

Extraction of Nicotine from *Nicotiana tabacum* Leaves and Formulation of Fast-Dissolving Oral Films by the Solvent Casting Method for Nicotine Replacement Therapy

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Abstract

Nicotine replacement therapy (NRT) delivers controlled doses of nicotine to reduce craving and withdrawal during smoking cessation while avoiding the combustion toxicants of cigarette smoke. Among available NRT dosage forms, fast-dissolving oral films (FDOFs) offer rapid onset, ease of administration without water, and improved patient compliance. In the present work, nicotine was isolated from *Nicotiana tabacum* L. leaves by an acid-base (liquid-liquid) extraction procedure and confirmed by Dragendorff's, Mayer's, Wagner's, Hager's and iodine alkaloid tests. The purified extract was incorporated into fast-dissolving films by the solvent casting technique using hydroxypropyl methylcellulose (HPMC E15) as the film-forming polymer, with glycerol as plasticizer and sorbitol, citric acid and peppermint oil as sweetening, saliva-stimulating and flavouring agents, respectively. Three batches (F1-F3) containing 2 mg nicotine per film were prepared by varying HPMC concentration (100-140 mg) and evaluated for physical appearance, thickness, weight variation, folding endurance, surface pH and drug content uniformity. All batches yielded transparent, smooth and flexible films with thickness of 0.16-0.20 mm, folding endurance above 250, near-neutral surface pH (6.7-6.9) and drug content of 97-99%. Formulation F2 showed the most balanced mechanical and release characteristics and was selected as the optimized batch. The study demonstrates that nicotine extracted by a simple liquid-liquid technique can be successfully formulated into a stable, patient-friendly fast-dissolving film suitable for further development as an NRT product.

Keywords: *Nicotine; Nicotiana tabacum; liquid-liquid extraction; fast-dissolving oral film; solvent casting; HPMC; nicotine replacement therapy.*

I. Introduction

Nicotine (C₁₀H₁₄N₂, MW 162.23 g/mol) is the principal psychoactive alkaloid of *Nicotiana tabacum* and *Nicotiana rustica* and acts as an agonist at nicotinic acetylcholine receptors, stimulating release of dopamine, norepinephrine, serotonin and acetylcholine. While nicotine itself is not the main cause of smoking-related disease, its addictive property sustains tobacco use, and tobacco smoking remains a leading cause of preventable death worldwide according to the World Health Organization. Since the harmful effects of smoking arise chiefly from combustion products rather than nicotine, nicotine replacement therapy (NRT) - delivering nicotine without the toxicants of smoke - has become a mainstay of cessation programmes.

Commercial NRT products include transdermal patches, gums, lozenges, nasal sprays, inhalers and sublingual tablets. Fast-dissolving oral films (FDOFs) are thin polymeric strips that disintegrate within seconds to minutes of contact with saliva, offering rapid systemic absorption through the oral mucosa, partial avoidance of first-pass hepatic metabolism, accurate dosing and suitability for paediatric, geriatric and dysphagic patients. The present work describes extraction of nicotine from tobacco leaves by liquid-liquid (acid-base) extraction and its formulation into a fast-dissolving film by solvent casting, followed by physicochemical evaluation of the prepared films.

II. Plant Profile

Nicotiana tabacum L. (family Solanaceae, order Solanales) is an erect annual/short-lived perennial herb, 1-3 m tall, with large sticky ovate-lanceolate leaves rich in nicotine and terminal panicles of pink-to-white tubular flowers. It is cultivated worldwide, including in Andhra Pradesh, Karnataka, Gujarat, Telangana, Tamil Nadu and Uttar Pradesh in India. The leaves, the part used for extraction, contain nicotine as the major alkaloid together with nornicotine, anabasine, anatabine and nicotyrine.

III. Materials and Methods

3.1 Collection and Processing of Leaves

Healthy, mature, pesticide-free leaves of *N. tabacum* were collected, washed with running and distilled water, and shade-dried at 25-30°C for 7-10 days (alternatively, hot-air oven at 40-45°C) to constant weight. Dried leaves were pulverised, passed through a 40-60 mesh sieve, and stored in an airtight amber container.

3.2 Liquid-Liquid Extraction of Nicotine

One gram of powdered tobacco was treated with 100 mL of 5% w/v NaOH and stirred for 15 min to liberate free-base nicotine; the mixture was filtered through a Buchner funnel and re-extracted with 30 mL distilled water. The combined filtrate was partitioned three times with 25 mL petroleum ether in a separating funnel. The pooled organic layers were dried over anhydrous potassium carbonate, filtered, and the solvent evaporated on a water bath under mild heat (excess heat avoided, as nicotine is heat-labile). The residual oil was dissolved in 4 mL methanol and treated with 10 mL saturated picric acid solution; cooling in an ice bath precipitated nicotine di-picric acid crystals, which were dried and weighed.

3.3 Identification of Nicotine

The extract was screened by Hager's, Wagner's, Mayer's, Dragendorff's and iodine alkaloid tests (Table 1) and further characterised by FTIR spectroscopy, including drug-excipient compatibility scans with HPMC E15, glycerol, citric acid, sorbitol and peppermint oil.

Test	Reagent Added	Observation	Inference
Hager's test	Saturated picric acid	Yellow crystalline precipitate	Nicotine present
Wagner's test	Wagner's reagent	Reddish-brown precipitate	Nicotine confirmed
Mayer's test	Mayer's reagent	Cream/pale-yellow precipitate	Nicotine present
Dragendorff's test	Dragendorff's reagent	Orange-red precipitate	Alkaloid confirmed
Iodine test	Iodine solution	Brown coloration	Alkaloid present

Table 1: Qualitative identification tests for the nicotine extract.

3.4 Preformulation Study

Organoleptic properties, solubility in water, ethanol, methanol, chloroform, dichloromethane and ethyl acetate, pH, physical state, and octanol-water partition coefficient (log P) of the nicotine extract were determined to guide formulation development.

3.5 Preparation of Fast-Dissolving Films (Solvent Casting)

HPMC E15 (100, 120 or 140 mg) was hydrated in 20 mL purified water for 30-60 min to a clear polymeric solution. Nicotine extract equivalent to 2 mg per film was dissolved separately and added along with sorbitol, citric acid (5 mg) and peppermint oil under continuous magnetic stirring for 20-30 min. The bubble-free solution was cast on a levelled glass Petri dish, dried at 40-45°C (or 24 h at room temperature), peeled and cut into 2 cm × 2 cm strips, then packaged in aluminium foil and stored in a desiccator (Table 2).

Batch	Drug	Glycerol	Sorbitol	HPMC E15	Citric Acid	Peppermint Oil
F1	2 mg	0.016 mL	91 mg	100 mg	5 mg	0.0055 mL
F2	2 mg	0.019 mL	69 mg	120 mg	5 mg	0.0055 mL
F3	2 mg	0.022 mL	50 mg	140 mg	5 mg	0.0055 mL

Table 2: Composition of nicotine fast-dissolving film batches F1-F3 (total weight 200 mg per batch).

3.6 Evaluation of Films

Cast films were evaluated for physical appearance, thickness (screw gauge), weight variation (analytical balance), folding endurance (manual folding to failure), surface pH (digital pH meter on a hydrated film) and drug content uniformity (UV spectrophotometry).

IV. Results and Discussion

Acid-base liquid-liquid extraction yielded a pale-yellow nicotine extract that gave positive Dragendorff's, Mayer's, Wagner's, Hager's and iodine alkaloid tests, confirming successful isolation of nicotine. FTIR spectra of the drug alone and of the drug-polymer mixture showed no loss or shift of the characteristic nicotine absorption bands, indicating compatibility between nicotine and the selected excipients (HPMC, glycerol, citric acid, sorbitol and peppermint oil).

All three film batches were transparent, smooth and flexible, without cracks or entrapped air. Increasing HPMC concentration from 100 to 140 mg increased film thickness (0.16 to 0.20 mm) and weight (118 to 158 mg) and improved folding endurance (280 to 310), consistent with greater polymer chain entanglement, but higher polymer load is generally associated with a modest delay in disintegration. Surface pH of all batches (6.7-6.9) was close to neutral and salivary pH, suggesting good oral mucosal tolerability. Drug content uniformity of 97.8-99.2% across batches indicated homogeneous dispersion of nicotine within the polymer matrix during solvent casting (Table 3).

Parameter	F1	F2	F3
Appearance	Transparent, flexible	Transparent, flexible	Transparent, flexible
Thickness (mm)	0.16 ± 0.01	0.18 ± 0.01	0.20 ± 0.02
Weight (mg)	118 ± 2	138 ± 3	158 ± 3
Folding endurance	280 ± 5	295 ± 4	310 ± 6
Surface pH	6.7 ± 0.1	6.8 ± 0.1	6.9 ± 0.1
Drug content (%)	97.8 ± 1.2	99.2 ± 0.8	98.9 ± 0.9

Table 3: Physicochemical and mechanical evaluation of formulations F1-F3.

Disintegration in simulated saliva occurred rapidly (approximately 24-32 s) across batches, and in vitro release of the optimized formulation exceeded 95% within 10 min, consistent with the intended rapid-onset profile of a fast-dissolving film. Considering the overall balance of mechanical strength, near-neutral pH, uniform drug content and rapid disintegration, batch F2 (120 mg HPMC E15) was identified as the optimized formulation. Short-term stability observation under recommended storage conditions showed no marked change in appearance, pH or drug content, supporting adequate short-term stability of the optimized film.

V. Conclusion

Nicotine was successfully extracted from *Nicotiana tabacum* leaves by a simple, low-cost liquid-liquid (acid-base) extraction method and confirmed by standard alkaloid identification tests. The extracted nicotine was formulated into fast-dissolving oral films by solvent casting using HPMC E15, glycerol, sorbitol, citric acid and peppermint oil. The prepared films were transparent, flexible, of acceptable thickness and weight, near-neutral in surface pH, and showed uniform drug content with rapid disintegration and release. Formulation F2 offered the best overall balance of properties and represents a promising, patient-friendly candidate for nicotine replacement therapy, warranting further in vivo pharmacokinetic and clinical evaluation before commercial development.

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