International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 7, July 2025 ijppr.humanjournals.com ISSN: 2349-7203

Development and Evaluation of Nicotine-Loaded Mouth Dissolving Films: From Extraction to Optimized Formulation

Kalyani Sahare[1], Maruf Shikalgar[2], Manmohan Singh[2], Gayatri Sonawane[2], Vibha Shetiya[2]

1) Assistant Professor, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, India
2) Students of Final Year Bachelor of Pharmacy, Dr. D. Y. Patil College of Pharmacy, Akurdi, Pune 411044, India

Received: 2025-06-25 Revised: 2025-07-10 Accepted: 2025-07-25

ABSTRACT

This research concentrates on the formulation and testing of the nicotine mouth dissolving films as a drug delivery system. It included the steps of nicotine extraction from tobacco leaves via alkaline extraction method by using 15 percent sodium hydroxide followed by organic solvent partitioning with diethyl ether. Nicotine was then transformed into mouth dissolving films using hydroxypropyl methylcellulose (HPMC) grades E-50 and E-05 as film forming polymers with glycerine and polyethylene glycol as plasticizers. The solvent casting method was used for the films preparation and Tween 80, citric acid and aspartame were used as excipients to improve the physicochemical properties and taste of the films. The formulation developed was optimized for the efficient mechanical properties and drug content uniformity as well as rapid drug release. The films were also stored in specified conditions for evaluation of stability and could likely serve as useful option for nicotine replacement therapy.

Keywords: Nicotine-Loaded Mouth Dissolving Films, Extraction to Optimized Formulation

1. INTRODUCTION

Background on Nicotine: Significance and Applications

Nicotine (C10H14N2) is an alkaloid that is mainly obtained from the Solanaceae family of plants, the major source being Nicotiana tobacco. It is a psychoactive compound comprising a pyridine and a pyrrolidine ring which gives it certain uniqueness in terms of its chemical and pharmacological characteristics. Nicotine is a powerful agonist for nicotinic acetylcholine receptors (nAChRs) located throughout the central nervous system as well as in the periphery. This response results in activation of the metabolites dopamine, norepinephrine and serotonin thus contributing to its several physiological activities.

The role of nicotine is much wider than its usual implication with tobacco products. The tobacco product was extensively used for centuries but with emerging pharmaceutical research it has be established that nicotine has several potential therapeutic applications in a number of disease states. Nicotine replacement therapies have been shown to be effective in alleviating abstinence syndrome in patients trying to stop using tobacco posts smoking and helping to decrease the dependence on the drug. In addition, there have been results portraying strong potential in the treatment of neurodegenerative diseases. For example, nicotine has been shown to possess strong potential in the treatment of Parkinson's disease since it has neuroprotective effects in preserving the dopaminergic neurons. The cognitive enhancement of nicotine and its capability to lower β-amyloid buildup have received interest in relation with Alzheimer's disease. Besides, the efficacy of nicotine in ADHD management has also been investigated, and the results appear to be positive where improvement in attention and cognition are concerned.

Rationale for Using Mouth Dissolvable Films

Oral dissolvable films are a novel form of nicotine delivery devices which offer a greater range of benefits in comparison to traditional delivery mechanisms. These films usually consist of hydrophilic polymer which upon interaction with saliva, instantly dissolve and create a solution or suspension of the active pharmaceutical ingredient. The oral cavity which is rich in blood vessels and has good absorption is ideal for the drugs to be administered. Compared to oral administration, intake through the buccal mucosa, which has a surface area of 50.2 cm made, can achieve effective drug absorption without undergoing the first pass metabolism in the liver resulting in potentially higher bioavailability.

Given the following attributes, mouth dissolvable films are ideally suited for delivering nicotine:

1. Rapid Onset of Action: The quick dissolution and direct absorption through the oral mucosa ensure much quicker therapeutic responses as compared to conventional formulations.

2. Precise Dosing: Films as a solid dosage form can be manufactured with exact drug content unlike gums or lozenges which give unpredictable dosing.

3. Enhanced Stability: Being a solid state, films enjoy better stability against chemical degradation compared to liquid formulations.

4. Better Patient Compliance: The dosage form is discreet, can be administered without water, and has pleasant organoleptic properties—all of which improve acceptance and adherence to therapy.

5. Manufacturing Benefits: Manufacturing films in a continuous process gives better opportunities for scaling up and cost-effectiveness in production.

Objectives of the Study

The purpose of this study is to design a procedure to extract nicotine and add it to a mouth-dissolving strip. This study has the following goals:

1. To maximize the efficiency of and improving the pharmacological purity of the nicotine extraction process.

2. To incorporate the extracted nicotine into a more dissolvable film that is stable and can last longer.

3. To assess the physical and chemical properties as well as the strip's stability and how long it takes infusing to dissolve.

4. To determine how long it takes to the strip to get absorbed in the body, maintaining the uniformity of drug content and the release rate of medication.

2. MATERIAL AND METHODS

2.1 Materials Used

All chemicals and excipients used were of pharmaceutical grade. Tobacco leaves (Nicotiana tabacum) were obtained from local cultivators.

Extraction Materials:

- Sodium hydroxide (NaOH, 98% purity)

- Diethyl ether (anhydrous, ≥99.7%)

Film Formulation Materials:

- Hydroxypropyl methylcellulose (HPMC E-50)

- Hydroxypropyl methylcellulose (HPMC E-05)

- Glycerine (99.5% purity)

- Polysorbate 80 (Tween 80)

- Polyethylene glycol (99.5% purity)

- Citric acid (anhydrous)

- Aspartame

- Purified water

- Ethanol

Equipment:

- Whatman filter paper No. 1

- Separating funnel (1000 mL)

- Heating mantle

- Analytical balance

- pH meter

- Hot plate magnetic stirrer

- Digital thermometer

- Film casting equipment

- Digital micrometre

2.2 Extraction of Nicotine

2.2.1 Source Material Preparation

Newly harvested tobacco leaves were cleaned to remove all impurities. The leaves were sun-cured for seven days at room temperature (25 ± 2°C) in a well-ventilated shed, excluding direct sunlight. Coarse powder was obtained by grinding the dried leaves using a mechanical grinder and sieving through a 40-mesh sieve for uniformity in particle size. This powdered material was kept at room temperature in an airtight container until use.

2.2.2 Extraction Process

The nicotine extraction was performed following a modified alkaline extraction method. The procedure was carried out as follows:

1. Alkaline Treatment:

- 100g of powdered tobacco leaves was weighed.

- Powder soaked in 500 mL of 15% w/v sodium hydroxide solution.

- Mixture kept at room temperature (25 ± 2°C) for 4 hours; stirring done occasionally.

- pH monitored and kept above 12 for duration of process.

2. Filtration:

- Whatman No. 1 filter paper was used to filter the alkaline mixture.

- The residue was further washed with 15% NaOH solution to ensure that extraction had been done completely.

3. Liquid-Liquid Extraction

- Filtrate was subjected to liquid-liquid partitioning with diethyl ether.

- Three extractions were performed using 50 mL of diethyl ether for each.

- Extractions were done for 10 minutes with gentle agitation

- The layers were carefully separated in a separating funnel organic.

4. Concentration

- All organic layers got merged

- The merged extract was dried using anhydrous sodium sulfate to eliminate any water droplet

- This solution was filtered to get rid of the drying agent

- The solvent was allowed to evaporate by placing a heating mantle at 35 degrees celcius under reduced pressure

5. Final Product

- Liquid nicotine was obtained and stored in amber-colored bottles

- Storage was kept at 4°C under nitrogen to avoid oxidation[1,2]

2.3 Formulation of Mouth Dissolvable Film

2.3.1 Components of the Film

The mouth dissolvable films were formulated using the following components:

1) Film-Forming Polymers:

- Hydroxypropyl methylcellulose (HPMC E-50; 4-6% w/v)

- Hydroxypropyl methylcellulose (HPMC E-05; 2-3% w/v)

2) Plasticizers and Surfactants:

- Glycerine (99.5% purity; 1-2% w/v)

- Polysorbate 80 (Tween 80; 0.5-1% w/v)

- Polyethylene glycol (99.5% purity; 1-2% w/v)

3) Taste Modifiers and Sweeteners:

- Citric acid (anhydrous; 0.1-0.2% w/v)

- Aspartame (0.2-0.3% w/v)

4) Solvents:

- Purified water

- Ethanol (solvent for active ingredient)

5) Active Ingredient:

- Extracted nicotine (dose as per formulation requirement)

Table 1 Formulation table

COMPONENTS	CONCENTRATION	FUNCTION
Nicotine	0.3 gm	API
HPMC E-05	5 gm	Primary film-forming polymers
HPMC E-50	0.5 gm	Primary film-forming polymers
PEG-400	3.5 ml	Plasticizer
Aspartame	0.1 gm	Sweetening agent
Citric acid	0.1 gm	Saliva stimulant
Tween 80	2 ml	Plasticizer
Glycerine	2 ml	Humectant
Ethanol	70 ml	Solvent
Purified water	30 ml	Solvent
Green food dye	3 drops	Colouring agent
Mint oil	3 drops	Flavouring agent

2.3.3 Method of Film Preparation (Solvent Casting)

Procedure:

1. Preparation of Polymer Solution (Phase A):

- HPMC E-50 and HPMC E-05 were accurately weighed.

- Purified water was heated to 80°C.

- The HPMC polymers were added gradually to hot water under continuous stirring.

- The stirring was continued at 500 rpm until a clear solution was obtained and then allowed to cool to room temperature, 25 ± 2°C.

2. Plasticizer Mixture Preparation (Phase B)

- Glycerine and PEG Glycerine and PEG will be mixed.

- Tween 80 Tween 80 will be added.

- Stir for 15 minutes for proper uniformity In this step, a mixture of all the above components shall be prepared and stirred for 15 minutes to achieve uniformity.

3. Active Ingredient Solution Preparation (Phase C)

- Nicotine Dissolution The required amount of nicotine shall be dissolved in ethanol.

- Aspartame and citric acid Aspartame and citric acid will be added.

- Mix until complete dissolution a mixture shall be made until complete dissolution occurs, the time for this operation is not defined but will depend on visually observing when dissolution is complete.

4. Final Mixing A final mixture shall be done.

- Add Phase B to Phase A while stirring continuously.

- Mix for 10 minutes at 300 rpm.

- Gradually add Phase C into the mixture, continue stirring for 10 minutes at room temperature.

Sonicate the solution for 10 minutes to remove air bubbles that have been entrapped.

5. Film casting

- Wash the glass plate well and wipe it dry.

- Set the thickness to 1 mm using the film applicator.

- Pour the solution onto the glass plate.

- Use the film applicator to draw down the solution at a constant rate.

- Achieve uniform spreading with no air bubbles.

6. Drying:

- Place the cast film in a dust-free drying chamber.

- Maintain temperature at 25 ± 2°C and relative humidity at 45 ± 5%.

- Allow to dry for 24 hours.

7. Post-Drying Operations:

- Peel off the film while taking care not to damage it.

- Cut into desired sizes, e.g. 2 × 3 cm.

- Measure thickness using a digital micrometre.

- Immediately package in a clean glass container.[3–6]

2.4 Evaluation Methods

2.4.1 Organoleptic property evaluation

Prepared films are analysed for its organoleptic properties such as colour, odour, texture, transparency etc.[7,8]

2.4.2 Test for mechanical strength of film

Film Thickness

The thickness of the films was measured using a standard calibrated micrometre screw gauge at different strategic locations and the mean value was calculated. [9,10]

Surface pH

The pH value of a film was determined by putting the prepared film in petri dish and subsequently the film was made wet by using distilled water and the pH was noted by touching the film surface with a pH meter electrode. [11]

Tensile Strength

Tensile strength of 10 films were calculated using a hooked weight apparatus. This test was performed by increasing the micro weights till the film break and the breaking point weight was calculated.[12,13]

Percentage Elongation

The same apparatus that was used to calculate the tensile strength of 10 films was also used to calculate the percentage elongation. (13,14)

% Elongation = (Increase in strip length / Initial strip length)×100

Folding Endurance

This test was conducted manually by folding the films repeatedly using the same plane until they broke. The folding endurance value is the number of times the film can be folded without breaking.(15)

2.4.3 Test for physicochemical property of film

Disintegration test

The 10 films were placed in 10 different petri dishes along with 10ml of water and the time taken for them to disintegrate was notes using a stopwatch.(16,17)

Weight variation test

The average weights are determined by weighing each film, and then, the average weight of the films is subtracted from the individual film weight.(10,18)

Moisture content

The amount of moisture present in the film affects the brittleness and friability of films. The amount of moisture present in the film can be determined by weighing method, a specific size of pre-weighed film is dried to 100–120°C until it attains constant weight and the difference in weight gives the amount of moisture present in the film. Moisture content can be calculated by following formula.(12,14):

% Moisture content = [(Initial weight-Final weight)×100/initial weight]

Drug content uniformity

The assay method described in pharmacopeia is followed. It is determined by measuring the drug absorbance in the individual film using a U.V. Spectrophotometer.(19)

3 RESULTS AND DISCUSSION

3.1 Organoleptic property evaluation

Table 2 Organoleptic property result

Parameter	Observation
Colour	Greenish colour film is produced
Odour	Fresh mint like odour
Taste	Fresh mint like taste
Transparency	Film is transparent in nature
Texture	Clear and smooth

3.2 Test for mechanical strength of film

Table 3 Mechanical strength property result

Parameter	Observation
Film Thickness	0.075 mm
Surface pH	6.8 (slightly acid)
Tensile strength	210 gm
Percentage elongation	12%
Folding endurance	96 folds

3.3 Test for physicochemical property of film

Table 4 Physicochemical property of film result

Film no.	Disintegration test (sec)	Weight of films (gm)	Weight variation (gm)	% Moisture content	Drug content uniformity (absorbance at 263 nm)
1.	14	0.196	0.001	1.5	0.112
2.	14	0.198	0.003	1.5	0.119
3.	16	0.196	0.001	1.5	0.112
4.	15	0.194	0.001	1.6	0.117
5.	14	0.196	0.001	1.5	0.112
6.	15	0.196	0.001	1.6	0.116
7.	14	0.192	0.003	1.6	0.115
8.	16	0.194	0.001	1.5	0.115
9.	16	0.194	0.001	1.5	0.117
10.	14	0.196	0.001	1.5	0.113

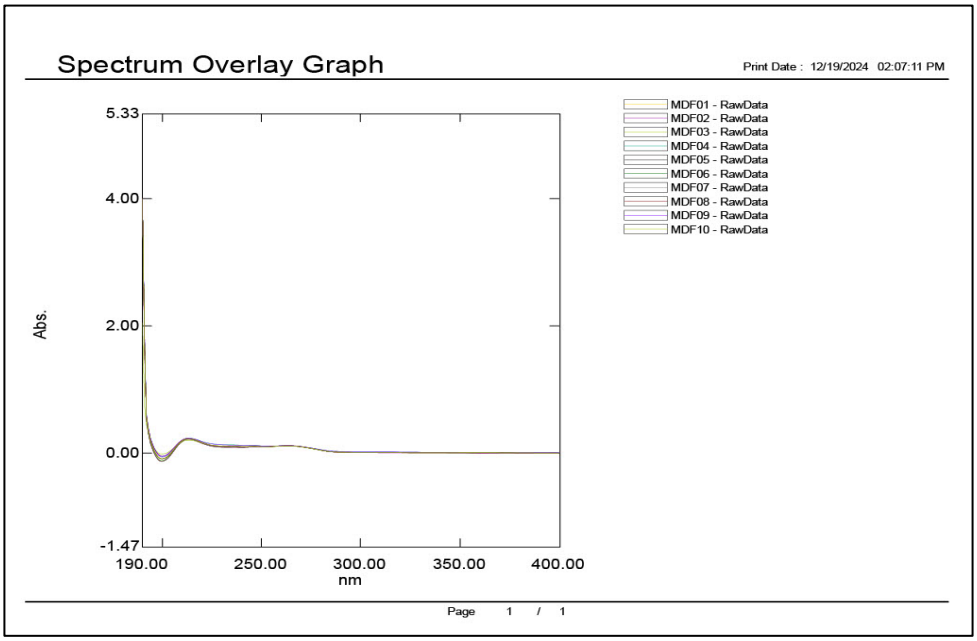

Image 1 Graph of nicotine absorbance

4 CONCLUSION

The current research effectively highlighted the formulation of nicotine-imbued mouth dissolving films as an innovative approach toward nicotine delivery. The alkaline extraction technique was found efficient in recovering nicotine from the tobacco leaf with an appreciable yield and purity. HPMC E-50 and E-05 combinations were found to give optimum film-forming properties. Films

showed favorable physical and mechanical properties due to the addition of plasticizers and other excipients. Solvent casting was illustrated as both reproducible and suited for consistent film production.

The optimized formulation showed several good properties: Drug content distribution is uniform. The thickness and mechanical strength are appropriate. The disintegration time is quick. The taste and mouthfeel are acceptable. Stability under the specified storage conditions is good.

These findings suggest that the nicotine mouth dissolving films developed would offer a convenient and effective alternative to the existing nicotine replacement therapies. Rapid dissolution and the ease of administration could help modify patient compliance positively, thereby improving therapeutic outcomes in smoking cessation programs. Further in vivo studies are therefore recommended to confirm the pharmacokinetic profile and therapeutic efficacy of the formulation. Long-term stability studies and clinical trials will also come in handy to fully validate these films' potentials for commercial applications.

REFERENCE:

1. Qayyum I, Fazal-ur-Rehman M, Ibrahim MS. Extraction of Nicotine (3-(1-methyl-2-pyrrolidinyl) pyridine) from Tobacco Leaves Separated from Gold Live Classic Brand™ Cigarettes by Solvent Extraction Approach and Characterization via IR Analysis. Biosci Biotechnol Res Asia. 2018 Dec 28;15(4):799–804.
2. Extraction and Determination of Nicotine in Tobacco from Selected Local Cigarettes Brands in Iraq. Lett Appl NanoBioScience. 2021 Jun 27;11(1):3278–90.
3. Deokule HA, Pimple SS, Chaudhari PD, Kulkarni AS. Fabrication and Evaluation of Mouth Dissolving Strips of Metoclopramide Hydrochloride by Using Novel Film Former. Res J Pharm Technol. 2021 Oct 31;5515–20.
4. Bala R, Khanna S, Pawar P, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. Int J Pharm Investig. 2013;3(2):67.
5. Kheawfu K, Kaewpinta A, Chanmahasathien W, Rachtanapun P, Jantrawut P. Extraction of Nicotine from Tobacco Leaves and Development of Fast Dissolving Nicotine Extract Film. Membranes. 2021 May 28;11(6):403.
6. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. J Controlled Release. 2011 Jul;153(2):106–16.
7. Anand V, Kataria M, Kukkar V, Saharan V, Choudhury PK. The latest trends in the taste assessment of pharmaceuticals. Drug Discov Today. 2007 Mar;12(5–6):257–65.
8. Ms A, C V. Formulation and Evaluation of Fast Dissolving Oral Films of Diazepam. J Pharmacovigil [Internet]. 2016 [cited 2025 Jan 16];4(3). Available from: http://www.esciencecentral.org/journals/formulation-and-evaluation-of-fast-dissolving-oral-films-of-diazepam-2329-6887-1000210.php?aid=74795
9. Ruchi Sharma, Deepika Joshi, Bhavana Singh, Nidhi Semwal. A review on orodispersible film a novel approach of drug delivery system. World J Biol Pharm Health Sci. 2022 Oct 30;12(1):001–11.
10. Peh KK, Wong CF. Polymeric films as vehicle for buccal delivery: swelling, mechanical, and bioadhesive properties. J Pharm Pharm Sci Publ Can Soc Pharm Sci Soc Can Sci Pharm. 1999;2(2):53–61.
11. Betz G. Power consumption profile analysis and tensile strength measurements during moist agglomeration. Int J Pharm. 2003 Feb 18;252(1–2):11–25.
12. Kathpalia H, Gupte A. An Introduction to Fast Dissolving Oral Thin Film Drug Delivery Systems: A Review. Curr Drug Deliv. 2013 Nov 31;10(6):667–84.
13. Repka MA, Prodduturi S, Stodghill SP. Production and Characterization of Hot-Melt Extruded Films Containing Clotrimazole. Drug Dev Ind Pharm. 2003 Jan;29(7):757–65.
14. R KD, Keerthy HS, Yadav RP. A Review on Fast Dissolving Oral Films. Asian J Pharm Res Dev. 2021 Jun 15;9(3):122–8.
15. Panda BP, Dey NS, Rao MEB. Development of Innovative Orally Fast Disintegrating Film Dosage Forms: A Review. Int J Pharm Sci Nanotechnol. 2012 Aug 31;5(2):1666–74.
16. El-Setouhy DA, El-Malak NSA. Formulation of a Novel Tianeptine Sodium Orodispersible Film. AAPS PharmSciTech. 2010 Sep;11(3):1018–25.
17. Joshi R, Akram W, Chauhan R, Garud N. Thin Films: A Promising Approach for Drug Delivery System. In: Jesús Villarreal-Gómez L, editor. Drug Carriers [Internet]. IntechOpen; 2022 [cited 2025 Jan 16]. Available from: https://www.intechopen.com/chapters/80982
18. Nair AB, Kumria R, Harsha S, Attimarad M, Al-Dhubiab BE, Alhaider IA. In vitro techniques to evaluate buccal films. J Controlled Release. 2013 Feb;166(1):10–21.
19. Satishbabu BK, Srinivasan BP. Preparation and evaluation of buccoadhesive films of atenolol. Indian J Pharm Sci. 2008;70(2):175–9.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 7, July 2025 **ijppr.humanjournals.com** ISSN: 2349-7203

How to cite this article:
Kalyani Sahare et al. Ijppr.Human, 2025; Vol. 31 (7): 217-226.

Conflict of Interest Statement: All authors have nothing else to disclose.