

FORMULATION AND EVALUATION OF TRANSDERMAL PATCH CONTAINING TURMERIC OIL

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ABSTRACT

The objective of the present project work was to extract turmeric oil and to incorporate it into transdermal drug delivery system. Turmeric oil was obtained from the rhizomes of *Curcuma longa* collected from northeast region of India (26°55'30"N, 83°44'53"E). Extraction was carried out by hydro distillation using Clevenger's apparatus following the method of Guenther (1948) at room temperature. The Rf value for curcumin determined by TLC was 0.70 that assures the purity of turmeric oil. Transdermal patches containing turmeric oil was formulated and evaluated for various parameters. The oil extracted was further incorporated into the polymers and examined for the compatibility issues. The transdermal patches were prepared using HPMC E50 and Poly Vinyl Alcohol in different ratio using Polyethylene glycol as plasticizer. The patches were evaluated for their physical properties like moisture content, flatness and thickness, weight variation, percentage elongation-break test. The physical properties of the prepared batches did not show any significant variations ($p > 0.05$) and were found to have good physical integrity. Stability studies showed that the physical and chemical properties of the tested batches were not altered significantly and all the test formulations were found to be stable. The evaluation tests of fresh and aged transdermal patch showed no significant effect on drug release ($p > 0.05$).

Keywords: Transdermal Patch, *Curcuma longa*, Turmeric Oil, HPMC, Clevenger Apparatus.

INTRODUCTION

The plant *Curcuma longa* linn (Zingiberaceae) commonly called as Indian saffron. The whole plant of turmeric mainly rhizomes, roots and leaves are used for medicinal purposes. Rhizomes and roots are playing an important role in ayurvedic and unani medicines. In the latter half of the 20th century, Curcumin was identified as responsible for most of the biological effects of turmeric. The rhizomes contain curcuminoids, curcumin, demethoxy curcumin, bis-demethoxycurcumin, 5'-methoxycurcumin and dihydrocurcumin which are found to be natural antioxidants. The fresh rhizomes also contain two new natural phenolics, which possess antioxidant and anti-inflammatory activities and two new pigments also.¹

The volatile oil as well as the petroleum ether, alcohol and water extracts of *C. longa* show anti-inflammatory effects.² The suppression of activation of transcription factors like NF-kB which regulates most of the pro-inflammatory gene expression, down regulation of activity and synthesis of cyclo-oxygenase-2 (COX-2).³

Different in-vitro and clinical studies with curcumin and volatile oil of *C. longa*, suppresses symptoms associated with arthritis by suppressing TNF production⁴ and blocking action of TNF. Topical application of curcumin also shows activity for arthritis.⁵ Cytokine macrophage migration inhibitory factor (MIF) has recently emerged as a crucial factor in the pathogenesis of rheumatoid arthritis.⁶

For the treatment of arthritis, acetaminophen and other NSAIDs are used to reduce the symptoms of inflammation. Since turmeric oil is traditionally used as an anti-inflammatory agent, it can be incorporated into the polymers for transdermal delivery.

MATERIALS AND METHODS

Materials

Turmeric oil was extracted from rhizomes of *Curcuma longa* by hydro-distillation and examined for the presence of curcumin by TLC technique.

The excipients as polymer, Polyvinyl Alcohol, HPMC-50CPS, Polyethylene Glycol-400, Ethanol, and Chloroform used, were of analytical reagent grade.

Method

Extraction of turmeric oil

The fresh plant of *Curcuma longa* was collected from Northeast region of India (Kushinagar). The rhizomes were collected and washed under running tap water followed by distilled water. Rhizomes were sliced and peeled. 250 gm of sliced and peeled rhizome were mixed with 400 ml of distilled water into the 1000 ml round bottom flask. Extraction was carried out by hydro distillation following the method of Guenther (1948) out at room temperature.⁷ The homogenate mixture in the RBF was heated for 6-8 hours. The oil, present at the upper layer in the ependroff tube, was separated from the water using separating funnel and examined for the presence of curcumin.

Preparation of transdermal film

Transdermal patch of turmeric oil was prepared with the polymer Polyvinyl Alcohol as backing membrane and HPMC-50CPS as dispersion polymer (Table-1).

Table 1: Composition of Transdermal Patch

Formulation Code	Composition of Transdermal Patch				Solvent Used
	PVA %w/v	HPMC-50 CPS %w/v	PEG-400 % of polymer weight	Drug % of polymer weight	
TOP-I	4	7	10	5	Water
TOP-II	4	6	10	5	Water
TOP-III	4	5	10	5	Water
TOP-IV	4	4	10	5	Water
TOP-V	4	4	10	5	EtOH
TOP-VI	4	5	10	5	EtOH
TOP-VII	4	6	10	5	EtOH
TOP-VIII	4	7	10	5	EtOH

The matrix type patches were prepared by preparing the backing membrane of Polyvinyl Alcohol and dispersing Hydroxy Propyl

Methyl Cellulose - 50CPS in different proportion in water and ethanol. The backing membrane was prepared and allowed to

dry for 24 hour at room temperature. Weighed quantity of turmeric oil and HPMC with suitable solvent was continuously stirred for 1 hour, then poly ethylene glycol was added as plasticizer and the stirring was continued for another 1 hour. Then 5ml dispersion containing turmeric oil was withdrawn by

using pipette and slowly poured over the previously prepared backing of PVA. The solvent was allowed to evaporate at a controlled rate by placing an inverted funnel over the glass plate. After 24 hours of drying at room temperature, the film was collected and evaluated.



Fig. 1: Preparation of Transdermal Patch

Evaluation of Formulations

Percentage Moisture Content

The prepared films were weighed individually and kept in desiccators containing fused calcium chloride at room temperature for 24 hrs. After 24 hrs, the films were re-weighed and percentage moisture content was determined.

Thickness

The thickness of the film was measured using a screw gauge.

Weight Uniformity

The prepared patches were dried at 60°C for 4hrs before testing. A specified area of patch were cut in different parts of the patch and weighed on digital balance. The average weight and standard deviation values were calculated from the individual weights.⁸

Percentage Elongation Break Test

The percentage elongation break was determined by measuring the length just before the break point.⁹

Flatness test

Three longitudinal strips were cut from each film at different portion like one from the center, other one from the left side, and another one from the right side. The length of each strip was measured and the variation in length because of non-uniformity in flatness was measured by determining percent constriction, with 0% constriction equivalent to 100% flatness.¹⁰

Statistical Analysis

Each patch formulations were prepared in duplicate and each analysis was duplicated. Evaluation test of all the batches were

tested for significance by using independent t-test with the aid of SPSS-12.0. Difference was considered significant when $p < 0.05$.

Stability Studies

The stability of selected formulations was tested according to International Conference on Harmonization guidelines for zones III and IV. The formulations were stored at accelerated (40 ± 2°/75 ± 5% RH) and long-term (30 ± 2°/65 ± 5% RH) test conditions in stability chambers (Thermotech TH-7007, India) for three months following open dish method. Stability studies indicate that, there was no major difference in moisture content and weight uniformity after storing formulations for three months. Stability studies showed that the physical and chemical properties of the tested batches were not altered significantly and all the test formulations were found to be stable. The evaluation tests of fresh and aged transdermal patch showed no significant effect on drug release ($p > 0.05$).

RESULT AND DISCUSSION

Monolithic device of turmeric oil was attempted to prepare. The placebo films were studied for flexibility, clarity, elasticity and ease of removal of films from molds. The study showed that Polyvinyl Alcohol and HPMC along with plasticizer PEG-400 10% w/v polymer weight were suitable for good flexibility and elasticity. The composition of various transdermal patches is shown in **Table-1**. Drug loaded patches were evaluated for various mechanical and physical properties and the results are shown in **Table-2**. The matrix transdermal drug delivery system bearing turmeric oil was fabricated using various concentration ratios of polyvinyl alcohol and hydroxy propyl methylcellulose and the solvent water and ethyl alcohol.

From the preparation, it was optimised that formulation with 4% and 5% HPMC showed the good result. The evaluation parameters are in range and may be acceptable.

Table 2: Characteristic of Transdermal Patch

S. No	Formulation Code	%Moisture Content ± SD	Thickness (mm.) ± SD	Flatness (%) ± SD	Weight Uniformity (gm.) ± SD	% Elongation at Break
1	TOP-I	1.695 ± 0.0145	0.35 ± 0.0115	94.74 ± 0.4686	0.91 ± 0.0153	65
2	TOP-II	2.424 ± 0.0422	0.37 ± 0.0058	97.43 ± 0.3143	0.93 ± 0.0058	75
3	TOP-III	2.312 ± 0.0200	0.36 ± 0.0153	88.89 ± 0.2318	0.93 ± 0.0100	55
4	TOP-IV	1.156 ± 0.0068	0.33 ± 0.0115	88.89 ± 0.2318	0.96 ± 0.0152	60
5	TOP-V	2.367 ± 0.0748	0.40 ± 0.0100	91.90 ± 0.6033	0.89 ± 0.0115	80
6	TOP-VI	2.941 ± 0.1175	0.39 ± 0.0058	94.74 ± 0.1379	0.90 ± 0.0173	70
7	TOP-VII	2.381 ± 0.0448	0.41 ± 0.0152	97.43 ± 0.3988	0.94 ± 0.0208	85
8	TOP-VIII	2.409 ± 0.0577	0.36 ± 0.0153	94.74 ± 0.1709	0.93 ± 0.1528	60

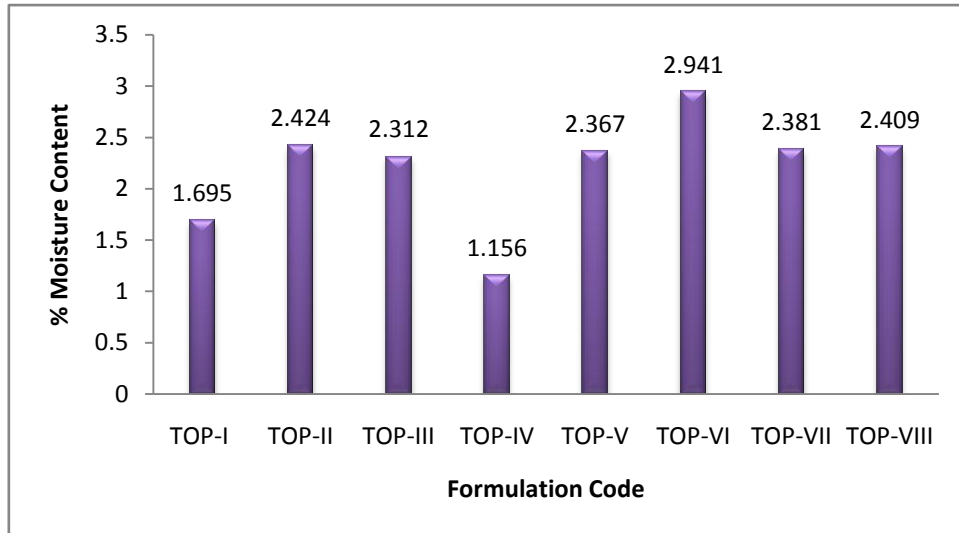


Fig. 2: Percentage Moisture Content of Transdermal Patch

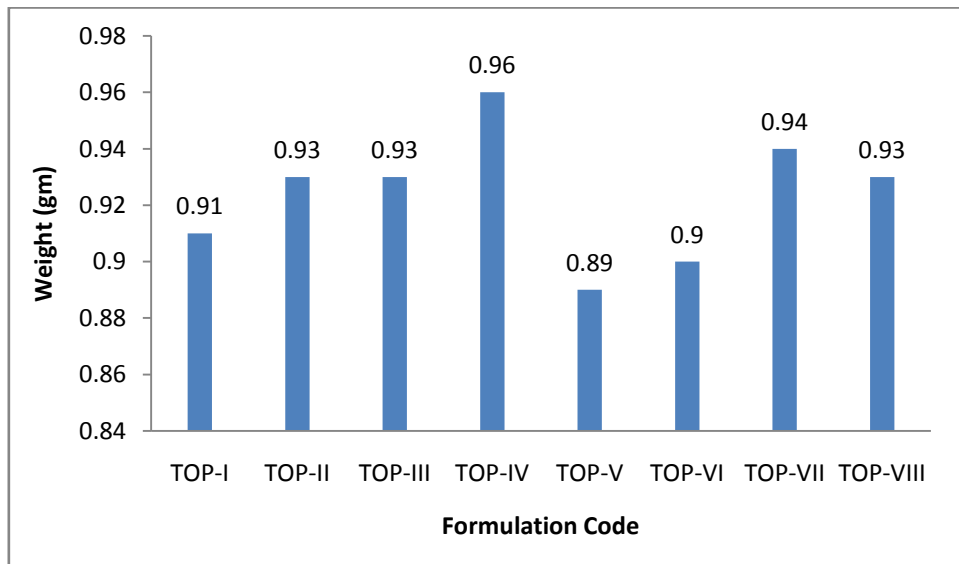


Fig. 3: Weight Uniformity of Transdermal Patch

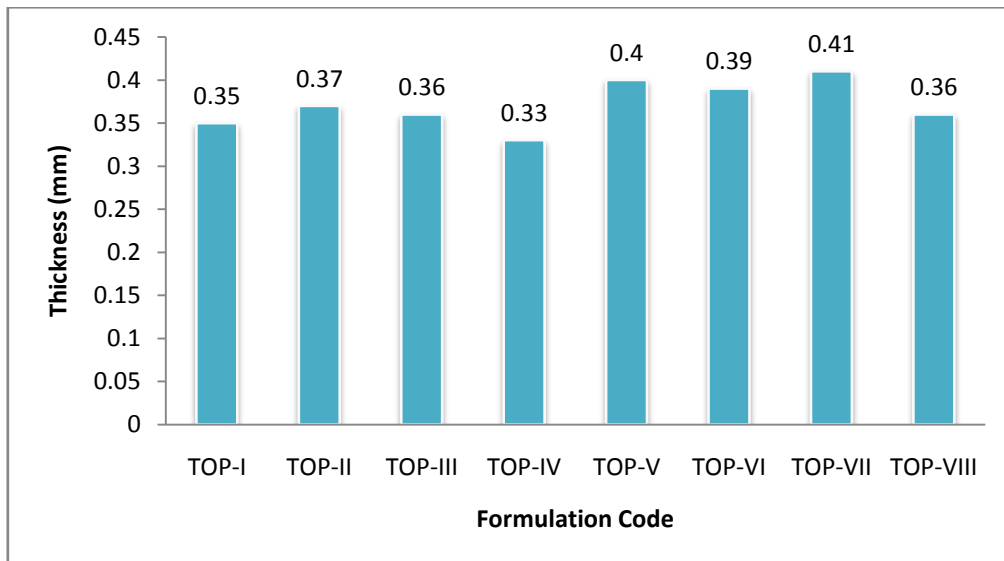


Fig. 4: Thickness of transdermal patches

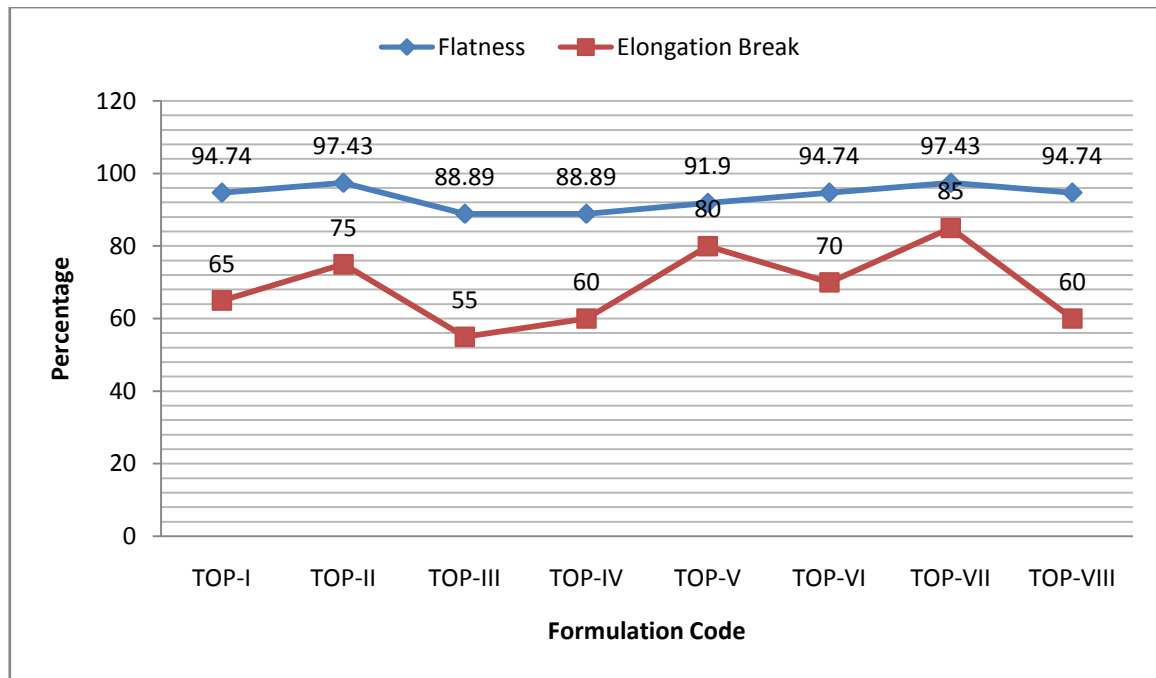


Fig. 5: Percentage Flatness and Elongation Break of transdermal patches

CONCLUSION

From the above results and discussion, it can be concluded that TOP-III (PVA 4% and HPMC 3%) and TOP-IV (PVA 4% and HPMC 4%) showed the best result. This research work highlights that turmeric oil may be incorporated into the transdermal drug delivery system for their suitable and convenient use. Studies have shown promising results; hence, there is a scope for further pharmacodynamic and pharmacokinetic evaluation.

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