e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
(Peer-Reviewed, Open Access, Fully Refereed International Journal)
Volume:05/Issue:10/October-2023 Impact Factor- 7.868 www.irjmets.com

A BRIEF OVERVIEW ON FORMULATION AND EVALUATION OF TRANSDERMAL PATCHES OF ACECLOFENAC

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ABSTRACT

The goal of this study was to create a transdermal treatment system of the matrix type. Using a solvent evaporation approach, the medication Aceclofenac is included in various ratios of hydrophilic (hydroxyl propyl cellulose) and hydrophobic (ethyl cellulose) polymeric systems. A plasticizer, 15% w/w dibutyl phthalate, is added to the polymer weight. Aceclofenac's transdermal penetration was increased by varying the amounts of isopropyl myristate and oleic acid. There was no evidence of any incompatibility between the medicine and the polymers based on their physicochemical compatibility, which was examined using differential scanning calorimetry and infrared spectroscopy. The transdermal films that were prepared were examined physically in terms of their thickness, weight fluctuation, drug content, flatness, tensile strength, folding durability, moisture content%, and rate of water vapour transmission. Good physical stability was indicated by all the formulations produced.

Human societies have been applying substances to the skin as cosmetic and medical agents for thousands of years. However, the use of the skin as a medicine delivery system did not begin until the 20th century. The term "transdermal" is actually dated by Merriam-Webster to 1944, indicating that it is a relatively new idea in pharmaceutical and medical practice. Transdermal medications come in a discreet, self-contained dose form. medication distribution via the skin to provide a systemic effect without causing variations in the drug's plasma concentration. The topical distribution of therapeutic agents presents numerous benefits in comparison to traditional oral and invasive drug delivery techniques.

Keywords: Aceclofenac, Transdermal Patch, Drug Delivery.

I. INTRODUCTION

Transdermal medication delivery has been able to fulfil a number of goals, including more constant and longer-lasting blood levels, improved patient compliance, and a painless and convenient way of drug delivery. Patients and doctors embraced the technology quickly, and patches were seen as a promising platform for a range of therapeutic applications, such as pain management, hormone treatment, motion sickness, angina, and hypertension (1).

Aceclofenac is a nonsteroidal anti-inflammatory medication (NSAID) derived from phenylacetic acid that exhibits strong analgesic and anti-inflammatory effects (2).

Aceclofenac (ACF) mainly inhibits prostaglandin synthesis as part of its method of action. The cyclooxygenase (Cox) enzyme, which is involved in the synthesis of prostaglandins, is strongly inhibited by ACF. According to in vitro results, ACF inhibits both Cox-1 and Cox-2 in whole blood assays, with clear selectivity for Cox-2 (3).

ACF has demonstrated stimulatory effects on the synthesis of cartilage matrix, which may be related to the medication's capacity to block IL-1 activity. Data obtained in vitro suggest that the medication stimulates the synthesis of glycosaminoglycan in osteoarthritic cartilage. ACF improves spine mobility and shortens the length of morning stiffness and pain in ankylosing spondylitis patients (4). Transdermal drug delivery systems (TDDS), sometimes referred to as "patches," are dosage forms intended to distribute a medication dosage that is therapeutically efficacious through a patient's skin. To administer therapeutic drugs for systemic effects via the human skin, it is necessary to take into account the skin's complete morphological, biophysical, and physicochemical features. Transdermal administration offers a significant advantage over oral and injectable methods due to its ability to prevent first-pass metabolism and increase patient compliance, respectively. With the evidence of numerous medications' percutaneous absorption, transdermal drug delivery systems (TDDS) are becoming more and more popular. TDDS and prodrugs were created with the intention of providing systemic medication by application. Making a wise drug ingredient selection is the most crucial choice for the

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effective growth of transdermal formulation. Good possibilities include drugs with low biological half-lives, broad therapeutic indices, short effective concentrations, extensive presystemic metabolism, minimal molecular weight, no skin irritation, and lipid-water penetration coefficients of two or higher. One of the main prototypes of rheumatic diseases and a frequent source of disability is rheumatoid arthritis (RA). As of right now, synthetic medications are a mainstay of arthritis care. Non-steroidal anti-inflammatory medicines (NSAIDs) and analgesics are the mainstay medications used to treat RA. (5)

II. MATERIALS AND METHOD

Finar Ltd. (Gujarat, India) kindly donated hydroxypropyl methyl cellulose, whereas Research-Lab Fine Chem Industries (Mumbai, India) kindly donated methyl cellulose. Finar Ltd.'s chloroform (Gujarat, India) The solvent casting procedure was used to prepare the patches. Getting Transdermal Patches Ready A measured amount of polymer was taken, and various solvent additions and vortex techniques were applied to it. The boiling tube was left aside for an hour to allow the polymer to swell, and adequate precautions were taken to prevent the formation of lumps. Following swelling, a measured amount of HPMC and propylene glycol was added to this mixture and vortexed.

Lastly, measure the amount. The leftover solvent was added to the polymer solution, aceclofenac was dissolved in it, and everything was thoroughly mixed. It was done in an oven that was put over a horizontal glass surface and kept at 40°C for 15 minutes in order to release any trapped air. The film took roughly 12 hours to dry.(6).

Table no. 1. Formulation and preparation of transdermal patches.(6)

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Drug (mg)	50	50	50	50	50	50	50	50	50	50
HPMC K15M (MG)	250	500	750	1000	-	-	-	-	-	-
Methyl Cellulose (mg)	-	-	-	-	250	500	750	1000	-	-
HPMCK15M& MC(mg)	-	-	-	-	-	-	-	-	500 500	750 250
Chloroform(ml)	1	1	1	1	1	1	1	1	1	1
Glycerine (ml)	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Ethanol (ml)	5	10	15	20	5	10	15	20	20	20

Development of calibration curve of aceclofenac: The 10 mg of aceclofenac was dissolved in methanol to create the primary stock solution. One millilitre of this stock solution was taken out and diluted with pH 6.8 phosphate buffer to make ten millilitres. From this, phosphate buffer was used to create a series of dilutions in the range of 2–12 µg/ml, which were then examined using a UV-visible spectrophotometer.(7)

Compatibility studies by FTIR spectroscopy: The Fourier transform infrared spectrophotometer, or FTIR, is a useful tool for identifying drug samples and observing interactions between the drug and its surfactants. Aceclofenac's FTIR spectra and the physical combination of the medication with lipid, surfactant, and chitosan were recorded with a resolution of 4 cm1 in the scanning range of 400 to 4000 cm1 [IR-Affinity1, Shimadzu, Japan].(8)

Preparation of aceclofenac loaded transferosome: Using rotary evaporation and thin film hydration, transferosomes were created. An organic solvent mixture of methanol and chloroform was used to dissolve 100 mg of the medication, as well as a mixture of lipid and surfactant in four different ratios [Table 1]. To create a thin lipid coating, the mixture was carefully evaporated using rotary evaporation (Buchi rotavapor R-3000) at reduced pressure and 60 rpm. The mixture was then transferred into a clean, dry round-bottom flask. The flask was placed under vacuum for the entire night in order to eliminate any remaining solvent. After drying, the thin lipid film was rotated at room temperature and hydrated with 10 ml of phosphate buffer solution (pH 6.8). The

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resulting vesicles were stored after being subjected to five-minute cycles of sonication using a probe sonicator (Rivotex) to further reduce their size. (9)

Differential scanning calorimetry: On a DSC-60 detector (Shimadzu, Japan), differential scanning calorimetry (DSC) analysis was carried out. A hermetically sealed aluminium pan containing 4 mg of aceclofenac medication and a physical mixture of the drug with additional excipients was weighed. Under nitrogen purge, a DSC scan was recorded from 30 to 3000 at a heating rate of 100/min.(10)

Physicochemical characterization of films -

Thickness - Using a micrometre (Mitutoyo Co., Japan) at three distinct locations, the patches' thickness was measured, and the mean values were computed.(11)

Weight Variation

Using a micrometre (Mitutoyo Co., Japan) at three distinct locations, the patches' thickness was measured, and the mean values were computed.(12)

Flatness

From each film, three longitudinal strips were removed: one from the left side, one from the right side, and one from the centre. Every strip's length was measured, and the percentage of constriction (0% constriction = 100% flatness) was used to calculate the length variation resulting from non-uniformity in flatness.(13)

Folding Endurance

One film was folded repeatedly in the same spot until it broke in order to ascertain this. The value of folding endurance was determined by counting how many times the film could be folded in the same direction without cracking or breaking. (14)

Percentage of Moisture Content

One film was folded repeatedly in the same spot until it broke in order to ascertain this. The value of folding endurance was determined by counting how many times the film could be folded in the same direction without cracking or breaking.(15)

Permeation Data Analysis

Using linear regression analysis, the flux (µg cm-2 hr-1) of ACF was determined from the slope of the plot of the cumulative quantity of ACF penetrated per cm2 of skin in steady state against time. (16,17).

Using the following formula [26], the drug's steady-state permeability coefficient (Kp) through the rat epidermis was determined: B J Kp = (1), where J is the patch's ACF concentration and C is its flow. Using the following formula, the penetration enhancer's penetration-enhancing impact was determined in terms of enhancement ratio (ER) (18).

$$Kp = J/C \quad (1)$$

Using the following formula [26], the drug's steady-state permeability coefficient (Kp) through the rat epidermis was determined: B J Kp = (1), where J is the patch's ACF concentration and C is its flow. Using the following formula, the penetration enhancer's penetration-enhancing impact was determined in terms of enhancement ratio (ER). (19).

ER = Kp with penetration enhancer

Kp withought penetration enhancer (2)

Weight Consistency Weighing three randomly chosen patches separately will allow weight fluctuation to be examined. This decision ought to be The International Journal of Pharma Research and Health Sciences, Volume 5, Issue 4, pages 1743–1746, is published quarterly. Performed with all rights reserved for each formulation. Every batch's patches were weighed separately, and the average weight was determined. (20).

III. RESULT

Investigation of Physicochemical Compatibility of Drug and Polymer. All processes that demand or produce energy can be quantitatively detected with differential scanning calorimetry (i.e., endothermic or exothermic phase changes). Figure 1 displays the thermograms of the following: EC (D), ACF (A), HPC (B), a physical mixture of ACF with an excipient of HPC patch formulation (C), and a physical mixture of ACF with an excipient

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of EC patch formulation (E). A melting peak was observed by the ACF at 158.22 °C. A peak ACF temperature of 158.22 °C was observed in the physical mixture of medication containing both HPC and EC patch formulation excipients at the same location, or close to 160 °C. This verified the drug's physicochemical stability when the formulation excipient utilised in the investigation was employed.

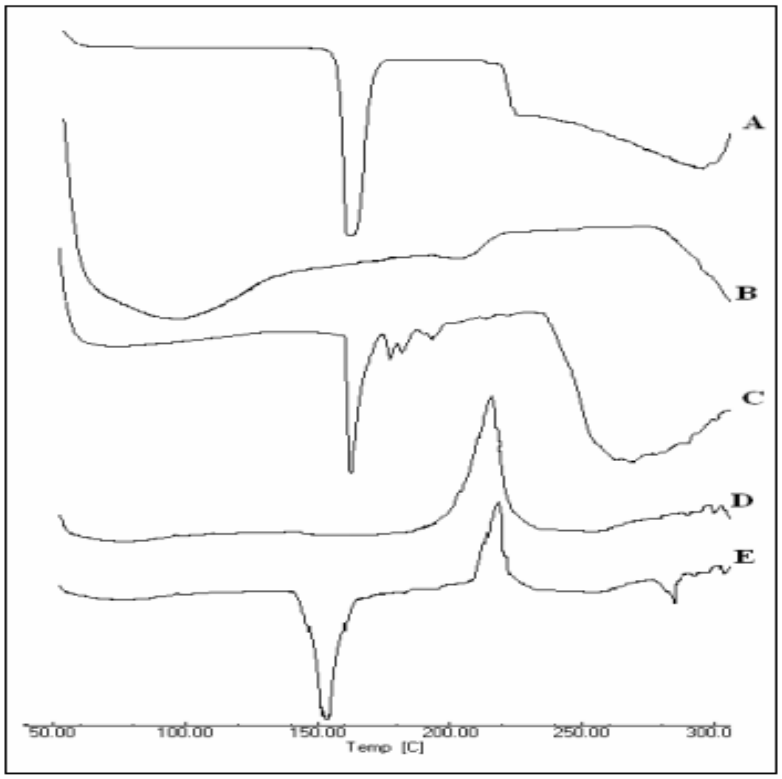

Figure 1: DSC study of ACF (A), HPC (B), physical mixture of

Physical mixture of EC formulation excipients with ACF (E), EC (D), and HPC formulation excipient with ACF (C) Drug-excipient interactions are important for the drug's release from the formulation, among other reasons. Here, the physical and chemical interactions between the medication and the excipients have been investigated using FTIR techniques. Figure 2 displays the infrared (IR) spectra of ACF (A), ACF's physical mixture with excipients from an HPC patch formulation (B), and ACF's physical mixture with excipients from an EC patch formulation (C). Sharp bands were seen in the infrared absorption spectroscopy (IR) of ACF at 3319, 3278, and 1770 cm1, corresponding to the stretching vibration bands of OH, N-H, and C=O.

The IR spectra of the drug and polymer mixture showed no changes in these key peaks, as displayed in the figure. This suggests that there were no physical interactions resulting from the development of bonds between the drug and polymers.

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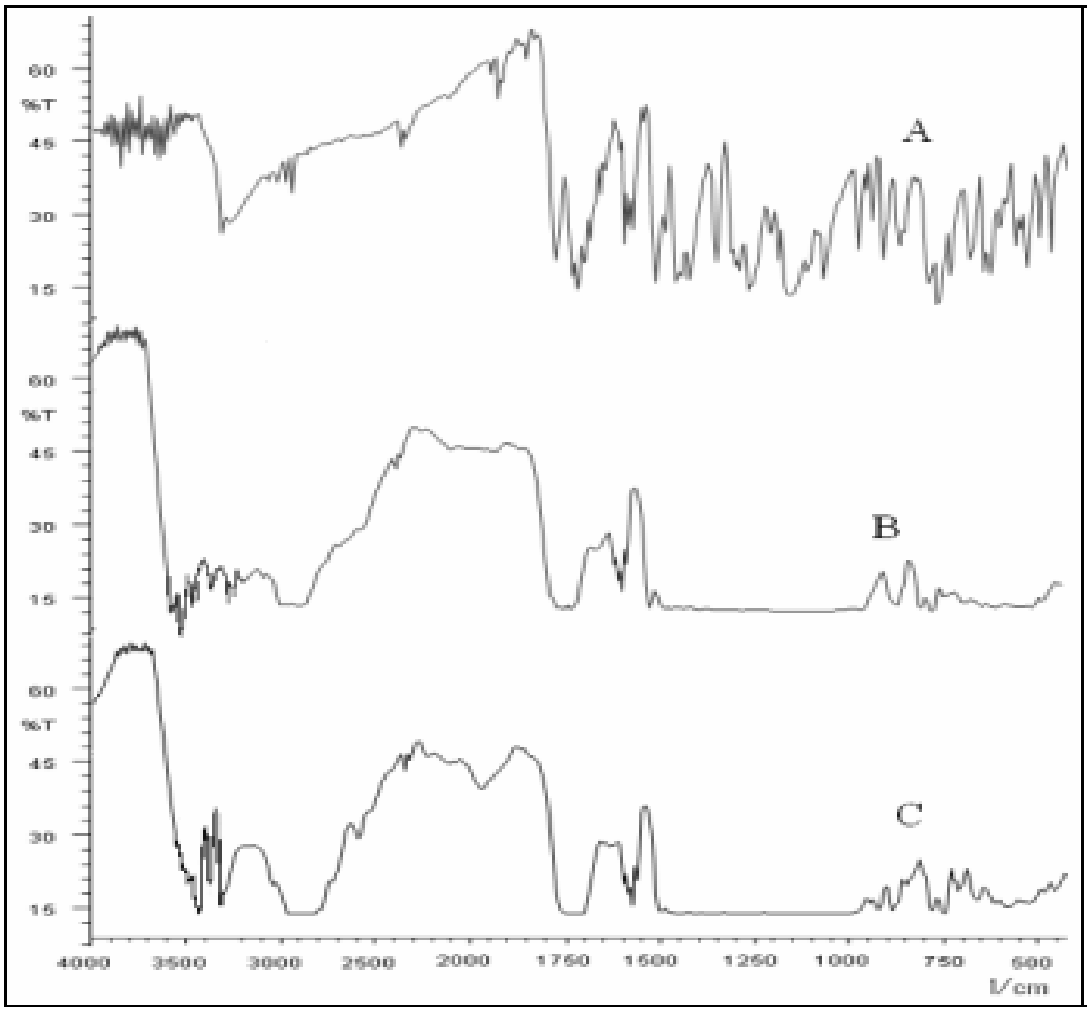

Figure 2: FTIR spectra of ACF (A), physical mixture of HPC with ACF (B), physical mixture of EC with ACF (C)

Table 2: Kinetic modeling of drug release (21)

Formulation code	Zero order	First order	Higuchi
F1	0.9975	0.9966	0.9365
F2	0.9928	0.9925	0.9660
F3	0.9884	0.9901	0.9741
F4	0.9955	0.9951	0.9604
F5	0.9834	0.9838	0.9802
F6	0.9781	0.9809	0.9847
F7	0.9902	0.9885	0.9692
F8	0.9692	0.9669	0.9901
F9	0.9595	0.9576	0.9935

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Using the solvent casting approach, thirteen distinct transdermal patches containing aceclofenac were created using polymers such as ethyl cellulose, HPMC, and Na-CMC. Table 1 displays the components of different transdermal patch formulations. The prepared patches were divided into 2.2-cm-diameter circular pieces and put through a battery of evaluation tests. An assessment of transdermal aceclofenac patches Table 2 lists the physical attributes of the different patches. The findings of the folding endurance test showed that when the patches were utilised, they would not break and would keep their strength and integrity when the skin folded.

With the exception of F7, which had a decent folding endurance, the majority of the patches containing glyceryl triacetate (F8–F13) as plasticizers had higher folding endurances than those using PEG-400 (F1–F6). The weight variations of the various patches were very similar, ranging from 78.00 ± 1.00 mg to 129.66 ± 3.21 mg. The consistency of the patches was assured by low standard deviation values in the film thickness measurements, with patch thicknesses ranging from 0.119 ± 0.002 mm to 0.188 ± 0.001 mm. Each patch of a single batch had weights that were fairly close to one another. In comparison to other formulations, the weight of the formulation with the highest HPMC concentration was higher. It might be because HPMC has a greater capacity to absorb moisture.

All of the transdermal patches had thicknesses between 0.119 and 0.188 mm. This thickness variation may be explained by the concentrations of the polymers; that is, a rise in polymer concentration led to an increase in patch thickness. Between 1.06 ± 0.00% and 7.23 ± 0.45% of moisture was lost. There was a slight variation in the moisture content across all formulas. When the concentration of hydrophilic polymer (HPMC) increased in matrix transdermal patches F3, F6, F9, or F10 in Table 2, the moisture content increased as well. A small amount of moisture left in the formulation could aid in the film's stability and prevent it from drying completely. In phosphate buffer solution (pH 7.4), patches were seen to enlarge, and this swelling was accompanied by an increase in weight. The combination of HPMC and EC in F9 reached its peak, and F13, which contained HPMC and Na-CMC, came next. Because EC, a hydrophobic polymer, was the only component present, F11 showed the least amount of swelling. An increase in swelling was observed in the series of F1 to F3, F4 to F6, and F7 to F9, with corresponding doses of 300, 400, and 500 mg of EC and rising HPMC concentrations. Thus, it can be said that swelling was mostly caused by the concentration of the hydrophilic polymer HPMC. The drug content data for each manufactured patch showed that the medicine had been distributed evenly. There was a range of 94.37% to 98.55% drug content.

Table 3: Results of physical evaluation tests conducted on aceclofenac transdermal patches

(average ± SD, n = 3)

Formulation Code	Weight (mg)	Thickness (mm)	Folding Endurance	Swelling Index (%)	Moisture content (%)	Drug content (%)
F1	80.33 ± 1.5	0.121 ± 0.001	190.66 ± 0.57	36.25 ± 1.25	1.66 ± 0.72	94.37 ± 1.52
F2	94.00 ± 2.0	0.127 ± 0.003	212.33 ± 2.08	51.76 ± 0.61	1.06 ± 0.00	95.71 ± 0.38
F3	109.00 ± 5.0	0.151 ± 0.001	242.00 ± 5.56	74.30 ± 0.91	3.05 ± 0.5	97.75 ± 0.70
F4	90.00 ± 1.00	0.128 ± 0.001	217.00 ± 1.00	41.85 ± 0.64	2.59 ± 0.641	98.57 ± 0.43
F5	105.66 ± 3.21	0.163 ± 0.001	243.66 ± 5.68	54.60 ± 1.98	2.85 ± 0.00	98.75 ± 0.30
F6	118.66 ± 1.15	0.170 ± 0.002	272.00 ± 6.00	81.35 ± 0.85	5.08 ± 0.85	98.71 ± 1.37
F7	108.00 ± 1.00	0.158 ± 0.001	247.33 ± 3.05	37.34 ± 0.53	2.15 ± 0.53	97.09 ± 2.16
F8	116.66 ± 1.15	0.175 ± 0.002	274.00 ± 3.60	62.35 ± 0.50	4.02 ± 0.50	96.94 ± 0.72
F9	129.66 ± 3.21	0.188 ± 0.001	296.33 ± 4.50	98.70 ± 0.45	7.23 ± 0.45	98.85 ± 0.93
F10	83.33 ± 1.52	0.119 ± 0.002	245.00 ± 5.56	92.76 ± 1.20	6.46 ± 1.43	98.51 ± 0.29
F11	78.00 ± 1.00	0.123 ± 0.003	262.33 ± 4.50	28.20 ± 1.28	1.25 ± 0.05	95.95 ± 0.65
F12	110.33 ± 3.51	0.157 ± 0.002	264.33 ± 15.56	86.66 ± 0.52	3.93 ± 0.52	97.13 ± 1.36
F13	113.66 ± 1.15	0.165 ± 0.002	254.66 ± 2.51	92.91 ± 2.34	3.23 ± 0.50	97.37 ± 1.15

In vitro diffusion and skin permeability studies : Figure 2a shows the drug diffusion pattern from semisolid formulations AF (AF1–AF8). Carbopol gel formulations (AF2) showed superior in vitro diffusion and permeation in comparison to formulations containing different dermatological bases. The impact of the dermatological base on the drug release profile has been well documented.

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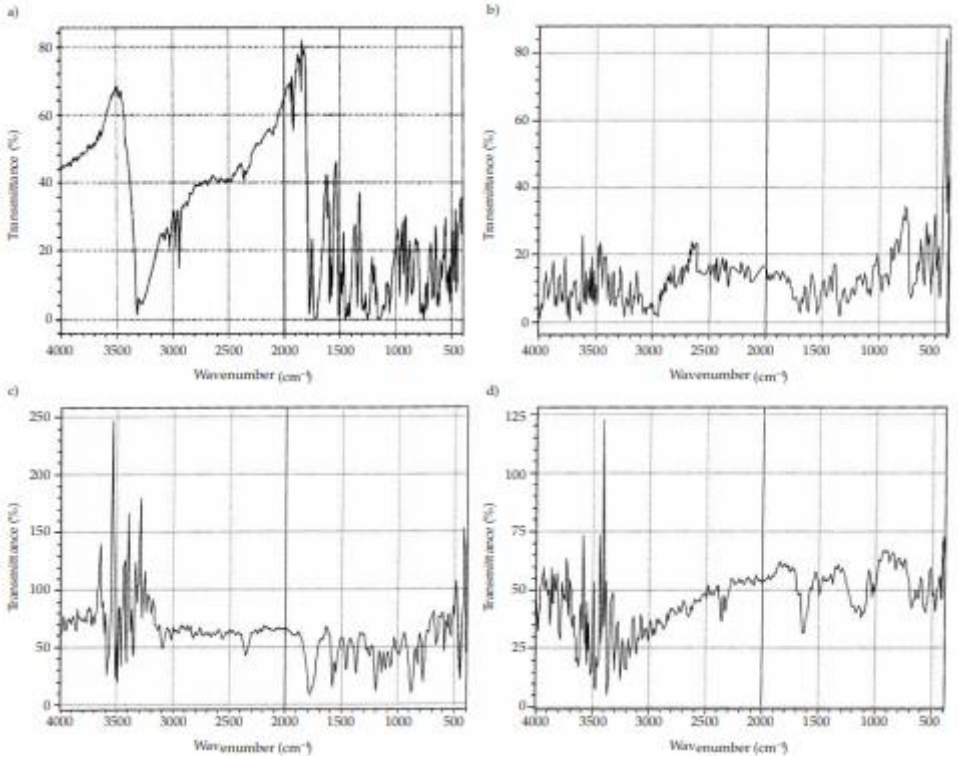

Figure. 3. FTIR spectra of: a) AF, b) AF-Carbopol formulation (AF2), c) AF-HPMC formulation (AF6), d) AF-PEG formulation (AF7).(24)

documented (22,23). For AF2, cumulative drug diffusion after 6 hours was 88.2 ± 2.4%, and cumulative drug permeation in the same period was 17.3 ± 0.8%. The carbopol gel base's pores and the absence of over-solubilization of the lipophilic drug in the aqueous vehicle may be responsible for the enhanced drug diffusion and permeation. These factors allow for relatively free drug diffusion to the vehicle and, consequently, faster release. (24).

IV. CONCLUSION

By employing chitosan, PVA, and PVP polymers in the solvent casting process, an aceclofenac-loaded transfersomal patch was created. When combined with hydrophilic polymers like PVA and PVP, chitosan in the patch formulation showed minimal swelling in water, but the patch's homogeneity, thickness, and tensile strength were still good. When it came to aceclofenac-loaded transfersomes, Tween 80 surfactant outperformed Span 80 in terms of maximum percentage drug release and smaller vesicles. Transfersomes were dispersed evenly over the patch.

Good physicochemical characteristics, such as thickness, weight variation, drug content, swelling index, folding endurance, and moisture content, were displayed by all produced formulations. The in-vitro release data demonstrated that the kinds and concentrations of polymers had an impact on the drug release from various patch formulations.

V. REFERENCES

[1] P. Anitha, S. Ramkanth, M. T. S. Saleem, K. Umasankari, B. P. Reddy, and M. Chetty. Preparation, in-vitro and in-vivo characterization of transdermal patch containing glibenclamide and atenolol: a combinational approach, Pak. J. Pharm. Sci. 24: 155-163 (2011).

[2] Dooley M, Spencer CM, Dunn CJ. Aceclofenac: a reappraisal of its use in the management of pain and rheumatic disease. Drugs. 2001;61(9):1351–1378. doi:10.2165/00003495-200161090-00012

[3] FitzGerald GA, & Patrono, C. The coxibs, selective inhibitors of cyclooxygenase-2. N Engl J Med. 2001;345(6):433-42.

[4] Laurent B, Annette M, Jean-Pierre D Daniel-Henri M. Effects of diclofenac, aceclofenac and meloxicam on the metabolism of proteoglycans and hyaluronan in osteoarthritic human cartilage. Br J Pharmacol 2000;131: 1413-1421.

[5] M. Verma, P. K. Gupta, V. B. Pokherkar, and A. P. Purohit. Development of transdermal drug dosage formulation for the anti-rheumatic ayurvedic medicinal plants, http://www.ayurvedam.com/pdf/deverhematic.pdf. Accessed on 21st March 2014.

[6] Gopal Rao M: "Formulation and evaluation of TDDS of "Propranolol HCL".IJPSR, 2001: 4(1); 44-49

[7] Shivani Kala, Divya Juyal. Preformulation and characterization studies of aceclofenac active ingredient. Pharma Innovation 2016; 5(25):110-19.

[8] Dandagi P, Gayatri D, Gadad A, Vaibhav B Formulation and Evaluation of Nanostructured Lipid Carrier (NLC) of Lornoxicam. Int J Pharm Pharm Sci 2014; 6(5): 73-7.

[9] Surti N, Parmar N, Bhadsavle S, Patel V. Transfersomes loaded transdermal drug delivery system of methotrexate for rheumatoid arthritis. World J. Pharm. Pharm. Sci. 2015; 4:58–68.

[10] Dandagi P, Gayatri D, Gadad A, Vaibhav B Formulation and Evaluation of Nanostructured Lipid Carrier (NLC) of Lornoxicam. Int J Pharm Pharm Sci 2014; 6(5): 73-7.

[11] Amnuaikit C, Ikeuchi I, Ogawara K, Higaki K, Kimura T. Skin permeation of propranolol from polymeric film containing terpene enhancers for transdermal use, Int. J. Pharm. 2005;289:167–178.

[12] Verma PRP, Iyer SS. Transdermal delivery of propranolol using mixed grades of Eudragit: design and in-vitro and in vivo evaluation. Drug Dev. Ind. Pharm. 2000;26: 471–476.

[13] Arora P, Mukherjee P. Design, development, physicochemical, and invitro and in-vivo evaluation of transdermal patches containing diclofenac diethylammonium salt. J Pharm Sci. 2002; 91: 2076-2089.

[14] Devi VK, Saisivam S, Maria GR, Deepti PU. Design and evaluation of matrix diffusion controlled transdermal patches of verapamil hydrochloride, Drug Dev. Ind. Pharm.2003; 29:495–503.

[15] Gupta R, Mukherjee B. Development and in-vitro evaluation of diltiazem hydrochloride transdermal patches based on povidone-ethyl cellulose matrices. Drug Dev Ind Pharm. 2003; 29:1 – 7

[16]] Julraht K, Keith AP, James AW. Development of a Transdermal Delivery Device for Melotoin In-vitro Study. Drug Dev. Ind. Pharm. 1995; 21:1377–1387.

[17] Ho HO, Chen LC, Lin HM, Sheu MT. Penetration Enhancement by Menthol Combined with a Solubilization Effect in a Solvent System. J. Control. Release, 1998; 51: 301–311.

[18] Yamune M, Williams A, Barry B. Terpenes Penetration Enhancers in Propylene Glycol/Water Co-solvent Systems: Effectiveness and Mechanism of Action. J. Pharm. Pharmacol. 1995; 47: 978–989.

[19] Williams, A., & Barry, B. Terpenes and the Lipid–Protein Partitioning Theory of Skin Penetration Enhancement. Pharm. Res. 1991; 8: 17–24.

[20] Patel HJ, Patel JS, Desai BG, Patel KD. Design and evaluation of amlodipine besilate transdermal patches containing film former. Int J Pharma Res Dev. 2009; 7: 1-12.

[21] Mutalik S, Udupa N. Glibenclamide transdermal patches: physicochemical, pharmacodynamic, and pharmacokinetic evaluations. J Pharm Sci. 2004; 93: 1577- 1594.

[22] J. Aukunuru, C. Bonepally and V. Guduri, Preparation, characterization and optimization of ibuprofen ointment intended for topical and systemic delivery, Trop. J. Pharm. Res. 6 (2007) 855–860

[23] Z. Gürol, S. Hekimo Lu, R. Demirdamar and M. Umnu, Percutaneous absorption of ketoprofen. I. In vitro release and percutaneous absorption of ketoprofen from different ointment bases, Pharm. Acta Helv. 71 (1996) 205–212; DOI: 10.1016/0031-6865(96)00011-8.

[24] V. V. Dhavse and P. D. Amin, Formulation and evaluation of topical bases of ketoprofen, East Pharm. 40 (1997) 133–135.