ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

Formulation and Evaluation of Nortriptyline Mucoadhesive Buccal Film Using Xanthan Gum for Smoking Cessation Therapy

S. Radhakrishnan[1*]; R. Sambathkumar[2]; C. Kannan[2]; R. K. Hariprasath[3]; S. Govindaraj[3]; R. Hari Vigneshwaran[3]; C. Santhosh[3]; R. Vishnu[3]

[1,2,3]The Erode College of Pharmacy, Veppampalayam, Erode – 638112, Tamil Nadu, India

Corresponding Author: S. Radhakrishnan[1*]

Publication Date: 2026/06/30

Abstract: Cigarette smoking continues to rank among the leading avoidable causes of mortality across the globe, responsible for millions of deaths every year. The persistence of nicotine dependence is driven mainly by two neurochemical pathways: activation of nicotinic acetylcholine receptors and glutamate-mediated signalling. Because nortriptyline, a tricyclic antidepressant, acts on several of the neurotransmitter systems tied to addiction, it has drawn interest as a smoking-cessation aid. A drawback of the conventional oral route, however, is that the drug is heavily metabolised on first pass through the liver, which sharply curtails how much reaches the circulation. This investigation therefore focused on preparing and assessing nortriptyline-loaded mucoadhesive buccal films. Two polysaccharides, xanthan gum and sodium alginate, served as the film-forming and mucoadhesive components, helping the film cling to the mucosa and regulating the rate at which the drug was liberated. The films were cast by solvent evaporation and then examined for appearance, thickness, weight consistency, folding endurance, surface pH, disintegration time, drug loading and release behaviour. Formulation variables were narrowed down with a design-of-experiments (DoE) scheme. Every batch proved uniform and mechanically sound, and the lead formulation maintained release for as long as 7 h. Of the five, batch F3 performed best, liberating close to 97% of its drug load while adhering most strongly to the mucosal surface.

Keywords: *Buccal Film; Nortriptyline; Mucoadhesion; Xanthan Gum; Smoking Cessation; Drug Delivery.*

How to Cite: S. Radhakrishnan; R. Sambathkumar; C. Kannan; R. K. Hariprasath; S. Govindaraj; R. Hari Vigneshwaran; C. Santhosh; R. Vishnu (2026) Formulation and Evaluation of Nortriptyline Mucoadhesive Buccal Film Using Xanthan Gum for Smoking Cessation Therapy. *International Journal of Innovative Science and Research Technology*, 11(6), 1766-1776. https://doi.org/10.38124/ijisrt/26jun964

I. INTRODUCTION

Delivering drugs through the lining of the cheek has become an appealing option for treatment aimed at both local and whole-body effects. The buccal mucosa carries a dense network of blood vessels, so molecules absorbed there can reach the bloodstream quickly and, in doing so, sidestep the metabolism that the liver would otherwise impose on a first pass.[1,2] A further practical benefit is that devices made for this site can be put in place and taken out with ease, and this simplicity tends to encourage adherence — a point that matters greatly for people who struggle to swallow tablets or capsules.[1,5]

Of the buccal dosage forms in use, mucoadhesive films have become a particular focus of attention. These slim polymeric sheets stick to the damp inner surface of the cheek and, compared with ordinary oral preparations, can raise bioavailability, hasten the onset of effect and stretch drug release out over time in a controlled fashion.[2,3] Being pliable and comfortable, they sit well within the mouth yet still allow the drug to pass efficiently across the mucosa.[4,16]

Smoking ranks among the most preventable contributors to illness and early death across the world, and is linked to millions of fatalities annually.[23] The nicotine taken in from tobacco acts on nicotinic acetylcholine receptors in the brain and switches on the dopamine-driven reward pathway, and it is this chain of neurochemical events that underpins dependence.[22] For a great many smokers, the odds of staying off cigarettes for good rise considerably when pharmacological support is provided.[25,26] Nortriptyline, a tricyclic antidepressant indicated for depression and neuropathic pain, has also been employed off-label to assist quitting; its principal action is to block the reuptake of norepinephrine and serotonin within the central nervous system, thereby tempering cravings and withdrawal.[25] Pooled analyses of placebo-controlled trials suggest that the drug

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

roughly doubles the chances of long-term abstinence, placing it on a par with bupropion and nicotine replacement therapy.[24]

The chief shortcoming of nortriptyline taken orally is the heavy first-pass metabolism it undergoes in the liver, which leaves only a small fraction systemically available. Administering it across the buccal mucosa offers a route to direct systemic uptake that can sidestep this obstacle, with potential gains in both efficacy and acceptability to the patient.[2,13]

Naturally derived polysaccharides have become favoured excipients in systems of this kind. Xanthan gum — a high-molecular-weight anionic polysaccharide obtained by fermenting *Xanthomonas campestris* — is prized for being biocompatible, biodegradable and notably mucoadhesive.[19,20] Once hydrated it sets into viscous gels that can draw out drug release, and it has served effectively as a mucoadhesive matrix in both buccal and gastroretentive systems.[20,21] Sodium alginate is, in much the same way, a biocompatible polysaccharide that forms films, binds to mucin and has found broad use in oromucosal film products.[6,18]

With this background, the present work set out to prepare and assess nortriptyline mucoadhesive buccal films built on xanthan gum and sodium alginate, and to profile their physicochemical attributes alongside their in vitro release performance.

II. MATERIALS AND METHODS

➢ *Materials*

Nortriptyline was received as a gift sample from Linux Pharma. Sodium alginate, xanthan gum, glycerine and citric acid were procured from Yarrow Chemicals. All reagents used were of analytical grade.

➢ *Drug–Excipient Compatibility Studies*

Possible interactions between nortriptyline and the chosen excipients were assessed by Fourier-transform infrared (FT-IR) spectroscopy using a Shimadzu infrared spectrophotometer. Each sample was blended with potassium bromide in an approximate 1:10 ratio and compressed into pellets on a KBr press, and spectra were acquired over the range 4000–400 cm^{-1}. No appreciable shift in the position or intensity of the characteristic peaks was observed, indicating that the drug remained compatible with the excipients (Figure 1).[7]

➢ *Optimisation by Design of Experiments (DoE)*

Design of experiments (DoE) is a structured statistical framework used to examine how formulation variables affect the responses of a pharmaceutical process. By varying controllable input factors in a systematic manner and recording the resulting outputs, the approach reveals cause-and-effect relationships and reduces the number of experimental runs needed for optimisation.[27,29] In this study, three independent variables were selected: sodium alginate concentration (factor A), xanthan gum concentration (factor B) and glycerine concentration (factor C). These were chosen because they strongly influence film formation, flexibility and mucoadhesion. Sodium alginate and xanthan gum function as film-forming and mucoadhesive polymers, whereas glycerine acts as a plasticiser that improves the flexibility and mechanical strength of the film. Two responses were monitored: dissolution (%), reflecting the extent of drug release and hence therapeutic effectiveness, and mucoadhesion strength (N), reflecting the capacity of the film to adhere to the mucosa and maintain prolonged contact. Systematic variation of the factors across the design runs enabled the optimal formulation conditions to be identified.[8,28]

➢ *Preparation of the Mucoadhesive Buccal Films*

The films were prepared by the solvent casting (solvent evaporation) method, which is widely used for polymer-film production owing to its simplicity and low cost.[14,15] A suitable solvent for the polymer and the active substance was first selected, and the polymer solution was prepared with attention to mixing viscosity and temperature. Air bubbles entrapped during mixing were removed before casting to ensure a homogeneous product. Once a uniform polymer mass had been obtained, the drug and additives were incorporated to achieve even distribution throughout the film; the rheological properties at this stage represent an important control parameter affecting drying, thickness and morphology. A thin layer of the mixture was then poured onto a prepared casting surface and dried with hot air under controlled temperature, time and humidity. After drying, the film was cut into portions of appropriate weight and drug dose and packed.

➢ *Evaluation of the Films*

- *Physical Appearance*

The films were examined visually and by touch for colour uniformity, surface smoothness, transparency and the absence of defects such as bubbles, cracks or entrapped particles.

- *Thickness*

Film thickness was measured with a screw gauge (least count 0.01 mm) at several randomly selected points across each film, and the mean and standard deviation were calculated.

- *Weight Uniformity*

Five films (3.2 cm × 2.2 cm) from each batch were weighed individually and the average weight determined. Differences between groups were analysed by one-way ANOVA in R software.

- *Folding Endurance*

Flexibility was quantified by folding a small strip (2 cm × 2 cm) repeatedly at the same point until it broke. The number of folds withstood without breaking was recorded as the folding endurance, and the determination was performed in triplicate.[7]

- *Microenvironment (Surface) pH*

Surface pH was measured to gauge the likelihood of mucosal irritation. Films were allowed to swell in distilled

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

water (pH 6.8); the surface was then brought into contact with phosphate buffer for 1–3 min and the pH read with a pen-type pH meter. The mean of five determinations was reported.[6]

- *Tack Tests*

Initial adhesiveness ("tackiness") was assessed by two simple, non-compendial procedures: a paper-press test, in which a paper substrate was pressed between two film strips for a short fixed time, and a finger/thumb test, a qualitative check classifying the film as tack-free, slightly tacky or tacky.

- *Dissolution*

Films (2 cm × 2 cm) were tested in an Erweka DT700 dissolution apparatus at 100 rpm using 900 mL of phosphate buffer (pH 6.8) maintained at 37 °C. Aliquots (5 mL) withdrawn at predetermined intervals were assayed by UV–visible spectrophotometry (Genesys 10S, Thermo Fisher Scientific) at 207 nm.

- *Disintegration*

Films (3.2 cm × 2.2 cm) were placed in a Petri dish containing 10 mL of purified water at 37 °C and swirled manually every 5 s until disintegration. The time was recorded and averaged over three samples.

- *Ex Vivo Permeation*

Permeation across freshly excised porcine buccal mucosa (< 2 h) was studied at 37 °C in Franz diffusion cells (n = 3; diffusion area 2.54 cm²). The receptor chamber was filled with phosphate-buffered saline (pH 7.4) and the tissue mounted between donor and receptor compartments. The film was applied to the mucosa, wetted with simulated salivary fluid, and 1 mL aliquots were withdrawn at intervals and replaced with fresh pre-warmed buffer. Drug was quantified by HPLC. Steady-state flux (Jss) was obtained from the slope of the linear portion of the cumulative-mass–time plot, and the apparent permeability coefficient was calculated as Papp = Jss/Cd, where Cd is the initial donor concentration.[13]

- *In Vitro Drug Release*

Release was determined using a modified Franz diffusion cell containing 30 mL of phosphate buffer (pH 6.8) with 20% PEG-400 in the receptor compartment, maintained at 37 ± 0.5 °C and stirred at 100 rpm. Samples (3 mL) were withdrawn over 8 h and replaced with an equal volume of equilibrated medium. After filtration (0.45 µm), drug concentration was measured by UV–visible spectrophotometry at 239 nm.

III. RESULTS AND DISCUSSION

➢ *Drug–Excipient Compatibility (FT-IR)*

Comparing the FT-IR traces of nortriptyline with those of the drug–excipient blends revealed no meaningful change in the location or strength of the main absorption bands, which rules out any incompatibility between the drug and the chosen excipients (Figure 1).[7]

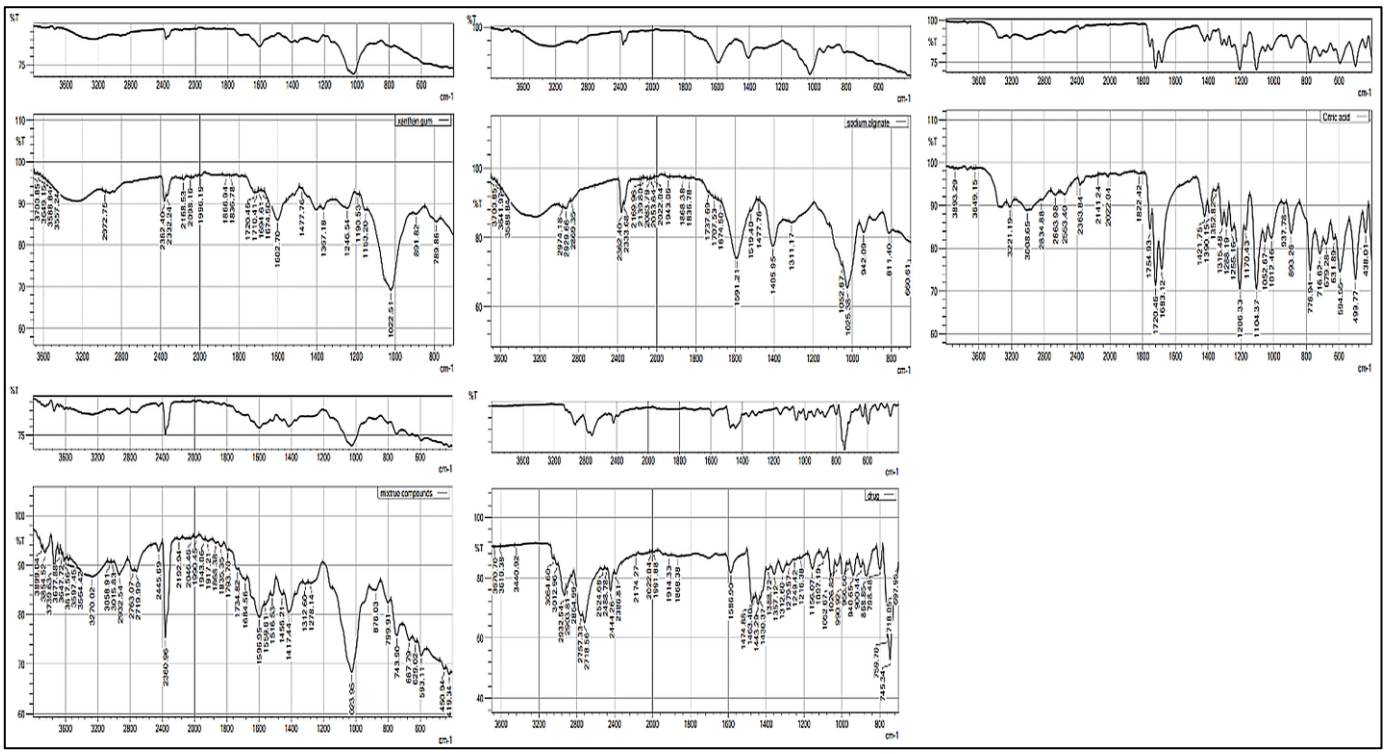


Fig 1 FT-IR Compatibility Study.

➢ *Formulation Design*

Five formulations (F1–F5) were prepared by systematically varying the polymer and plasticiser concentrations, as summarised in Table 1.

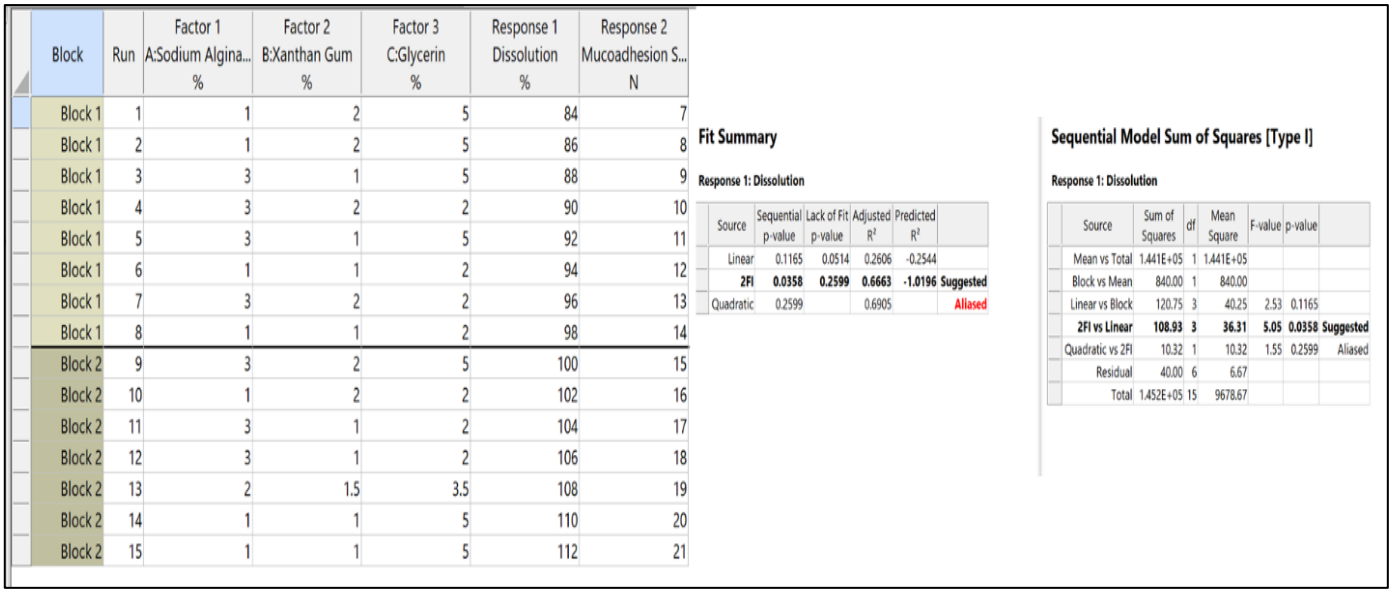
ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

Table 1 Composition of the Nortriptyline Buccal Film Formulations.

S. No	Formulation	Drug (%)	Sodium alginate (%)	Xanthan gum (%)	Glycerine (%)	Citric acid (%)	Distilled water (%)
1	F1	0.5	1.00	0.50	1.50	0.5	96
2	F2	0.5	1.50	1.00	2.50	0.5	94
3	F3	0.5	2.00	1.50	3.50	0.5	92
4	F4	0.5	2.50	2.00	4.50	0.5	90
5	F5	0.5	3.00	2.50	5.50	0.5	88

➢ *DoE Optimisation*

Analysis of the design table and fit summary, together with the contour, three-dimensional and perturbation plots, was used to relate the three factors to the measured responses (dissolution and mucoadhesion strength) and to define the constraints and optimal solution (Figures 2–5). A calibration curve for nortriptyline (Figure 6) was constructed for quantification.[30,33,35]



Block	Run	Factor 1 A:Sodium Algina... %	Factor 2 B:Xanthan Gum %	Factor 3 C:Glycerin %	Response 1 Dissolution %	Response 2 Mucoadhesion S... N
Block 1	1	1	2	5	84	7
Block 1	2	1	2	5	86	8
Block 1	3	3	1	5	88	9
Block 1	4	3	2	2	90	10
Block 1	5	3	1	5	92	11
Block 1	6	1	1	2	94	12
Block 1	7	3	2	2	96	13
Block 1	8	1	1	2	98	14
Block 2	9	3	2	5	100	15
Block 2	10	1	2	2	102	16
Block 2	11	3	1	2	104	17
Block 2	12	3	1	2	106	18
Block 2	13	2	1.5	3.5	108	19
Block 2	14	1	1	5	110	20
Block 2	15	1	1	5	112	21

Fit Summary

Response 1: Dissolution

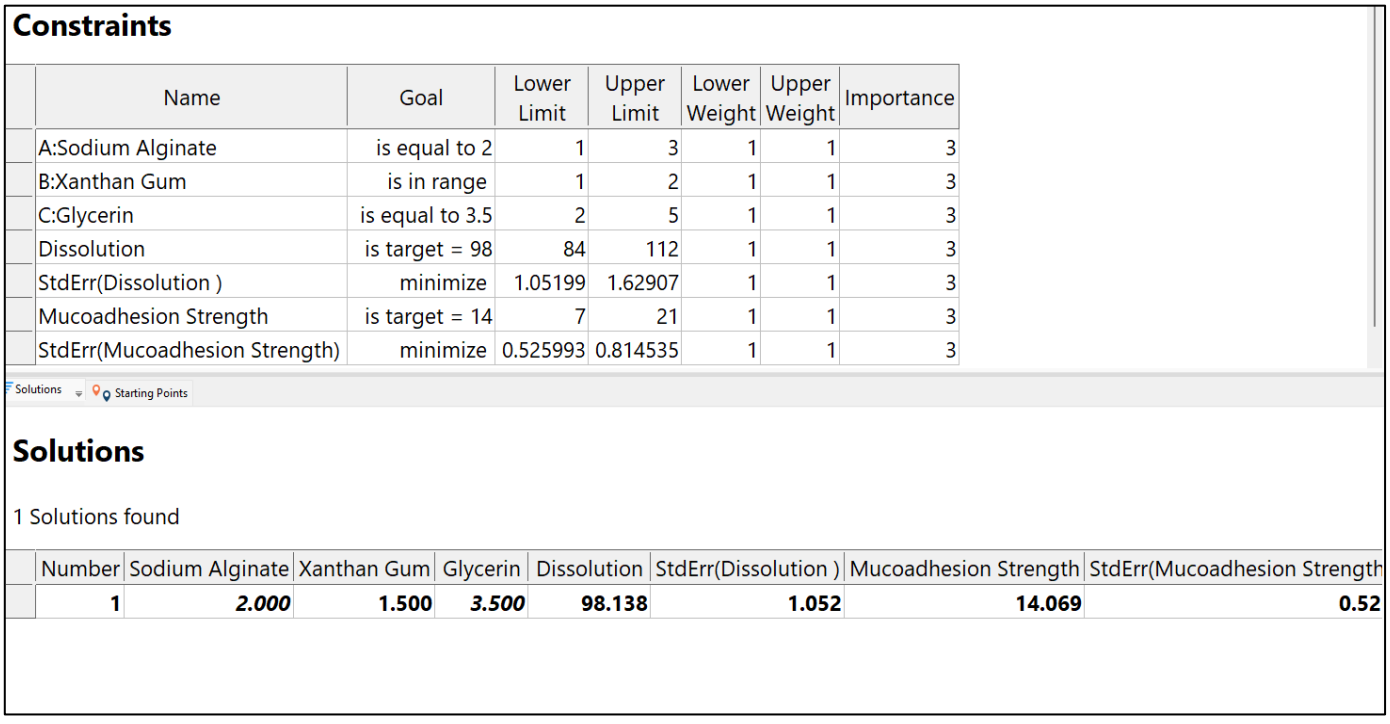
Source	Sequential p-value	Lack of Fit p-value	Adjusted R^2	Predicted R^2	
Linear	0.1165	0.0514	0.2606	-0.2544	
2FI	**0.0358**	**0.2599**	**0.6663**	**-1.0196**	**Suggested**
Quadratic	0.2599		0.6905		Aliased

Sequential Model Sum of Squares [Type I]

Response 1: Dissolution

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Mean vs Total	1.441E+05	1	1.441E+05			
Block vs Mean	840.00	1	840.00			
Linear vs Block	120.75	3	40.25	2.53	0.1165	
2FI vs Linear	**108.93**	**3**	**36.31**	**5.05**	**0.0358**	**Suggested**
Quadratic vs 2FI	10.32	1	10.32	1.55	0.2599	Aliased
Residual	40.00	6	6.67			
Total	1.452E+05	15	9678.67			

Fig 2 Design Table and Fit Summary.



Constraints

Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
A:Sodium Alginate	is equal to 2	1	3	1	1	3
B:Xanthan Gum	is in range	1	2	1	1	3
C:Glycerin	is equal to 3.5	2	5	1	1	3
Dissolution	is target = 98	84	112	1	1	3
StdErr(Dissolution)	minimize	1.05199	1.62907	1	1	3
Mucoadhesion Strength	is target = 14	7	21	1	1	3
StdErr(Mucoadhesion Strength)	minimize	0.525993	0.814535	1	1	3

Solutions | Starting Points

Solutions

1 Solutions found

Number	Sodium Alginate	Xanthan Gum	Glycerin	Dissolution	StdErr(Dissolution)	Mucoadhesion Strength	StdErr(Mucoadhesion Strength
1	***2.000***	**1.500**	***3.500***	**98.138**	**1.052**	**14.069**	**0.52**

Fig 3 Constraints and Solutions.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

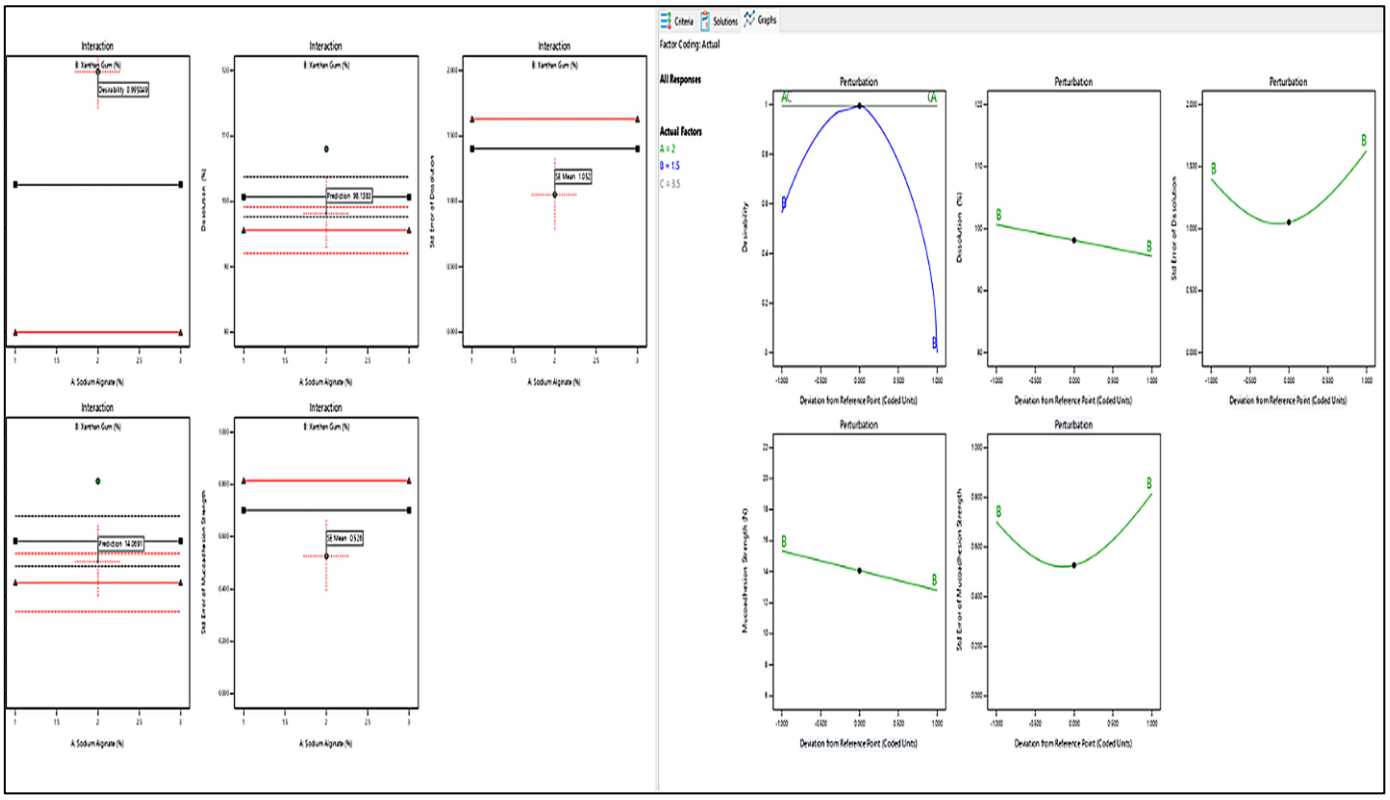


Fig 4 Interaction and Perturbation Plots.

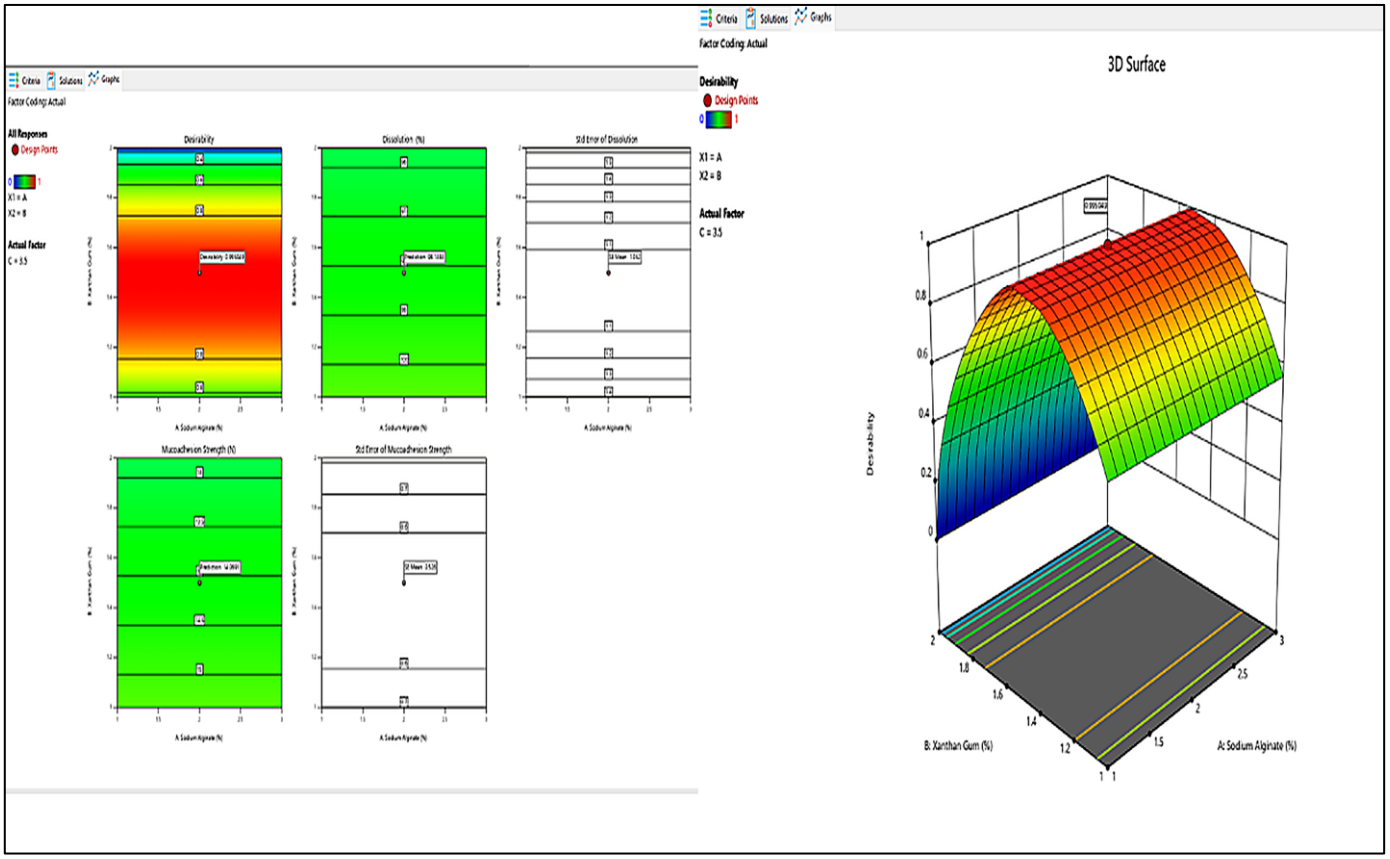


Fig 5 Contour and 3D Response Plots.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

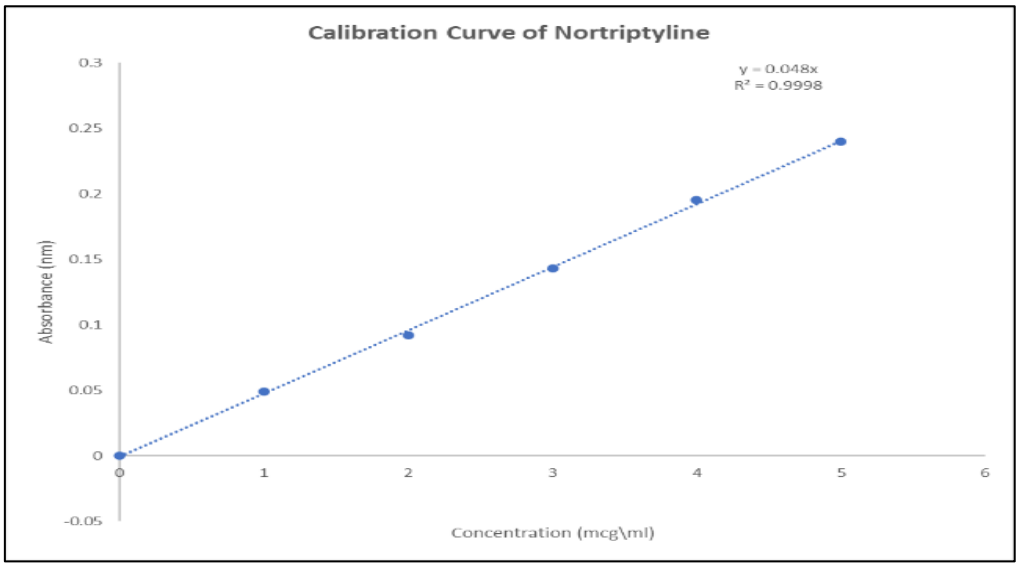


Fig 6 Calibration Curve of Nortriptyline.

➢ *Physicochemical Characterisation*

Table 2 sets out the physicochemical parameters of the five batches. Thickness fell between 0.62 and 0.66 mm and the weights held steady from batch to batch, both signs of even casting. Surface pH in every case sat near neutral (6.60–6.92), implying little tendency to irritate the mucosa. Folding-endurance figures showed the films to be flexible enough for buccal use, with F3 returning the highest value.[9,10]

Table 2 Physicochemical Properties of Formulations F1–F5.

S. No	Formulation	Thickness (mm)	Weight (mg)	Folding endurance	Surface pH
1	F1	0.65	18	10	6.92
2	F2	0.64	20	9	6.87
3	F3	0.62	20	12	6.80
4	F4	0.66	20	6	6.60
5	F5	0.64	21	8	6.72

Microscopic examination of the optimised films revealed smooth, uniform surfaces without cracks or phase separation (Figure 7).

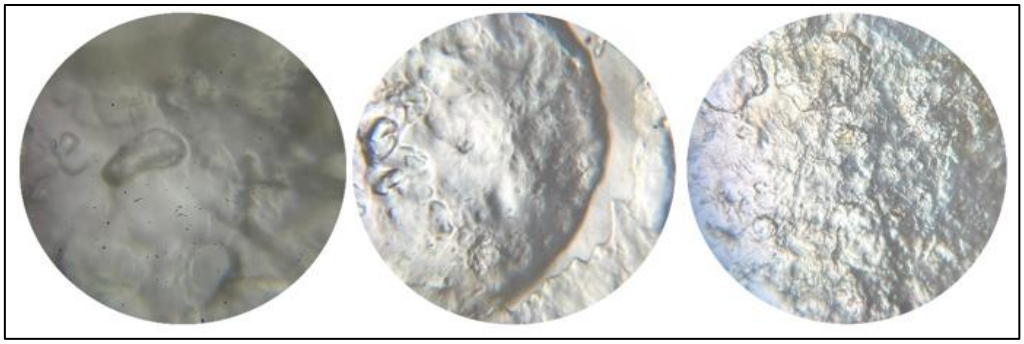


Fig 7 Microscopic Examination of the Films.

➢ *Disintegration*

Disintegration times were comparable across the batches (12–14 min; Table 3), consistent with the uniformity observed in the physicochemical evaluation.

Table 3 Disintegration Times of Formulations F1–F5.

S. No	Formulation	Disintegration time (min)
1	F1	12
2	F2	13
3	F3	12
4	F4	12
5	F5	14

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

➢ *In Vitro Drug Release*

Table 4 lists the comparative release profiles of all five batches, which are plotted in Figure 8. In each instance release carried on steadily across the 7 h window. F3 gave the greatest cumulative release, attaining roughly 97% by 7 h, which indicates that its polymer proportion hit an optimal middle ground between keeping the film intact and allowing the drug to diffuse.[19,20]

Table 4 Comparative Cumulative Drug-Release Profiles (% Drug Released).

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
0	0	0	0	0	0
0.15	4	4	5	4	3
0.30	7	7	10	7	6
0.45	10	10	14	10	8
1	15	14	19	16	11
2	28	27	33	29	22
3	40	38	47	42	33
4	52	50	61	55	44
5	66	63	75	67	55
6	79	76	88	80	67
7	90	86	97	91	79

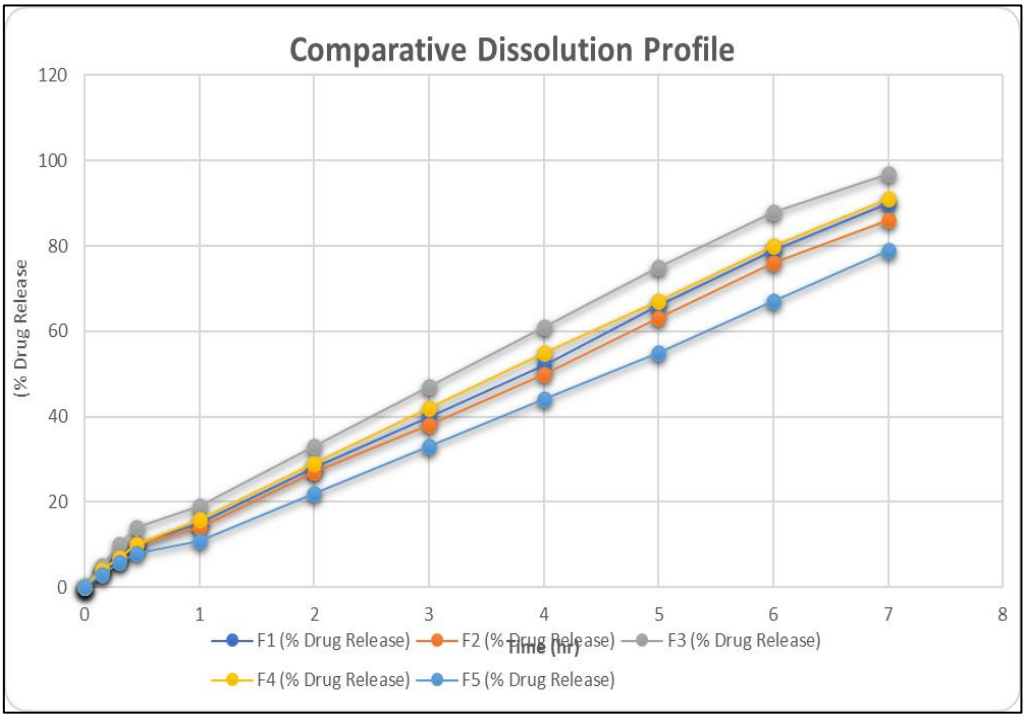


Fig 8 Comparative Dissolution Profile of Formulations F1–F5.

➢ *Release Kinetics*

To probe the mechanism behind release, the figures for the lead batch (F3) were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models.[31,32] Table 5 carries the kinetic data and Table 6 the correlation coefficients, while the matching model plots appear in Figure 9. First-order kinetics gave the tightest fit ($R^2 = 0.9952$), with the zero-order model close on its heels ($R^2 = 0.9942$); the Higuchi and Korsmeyer–Peppas fits were comparatively weak. That first-order behaviour dominates suggests the release rate hinges chiefly on how much drug is left within the matrix.

Table 5 Release-Kinetic Data for the Optimised Formulation F3.

Time (h)	√Time	Log time	% released	% remaining	Log % remaining	Log % released
0	0.000	—	0	100	2.000	0
0.15	0.387	-0.824	5	95	1.978	0.778
0.30	0.548	-0.523	10	90	1.954	1.041
0.45	0.671	-0.347	14	86	1.934	1.204
1	1.000	0.000	19	81	1.908	1.342
2	1.414	0.301	33	67	1.826	1.602

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

3	1.732	0.477	47	53	1.724	1.763
4	2.000	0.602	61	39	1.591	1.857
5	2.236	0.699	75	25	1.398	1.924
6	2.449	0.778	88	12	1.079	1.624
7	2.646	0.845	97	3	0.477	1.987

Table 6 Correlation Coefficients for the Kinetic Models (Formulation F3).

Model	**R^2**	**Interpretation**
Zero-order	0.9942	Very good fit
First-order	0.9952	Best-fit model
Higuchi	0.693	Moderate fit
Korsmeyer–Peppas	0.6114	Poor fit

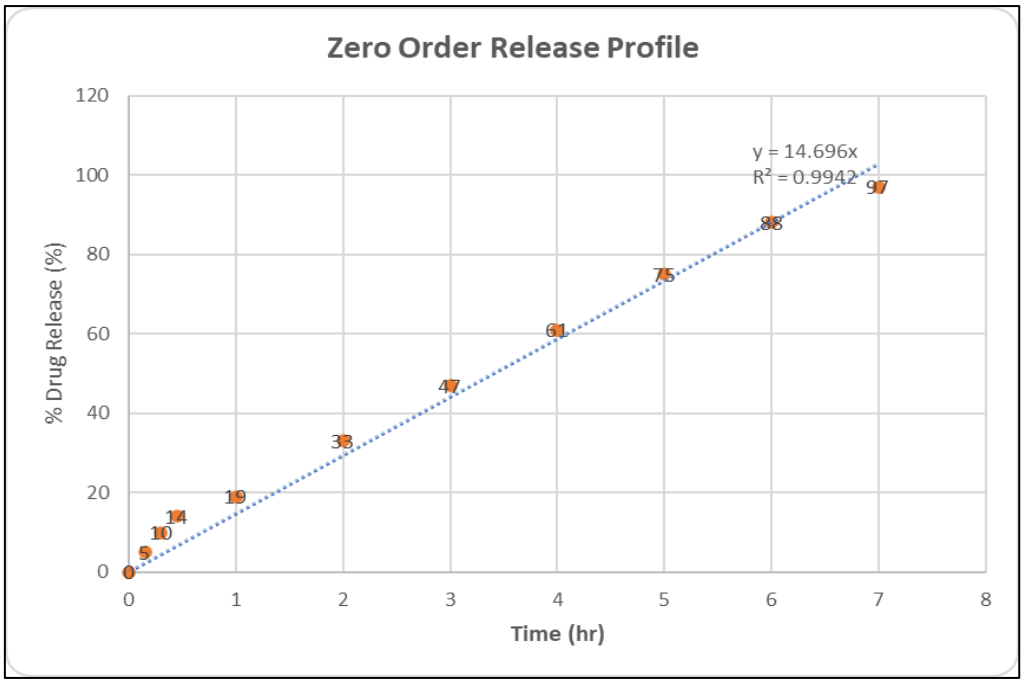


Fig 9a. Zero-Order Release Plot.

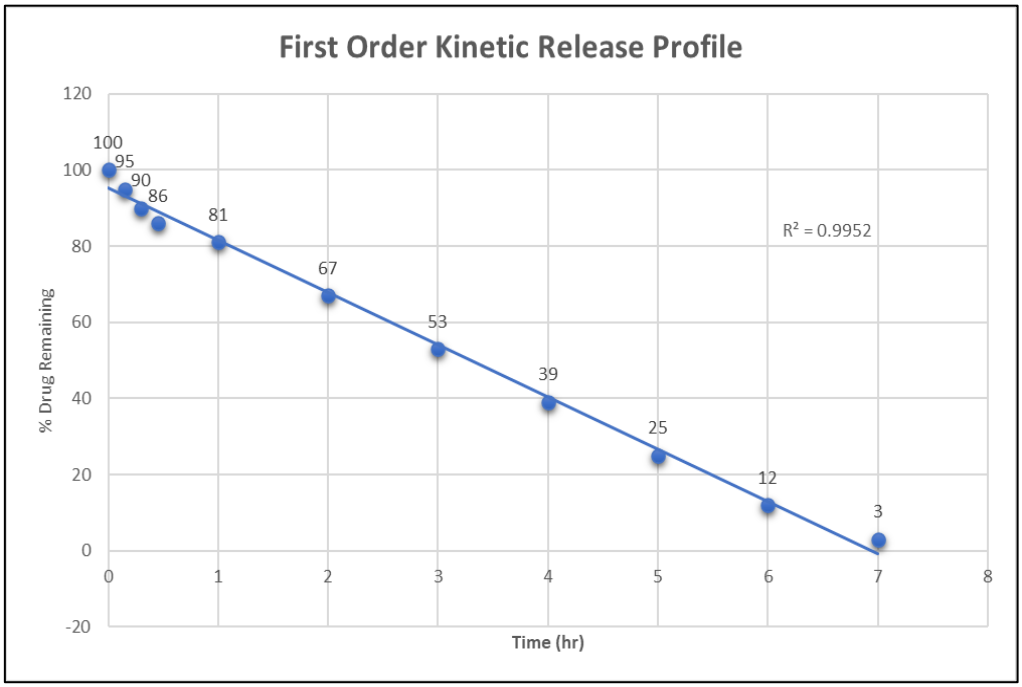


Fig 9b First-Order Release Plot.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

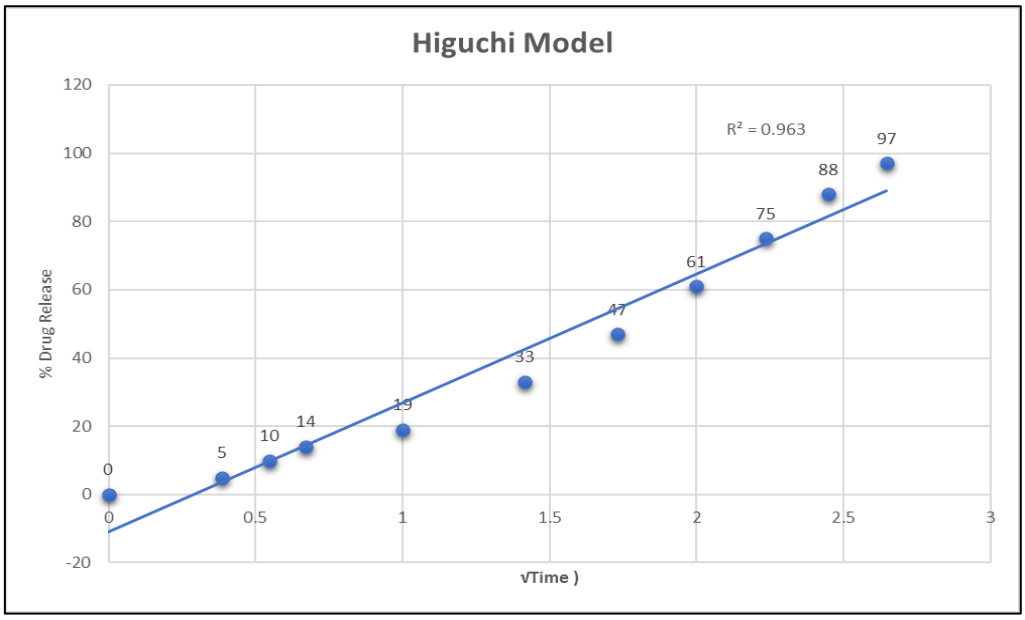


Fig 9c Higuchi Plot.

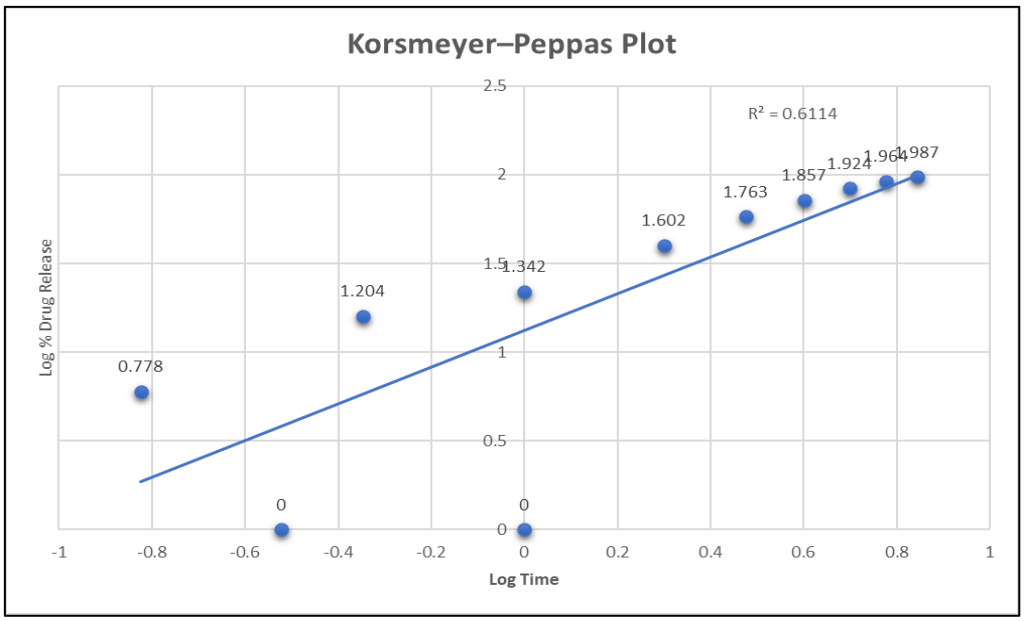


Fig 9d Korsmeyer–Peppas Plot.

➢ *Discussion*

Buccal films were obtained by solvent casting, with sodium alginate and xanthan gum acting as the polymers and glycerine as the plasticiser. Five batches (F1–F5) arose from varying the polymer levels, and each underwent assessment of thickness, weight variation, folding endurance, surface pH and in vitro release. The findings confirmed that the films were uniform, flexible and fit for buccal use, their near-neutral surface pH pointing to a slim chance of mucosal irritation.[9,11] Batch F3 was the standout: it married sound mechanical strength with the largest cumulative release (≈97% over 7 h), signalling that the polymer proportion in F3 struck an optimal compromise between holding the film together and letting the drug diffuse out.

Fitting the release data to kinetic models gave the closest agreement with first-order behaviour, which implies that the rate of release tracks the quantity of drug still held in the matrix.[31] The viscous gel mesh that xanthan gum builds on hydration fits neatly with this sustained pattern, and the mucin-binding nature of sodium alginate adds further weight to the prospect of extended contact with the mucosa.[19,34] Working through a DoE design made it possible to weigh several formulation factors and their interplay at once, which underpinned the methodical search for an optimised make-up; subsequent work might push this further to fine-tune polymer levels and processing settings.[28,33]

On balance, the nortriptyline buccal film developed here shows real promise as a vehicle for sustained delivery across the mucosa, and could serve as an effective alternative dosage form — one offering better therapeutic performance and greater patient acceptability — within smoking-cessation therapy.[25,26]

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

IV. CONCLUSION

Mucoadhesive buccal films of nortriptyline were prepared with success from xanthan gum and sodium alginate and then fine-tuned through a design-of-experiments approach. All of the batches turned out uniform, flexible and non-irritant, and the lead film (F3) held its release across 7 h, reaching close to 97% cumulative drug liberation with first-order kinetics and firm mucoadhesion. By ferrying the drug across the buccal mucosa and sparing it the liver's first-pass metabolism, the system presents an encouraging alternative for lifting both the bioavailability and the patient acceptability of nortriptyline in smoking-cessation therapy. Confirmatory in vivo and stability work is the logical next step toward establishing its clinical value.

- *Declaration of Competing Interest*

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- *Funding*

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

REFERENCES

[1]. Jacob S, Nair AB, Boddu SHS, Gorain B, Sreeharsha N, Shah J. An updated overview of the emerging role of patch and film-based buccal delivery systems. Pharmaceutics. 2021;13(8):1206.
[2]. Nair VV, Cabrera P, Ramírez-Lecaros C, Jara MO, Brayden DJ, Morales JO. Buccal delivery of small molecules and biologics: of mucoadhesive polymers, films, and nanoparticles — an update. Int J Pharm. 2023;636:122789.
[3]. Müller L, Rosenbaum C, Krause J, Weitschies W. Characterization of an in vitro/ex vivo mucoadhesiveness measurement method of PVA films. Polymers (Basel). 2022;14(23):5146.
[4]. Korelc K, Larsen BS, Gašperlin M, Tho I. Water-soluble chitosan eases development of mucoadhesive buccal films and wafers for children. Int J Pharm. 2023;631:122544.
[5]. Sevinç Özakar R, Özakar E. Current overview of oral thin films. Turk J Pharm Sci. 2021;18(1):111–122.
[6]. Pamlényi K, Kristó K, Jójárt-Laczkovich O, Regdon G Jr. Formulation and optimization of sodium alginate polymer film as a buccal mucoadhesive drug delivery system containing cetirizine dihydrochloride. Pharmaceutics. 2021;13(5):619.
[7]. Kristó K, Módra S, Hornok V, Süvegh K, Ludasi K, Aigner Z, et al. Investigation of surface properties and free volumes of chitosan-based buccal mucoadhesive drug delivery films containing ascorbic acid. Pharmaceutics. 2022;14(2):345.
[8]. Hassan AAA, Kristó K, Ibrahim YHEY, Regdon G Jr, Sovány T. Quality by design-guided systematic development and optimization of mucoadhesive buccal films. Pharmaceutics. 2023;15(9):2375.
[9]. Pamlényi K, Rayya H, Hassan AAA, Jójárt-Laczkovich O, Sovány T, Pintye-Hódi K, et al. Development and optimization of chitosan-ascorbate-based mucoadhesive films for buccal delivery of captopril. Pharmaceutics. 2025;17(4):401.
[10]. Jovanović M, Tomić N, Cvijić S, Stojanović D, Ibrić S, Uskoković P. Mucoadhesive gelatin buccal films with propranolol hydrochloride: evaluation of mechanical, mucoadhesive, and biopharmaceutical properties. Pharmaceutics. 2021;13(2):273.
[11]. Papakyriakopoulou P, Rekkas DM, Colombo G, Valsami G. Development and in vitro–ex vivo evaluation of novel polymeric nasal donepezil films for potential use in Alzheimer's disease using experimental design. Pharmaceutics. 2022;14(8):1742.
[12]. Ciurba A, Sipos E, Todoran N, Hancu G, Rusu A, Bíró R. Preparation and evaluation of caffeine orodispersible films: the influence of hydrotropic substances and film-forming agent concentration on film properties. Polymers (Basel). 2023;15(9):2034.
[13]. Rajabi A, Idrees M, Rahman A, Iyire A, Wyatt D, Koner J, et al. Evaluating the role of amino acids and isothermal dry particle coating in modulating buccal permeation of large molecule drug vancomycin. Sci Rep. 2024;14(1):19678.
[14]. Farooqui P, Gude R. Formulation development and optimisation of fast dissolving buccal films loaded glimepiride solid dispersion with enhanced dissolution profile using central composite design. Int J Pharm Pharm Sci. 2023;15(6):28–38.
[15]. Haju SS, Yadav S. Formulation and evaluation of cilnidipine mucoadhesive buccal film by solvent casting technique for the treatment of hypertension. Int J Pharm Pharm Sci. 2021;13(9):34–43.
[16]. Badekar R, Bodke V, Tekade BW, Phalak SD. An overview on oral thin films — methodology, characterization and current approach. Int J Pharm Pharm Sci. 2024;16(4):1–9.
[17]. Aashmeen S, Lal N, et al. Therapeutic potential and formulation considerations of orally disintegrating films in acute disorders. Discov Pharm Sci. 2025;3(1):30.
[18]. Mishra UK, et al. Advancement in sodium alginate-based drug delivery systems: applications and future prospects. AAPS PharmSciTech. 2026;27(4):196.
[19]. Layek B. A comprehensive review of xanthan gum-based oral drug delivery systems. Int J Mol Sci. 2024;25(18):10143.
[20]. Kulhari H, et al. Advances in xanthan gum-based systems for the delivery of therapeutic agents. Pharmaceutics. 2023;15(2):402.
[21]. Bhardwaj BY, Vihal S, Pahwa R. Recent advancements in xanthan gum-based gastroretentive floating formulations: chemical modification, production and applications. Carbohydr Polym. 2024;344:122548.
[22]. Jiang J, Li X, Hu AF, Zhou GJ, Gao YH, Xu C, et al. Nicotine and neuronal nicotinic acetylcholine receptors: unraveling the mechanisms of nicotine addiction. Front Neurosci. 2025;19:1670883.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/26jun964

[23]. World Health Organization. Tobacco [fact sheet]. Geneva: World Health Organization; 2024.
[24]. Hajizadeh A, Howes S, Theodoulou A, Klemperer E, Hartmann-Boyce J, Livingstone-Banks J, et al. Antidepressants for smoking cessation. Cochrane Database Syst Rev. 2023;(5):CD000031.
[25]. Pajai DD, Paul P, Reche A. Pharmacotherapy in tobacco cessation: a narrative review. Cureus. 2023;15(2):e35086.
[26]. Meng Y, Xiang S, Qu L, Li Y. The efficacy and acceptability of pharmacological monotherapies and e-cigarette on smoking cessation: a systematic review and network meta-analysis. Front Public Health. 2024;12:1361186.
[27]. Sovány T, Kristó K, Csóka I. Aspects and implementation of pharmaceutical quality by design. Pharmaceutics. 2024;16(6):832.
[28]. Priani SE, Fakih TM, Wilar G, Chaerunisaa AY, Sopyan I. Quality by design and in silico approach in SNEDDS development: a comprehensive formulation framework. Pharmaceutics. 2025;17(6):701.
[29]. Demiralp B. Experimental design in pharmaceutical formulation development: achievements, limitations and the transition toward intelligent optimization. Sci Pharm. 2026;94(2):38.
[30]. Maneewattanapinyo P, et al. Quality by design integration of design of experiments for tablet formulation optimization and process validation. AAPS PharmSciTech. 2026;27(2):94.
[31]. Askarizadeh M, et al. Kinetic modeling to explain the release of medicine from drug delivery systems. ChemBioEng Rev. 2023;10(6):1006–1049.
[32]. Patel AJ, Singh RP, Patel V, Goswami S. Application of mathematical models in drug release kinetics of Lagerstroemia speciosa extract–phospholipid complex. Res J Pharm Technol. 2022;15(3):1257–1262.
[33]. Vora LK, Gholap AD, Jetha K, Thakur RRS, Solanki HK, Chavda VP. Artificial intelligence in pharmaceutical technology and drug delivery design. Pharmaceutics. 2023;15(7):1916.
[34]. Wang H, Yang L, Yang Y. A review of sodium alginate-based hydrogels: structure, mechanisms, applications, and perspectives. Int J Biol Macromol. 2025;292:139151.
[35]. Kapoor DU, Kukkar RR, Gaur M, Prajapati BG, Malviya R. The potential of quality target product profile in the optimization of nanoemulsions. Curr Nanomed. 2025;15(1):4–17.