ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

STUDYING INFLUENCE OF VARIOUS PERMEATION ENHANCERS ON CURCUMIN TRANSDERMAL PATCHES

Vidya Birajdar[1], Ayesha Sultana[*1], K. Venu Madhav[2], M. Kiranmai[3], P. Naga Haritha[4]

Department of Pharmaceutics, St. Pauls College of Pharmacy, Turkayamjal, Hyderabad.

Corresponding Author E-mail: vidyabirajdar0608@gmail.com

ARTICLE INFO

Key words:
Curcumin, Formulations, Evaluation, Permeation enhancers, Transdermal patches.

Access this article online Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

This research was conducted to study the influence of natural permeation enhancers by formulating Curcumin patches. Preformulation studies on the drug curcumin were done which included description, melting point, solubility and preparation of standard curve. Solvent casting technique is used to prepare the transdermal patches. Six formulations were made with 10 mg of curcumin by using polymers namely HPMC and EC, chloroform and ethanol as solvents, PEG 400 as plasticizer at various ratios and eucalyptus oil, basil oil and fennel oil as permeation enhancer. Curcumin was physically examined for color and odor. Solubility was determined in water, phosphate buffer pH 7.4, and ethanol. Based on this further evaluation was carried out. In-vitro drug diffusion study was carried out using Franz diffusion cell. Transdermal patches were evaluated for pH evaluation, thickness uniformity, weight uniformity, % moisture loss and in-vitro diffusion study. This was done for 6 formulations F1, F2, F3, F4, F5, and F6. It was found that the formulation F6 has shown highest penetration about 88.2 % in 300 mins. Formulation F6 i.e., combination of eucalyptus oil and basil oil has shown better characteristics than other oils.

INTRODUCTION

A transdermal patch is defined as medicated adhesive patch which is placed on the skin to deliver a selected dose of medication through the skin with a pre-determined rate of release to reach into the blood stream. Transdermal drug delivery is theoretically ideal for several injected and orally delivered drugs, but many drugs cannot pass through the skin due to skin's low permeability. Transdermal administration of drug undergo first pass metabolism which will improve the bioavailability and reduce the dosing frequency compared with oral route. [1, 2] One example of transdermal preparation is a patch. Patch preparations have several advantages, namely greater safety and convenience in usage, painless usage and better precision in dosage than Other transdermal preparations. Permeation enhancers by interacting with skin constituents improve the flux of drug molecules. Thus the use of enhancers in transdermal preparations is for enhancing the permeability of small lipophilic molecules. [3] Permeation enhancers are the substances which promote the absorption of drug through the skin temporarily by transiently enhancing the skin permeability. [4] They are employed to transfer the delivery of medication which is ionizable and impermeable to maintain drug levels in blood, to produce higher dose of less potentially active drugs, to deliver high molecular weight hormones and peptides and to lesser the lag time of TDDS. [5, 6]

Curcumin is the product obtained by solvent extraction of turmeric and purifying the

extract by crystallization. Curcumin is chemical (1E, 6E)-1, 7 bis (4-hydroxy-3-methoxy phenyl) hepta-1,6-dione-3,5-Dione. Curcumin is employed for the treatment of anti-cancer, anti-oxidant, anti-inflammatory, anti-viral, anti-fungal, hyperlipidemic, anti-bacterial, wound healing and hepato protective activities. Despite the presence of enormous number of pharmacological actions, the therapeutic efficacy of curcumin is restricted because of its poor oral bioavailability of curcumin has been attributed to its poor aqueous solubility as its partition coefficient 3.2 and extensive first pass metabolism. [7]

The plant *Curcuma longa linn* [Zingiberaceae] commonly called as 'Indian saffron'. The entire plant of turmeric mainly rhizomes, roots and leaves are used for medicinal purpose. Studies have shown that curcumin is non toxic to humans. Curcumin exerts anti-inflammatory activity by inhibition of number of various molecules that play a crucial role in inflammation. Turmeric is effective in reducing post-surgical inflammation. [8]

Curcumin protects skin by quenching free radicals and reducing inflammation through nuclear factor – KB inhibition. Curcumin treatment also reduced wound- healing time, improved collagen deposition and increased fibroblast and vascular density in wounds thereby enhancing both normal and impaired wound healing. [9]

MATERIALS AND METHODS

Materials

Curcumin was taken from the laboratory of Pharmaceutics. St. Pauls College of Pharmacy, Hyderabad, India.

Polymers and excipients namely hydroxypropyl methyl cellulose (HPMC), ethyl cellulose (EC), polyethylene glycol-400(PEG-400), chloroform, ethanol, eucalyptus were from Qualikems Fine chem. Pvt.Ltd. Fennel oil from Blossom Kochhar Beauty products Pvt.Ltd. Basil oil from Naturveda Pvt.Ltd. All chemicals & reagents used were of analytical grade.

Method of Preparation

The transdermal patches were prepared by solvent casting technique. The casting solutions for transdermal patches were prepared as per composition stated in table no: 1. Weighed quantities of HPMC and EC were dissolved in measured quantities of chloroform and ethanol (1:1). The drug curcumin 10mg is dissolved in the solvent mixture along with natural oils as permeation enhancer and PEG 400 as plasticizer. This mixture is stirred for 10 mins using stirrer. Before pouring the polymeric solution, few drops of glycerin is poured on petridish. This mixture was then poured in the petridish and glass funnel was placed on it and allowed to dry at room temperature for 24 hrs for solvent evaporation.

The patches are kept in desiccator, wrapped in aluminum foil and then packed in self sealing covers for further evaluation.

PREFORMULATION STUDY OF THE DRUG: Curcumin

Preformulation study is defined as a study of physical and chemical properties of a drug substance alone. Organoleptic properties, melting point, solubility studies and preparation of std. curve of curcumin was done

A. Description

Curcumin was physically examined for color and odor etc.

B. Melting Point

Melting point of drug sample was performed by using capillary tube method. A fine powder of curcumin was filled in a capillary tube, sealed at one end the capillary tube was tied to the bottom of the thermometer. The thermometer and capillary tube was heated gently by means of burner. When sample starts melting the reading was recorded. [10]

C. Solubility

Solubility of curcumin was determined in water, ethanol, phosphate buffer, acetone, DMSO, chloroform, acetic acid etc.

D. Preparation of standard curve for curcumin

Primary stock solution: 100 mg of curcumin was accurately weighed and dissolved in 30ml of ethanol and diluted to 100ml with distilled water.

Secondary stock solution: 1 ml of primary solution was diluted to 100ml distilled water. From this 1 ml was pipette out diluted to 10 ml. Aliquots of 1 ml, 2 ml, 4 ml, 6 ml, 8 ml and 10 ml were pipette out and diluted to 10

ml with distilled water. Standard graph was plotted by concentration on X- axis and obtained absorbance on Y-axis. [11]

EVALUATION OF TRANSDERMAL PATCHES

I. Organoleptic evaluation

The organoleptic evaluation was conducted by observing the color, odor, and texture of the patch.

II. pH evaluation

The patches were cut [1×1 cm^2] and immersed into 1 ml of distilled water for 2 h at room temperature. pH evaluation was performed by placing a litmus paper on the patches surfaces for 1 min. pH was then determined. [12]

III. Uniformity of Thickness

The thickness of the drug loaded patch is measured in different points by using a Vernier caliper and determines the average thickness and standard deviation for the same to ensure the thickness of the prepared patch. [13]

IV. Uniformity of Weight

A specified area of the patch is to be cut in different parts of the patch and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weights. [14]

V. Percentage Moisture content

The prepared films are to be weighed individually and to be kept in a desiccator containing calcium chloride at room temperature for 24 hrs. After 24 hrs the films are to weighed and determine the percentage of moisture content from the below formula. [15]

% moisture content = [Initial wt- final wt / final wt] × 100.

VI. *In- Vitro* Diffusion study

An in-vitro permeation study has been carried out using Franz diffusion cell. Egg membrane is taken as semi-permeable membrane for diffusion. The egg membrane is mounted between the donor and the receptor compartment. A weighed amount of transdermal patch is placed on one side of membrane. The receptor medium is phosphate buffer 7.4. The temperature of the cell was maintained at 32±0.5°C. Heat is provided using thermostatic hot plate with a magnetic stirrer. The receptor fluid is stirred by Teflon coated magnetic beat which is placed in the diffusion cell. Samples are withdrawn at regular time intervals and replaced by equal volumes of fresh receptor fluid on each occasion. Samples are analyzed spectrophotometrically at 429 nm. The drug release was performed. [16]

RESULTS

PREFORMULATION STUDY OF THE DRUG: Curcumin

A. Organoleptic properties:

Curcumin was physically examined for color, odor etc. It is an orange yellow powder with pungent taste and characteristic aroma odor.

B. Melting Point:

The melting point of curcumin was found to be 180°C.

C. Solubility:

The solubility profile of curcumin was found to be

D. Standard curve of curcumin:

Calibration curve of curcumin at 429 nm is taken and curve shown in Graph 1

Correlation co-efficient [r^2] = 0.985

Equation of regressed line y = 0.075 + 0.005

Slope of regressed line = 0.075

Where, X = Concentration [µg/ml], Y = Absorbance [nm]

EVALUATION OF TRANSDERMAL PATCHES

Organoleptic evaluation

The results of the organoleptic evaluation of all the six formulations showed that it generated a smooth surface textured, dry, elastic, yellow, characteristic odor and transparent properties. All the physical characterization of the transdermal patches, including thickness, weight uniformity, pH, percentage of moisture content are shown are shown in table no:3.

KINETICS OF DRUG RELEASE

To examine the drug release kinetics and mechanism, the cumulative release data were fitted to model representing Zero order, First order, Higuchi's square root of time and Korsemeyer Peppas log plot.

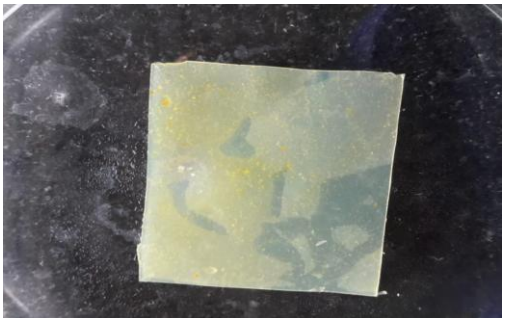


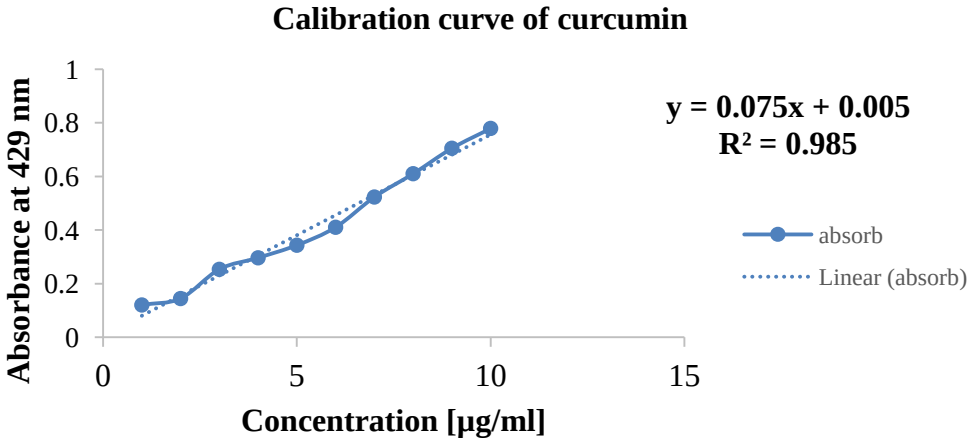
Figure 1: The prepared transdermal patch of curcumin.

Table no: 1-Transdermal patches formulation

Formulations	Polymer		Solvents		Plasticizers	Drug	Permeability Enhancer
	HPMC (mg)	EC (mg)	Ethanol (ml)	Chloroform (ml)	PEG 400 (%)	Curcumin (mg)	Essential Oils (%)
F1	300	100	10	10	0.5	10	Eucalyptus oil [0.5]
F2	250	150	10	10	0.5	10	Fennel oil [0.5]
F3	200	200	10	10	0.5	10	Basil oil [0.5]
F4	300	200	10	10	0.5	10	Basil [0.5]+ Fennel [0.5]
F5	300	200	10	10	0.5	10	Eucalyptus[0.5] + Fennel [0.5]
F6	300	200	10	10	0.5	10	Eucalyptus [0.5] + Basil [0.5]

Table no: 2- Solubility of Curcumin

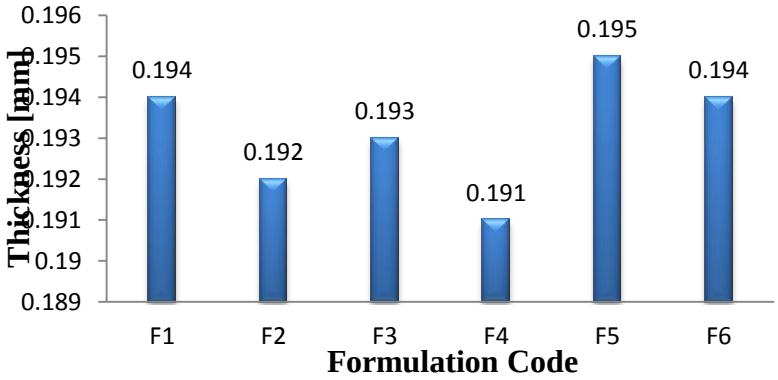
THEORETICAL	MEDIUM
Insoluble	Water, Chloroform, Acetic acid, Phosphate buffer.
Soluble	Ethanol, DMSO
Poorly Soluble	Acetone, Sodium hydroxide, Sodium Carbonate.



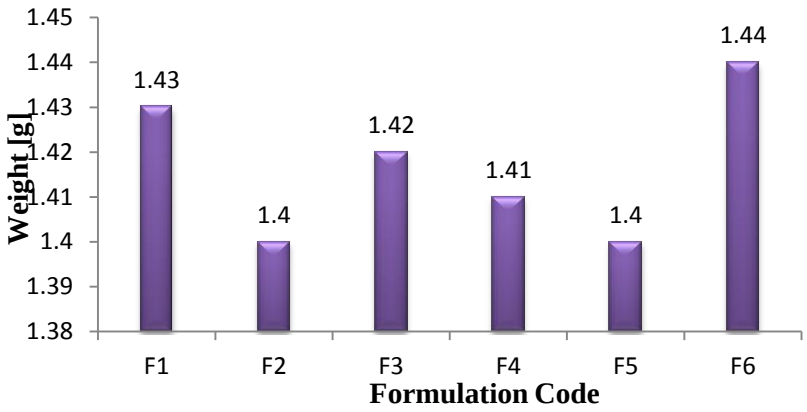
Graph 1: Calibration curve of curcumin

Table no: 3-Physico-chemical properties of prepared Transdermal Patch

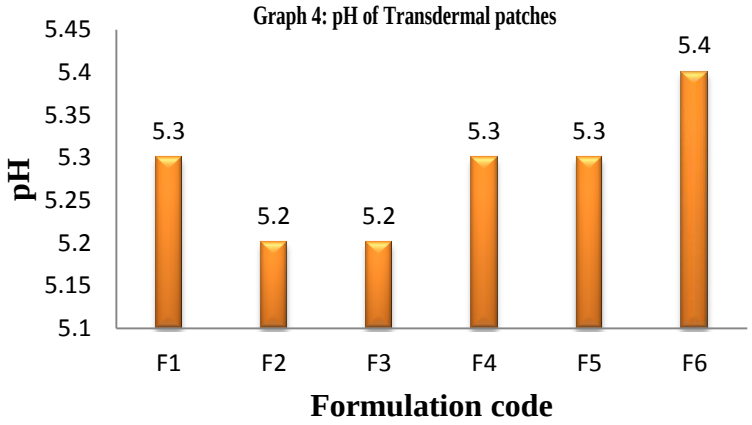
S.No	Formulation Code	Thickness [mm] ±SD	Weight [g] ±SD	pH	% Moisture content [%] ±SD
1	F1	0.194±0.0058	1.43±0.0158	5.3	3.215±0.0200
2	F2	0.192±0.0115	1.40±0.0208	5.2	3.424±0.0175
3	F3	0.193±0.0193	1.42±0.0100	5.2	3.367±0.0120
4	F4	0.191±0.0159	1.41±0.0173	5.3	3.409±0.0448
5	F5	0.195±0.0058	1.40±0.0155	5.3	3.321±0.0377
6	F6	0.194±0.0100	1.44±0.0078	5.4	3.541±0.0068

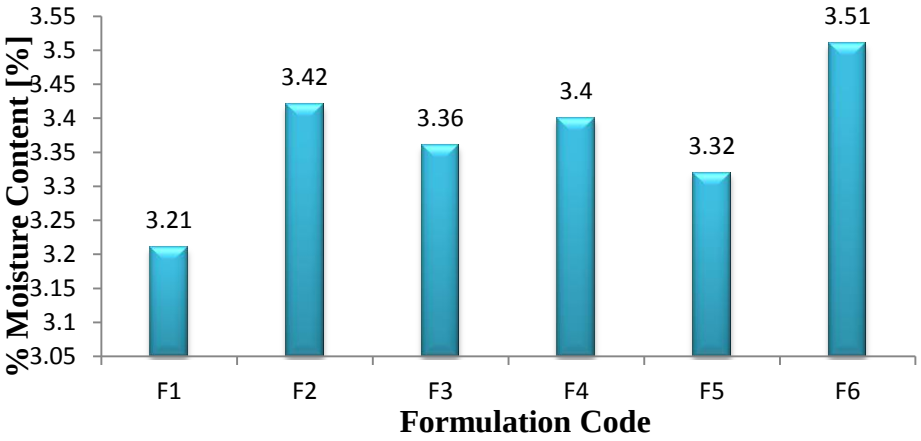


Graph 2: Thickness of Transdermal Patch



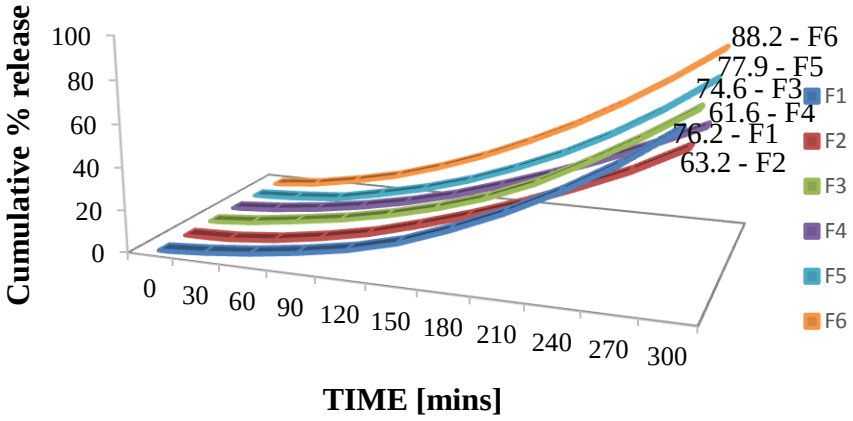
Graph 3: Weight of Transdermal Patch





Graph 5: Percentage Moisture Content of Transdermal Patch

COMPARISON OF *IN VITRO* RELEASE STUDIES



Graph 6: Comparison of in-vitro release of various formulations

Table no: 4- *In-vitro* release data of drug permeation through egg membrane for formulation F1 – EUCALYPTUS OIL

Time [mins]	Square root of time	Log [time]	% Cumulative amount released	Log cumulative % drug released	% of drug remaining in the matrix	Log % of drug remaining in the matrix
0	0	0	-	-	100	2
30	5.47	1.47	1.6	0.21	98.3	1.99
60	7.74	1.77	3.9	0.59	96.0	1.98
90	9.48	1.97	7.1	0.85	92.9	1.96
120	10.97	2.07	11.1	1.04	88.8	1.94
150	12.24	2.17	16.9	1.22	83.0	1.91
180	13.41	2.25	25.3	1.4	74.6	1.87
210	14.49	2.32	35.1	1.54	64.8	1.81
240	15.49	2.38	46.7	1.66	53.3	1.72
270	16.43	2.43	60.1	1.77	39.8	1.60
300	17.32	2.47	76.2	1.88	23.7	1.37

Table no: 5- *In-vitro* release data of drug permeation through egg membrane for formulation F2 – FENNEL OIL

Time [mins]	Square root of time	Log [time]	% Cumulative amount released	Log cumulative % drug released	% of drug remaining in the matrix	Log % of drug remaining in the matrix
0	0	0	-	-	100	2
30	5.47	1.47	0.7	0.11	99.2	1.99
60	7.74	1.77	2.9	0.46	97.1	1.98
90	9.48	1.97	6.5	0.81	93.4	1.97
120	10.97	2.07	11.1	1.04	88.9	1.94
150	12.24	2.17	17.4	1.24	82.6	1.91
180	13.41	2.25	24.4	1.38	75.6	1.87
210	14.49	2.32	32.3	1.50	67.7	1.83
240	15.49	2.38	41.4	1.61	58.6	1.76
270	16.43	2.43	51.2	1.70	48.8	1.68
300	17.32	2.47	63.2	1.80	36.8	1.56

Table no: 6- *In-vitro* release data of drug permeation through egg membrane for formulation F3 – BASIL OIL

Time [mins]	Square root of time	Log [time]	% Cumulative amount released	Log cumulative % drug released	% of drug remaining in the matrix	Log % of drug remaining in the matrix
0	0	0	-	-	100	2
30	5.47	1.47	1.9	0.27	98.1	1.99
60	7.74	1.77	5.0	0.70	94.9	1.97
90	9.48	1.97	8.4	0.92	91.5	1.96
120	10.97	2.07	13.0	1.11	86.9	1.93
150	12.24	2.17	18.7	1.27	81.2	1.90
180	13.41	2.25	25.8	1.41	74.1	1.86
210	14.49	2.32	35.1	1.54	64.8	1.81
240	15.49	2.38	47.1	1.67	52.8	1.72
270	16.43	2.43	60.1	1.77	39.8	1.59
300	17.32	2.47	74.6	1.87	25.4	1.40

Table no: 7 In-vitro release data of drug permeation through egg membrane for formulation F4 – BASIL + FENNEL

Time [mins]	Square root of time	Log [time]	% Cumulative amount released	Log cumulative % drug released	% of drug remaining in the matrix	Log % of drug remaining in the matrix
0	0	0	-	-	100	2
30	5.47	1.47	1.7	0.23	98.3	1.99
60	7.74	1.77	4.3	0.64	95.6	1.98
90	9.48	1.97	7.9	0.90	92.0	1.96
120	10.97	2.07	12.5	1.09	87.4	1.94
150	12.24	2.17	18.2	1.26	81.7	1.91
180	13.41	2.25	25.3	1.40	74.6	1.87
210	14.49	2.32	33.0	1.51	66.9	1.82
240	15.49	2.38	41.7	1.62	58.2	1.76
270	16.43	2.43	51.3	1.71	48.7	1.68
300	17.32	2.47	61.6	1.79	38.4	1.58

Table no: 8- *In-vitro* release data of drug permeation through egg membrane for formulation F5 – EUCALYPTUS + FENNEL

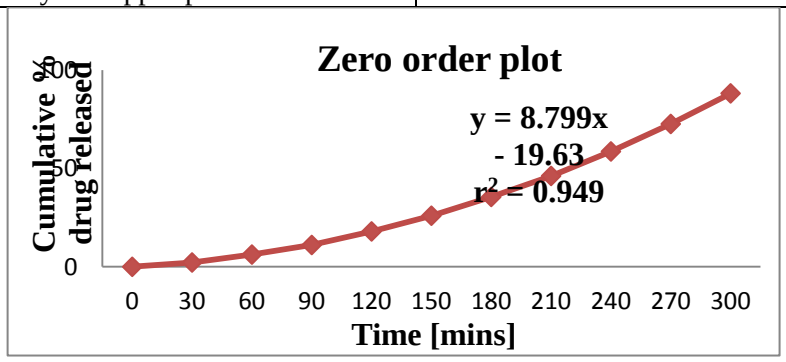
Time [mins]	Square root of time	Log [time]	% Cumulative amount released	Log cumulative % drug released	% of drug remaining in the matrix	Log % of drug remaining in the matrix
0	0	0	-	-	100	2
30	5.47	1.47	1.2	0.07	98.8	1.99
60	7.74	1.77	3.0	0.47	97.0	1.98
90	9.48	1.97	7.6	0.88	92.4	1.96
120	10.97	2.07	12.7	1.10	87.3	1.94
150	12.24	2.17	19.3	1.28	80.7	1.90
180	13.41	2.25	27.6	1.44	72.4	1.85
210	14.49	2.32	37.1	1.56	62.9	1.89
240	15.49	2.38	48.6	1.68	51.4	1.71
270	16.43	2.43	62.1	1.79	37.9	1.57
300	17.32	2.47	77.9	1.89	22.1	1.34

Table no: 9In-vitro release data of drug permeation through egg membrane for formulation F6 – EUCALYPTUS + BASIL

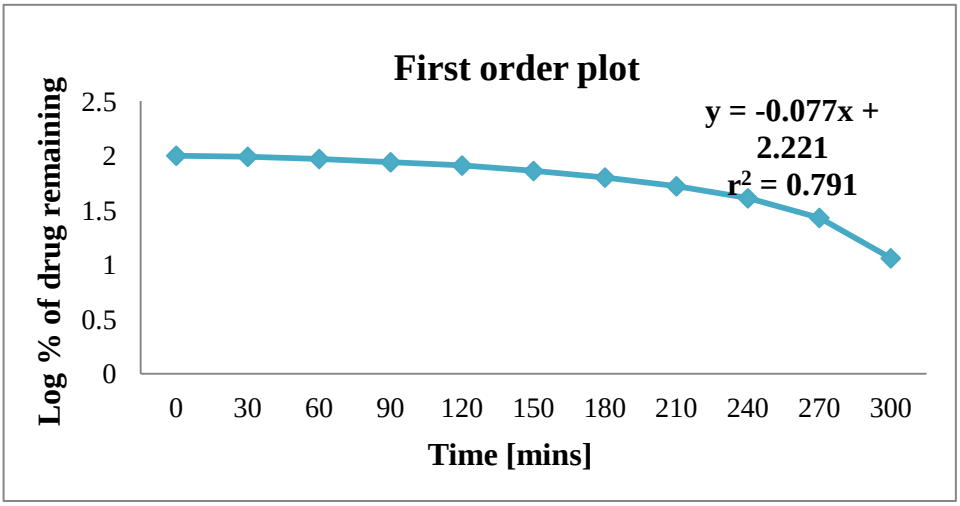
Time [mins]	Square root of time	Log [time]	% Cumulative amount released	Log cumulative % drug released	% of drug remaining in the matrix	Log % of drug remaining in the matrix
0	0	0	-	-	100	2
30	5.47	1.47	2.2	0.34	97.8	1.99
60	7.74	1.77	6.2	0.79	93.7	1.97
90	9.48	1.97	11.1	1.04	88.9	1.94
120	10.97	2.07	17.9	1.25	82.1	1.91
150	12.24	2.17	25.9	1.41	74.1	1.86
180	13.41	2.25	35.5	1.55	64.4	1.80
210	14.49	2.32	46.2	1.66	53.7	1.72
240	15.49	2.38	58.6	1.76	41.3	1.61
270	16.43	2.43	72.6	1.86	27.3	1.43
300	17.32	2.47	88.2	1.94	11.7	1.06

Table no: 10-Curve fitting data for the release rate profile of optimized formulation F6

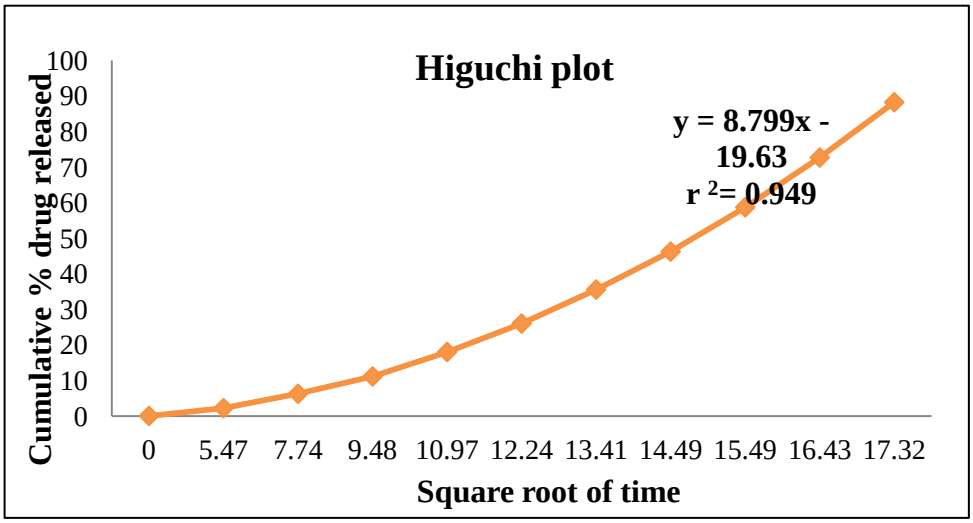
Model	r^2 value
Zero order	0.949
First order	0.791
Higuchi plot	0.949
Korsemeyer- Peppas plot	0.921



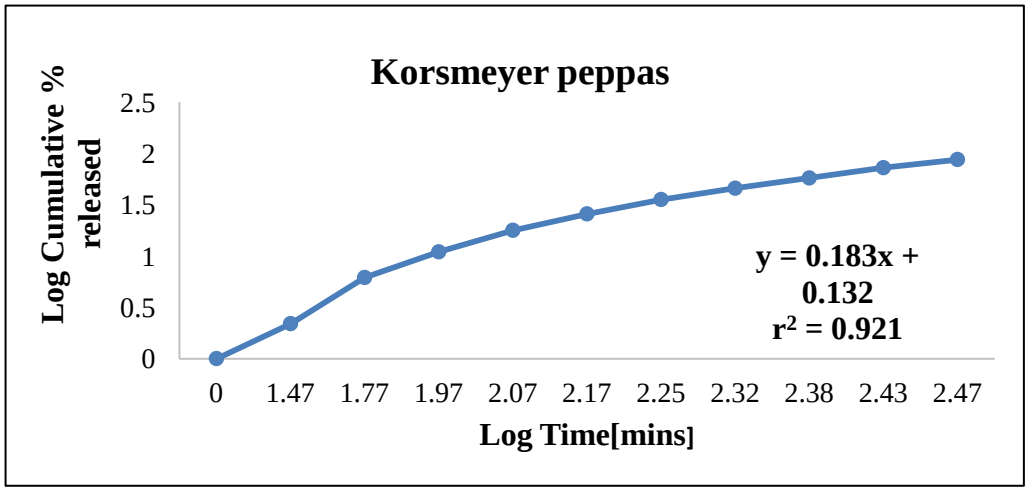
Graph 7: Zero order plot for drug release kinetics



Graph 8: First order plot for drug release kinetics



Graph 9: Higuchi plot for drug release kinetics



Graph 10: Korsmeyer-Peppas plot for drug release kinetics

CONCLUSION

Curcumin is a bright yellow chemical produced by plant of the curcuma longa species, a member of the Zingerberaceae family. Curcumin is an anti-inflammatory agent was selected for the formulation of transdermal drug delivery system. Transdermal patches of curcumin were prepared by polymer combination of HPMC and EC. The patches were prepared by solvent casting technique. The patches were subjected to various evaluation parameters. All parameters were within the limits. They showed good physicochemical and mechanical properties as well as enhanced permeation characteristics. The uniformity of weight and thickness indicates that the polymeric solution of the drug is well dispersed in the patches.

The moisture content did not affect the patch strength and integrity, they helped the patches to remain stable and protected from being completely dried patches. The in-vitro permeation studies of patches using egg membrane as barrier was carried out using phosphate buffer 7.4 in the receptor compartment. The cumulative % of drug release of patch F1- 76.22%, F2- 63.2%, F3- 74.66%, F4- 61.67%, F5- 77.9%, F6- 88.21%. As a result the combination of eucalyptus oil and basil oil showed better in-vitro permeation compared to other formulated patches. The release kinetics was evaluated by making use of Zero order, First order, Higuchi plot and Korsemeyer-Peppas plot. The drug release through the transdermal patches of curcumin follows Zero order kinetics and Higuchi's kinetics.

BIBILOGRAPHY

1. Deepak kumar, Jyoti sahu, Dr.Chanchal Deep Kaur. Formulation and evaluation of Transdermal patch using antioxidant phytoconstituent. International journal of research and development organization. 2016; 2(4): 1-9.
2. Rahika Gadekar, Manoj Kumar Saurabh, Gulab S.Thakur, Avinash Saurabh. Study of formulation, characterization on wound healing potential of transdermal patches of Curcumin. Asian journal of pharmaceutical and clinical research. 2012; 5(4): 225-230.
3. Pankaj Karande, Amit Jain, Samir Mitragotri. Insights into synergistic interactions in binary mixtures of chemical permeation enhancers for transdermal drug delivery. Journal of controlled release. 2006; 115(1): 85-93.
4. Bhawana Sethi, Rupa Mazumdar. Comparision of effect of penetration enhancer on different polymers for drug delivery. Int J app pharm. 2019; 11(1): 89-93.
5. Nimisha Roy, Mehul Agarwal, Shubhangi Chaudhary, Vipin Tirkey, Amar Dhwaj and Nidhi Mishra. Review article on permeation enhancers: A major breakthrough in drug delivery technology. International journal of pharmaceutical sciences and research. 2016; 8(3): 1001-1011.
6. Adrian C. Williams, Brain W.Barry. Penetration enhancers. Advanced drug delivery reviews. 2004; 56: 603-618
7. R.Patel, S.K.Singh, Dr.N.R.Sheth, R. Gendle. Development and characterization of curcumin loaded transfersome for transdermal delivery. Journal of pharmaceutical sciences and research. 2009; 1(4): 71-80.
8. Amit K Vishwakarma, Om P Maurya, Nimsha,Dipti Srivastava. Formulation and evaluation of transdermal patch containing Turmeric oil. International journal of pharmacy and pharmaceutical sciences. 2012; 4(5): 358-361.
9. Rjaesh Thangapazham, Anuj Sharma, Radha K Maheshwari. Beneficial role of curcumin in skin disease. Advances in experimental medicine and biology. 2007; 595: 343-357.
10. Wade. A, Martindale- The extra pharmacopoeia, 27th Ed. The press, pharmaceutical London, 1977.
11. Saraswathi. R, Krishnan. P.N, Dilip. C, Shabir Ali.t.k. Formulation and

evaluation transdermal patches of curcumin. Scholar research library. Der Pharmacia letter, 2010; 2(5): 117-126.
12. Rajesh. N, Siddarmaiah, D.V.Gowda, Somashekar. C.N. Formulation and evaluation of biopolymer based transdermal drug delivery system. Int J pharmacy and pharm.sci. 2010; 2: 142-147.
13. Saini T.R, Seth AK, Agarwal GP. Evaluation of free films. Indian drugs. 1985; 23(1): 45-47.
14. Gannu. R, Vishnu. Y V, Kishan V rao Y M. Development of Nitrendipine transdermal patches; in-vivo and ex-vivo characterization. Current drug delivery 2007; 4: 69-76.
15. Mamatha. T, Rao V J, Mullanti K and Ramesh G. Development of matrix type transdermal patches of Lercanidipine hydrochloride: physicochemical and in-vitro characterization. Daru. 2010; 18(1): 9-16.
16. Mohd. Amjad, Mohd. Ehtheshamuddin, S. Chand, Hanifa, M. Sabreesh, R. Asia and G.S.Kumar. Formulation and evaluation of transdermal patches of atenolol. Advance research in pharmaceuticals and biological. 2011; 1(2): 109-119.