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# THE FORMULATION & EVALUATION OF MOUTH DISSOLVING FILM OF PROCYCLIDINE HCL

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**ABSTRACT**

The pharmaceutical company relies heavily on oral drug delivery technology. The market has moved from the traditional tablet/capsule form to the modern fast-dissolving tablet/capsule form. Oral solids have lower bioavailability, which makes it difficult. Errors in the use of injections and dosages of liquid drugs changed the focus of the study. Pharmaceutical companies need to create new oral dosage forms to remove some limitations on known side effects. Most of these problems can be solved with oral thin films. Currently, on the market, there are not many prescriptions for oral thin film. Despite the uncertainty surrounding the development, approval, and penetration, the market is expected to grow steadily over the next decade. Many people have difficulty swallowing, especially children, the elderly, and people with dysphagia. In addition, some disorders require a quick response. The main objective of this work was to develop a palatable film using procyclidine HCl, as well as base ingredients such as polymers, plasticizers, sweeteners, salivary stimulants, and flavors. The films are prepared by solvent casting method. HPMC E5 cps, can't pass film thickness. HPMC E15 has good flexibility. The plasticizer propylene glycol cannot give the film flexibility and resistance to folding. PEG 400 produces good flexural strength, good tensile strength, and good percent elongation. The optimized formulation (F3) exhibits palatability, surface pH, folding resistance, instant drug release as well as good mechanical properties.

**Keyword: Mouth Dissolving Film, Immediate Release, Procyclidine HCL, Fast Degrading Membranes, Water-Soluble Polymer**

## INTRODUCTION

The new technology for rapid-dispersing dosage forms is called quick-dissolving, quick-dissolving, quick-dissolving, and rapid-dissolving tablets. However, the

functions and Concepts of all these dosage forms are similar. By definition, the solid dosage form dissolves or breaks down rapidly in the oral cavity to form a solution or suspension without the need for water infusion. This is called a rapid-dispersing oral drug dosage form **[1]**.

Dysphagia (dysphagia) is common in all age groups, particularly in the elderly, and can also occur with regular tablets and capsules. Dysphagia is associated with many diseases, including stroke, Parkinson's disease, AIDS, thyroidectomy, thyroid therapy head, and neck, and other neurological diseases, including cerebral palsy. The most common complaint is pellet size, followed by surface, shape, and taste **[2]**.

The problem with swallowing tablets is that is most pronounced in elderly patients and children, as well as those who are often agitated and do not have easy access to water. The oral membrane is the latest technology in oral disintegrating dosage production shape. They are thin, glossy films of edible water-soluble polymers of various kid's sizes, and shapes (such as a square, rectangle, or disc) **[3]**.

The stripes can be soft or brittle, opaque, or transparent. They are designed to break the quickly tongue without water. Fast Degrading Membranes (FDF) have a large amount of decomposition surface. These films reduce the danger/fear of suffocation, they are easy to handle and manage, and at the same time, they maintain a simple, traditional container manufactured, thus overcoming the short-term failure of rapid oral decomposition tablet **[4, 5]**.

The flexibility and strength of the film were chosen to facilitate the production of processes such as rewinding, cutting, and packaging. The rapidly disintegrating film is placed on the blade and film the patient's mucus, and immediately sink into saliva. The membrane rapidly hydrates and adheres firmly to the application site. It is disrupted and then rapidly dissolves to release the drug for Absorbed through the oral mucosa or absorbed from the stomach if taken orally **[6, 7]**.

**OVERVIEW OF THE ORAL MUCOSA-**

The oral mucosa consists of an outer layer of stratified squamous epithelium. Below is the basement membrane, the stroma, followed by the submucosa, such as the innermost layer. The epithelium resembles stratified squamous epithelium. is found in other parts of the body because it has a mitotically active basal cell layer, reaches the surface via several distinct mediators, and cells are secreted from the epithelial surface. Tissue **[8-10]**.

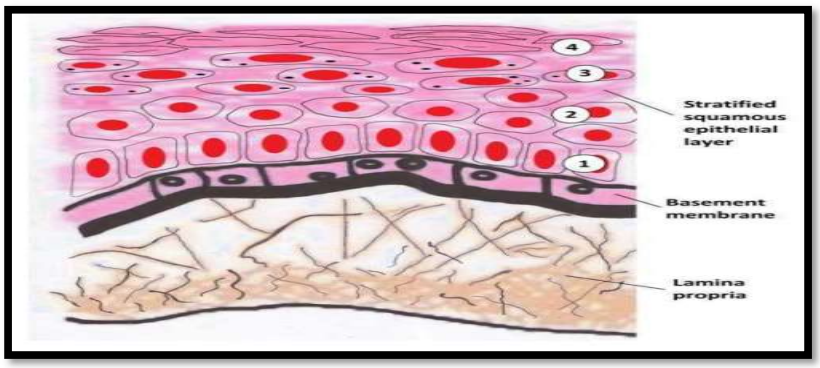



**Figure 1: Various layers of the oral mucosa**

## MATERIALS & METHODS-

The API- Procyclidine HCL was received in the form of a gift sample from Invo-chem Laboratories, Mumbai, Where HPMC E15, HPMC E5, PEG 400, Sodium saccharin was collected from Fine Chem Industries, Mumbai & Propylene glycol was collected from Loba chemicals, Mumbai.

Digital balance (Mettler Toledo PR203), Hot air oven (Thermo lab), UV Spectrometer (Shimadzu, UV 1800), Dissolution test Apparatus (Lab India D5 8000), Micrometer screw gauge (Mitutoyo, china), FTIR Spectrophotometer (Bruker Alpha 200881), pH meter (Electro Lab), Stability chamber (Thermo lab Pvt ltd). With the help of this instrument, the formulation and evaluation of mouth dissolving film of Procyclidine HCL has been done.

## DOSE CALCULATION-

For the preparation of mouth dissolving film initially, the dose calculation is important this calculation is as mentioned below.

Inner radius of glass plate = 5.65 cm.

Inner Area of the plate ($\pi r^2$) = 3.14 x 5.65 x 5.65 = 100 cm2. No. of 4 cm2 films present whole plate =100/4 =25 films.

**Each films contains 5 mg of drug.**

25 films contain 125 mg drug (25×5). Labelled claim= 5 mg.

## FORMULATION-

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Procyclidine HCL (mg) | 125 | 125 | 125 | 125 | 125 | 125 | 125 | 125 | 125 |
| HPMC E15 (g) | 1.0 | 1.25 | 1.5 | - | - | - | 1.25 | - | 1.25 |
| HPMC E5 (g) | - | - | - | 1.0 | 1.25 | 1.5 | - | 1.25 | 1.25 |
| PEG 400 (ml) | 1.5 | 1.25 | 1.0 | - | - | - | - | 1.25 | - |
| Propylene glycol (ml) | - | - | - | 1.5 | 1.25 | 1.0 | 1.25 | - | - |
| Citric acid (g) | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 | 0.10 |
| Sodium Saccharin (g) | 0.125 | 0.125 | 0.125 | 0.125 | 0.125 | 0.125 | 0.125 | 0.125 | 0.125 |
| Flavour (g) | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| Distilled water (ml) | QS | QS | QS | QS | QS | QS | QS | QS | QS |

**METHOD OF PREPARATION-**

The water-soluble polymer and plasticizer are dissolved in distilled water. Stir the solution on a magnetic stirrer for 2 hours and set aside to remove all trapped air bubbles. At the same time, dissolve the excipients and drugs and fully stir for 30 minutes. After the stirring is completed, mix the two solutions **[11-13]**.

Finally, the solution is poured on a suitable petrochemical plate to form a thin film. The plate was kept in a hot air oven at 45°C for 12 hours. The dried film is gently peeled from the glass plate and cut to the required size. With the help of this method of preparation, the formulation has been done **[14, 15]**.

**Figure 2: The Prepared Fast Dissolving Film**

**PREFORMULATION STUDY-**

Pre-formulations can be described as the development phase that characterizes the physicochemical and biopharmaceutical properties of drugs. It is an important part of the drug development process. The information related to drug development obtained at this stage is used to make key decisions in the later stages of development. A variety of information must be generated to develop formulas reasonably. In the preformulation stage of product development, drug characterization is a very important step, followed by the study of the compatibility characteristics of excipients **[16, 17]**.

1. **Solubility-**

   The solubility of Procyclidine HCL was determined in various solvents. In the test tube, 10 ml required solvent was transferred and 1 gm of Procyclidine HCL was added to the solvent. The

mixture was then sonicated for 10 min and observation was done for the particles remain if any. As per observation, the solubility of Procyclidine HCL is freely in ethanol & water **[18-20]**.

**2. Heavy metal content-**

The part of Lead per million parts of powder was examined by comparing the sample

solution with 10 ppm lead standard solution for 2 gm material **[21]**.

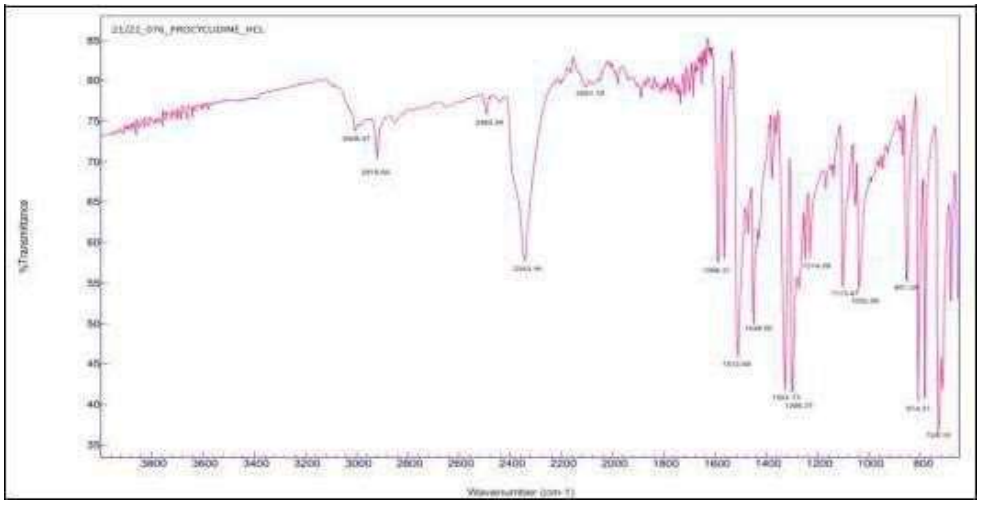
**3. Melting point-**

The melting point was carried out by using the open capillary tube method. Procyclidine

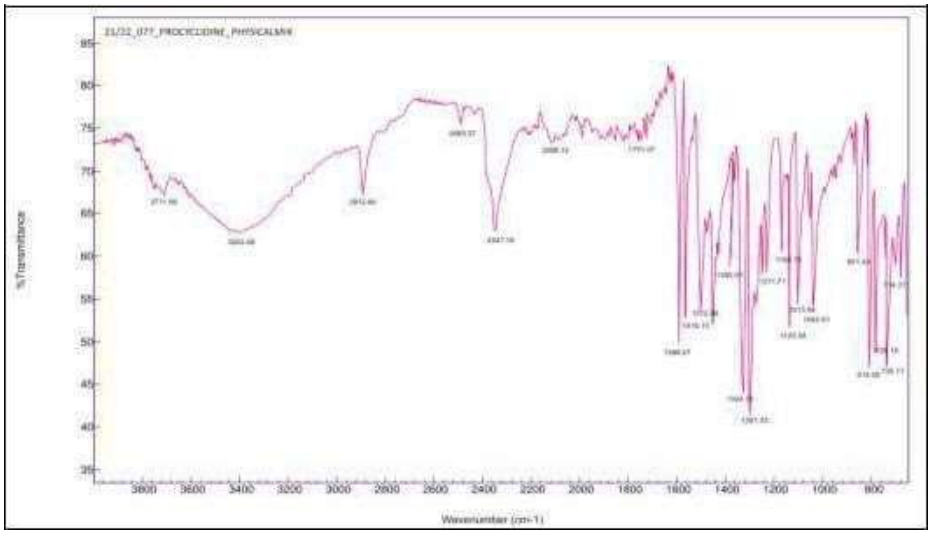
HCL was taken in a glass capillary whose one end was sealed by flame. The capillary was then dipped into the liquid paraffin, placed inside the melting point apparatus and the melting point was noted at that time observe that the melting point is 184℃ **[22]**.

**4. Compatibility Studies-**

An FTIR study was conducted to check the compatibility of the drug with the polymer. The infrared spectrum of Procyclidine hydrochloride was measured on a Fourier transform infrared spectrophotometer using the KBr scattering method. Use dry potassium bromide for baseline correlation. Subsequently, an FTIR spectrophotometer was used to analyze the spectra of the drug, potassium bromide, and the dry mixture of the drug and various polymers. The maximum absorption in the spectrum obtained with the test substance corresponds to the maximum absorption of the reference spectrum in position and intensity **[23-25]**.




**Graph 1: IR Spectra of Procyclidine HCL**



**Graph 2: IR Spectra of Physical Mixture**

**Table 2: Principal peak and functional group present FTIRSpectra of Procyclidine HCl**

| Functional Group | Reported Peak($cm^{-1}$) | Observed Peak ($cm^{-1}$) |
|---|---|---|
| N-H Stretch | 2900-2945 | 2919.64 |
| C-N Stretch | 2235-2255 | 2243.16 |
| C=C Stretching | 1510-1538 | 1512.64 |
| C-H bending | 1300-1340 | 1324.73 |
| C-H bending (Aromatic) | 1425-1470 | 1448.56 |

**Table no 3- Interpretation of FTIR Spectrum of physical mixture**

| Functional Group | Peaks | |
|---|---|---|
| | Pure Drug | Physical Mixture |
| N-H Stretch | Yes | Yes |
| C-N Stretch | Yes | Yes |
| C=C Stretching | Yes | Yes |
| C-H bending | Yes | Yes |
| C-H bending (Aromatic) | Yes | Yes |

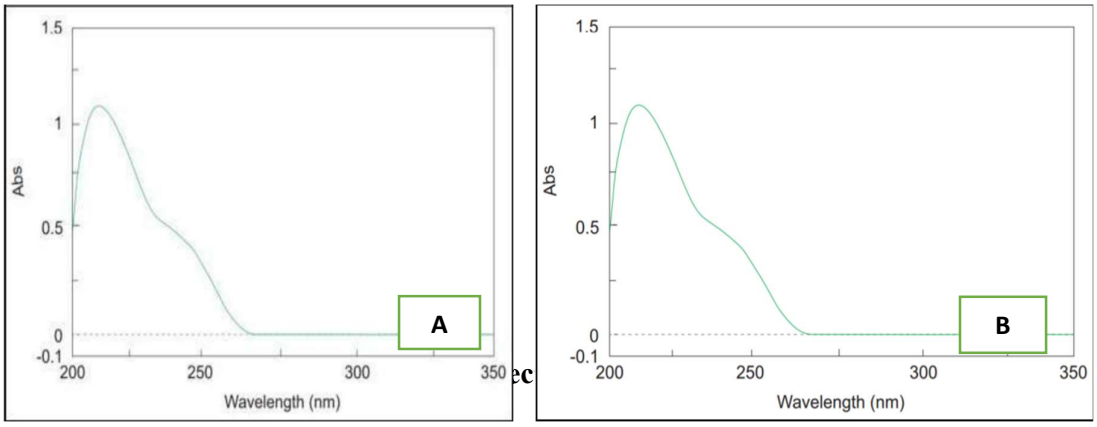
From the Infrared spectrometer it was found that all the principal peaks in Procyclidine HCl is represent in FTIR of physical mixture; Hence it is concluded that no significant interaction was found in drug and excipients and both compatible with each other.

**5. UV analysis-**

**A.** Spectra analysis-

The stock solution was prepared with 10 mg Procyclidine hydrochloride in 10 ml water. Extract 10 ml from this stock solution and dilute to 100 ml with water. Prepare the calibration curve by appropriately diluting the stock solution and using different concentrations (20 µg/ml-100 µg/ml). The absorbance is measured at 212 & 213 nm.

In Below Graphs the 'A' graph contain the water medium while 'B' Contain the basic medium **[26-28]**.



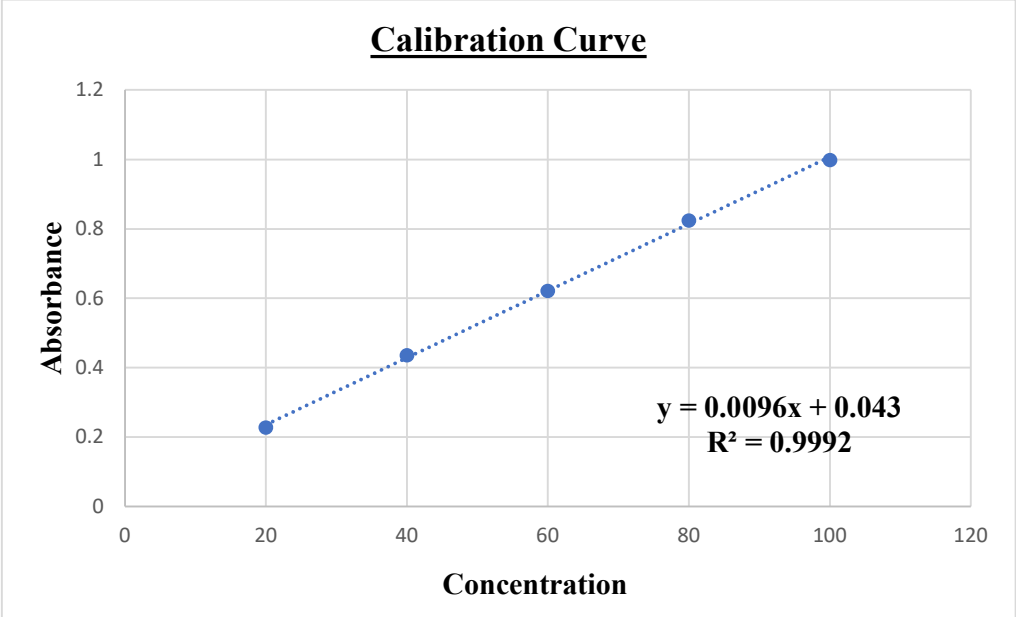

**B. Calibration Study of API-**

The absorbance of various concentrations measured at 212 & 213 nm is shown now for the calibration study serial dilution takes place as shown below table in two different media i.e., water media & basic media (pH 6.8) **[29]**-

**A) Water media-**

**Table 4: Standard graph of Procyclidine HCL**

| Sr. No | Concentration (µg/ml) | Absorbance (212 nm) |
|---|---|---|
| 1 | 20 | 0.228 |
| 2 | 40 | 0.436 |
| 3 | 60 | 0.621 |
| 4 | 80 | 0.824 |
| 5 | 100 | 0.998 |



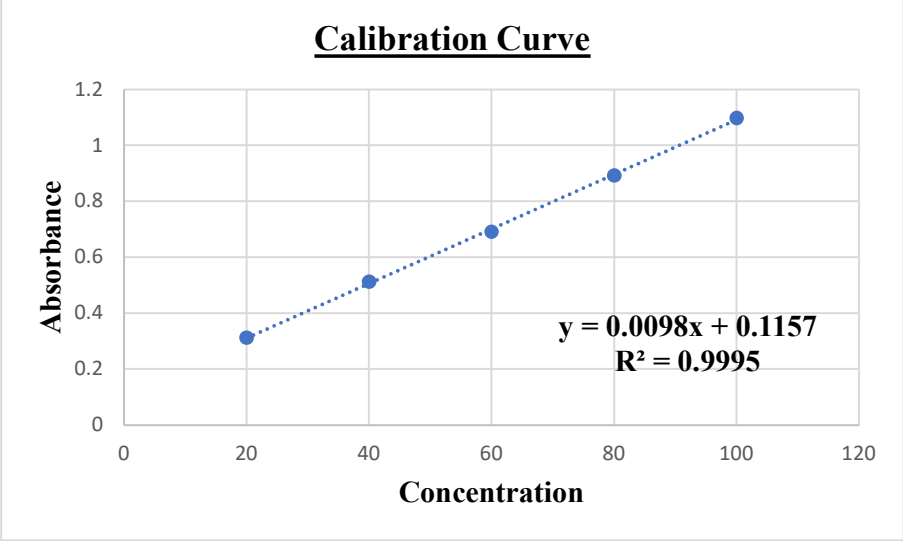

**Graph 4: Standard graph of Procyclidine HCL**

From the calibration curve, the regression equation was found to be y = 0.0096x + 0.043 and $R^2$= 0.9992 which will be helpful in drug content and % CDR determination on UV spectrophotometer.

**B) For the Basic Media-**

**Table 5: Standard graph of Procyclidine HCL**

| Sr. No | Concentration µg/ml | Absorbance (213 nm) |
|---|---|---|
| 1 | 20 | 0.312 |
| 2 | 40 | 0.512 |
| 3 | 60 | 0.691 |
| 4 | 80 | 0.892 |
| 5 | 100 | 1.0973 |




**Graph 5: Standard graph of Procyclidine HCL**

From the calibration curve the regression equation was found to be y = 0.0098x + 0.1157and $R^2$= 0.9995 which will helpful in drug content and % CDR determination on UV spectrophotometer.

**EVALUATION-**

**Thickness**

To determine the film's thickness, use a micrometer. The thickness of the film was measured five separate at locations in order to determine its homogeneity **[30, 31]**. The film must have a thickness of less than 5%. The thickness range for the F1 to F9 batch evaluation was 0.52 mm to 0.56 mm. The thickness of the fast-dissolving film for each formulation is shown in Table.

**Folding endurance-**

To determine the bending resistance, the film was cut and quickly bent at the same location until it broke. The number of times the film can be bent at the same position without breaking gives the value of the bending strength **[32, 33]**. From the evaluation of Folding endurance of F1 to F9 batches was found in between **8 to 14.** The folding resistance of the fast-dissolving film of all the formulations

**Tensile strength**

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the formula **[34]**.

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Strip thickness} \times \text{strip width}}$$

From the evaluations of tensile strength of F1 to F9 batches was found between 47.86 to 59.36 gm/cm The tensile strength of fast dissolving films of all formulations is given in Table.

**Percentage elongation**

It was calculated by **[35]**-

$$\text{Percentage elongation} = \frac{\text{Increase in length of strip} \times 100}{\text{The initial length of the strip}}$$

From the evaluation of % elongation of F1 to F9 batches was found in between 8 to12. The percentage elongation of fast dissolving films of all formulations

**In-vitro disintegration (Petri dish method)-**

Put 2ml of distilled water into a Petri dish, add a film on the water surface, and measure the time for the oral film to completely dissolve **[36]**. From the evaluations of in-vitro evaluation of F1 to F9 batches was found in between **23** to **33 sec**. The in-vitro disintegration time of the fast-dissolving film of all formulations is given in Table.

**Table 5: Evaluation parameters**

| Formulations | Thickness (mm) | Folding endurance | Tensile strength (gm/cm2) | % Elongation | In-vitro disintegration time(sec) |
|---|---|---|---|---|---|
| $F_1$ | 0.53 | 11 | 51.34 | 9 | 26 |
| $F_2$ | 0.55 | 9 | 49.28 | 11 | 26 |
| $F_3$ | 0.53 | 14 | 54.15 | 12 | 24 |
| $F_4$ | 0.56 | 12 | 55.36 | 10 | 26 |
| $F_5$ | 0.53 | 9 | 58.30 | 11 | 31 |
| $F_6$ | 0.55 | 10 | 51.40 | 8 | 23 |
| $F_7$ | 0.54 | 12 | 59.36 | 10 | 24 |
| $F_8$ | 0.56 | 11 | 50.36 | 12 | 31 |
| $F_9$ | 0.52 | 8 | 47.86 | 11 | 33 |

**Weight variation-**

Ten films are selected and their average weight is weighed. Weigh a single film & calculate the percentage weight variation **[38]**. weight variation of F1 to F9 batches was found in between 2.1±.05 to 7.5±.08 %. The weight change of the instant film of all the formulations shown in **Table 6**.

**Surface pH-**

The pH was determined by dissolving a film in 1-2 ml of distilled water and then the PH of the obtained solution was measured by the pH meter **[39]**. From the evolutions of surface pH of F1 to F9 batches was found in between 6.0 to 6.98. The Surface pH of the film of all the formulations shown in **Table 6**.

**Table 6: Weight Variation and Surface pH**

| Formulations | Weight variation (%) | Surface pH |
|---|---|---|
| $F_1$ | 7.5±.08 | 6.35 |
| $F_2$ | 5.1±. 03 | 6.90 |
| $F_3$ | 2.1±.05 | 6.87 |
| $F_4$ | 4.5±.03 | 6.94 |
| $F_5$ | 5.1±.06 | 6.95 |
| $F_6$ | 4.1±.03 | 6.0 |
| $F_7$ | 5.6±.04 | 6.97 |
| F8 | 6.1±.05 | 6.98 |
| $F_9$ | 3.3±.06 | 6.89 |

**Drug content-**

The test is performed by dissolving a 4 cm2 area film in 50 ml of Phosphate buffer 6.8 under stirring. Filter the solution using Whatman filter paper and dilute the filtrate to 100 ml with the same buffer in a volumetric flask. The solution was analyzed using an ultraviolet spectrometer **[40]**. From the evaluations of Drug content of F1 to F9 batches was found in between 4.82 to 5.24 mg. The results of the drug content of all formulations.

**Assay-**

The test is performed by dissolving a 4 cm2 area film in 50 ml pH 6.8 phosphate buffer under stirring. Filter the solution using Whatman filter paper and dilute the filtrate to 100 ml with the same buffer in a volumetric flask **[39, 40]**. The solution was analyzed using an ultraviolet spectrophotometer. From the % assay evaluations of F1 to F9 batches was found in between 96.4 to 104.8 %.

**Table 7: Drug content and Assay**

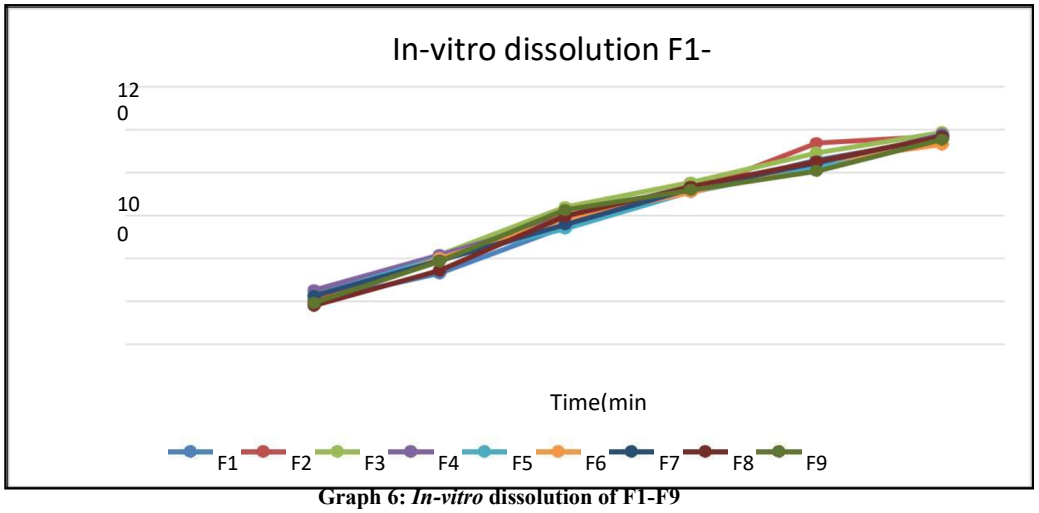
| Formulations | Drug content (mg) | Assay (%) |
|---|---|---|
| $F_1$ | 5.24 | 104.8 |
| $F_2$ | 4.82 | 96.4 |
| $F_3$ | 5.1 | 102 |
| $F_4$ | 4.85 | 97 |
| $F_5$ | 5.07 | 101.4 |
| $F_6$ | 4.91 | 98.2 |
| $F_7$ | 4.89 | 97.8 |
| $F_8$ | 5.02 | 100.4 |
| F9 | 4.87 | 97.4 |

**In-vitro dissolution-**

Use 900 ml Phosphate buffer 6.8 as the medium and keep it at 37±0.5°C while settingthe basket to 100 rpm. Cut 4 cm2 (2 x 2 cm) film sample and place five films in the basket. Take 5 ml samples every 30 seconds and replace the same amount of samples with fresh Phosphate buffer 6.8. The extracted samples were filtered and analyzed using an ultraviolet spectrometer at a wavelength of 212 nm.

**Table 8: In-vitro dissolution of F1-F9**

| Percentage drug released | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Time (min) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 0.5 | 19.91 | 20.35 | 23.07 | 25.13 | 22.5 | 19.08 | 22.5 | 18.11 | 19.3 |
| 1 | 32.98 | 38.6 | 41.58 | 41.58 | 40.31 | 40.04 | 39.04 | 34.3 | 38.68 |
| 1.5 | 54.69 | 59.96 | 63.82 | 58.82 | 53.9 | 58.42 | 55.88 | 59.65 | 62.46 |
| 2 | 71.54 | 71.14 | 75.39 | 71.01 | 71.1 | 70.96 | 72.5 | 73.33 | 71.89 |
| 2.5 | 85.92 | 93.77 | 89.21 | 82.98 | 81.8 | 84.87 | 84.39 | 85.18 | 80.79 |
| 3 | 95.7 | 97.02 | 98.82 | 97.72 | 96.18 | 93.2 | 97.02 | 96.67 | 95.39 |




**Graph 6: *In-vitro* dissolution of F1-F9**

## Comparison of in-vitro drug release data of marketedformulation and formulation $F_3$

**Table 9: Comparison of in-vitro drug release data ofMarketed tablet formulation and formulation $F_3$**

| Time (mins) | % CDR Marketed Formulation | % CDR $F_3$ |
|---|---|---|
| 0.5 | 0 | 23.07 |
| 1 | 0 | 41.58 |
| 1.5 | 0 | 63.82 |
| 2 | 0 | 75.39 |
| 2.5 | 0 | 89.21 |
| 3 | 0 | 98.82 |
| 10 | 18.07 | - |
| 20 | 38.11 | - |
| 30 | 61.97 | - |
| 40 | 73.38 | - |
| 50 | 86.10 | - |
| 60 | 98.29 | - |

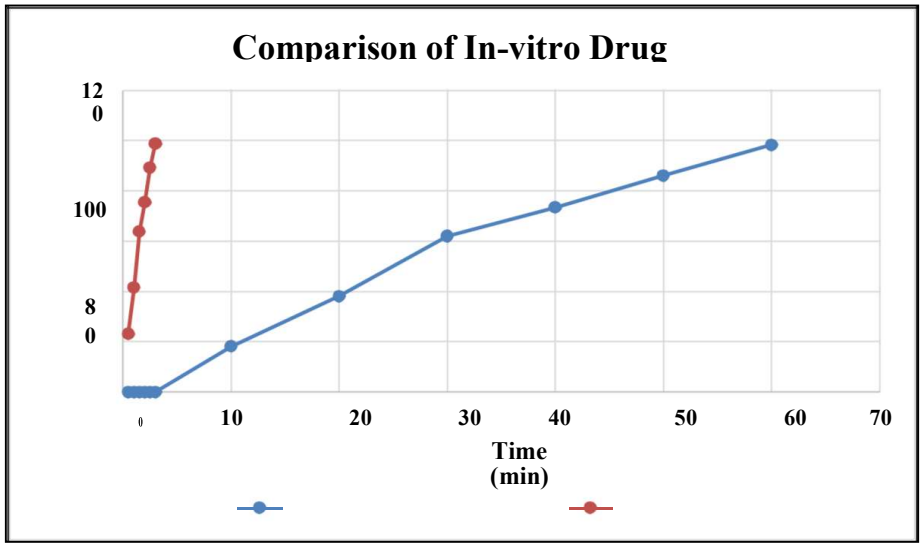



**Figure 7: Comparison of in-vitro drug release data of Marketed Tablet formulation and formulation 3**

## STABILITY STUDIES ($F_3$)

Stability studies are conducted according to ICH to evaluate the stability of pharmaceutical preparations. The optimized formula of F3 is sealed in polyethylene laminated aluminum packaging. The samples were kept at 40 degrees Celsius and 75% RH for 3 months. At the end of the study period, changes in the physical appearance, colour, drug content, and drug release characteristics of the preparation were observed **[40]**.

**Table 10: Stability studies of F3 Batch [Condition (40°C/75%RH)]**

| Parameters | Initial | 1 month | 3 months |
|---|---|---|---|
| Thickness (mm) | 0.53 | 0.52 | 0.52 |
| Folding endurance | 14 | 12 | 12 |
| Tensile strength (gm/cm$^2$) | 54.15 | 54.11 | 53.27 |
| *in-vitro* disintegration time (sec) | 24 | 23 | 21 |
| *in-vitro* dissolution (%) | 98.82 | 97.56 | 96.45 |

## RESULTS

The preparation & evaluation of mouth dissolving film (130mg) take place & With the help of all evaluation observations, optimized formulation (F3) was shown good mouthfeel, surface pH, folding endurance, instant drug release as well as good mechanical properties. Formulation number F3 showed less disintegration time of 24 seconds and, 98% of drugs were released within 3 minutes while the marketed formulation took 1 hour. Therefore, the rapid drug release was achieved for the immediate onset of action which is the benefit when compared to the conventional dosage form.

## CONFLICTS OF INTEREST

There are no conflicts of interest and disclosures regarding the manuscript.

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