FORMULATION AND EVALUATION OF TADALAFIL SUBLINGUAL FILM USING 3² FACTORIAL DESIGN

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Abstract

Background: Tadalafil is a phosphodiesterase type 5 (PDE5) inhibitor used for the treatment of erectile dysfunction. Conventional oral tablets exhibit delayed onset of action due to hepatic first-pass metabolism and slow dissolution. Sublingual films offer advantages including rapid disintegration in the oral cavity, enhanced bioavailability through sublingual absorption, and convenient administration without water.

Objective: The present study aimed to formulate and optimize sublingual films of Tadalafil using 3² factorial design to achieve rapid disintegration with adequate mechanical properties for the management of erectile dysfunction requiring faster onset of action.

Methods: Sublingual films were prepared by solvent casting technique using HPMC E15 and polyvinyl alcohol (PVA) as film-forming polymers, propylene glycol as plasticizer, and mannitol as sweetener. A 3² full factorial design was employed to study the effect of two independent variables (HPMC E15 and PVA concentrations) on dependent variables including disintegration time and tensile strength. Films were evaluated for mechanical properties, surface pH, drug content, and in-vitro drug release.

Results: FTIR studies confirmed the absence of drug-excipient incompatibility. Preliminary trials established propylene glycol (20% w/w) as the optimal plasticizer and HPMC E15-PVA combination as the optimal polymer system. Among the nine factorial batches, formulation F4 containing HPMC E15 (14 mg) and PVA (4 mg) demonstrated optimal characteristics with disintegration time of 14.66±1.52 seconds, tensile strength of 10.12±0.48 g/cm², folding endurance of 265, and drug release of 92.78±0.75% within 5 minutes. Statistical analysis confirmed the significant effects of both polymers on response variables.

Keywords: Tadalafil, sublingual film, solvent casting, factorial design, HPMC E15, polyvinyl alcohol, erectile dysfunction.

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1. INTRODUCTION

Oral thin films, also known as orodispersible films or mouth-dissolving films, have emerged as an innovative drug delivery system offering several advantages over conventional solid dosage forms. These films are designed to disintegrate rapidly when placed on the tongue or in the sublingual region, releasing the drug for local or systemic absorption (Arya et al., 2010). The sublingual route is particularly advantageous for drugs susceptible to first-pass metabolism, as it allows direct absorption into the systemic circulation through the highly vascularized sublingual mucosa (Barnhart & Sloboda, 2007).

Oral thin films offer numerous benefits including ease of administration without water, rapid onset of action, improved patient compliance, accurate dosing, and suitability for patients with swallowing difficulties such as pediatric, geriatric, and dysphagic patients (Bhyan et al., 2011). The thin film dosage form also provides better stability compared to liquid formulations and offers opportunities for taste masking of bitter drugs. These characteristics make oral films an attractive alternative for drugs requiring rapid therapeutic effect (Gavaskar et al., 2010).

Tadalafil is a potent and selective inhibitor of phosphodiesterase type 5 (PDE5), which is responsible for degradation of cyclic guanosine monophosphate (cGMP) in the corpus cavernosum (DrugBank, 2023). By inhibiting PDE5, Tadalafil enhances the effect of nitric oxide, resulting in smooth muscle relaxation and increased blood flow to the penis, thereby facilitating penile erection. Tadalafil is currently available as conventional oral tablets with doses ranging from 2.5 to 20 mg, indicated for the treatment of erectile dysfunction and benign prostatic hyperplasia.

Despite its therapeutic efficacy, conventional Tadalafil tablets may not provide sufficiently rapid onset of action for patients requiring immediate therapeutic effect. The drug undergoes hepatic metabolism and exhibits variable absorption depending on food intake. Development of a sublingual film formulation could potentially overcome these limitations by providing rapid drug release and absorption through the sublingual mucosa, bypassing first-pass metabolism and offering more predictable pharmacokinetics (Gupta et al., 2010).

The formulation of oral thin films requires careful selection of film-forming polymers, plasticizers, and other excipients to achieve desired mechanical properties and disintegration characteristics. Hydroxypropyl methylcellulose (HPMC) is widely used as a film-forming polymer due to its excellent film-forming ability, good mechanical properties, and compatibility with a wide range of drugs (Jha et al., 2011). Polyvinyl alcohol (PVA) is another commonly used polymer that provides flexibility and improves film properties when used in combination with other polymers. Plasticizers such as propylene glycol, polyethylene glycol, and glycerin are incorporated to improve film flexibility and reduce brittleness (Noushin et al., 2009).

Factorial design is a systematic approach for studying the effects of multiple variables on response parameters simultaneously. A 3^2 factorial design allows evaluation of two factors at three levels, providing information about linear and quadratic effects as well as interaction

effects (Arora & Gupta, 2007). This statistical approach enables optimization of formulation parameters with minimum number of experimental runs while maintaining statistical validity.

The present investigation aimed to develop and optimize sublingual films of Tadalafil using 3^2 factorial design. The study involved systematic screening of plasticizers and polymers through preliminary trials, followed by optimization of polymer concentrations using factorial design approach. The optimized formulation was evaluated for mechanical properties, disintegration time, drug content, and in-vitro dissolution characteristics.

2. MATERIALS AND METHODS

2.1 Materials

Tadalafil was obtained from Vapi Care Pharma Private Ltd., India. Hydroxypropyl methylcellulose E15 (HPMC E15), polyvinyl alcohol (PVA), polyvinyl pyrrolidone K30 (PVP K30), propylene glycol, polyethylene glycol 400 (PEG 400), glycerin, mannitol, citric acid, and Tween 80 were procured from K.J. Faculty of Pharmacy, SSSRGI. Xanthan gum and guar gum were also obtained from the same source. All other chemicals and reagents used were of analytical grade. Simulated salivary fluid (SSF) pH 6.8 was prepared according to standard procedures.

2.2 Instruments and Equipment

The study utilized UV-Visible Spectrophotometer (Shimadzu UV 1800), FTIR Spectrophotometer (Shimadzu), digital pH meter (Chemline Technology), electronic digital weighing balance (ACZET Pvt. Ltd., CY 224), micrometer screw gauge (Micro Teknik), tensiometer (Vision International Company), magnetic stirrer (Sky Bound), and sonicator (Althea Technology).

2.3 Preformulation Studies

2.3.1 Identification of Drug

The identity of Tadalafil was confirmed using UV spectroscopy and melting point determination. The drug was dissolved in simulated salivary fluid pH 6.8 and the UV spectrum was recorded in the range of 200-400 nm to determine the wavelength of maximum absorption (λmax). The melting point was determined using digital melting point apparatus and compared with reported literature values (Prajapati et al., 2014).

2.3.2 Drug-Excipient Compatibility Study

Fourier Transform Infrared (FTIR) spectroscopy was employed to investigate potential interactions between Tadalafil and the selected excipients (D'Souza et al., 2008). Physical mixture of drug with polymers (HPMC E15 and PVA) in 1:1 ratio was prepared and FTIR

spectra 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.

2.4 Analytical Method Development

A calibration curve for Tadalafil was constructed in simulated salivary fluid pH 6.8 at 285 nm. Stock solution was prepared by dissolving accurately weighed quantity of drug in SSF pH 6.8. Serial dilutions were made to obtain concentrations ranging from 5-25 µg/mL. The absorbance was measured at 285 nm against blank, and the calibration curve was plotted (Benajeer et al., 2012).

2.5 Preparation of Sublingual Films

Sublingual films were prepared by solvent casting technique (Dandagi & Gayakwad, 2005). The required amount of film-forming polymer was allowed to hydrate in minimum amount of distilled water for 1-2 hours until a clear viscous solution was obtained. The plasticizer was then added to the polymer solution (Solution A). In a separate beaker, the drug and other ingredients including sweetener and saliva stimulating agent were dissolved in minimum amount of water (Solution B). Solution B was added to Solution A with constant stirring to obtain a homogeneous viscous solution (Solution C).

The resulting solution was set aside until entrapped air bubbles were removed. The bubble-free solution was cast onto glass Petri dishes (62.17 cm^2 area) and dried in a hot air oven at 40-45°C for 8-10 hours. The dried films were carefully peeled from the Petri dishes, checked for any imperfections, and cut into 2×2 cm^2 pieces (4 cm^2 area) each containing 10 mg of Tadalafil. The films were stored in aluminum foil pouches until further evaluation (Tayel et al., 2010).

2.6 Preliminary Trials

Preliminary trials were conducted systematically to optimize the plasticizer type and concentration, and to select the optimal polymer or polymer combination for film formulation.

Plasticizer Optimization (B1-B5): Five batches were prepared using HPMC E15 (35% w/w) and PVP K30 (15% w/w) as polymers with different plasticizers: glycerin (15% w/w) in B1, PEG 400 (15% w/w) in B2, and propylene glycol at 15%, 20%, and 10% w/w in batches B3, B4, and B5, respectively.

Single Polymer Optimization (B6-B10): Five batches were prepared using individual polymers at 50% w/w concentration: PVP K30 (B6), PVA (B7), HPMC E15 (B8), xanthan gum (B9), and guar gum (B10), with propylene glycol (20% w/w) as plasticizer.

Polymer Combination Optimization (B11-B14): Four batches were prepared using HPMC E15 (40% w/w) in combination with different secondary polymers at 10% w/w: PVA (B11), PVP K30 (B12), xanthan gum (B13), and guar gum (B14).

2.7 Experimental Design

Based on preliminary trials, a 3^2 full factorial design was employed to optimize the formulation. The two independent variables selected were: X1 - HPMC E15 concentration (14, 16, and 18 mg) and X2 - PVA concentration (2, 4, and 6 mg). The dependent variables evaluated were disintegration time and tensile strength. Nine formulations (F1-F9) were prepared according to the factorial design matrix presented in Table 1.

Table 1: 3^2 Factorial Design Matrix with Coded and Actual Values

Batch	X1 Coded	X2 Coded	HPMC E15 (mg)	PVA (mg)	Total Polymer (mg)
F1	-1	-1	14	2	16
F2	-1	0	16	2	18
F3	-1	+1	18	2	20
F4	0	-1	14	4	18
F5	0	0	16	4	20
F6	0	+1	18	4	22
F7	+1	-1	14	6	20
F8	+1	0	16	6	22
F9	+1	+1	18	6	24

All formulations contain: Tadalafil 10 mg, Propylene glycol 4 mg, Mannitol 2.4 mg, Citric acid 2.4 mg, Tween 80 q.s., Water q.s.

2.8 Evaluation of Sublingual Films

Visual Appearance: Films were visually inspected for clarity, color, homogeneity, and surface texture. The ease of film separation from the mold was also assessed (Vineet et al., 2010).

Thickness: Film thickness was measured using a micrometer screw gauge at five different locations (center and four corners) for each film. The mean thickness was calculated and expressed in millimeters (Rameshwari & Jeya, 2009).

Folding Endurance: Folding endurance was determined by repeatedly folding the film at the same place until a visible crack was observed. The number of times the film could be folded without breaking was recorded as folding endurance (Suresh et al., 2011).

Tensile Strength: Tensile strength was measured using a tensiometer (Ponco Machine Tools). Film strips free from air bubbles were held between two clamps at a fixed distance. Force was applied by pulling one clamp until the film broke. Tensile strength was calculated as: Tensile Strength = Load at break (g) / Cross-sectional area (cm^2) (Sindhu et al., 2010).

Percent Elongation: The percent elongation was determined simultaneously with tensile strength measurement and calculated as: % Elongation = [(Final length - Original length) / Original length] × 100 (Narendra et al., 2005).

Surface pH: A 2×2 cm² film was placed in a Petri dish and moistened with 0.5 mL of distilled water for 30 seconds. The pH was measured by bringing the electrode of a calibrated pH meter in contact with the film surface and allowing equilibration for 1 minute (Abeer et al., 2006).

Disintegration Time: The film was placed in a Petri dish containing 10 mL of simulated salivary fluid pH 6.8 with gentle swirling. The time required for the film to completely disintegrate was recorded as disintegration time (Yildiz et al., 2015).

Drug Content (Assay): A 2×2 cm² film was dissolved in 100 mL of simulated salivary fluid pH 6.8. After complete dissolution, the solution was filtered, diluted appropriately, and analyzed at 285 nm using UV-Visible Spectrophotometer (Godbole et al., 2014).

In-Vitro Drug Release: Dissolution studies were performed using USP Type II (paddle) apparatus with 300 mL of simulated salivary fluid pH 6.8 at 37±0.5°C and 50 rpm. Samples were withdrawn at 1, 2, 3, 4, and 5 minutes and replaced with fresh medium. The samples were analyzed spectrophotometrically at 285 nm and cumulative drug release was calculated (Al-Madhagi et al., 2016).

2.9 Statistical Analysis

The experimental data were analyzed using Design Expert software. Multiple regression analysis was performed to establish polynomial equations relating independent variables to response parameters. Response surface methodology (RSM) and contour plots were generated to visualize the effects of variables and their interactions on responses. Checkpoint batches were prepared to validate the design model.

3. RESULTS AND DISCUSSION

3.1 Preformulation Studies

The UV spectrum of Tadalafil in simulated salivary fluid pH 6.8 exhibited maximum absorption at 285 nm, which is consistent with the reported literature value of 284 nm. The melting point of Tadalafil was found to be 290°C, which corresponds well with the reported range of 289-293°C, confirming the identity and purity of the drug sample.

3.2 FTIR Compatibility Studies

The FTIR spectrum of pure Tadalafil displayed characteristic absorption bands at 3601.10 cm^{-1} (O-H stretching), 1433.11 cm^{-1} (C-H stretching), and 1510.26 cm^{-1} (aromatic C=C stretching). The physical mixture of drug with polymers (HPMC E15 and PVA) exhibited similar peaks at 3684.04 cm^{-1}, 1423.47 cm^{-1}, and 1512.19 cm^{-1}, respectively, as shown in Table 2. The peaks

observed in the drug spectrum were not hindered in the drug-excipient mixture spectrum, indicating the absence of any physicochemical interaction between Tadalafil and the selected excipients.

Table 2: FTIR Spectral Interpretation of Tadalafil

Functional Group	Standard (cm^{-1})	Drug (cm^{-1})	Drug + Excipients (cm^{-1})
O-H stretching	3650-3584	3601.10	3684.04
C-H stretching	1480-1380	1433.11	1423.47
Aromatic C=C	1500-1600	1510.26	1512.19

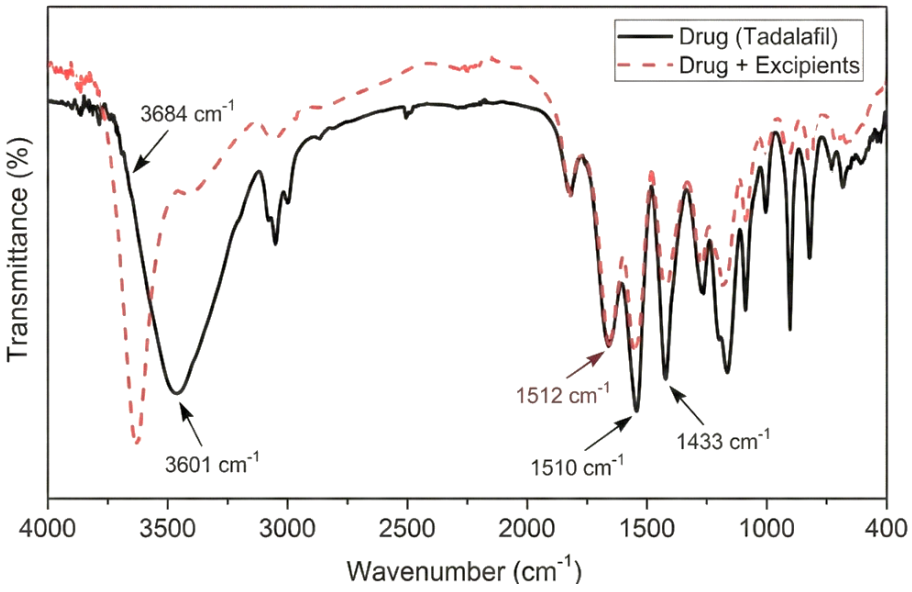

Fig.1- FTIR Spectral Interpretation of Tadalafil

3.3 Calibration Curve

The calibration curve of Tadalafil in simulated salivary fluid pH 6.8 was found to be linear over the concentration range of 5-25 µg/mL at 285 nm. The regression equation was $y = 0.0212x + 0.0983$ with a correlation coefficient (R^2) of 0.9956, indicating excellent linearity suitable for analytical determination of drug content and dissolution studies.

3.4 Preliminary Trial Results

Plasticizer Optimization: The results of plasticizer optimization trials (B1-B5) are summarized in Table 3. Batch B1 containing glycerin produced films with good appearance but moderate plasticity and high disintegration time (73 seconds). Batch B2 with PEG 400 produced sticky films with white spots and poor folding endurance (89). Batches B3, B4, and B5 containing propylene glycol at different concentrations produced transparent, non-sticky films with good mechanical properties. Among these, batch B4 containing propylene glycol at

20% w/w demonstrated optimal characteristics with highest folding endurance (211), tensile strength (13.54 g/cm²), and acceptable disintegration time (44 seconds). Therefore, propylene glycol at 20% w/w was selected as the optimal plasticizer for subsequent formulations.

Table 3: Evaluation Results of Plasticizer Optimization Batches (B1-B5)

Parameter	B1 (Glycerin)	B2 (PEG 400)	B3 (PG 15%)	B4 (PG 20%)
Appearance	Good	Poor	Good	Good
Folding endurance	128	89	177	211
Tensile strength (g/cm²)	10.04	9.03	11.97	13.54
Surface pH	6.47	6.56	6.50	6.57
DT (sec)	73	43	49	44

PG: Propylene glycol; DT: Disintegration time

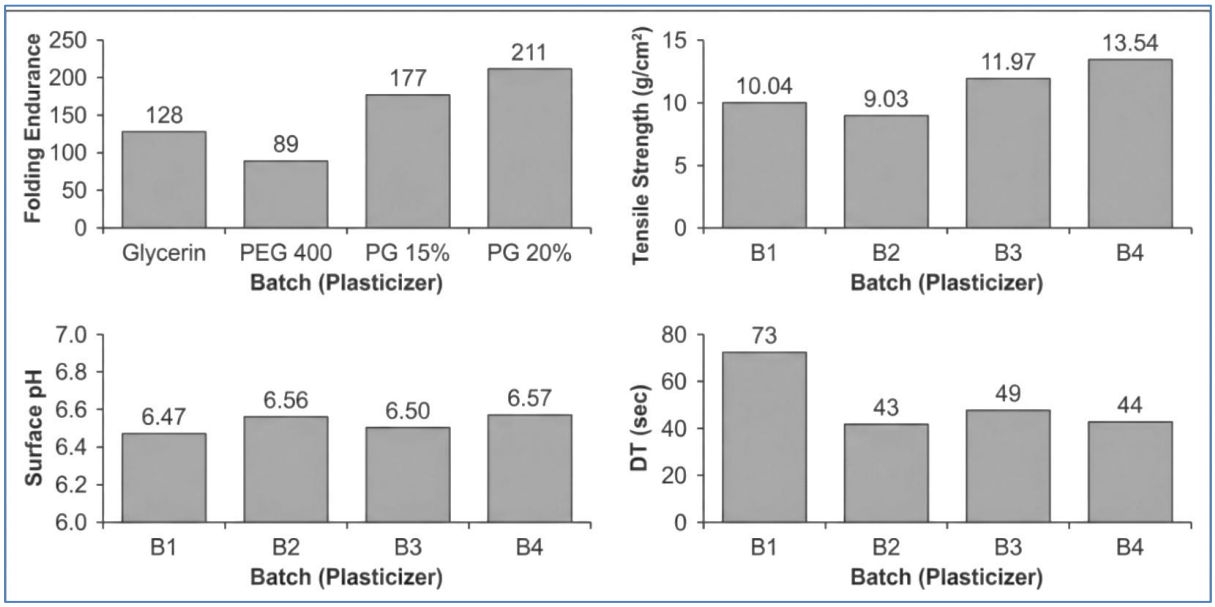

Fig.2- Evaluation Results of Plasticizer Optimization Batches (B1-B5)

Single Polymer Optimization: Evaluation of single polymer batches (B6-B10) revealed that none of the individual polymers produced films with all desired properties. Batch B6 (PVP K30) produced sticky films that could not be peeled from the Petri dish. Batch B7 (PVA) produced soft films with good drug release but lower mechanical strength. Batch B8 (HPMC E15) produced thin, plastic-like films with fast disintegration (37-40 seconds) but moderate tensile strength. Batches B9 (xanthan gum) and B10 (guar gum) produced films with poor mechanical properties and inconsistent drug release.

Polymer Combination Optimization: Evaluation of polymer combination batches (B11-B14) demonstrated that batch B11 containing HPMC E15 and PVA combination produced films

with optimal characteristics including good appearance, smooth texture, moderate tensile strength (11.20-12.53 g/cm²), high folding endurance (240-251), acceptable disintegration time (30-32 seconds), and good drug release profile (88.09% at 5 minutes). Therefore, the combination of HPMC E15 and PVA was selected for factorial design optimization.

3.5 Evaluation of Factorial Design Batches

The evaluation parameters of factorial design batches (F1-F9) are presented in Table 4. All formulations exhibited acceptable physical characteristics with good to moderate appearance and adequate spreadability. The folding endurance ranged from 171 to 322, with higher values observed in batches containing higher polymer concentrations. Film thickness ranged from 0.073±0.011 to 0.123±0.005 mm, showing direct correlation with total polymer content. Surface pH values were in the acceptable range of 5.87 to 6.52, ensuring compatibility with the oral mucosa.

Table 4: Evaluation Parameters of Factorial Design Batches (F1-F9)

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Folding endurance	171	203	180	265	242	285	252	310	322
Tensile strength (g/cm²)	9.41	10.65	12.09	10.12	11.29	12.95	12.79	13.69	14.97
% Elongation	10	10	15	15	10	25	20	20	25
Thickness (mm)	0.073	0.086	0.09	0.096	0.10	0.106	0.116	0.123	0.12
Surface pH	6.27	6.48	5.95	6.52	5.87	6.50	6.32	5.98	6.29
Assay (%)	86.43	81.39	91.65	94.26	89.56	92.86	84.34	95.13	89.04
DT (sec)	11.66	20.33	30.33	14.66	23.33	34.33	19.66	30.33	36.33

DT: Disintegration time; Values represent mean of three determinations

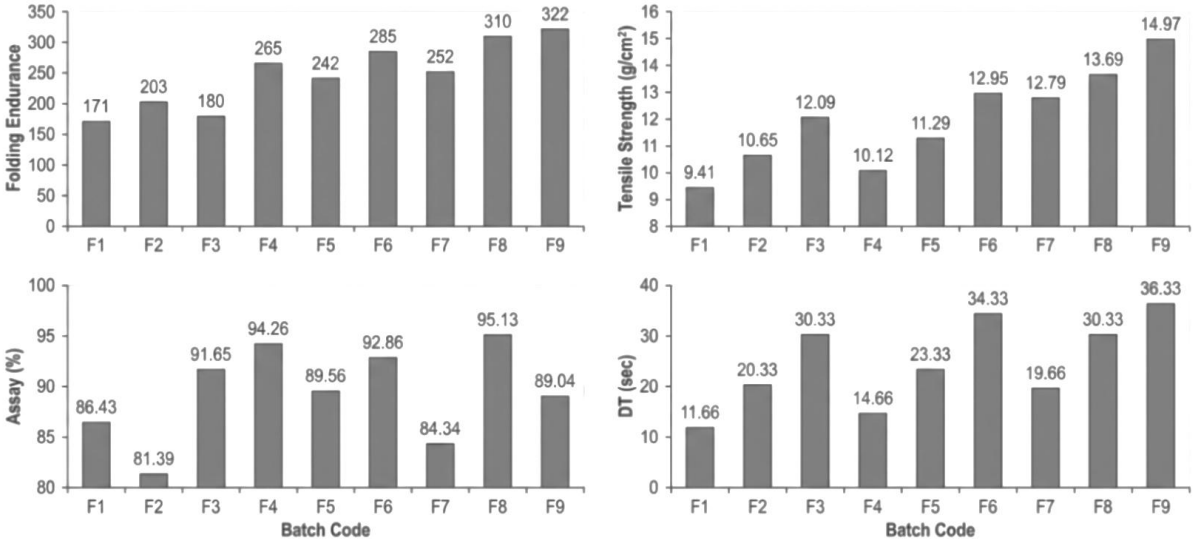

Fig.3- Evaluation Parameters of Factorial Design Batches (F1-F9)

Tensile strength values ranged from 9.41±0.57 to 14.97±0.81 g/cm², demonstrating adequate mechanical strength for handling and packaging. The disintegration time varied from 11.66±0.57 to 36.33±1.52 seconds, showing a clear relationship with polymer concentration. Drug content (assay) ranged from 81.39% to 95.13%, indicating satisfactory uniformity of drug distribution in the films.

3.6 In-Vitro Drug Release Studies

The in-vitro drug release profiles of factorial design batches are presented in Table 5 and illustrated in Figure 1. All formulations demonstrated rapid drug release characteristics suitable for sublingual delivery, with substantial drug release achieved within 5 minutes.

Table 5: Cumulative Drug Release (%) of Factorial Design Batches

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	41.94	40.23	46.65	51.40	48.69	45.97	43.38	55.82	54.83
2	48.99	47.17	53.28	68.03	64.90	67.98	64.90	66.83	71.36
3	57.03	60.91	73.26	78.69	71.01	75.58	75.78	73.02	79.25
4	69.10	67.02	80.83	84.38	78.98	81.03	83.22	80.62	83.09
5	85.63	84.95	86.33	92.78	83.82	86.77	87.69	82.16	87.14

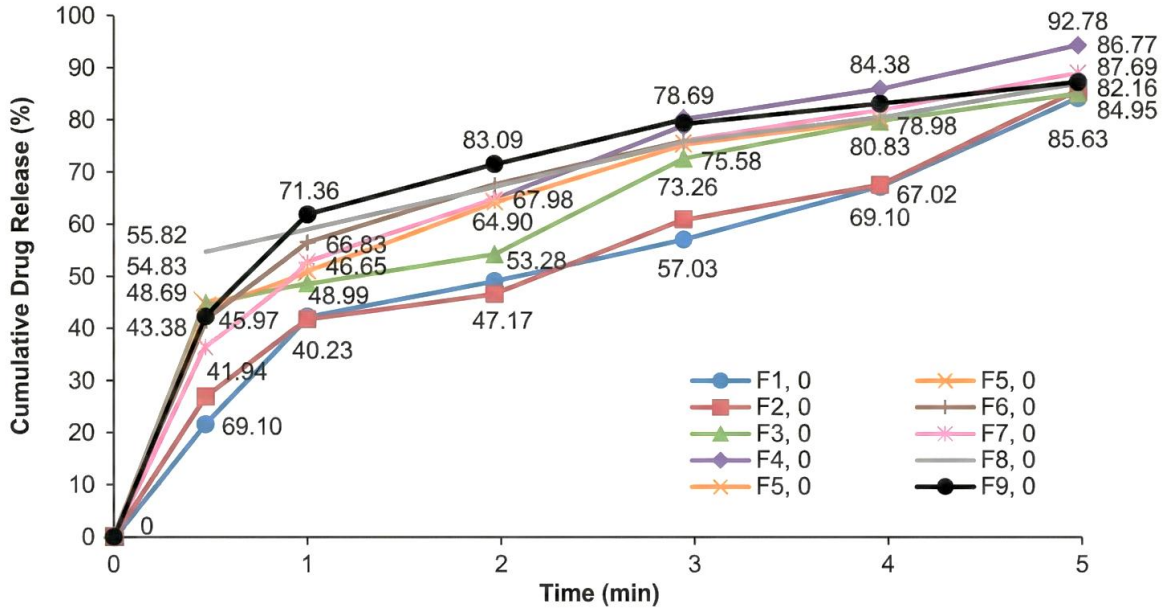

Fig.4- Cumulative Drug Release (%) of Factorial Design Batches

The drug release data demonstrated that formulation F4 exhibited the highest drug release of 92.78±0.75% at 5 minutes, which correlates well with its optimal disintegration time. Batch F4 also showed rapid initial release with 51.40±0.51% drug released within the first minute, indicating immediate disintegration and drug dissolution. The superior performance of F4 can be attributed to the optimal balance of HPMC E15 and PVA concentrations, which provides adequate film integrity while allowing rapid disintegration and drug release.

3.7 Statistical Analysis and Optimization

Multiple regression analysis of the factorial design data was performed to establish polynomial equations relating independent variables to response parameters. For tensile strength, the polynomial equation was: Tensile Strength = 11.33 + 1.28X1 + 1.55X2 + 0.178X1X2 + $0.813X1^2$ - $0.125X2^2$

The analysis revealed that variable X2 (PVA) had the highest magnitude coefficient among all factors, indicating it was the most significant variable affecting tensile strength. The positive coefficients for both X1 (HPMC E15) and X2 (PVA) indicated that increasing either polymer concentration resulted in increased tensile strength. The positive coefficient for the interaction term (X1X2) suggested a synergistic effect between the two polymers on tensile strength.

For disintegration time, increasing polymer concentrations resulted in longer disintegration times, as expected due to greater film thickness and polymer content. Response surface plots and contour plots were generated to visualize the relationship between variables and responses, confirming that intermediate polymer concentrations provided the optimal balance between mechanical properties and disintegration characteristics.

Checkpoint batches were prepared to validate the model predictions. The predicted and observed values showed good agreement (Table 6), confirming the validity of the factorial

design model. Based on comprehensive evaluation of all parameters, formulation F4 containing HPMC E15 (14 mg) and PVA (4 mg) was identified as the optimized formulation, demonstrating optimal disintegration time (14.66±1.52 seconds), adequate tensile strength (10.12±0.48 g/cm²), good folding endurance (265), and excellent drug release (92.78% at 5 minutes).

Table 6: Validation of Factorial Design Model - Checkpoint Batches

Checkpoint	Response	Predicted	Observed
CP1 (HPMC 15.77, PVA 3.03)	DT (sec)	22	21.31
	Tensile strength	9.91	10.62
CP2 (HPMC 16.30, PVA 2.94)	DT (sec)	24	23.65
	Tensile strength	11.19	10.94
CP3 (HPMC 17.95, PVA 4.99)	DT (sec)	35	35.04
	Tensile strength	14.05	13.66

DT: Disintegration time; CP: Checkpoint

4. CONCLUSION

The present study successfully developed and optimized sublingual films of Tadalafil using 3^2 factorial design with solvent casting technique. Preliminary trials established propylene glycol (20% w/w) as the optimal plasticizer and the combination of HPMC E15 and PVA as the optimal polymer system for producing films with desired mechanical and disintegration properties.

The factorial design approach enabled systematic optimization of polymer concentrations. Among the nine factorial batches, formulation F4 containing HPMC E15 (14 mg) and PVA (4 mg) demonstrated optimal characteristics with rapid disintegration (14.66±1.52 seconds), adequate tensile strength (10.12±0.48 g/cm²), excellent folding endurance (265), and rapid drug release (92.78% at 5 minutes). Statistical analysis confirmed the significant effects of both polymers on response variables, with PVA showing the most pronounced effect on tensile strength.

The developed sublingual film formulation of Tadalafil offers potential advantages for the management of erectile dysfunction, including rapid drug release, convenient administration without water, avoidance of first-pass metabolism, and improved patient compliance. The findings suggest that sublingual films represent a promising alternative dosage form for drugs requiring rapid onset of action. Further in-vivo pharmacokinetic studies and clinical investigations would be warranted to establish the bioavailability advantages and therapeutic efficacy of the developed formulation compared to conventional tablets.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Abeer, M. A., Ahmad, H. M., & Peter, A. C. (2006). Effect of pH on sublingual absorption of oxycodone hydrochloride. *AAPS PharmSciTech, 7*(1), E1-E5.

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.

Arora, V., & Gupta, B. (2007). Advances in direct compression technology. *Pharma Times, 74*, 26-27.

Arya, A., Chandra, A., Sharma, V., & Pathak, K. (2010). Fast dissolving films: An innovative drug delivery system and dosage form. *International Journal of ChemTech Research, 2*, 576-583.

Barnhart, S. D., & Sloboda, M. S. (2007). The future of dissolvable films. *Drug Delivery Technology, 7*(8), 34-37.

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.

Bhyan, B., Jangra, S., Kaur, M., & Singh, H. (2011). Orally fast dissolving films: Innovations in formulation and technology. *International Journal of Pharmaceutical Sciences Review and Research, 9*(2), 50-57.

Dandagi, P. M., & Gayakwad, V. M. (2005). Taste masked ofloxacin mouth disintegrating tablets. *Indian Drugs, 17*, 52-54.

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.

DrugBank. (2023). Tadalafil. Retrieved September 13, 2023, from https://go.drugbank.com/drugs/DB00820

Gavaskar, B., Vijayakumar, S., & Sharan, G. (2010). Overview on fast dissolving films. *International Journal of Pharmacy and Pharmaceutical Sciences, 2*(3), 29-33.

Godbole, A. M., D'Mello, P. M., & Bhatia, M. 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.

Gupta, A., Mishra, K., & Gupta, V. (2010). Recent trends of fast dissolving tablet - An overview of formulation technology. *International Journal of Pharmaceutical and Biosciences, 42*, 1-10.

Jha, K., Geethalakshmi, A., Bhatia, V., & Shukla, T. (2011). Orally disintegrating tablets - Technology for mankind. *Journal of Global Pharma Technology, 74*, 11-17.

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.

Noushin, B., Naghmeh, H., Seyed, M., & Bijan, S. (2009). Development and optimization of a sublingual tablet formulation for physostigmine salicylate. *Acta Pharmaceutica, 45*, 301-312.

Prajapati, S. T., Patel, M. V., & Patel, C. N. (2014). Preparation and evaluation of sublingual tablets of zolmitriptan. *International Journal of Pharmaceutical Investigation, 4*(1), 27-31.

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

Sindhu, A., Basavaraj, B. V., Bharath, S., Deveswaran, R., Sharon, F., & Madhavan, V. (2010). Formulation and optimization of sublingual tablets of rabeprazole sodium. *International Journal of Pharmaceutical Sciences and Research, 5*(2), 50-54.

Suresh, V. K., Ranjit, K. P., Basavaraj, S., & 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.

Tayel, S. A., Soliman, I. I., & Louis, D. (2010). Formulation of ketotifen fumarate fast-melt granulation sublingual tablet. *AAPS PharmSciTech, 11*(2), 679-685.

Vineet, B., Vikesh, S., Narendra, G., Salim, M. D., & 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.

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