ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

# DEVELOPMENT AND EVALUATION OF ORAL FILM OF SUMATRIPTAN SUCCINATE

**Gurleen Kaur*, Priyanka, Kapil Kumar, Deepak Teotia**

*Global Institute of Pharmaceutical Education and Research, Kashipur, Uttarakhand, India*

**Corresponding author: gurleensandhu1991@gmail.com*

## ABSTRACT

The development of fast dissolving dosage form consisted in film form and the rapid disintegrating properties were obtained through a special procedure or formulation modification, recently fast dissolving film are gaining as an alternative to fast dissolving film rapid absorbed.

The present work aimed at preparing mouth dissolving film of Sumatriptan Succinate with the purpose of developing a dosage form a very quick onset of action. Sumatriptan Succinate is a 5-$HT_{1B/1D}$ receptor agonist used in the treatment of migraine. The bioavailability of Sumatriptan is approximately 15% so by delivering the drug through sublingual route will enhance bioavailability of the drug and provide quick onset of action to treat acute migraine attack. It allows the drug to directly enter into the systemic circulation and bypass the first pass metabolism. The main purpose of doing this study is to enhance the bioavailability and efficacy of sumatriptan because according to literature review this drug comes under the category of low efficacy drug used in management of acute attack of migraine due to its limitation to achieve pain free response within 2 hours of administration of oral dosage form of drug. This route by passes the first pass effect and due to this drug degradation will also not take place and it proves to be better option for dysphagic patients, pediatric, geriatric patients. The fast dissolving films are more beneficial in comparison to the tablet and capsules because sublingual films tend to dissolve within a minutes/ second safter placing below the tongue.

**Keywords:** Sumatriptan Succinate, Brachiocephalic veins, Bioavailability, Fast dissolving, systemic circulation

## 1. INTRODUCTION

In sublingual drug delivery, the delivery of drug take place beneath the tongue from where it directly reaches to the systemic circulation by passing through the ventral surface of the tongue and also through the floor of the oral cavity [1]. Drugs are rapidly absorbed into the oral mucosa, and get transported through the different veins like facial veins, internal jugular vein, and brachiocephalic veins [3-6]. The drug administration through this route is 3 to 10 times more beneficial than oral route. For sublingual delivery, a small volume of saliva is required to break the dosage form into the oral cavity [7]. Dysphagia a kind of trouble in gulping is very common issue for all age group particularly kids, elders and also those patients who are not cooperative or having lesser liquid diet they experience gulping issues to these dose shapes [2]. Sublingual drug delivery system is a kind of delivery system in which drug is kept under the tongue so it directly reaches to the systemic circulation by passing through the ventral surface and the floor of the oral mucosa [8-10]. This route by passes the first pass effect and due to this drug degradation will also not take place and it proves to be better option for dysphagic patients, pediatric, geriatric patients. This occurs because of more permeability of sublingual route than buccal area. The sublingual drug delivery is an effective route but having a challenging task because all drug molecules cannot be administered through this route [11]. The sublingual film approach can improve the drug targeting to brain due to which the adverse effects of drug will be minimized and bioavailability of drug will be further enhanced. HPMC K4M and NaCMC are used as film forming polymer in the preparation of sublingual films so that the film dissolved rapidly in the sublingual cavity and directly deliver the drug to the systemic circulation. PEG 400 was used as plasticizers as it provides flexibility and mechanical properties to film [12].

Sumatriptan is a Serotonin agonist that acts selectively at 5HT1 receptors. It is used in the treatment of migraine disorders. The 5-$HT_{1B}$ and 5-$HT_{1D}$ receptor function as autoreceptors, which inhibit the firing of serotonin neurons and a reduction in the synthesis and release of serotonin upon activation [13, 14]. After sumatriptan binds to these receptors, adenylate cyclase activity is

inhibited via regulatory G protein, increases intracellular calcium, and affects other intracellular calcium, and affects other intacellular events. The elimination half-life of sumatriptan is approximately 2.5 hours. Radio labeled 14C-Sumatiptan administered orally is largely renally excreted (about 60%) with about 40% found in the feces [15].

Sumatriptan succinate has bioavailability 45% which would not be affected even if the dosage form is taken with food [16]. It is not completely absorbed when given orally and follows first pass metabolism, resulting in low bioavailability due to its extensive first pass effect. The aim of this work was to prepare Sumatriptan Succinate fast dissolving thin films allowing the drug to directly enter the systemic circulation and bypassing the first-pass metabolism.

## 2. MATERIAL AND METHODS

Sumatriptan was obtained from Orchid Chemicals and Pharmaceuticals Ltd., Chennai, India as gift sample. HMPC K4 and Sodium Carboxymethyl cellulose were obtained from Central Drug House Pvt. Ltd., New Delhi, India. Other reagents used were of analytical grade.

### 2.1. Preparation of dummy sublingual films

The method used for the preparation of films was solvent casting method. Formulation code A was prepared by dissolving HPMC K4M and Sodium carboxy methylcellulose (Na CMC) in specific proportion in distilled water. For formulation code Baqueous solution I was prepared by dissolving the HPMC K4M and Sodium carboxy methyl cellulose (Na CMC) in specific proportion in distilled water and was allowed to stir for 1 hour. Aqueous solution II was prepared by mixing PEG-400 in specific proportion in distilled water. Then the aqueous solution II was added to aqueous solution I slowly while stirring and further stirred for 1 hour after addition as shown in table 1. Then it was kept for 2 hours to remove all the entrapped air bubbles. The mixture solution was then casted on a 9 cm teflon coated petri plate and was dried at 40°C for 24 hours in hot air oven. The film was carefully removed from petri plate and was cut into required dimensions of 3×1cm$^2$. The samples of film with air bubbles, tears or having mean thickness variations of greater than 5 % were excluded from analysis [17]. The selected samples were stored in desiccator until further analysis. The composition of various batches sublingual films are given in Table 1.

### 2.2. Preparation of drug loaded sublingual films:

The best dummy formulations were selected for the incorporation of the pure drug based on visual appearance, disintegration time, folding endurance, wetting time and some other parameters to form drug loaded sublingual film [18][18]. Mannitol, DMSO and tween 80 were added in different concentration before the addition of PEG-400 aqueous solution as shown in Table 2.

### 2.3. Evaluation of sublingual film

#### *2.3.1. Appearance of film*

The appearance of the prepared films was evaluated visually.

#### *2.3.2. Mean Thickness*

The thickness of each film of all the prepared batches was measured from five different locations (four corners and centre) using digital vernier caliper having a least count of 0.01 mm. The data were represented as a mean and standard deviation was calculated [19].

#### *2.3.3. Folding Endurance*

Folding endurance is defined as the number of times a film could be folded manually at the same place without a visible sign of crack. It was determined by folding each film repeatedly at the same place until it breaks [8, 9]. The study was done in triplicate for all batches [20].

#### *2.3.4. In-vitro Disintegration time*

The *in-vitro* disintegration time gives an idea about the disintegration and dissolution characteristics of the film [10]. The films from each batch of dimensions 3x1 cm$^2$ was placed in a glass petridish (around 9 cm diameter) containing 25 ml of simulated saliva, maintained at 37°C, with swirling at every 10 s. The disintegration time was recorded as the time when the film starts to break or disintegrate [11]. The study was done in triplicate for all batches [21].

#### *2.3.5. In -vitro* wetting time

A circular tissue paper 7cm in diameter was placed in the petri plate. 10 ml of 0.05% w/v eosin dye solution in water was added to the petri plate. A 3×1 cm$^2$ film was placed on the surface of the tissue paper. The time required for the dye solution to appear on the surface of the film was noted as the wetting time [22]. The study was done in triplicate for all batches.

#### *2.3.6. Surface pH*

The surface pH of film was determined in order to investigate the possibility of any in vivo side effect. As an

acidic or alkaline pH may cause irritation of the mucosa, the surface pH of the films was determined to check whether it is neutralizing or not. A pH electrode was used for this purpose. The film was cut in size of 3 x 1 $cm^2$ and placed in a petridish. It was moistened with 1 ml of simulated saliva (pH 6.8) and kept for 1 min, and then pH was measured by bringing the electrode in contact with the surface of the sublingual film. The procedure was performed in triplicate and average value with standard deviation was reported [22]. The study was done in triplicate for all batches.

### *2.3.7.* Content uniformity

The drug content uniformity of drug loaded films was determined by dissolving film of 3 x 1 cm in 100 ml of simulated saliva (pH 6.8). The sample was filtered through 0.45 µm membrane filter after suitable dilution. The drug content was analyzed at 245 nm using double beamed UV spectrophotometer [14]. The study was done in triplicate for all batches [23].

### *2.3.8. In-vitro* drug release

The *in-vitro* drug release of the film samples of prepared batches was carried out in 250 ml of simulated saliva as dissolution medium using USP dissolution apparatus I, maintained at 37±0.5°C with 50 rpm. 5 ml samples were withdrawn at different pre-determined time intervals and an equal volume of fresh dissolution medium maintained at same temperature was added to maintain the sink condition in the dissolution vessel. Samples were filtered through 0.45 µm membrane filter after suitable dilutions, if required and then analyzed spectrophotometrically at 245 nm. The test was performed in triplicate for each film formulation and the average value was taken. The study was done in triplicate for all batches [24].

### *2.3.9. In-vitro* permeation study

*In-vitro* permeation study was performed to determine the permeability of drug across dialysis membrane by using franz diffusion cell of radius 2.5 cm. With the help of clamps, the dialysis membrane after activation was fixed in between the donor and receptor compartment. The receptor compartment was filled with 20 ml of phosphate buffer pH 7.4. The film strip was placed in donor compartment on the dialysis membrane and the donor compartment was filled with 3 ml of simulated saliva pH 6.8. The whole study was carried out by maintaining the temperature of buffer at 37±0.5°C by keeping the franz diffusion cell over magnetic stirrer and stirring the media throughout the study. 1 ml samples were withdrawn from the receptor compartment at time intervals of 15, 30, 60, 75, 90, 105, 120 min and replaced with an equal amount of freshly prepared simulated saliva pH 6.8 maintained at same temperature of 37±0.5°C. The samples were then filtered using 0.45-µm membrane filter and then analyzed spectrophotometrically at 245 nm. The graph of % drug permeated v/s time was plotted and slope of the linear portion of graph was used Jss (steady state flux). The permeability coefficient (Kp) was calculated for each batch using equation in which Cv is the total concentration of drug in receptor compartment. The test was performed in triplicate for each film formulation and the average value was taken [25].

## 3. RESULTS AND DISCUSSION

The authenticity of drug was performed by various different test i.e. solubility, melting point, test according to Indian Pharmacopoeia and some analytical tests were also performed on sample to justify the authenticity of sample. The melting point of obtained drug sample was found to be 164-166°C, which complies with the one specified in Indian pharmacopoeia. This justifies the authenticity of given sample of Sumatriptan succinate was found to be soluble in water, alcohol and chloroform and slightly soluble in ether. Solubility profile justifies the authenticity of given sample of Sumatriptan succinate.

The melting point of Sumatriptan succinate was determined using melting point apparatus. The sample was placed in capillary which was placed in apparatus and the temperature at which the sample is starting to melt at 164°C.

**Batch F6** **Batch F7**

**Fig. 1: Sublingual Film of Sumatriptan formulations**

Sumatriptan succinate sample was identified and characterized by the parameters listed in Table 2. No variations were found in its specification in Certificate of Analysis (COA) and observations recorded at the time of experimentation.

Experimentally observed melting point complies with reported melting point in literature. The calibration plot of sumatriptan succinate has been developed in simulated saliva pH 6.8 and phosphate buffer pH 7.4. These buffers were selected because of their pH resemblance with the characteristics sites i.e. sublingual region and blood plasma dosage form. Linear regression coefficient and linear regression equation were also established. The calibration plots in different buffers have been shown in (Figure 2).

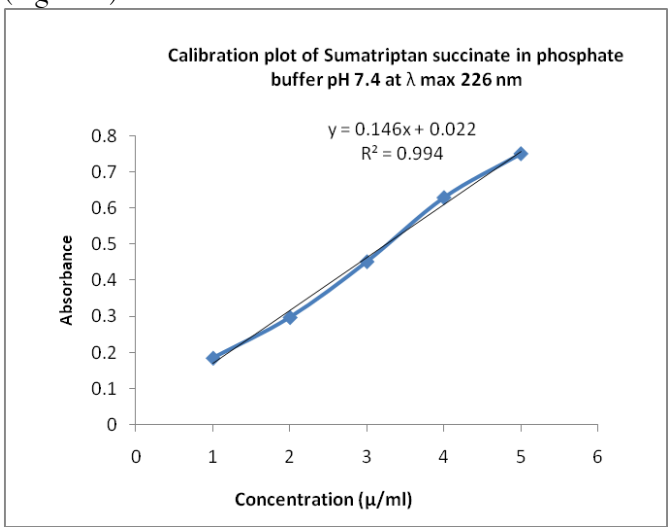


**Fig. 2: Calibration plots of SS in different buffers (A) stimulated saliva pH 6.8 (B) phosphate buffer pH 7.4.**

By using solvent casting method of film formation, 18 dummy formulations have been prepared. These formulations were evaluated for mean thickness, folding endurance, wetting time, disintegration time and surface pH Based on these parameters with desired values like folding endurance >150, disintegration time <1 minute, low wetting time and pH 6.2-7.2 certain formulations was selected, which were further incorporated with drug.

All the films were analyzed visually. The films were found to be transparent and free from bubbles. All prepared films were peeled out easily and stored in desiccator till further use.

All the films were evaluated for thickness by using calibrated digital vernier caliper. As all the formulations contain different amount of polymers, hence the thickness was gradually increases with the amount of polymers. All the batches were found to have thickness in the range of 0.09 mm to 0.17 mm. The results for the same are listed in Table 3.

The folding endurance was measured manually. A film of 3 x 1 cm was cut and subjected for the folding endurance studies until it broke at the same place. Endurance increases with increase in the polymer concentration as shown for all the batches of formulation code A and B. The number of times the film could be folded at the same place without breaking.

**Table 1: Composition of different batches of dummy films**

| **Formulation code A (For selection of Polymer)** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Components** | **A1** | **A2** | **A3** | **A4** | **A5** | **A6** | **A7** | **A8** | **A9** |
| HPMC K4M (mg) | 100 | 200 | 300 | 100 | 200 | 300 | 100 | 200 | 300 |
| Na CMC (mg) | 10 | 10 | 10 | 20 | 20 | 20 | 30 | 30 | 30 |
| Water (ml) | q.s to 20 ml | | | | | | | | |
| **Formulation code B (For selection of Plasticizer)** | | | | | | | | | |
| **Components** | **B1** | **B2** | **B3** | **B4** | **B5** | **B6** | **B7** | **B8** | **B9** |
| HPMC K4M (mg) | 100 | 200 | 300 | 100 | 200 | 300 | 100 | 200 | 300 |
| Na CMC (mg) | 10 | 20 | 30 | 10 | 20 | 30 | 10 | 20 | 30 |
| PEG-400 (ml) | 0.10 | 0.10 | 0.10 | 0.15 | 0.15 | 0.15 | 0.20 | 0.20 | 0.20 |
| Water (ml) | q.s to 20 ml | | | | | | | | |

*In-vitro* wetting time of the films was done and wetting time was noted. The wetting time of all films was found to be from 31 sec to 39 sec. as shown in Table 4.

The disintegration time of the films was evaluated using simulated saliva pH 6.8.

The readings for each batch were recorded, at which disintegration started. The disintegration time of the dummy films ranges from 36 to 55 seconds depending upon the polymer concentration and plasticizer.

The surface pH of the films was evaluated using simulated saliva pH 6.8. The pH of the films was found to be in the range of 6.21 - 7.13, which proves that the films will not cause any irritation in the sublingual mucosa as the pH was found to be almost neutral.

**Table 2: Composition of drug loaded sublingual films**

| Components | F0 | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Sumatriptan succinate (mg) | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 |
| HPMC K4M (mg) | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| Na CMC (mg) | 20 | 10 | 20 | 30 | 20 | 20 | 20 | 20 | 20 | 20 |
| Mannitol (mg) | -- | 95.37 | 95.37 | 95.37 | -- | -- | -- | -- | -- | -- |
| Tween 20 (% v/v) | -- | -- | -- | -- | 1 | 2 | 3 | -- | -- | -- |
| DMSO (%w/w) | -- | -- | -- | -- | -- | -- | -- | 1 | 2 | 3 |
| PEG 400 (ml) | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 | 0.15 |
| Water (ml) | q.s to 20 ml | | | | | | | | | |

**Table 3: Physicochemical characteristics of dummy sublingual films**

| Formulation code | Mean Thickness (mm) | Folding Endurance | Wetting Time(sec) | Disintegration Time(sec) | Surface pH | Visual appearance |
|---|---|---|---|---|---|---|
| **A1** | 0.09 ± 0.003 | 132±3 | 33.66±2.05 | 46±2.08 | 6.21 ± 0.34 | Good |
| **A2** | 0.10 ± 0.002 | 138±2 | 35.66±2.05 | 45±3.05 | 6.92 ± 0.73 | Good |
| **A3** | 0.14 ± 0.007 | 140±3 | 31.66±2.35 | 44±2.64 | 6.82 ± 0.67 | Sticky |
| **A4** | 0.13 ± 0.10 | 136±4 | 36.66±0.94 | 45±3.60 | 7.1 ± 1.2 | Good |
| **A5** | 0.14 ± 0.004 | 138±3 | 33±2.44 | 50±2 | 6.45 ± 0.92 | Good |
| **A6** | 0.16 ± 0.003 | 146±2 | 37±2.94 | 49±3.51 | 6.98 ± 0.91 | Sticky |
| **A7** | 0.13 ± 0.005 | 131±2 | 34±2.86 | 48±4.50 | 7.01 ± 1.3 | Good |
| **A8** | 0.15 ± 0.13 | 135±2 | 33±0.94 | 55±3.05 | 6.54 ± 0.88 | Good |
| **A9** | 0.17 ± 0.009 | 140±3 | 36.33±0.94 | 52±4.16 | 6.84 ± 0.93 | Sticky |
| **B1** | 0.10±0.002 | 155±4 | 39±3.39 | 44±2.51 | 6.9 ± 0.65 | Good |
| **B2** | 0.13±0.10 | 156±4 | 37.33±2.49 | 46±2 | 6.05 ± 1.4 | Good |
| **B3** | 0.14±0.004 | 161±3 | 33±2.44 | 39±2.51 | 7.08 ± 0.67 | Good |
| **B4** | 0.15±0.13 | 153±2 | 32±2.94 | 41±3 | 7.13 ± 1.20 | Good |
| **B5** | 0.16±0.003 | 165±3 | 35±0.94 | 43±1.52 | 7.06 ± 0.86 | Good |
| **B6** | 0.17±0.009 | 169±2 | 35±2.16 | 36±2.08 | 6.83 ± 0.91 | Sticky |
| **B7** | 0.12±0.002 | 156±5 | 33±0.94 | 44±3.05 | 6.48 ± 0.61 | Brittle |
| **B8** | 0.15±0.13 | 158±3 | 37.33±2.49 | 47±2 | 6.99 ± 0.99 | Brittle |
| **B9** | 0.17±0.009 | 164±4 | 39±3.39 | 45±3 | 6.90± 0.88 | Brittle |

*Data are represented as mean ± S.D (n=3), mean thickness (n= 5)*

### 3.1. Evaluation of sublingual films containing SS

The best selected dummy formulation was incorporated with drug. They were evaluated for physiochemical characteristics like visual appearance, mean thickness, folding endurance, wetting time, disintegration time and surface pH.

Appearance of the films was analyzed visually. All films were homogenous, transparent, and easily peeled out from petri plate for all batches except batches F1 to F3 containing mannitol, which were opaque and not peeled out easily from petri plate.

The thickness of the films is measured by using calibrated digital vernier caliper. The thickness of all the films ranges from 0.13 to 0.16 mm. The values of thickness of various batches are shown in (Table 4).

The folding endurance was measured manually. A film of 3x1 $cm^2$ was cut and subjected for the folding endurance studies until it broke at the same place. The folding endurance of all the formulations was found to be 156 to 200.

The thickness of the films is measured by using calibrated digital vernier caliper. The thickness of all the films ranges from 0.13 to 0.16 mm. The values of thickness of various batches are shown in Table 4. The thickness of the films is measured by using calibrated digital vernier caliper. The thickness of all the films ranges from 0.13 to 0.16 mm. The folding endurance was measured

manually. A film of 3 x 1 cm was cut and subjected for the folding endurance studies until it broke at the same place. The folding endurance of all the formulations was found to be 156 to 200. The wetting time of all the prepared batches was noted. There was no significant difference ($p<0.05$) in wetting time of dummy films and the drug loaded films. The values are found in between 30 sec to 39 sec.. The disintegration time of all the drug loaded formulations did not show much difference from the dummy formulations but batches F4, F5 and F6 shows disintegration time greater than 1 min.

**Table 4: Physicochemical characteristics of drug loaded sublingual films**

| Batch code | Mean Thickness (mm) | Folding Endurance | Wetting Time(sec) | Disintegration Time(sec) | Surface pH | Content uniformity (%) |
|---|---|---|---|---|---|---|
| F0 | 0.14±0.08 | 165±2 | 32±2.39 | 43.33±1..52 | 6.8±0.05 | 96.76±0.70 |
| F1 | 0.14±0.01 | 162±2.64 | 33±2.44 | 39.33±3.05 | 6.8±0.05 | 97.9± 1.36 |
| F2 | 0.13±0.01 | 156±2 | 30.66±1.24 | 43±2.64 | 7±0.01 | 96.76±0.70 |
| F3 | -- | -- | -- | -- | -- | 103.4±0.55 |
| F4 | 0.14±0.01 | 194±3.60 | 34.33±1.24 | 95±2 | 6.9±1.52 | 96.73±0.72 |
| F5 | 0.14±0.01 | 195±2 | 33±1.64 | 98.33±2.51 | 6.9±1.52 | 98.26±1.35 |
| F6 | 0.16±0.01 | 200±4 | 34.33±1.69 | 92.33±3.05 | 6.9±1.52 | 102.06 ± 0.76 |
| F7 | 0.13±0.01 | 164±2 | 32.66±2.49 | 46.66±3.05 | 6.6±0.1 | 97.13 ±1.13 |
| F8 | 0.14±0.01 | 165±2 | 35±1.63 | 46±2 | 6.8±0.1 | 95.1 ± 1.15 |
| F9 | 0.13±0.01 | 166±2 | 36±1.63 | 51±2 | 6.9±0.15 | 97.36±1.35 |

**Data are represented as mean ± S.D (n=3), mean thickness (n= 5)*

### 3.2. Drug content uniformity

Content uniformity test for all the prepared batches were performed as per USP guidelines. Actual drug content in the prepared films was in the range of 95.1%-103.4% of the claimed content. This indicates the even distribution of the drug in the prepared matrix of the films of different batches.

### 3.3. *In-vitro* dissolution profile

Figure 3 and Figure 4 show the dissolution profile of all the formulated batches in simulated saliva pH 6.8.

According to literature, the amount of drug dissolved from sublingual tablet must be more than 80% within 15 minutes.

The same criteria were followed for prepared sublingual films. The *in-vitro* drug release of all batches is shown in figures. The *in-vitro* drug of the batch F3 was not carried out because that batch was not peeled out from the Petri plate because it contains mannitol that precipitated out while drying. The batches F1, F2, F4, F6 and F8 showed more than 80% drug release in 15 min.

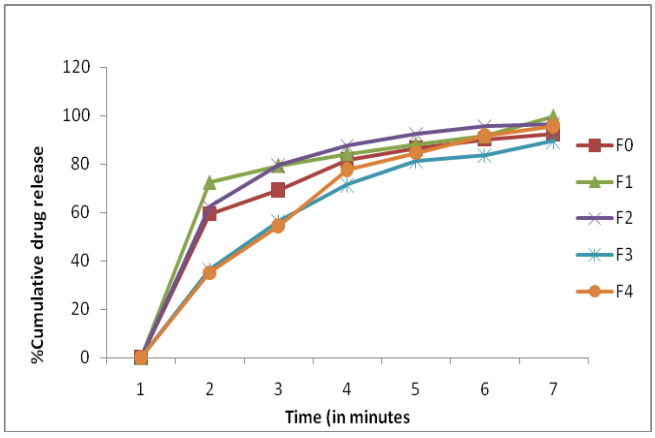


**Fig. 3: Dissolution profile of sublingual films of batch F0 to F6**

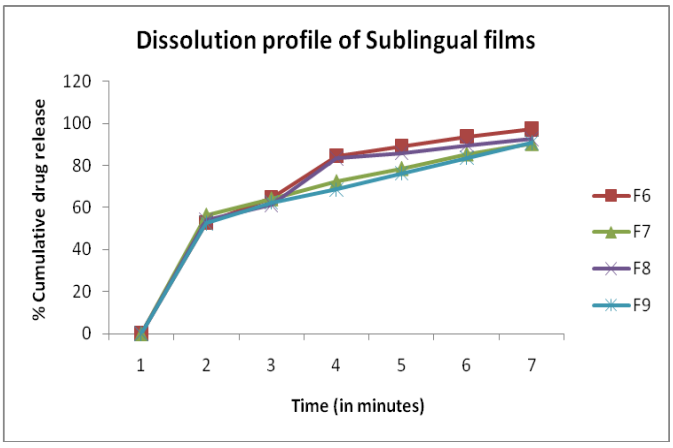


**Fig. 4: Dissolution profile of sublingual films of batch F6 to F9**

### 3.4. *In-vitro* permeation study

The prepared batches were analyzed further by performing *in-vitro* permeation studies using dialysis membrane. The prepared batches were analyzed further by performing *in-vitro* permeation studies using dialysis membrane. Permeation study of batch F3 was not performed because film was not peeled off from the petriplate. DMSO and tween 20 were used as permeation enhancer in the concentration of 1% v/v, 2% v/v and 3% v/v. From the results of the study it was found that batch F8 containing 2% v/v DMSO has highest % permeation in 2 hours. Based on the results F8 batch was selected as an optimized batch.

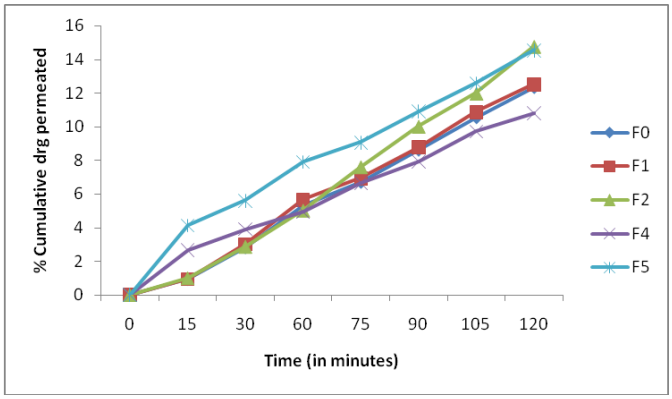


**Fig. 5: *In-vitro* permeation study of sublingual films of batch F0 to F6**

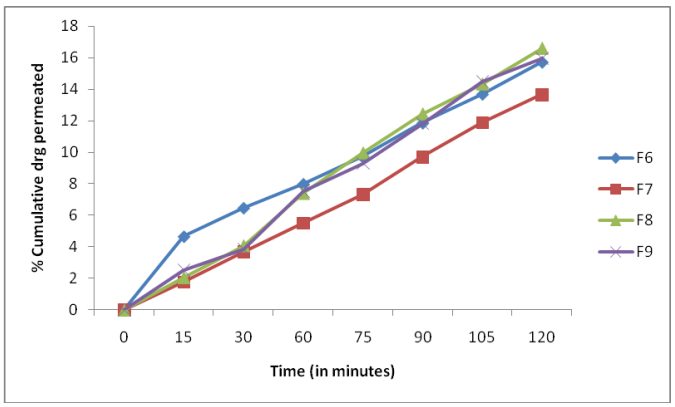


**Fig. 6: *In-vitro* permeation study of sublingual films of batch F6 to F9**

## 4. CONCLUSION

Drug chosen for study is Sumatriptan succinate which is serotonin 5-$HT_1$ receptor agonist that ptently and selectively binds to 5-$HT_{1B/1D}$ subtype present mainly in brain. It used mainly in acute attack of migraine. The identification of Sumatriptan succinate was confirmed by melting point and IR spectra. In the present study fast dissolving sublingual films of Sumatriptan succinate were prepared by solvent casting method using polymer HPMC K4M and their combinations along with different concentration of plasticizer. Sumatriptan succinate is considered to be potentially useful for treatment of acute migraine patients especially for pediatrics and elderly patients due to its convenience. Studies were carried out using different concentration of the polymer HPMC K4M. Promissing formulation for the immediate release of Sumatriptan Succinate in formulation of F8 through Sublingual route since they exhibited Maximum drug release and permeation. Sumatriptan Succinate oral film were prepared by solvent casting method with using different film forming agents like, HPMC K4M, PEG 400, NaCMC are used as a thickning agent and mannitol as filled and sweetner. Fast Disintegration film was placing in oral cavity quickly gets hydrated, sticks into the side of application and then release of the drug after disintegration. These formulations were evaluated for mean thickness, folding endurance, wetting time, disintegration time and surface pH. Based on these parameters with desired values like folding endurance >150, disintegration time <1 minute, low wetting time and pH 6.2-7.2 certain formulations was selected, which were further incorporated with drug. The folding endurance was measured manually. A film of 3x1 $cm^2$ was cut and subjected for the folding endurance studies until it broke at the same place. The folding endurance of all the formulations was found to be 156 to 200. The thickness of the films is measured by using calibrated digital vernier caliper. The thickness of all the films ranges from 0.13 to 0.16 mm. The wetting time of all the prepared batches was noted. There was no significant difference ($p<0.05$) in wetting time of dummy films and the drug loaded films. The values are found in between 30 sec to 39 sec. The sublingual film approach can improve the drug targeting to brain due to which the adverse effects of drug will be minimized and bioavailability of drug will be further enhanced. HPMC K4M and NaCMC are used as film forming polymer in the preparation of sublingual films so that the film dissolved rapidly in the sublingual cavity and directly deliver the drug to the systemic circulation. PEG 400 was used as plasticizers as it provides flexibility and mechanical properties to film. SS loaded sublingual film was prepared by using solvent casting method. The formulation F8 (HPMC K4M 1 % w/v, NaCMC 0.1% w/v and 2 % v/v DMSO) was selected as best optimized batch as it gives maximum percent cumulative drug

release of 83.3 % after 15 minutes. It also showed maximum percent drug permeation of 16.59 % after 120 minutes with $J_{ss}$ and Kp value of 10.93 μg/cm$^2$mins and 0.10 respectively. Future prospective of the present work can be combination of different polymers with distinct permeation enhancers and their *in-vivo* studies. May be they enhance the bioavailability and efficacy of SS to a further greater extent. The thickness of the films is measured by using calibrated digital vernier caliper. The thickness of all the films ranges from 0.13 to 0.16 mm.

## 5. REFERENCES


1. Narang N and Sharma J. *Int J Pharm Pharm Sci*, 2011; **3:**18-22
2. Lam JKW, Y, Xu, Worsley A, Wong ICK. *Adv Drug Deliv Rev*., 2014; **73:**50-62.
3. Parmar D, Patel D, Bhimani B, Tripathi A, Daslaniya D, Patel G. *Int. J. Pharm. Res. Biosci*., 2012; **1:**27- 41.
4. Parmar D, Patel D, Bhimani B, Tripathi A, Daslaniya D, Patel G. *Int. J. Pharm. Res. Biosci.,* 2012; **1:**27- 41.
5. Prakruthi M. Amin, Gangurde AB, Pranali V. *International Journal of Pharmacy and Pharmaceutical Research*, 2015; **3(3):**183-203.
6. Mashru RC, Sutariya VB, Sankalia MG, and Parikh PP. *Drug development and Industrial Pharmacy, 2005;* **31(1):**25-34.
7. Boateng J, Mani J, Kianfar F. *Biomed. Res. Int.*; 2013; 1-8.
8. Singh AK, Singh A, Madhav NVS. *Universal Journal of Pharmaceutical Research,* 2017; **2(6):**25-34.
9. Cilurzo F, Cupone IE, Minghetti P, Buratti S, Gennari CG, Montanari L. *Drug Dev. Ind. Pharm.*, 2008; **37:**52-59.
10. El Meshad AN, El Hagrasy AS, *AAPS Pharm Sci Tech.,* 2011; **12:**1384-1392.
11. Sharma R, Kamboj S, Singh G, Rana SK. *Eur J Pharm Sci*., 2016; **84:**55-69.
12. Mathur P, Mathur CK, Mathur K. *Universal Journal of Pharmaceutical Research,* 2018; **3(6):**49-52.
13. Pakalnis A, Kring D, Paolicchi J. *J. Child. Neurol.*, 2003; **18:**772-775.
14. Villalon CM, Centurion D, Valdivia LF, de Vries P, Saxena PR. *Curr. Vasc. Pharmacol.,* 2003; **1:**71-84.
15. Ahonen K, Hamalainen ML, Rantala H, Hoppu K, *Neurology,* 2004; **62:**883-887.
16. Pierce MW. *Neurotherapeutics,* 2010; **7:**159-163.
17. Edenta Chidi, Nwobodo Ndubuisi Nwobodo, Offiah Raymond O. *Universal Journal of Pharmaceutical Research*, 2017; **2(5):**23-27.
18. Bayrak Z, Tas C, Tasdemir U, Erol H, Ozkan CK, Savaser A, and Ozkan Y. *European Journal of Pharmaceutics and Biopharmaceutics,* 2011; **78(3):**499-505.
19. Bhartee Pathak, Kapil Kumar. *Universal Journal of Pharmaceutical Research,* 2017; **2(3):**20-25.
20. Abdelbary A, Bendas E., Ramadan AA, Mostafa DA. *AAPS Pharm Sci Tech*., 2014; **15:**103-110.
21. Dixit RP, Puthli SP. *J. Control Rel.,* 2009; **139:**94-107.
22. Satbir Singh, Tarun Virmani, Reshu Virmani, Pankaj Kumar, Geeta Mahlawat. *Universal Journal of Pharmaceutical Research*, 2018; **3(4):**60-69.
23. Parejiya, PB, Patel RC, Mehta DM, Shelat PK, Barot BS. *J Pharm Invest*., 2013; **43:**343-351.
24. Sharma R, Kamboj S, Singh G, Rana SK. *Eur J Pharm Sci.,* 2016; **84:**55-69.
25. Saifullahi Umar, Moh Kingsley Onyekachi. *Universal Journal of Pharmaceutical Research*, 2017; **2(1):**17-20.