

## Design and development of transdermal drug delivery systems of metoprolol succinate

DMK. Chakradhar<sup>1\*</sup>, A. Sunitha<sup>2</sup>, B. Sofia<sup>3</sup>, Grandhi Srikar<sup>4\*</sup>

<sup>1,4</sup>Assistant Professor, <sup>2</sup>HOD, <sup>3</sup>Student, <sup>1</sup>Raghu College of Pharmacy, Dakamarri, Visakhapatnam, Andhra Pradesh, <sup>2</sup>Hindu College of Pharmacy, Guntur, Andhra Pradesh, <sup>3</sup>Emmanuel College of Pharmacy, Visakhapatnam, Andhra Pradesh, <sup>4</sup>University College of Pharmaceutical Sciences, <sup>4</sup>Acharya Nagarjuna University, Nagarjuna nagar, Guntur, Andhra Pradesh, India

### Abstract

**Introduction:** Most of the drugs taken orally are found to be not as effective as desired. To overcome such problems transdermal drug delivery system has been developed. Transdermal drug delivery systems (TDDS) are dosage forms which involve in the drug transport to viable epidermal and or dermal tissues of the skin for local therapeutic effect while a very major fraction of drug is transported into the systemic blood circulation. Several important advantages of transdermal drug delivery are limitation of hepatic first pass metabolism, enhancement of therapeutic efficacy and maintenance of steady plasma level of the drug.

**Materials and Methods:** The current research work includes the development of Metoprolol succinate transdermal patches and their evaluation. The transdermal patches were formulated by solvent casting method varying the concentrations of Eudragit NE 30D (%v/w) and DMSO (%w/w of dry polymer).

**Results:** Among the nine formulations of the transdermal patches F3 formulation was considered as the optimized formulation considering its tensile strength, percentage elongation, percentage drug content and mainly cumulative percentage drug diffusion. The cumulative percentage drug diffused from F3 formulation was found to be 97.36 at the end of 24<sup>th</sup> hour.

**Conclusion:** Stable and effective transdermal drug delivery systems of metoprolol succinate for once daily administration were prepared for better patient compliance.

**Keywords:** Transdermal drug delivery, Solvent casting method, Metoprolol succinate, Therapeutic efficacy, Steady plasma level.

### Introduction

Discovery of new medicinal agents and related innovation in drug delivery system have enabled not only the successful implementation of novel pharmaceutical, but also permitted the development of new medical treatment with existing drugs. One of the most controversial methods among the drug delivery through skin is the use of vehicle formulations. Optimization of drug delivery through human skin is one of the important methods in modern therapy. Although the skin as a route for drug delivery can offer many advantages, the barrier nature of the skin

makes it difficult for most drugs to penetrate into and permeate through it. Human skin effectively inhibits drug permeation mainly because of the upper most horny layer stratum corneum. Thus to maximize drug flux, formulations reduce the hindrance of this barrier, although sometimes drug transport via the hair follicle might also be involved. There has been wide interest in exploring new techniques to increase drug absorption through the skin. Over the past two decades, the transdermal drug delivery has become a proven technology holding the promise that new compound could be delivered in a convenient way

\*Corresponding Author: Grandhi Srikar, University College of Pharmaceutical Sciences, Acharya Nagarjuna University, Nagarjuna nagar, Guntur, Andhra Pradesh, India  
Email: [srikar.grandhi@gmail.com](mailto:srikar.grandhi@gmail.com)  
<http://doi.org/10.18231/j.ijpca.2019.015>

through the skin. The mitigation of the psychological, physical suffering and the cure or at least amelioration of disfiguring diseases such as eczema, psoriasis, ichthyosis and the skin cancers are noble aims of dermal and trans dermal delivery of drugs.<sup>1</sup>

Dermal drug delivery is the topical application of drugs to the skin in the treatment of skin diseases which maybe a disadvantage because the topical application of these dosage forms may not last for a longer periods of time on the skin as they are exposed to the environment directly. Transdermal delivery is an important delivery route that delivers precise amount of drug through the skin to attain systemic action. Transdermal route of drug administration have several advantages like circumvention of hepatic metabolism variables, and effects P<sup>H</sup>, food intake, gastrointestinal motility that is normally seen with gastrointestinal administration. Constant drug input from the transdermal formulation decreases the variations in the drug plasma levels, reducing the side effects particularly of drugs with narrow therapeutic window.<sup>2</sup>

Metoprolol succinate is a cardio selective  $\beta$ 1-adrenergic blocking agent used for acute myocardial infarction (MI), heart failure, angina pectoris and mild to moderate hypertension. It may also be used for supra ventricular and tachy arrhythmias and prophylaxis for migraine headaches. Metoprolol succinate competes with adrenergic neurotransmitters such as catecholamines for binding at beta (1)-adrenergic receptors in the heart. Beta (1)-receptor blockade results in a decrease in heart rate, cardiac output, and blood pressure. It is a BCS class 1 drug with high solubility and high permeability and is similar to atenolol in its moderate lipid solubility.<sup>3</sup> The current research work involves the development of transdermal patches of metoprolol succinate by solvent casting method<sup>4,5</sup> and the evaluation studies for the developed transdermal patches.

## Materials and Methods

Metoprolol Succinate was purchased from Sravani pharma pvt.Ltd, Navi Mumbai, HPMC K 15M was obtained as a gift sample from Central Drug House(P).Ltd, New Delhi, Eudragit NE 30D was obtained as a gift sample from Evonik Degussa India Pvt. Ltd, Mumbai. Poly Ethylene Glycol (PEG 400),

DMSO, Methanol, Sodium Hydroxide and Potassium dihydrogen phosphate were obtained as gift samples from Qualigens fine chemicals, Mumbai.

## Drug Polymer Interaction Studies

Drug and the excipients are studied for their compatibility using FT- IR spectrophotometry. Metoprolol succinate was mixed with potassium bromide (1:10 parts) and is compressed into pellet. Similarly drug, excipient mixture is also mixed with potassium bromide (1:10 parts) and is compressed into pellet. These are then analyzed with FT-IR.

## Preparation of transdermal patch of metoprolol succinate

In this study, two factors were evaluated each at three levels and experimental trials were performed at all nine possible combinations. The amounts of Eudragit NE30D (X1) and DMSO (X2) were selected as independent variables. Transdermal films were prepared by solvent casting method<sup>6</sup>.

## Solvent casting method

Polymers Eudragit NE 30D (7%, 8%, 9%) and HPMC K15M (3%) were weighed accurately and dispersed with stirring in water. Metoprolol Succinate (30 mg) was weighed accurately and dissolved with stirring in methanol add varying amounts of DMSO (5%, 10%, 15%) as shown in Table 1. The polymeric dispersion was added to drug solution with gentle stirring, followed by addition of PEG 400 (30%) to the solution. The solutions were subjected to sonication for 20 min. Then drug-polymeric mixtures were poured on the surface of mercury in a petri-dish. The rate of evaporation of the solvent was controlled by inverting the cut funnel over the petri-dish. The film formation was noted by observing the mercury surface after complete evaporation of the solvent and further dried at room temperature for 24 hours. The dried films were carefully removed from the petri dish, checked for any imperfections or air bubbles and cut in to pieces of 4 cm<sup>2</sup>.

## Evaluation tests for metoprolol succinate transdermal patches

### Thickness

The thickness of the patch was determined using a vernier calliper at three separate points of each patch. From each formulation, three randomly selected patches were tested for their thickness.<sup>7</sup>

### Tensile strength and % elongation

A tensile strength of patch is the total weight necessary to break or rupture the dosage form and this was done using a rectangular frame with two plates made up of iron. The 4 cm<sup>2</sup> patch from each formulation was taken. One end of the patch was sandwiched between the iron plates and fixed. Other end was connected to a freely movable thread over a pulley. The weights were added gradually to the pan which was attached with the hanging end of the thread. The force needed to fracture the patch was determined by measuring the total weight loaded in the pan.<sup>8, 9</sup> The following equation was used to calculate the tensile strength

$$\text{Tensile Strength (TS)} = \frac{\text{Load} * 100}{\text{thickness} * \text{width}}$$

The percentage elongation of the transdermal patch was determined by measuring the initial length of the patch using a scale and a pointer is attached to freely movable thread. Increase in length at the time of break of the patch was recorded and the percentage elongation was calculated by following formula.

$$\text{Percentage elongation} = \frac{\text{initial length} - \text{final length}}{\text{initial length}} * 100$$

### Folding endurance

Folding endurance was determined by repeated folding of the patch at the same place till the strip breaks. The number of times the patch was folded without breaking was computed as the folding endurance value.<sup>10</sup>

### Weight uniformity

The prepared patches were dried at 60°C for 4hrs before testing. A specified area of patch is to be cut at different parts of the patch and their individual weight was measured on a digital balance. The average weight and standard deviation values were calculated from the individual weight.<sup>11</sup>

### Drug Content

A specified area (4 cm<sup>2</sup>) of patch was dissolved in 10 ml phosphate buffer pH 7.4 and filtered through a filter medium. 1 ml solution was taken and diluted upto 10ml. The sample was analyzed in the UV spectroscopy at a  $\lambda_{\text{max}}$  of 224nm against blank for its absorbance and the drug content was calculated.

### Percentage Moisture loss

The prepared patches were weighed individually and kept in desiccators containing fused calcium chloride at room temperature for 24 hrs. After 24 hrs the patches were reweighed and the percentage moisture content was determined using the below mentioned formula<sup>12</sup>

$$\text{Percentage moisture loss} = \frac{(\text{initial weight} - \text{final weight})}{\text{initial weight}} * 100$$

**Table 1:** Formulation codes of metoprolol succinate transdermal patches

S. No.	Ingredients	Formulation Codes								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Metoprolol Succinate(gm)	30	30	30	30	30	30	30	30	30
2	Eudragit NE 30D (% v/w)	7	7	7	8	8	8	9	9	9
3	HPMC k15M (% w/w)	3	3	3	3	3	3	3	3	3
4	PEG 400 (% w/w of dry polymer)	30	30	30	30	30	30	30	30	30
5	DMSO (% w/w of dry polymer)	5	10	15	5	10	15	5	10	15
6	Methanol: Water	7:3	7:3	7:3	7:3	7:3	7:3	7:3	7:3	7:3

### Percentage Moisture absorption & Moisture absorption rate:

The water vapour transmission data through transdermal patches are important in knowing the permeation characteristics. Glass vials of equal diameter were used as transmission cells. These transmission cells were washed thoroughly and dried to constant weight in an oven. About 1 gm of fused calcium chloride as a desiccant was taken in the vials and the polymeric patches were fixed over the brim with the help of an adhesive tape. These pre weighed vials were stored in a humidity chamber at a relative humidity of 80% with the temperature set to 30°C for a period of 24 hours. The weight gained was determined every hour up to a period of 24 hours<sup>12</sup>. The percentage moisture absorption and moisture absorption rate of the transdermal patch were determined by the following formulae.

$$\text{Percentage moisture absorption} = \frac{(\text{initial weight} - \text{final weight})}{\text{initial weight}}$$

$$\text{Moisture absorption rate} = \frac{(\text{initial weight} - \text{final weight}) \times \text{Thickness}}{\text{Surface area exposed}}$$

### Surface pH

Transdermal films were allowed to swell for 2hr at 37 °C on the surface of an agar plate (Prepared by dissolving 2% (w/v) agar in worm isotonic phosphate buffer of pH 7.4 with constant stirring and then allowing it to solidify at room temperature). The surface pH was measured using pH meter by placing the electrode in contact with the surface of the swollen films and allowed to equilibrate for 1 min. The experiments were performed in triplicate and average pH of three determinations was reported<sup>13</sup>.

### In vitro diffusion study

The invitro diffusion studies were carried by using goat skin. The transdermal permeation was performed in modified Franz Diffusion cell (surface area 3.14 cm<sup>2</sup>). The patch is placed on the stratum corneum side of skin such that the patch is exposed to the donor compartment and dermis side was placed facing receptor compartment. Receptor compartment contains phosphate buffer pH 7.4 and samples were withdrawn at regular time intervals and replaced with the same

buffer. The samples were analyzed at a  $\lambda_{\text{max}}$  of 224nm against blank by UV spectrophotometer.<sup>14-15</sup>

### Kinetic modelling of release data

Data obtained from in-vitro release studies<sup>16</sup> are fitted to various kinetic equations to find out the mechanism of drug release. The kinetic models used were:

$$Q_t = K_0 t \text{ (zero-order equation)}$$

$$\ln Q_t = \ln Q_0 - K_1 t \text{ (first-order equation)}$$

$$Q_t = K_h t_{1/2} \text{ (Higuchi equation)}$$

Where  $Q_t$  is the amount of drug release in time  $t$ ,  $Q_0$  is the initial amount of drug in the microsphere, and  $K_0$ ,  $K_1$ , and  $K_h$  are rate constants of zero order, first order and Higuchi equations respectively. Further to confirm the mechanism of drug release, the first 60% of drug release, it was fitted in Korsmeyer-Peppas model.

$$M_t / M_\infty = k t^n$$

where  $M_t$  is the amount of drug release at time  $t$  and  $M_\infty$  is the amount release at time  $t = \infty$ , thus  $M_t / M_\infty$  is the fraction of drug released at time  $t$ ,  $k$  is the kinetic constant, and  $n$  is the diffusion exponent which can be used to characterize both mechanism for both solvent penetration and drug release.

### Stability studies

Short-term stability studies were performed at a temperature of 45°±1°C over a period of seven weeks (45 days) on the promising optimized formulation. Sufficient number of tablets (15) were packed in amber coloured screw capped bottles and kept in humidity chamber and maintained at 45°±1°C. Samples were taken at weekly intervals for drug content estimation. At the end of three weeks period, colour, dissolution test and in vitro studies were performed to determine the drug release profiles.

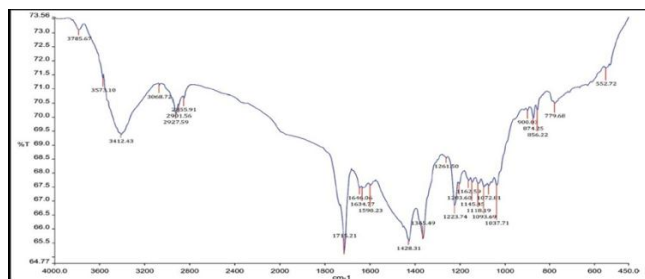
### Results and Discussion

Matrix type transdermal patches of metoprolol succinate were prepared using Eudragit NE 30D, HPMC K15M as film formers by solvent casting method and subjected to further evaluation tests. Incorporation of PEG 400 at a concentration of 30% w/w of dry polymers yielded smooth and flexible patches. Decreasing or increasing the concentration of

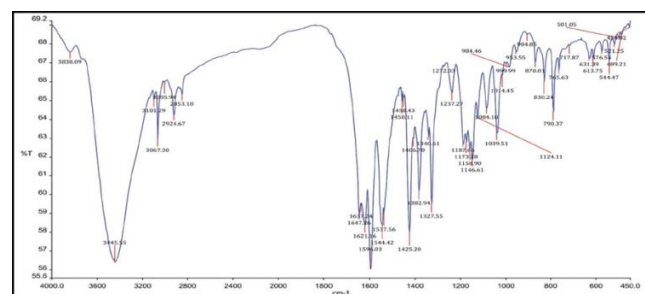
PEG 400 from the above mentioned value resulted in the formation of brittle or soft patches respectively.

### Drug Polymer Interaction Studies

From the Fig. 1 & 2, it was inferred that there were no significant variations in the major peaks of both the spectra indicating that the drug and excipient are compatible with each other and are non-interacting.



**Fig. 1:** FT-IR Plot for pure drug of Metoprolol Succinate



**Fig. 2:** FT-IR Plot for pure drug of Metoprolol Succinate + Excipients

### Evaluation parameters of the transdermal patches

#### Thickness

Thickness of the various formulations (F1 to F9) is given in table 2. Patches was in the range from 0.123 - 0.238 mm. The physicochemical evaluation study reveals that all formulations measured weight and thickness with low standard deviation values.

#### Tensile strength

The results of tensile strength from various formulations (F1 to F9) are given in table 2. Tensile strength of all the patches was in the range of  $605 \pm 6.3$  to  $759 \pm 5.7$  gm/cm<sup>2</sup> suggesting all films were having good mechanical strengths to withstand mechanical damage during, production and application.

### Percentage elongation

The results of Percentage elongation from various formulations (F1 to F9) are given in table 2. The results revealed that Percentage elongation was in the range of 11.24 to 22.56. This represents the elasticity of the patch. Increase in concentration of Eudragit NE30D results in enhancement of elasticity of patch.

### Folding endurance

The results of folding endurance of various formulations (F1 to F9) are given in table 2. All the patches were showing folding endurance in the range of  $256 \pm 08$  to  $309 \pm 04$ . Results revealed that as the concentration of polymers increases folding endurance increases. The folding endurance measures the ability of patch to withstand rupture. It was found to be satisfactory. The result indicated that the patches would not break and would maintain their integrity with general skin folding when used. The folding endurance of Eudragit patches is higher than patches containing more concentration of Eudragit NE 30D. The surface pH of all the formulations was in the range of 5.1-5.8, the pH range of skin and hence no skin irritation was expected.

### Uniformity of weight

The weight of prepared films was in the range of 0.134 to 0.179 mg given in table 2. In all the cases the calculated standard deviation values were very low which suggest that the prepared films were uniform in weight. The weight of the films increases as the concentration of polymer increases.

### Drug content

The results of drug content of various films are given in table 2. The results indicate that drug content of films were in the range of 92.53 to 97.73. Homogeneous uniform drug distribution is one of the important characteristics of a transdermal patch that ensures the uniform reproducible sustained release of the drug from the patch. Estimation of drug content indicated that the drug is uniformly distributed throughout the patches, evidenced by the low values of the SD.

### Percentage moisture loss

The results of Percentage moisture loss of various films are given in table 2. The results indicate that Percentage moisture loss of films were in the range of  $2.43 \pm 0.12$  to  $3.01 \pm 0.18$ . From the result we conclude that as the concentration of polymer was increase there was increase in moisture loss.

### Percentage moisture absorption

The results of Percentage moisture absorption of various films are given in table 2. The results indicate that Percentage moisture absorption of films were in the range of 4.22 to 6.42. From the result we conclude that as the concentration of polymer was increase there was increase in moisture absorption. The enhancement of water vapour permeation with increase of PEG 400 is due to the irregular arrangement of molecules in the amorphous state, which usually causes the molecules to be spaced further apart than in a crystal. Hence, the specific volume is increased and the density is decreased compared to that of crystal, which leads to

the absorption of vapour into their interstices. All the formulations were permeable to water vapour

### Moisture permeability Rate

The results of moisture permeability rates from various films are given in table 2. The results indicate that Percentage moisture absorption of films were in the range of  $4.81 \times 10^{-4}$  to  $6.53 \times 10^{-4}$ . From the result we conclude that as the concentration of polymer was increase there was increase in moisture absorption. The consequence of water uptake could be the formation of empty spaces within the patch that could make its structure less resistant to mechanical stresses.

### Surface pH

The surface pH of prepared films was in the range of 5.1 - 5.7 with a very low value of standard deviation given in table 2. All the films were having surface pH close to skin pH suggesting that they will not irritate the skin.

**Table 2.1:** Evaluation parameters of Metoprolol succinate transdermal films

Formulation Code	Thickness (mm)	Tensile Strength (gm/cm <sup>2</sup> )	Elongation (%)	Folding endurance	Weight Variation
F1	$0.123 \pm 0.011$	$615 \pm 6.6$	$16.25 \pm 3.52$	$256 \pm 08$	$138 \pm 0.013$
F2	$0.125 \pm 0.011$	$605 \pm 6.8$	$22.56 \pm 3.26$	$267 \pm 07$	$134 \pm 0.020$
F3	$0.155 \pm 0.012$	$648 \pm 7.0$	$19.23 \pm 4.25$	$279 \pm 12$	$149 \pm 0.014$
F4	$0.165 \pm 0.011$	$684 \pm 5.6$	$20.12 \pm 4.62$	$278 \pm 13$	$143 \pm 0.013$
F5	$0.200 \pm 0.013$	$695 \pm 4.2$	$17.26 \pm 4.12$	$281 \pm 11$	$152 \pm 0.015$
F6	$0.215 \pm 0.013$	$713 \pm 7.6$	$19.58 \pm 3.65$	$298 \pm 07$	$157 \pm 0.020$
F7	$0.220 \pm 0.012$	$722 \pm 4.0$	$13.56 \pm 3.45$	$309 \pm 05$	$170 \pm 0.022$
F8	$0.232 \pm 0.013$	$735 \pm 3.1$	$15.69 \pm 3.78$	$298 \pm 06$	$174 \pm 0.021$
F9	$0.238 \pm 0.013$	$758 \pm 3.9$	$11.25 \pm 3.55$	$294 \pm 06$	$179 \pm 0.019$

**Table 2.2:** Evaluation parameters of Metoprolol succinate transdermal films

Formulation code	Drug Content	Moisture loss (%)	Moisture absorption (%)	Moisture permeability rate (gm.cm/ cm <sup>2</sup> .24 h)	pH
F1	92.53 ± 0.12	2.43 ± 0.12	4.22 ± 0.12	4.81 x 10 <sup>-4</sup>	5.5 ± 0.14
F2	91.12 ± 0.22	2.52 ± 0.15	4.28 ± 0.15	4.93 x 10 <sup>-4</sup>	5.6 ± 0.08
F3	94.47 ± 0.17	2.64 ± 0.11	4.85 ± 0.20	5.19 x 10 <sup>-4</sup>	5.3 ± 0.14
F4	92.36 ± 0.15	2.65 ± 0.20	4.83 ± 0.18	5.56 x 10 <sup>-4</sup>	5.8 ± 0.16
F5	93.14 ± 0.16	2.87 ± 0.12	5.25 ± 0.25	5.93 x 10 <sup>-4</sup>	5.7 ± 0.07
F6	94.78 ± 0.12	2.91 ± 0.12	5.56 ± 0.15	5.99 x 10 <sup>-4</sup>	5.3 ± 0.14
F7	95.62 ± 0.11	2.98 ± 0.14	6.12 ± 0.17	6.25 x 10 <sup>-4</sup>	5.4 ± 0.11
F8	96.48 ± 0.10	3.01 ± 0.15	6.25 ± 0.24	6.36 x 10 <sup>-4</sup>	5.2 ± 0.13
F9	97.73 ± 0.17	2.97 ± 0.12	6.42 ± 0.18	6.53 x 10 <sup>-4</sup>	5.1 ± 0.18

### In vitro drug diffusion

*In vitro* drug permeation profiles of Metoprolol Succinate of all prepared films are shown in table 3. The results suggest that Eudragit NE30D and DMSO play an important role in the release of drug from the films. Films having higher concentration of Eudragit NE30D showed lower values of drug permeation as compared to films having lower amount of Eudragit NE30D. The cumulative percent drug permeation at the end of 24<sup>th</sup> hour was higher in the formulation with low concentration of Eudragit and high percentage of DMSO. This might be attributed to the high release from formulation with Eudragit and high percentage of DMSO, polymer could be explained by the hydrophilic nature of this polymer. Eudragit is known to have larger cavity size in its polymeric network and thus it may involve a faster mode of diffusion of Metoprolol succinate from the formulations.

The increase of release with increase of PEG 400 content in the patch may be due to the leaching of PEG 400 and pore formation. This leads to an increase in the external film area exposed to the solvent, increased internal porosity and decreased the tortuosity. The possible mechanism of enhancement of skin flux with increase of PEG 400 in the patches may be due to its co-enhancing property in aqueous vehicle system. The rapid leaching of hydrophilic fraction of polymers resulted in the formation of pores and thus leads to the decrease of mean diffusional path length of the drug molecules to permeate into dissolution medium.

### Kinetic modeling of the drug release data

The *in vitro* permeation data were fit to different equations and kinetic models to explain permeation profiles. The coefficient of correlation of each of the kinetics was calculated and compared as shown in Table 3. The *in vitro* permeation profiles of all the different formulations of transdermal patches fit to zero order kinetics and they could also be best expressed by Higuchi's equation for the release of drug from a homogeneous polymer matrix type delivery system that depends mostly on zero order diffusion characteristic. The data was further treated as per Korsmeyer's equation. It could be inferred from the slope (n) values obtained by this equation that the drug release was by non-fickian or anomalous diffusion predominated in all formulations.

**Table 3:** Table representing Percentage Drug release at 24<sup>th</sup> hour and the kinetic modelling of release data of formulations (F1 – F9)

Formulation Code	Cumulative drug release at 24 <sup>th</sup> hour	Zero order (r <sup>2</sup> -value)	First order (r <sup>2</sup> -value)	Higuchi's (r <sup>2</sup> -value)	Peppas's n-value
F1	90.36	0.987	0.925	0.929	0.776
F2	94.58	0.985	0.898	0.939	0.770
F3	97.36	0.997	0.885	0.946	0.792

F4	80.46	0.990	0.826	0.898	0.793
F5	83.76	0.991	0.870	0.922	0.774
F6	87.13	0.992	0.892	0.931	0.698
F7	72.68	0.992	0.873	0.907	0.914
F8	75.56	0.993	0.862	0.914	0.798
F9	80.79	0.992	0.884	0.917	0.804

**Table 4:** Table representing stability data for optimized formulation (F3)

S. No	Parameter	Day 1	Day 15	Day 30
1	Thickness	0.155 ± 0.012	0.153 ± 0.010	0.157 ± 0.017
2	Tensile strength (gm/cm <sup>2</sup> )	648 ± 1.17	650 ± 1.18	656 ± 1.21
3	Percentage elongation	19.23 ± 0.15	20.13 ± 0.21	20.17 ± 0.20
4	Folding endurance	279 ± 0.42	282 ± 0.76	276 ± 0.35
5	Percentage moisture absorbance	4.85 ± 0.14	4.95 ± 0.50	4.80 ± 0.48
6	Percentage moisture loss	2.46 ± 0.10	2.45 ± 0.12	2.44 ± 0.15
7	Drug content	94 ± 0.15	92.45 ± 0.37	93.02 ± 0.55
8	Surface pH	5.3 ± 0.021	5.1 ± 0.011	5.1 ± 0.019
10	Weight variation (mg)	149 ± 1.33	146 ± 1.41	144 ± 1.29

### Stability study

The promising formulation F3 was subjected at 40 ± 0.5 °C temperature and 75 ± 5% RH for 1 month to check the stability. From the results of the stability study shown in Table 4, it can be concluded that the films can be stored at 40 °C and 75% RH without any significant stability problems.

### Conclusion

In the present investigation, formulations F1-F9 were prepared using 7%, 8% and 9% of Eudragit NE30D and 5% 10% and 15% (w/w of dry polymer) of DMSO (Dimethyl sulphoxide). HPMC K15M was incorporated as hydrophobic copolymer at concentration of 3%. Among which formulation **F3** was selected as the promising formulation on the basis of its tensile strength, percentage elongation, percentage drug content and mainly cumulative percentage drug diffusion. The cumulative percentage drug diffused of F3 was found to be 97.36. The tensile strength of the patches was found to vary with the plasticizer.

Hence the controlled release matrix transdermal patches of Metoprolol succinate which are used mainly in minimizing dose and help to improve the patient

compliance and Metoprolol succinate is a drug of choice for delivery through the control release via matrix transdermal patches. Benefits such as sustained drug release, reducing frequency administration, improving bioavailability, and thereby may help to improve patient compliance.

### Source of Funding

None.

### Conflict of interest

None.

### References

1. Shaw J. E., Chandrasekharan S. K. and Campbell P. Percutaneous Absorption: Controlled Drug Delivery for Topical or Systemic Therapy. *J Invest Dermatol* 1976;67(5-2):677-8.
2. Jain, N. K., Controlled and Novel Drug Delivery, CBS Publishers and Distributors, 107, 2002.
3. <http://www.drugbank.ca/drugs/DB00461>. Date of access: 14/06/2019.s
4. Subash SP, Muneer TK, Panneerselvam T, Mohd Azharuddin, Shabaraya AR. Controlled drug delivery of Diltiazem hydrochloride as transdermal patches: a novel approach on formulation evaluation in vitro and in vivo parameters. *Res Pharm* 2011;1(2):17-9.



5. Nilesh BR, Hardikar SR, Ashok BV. Formulation and evaluation of transdermal patches of Ropinirole HCL. *Res J Pharm, Biol Chem Sci* 2011;2(1):138-148.
6. Munden BJ, Dekay HG, Banker GS. Evaluation of polymeric materials and screening of film coating agents. *J Pharm Sci* 1964;53(4):395-401.
7. Ramarao P, Ramakrishna S, Diwan PV. Drug release kinetics from polymeric films containing Propranolol hydrochloride for transdermal use. *Pharm Dev Technol* 2000;5(4):465-72.
8. Samanta MK, Dube R, Suresh B. Transdermal drug delivery system of Haloperidol to overcome self-induced extrapyramidal syndrome. *Drug Deliv Ind Pharm* 2003;29(4):405-15.
9. Saini TR, Seth AK, Agrawal GP. Evaluation of free films. *Indian drug* 1985;23(1):45-7.
10. Raghuraman S, Velrajan R, Ravi B, Jeyabalan D, Benito J, Sankar V et al. Design and evaluation of Propranolol hydrochloride buccal films. *Indian J Pharm Sci* 2002;64(1):32-6.
11. Mamatha T, Venkateswara RJ, Mukkanti K, Ramesh G. Transdermal drug delivery for Atomoxetine hydrochloride- in vitro and ex vivo evaluation. *Curr Trends Biotechnol Pharm* 2009;3(2):188-96.
12. Murthy SN, Hiremath SSR. Preformulation studies of transdermal films of hydroxy propyl methyl cellulose and sodium carboxy methyl cellulose. *Int J Pharm Excipients* 2002;34-8.
13. Bottenberg P, Cleymact R, Muynck CD, Remon JP, Coomans D, Michotte Y et al. Development and testing of bioadhesive fluoride containing slow release tablets for oral use. *J Pharm Pharmacol* 1991;43:457-64.
14. Keshary PR, Chien YW. Mechanism of transdermal nitroglycerin administration: development of finite dosing skin permeation system. *Drug Deliv Ind pharm* 1984;10(6):883-913.
15. Chandrashekar NS, Shobharani RH. Design, fabrication and calibration of modified diffusion cell for transdermal diffusion studies. *Int J Pharm Excipients* 2005;105.
16. Negia R, Goswamia L, Kothiyalb. Microballoons for drug delivery: A review. *Indian J Pharm Biol Res* 2014;2(2):100-7.

**How to cite this article:** Chakradhar DMK, Sunitha A, Sofia B, Srikar G. Design and development of transdermal drug delivery systems of metoprolol succinate. *Int J Pharm Chem Anal* 2019;6(3):76-84.