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FORMUALTION AND IN VITRO CHARACTERIZATION OF SUSTAINED RELEAE MUCOADHESIVE BUCCAL TABLET

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Abstract:

Ropinirole HCL is a para-sympathomimetic or cholinergic agent, used to treat mild to moderate dementia caused by Parkinson disease. It is subjected to an extensive hepatic first pass metabolism with systemic bioavailability of 36%. Its short half-life being 3-4 hours. The objective of the present study is to develop sustained release mucoadhesive buccal tablet for Ropinirole HCL to overcome poor bioavailability (below 50%) due to extensive first pass metabolism, poor permeability from the GIT and shorter half-life (2-6 hr.) by reducing the dosing frequency. Direct compression method was used to prepare buccal tablet. The prepared formulations were characterized for pre & post compression studies. The results of FTIR study revealed that there is no physical or chemical interaction between drug and polymer. Formulation Batch C-7 was selected as optimized batch which contain Ropinirole HCL (1 mg), HPMC-K4M (120 mg), HPMC -K100 (140mg), Mannitol (100 mg), Magnesium stearate 2%. The optimized batch was showed evaluation result as, Weight Variation (251.6±1.712), Hardness (8.36±0.05) kg/cm^2, Diameter (12.27±0.115), Thickness (3.12±0.002) mm, Friability (0.50±0.01), Drug Content (98.93±0.92) %, Muccoadhesive strength (38.34±0.205) gm and Muccoadhesive force studies (3.76±0.136) Dyne and cumulative drug release for 8 hours (43.60±0.122). It was concluded that the prepared of Sustained release Muccoadhesive Buccal tablet of Ropinirole HCL may prove to be potential candidate for safe and effective Sustained release drug delivery over an extended period of time which can reduce dosing frequency.

Key World: Buccal Tablet, Polymers, Muccoadhesive tablets, Buccal Administration.

INTRODUCTION:

Among the various routes of drug delivery, oral route is the most suitable and most widely accepted one by the patients for the delivery of the therapeutically active drugs. But, after oral drug administration many drugs are subjected to presystemic clearance in liver, which often leads to a lack of correlation between membrane permeability, absorption and bioavailability. In recent years, significant interest has been shown in the development of controlled drug delivery to, or via mucous membranes by the use of mucoadhesive polymers. Within the oral mucosal cavity, the buccal region offers an attractive route for administration of the drug of choice. Buccal routes of drug delivery offer distinct advantages over oral administration for systemic drug delivery. Such as possible bypass of first pass effect, avoidance of pre-systemic elimination within the GI tract. These factors make the oral mucosal cavity a very attractive and feasible site for systemic drug delivery. Moreover, rapid onset of action can be achieved relative to the oral route and the formulation can be removed if therapy is required to be discontinued. It is also possible to administer drugs to patients who are unconscious and less co-operative Considering the low patient compliance of rectal, vaginal, sublingual and nasal drug delivery for controlled release, the buccal mucosa has rich blood supply and it is relatively permeable.

Mucoadhesive drug delivery systems are delivery systems, which utilize the property of bioadhesion of certain polymers. Bioadhesion is defined as an ability of a material to adhere a particular region of the body for extended period of time not only for local targeting of drugs but also for better control of systemic delivery. Successful buccal drug delivery using buccal adhesive system requires at least three of the following.

(a)A mucoadhesive to retain the system in the oral cavity and maximize the in timacy of contact with mucosa,

(b) A vehicle that release the drug in a controlled fashion under the condition sprevailing in them out hand

(c) Strategies for overcoming the low permeability of the oral mucosa.

The buccal mucosa lines the inner check and buccal formulations are placed in them out between the upper gingival (gums) and cheek to treat local and systemic conditions. The buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotides and polysaccharides, as well as conventional small drug molecules. Various mucoadhesive devices such as tablets, film, patches, discs, strips, ointments and gel have been recently developed.[5]

1. Oral Mucosal Sites [2,3,4] :Within the oral mucosal cavity, delivery of drugs is classified into three categories,
2. Sublingual Delivery: is the administration of the drug via the sublingual mucosa (the membrane of the ventral surface of the tongue and the floor of the mouth) to the systemic circulation.
3. Buccal Delivery: is the administration of drug via the buccal mucosa (the lining of the cheek) to the systemic circulation.
4. Local Delivery: for the treatment of conditions of the oral cavity, principally ulcers, fungal conditions and periodontal disease

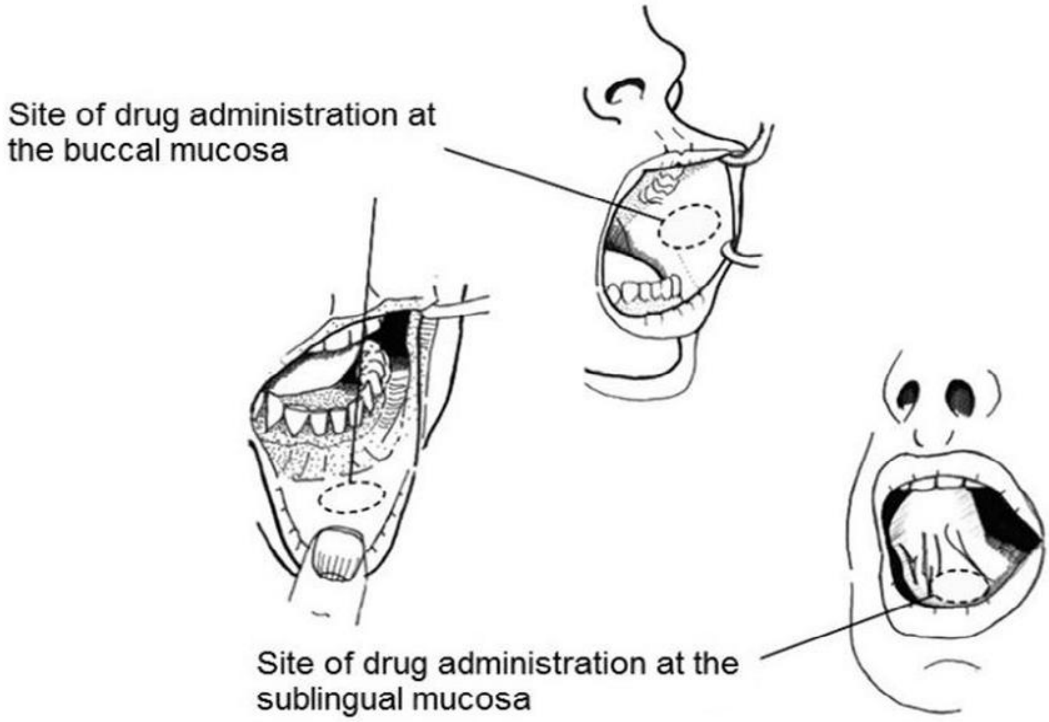


Figure1. The administration of tablet via buccal route

5. Advantages of Buccal Drug Delivery System [2,3,4]

The advantages of buccal drug delivery system are[2]

1. Enhancement of Bioavailability:

   Oral route is the most suitable and most widely accepted one by the patients for the delivery of the therapeutically active drugs. But, after oral administration many drugs are subjected to presystemic clearance in liver, which often leads to decreased in oral bioavailability. The buccal drug delivery system enhance the oral bioavailability by avoiding the first pass hepatic metabolism of the drug and providing the intimate contact between tablet and the buccal mucosa,resulting there by in high drug flux and reduce the amount of drug required to achieve therapeutic efficacy. Therefore drugs, which show poor bioavailability via the oral route, can be administered conveniently.

   Ex. Drugs, which are unstable in the acidic environment of the stomach or are destroyed by the enzymatic oral alkaline environment of the intestine.

2. Sustained Drug Delivery: -

   Some active pharmaceutical ingredients' (API's) have intrinsically long halflives and are thus inherently long lasting and may only require once daily oral dosing to achieve a suitable therapeutic effect. However the vast majorities of API'shave relatively short half-lives and are thus shorter acting and require multiple daily dosing from conventional immediate release dosage forms to achieve a constant and sustained therapeutic effect. If doses are administered too frequently minimum toxic concentrations may be reached with the result that unwanted side effects become prevalent, whereas infrequent dosing may lead to sub-therapeutic blood levels being achieved. The term sustained release is a broad expression that describes drug delivery in systems where the API is released in a controlled manner, at a predetermined rate, duration or location to achieve and

maintain optimum therapeutic blood levels of an API. The API is either dispersed in a soluble or insoluble matrix or as solid particles, or as a solution that has been encapsulated by an outer rate controlling polymeric membrane from which the drug will be release in a controlled fashion.

3. Rapid Onset of Action:

   A relatively rapid onset of action can be achieved relative to the oral route and the formulation can be removed if therapy is required to be discontinued. The buccal mucosa has rich blood supply and is relatively permeable and large contact surface of the oral cavity contributes to rapid and extensive drug absorption. The extent of perfusion is more therefore quick and effective absorption is possible. It is useful particularly for administration of antianginal drugs.

4. Improved Patient Compliance:

   Poor patient compliance increases the chances of missing the dose of a drug with short half life for which frequent administration is necessary. The buccal drug delivery systems have added advantages over immediate release dosage form. These include reduction of dosing frequency by administering the drug once or twice a day. Since thefrequency of drug administration is reduced, patient compliance can be improved and drug administration can be more convenient due to reduction of gastrointestinal side effects. Also causes less fluctuation of plasma drug level and leads to more uniform drug effect and lesser total dose. Improve the patient compliance due to the elimination of pain associated with injections. Nausea and vomiting are greatly avoided.

5. Increased Ease of Drug Administration: -

   The buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotides and polysaccharides, as well as conventional small drug molecules. Easy access to the membrane sites so that the delivery system can be applied, localized and removed easily.

6. Reduction of GI Irritation:

   Several drugs cause irritation and damage to the gastric mucosa through direct contact, increased stimulation of acid secretion or through interference with the protective mucosal layer

   e.g. NSAIDs, especially the salicylates.

   Such problems can be overcome by non-exposure of the drugs to the gastrointestinal fluids.

7. Enhancement of Solubility and Dissolution Rate:-

   Presence of saliva facilitates both drug dissolution and subsequent permeation by keeping the oral mucosa moist. The buccal mucosa has been supplied with dense network of blood capillaries and having large contact surface of the oral cavity contributes to rapid and extensive drug absorption. Moreover the use of permeation enhancers in buccal dosage forms enhances the solubility and dissolution rate through the buccal mucosa.

8. High Margin of Safety: -

   Increased margin of safety of highly potent drugs due to better control of plasma levels. Reduction in fluctuation in steady state levels and thus maintaining drug concentration within a therapeutically effective window, therefore better control of disease condition and reduced intensity of local or systemic side effects.

Can be used in case of unconscious and less co-operative patients.

9. Economical: - Reduction in health care costs through improved therapy, shorter treatment period, less frequency of dosing and reduction in personnel time to dispense, administer and monitor patients made the buccal drug delivery systems cheaper.

10. Limitations of Buccal Drug Delivery System [2,3,4] The limitations of buccal drug delivery system are:

- ❖ Low permeability of the buccal membrane, specifically when compared to the sublingual membrane results in low bioavailability. The buccal mucosa is considerably less permeable than the sublingual area, and is generally not able to provide the rapid absorption and good bioavailability seen with sublingual administration. The total surface area of the membranes of the oral cavity available for drug absorption is 170 cm^2 of which -50 cm^3 represents non-keratinized tissues, including buccal membrane.
- ❖ One of the major disadvantages associated with buccal drug delivery is the low flux which results in low drug bioavailability. Various compounds have been investigated for their use as buccal penetration enhancers in order to increase the flux of drugs through the mucosa. Since the buccal epithelium is similar in structure to other stratified epithelia of the body, enhancers used to improve drug permeation in other absorptive mucosa have been shown to work in improving buccal drug penetration.
- ❖ Only those drugs which are absorbed by passive diffusion can be administered by this route. e.g. Small molecules such as butyric acid and butanol, ionizable low molecular weight drugs such as acyclovir, propranolol, Rivastigmine and salicylic acid, large molecular weight hydrophilic polymers such as dextrans, and a variety of peptides including octreotide, leutinizing hormone releasing hormone (LHRH), insulin, and interferon have all been studied.
- ❖ Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug

and ultimately the involuntary removal of the dosage form. The continuous secretion of the saliva (0.5-2 1/day) leads to subsequent dilution of the drug.

- ❖ The patient cannot eat/drink/speak.

- **OBJECTIVES:**

The objectives of present study are as follows;

1. To screen and select suitable polymer for buccal drug delivery.

2. To prepare buccoadhesive tablets using suitable polymer.

3. To perform in vitro characterization for buccoadhesive tablets.

4. To study mucoadhesive time for buccoadhesive tablets.

5. To perform dissolution study and observe release profile of buccoadhesive tablet.

❖ **DRUG PROFILE:**

- **Ropinirole hydrochloride –** Ropinirole hydrochloride is the hydrochloride salt form of ropinirole, a non - ergot dopamine agonist with antiparkinsonianproperty. Acting as a substitute for dopamine, Ropinirole hydrochloride bindsand activates dopamine D_2 and D_3 receptors within the caudate putamen in the brain, thereby improving motor function. Ropinirole hydrochloride is used alone or with other medicines to treat parkinson's disease. Ropinirole tablets are also used to treat a condition called Restless Legs Syndrome.
- **Synonyms –** ReQuip
- **Chemical Structure -**

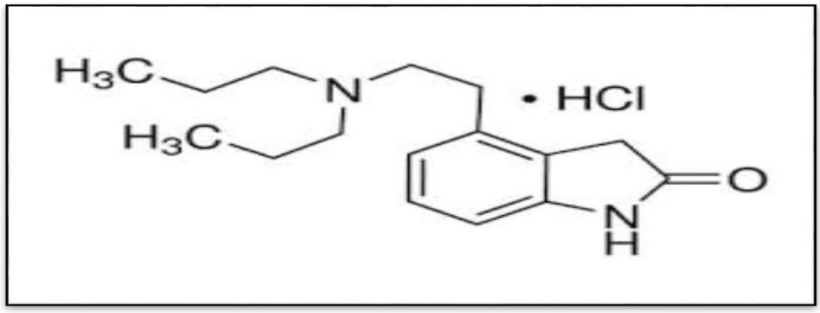


Figure No. 1 – Structure of Ropinirole Hydrochloride

- **Chemical Name –** 4-[2-(dipropylamino)ethyl]-1,3-dihydroindol-2-one
- **Category –** Ropinirole hydrochloride belongs to the class called dopamineagonists.
- **Molecular Formula –** $C_{16}H_{24}N_2O.HCl$
- **Molecular Weight –** 296.83 g/moles
- **Melting Point –** 243 – 250°C
- **Description –**
- **Colour –** Off White to Yellow
- **Odour –** Odourless
- **Texture –** Fine Powder

❖ **Method and Material :**

❖ **Material :**

Ropinirole hydrochloride are collected as a gift sample from Alembic pharmaceuticals limited, Vadodara and HPMC K4M, HPMC K15M, HPMC K100M all are collected from Colorcon Asia Pvt.Ltd., Goa. And microcrystalline cellulose, Magnesium stearate, Mannitol,Talc are collected from S. D. Fine chemicals Ltd. Mumbai.

❖ **Method:**

- **Selection of Method: -**

  Preparation Of Muccoadhesive Buccal Tablet was done by Direct Compression Method. Direct compression method can prepare good buccal tablet as compare to wet granulation technique.

- **Selection of polymers:**

  For the preparation of Mucoadhesive Buccal tablet large amount of synthetic as well as natural polymers are available. From that polymer we use natural polymer HPMC, Mannitol, MCC. This polymer gives good Sustained release of drug and mucoadhesive property as compare to the other polymer.

- **Selection Of Directly compressible Diluent :**

  In Mucoadhesive Buccal Tablet we use Microcrystalline Cellulose as Directly Compressible Diluent. It will give good compressible property.

- **Selection of Glidants:**

  In mucoadhesive buccal tablet we use talc as Glidants.

- **Selection of sweetening agent:**

  In Mucoadhesive buccal tablet we use mannitol as sweetening agent.

- **Preliminary batch for formulation of mucoadhesive buccal tablet:**

  Mucoadhesive Buccal tablets of Ropinirole hydrochloride were prepared by a direct compression method. Before going to direct compression, all the ingredients (drug, polymers, and excipients) were screened through sieve no. 60. All the ingredients were thoroughly blended in a glass mortar with a pestle for 15 minutes. After sufficient mixing magnesium stearate was added and again mixed for additional 2-3 minutes. The mixture is compressed using a g 9mm punch on a rotary tablet punching machine.

1. Weighing: – The amount of API Ropinirole hydrochloride and excipients required for the batch of tablet formulation were weighed using electronic weighing balance.
2. Screening: After weighing the Ropinirole hydrochloride and excipients were passed through sieve no. 60 to break agglomerates if any are present in the raw materials for uniform distribution.
3. Mixing: All polymer and excipients except magnesium stearate and talc were mixed manually with metoprolol succinate (API) by using a mortar pestle.
4. Blend lubrication: The prepared blend was lubricated using magnesium stearate and talc in a mortar pestle for 15 minutes.
5. Compression: The prepared blend was compressed using a standard 9 mm round, flat punch.

➢ **Factorial Batch: -**

A factorial design is used to evaluate two or more factor simultaneously. The treatment is combination of level of factors. The advantages of factorial design over one factor at-a-time experiments includes their efficiency and deletion of interaction. Intervention studies with two or more categorical explanatory variable leading to numerical outcome variable with two or more value refers as levels. A study in which there are two factors with theirs three levels called 32 factorial was selected. The two independent variables were selected HPMC K4M (X1) and ratio of HPMC K4M: HPMC K100M(X2) nine formulations formulated as per experimental design.

Table No: Amount of variable in factorial designs batches

Coded Val	**Actual Value**	
	X1 **HPMC K4M**	**X2** **HPMC K100M**
-1	**70**	**100**
0	**90**	**120**
+1	**120**	**140**

Table No. : - Experimental Design

Formulation Code	**Coded value**	
	X1	**X2**
F1	-1	+1
C8	-1	0
F3	-1	-1
F4	0	+1
F5	0	0
F6	0	-1

F7	+1	+1
F8	+1	0
F9	+1	-1

➢ **Factorial Batch of Formulation for Sustained Release Mucco- adhesive Buccal Tablet:**

- **Formulation of sustained Release Mucoadhesive Buccal Tablet By using of different polymer.**

Name of Ingredient	**Quantity taken (mg)**								
	C1	C2	C3	C4	C5	C6	C7	C8	C9
Drug	1	1	1	1	1	1	1	1	1
HPMC K4M	70	70	70	90	90	90	120	120	120
HPMC K 100M	100	120	140	100	120	140	100	120	140
Mannitol	100	100	100	100	100	100	100	100	100
Microcrystalline cellulose	10	8	5	10	8	5	10	8	5
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
Total	290	310	330	310	330	350	340	360	380

➢ **Evaluations –**

1. Pre – compression study:

- **Determination of Bulk density-**

Apparent bulk density can be determined by pouring preserved bulk powder into a graduated measuring cylinder via a large funnel and measuring the volume and weight of the powder. Bulk density can be calculated by the following formula.[88]

Where,

V_o – Bulk Volume

$$\text{Bulk Density} = \frac{\text{Weight}}{\text{Bulk Volume (Vo)}}$$

- **Determination of Tapped density-**

Tapped density can be determined by pouring preserved powder into a graduated measuring cylinder via a large funnel and tapping 100 times on a wooden plank and measuring the volume and weight of the powder. Tapped density can be calculated by the following formula.[88]

$$\text{Tapped Density} = \frac{\text{Weight}}{\text{Tapped Volume (Vt)}}$$

Where,

V_t – Tapped Volume

1. Compressibility Index (or) Carr's index (I) –

An indirect method of measuring powder flow from bulk densities was developed by Carr. The percentages compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability. Carr's index of each formulation was calculated according to the equation given below.[88]

$$\text{Carr's Index (\%)} = \frac{TD - BD}{TD} \times 100$$

Where,

TD = Tapped density BD = bulk density

2. Hausner's ratio –

Hausner's ratio indicates the flow properties of the powder and is measured by the ratio of Tapped density to bulk density. It is the ratio of tapped density and bulk density. Hausner's found that this ratio was related to interparticle friction and, as such, could be used to predict powder flow properties. Generally, a value less than 1.25 indicates good flow properties, which is equivalent to 20% of Carr's index.[88]

$$\text{Hausners Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

1. Angle of repose-

The angle of repose is the maximum angle that the plane of powder makes with the horizontal surface on rotation. The angle of repose is helpful in the assessment of flow properties of particles which could be further related to packing densities and mechanical arrangements of particles. The angle of repose of granules was determined by the fixed funnel and free-standing cone method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surfaces. The diameter of the powder cone was measured and the angle of repose was calculated using the following equation[88].

$$\text{Tan } \theta = \frac{h}{r}$$

Where,

h = height of the powder heap

r = radius of the powder heap

θ = is the angle of repose

4.4.4.3 Post Compression Parameters:

1. Weight Variation-

Twenty tablets are selected at random, individually weighed in a single pan electronic balance and the average weight is calculated. The uniformity of weight is determined according to I.P. specification. As per IP not more than two of individual weights should Deviate from average weight by more than 5% and none deviate more than twice that Percentage.[88]

2. Hardness-

The Monsanto hardness tester was used to determine the hardness of the tablet. The tablet was held between a fixed and moving jaw. The scale was adjusted to zero; the load was gradually increased until the tablets fractured. The value of the load at that point gives a measure of the hardness of the tablet. Tablet requires a certain amount of strength or hardness and resistance to friability to withstand mechanical shocks of handling in manufacture, packing, and shipping. Three tablets from each batch are used for the hardness test and the results are expressed in Kg/cm2.[88]

3. Friability-

Friability is the measure of tablet strength. Roche-type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed and the percentage loss was determined.[88]

$$\% \text{ Friability} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Final Weight}} \times 100$$

4. Thickness-

The thickness of three randomly selected tablets from each formulation was determined in mm using a Digital thickness tester. The average values were calculated.[88]

5. Drug Content Uniformity-

Ten tablets from each formulation were taken, crushed, and mixed. From the mixture 10 mg of Ropinirole hydrochlorideequivalent of the mixture was extracted thoroughly with 100 mL of pH 6.8 phosphate buffer. The amount of drug present in each extract was determined using a UV spectrophotometer at 279 nm. This procedure was repeated thrice and this average was chosen.[88]

$$\% \text{ Drug Content} = \frac{\text{Absorbance}}{\text{Weight Taken}} \times 100$$

4.4.4.4 Bioadhesive Parameters

1. Surface pH-

The microenvironment pH (surface pH) of the buccal tablets was determined to investigate the possibility of any side effects in vivo. As an acidic or alkaline pH may irritate the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible. A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping it in contact with 5 mL of distilled water (pH 6.5 ± 0.05) for 2 h at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablets and allowing it to equilibrate for 1 min.[88]

2. Mucoadhesive Strength-

Mucoadhesive strength of the tablet was measured on a modified physical balance. The fresh goat buccal mucosa was collected from a local slaughterhouse and used within 2 h of slaughter. Cut into a piece of 3 cm and washed with phosphate buffer pH 6.8. A piece of buccal mucosa was stuck to the inverted 50ml beaker which is placed in the center of a 250ml beaker containing phosphate buffer (pH 6.8). The tablet was stuck to the lower side of the glass vial with cyanoacrylate adhesive. Two pans of the balance were balanced with 5 gm weight on the right-hand side pan. A weight of 5 gm was removed from the right- h a n d side pan, which lowered the pan along with the tablet over the mucosa. The balance was kept in this position for 5 min. contact time. The water was added slowly by hand (100 drops/min.) to the right-hand side pan until the patch detached from the mucosal surface. The weight in grams required to detach the tablet from the mucosal surfaces gave the measure of mucoadhesive strength. The weight, in grams, needed to detach the tablet from the mucosal surface (goat buccal mucosa) results in the measure of mucoadhesive strength. The following parameters were calculated from the mucoadhesive strength. [88]

Force of adhesion (N) = (Bioadhesive strength/1000) × 9.81

3. Mucoadhesive Time

A USP disintegration device was used to determine the in vitro residence time. The disintegration media was 500 ml of pH 6.8 phosphate buffer kept at 370.5°C. A 3 cm long goat buccal mucosa was pasted to the surface of a glass slab and vertically affixed to the equipment. The mucoadhesive patch was hydrated from one surface with 15l pH 6.8 PB before being brought into contact with the mucosal membrane. The glass slab was secured vertically to the apparatus and allowed to move up and down so that the patch was entirely submerged in the buffer solution at the lowest position and was completely out at the highest point. The amount of time required for complete erosion or separation of the patch of each set of the mucosal surface.[88]

4.4.4.1 In - Vitro Drug Release Studies-

Dissolution characteristics of the formulated Bucco-adhesive tablets of Ropinirole hydrochloridewere carried out using USP Type II (paddle) dissolution test Apparatus for 8 hrs. Method: 500 ml of 6.8 phosphate buffer was filled in the dissolution vessel and the temperature of the medium is set at 37°C ± 0.5°C. One tablet of the different batch is placed in each dissolution vessel and the rotational speed of the paddle was set at 50 pm. 10 ml of sample is withdrawn at a pre-determined time interval of every one hour for up to 8 hours and the same volume of fresh medium is replaced immediately. The withdrawn sample is diluted to 10 ml in a volumetric flask and filtered through a 0.45µ membrane filter. [88]

4.4.4.1 In Vitro drug permeation study-

The extent and rate of mucosal permeation of ropinirole hydrochloridethrough the goat buccal mucosa were carried out using Franz diffusion cell. The effective diffusion area was 1.8 $cm^{2.}$ The receptor compartment (40 ml) was filled with PBS, pH 7.4, and its temperature was maintained at 37 ± 0.5°C. A 50 rpm stirring speed was applied usinga magnetic stirrer to simulate a buccal cavity environment. The patch was applied underocclusion on the buccal mucosal surface of the goat fitted between the donor and receptor compartments of the diffusion cell. Five milliliters of the sample from the receptor medium were withdrawn at regular intervals and replaced immediately with an equal volume of PBS, pH 7.4. The amount of ropinirole hydrochloridereleased into the receptor medium was quantified by using UV–a visible spectrophotometer at 274 nm against a blank.[88]

4.4.4.1 Swelling Study-

Swelling of tablet excipient particles involves the absorption of a liquid increasing weight and volume. Liquid uptake by the particle may be due to saturation of capillary spaces within the particles or hydration of macromolecule. The liquid enters the particles through pores and binds to large molecules, breaking the hydrogen bond and resulting in the swelling of particles. The extent of swelling can be measured in terms of % of weight gain by the tablet. [88]

$$\text{Swelling Index} = \frac{Wt - Wo}{Wo}$$

Where S.I. = Swelling index Wt = Weight of tablet at time t

Wo = Weight of tablet before placing in the beaker

4.4.5 KINETICS DRUG RELEASE

In vitro dissolution has been recognized as an important element in drug development, to analyze the mechanism for the release and release rate kinetics of the formulated dosage form, the data obtained from conducted studies were fitted into zero-order, first-order, Higuchi matrix, Korsmeyer - Peppas and Hixson Crowell model. By comparing the r – values obtained, the best fit model was selected.

1. Zero-order kinetics -

The following equation represents 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.

Qt = Qo + Kot

Where Qt = amount of drug dissolved in

time t, Qo = initial amount of drug in the solution

and Ko = zero-order release constant.

This relation can be used to describe the drug dissolution of several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems, as well as matrix tablets with low soluble drugs, coated forms, osmotic systems, etc. The pharmaceutical dosage forms following this profile release the same amount of drug by a unit of time and it is the ideal method of drug release to achieve a pharmacological prolonged action. To study the release kinetics, data obtained from in vitro drug release studies were plotted as the cumulative amount of drug release versus time.[89]

2. First-order kinetics –

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

Log Qt = log Q0 + K1t / 2.303

Where Qt = amount of drug released in time t, Q0 = initial amount of drug in the solution and K1 = first-order release rate constant.

The pharmaceutical dosage forms following this dissolution profile, such as those containing water-soluble drugs in porous matrices release the drug in a way that is proportional to the amount of drug released by a unit of time diminished. The data obtained are plotted as a log cumulative percentage of drug remaining versus time which would yield a straight line with a slope of –k/2.303. [89]

3. 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 media. To study the Higuchi model the release rate was fitted to the following equation,

Qt = KH t1/2

Where, Qt = amount of drug released in time t and KH = Higuchi dissolution constant.

Higuchi describes drug release as a diffusion process based on Fick's law, square root time- dependent. This relation can be used to describe the drug dissolution from several types of modified release pharmaceutical dosage forms, as in the case of some transdermal systems and matrix tablets with water-soluble drugs. The data obtained were plotted as cumulative percentage drug release versus square root of time. [89]

4. Korsmeyer – Peppas model –

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

Mt /M∞ = k.tn

Where Mt /∞ = fraction of drug released at time t, K = release rate constant and n = release exponent.

In this model, the value of n characterizes the release mechanism of the drug. For the case of cylindrical tablets, 0.45< n corresponds to a Fickian diffusion mechanism, 0.45 < n < 0.89 to non – Fickian transport, n = 0.89 to case II (relaxation) transport, and n > 0.89 to super case II transport. To find out the exponent of n the proportion of the release curve, where Mt / M, < 0.6 should only be used. To study the release kinetics, data obtained from in vitro drug release studies were plotted as long cumulative percentages of drug release versus log time. [89]

5. Hixson – Crowell model –

To study the Hixson - Crowell model the release rate data are fitted to the following equation, W01/3- Wt1/3 = st

Where W0 = initial amount of drug in the pharmaceutical dosage form, Wt = remaining amount of drug in the pharmaceutical dosage form at time t, Ks = constant incorporating the surface–volume relation.

This expression applies to pharmaceutical dosage forms such as tablets, where the dissolution occurs in planes that are parallel to the drug surfaces if the dimensions of the tablet diminish proportionally, in such a manner that the initial geometrical form keeps constant all the time. To study the release kinetics, data obtained from in vitro drug release studies were plotted as the cube root of drug percentage remaining in the matrix versus time. [89]

4.4.5.1 Stability Study

The stability of the drug has been defined as the ability of a particular formulation, in a specific container, to remain within its physical, chemical, therapeutic, and toxicological specifications. A drug formulation is said to be stable if it fulfills the following requirements,

- It should contain at least 90% of the stated active ingredient.
- It should contain an effective concentration of added preservatives if any.
- It should not exhibit discoloration or precipitation, nor develops a foul odor.

The purpose of stability testing is to provide evidence on how the quality of a drug substance varies with the time under the influence of a variety of environmental factors such as temperature, humidity, and light and enables recommended storage conditions, retest periods, and shelf lives to be established.

International Conference on Harmonisation (ICH) specified the length of study and storage conditions as,

Long term testing – 25°C ± 2°C / 60 RH ± 5% for 12 months. Accelerated testing – 40°C ± 2°C / 75 RH ± 5% for 6 months.

In the present study, a stability study was carried out at 40°C ± 2°C / 75 RH ± 5% for 28 days (4 weeks) for the optimized formulation. The optimized formulation was analyzed for the drug entrapment efficiency, In vitro drug release study, and % Drug content.[90]

The parameters for the stability study are,

1. Physical appearance
2. Drug content
3. Lag time
4. In vitro drug release

Prepared buccoadhesive tablets were evaluated for stability study as per the procedure discussed in section **4.4.4.2.6**. The stability study was shown in **Table no. 14** at **40°C ± 2°C / 75 ± 5% RH, Table no. 27** at **25°C ± 2°C / 75 ± 5% RH** and **Table no. 28** at **10°C ± 2°C / 75 ± 5% RH**, discussed in section **5.2.8.**

RESULTS AND DISCUSSION:

- **Characterization of Ropinirole Hydrochloride**

1. Description –

- **Colour –** Yellowish white
- **Odour –** Odourless
- **Texture –** Fine powder
- **Solubility study -** The solubility of ropinirole hydrochloride was found to be,

Table No. – Solubility profile of Ropinirole hydrochloride

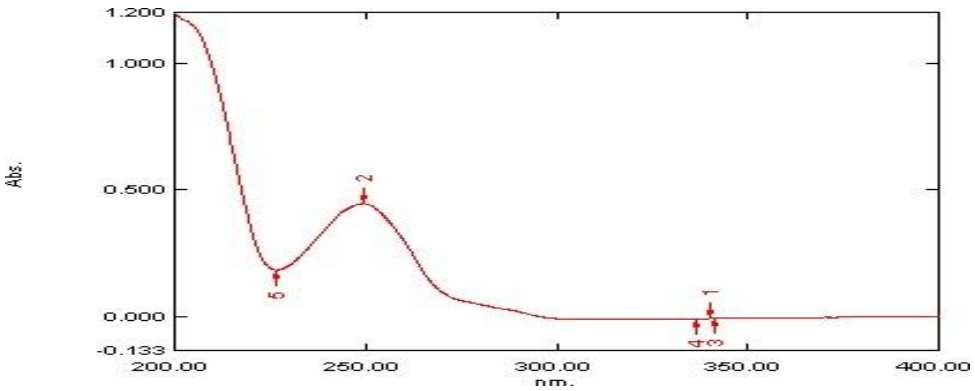
Sr. No.	Name of solvents	Solubility (Descriptive Terms)	Standard Reference
01	Water	Freely Soluble	Freely Soluble
02	0.1 N HCl	Freely Soluble	Freely Soluble
03	PBS pH – 7.4	Freely Soluble	Freely Soluble
04	DMSO	Freely Soluble	Freely Soluble
05	Ethanol	Insoluble	Insoluble

- **Melting point determination**

The melting point of ropinirole hydrochloride was found to be in the range of 244 - 248°C which lies within the reported range of 245 - 250°C. It complies with the purity of the drug sample and literature values.

RESULT – Procured drug sample of ropinirole hydrochloride has same melting point range as mentioned in referred reference research articles and books.

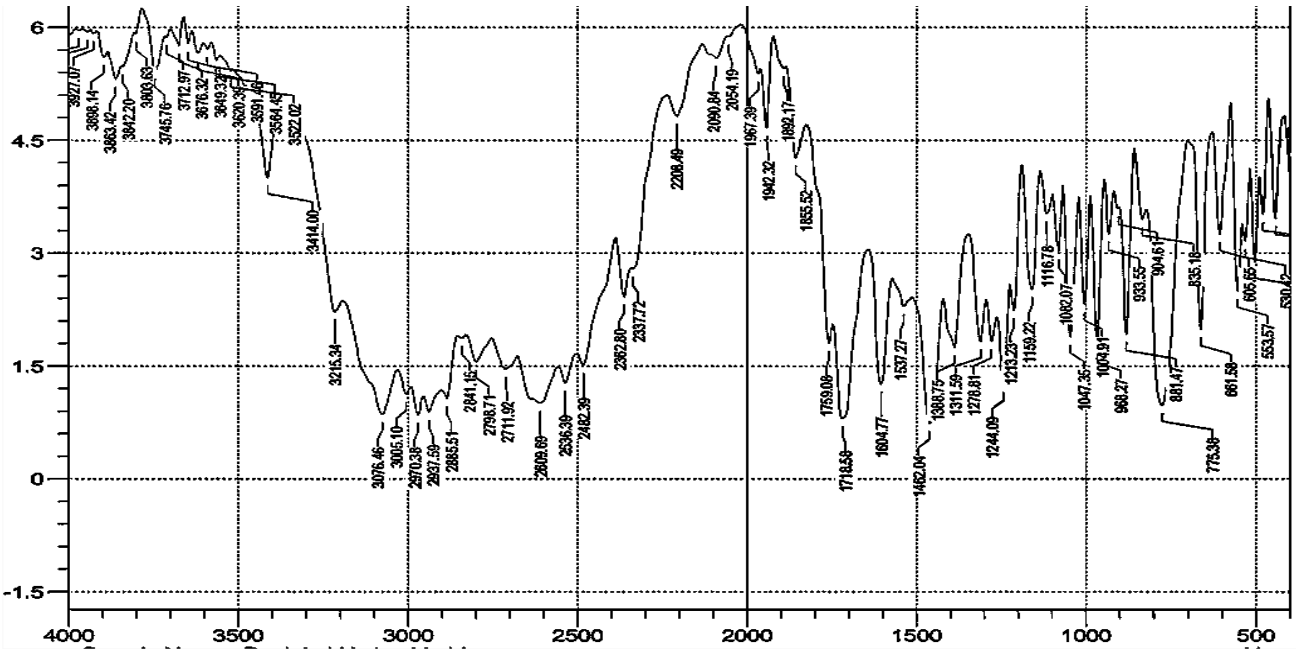
- ***Spectrophotometric Methods for Estimation of Ropinirole Hydrochloride***
- Determination of Lambda max –



Graph No. 1 - UV Spectrum of Ropinirole Hydrochloride

RESULT – This is confirmatory analytical test for drug, showing UV spectrum as described in reference books and the absorbance curve showed characteristic absorption maxima at **250 nm** for ropinirole hydrochloride.

- **FTIR Spectroscopy –**

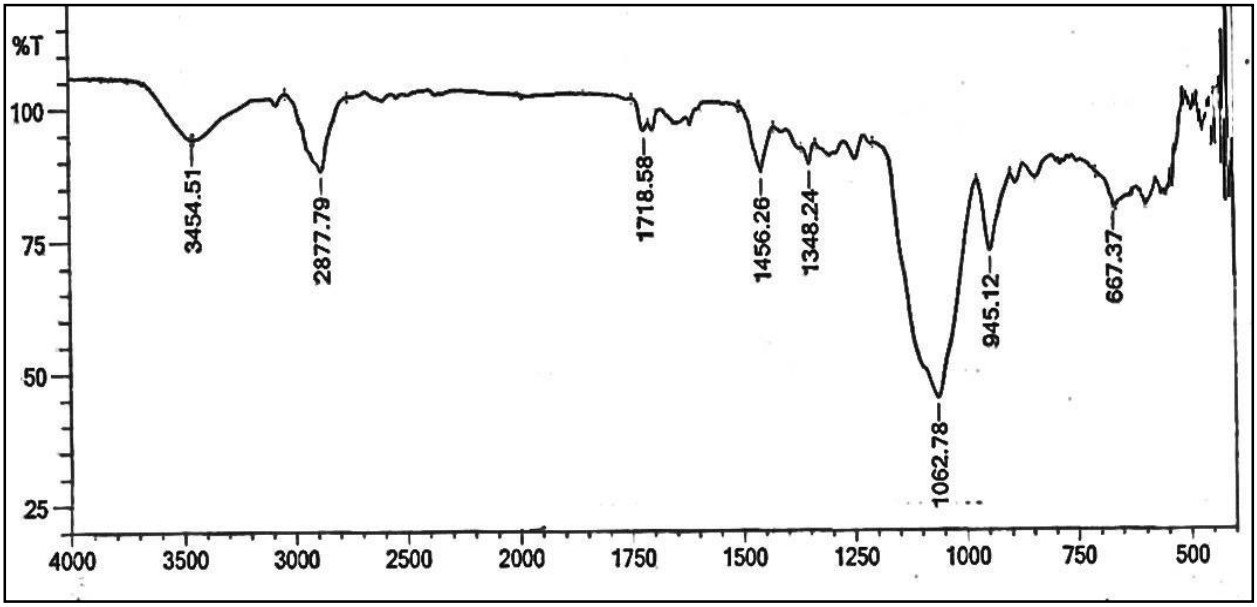


Graph No. 2 - FTIR Spectrum of Ropinirole Hydrochloride

RESULT - The spectra studied at 4000 to 400 cm^{-1}. The spectrum of ropinirole hydrochloride showed the above functional groups at their frequencies mention in Table No. 11. The FTIR of drug was found to be similar to the standard FTIR spectrum of ropinirole hydrochloride.

Table No 2. Functional groups and their frequencies with pure drug

Assignments	IR Frequency (cm^{-1})
-C-H Stretching (Aliphatic)	2937.59
-C=O Stretching (Aromatic)	1718.58
-C=C Stretching (Aromatic)	1462.04
-N-H Stretching (2°)	3414.00

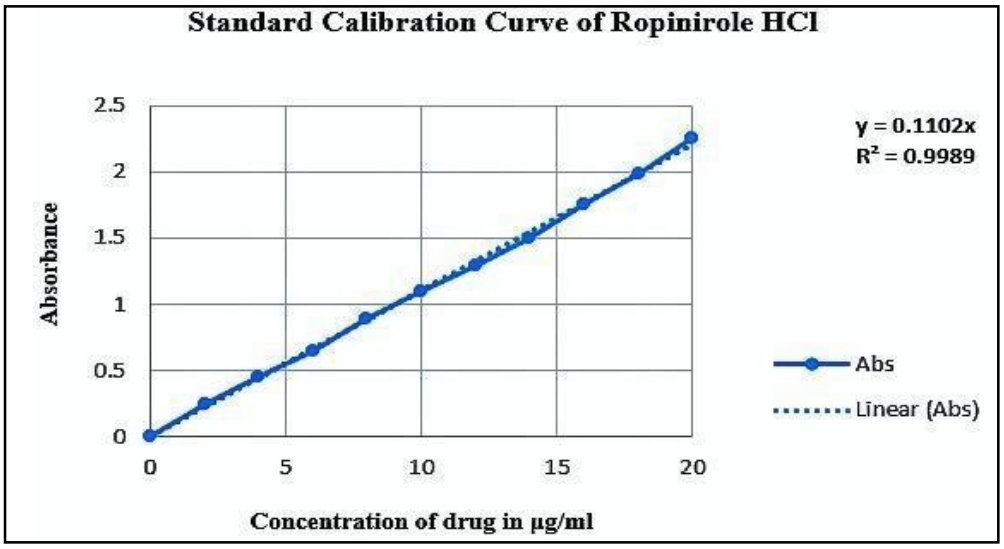


Graph No. 3 – Polymeric picture of Ropinirole Hydrochloride + polymer

RESULT – Drug excipient interaction study by FTIR spectroscopy was carried out as per standard procedure. FTIR spectra of physical mixture of API and polymers i.e. HPMC K100M and HPMC K4M was shown in Graph No.3. It was observed that principle peaks of drug was found in FTIR spectra of physical mixture of drug and excipients. It was suggested that, there was no physical and chemical interaction between drug and polymers.

- **Standard calibration curve of Ropinirole HCl in 0.1 N HCl at 250 nm.**

Sr. No.	Concentration (µg/ml)	Absorbance ± SD
1	0	0 ± 0
2	2	0.245 ± 0.0008
3	4	0.453 ± 0.0012
4	6	0.652 ± 0.0009
5	8	0.887 ± 0.0019
6	10	1.103 ± 0.0011
7	12	1.297 ± 0.0005
8	14	1.501 ± 0.0008
9	16	1.751 ± 0.0006
10	18	1.988 ± 0.0015
11	20	2.251 ± 0.0007



Graph No. 5 – Standard calibration curve of Ropinirole HCl

Discussion – From the standard curve it was observed that, the drug obeys beers law in concentration range of 2.0 – 20 µg/ml in 0.1 N HCl. Drug has shown good linearity with regression of coefficient R^2 = 0.9989 and equation for line was found to be y = 0.1102x which is used for calculation drug release and also in the calculation of dissolution study.

- **Pre compression Study**

Table No.4 - Pre - compression study of preliminary batch

Batch	**Bulk Density (g/cm^3 ± SD)**	**True Density (g/cm^3 ± SD)**	**Carr's Index (% ± SD)**	**Hausners Ratio (± SD)**	**Angle of Repose (θ ± SD)**
C1	0.460 ± 0.013	0.523 ± 0.017	12.52 ± 0.72	1.14 ± 0.06	31.26 ± 1.19
C2	0.453 ± 0.012	0.523 ± 0.019	12.24 ± 0.98	1.15 ± 0.04	31.60 ± 1.44
C3	0.469 ± 0.009	0.542 ± 0.023	14.39 ± 0.71	1.16 ± 0.07	32.19 ± 1.61
C4	0.450 ± 0.017	0.519 ± 0.012	12.32 ± 0.67	1.16 ± 0.05	33.17 ± 1.26
C5	0.456 ± 0.021	0.521 ± 0.008	13.10 ± 0.44	1.16 ± 0.09	33.69 ± 1.38
C6	0.441 ± 0.008	0.513 ± 0.006	13.54± 0.33	1.20 ± 0.04	32.45 ± 1.14
C7	0.454 ± **0.**019	0.514 ± 0.013	13.81 ± 0.42	1.18 ± 0.08	31.42 ± 1.26
C8	0.463 ± 0.005	0.530 ± 0.011	12.76 ± 0.32	1.16 ± 0.09	32.15 ± 1.24
C9	0.460 ± 0.002	0.521 ± **0**.003	12.17 ± 0.74	1.22 ± 0.02	31.85 ± 1.45

Discussion –

It was observed that the **Bulk Density** of formulations from F1 to F9 was in the range of (0.460 ± 0.002-0.462± 0.002) gm/cm^3. All formulations have good flow properties.

It was observed that, **Tapped Density** of formulations from F1 to F9 was in the range of (0.525 ± 0.010-0.525 ± 0.007) gm/cm^3. All formulations have good flow properties.

It was observed that **Carr's Index** of formulations from F1 to F9 was in the range of (12.52 ± 0.78- 13.71 ± 0.49) %. All formulatihave has good flow properties.

It was observed that **Hausner's Ratio** of formulations from F1 to F9 was in the range of (1.14 ± 0.05- 1.15 ± 0.03). All formulations have good flow properties.

It was observed that the **Angle of Repose** of formulations from F1 to F9 was in the range of (31.25 ± 1.17-31.43 ± 1.20) θ. All formulations have good flow properties.

Post Compression Study

Result

Table no. 9 – Post–compression study.

Batch	Wt. variation (± SD)	Hardness (± SD)	Diameter (± SD)	Thickness (±SD)	Friability (± SD)	Drug Content
C1	249.96±0.598	5±0.051	9.013±0.156	2.730±0.010	0.36±0.0025	86.20±2.34
C2	249.81±0.601	4.6±0.059	9.014±0.156	2.741±0.005	0.40±0.0018	93.81±1.45
C3	249.82±0.564	5.16±0.05	9.014±0.156	2.745±0.018	0.52±0.0019	91.48±143
C4	249.76±0.578	5±0.054	9.014±0.156	2.752±0.013	0.36±0.0025	83.68±1.43
C5	249.87±0.503	5±0.055	9.013±0.156	2.744±0.011	0.38±0.0021	91.46±1.46
C6	250.56±0.616	4.8±0.059	9.014±0.156	2.739±0.008	0.41±0.0025	91.13±086
C7	249.78±0.548	5±0.057	9.014±0.156	2.748±0.017	0.40±0.0018	90.57±067
C8	249.43±0.532	4.8±0.055	9.013±0.156	2.752±0.015	0.39±0.0017	88.72±1.54
C9	250.12±0.628	5.16±0.05	9.013±0.156	2.748±0.019	0.42±0.009	91.03±1.38

Discussion –

The **Average Weight** of all Bucco-adhesive tablets within formulation was found to be uniform. This indicates uniform filling of the die cavity during tablet compression. Since the average weight of all tablets was almost 250 mg, the test requirements are met if none of the individual tablet weights is less than 95% or more than 105% of the average weight.

The **Hardness** of all Bucco-adhesive tablets was found to be in the range of 5±0.051to 5.12±0.05 kg/cm2. This ensures good mechanical strength.

The **Thickness** of all Bucco-adhesive tablets was found in the range of 2.730±0.010 to 2. .745±0.018mm. There were no marked variations in the thickness of all formulations indicating uniform behavior of powder throughout the compression process.

The **Friability** of all Bucco-adhesive tablets was found to be in the range one 0.36±0.0025 to 0.36±0.0025 which indicates good friability.

The **Drug Content** of all formulations was found to be between 86.20±2.34 to 90.38±2.35. The values ensure good uniformity of drug content in the tablet.

- **Bioadhesive Parameters**

Table: Surface pH, Mucoadhesive strength, Force of adhesion, Mucoadhesive Time

Batch	Surface pH	Drug Content (%)	Mucoadhesive strength (gms)	Force of adhesion (N)	Mucoadhesive Time
C1	6.68±0.13	86.20±2.34	08.52±0.76	0.08±0.1	7.40 ± 0.3
C2	6.56±0.11	93.81±1.45	11.69±0.24	0.10±0.1	8.53 ± 0.3
C3	6.48±0.16	91.48±143	09.54±0.75	0.09±0,2	7.48 ± 0.2
C4	6.44±0.13	83.68±1.43	08.96±0.88	0.08±0.1	7.54 ± 0.12
C5	6.74±0.15	91.46±1.46	11.28±0.88	0.11±0.1	8.05 ± 0.24
C6	7.3±0.22	91.13±086	04.13±0.30	0.04±0.2	7.43 ± 0.27
C7	6.44±0.13	90.57±067	05.67±0.32	0.05±0.2	7.45 ± 0.30
C8	6.34±0.18	88.72±1.54	08.02±0.85	0.07±0.1	7.45 ± 0.31
C9	7.07±0.15	91.03±1.38	10.56±0.35	0.10±0.3	7.50 ± 0.32

Discussion

The **surface pH** of all Bucco-adhesive tablets was found to be in the range of 6.68±0.13 to 6.40±0.15 This ensures good surface pH.

The **Drug Content** of all formulations was found to be between 86.20±2.34 to 90.38±2.35. The values ensure good uniformity of drug content in the tablet.

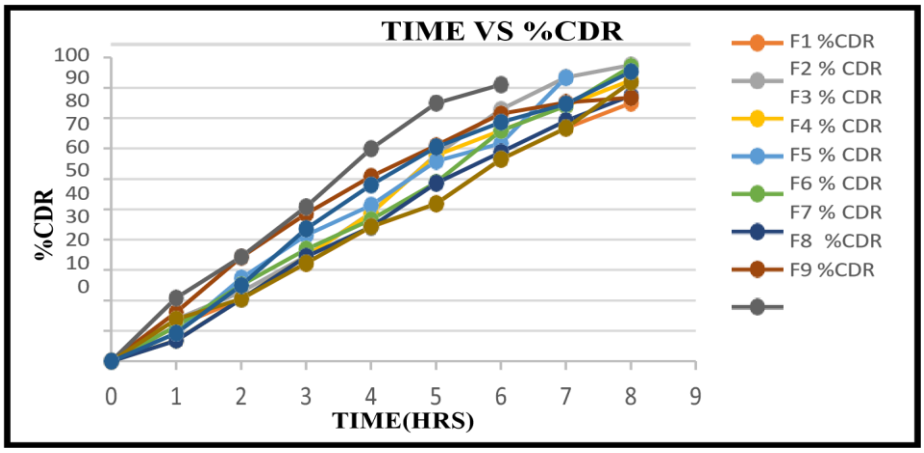
The **Mucoadhesive strength** of all Bucco-adhesive tablets was found to be in the range of 08.52±0.76 to 14.21±0.71. This ensures good mucoadhesive strength.

The **Force of adhesion** of all Bucco-adhesive tablets was found to be in the range of 0.08±0.1 to 0.14±0.2. This ensures a good force of adhesion.

The **Mucoadhesive time** of all Bucco-adhesive tablets was found to be in the range of 7.40 ± 0.3 to 8.05 ± 0.25. This ensures good mucoadhesive time.

- **In- Vitro Drug Release Study**

TIME (HRS)	CUMULATIVE % DRUG RELEASE								
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**
0	0± 0	0±0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
1	11.53 ± 0.198	13.846 ± 0.169	6.92± 0.165	9.23± 0.191	11.53± 0.175	6.92± 0.198	16.15± 0.195	20.76± 0.191	13.84± 0.188
2	20.48± 0.185	22.895 ± 0.199	20.49± 0.174	27.33± 0.148	25.12± 0.177	20.49± 0.191	34.25± 0.194	34.45± 0.194	20.63± 0.147
3	32.3± 0.191	34.66± 0.146	34.47± 0.184	41.45± 0.184	36.92± 0.177	34.57± 0.174	48.6± 0.175	50.75± 0.174	32.35± 0.185
4	44.35± 0.197	48.914 ±0.187	48.73± 0.195	54.31± 0.185	46.69± 0.174	44.21± 0.134	60.74± 0.186	68.95± 0.188	44.31± 0.191
5	51.25± 0.174	67.64± 0.164	65.84± 0.184	58.48± 0.191	58.41± 0.169	70.99± 0.184	84.75± 0.181	53.94± 0.185	70.54± 0.189
6	66.47± 0.179	82.83± 0.176	75.88± 0.199	71.64± 0.165	75.48± 0.174	68.49± 0.198	81.42± 0.186	97.04± 0.174	78.64± 0.195
7	76.78± 0.177	93.412 ± 0.189	84.12± 0.181	93.12± 0.149	84.12± 0.178	79.18± 0.169	85.12± 0.167		76.83± 0.185

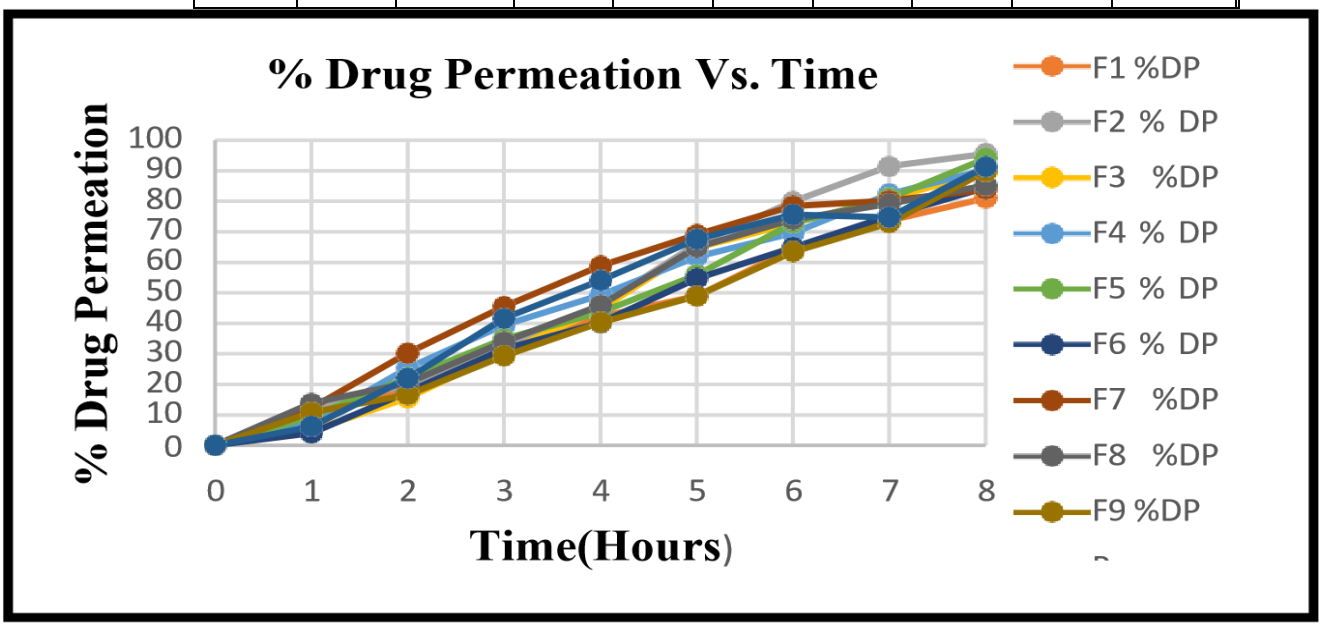


Graph No. 8. Time vs. % CDR of F1 to F9 Batch

- In Vitro Drug Permeation Study

TIME (HRS)	% DRUG PERMEATION								
	C1	**C2**	**C3**	**C4**	**C5**	**C6**	**C7**	**C8**	**C9**
0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
1	9.53 ± 0.42	11.846 ± 0.57	4.92 ± 0.80	7.23 ± 0.34	9.53 ± 0.35	3.92 ± 0.65	12.15 ± 0.74	13.76 ± 0.45	10.84 ± 0.34
2	18.58 ± 0.65	19.895 ± 0.49	15.49 ± 0.81	25.33 ± 0.79	22.11 ± 0.65	17.49 ± 0.65	30.25 ± 0.68	20.34 ± 0.63	16.63 ± 0.35
3	30.3 ± 0.65	31.66 ± 0.30	30.47 ± 0.81	39.44 ± 0.86	34.92 ± 0.87	31.47 ± 0.65	45.5 ± 0.83	33.85 ± 0.68	29.35 ± 0.75
4	42.25 ± 0.35	45.914 ± 0.25	44.73 ± 0.23	49.31 ± 0.70	43.69 ± 0.70	40.2 ± 0.84	58.76 ± 0.85	45.95 ± 0.39	40.29 ± 0.45
5		65.963	64.78	61.88	55.91	54.64	68.99	64.88	48.94

	48.9 ± 0.40	± 0.40	± 0.54	± 0.88	± 0.54	± 0.89	± 0.70	± 0.78	± 0.68
6	64.47 ± 0.35	79.85 ± 0.60	72.88 ± 0.89	69.67 ± 0.79	72.88 ± 0.39	64.82 ± 0.94	78.4 ± 0.81	74.04 ± 0.81	63.51 ± 0.62
7	73.78 ± 0.15	91.484 ± 0.50	81.11 ± 0.15	82.39 ± 0.75	81.11 ± 0.50	75.18 ± 0.93	80.2 ± 0.55	79.2± 0.62	72.83 ± 0.15
8	81.02 ± 0.75	95.511 ± 0.70	89.48 ± 0.75	90.35 ± 0.91	94.01 ± 0.81	84.46 ± 0.95	83.78 ± 0.14	85.2± 0.64	89.85 ± 0.70



Graph No. 9 % Drug Permeation Vs. Time

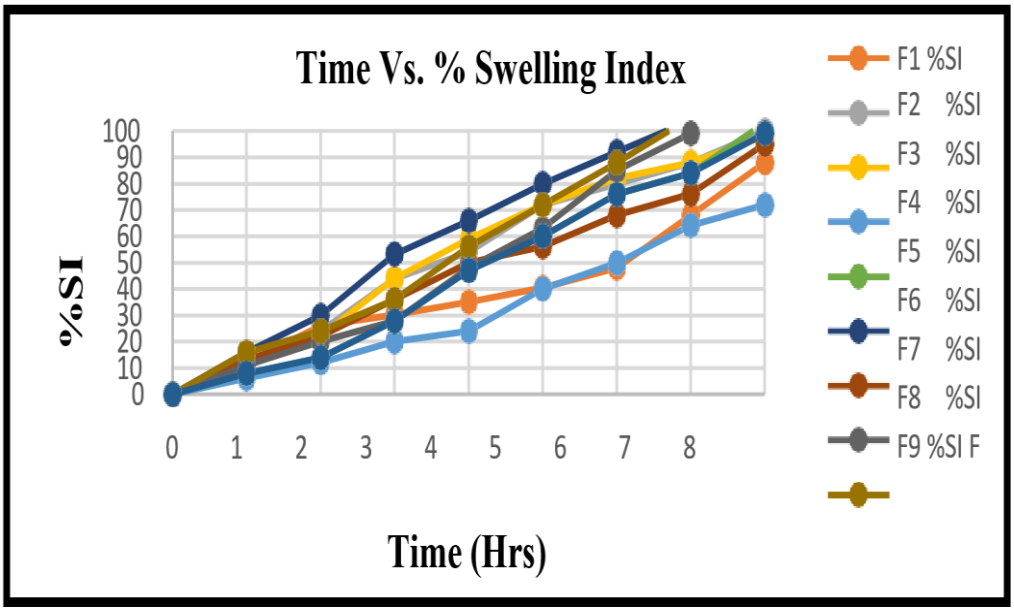
- **Determination of Swelling Index**

Table: – % Swelling Index

Time	F1± SD	C8 ± SD	F3 ± SD	F4 ± SD	F5±SD	F6 ± SD	F7 ± SD	F8 ± SD	F9± SD
0	0±0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
1	12± 0.895	12 ± 0.895	12 ± 0.895	6±0.895	8 ± 0.895	16 ± 0.895	13 ± 0.895	11 ± 0.895	16 ± 0.895
2	26 ± 0.605	24 ± 0.895	22 ± 0.895	12 ± 0.895	14 ± 0.895	30 ± 0.895	22 ± 0.895	20 ± 0.895	24 ± 0.895
3	30.2 ± 0.712	44 ± 0.895	44 ± 0.895	20 ± 0.895	28 ± 0.895	53.2 ± 0.895	36 ± 0.895	28 ± 0.895	36 ± 0.895
4	35.2 ± 0.887	54 ± 0.895	59 ± 0.895	24 ± 0.895	47.2 ±0.895	66 ± 0.895	50 ± 0.895	48 ± 0.895	56 ± 0.895
5	40.4 ± 0.568	72 ± 0.895	72 ± 0.895	40 ± 0.895	60 ± 0.895	80 ± 0.895	56 ± 0.895	63 ± 0.895	72 ± 0.895
6	48.4 ± 0.897	80 ± 0.895	82 ± 0.895	50 ± 0.895	76 ± 0.895	92 ± 0.895	68 ± 0.895	85 ± 0.895	88 ± 0.895
7	68 ± 0.689	88 ± 0.895	88 ± 0.895	64 ± 0.895	84 ± 0.895	104 ± 0.895	76 ± 0.895	99 ± 0.895	105 ± 0.895

8	88 ± 0.895	100 ± 0.895	1 ± 0.895	72 ± 0.895	103 ± 0.895	119 ± 0.895	95 ± 0.895	118 ± 0.895	120 ± 0.895

n=3



Graph No. 10 Time vs. % Swelling Index of F1 to F9 Batch

Kinetics of Drug Release:

Table no. 15: Model Fitting Release Profile of Sustained Release Mucco-Adhesive Buccal Tablet.

Formulation Batches	**Mathematical models (kinetics)**						**Best fit model**
	Zero order	**First order**	**Higuchi model**	**Korsmeyer peppas**		**Hixson crowell**	
	R	**R**	**R**	**R**	**N**	**r**	
C-1	0.997	0.867	0.946	0.989	0.989	0.915	Zero order
C-2	0.996	0.912	0.932	0.960	0.994	0.809	Korsmeyer peppas
C-3	0.984	0.901	0.956	0.996	1.005	0.908	Korsmeyer peppas

C-4	0.993	0.846	0.955	0.998	0.911	0.964	Korsmeyer peppas
C-5	0.991	0.932	0.953	0.990	0.987	0.960	Zero order
C-6	0.886	0.900	0.980	0.978	0.984	0.916	First order
C-7	0.900	0.919	0.945	0.947	0.911	0.984	First order
C-8	0.988	0.915	0.938	0.877	0.985	0.983	Zero order
C-9	0.916	0.938	0.978	0.891	0.955	0.916	Korsmeyer peppas

n=3

- **Stability Study**

Table : Stability study at 40°C ± 2°C / 75 ± 5% RH

Time	**Drug Content (%)**	**Mucoadhesive strength (gm)**	**Surface PH Mean ± SD**	**%Drug Release (After 8hrs)**
0 Day	93.81±1.45	11.69±0.24	6.56±0.1 1	93.71±0.61
1 Week	93.75±0.85	11.30±0.50	6.46±0.1 5	93.54±0.60
2 Week	93.57±0.49	10.74±0.81	6.32±0.1 5	93.32±0.45
3 Week	93.30±0.41	10.38±0.88	6.27±0.1 5	93.21±0.32
4 Week	93.20±0.35	11.68±0.73	6.17±0.	92.40±0.21

Table No. 16 Stability study at 25°C ± 2°C / 75 ± 5% RH

Time	Drug Content (%)	Mucoadhesive strength (gm)	Surface PH Mean ± SD	%Drug Release (after 8hrs)
0 Day	93.81±1.45	11.69±0.24	6.56±0.11	93.60±0.12
1 Week	93.49±0.41	11.51±0.73	6.43±0.75	93.51±0.30
2 Week	93.38±0.37	10.64±0.82	6.47±0.28	93.48±0.10
3 Week	93.29±0.21	10.61±0.82	6.46±0.50	93.41±0.45
4 Week	93.21±0.27	10.49±0.61	6.45±0.11	92.35±0.45

n=3

Table No. 17 Stability study at 10°C ± 2°C / 75 ± 5% RH

Time	Drug Content (%)	Mucoadhesive strength (gm)	Surface PH Mean ± SD	%Drug Release(after 8hrs)
0 Day	93.81±1.45	11.69±0.24	6.56±0.11	93.60±0.12
1 Week	93.50±0.67	11.94±0.56	6.44±0.15	93.51±0.16
2 Week	93.46±0.20	10.81±0.56	6.36±0.15	92.42±0.45
3 Week	93.41±0.15	10.78±0.56	6.30±0.15	93.38±0.68
4 Week	93.35±0.11	10.24±0.56	6.25±0.15	92.30±0.45

n=3

Result– The stability studies of evaluated formulation C8 revealed that there is a slight reduction in drug content was observed over 4 weeks. No significant changewas observed in % Drug Content, Mucoadhesion Strength, and % Cumulative Drug Release (After 8 Hours) at various storing conditions 40+2", 75+5 % RH, 25+2º, 75+5% RH, and 10 +2°C, 75+5 RH. Hence formulation C8 was found to be stable for 4 weeks.

- **Conclusion:**

  The present study has been a satisfactory attempt to formulate Sustained release Muccoadhesive Buccal tablet of Ropinirole HCL with a view of improving sustained release of the drug. From the experimental results it can be concluded that, The various polymers were used for screening amongst them the Buccal tablet prepared by Hyadroxypropylmethylcellulose, shows good Muccoadhesive strength and Muccoadhesive Force.

  Prior to formulation, preformulation studies were carried out in order to establish compatibility between drug and polymers by FTIR spectroscopy. The results of FTIR study revealed that there is no physical or chemical interaction between drug and polymer.

  For the formulation biocompatible polymers Hydroxypropylmethylcellulose, was chosen in varying proportions with the drug. Direct compression method was used to prepare buccal tablet

  The prepared formulations were characterized for their postcomprenion staties te. Wt. Vition, Hardness, Diameter, Thickness, Friability. Drug Content, Moccoadhesive e and Maccoadhesive force studies. Almost all the formulations showed fairly agtable values for all the parameters evaluated.

  Formatted Buccal tablet were stable at the selected temperature and humidity in storage be 28 days. From the stability studies it was found that there was no significant change in the drug content and release characteristics.

  Hence, finally it was concluded that the prepared Sustained release Maccoadhesive Bucal tablet of Rivastigmine Tartrate may prove to be potential candidate for safe and effective Sustained release drug delivery ever an extended period of time which can mdace dosing frequency.

- **Future Scope:**

  The design drug delivery system hold promises to further study ie. In vivo studie leading to IVIVC for commercialization.

  There is hope for its scale up technology for commercialization as it can easily applicable for large scale production.

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