



PREPARATION AND OPTIMIZATION OF ITRACONAZOLE MUCOADHESIVE BUCCAL TABLET

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DOI: <https://doi.org/10.5281/zenodo.18875733>

How to cite this Article: Arun Singh Yadav¹, Abhishek Kumar Jain², Umesh Kumar Jain^{3*} (2026). Preparation And Optimization Of Itraconazole Mucoadhesive Buccal Tablet. World Journal of Pharmaceutical and Life Sciences, 12(3), 131–142. This work is licensed under Creative Commons Attribution 4.0 International license.



Article Received on 04/02/2026

Article Revised on 25/02/2026

Article Published on 01/03/2026

ABSTRACT

Itraconazole exhibits low aqueous solubility and short biological half-life, leading to poor bioavailability and the need for frequent dosing when administered through conventional dosage forms. The present study was undertaken to develop and optimize a mucoadhesive buccal tablet of itraconazole using different ratios of polysaccharide polymers to enhance mucoadhesion, prolong gastric residence time, and improve bioavailability. Preliminary screening studies were conducted with various polymers, among which guar gum and xanthan gum demonstrated superior swelling behavior, controlled drug release, and mucoadhesive properties. Based on these findings, final batches of mucoadhesive buccal tablets were prepared by the direct compression method. The prepared formulations were evaluated for swelling index, drug content, ex-vivo mucoadhesive strength, and in-vitro dissolution studies. Among all the formulations, IBT4 exhibited the most desirable sustained drug release profile. Drug release kinetic studies were carried out using zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The regression coefficient (r^2) values indicated that the drug release followed a non-Fickian diffusion mechanism with Super Case-II transport. The results of the study demonstrate that the developed mucoadhesive buccal tablet formulation is a promising approach for improving the bioavailability of itraconazole and reducing dosing frequency.

KEYWORDS: Itraconazole; Mucoadhesive buccal tablets; Guar gum; Xanthan gum; Sustained drug release; Non-Fickian diffusion.

1. INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to its convenience, patient compliance, and cost-effectiveness (Alqahtani *et al.*, 2021). However, conventional oral dosage forms often suffer from several limitations such as variable gastrointestinal absorption, short gastric residence time, enzymatic degradation, and extensive first-pass metabolism, which can significantly reduce the bioavailability of many drugs. These limitations are more pronounced in drugs exhibiting poor aqueous solubility and short biological half-life, necessitating frequent dosing and resulting in suboptimal therapeutic outcomes (Wen *et al.*, 2015).

Itraconazole is a broad-spectrum triazole antifungal agent widely used for the treatment of systemic and superficial fungal infections (Seyedmousavi *et al.*, 2015). Despite its high therapeutic potential, itraconazole exhibits poor water solubility, pH-dependent absorption, and low oral bioavailability. The drug demonstrates erratic absorption in the gastrointestinal tract, leading to wide interpatient variability. Moreover, its short effective residence time in the upper gastrointestinal tract reduces the extent of absorption, thereby requiring repeated dosing for maintaining therapeutic drug levels (Awasthi and Kulkarni 2016).

Mucoadhesive drug delivery systems have gained significant attention as an effective strategy to overcome

these challenges by increasing the residence time of dosage forms at the site of absorption (Homayun *et al.*, 2019). Buccal mucoadhesive tablets are designed to adhere to the buccal mucosa, allowing intimate contact with the absorptive surface and enabling prolonged drug release. This approach offers several advantages, including improved bioavailability, sustained therapeutic effect, reduction in dosing frequency, avoidance of firstpass metabolism, and enhanced patient compliance (Bhandare and Nannor 2024). Polysaccharide-based polymers are widely used in mucoadhesive formulations owing to their excellent swelling characteristics, biocompatibility, biodegradability, and mucoadhesive properties. Polymers such as guar gum and xanthan gum have been extensively explored due to their ability to form strong hydrogen bonds with mucin, thereby enhancing mucoadhesion. Additionally, these polymers can modulate drug release by forming a gel-like matrix upon hydration, making them suitable for sustained-release formulations (Zhang *et al.*, 2023). Optimization of polymer type and polymer ratio is a crucial step in the development of an effective mucoadhesive buccal tablet. Variations in polymer concentration significantly influence key formulation characteristics such as swelling index, mucoadhesive strength, drug release rate, and mechanical integrity of tablets. Therefore, a systematic approach is required to identify an optimal polymeric combination capable of providing strong mucoadhesion and controlled release of itraconazole (Agarwal and Murthy 2015). In the present study, an attempt has been made to prepare and optimize mucoadhesive buccal tablets of itraconazole using different ratios of polysaccharide polymers. The formulations were prepared by the direct compression method, which is a simple, cost-effective, and scalable manufacturing process. Preliminary screening studies were carried out to select suitable polymers based on their mucoadhesive and release-retarding properties (Al-Zoubi *et al.*, 2021). The prepared mucoadhesive buccal tablets were evaluated for pre-compression and post-compression parameters, swelling behavior, drug content uniformity, ex-vivo mucoadhesive strength, and in-vitro drug release profiles. Furthermore, the drug release mechanism was analyzed using various kinetic models to understand the release behavior of itraconazole from the formulated tablets (Shruthi, 2017). Thus, the study aims to develop a promising mucoadhesive buccal tablet formulation of itraconazole that enhances residence time, improves bioavailability, and provides sustained drug release, thereby offering an effective alternative to conventional oral dosage forms.

2. MATERIAL AND METHODS

2.1 UV spectrophotometric analysis for absorption maxima (λ_{max})

Accurately weighed 50 mg of drug sample was soluble in 50 ml of phosphate buffer pH 6.8 in 50 ml volumetric flask. The mixture was sonicated with the help of sonication in bath sonicator for 20 min to get 1000 $\mu\text{g/ml}$ solution. The prepared solution was named as **Stock I**.

Withdrawn 1 ml of prepared solution was again diluted up to 100 ml with same solvent separately with sonication for 20 min to obtain 10 $\mu\text{g/ml}$ solution. The spectrum of these solutions was run in 200 – 400 nm range in double beam UV spectrophotometer.

2.2 The calibration curve of drug in phosphate buffer pH 6.8

Accurately weighed 50 mg of drug sample was soluble in 50 ml of phosphate buffer pH 6.8 in 50 ml volumetric flask. The mixture was sonicated with the help of sonication in bath sonicator for 20 min to get 1000 $\mu\text{g/ml}$ solution. The prepared solution was named as Stock-I. From the above stock solution 10 ml was again diluted with 100 ml of dissolution medium to obtain 100 $\mu\text{g/ml}$ solution. From above prepared solution was withdrawn as 1 ml, 2 ml, 3 ml upto 5 ml and diluted up to 10 ml with respective solvent in 10 ml volumetric flasks to get concentration of 10 $\mu\text{g/ml}$, 20 $\mu\text{g/ml}$, 30 $\mu\text{g/ml}$, upto 500 $\mu\text{g/ml}$ respectively. The absorbance of each solution was measured separately at 261 nm for phosphate buffer pH 6.8.

2.3 Preformulation Studies

2.3.1 Organoleptic properties

The organoleptic characteristics of drug sample were determined by using sensory organs of body (Clapham *et al.*, 2023).

2.3.2 Microscopic examination

The drug sample itraconazole was studied as the nature / texture of the powder. A pinch of drug powder was spread on a glass slide and observed under phase contrast microscope and it was crystalline in nature (Albaraki, 2015).

2.3.3 Physical Characteristics

The density of drug powder was exactly weighed (M) and poured gently through a glass funnel into graduated cylinder and the volume was noted and bulk density was determined (Akseli *et al.*, 2019).

2.3.4 Particle size

The drug particle size was determined by using a microscope fitted with ocular micrometer and stage micrometer (Ding *et al.*, 2018).

2.3.5 Flow properties

The flow properties of drug powder were distinguished in terms of carr's index, hausner's ratio and angle of repose. The Carr's index ((IC)) and Hausner's ratio (HR) of drug powders were calculating according to following equation:

$$\text{Carr's Index (IC)} = \frac{\rho_{\text{Tapped}} - \rho_{\text{Bulk}}}{\rho_{\text{Tapped}}}$$

$$\text{Hausner's ratio (HR)} = \frac{\rho_{\text{Tapped}}}{\rho_{\text{Bulk}}}$$

The angle of repose (θ) was measured by fixed height method. This was calculated by following equation:

$$\text{Angle of repose } (\theta) = \tan^{-1} 2 H / D$$

Where H is the surface area of the free-standing height of the powder heap and D is diameter of heap that formed after powder flow from the glass funnel.

2.3.6 Solubility analysis

The solubility of drug was determined in various solvents (Water, 0.1 N HCl, phosphate buffer 6.8 and phosphate buffer 7.4). The excess amount of drug was added to 50 ml of solvent and mixed continuously till to morning at $37 \pm 0.5^\circ\text{C}$. The solubility value of drug in different medium was determined by above UV-Visible spectrophotometric method (Fereja *et al.*, 2015).

2.3.7 Partition coefficient

The partition coefficient of drug was determined in n-octanol: phosphate buffer pH 6.8 medium. The weighed amount 50 mg of drug was mixed into 25 ml each of an n-octanol and phosphate buffer pH 6.8 phase in a separating funnel and shaken for upto 24h. All phases were separated and drug solubilized was determined by UV-Visible spectrophotometric method. The partition coefficient of drug was calculated using following equation (Khan *et al.*, 2017).

$\text{Log } P (\text{n-oct} / \text{phosphate buffer pH 6.8}) = \text{Log} (C_{\text{n-Oct}} / C_{\text{phosphate buffer pH 6.8}})$ equilibrium. The partition coefficient of itraconazole was found to be ($\text{log}P=5.66$).

2.3.8 Drug-exciipient compatibility studies

The compatibility i.e. drug-exciipient interaction studies are useful for dosage form design. For compatibility studies drug / excipients ratio are chosen and investigated based on the reasonable drug / excipient's ratio in the final product. The drug sample mixture was determined by FTIR spectrums study for identification of drug excipients compatibility study (Shakir *et al.*, 2022).

2.4 Preparation of buccal mucoadhesive tablets

The tablets were prepared by direct compression method. Itraconazole, Guargum, Xanthan gum and Carragennan were sieved through #30 sieves. Magnesium stearate and MCC were sieved through #60 sieves before the use. All the materials were accurately weighed and blended using hand blender and directly compressed on a manual single punch tablet compression machine into 100mg tablets using flat-faced, round punches 8 mm in diameter. 9 batches of the formulation were prepared using guargum, xanthan gum and carragennan as polymers, with the ratio of drug to polymer kept as 1:3 (O'Brien, 2025).

Table 1: Various composition of buccal mucoadhesive tablets.

F. Code	Drug (mg)	Guargum (mg)	Xanthan gum (mg)	Carragennan (mg)	Magnesium stearate (mg)	MCC (mg)
IBT1	150	35	20	10	5	15
IBT2	150	30	25	10	5	15
IBT3	150	20	35	10	5	15
IBT4	150	35	20	7.5	5	15
IBT5	150	30	25	7.5	5	15
IBT6	150	20	35	7.5	5	15
IBT7	150	35	20	5	5	15
IBT8	150	30	25	5	5	15
IBT9	150	20	35	5	5	15

2.5 Characterization

2.5.1 Flow properties

Flow properties depend on particle size, shape, porosity and density of the bulk powder. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane (Müller *et al.*, 2021). $\tan\Theta = h/r$

Where h=height of pile, r = radius of the base of the pile, Θ =angle of repose.

2.5.2 Weight variation

The average weight by more than the percent shown below and none deviates by more than twice that percent (Wei *et al.*, 2020).

2.5.3 Hardness

Hardness of tablet is defined as the force required to break a tablet a in a diametric direction. A tablet was placed between two anvils. Hardness is thus the tablet crushing strength.

Monsanto tester is used for hardness testing (Awofisayo *et al.*, 2015).

2.5.4 Friability

Weigh 10 tablets and place in a friabilator chamber rotated at 25 rpm and they are dropped on distance of 6 inches and allowed to rotate for 100 revolutions. The difference in the weigh is calculated and the weight loss should not be more than 1% (Shimu, 2024).

2.5.5 Thickness

The thickness of tablets was performed on 20 tablets from each formulation by using Vernier caliper (Diara *et al.*, 2015).

2.5.6 Swelling index (%)

Swelling ratio was determined using following equation: $\text{Swelling Ratio (\%)} = (A_t - A_0) / A_{\text{tablet}} * 100$
 A_t , weight of the tablet and basket at time t (g);
 A_0 , weight of the tablet and basket at the beginning (g);
 A_{tablet} , weight of the dry tablet (g). The prepared tablets

were placed in the wire basket of six basket dissolution apparatus. The basket was immersed in a beaker containing phosphate buffer pH 6.8 for 2 h and allowed to swell at 37 °C. The tablets were removed and changes in weight were measured before and after swelling.

2.5.7 Percent Drug content estimation

Crushed 10 tablets from all batches in pestle- mortar and weighed equivalent 150 mg as drug dose using for single tablet was taken in volumetric flask (100ml) and dissolved in phosphate buffer pH 6.8 and filtered. This solution was analyzed in UV spectrophotometer at λ_{max} 261 nm (Thong *et al.*, 2018).

2.5.8 *in-vitro ex-vivo* mucoadhesive strength

The mucoadhesive strength of the prepared tablet was determined by modified physical balance. The assembly consist of a modified double beam physical balance in which left sided pan is removed and attached with glass slide with an additional weight is added with slide to balance the weight of both the pan. Fresh intestine mucosa of goat was used as membrane obtained from local slaughter house and kept in kerb solution during transportation and phosphate buffer pH 6.8 CL was use for moistening the mucosa. The underlying mucous membrane was separated by the help of surgical blade and tied with the glass slide with the help of thread. Now the tablet was made to stick with the wooden block and made contact with the mucous membrane and the tablet. The additional weight was increased on the right pan until the tablet detaches from the membrane and the weight used was noted as mucoadhesive strength in grams and force of adhesion was calculated (Adetunji *et al.*, 2015).

2.5.9 *In vitro* Dissolution study: In vitro dissolution study was carried out using USP type II (basket type) apparatus with phosphate buffer pH 6.8 as a dissolution medium. The temperature was maintained at $37 \pm 0.5^\circ\text{C}$ with 50 rotations per minute. 1ml of aliquots were

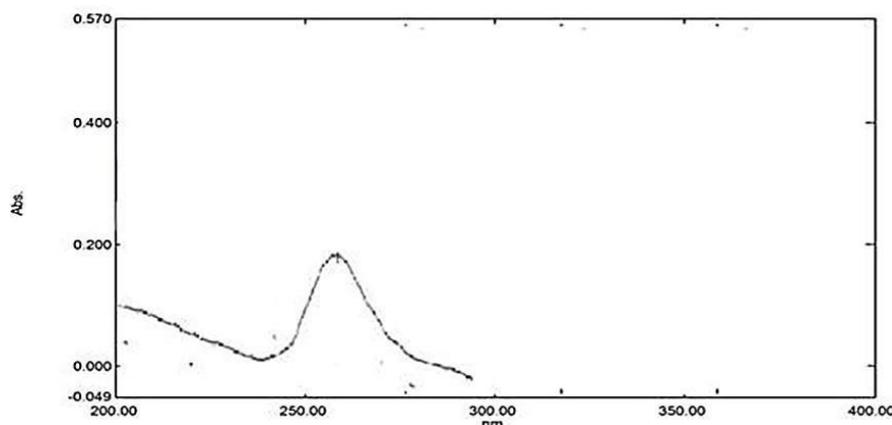
withdrawn at different time intervals and same amount of fresh dissolution medium was replaced to maintain sink condition. The aliquots were analyzed for drug content at λ_{max} 261 nm wavelength using UV-spectrophotometer. The cumulative percentage drug release was calculated and reported (Alvebratt *et al.*, 2020).

2.5.10 *in-vitro* drug release kinetic study: In vitro drug release kinetic study:

The drug release and mechanism it follows to release can be determined by matching the data with various release models like Higuchi, Korsmeyer-Peppas, zero order and first order plots. The kinetics of drug release was studied in various kinetic models by plotting the data obtained from in vitro drug release study. The zero-order kinetics was studied by plotting cumulative amount of drug released versus time. Whereas first order kinetics was studied by plotting log cumulative percentage of drug remain versus time. Higuchi's model of kinetics was studied by plotting cumulative percentage of drug released versus square root of time. The mechanism of drug release from the formulation was confirmed by fitting the in vitro drug release data with the Korsmeyer-Peppas model by plotting log cumulative percentages of drug release versus log time. The release exponent 'n' and 'k' values were calculated from the Y intercept and slope of a straight line respectively (Askarizadeh *et al.*, 2023).

3. RESULT AND DISCUSSION

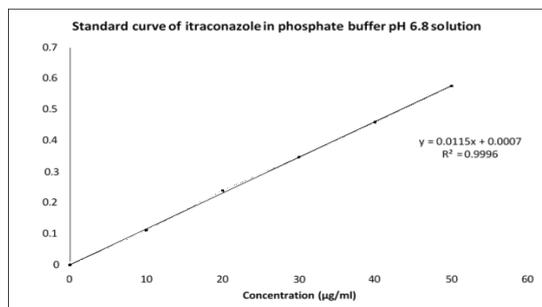
3.1 UV spectrophotometric study: The maximum absorption (λ_{max}) of drug sample itraconazole in phosphate buffer pH 6.8 solutions were found to be at 261 nm. The calibration curves in phosphate buffer pH 6.8 were prepared with drug solutions of known concentrations. The absorbance was measured and plotted against drug concentration. The calibration curves show excellent linearity of data as evidenced by the values of correlation coefficients that were found to be greater than 0.99.



Graph 1: Maximum absorption wavelength (λ_{max}) of drug in phosphate buffer pH 6.8 solution (20 $\mu\text{g/ml}$).

Table 2: Standard curve of drug itraconazole in phosphate buffer pH 6.8 solution (20 µg/ml).

Concentration	Absorbance
0	0
10	0.111
20	0.238
30	0.346
40	0.459
50	0.574

**Graph 2: Standard curve of itraconazole in phosphate buffer pH 6.8 solution (261 nm).**

3.2 Preformulation Studies

Preformulation studies are the first step for the rational development of dosage forms of model drug substances. It is an investigation of physical and chemical properties of drug substances alone and in combination with excipients in research. The overall objective of preformulation studies is to produce information constructive to the formulator in development of stable and bioavailable dosage forms.

3.2.1 Organoleptic Characteristics

Itraconazole is Whitish yellow, slightly pungent odor, slightly sweet taste and crystalline powder in nature.

3.2.2 Micromeritic Properties

The tapped density was determined using tapped density apparatus. A bulk and tapped density of itraconazole is to be 0.221 gm / cm³ to 0.229 gm / cm³. The particle size of drug powder was 93 µm.

3.2.3 Flow Properties

The drug showed carr's index (%) 12.28±0.011; hausner's ratio 1.13±0.011 and angle of repose θ 26.6±0.10, thus showed excellent flow properties.

3.2.4 Solubility Studies (25 ± 2 °C)

The solubility of drug was determined in various solvents (Water, 0.1 N HCl, Phosphate buffer pH 4.5, pH 6.8, pH 7.4) at room temperature (25±2 °C). The solubility in water is 18.93 (mg / ml); 0.1 N HCl 22.33 (mg / ml); Phosphate buffer pH 6.8 is 13.01 (mg / ml) and in Phosphate buffer pH 7.4 is 17.94 (mg / ml). The results indicated that the drug have maximum solubility water, and also soluble in 0.1 N HCl.

3.2.5 Partition Coefficient

The partition coefficient of drug was found to be (5.22).

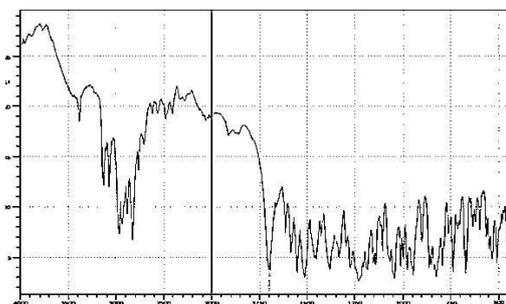
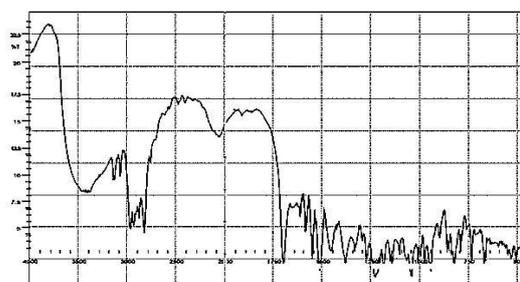
3.2.6 FTIR Spectral Analysis

□ FTIR Peaks of Chitosan

In FTIR spectrum chitosan exhibited a broad peak at 3431 cm⁻¹, which is assigned to the N-H and hydrogen bonded O-H stretch vibrational frequencies, while a sharp peak at 3610 cm⁻¹ is that of free O-H bond stretch of glucopyranose units. Further, in the C-H stretch region of FTIR spectrum, the higher intensity peak at 2923 cm⁻¹ is assigned to the asymmetric and the lower intensity peak at 2857 cm⁻¹ is assigned to the symmetric modes of CH₂. The peaks at 1550 and 1599 cm⁻¹ were assigned to strong N-H bending vibrations of secondary amide, which usually occur in the range of 1640 to 1550 cm⁻¹ as strong band.

□ FTIR Peaks of Pure Itraconazole

The characteristic IR peak of drug alone over the frequency range 500 – 4000 cm⁻¹ occurred at 3439, 3126 and 3069 cm⁻¹ due to the absorption of NH₂ groups, 2964 cm⁻¹ resulted from CH₂ stretching frequency band and a sharp peak occurred at 1698 cm⁻¹ due to C=O stretching vibration. The peaks observed at 1609 cm⁻¹ and 1429 cm⁻¹ may be assigned to the C=N and CN bonds, respectively. The characteristic peaks occurred at 1510 and 1451 cm⁻¹ owed to CH deformation. The IR region from 600- 1400 cm⁻¹ which is called the fingerprint, usually contains a large number of unassigned vibrations characteristic of the molecule. The IR spectra of the physical mixtures of drug with polymers did not show any significant differences in the characteristic bands of the respective spectra of the pure components and the functional groups still showing their characteristic bands indicating that there is no complex formation.

**Graph 3: FTIR of itraconazole drug (Sample and pure drug).****Graph 4: FTIR of itraconazole drug (Drug excipients).**

3.3 Characterization of buccal mucoadhesive tablets

3.3.1 Formulation Method

Buccal mucoadhesive tablets were prepared by the direct compression method, using guar gum, xanthan gum and carragennan as swellable polymers. The effect of the nature of polymers was studied by preparing various formulations of buccal mucoadhesive tablets. In all these formulations, a constant amount of drug (150 mg) was maintained and it was initially characterized for flow properties and all other parameters.

3.3.2 Pre-Compression Parameters (Powder Blend Characteristics)

The different characterization as angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio includes angle of repose (26.71°), bulk density (0.274 g/cm³), tapped density (0.273 g/cm³), carr's index (26.31 %) and hausners ratio was found to be (1.58).

3.3.3 Post-Compression Parameters

• Physical Properties

The other characterization includes thickness, hardness, friability, weight variation, drug content, buoyancy lag time and in-vitro drug release. The thickness of all the tablets was in the range of 4.01 to 4.09 mm. The average weights of the entire prepared tablet were 240.17 mg to 240.71 mg which was within the specified limit. The hardness of all the formulated tablets was found to be in the range of 5.04 to 5.36 kg/cm². Friability was found to be 0.31 to 0.38 %.

• Swelling and Mucoadhesive Properties

In-vitro mucoadhesion time of all the prepared formulation was found between 1.12 h to 1.31 h. The swelling Index for all tablets was found in the range of 150.23 % to 159.55 %.

• Drug Content

The drug content of the entire prepared tablet was found to be 98.65 to 101.32.

3.3.4 In-Vitro Drug Release Studies

From the in vitro drug release studies, it was found that in formulations IBT4 showed best sustained release profile. The retarded drug release was found to be in the following order.

Order of retarded drug release

IBT4 > IBT5 > IBT7 > IBT6 > IBT3 > IBT8 > IBT2 > IBT1 > IBT9.

3.3.5 Drug Release Kinetics

Among the nine formulations (IBT1 to IBT9) prepared formulations F4 was found to be the best formulations in terms of sustained drug release. Drug release kinetics was performed by using various kinetic models such as Zero order, First order, Korsmeyer- Peppas and Higuchi's equation. The regression coefficient (r²) value of various models was found to be non-fickinon drug release diffusion mechanism and followed supercase II transport mechanism respectively.

Table 3: Flow properties of various buccal mucoadhesive tablets.

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's index (%)	Hausner Ratio	Angle of Repose
IBT1	0.252	0.233	19.32	1.10	26.71
IBT2	0.263	0.257	20.33	1.17	22.33
IBT3	0.285	0.271	23.21	1.12	26.12
IBT4	0.243	0.237	22.51	1.17	24.81
IBT5	0.262	0.265	22.24	1.21	21.25
IBT6	0.274	0.220	23.21	1.31	27.24
IBT7	0.291	0.273	26.31	1.58	22.22
IBT8	0.243	0.212	23.21	1.16	25.15
IBT9	0.231	0.222	23.30	1.16	26.14

Table 4: The various characterization of buccal mucoadhesive tablets.

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness 2 (kg/cm ²)	Friability (%)	Swelling Index	Percent Drug content	io adhesive strength (gm)
IBT1	241.21±.49	4.09±.01	5.51±.11	0.36±.13	150.23±0.17	99.52±0.26	21.03±0.5
IBT2	240.17±.01	4.01±.02	5.54±.12	0.31±.16	159.55±0.28	99.08±0.18	24.52±0.1
IBT3	241.12±.02	4.06±.01	5.31±.13	0.38±.11	156.17±0.21	99.29±0.98	29.36±0.4
IBT4	240.19±.04	4.04±.01	5.04±.18	0.32±.19	158.18±0.22	99.15±0.15	31.02±0.5
IBT5	241.21±.01	4.03±.03	5.14±.11	0.34±.17	157.62±0.03	98.65±0.14	23.12±0.1
IBT6	240.15±.05	4.01±.02	5.36±.10	0.38±.16	156.71±0.31	99.91±0.32	20.17±0.2
IBT7	241.11±.01	4.06±.03	5.25±.44	0.35±.17	157.58±0.11	99.16±0.44	22.24±0.4
IBT8	241.73±.03	4.09±.03	5.11±.27	0.32±.13	156.59±0.25	99.14±0.08	21.25±0.2
IBT9	240.21±.06	4.06±.02	5.10±.21	0.34±.13	156.25±0.19	101.32±0.16	28.56±0.2

Table 5: In vitro drug release study of the prepared buccal mucoadhesive tablets.

Time (h)	ITB1	ITB2	ITB3	ITB4	ITB5	ITB6	ITB7	ITB8	ITB9
0	0	0	0	0	0	0	0	0	0
1	3.2	4.3	3.1	2.1	2.5	2.8	3.1	3.5	3.8
2	14.6	14.8	12.2	10.5	11.4	11.1	10.5	12.5	15.4
3	25.3	24.3	23.3	21.4	21.6	20.8	22.2	25.6	28.6
4	40	39.1	37.4	33.6	35.3	32.3	38.7	38.2	42.7
5	46.4	46.2	46.3	41.7	45.5	45.5	44.4	45.9	48.4
6	54.1	56.2	53.1	49.3	52.6	52.2	54.3	52.8	55.3
7	66.2	63.2	61.1	57.3	61.5	62.2	60.6	64.7	68.4
8	72.4	70.2	67.6	60.4	68.4	67.9	68.2	69.5	73.6
9	80.5	79.8	75.4	69.2	75.1	74.6	76.7	76.4	82.7
10	85.1	85.3	82.2	76.5	80.3	82.6	81.4	84.3	88.3
11	90.6	89.3	89.5	84.3	87.4	87.3	88.3	88.3	90.6
12	98.6	98.1	97.1	95.5	96.1	96.9	96.6	97.7	99.7

Table 6: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB1)

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	4.800	3.2	0.505	96.80	1.986
2	1.414	0.301	21.900	14.6	1.164	85.40	1.931
3	1.732	0.477	37.950	25.3	1.403	74.70	1.873
4	2.000	0.602	60.000	40	1.602	60.00	1.778
5	2.236	0.699	69.600	46.4	1.667	53.60	1.729
6	2.449	0.778	81.150	54.1	1.733	45.90	1.662
7	2.646	0.845	99.300	66.2	1.821	33.80	1.529
8	2.828	0.903	108.600	72.4	1.860	27.60	1.441
9	3.000	0.954	120.750	80.5	1.906	19.50	1.290
10	3.162	1.000	127.650	85.1	1.930	14.90	1.173
11	3.317	1.041	135.900	90.6	1.957	9.40	0.973
12	3.464	1.079	147.900	98.6	1.994	1.40	0.146

Table 7: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB2).

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	6.450	4.3	0.633	95.70	1.981
2	1.414	0.301	22.200	14.8	1.170	85.20	1.930
3	1.732	0.477	36.450	24.3	1.386	75.70	1.879
4	2.000	0.602	58.650	39.1	1.592	60.90	1.785
5	2.236	0.699	69.300	46.2	1.665	53.80	1.731
6	2.449	0.778	84.300	56.2	1.750	43.80	1.641
7	2.646	0.845	94.800	63.2	1.801	36.80	1.566
8	2.828	0.903	105.300	70.2	1.846	29.80	1.474
9	3.000	0.954	119.700	79.8	1.902	20.20	1.305
10	3.162	1.000	127.950	85.3	1.931	14.70	1.167
11	3.317	1.041	133.950	89.3	1.951	10.70	1.029
12	3.464	1.079	147.150	98.1	1.992	1.90	0.279

Table 8: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB3).

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cumulative % drug released	Cummulative % drug retained	Log cumulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	4.650	3.1	0.491	96.90	1.986
2	1.414	0.301	18.300	12.2	1.086	87.80	1.943
3	1.732	0.477	34.950	23.3	1.367	76.70	1.885
4	2.000	0.602	56.100	37.4	1.573	62.60	1.797
5	2.236	0.699	69.450	46.3	1.666	53.70	1.730
6	2.449	0.778	79.650	53.1	1.725	46.90	1.671
7	2.646	0.845	91.650	61.1	1.786	38.90	1.590
8	2.828	0.903	101.400	67.6	1.830	32.40	1.511
9	3.000	0.954	113.100	75.4	1.877	24.60	1.391
10	3.162	1.000	123.300	82.2	1.915	17.80	1.250
11	3.317	1.041	134.250	89.5	1.952	10.50	1.021
12	3.464	1.079	145.650	97.1	1.987	2.90	0.462

Table 9: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB4).

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cumulative % drug released	Cummulative % drug retained	Log cumulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	3.150	2.1	0.322	97.90	1.991
2	1.414	0.301	15.750	10.5	1.021	89.50	1.952
3	1.732	0.477	32.100	21.4	1.330	78.60	1.895
4	2.000	0.602	50.400	33.6	1.526	66.40	1.822
5	2.236	0.699	62.550	41.7	1.620	58.30	1.766
6	2.449	0.778	73.950	49.3	1.693	50.70	1.705
7	2.646	0.845	85.950	57.3	1.758	42.70	1.630
8	2.828	0.903	90.600	60.4	1.781	39.60	1.598
9	3.000	0.954	103.800	69.2	1.840	30.80	1.489
10	3.162	1.000	114.750	76.5	1.884	23.50	1.371
11	3.317	1.041	126.450	84.3	1.926	15.70	1.196
12	3.464	1.079	143.250	95.5	1.980	4.50	0.653

Table 10: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB5)

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cumulative % drug released	Cummulative % drug retained	Log cumulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	3.750	2.5	0.398	97.50	1.989
2	1.414	0.301	17.100	11.4	1.057	88.60	1.947
3	1.732	0.477	32.400	21.6	1.334	78.40	1.894
4	2.000	0.602	52.950	35.3	1.548	64.70	1.811
5	2.236	0.699	68.250	45.5	1.658	54.50	1.736
6	2.449	0.778	78.900	52.6	1.721	47.40	1.676
7	2.646	0.845	92.250	61.5	1.789	38.50	1.585
8	2.828	0.903	102.600	68.4	1.835	31.60	1.500
9	3.000	0.954	112.650	75.1	1.876	24.90	1.396
10	3.162	1.000	120.450	80.3	1.905	19.70	1.294
11	3.317	1.041	131.100	87.4	1.942	12.60	1.100
12	3.464	1.079	144.150	96.1	1.983	3.90	0.591

Table 11: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB6)

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummul active % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	4.200	2.8	0.447	97.20	1.988
2	1.414	0.301	16.650	11.1	1.045	88.90	1.949
3	1.732	0.477	31.200	20.8	1.318	79.20	1.899
4	2.000	0.602	48.450	32.3	1.509	67.70	1.831
5	2.236	0.699	68.250	45.5	1.658	54.50	1.736
6	2.449	0.778	78.300	52.2	1.718	47.80	1.679
7	2.646	0.845	93.300	62.2	1.794	37.80	1.577
8	2.828	0.903	101.850	67.9	1.832	32.10	1.507
9	3.000	0.954	111.900	74.6	1.873	25.40	1.405
10	3.162	1.000	123.900	82.6	1.917	17.40	1.241
11	3.317	1.041	130.950	87.3	1.941	12.70	1.104
12	3.464	1.079	145.350	96.9	1.986	3.10	0.491

Table 12: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB7)

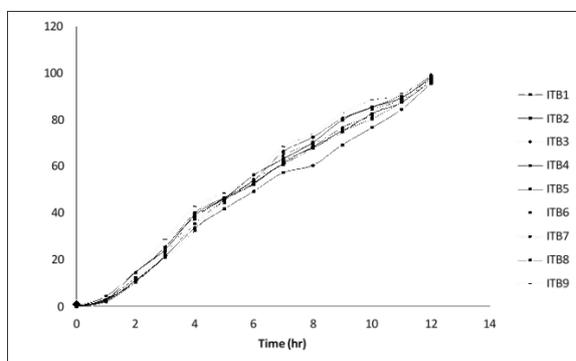
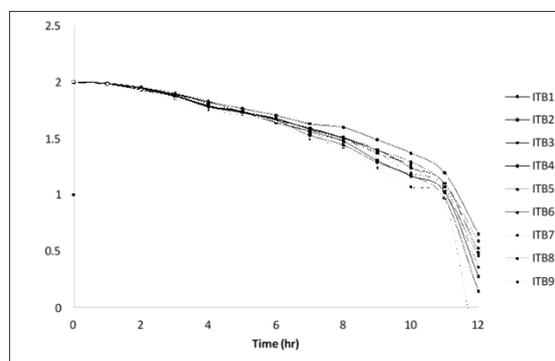
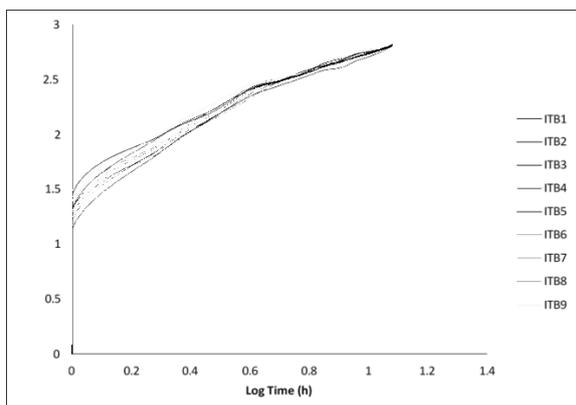
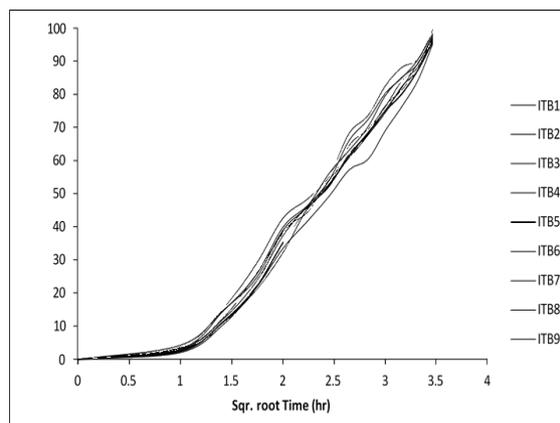
Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummulative % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	4.650	3.1	0.491	96.90	1.986
2	1.414	0.301	15.750	10.5	1.021	89.50	1.952
3	1.732	0.477	33.300	22.2	1.346	77.80	1.891
4	2.000	0.602	58.050	38.7	1.588	61.30	1.787
5	2.236	0.699	66.600	44.4	1.647	55.60	1.745
6	2.449	0.778	81.450	54.3	1.735	45.70	1.660
7	2.646	0.845	90.900	60.6	1.782	39.40	1.595
8	2.828	0.903	102.300	68.2	1.834	31.80	1.502
9	3.000	0.954	115.050	76.7	1.885	23.30	1.367
10	3.162	1.000	122.100	81.4	1.911	18.60	1.270
11	3.317	1.041	132.450	88.3	1.946	11.70	1.068
12	3.464	1.079	144.900	96.6	1.985	3.40	0.531

Table 13: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB8).

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cummulative % drug released	Cummulative % drug retained	Log cummul active % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	5.250	3.5	0.544	96.50	1.985
2	1.414	0.301	18.750	12.5	1.097	87.50	1.942
3	1.732	0.477	38.400	25.6	1.408	74.40	1.872
4	2.000	0.602	57.300	38.2	1.582	61.80	1.791
5	2.236	0.699	68.850	45.9	1.662	54.10	1.733
6	2.449	0.778	79.200	52.8	1.723	47.20	1.674
7	2.646	0.845	97.050	64.7	1.811	35.30	1.548
8	2.828	0.903	104.250	69.5	1.842	30.50	1.484
9	3.000	0.954	114.600	76.4	1.883	23.60	1.373
10	3.162	1.000	126.450	84.3	1.926	15.70	1.196
11	3.317	1.041	132.450	88.3	1.946	11.70	1.068
12	3.464	1.079	146.550	97.7	1.990	2.30	0.362

Table 14: In vitro drug release study of the prepared buccal mucoadhesive tablets (ITB9)

Time (h)	$\sqrt{\text{Time}}$	Log time	Cummulative drug released	Cummulative % drug released	Log cummulati ve % drug released	Cummulative % drug retained	Log cummulati ve % drug retained
0	0.000	#NUM!	0.000	0	#NUM!	100.00	2.000
1	1.000	0.000	5.700	3.8	0.580	96.20	1.983
2	1.414	0.301	23.100	15.4	1.188	84.60	1.927
3	1.732	0.477	42.900	28.6	1.456	71.40	1.854
4	2.000	0.602	64.050	42.7	1.630	57.30	1.758
5	2.236	0.699	72.600	48.4	1.685	51.60	1.713
6	2.449	0.778	82.950	55.3	1.743	44.70	1.650
7	2.646	0.845	102.600	68.4	1.835	31.60	1.500
8	2.828	0.903	110.400	73.6	1.867	26.40	1.422
9	3.000	0.954	124.050	82.7	1.918	17.30	1.238
10	3.162	1.000	132.450	88.3	1.946	11.70	1.068
11	3.317	1.041	135.900	90.6	1.957	9.40	0.973
12	3.464	1.079	149.550	99.7	1.999	0.30	-0.523

**Graph 5: Zero-order kinetic plot of prepared buccal mucoadhesive tablets (ITB1- ITB9)****Graph 6: First-order kinetic plot of prepared buccal mucoadhesive tablets (ITB1- ITB9)****Graph 7: Korsmeyer-peppas kinetic plot of prepared buccal mucoadhesive tablets (ITB1- ITB9).****Graph 8: Higuchi kinetic plot of prepared buccal mucoadhesive tablets (ITB1- ITB9).**

4. CONCLUSION

The present study successfully developed mucoadhesive buccal tablets of itraconazole using different polysaccharide polymer combinations to enhance gastric residence time and bioavailability. Preliminary studies identified guar gum and xanthan gum as suitable polymers for providing effective mucoadhesion and controlled drug release. All formulations prepared by

direct compression were evaluated for key parameters, and formulation IBT4 demonstrated the most optimal sustained drug release profile. Drug release kinetic analysis indicated a nonFickian diffusion mechanism following Super Case-II transport. Overall, the optimized mucoadhesive tablet formulation shows potential for improving therapeutic efficacy and reducing dosing frequency.

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