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RESEARCH ARTICLE

Formulation and Evaluation of *Amomum sublatum* Leaf Oil Incorporated Pluronic Matrix Type Transdermal Patches in Percutaneous Absorption

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Abstract

A matrix type of transdermal patch formulations having different types of hydrophilic, hydrophobic polymer components Diclofenac potassium (Diclofenac K) served as the model drug and penetration enhancer for topical delivery in this research, employing the USP7 apparatus for dissolution studies. Transdermal patches loaded with *Amomum sublatum* leaf volatile oil (utilized penetration enhancer) were formulated using the solvent evaporation technique, incorporating varying amounts of pluronic F-127 and ethyl cellulose based on 15 formulations designed by the Box Behnken model. The prepared patches underwent evaluation for various physicochemical parameters, including tensile toughness, moisture content, and moisture uptake. *In vitro* diffusion studies were conducted using the USP7 apparatus dedicated totransdermal drug release investigations. The optimized formulation, F10, exhibited a drug releaseof 82% over 24 hours in the *in vitro* diffusion study. All the transdermal matrix-type formulations demonstrated satisfactory results, indicating that the developed matrix-type transdermal patch, containing different polymers and the *A. sublatum* leaf volatile oil penetration enhancer, holds potential for transdermal delivery in the treatment of pain and swelling.

Keywords: *Amomum* Leaf Oil, Box Behnken Model, Pluronic, USP 7 Dissolution Apparatus

1. Introduction

The transdermal system, in particular, research and development and QC may not always use the same methodology or have the same goals while executing the drug release test. The USP apparatus 7 or Franz diffusion apparatus is commonly employed to provide a reliable prognostication of bioavailability for an NDA or bioequivalence for an ANDA. This utilization is crucial for anticipating the *in vivo* carrying out the therapeutic outcome[1]. The USP 7 reciprocating holder is used to determine the transdermal system's drug release rate for quality control[1]. The Diclofenac potassium patch is made for uninterrupted release of the drug after application to the skin. The USP Apparatus 7 was used to evaluate the *in vitro* release of the drug in the Diclofenac potassium transdermal patch. The most recent edition of the United States Pharmacopoeia describes the design of the USP 7 apparatus. The assembly be made up of a set of glass or another appropriately inert material with volumetric calibration, motor, and drive assembly are utilized to vertically reciprocate the arrangement and automatically shift it to another row of containers, if long for, several appropriate sample holders. For drug-release testing, choose conventional 50 ml. tubes or optional 100 and 300 ml. tubes to suit your unique requirements. The dissolution test apparatus of formulation having a transform of media decreases the volume and increases violent agitation, the Agilent reciprocating holding instrument (USP7) is perfect. Products like transdermal formulations, osmotic pumps, extended-release pills, capsules, and artery stents are frequently investigated. Agilent reciprocating holder USP 7 apparatus is excellent for testing the automatic dissolving of formulation which requires be change in media, a reduced volume or more violent agitation. Extensive-release capsules, tablets, transdermal formulations, osmotic pumps,

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and vascular stents are examples of typical products evaluated. For consistent batch-to-batch evaluation, the holders reciprocate through a 2 cm duration. Inside the water bath, the containers for the solution are of any reasonable size that allows the temperature to be kept constant. The design of the Agilent Technologies reciprocating apparatus 7 (holders) is the same as that defined in the USP. 7 sample tubes travel up to 7 rows automatically. The temperature is adjusted by a water bath, and the dissolution heater/circulator. To reduce evaporation, a loosely fitting plastic sheet is employed to cover the test tubes[2]. Plurenic F127 and ethyl cellulose are the hydrophilic and hydrophobic polymers used in the matrix-type transdermal patch formulation for the release of medicament in a controlled way.

Aromatic compounds known as essential oils are extracted from natural sources, specifically plants. When used as skin penetration enhancers, these oils partition into the stratum corneum and engage with various tissue components lowering the blockade function of the skin layer (stratum corneum) while causing no damage to the skin cells beneath. In this quest to examine the effectiveness of essential oils as permeation enhancers, *Amomum* oil, an essential oil was chosen to examine its ability to penetrate -boosting impact on transdermal patches using Diclofenac potassium as a model medication[3].

Amomum leaf oil was extracted from *A. sublatum*. of the family Zingiberaceae GC and GC-MS examination results show that it has 39 components, of which terpinene-4-ol (29.87%), eucalyptol (18.69%), β-phellandrene (7.97%), γ-terpinene (6.67%), p-cymene (6.20%), were found as significant constituents. Oxygenated monoterpenes were the predominant constituents in the essential oil of *A. subulatum*, accounting for 59.03% of the total oil content[4].

2. Materials and Methods

2.1 Determination of Essential Oil using the Clevenger Apparatus

The Clevenger device serves to find out the % of volatile oils in the oil-bearing component. About 500 gm of fresh leaf material into a sample flask and filled with water, maintaining a substance-to-water ratio of 1:8. Attached the flask was to the Clevenger apparatus and initiated the flow of water through the condenser by opening the water tap. Apply heat using a heating mantle and regulate it to allow oil-containing water vapors to enter the graded distillate receiving tube, while excess water returns to the flask. After 8 hours, cool the setups, extract water from the distillate collection tube and then transfer the oil to the rotary evaporator to remove any remaining water and use a desiccator to cool the flask. The volatile oil was stored tightly closed glass container for further use[5].

2.2 Preparation of the Transdermal Patches

The solvent evaporation process in cylindrical two sides opening glass moulds was taken. The matrix-type transdermal patches having Diclofenac K were made utilizing different ratios of polymers such as EC and plurenic F127. The bottom end of the glass mould was covered with an aluminium sheet, and the backing membrane was diffused by pouring 4% (w/v) PVA solution and drying in a hot air oven for 6 hours at 60ºC. Measure the weight of two polymers in the appropriate ratio, the drug Diclofenac potassium and then become a solution in ethanol. As a plasticizer, dibutyl phthalate was utilized. *Amomum* leaf oil was used as a penetration enhancer. A slow stir with a magnetic stirring was then added 20% w/w of the total weight of the polymers to the homogenous dispersion. The consistent dispersion was cast on the previously cast Polyvinyl alcohol backing membrane and air-dried at room temperature[6]. Formulations were removed from the mould. Then it was stored in an aluminium foil and kept inside the desiccators until further study (Table 1).

2.3 Evaluation of Transdermal Patches

2.3.1 Drug Polymer Interaction Study (FT-IR Spectroscopy)

An FT-IR spectroscopy investigation of Diclofenac potassium alone and in ethyl cellulose and plurenic F127, *Amomum* oil combination was also performed[7].

2.3.2 Folding Endurance

After the formulation of patches, the folding endurance study was manually determined. The formulations were turned under repeatedly in the same spot until broken, total number of folding of the patches in the same area repeatedly provides an appropriate number for this study.

Table 1. Different formulation chart

Formulation No	EC	PL	Penetration enhancer	Plasticizer (% w/w)	Ethanol (ml)	Drug (mg)
F1	250	444	3	30	10	50
F2	56	250	3	30	10	50
F3	56	56	4.5	30	10	50
F4	250	250	4.5	30	10	50
F5	56	444	4.5	30	10	50
F6	444	250	6	30	10	50
F7	250	56	3	30	10	50
F8	250	444	6	30	10	50
F9	444	250	3	30	10	50
F10	444	56	4.5	30	10	50
F11	56	250	6	30	10	50
F12	250	250	4.5	30	10	50
F13	250	56	6	30	10	50
F14	250	250	4.5	30	10	50
F15	444	444	4.5	30	10	50

2.3.3 Weight Variation Study

The experiment was conducted on a formulated patch made from a blend of two polymers in a casting solution. The average weight of the film, along with its deviation from the mean, was calculated and documented. The mass of individual patches was measured using a digital balance with a precision of 0.001 mg.

2.3.4 Tensile Strength

The modified spring balancing method was used to determine the results of this investigation. From the centre of the circular patch, 26cm long rectangular strips of transdermal patches were cut out. The patches were fastened to a hook on the spring balance at one end and a progressively expanded load was applied to the other. The measurement now the patch pulled apart from the centre was recorded and then divided by the transdermal strip's area to determine the tensile strength in Newton/cm^2.

2.3.5 Water Vapour Transmission Rate

The film was attached to a glass vial using adhesive, and the vial contained calcium chloride (3g), serving as a drying agent or desiccant. Subsequently, the vials were kept in a desiccator containing a saturated KCl solution. At regular intervals over 72 hours, the vial was taken out and weighed. The experiment was conducted three times; the average results were computed and documented[8].

$$W.\ V.\ T. = WL/S$$

Where, W = water vapour transmitted in gm, L = thickness in cm, S = exposed surface area in cm^2.

2.3.6 Moisture Content and Moisture Uptake

The formulation was labelled, weighed individually, stored at room temperature placed in a vacuum desiccator having Diphosphorus pentoxide for 24 hours. Every patch was weighed individually until a consistent and stable weight was obtained. The moisture content percentages were computed by subtracting the initial weights from the final weights about the final weight values.

$$\%\ \text{Moisture content} = (A\text{-}B\ /\ B) \times 100$$

Where, A = Initial weight and B = Final weight.

The moisture uptake test was conducted as follows: The formulations were weighed and then dried to a consistent weight at room temperature in a vacuum

desiccator (24 hours), left unprotected to 84% relative humidity (saturated potassium chloride)[9].

$$\% \text{ of moisture uptake} = (Y\text{-}X/X) \times 100$$

Where, X = initial weight, Y = final weight.

2.3.7 Uniformity of Thickness

In this experiment micrometer (Mitutoyo) was used with the smallest increment (0-0.1mm). Measurements were held at five different locations on each patch, and the mean, along with the standard deviation, was calculated from these five values.

2.3.8 Percent Flatness Study

Formulation strips from each transdermal patch were cut out, with one taken from the middle of the formulation and two from each side. Next, the length (strip) was determined, and the discrepancy in length due to rough flatness was found by the percentage of squeezing, keeping in mind that if 0% constriction happened, that is equivalent to 100% flatness.

$$\% \text{ of constriction} = L1\text{-}L2 / L2$$

Where, the L1 = Initial length of each strip and L2 = Final length of each strip.

2.3.9 Drug Content Study

The drug content study was conducted in the following manner, 1 – 2 cm cut of transdermal patch pieces were taken separately, crushed, and took hold of a volumetric flask (100 ml) which contained phosphate buffer (pH 7.4). A magnetic bead was used to agitate the liquid mixture for five hours. The patch liquids mixture was filtered using. The filtrate obtained through Whatman filter paper was studied for drug content using spectrophotometry at 276nm, comparing it against a reference solution composed of placebo films without any drug[10].

2.4 *In Vitro* Study

This study was brought about by utilising the USP -7 dissolution apparatus according to the previous limitation with some modification the vessel volume capacity of the reciprocating apparatus is 300 mL. The temperature was maintained at 37 ± 0.3 °C. The reciprocating discs have a 2.5 cm stroke depth. A 45-dips-per-minute dipping (or stroking) rate was maintained. There were 7 patches used in each test. Each patch holder contains all additional dissolution circumstances. Place the vessel inside the water bath. The vessels contain 7.4 phosphate buffer. The vessel was placed in the water bath. The patch was kept on the upper portion of the dialysis membrane, and both are placed properly on the open side of the reciprocating cylinder then the cap was closed properly to keep it perfectly in its position now the cylinder was on the end of the agitator rod screwed. After switching on the dissolution apparatus, the reciprocating cylinder came down inside the vessel containing phosphate buffer (7.4). The dialysis membrane was in contact with the buffer solution so that drugs from the patch could be released through the membrane to the buffer solution. Now the sample was collected (every one hour) for 24 hours. To reduce evaporation after the medium was changed and while the drug release test was being conducted, the vessels were covered. Before testing, the transdermal system's liner was taken off. The test tube solutions were set aside for spectrophotometric analysis[11].

3. Results and Discussion

According to Table 2 the patches made with various amounts of EC- PL had a percent moisture content ranging from 1.78 to 4.80 % w/w. This result showed that when the concentration of hydrophilic polymer in various formulations increased, so did their moisture content. F10 has low moisture content since it contains the most EC. However, the formulations' modest moisture level aids in keeping the material stable and prevents it from drying out completely and becoming brittle. The percentage moisture uptake of the patches made with various EC and PL proportions ranged from 2.54 to 6.92 % (Table 3). The maximum moisture uptake is found in F5, which has the highest concentration of PL and lower amount of EC, however, this is reversed in F10. The patches are safeguarded from microbiological contamination and bulkiness by concurrently reduced moisture uptake[12]. Uniformity of thickness study micrometres with the least count of 0 - 0.01 mm was utilized to measure the homogeneity of the film's thickness. The film's thickness was estimated at 5 distinct locations, and the average value was computed and the standard error value of the mean[13].

Table 2. Results of formulated patches

Formulation	Folding Endurance	Weight variation	Tensile strength	Water vapour transmission (gm/cm/h)	Moisture content
F1	78 ± 1.32	0.21	220.10 ± 0.02	$1.65624 \times 10^{-4} \pm 0.02$	3.80 ± 0.002
F2	79 ± 1.09	0.20	237.39 ± 0.02	$1.53121 \times 10^{-4} \pm 0.03$	3.40 ± 0.003
F3	78 ± 1.32	0.20	227.36 ± 0.01	$1.11259 \times 10^{-4} \pm 0.02$	1.80 ± 0.002
F4	78 ± 1.31	0.20	225.83 ± 0.02	$1.43121 \times 10^{-4} \pm 0.04$	3.42 ± 0.002
F5	88 ± 1.31	0.21	209.56 ± 0.01	$1.86157 \times 10^{-4} \pm 0.04$	4.01 ± 0.002
F6	92 ± 1.13	0.21	251.23 ± 0.02	$1.10012 \times 10^{-4} \pm 0.02$	3.89 ± 0.002
F7	85 ± 1.02	0.20	240.19 ± 0.01	$1.10234 \times 10^{-4} \pm 0.03$	1.80 ± 0.003
F8	78 ± 1.40	0.20	216.12 ± 0.02	$1.81012 \times 10^{-2} \pm 0.02$	3.82 ± 0.002
F9	90 ± 1.31	0.20	249.57 ± 0.03	$1.76693 \times 10^{-4} \pm 0.02$	3.72 ± 0.001
F10	90 ± 1.09	0.20	252.31 ± 0.03	$1.06029 \times 10^{-4} \pm 0.02$	1.78 ± 0.001
F11	79 ± 1.05	0.20	224.83 ± 0.02	$1.59132 \times 10^{-4} \pm 0.02$	3.69 ± 0.002
F12	78 ± 1.32	0.20	224.83 ± 0.02	$1.43122 \times 10^{-4} \pm 0.02$	2.42 ± 0.002
F13	85 ± 1.02	0.20	242.19 ± 0.01	$1.10312 \times 10^{-4} \pm 0.02$	2.20 ± 0.002
F14	78 ± 1.32	0.21	224.83 ± 0.02	$1.43119 \times 10^{-4} \pm 0.02$	3.41 ± 0.002
F15	94 ± 1.02	0.20	229.31 ± 0.01	$1.55628 \times 10^{-4} \pm 0.02$	4.80 ± 0.002

Mean value ±SD (n=3)

According to the flatness study's findings (Table 3), none of the formulations had any dissimilarity in the lengths of the strips before and after their cuts designated that they were more than 99% flat. It suggests that the films have no constriction, which would allow them to keep a flat surface when used to the human skin, allowing for closer exposure and improved medication penetration[14]. After the drug content study, it was observed that more than 97% of the drugs were present in the prepared patches, it was observed. The range of drug concentration in various formulations made with EC-PL was observed to be between 97.00 to 99.2 %. Adequate drug content was observed in all formulations[15]. In the *in-vitro* skin permeation experiment of the formulated patches, drug release data were treated to fit with numerous kinetic models, including zero order, first order, Higuchi model, and Korsemeyer Peppas release kinetics. A comparative plot of cumulative % drug release per cm^2 against the square root of time was generated for patches containing EC-PL (Figure 1). The first-order kinetics of EC-PL patches were expressed by plotting Log ARA against time (Table 4). Additionally, the diffusion kinetics of the drug release study, represented by the Korsemeyer- Peppas model, were illustrated by plotting log Mt/M∞ against log time for EC-PL (Table 4)[16]. The degrees of regression ment for all kinetic models were computed by incorporating *in vitro* permeation results from different transdermal patch formulations through a dialysis membrane[17]. The drug release study indicated a burst release for all patch formulations.

The folding endurance numbers of all patches were deemed satisfactory, signifying that the patch formulated with dibutyl phthalate (plasticizer) exhibited optimal flexibility (Figures 2 and 3). The weight-prepared patches ranged between 0.20 to 0.21 gm. All the patches showed uniformity in weight which is indicative of the efficiency of the solvent-casting process.

The drug was subjected to an FT-IR analysis to identify the compounds. The drug was carefully put over the sample holder for scanning. Figure 4 displays the FT-IR spectrum for a pure drug and drug-polymer. Drug-excipient interactions are important for the formulation, there is no interaction. Figure 4 depicts the infrared (IR) spectra of the physical mixture of DI-K with excipients of Pluronic and Ethyl cellulose formulation (B). The Infrared absorption spectroscopy (IR) of Diclofeanac-K

Table 3. Results of formulated patches

Formulation code	Moisture uptake	Uniformity thickness	% Flatness	Drug content
F1	6.54 ± 0.001	109 ± 1.2	99.4 ± 0.003	97.6
F2	5.60 ± 0.001	110 ± 1.2	99.6 ± 0.002	99.2
F3	2.84 ± 0.001	113 ± 1.3	99.4 ± 0.003	98.6
F4	5.82 ± 0.002	109 ± 0.8	99.2 ± 0.005	98.1
F5	6.92 ± 0.002	109 ± 1.4	99.2 ± 0.003	97.00
F6	5.71 ± 0.001	113 ± 1.3	99.9 ± 0.002	98.2
F7	2.81 ± 0.003	109 ± 1.3	99.8 ± 0.003	98.93
F8	6.54 ± 0.002	110 ± 1.1	99.6 ± 0.004	98.93
F9	3.91 ± 0.002	110 ± 0.9	99.8 ± 0.002	97.33
F10	2.54 ± 0.002	108 ± 0.8	99.2 ± 0.005	99.26
F11	4.92 ± 0.001	102 ± 0.8	99.2 ± 0.005	99.51
F12	5.81 ± 0.002	109 ± 0.8	99.2 ± 0.005	98.65
F13	2.80 ± 0.002	110 ± 0.8	99.0 ± 0.005	99.01
F14	5.82 ± 0.001	109 ± 0.8	99.2 ± 0.005	99.47
F15	6.41 ± 0.002	109 ± 0.8	99.1 ± 0.005	98.07

Value represent mean±SD (n = 3)

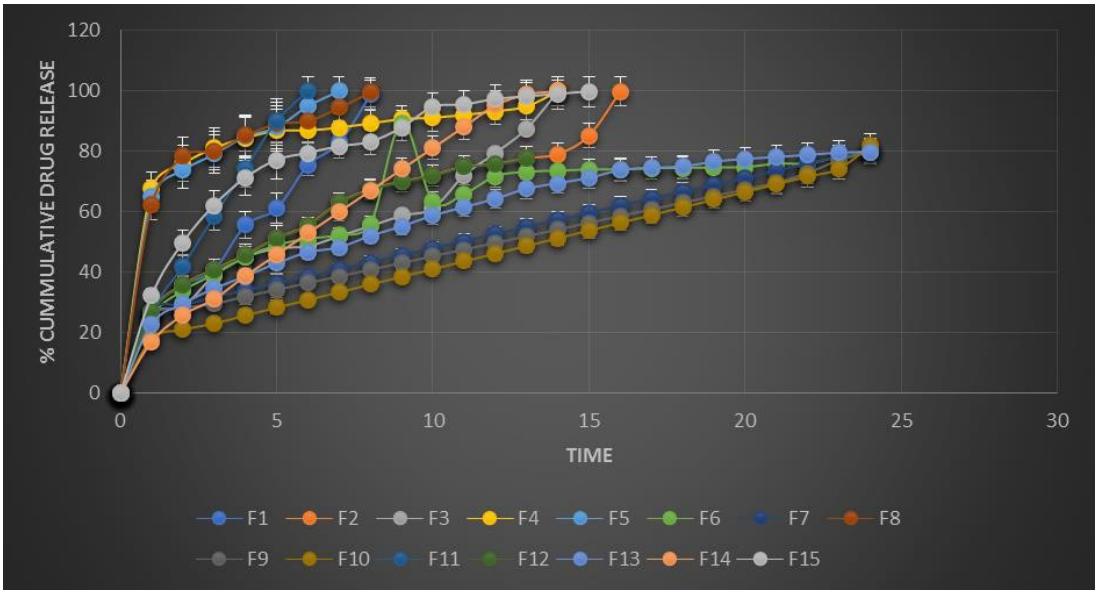

Figure 1. Graphical representation of drug release.

Table 4. Pharmacokinetic data of the formulations

	R^2														
Kinetics	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**
Zero	0.9759	0.8985	0.8324	0.5135	0.6847	0.8187	0.7153	0.6307	0.7174	0.8358	0.986	0.8985	0.8565	0.9804	0.8179
First	0.689	0.97	0.86	0.83	0.931	0.62	0.96	0.91	0.95	0.94	0.9	0.97	0.9	0.78	0.96
Higu	7970	8792	9093	4961	8442	7694	9977	8337	4386	8527	2631	8818	7697	7397	0582
chi	0.9492	0.9701	0.9633	0.9315	0.9913	0.8032	0.9702	0.9486	0.96	0.9623	0.9906	0.9893	0.9864	0.9821	0.9404
Kosmeyer Peppas	0.9551	0.9641	0.9319	0.9672	0.9304	0.9049	0.9982	0.8107	0.9314	0.9533	0.9141	0.9644	0.9943	0.9923	0.8831

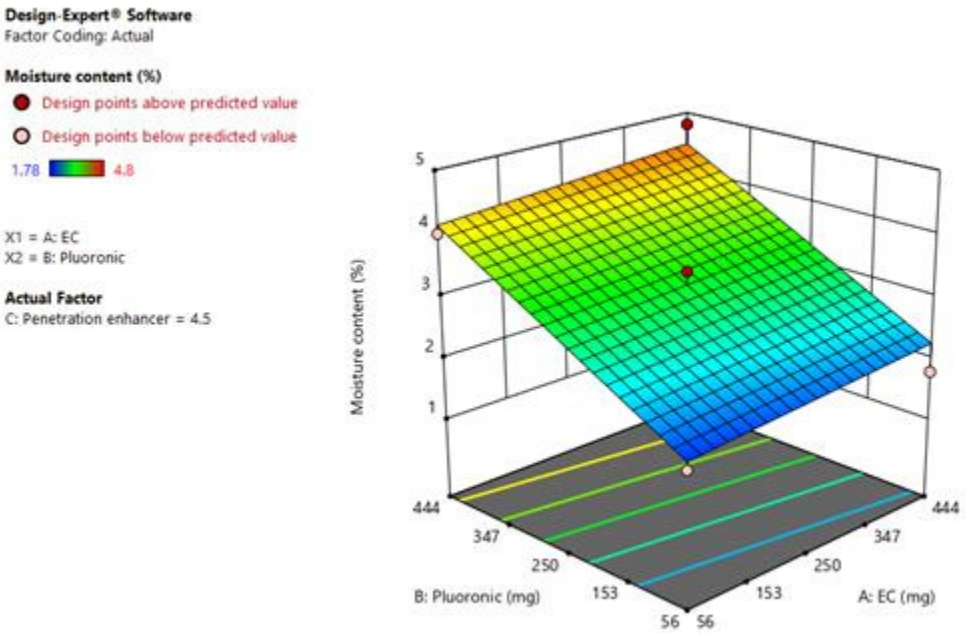

Figure 2. 3D response surface plot showing the influence of polymer concentration, plasticizer concentration and permeation enhancer concentration on moisture content.

revealed sharp bands at 3439.66, 3377.68, and 882.90 cm^{-1}, which were caused by the stretching of the vibration bands of OH, N-H, and C-Cl, respectively (Figure 4). The sharp peak of the IR spectra is the drug and polymer mixture did not change, as seen in the image, indicating that there were no physical interactions due to the bond formation between the drug and polymer.

The tensile strength of patches comprising EC and PL ranged from 209.50 gm/cm2 to 252.31 gm/cm^2. An observed trend revealed that polymer concentration increases PL arises in a gradual decrease in the tensile strength of the formulation. The Water Vapour Transmission Rates (WVTR) for EC-PL patches ranged from 1.05259 x 10^{-4} to 1.86157 x 10^{-4}, indicating permeability to water. An increase in the hydrophilic polymer concentration was associated with elevated WVRT, and F5 exhibited the least water vapour transmission, possibly due to its lower hydrophilic polymer content. The % moisture content of formulated patches prepared with different EC-PL ratios ranged from 1.78% to 4.80%. The results indicated that an increase in the hydrophilic polymer concentration led to a corresponding increase in moisture content. F10, with the highest EC content, demonstrated lower moisture content differentiating from F5. However, the modest moisture content in formulations helps maintain

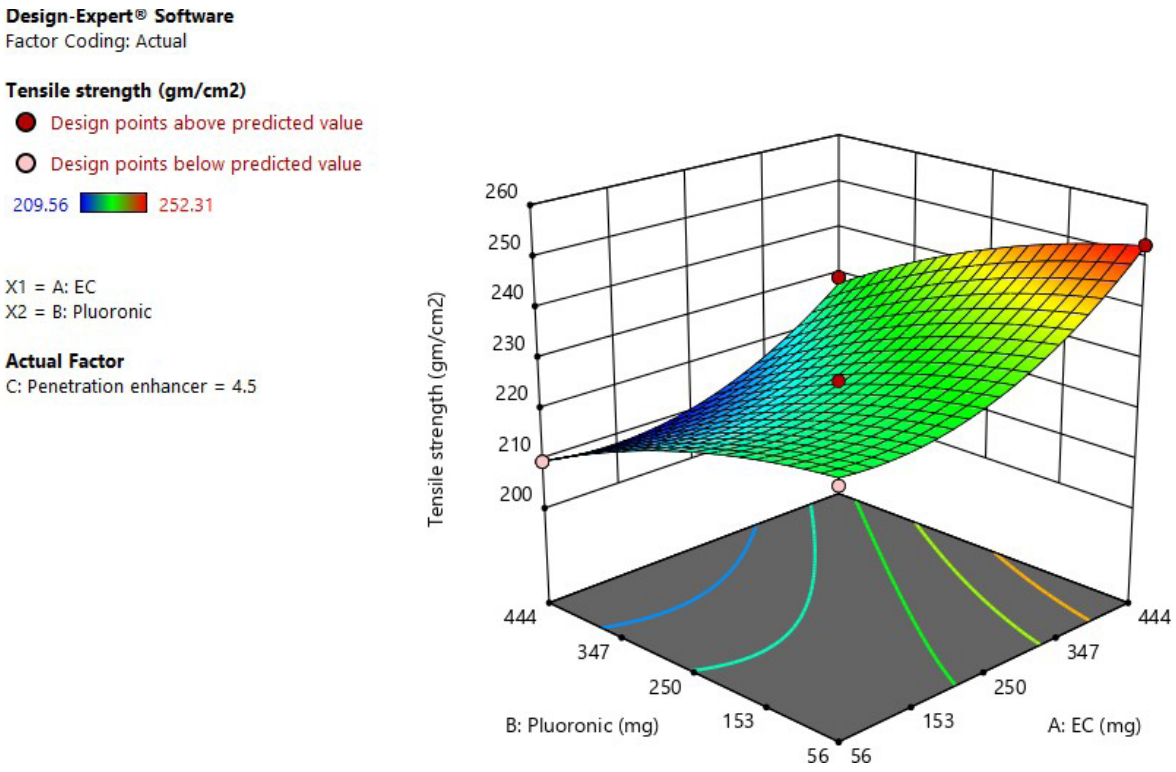

Figure 3. 3D response surface plot showing the influence of polymer concentration, plasticizer concentration and permeation enhancer concentration on tensile strength.

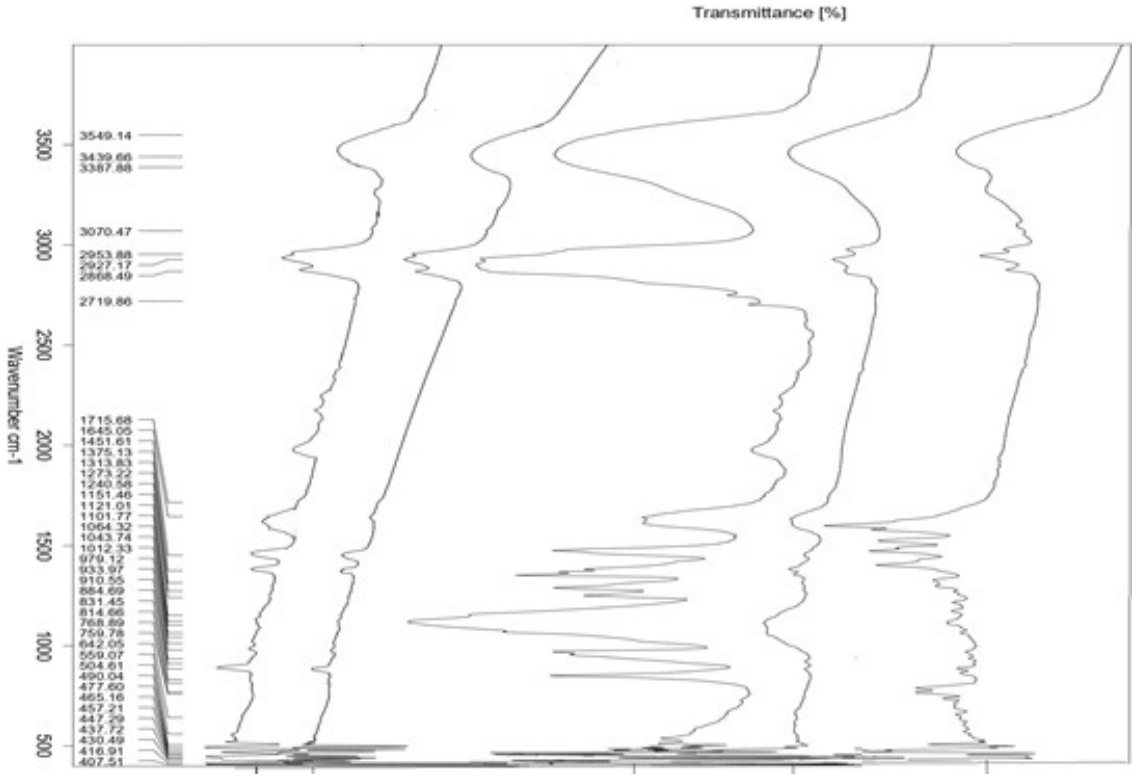

Figure 4. FT-IR data for formulation with active drug and excipients.

Table 5. Fit Summary: ANOVA for quadratic model

SL.NO	Factor 1	Factor 2	Factor 3	Response 1	Response 2
Run	A: EC (mg)	B: Pluoronic (mg)	C: Penetration enhancer (ml)	Tensile strength (gm/cm^2)	Moisture content (%)
1	250	444	3	220.1	3.8
2	56	250	3	237.39	3.4
3	56	56	4.5	227.36	1.8
4	250	250	4.5	225.83	3.42
5	56	444	4.5	209.56	4.01
6	444	250	6	251.23	3.89
7	250	56	3	240.19	1.8
8	250	444	6	216.12	3.82
9	444	250	3	249.57	3.72
10	444	56	4.5	252.31	1.78
11	56	250	6	224.83	3.69
12	250	250	4.5	224.83	2.42
13	250	56	6	242.19	2.2
14	250	250	4.5	224.83	3.41
15	444	444	4.5	229.31	4.8

Table 6. Response for tensile strength: ANOVA for linear model

Source	Sum of Squares	df	Mean Square	F-value	p-value
Model	2389.21	9	265.47	70.28	< 0.0001 significant
A-EC	866.94	1	866.94	229.53	< 0.0001
B-Pluoronic	945.26	1	945.26	250.26	< 0.0001
AC	50.55	1	50.55	13.38	0.0146
A^2	223.97	1	223.97	59.30	0.0006
B^2	40.62	1	40.62	10.75	0.0220
C^2	224.83	1	224.83	59.53	0.0006
Residual	18.89	5	3.78		
Lack of Fit	18.22	3	6.07	18.22	0.0525 not significant
Pure Error	0.6667	2	0.3333		
Cor Total	2408.10	14			

Factor coding is coded; the Sum of squares is Type III – Partial; Fit Statistics

Table 7. Response for moisture content

Source	Sum of Squares	df	Mean Square	F-value	p-value
Model	10.10	3	3.37	14.64	0.0004 significant
B-Pluoronic	9.79	1	9.79	42.58	< 0.0001
Residual	2.53	11	0.2299		
Lack of Fit	1.87	9	0.2077	0.6293	0.7436 not significant
Pure Error	0.6601	2	0.3300		
Cor Total	12.62	14			

Factor coding is coded; the Sum of squares is Type III – Partial

material stability, preventing complete dryness and brittleness. The percentage moisture uptake for patches with various EC and PL proportions ranged from 2.54% to 6.92%. Higher moisture uptake was observed with increased hydrophilic polymer concentration, with F5, containing the highest PL amount, exhibiting the highest moisture uptake. Simultaneously, low moisture uptake protects patches from microbial contamination and excessive bulkiness. The patch thickness was determined to be between 102 and 113 microns. A lower value of Standard Deviation (SD) of the formulation thickness confirmed consistency in patches prepared through the solvent evaporation method. Flatness experiment results indicated more than 99% flatness for all formulations, suggesting no constriction in the films and ensuring a smooth surface upon application to the skin for better drug permeation. Scanning electron microscope analysis using JEOL, JSM-6360, at 7 Kv, revealed the surface morphologies of the films, with patch pieces gold-coated for electrical conductivity before the study.

Model F-value of 14.64 suggests the significance of the model (Table 7). There is only a 0.04% probability that an F-value of this magnitude could appear from random disparity. P-values under 0.0500, with term B is significant. Values exceeding 0.1000 indicate a lack of significance in model terms. If a lot of model terms are insignificant, the model depletion may be intense. A fit F-value of 0.63 indicates a lack of fit which is not significant. The value of 74.36% probability be need of the size could be a random variation. A non-significant is required to fit, it is desirable as it implies a good fit for the model.

The divine R^2 value standing at 0.6260 ranges are adjusted R^2 of 0.7450, a difference of less than 0.2. With a ratio of 10.238, your signal is deemed adequate. This model is suitable for exploring the design space[12].

The F-value of 70.28 shows the significance of the model (Tables 5 and 6). P-values below 0.0500 mark the significance of model terms, with A, B, AC, A^2, B^2, and C^2 being significant in this case. Remarkable values of 0.1 suggest inconsequentiality in the model. If there are numerous inconsequential model terms essential for pecking order), a lower value may increase its presentation. The lack of fit F-value of 18.22 value suggested that a 5.25% chance that such a large lack of fit F-value could be due to noise. Lack of fit is unacceptable, as we focus on the model to fit effectively. This relatively low probability (<10%) raises concerns.

The divine R^2, at 0.8783, aligns fitting well calibrated, R^2 of 0.9780, the difference is lower than 0.2. Assessing the signal-to-noise ratio suggests the ratio increasing by 4, and our model's ratio of 27.385 surpasses this threshold, indicating a satisfactory signal.

Representation of F-value of 14.64 indicates the model is significant that values 0.04% possibility of F-value is getting due to noise. The P-value is below 0.0500. It signifies the significance of model terms; the term B is considered as significant. Reverse, values distinct 0.1000 indicates inconsequentiality of model terms, and addressing many such terms could enhance the model. The deficiency of the fit F-value, at 0.63, implies non-significance, with a 74.36% chance of this F-value arising due to noise. A non-remarkable need for fit is desirable, indicating the best fit for this model.

The forecast R^2, registering at 0.6260, aligns reasonably with the modified R^2 of 0.7450, exhibiting a differentiation is less than 0.2. A ratio surpassing 4 is thinking about favourable. With a ratio of 10.238, this

model presents an ample signal, indicating its suitability for navigating the design space.

The folding endurance experiment was manually measured; films could be folded without cracking for 78 to 94 folds before the fold was complete. All the patches show good flexibility and strength. (Table 2) The weight variation of the patch's area was meticulously divided into several pieces and then weighed in a digital balance. It was discovered that the values fell within the permitted range and the weight ranged from (0.20g to 0.21 g). Therefore, this uniformity in weight ensures that the method is repeatable and that the drug will be distributed uniformly (Table 2). The tensile strength of the patches' strength ranged from 209.50 gm/cm^2 to 252.31 gm/cm^2, when the concentration of hydrophilic polymer (PL) was increased, the patches' tensile strength steadily decreased. Water vapour transmission: In the instance of EC the patches' water vapour transmissions ranged from 1.05259 x10^{-4} to 1.86157 X 10^{-4}, indicating that they were permeable to water. It was noticed that the WVRT rose with the addition of hydrophilic polymer and that TEP10 had the lowest water vapour transmission profiles, possibly because of the absence of hydrophilic polymer.

4. Conclusion

The Diclofenac potassium Transdermal patch of using plurenic F127 and ethyl cellulose as rate- controlling polymers and *A. sublatum* oil as a natural penetration enhancer were prepared and optimized using central composite statistical design. A patch containing a higher concentration of polymer ethyl cellulose and plurenic F127 of formulation F10 showed drug releases to 82%, respectively, and up to 24 h of polymers showed maximum values of the drug release. *In vitro,* work concluded that the drug release from the patch containing *Amomum* oil as a penetration enhancer gives better results up to 24h. Hence present study demonstrates that plurenic F127 polymer and natural permeation enhancer with drug may be successfully employed as a drug carrier and permeation enhancer for controlled and desirable drug delivery applications with additional health benefits.

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