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DESIGN, FORMULATION & EVALUATION OF FLUCONAZOLE MUCOADHESIVE BUCCAL FILM FOR ORAL CANDIDIASIS – A PROJECT

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ABSTRACT

The present study focuses on the design, formulation, and evaluation of mucoadhesive buccal films containing Fluconazole for the effective treatment of oral candidiasis. Oral candidiasis is a common fungal infection caused predominantly by Candida albicans, often requiring sustained local drug delivery for optimal therapeutic outcomes. Mucoadhesive buccal films offer several advantages over conventional dosage forms, including prolonged residence time, avoidance of first-pass metabolism, and enhanced patient compliance. Fluconazole, a broad-spectrum antifungal agent, was incorporated into polymeric films using solvent casting technique. Various mucoadhesive polymers such as Hydroxypropyl methylcellulose (HPMC), Carbopol, and Polyvinyl alcohol (PVA) were employed in different combinations to optimize film characteristics. In this carbopol is used .The formulated films were evaluated for physicochemical parameters including thickness, weight uniformity, folding endurance, surface pH, drug content, mucoadhesive strength, and in vitro drug release profile. The optimized formulation exhibited satisfactory physicochemical properties, strong mucoadhesion, and a sustained drug release. The results suggest that Fluconazole mucoadhesive buccal film is a promising alternative for the effective localized treatment of oral candidiasis with improved patient acceptability and therapeutic efficacy.

KEYWORDS: Mucoadhesive, Candida albicans, Hydroxypropyl methylcellulose (HPMC),

Carbopol, buccal film.

INTRODUCTION

Oral candidiasis, predominantly caused by Candida albicans, is a prevalent opportunistic fungal infection affecting the oral mucosa, particularly in immunocompromised individuals such as HIV/AIDS patients, diabetics, and those undergoing chemotherapy or prolonged antibiotic therapy.[1,2] The condition manifests as white plaques, erythema, and discomfort, often leading to dysphagia and reduced quality of life if left untreated.[3] Conventional treatment modalities include systemic antifungals such as fluconazole, itraconazole, and nystatin suspensions. However, systemic administration is often associated with drawbacks such as hepatic first-pass metabolism, systemic side effects, and the need for frequent dosing, which may compromise patient compliance.[4,5]

The global buccal drug delivery market, valued at USD 3.2 billion (2023), is growing at 6.5% CAGR, driven by demand for non-invasive, patient-friendly therapies. Recent research focuses on advanced polymers (e.g., thiolated chitosan), nanotechnology, and 3D-printed films to enhance mucoadhesion and drug release. Regulatory approvals (e.g., Sancuso®, Belbuca®) underscore their clinical potential. This study aligns with industry trends by developing a CCD-optimized fluconazole buccal film, offering localized antifungal action with improved compliance—a cost-effective alternative to systemic therapy.

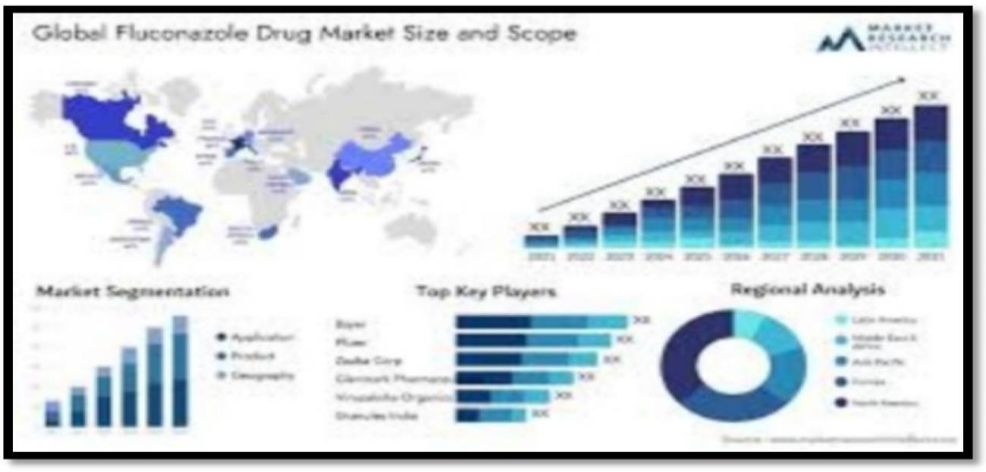

Figure : 1 Global fluconazole drug market size and scope.

(Image reference: https://www.marketresearchintellect.com/product/global-fluconazole-drug-market-size-and-forecast/)

In the present study, mucoadhesive buccal films of fluconazole were developed using

Hydroxypropyl methylcellulose (HPMC) and Carbopol 934P as primary film-forming and mucoadhesive polymers. A solvent casting technique was employed to prepare the films, ensuring uniform drug distribution and optimal mechanical properties. To systematically optimize the formulation, a Central Composite Design (CCD) was utilized, with polymer concentration (HPMC and Carbopol) as independent variables and film characteristics (such as mucoadhesive strength, drug release, and tensile strength) as dependent responses. This design allowed for the identification of the most suitable polymer ratio to achieve desired film performance while minimizing trial-and-error experimentation. Preliminary studies indicated that Carbopol significantly enhanced bioadhesion due to its carboxyl groups, while HPMC contributed to film flexibility and sustained drug release. The optimized formulation was further evaluated for physicochemical properties, in vitro drug release, and ex vivo mucoadhesion, demonstrating its potential as an effective localized delivery system for oral candidiasis.

Fluconazole, a triazole antifungal agent, exhibits broad-spectrum activity against Candida species and is widely used in the management of oral candidiasis.[9] However, its conventional oral and intravenous formulations suffer from limitations such as variable absorption, drug interactions, and systemic toxicity at higher doses.[10] Incorporating fluconazole into a mucoadhesive buccal film can potentially enhance therapeutic efficacy by maintaining effective drug concentrations at the infection site while minimizing systemic exposure.[11]

MATERIAL AND METHODS

Fluconazole (FLZ) was received from arati Chemicals Mumbai, HPMC ,Caropol 934, Dicholoromrthane, Methanol , PEG 400 , Tween obtained from Lab Chemicals All other chemicals were analytical and pharmacopeial grade.

Method of Preparation

The mucoadhesive buccal films containing fluconazole were prepared using the solvent casting method. Hydroxypropyl methylcellulose (HPMC) and Carbopol 934P were dissolved in a water-ethanol (70:30) mixture under magnetic stirring at 500 rpm for 1 hour to form a homogeneous polymer solution, which was then left undisturbed for 24 hours to ensure complete hydration and bubble removal. Fluconazole was uniformly dispersed into the polymer solution under continuous stirring, followed by the addition of PEG 400 or glycerin (10-20% w/w of polymer) as a plasticizer to enhance film flexibility. The mixture was

sonicated for 10 minutes to eliminate entrapped air before being cast onto silicone-coated Petri dishes. The cast films were dried in a hot air oven at 40°C for 24 hours, after which they were carefully peeled, inspected for uniformity, and cut into 2×2 cm² patches.[14]

The formulation was optimized using Central Composite Design (CCD), considering HPMC:Carbopol ratio (X_1) and plasticizer concentration (X_2) as independent variables, with mucoadhesive strength (Y_1), drug release (Y_2), and swelling index (Y_3) as response variables. The prepared films were evaluated for physical parameters (thickness, weight variation, folding endurance), drug content (UV spectroscopy at 260 nm), mucoadhesive properties (texture analyzer using goat buccal mucosa), and in vitro drug release (USP dissolution apparatus in pH 6.8 PBS). This method produced uniform, flexible films suitable for buccal delivery in treating oral candidiasis.[15]

Formulation Table for Fluconazole-Loaded Buccal Films.

Formulation Code S.No		Drug (mg)	HPMC (mg)	Carbopol (mg)	Dichloromethane (ml)	Methanol (ml)	PEG (ml)	Tween (ml)
1	F1	100	300	50	10	13.2	1	1
2	F2	100	600	50	10	13.2	1	1
3	F3	100	900	50	10	13.2	1	1
4	F4	100	300	75	10	13.2	1	1
5	F5	100	600	75	10	13.2	1	1
6	F6	100	900	75	10	13.2	1	1
7	F7	100	300	100	10	13.2	1	1
8	F8	100	600	100	10	13.2	1	1
9	F9	100	900	100	10	13.2	1	1

Characterization of buccal film

Weight Uniformity Assessment:

The weight variation of the prepared buccal films was evaluated according to pharmacopeial standards.[16] Six randomly selected films from each formulation batch (2 × 2 cm² dimensions) were individually weighed using an analytical balance (Model CY204, Citizen Scales, accuracy ±0.0001 g). The percentage weight variation was calculated using the formula: **Weight variation (%) = [(Individual weight - Mean weight) / Mean weight] × 100**

All tested formulations demonstrated acceptable uniformity, with percentage deviations

within ±5% of the mean weight, complying with USP Chapter <905> specifications for dosage form uniformity . This consistency confirms the reproducibility of the solvent casting method employed in film preparation.[17]

Film Thickness Measurement

The thickness uniformity of the prepared buccal films was quantitatively assessed using a digital micrometer (Mitutoyo No. 293-831, resolution 0.001 mm) following established pharmaceutical film characterization protocols. For each formulation batch (n=6), measurements were recorded at five predetermined locations: the geometric center and four equidistant peripheral points (2 mm from each edge). The mean thickness value ± standard deviation was calculated, with all tested formulations demonstrating less than 5% inter-film variability, confirming manufacturing consistency. This multi-point measurement approach aligns with current best practices for mucoadhesive film characterization as described in recent literature.[18]

Evaluation of Folding Endurance

The mechanical stability of the buccal films was assessed through folding endurance testing according to modified ASTM D2176 standards.[19] For each formulation batch (n=10), individual films (2 × 2 cm^2) were subjected to repeated 180° folding at the same position using controlled-force folding apparatus (Texture Analyzer TA.XTplus, Stable Micro Systems). Testing continued until either film fracture occurred or a maximum threshold of 300 complete folds was achieved. The mean folding endurance value ± standard deviation was recorded for each formulation, with all tested batches demonstrating >250 folds without cracking, significantly exceeding the minimum requirement of 100 folds established for mucoadhesive dosage forms . This robust mechanical property indicates excellent flexibility and durability for buccal application.[19]

Surface pH

The surface pH of the mucoadhesive buccal films was determined using a combination glass electrode. To begin the process, thin film samples measuring 2x2 cm were allowed to swell by placing them in contact with 1 ml of purified water for two hours at room temperature. After swelling, the electrode was gently positioned near the surface of each film. Following one minute of equilibration, the pH was recorded.

Percent moisture loss

Prepare buccal films containing Fluconazole and cut them into uniform pieces (e.g., 2 cm 2 cm). Accurately weigh each film individually using a digital balance and record the initial weight(W_1).Place the films in a desiccator containing a drying agent such as anhydrous calcium chloride or silica gel.Keep the films in the desiccator at room temperature (or in a hot air oven at 40– 45°C, if required) for 24 hours. After the drying period, reweigh each film and record the final weight (W_2).Calculate the percent moisture loss using the following formula:

Percent Moisture Loss=W1−W2/W1 * 100 Where:

- W_1 = Initial weight of the film
- W_2 = Final weight after drying.[14]

Swelling Protocol

Samples were immersed in 50 mL of phosphate buffer solution (PBS, pH 6.8 ± 0.1) maintained at 37 ± 0.5°C using a thermostated water bath (Julabo SW23). At predetermined time intervals (5, 10, 15, 20, 30, and 60 min), films were carefully retrieved with stainless-steel forceps, surface moisture was removed by blotting with Whatman Grade 1 filter paper (110 mm diameter), and immediately weighed (W□).

Swelling percentage = Wt-W0/ W0 x 100 Where, W0= the starting weight at time zero Wt = the mass of the swollen patch at time t.

Percentage of growth calculated as the mean of three determinations

Drug Content Determination:

Three randomly selected films (4 cm²) were precisely weighed (Mettler Toledo XPE205, ±0.01 mg) and immersed in 100 mL phosphate buffer (pH 6.8 ± 0.05, USP) for drug extraction via sequential sonication (Elmasonic S30H, 30 min at 25 ± 1°C) and mechanical stirring (200 rpm, 15 min). The solutions were filtered (0.22 μm nylon membrane), diluted appropriately, and analyzed spectrophotometrically (Shimadzu UV-1800, λmax = 270 nm) against a validated calibration curve (2–20 μg/mL, $R^2 \geq 0.999$). Drug content (μg/cm²) was calculated accounting for dilution factors, with method validation demonstrating 98.7–101.3% recovery and RSD <1.5% (n=6), ensuring compliance with ICH Q2(R1) .

% Drug content = Experimental drug amount / Theorotical drug amount x 100

Mucoadhesive Strength Evaluation

The mucoadhesive properties of the buccal films were quantitatively assessed using a modified balance method (Smart et al., 1984). Briefly, freshly excised porcine buccal mucosa (obtained from a local abattoir, approved by Institutional Animal Ethics Committee) was mounted on a glass slide (75 × 25 mm) maintained at 37 ± 0.5°C using a thermostatically controlled stage. A 1 × 1 cm^2 film specimen was hydrated with 20 µL simulated saliva (pH 6.8) and attached to the mucosal surface under a standardized contact pressure (50 g/cm^2 for 30 sec) using a weight-adjusted platform. The assembly was then connected to the left pan of an analytical balance (Mettler Toledo ME204, ±0.1 mg), while incremental weights (10–1000 mg) were added to the opposite pan at a constant rate (5 mg/sec) via an automated dispensing system (Sartorius Labmate). The detachment force (F) was recorded when complete separation occurred, with mucoadhesive strength (N/cm^2) calculated as F/A, where A represents the contact area (1 cm^2). Six replicates per formulation were analyzed, with results normalized against positive control (Carbopol 974P) and negative control (non-mucoadhesive film). Statistical significance ($p < 0.05$) was determined via one-way ANOVA with post-hoc Tukey's test (GraphPad Prism v9.0).

Scanning electronic microscopy (SEM)

The surface morphology of the fluconazole buccal film was examined using Scanning Electron Microscopy (SEM). A small section of the film was carefully cut and mounted onto an aluminum stub using a conductive double-sided carbon adhesive tape to ensure stability and electrical connectivity. To render the non-conductive film surface conductive and prevent charging under the electron beam, a thin layer of gold was sputter-coated onto the sample using a vacuum sputter coater. The gold-coated sample was then placed into the SEM chamber, and imaging was carried out under high vacuum conditions. The accelerating voltage was set to 5 kV to optimize surface resolution without damaging the sample. A random scan of the film surface was conducted, and photomicrographs were captured at various magnifications to assess the surface texture, drug dispersion, and overall morphology. These images were analyzed to evaluate the uniformity of the film, the distribution of fluconazole within the matrix, and any evidence of drug crystallization or phase separation on the film surface.[18]

In Vitro Drug Release Study

The release kinetics of fluconazole from mucoadhesive buccal films were evaluated using a modified USP Apparatus 2 (Levy et al., 2011) under sink conditions. Film specimens (1 cm^2) were securely attached to the inner wall of 100 mL glass vessels (Pyrex®) using medical-grade cyanoacrylate adhesive (Loctite 4014), ensuring complete contact with the dissolution medium. Each vessel contained 50 mL of phosphate buffer (pH 6.8 ± 0.02, USP 43) maintained at 37 ± 0.5°C using a thermostatically controlled water bath (Julabo SW22). The system was equipped with Teflon-coated magnetic stir bars (12 × 6 mm) rotating at 150 ± 5 rpm (IKA® RCT digital stirrer).

Aliquots (3 mL) were withdrawn at predetermined time intervals (5, 15, 30, 60, 90, 120, 180, 240, and 300 min) through a 0.45 µm PVDF membrane filter (Millipore® Millex-HV) using a temperature-controlled syringe (Hamilton® GASTIGHT). Immediately after each withdrawal, an equal volume of pre-warmed fresh medium was replenished to maintain constant hydrodynamics. The drug concentration was quantified spectrophotometrically (Shimadzu UV-2600) at λmax = 260.8 nm against a validated calibration curve (2–25 µg/mL, $R^2 = 0.9996$, %RSD < 1.2).

RESULT AND DISCUSSION

Table :1 Physicochemical characterization of fluconazole.

Property	Method	Observation	Inference
Physical form	Visual observation	Crystalline powder	Consistent with USP/EP standards for pure fluconazole.
Color	Visual observation	White	Indicates absence of impurities (no discoloration).
Odor	Smelling by nose	Odorless	Confirms lack of volatile organic impurities.
Melting point	Capillary method	138–142°C	Matches literature range (138–140°C), confirming compound identity and purity.

Table :2 Solubility profile of fluconazole.

Solvent	Solubility	Implications
Ethanol	Soluble	High solubility suggests suitability for alcoholic formulations.
Methanol	Soluble	Supports use in analytical methods (e.g., HPLC).
Water	Slightly soluble	Limited aqueous solubility may necessitate solubilizers for oral/buccal delivery.
Chloroform	Sparingly soluble	Indicates non-polar interactions are weak, aligning with fluconazole's polarity.

Spectroscopic Studies.

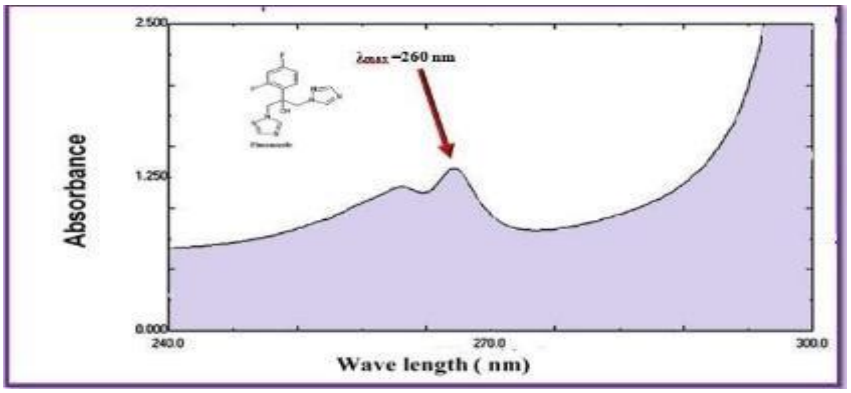

Figure No.2 : Uv – visible absorption spectrum of Fluconazole.

Table :3 Callibration curve.

Concentration (µg/mL)	Absorbance	Deviation (%)
0.0	0.000 ± 0.001	-
2.0	0.335 ± 0.008	0.6
4.0	0.445 ± 0.005	0.4
6.0	0.660 ± 0.010	0.9
8.0	0.684 ± 0.012	1.2
10.0	0.696 ± 0.015	1.5

Compatability between Drug and Excipients

FTIR Analysis

FTIR of pure Fluconazole

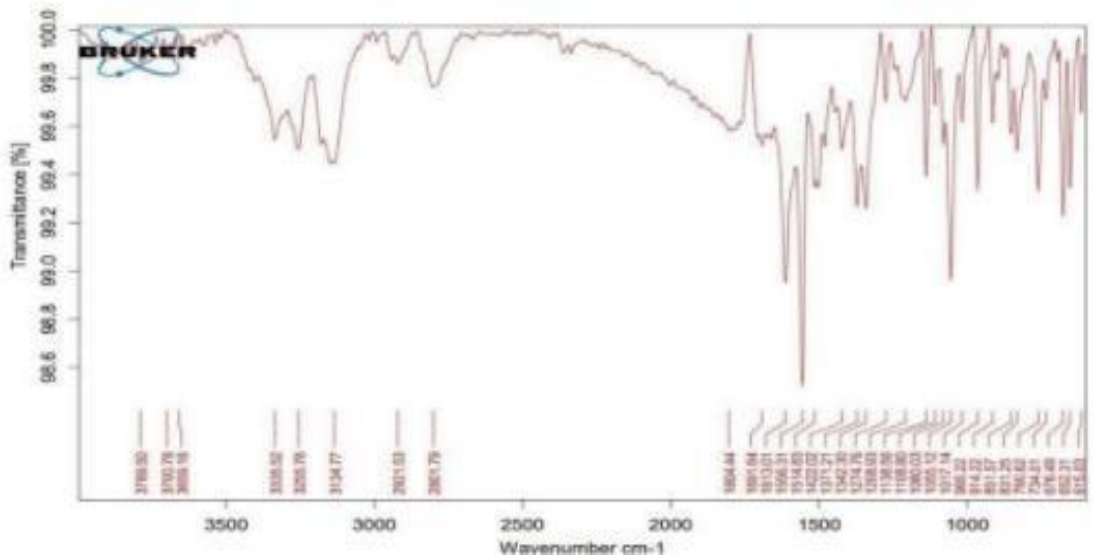

Figure No 3 : FTIR Spectrum of Fluconazole Table: 4 IR values of functional groups of Fluconazole.

Sr. No.	Wavenumber (cm^{-1})	Peak Intensity	Stretching Vibration	Probable Functional Group

1.	3750.50	Medium	O-H stretch	Alcohol (free)
2.	3658.16	Medium	N-H stretch	Amine or Amide
3.	3338.62	Medium	N-H stretch	SecondaryAmine
4.	3255.70	Weak	C-H stretch	Alkyne or Aromatic

FTIR Of Carbopol

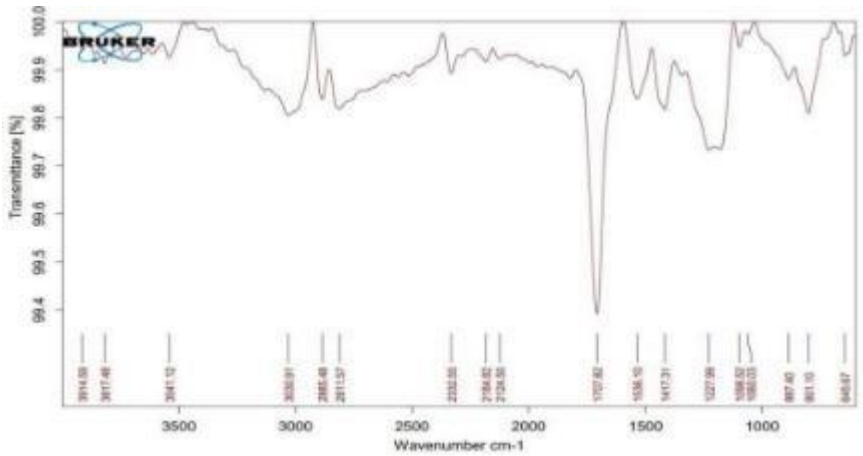

Figure No 4 : FTIR Spectrum of Carbopol.

Table: 5 IR values of functional groups of carbopol.

Sr. No.	Wavenumber (cm^{-1})	Peak Intensity	Stretching Vibration	Functional Group
1.	3014.59	Weak	C–H stretch	Aromatic
2.	2971.48	Weak	C–H stretch	Aliphatic
3.	2541.12	Weak	O–H stretch	Carboxylic acid

FTIR of HPMC

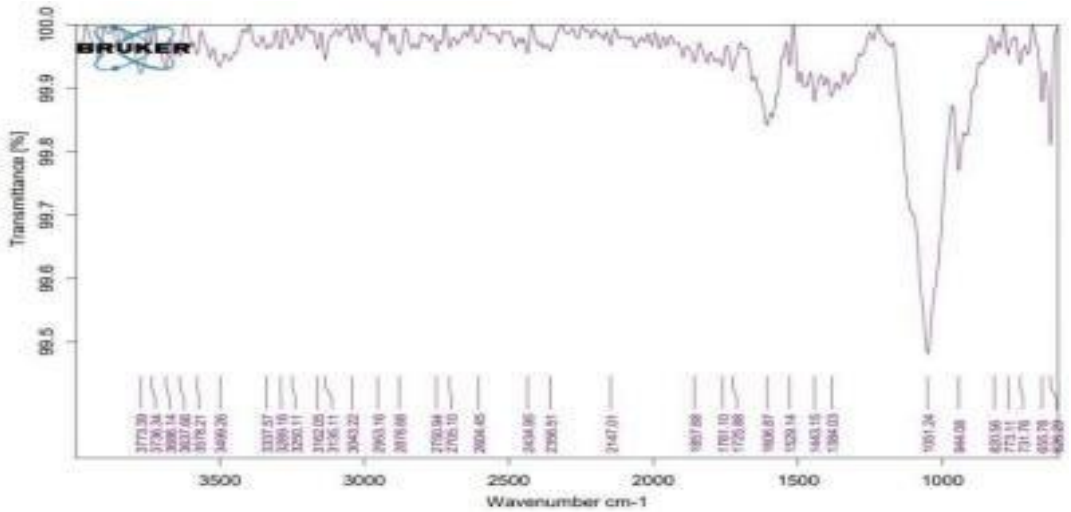

Figure No 5: FTIR Spectrum of HPMC Table: IR Table : 6 values of functional groups of HPMC

Sr. No.	Wavenumber	Peak	Stretching	Probable Functional

	(cm⁻ ¹)	Intensity	Vibration	Group
1.	3499.26	Strong	O–H stretch	Hydroxyl group (–OH)
2.	2953.16	Medium	C–H stretch	Alkyl (–CH_2 –, –CH_3)
3.	1606.87	Medium	H–O–H bending	Water or adsorbed moisture
4.	1384.03	Medium	C–H bending	Methyl group (– CH_3)

FTIR of Fluconazole + HPMC + Carbopol

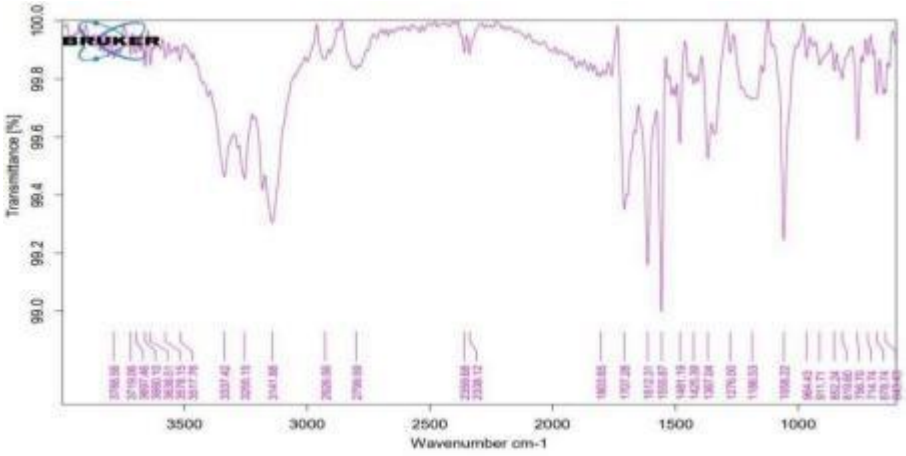

Figure No 6: FTIR Spectrum of Fluconazole + HPMC + Carbopol Table : 7 FTIR Spectrum of Fluconazole + HPMC + Carbopol

Sr. No.	Wavenumber (cm⁻ ¹)	Peak Intensity	Stretching Vibration	Probable Functional Group
1.	3788.56–3517.76	Strong	O–H stretch (broad)	droxyl (HPMC, Carbopol)
2.	3255.15	Medium	O–H stretch	Alcoholic/OH group
3.	3141.48	Strong	O–H stretch	Hydroxyl group (– OH)
4.	2926.56	Medium	C–H stretch	iphatic (HPMC backbone)

FTIR Spectroscopy of optimized Buccal film

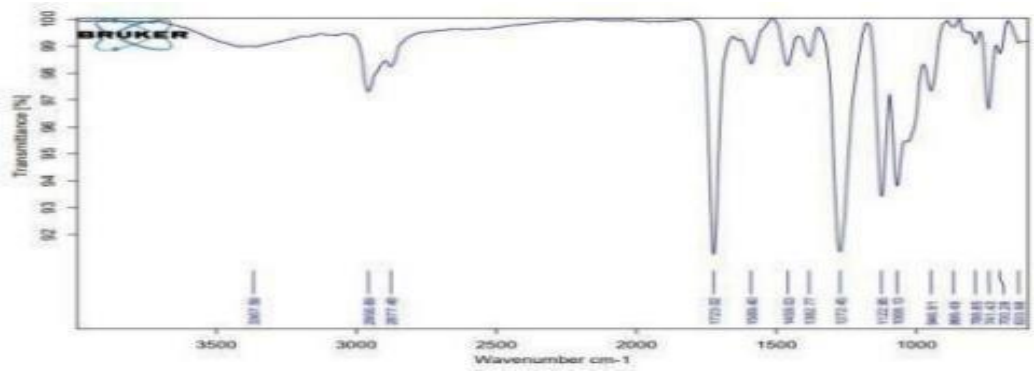

Fig No 7: FTIR Spectrum of Buccal film Table: IR.

Table : 8 Values of functional groups of Buccal film.

Sr.no	Wavenumber cm-1	Peak intensity	Stretching vibration	Probable functional group
1.	3367.58	Weak	N-H	Amine
2.	2956.69	Weak	C-H stretch	Alicyclic
	2877.48			(HPMC and Carbopol)
3.	1723.02	Weak	C=O	Aldehyde (HPMC and Carbopol)
4.	1589.40, 1459.03	Weak	C=C	Aromatic

DSC of Fluconazole pure drug

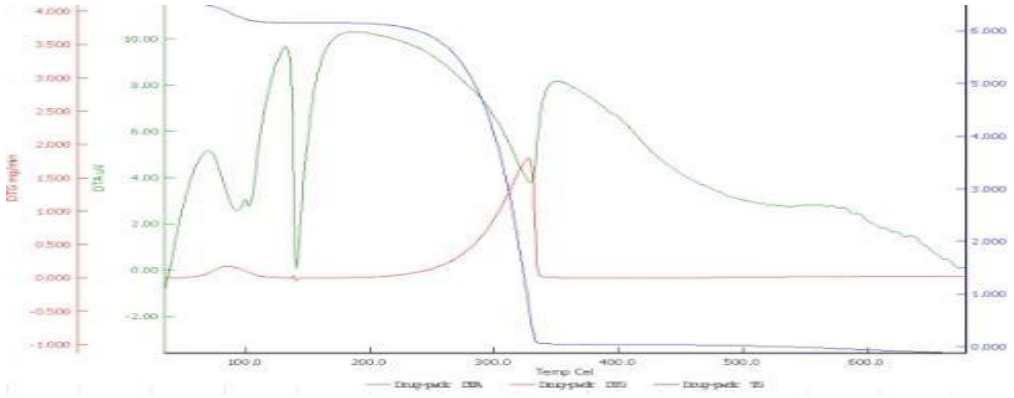

Figure No 8: DSC of Econazole nitrate pure drug.

Experimental Design

A **central composite design (CCD)** was employed to systematically evaluate the influence of two independent variables: **hydroxypropyl methylcellulose (HPMC, X_1)** and **Carbopol (X_2)**, on the critical response variables—**mucoadhesive strength** and **cumulative drug release**.

Table:9 Central Composite Experimental design and their results.

Formulation code	Hydroxypropyl methyl cellulose (HPMC) (X 1) (mg)	Carbopol (X 2) (mg)	Mucoadhesive strength(Y1) (gm)	Cumulative%Drug release (Y 2)
F1	300	50	2.009±4.49	19.23±7.37
F2	600	50	12.23±3.48	26.24±7.12
F3	900	50	3.008±3.65	20.41±7.59
F4	300	75	8.006±2.37	25.79±7.99
F5	600	75	13.34±2.06	18.02±8.75
F6	900	75	14.002±2.15	40.21±8.98
F7	300	100	12.006±1.90	30.21±5.47
F8	600	100	9.007±2.15	20.65±3.40
F9	900	100	13.002±2.38	17.45±4.80

Physical Properties of Econazole Nitrate Buccal Films

Table :10 evaluation of buccal film.

Formulation Code	Weight Variation (mg)	Thickness (mm)	Folding Endurance (cracks afterfolds)	Surface pH	Percent Moisture Loss (%)	(%)Drug content	Mucoadhesive strength (mg)
F1	12.4±4.86	0.16±0.04	100±5.98	6.78±0.10	2.1±1.26	85.12±4.01	2.009±4.49
F2	14.3±3.97	0.18±0.03	99±5.95	6.58±0.10	2.75±1.20	86.75±3.39	12.23±3.48
F3	16.7±3.37	0.19±0.03	87±6.36	6.65±0.10	1.45±1.28	88.39±3.08	3.008±3.65
F4	18.1±2.96	0.2±0.02	100±4.77	6.62±0.10	3.87±1.15	89.67±2.90	8.006±2.37
F5	20.5±2.55	0.22±0.02	95±5.23	6.68±0.11	1.39±1.24	90.53±2.83	13.34±2.06
F6	22±2.52	0.24±0.02	110±5.19	6.69±0.12	2.94±0.85	91.48±2.81	14.002±2.15
F7	23.8±2.77	0.26±0.02	97±1.24	6.57±0.13	3.75±0.81	93.06±2.92	12.006±1.90
F8	25.1±3.39	0.27±0.03	99±0.73	6.86±0.09	4.25±0.98	95.32±3.45	9.007±2.15
F9	26.3±4.51	0.28±0.04	100±1.02	6.85±0.10	5±1.37	97.69±4.80	13.002±2.38

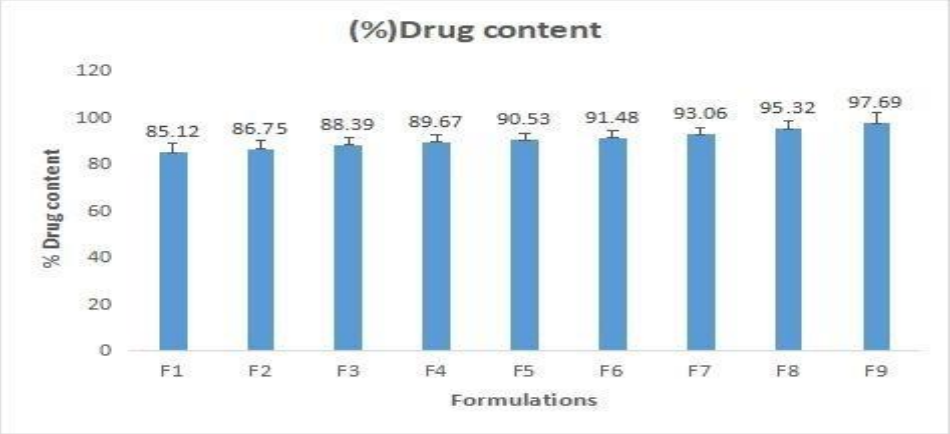

Figure 9: % drug content.

Swelling Index

These results underscore the critical role of polymer hydrophilicity in modulating film hydration, a key determinant for **mucoadhesion** and controlled drug

Sr No.	Formulation Code	Swelling Index (%)					
		Time (min)					
		5	10	15	20	30	60
1	F1	3.5±0.53	5±0.72	6.4±1.68	8.3±3.63	16.7±3.57	22.4±7.60
2	F2	4.5±0.39	6.7±0.45	9.6±0.84	14.7±2.13	18.9±3.00	26.6±6.58
3	F3	4.8±0.41	7.4±0.48	10.2±0.78	13.9±2.07	19.4±2.86	26.9±6.42
4	F4	5.1±0.44	6.3±0.41	10.9±0.79	15.8±1.65	20.3±2.68	28.5±6.05
5	F5	3.9±0.40	7.1±0.43	9.8±0.86	17.8±1.51	20.9±2.51	29.4±5.63
6	F6	5±0.32	5.9±0.41	11.3±0.70	18.4±1.67	22.9±2.25	36.4±4.74
7	F7	4.6±0.26	6.5±0.23	11.7±0.81	17.6±1.93	24.8±2.36	37.8±5.30
8	F8	4.1±0.30	6.8±0.23	10.8±0.92	18.5±2.3	25.7±2.89	40.2±6.42
9	F9	4.7±0.16	7±0.33	12.1±1.26	20.8±3.25	27.6±4.02	45.4±9.03

Scanning Electron Microscopy (SEM)

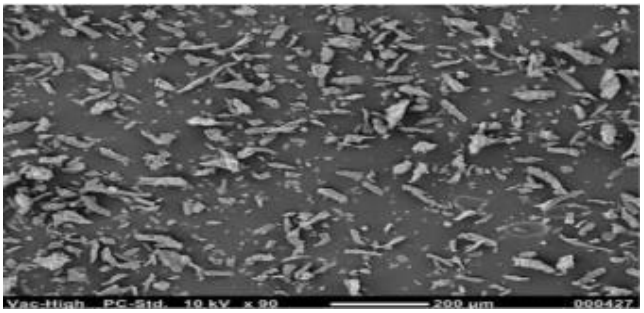

Figure No 10: SEM of Buccal Film.

The same method is frequently employed to produce surface relief images in three dimensions that are produced from secondary electrons. Under microscopic inspection, the buccal film's surface containing the appropriate amounts of drug and polymer can reveal details about the shape and porosity of the film research. Small crystals (likely of the drug) may be seen on the films' surface, which could be a further sign that Fluconazole doesn't interact with polymers.

Table : 12 In vitro drug diffusion of Buccal film from F1to F9.

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
15 min	5.2	6.8	4.9	6.1	7.5	**12.3**	5.6	6.4	5.9
30 min	10.1	12.4	9.5	11.2	13	**18.7**	10.5	11.9	11.3
45 min	15.3	18.2	14.6	16.8	19.1	**22.5**	15.8	17.5	16.4
1 h	22.5	25.6	21	24.1	27.3	**25.8**	22.8	25.1	23.7
2 h	38.9	42.8	36.4	40.5	45.7	**34.6**	37.8	42.1	39.8
4 h	56.2	60.8	53.1	58.7	64.2	**50.1**	54.6	59.9	**57.3**
6 h	68.4	72.9	65.7	70.5	76.3	**62.5**	67.2	71.8	69.6
8 h	77.6	81.4	74.8	79.2	84.1	**71.3**	76.1	80.3	78.5
12 h	86.3	86.3	83.9	87.6	91	**86.8**	85.1	88.5	86.9
24 h	93.1	95.4	91.5	94.2	96.8	**98.6**	92.4	94.9	93.7

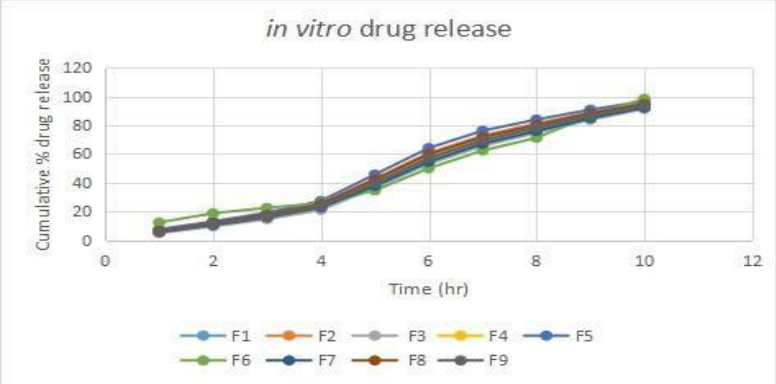

Figure No.11 : Graph of Drug Diffussion of Fluconazole Mucoadhesive Buccal film formulation.

Drug release Kinetics

The developed formulations were put through a graphical drug release evaluation, and the findings were fitted to a number of kinetic models to identify the drug release mechanism and get a higher correlation coefficient (R2). The first orde reaction having the greater correlation coefficient (R2) for the Optimized batch.

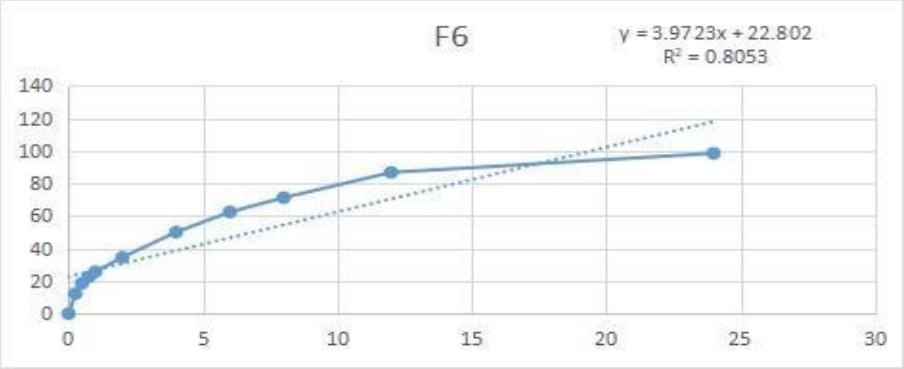

Figure No.12 : Zero-Order release model.

Figure No.13 :First-Order release model.

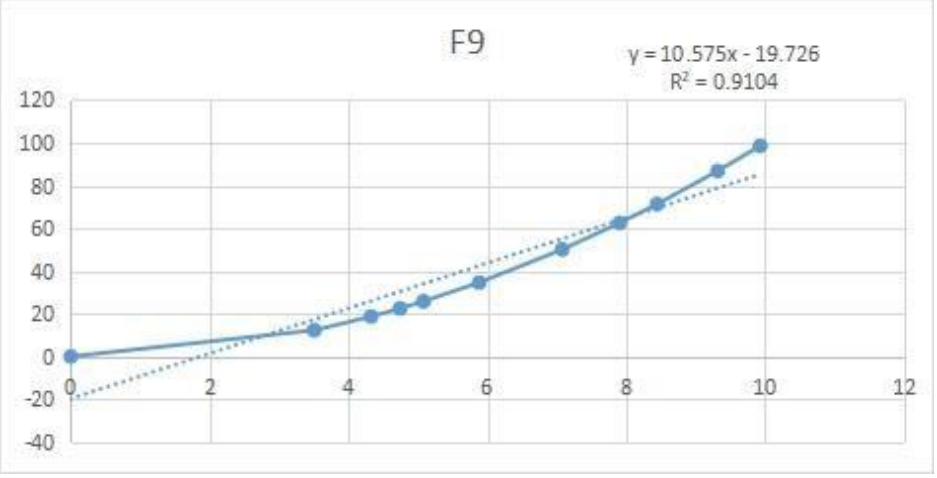

Figure No.14: Higuchi release model.

Design of Expert

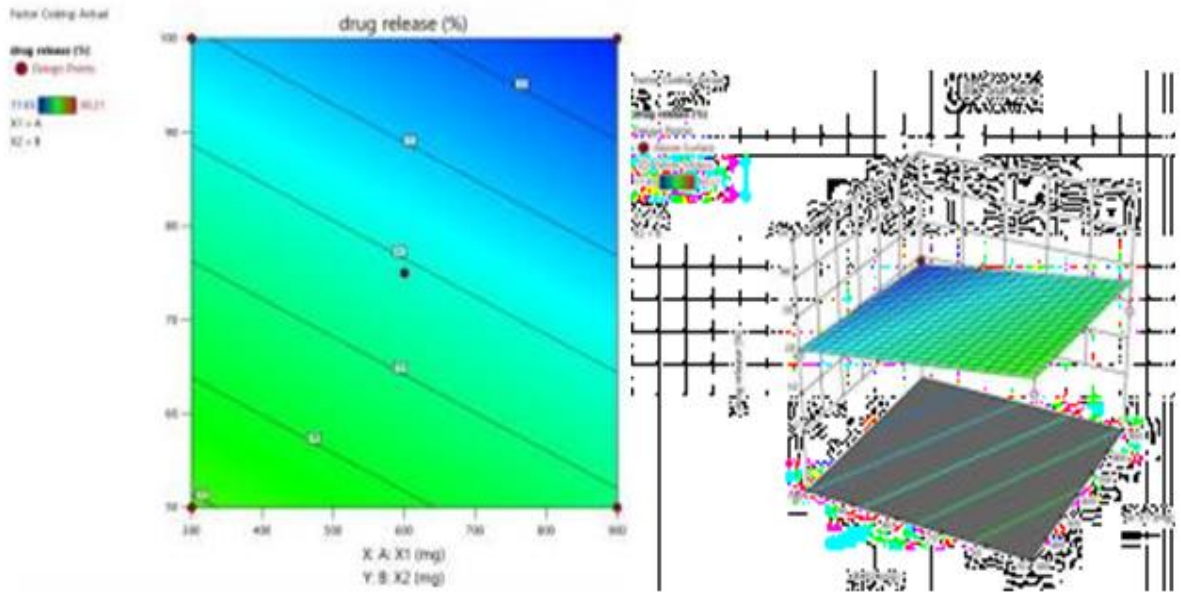

Figure 15 : Design of expert graphs.

Antifungal activity

Table : 13Antifungal Activity of Samples against Candida albicans.

Sr. No.	Samples	Conc.	Zone in diameter (mm) Against Candida albicans
	Control	-	-
1.	STD	1 mg	20
2.	Sample – F6	1mm	15
		1mm	17

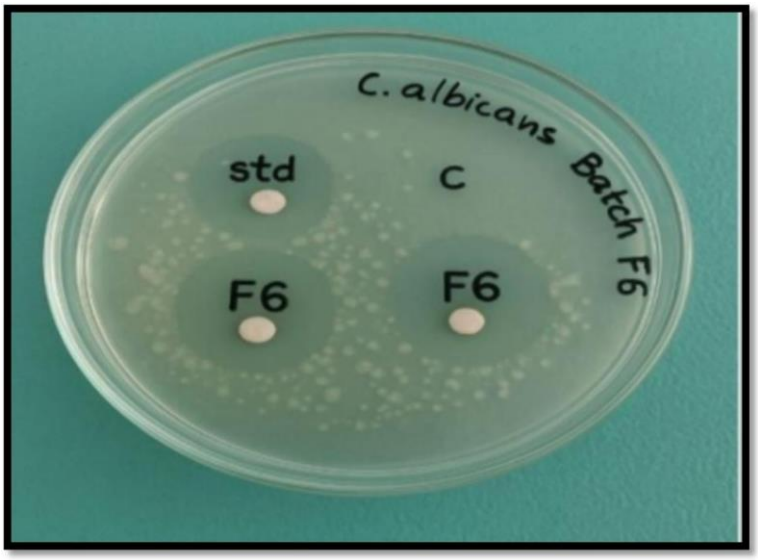

Figure No.16: Antifungal activity for Optimized Batch.

CONCLUSION

This study successfully formulated and characterized mucoadhesive buccal films of Fluconazole, offering a targeted therapeutic approach for oral candidiasis. Utilizing optimized polymer-plasticizer combinations, the developed films exhibited excellent mucoadhesive strength, uniform drug distribution, mechanical flexibility, and enhanced patient compliance. The optimized formulation demonstrated favorable physicochemical properties, sustained drug release kinetics, and prolonged buccal retention, ensuring localized antifungal efficacy while minimizing systemic adverse effects. *In vitro* release studies confirmed a controlled drug diffusion profile, supporting its potential for prolonged therapeutic action. These findings suggest that Fluconazole-loaded mucoadhesive buccal films present a clinically viable and patient-friendly alternative to conventional antifungal delivery systems, warranting further *in vivo* and clinical validation.

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