FORMULATION AND EVALUATION OF OLANZAPINE SUBLINGUAL TABLETS USING SOLID DISPERSION TECHNIQUE

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Abstract

Background: Olanzapine belongs to BCS Class II drugs characterized by low solubility and high permeability, which limits its therapeutic efficacy when administered orally. The sublingual route offers advantages including rapid absorption, avoidance of first-pass metabolism, and quick onset of action, making it particularly suitable for psychiatric emergencies.

Objective: The present study aimed to formulate and evaluate sublingual tablets of Olanzapine using solid dispersion technique to enhance solubility and achieve rapid drug release for the management of schizophrenia.

Methods: Solid dispersions were prepared using solvent evaporation method with PEG 6000 and propylene glycol as carriers. Sublingual tablets were formulated by direct compression method using various superdisintegrants including croscarmellose sodium (CCS), crospovidone (CP), and sodium starch glycolate (SSG). The formulations were evaluated for preformulation parameters, physical characteristics, in-vitro disintegration time, wetting time, and drug release studies.

Results: FTIR studies confirmed the absence of drug-excipient incompatibility. Solid dispersion with propylene glycol at 1:2 ratio showed maximum solubility enhancement (0.24 mg/mL). Among all formulations, batch F8 containing 5% sodium starch glycolate exhibited optimal characteristics with disintegration time of 15±3 seconds, wetting time of 15±1 seconds, and drug release of 98.19±0.44% within 10 minutes. Stability studies at 40°C/75% RH for 30 days confirmed the formulation stability.

Keywords: Olanzapine, sublingual tablets, solid dispersion, superdisintegrants, sodium starch glycolate, BCS Class II.

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1. INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to its convenience, patient compliance, and cost-effectiveness. However, drugs administered through the conventional oral route undergo first-pass hepatic metabolism, which can significantly reduce their bioavailability (Banker & Anderson, 1991). The sublingual route of drug administration offers a promising alternative by allowing drug absorption directly into systemic circulation through the highly vascularized sublingual mucosa, thereby bypassing hepatic first-pass metabolism (Sudhakar et al., 2006).

The sublingual mucosa presents favorable characteristics for drug absorption, including a rich blood supply, relatively thin epithelium, and the presence of immobile mucus layer that can retain drug formulations (Collins & Dawes, 1987). The surface area of the adult human oral mucosa is approximately 200 cm^2, with the sublingual region being particularly suitable for rapid drug absorption due to its non-keratinized nature and high permeability (Goswami et al., 2009). These anatomical and physiological features make sublingual delivery an attractive option for drugs requiring rapid onset of action, such as antipsychotic medications used in psychiatric emergencies.

Olanzapine, a thienobenzodiazepine derivative, is an atypical antipsychotic agent widely used in the treatment of schizophrenia and bipolar disorder (Timmer & Sitsen, 2000). According to the Biopharmaceutics Classification System (BCS), Olanzapine belongs to Class II drugs, characterized by low aqueous solubility and high permeability. This solubility limitation poses a significant challenge in achieving optimal therapeutic plasma concentrations following oral administration. Various formulation strategies have been explored to enhance the dissolution rate and bioavailability of poorly water-soluble drugs, including solid dispersion technique, particle size reduction, and use of surfactants (Setty et al., 2008).

Solid dispersion represents a promising approach for improving the dissolution characteristics of poorly soluble drugs. In this technique, the drug is dispersed in an inert carrier matrix, which can enhance wettability, reduce particle size, and improve drug release kinetics (Ishikawa et al., 2000). Carriers such as polyethylene glycol (PEG) 6000 and propylene glycol have been widely investigated for preparing solid dispersions due to their safety profile, good compatibility with drugs, and ability to enhance dissolution (Jeong et al., 2008).

The formulation of sublingual tablets requires careful selection of excipients, particularly superdisintegrants, to ensure rapid tablet disintegration and drug release in the limited salivary fluid available in the sublingual cavity (Prathusha, 2017). Superdisintegrants such as croscarmellose sodium (CCS), crospovidone (CP), and sodium starch glycolate (SSG) function through different mechanisms including swelling, wicking, and strain recovery to facilitate rapid tablet disintegration (Ölmez & Vural, 2009). The concentration and type of superdisintegrant significantly influence the disintegration time and consequently the drug release profile of sublingual formulations.

The present investigation aimed to develop sublingual tablets of Olanzapine using solid dispersion technique to overcome the solubility limitation of the drug and achieve rapid drug release suitable for emergency psychiatric interventions. The study involved systematic evaluation of different carriers for solid dispersion preparation, screening of various superdisintegrants, and optimization of the formulation to achieve rapid disintegration and enhanced drug dissolution.

2. MATERIALS AND METHODS

2.1 Materials

Olanzapine was obtained from K.J. Faculty of Pharmacy, SSSRGI, India. Polyethylene glycol (PEG) 6000, propylene glycol, croscarmellose sodium (CCS), sodium starch glycolate (SSG), lactose monohydrate, sucralose, and magnesium stearate were procured from the same source. All other chemicals and reagents used were of analytical grade. Phosphate buffer pH 6.8 was prepared according to standard pharmacopoeial procedures.

2.2 Instruments and Equipment

The study utilized UV-Visible Spectrophotometer (Shimadzu UV 1800), FTIR Spectrophotometer (Alpha-E, Shimadzu Corporation), dissolution apparatus (Labindia Analytical Instrument Pvt. Ltd., Li-pe-129), tablet compression machine (Shaktipharmatech Pvt. Ltd., SLp-1), disintegration tester (Electrolab EDI-3X), friability tester (Sentwin India, Veego), hardness tester (Score Testing Instrument 1010B), electronic digital weighing balance (XB 220A, Swizzer), and pH meter (Chemline Technologies Cl 120).

2.3 Preformulation Studies

2.3.1 Identification of Drug

The identity of Olanzapine was confirmed using UV spectroscopy. The drug was dissolved in phosphate buffer pH 6.8 containing methanol, and the UV spectrum was recorded in the range of 200-400 nm using UV-Visible spectrophotometer to determine the wavelength of maximum absorption (λmax). The melting point of Olanzapine was determined using melting point apparatus and compared with the reported literature values.

2.3.2 Drug-Excipient Compatibility Study

Fourier Transform Infrared (FTIR) spectroscopy was employed to investigate potential interactions between Olanzapine and the selected excipients (D'Souza et al., 2008). FTIR spectra of pure drug, individual excipients, and physical mixtures of drug with excipients were recorded in the range of 4000-400 cm^{-1} using KBr pellet method. The spectra were analyzed for any significant shifts in characteristic peaks that would indicate drug-excipient incompatibility.

2.4 Analytical Method Development

A calibration curve for Olanzapine was constructed in phosphate buffer pH 6.8 at 252 nm. Stock solution was prepared by dissolving accurately weighed quantity of drug in phosphate buffer containing methanol. Serial dilutions were made to obtain concentrations ranging from 5-30 µg/mL. The absorbance was measured at 252 nm against blank, and the calibration curve was plotted (Benajeer et al., 2012).

2.5 Preparation of Solid Dispersions

Solid dispersions were prepared using two different carriers: PEG 6000 and propylene glycol, at various drug-to-carrier ratios (1:1, 1:2, 1:3, and 1:4) as shown in Table 1. For PEG 6000-based solid dispersions (S1-S4), solvent evaporation method was employed. The drug and carrier were dissolved in ethanol as a common solvent and stirred continuously for 30 minutes. The solvent was evaporated in a hot air oven at 40°C for 1 hour. The dried mass was passed through a 30# sieve to obtain uniform powder (Rameshwari & Jeya, 2009).

For propylene glycol-based solid dispersions (S5-S8), the drug was dissolved in propylene glycol under continuous stirring for 30 minutes. Since propylene glycol is a liquid non-volatile solvent, the drug-carrier solution was adsorbed onto lactose monohydrate using geometric mixing method. The resulting powder was passed through 30# sieve to ensure uniformity.

Table 1: Composition of Solid Dispersion Formulations

Ingredients (mg)	S1	S2	S3	S4	S5	S6	S7
Olanzapine	15	15	15	15	15	15	15
PEG 6000	15	30	45	60	-	-	-
Propylene glycol	-	-	-	-	30	45	60
Lactose monohydrate	-	-	-	-	60	90	120
Total weight	30	45	60	75	105	150	195

2.6 Evaluation of Solid Dispersions

Drug Content: An accurately weighed quantity of solid dispersion equivalent to 15 mg of Olanzapine was triturated and dissolved in phosphate buffer pH 6.8 under stirring for 10 minutes. The solution was filtered through 0.45 µm membrane filter, suitably diluted, and the absorbance was measured at 252 nm using UV-visible spectrophotometer.

Saturation Solubility: Solubility studies were performed by adding excess amount of solid dispersion to phosphate buffer pH 6.8 and shaking at 37±0.5°C for 24 hours. The samples were

filtered and analyzed spectrophotometrically at 252 nm after suitable dilution (Aburahma et al., 2010).

2.7 Preparation of Sublingual Tablets

Sublingual tablets were prepared by direct compression method using the optimized solid dispersion (Bhardwaj et al., 2010). Nine formulations (F1-F9) were prepared using three different superdisintegrants at three concentration levels (3.5%, 5%, and 7% w/w) as detailed in Table 2. All ingredients were individually passed through 40# sieve. The solid dispersion equivalent to 15 mg Olanzapine, sweetener (sucralose), and diluent (lactose) were mixed thoroughly using geometric dilution technique. The superdisintegrant was added to the mixture and blended uniformly. Magnesium stearate, previously passed through 60# sieve, was added as a lubricant and gently mixed for 2-3 minutes. The final blend was compressed into tablets weighing 200 mg using tablet compression machine with suitable tooling.

Table 2: Composition of Sublingual Tablet Formulations

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Solid dispersion*	105	105	105	105	105	105	105	105	105
CCS	7	10	14	-	-	-	-	-	-
CP	-	-	-	7	10	14	-	-	-
SSG	-	-	-	-	-	-	7	10	14
Sucralose	10	10	10	10	10	10	10	10	10
Mg stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Lactose (q.s.)	76.5	73.5	69.5	76.5	73.5	69.5	76.5	73.5	69.5
Total	200	200	200	200	200	200	200	200	200

**Solid dispersion equivalent to 15 mg Olanzapine; CCS: Croscarmellose sodium; CP: Crospovidone; SSG: Sodium starch glycolate*

2.8 Evaluation of Sublingual Tablets

Weight Variation: Twenty tablets were randomly selected and weighed individually using analytical balance. The average weight and percentage deviation were calculated according to USP specifications (Godbole et al., 2014).

Hardness: Tablet hardness was determined using Monsanto hardness tester. Ten tablets were tested and the average hardness was expressed in kg/cm² (Narendra et al., 2005).

Thickness: The thickness of tablets was measured using vernier caliper. Ten tablets were measured and the average thickness was recorded in millimeters.

Friability: Friability was determined using Roche friabilator. Pre-weighed tablets equivalent to 6.5 g were placed in the friabilator drum and rotated at 25 rpm for 4 minutes (100 revolutions). The tablets were dedusted, reweighed, and the percentage friability was calculated using the formula: % Friability = $[(W_1 - W_2) / W_1] \times 100$, where W_1 and W_2 are the initial and final weights, respectively (Kulkarni et al., 2011).

Drug Content: One tablet was triturated and dissolved in 100 mL phosphate buffer pH 6.8 under stirring for 10 minutes. The solution was filtered through 0.45 µm membrane filter, diluted appropriately, and the absorbance was measured at 252 nm using UV-visible spectrophotometer.

In-Vitro Disintegration Time: The disintegration time was determined using USP disintegration apparatus in 500 mL phosphate buffer pH 6.8 maintained at 37±0.5°C. Six tablets were placed in the disintegration tubes and the time required for complete disintegration was recorded (Yıldız et al., 2015).

Wetting Time: Wetting time was determined by placing a tablet on tissue paper moistened with phosphate buffer pH 6.8 containing eosin dye. The time required for the dye to reach the upper surface of the tablet was recorded as wetting time (Bayrak et al., 2011).

In-Vitro Drug Release: Dissolution studies were performed using USP Type II (paddle) dissolution apparatus in 500 mL phosphate buffer pH 6.8 at 37±0.5°C and 50 rpm. Samples were withdrawn at predetermined time intervals (2, 4, 6, 8, 10, and 15 minutes) and replaced with an equal volume of fresh medium. The samples were filtered and analyzed spectrophotometrically at 252 nm. The cumulative percentage drug release was calculated (Al-Madhagi et al., 2016).

2.9 Stability Studies

The optimized formulation was subjected to accelerated stability studies according to ICH guidelines. The tablets were packed in aluminum foil and stored at 40±2°C and 75±5% RH for 30 days. Samples were withdrawn at predetermined intervals and evaluated for physical appearance, drug content, disintegration time, and in-vitro dissolution (Yadav et al., 2015).

3. RESULTS AND DISCUSSION

3.1 Preformulation Studies

The UV spectrum of Olanzapine in phosphate buffer pH 6.8 exhibited maximum absorption at 252 nm, which is consistent with the literature values. The melting point of Olanzapine was found to be 191-195°C, which corresponds well with the reported range of 192-195°C, confirming the identity and purity of the drug sample.

3.2 FTIR Compatibility Studies

The FTIR spectrum of pure Olanzapine displayed characteristic absorption bands at 3016 cm^{-1} (C-H stretching), 1597 cm^{-1} (C-C stretching), 1240 cm^{-1} and 1026 cm^{-1} (C-O-C stretching), 1730 cm^{-1} (C=O stretching), and 3510 cm^{-1} (O-H stretching). The physical mixture of drug with polymers exhibited similar peaks without any significant shifts or disappearance of characteristic peaks, as shown in Table 3. This indicates the absence of any physicochemical incompatibility between Olanzapine and the selected excipients.

Table 3: FTIR Spectral Interpretation of Olanzapine

Functional Group	Standard (cm^{-1})	Observed (cm^{-1})	Mixture (cm^{-1})
C-H stretching	~3030	3016	3016
C-C stretching	~1600	1597	1597
C-O-C stretching	1234, 1075-1020	1240, 1026	1240, 1026
C=O stretching	1725-1705	1730	1727
-OH stretching	2590-3650	3510	3363

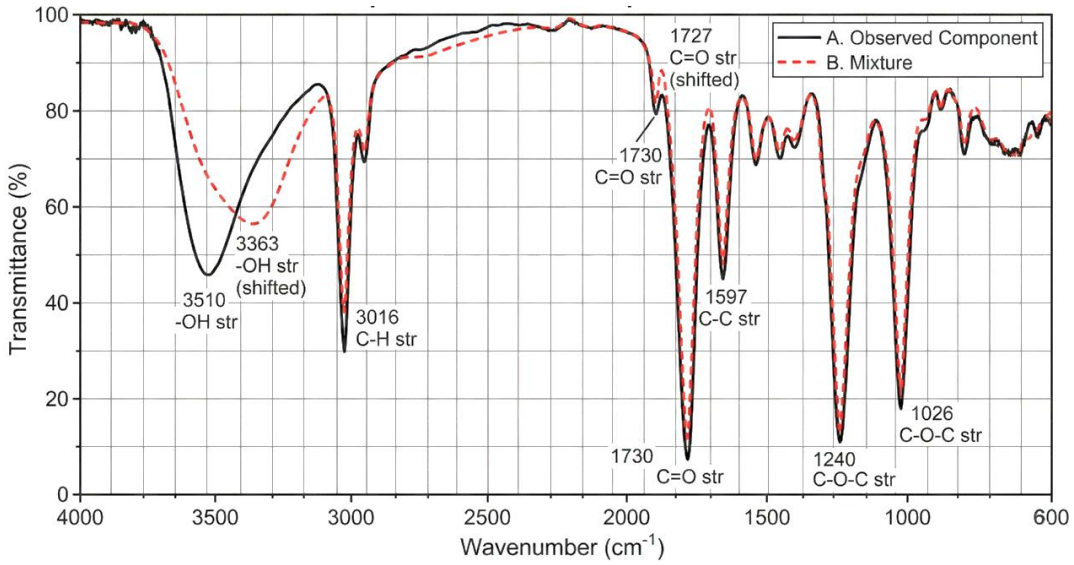

Fig.1- FTIR Spectral Interpretation of Olanzapine

3.3 Calibration Curve

The calibration curve of Olanzapine in phosphate buffer pH 6.8 was found to be linear over the concentration range of 5-30 µg/mL at 252 nm. The regression equation was y = 0.1257x + 0.0274 with a correlation coefficient (R^2) of 0.9972, indicating excellent linearity suitable for analytical determination of drug content and dissolution studies.

3.4 Evaluation of Solid Dispersions

The results of solid dispersion evaluation are presented in Table 4. All formulations exhibited acceptable drug content ranging from 97.22% to 101.26%, indicating uniform distribution of

drug within the carrier matrix. The solubility studies revealed a progressive enhancement in drug solubility with increasing carrier concentration for both PEG 6000 and propylene glycol-based formulations.

Table 4: Evaluation Parameters of Solid Dispersions

Parameter	S1	S2	S3	S4	S5	S6	S7
Solubility (mg/mL)	0.01	0.02	0.04	0.08	0.12	0.16	0.24
Drug content (%)	99.24	100.02	98.56	101.26	97.22	98.79	99.45

Propylene glycol-based solid dispersions demonstrated superior solubility enhancement compared to PEG 6000 formulations. At 1:4 drug-to-carrier ratio (S7 with propylene glycol and lactose monohydrate), maximum solubility of 0.24 mg/mL was achieved, representing approximately 24-fold enhancement compared to pure drug solubility. This significant improvement can be attributed to the liquid nature of propylene glycol, which improves drug wettability and molecular dispersion within the carrier matrix. Based on these findings, the solid dispersion S6 (1:2 ratio with propylene glycol) was selected for further tablet formulation studies as it provided substantial solubility enhancement with acceptable solid dispersion weight.

3.5 Physical Evaluation of Sublingual Tablets

The physical evaluation parameters of all sublingual tablet formulations are summarized in Table 5. All formulations exhibited uniform weight with acceptable variation within ±5% of the average weight, complying with pharmacopoeial limits. The hardness values ranged from 4.15±0.15 to 4.39±0.12 kg/cm², which is considered optimal for sublingual tablets as it ensures adequate mechanical strength while permitting rapid disintegration in the oral cavity.

Table 5: Physical Evaluation Parameters of Sublingual Tablets

Batch	Weight (mg)	Hardness (kg/cm²)	Thickness (mm)	Friability (%)	Drug content (%)
F1	200.32±0.22	4.34±0.21	3.47±0.08	0.12±0.03	100.32
F2	200.54±1.16	4.32±0.11	3.37±0.06	0.16±0.02	99.74
F3	201.44±0.27	4.21±0.14	3.45±0.04	0.24±0.03	98.69
F4	199.24±1.08	4.15±0.15	3.46±0.08	0.22±0.01	99.15
F5	200.17±1.01	4.27±0.17	3.47±0.11	0.29±0.03	98.74
F6	201.15±1.16	4.36±0.18	3.45±0.07	0.32±0.00	98.45
F7	201.21±0.34	4.39±0.12	3.46±0.02	0.27±0.03	99.75

Batch	Weight (mg)	Hardness (kg/cm²)	Thickness (mm)	Friability (%)	Drug content (%)
F8	200.16±0.28	4.25±0.24	3.44±0.07	0.15±0.02	101.22
F9	199.36±1.08	4.34±0.15	3.42±0.03	0.14±0.01	100.45

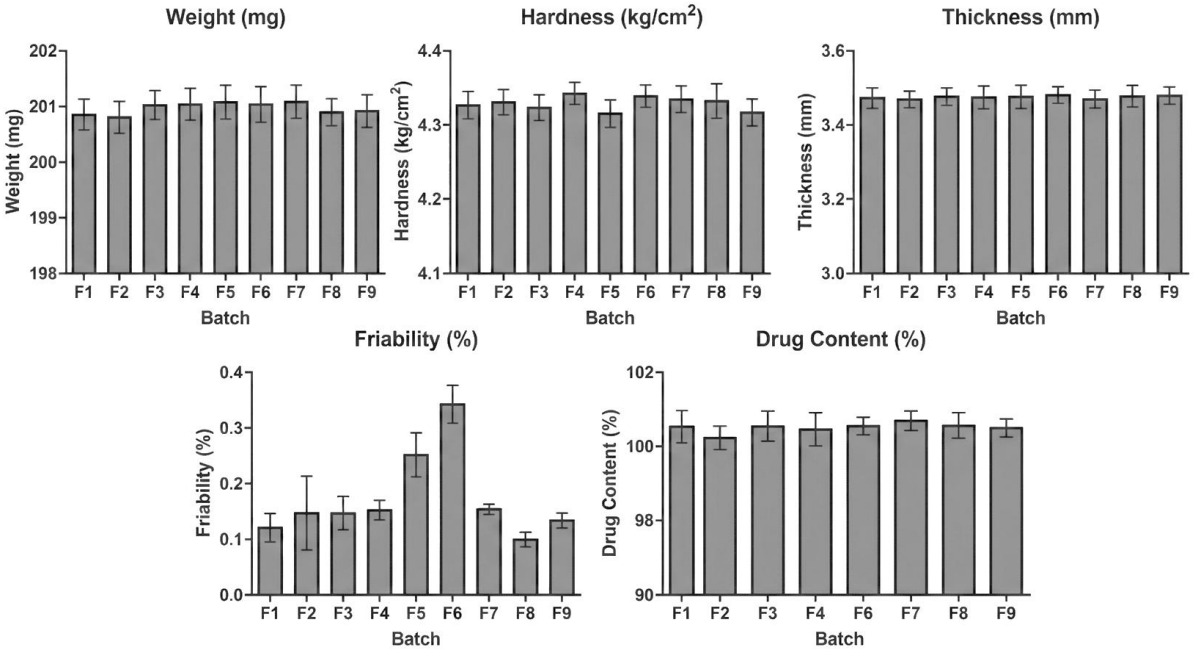

Fig.2- Physical Evaluation Parameters of Sublingual Tablets

Tablet thickness was consistent across all batches, ranging from 3.37±0.06 to 3.47±0.11 mm. The friability values were well below the pharmacopoeial limit of 1%, ranging from 0.12±0.03% to 0.32±0.00%, indicating adequate mechanical integrity of the tablets to withstand handling during manufacturing, packaging, and transportation. Drug content uniformity was satisfactory for all formulations, with values ranging from 98.45% to 101.22%, demonstrating uniform distribution of drug within the tablet matrix.

3.6 Disintegration and Wetting Time

The disintegration time and wetting time data are presented in Table 6. Disintegration time is a critical parameter for sublingual tablets as it directly influences the rate of drug release and subsequent absorption. All formulations exhibited disintegration time less than 30 seconds, which is considered acceptable for sublingual delivery systems.

Table 6: Disintegration Time and Wetting Time of Sublingual Tablets

Batch	Superdisintegrant	Disintegration Time (sec)	Wetting Time (sec)
F1	CCS 3.5%	22±1	9±1
F2	CCS 5%	23±2	14±2

Batch	Superdisintegrant	Disintegration Time (sec)	Wetting Time (sec)
F3	CCS 7%	18±1	17±1
F4	CP 3.5%	21±1	21±1
F5	CP 5%	23±2	11±1
F6	CP 7%	24±1	9±2
F7	SSG 3.5%	12±1	17±1
F8	SSG 5%	15±3	15±1
F9	SSG 7%	14±1	19±1

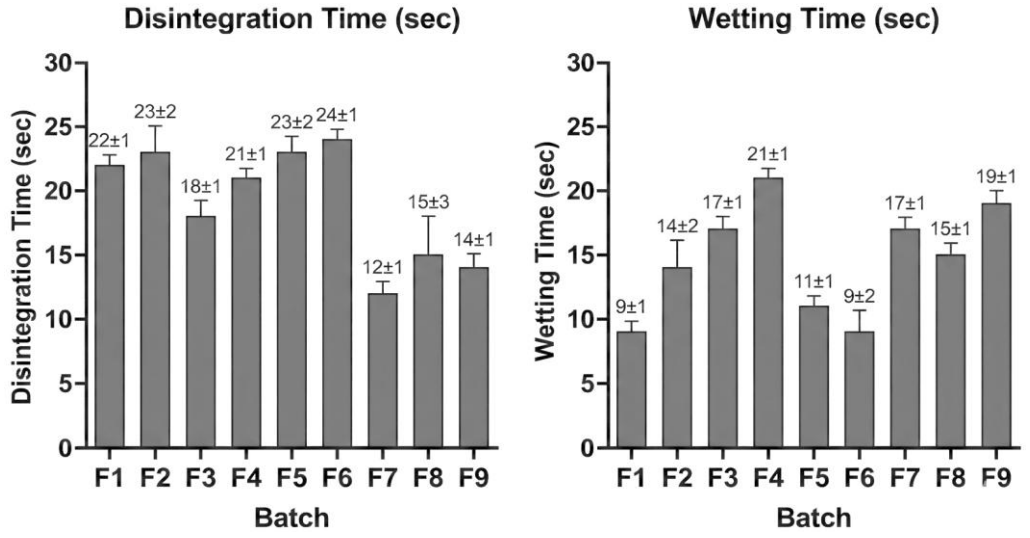

Fig.3- Disintegration Time and Wetting Time of Sublingual Tablets

Among the three superdisintegrants evaluated, sodium starch glycolate (SSG) demonstrated superior disintegration performance. Formulations F7, F8, and F9 containing SSG exhibited the shortest disintegration times of 12±1, 15±3, and 14±1 seconds, respectively. This enhanced performance can be attributed to the unique mechanism of action of SSG, which involves rapid swelling upon contact with aqueous medium, generating sufficient pressure to break apart the tablet matrix (Balusu et al., 2012). Croscarmellose sodium (CCS) showed intermediate performance with disintegration times ranging from 18-23 seconds, while crospovidone (CP) exhibited relatively longer disintegration times of 21-24 seconds.

3.7 In-Vitro Drug Release Studies

The in-vitro drug release profiles of all formulations are illustrated in Figure 1, and the cumulative percentage drug release data are presented in Table 7. All formulations demonstrated rapid drug release characteristics suitable for sublingual delivery, with complete drug release achieved within 15 minutes.

Table 7: Cumulative Drug Release (%) of Sublingual Tablet Formulations

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
2	38.62	42.51	43.57	30.22	32.14	34.91	45.35	48.12	50.11
4	67.54	69.71	71.22	55.32	58.19	60.14	77.12	80.14	82.14
6	83.18	84.32	86.47	71.21	68.19	70.74	84.14	86.19	88.74
8	94.58	95.11	96.87	86.12	83.17	85.04	90.14	92.64	94.99
10	95.12	96.14	97.22	94.18	90.21	92.45	96.14	98.19	99.14
15	96.11	97.12	99.81	95.19	94.33	96.77	99.28	100.02	100.01

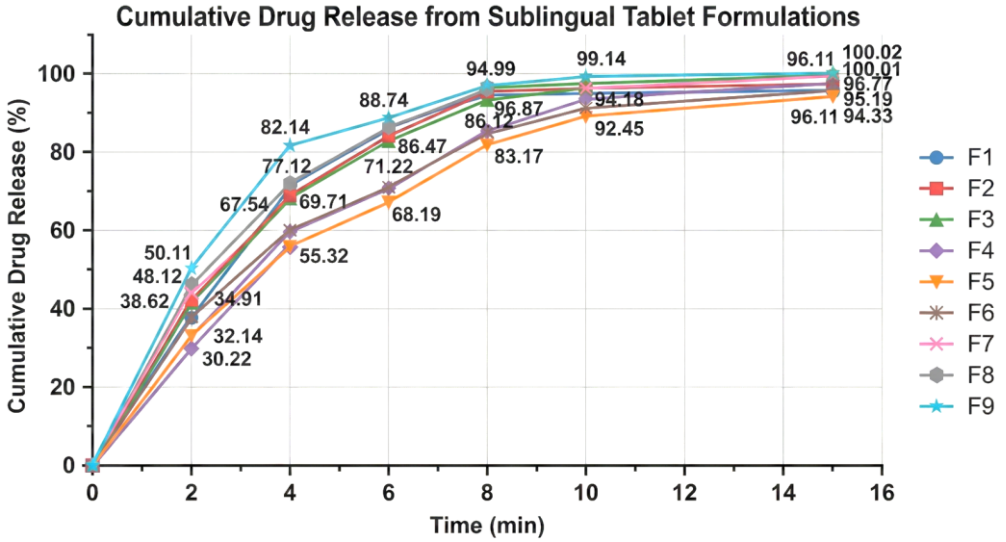

Fig.4- Cumulative Drug Release (%) of Sublingual Tablet Formulations

The drug release data demonstrated a clear relationship between the type of superdisintegrant and dissolution rate. Formulations containing SSG (F7-F9) exhibited the highest initial drug release, with approximately 45-50% drug released within the first 2 minutes. This rapid initial release correlates well with the shorter disintegration times observed for SSG-containing formulations. At 10 minutes, formulations F8 and F9 achieved nearly complete drug release of 98.19±0.44% and 99.14±0.34%, respectively.

Croscarmellose sodium-containing formulations (F1-F3) showed intermediate dissolution performance with drug release values ranging from 95-97% at 10 minutes. Crospovidone-based formulations (F4-F6) exhibited relatively slower dissolution rates, achieving 90-94% drug release at 10 minutes. The superior performance of SSG can be explained by its rapid and extensive swelling capacity, which facilitates faster tablet disintegration and subsequent drug dissolution from the solid dispersion matrix.

Based on the comprehensive evaluation of disintegration time, wetting time, and drug release characteristics, formulation F8 containing 5% sodium starch glycolate was identified as the optimized formulation. This batch demonstrated an optimal balance between disintegration time (15±3 seconds), acceptable friability (0.15±0.02%), and excellent drug release (98.19±0.44% at 10 minutes and complete release at 15 minutes).

3.8 Stability Studies

The optimized formulation F8 was subjected to accelerated stability testing at 40±2°C and 75±5% RH for 30 days. The stability study results are presented in Table 8. No significant changes were observed in the physical appearance, hardness, weight variation, thickness, or friability of the tablets during the storage period.

Table 8: Accelerated Stability Study Results of Optimized Formulation (F8)

Parameter	Initial	After 30 days
Hardness (kg/cm²)	4.25±0.24	4.22±0.21
Weight (mg)	200.16±0.28	201.26±0.14
Thickness (mm)	3.44±0.07	3.42±0.11
Friability (%)	0.15±0.02	0.17±0.03
Disintegration time (sec)	13±2	14±2
Wetting time (sec)	9±2	10±1
Assay (%)	99.89	99.09
Drug release at 15 min (%)	98.17±1.11	97.11±1.36

The drug content remained stable with only a marginal decrease from 99.89% to 99.09%, which is within acceptable limits. The disintegration time showed a slight increase from 13±2 to 14±2 seconds, while the drug release at 15 minutes decreased marginally from 98.17±1.11% to 97.11±1.36%. These minor changes are not statistically significant and demonstrate that the formulation maintains its quality attributes under accelerated storage conditions. The results indicate that the developed sublingual tablet formulation possesses adequate stability and can be expected to maintain its pharmaceutical quality during normal storage conditions.

4. CONCLUSION

The present study successfully developed sublingual tablets of Olanzapine using solid dispersion technique combined with superdisintegrants to achieve rapid drug release. The preformulation studies confirmed the identity of the drug and established compatibility between Olanzapine and the selected excipients. Solid dispersion prepared with propylene glycol and lactose monohydrate at 1:2 ratio provided significant enhancement in drug solubility.

Among the three superdisintegrants evaluated, sodium starch glycolate demonstrated superior performance in terms of disintegration time and drug release. The optimized formulation F8

containing 5% SSG exhibited rapid disintegration (15±3 seconds), acceptable wetting time (15±1 seconds), and nearly complete drug release (98.19% at 10 minutes). Accelerated stability studies confirmed that the formulation maintains its quality attributes under stressed conditions.

The developed sublingual tablet formulation offers potential advantages for the management of schizophrenia, particularly in situations requiring rapid onset of drug action. The sublingual route bypasses first-pass metabolism and provides rapid drug absorption, which may translate to improved therapeutic outcomes. Further in-vivo studies and clinical investigations would be warranted to establish the pharmacokinetic advantages and therapeutic efficacy of the developed formulation.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Aburahma, M. H., El-Leithy, I. S., & Elkheshen, S. A. (2010). Preparation and in vitro/in vivo characterization of porous sublingual tablets containing ternary kneaded solid system of vinpocetine with β-cyclodextrin and hydroxy acid. *Scientia Pharmaceutica, 78*(2), 363-379.

Al-Madhagi, W., Fayed, M. H., & Abdel-Aty, A. M. (2016). Formulation and evaluation of new glimepiride sublingual tablets. *Journal of Pharmaceutics, 2016*, 1-5.

Balusu, H., Jayanthi, G., & Swamy, S. M. (2012). Formulation and evaluation of fast disintegrating zolmitriptan sublingual tablets. *Current Trends in Biotechnology and Pharmacy, 10*, 84-98.

Banker, G. S., & Anderson, N. R. (1991). Tablets. In L. Lachman, H. A. Lieberman, & J. L. Kanig (Eds.), *The theory and practice of industrial pharmacy* (3rd ed., pp. 293-345). Varghese Publishing House.

Bayrak, Z., Tas, C., Tasdemir, U., Erol, H., & Kose Ozkan, C. (2011). Formulation of zolmitriptan sublingual tablets prepared by direct compression with different polymers: In vitro and in vivo evaluation. *European Journal of Pharmaceutics and Biopharmaceutics, 78*, 499-505.

Benajeer, S., Naseeb Basha, S., & Shanmugam, S. (2012). New simple UV spectrophotometric method for determination of mirtazapine in bulk and pharmaceutical dosage forms. *International Journal of Pharma Sciences and Research, 3*(10), 482-486.

Bhardwaj, V., Shukla, V., Goyal, N., & Sharma, P. K. (2010). Formulation and evaluation of fast disintegrating sublingual tablets of amlodipine besylate using different superdisintegrants. *International Journal of Pharmacy and Pharmaceutical Sciences, 2*(3), 89-92.

Collins, L. M., & Dawes, C. (1987). The surface area of the adult human mouth and thickness of the salivary film covering the teeth and oral mucosa. *Journal of Dental Research, 66*(8), 1300-1302.

D'Souza, L., Devi, P., Divya Shridhar, M. P., & Naik, C. G. (2008). Use of Fourier Transform Infrared (FTIR) spectroscopy to study cadmium-induced changes in Padina tetrastromatica (Hauck). *Analytical Chemistry Insights, 3*, 135-143.

Godbole, A. M., D'Mello, P. M., Bhatia, M. S., & Kulkarni, S. (2014). Formulation and in-vitro evaluation of sublingual tablets of ondansetron hydrochloride using coprocessed excipients. *Indian Journal of Pharmaceutical Education and Research, 48*, 7-17.

Goswami, T., Jasti, B. R., & Li, X. (2009). Estimation of the theoretical pore sizes of the porcine oral mucosa for permeation of hydrophilic permeants. *Archives of Oral Biology, 54*(6), 577-582.

Ishikawa, T., Watanabe, Y., Takayama, K., Endo, H., & Matsumoto, M. (2000). Effect of hydroxypropylmethylcellulose (HPMC) on the release profiles and bioavailability of a poorly water-soluble drug from tablets prepared using macrogol and HPMC. *International Journal of Pharmaceutics, 202*(1-2), 173-178.

Jeong, S. H., Takaishi, Y., Fu, Y., & Park, K. (2008). Material properties for making fast dissolving tablets by a compression method. *Journal of Materials Chemistry, 18*(30), 3527-3535.

Kulkarni, S., Ranjit, K. P., Basavaraj, Someshwara, R. B., & Ashok, K. P. (2011). Effect of superdisintegrants on formulation of taste masked fast disintegrating lisinopril tablets. *International Journal of Current Pharmaceutical Research, 3*(1), 11-14.

Narendra, C., Srinath, M. S., & Prakash, B. R. (2005). Formulation and evaluation of sublingual tablet containing terbutaline sulphate optimisation and in vivo studies. *Ars Pharmaceutica, 46*(2), 139-158.

Ölmez, S. S., & Vural, I. (2009). Advantages and quality control of orally disintegrating tablets. *FABAD Journal of Pharmaceutical Sciences, 34*(3), 167-172.

Prathusha, P. (2017). A review on sublingual tablets. *Journal of Formulation Science & Bioavailability, 1*(1).

Rameshwari, S., & Jeya, A. J. (2009). Formulation and evaluation of nifedipine sublingual tablets. *Asian Journal of Pharmaceutical and Clinical Research, 2*(3), 44-48.

Setty, C. M., Prasad, D. V. K., Gupta, V. R. M., & Sa, B. (2008). Development of fast dispersible aceclofenac tablets: Effect of functionality of superdisintegrants. *Indian Journal of Pharmaceutical Sciences, 70*(2), 180-185.

Sudhakar, Y., Kuotsu, K., & Bandyopadhyay, A. K. (2006). Buccal bioadhesive drug delivery—A promising option for orally less efficient drugs. *Journal of Controlled Release, 114*(1), 15-40.

Timmer, C. J., & Sitsen, J. M. A. (2000). Clinical pharmacokinetics of mirtazapine. *Clinical Pharmacokinetics, 38*(6), 461-474.

Yadav, S., Sharma, D., & Singh, G. (2015). Formulation and optimization of sublingual tablet of ramipril. *Journal of Chemical and Pharmaceutical Research, 7*(8), 1077-1086.

Yıldız, S., Aytekin, E., & Yavuz, B. (2015). Formulation studies for mirtazapine orally disintegrating tablets. *Drug Development and Industrial Pharmacy*, 1-10.