Advances in Bioresearch
Adv. Biores., Vol 13 (3) May 2022: 18-25

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.13.3.1825

Advances in Bioresearch

ORIGINAL ARTICLE

Formulation and Development of Herbal Transdermal Patch of *Curcuma Longa L.* and *Vitus negundo L.* with *In-Vitro* Evaluation

Poojashree Verma[1]*, Niharika Gokhale[2]
[1,2]Oriental College of Pharmacy and Research, Oriental University, Indore, Madhya Pradesh 452003

ABSTRACT

The main aim of this present study is to formulate and develop nathropathic transdermal path of Curcuma longa L. (Curcumin) and Vitax negundo L.(Casticin) for the anti-inflamatory, anti-oxidant, hormal imbalance, Antidibetic, and Immunomudulator activity. As both the drugs contains high amount of flavanoids, iridoide glycosides, alkaloids, and essential oils. The transderma patches of both the drugs were prepared by using three different polymers like hydroxypropyl methylcellulose, ethylcellulose and polyvinylpyrrolidone by solvent casting method. The prepared transdermal patches were evaluated for their physicochemical characteristics such as physical appearance, weight uniformity, thickness, folding endurance, moisture content, surface pH, tensile strength. The in-vitro diffusion study was carried out using rat membrane. These parameters indicate the successful release of drug from the fabricated patch. With the overall observation it was concluded that the fabrication of transdermal patch is successfully worked and subjected to diffusion study. Ethanol and Water is used as a solvent and samples are collected for 24h and absorbance is measured by using UV spectrophotometer at 256 nm and 424. It showed the successful release of drug from the fabricatd patch.

Keywords: *Transdermal patch; in-vitro; Curcuma longa L.; Vitax negundo L.; Anti-oxidant*

Received 04.03.2022 Revised 22.04.2022 Accepted 14.05.2022

How to cite this article:
P Verma, N Gokhale. Formulation and Development of Herbal Transdermal Patch of *Curcuma Longa L.* and *Vitus Negundo L.* with *In-Vitro* Evaluation. Adv. Biores. Vol 13 [3] May 2022. 18-25

INTRODUCTION

Transdermal drug delivery system (TDDS) is really a extensively accepted ways drug delivery, and transdermal spots tend to be developed to deal with various conditions. TDDS are extended release quantity forms that may give you a steady systemic drug concentration and prevent pass metabolic process that is initially. They may be able even avoid intestinal problems associated with drugs and reasonable absorption.[1,2] Lots of transdermal patches have been produced by different detectives to realize manage launch for longer duration, as an example, anti-oxidant, anti-inflammatory, contraceptive path containing estrogen, and antirheumatic area. Hence, they might change the need for multiple and dosing that is regular. Local drug launch would offer added advantage as being a reduced dose of the medicine at the target site will probably be needed in place of higher amounts needed by entire body management. This will provide optimum efficacy with minimum negative effects. Hence, turning to safe, efficient and time-tested ayurvedic medication that is herbal will probably be preferable choice and prime issue this is certainly regarding of research. The winds of improvement in the dru scenario are blowing forcefully around the globe. The introduction of brand new technologies provides unique opportunities to take advantage of book techniques in medicine delivery. A move from standard medication distribution to novel medicine delivery is seen a move from conventional drug delivery suffers from various disadvantages, for instance, pulsating blood levels, frequent dosing, patient noncompliance, more complications, whereas novel drug distribution system is system that is tailor-made. The rate managed drug delivery system resut in: constant and output that is continuous, maintenance of constant plasma medication amount, lesser part impacts. [3] Phytochemicals such as alkaloids, flavonoids, phenolic compounds, glycosides etc. play a significant role in pharmacological properties of plants *Vitex negundo L.* belongs to the family Verbenanceae. It is used in the treatment of asthma, cancer, jaundice, liver disorders, wounds, rheumatism, joint pains, antiallergic, extract of nirgudi has been shown various

biological activities such as antibacterial, antifeedant, antifungal, insecticidal, antioxidant activity etc. parts of nirgundi like leaves, roots, bark, fruits, flowers, and seeds are used for medicinal purpose. Curcumine is a constituent extracted from *Curcuma longa* L. belonging to the family Zingiberacae. Topical application of turmeric extract has limitations due to its low absorption of active ingredients. The potential use of topical turmeric extract in the form of nanoparticles for inflammatory skin diseases. It contains curcuminoid, a nonenzymatic antioxidant polyphenol group. Curcuminoid consists of diferuloylmethane (curcumin/CUR), demethoxycurcumin, bis-demethoxycurcumin, and cyclic curcumin. It has proven the medicinal properties like anti-infflamtory, anti-oxidant, anti-microbial, immunostimulant, hepatoprotective, and antimutagenic. [4]

According to the literature survey the anti-oxidant, anti-inflammatory, hepatoprotactive, antimutagenic, anti-daibetic and for hormonal imbalance the formulation of cucumin like tablet, capsule, nanoparticles, microemulsion, and transdermal patch is reported. For vitex anti-fungal, anti-bacetrial, anti-oxidant, insecticidal, antifeedant, estrogen enhancing ability, menstruation, male libido and rejunivative activity the formulation like capsule, tablet, nanoemulion, and drop is reported. Till now no formulation is reported in the combination of cucumin and vitex. Hence, the main objective of the present research work is to formulate and evaluate the transdermal patch of curcumin and vitex for the treatment of women hormonal disorder.[10]As both the drugs have best combination for the treatment of inflammation, menstruation problem, polycystic ovarian syndrome (PCOS).

MATERIAL AND METHODS

Materials

Curcumin and Turmeric extract were obtained as gift sample from Amsar Pvt. Ltd. form Indore, Hydroxypropyl methyl cellulose (HPMC) and polyvinylpyrolidine, Oleic acid were obtained from Oriental University, Indore. Polyethylene glycol 400 (PEG 400), Ethyl Cellulose and Ethanol were obtained from SD fine chemicals.

Methods

Preformulation Studies

It is one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the drug, which included solubility and compatibility studies.

Solubility Studies

Curcumin and Casticin was physically examined for colour, odour, taste etc. Solubility of curcumin was determined in water, phosphate buffer 7.4, ethanol, DMSO, tetra hydro furan, etc.

Preparation of standard calibration curve for Turmeric (Curcumin) and *Vitex Nigundo* (Casticin)

Primary stock solution of curcumin (100 mg) was accurately weighed and dissolved in 30 ml ethanol and diluted to 100 ml with distilled water. Secondary stock solution 1 ml of primary solution was diluted to 100 ml distilled water to get a concentration of 10 µg /ml. Aliquots of 1 ml, 2 ml, 4 ml, 6 ml, 8 ml, and 10 ml were pipette out from 10µg/ml and diluted to 10 ml with distilled water to get a 1µg, 2µg, 4µg, 6µg, 8µg, and 10µg concentration of curcumin. Standard graph was plotted by keeping the known concentration on X-axis and obtained absorbance on Y-axis. Casticin stock solution and aliquots were prepared same as that of Curcumin.

FT-IR of Turmeric (Curcumin) and *Vitex Nigundo* (Casticin)

The FTIR of turmeric (Curcumin) and *Vitex Nigundo* (Casticin) and different inclusion complexes were analysed using the FT-IR spectrophotometer (Shimadzu) at a broad range of 4000-400 cm^{-1}. The sample was kept at the diamond substrate, and the pressure was applied with a compression bar. The software scan the graph. The characteristic peak were analysed compared with pure and the complex mixture to check the interaction between them.

DSC of Turmeric (Curcumin) and *Vitex Nigundo* (Casticin)

The thermal analysis of Turmeric (Curcumin) and Vitex Nigundo (Casticin) and the inclusion complex was studied using Mettler Toledo's DSC. An empty aluminium plate was used as reference. Around 5mg of each test sample were pursed in an aluminium plate, and thermograms were found under a nitrogen gas flow of 10ml/min. The thermal analysis was conducted at a heating rate of 10 °C/min from 30-300°C.

Formulation Studies

Optimization and Formulation of Transdermal Patch

Preparation of matrix patch of Turmeric (Curcumin) and Vitex (Casticin)transdermal patches were fabricated by the solvent Casting technique utilizing different ratios of HPMC, ethyl cellulose, and PVP respectively. In the process of formulation, initially, the polymer (HPMC) was taken in a beaker with a solvent ethanol: water (6:4) and was allow to solublize completely for a duration of 30 min. Subsequently, with continuously stirring, ethyl cellulose was added. Afterward, the plasticizer (Dibutylphthalate) and

permeation enhancer (Oleic acid) were added and mixed uniformly for the five minutes. Finally, both the drug was incorporated with continuous stirring to mix well. The resultant homogenous dispersion was spread over a petriplate. Later, the controlled solvent evaporation was achieved by heating and the fabricated dried film was cut into 10cm^2 dimension. The prepared films were wrapped in aluminum foil and stored in the desiccator for further study.

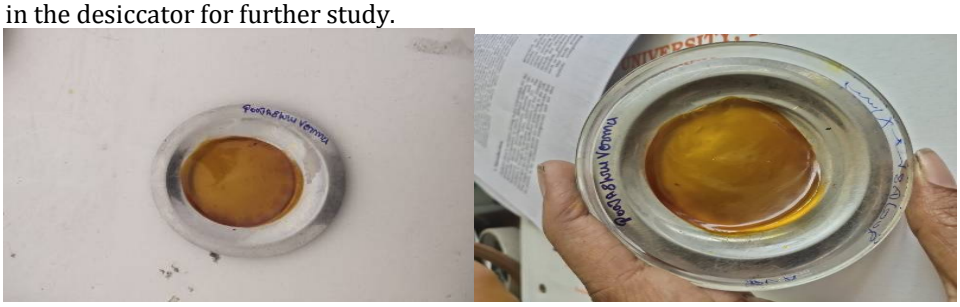

Figure 1: Transdermal patch

Table 1: Formulation of Transdermal Patch

S. No.	Formulation Code	Curcumin: Casticin	HPMC	Ethyl Cellulose	PVP	Ethanol: Water
1	F1	200mg: 50mg	100	100	50	6:4
2	F2	200mg: 50mg	100	200	50	6:4
3	F3	200mg: 50mg	100	300	50	6:4
4	F4	200mg: 50mg	200	100	50	6:4
5	F5	200mg: 50mg	200	200	50	6:4
6	F6	200mg: 50mg	200	300	50	6:4
7	F7	200mg: 50mg	300	100	50	6:4
8	F8	200mg:50mg	300	200	50	6:4
9	F9	200mg:50mg	300	300	50	6:4

Evaluation of Transdermal Patch

Uniformity of Weight

Weight variation is studied by individually weighing 10 randomly selected patches and calculating the average weight. The individual weight should not deviate significantly from the average weight.[9]

Thickness

The thickness of film was determined by measuring the thickness at centre and side on the formulated polymeric film using (micrometer) screw gauge and the average thickness was determined. [6]The least count of screw gauge and average thickness was determined. The least count of screw gauge was found to be 0.01cm.

Folding endurance

Folding endurance of the film was determined by repeatedly folding a small strip of film (2cm×2cm) 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 folding endurance.

Moisture content

The film were weighed individually and kept at desiccators containing activated silica at room temperature for 24hours. Individual film was weighed repeatedly until they show the constant weight. The percentage of moisture content was calculated as the difference between the initial and final weight with respect to final weight.

Drug Content

The drug content of the transdermal film was determined by means of UV\Vis spectrophotometer method. The formulated patch was cut into piece and dissolved in 10 ml of methanol. The resulting solution was quantitavely transferred to volumetric flask, and appropriate dilution were made with phosphate buffer pH 7.4and filtered through whatmann filter paper and analyzed for drug content at 256nm and 424 nm by using UV\Vis spectrometer.

Surface pH

The patches surface pH was determined by Labman digital pH meter. The patches were kept in 5ml of distilled water and allowed to swell for one hour at room temperature. The glass electrode was kept near the patches surface. Readings were allowed to equilibrate for a minute and then recorded.

Percent moisture absorption

A weighed film kept in desiccators at room temperature for 24 hrs was taken out and exposed to 84% relative humidity (a saturated solution of aluminum chloride) in dessicator until a constant weight for the

film was obtained. The percentage of moisture uptake was calculated as the difference between final and initial weight with respect to initial weight.[4]

Flatness

Longitudinal strips were cut out from each film. One from the each film one from the center and two from either side. The length of each strip was measured and the variation in the length because of non-uniformity flatness was measured.

***In vitro* permeation study**

The *in vitro* permeation study of herbal fabricated transdermal patch of Curcumin and Casticin was carried out by using cellophane membrane and Franz diffusion cell. A diameter patch was placed in initiate contact with the membrane the back side was covered with aluminum foil act as a backing membrane was place in the receptor compartment filled with 17 ml of phosphate buffer pH 7.4.The cell content were stirred with a magnetic stirred with a magnetic stirrer and a temperature of 37±5˚C was maintained during experiment. Withdraw 1 ml of sample through the sampling post different time interval for a period 24 hr, simultaneously replacing equal volume of phosphate buffer pH 7.4 to maintained an ink condition. The sample was analyzed spectrophotometer at256 nm and 424 nm respectively.

Primary Skin Irritation Study

Three albino rabbits of either sex weighing 2-2.5 kg were used for the test. The intact skin was used. The skin from the back of each rabbit was depilated 24 hours prior to application of the patch. Two areas of the back of each rabbit, approximately 10 cm apart were designated for the position of the patches. One area was used for application of plain polymeric patch and the other was used for drug patch. The animals were immobilized using rabbit holder during 24 hours exposure. Upon removal of the patches, the resulting reaction was evaluated using weighed scores. Reading was also made after 72 hours and the final scores represent an average of the 24 and 72 hour reading.

RESULT AND DISCUSSION

Performulation Studies

Solubility Studies

Curcumin and Casticin were souble in phosphate buffer 7.4, ethanol and water.

Preparation of standard calibration curve for Turmeric (Curcumin) and Vitex Nigundo (Casticin)

The standard calibration curve of turmeric and *Vitex nigundo* is prepared which is given in Figure 2. The regration of Curcumin and *Vitex Nigondu* was found to be 0.9981 and 0.998 respectively.

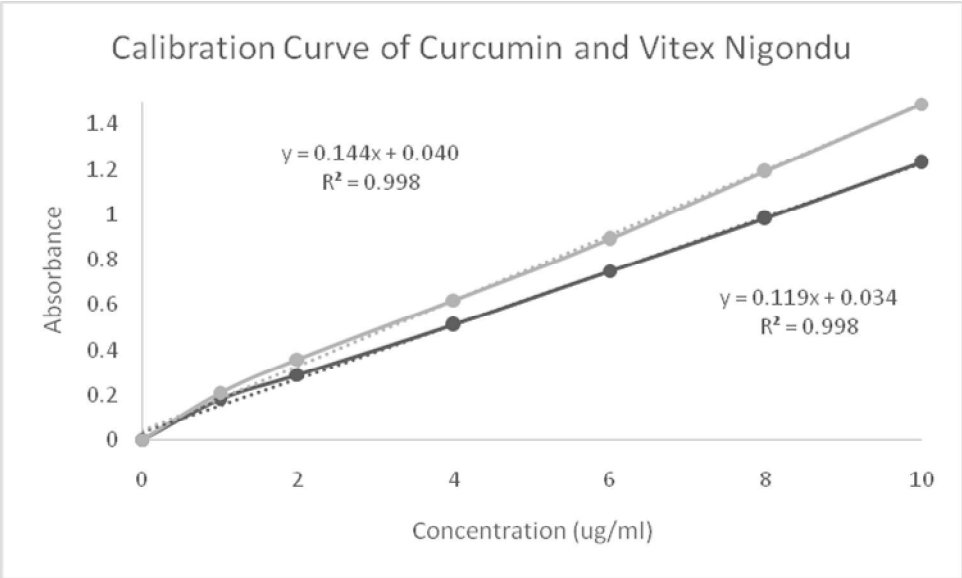

Figure 2: Standard Calibration Curve of Curcumin and Vitex Nigondu

FT-IR of Turmeric (Curcumin) and *Vitex Nigundo* (Casticin)

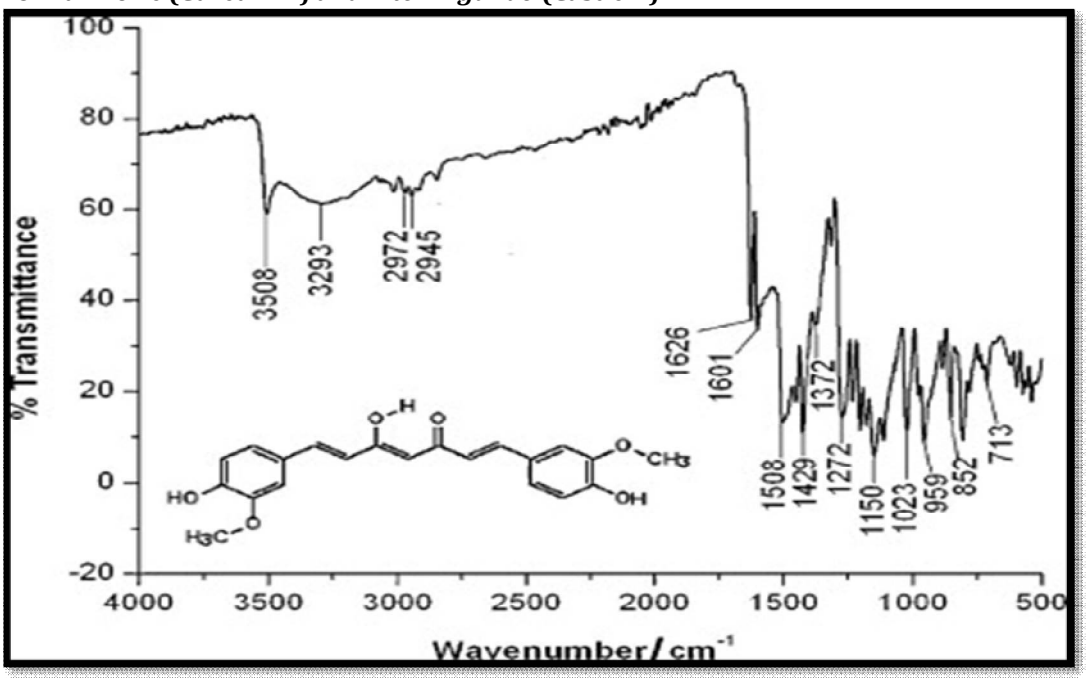

Figure 3(a): FT-IR of Curcumin

The FTIR of turmeric (Curcumin) and Vitex Nigundo (Casticin) is given in Figure 3 (a) and (b). The IR sepectrum of Curcumin demonstrated stretching vibrations due to phenolic hydroxyl groups at 3200-3500cm^{-1}, stretching viratio at 1490cm^{-1}associated with the aromatic C=C bond and a bending vibration at 1246cm^{-1} attributed to the phenolic C-O group. The IR spectrum of Vitex Nigundo demonstrated stretching due to O-H group at 3200-3400cm-^{1}, C-H vibration at 2915-2935, stretching of C=O at 1210-1320 and stretching of C-H at 1350-1480.

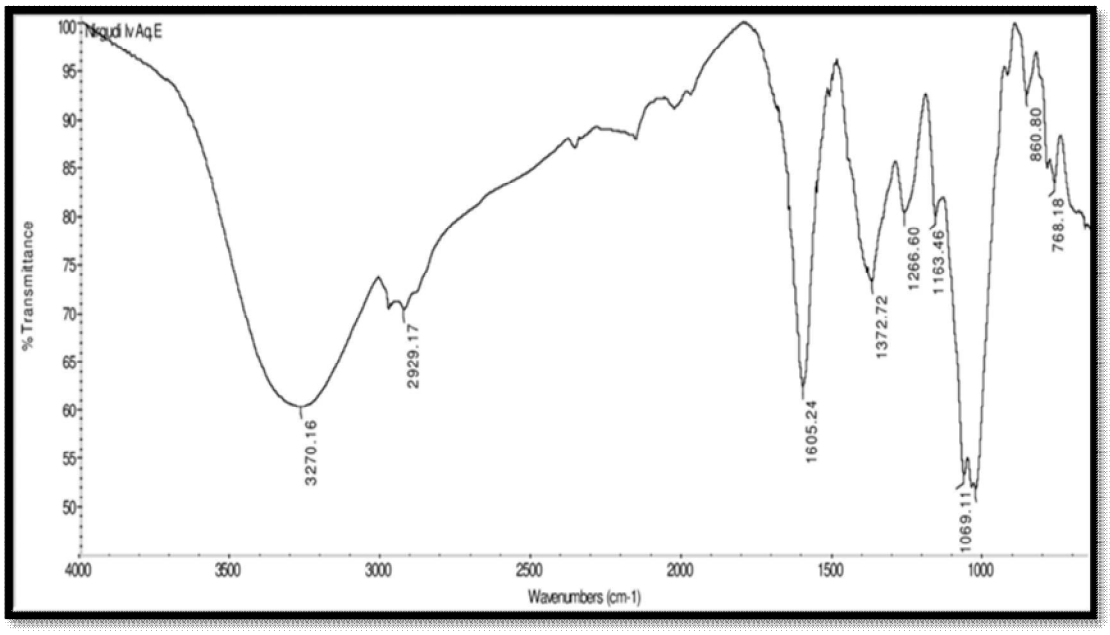

Figure 3(b) FT-IR of Vitex Nigondu

DSC of Turmeric (Curcumin) and *Vitex Nigundo* (Casticin)

The DSC of Curcumin and Vitex Nigundo is given in Figure 4(a) and (b).

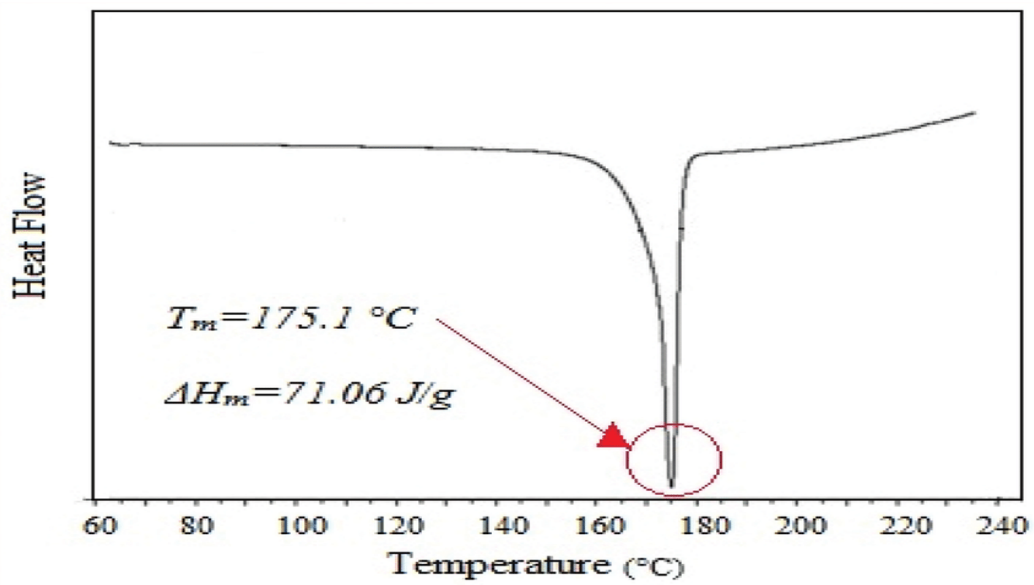

Figure 4(a): DSC of Curcumin

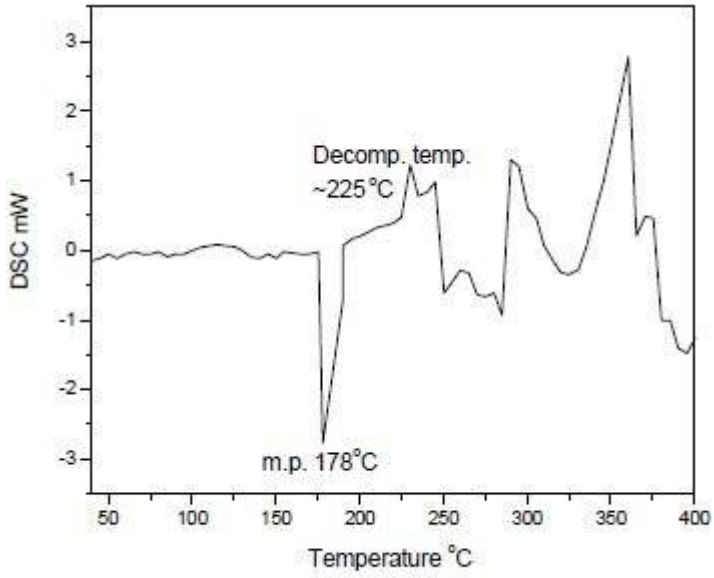

Figure 4(b): DSC of Vitex Nigundo

Formulation Studies

Evaluation of Transdermal Patch

Uniformity of Weight

The uniformity of weight was found to be in the range of 1.8±0.1 to 2.18±0.42. The result of uniformity of weight for all the formulations from F1 to F9 is given in Table 2.

Thickness

The thickness of the patches were found to be in the range of 0.11±0.2 to 0.22±0.54mm. The result of thickness for all the formulations from F1 to F9 is given in Table 2.

Folding endurance

Folding endurance of the patches were found be to in the range of 89±0.23 to 100±0.45. The result of folding endurance for all the formulations from F1 to F9 is given in Table 2.

Moisture content

The moisture content of patches were found to be in the range of 2.22±0.23 to 4.81±0.23. The result of moisture content for all the formulations from F1 to F9 is given in Table 2.

Drug Content

The drug content of the transdermal film was determined by means of UV\Vis spectrophotometer method. The drug content of patches were found to be in the range of 80.12±0.12 to 95.02±0.12. The result of drug content for all the formulation is given in Table 2.

Surface pH

The surface pH of the transdermal patches were in the range of 7.1±0.12 to 7.4±0.76. The result of surface pH for all the formulations is given in Table 2.

Percent moisture uptake

The percent moisture uptake were ranged between 22.12±0.34 to 27.46±0.10. The result of percent moisture uptake is given in Table 2.

Flatness

The flatness of the transdermal patches were in the range of 76±0.34 to 100±0.12. The result of flatness is given in Table 2.

***In vitro* permeation study**

The formulation F9 exhibited 97.5 % of drug permeation in 24h with a flush of 8.65µg/cm^2/h given in Figure 4 and Table 3. The result of in vitro drug permeation from Curcumin and Vitex nigundo transdermal patches through cellophane membrane shows that it could possibly permeated through the human skin. [2,3]

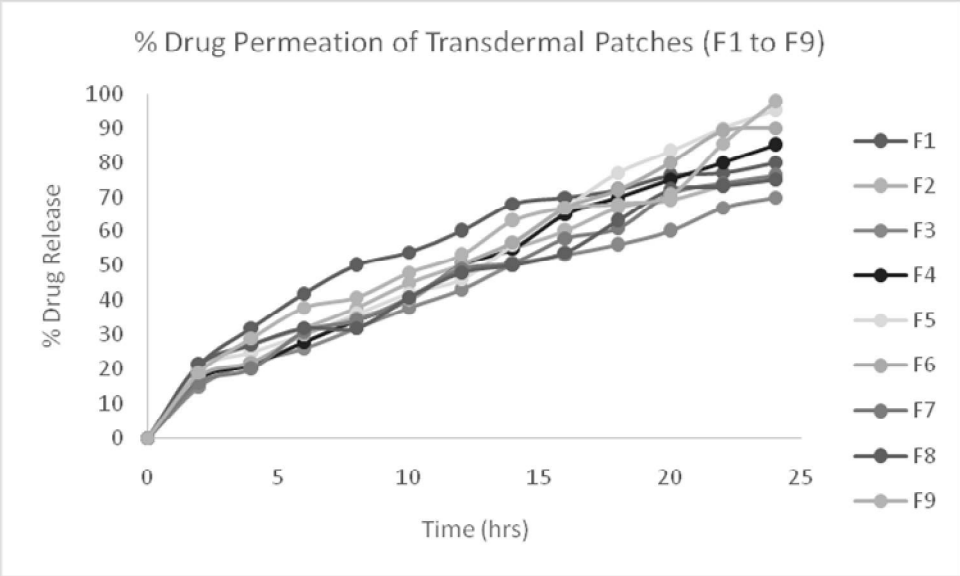

Figure 5: % Drug Permeation of transdermal Patches (F1-F9)

Table 2: Evaluation Parameters for optimized formulation

S. No.	Formulation	Uniformity of weight±SD	Thickness(mm)± SD	Folding endurance± SD	Moisture content± SD	Drug content ± SD	Surface pH± SD	Percent moisture uptake ± SD	Flatnes ± SD
1	F1	2.11±0.1	0.11±0.2	100± 0.16	2.81± 0.14	84.12±0.23	7.2± 0.23	25.56±0.78	77±0.11
2	F2	2.16±0.12	0.16±0.4	102±0.18	2.84±0.75	83.35±0.14	7.1±0.12	27.46±0.10	76±0.34
3	F3	2.18±0.42	0.18±0.3	100±0.14	3.83±0.23	88.98±0.34	7.4±0.24	26.12±0.6	81±0.67
4	F4	2.15±0.1	0.11±0.6	98±0.11	4.81±0.23	85.23±0.65	7.1±0.54	25.12±0.32	85±0.87
5	F5	2.17±0.11	0.16±0.15	130±0.23	3.32±0.54	90.64±0.87	7.4±0.76	23.87±0.11	86±0.24
6	F6	2.16±0.045	0.18±0.18	135±0.56	4.12±0.78	85.23±0.34	7.3±0.34	26.14±0.12	87±0.56
7	F7	2.12±0.065	0.22±0.4	123±0.11	3.11±0.12	80.12±0.12	7.4±0.34	23.12±0.23	100±0.11
8	F8	2.11±0.13	0.21±0.2	89±0.23	4.11±0.45	91.22±0.23	7.3±0.56	24.12±0.12	100±0.12
9	F9	1.8±0.11	0.22±0.54	150±0.45	2.22±0.23	95.02±0.12	7.4±0.12	22.12±0.34	100±0.11

Table 3: *In-vitro* permeation study of all the formulations

S. No.	Time (hrs)	Percent Drug Permeation								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	2	21	20	15	17	20	18	16	21	19
3	4	32	27	22	21	25	22	20	27	29
4	6	42	32	26	28	30	30	31	32	38
5	8	50	38	32	34	36	35	34	32	41
6	10	54	45	38	40	42	40	41	41	48
7	12	60	50	43	50	46	50	49	48	53
8	14	68	55	50	55	56	57	51	50	63
9	16	70	60	53	65	67	67	58	54	67
10	18	72	67	56	70	77	72	61	63	68
12	20	76	69	60	75	83	80	71	72	70.4
13	22	77	73	67	80	90	89	74	73	85.4
14	24	80	75	70	85	95	90	76	75	97.5

Primary Skin Irritation Study

Skin irritation studies show no sign of erythema or any other skin irritation reaction, so it can be concluded that neither any drug nor any polymer or excipient was found to cause adverse effects on skin, hence patch was found to be compatible with skin.

REFERENCES

1. Cherukuri, S., Batchu, U. R., Mandava, K., Cherukuri, V., & Ganapuram, K. R. (2017). Formulation and evaluation of transdermal drug delivery of topiramate. International journal of pharmaceutical investigation, 7(1), 10.
2. Balaji P, Thirumal M, Gowri R, Divya V, Ramaswamy V. Design and evaluation of matrix type of transdermal patches of methotrexate. Int J Pharm Chem Biol Sci. 2012; 2:464–71.
3. Chauhan, L., & Vashisht, S. (2018). Formulation and evaluation of Novel herbal antidiabetic transdermal patch. Inno Pharm Pharmacother, 6(4).170-177
4. Das, A., Ghosh, S., Das, S., Dey, B. K., & Ghosh, T. K. (2011). Formulation and In Vitro Evaluation of Transdermal Patches of Metformin Hydrochloride Using Hydrophilic and Hydrophobic Polymer Complex. Research Journal of Pharmacy and Technology, 4(4), 561-565
5. Agrawal S, Balamurugan S. (2013). Formulation and Evaluation of Chitosan Based Bioadhesive Transdermal Drug Delivery Systems of Lisinopril for Prolonged drug delivery.Der Pharmacia Sinica, 4(3):1-7.
6. Verma, M., Gupta, P. K., Varsha, B. P., & Purohit, A. P. (2007). Development of transdermal drug dosage formulation for the antirheumatic ayurvedic medicinal plants. *Ancient Sci Life*, *1*, 66-69.
7. Aranaz I, Mengíbar *M,* Mengíbar M .(2009). Functional Characterization of Chitin and Chitosan.Current Chemical Biology, *3:*203-230
8. Bharkatiya M, Nema N.K, Bhatnagar M, (2010).Designing and Characterization of Drug Free Patches for Transdermal Application. International Journal of Pharmaceutical Sciences and Drug Research; 2(1): 35-39
9. Mahajan, N. M., Zode, G. H., Mahapatra, D. K., Thakre, S., Dumore, N., & Gangane, P. S. (2018). Formulation development and evaluation of transdermal patch of piroxicam for treating dysmenorrhoea. *Journal of Applied Pharmaceutical Science*, *8*(11), 035-041.
10. Lans, C., Taylor-Swanson, L., & Westfall, R. (2018). Herbal fertility treatments used in North America from colonial times to 1900, and their potential for improving the success rate of assisted reproductive technology. *Reproductive biomedicine & society online*, *5*, 60-81.