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Research Article

Formulation and *In-Vitro* evaluation of Nortriptyline Hydrochloride mucoadhesive buccal films

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Abstract

This contemporaneous research was aimed to formulate buccal mucoadhesive DDS to enhance bioavailability and avoid pre systemic metabolism. The mucoadhesive film was fabricated by solvent casting method with base polymer chitosan and a combination of hydrophilic polymer like PVP or Gelatin. The films were then evaluated. All the formulations were found to have optimum strength to withstand folding endurance. The films' consistent size, thickness, and weight variation were discovered. The drug content uniformity of films was exceptionally well. Given that the film's surface pH falls between 6.6 and 6.7, buccal administration is appropriate for it. The pH near to the neutral region decreases the chances of mucosal irritation. The invitro adhesion ability of the formulations were affected by the composition of chitosan and PVP or Gelatin. The lower and higher concentration of chitosan was not sufficient for *invitro* adhesion of films. The formulation having chitosan and hydrophilic polymers in the ratio 1:1.5 showed strong invitro adhesion. The *invitro* bioadhesion time of the formulations containing chitosan and gelatin or PVP was less due to poor ionization of gelatin. On increasing the concentration of hydrophilic polymers, the *invitro* bioadhesion time increased. The highest concentration of the polymers decreased the adhesion time. The formulation NF5 with chitosan and gelatin within the proportion of 1:1.5 exhibited drug release of 98.1% at 6 hours. The sole purpose of this work is to adhere the buccal film with the mucosa, hence formulation NF5 was selected as best formulation. Thus, current investigation's goal to develop a buccal mucoadhesive drug delivery was fulfilled.

Keywords: Buccal film, Nortriptyline HCl, depression, *in vitro* studies, mucoadhesive

INTRODUCTION

Nowadays, requirement of design and development of novel dosage form is created to improve patient compliance, safety and efficacy. The mucosa is relatively permeable with a rich blood supply. The oral transmucosal drug delivery bypasses liver and avoids pre-systemic elimination in the GI tract and liver. Oral mucosa is a good choice for systemic delivery of drug due to above reasons. Example of such drugs include buprenorphine, propranolol, salbutamol sulphate, diclofenac sodium, flurbiprofen, and fexofenadine. The buccal mucosa is relatively permeable, robust in comparison to the other mucosal tissues and is more tolerant to potential allergens which have a reduced tendency to irreversible irritation or damage. The buccal mucosa is a useful route for the treatment of either local or systemic therapies overcoming the drawbacks of conventional administration routes. However, salivary production and composition may contribute to chemical modification of certain drugs. Moreover, involuntary swallowing can result in drug loss from the site of absorption. Furthermore, constant salivary scavenging within the oral cavity makes it very difficult for dosage forms to be retained for an extended period, in order to facilitate absorption in this site. [1]

Buccal film is administered through buccal drug delivery system. Buccal film is small, with low dose, easily administered so that it is more palatable and acceptable dosage from than other buccal drug delivery system like wafers, lozenges, microparticles, gel, tablets. Buccal film is effective dosage form which improves bioavailability as it bypasses first pass metabolism. It is satisfactorily adhered to buccal layer of oral cavity, so it is more convenient than other dosage form. It is cost effective, biodegradable, fast absorption, elegant, easy to handle, non-irritating and no requirement of swallowing of drug henceforth it is more accepted dosage form by geriatric and paediatric patients.[2]

Nortriptyline HCl is a strong norepinephrine reuptake inhibitor and a moderate serotonin reuptake inhibitor. Nortriptyline hydrochloride blocks the reuptake of both noradrenaline and serotonin into the presynaptic terminals by binding to the transporters, viz. serotonin transporter (SERT) and norephedrine transporter (NET). The synaptic level of this mono amine is increased and there by prolong the action on the receptor. Nortriptyline hydrochloride potentiates amine, neurotransmitter in the CNS.[3]

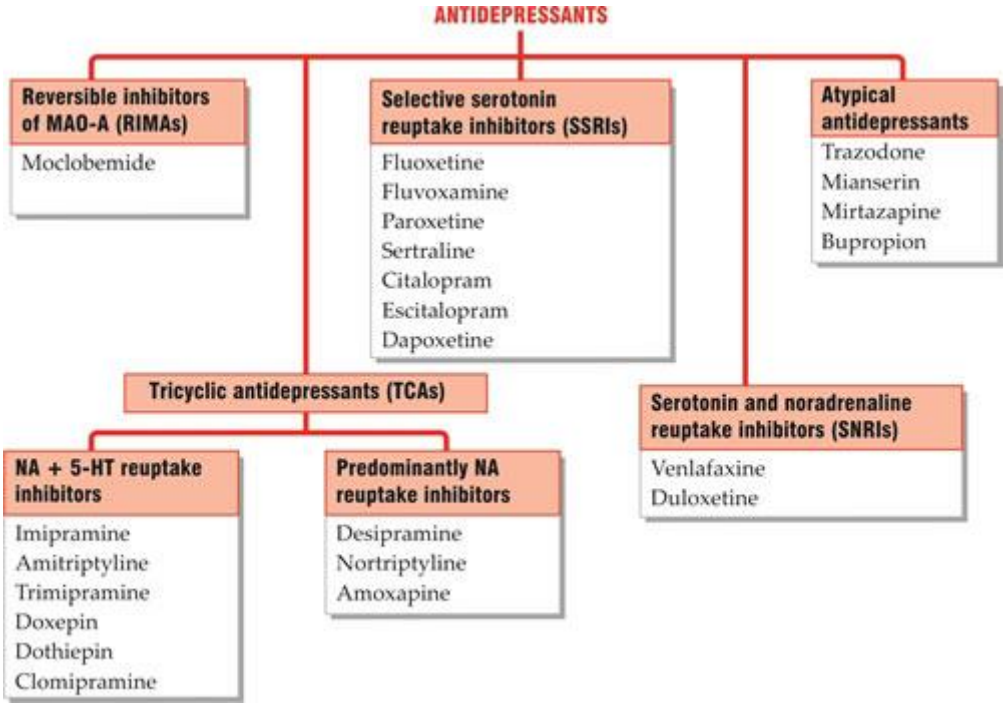


Figure 1: classification of antidepressants

MATERIALS AND METHODS:

Nortriptyline HCl was procured from R L Fine chem, Bengaluru, Chitosan (Tamil Nadu fisheries limited), Glacial acetic acid (Finar chemicals), Gelatin (Hi Media), Whatmann filter paper (Finar chemicals), anhydrous Calcium Chloride (Universal Laboratories pvt Ltd, Mumbai).

Preparation of nortriptyline HCl buccal films by solvent casting technique: -It was decided to formulate mucoadhesive buccal films using chitosan along with gelatin or Poly vinyl pyrrolidone (PVP). Chitosan solution in Glacial acetic acid was mixed with various proportions of Gelatin or PVP. Amount of drug equivalent to 10mg per 10mm film was added to the solution. The drug containing polymer solutions were casted on a glass plate containing a round shaped bangle stuck to it. It was then dried at 40°C for 6 hours. The dried films were then cut into circular shaped films of 10mm diameter. Various formulations containing Chitosan and Gelatin or PVP in the weight ratio of 1:1, 1:1.5 and 1:2 was prepared. Attempts were made to optimize the concentration of GAA used for dissolving chitosan. 2% GAA was found to be suitable as it gave stable films. The mixing ratio (r) defined as the percentage of gelatin in the mixture is calculated as:

$$\text{Mixing ratio (r)} = \frac{wc}{wc+wg}$$

Wc and Wg were the weights of chitosan and gelatin, respectively.

Table 1: Formulation table of Nortriptyline HCl mucoadhesive buccal films:

INGREDIENTS	F1	F2	F3	F4	F5	F6
Nortriptyline HCl	25mg	25 mg	25 mg	25 mg	25 mg	25 mg
Chitosan	50mg	50mg	50mg	50mg	50mg	50mg
Gelatin	20mg	40mg	60mg	-	-	-
PVP	-	-	-	20mg	40mg	60mg
Methanol	10 ml	10 ml	10 ml	10 ml	10 ml	10 ml
Glacial acetic acid	2%	2%	2%	2%	2%	2%

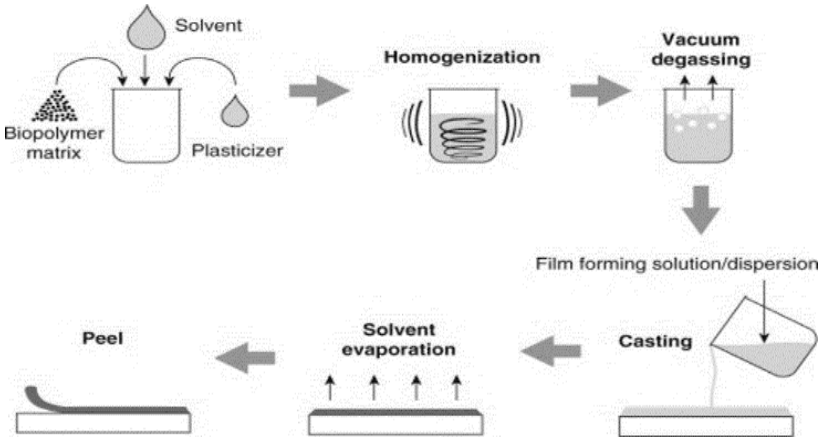


Figure 2: solvent casting technique

Evaluation of buccal films: -

Physical appearance: - All the prepared patches were visually inspected for colour, clarity, flexibility, and smoothness.

Weight of the film: - A weighing balance is used to weigh the films. Three films of individual compositions (1.75 square inch) were weighed separately in order to assess the film weight. Film weight is computed and analysed to determine its average weight.[4]

Thickness: **-** A calibrated digital Vernier caliper was utilized to measure the thickness of buccal film. thickness is assessed three times, and the mean value is computed. This ensures consistency in the thickness of the film, which would be connected to definiteness of the dosage within film and protects the repeatability of the formulation procedure.[5]

Tensile strength: **-** It the finest tension that would be applied to a film before it snaps, which could be achieved with the help with of a texture analyzer AG/MC1 (Acquati, Italy) outfitted with a 5 N load cell. Distinctive film strips are secured between two clamps spaced at a certain distance. Calculation is performed using:

Tensile strength (N/mm^2) = breaking force (N)/ cross sectional area of sample (mm^2)

Films in triplicate were casted having 2x2 dimensions. The width along with breadth were noted at three sites and average value was taken for calculation. The variation of stress was kept constant at 0.5g every 2 mins. Elongation is estimated and weight values derived.[6]

Surface pH of the film: - The films are confirmed to swell for 2 h at 37 ° c by contacting 1 ml. of distilled water. The electrode is then placed in contact with the film's surface for 60 seconds before the pH is determined.[7]

Folding endurance: - It is tested by folding in the very same film site multiple times up till it tears. The amount of times this can be done same way before tearing determines result of folding endurance.[8]

Mucoadhesive strength: - Through the use of a modified analytical balance, the mucoadhesive strength is established. By adding a tiny droplet of water to slide on one side of the analytical balance and attaching the other end of the weighing pan, film is applied to the glass-slide. The pan was gradually filled with weight until the glass slide separated from film. Mucoadhesive strength of a film is the weight required to separate it from the glass slide.

Drug content uniformity: - The mucoadhesive film was set in a volumetric flask and evenly diluted in pH 6.8 buffer. After diluting, 5 ml solution along 20 ml of pH 6.8 PBS, the mixture is filtered. A spectrophotometer (249 nm) is used to measure the absorbance of the drug in the film. one It is calculated to find the average drug content. The standard graph was used to calculate the drug content percentage.[9]

In-vitro disintegration time: **-** It is estimated utilizing a USP disintegration setup. The sol^n selected is 800 ml pH 6.8 IPB (at 37° ± 0.5°C). A sheep cheek mucosal membrane, (3cm L), was attached to glass slab, vertically planted in the apparatus. This system is made wet at one surface using 15µl IPB and then placed with mucosa membrane. Slab was let to motion up and down such as dosage form absolutely submerged in the buffer at the base point and was out at the high point.[10]

In vitro diffusion study: - Only the optimised batch will be examined. The test is done using sheep buccal mucosa. The Franz diffusion cell was utilized (constant at 37 degrees Celsius) with pH 6.8 phosphate buffer for 6 h. The samples were spectrophotometrically inspected at 239 nanometers.[11]

Moisture uptake studies (or) swelling index: This is analysed as weight and swelling area growth. Weight increases due to swelling**:** A film of 10 mm size of individual batch is weighed on pre-weighed glass cover.It is set in a pH 6.8(10 ml) buffer containing petri dish. At intervals of 5 mins, up till 1 h,weight is determined by removing cover slip. The variation in weights represents the increase caused by water uptake and film expansion. Area increase**:** Similar procedure is carried out for calculation of variation in area. For this, measuring scale was used to evaluate increase in the area. The area of the film's diameter enhanced at 1 h intervals for 6 hours, and the area was quantified. [12]

The percentage weight and area swelling value derived from the mean of triplicates by:

Percentage swelling = $(X_t - X_o / X_o) \times 100$

Percentage moisture loss: **-** To test the durability of films in dry environments, percentage moisture loss is executed. It is situated in a desiccator holding fuse anhydrous calcium chloride. It is removed and weighed after 72 h.[13] The algorithm below represents the avg % moisture loss.: -

$$percentage\ moisture\ loss = \frac{initial\ weight - final\ weight}{initial\ weight} x\ 100$$

Dissolution kinetics study: - It is performed utilizing zero and first order, Peppa's and Higuchi's models. Dissolution data is useful in determining these studies. Model showing the highest R value is regarded as the best fit. n value determines diffusion patterns.[14]

Stability study: - The stability testing was conducted at varying temperatures in conformity with ICH recommendations. It was done by subjecting the Optimized formulation in their final packaging mode to 25±2°C / 40±2°C and 65%±5% / 75%±5 relative humidity in a programmed environmental sample chamber. At thirty, sixty and ninety days, samples were removed and evaluated for variations.[15]

RESULTS AND DISCUSSION:

Organoleptic properties: -

These tests were performed, and the results were as follows- colour appeared ads white to off white, appearance as crystalline powder, it is odourless and has a characteristic taste.

Melting point: - The Melting point of Nortriptyline hydrochloride was found to be in the range of 200-220°c. The observed melting point was found to be 218⁰c. This indicates the purity of the drug sample. Any impurity if present will cause variation in the melting point of the given drug substance. The Result was found to be within limit.

Solubility: - Nortriptyline HCl was found to be soluble in Methanol and ethanol, Soluble in Phosphate buffer (6.8) and chloroform and sparingly soluble in water.

UV-spectroscopy-analysis of drug:

Table 2: Standard curve of Nortriptyline HCl in 6.8pH phosphate buffer

Sr. No.	Conc.(µg/ml)	Absorbance (nm)
1	0	0
2	2	0.176 ±0.064
3	4	0.361±0.074
4	6	0.528±0.043
5	8	0.704±0.058
6	10	0.912±0.042

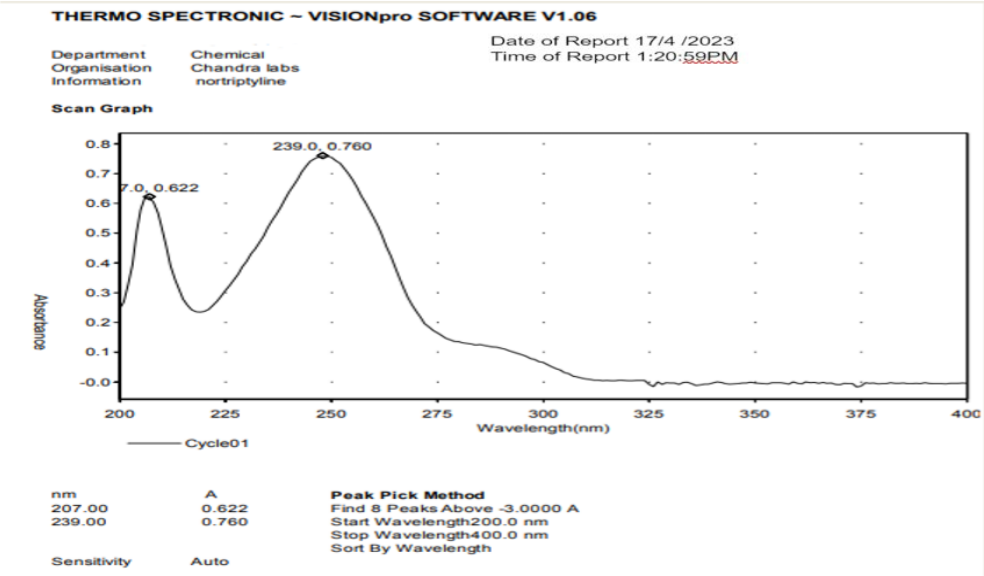


Figure 3: UV spectrum of Nortriptyline HCl.

Calibration curve of Nortriptyline HCl:

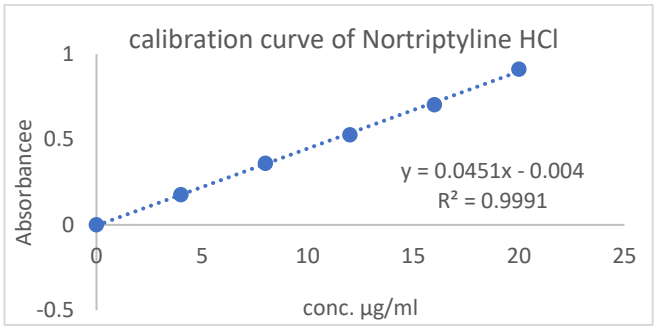
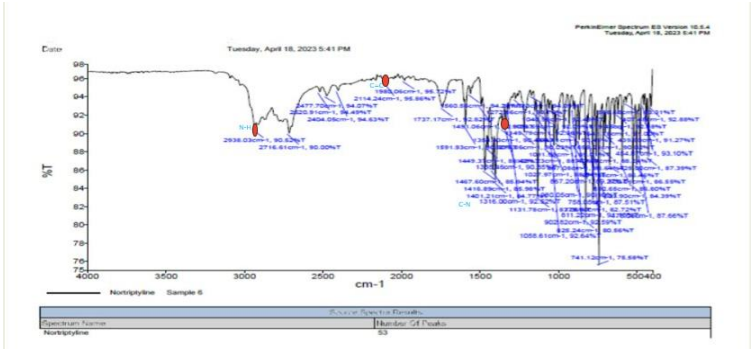


Figure 4: calibration curve of Nortriptyline HCl

Observation: - It was observed that the drug obeys beer's law in concentration range of 2-10 µg/ml in 6.8pH phosphate buffer. The drug exhibited λ max at 239nm.

Drug and excipient compatibility studies: -Fourier Transform Infrared spectrophotometry (FTIR): - Compatibility study of drug with the excipients was performed by FTIR spectroscopy using SHIMADZU-FTIR 410 model. The FTIR Spectra of the pure drug, and the binary mixture were compared. There was no appearance of new peak or disappearance of peak in the spectra of the mixture which implies absence of incompatibility between the drug and the polymer under study.[16]



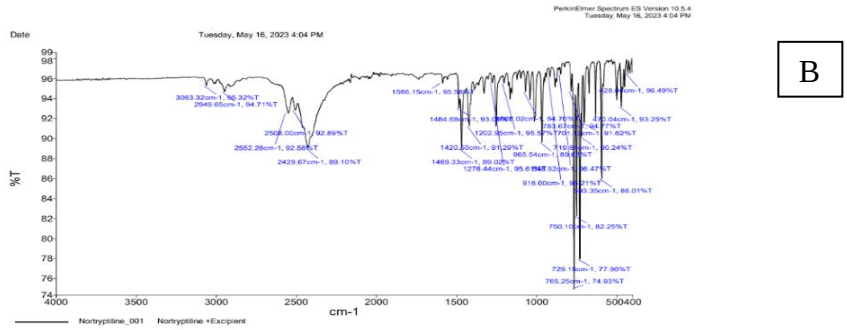


Figure 5: - A) FTIR Spectra of Nortriptyline HCl pure drug, B) FTIR Spectra of Nortriptyline HCl drug with optimized formulation

Observation: - The correlation between the pure drug and excipients indicated that the drug was compatible with the formulation excipients. FTIR spectra was compared and checked for the shifting in functional peaks and non-involvement of functional group. From the spectra there is no interaction between the selected carriers, drug and mixtures. Hence the selected carrier was found to be compatible in entrapping the selected Nortriptyline HCl with carriers without any mutual interactions

Evaluation of Buccal Films:

Film weight variation and thickness: Weight and thickness of the prepared formulations were recorded and found to be consistent and uniform. Three Films each of 1.75 square inch were cut at three different places from casted films and weight variation was measured. Weight variation varies from 135.20±0.12 to 152.35±0.17 The thickness of the film was measured using digital vernier callipers with at least count of 0.01 mm at different spots of the film. The thickness was measured at three different spots of the film and average was taken and SD was calculated. It was observed that as the polymer concentration increases the thickness of the film also increases.

Tensile strength: Tensile strength of prepared buccal film varies from 3.41±0.05 to 6.46±0.83 N/mm^2 revealing that the films had good mechanical strength and flexibility. Tensile strength of buccal film increases with the increase in the polymeric concentration. Formulation NF1 showed the lowest tensile strength.

Folding endurance: As the concentration of PVP or gelatin to Chitosan increases, the folding endurance of the films increases. Formulation with low concentration of gelatin or PVP showed a large deviation when compared to that of high concentrations. High concentration of polymers increases strength of film to withstand folding endurance test.

Drug Content Uniformity of Films: The buccal films dissolved in phosphate buffer pH 6.8 was taken for determination of drug content by using double beam UV-Visible spectrophotometer. The values evidently proved that the drug loading per film is uniform within the limits.

Surface pH of the Nortriptyline HCl films: The surface pH of the Nortriptyline buccal films was determined by using combined pH electrode. The pH values were found to be in the range of 6.2 to 6.5 making it suitable to be administered in the buccal mucosa. The pH of the film nearer to the neutral region makes them comfortable for use.

Swelling Index/moisture uptake: The formulation containing increased concentration of Gelatin found to have higher swelling index. This is since gelatin swells to a large extent than chitosan when exposed to water. The formulation NF6 containing Chitosan and Gelatin in the ratio 1:2 registered 40% increase in weight as against NF4 containing chitosan and Gelatin in the ratio of 1:1. Likewise formulation NF1containing Chitosan and PVP in the ratio of 1:1 showed 22% rise in weight as against NF3 having equal ratio of chitosan and PVP. Formulations NF3 and Formulations NF6 with chitosan and PVP or Gelatin in the ratio of 1:2 had the highest value for increase in area due to swelling.

Percentage Moisture Loss: Checking the physical stability of the patch at high humid conditions and integrity of the patch at dry conditions, the patches were evaluated for PML. The formulation NF1 shows higher value of Moisture loss.

Measurement of Mucoadhesive Strength: The mucoadhesive strength exhibited by Nortriptyline buccal films was satisfactory for maintaining them in oral cavity. The formulation NF5 shows good adhesion. The highest mucoadhesive strength was found to be in formulation NF5.

Determination of *in vitro* residence time (Disintegration time): The in-vitro residence time demonstrates the ability of the film to adhere with the mucosal surface. Longer in-vitro residence

times were registered for the formulations having chitosan and Gelatin or PVP in the ratio 1:1.5. The formulations NF2 and NF5 having low concentration of PVP or Gelatin had low adherence with the mucosa because the chitosan was not properly ionized. The formulations NF3 and NF6 having higher amount of PVP or Gelatin had less invitro residence time. The hydrophilic nature of gelatin and PVP decreases the effect of chitosan and makes it easily removed from mucosa.

Table 3: results of evaluation of buccal films

Formulation code	Evaluation parameter				
	Weight Variation *in mg	Thickness *in mm	Tensile strength (N/mm^2)	Surface ph	Folding endurance
Nf1	135.20±0.12	0.30±0.05	3.41±0.05	6.46±0.4	172±1.12
Nf2	142.30±0.27	0.44±0.07	5.40±0.65	6.50±0.6	231±8.42
Nf3	151.23±0.14	1.42±0.19	6.46±0.83	6.42±0.4	290±7.24
Nf4	137.42±0.17	0.25±0.11	3.80±0.20	6.48±1.4	183±1.19
Nf5	143.41±0.20	0.40±0.05	4.66±0.89	6.40±0.7	230±6.46
Nf6	152.35±0.17	1.22±0.17	6.41±1.63	6.59±0.4	296±9.28

Table 4: evaluation results of buccal film:

Formulation code	Evaluation parameter						
	Percentage moisture loss	Mucoadhesive strength ($dyne/cm^2$)	Drug content uniformity in %	Mucoadhesive strength	% weight increase (swelling index)	% area increase (swelling index)	*Invitro* residence time *in min
Nf1	5.76±0.12	34.64±0.30	92.37±0.06	34.60±0.30	22	75	280
Nf2	5.40±0.68	35.2±0.21	94.25±0.14	35.2±0.21	24	90	315
Nf3	4.64±0.11	31.7±0.75	95.16±0.25	31.7±0.75	32	140	230
Nf4	3.72±0.02	37.2±0.38	96.08±0.09	37.2±0.38	23	80	260
Nf5	4.10±0.21	38.4±0.39	97.17±0.10	38.4±0.39	31	78	350
Nf6	5.21±0.038	36.5±0.28	97.10±0.05	36.5±0.28	40	150	210

In vitro drug release diffusion study: The in-vitro drug release from the formulations was studied using Franz diffusion cell for a period of 6 hours. The cumulative % drug release was calculated. Among the formulations containing PVP, the formulation NF1 having chitosan and PVP in the ratio 1:1 registered drug release of 86.2%. The drug release consequently increased on increasing the amount of PVP in the formulations NF2 and NF3. Being hydrophilic in nature the PVP absorbed water and increased the drug release. The formulation NF2 had drug release of 97.88% in 5 hours and formulation NF3 with 85.39% after 4 hours. The presence of PVP decreases invitro residence time.

Table 5: *In-vitro* drug release data for formulations.

Time in hrs	NF1 (%)	NF2 (%)	NF3 (%)	NF4 (%)	NF5 (%)	NF6 (%)
0	0	0	0	0	0	0
1	29.34±0.74	35.71±0.28	49.95±0.26	16.32±0.22	34.13±0.22	28.7±0.35
2	46.52±0.06	54.08±0.73	67.07±0.58	28.26±0.34	56.12±0.29	65.34±0.41
3	64.48±0.44	71.9±0.91	71.88± 0.19	42.35±0.85	69.34±0.53	82.18±0.77
4	71.25± 0.061	83.87±0.81	77.15± 0.76	61.58±0.57	88.53±0.74	96.6±0.21
5	81.15± 0.24	88.48±0.59	80.12±0.71	78.26±0.63	92.41±0.82	--
6	86.2±0.92	97.88±0.12	85.39±0.74	81.23± 0.66	98.1±0.78	--

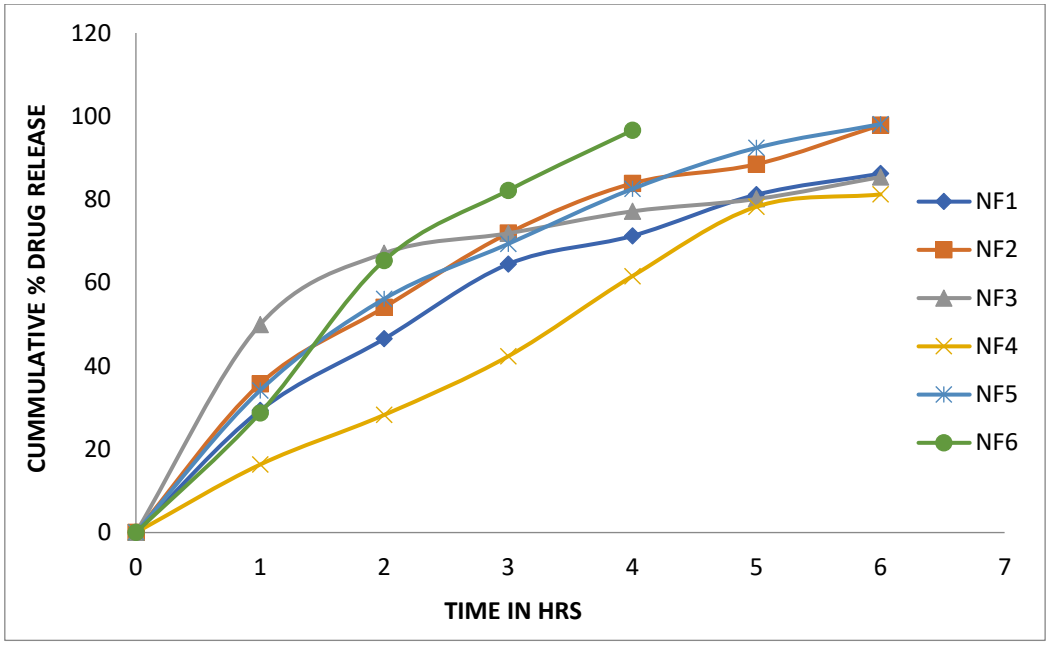


Figure 6: Dissolution graph of Mucoadhesive Buccal films of Nortriptyline HCl.

The formulation NF4 belonging to gelatin series with chitosan to gelatin ratio1:1 showed drug release of 78.26% after 5 hours. The poor drug release might be due to the influence of chitosan. The amount of hydrophilic polymer gelatin is increased in formulations NF5 and NF6. The gelatin swells in presence of water thereby increases the drug release but at the same time it influences the bio-adhesion of the formulation with mucosa. The formulation NF5 with chitosan and gelatin in the ratio 1:1.5 showed drug release of 98.1% in 6 hours. The formulation NF6 having chitosan and gelatin ratio 1:2 had the highest drug release of 96.6% in 4 hours. Formulation NF6 had the better release but it had less in-vitro residence time. The sole purpose of this work is to adhere the buccal film with the mucosa, hence formulation NF5 was selected as best formulation. The higher in-vitro residence time of NF5 made it most favoured formulation of gelatin series.Summarizing the data, it was found that drug release was slower for the buccal films with chitosan and gelatin or PVP in equal ratio. As the concentration of hydrophilic polymer increases the drug release also found to increase. The swelling nature of the polymers affected the in-vitro bioadhesion time.

Kinetic studies for optimized formulation:

Table 6: kinetic studies for optimized formulation NF5:

	ZERO	FIRST	HIGUCHI	PEPPA'S
	% CDR Vs T	Log % Remain Vs T	%CDR Vs √T	Log C Vs Log T
Slope	15.6105	-0.2654809	41.550095	1.69649835
Intercept	14.95333	2.1322266	-2.4942732	2.02816255
Correlation	0.995458	-0.9261964	0.9317277	0.91635594
R^2	0.968135	0.9102379	0.9943047	0.82420813

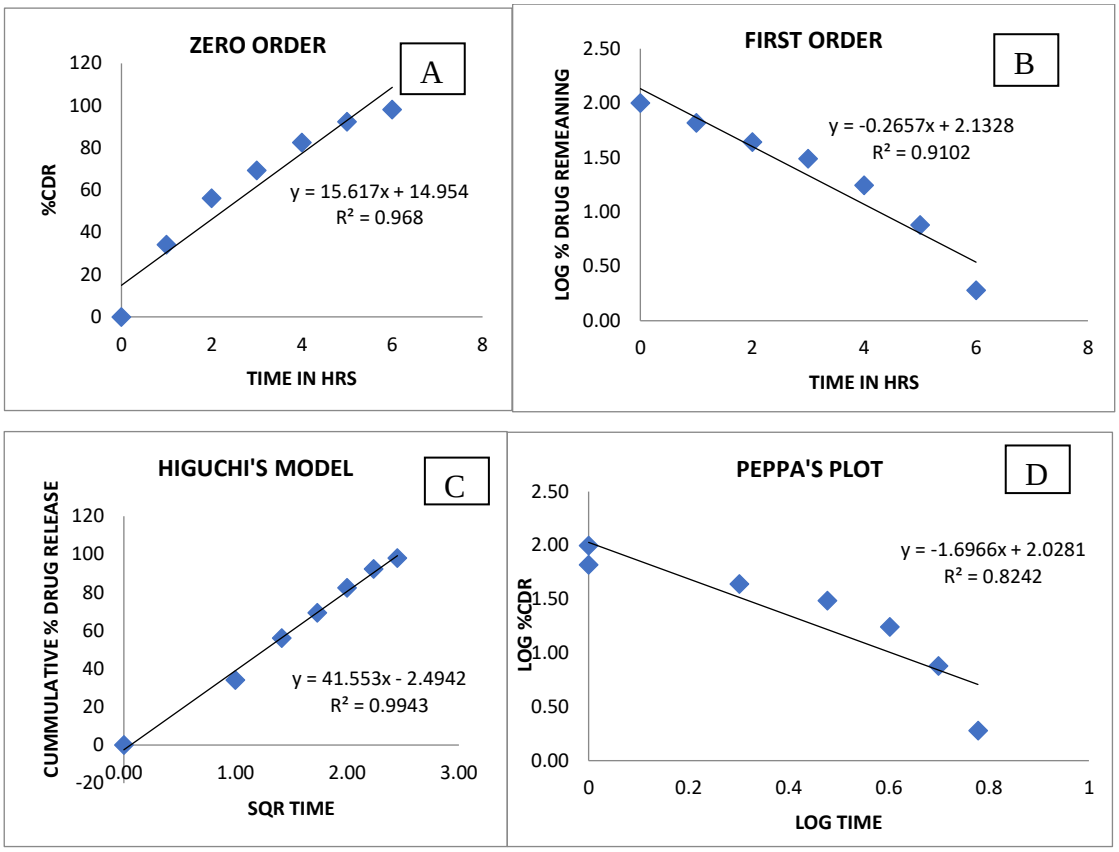


Figure 7: A) Zero Order plot for Formulation NF5, B) First Order Plot for Formulation NF5, C) Higuchi's plot for formulation NF5, D) Peppa's plot for formulation NF5

Mechanism of drug release: To find out the mechanism of drug release from hydrophilic matrices, the *invitro* dissolution data of each formulation with different kinetic drug release equations. Namely Zero order: $Q=K_0t$; Higuchi's square rate at time: $Q=K_Ht^{1/2}$ and Peppas: $F=K_mt^n$, where Q is amount of drug release at time t, F is Fraction of drug release at time t, K_0 is zero order kinetic drug release constant, K_H is Higuchi's square root of time kinetic drug release constant, K_m is constant incorporating geometric and structural characteristic of the films and n is the diffusion exponent indicative of the release mechanism. The correlation coefficient values (R) indicate the kinetic of drug release was zero order. The mechanism of drug release was by Peppa's model indicates the super case II transport evidenced with diffusion exponent values (n)

Stability studies for NF5:

Table 7: stability studies for optimized formulation NF5:

Time	Colour	Assay.		Cumulative % drug release at 6 hrs	
		25±2⁰c and 65±5%RH	40±2˚c and 75±5%RH	25±2⁰c and 65±5%RH	40±2⁰c and 75±5%RH
First day	White	100.45	100.14	98.1	98.1
30 days	White	101.82	99.15	97.54	97.12
60 days	White	100.80	98.75	97.24	96.56
90 days	White	99.30	98.26	96.65	96.12

DISCUSSION:

- The pre-formulation research has been accomplished for Nortriptyline HCl and analyzed the use of UV- Visible Spectrophotometer.
- The absorption spectrum of Nortriptyline HCl was found to be sharp and maximum at wavelength of 239 nm, consequently it was selected as the wavelength for detection.
- The melting point was decided using capillary tube method, the observed melting point was discovered to be 218 ºC.
- The standard graph of Nortriptyline HCl confirmed desirable linearity with R^2 of 0.9991, which shows that it obeys Beer- Lamberts law.
- The FTIR studies of pure drug and physical combination were conducted. The spectra of the drug and physical mixture discovered all the distinctive peaks. There were no drug-Excipients interactions in the physical mixture.

- Different formulations have been organized with the aid of using various concentrations of chitosan, gelatin and PVP with the aid of using solvent casting technique.
- The prepared formulations have been evaluated for numerous parameters like FTIR, Organoleptic evaluation, Swelling properties, weight of the films, pH of films, thickness of the films, Folding endurance, Tensile strength, Drug Content uniformity, Disintegration time, In-vitro Diffusion study, percentage moisture loss, Stability testing, Kinetic studies.
- The optimized formulation NF5 confirmed thickness of 0.40 mm, weight of 143.41 mg, pH of 6.40, mucoadhesive strength of 38.4 dyne/cm^2 , disintegration time of 350 mins, and the drug release data of selected buccal film NF5 confirmed desirable fit into zero order and Higuchi's release Kinetics.
- Therefore, developing the drugs as buccal films can give quicker release of drug and can also additionally prove to be a potential approach to enhance bioavailability of drug.

CONCLUSION

The present study was aimed to formulate mucoadhesive drug delivery system to enhance bioavailability and avoid pre systemic metabolism. The mucoadhesive film was fabricated by solvent casting method with base polymer chitosan and a combination of hydrophilic polymer like PVP or Gelatin. The films were then evaluated. All the formulations were found to have optimum strength to withstand folding endurance. The films were found to have uniform size, thickness and weight. The drug content uniformity of films was exceptionally well. The surface pH was found to be in the range of 6.6 which makes the film suitable for buccal administration. The pH near to the neutral region decreases the chances of mucosal irritation. The invitro adhesion ability of the formulations were affected by the composition of chitosan and PVP or Gelatin. The lower and higher concentration of chitosan was not sufficient for invitro adhesion of films. The formulation having chitosan and hydrophilic polymers in the ratio 1:1.5 showed strong invitro adhesion. The invitro bioadhesion time of the formulations containing chitosan and gelatin or PVP was less due to poor ionization of gelatin. On increasing the concentration of hydrophilic polymers, the invitro bioadhesion time increased. The highest concentration of the polymers decreased the adhesion time. The formulation NF5 with chitosan and gelatin in the ratio 1:1.5 showed drug release of 98.1% in 6 hours. The sole purpose of this work is to adhere the buccal film with the mucosa, hence formulation NF5 was selected as best formulation.

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