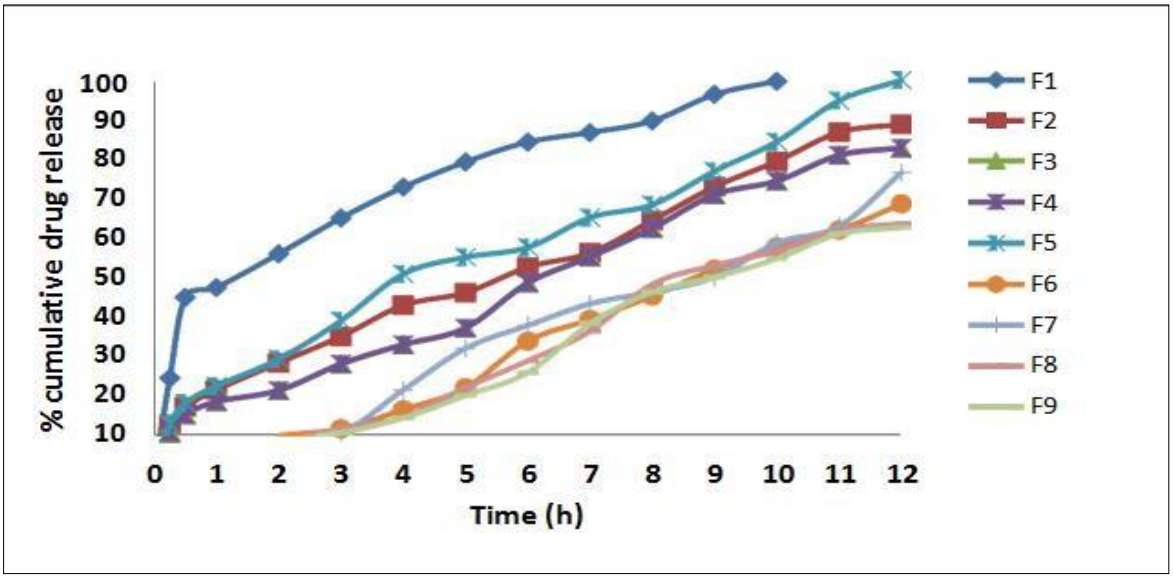

Figure No.8: In-vitro drug release of posaconazole buccal tablets F1 to F9

Stability study

From the data obtained it can be inferred that there was no change in physical parameters of the buccal tablets. Also, the tablets did not show any significant loss in their drug content, Mucoadhesive strength and percent drug release at 12 h. Therefore, it was ascertained that, the Mucoadhesive buccal tablets of posaconazole could be stored for a period of at least 2 years.

Table No. 10: Stability study for optimized formulation F 5 at 40^0C+75%RH

Frequency of testing	Drug content (% ± S.D.)	Mucoadhesive strength (gm± S.D.)	% Drug release at 12 h (% ± S.D.)
	Formulation F5		
0	98.68±0.26	26.61±1.02	96.10±1.75
8 days	98.12±0.10	27.12±1.23	96.20±0.99
15 days	99.52±0.25	26.10±1.12	97.74±1.74
1 month	98.25±0.10	27.00±0.98	98.45±1.35
2 months	98.56±0.56	27.10±1.04	99.12±2.15
3 months	99.02±0.45	26.31±1.12	99.46±1.14

Conclusion

Mucoadhesive dosage forms have long been employed to improve the bioavailability of drugs undergoing significant hepatic first-pass metabolism. Posaconazole has been selected as model drug because it exhibits pharmacokinetic and physicochemical properties justified for buccal delivery. It was planned in this investigation to develop Mucoadhesive buccal tablets containing an antifungal agent, posaconazole to release the drug in buccal cavity for extended period of time in order to avoid first-pass metabolism for improvement in bioavailability, to reduce the dosing frequency and to improve the patient compliance to treat the oral candidiasis.

References

1. *Shojaei AH. Buccal Mucosa as A Route for Systemic Drug Delivery: A Review. J Pharm Pharmaceut. Sci.1998; 1(1):15-30.*
2. *Sharma R, Kumar S, Malviya R, Prajapati BG, Puri D, Limmatvapirat S, Sriamornsak P. Recent advances in biopolymer-based mucoadhesive drug delivery systems for oral application. Journal of Drug Delivery Science and*

Technology. 2023 Dec 3:105227.

3. *Sampath Kumar KP, Bhowmik D, Amitsankar D, Paswan S, Deb. Recent advances in mucoadhesive buccal drug delivery systems and its marketed scope and opportunities, critical review in pharmaceutical sciences; 2012, 1: 79-93.*
4. *Kurcubic I, Cvijic S, Filipcev B, Ignjatovic J, Ibric S, Djuris J. Development of propranolol hydrochloride bilayer mucoadhesive buccal tablets supported by in silico physiologically-based modeling. Reactive and Functional Polymers. 2020 Jun 1;151:104587.*
5. *Smart JD. Drug delivery using buccal-adhesive systems. Advanced drug delivery reviews. 1993 Sep 1;11(3):253-70.*
6. *Venkatlakshmi R, Sudhakar Y, Chetty M, Sasikala C, and Mohan verma M. Buccal drug delivery using adhesive polymeric patches. International J pharmacy science & research. 2012, 3(1)56-66.*
7. *Russo E, Selmin F, Baldassari S, Gennari CG, Caviglioli G, Cilurzo F, Minghetti P, Parodi B. A focus on mucoadhesive polymers and their application in buccal dosage forms. Journal of drug delivery Science and Technology. 2016 Apr 1;32:113-25.*
8. *Al-Dhubiab BE, Nair AB, Kumria R, Attimarad M, Harsha S. Formulation and evaluation of nano based drug delivery system for the buccal delivery of acyclovir. Colloids and Surfaces B: Biointerfaces. 2015 Dec 1;136:878-84.*
9. *Phanindra B, Krishna Moorthy B and Muthukumaran M. Recent advances in mucoadhesive/bioadhesive drug delivery system: A review. Int. J. Pharm. Med. & Bio. Sci. 2013; 2(1): 68-84.*
10. *Patil H, Tiwari RV, Repka MA. Recent advancements in mucoadhesive floating drug delivery systems: A mini-review. Journal of Drug Delivery Science and Technology. 2016 Feb 1;31:65-71.*
11. *Sharma R, Kumar S, Malviya R, Prajapati BG, Puri D, Limmatvapirat S, Sriamornsak P. Recent advances in biopolymer-based mucoadhesive drug delivery systems for oral application.*

Journal of Drug Delivery Science and Technology. 2023 Dec 3:105227.

12. *Patel M, Karigar A, Savaliya P, Ramana M, Dubal A. Buccal drug delivery system: the current interest. Int. res. J. of pharm. 2012; 2(12):4-11.*
13. *Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. Adv. Drug. Del. Rev. 2005; 57 (11): 1666– 1691.*
14. *Hagerstrom H, Paulsson M, Edsman K. Evaluation of mucoadhesion for two polyelectrolyte gels in simulated physiological conditions using a rheological method. Eur. J. Pharm. Sci. 2000; 9 (3): 301–309.*
15. *Roy S ,Pal K, Anis A, Pramanik K, Prabhakar B. Polymers in Mucoadhesive Drug Delivery System: A Brief Note. Designed Monomers and Polymers.2009; 12: 483-495.*
16. *Punitha S, Girish Y. Polymers in mucoadhesive buccal drug delivery system – A review. Int. J. Res. Pharm. Sci. 2010; 1(2): 170-186.*
17. *Alopaeus JF, Hellfritzsch M, Gutowski T, Scherließ R, Almeida A, Sarmento B, Škalko-Basnet N, Tho I. Mucoadhesive buccal films based on a graft co-polymer–A mucin-retentive hydrogel scaffold. European Journal of Pharmaceutical Sciences. 2020 Jan 15;142:105142.*
18. *Balakrishna T. Formulation and Evaluation of Lansoprazole Fast Dissolving Buccal Films. AJP [Internet]. 2018;12(02).*
19. *Dubey AK, Singla RK. Current Trends in Anti-Candida Drug Development. Curr Top Med Chem. 2019;19(28):2525-2526.*
20. *Szekalska M, Wróblewska M, Trofimiuk M, Basa A, Winnicka K. Alginate oligosaccharides affect mechanical properties and antifungal activity of alginate buccal films with posaconazole. Marine Drugs. 2019 Dec 9;17(12):692.*
21. *Wiederhold NP. Pharmacokinetics and safety of posaconazole delayed-release tablets for invasive fungal infections. Clinical Pharmacology: Advances and Applications. 2015 Dec 23:1-8.*