e-ISSN: 2320-4230, p-ISSN: 2961-6085

Journal of Drug Discovery and Therapeutics

Available Online at www.jddt.in

CODEN: - JDDTBP (Source: - American Chemical Society)

Volume 14, Issue 3; 2026, 31-38

Pharmaceutical Development and Analytical Method Validation of a Nicotine Polacrilex-Containing Pouch Formulation

Aakriti Raj[1], Mayank Bansal[2], Ashutosh Sharma[3], Yogesh Kumar Garg[4]

[1]Research Scholar, Jaipur College of Pharmacy, Jaipur
[2]Principal & Professor, Jaipur College of Pharmacy, Jaipur
[3]Associate Professor, Jaipur College of Pharmacy, Jaipur
[4]Professor, Jaipur College of Pharmacy, Jaipur

Received: 20-03-2026/ Revised: 07-04-2026/ Accepted: 27-04-2026
Corresponding author: Aakriti Raj
Conflict of interest: No conflict of interest.

Abstract:

Nicotine Polacrilex is a most commonly used active pharmaceutical ingredient in the treatment of tobacco dependence as a nicotine replacement therapy (NRT) in adult patients. This paper demonstrates the pharmaceutical development and analytical method validation of a novel nicotine polacrilex-containing pouch formulation through buccal nicotine delivery. This formulation was designed to deliver 2 mg of nicotine per pouch through controlled buccal absorption, providing a smokeless, tar-free alternative to cigarettes.

Keywords: Nicotine polacrilex, nicotine replacement therapy, pouch formulation, buccal drug delivery, HPLC method validation, ICH Q2, smoking cessation, tobacco dependence.

Introduction

Background and Rationale

Tobacco use is one of the leading causes of morbidity and mortality worldwide. studies has established that tobacco smoke exposure actively of passively can causes death, illness, and disability affecting multiple organ systems including the lungs, oral cavity, larynx, oesophagus, stomach, pancreas, liver, kidney, urinary bladder, uterine cervix, and bone marrow.

Smoking is the leading cause for approximately 90% of lung cancer deaths in men and 80% in women and it is directly linked to cardiovascular disease, chronic obstructive pulmonary disease (COPD), and adverse reproductive outcomes. Cigarette smoking has long been one of the leading causes of premature death and disease in many industrialized countries worldwide, with the United States alone recording more than 400,000 deaths annually [1]Nicotine acts on nicotinic acetylcholine receptors in the brain, stimulating dopaminergic pathways in the nucleus accumbens and frontal cortex. This dopamine release enhancing craving for tobacco use and allow the person to develop dependence. Monoamine oxidase enzymes (MAO-A and MAO-B), which break down dopamine, are also tempered by nicotine, contributing to the neurochemical cycle of addiction. [2]

Nicotine Replacement Therapy (NRT)

Nicotine replacement therapy (NRT) is a well-established, evidence-based first-line

pharmacological intervention for tobacco cessation. It is functioned by delivering controlled, sub-therapeutic doses of nicotine which alleviate withdrawal symptoms of nicotine and reduce cravings without exposing the user to the harmful combustion byproducts of cigarettes such as tar and carbon monoxide. Various forms of NRT are commercially available in India and internationally:

By providing you with a modest, regulated dose of nicotine, NRT lessens withdrawal symptoms without exposing you to any of the other harmful compounds included in cigarettes. This tiny quantity of nicotine lessens your desire to smoke and helps you meet your nicotine appetite.

Different kinds of NRT are employed for different purposes. Which forms you like is up to you. For some person, certain NRT products are more effective than others. Certain NRT products may be preferred by some individuals over others [3]

Different forms of NRT available in India
Gum: Chewing gum was the first type of NRT which was widely accessible by enabling the direct absorption of nicotine by buccal mucosa, these chewing gums result in plasma concentrations that are about half of those caused by cigarette smoking. These gums are present in market in different strengths that can be taken as needed or after pre-determined intervals. [4]

Lozenge

Lozenges, has shown commendable results in boosting tobacco cessation rates while minimizing withdrawal symptoms in cigarette smokers. The peak plasma concentrations that are produced by lozenge is 8%–10% greater than those of the gum. [5]

Patches

Patches are applied topically, at a comparatively constant pace nicotine is delivered through the skin. Because patches come in a several of dosages, Chian smokers or the smokers who are severely addicted can use the strongest patches, and those who are less dependent can use a lower dosage. Because of the presence of different dosages, consumers can gradually cut back on nicotine consumption over a few days or more, allowing consumers' body to progressively adjust to lesser nicotine levels and eventually to reach a nicotine-free state. [6]

Formulation to be developed: Nicotine pouches

Pouch is a specific kind of dosage form used in nicotine replacement therapy. They give nicotine to the body by momentarily lowering cravings and the symptoms of nicotine withdrawal after stopping smoking.

However, Pouch provide a more consistent and lower dose of nicotine to blood than cigarettes do. Pouch helps in managing, control, and progressively lessen body's desire for nicotine when taken as prescribed

Nicotine Polacrilex

This primarily works on nicotinic acetylcholine receptors in the brain. By activating presynaptic acetylcholine receptors it increases Acetylcholine release and metabolism. Dopamine levels in the nucleus accumbens rises which is result of its stimulation of the dopaminergic system [7]

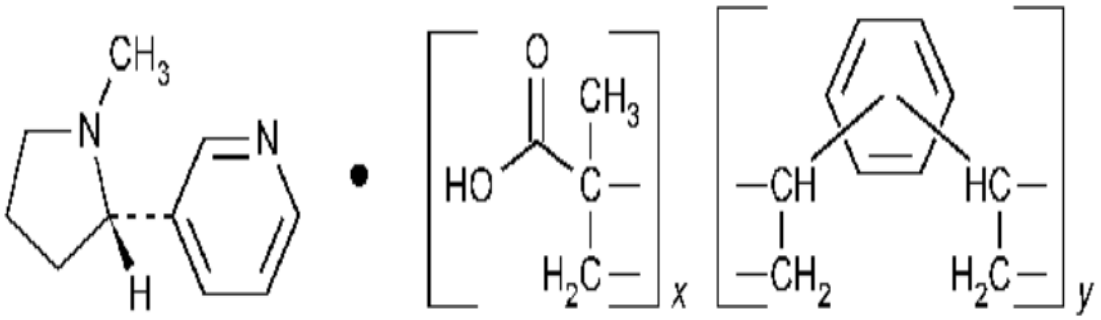

Figure 1:

Molecular Formula:

[(C4H6O2)x(C10H10)y](C10H14N2)

Synonyms: Nicorette

3(1-methyl-2-pyrrolidinyl) pyridine

1-methyl-2-(3-pyridyl) pyrrolidine

β-pyridyl-α-N-methyl-pyrrolidine

Mol. Weight: 162.23 g/mol

T ½ : 2 hours.

Methodology

Literature Search Strategy

The literature search was conducted using electronic databases including PubMed, ScienceDirect, Scopus, Web of Science, and Google Scholar

Inclusion and Exclusion Criteria

Include:

peer-reviewed articles, regulatory guidelines (FDA, EMA, ICH), pharmacopeial monographs, and articles related to nicotine replacement formulations and method validation.

Exclude: non-scientific reports, conference abstracts without data, non-peer-reviewed articles.

Insights of Formulation

Formulation strategies for nicotine polacrilex Pouch Formulation:

Pre formulation:

- Choice of Excipient
- Drug- Excipient compatibility

Formulation Development:

The batch formula is divided into the following steps:

- Weighing of drug
- Mixing of excipient and API.
- Addition of flavors
- Packaging

Pre validation parameters

- Instrumentation
- Chemicals and Reagents
- Preparation of Standard Solution
- Preparation of Sample Solution

Validation parameters

Validation parameters (as per ICH Q2 guidelines)

- System suitability
- Specificity
- Linearity
- Precision
- Accuracy
- Robustness
- Stability of analytical solution

Results

Drug-Excipient Compatibility Study

All Drug-Excipient combinations of Nicotine Polacrilex with the selected excipients shows an off-white powder appearance under all storage conditions i.e. 40°C/75% RH open and closed; 30°C/75% RH open and closed after one month. The Drug and excipients shows full physicochemical compatibility, confirming suitability for use in the final formulation.

Table 1: Trial Batch Composition

Ingredient	DB-F1 (mg/pouch)	DB-F2 (mg/pouch)	DB-F3 (mg/pouch)
Nicotine Polacrilex	10.00	10.000	10.000
Microcrystalline Cellulose	50.000	60.000	65.100
Peppermint SD Powder Flavour	18.400	18.400	18.400
Mannitol	49.000	39.900	52.900
Pregelatinized Starch	23.000	32.100	23.000
Mint SD Powder Flavour	12.000	12.000	12.000
Sodium Carbonate	10.600	10.600	10.600
Erythritol	50.800	40.800	31.800
Sodium Bicarbonate	8.600	8.600	8.600
Acesulfame-K	9.800	9.800	9.800
Propylene Glycol	7.800	7.800	7.800
Total Weight	250.000mg	250.000 mg	250.000 mg

Table 2: Physicochemical Evaluation of Trial Batches

Parameter	DB-F1	DB-F2	DB--F3
Description	Pouches filled with off-white color powder	Pouches filled with off-white color powder	Pouches filled with off-white color powder
Average Weight (250 mg ± 7.5%)	250.20 mg	254.09 mg	248.45 mg
Assay (Spec: 95–115%)	100.5%	89.2%	98.1%

DB-F1 demonstrated optimal performance across all parameters and was selected as the finalized formulation. The final formulation composition is based on DB-F1.

Table 3: In-Process Checks

Parameter	Specification
Description	Off-white color powder
pH	7.80
Bulk Density	0.8 g/cm3
Tap Density	0.7g/cm3
Blend Uniformity	BU: 100.01% RSD: 1.0%
Assay	100.5%

Method Validation Results

Table 4: System Suitability

Injection	Peak Response of Nicotine	Tailing factor
1.	1516716	1.05
2.	1515939	0.99
3.	1517804	1.03
4.	1515498	1.05
5.	1520567	1.04
Average	1517305	1.03
SD	1809.30	-
% RSD	0.12	-

The %RSD of 0.12 which is within the acceptance limit of NMT2.0%, confirming adequate system performance.

Table 5: Specificity

Name of solution	Peak Response of Nicotine	Retention time (Min)
Blank	Nil	Nil
Placebo	Nil	NIL
Standard	1660415	8.01
Test	1660381	8.04

At the nicotine retention period, no interference was seen from blank solution, placebo, or standard and test solution.

Table 5: Repeatability (Method Precision)

Preparation	Avg. Peak Response	% Assay
Set-1	1,432,838	101.62
Set-2	1,431,807	101.57
Set-3	1,433,442	101.87
Set-4	1,432,587	101.84
Set-5	1,434,515	101.83
Set-6	1,434,338	101.90
Average	—	101.77
Standard Deviation	—	0.14
% RSD	—	0.13

Table 6: Intermediate Precision (Ruggedness)

Preparation	Avg. Peak Response	% Assay
Set-1	1,371,583	100.01
Set-2	1,374,009	100.22
Set-3	1,374,873	100.28
Set-4	1,372,470	100.12
Set-5	1,376,445	100.46
Set-6	1,375,173	100.24
Average	—	100.22

Standard Deviation	—	0.16
% RSD	—	0.16

Cumulative %RSD of method precision and intermediate precision all 12 results combined is 0.77% which is well within the acceptance limit of ≤2.0%.

Table 7: Linearity

Linearity Level	Concentration (ppm)	Avg. Peak Response	R^2
50%	40.14	719,514	0.9999
80%	64.22	1,170,011	
100%	80.28	1,474,993	
120%	96.33	1,761,527	
150%	120.42	2,210,421	

Over the 50–150% concentration range, the correlation value R2 = 0.9999 demonstrates a strong linear connection between concentration and peak area response.

Table 8: Accuracy

Level	Preparation	Area	% Recovery	Avg. Recovery	% RSD
50%	Accuracy Level-1	713,767	96.86	96.79	0.08
50%	Accuracy Level-2	714,188	96.81		
50%	Accuracy Level-3	716,112	96.70		
100%	Accuracy Level-1	1,438,293	97.34	97.19	0.26
100%	Accuracy Level-2	1,435,676	97.34		
100%	Accuracy Level-3	1,434,667	96.91		
150%	Accuracy Level-1	2,188,869	98.97	98.90	0.09
150%	Accuracy Level-2	2,188,472	98.94		
150%	Accuracy Level-3	2,187,893	98.80		

Stability of Analytical Solutions: Solution stability data demonstrated %RSD values for peak responses at all time intervals below 2.0% for both reference and test solutions, confirming adequate stability throughout the analytical run.

Table 9: Robustness

Condition	Results (% Assay)	Cumulative %RSD
Method Precision (baseline)	101.77	—
Column Temp: 23°C	102.85	0.42
Column Temp: 27°C	102.93	0.45
Buffer pH: 9.8	102.75	0.38
Buffer pH: 10.2	102.61	0.33

All %RSD values remain below 0.5% under modified conditions, confirming the method's robustness to minor variations in chromatographic parameters.

Discussion: A nicotine polacrilex pouch formulation with acceptable physicochemical and organoleptic qualities was successfully produced and assessed in

this study. Uniform nicotine distribution (blend uniformity between 90–110%, %RSD < 5.0%) was guaranteed by the improved production process, which included premixing, sieving, sandwich blending, and controlled pouch filling. For the assay detection of nicotine in pouch formulations, a reliable, accurate, linear, specific, and stable HPLC analytical technique was created and verified. The method's appropriateness for regular pharmaceutical quality control was confirmed by its outstanding linearity (R^2 = 0.9999), repeatability (%RSD = 0.13), and moderate precision (%RSD = 0.16).All of the findings point to nicotine polacrilex pouches' potential as a stable, evidence-based substitute nicotine delivery method for smoking cessation, with reliable product quality guaranteed by validated analytical method.

The results collectively support the potential of nicotine polacrilex pouches as a viable, evidence-based alternative nicotine delivery system for smoking cessation therapy, with consistent product quality ensured through validated analytical method. These findings provide a scientific foundation for further scale-up, clinical investigation, and regulatory submission of the developed formulation in the Indian pharmaceutical market.

Summary and conclusion

The developed formulation process and analytical method shoes satisfactory performance. All the performed validation parameters including specificity, precision, accuracy, linearity, robustness, and solution stability met the acceptance criteria. Additionally, no deviationns were observed during the study, indicating that the experimental procedures were carried out as planned by chemist. Based on the obtained result, the developed HPLC method is suitable for routine quality control analysis of nicotine in nicotine pouch formulations. Furthermore, the optimized formulation and development process ensure a consistent product quality and uniform nicotine distribution that makes the developed nicotine pouch formulation suitable for further development and potential commercial production.

Reference

1. Saurabh Ravi, Sharma P. K., Bansal M. Transdermal Drug Delivery of Nicotine", International Journal of Drug Development & Research, Vol. 3(2), 01-08, 2011.
2. Fowler, J. S., et al. (2003). Inhibition of monoamine oxidase B in the brains of smokers. Nature, 379, 733–736
3. Nemeth-Coslett R, 1989 Physiologic effects of nicotine polacrilex. Biomed Pharmacother. 1989;43(1):5-10.
4. Helena Digard, Nathan Gale, Graham Errington, Nicola Peters & Kevin mcadam : Multi-analyte approach for determining the extraction of tobacco constituents from pouched snus by consumers during use, 2013
5. Mendelsohn C. 2013 Optimising nicotine replacement therapy in clinical practice. Aust Fam Physician. 2013 May;42(5): 305-9.
6. The MPOWER packge, warning about the dangers of tobacco. Geneva: WHO; 2011. WHO Report on The Global Tobacco Epidemic, 2011
7. Jain, N. ., Sharma, A. ., Srivastava, A. K. ., & Bansal, M. (2025). Evaluation of Antifungal Potential of Syzygium cumini Ethosomal Gel. Journal of Biomedical and Pharmaceutical Research, 14(3), 32–37.https://doi.org/10.32553/jbpr.v14i3.1318
8. Deeksha Singh, Shambhavi Dwivedi, Nivedita Singh, Prabodh Kumar Trivedi, HY5 and COP1 function antagonistically in the regulation of nicotine biosynthesis

in Nicotiana tabacum, Plant Physiology and Biochemistry, Volume 214, 2024, 108916, ISSN 0981-9428, https://doi.org/10.1016/j.plaphy.2024.108916.

9. Miditana, S.R., Korlam, S., Babu, A.R., Rao, V.P. and Kumari, M.A. (2025). Adverse Effects and Therapeutic Potential of Nicotine: A Review. Advances in Pharmacology and Pharmacy, 13(3), pp.448–457. doi:https://doi.org/10.13189/app.2025.130315.
10. Chatterjee A, Pandey A, Sharma A, Bansal M, Gupta RK. Preparation and Characterization of Sustained Release Risperidone Loaded Eudragit Microparticles by Spray-Drying Technique. International Journal of Drug Delivery Technology. 2024;14(2):978-983.DOI: 10.25258/ijddt.14.2.57
11. S., Bansal, M. and Kaushik, D. 2020. Optimization & Validation of Bilayer Tablet Fabricated By Antihypertensive Drugs. International Journal of Medical and Biomedical Studies. 4, 7 (Jul. 2020). DOI:https://doi.org/10.32553/ijmbs.v4i7.1262.
12. Nagpal P, Kaushik K, Bansal M, Analytical Estimation and Validation of Ciprofloxacin HCl by using new strategies" Journal of Emerging Technologies and Innovative Research, Vol. 11 (12), b513-b536, 2024
13. Adams, T. and Morris, J. (2023). Nicotine Addiction and Smoking: Health Effects and Interventions. Available at: https://www.ncbi.nlm.nih.gov/books/NBK537066/
14. Kalkhoran, S., & Glantz, S.A. (2016). E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. The Lancet Respiratory Medicine, 4, 116–128. https://doi.org/10.1016/S2213-2600(15)00521-4