Research Article

# Formulation and Evaluation of Fast Disintegrating Sublingual Tablets of Ropinirole Hydrochloride

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**ABSTRACT**

Ropinirole is rapidly absorbed in humans; however it undergoes extensive first-pass metabolism and having only 50% bioavailability. Therefore, the sublingual delivery of Ropinirole hydrochloride would be major improvement in the clinical use of Ropinirole. The Sublingual tablets were prepared by direct compression procedure using different concentration of Crospovidone and Croscarmellose Sodium. Compatibility studies of drug and polymer were performed by FTIR spectroscopy. Preformulation property of API was evaluated. Post-compression parameters such disintegration time, wetting time, water absorption ratio *in vitro* drug release and *ex vivo* permeability study of optimized formulation were determined. FTIR spectroscopy study revealed that there was no possible interaction between drug and polymers. The pre-compression parameters were in acceptable range of pharmacopoeia specification. The disintegration time of optimized formulation (F5) was up to 40 sec. The *in vitro* release of Ropinirole hydrochloride was up to 9 minutes. The percentage relative permeability of Ropinirole hydrochloride from optimized sublingual tablets was found to be 90.51% after 30 minutes. Sublingual tablets Ropinirole hydrochloride of were successfully prepared with improved bioavailability.

**Keywords:** $3^2$ factorial designs, Croscarmellose Sodium, Crospovidone, Direct compression method, Fast disintegrating tablets, Ropinirole Hydrochloride.

## INTRODUCTION

First pass metabolism can be overcome by sublingual drug delivery, and quick drug delivery into the systemic circulation can be obtained. Sublingual administration can offer an attractive alternative route of administration. The advantage of the sublingual drug delivery is that the drug can be directly absorbed into systemic circulation bypassing enzyme degradation in the gut and liver. These formulations are particularly beneficial to pediatric and geriatric patients. In addition sublingual mucosa and abundance of blood supply at the sublingual region allow excellent drug penetration to achieve high plasma drug concentration with rapid onset of an action.[1, 2]

Oral mucosal drug delivery is an alternative method of systemic drug delivery that offers several advantages over both injectable and enteral 11methods. Because the oral mucosa is highly vascularized, drugs that are absorbed through the oral mucosa directly enter the systemic circulation, bypassing the gastrointestinal tract and first-pass metabolism in the liver. For some drugs, this results in rapid onset of action via a more comfortable and convenient delivery route than the intravenous route. Not all drugs, however, can be administered through the oral mucosa because of the characteristics of the oral mucosa and the physicochemical properties of the drug.[3, 4]

The mucosal lining of the oral cavity are readily accessible, robust, and heal rapidly after local stress or damage. Oral mucosal drug delivery systems can be localized easily and are well accepted by patients. Therefore, it is evident that the oral cavity can serve as a site for systemic drug delivery. The total surface area of the oral cavity is about 100 cm. The mucosal membranes of the oral cavity can be divided into five regions: the floor of the mouth (sublingual), the buccal mucosa (cheeks), the gums (gingiva), the palatal mucosa, and the lining of the lips.[5]

## FAST DISINTEGRATING SUBLINGUAL TABLETS[1]

FDT is defined as a solid dosage form that contains medicinal substances and disintegrates rapidly (within few seconds) without water when kept on the tongue. Tablets that disintegrate or dissolve rapidly in the patient's mouth are convenient for young children, the elderly and patients with swallowing difficulties and in situations where potable liquids are not available. Direct compression is one of the techniques which require the incorporation of a super disintegrates into the formulation, or the use of highly water soluble excipients to achieve fast tablet disintegration. Compared to conventional dosage form the drug dissolution, its absorption as well as onset of clinical action and its bioavailability may be significantly greater. Though chewable tablets are available in the market, they are not same as the new FDTs. Patients for whom chewing is difficult or painful can use these FDTs. It can be used easily in infants and in children who have lost their primary teeth and who do not have full use of their permanent teeth.

### Criteria for Fast Disintegrating Drug Delivery System[1]

The tablets should

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be harder and less friable.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.

**Criteria for excipient used in the formulation of FDTs**[6]

- It must be able to disintegrate quickly.
- Their individual properties should not affect the FDTs.
- It should not have any interactions with drug and other excipients.
- It should not interfere in the efficacy and organoleptic properties of the product.
- When the final integrity and stability of the product.
- The melting points of excipients used will be in the range of 30-35$^0$C.
- The binders may be in liquid, semi liquid, solid or polymeric mixtures.
- (Ex: Polyethylene glycol, coca butter, hydrogenated vegetable oils)

**Advantages of FDDDTs**[4]

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric, geriatric patients and psychiatric patients.
- Convenience in administration of drug and accurate dosing as compared to liquid formulations.
- Water is not required for swallowing the dosage form, which is convenient feature for patients who are traveling and do not have immediate access to water.
- Good mouth feels property helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Fast dissolution of medicament and absorption which will leads to rapid, onset of action.
- Some drugs are absorbed from the mouth pharynx and esophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- It provides advantages of liquid formulations in the form of solid dosage form.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects. There is no reported literature on the fast disintegrating sublingual tablets of Ropinirole so far. Ropinirole HCl (4-[2-dipropylamino)ethyl]-1,3-dihydro-2-H-indol-2-one-monohydrochloride) is a new non-ergoline dopamine agonist recently introduced into Parkinson's disease therapy. The Ropinirole is a non-ergoline dopamine agonist with high relative specificity and full intrinsic activity at the D2 and D3 dopamine receptor subtypes. Ropinirole is absorbed rapidly and almost completely. Due to the extensive first pass metabolism of Ropinirole, the mean bioavailability of the dugs is 50%. So, it is considered very useful to design and optimize the fast disintegrating sublingual tablets of Ropinirole. [7, 8]

## MATERIALS AND METHODS

Ropinirole hydrochloride Gifted from Intas pharmaceuticals Ltd. Ahmadabad. Sodium starch glycolate, Crosspovidone, Crosscarmellose Sodium, and Aspartame from Yarrow chem. Ltd, Mumbai. Magnesium stearate, Talc, and Lactose from Chem dyes Corporation.

**Pre-compression properties**

The properties of the tablets like weight variation, hardness, friability, disintegration time, dissolution profile and content uniformity depends on the powder parameters. Properties of powder, which are of most importance, are Bulk density, Hausner's ratio and Compressibility index etc. These parameters were evaluated on a laboratory scale for optimum production with respect to quality and quantity.

Prior to compression into tablets, the blend was evaluated for following properties such as;

***Angle of Repose***[9]

Angle of repose was determined by funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone height, h, was obtained. Diameter of heap, D, was measured. The angle of repose, θ, was calculated by formula

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

$$\theta = \tan^{-1} (h / r)$$

Where, **θ** is the angle of repose,

h is the height in cm and r is the radius.

***Bulk Density***[9]

Apparent bulk density was determined by pouring pre-sieved drug excipient blend into a graduated cylinder and

measuring the volume and weight "as it is". It is expressed in g/mL and is given by;

$$D_b = M / V_0$$

Where, M is the mass of powder,

$V_0$ is the Bulk volume of the powder

***Tap Density***[9]

It was determined by placing a graduated cylinder, containing a known mass of drug- excipient blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/mL and is given by;

$$D_t = M / V_t$$

Where, M is the mass of powder,

$V_t$ is the tapped volume of the powder.

***Carr's Index (Compressibility Index)*** [9]

It is expressed in percentage and is expressed by;

$$I = D_t - D_b / D_t$$

Where, $D_t$ is the tapped density of the powder

$D_b$ is the bulk density of the powder.

***Hausner's Ratio***[9]

It is expressed in percentage and is expressed by;

$$H = D_t / D_b$$

Where, $D_t$ is the tapped density of the powder

$D_b$ is the bulk density of the powder.

**Preparation of Fast Disintegrating Sublingual Tablets**

Each tablet containing 4 mg of drug was prepared by direct compression method. Three superdisintegrant Crospovidone, Croscarmellose sodium, and Sodium starch glycolate used in the different concentration range. All the ingredients were passed through sieve 100# and then geometrical mixing of all the ingredients were done except magnesium stearate and talc. They were added at the end. The mixed blend of drug and the excipients was compressed using RIMEK 10 station rotary punching machine to produce tablet weighing 100mg.

**Experimental Design**

$3^2$ Full Factorial Design was applied to check the effect of the superdisintegrants on various parameters of tablets while superdisintegrants were used in combination. {Concentration of Superdisintegrants were 2%(+1), 3%(0), 4%(-1)}.

**Evaluation of Fast Disintegrating Sublingual Tablet of Ropinirole Hydrochloride**

***General Appearance and Organoleptic Properties***

The control of a general appearance of a tablet involves the measurement of a number of attributes such as a tablet's size, shape, color, presence or absence of an odor.

***Weight Variation***[9]

It was performed as per the method given in the United State Pharmacopoeia. Tablets were randomly checked to ensure that uniform weight tablets were being made. Twenty tablets were selected randomly from each formulation, weighed individually and the average weight and % variation of weight was calculated.

***Friability*** [9]

10 tablets were weighed and placed in the Roche Friabilator test apparatus, the tablets were exposed to rolling and repeated shocks, resulting from free falls within the apparatus. After 100 evolutions the tablets were de-dusted and weighted again. The friability was determined as the percentage loss in weight of the tablets.

***Hardness***[9]

Hardness was measured using the Monsanto hardness tester. Measured the pressure required to break diametrically placed tablet, by a coiled spring.

***In-vitro* Disintegration Studies**

A Modified Method was used to check the disintegration time. In about 6-8mL of phosphate buffer 6.8pH was taken in 10mL of measuring cylinder. Tablet was placed in the cylinder and complete dispersion of tablet in the cylinder was recorded as the disintegration time.

***Wetting Time***[5]

A piece of tissue paper folded twice was placed in a small Petri dish (ID =6.5 cm) containing 6mL of simulated saliva pH, a tablet was put on the paper containing amaranth powder on the upper surface of the tablet, and the time required for formation of pink color was measured as wetting time. Three trials for each batch were performed and standard deviation was also determined.

***Drug Content Uniformity***[10]

Five tablets were accurately weighed and finely powdered. A quantity equivalent to 5 mg of Ropinirole hydrochloride was transferred to a 100mL volumetric flask. To it, 50mL of Phosphate buffer 6.8 was added and shaken for 1 hour to dissolve drug. The solution was filtered and residue was washed with 25mL of Phosphate buffer 6.8. The washing obtained was added to initial filtrate and volume was made up to 100mL with Phosphate buffer 6.8. From above solution 1mL of stock solution was diluted to 10mL. The drug content was determined spectrophotometrically at 249 nm.

***In-vitro Dissolution Studies***[11]

Dissolution studies were carried out for all the formulation in USP paddle method (Apparatus 2) using Phosphate buffer 6.8, in the dissolution medium (250mL) at 50 Rpm and 37±0.5ºC. Samples were periodically

withdrawn at suitable time intervals and volume replaced with equivalent amounts of plain dissolution medium. The samples were analyzed spectrophotometrically at 249 nm.

### *Ex-Vivo* Permeability Study [5, 12]

- Ex vivo permeation studies through porcine oral muc osa is carried out using the modified Franzdiffusion c ell.
- The buccal mucosa was excised and trimmed evenly f rom the sides and then washed in isotonic phosphate buffer of pH 6.8 and used immedi ately. The membrane was stabilized before mounting to remove the soluble component. The mucosa was mounted between the donor and receptor compartments. The receptor compartment was filled with of isotonic phosphate buffer of pH6.8 which was maintained at 37±0.2°C and hydrodynamics were maintained by continuous flow of water through cell, maintained at 37± 0.5$^0$C.
- One Formulation (Sublingual tablet) firstly moistened with a few drops of phosphate buffer 6.8 kept on the mucosal membrane in donor compartment.
- The receptor compartment was filled with phosphate buffer of pH 6.8.
- Samples were withdrawn at suitable interval replacin g the same amount with fresh medium.
- The percentage of drug permeated was determined b y measuring the absorbance inUV-Visiblespectrophot ometer at 249nm.

**Table 1:** Formulation of Final Batches F1-F9 by Direct Compression Method

| Ingredients (mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Ropinirole HCL | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| CP | 2 | 2 | 2 | 3 | 3 | 3 | 4 | 4 | 4 |
| CCS | 2 | 3 | 4 | 2 | 3 | 4 | 2 | 3 | 4 |
| Aspartame | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Mg. Stearate | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| D-Mannitol | 86 | 85 | 84 | 85 | 84 | 83 | 84 | 83 | 82 |
| Wt. of tablet fixed | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

**Table 2:** Preformulation Study of Final Batches F1-F9

| Batch | Bulk Density (g/cm$^3$) | Tap Density (g/cm$^3$) | Carr's Index | Hausner's ratio | Angle of repose |
|---|---|---|---|---|---|
| **F1** | 0.22 ± 0.016 | 0.25 ± 0.021 | 12.00 ± 0.44 | 1.13 ± 0.012 | 28°.31' ± 0.23 |
| **F2** | 0.23 ± 0.021 | 0.27 ± 0.025 | 14.81 ± 0.71 | 1.17 ± 0.019 | 28°.96' ± 0.17 |
| **F3** | 0.25 ± 0.018 | 0.29 ± 0.020 | 13.79 ± 0.46 | 1.16 ± 0.011 | 28°.02' ± 0.22 |
| **F4** | 0.28 ± 0.020 | 0.32 ± 0.021 | 12.50 ± 0.59 | 1.14 ± 0.012 | 29°.12' ± 0.31 |
| **F5** | 0.24 ± 0.017 | 0.27 ± 0.022 | 11.11 ± 0.63 | 1.13 ± 0.019 | 29°.83' ± 0.28 |
| **F6** | 0.21 ± 0.021 | 0.24 ± 0.019 | 12.50 ± 0.58 | 1.14 ± 0.009 | 29°.66' ± 0.21 |
| **F7** | 0.26 ± 0.018 | 0.30 ± 0.022 | 13.33 ± 0.38 | 1.15 ± 0.012 | 29°.45' ± 0.19 |
| **F8** | 0.22 ± 0.017 | 0.26 ± 0.014 | 15.38 ± 0.33 | 1.18 ± 0.011 | 29°.24' ±0.28 |
| **F9** | 0.24 ± 0.020 | 0.29 ± 0.017 | 17.24 ± 0.41 | 1.20 ± 0.013 | 29°.64' ±0.28 |

**Note:** Values are mean value of 3 observation (N=3), and values in parenthesis are standard deviation (±SD)

## RESULTS AND DISCUSSION

### Evaluation of Fast Disintegrating Sublingual Tablet for Designed Formulations

#### *Pre compression evaluation of Fast Disintegrating Sublingual tablet for designed formulations*

#### *Angle of Repose*

Table no. 2 shows the results obtained for angle of repose for all the formulations. The values were found to be in the range of 28°.02' to 29°.83'. All the formulations showed the angle of repose within 30°, which indicates good flow for all the formulation.

#### *Density*

Both loose bulk density (LBD) and tapped bulk density results are shown in Table no.2. The loose bulk density and tapped bulk density for all the formulations varied from 0.21 gm/cm3 to 0.28 gm/cm3 and 0.24 gm/cm3 to 0.32 gm/cm3 respectively. The values obtained lies within the acceptable range and no large differences found between loose bulk density and tapped bulk density. These results help in calculating the % compressibility of the powder.

***Percentage Compressibility (Carr's Consolidation Index)***

Table 2 shows the results obtained for percentage compressibility. The percentage compressibility of powder mix was determined by the equation given for Carr's Consolidation Index in methodology section. The percentage compressibility for all the formulations lies within the range of 11.11 to 17.24; hence they are showing good compressibility.

***Hausner's Ratio***

Table 2 shows the results obtained for Hausner's ratio. The Hausner's ratio of powder mix was determined by the equation given in methodology section using the data obtained for loose bulk density and tapped bulk density. The Hausner's ratio for all the formulations lies within the range of 1.13 to 1.20, which is nearer to optimum Hausner's ratio of 1.25.

**Post compression evaluation of Fast Disintegrating Sublingual tablet for designed formulations**

***Hardness***

The hardness of all the formulations was checked using Monsanto Hardness Tester. The average hardness of all the batches is in the range of 2.4 to 3.6 kg/cm$^2$. The lower standard deviation values indicated that the hardness of all the formulations were almost uniform in specific method and possess good mechanical strength with sufficient hardness.

***Friability***

Friability testing of formulations was done as described in the methodology section. All tablets showed % friability below 1% and thus were in acceptable range and passed the test. The results are given in table 3.

***Weight Variation Test***

Twenty tablets were taken for weight variation testing. All the tablets passed the weight variation test and were in the permissible range of percentage deviation ± 10. The values are given in table 3.

***Wetting Time***

Wetting is closely related to inner structure of tablets. The wetting time in different formulations vary according to the ability of superdisintegrants for swelling and capacity of absorption of water. It was in the range of 17.0 seconds to 52.0 seconds.

***Drug Content Estimation***

The % drug content of all the formulations is mentioned in Table no.3. The drug content values for all the formulations are in the range of 97.11 ± 0.41 to 99.87 ± 0.87.

***In vitro Disintegration Test***

All the formulations were evaluated and results obtained are given in Table no 3. The average in vitro disintegration time for all the formulations lies within the range of 30.0 ± 1.5 seconds to 50 ± 2.6 seconds. This in vitro disintegration time gives direct information regarding super disintegrating nature of disintegrates used.

***Dissolution studies***

*In vitro* drug release studies were performed as per the procedure described in methodology section. Formulation which having a lower disintegration time are best preferred for the formulation of fast disintegrating sublingual tablets. The samples were withdrawn at specified time intervals and analyzed by UV method. % cumulative drug release was calculated on the basis of mean amount of Ropinirole hydrochloride present in the respective formulation. In vitro drug release data for formulation (F1-F9) shown in table 3. The percentage cumulative drug release of sublingual formulations of Ropinirole hydrochloride was plotted against time to obtain drug release profiles as shown in Figure 1.

**Table 3:** Hardness, Friability, Weight variation, & Wetting Time, Disintegration Time, Drug Content & % Cumulative Drug Release of Final Batches F1-F9

| Batch | Hardness (kg/cm$^2$) MEAN ± SD | Friability (%) MEAN ± SD | Weight Variation (mg) MEAN ± SD | Wetting Time (Seconds) MEAN ± SD | Disintegration Time (Seconds) | Drug Content (%) | % Cumulative Drug Release |
|---|---|---|---|---|---|---|---|
| **F1** | 3.2 ± 0.2 | 0.50 ± 0.03 | 102.56 ± 1.6 | 52.0 ± 1.0 | 45.0 ± 1.5 | 97.11 ± 0.41 | 97.68 ± 1.46 |
| **F2** | 3.0 ± 0.4 | 0.53 ± 0.05 | 100.83 ± 2.4 | 44.3 ± 1.5 | 47.0 ± 2.5 | 99.41 ± 0.98 | 98.24 ± 1.02 |
| **F3** | 2.8 ± 0.2 | 0.49 ± 0.05 | 101.36 ± 1.7 | 27.7 ± 1.5 | 50.0 ± 2.6 | 99.87 ± 0.87 | 96.04 ± 1.12 |
| **F4** | 3.0 ± 0.4 | 0.51 ± 0.09 | 102.35 ± 1.6 | 38.3 ± 0.6 | 43.0 ± 1.5 | 97.54 ± 0.53 | 98.85 ± 0.56 |
| **F5** | 3.2 ± 0.2 | 0.52 ± 0.02 | 101.78 ± 1.4 | 21.0 ± 1.7 | 40.0 ± 0.6 | 97.28 ± 0.77 | 97.42 ± 0.92 |
| **F6** | 2.8 ± 0.4 | 0.48 ± 0.06 | 104.40 ± 1.6 | 25.7 ± 2.1 | 41.0 ± 1.0 | 98.76 ± 1.20 | 93.56 ± 1.24 |
| **F7** | 2.8 ± 0.2 | 0.54 ± 0.02 | 102.88 ± 1.8 | 22.0 ± 1.0 | 35.0 ± 1.5 | 99.83 ± 2.21 | 97.01 ± 0.56 |
| **F8** | 3.0 ± 0.2 | 0.51 ± 0.05 | 100.95 ± 1.9 | 19.7 ± 0.6 | 32.0 ± 0.6 | 99.32 ± 1.30 | 96.23 ± 0.39 |
| **F9** | 3.2 ± 0.4 | 0.55 ± 0.03 | 102.79 ± 1.3 | 17.0 ± 1.0 | 30.0 ± 1.5 | 98.51 ± 0.98 | 99.38 ± 0.68 |

**Table 4:** $3^2$ Full Factorial design with corresponding response of DT and T90

| Parameter | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Disintegration Time (seconds) | 45.0 | 47.0 | 50.0 | 43.0 | 40.0 | 41.0 | 35.0 | 32.0 | 30.0 |
| T90 (minutes) | 7.78 | 8.01 | 8.57 | 7.75 | 8.19 | 8.23 | 7.46 | 7.68 | 7.37 |

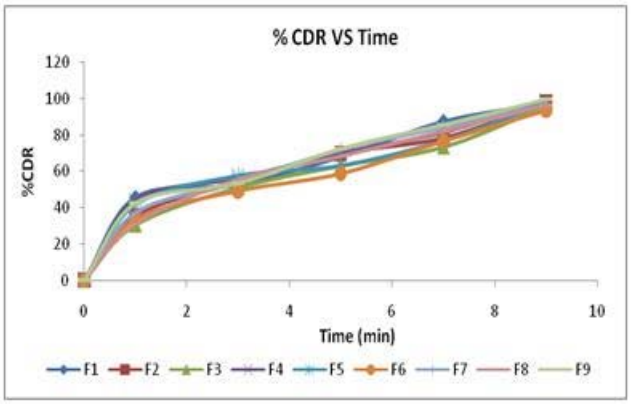


**Figure 1:** *In- vitro* drug release of Ropinirole Hydrochloride from formulation F1-F9

**Statistical Analysis of Experimental Data by Using Design Expert 9.0 Software**

In this study, amount of Crospovidone and CCS were chosen as the independent formulation variables. The dependent variables included Disintegration time and in vitro T90. The effect of formulation variables on the response variables were statically evaluated by applying one-way ANOVA using Design-Expert® 9.0.2 (Stat Ease, USA). The design was evaluated using a quadratic model, which bears the form of the equation:

$$Y = b_0 + b_1 X_1 + b_2 X_2 + b_3 X_1 X_2 + b_4 X_1^2 + b_5 X_2^2$$

Where Y is the response variable, $b_0$ the constant and $b_1, b_2, b_3 \ldots b_5$ is the regression coefficient. $X_1$ and $X_2$ stand for the main effect; $X_1X_2$ are the interaction terms that shows how the response changes when two factors are simultaneously changed. $X_1^2$ and $X_2^2$ are quadratic terms of the independent variables to evaluate the nonlinearity.

The dependent variables were tested for all the 9 batches and the results are shown in Table 4.

A numerical optimization procedure using desirability approach was used to identify the optimal settings of the formulation variables to obtain the target response. The data of pure error are summarized in ANOVA table which can provide a mean response and an estimate of pure experimental uncertainty. F5 is the optimized formula.

**Disintegration Time**

The Model F-value of 95.06 implies the model is significant. There is only a 0.17% chance that a F-Value this large could occur due to noise. Values of "Prob> F" less than 0.0500 indicate model terms are significant. In this case A and AB are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. The "Pred R-Squared" of 0.9363 is in reasonable agreement with the "Adj R-Squared" of 0.9594.

**T90**

The Model F-value of 65.01 implies the model is significant. There is only a 0.29% chance that a F-Value this large could occur due to noise. Values of "Prob> F" less than 0.0500 indicate model terms are significant. In this case A, B, AB, $A^2$ are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. The "Pred R-Squared" of 0.8885 is in reasonable agreement with the "Adj R-Squared" of 0.756.

**Table 5:** Comparison chart of predicted and experimental values for optimized formulation

| Dependent Variables | Optimized Formulation | | |
|---|---|---|---|
| | Predicted Value | Experimental Value | Error |
| Disintegration Time (Sec) | 40.0 | 38.0 | 2.0 |
| T90 (minutes) | 8.10 | 8.23 | 0.13 |

**Table 6:** % Cumulative Drug Release of Ropinirole HCl Sublingual Tablet by using Modified Franz Diffusion Cell

| Time(min) | %CDR |
|---|---|
| 1 | 2.28 ± 0.69 |
| 3 | 4.2 ± 1.15 |
| 5 | 7.11 ± 1.32 |
| 7 | 12.77 ± 1.29 |
| 9 | 23.08 ± 2.09 |
| 12 | 48.97 ± 1.94 |
| 15 | 67.11 ± 1.89 |
| 20 | 71.36 ± 1.31 |
| 25 | 80.02 ± 2.17 |
| 30 | 90.51 ± 2.61 |

**Note:** Values are mean value of 3 observation (N=3), and values in parenthesis are standard deviation (± SD)

The results in Table 5 demonstrated a good relationship between the predicted and experimental values, confirming the validity of the model. The hardness of formulation batch F5 was found to be 3.0 kg/cm$^2$. The percentage friability of F5 was 0.51%. The drug content was found to be 97.28 % of the theoretical value. The percentage deviation for 20 tablets was within the acceptable pharmacopeia limits (±10%). The formulation

F5 showed rapid dissolution rate and the cumulative drug release was found to be 97.42% and complete dissolution was achieved in 9 minutes. The response surface plots showing the effect of amount of Crospovidone ($X_1$) and amount of CCS($X_2$) on the response Disintegration Time (Y1) and T90 (Y2) are shown in Figure 2.

### *Ex-Vivo* Permeability Study

It can also be concluded that Formula F5 shows lesser drug release in Diffusion as compared to that of in-vitro drug release study.

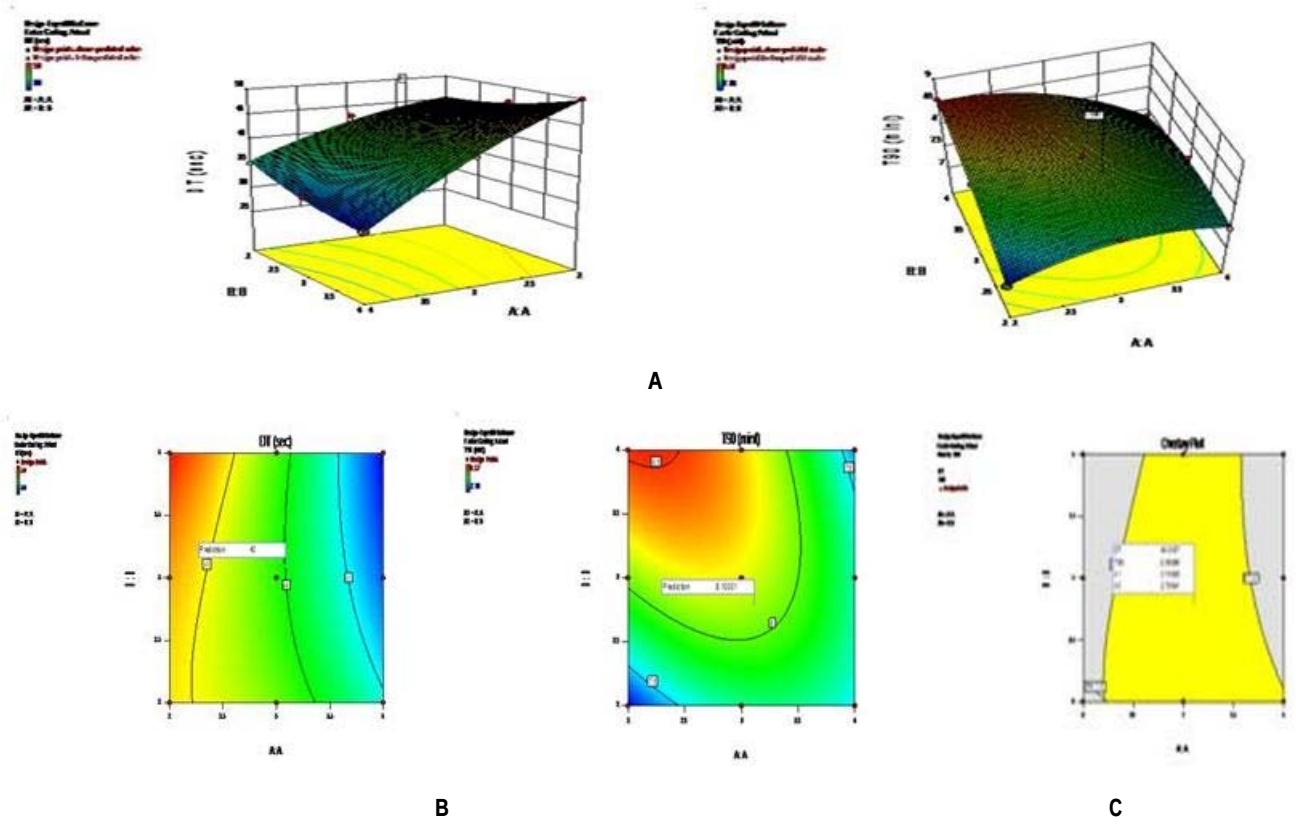

**Figure 2:** Response surface plot (A) and Contour Plot (B) of Disintegration Time (Seconds) and T90 (minutes), & Combined Contour Optimization Plot of T90 & disintegration Time(C).

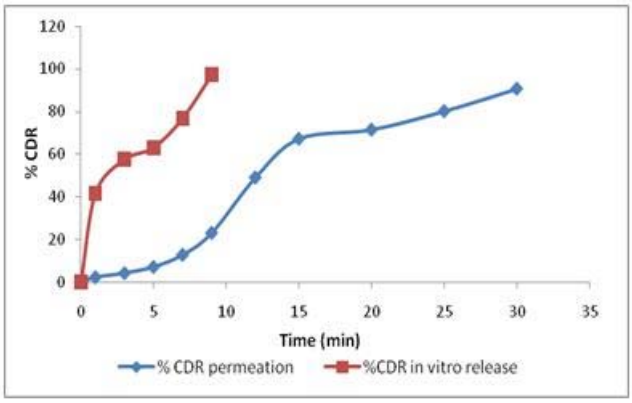


**Figure 3:** Comparison of *In-vitro* drug release of Ropinirole Hydrochloride

## CONCLUSION

Fast dissolving tablets of Ropinirole hydrochloride was satisfactorily formed with appropriate physical characteristic. The Fast dissolving tablets of Ropinirole hydrochloride was found appropriate for the fast release of Ropinirole hydrochloride with acceptable in vitro disintegration time. The Ropinirole hydrochloride release from the tablets was within 9 minutes by optimizing amount Crospovidone and Croscarmellose Sodium. So Sublingual tablets Ropinirole hydrochloride of were successfully prepared with improved bioavailability.

## REFERENCES

1. Gupta A, Mishra AK, Gupta V, Bansal P, Singh R and Singh AK, Recent Trends of Fast Dissolving Tablet - An Overview of Formulation Technology, Int. J. Pharmaceutical & Biological Archives, 1, 2010, 1-10.
2. Tas Z, Bayrak Z, Tasdemir U, Erol H, Ozkan CK, Savaser A, Ozkan Y, Formulation of Zolmitriptan Sublingual Tablets prepared by Direct Compression with different polymer: In vitro and in vivo evaluation, Euro. J. Pharmaceutics and Biopharmaceutics, 78, 2011, 499-505.
3. Paderni C, Compilato Z, Giannola LI, Campisi G, Oral local drug delivery and new perspectives in oral drug formulation, Oral Surg OralMed Oral Pathol Oral Radiol, 114, 2012, 25-34.
4. Patel N, Pancholi SS, An Overview on: Sublingual Route for Systemic Drug Delivery, Int. J. Research in Pharmaceutical and Biomedical Sciences, 3, 2012, 913-923.
5. Narang N, Sharma J, Sublingual Mucosa as a Route for Systemic Drug Delivery, Int. J. Pharmacy and Pharmaceutical Sciences, 3, 2011, 18-22.

6. Manivannan R, Oral Disintegrating Tablets: A Future Compaction, Int. J. of Pharma Research and Development, 1, 2009, 1-10.

7. "Ropinirole", 2013, www.drugs.com/mmx/ropinirole-hydrochloride.html

8. "Ropinirole", 2013, http://drugbank.ca/drugs/DB00268.

9. Lachman L, Lieberman H, Kanig J, The theory and practice of industrial pharmacy, 4th ed. Bombay: Varghese publishing house, 1986, 296-303.

10. Rameshwari S, Sheeba FR, Acharya GD, Anandhi J, Formulation and Evaluation of Nifedipine Sublingual Tablets, Asian J. Pharmaceutical and Clinical Research, 2, 2009, 44-48.

11. Sharma R, Yasir M, Gupta A, Formulation and Evaluation of Fast Disintegrating Sublingual Tablets of Glipizide: An Attempt to Treat Diabetic Coma, Int. J. ChemTech Research, 2, 2010, 2026-2033.

12. Prajapati S, Patel P, Patel C, Formulation and Evaluation of Sublingual Tablets containing Sumatriptan Succinate, Int. J.Pharmaceutical Investigation, 2, 162-168.

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