



## FORMULATION DEVELOPMENT AND EVALUATION OF SUBLINGUAL FILM OF NADOLOL

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### ABSTRACT

Fast dissolving films have been played an important role in the current pharmaceutical research. The present study was aimed to formulate develop and evaluate Sublingual film of Nadolol using Polyvinyl Alcohol, Polyvinyl Pyrrolidone K-30, Polyethylene Glycol-400 and Sodium saccharin. Nadolol is an antihypertensive agent used in the management of hypertension and treatment of angina pectoris and heart failure. Present work aimed at preparing quick onset of action which is beneficial in hypertension, aiding in the enhancement of bioavailability and is very convenient for administration without the problem of swallowing and using water. Fast dissolving oral films are useful in patients such as pediatric, geriatric, bedridden or developmentally disabled who face difficulty in swallowing conventional tablets or capsules and liquid orals or syrups leading to ineffective therapy. Solvent casting method are used to prepared sublingual film of Nadolol and The prepared films were evaluated for Average thickness, Weight variation, disintegration time, content uniformity, *In-vitro* dissolution studies and Mechanical strength such as Folding endurance, Tensile Strength and percent elongation. Films in vitro drug release studies also done by using USP dissolution apparatus. The in vitro drug release in optimized formulation F6 was found to be 98.58% in 5 min.

**KEYWORDS:** Nadolol, Sublingual film, Polyvinyl Alcohol, Polyvinyl Pyrrolidone K-30, Solvent casting method.

### INTRODUCTION

Sublingual Films or oral thin films (OTF) are the most advanced form of oral solid dosage form due to more flexibility and comfort.<sup>[1]</sup> It improves the efficacy of APIs by dissolving within minute in oral cavity after the contact with saliva without chewing and no need of water for administration. It gives quick absorption and Fast dissolving films for oral administration was a novel approach, for the patients who experience difficulties in swallowing tablets or capsules. Geriatric, pediatric and dysphasic patients associated with many medical conditions face a problem of difficulty in swallowing the solid dosage forms.<sup>[2]</sup>

Nadolol is Antihypertensive drug, it is a nonselective beta-adrenergic receptor blocking agent. Nadolol specifically competes with beta-adrenergic receptor agonists for available beta receptor sites; it inhibits both the beta-1 receptors located in cardiac muscle and the beta-2 receptor located in the bronchial and vascular musculature, inhibiting the chronotropic, inotropic and vasodilator responses to beta-adrenergic stimulation

proportionately. Nadolol competes with adrenergic neurotransmitters such as catecholamines for binding at sympathetic receptor sites. Nadolol binds at beta-1 adrenergic receptors in the heart and vascular smooth muscle, inhibiting the effects of the catecholamines epinephrine and norepinephrine and decreasing heart rate, cardiac output and systolic and diastolic blood pressure.<sup>[4,5]</sup>

Justification and novelty behind this research work is following:<sup>[3]</sup>

- No Marketed Nadolol film is available in India.
- Less excipients are required to manufacturing of film, ultimately cost of film decreases.
- Hypertension markedly reduces functional ability and extremely restlessness in such cases rapid onset of action required.
- In case of high blood pressure quick onset of action required because uncontrolled high blood pressure create Strokes, Heart attack, Kidney Problem.
- Specially intended to geriatric patients who have problem of dysphagia.

- Administered without water, anywhere, any time (after or before meal).
- Avoid the problem of disintegration.

pyrrolidone, Polyethylene glycol-400 and Sodium saccharin used were of analytical grade.

## MATERIALS AND METHODS

Nadolol was obtained as gift sample from Yarrow chem Laboratory, Mumbai. Polyvinyl Alcohol, polyvinyl

**Table No. 1 The different functional categories of ingredients used in formulation.**

| Sr. No. | Ingredients                | Functional category                   |
|---------|----------------------------|---------------------------------------|
| 1       | Nadolol                    | Anti-Hypertensive Agent.              |
| 2       | Polyvinyl alcohol          | Film forming agent.                   |
| 3       | Polyvinyl pyrrolidone K-30 | Super disintegrating agent.           |
| 4       | Polyethylene Glycol-400    | Plasticizer                           |
| 5       | Sodium Saccharin           | Sweetener & saliva stimulating agent. |
| 6       | Distilled water            | Vehicle.                              |

## PREPARATION OF SUBLINGUAL FILM

The sublingual film of Nadolol were prepared by the solvent casting method using PVA and PVP K-30 as a

film forming polymer and PEG as a plasticizer. Sodium saccharin is used as sweetener and saliva stimulating agent.

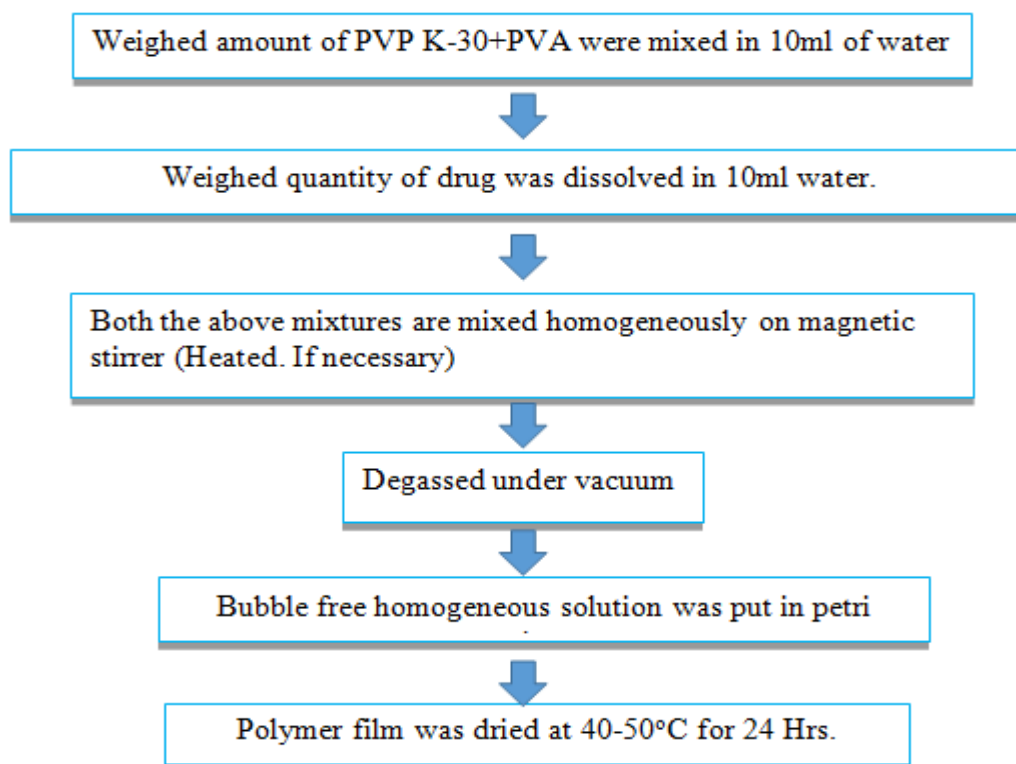


**Fig. 1. Preparation of the film**

## DOSE CALCULATION

The area and number of films prepared for each batch can be calculated as follows:

Total area of petri plate = 68 cm<sup>2</sup>

Each film area = 2x2 = 4cm<sup>2</sup>

Number of film in petri plate = 68 / 4 = 17 Films

Dose of the drug for 2x2 film = 20mg

Total dose in petri plate = 17 x 20 = 340 mg

**Table No.2. Variables in optimization study.**

| Variables               | Factors                    |
|-------------------------|----------------------------|
| Independent<br>X1<br>X2 | Polyvinyl Alcohol          |
|                         | Polyvinyl Pyrrolidone K-30 |
| Dependent<br>Y1         | Release (%)                |

Table No.3. Ranges of independent variables used in factorial design.

| Formulation Code | Coded Value |     |     |     |
|------------------|-------------|-----|-----|-----|
|                  | X 1         | Mg  | X 2 | Mg  |
| F1               | -1          | 200 | +1  | 150 |
| F2               | 0           | 250 | +1  | 150 |
| F3               | +1          | 300 | +1  | 150 |
| F4               | -1          | 200 | 0   | 200 |
| F5               | 0           | 250 | 0   | 200 |
| F6               | +1          | 300 | 0   | 200 |
| F7               | -1          | 200 | -1  | 250 |
| F8               | 0           | 250 | -1  | 250 |
| F9               | +1          | 300 | -1  | 250 |

Table No.4. Composition of Nadolol sublingual Films.

| Ingredients (Mg) | F1   | F2   | F3   | F4   | F5   | F6   | F7   | F8   | F9   |
|------------------|------|------|------|------|------|------|------|------|------|
| Nadolol          | 340  | 340  | 340  | 340  | 340  | 340  | 340  | 340  | 340  |
| PVP              | 150  | 150  | 150  | 200  | 200  | 200  | 250  | 250  | 250  |
| PVA              | 200  | 250  | 300  | 200  | 250  | 300  | 200  | 250  | 300  |
| PEG-400          | 0.18 | 0.18 | 0.18 | 0.18 | 0.18 | 0.18 | 0.18 | 0.18 | 0.18 |
| Sodium Saccharin | 40   | 40   | 40   | 40   | 40   | 40   | 40   | 40   | 40   |
| Water.           | q.s  | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. | q.s. |

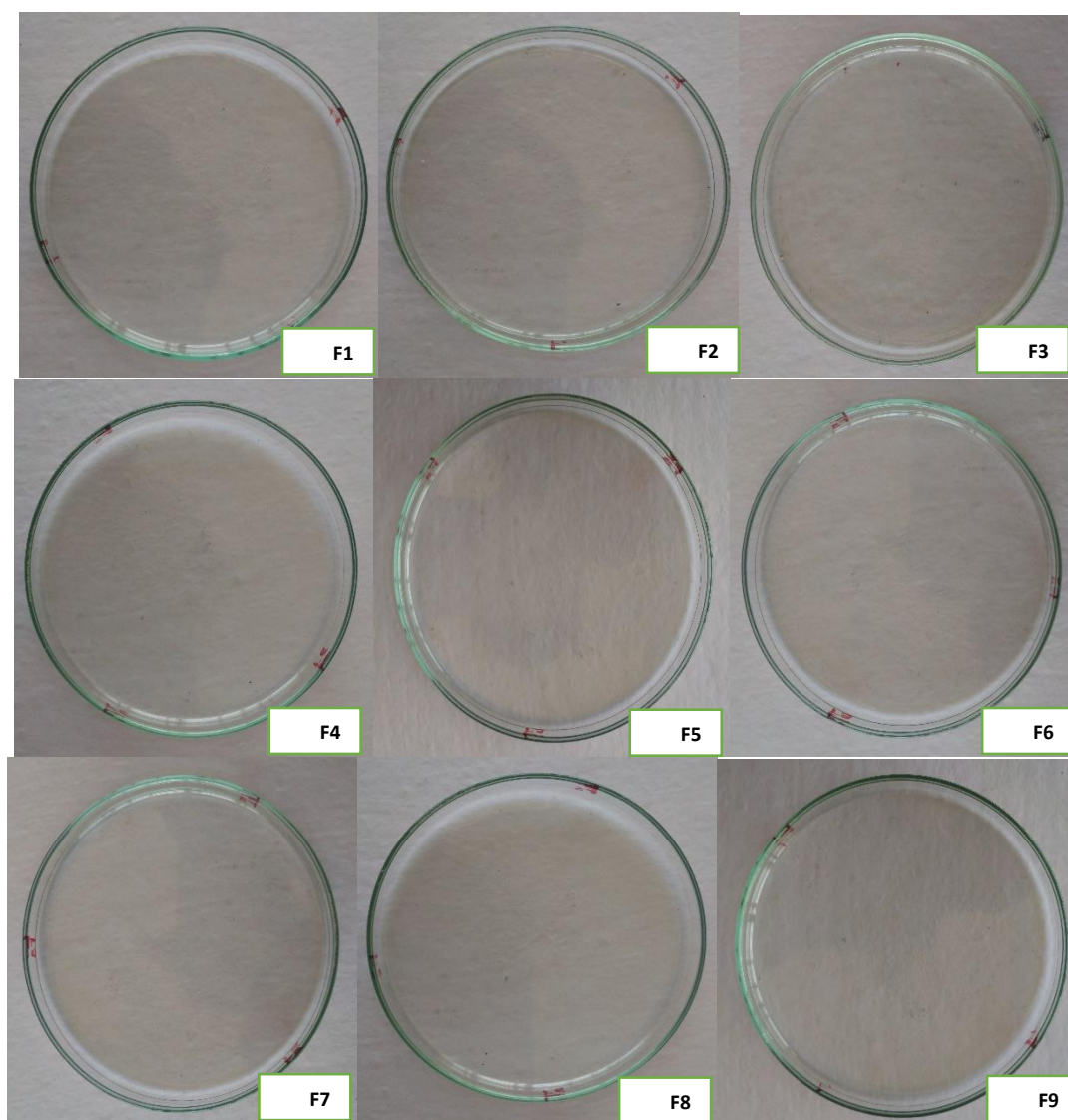


Fig. 2-. Formulation of Sublingual Film of Nadolol

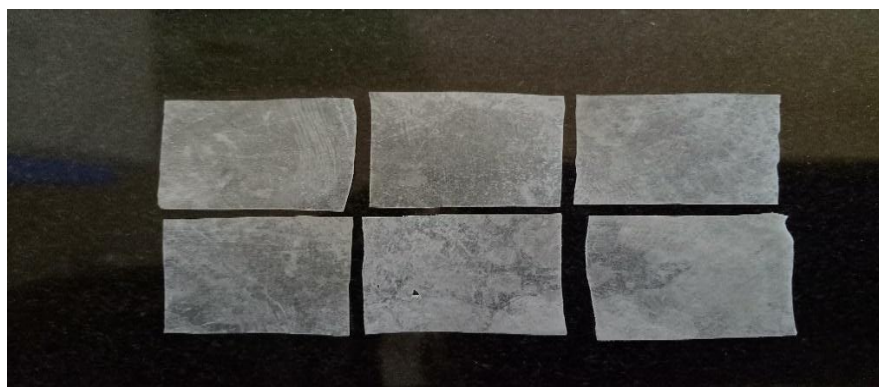


Fig.3. Cutted Desired shape of Sublingual Film of Nadolol (4cm<sup>2</sup>)

### DRUG EXCIPIENT COMPATIBILITY STUDIES

The DSC thermo grams of the pure drug and drug: HPMC E5 mixture were shown in Figure1 sharp peak at 131.97°C and good compatibility with polymers. These study concluded that no excipient incompatibility.

### EVALUATION OF SUBLINGUAL FILM

**1. Organoleptic Evaluations:** Formulated films were evaluated for organoleptic evaluations like Color, odor and taste.

#### 2. Physical Appearance and Surface Texture

Physical appearance was checked by visual inspection and surface texture was evaluated by touch or feel of the film.

#### 3. Thickness of Films

The thickness of three randomly selected films from every batch was determined using a standard Digital Vernier Caliper and average values were reported.<sup>[8]</sup>

#### 4. Weight Uniformity

The cast film was cut at different places and the weight of each film was checked with the help of an electronic balance and the average weight was calculated.<sup>[7]</sup>

#### 5. Surface pH

The surface pH of the film was calculated in order to investigate any side effects in vivo. A combined pH electrode was used for this purpose The cutted film 4cm<sup>2</sup> film has to be kept in the oral cavity, pH of the saliva ranging from 5.5-7.5. So, to dissolve and solubilize the drug in saliva present in the oral cavity the pH of film should keep near to neutral. Since acidic or alkaline pH may leads to irritation to the buccal mucosa. The film preparation to be tested was placed in petri plate and was slightly moistened with 0.5 ml distilled water introduced drop wise. The pH is measured by bringing the electrode in contact with the surface of the oral film and allowing equilibrating for 1 min. The study performed on three films of each formulation and mean ±SD was calculated.

#### 6. Folding Endurance

Folding endurance was determined by repeatedly folding the film at the same position until it breaks. The number

of times the films can be folded without breaking is termed as the folding endurance value.<sup>[7]</sup>

#### 7. Tensile Strength

Tensile strength of films was determined using an apparatus fabricated in laboratory. A small film strip (2 × 2 cm<sup>2</sup>) was cut and fixed to assembly. The weight required to break the film was noted and simultaneously film elongation was measured with the help of pointer mounted on the assembly. Measurements were done in triplicate for each batch. The mechanical properties tensile strength and % elongation were calculated for the fast dissolving film from the above measurements. Tensile strength is the ratio of maximum stress applied to a point at which the film specimen breaks and can be computed from the applied force at rupture to the cross sectional area of the fractured film as a mean of three measurements and described in the equation-<sup>[8]</sup>

$$\text{Tensile strength} = \frac{\text{Load at Failure} \times 100}{\text{Strip thickness} \times \text{Strip Width}}$$

#### 8. Percentage Elongation

When stress is applied, a film sample stretches and this is referred to as a strain. Strain is basically the deformation of film divided by the original dimension of the sample.<sup>[8]</sup>

$$\text{Percentage elongation} = \frac{\text{Increase in length} \times 100}{\text{original length}}$$

1.

#### 9. Drug content

For determination of the drug content of Nadolol Sublingual film equivalent to dose of 20 mg was dissolved in 50 ml of pH 6.8 buffer. The solution was sonicated for 10 minutes and then filtered through Whatmann filter paper no. 41, to separate out the insoluble excipients. 1ml of filtrate was diluted to 100 ml with pH 6.8 buffer. The absorbance of resultant solution was measured using U. V. spectrophotometer at 269 nm and drug content was calculated.<sup>[3]</sup>

#### 10. Disintegration time

The disintegration for orally disintegrating tablets described in CDER guidance can be applied to oral film. Although, no official guidance is available for FDOF, this may be used as a qualitative guideline for quality

control test or at development stage. But for the present work disintegration was measured by taking the 25 ml of distilled water in 50 ml beaker and individual film is dipped into that solution and disintegration time was recorded.<sup>[3]</sup>

### 11. In Vitro Dissolution study

The in vitro release of drug from all formulations was determined using USP apparatus type II (Paddle method). The following conditions were followed to study the in-vitro dissolution study of Nadolol sublingual Film.

1. USP dissolution apparatus: Type II (Paddle method)

2. Volume of dissolution medium: 900 ml
3. Speed: 50 rpm
4. Temperature:  $37 \pm 0.50^\circ\text{C}$
5. Dissolution medium: pH 6.8 buffer
6. Sampling interval: 1 min
7. Quantity of sample withdrawn: 5ml

Aliquots of dissolution medium of 5 ml were withdrawn at 1 min interval for 4 min. The volume withdrawn was replaced by fresh volume of dissolution medium. The filtered samples were analyzed spectrophotometrically at 225 nm and absorbance was noted. Cumulative percent drug release was calculated.<sup>[3]</sup>

## RESULT AND DISCUSSION

### Infra-Red Spectrum

The Infra-Red spectrum of Nadolol is shown in Figure 4.

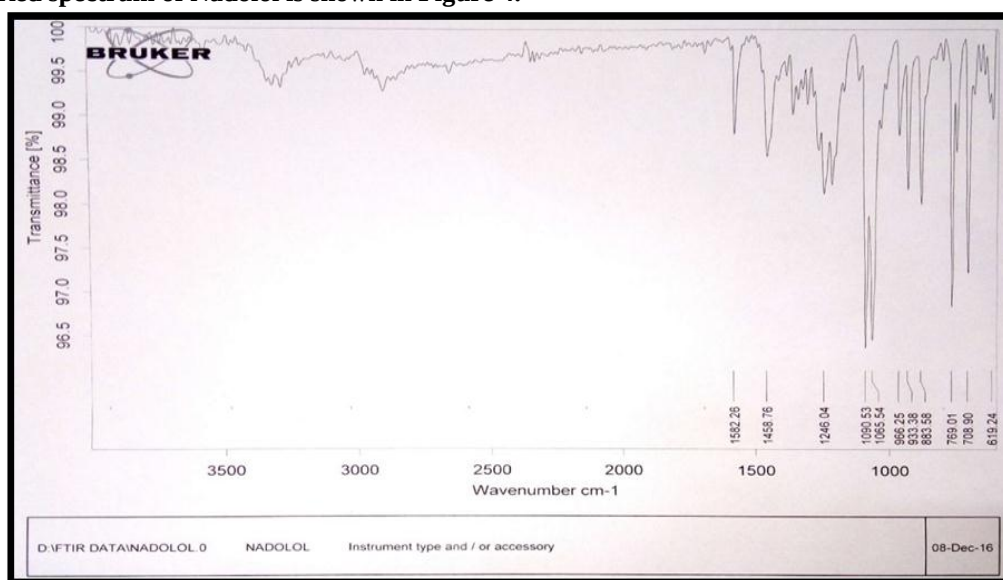


Fig No: 4. FTIR of Nadolol

The FTIR spectra of pure Nadolol showed the peaks at wave numbers ( $\text{cm}^{-1}$ ) which correspond to the functional groups present in the structure of the drug.

Table No.5. Ranges of the functional groups present in I.R. of Nadolol

| Functional groups      | Observed value ( $\text{cm}^{-1}$ ) | Reported value ( $\text{cm}^{-1}$ ) |
|------------------------|-------------------------------------|-------------------------------------|
| C=C Bending (Aromatic) | 1582.26                             | 1585                                |
| -C-H(Aromatic stretch) | 1458.76                             | 1460                                |
| C-O(Stretch)           | 1090.53                             | 1092                                |
| Out of plane C-H       | 933.38                              | 935                                 |
| N-H                    | 782.40                              | 770                                 |

### COMPATIBILITY STUDY

#### Fourier Transform Infrared Spectroscopy

Overlay FT-IR spectra of physical mixture of drug with PVA and PVP K-30, showed matching peaks with the

pure drug spectra. The characteristic peaks of drug were also seen in the spectra of drug in combination with polymers (Figure-5) which indicate compatibility of drug with polymers.<sup>[15]</sup>

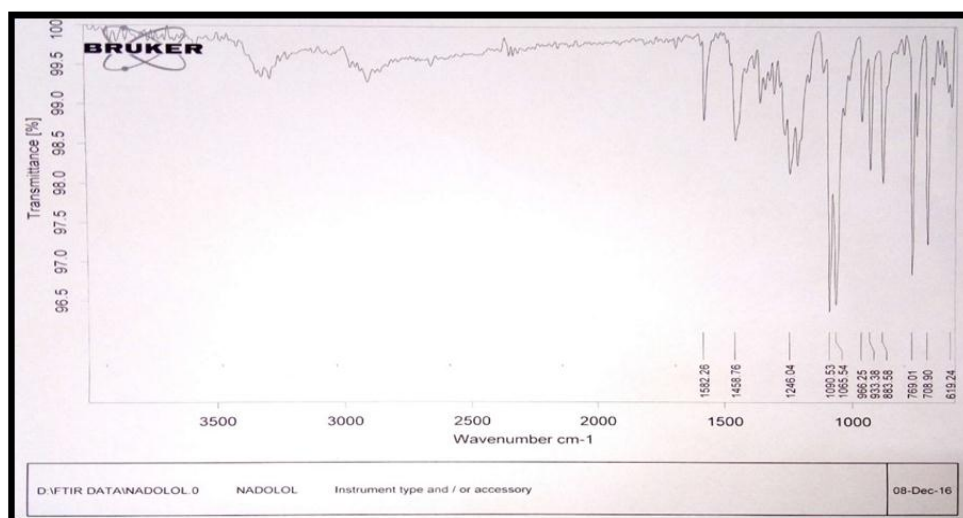


Fig No: 5. FTIR of mixture of Nadolol

Table No. 6. Ranges of the functional groups present in FTIR Nadolol of Physical mixture of with Excipients

| Sr. No. | Functional group (cm) <sup>-1</sup> | Observed Frequency in (cm) <sup>-1</sup> | Pure drug | Drug with PVA and PVP. |
|---------|-------------------------------------|------------------------------------------|-----------|------------------------|
| 01.     | C=C Bending (Aromatic)              | 1582.07                                  | Yes       | Yes                    |
| 02.     | -C-H(Aromatic stretch)              | 1458.75                                  | Yes       | Yes                    |
| 03.     | C-O(Stretch)                        | 1090.51                                  | Yes       | Yes                    |
| 04.     | Out of plane C-H                    | 933.48                                   | Yes       | Yes                    |
| 07.     | N-H                                 | 769.17                                   | Yes       | Yes                    |

Table 7. Evaluation of physico-mechanical parameters of fast dissolving film

| TIME IN MIN | % CUMULATIVE DRUG RELEASE ± S.D |               |               |               |             |             |               |             |             |
|-------------|---------------------------------|---------------|---------------|---------------|-------------|-------------|---------------|-------------|-------------|
|             | F1                              | F2            | F3            | F4            | F5          | F6          | F7            | F8          | F9          |
| 1           | 76.03±0.10                      | 54.99 ± 0.537 | 50.56 ± 0.756 | 54.91 ± 0.212 | 67.04±0.325 | 77.86±0.106 | 65.81 ± 0.732 | 67.95±0.342 | 58.42±0.829 |
| 2           | 80.54 ± 0.21                    | 63.08±0.32    | 59.56±0.786   | 62.54±0.643   | 73.14±0.116 | 85.19±0.166 | 70.09±0.318   | 70.93±0.643 | 65.59±0.443 |
| 3           | 83.91±0.431                     | 68.95±0.63    | 66.06±0.232   | 67.28±0.862   | 84.29±0.547 | 91.61±0.318 | 77.50±0.431   | 78.34±0.724 | 73.38±0.445 |
| 4           | 88.57±0.32                      | 80.10±0.86    | 78.04±0.749   | 76.89±0.673   | 88.64±0.461 | 94.91±0.014 | 85.36±0.318   | 83.76±0.283 | 82.24±0.828 |
| 5           | 93.46±0.75                      | 86.67±0.21    | 84.38±0.650   | 85.67±0.106   | 94.07±0.73  | 98.57±0.219 | 91.86±0.650   | 90.79±0.650 | 89.11±0.932 |

## EVALUATION PARAMETERS OF SUBLINGUAL FILM

Table No 8. In-vitro drug release study of all formulations

| Batch no | Tensile Strength (kg/mm <sup>2</sup> ) | Elongation at break (%) | Thickness (mm) | Weight variation (mg) | Folding Endurance | Surface pH   | % Drug content | Disintegration time (sec) |
|----------|----------------------------------------|-------------------------|----------------|-----------------------|-------------------|--------------|----------------|---------------------------|
| F1       | 1.1567 ± 0.032                         | 26.50 ± 0.500           | 0.090 ± 0.020  | 41.00±0.707           | 153 ± 0.577       | 6.27 ± 0.067 | 91.16 ± 1.280  | 20.33 ± 0.577             |
| F2       | 1.4191 ± 0.025                         | 28.66 ± 0.763           | 0.096 ± 0.019  | 44.40±0.894           | 176 ± 1.527       | 7.19 ± 0.106 | 95.00 ± 0.433  | 27.00 ± 2                 |
| F3       | 1.6333 ± 0.031                         | 30.66 ± 0.750           | 0.112 ± 0.018  | 48.80±1.946           | 212 ± 3.055       | 6.24 ± 0.091 | 92.25 ± 1.500  | 18.33±0.577               |
| F4       | 1.1875 ± 0.028                         | 27.00 ± 0.530           | 0.114 ± 0.026  | 46.00±1.414           | 160 ± 1.006       | 6.80 ± 0.055 | 92.16 ± 2.126  | 17.33±1.527               |
| F5       | 1.3800 ± 0.050                         | 29.66 ± 0.288           | 0.110 ± 0.042  | 47.00±1.428           | 181 ± 2.309       | 6.87 ± 0.057 | 95.66 ± 2.980  | 22.33±0.577               |
| F6       | 1.7483 ± 0.045                         | 32.83 ± 0.252           | 0.080 ± 0.014  | 50.40±0.547           | 223 ± 2.516       | 6.43 ± 0.064 | 98.16 ± 1.010  | 17.00±1                   |
| F7       | 1.1875 ± 0.049                         | 27.67 ± 0.773           | 0.084 ± 0.007  | 44.00±2.121           | 147 ± 1           | 7.45 ± 0.080 | 90.33±1.700    | 23.00±1.730               |
| F8       | 1.4966 ± 0.036                         | 27.83 ± 0.763           | 0.114±0.010    | 49.00±1.870           | 172 ± 1.527       | 6.46 ± 0.095 | 96.75±2.460    | 20.66±1.150               |
| F9       | 1.6783 ± 0.036                         | 32.66 ± 0.288           | 0.104 ± 0.015  | 51.60±2.190           | 221 ± 1.154       | 6.61 ± 0.011 | 88.25±2.220    | 23.00±0                   |

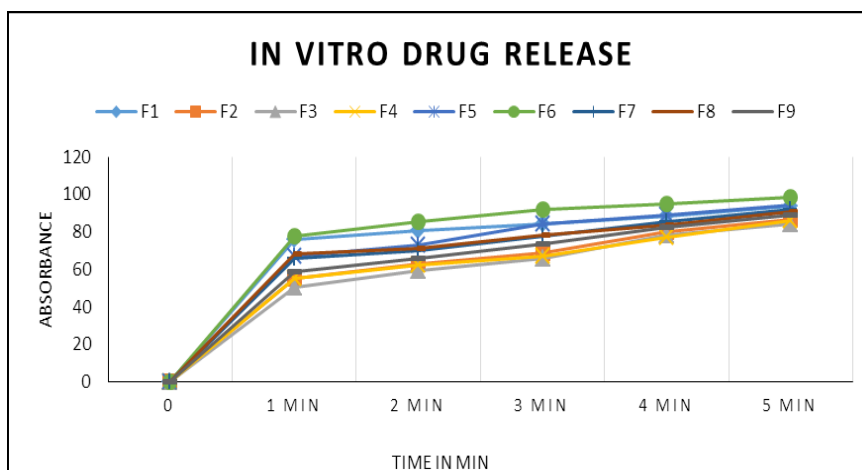


Fig 6. Comparative Evaluation of In-vitro drug release study of sublingual film of Nadolol

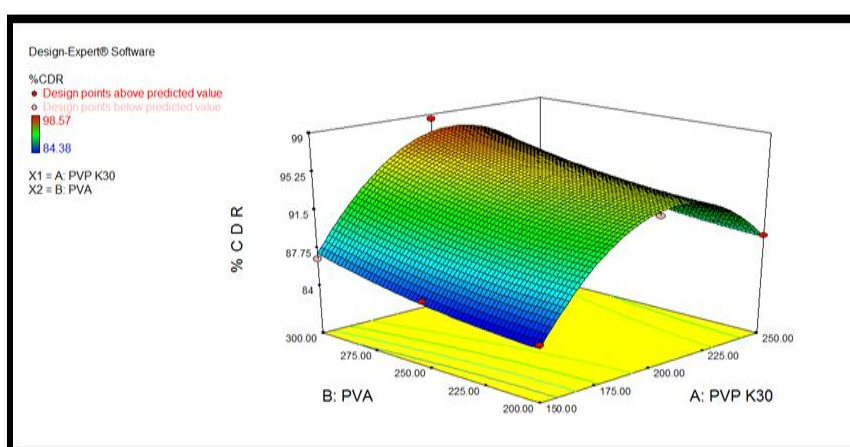


Fig.7 Surface Response plot showing effect of polyvinyl alcohol and polyvinyl pyrrolidone K-30 on release

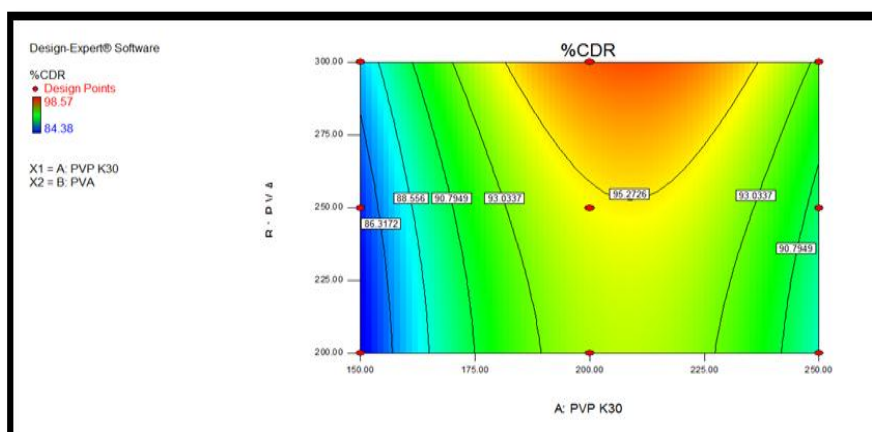


Fig. 8: The countour plot showing effect of polyvinyl alcohol and polyvinyl pyrrolidone K-30 on Release

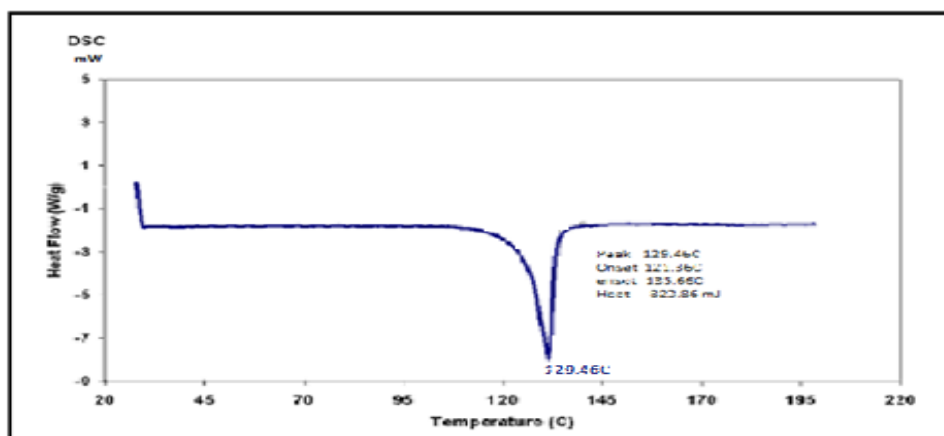


Fig 9. DSC spectra of Nadolol

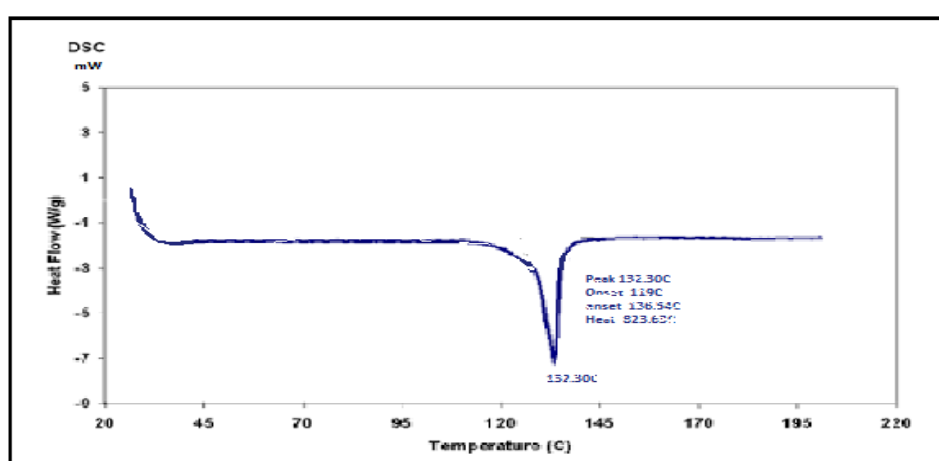


Fig 10. DSC spectra of Nadolol film

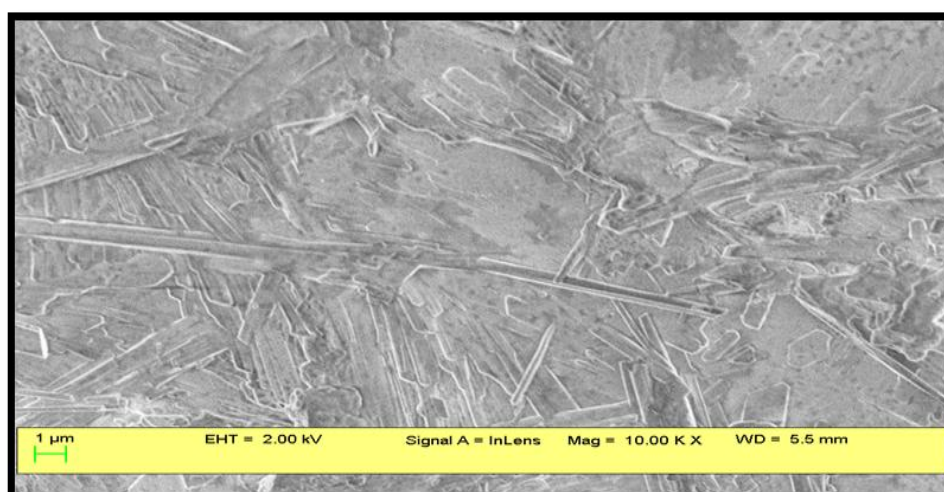


Fig 11. Scanning electronic microscopy of F6 batch

#### ACCELERATED STABILITY STUDY FOR OPTIMIZED FORMULATION

Optimized formulation F6 at 40°C, 75% RH  $\pm$  5% was found to be stable up to 90 days. There was no significant change in drug content, visual appearance i.e.

change in colour. All Formulations stored at elevated temperature showed slight change in pH and disintegration time, other parameters were found to be unchanged.

Table 9. Stability data for F6 formulation

| SR. NO | OBSERVATION                        | BERFOR STABILITY TESTING | AFTER STABILITY TESTING |
|--------|------------------------------------|--------------------------|-------------------------|
| 1.     | Drug content                       | 98.57%                   | 98.55%                  |
| 2.     | Visual appearance (Colour changes) | Light yellow             | Light yellow            |
| 3.     | pH                                 | 6.4                      | 6.4                     |
| 4.     | Disintegration time                | 17 Sec                   | 18 Sec                  |

## CONCLUSION

The prepared films were found to be uniform, flexible and 98.57% of drug was released from F<sub>6</sub> film within 5 minutes which was desirable for fast absorption. Later stability studies of this formulation were indicating that there was no degradation of the formulation at high temperature and humidity conditions. It was indicating that this formulation was stable.

From the present investigation it can be concluded that oral thin film formulation can be a potential novel drug dosage form for pediatric, geriatric and also for general population. Hence Nadolol were found to be suitable for eliciting better therapeutic effect in the treatment of Hypertension.

## REFERENCES

- Priyanka Nagar, Iti Chauhan and Mohd Yasir. Insights into Polymers: Film Formers in Mouth Dissolving Films. *Drug Invention Today*, 2011; 3(12): 280-289.
- Arya A, Chandra A, Sharma V, Pathak K (2010) Fast Dissolving Oral Films: An Innovative Drug Delivery System And Dosage Form. *Int J of Chem Tech Research*, 2: 576-583.
- Poonam A. Padamwar, Poonam P. Phasate, Formulation and evaluation of Fast dissolving oral film of Bisoprolol fumarate, *Int J of Pharma Sci. and Research.*, 01 Jan 2015; 6: 135-143.
- British Pharmacopoeia 2013, Published by British Pharmacopoeia Commission; vol-II; 1503.
- The United State Pharmacopeia, The national Formulary, Vol-III, The official compendia of standards, Asian Edition-2015; 4475.
- Shri Rekha M., SK. Shaheda Sultana, K. Mahathi, P. parveen, B. Prathima, A. Seetha, Formulation and evaluation of Fast dissolving Buccal film containing Isradipine Solid Dispersion, *Am. J Pharm Tech Res.* 2015; 5(2): 222-231.
- DK Yatin, AT Dipen, VP Amit, PP Vipul. Formulation And Evaluation Of Fast Dissolving Sublingual Film of Metoprolol Succinate *Int. J. Pharma. Sci*, 2013; 4(3): 140-54.
- SC Prabhu, S Parsekar, A Shetty, SS Monteiro, M Azharuddin, AR Shabaraya. Design And Characterisation of Fast Dissolving Sublingual Films of Montelukast Sodium. *Int. J. Pharma. Res. Bio-Sci*, 2014; 3(3): 268-81.
- Naziya Khatoon NG, Raghavendra Rao B, Mahipal Reddy (2013) Overview on fast dissolving oral films. *International Journal of Chemistry and Pharmaceutical Sciences*, 1: 63-75.
- Bhyan B, Sarita J (2012) Formulation and evaluation of fast dissolving sublingual films of Rizatriptan Benzoate. *International Journal of Drug development and Research*, 4: 133-143.
- Karen HD, Patel DM, Jasakiya AR, Patel CN (2013) Development of oral strip for Loratadine and in vitro evaluation. *International Journal of Pharmacy and Pharmacology*, 2: 125-130.
- Dixit RP, Puthli SP (2009) Oral strip technology: overview and future potential. *J Control Release*, 139: 94-107.
- Gupta M, Patel M, Madhulika K (2011) Enhancement of Dissolution Rate of Rapidly Dissolving Film of Meclizine hydrochloride By Complexation of Meclizine Hydrochloride with beta Cyclodextrine. *Journal of Applied Pharmaceutical Science*, 1: 150-153.
- Kulkarni AS, Deokule HA, Mane MS, Ghadge DM (2010) Exploration of different polymers for use in the formulation of oral fast dissolving strips. *Journal of Current Pharmaceutical Research*, 2: 33-35.
- Manish Kumar, Amit Sinhal, Pravin Kumar, Anil Kumar, Mayank Chaturvedi, et al. (2011) Formulation and in vitro evaluation of periodontal films containing ofloxacin. *Journal of Chronotherapy & Drug Delivery*, 2: 37-41.
- Margareth RC, Raimar L, May A (2011) Simulated biological fluids with possible application in dissolution testing, *Dissolution Technologies*, 18: 15-28.
- Nishigaki M, Kawahara K, Nawa M, Futamura M, Nishimura M, et al. (2012) Development of fast dissolving oral film containing dexamethasone as an antiemetic medication: Clinical usefulness, *International Journal of Pharmaceutics*, 424: 12-17.
- Mital SP, Hiren P, Aarti B, Vadalala KR (2012) Formulation and Evaluation of Mouth Dissolving Film of Ropinirole Hydrochloride by Using Pullulan Polymers. *IJPRAS*, 1: 60-72.
- Nehal S, Garg G, Pramod Kumar S (2011) A Short Review on A Novel Approach in Oral Fast Dissolving Drug Delivery System and their Patents. *Advances in Biological Research*, 5: 291-303.