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Pharmacy Practice and Research
Volume 2 Issue 2, 2022

Effect of Penetration Enhancers on the Development and Evaluation of Matrix Type Transdermal Patch of Diclofenac Sodium

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ABSTRACT

The main objective of the present work was to develop transdermal patch of diclofenac sodium using different concentration of various penetration enhancers by using solvent casting method. Transdermal patch of diclofenac was prepared by using polymer hydroxyl-propyl-methyl cellulose in all preparation altering the concentration of penetration enhancer like tween 80, sodium lauryl sulfate, dimethyl-sulfoxide in different concentration. In the present study, the ten formulations were developed and these formulation batches were evaluated for pre-formulation study like solubility, melting point detection, drug compatibility study and evaluation of patch like weight variation, thickness, moisture loss, moisture absorb, surface pH, swelling index, percentage elongation, tensile strength, drug content uniformity, drug permeation study of all formulations were found to be within limit.Effects of various penetration enhancers – Tween80, SLS, DMSO at varying concentration has been checked on in-vitro permeation of drugs and was found to be effective.Based on the evaluation parameters, F9 formulation containing 65 % of di-methyl-sulfoxide shows significant increase in permeation with 93.28%, in-vitro drug release of 84.12% in 12 hrs, The rank order of the penetration enhancers along with PEG400 was found to be: DMSO (65%)> SLS (5%)> DMSO (60%)>SLS (10%)>Tween80(15%)> Tween(10%)> DMSO (55%) >Tween80 (5%)> SLS(15%)> blank.

Keywords: *Transdermal patch, Diclofenac sodium, penetration enhancer, di-methyl sulfoxide, sodium lauryl sulfate, tween 80.*

INTRODUCTION

In the area of drug delivery system innovations are taking place at a much faster pace as compared with the last two decades. Inextricable aspects of new drug delivery system are improved patient compliance and effectiveness of drug [1,2]. A more radical approach to explore newer interfaces on the body for introducing therapeutics one of which is transdermal drug delivery makes use of human skin as a port of entry for systemic delivery of drug molecules [3]. Transdermal drug delivery system (TDDS) is one of the systems lying under the category of controlled drug delivery, in which the aim is to deliver the drug through the skin in a predetermined and controlled rate. TDDS are adhesive drug-containing devices of defined surface area that deliver a predetermined amount of drug to the surface of intact skin at a programmed rate to reach the systemic circulation [4, 5, 6, 7, 8].

Diclofenac sodium is Non-steroidal anti-inflammatory agent (NSAIDS), widely used in musculoskeletal disorders, arthritis, toothache, etc., for symptomatic relief of pain and inflammation. Diclofenac sodium is reportedly used for topical applications. The drug undergoes substantial hepatic first-pass metabolism and only about 50% of administered dose

reaches systemic circulation. In Rheumatoid Arthritis patients are advised to take the NSAIDs for prolong period but the side effects such as systemic toxicity, GIT irritation, nausea, vomiting, gastric erosion, headache are the main drawbacks of Diclofenac sodium. Because of its short biological half-life and frequent administration, it is considered as a suitable candidate to formulate it into a sustained release matrix type transdermal patch system. Main objective of study is to develop transdermal patch of Diclofenac sodium to achieve more patient compliance, to reduce the dosing frequency, to enhance the release rate of drug for quick onset of action, to avoid the oral administration of drug to omit the GIT related bioavailability problems and to improve local availability of drug to site of action in arthritis [9].

ADVANTAGE OF TDDS [10, 11, 12]

1) Can avoid gastrointestinal drug absorption difficulties covered by gastrointestinal pH, enzymatic activity and drug interaction with food, drink and other orally administered drug.
2) Can be a substitute for oral administration of medication when the route is unsuitable as with vomiting and diarrhea.
3) To avoid the first pass effect *e.g.* Transdermal Nitroglycerin. It is rapidly metabolized by the liner when taken orally.
4) Noninvasive, avoiding the inconvenience of parenteral therapy.
5) They provided extended therapy with a single application, improving compliance over other dosage forms requiring more frequent dose administration *e.g.* Transdermal clonidine 7 day.
6) The activity of drugs having a short half-life is extended through the reservoir of drug in the therapeutic delivery system and its controlled release.
7) Drug therapy may be terminated rapidly by removal of the application from the surface of the skin.

DISADVANTAGE OF TDDS [12]

- Some patients develop contact dermatitis at the site of application from one or more of the system components, necessitating discontinuation.
- Only potent drugs are suitable candidates for transdermal patch because of the natural limits of drug entry imposed by the skin impermeability.
- Some drugs *e.g.* scopolamine transdermal patch placed behind the ear, it is uncomfortable.
- Not suitable for high drug doses.

COMPONENTS OF TRANSDERMAL DRUG DELIVERY SYSTEM

a) Backing Layer

It protects the polymeric drug reservoir from the external environment, provides support to it and accepts printings. Backing membrane must have optimum elasticity, flexible and impermeable to drug diffusion to prevent drug loss. It should be compatible with polymer, excipients and drug and should not cause any reaction. It is fabricated of aluminium foil, polyethylene, polyester, polyvinyl chloride, heat sealed layers, polyurethane and includes adhesive foam pad [`13, 14, 15].

b) Drug containing Layer

The drug should have some desirable physicochemical properties favorable for drug transport across the skin. Drug should have low molecular weight (up to 1000 Dalton),

low melting point, short half-life, affinity for lipophilic and hydrophilic, potent, and non-irritant.

c) Rate controlling Membrane

Rate controlling membranes determine the rate at which drug is to be delivered from dosage form. Various types of polymers from natural and synthetic origin are used to prepare a rate controlling membrane. Examples for rate controlling membranes are chitosan, poly-2-hydroxyethyl methacrylate etc. [15, 16].

- ✓ It should fulfill the following criteria for becoming ideal membrane as it is a critical component of the transdermal drug delivery system.
- ✓ The diffusion coefficient of the drug should range from 10-7 to 10-9.
- ✓ Film should be such that it can be fabricated into 1 to 5 mil (mil= one-thousand of an inch) thickness.
- ✓ It should have low solubility for the drug as well as the excipients.
- ✓ It should have the property to laminate with both adhesive drugs containing layer.
- ✓ It should have softened temperature above the shipping temperature so that it will become soft during transportation.

1) Adhesive

Adhesive maintains the patch in continuous contact with the skin. It should adhere to the skin with a finger pressure and should retain the patch in place for prolonged period. The selection criteria for patch include type and design of patch, adhesive properties. It should be non-irritant, compatible with the other ingredients of the formulation and skin and easily removable. E.g., poly-iso-butadiene, poly-acrylate and silicon based adhesive polymer

2) Release liner

Release liner is the part of primary packaging and prevents the loss of drug from the polymer matrix and prevents contamination of the patch from outside environment during storage and transport. It is peeled off at the time of use. Release liner may be occlusive (e.g., polyethylene, PVC) or non-occlusive (paper fabric). Polyester foil and metallic foil are also used for release liner [17].

Different approaches for transdermal drug delivery[17, 18, 19, 20]

Transdermal drug delivery system can be classified into two type on the basis for different approaches on penetration either by skin or using device.

Skin-controlled device

The device is designed to reply on the skin to control the rate at which the drug diffuses into the body. A drug in matrix layer between frontal and backing layers are typically skin controlled. The polymer matrix controls the release rate which is generally greater than the permeation rate across the skin.

System-controlled device

Rate controlling membranes and the drug usually in a form of liquid or gel i.e. reservoir are used for the system-controlled devices. The membrane controls the diffusion of drug from reservoir to the skin. The other components of these systems are backing, adhesive and release liners which are the general functional components.

Types of Transdermal Patches

Single layer drug in adhesive

In this type the adhesive layer contains the drug. The adhesive layer not only serves to adhere the various layers together and this type of layer is responsible for the releasing the drug to the skin. The adhesive layer is surrounded by a temporary liner and a backing.

Multi -layer drug in adhesive

This type is also similar to the single layer but it contains a immediate drug release layer which is different from other layer which will be a controlled release along with the adhesive layer. The adhesive layer is responsible for the releasing of the drug. This patch also has a temporary liner-layer and a permanent backing.

Vapour patch

In this type of patch, the role of adhesive layer not only serves to adhere the various layers together but also serves market, commonly used for releasing of essential oils in decongestion. Various other types of vapor patches are also available in the market which are used to improve the quality of sleep and reduces the cigarette smoking conditions.

Reservoir system

In this system the drug reservoir is embedded between the two layers; an impervious backing layer and a rate controlling membrane. The drug releases only through the rate controlling membrane, which can be micro porous or non- porous. In the drug reservoir compartment, the drug can be in the form of a solution, suspension, gel or dispersed in a solid polymer matrix. Hypoallergenic adhesive polymer can be applied as outer surface polymeric membrane which is compatible with drug.

Micro reservoir system

In this type the drug delivery system is a combination of reservoir and matrix-dispersion system. The drug reservoir is formed by first suspending the drug in an aqueous solution of water soluble polymer and then dispersing the solution homogeneously in a lipophilic polymer to form thousands of unreachable, microscopic spheres of drug reservoirs. This thermodynamically unstable dispersion is stabilized quickly by immediately cross-linking the polymer in-situ by using cross linking agents.

Matrix system

In matrix diffusion system drug is uniformly dispersed in hydrophilic or lipophilic polymeric material. The rate of erosion of the polymer, thickness of the layer and surface area of the film determines the release rate of the drug. No other rate controlling membrane is present in the matrix system.

These are also known as the monolithic systems. Adhesive layer is spreaded around the circumference of the polymer disc instead of spreading on the surface of the patch. Matrix system of drug delivery can be modified by adding drug directly in the adhesive layer. This may be formulated in single layer drug in adhesive system or multilayer drug in adhesive system.

MATERIALS AND METHODS

Table 1: List of Chemicals Used With Supplier

S.N.	Materials	Source
1.	Diclofenac Sodium	Gifted by Deurali Janata Pharmaceutical Pvt. LTD.
2.	HPMC K4M	Gifted by Deurali Janata Pharmaceutical Pvt. LTD.
3.	Ethyl Cellulose	Gifted by Deurali Janata Pharmaceutical Pvt. LTD.
4.	Pectin	Gifted by Deurali Janata Pharmaceutical Pvt. LTD.
5.	Poly Ethylene Glycol 400	Thermo Fisher scientific India Pvt. Ltd
6.	Tween 80	Gifted by Deurali Janata Pharmaceutical Pvt. LTD.
7.	Methanol	Thermo Fisher scientific India Pvt. Ltd
8.	Potassium dihydrogen phosphate	Merck Limit, Mumbai

Table 2: List of Equipment, Instrument and Machineries Used

S.N.	Instrument	Manufacturer
1.	Dissolution Test Apparatus	Aastha International / PDA-65
2.	Digital Electronic Balance	Kern and Sohn GmbH/D-72335
3.	UV spectrophotometer (double beam)	ELICOR/SL210UV SPECTROPHOTOMETER
4.	pH Meter	SimtronicsR
5.	Vernier caliper	Stainless hardened
6.	Hot air oven	Universal Hot air oven, VITCO Company
7.	Cellophane membrane	Gifted by Kathmandu University
8.	Franz Diffusion Cell	Self- Fabricated
9.	Magnetic Stirrer (2 liter)	Accuma X India, Model (Al- 169-55)
10.	Petri disc	Locally Fabricated
11.	Glass Wares	Borosilicate Grade
12.	Digital Ultrasonic Mixture	Ambala cantt India
13.	Desicator	Borosilicate Glass
14.	Sonicator (6 L)	HL Scientific Industries
15.	Melting point apparatus	Bio Technics India

METHODS

Drug-Excipient Compatibility: Drug-Excipient compatibility was assured by FT-IR spectroscopy.

Formulation of Transdermal Patch: The transdermal patches were developed by a solvent casting method using different concentration of penetration enhancer like tween 80, sodium lauryl sulfate and di-methyl sulfo-oxide.

Table 3: Formulation Chart of Diclofenac Sodium Transdermal Patch

Ingredients/formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Diclofenac (mg)	500	500	500	500	500	500	500	500	500	500
HPMC (mg) (1:1)	500	500	500	500	500	500	500	500	500	500
PEG400(10%w/w)	90µl	90µl	90µl	90µl	90µl	90µl	90µl	90µl	90µl	90µl
Tween80(%w/w)	51 µl	102 µl	153 µl	---	---	---	---	---	---	---
SLS(%w/w)	----	---	----	55 mg	110 mg	165 mg	----	----	---	---

DMSO(%w/w)	----	---	---	---	---	---	605 µl	660 µl	715 µl	----
Drugs/petri-disc(mg)	500	500	500	500	500	500	500	500	500	500
Drug/ patches(mg)	50	50	50	50	50	50	50	50	50	50
Petri-disc area(cm2)	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5
Area of patches(cm2)	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Methanol (ml)	10	10	10	10	10	10	10	10	10	10
Water (ml)	15	15	15	15	15	15	15	15	15	15

F1=Tween 80 5%
F2=Tween80 10%
F3=Tween80 15%
F4=SLS 5%
F5=SLS10%
F6=SLS15%
F10=BLANK
F7=55%
F8=60%
F9=65%

Evaluations of transdermal patch [20, 21, 22, 23, 24, 25,26]

Physical appearance

All the prepared patches were visually inspected for color, clarity, flexibility, and smoothness.

Weight variation

The matrix film was cut into 6.25cm2 patch. Weight of five patches was taken individually and value were averaged. The data were presented as mean ± standard deviation.

Thickness variation

The matrix film was cut into 6.25cm2 patch. Thickness of five patches was measured individually by digital Vernier caliper. The values were averaged and the data were presented as mean ± standard deviation.

Folding endurance of the patches

A strip of film (6.25cm2) was cut evenly and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gave the value of the folding endurance.

Percentage of moisture absorbed

Accurately weighed patches ware placed in a desiccators containing saturated solution of aluminium chloride for 72 hours. After 72 hours, the patch were reweighed and the percentage moisture absorption will be calculated using the formula:

$$\% \text{ moisture absorption} = \frac{\text{Final weight-Initial weight}}{\textit{Initial Weight}} \times 100$$

Percentage of moisture Loss

Accurately weighed patches were placed in a desiccator containing fused anhydrous Calcium chloride for 72 hours. After 72 hours, the patch were reweighed and percentage moisture loss is calculated using the formula.

$$\% \text{ Moisture loss} = [(\text{Initial Weight-Final weight})/ \text{Initial weight}] X\ 100$$

Surface pH

Patch was kept in contact with 0.5 ml of phosphate buffer 5.8 for 1 hr at room temperature in glass tubes and were allowed to swell. A combined glass electrode was brought near the surface of patch and pH readings were taken after allowing an equilibration period of 1 min.

Swelling Index

Swelling study of prepared patch was performed by calculating the function of weight increase due to swelling, which was measured for each formulation. Patch were weighed individually and were placed separately in petridish and 1mL of phosphate buffer, pH 5.8. After 24 hours the patch was removed and weighed. The swelling index (SI) were calculated by given formula:

$$SI = \{[\text{Weight of swell Patch after 24 hours (W2)} - \text{Initial weight of Patch (W1)}] / \text{Weight of patch (W1)}\} X100$$

Percentage Elongation

The initial length of the patch was measured on scale and force was applied until the patch was broken and calculated the % elongation of patch by using the following formula:

$$\text{Percentage elongation} = (\text{Increase in length} / \text{Original length}) X 100$$

Tensile Strength

It is the maximum stress applied to a point of patch at which the strip specimen breaks. A patch should have good tensile strength. Weight at which the patch breaks is known as load failure. The test patch of size (2.5 ×2.5 cm2) was fixed between these cell grips and force was gradually applied till the film broke. Tensile strength was calculated by the given formula:

$$\text{Tensile strength} = \frac{\text{Load at breakage}}{\text{Strip thickness X Strip width}}$$

Drug Content Uniformity

Pieces of 2.5 × 2.5 size were cut from each type of formulation and put in 100 ml beaker of phosphate buffered pH 5.8 solution. The contents were magnetically stirred for 2 h. The solution was then filtered through Whatman filter paper (0.45 μ) and diluted suitably with phosphate buffer saline pH 5.8. The solution was then analyzed for its absorbance at 285 nm using placebo patch as blank. The drug content was calculated by using the equation obtained from standard calibration curve.

Drug Permeation Study

The in-vitro permeation study is carried out by using Franz Diffusion Cell. Cellophane membrane was taken as semi permeable membrane for diffusion. The Franz diffusion cell has receptor compartment with an effective volume 50ml and internal diameter of 4.5cm. A Transdermal patch was placed on one side of cellophane membrane. The medium on the receptor side was phosphate buffer pH 5.8. The receptor compartment was surrounded by water jacket to maintain the temperature at 37 ±2°C. Temperature was maintained using a thermostatic hot plate with a magnetic stirrer. The receptor fluid was stirred by Teflon coated magnetic bead which was placed in the diffusion cell. During each sampling interval, samples are withdrawn and replaced by equal volumes of fresh receptor fluid on each occasion. The samples (1 ml) was withdrawn at predetermined time interval and diluted in 25ml volumetric flask. The sample was analyzed spectrophotometrically at 285 nm.

RESULT AND DISCUSSION

Drug- excipients Compatibility Study

The IR spectral analysis of Diclofenac sodium patch with other excipients was carried out. The characteristic peaks appear for both API and its physical mixture shows that there is no interaction between API and excipients.

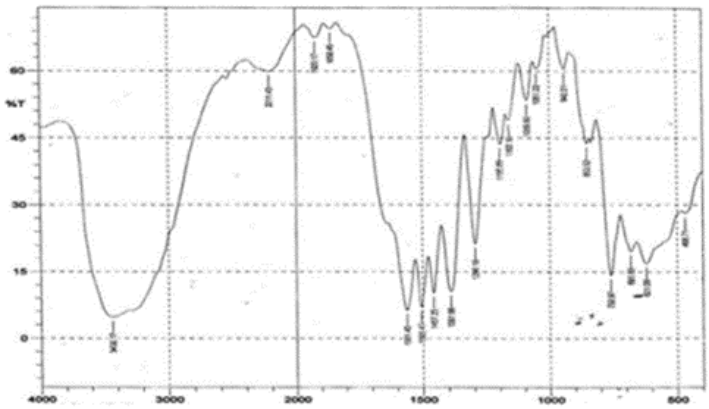

Fig. 1: FTIR of pure diclofenac sodium

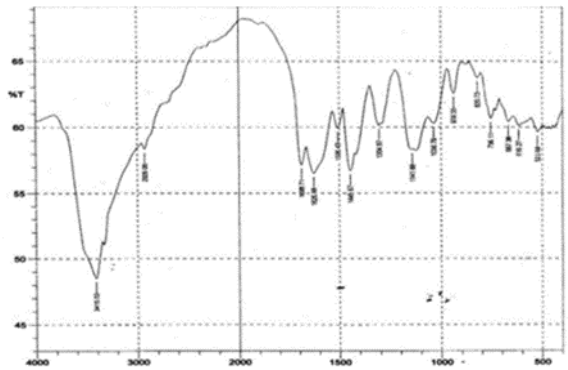

Fig. 2: FTIR ofdiclofenac sodium+ HPMC K4M + SLS

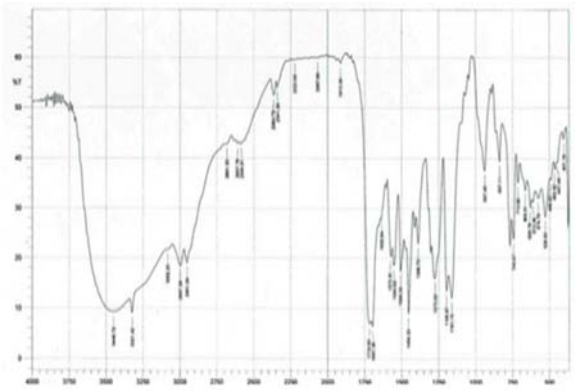

Fig. 3: FTIR of diclofenac sodium + HPMC K4M + DMSO

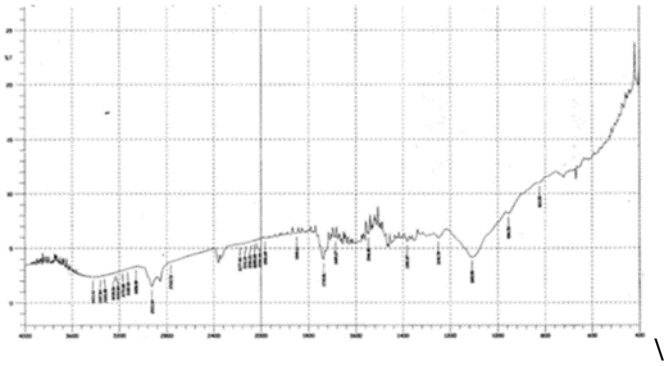

Fig. 4: FTIR of diclofenac sodium+ HPMC K4M+ Tween 80

Determination of λ max

λmax of diclofenac sodium was found to be 285nm. The result of λ max of diclofenac sodium is plotted as shown in figure 5.

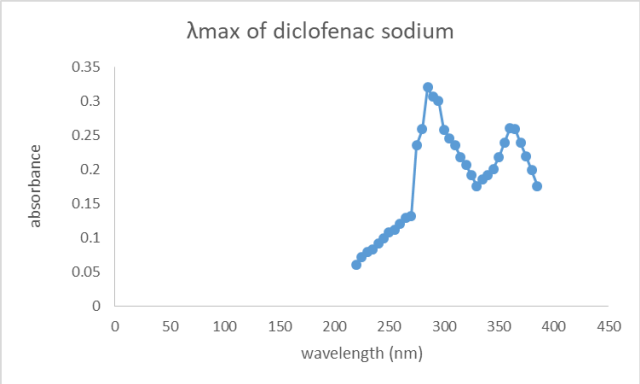

Fig. 5: Determination of λ max

Standard Calibration Curve for Diclofenac sodium

A standard calibration curve for diclofenac sodium was obtained by measuring absorbance at 285 nm and by plotting graph of absorbance vs concentration. The absorbance reading of diclofenac sodium with phosphate buffer were showed in table 2 and figure 6.

Table 4 Absorbance values of Diclofenac Sodium in Phosphate Buffer 5.8

S.N.	Concentration (µg/ml)	Absorbance (285nm)
1.	0	0
2.	5	0.15
3.	10	0.32
4.	15	0.49
5.	20	0.64
6.	25	0.79

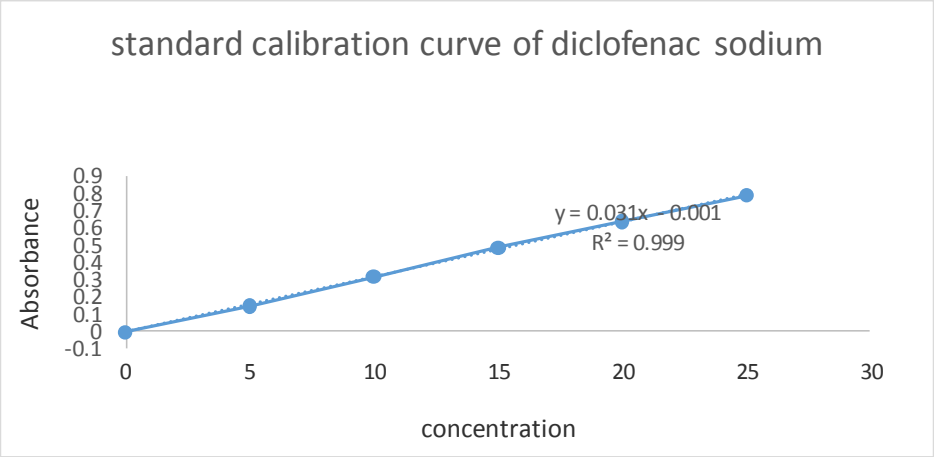

Fig. 6: Standard Calibration Curve of Diclofenac sodium on phosphate buffer at pH 5.8

Preliminary Characterization

The formulated patches were evaluated for preliminary character. The patches were semi-transparent, smooth and non-tacky and flexible.

Table 5: Organoleptic Properties of Transdermal Patch of Diclofenac Sodium

Formulation code	Transparency	Flexibility	Smoothness	Tacky Property
F1	Semi-transparent	Flexible	Smooth	Non-tacky
F2	Semi-transparent	Flexible	Smooth	Non-tacky
F3	Semi-transparent	Flexible	Smooth	Non-tacky
F4	Semi-transparent	Flexible	Smooth	Non-tacky
F5	Semi-transparent	Flexible	Smooth	Non-tacky
F6	Semi-transparent	Flexible	Smooth	Non-tacky
F7	Semi-transparent	Flexible	Smooth	Non-tacky
F8	Semi-transparent	Flexible	Smooth	Non-tacky
F9	Semi-transparent	Flexible	Smooth	Non-tacky
F10	Semi-transparent	Flexible	Smooth	Non-tacky

Physicochemical Properties

The thickness, weight, folding endurance, moisture lost and moisture absorbed of the patches containing penetration enhancer ranged from between 0.078±0.022 to 0.132±0.038 mm, of 0.200±0.021 to 0.324±0.048 gm, 82 to 96 times, 10.60 to 17.75% and 3.85 to 8.82% respectively. Similarly, the thickness, weight, folding endurance, moisture lost and moisture absorbed of blank was found to be 0.316±0.030 mm, 0.251±0.012 mg, 95 time, 18.26% and 9.23% respectively.

The surface pH, swelling index, percentage elongation, tensile strength ranged from 5.769 ±0.053 to 5.848±0.045, 9.874±1.716% to 40.569±1.901%, 150 to 325 %mm2, 0.005 to 0.03 kg /mm2 respectively.

Diclofenac sodium (50mg) was loaded in each patch. Drug content uniformity ranged from 46.64±1.80 to 53.91±0.87 mg. The possible reasons could be due to weighing error, laboratory condition, improper leveling of the petri-disc during solvent casting method and imperfect mixing.

Table 6: Thickness, Weight, Folding endurance, Moisture Loss, Moisture Absorb and Surface pH

Formulation Code	Thickness (n=5,mm)	Weight (n=5,gm)	Folding Endurance	Moisture Lost (%)	Moisture absorbed (%)	Surface pH (n=3)
F1	0.392±0.002	0.324±0.048	88	12.4	5.36	5.848±0.045
F2	0.248±0.011	0.200±0.021	83	17.75	6.10	5.840 ± 0.05
[F3	0.340±0.022	0.261±0.022	82	11.82	3.85	5.801 ±0.002
F4	0.348±0.026	0.272±0.014	89	16.73	5.1	5.769 ±0.053
F5	0.476±0.040	0.300±0.023	77	14.40	4.5	5.827 ±0.0058
F6	0.414±0.011	0.269±0.044	83	11.76	6.8	5.821 ±0.0338
F7	0.360±0.067	0.268±0.059	91	10.60	7.03	5.811 ±0.009
F8	0.426±0.065	0.280±0.032	79	13.30	7.6	5.817 ±0.014
F9	0.284±0.046	0.237±0.029	96	16.74	8.82	5.845 ±0.058
F10	0.316±0.030	0.251±0.012	95	18.26	9.23	5.803 ±0.005

Table 7: Swelling Index, Percentage Elongation and Tensile Strength

Formulation code	Swelling index	Percentage elongation (% mm2)	Tensile strength (kg/mm2)
F1	21.629±1.653	150	0.03
F2	9.874±1.716	200	0.0216
F3	40.569±1.901	200	0.0136
F4	22.128±1.649	150	0.008
F5	11.837±1.403	175	0.0052
F6	34.066±4.855	200	0.005
F7	18.482±1.615	250	0.005
F8	10.350±0.664	300	0.0051
F9	35.350±4.492	325	0.01
F10	21.086±0.939	150	0.0167

Drug Content Uniformity

The percentage drug content of all formulations was found to be in the range of 93.28% to 107.82% which complies with limits established in the official compendia. As per the USP requirements, the films found to meet the criteria for content uniformity (85- 115) % of the label claim.

Table 8: Assay for Transdermal Patch

Formulation code	Assay %
F1	103.64
F2	107.82
F3	102.5
F4	95.84
F5	105.72
F6	102.74
F7	94.44
F8	97.96
F9	93.28
F10	101.54

***In vitro* Permeation Study**

The in vitro permeation study was carried out by using cellophane membrane for 12 hours using phosphate buffer of pH 5.8 as a receiver fluid. The *In vitro* permeation study showed that drug permeation through the cellophane membrane from F1, F2, F3, F4, F5, F6, F7, F8, F9 and F10 was 70.57%, 73.06%, 75.27%, 82.54%, 76.12%, 67.19%, 72.40%, 80.43%, 84.12% and 62.38% respectively in 12 hours. The reason for different value of cumulative percentage permeation through cellophane membrane could be due to using different penetration enhancer in different concentration.

The rank order of the penetration enhancers along with PEG400 was found to be: DMSO (65%)> SLS (5%)> DMSO (60%)>SLS (10%)>Tween80(15%)> Tween(10%)>DMSO(55%) >Tween80 (5%)> SLS(15%)> blank.

The cumulative percentage permeation of Tween80 has shown significantly less than those of others as Tween80 can cause formation of micelles at very low concentration. Mere increase in the concentration of Tween doesn't significantly increase the permeation and the above mention property of could be the possible reason.

Increase in concentration of SLS lead to decrease in permeation, SLS form the micelles and due to the formation of the micelles the permeation after increasing the concentration decreases. From the data it shows that SLS with 5% have maximum permeation whereas permeation decreases significantly with increase in SLS concentration.

DMSO is used as penetration enhancer in a very high concentration. The concentration of DMSO as enhancers is used above 60 %. The increase in the concentration of DMSO increases the permeation and the data shows the increase of permeation with increase in DMSO concentration. The DMSO 65% shows the significant increase.

Table 9: Cumulative Drugs permeated through Cellophane Membrane

Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
1	9.49	11.43	10.44	12.11	11.43	9.21	10.20	12.23	14.16	7.25
2	18.32	20.60	20.60	22.43	18.72	16.80	20.60	23.44	24.23	13.56
3	28.46	32.52	31.76	32.44	29.34	27.20	30.40	34.98	36.59	24.65
4	39.56	47.95	46.44	50.16	47.98	36.40	48.61	52.33	54.55	32.76
5	45.62	55.43	54.38	60.54	57.65	46.81	57.19	62.22	65.87	40.79
6	52.62	61.46	60.95	63.76	63.67	51.20	62.81	65.46	68.76	47.79
8	61.61	65.94	66.56	68.56	68.32	59.21	67.60	71.44	75.22	52.21
10	63.31	69.12	71.17	74.32	70.26	62.52	68.99	76.98	80.34	58.32
12	70.57	73.06	75.27	82.54	76.12	67.19	72.40	80.43	84.12	62.38

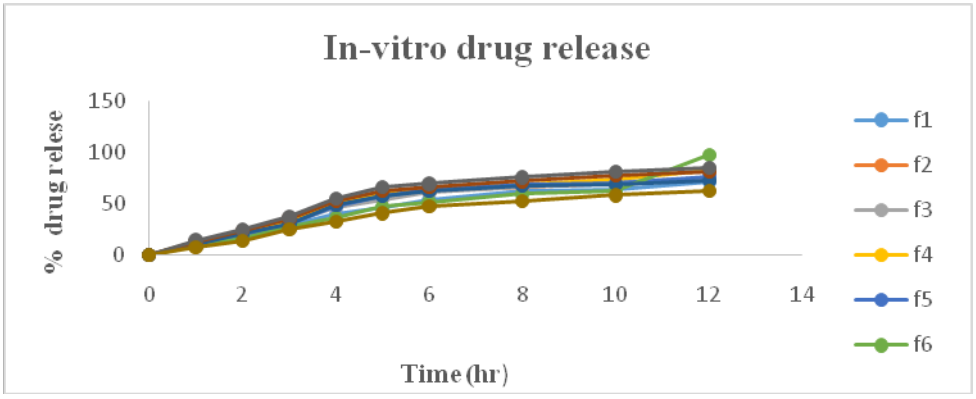

Fig. 7: In-vitro drug release of diclofenac sodium patch

CONCLUSION

Based on our laboratory study the following conclusion can be drawn. It was seen during our research that transdermal patches can be formed using HPMC K4M as a polymer. The polymer forms a matrix which retards the drug release from the formulation. At the same time addition of a permeation enhancer showed a change in release rate.

The various patches were prepared using HPMC K4M as polymer, PEG as a plasticizer and varying concentration of the penetration enhancer. The patches show good physicochemical properties. Effects of various penetration enhancers - Tween80, SLS, DMSO at varying concentration has been checked on in-vitro permeation of drugs and was found to be effective. The burst effects in drugs permeation profile have been shown in the present study; this indicates that drug therapeutic level can reach quickly relatively during the application of the penetration enhancers. Among 9 formulation DMSO 65% showed the highest penetration value compare to other whereas Tween 5% has lowest penetration value. Since, permeation was altered altering the penetration enhancer and its concentration which can be helpful for furthermore study.

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