International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Optimization Development and Characterization of Film-Forming Transdermal Spray

Miss.Swati Malkote[1], Dr.Kamlesh Wadher[2], Dr.Milind Umekar[3]

Smt.Kishoritai Bhoyar College of Pharmacy, Kamptee Dist.Nagpur, Pin 441002

Abstract:
Transdermal drug delivery system is widely used for the administration of various dosage forms such as gel, patch spray but they have some drawbacks to overcome these drawbacks new techniques for administering drugs to the skin were explored by creating film-forming polymeric solutions. The objective of this study was to develop a film-forming spray formulation to treat inflammation. The formulation was developed by combining polymers, penetration enhancer, plasticizer, and a suitable solvent system. The central composite design with 2 independent variables and 3 dependent variables is implemented to optimize the formulation and which was given 12 runs. The film-forming spray was put through its tests to assess formulation and container-related parameters such as, spray angle, volume delivered for one actuation and. From the study, it was observed that the concentration of ethyl cellulose and Eudragit l-100 has a greater influence on the viscosity of the spray solution, drying time, whereas the eutectic mixture has a greater influence on the drug permeation followed by the polymers. It also tested for anti-inflammatory activity with carrageenan induced paw edema volume and it was found that formulation showed better anti-inflammatory activity. The study has concluded that the formulated film-forming spray formulation is highly efficient in treating transdermal inflammation when compared to the traditional dosage forms.

Keywords: Transdermal drug delivery system, Film forming spray, Diclofenac potassium, Volume of a spray per each actuation.

1. INTRODUCTION

Transdermal drug delivery systems (TDDS) are a type of medication that is contained within discrete dosage forms and is capable of delivering drugs through the skin at a regulated rate and into the systemic circulation. The transdermal drug delivery system refers to the application of a drug, in the form of a patch, gel, or spray, to the skin to achieve a systemic effect. (1) The oral route is commonly used to administer drugs, but it has drawbacks such as first pass metabolism, drug degradation due to enzymes and pH in the gastrointestinal tract. To address these issues, various innovative drug delivery systems have been developed. One of these novel approaches is transdermal drug delivery, which involves the use of medicated film-forming sprays that deliver a therapeutic amount of the drug through the skin.(2) New techniques for administering drugs to the skin were explored by creating film-forming polymeric solutions. These solutions were analyzed for their mechanical properties and ability to allow water vapor to pass through. To create these solutions, changes were made to the plasticizer used, as well as the type and amount of film-forming polymer.

Mechanism of film forming spray

The drug release from a film is similar to that of a patch, where the medication is released gradually from a polymer matrix after the formation of a film. Films, unlike topical patches and medicines, conform to the pattern of the skin or wound and can cover deep indentations with tiny droplets of the film-forming solution. This makes drug delivery to the target tissue much simpler, and drug dosages can be administered via a film-forming spray.(3)

2. MATERIALS AND METHOD

Diclofenac Potassium was purchased from Zim Laboratories Ltd, Nagpur and Ethyl Cellulose, Eudragit L-100, Camphor Menthol, sodium hydroxide, Disodium hydrogen phosphate were obtained from Loba Chemie, Mumbai. Ethanol and acetone were obtained from Sigma Aldrich, Mumbai. Polyethylene Glycol-400 and Potassium dihydrogen phosphate was obtained from Merck Specialities Pvt.Ltd, Mumbai. Methanol was received from Research-lab Fine Chem Industries, Mumbai.

3. Characterization of FFTDs

1. Melting point: - Given sample of drug (Diclofenac potassium) was characterized for melting point and compared with standard range of melting point (307°C to 310°C).
2. UV-visible spectrophotometric analysis: The calibration curve of the Diclofenac potassium was plotted in methanol.

A. Determination of λ max for Diclofenac Potassium (in methanol)
10 mg of Diclofenac Potassium was accurately weighted and transferred into the 100ml volumetric flask and dissolved in minimum quantity of methanol and make up volume with 100 ml methanol resulting in 100 ug/ml of drug concentration. The solution was then scanned in UV range between 200 to 400 nm, from UV spectra 281.4 nm was selected as λmax for analysis of Diclofenac Potassium.

B. Standard calibration curve of diclofenac potassium in methanol.

Standard stock solution

The standard stock solution (100 ug/ml) of Diclofenac was prepared by weighing accurately 10 mg of pure Diclofenac into 100 ml of volumetric flask and dissolved in a minimum quantity of solvent and the final volume was made up to 100 ml mark with solvent separately. In above stock solution was taken 1ml of solution diluted with 10ml of solvent to prepared 10ug/ml solution. The solution was scanned between the wavelength regions of 200-400 nm

Working stock solution

To find out the wavelength maximum absorption (λmax) of Diclofenac potassium the standard stock solution (100 ug/ml) of Diclofenac was prepared by weighing accurately 10 mg of pure Diclofenac into 100 ml of volumetric flask and dissolved in a minimum quantity of solvent and the final volume was made up to 100 ml mark with solvent separately. In above stock solution was taken 1ml of solution diluted with 10ml of solvent to prepared 10ug/ml solution. The solution was scanned between the wavelength regions of 200-400 nm.

4. Experimental design

The 2-factorial Central composite design was chosen for the optimization by selecting the formulation factors Ethyl cellulose (X1), Eudragit L-100 (X2) and the response variables Drug permeation, Drug content and Drying Time. The total number of the batches is 12 batches, which includes 4 factorial point runs, 4 axial point runs and 4 centre point run, which includes a total of 12, 4-repeating combinations of

excipients. Two independent variables were chosen at one level and coded as -1 (low), and +1 (higher), yielding two factorial designs with 12 potential combinations. The dependent variables were established as Drug permeation (%), Drug content (%), Drying time(seconds). All 12 potential combinations of the specified variables were used in the experimental trials.

Table 1 : Independent formulation variables and their levels applied using Design Expert

Factor	Name	Low actual level	High actual level	Low coded level	High coded level
X1	Amount of Ethyl Cellulose	0.29 gm	1.7 gm	-1	+1
X2	Amount of Eudragit L-100	1 gm	3.4 gm	-1	+1

Table 2: Composition of Central composite design with measured responses of Film forming spray formulation

		Independent variables		Dependent variables		
Run	Batch code	Ethyl cellulose (X1,gm)	Eudragit L-100 (X2, gm)	Drug permeation (%)	Drug content (%)	Drying time (seconds)
1	F1	1	2	59.00±0.12	69.04±0.24	200±0.94
2	F2	1	2	58.5±0.76	71±0.98	200±2.85
3	F3	1	3.41421	38.20±0.35	58.01±0.8	317±0.54
4	F4	0.292893	2	82.00±1.42	77±1.23	130±0.21
5	F5	1.5	3	30.00±0.49	56.5±0.82	300±0.58
6	F6	1.5	1	58.01±1.92	73.5±0.72	178±0.45
7	F7	0.5	3	64.51±0.62	66±0.36	230±0.8
8	F8	1	0.585786	76.00±0.54	80.91±1.39	181±2.28
9	F9	1	2	57.09±0.91	69±0.81	200±2.86
10	F10	1.70711	2	41.03±0.65	63±0.54	238±0.26
11	F11	1	2	59.01±0.22	71±1.59	198±0.38
12	F12	0.5	1	91.00±0.18	83±0.94	132±0.42

5. PREPARATION OF FILM FORMING SPRAY

The Diclofenac potassium Film-forming spray solution were prepared by a simple solvent dissolving method. To prepare the camphor- menthol eutectic mixture, equal quantities of the camphor and menthol were weighed and kept in bath sonicator for 10 min to liquify.In another beaker Ethanol and ethyl cellulose blend was taken to this drug (Diclofenac potassium) and Plasticizer (polyethylene glycol 400) was added and stirred for 30 min on magnetic stirrer at room temperature to get a clear solution .Then the liquified camphor-menthol eutectic mixture was added to the solvent mixture under stirring. After that, the polymers (Eudragit L-100) were weighed and added to the above mixture. Then, this was kept under mechanical stirring for 20 min to get dispersed homogeneously. The prepared solution was kept in a bath

sonicator to disperse if there are any polymer aggregates. This final solution was transferred into a refillable suitable container.

6.Evaluation of Prepared Film Forming Spray

6.1 Spray angle

Piece of white paper was clipped on board Methyl red was dissolved in the formulation to get 1 % solution and sprayed on paper keeping nozzle of spray 15 cm away from paper. Spray dots formed were measured for its radius from different angle and spray angle was calculated by following equation:

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

Where h is the distance of paper from the nozzle and r is average radius of the circle (Huang Y et al.,2021).

6.3. The volume of spray solution delivered per each actuation

The volume of spray solution released can be used to calculate the amount of drug-delivering for one actuation. To calculate the amount of spray solution released for each actuation, the initial weight of the spray container with spray solution is checked (W1). Then the solution was sprayed once with a single actuation, and then it is again reweighed (W2). The amount of spray solution delivered for each actuation was calculated by the formula.

$$\text{Amount delivered for one actuation (A)} = \frac{(W1 - W2)}{D}$$

Where,

D = density of the spray solution

6.4 .In-vitro Drug Release

A) Procedure for dialysis membrane activation

Cut the dialysis membrane and immersed in a boiling 2% sodium bicarbonate ($NaHCO_3$) solution for 10 min and rinse with distilled water. Then this membrane immersed in boiling water for 10 min, rinsed with fresh distilled water and kept in distilled water for 24 hours before use.

***B*) Procedure for In-vitro diffusion study:**

An in vitro drug release test of the Film -forming spray was performed using Franz diffusion cells with dialysis membrane. A dialysis membrane (LA393-5MT, dialysis membrane -70, average flat width 29.31 mm, average diameter 17.5 mm and capacity 2.41 ml/cm; (HIMEDIA Laboratories, Mumbai, India), which used as diffusion barrier. The donor compartment contained a 2 ml of film forming spray contained (10mg diclofenac potassium) while receptor compartment was filled with 20 ml phosphate buffer solution (pH6.8, 20ml). The donor chamber was placed in such a way that it just touched the diffusion medium in the receptor chamber. The temperature was maintained constant at 37 ± 0.5˚c using magnetic stirrer (100 rpm). At predetermined time intervals, samples (1ml) were periodically withdrawn from the receptor compartment, replaced with the same amount of fresh pre-warmed buffer solution, and assayed using UV spectrophotometer (Model: V-630, JASCO International Co. Ltd., Tokyo, Japan) at 281 nm for diclofenac potassium. After suitable dilution and the concentration of diclofenac potassium were calculated using calibration curve (Bajaj H et al., 2016).

6.5.Ex-vivo permeation study

Ex vivo drug permeation studies of Film forming spray was carried out using Franz's diffusion cell (receptor capacity: 20.0 ml; permeation area 4.96 cm^2) and rat's skin as prototypical diffusion membrane. The rat skin was placed on the diffusion chamber. The rat's skin was placed on the diffusion chamber

directed toward supplier and receptor compartments, respectively. Film forming spray equivalent to 10 mg of Diclofenac Potassium were spread over the mucosal membrane in supplier compartment.

6.6.Anti-inflammatory activity in carrageenan induced paw edema

An inflammatory reaction is easily induced in rats in the form of paw edema using irritants. Substances such as formalin, bradykinin, histamine,5 – hydroxy tryptamine, mustard or egg white. When injected into the dorsum of the leg of rat's cause acute paw edema within minutes of injection. Carrageenan -induced paw edema is the most commonly used method. Carrageenan, a seaweed polysaccharide, is used as a proinflammatory agent in basic research. Thus, a well-documented acute inflammation model, established by plantar injection of carrageenan in rats, was used to induce paw edema. A micro-controlled water plethysmometer (UGO Basile) can be used to accurately measure rat/mouse paw swelling (edema). It consists of a Plexiglas cell filled with 0.05% wt./vol.sodium chloride solution to reduce the surface tension (adhesion of the water to skin of the paw). a surfactant provided by the manufacturer is added to water tank. The cell is available in different diameters into which the foot sinks. The transmitter records small differences in the water level caused by volume displacement. The digital readout shows the exact volume of the paw.

A) Animals

Healthy adult sprague dawley rats of either sex weighing 200g-300g were selected for the studies. The animals were housed in large, spacious, hygienic cages during the course of experimental period. The animal house was maintained and the animals were 12 ± 1 hour day and night schedule with a temperature [64-79°F] maintained at standard experimental condition. The animals were fed with standard rodent pellet feed and water *ad libitum*. The animals were fasted 12 hours prior to the experiment with free access to only water. The experimental procedure was approved by IAEC (Institutional animal ethical committee of KMCH, governed by CPCSEA, Government of India (Anter HM et al.,2018).

B) Experimental procedures:

1. Weigh the animals and number them. Make a mark on both hind paws (right and left) just behind the (tibio-tars) junction.so each time the paw dips into the mercury column up to the fixed mark to ensure a constant paw volume.
2. Record the initial paw volume (right and left) of each rat using mercury displacement method. Divide the animals into three groups. each containing at least 2 rats. Apply saline to the control group and diclofenac potassium of one to 3 spray transdermally to treatment group and in third that is disease group gives only carrageenan injection.
3. After 30 minutes. Inject 0.1 ml of 1% (w/v) Carrageenan into the plantar area of the left paw of the control group as well as the diclofenac potassium treated group. The right paw will serve as the reference non-inflamed paw for comparison. Record the paw volume of both legs of control and diclofenac -treated rats at 0.5 hr,1hr,2hr,3hr,4hr,5 hr after carrageenan exposure.
4. Calculate the percentage difference in the volume of the right and left paws of each animals from the control group and the diclofenac potassium-treated group. Compare the mean percent change in paw volume in control and drug -treated animals and express as percent inhibition of edema by the drug.

$$\%\ \textbf{Antiinflammatory activity} = \frac{\text{paw edema of control} - \text{paw edema of test}}{\text{paw edema of control}} \times 100$$

7.RESULTS AND DISCUSSION

7.1 PRELIMINARY STUDY OF DRUG AND EXCIPIENTS

The preliminary study of drug and excipients was used to determine the suitability of a drug and excipients for the practical purpose. Results for preliminary evaluation of Diclofenac Potassium, Ethyl Cellulose, and Eudragit L-100 are shown in table

7.1.1 Preliminary characterization of Drug

Table .3 : Preliminary characterization of Diclofenac potassium

Characteristics	**Observation**	**Remarks (as per IP)**
Description	White to off white crystalline powder	Complies
Melting point	207ºC to 210ºC	Complies
Solubility	Completely Soluble in Methanol, Ethanol, sparingly soluble in Water	Complies
UV absorption of solution in distilled water	Maxima at 281 nm	Complies

7.1.2 Preliminary study of Excipients:

Table.4 : Preliminary characterization of Ethyl Cellulose

Characteristics	**Observation**	**Remarks (as per MSDS)**
Description	White to yellowish powder	Complies
Melting point	250-255°c	Complies
Solubility	Soluble in water, glycerol and propane-1,2-diol	Complies
Odour	No odour	Complies

Table .5: Preliminary characterization of Eudragit L-100

Characteristics	**Observation**	**Remarks (as per MSDS)**
Description	White to off white	Passes
Melting point	209 to 211º	Passes
Solubility	Soluble in alcohol and insoluble in ethyl acetate, water	Passes
Odour	Odorless	Passes

The general preparation of the Diclofenac potassium Film-forming spray formulation is by dissolving the excipients in the blend of solvents and sonicating it until a homogenous solution forms. The formulation optimization was performed using the statistical tool, namely the design of experiments. The values of Y1 response (drug permeation) were found to be in the range of 30 % to 91 %, Y2 response (Drug content) in the range of 56 .5% to 83%, and Y3 response (drying time) in the range of 132 seconds to 317 seconds respectively. To demonstrate the effects and relationships between the excipients, computer design tools were used to create polynomial equations and interactive charts. The sequential model sum of squares, the

lack of fit test, and model summary statistics were used to choose the response analysis models. ANOVA was used to verify the polynomial equations statistically, with model terms deemed significant when 'Prob>F' 0.0500 and non-significant when 'Prob>F'>0.1000. For the observed data, three-dimensional response surface charts were constructed to determine the effect of the chosen independent factors on the responses.

7.2. Calibration curve for diclofenac potassium in methanol

Table 6.4: Calibration data for diclofenac potassium in methanol at 281 nm

Concentration (µg/ml)	Absorbance
0	0
20	0.1079
40	0.2001
60	0.3041
80	0.4088
100	0.5146
Slope	0.0051
Intercept	0.0002
Regression Equation	y = 0.0051x + 0.0002
Correlation Coefficients	R^2 = 0.9996

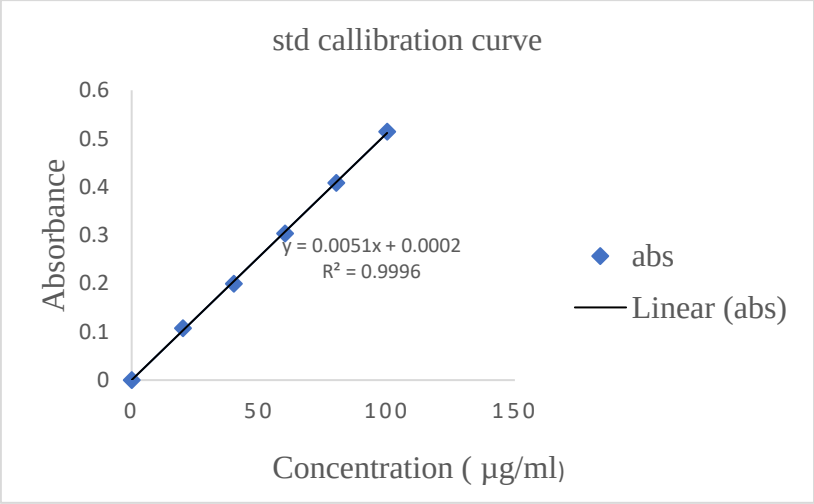


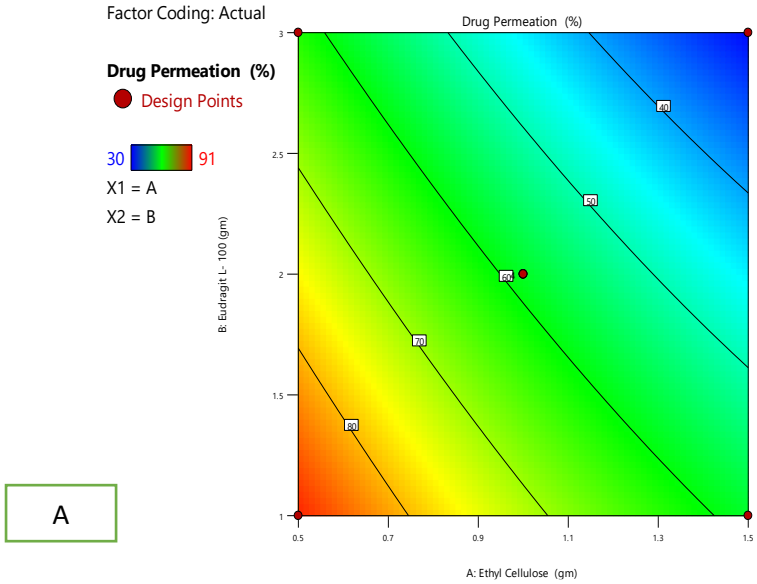
Figure 1 : Calibration curve of diclofenac potassium in methanol at 281 nm

Response 1: Drug Permeation

Table 6.5 : ANOVA for Quadratic model of Drug Permeation

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	3458.18	5	691.64	236.46	< 0.0001	significant

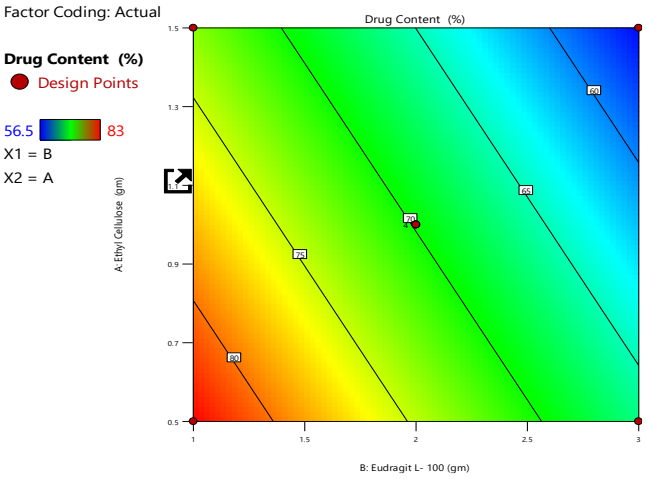
A-Ethyl Cellulose	1952.59	1	1952.59	667.56	< 0.0001	
B-Eudragit L- 100	1478.05	1	1478.05	505.32	< 0.0001	
AB	0.2500	1	0.2500	0.0855	0.7799	
A^2	24.03	1	24.03	8.21	0.0286	
B^2	0.6250	1	0.6250	0.2137	0.6602	
Residual	17.55	6	2.92			
Lack of Fit	14.86	3	4.95	5.53	0.0969	not significant
Pure Error	2.69	3	0.8958			
Cor Total	3475.73	11				



Response 2: Drug content

Table 6.6 :ANOVA for linear model of drug content

Source	**Sum of Squares**	**df**	**Mean Square**	**F-value**	**p-value**	
Model	739.05	2	369.52	690.90	<0.0001	significant
A-Ethyl Cellulose	188.17	1	188.17	351.82	<0.0001	
B-Eudragit L- 100	550.88	1	550.88	1029.97	<0.0001	
Residual	4.81	9	0.5348			
Lack of Fit	0.8924	6	0.1487	0.1138	0.9871	not significant
Pure Error	3.92	3	1.31			
Cor Total	743.86	11				

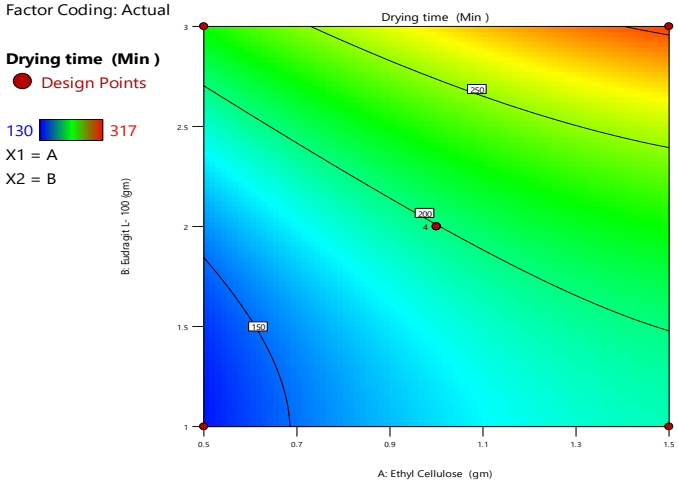


B

Response 3: Drying time

Table 6. 7 ANOVA for Quadratic model of Drying time

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	35152.80	5	7030.56	119.88	< 0.0001	significant
A-Ethyl Cellulose	9027.32	1	9027.32	153.93	< 0.0001	
B-Eudragit L- 100	21252.32	1	21252.32	362.39	< 0.0001	
AB	144.00	1	144.00	2.46	0.1682	
A^2	562.50	1	562.50	9.59	0.0212	
B^2	3422.50	1	3422.50	58.36	0.0003	
Residual	351.87	6	58.64			
Lack of Fit	348.87	3	116.29	116.29	0.0013	significant
Pure Error	3.00	3	1.0000			
Cor Total	35504.67	11				



7.3 Validation of RSM results

In order to evaluate the optimization capability of models generated according to the results of the RSM (central composite design), film forming spray formulation was prepared using the optimal process variables settings that X_1 and X_2 were equal 0.5:1 (gm). The response Y_1 (%DR at 6 hrs), Y_2 (%DC) and Y3(DT) obtained with predicted models.

Table 6.8 : Characteristics of optimum formula

Objects	EC in gm (X_1)	E l-100gm (X_2)	%DP (Y_1, %)	%DC (Y2, %)	DT(Seconds)	Desirability	
Predicted	0.500	1.000	91.920	83.978	134.116	0.981	Selected
Actual (F12)	0.500	1.000	91	83	132		

7.4 Spray angle

The average diameter of the spray pattern was found to be various depending on the ratio of polymers present in the film forming solution. from the spray pattern analysis, and then the radius (r) is calculated according to their diameter. The length (L) from the nozzle to the sheet is taken as 7 cm. The spray angle of prepared formulation was between 54.85±0.26to 66.77º±1.28. The spray angle (θ) for the optimized batch (F12) is found to be 54.85±0.26.

Table 6.9 : Spray angle

Batch code	Distance in Cm (L)	Radius(r)	Spray angle(±SD)
F1	7	4	60.26º±0.16
F2	7	3.9	60.81º±0.24
F3	7	1.86	61.74º±0.83
F4	7	4.25	58.63º±0.64
F5	7	3.2	65.36º±0.72
F6	7	1.62	58.74º±0.16
F7	7	3.15	66.77º±1.28
F8	7	3.05	65.75º±2.29
F9	7	4.8	55.41±0.92
F10	7	3.05	66.41±0.79
F11	7	4.6	56.66º±0.43
F12	7	4.9	54.85 º±0.26

7.5 The volume of spray solution delivered per each actuation

The initial weight of the container and the spray solution was found to be 201.527. The weight of the container and the formulation after one actuation was found to be 201.418. From the above studies, the density of the optimized batch solution is found to be 0.87116 gm/ml. The volume of the solution for the optimized batch delivered per actuation is found to be 0.125 ml.

Table 6.10 : Volume actuated upon each Spray

Formulation code	Volume of spray solution delivered per each actuation (ml)
F1	0.543±0.048
F2	0.8651±0.054
F3	0.1605±0.032
F4	0.345±0.29
F5	0.847±0.026
F6	0.2892±0.045
F7	0.732±0.025
F8	0.920±0.084
F9	0.1605±0.039
F10	1.225±0.046
F11	1.567±0.013
F12	0.125±0.028

*****Values expressed as mean ±SD, n=3, SD: Standard deviation

7.6 In-vitro drug release

7.6.1 In-vitro drug release

In-vitro drug release study was carried out the using the Franz diffusion cell in pH 6.8 phosphate buffer saline. In-vitro release profile of film forming spray was monitored for 6hrs. The release profile of Film forming spray (batch F1 to F12) were carried out separately as shown in table and. Film forming spray showed drug release in a range between 30.00± to 91.00±. 0 at 6 hrs with the highest % drug release was obtained for the batch F12 and the lowest one obtained was in the case of batch F5.

Table 6.11 : Drug diffusion of Film forming spray (F1 to F6)

Time (Hrs)	Percentage drug release (%)					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	8.25±0.6	7.12±0.16	11.79±0.43	9.64±0.73	4.23±0.8	9.64±0.56
2	16.48±0.85	18.98±0.92	14.05±0.29	17.75±0.24	6.39±0.25	11.01±0.42
3	28.19±0.36	29.42±0.4	15.40±0.18	34.64±0.62	11.44±0.27	21.99±0.49
4	39.52±0.75	35.13±0.31	17.38±0.45	64.65±1.92	16.93±0.16	35.84±0.66
5	47.31±2.09	46.37±2.90	28.51±0.62	72.43±2.89	21.26±0.95	41.93±0.91
6	59.00±0.12	58.5±0.76	38.20±0.35	82±1.42	30.00±0.49	58.01±1.92

*****Values expressed as mean ±SD, n=3, SD: Standard deviation

Table 6.12 : Drug diffusion of Film forming spray (F7 to F12)

Time (Hrs)	Percentage drug release (%)					
	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0

1	11.60±0.8	12.64±0.35	9.45±0.83	9.35±0.52	10.62±0.71	29.19±0.89
2	24.59±0.54	13.84±0.54	13.54±0.23	14.51±0.66	14.57±0.42	43.36±0.26
3	39.38±0.26	18.32±0.19	23.09±0.18	23.62±0.82	22.02±2.89	56.79±0.65
4	49.96±.92	20.05±0.44	35.81±1.32	27.18±0.14	33.42±1.38	76.46±0.49
5	57.16±0.39	36.59±1.28	40.13±0.97	32.73±1.25	44.75±1.44	86.23±0.96
6	64.51±0.62	76±0.54	57.09±0.91	41.03±0.65	59.01±0.22	91.00±0.18

*****Values expressed as mean ±SD, n=3, SD: Standard deviation

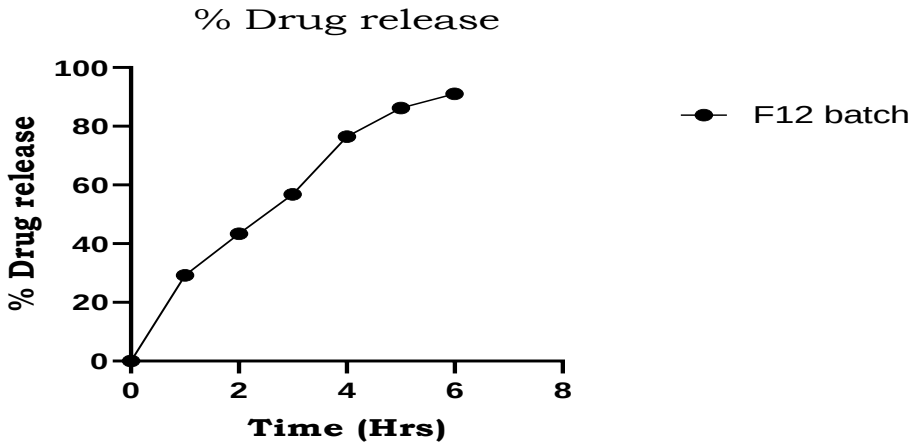


Figure 6.2 : In-vitro diffusion profile of batch F12

7.7. Ex-vivo permeation studies

The Ex-vivo permeation study was performed for the optimized formulation i.e., batch F12 based on the results of in vitro drug diffusion study. The permeation (drug release) of Film Forming spray of batch F12 was found to be 93.97% after 6 hrs.

Table 6.13 : Ex-vivo permeation data

Time (min)	Ex-vivo (%) of F12 batch
0	0
1	38.97±0.56
2	45.80±0.38
3	57.57±0.94
4	75.10±0.89
5	84.7±0.42
6	93.97±0.19

*****Values expressed as mean ±SD, n=3, SD: Standard deviation

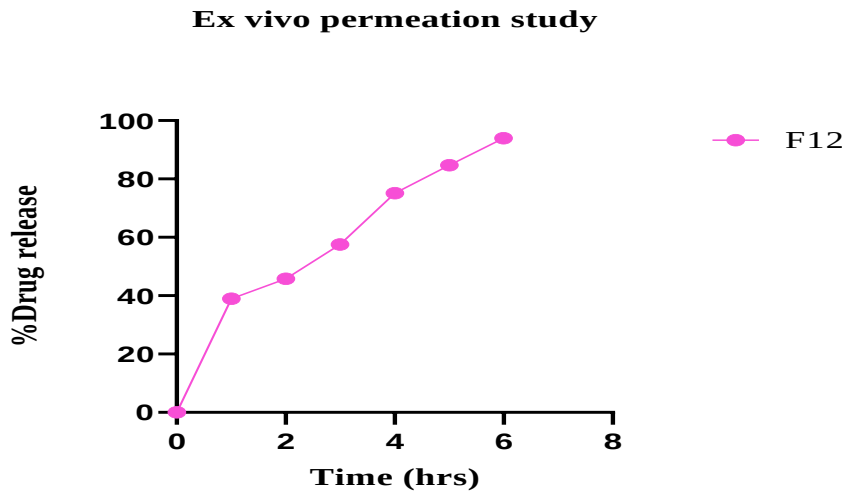


Figure 6.3 Ex vivo permeation study profile of optimized batch

7.8 Anti-inflammatory activity

Anti-inflammatory was carried for diclofenac film forming spray for the optimized batch (F12), in which three groups of animals was used as control in which only gives the saline solution, disease in which we give only the carrageenan in the sub-plantar region, and in the treatment group pre-treated with diclofenac film forming spray and after 30 minutes carrageenan was injected in plantar region for inducing paw edema taken the reading at various period of time.

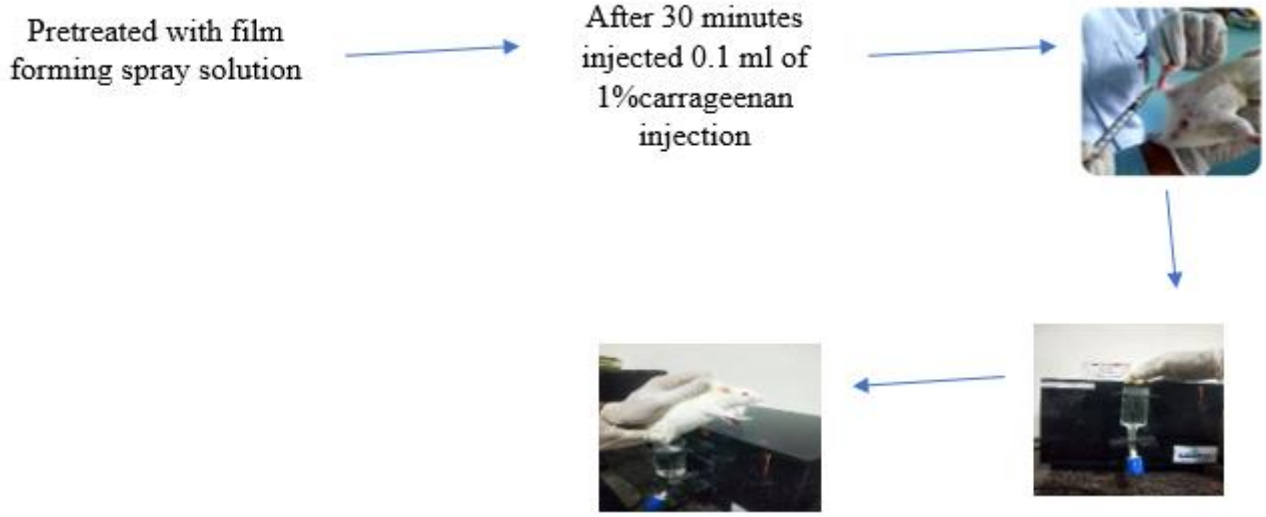


Figure 6.4 : Film forming spray transdermal administration

Table 6. 14 Animal paw edema volume

Reading period	Paw edema volume		
	Control	Disease	Treatment
0.5 hr	0.65	1.25	0.45

1 hr	0.50	1.00	0.25
2hr	0.75	1.15	0.32
3hr	1.10	1.28	0.38
4hr	0.96	1.16	0.34
5hr	0.87	1.05	0.24

Table 6. 14 Carrageenan induced paw edema (%)

Group	**Mean protection in (%)**					
	0.5 hr	1hr	2hr	3hr	4hr	5 hr
Control	-	-	-	-	-	-
Treatment	30.76	50.00	57.33	64.58	65.45	72.41

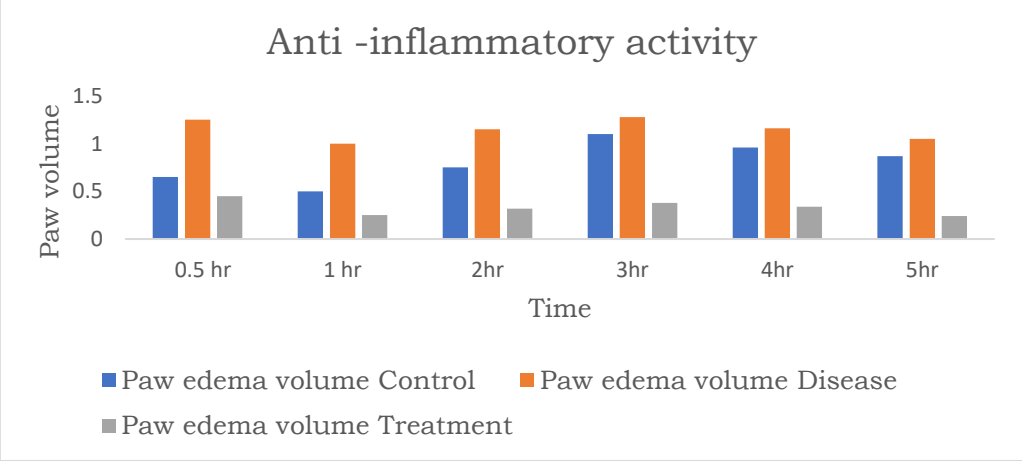


Figure 6.5 : Inhibition of edema (%, Optimized batch F12)

SUMMARY

The Diclofenac potassium is a non-steroidal anti-inflammatory drug. Along with ethyl cellulose, and eudragit l-100 were selected for the formulation of film forming spray, the selected diclofenac potassium and ethyl cellulose, eudragit l-100 sample were evaluated for Preformulation study i.e., melting point, solubility study, FTIR and DSC. Samples were shown to have good melting point, soluble in methanol, ethanol, water, glycerol and drug solubility studied was carried out in methanol, result was found to be good. The FTIR and DSC gives the compatibility data for the drug and physical mixture and it was found to be compatible with each other and there was interaction between them.

The optimized film forming spray formulation was confirmed by evaluation of , spray angle and volume of spray per each actuation. The final optimized batch of film forming spray was clear, the spray angle value was found to be 54.85 ±0.26° showed that minimum spray angle for the formulation which means it covers maximum surface area and volume of spray per each actuation was 0.125 ml

CONCLUSION

The spray angle and volume of spray per each actuation gives best results .The in vitro diffusion study of film forming spray formulation showed release of diclofenac potassium till 6hrs.The drug content and drying was also good. The anti-inflammatory was performed by using optimized batch and it gives better results within 5 hrs. And transdermal application of spray it is good for patient compliances and also

eliminated the problem of GIT degradation of drug. From the present experimental data, it can be concluded that the proposed objectives of the project are achieved.

REFERENCES

1. Ali S, Shabbir M, Shahid N. The structure of skin and transdermal drug delivery system-a review. Research journal of pharmacy and technology. 2015;8(2):103-9
2. Anter HM, Abu Hashim II, Awadin W, Meshali MM. Novel anti-inflammatory film as a delivery system for the external medication with bioactive phytochemical "Apocynin". Drug Design, Development and Therapy. 2018 Sep 13:2981-3001.
3. Anjana V, Jyothi V. A review article on anatomy of skin in Ayurveda.,2023
4. Asp MJ Pharma. 2016;1(1):6.
5. Bajaj H, Kumar T, Singh V. Film forming gels: a review. Research journal of pharmaceutical biological and chemical sciences. 2016 Jul 1;7(4):2085-91
6. Barbieri JS, Wanat K, Seykora J. Skin: basic structure and function.,2014
7. Bakhrushina EO, Shumkova MM, Sergienko FS, Novozhilova EV, Demina NB. Spray Film-Forming systems as promising topical in situ Systems: A review. Saudi Pharmaceutical Journal. 2022 Nov 23.
8. Barros ND, Chagas PA, Borges FA, Gemeinder JL, Miranda MC, Garms BC, Herculano RD. Diclofenac potassium transdermal patches using natural rubber latex biomembranes as carrier. Journal of Materials. 2015 Nov 8;2015:1-7.
9. Bornare SS, Aher SS, Saudagar RB. A review: Film forming gel novel drug delivery system. Int J Curr Pharm Res. 2018;10(2):25-8.
10. Casey G. Physiology of the skin. Nursing Standard (through 2013). 2002 May 8;16(34):47.
11. Chamsai B, Soodvilai S, Opanasopit P, Samprasit W. Topical Film-Forming Chlorhexidine Gluconate Sprays for Antiseptic Application. Pharmaceutics. 2022 May 25;14(6):1124.
12. Desai M, Godbole AM, Somnache S, Gajare P, Pednekar A, Manerikar S, Kudaskar K, Naik V. Design, Development, and Characterization of Film Forming Spray as Novel Antifungal Topical Formulation for Superficial Fungal Infections. INDIAN JOURNAL OF PHARMACEUTICAL EDUCATION AND RESEARCH. 2022 Oct 1;56(4): S651-8
13. De Oliveira FF, de Menezes LR, Tavares MI. Film-forming systems in topically administered pharmaceutical formulations. Materials Sciences and Applications. 2020 Aug 14;11(08):576
14. Deshmukh SN, Gade V, Garud A, Dumbre R, Warude B, Maharaj S, Girme S, Shewalkar S. Novel film forming spray from tea tree leaves with special emphasis on development, formulation and evaluation. Journal of Positive School Psychology. 2022 Jun 1:5179-84.
15. Devhadrao NV, Siddhaia M. Review on ocular insert drug delivery system. Journal of Drug Delivery and Therapeutics. 2018 Oct 15;8(5-s):115-21.
16. Duchesne E, Dufresne SS, Dumont NA. Impact of inflammation and anti-inflammatory modalities on skeletal muscle healing: from fundamental research to the clinic. Physical therapy. 2017 Aug 1;97(8):807-17
17. Durga KN, Bhuvaneswari P, Hemalatha B, Padmalatha K. A Review on Transdermal Drug Delivery System. Asian Journal of Pharmacy and Technology. 2022 May 25;12(2):159-66.
18. Edwards A, Qi S, Liu F, Brown MB, McAuley WJ. Rationalising polymer selection for supersaturated film forming systems produced by an aerosol spray for the transdermal delivery of methylphenidate. European Journal of Pharmaceutics and Biopharmaceutics. 2017 May 1;114:164-74.

19. Gaikwad AK. Transdermal drug delivery system: Formulation aspects and evaluation. Comprehensive Journal of Pharmaceutical Sciences. 2013 Feb;1(1):1-0.
20. Gennari CG, Selmin F, Minghetti P, Cilurzo F. Medicated foams and film forming dosage forms as tools to improve the thermodynamic activity of drugs to be administered through the skin. Current Drug Delivery. 2019 Jun 1;16(5):461-71
21. Gohel MC, Nagori SA. Fabrication of modified transport fluconazole transdermal spray containing ethyl cellulose and Eudragit® RS100 as film formers. AAPS Pharm SciTech. 2009 Jun; 10:684-91.
22. Holmgaard R, Nielsen JB. Dermal absorption of pesticides: evaluation of variability and prevention. Copenhagen, Denmark: Danish Environmental Protection Agency; 2009.
23. Huaytragul J, Chalitangkoon J, Monvisade P, Chotsaeng N. Enhancing chitosan solubility in alcohol: Water mixtures for film-forming systems releasing with turmeric extracts. Journal of the Taiwan Institute of Chemical Engineers. 2021 Jun 1; 123:293-301.
24. Huang Y, Wang M, Xu L, Deng J. Experimental study on a spray and falling-film cooling system. Case Studies in Thermal Engineering. 2021 Aug 1; 26:101057.
25. Jhawat VC, Saini V, Kamboj S, Maggon N. Transdermal drug delivery systems: approaches and advancements in drug absorption through skin. Int J Pharm Sci Rev Res. 2013 May;20(1):47-56
26. Jyothi VG, Pawar J, Fernandes V, Kumar R, Singh C, Singh SB, Madan J, Khatri DK. Film forming topical dermal spray of meloxicam attenuated pain and inflammation in carrageenan-induced paw oedema in Sprague Dawley rats. Journal of Drug Delivery Science and Technology. 2022 Apr 1;70:103195