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FORMULATION AND EVALUATION OF AMITRIPTYLINE HCL MUCOADHESIVE BUCCAL FILMS

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ABSTRACT

Buccal mucoadhesive systems among novel drug delivery systems have attracted great attention in recent years due to their ability to adhere and remain on the oral mucosa and to release their drug content gradually Buccal mucoadhesive films can improve the drug therapeutic effect by enhancement of drug absorption through oral mucosa increasing the drug bioavailability via reducing the hepatic first-pass effect. The aim of the current study was to formulate the drug as buccal bioadhesive film, which releases the drug at sufficient concentration with a sustained manner reducing the frequency of the dosage form administration. One of the advantages of this formulation is better patient compliances due to the ease of administration with no water to swallow the product. Dissolution profile as studied in USP dissolution apparatus type 1 using pH 6.8 simulated saliva. The influence of variables like polymer type, concentration, of Amitriptyline HCl release profile was studied. The formulation was optimized based on various evaluation parameters like drug content and in-vitro drug release. Formulation F6 successfully release of drug within 7 hrs. The IR spectra showed stable properties of Amitriptyline HCl in a mixture of polymers used and revealed the absence of interaction between drug and selected polymer, stability studies were as per ICH guidelines, and results indicated that the selected formulation was stable.

KEYWORDS - *Amitriptyline HCL, Mucoadhesive, Buccal films.*

INTRODUCTION

Mucoadhesive buccal films which binds to biological surfaces that are covered by mucus. Normally, drugs are administered via numerous routes and dosage forms. Although the oral route is the most desired way of drug delivery, drug solubility and first pass metabolism sensitivity are crucial characteristics that must be present for the drug to be absorbed by this route. Parental route is the most painful type of administration. Topical medications can only be used for local or topical therapy. Drugs with high molecular weight, low skin penetration, poor water solubility, and substantial first pass metabolism require alternate routes. Most drugs are increasingly being administered via mucoadhesive route. Mucoadhesive drug delivery systems, which uses both natural and synthetic polymers, is a technique for controlled drug release that enables close contact between the polymer and a target tissue. Mucoadhesive drug delivery systems utilise the bioadhesion of certain polymers, which in turn adhesive during hydration and are therefore able to be used for targeted drug delivery to a specific area of the body for a prolonged length of time. The mucoadhesive properties are known to extend the drug's duration in the body after administration. The direct drug absorption and the reduced excretion rate together have the effect of increasing the drug's bioavailability. Lower API concentrations may result from longer residence times and more adhesion.

MATERIALS AND METHODS

MATERIALS

The gift sample Amitriptyline HCl is from Sai Mirra Inno Pharm Pvt Ltd, and polymers such as HEC, HPMC K100, HPC,

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Polyethylene glycol (mL), Sodium saccharin (mg), and Vanillin (mg) are from Vopec Pharmaceuticals Pvt Ltd.

METHODS

PREFORMULATION STUDY

Compatibility study

FTIR Studies

FT-IR spectra of pure Amitriptyline HCl, and combination with HPMC K100, HEC, HPC, showed in (Figure). Pure Amitriptyline HCl showed principle absorption peaks at 3500-3000cm-1 (NH Stretch) and 1600-1475 cm-1 (C=C Strech) 1350-1000 cm-1 (C-N Strech), 900- 690 cm-1 (CH bend). The same peak of NH-Stretch, C=C Stretch, N-H stretch, CH Bend, bonds were present as that of the pure drug without much shifting in the spectra of Amitriptyline HCl along with the polymers. This suggested no chemical interaction between the drug and the polymer.

DSC study

DSC thermogram was carried out for thermal compatibility of the drug and physical mixtures were shown in (figure 5 to 8). The melting point of the pure drug was 224.25 0C whereas the melting point of drugs in the physical mixture of drugs with HPMC K100 was 219.29 0C and drug with HPC 217.63 0C and drug with HEC was 202.10 0C. There is no change in the melting point peak of the drug in the physical mixture was retained indicating there is no interaction between the drug and polymers.

Preparation of mucoadhesive buccal film

The films are preferably formulated using the solvent casting method. The required quantity of polymer was added in small quantities and mixed well to dissolve in distilled water. The small quantity of drug is dissolved in the above solution. Add plasticizers to the above solution and mixed well. The solution was then cast on the Petri dish and kept in a hot air oven for drying at 40° C. After drying films were removed with the help of a sharp blade and kept in a desiccator for 24 hrs then cut into pieces of the desired shape and size.

Table 1
Formulation details of Amitriptyline HCl mucoadhesive buccal films

Formulation Code	Drug (Mg)	Polymer And Its Composition (Mg)			Polyethylene Glycol (Ml)	Sodium Saccharin (Mg)	Vanillin (Mg)	Distilled Water (Ml)
		HEC	HPMC K 100	HPC				
F1	130	150			0.1	2	2	10
F2	130	200			0.1	2	2	10
F3	130	250			0.1	2	2	10
F4	130		250		0.1	2	2	10
F5	130		300		0.1	2	2	10
F6	130		350		0.1	2	2	10
F7	130			250	0.1	2	2	10
F8	130			300	0.1	2	2	10
F9	130			350	0.1	2	2	10

CHARATERIZATION OF MUCOADHESIVE BUCCAL FILMS

Scanning Electron Microscopy (SEM)

The shape and surface characteristics of felodipine co-crystals was assessed by Scanning Electron Microscopy (SEM)

IR spectroscopy

IR spectrum of the drug, co-former, and co-crystals were recorded using FTIR in order to determine predictable interaction between the drug and co-former. The co- crystals were mixed with potassium bromide (K-Br) and then pressed with hydraulic press to form pellets which were further subjected to scanning in between 4000 and 400 cm−1.

EVALUATION OF MUCOADHESIVE BUCCAL FILMS

Physical appearance and surface texture of films

This parameter was checked simply with a visual inspection of films and evaluation of texture by feel or touch.

a. Weight uniformity of films

Three films of the size 2×2 cm were weighed individually using digital balance and the average weights were calculated.

b. **The thickness of films**

Thickness of the films was measured using a screw gauge with a least count of 0.01mm at different spots of the films. The thickness was measured at three different spots of the films and the average was taken.

c. Folding endurance of patches

The flexibility of films can be measured quantitatively in terms of what is known as folding endurance. Folding endurance of the films was determined by repeatedly folding a small strip of the films (approximately 2x2 cm) at the same place till it broke. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

d. **Swelling property**

Simulated solution of saliva was prepared to check the swelling property of the patch. The initial weight of the patch was determined and placed in the pre-weighed

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stainless steel mesh. The system was dipped in the simulated saliva solution. The increase in the weight of the patch was noted by weighing the system at regular intervals. The degree of swelling was determined by the formula:

$$\text{Degree of swelling} = \frac{\text{[Final weight (Wt) – Initial weight (Wo)]}}{\text{[Initial weight (Wo)]}}$$

e. Drug content uniformity of films:

The films were tested for drug content uniformity by UV Spectrophotometric method. Films of 2×2 cm size were cut from three different places from the casted films. Each film was placed in a 100 mL volumetric flask and dissolved in simulated saliva pH 6.8 and 5 mL is taken and diluted with water up to 10 mL. The absorbance of the solution was measured at λ max 240 nm using a UV/ visible spectrophotometer (Shimadzu). The percentage of drug content was determined.

f. **Surface pH**

Patch was slightly wet with help of water. The pH was measured by bringing the electrode in contact with the surface of the patch. The study was performed on three patches of each formulation and average was taken.

g. **Moisture loss**

Percent moisture loss is a parameter that determines the hygroscopicity of a film. Usually, this parameter is determined by first finding the initial weight of the film, afterward, putting this film in a desiccator for three days. Desiccator contains calcium carbonate. After three days, strips are taken out and weighed again. Moisture loss is determined by applying the following formula

.

$$\text{\% Moisture loss} = \frac{\text{(Initial weight – Final weight)}}{\text{(Initial weight)}} \times 100$$

In vitro Mucoadhesive strength

The mucoadhesive strength of the mucoadhesive buccal patches was determined at room temperature using the two-arm balance with minor modifications. Fresh sheep buccal mucosa was obtained from a local slaughter house and used for the study within 2 h of slaughter. The mucosal membrane was separated by removing underlying fat and loose tissues, and thickness of 2 mm was obtained. The membrane was then washed with distilled water and then with BS pH 6.5 at 37 ◦C.

***In-vitro* dissolution studies**

The release rate of Amitriptyline HCl dissolving Buccal films was determined by using USP dissolution testing apparatus II at 50 RPM. The film with 2×2 cm was placed in the 300 mL of 6.8 pH simulated saliva as a dissolution medium, and the temperature was maintained at 37°C. From this dissolution medium, 2 ml of the sample solution was withdrawn at different time intervals. The samples were filtered through Whitman filter paper and absorbance was determined 240 nm using double beam UV- Visible spectrophotometer.

Permeation study

The prepared mucoadhesive buccal films are placed in the diffusion cell on the upper membrane of the (donor compartment) and the receptor compartment contains simulated saliva (20 ml) it can be contacted with the dialysis membrane upper side of the donor compartment contain a film attach the film of length and width (2×2) cm it contains 20 mg of the drug. And the receptor compartment it contains simulated saliva and magnetic bead and this diffusion compartment placed in the magnetic stirrer the drug permeation start through the dialysis membrane and enter into the receptor compartment the drug to be entered in the receptor compartment and this solution took 2 ml every one hour and maintain the sink condition by replacing the 2ml of simulated saliva into the receptor compartment and this every interval taken samples analyzed by (Shimadzu) UV-visible spectrophotometer.

PERMEATION KINETICS

The matrix systems were reported to follow the zero-order permeation rate and the diffusion mechanism for the permeation of the drug. To analyse the mechanism for the permeation and permeation rate kinetics of the dosage form, the data obtained was fitted into, Zero - order, First order, Higuchi matrix and Peppa's model. In this by comparing the r values obtained, the best fit model was selected.

Zero Order Kinetics

Drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly, assuming that the area does not change and no equilibrium conditions are obtained can be represented by the following equation

$$Qt = Qo + Kot$$

First order kinetics

To study the first order release kinetics the release rate data were fitted to the following equation.

$$\text{Log } Qt = \log Qo + k1t/2.303.$$

Higuchi model

Higuchi developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semisolids and or solid matrices. Mathematical expressions were obtained for drug particles dispersed in a uniform matrix behaving as the diffusion

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media. And the equation was

$$Qt = KH\text{-}t\ 1/2$$

Korsmeyer and Peppa's model

To study this model the release rate data are fitted to the following equation.

$$Mt/M\alpha = K.tn$$

Hixon and Crosswell erosion equation

$$QO^{1/3} - Qt^{1/3} = KHCt$$

Stability studies

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors. To assess the drug and formulation stability, stability studies were done as per ICH guidelines.

The formulated mucoadhesive buccal films were wrapped in aluminum foil and stored at 45 ± 0.5ºC for twelve weeks. After three months, films were tested for appearance, drug content, and in-vitro drug release.

RESULTS AND DISCUSSION

PREFORMULATION STUDIES

Compatibility study

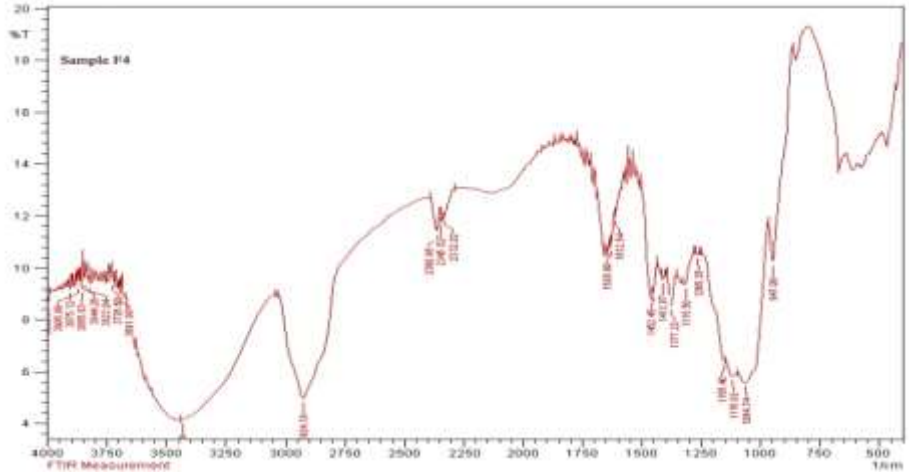

Figure 1
FTIR Spectra of Amitriptyline HCl

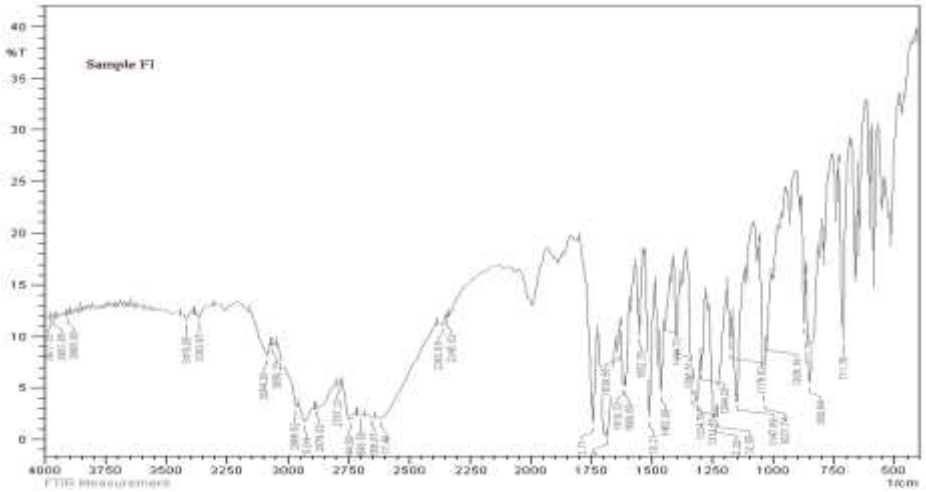

Figure 2
FTIR Spectra of Physical mixture of HEC

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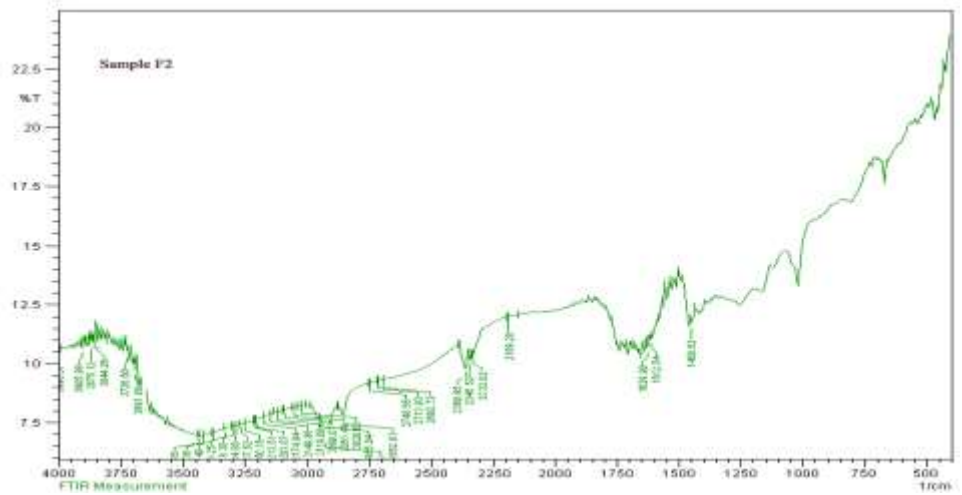

Figure 3
FTIR Spectra of Physical mixture of HPMC K100

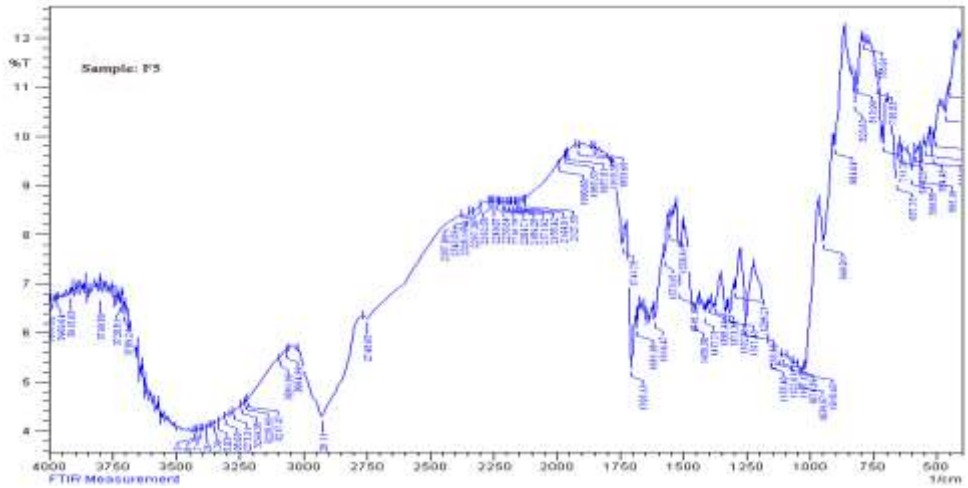

Figure 4
FTIR Spectra of Physical mixture of HPC

Table 2
IR Interpretations for Pure drug and Polymers

Functional Groups	Amitriptyline HCl	HEC	HPMC K100	HPC
OH (Alcohols)	3691.88	3632.92	2748.65	3244.38
CH (Alkane)	1315.50	3138.29	3174.94	3091.99
NH (2˚amines)	1116.82	3410.26	2692.72	2357.09
C=C (Alkynes)	2345.52	2359.02	2189.28	2328.16

The drug and polymers were characterized by FTIR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From the results, it was concluded that there was no interference in the functional groups as the principle peaks of the Amitriptyline HCl were found to be unaltered in the spectra of the drug-polymer mixture.

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Differential Scanning Calorimetry

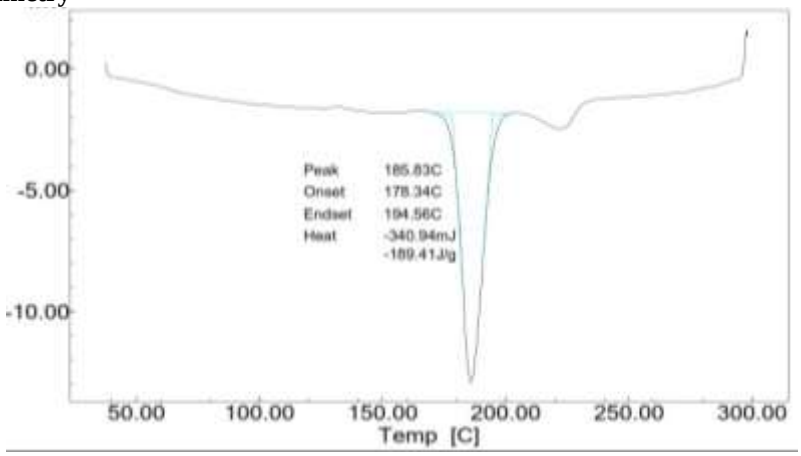

Figure 5
DSC thermogram of pure drug

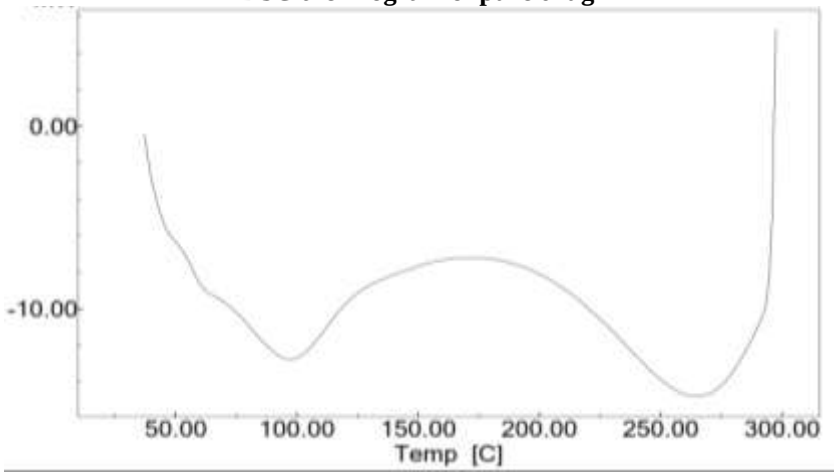

Figure 6
DSC thermogram of HEC

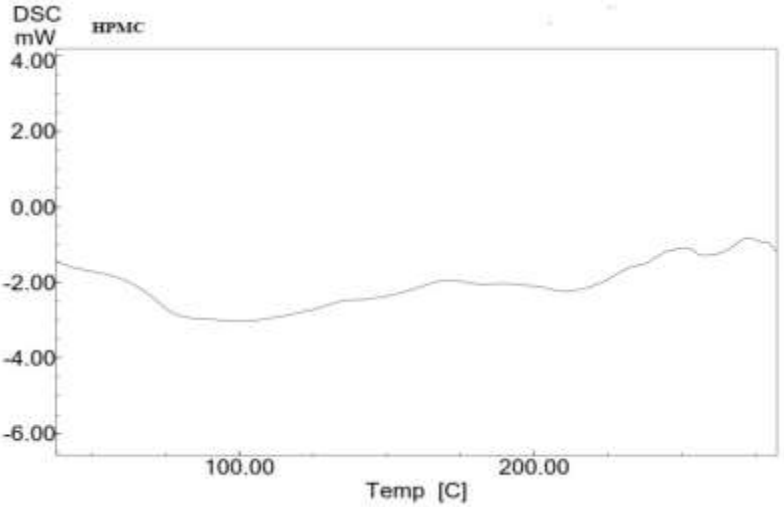

Figure 7
DSC thermogram of HPMC K100

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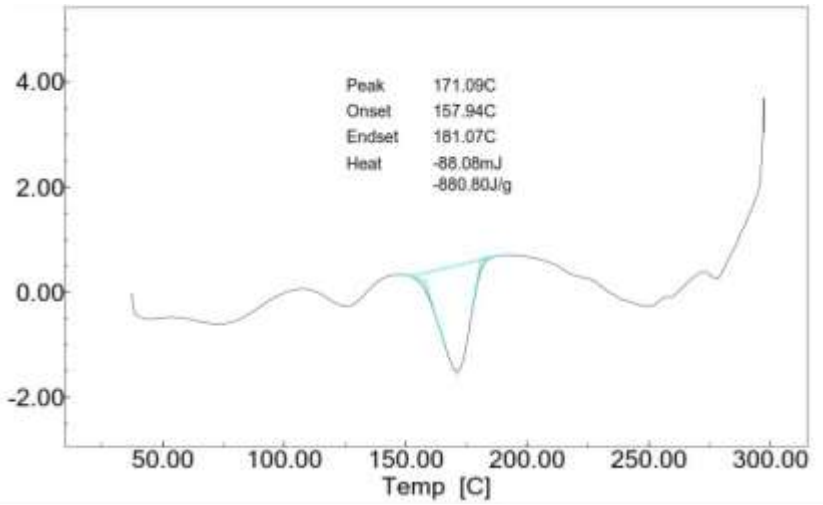

Figure 8
DSC thermogram of HPC

Preparation of mucoadhesive buccal film

The films are preferably formulated using the solvent casting method. The required quantity of polymer was added in small quantities and mixed well to dissolve in distilled water. The small quantity of drug is dissolved in the above solution. Add plasticizers to the above solution and mixed well. The solution was then cast on the Petri dish and kept in a hot air oven for drying at 40° C. After drying films were removed with the help of a sharp blade and kept in a desiccator for 24 hrs then cut into pieces of the desired shape and size.

CHARATERIZATION OF MUCOADHESIVE BUCCAL FILMS

Scanning Electron Microscopy (SEM)

Microscopic characterization of co-crystals:

Microscopic characteristics of prepared co-crystals were observed by light microscope.

Figure 9
Microscopic Images of Co-Crystals

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Morphological characteristics of co-crystals

The shape and surface characteristics of Amitriptyline HCl cocrystal was assessed by Scanning Electron Microscopy (SEM).

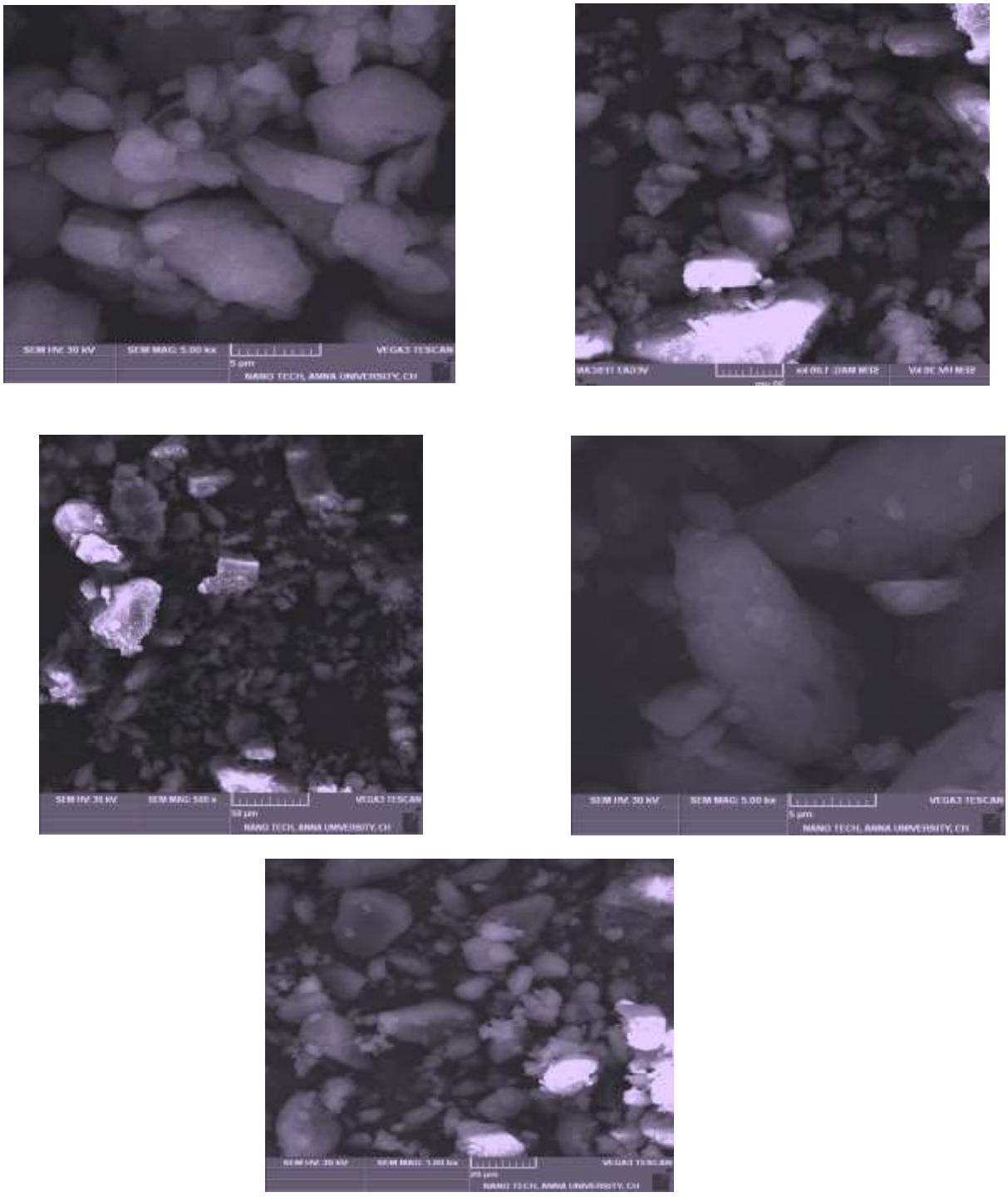

Figure 10
SEM Image of Amitriptyline HCl Cocrystals

IR- Spectroscopy:

The FTIR analysis of the pure drug and Amitriptyline HCl co-crystal was done. IR spectra are as shown in Figure 11.

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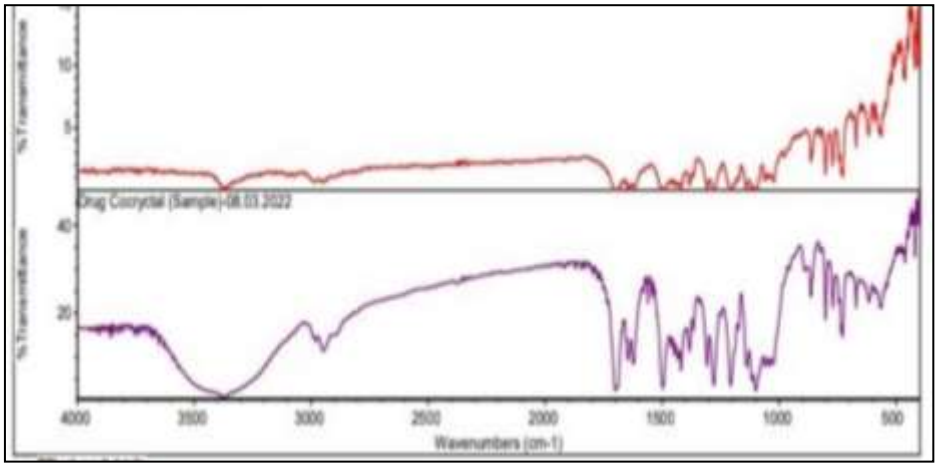

Figure 11
Comparison Between Pure Drug and Drug Cocrystal

FT-IR spectroscopy was used to detect the existence of interaction between Amitriptyline HCl and sorbitol coformer used during the preparation of cocrystal. When hydrogen bonding occurs between Amitriptyline HCl and the coformer, a shift in certain peaks, which OH affected by an interaction, can be observed in Amitriptyline HCl spectra. In Dosulepin HCl, the groups in which hydrogen bonding can occur are the amine group in the ring and the two carbonyl group. When this hydrogen bonding occurs, bond energy at the N-H or C=O bond decrease and peak shift to lower frequencies is observed. This peak shift was most noticeable at the N-H stretch peak at 3376.43cm^{-1}, C-H stretch at 2948.28cm^{-1} and the C=O stretch peak at 1699.72cm^{-1}. These peaks shifting may be the probable group which involved in the bond formation with sorbitol to synthesis co- crystal.

EVALUATION OF MUCOADHESIVE BUCCAL FILMS

Physical appearance and surface texture of films

The overall appearance was found to be clear and transparency was good which Shows that the drug has distributed uniformly.

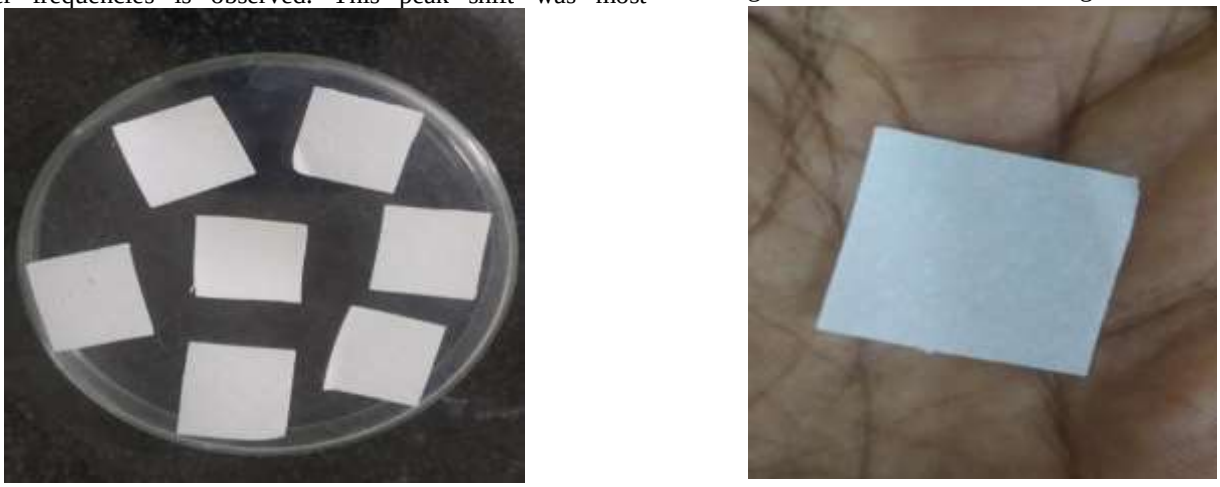

Figure 12
Images of Buccal Film

a. Weight uniformity of films: The weight uniformity of the films mentioned in table in which the values varied between a minimum of 42.63±0.150 to 45.96±0.152.

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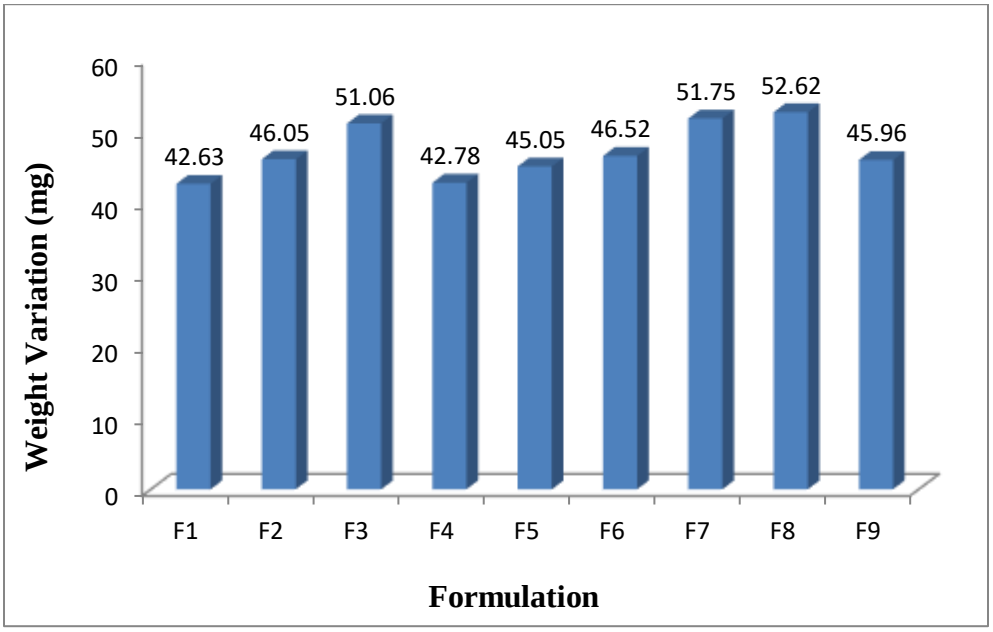

Figure 13
Weight uniformity of the film

b. The thickness of films:

As all the formulations contain different amounts of polymers, the thickness was gradually increased with the number of polymers. All the film formulations were found to have a thickness in the range of 0.12 to 0.19 mm and were observed within the limits.

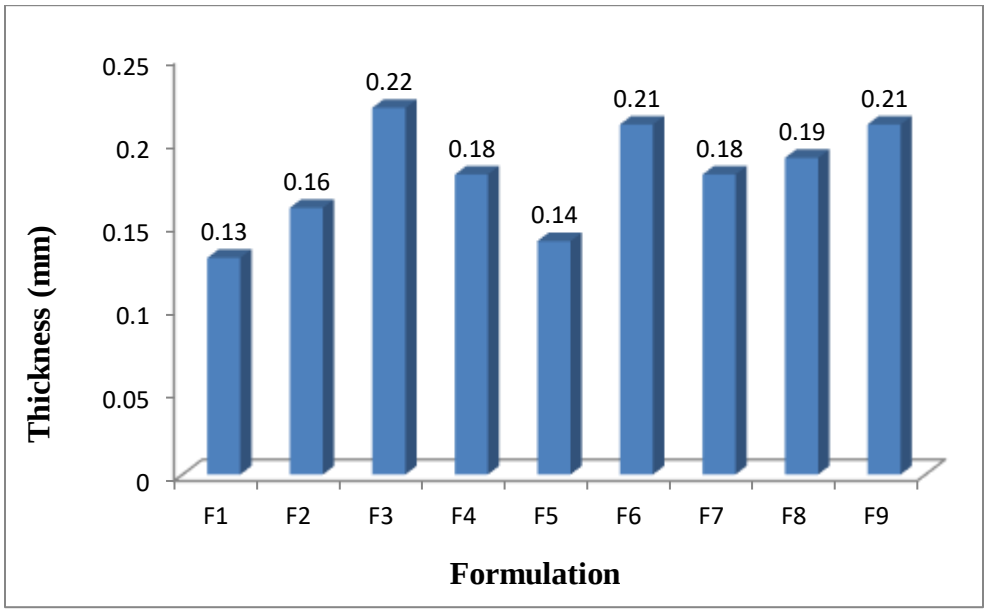

Figure 14
Thickness of the film

c. Folding endurance of patches:

The folding endurance was measured manually, by folding the mucoadhesive buccal film repeatedly at a point till it broke. The breaking time was considered as the endpoint. Folding endurance was found to be highest for F4 and lowest for F2. It was found that the folding endurance of the mucoadhesive buccal films was affected by the increase of carrier concentration. The folding endurance values of the mucoadhesive buccal films were found to be optimum and therefore, the mucoadhesive buccal films exhibited good physical and mechanical properties. The folding endurance of films was found to be in the range of 333 to 321 (Table 14).

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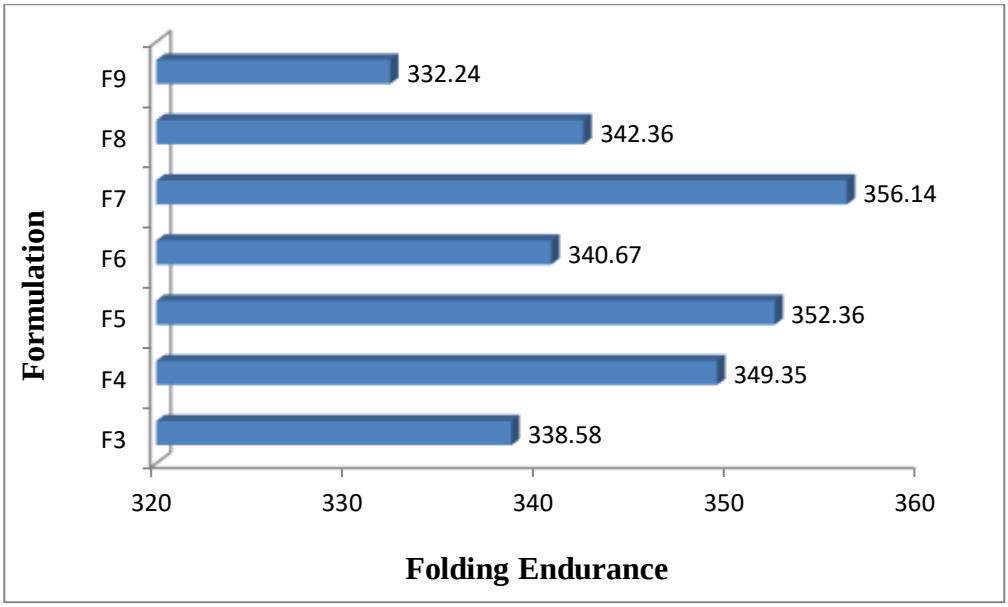

Figure 15
Folding endurance of the film

d. Swelling property

Simulated solution of saliva was prepared to check the swelling property of the patch. The initial weight of the patch was determined and placed in the pre-weighed stainless steel mesh. The system was dipped in the simulated saliva solution. The increase in the weight of the patch was noted by weighing the system at regular intervals. The degree of swelling was determined by the formula. The average swelling was found to be 6.63

$$\text{Degree of swelling} = \frac{[\text{Final weight (Wt)} - \text{Initial weight (Wo)}]}{[\text{Initial weight (Wo)}}$$

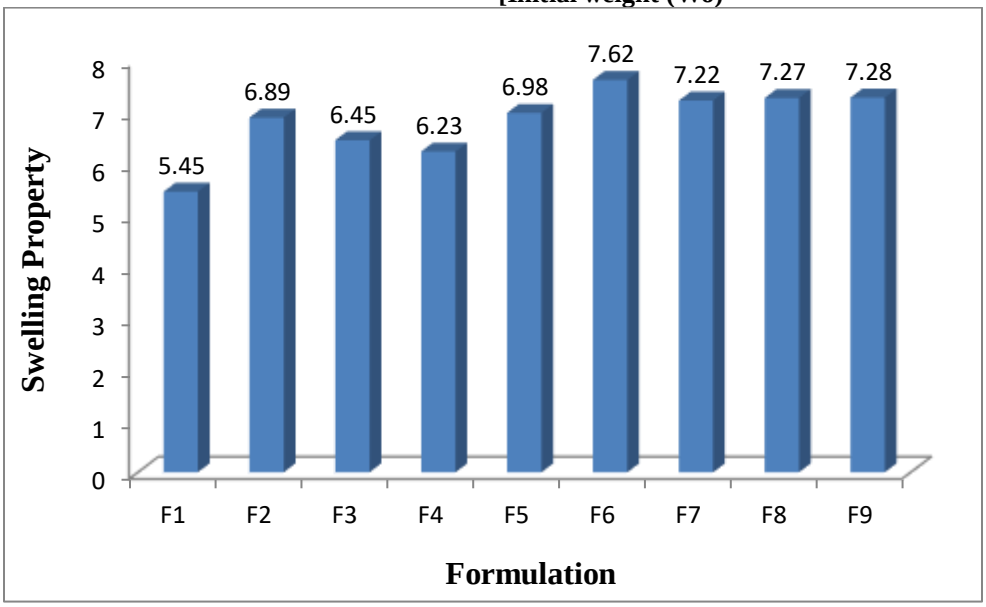

Figure 16
Swelling Property of the film

e. Drug content uniformity of films:

The prepared film formulations were studied for their drug content. The drug was dispersed in the range of 93.76 to 97.43 %. Suggesting that the drug was uniformly dispersed in all films.

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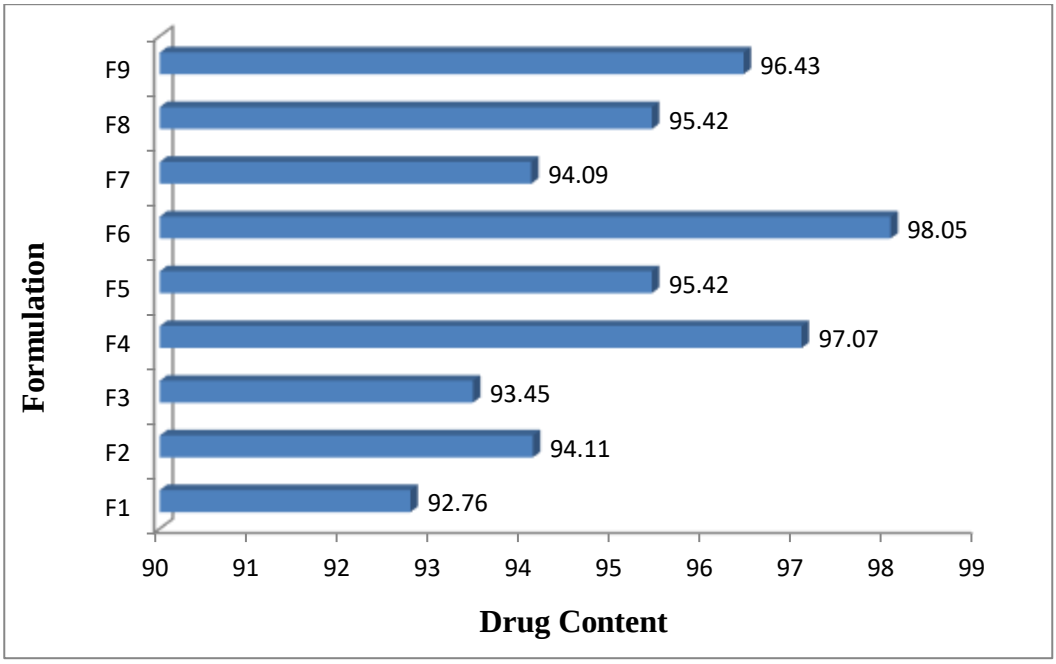

Figure 17
Drug content of the film

f. Surface pH

Patch was slightly wet with help of water. The pH was measured by bringing the electrode in contact with the surface of the patch. The study was performed on three patch of each formulation and average was taken. The surface pH was ranging from 6.4-6.5.

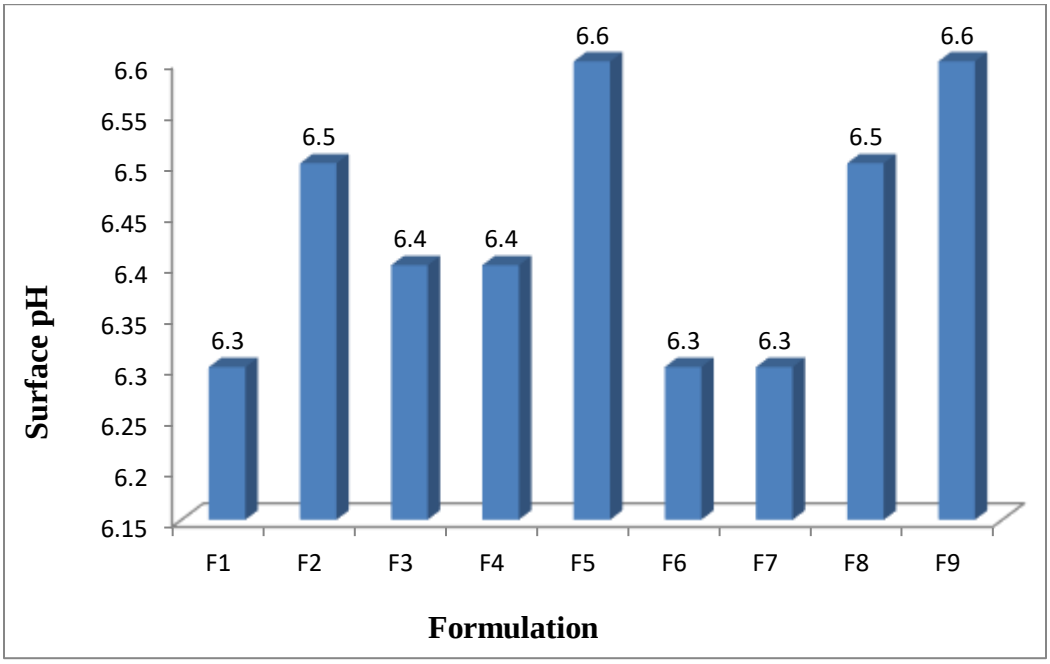

Figure 18
Surface pH of the film

g. Percent moisture loss

It was done to check the integrity of patch at dry condition and hygroscopicity of patch. Three patch of 2 x 2 cm^2 size were cut out and weighed accurately. Then the patch was rested in a desiccator Containing fused anhydrous calcium carbonate. After 3 days the patches are removed, weighed and percentage weight loss are calculated.

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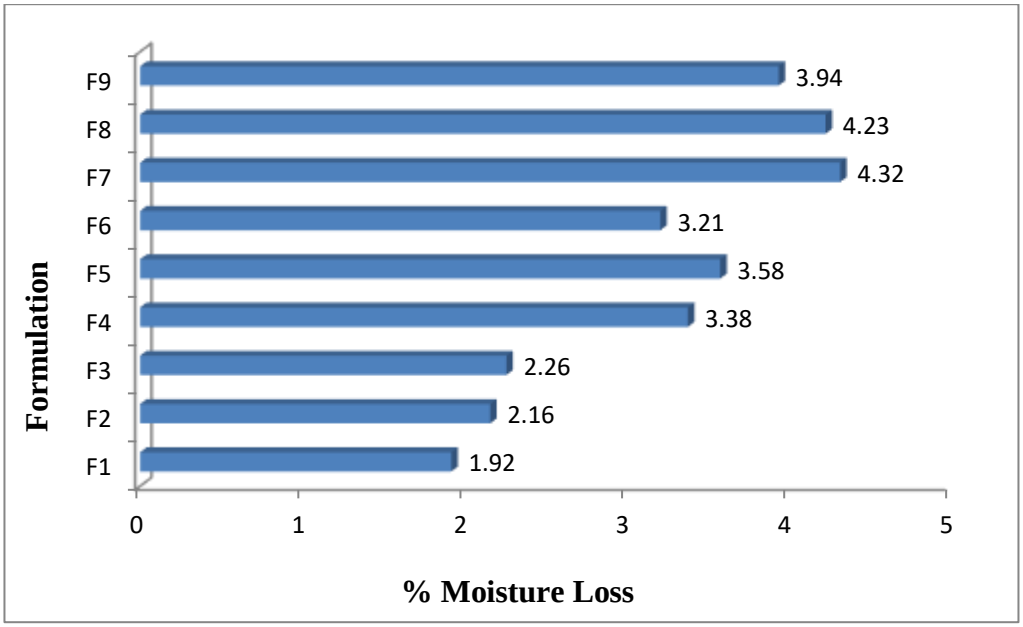

Figure 19
% Moisture Loss of the film

Table 3
Evaluation Parameters data for mucoadhesive buccal films

Formulation Code	Weight variation (mg)	Thickness (mm)	Folding endurance	Swelling Property
F1	42.63±0.150	0.13±0.0107	328.62±1.504	5.45
F2	46.05±0.075	0.16±0.0031	316.62±1.504	6.89
F3	51.06±0.165	0.22±0.0034	338.58±0.508	6.45
F4	42.78±0.178	0.18±0.0052	349.35±1.348	6.23
F5	45.05±0.267	0.14±0.0051	352.36±0.194	6.98
F6	46.52±0.152	0.21±0.0034	340.67±1.348	7.62
F7	51.75±0.176	0.18±0.0035	356.14±0.332	7.22
F8	52.62±0.309	0.19±0.0104	342.36±1.348	7.27
F9	45.96±0.152	0.21±0.0051	332.24±1.668	7.28

Formulation Code	Drug Content	Surface pH	% Moisture Loss
F1	92.76±0.83	6.3	1.92
F2	94.11±1.72	6.5	2.16
F3	93.45±0.48	6.4	2.26
F4	97.07±1.23	6.4	3.38
F5	95.42±1.68	6.6	3.58
F6	98.05±1.24	6.3	3.21
F7	94.09±2.08	6.3	4.32
F8	95.42±2.05	6.5	4.23
F9	96.43±1.68	6.6	3.94

In Vitro Mucoadhesive strength

Mucoadhesive strength was an important property to be determined because it ensures the attachment of dosage form and delivery of drug at the site of administration. The direct relationship between the swelling index and adhesion strength has been described by many authors. Formulation F9 and F6 therefore showed highest bioadhesion due to their highest swelling index, thus ensuring adhesion of patch at the site of administration. On applying factorial design, the quadratic model was suggested by software and found to be significant with model p value F" less than 0.0007 for each term was obtained which indicated that every model term was significant.

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Table 4
In Vitro Mucoadhesive strength data for mucoadhesive buccal films

Formulation	Mucoadhesive Strength
F1	4.6
F2	4.8
F3	6.5
F4	4.3
F5	5.6
F6	6.8
F7	7.3
F8	8.2
F9	9.4

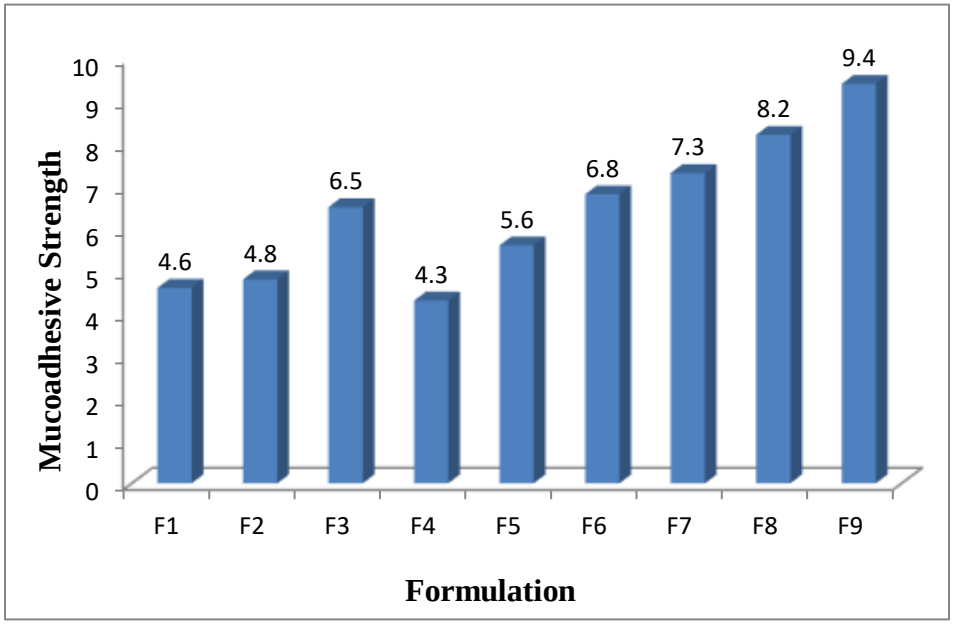

Figure 20
In Vitro Mucoadhesive strength of the film

***In-vitro* dissolution studies:**

Table 5
In-vitro release data of various Amitriptyline HCl mucoadhesive buccal films prepared using HPMC K100, HPC, HEC
Cumulative % drug release from buccal films F1 to F9 prepared from HEC, HPMC K100, HPC

Formulation Code	F1	F2	F3	F4	F5	F6	F7	F8	F9
15 mins	13.96	16.94	19.03	16.78	23.91	25.78	12.42	17.34	18.33
30 mins	28.08	24.08	34.13	31.98	37.05	42.98	28.46	32.47	35.43
1h	41.19	42.18	43.17	43.96	45.97	57.07	47.47	43.49	48.54
2h	48.22	52.21	55.18	55.05	57.08	65.08	54.52	47.54	59.58
3h	52.18	57.24	58.27	68.07	71.14	73.13	62.59	63.56	73.61
4h	64.24	68.28	71.28	72.13	78.16	81.15	68.61	72.62	73.62
5h	75.27	77.32	78.32	83.16	84.12	85.22	78.68	83.64	81.67
6h	79.34	83.32	88.36	91.22	91.21	92.18	84.65	87.72	88.72
7h	87.39	91.37	96.08	97.19	96.17	98.24	92.71	92.68	94.67

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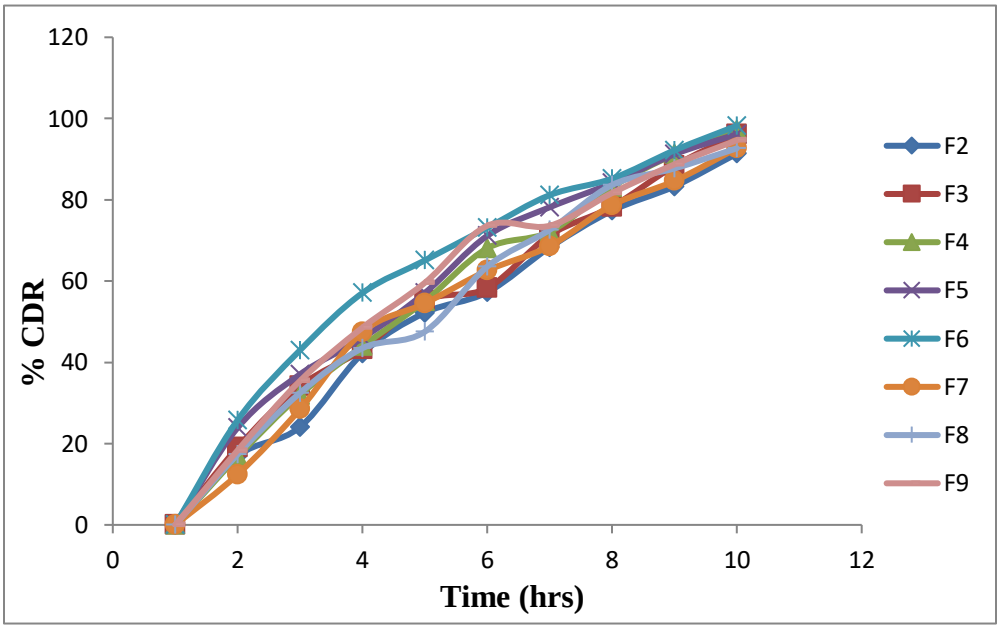

Figure 21
In-vitro release data of various mucoadhesive buccal film of Amitriptyline HCl (F1-F9)

Table 6
Permeability data of films

Formulation Code	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
0.5	18.72	22.82	23.23	26.35	28.54	33.22	24.84	28.08	28.53
1	33.25	36.21	42.08	42.73	46.95	52.85	42.09	45.92	44.92
2	44.08	42.89	45.85	54.98	53.88	59.65	45.91	56.74	58.74
3	47.86	54.72	56.72	63.54	65.18	72.32	56.72	64.56	68.54
4	57.71	62.51	68.54	68.48	74.32	82.18	68.54	72.38	75.32
5	65.52	72.31	79.36	74.33	75.29	85.14	69.52	75.35	82.16
6	72.34	73.34	75.29	83.16	86.13	85.95	77.32	82.18	86.15
7	76.31	86.15	89.13	87.14	88.95	91.97	81.19	85.15	88.97
8	84.16	87.98	88.99	86.95	92.95	97.75	82.13	87.95	92.98

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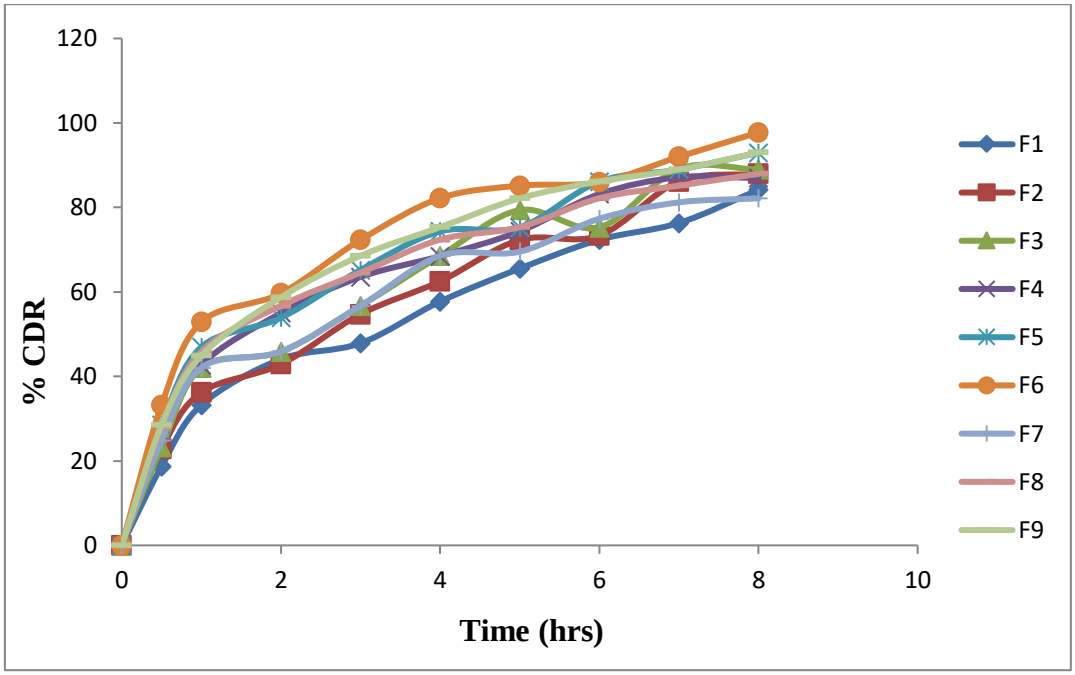

Figure 22
Permeability of various mucoadhesive buccal film of Dosulepin HCl

Table 7
Percentage drug content of optimized formulation F6 during stability studies

Trial No.	1st Day	After 4 weeks	After 6 weeks	After 12 weeks
I	96.22	97.32	97.96	98.15
II	98.26	97.41	98.06	98.06
III	98.23	97.43	98.11	98.18
Mean	98.23 ± 0.02	97.39 ± 0.04	98.04 ± 0.06	98.13 ± 0.05

Table 8
In vitro release data of optimized formulation F6 during stability studies

Time (in hours)	% CDR			
	1 st Day	After 4 weeks	After 6 weeks	After 12 weeks
15m	23.00	24.22	23.84	23.84
30m	43.92	44.46	42.12	43.74
1h	55.94	58.05	55.82	53.86
2h	69.89	69.95	67.96	65.96
3h	76.96	76.85	76.96	74.84
4h	84.26	85.96	83.88	84.89
5h	93.12	92.54	92.87	93.52
6h	95.68	96.88	96.71	98.00

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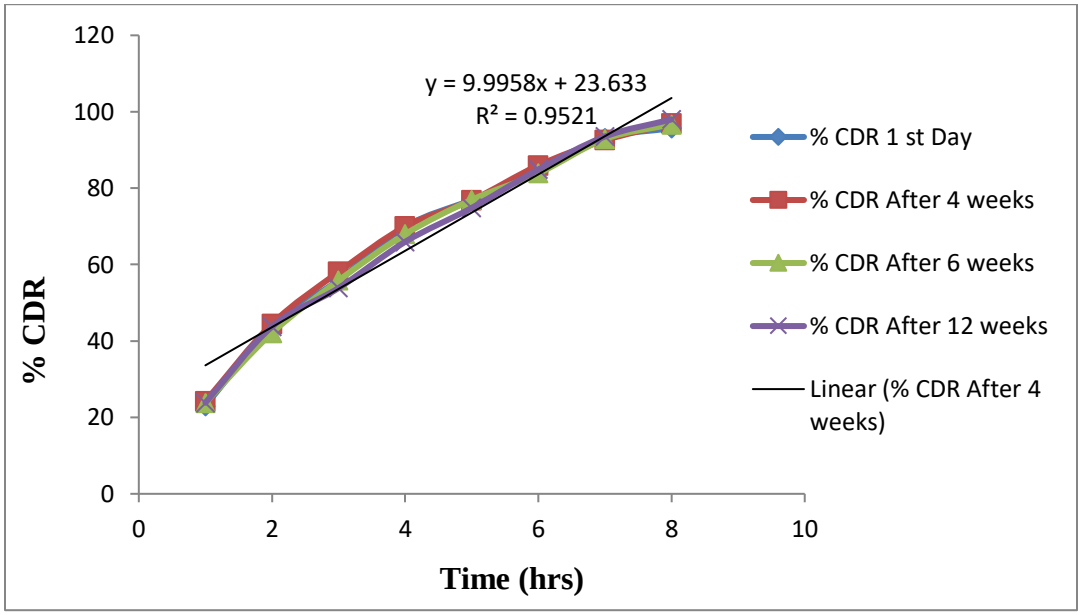

Figure 23
In vitro release of optimized formulation F6 during stability studies

Permeation Kinetics:

The drug release kinetics for the optimized formulation was calculated and the results obtained are presented in table .

Table 9
Release kinetics of Mucoadhesive buccal films of Amitriptyline HCl (F1 to F5)

Model	Equation	F 1		F 2		F 3		F 4		F 5	
		R^2	m	R^2	m	R^2	M	R^2	m	R^2	M
Zero order	Mo-Mt=kt	0.655	69.4	0.939	1123	0.007	15.93	0.202	72.88	0.928	1414
First order	InM=InMo	0.494	0.061	0.540	0.067	0.257	0.038	0.352	0.044	0.438	0.062
Higuchi's Matrix	$M_0-M_t = kt1/2$	0.516	4508	0.767	7420	0.023	212.0	0.189	515.5	0.803	9618
Korsmeyer-Peppar	log (M_0-M_t)= log k + n log$t$	0.835	2.354	0.884	2.545	0.572	1.709	0.663	1.813	0.806	2.517

Table 10
Release kinetics of Mucoadhesive buccal films of Amitriptyline HCl (F6 to F9)

Model	Equation	F 6		F 7		F 8		F 9	
		R^2	m	R^2	m	R^2	M	R^2	M
Zero order	Mo-Mt=kt	0.917	15.49	0.949	154.4	0.932	1603	0.812	1.312
First order	InM=InMo	0.481	0.052	0.465	0.051	0.379	0.060	0.248	0.231
Higuchi's Matrix	$M_0-M_t = kt1/2$	0.798	1057	0.848	1067	0.344	0.057	0.241	0.183
Korsmeyer -Peppar	log (M_0-M_t)= log k + n log$t$	0.835	2.032	0.827	2.033	0.910	11379	0.821	1.257

CONCLUSION

All the formulation showed acceptable quality control property formulation F6 having polymer concentration HPMC K100 showed better drug release rate over 7 hours thus formulation F6 was found to be the most promising formulation based on acceptable evaluation property and the In-vitro drug release rate of 98.24%. Based on the FTIR studies appear to be no possibility of interaction between the Amitriptyline HCl and polymers of other excipients used in the films. DSC Studies was confirmed that there is no interaction between drug and selected polymers. Stability studies were conducted for the optimized formulation as

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per ICH guidelines for 90 days which revealed that the formulation was stable. The result suggests that the developed mucoadhesive buccal film of Amitriptyline HCl could perform better than conventional dosage form leading to improved efficacy and better patient compliance.

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I would like to thank Principal sir (Dr. Kamal Has-san) St. Mary's Group of Institutions, Deshmukhi (Village), Pochampally (Mandal), Yadadri Bhuvanagiri (Dist), Telangana-508284, India.

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REFERENCES

1. *Shipp, L., Liu, F., Kerai-Varsani, L., & Okwuosa, T.C. (2022). Buccal films: A review of therapeutic opportunities, formulations & relevant evaluation approaches. Journal of Controlled Release, 352, 1071-92. https://doi.org/10.1016/j.jconrel.2022.10.058*
2. *Pradeep Kumar, M., & Naga Roopini, B. (2023). Formulation and Evaluation of Mucoadhesive Beads of Dexamethasone. International Journal of clinical Pharmacokinetics and Medical Sciences, 3(2), 63-71. http://dx.doi.org/10.26452/ijcpms.v3i2.504*
3. *Jagtap, V.D. (2020). Buccal film a review on novel drug delivery system. International Journal of Research and Reviews, 7, 17-28. http://www.ijrrjournal.com/*
4. *Dasari, V., Gujjula, P., & Angala Parameswari, S. (2021). Formulation Design and Evaluation of Olmesartan Mucoadhesive Buccal Tablets. Future Journal of Pharmaceuticals and Health Sciences, 1(4), 186-192. http://dx.doi.org/10.26452/fjphs.v1i4.184*
5. *Chatterjee, B., Amalina, N., Sengupta, P., & Mandal, U.K. (2017). Mucoadhesive polymers and their mode of action: A recent update. Journal of Applied Pharmaceutical Science, 7(5), 195-203. http://dx.doi.org/10.7324/JAPS.2017.70533*
6. *Venkateswarlu, I., Viswanatha Reddy, M., Jayashankar Reddy, V., & Ramesh, Y. (2011). Formulation and Evaluation of Fluconazole Transdermal Patches. International Journal of Institutional Pharmacy and Life Sciences, 1(1), 18-29*
7. *Salehi, S., & Boddohi, S. (2017). New formulation and approach for mucoadhesive buccal film of rizatriptan benzoate. Progress in biomaterials. 6, 175-187. https://doi.org/10.1007/s40204-017-0077-7*
8. *Verma S, Kaul M, Rawat A, Saini S. An overview on buccal drug delivery system. International journal of pharmaceutical sciences and research. 2011 Jun 1;2(6):1303. http://dx.doi.org/10.13040/IJPSR.0975-8232.2(6).1303-21*
9. *Rao, N.R., Shravani, B., & Reddy, M.S. (2013). Overview on buccal drug delivery systems. Journal of pharmaceutical sciences and research. 5(4):80.*
10. *Khade, A., Gadge, G., & Mahajan, U. (2020). An overview on natural polymer based mucoadhesive buccal films for controlled drug delivery. International Journal of Pharmacy Research & Technology (IJPRT), 10(1), 48-57. https://doi.org/10.31838/ijprt/10.01.10*
11. *Diaz-del Consuelo, I., Jacques, Y., Pizzolato, G.P, Guy, R.H., & Falson, F. (2005). Comparison of the lipid composition of porcine buccal and esophageal permeability barriers. Archives of oral biology, 50(12):981-987. https://doi.org/10.1016/j.archoralbio.2005.04.008*
12. *Shinkar, D.M., Dhake, A.S., & Setty, C.M. (2012). Drug delivery from the oral cavity: A focus on mucoadhesive. PDA Journal of Pharmaceutical Science and Technology, 66, 466-500. https://doi.org/10.5731/pdajpst.2012.00877*
13. *Ramesh, Y., Anjana, A., Karunasree, M., Manjula Devi, B., Sankeerthana, K., Sri Lakshmi, P., & Vasanthi, A. (2014). Formulation and Evaluation of Atenolol Transdermal Patches. Cre. J. Pha. Res, 2(1), 16-22.*
14. *M.Pradeep Kumar, Karthickeyan Krishnan, Satyabrata Bhanja, Uttam Prasad Panigrahy. (2022). Formulation And Evaluation Of Etodolac Buccal Films By Using Different Polymers And Permeation Enhancers. Chinese Journal Of Medical Genetics, 32(4), 681-687.*
15. *Kumar, R.S., & Nuvati, K. (2019). Mucosal Drug Delivery Systems: An Overview. Journal of Drug Delivery and Therapeutics, 9(4):629-634. https://doi.org/10.22270/jddt.v9i4.3172*