

## FORMULATION AND EVALUATION OF METHOTEXATE TRANSDERMAL PATCH BY USING VARIOUS POLYMERS RESEARCH ARTICLE

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Article Received on 29 Jan. 2026,  
Article Revised on 19 Feb. 2026,  
Article Published on 01 March 2026,

<https://doi.org/10.5281/zenodo.18798243>

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**How to cite this Article:** G. Himaja<sup>\*</sup>, L. Nikhitha P., Chitra A. Akshaya M. Sindhu. (2026). Formulation and Evaluation of Methotexate Transdermal Patch By Using Various Polymers Research Article. World Journal of Pharmaceutical Research, 15(5), 740-748.

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### ABSTRACT

The aim of this research is to prepare Methotrexate transdermal patches were formulated using HPMC and PVP as film forming polymers. patches were prepared by solvent casting method and evaluated for physicochemical properties. In order to obtain best optimised products. 9 different formulations were developed different polymers like HPMC, PVP, ethanol, glycerine dissolving in minimal amount of acceptable solvent. the prepared patches evaluate to physical appearance, determination of drug content, in vitro drug release. formulation F9 contain HPMC and PVP (500) shows maximum drug release, produced flexible, smooth films with good mechanical properties. compared to other formulations.

**KEYWORDS:** Methotrexate, Hydroxypropyl methyl cellulose (HPMC), Polyvinylpyrrolidone (PVP), Ethanol, glycerine.

### Novel Drug delivery system

Novel drug delivery system [NDDS] refers to the approaches formulation technologies and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effects. NDDS is a system for delivery of drug other than conventional drug delivery system. NDDS is a combination of advance technique and new dosage form which are far better than conventional dosage form. A novel drug delivery system plays

important role to enhancing the therapeutic efficacy, reducing toxicity increasing patient compliance and enabling entirely new medical treatment.<sup>[1]</sup>

### **Transdermal Patches**

A **transdermal patch** is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. An advantage of transdermal drug delivery route over other types of medication delivery (such as oral, topical, intravenous, or intramuscular) is that the patch provides a controlled release of the medication into the patient, usually through either a porous membrane covering a reservoir of medication or through body heat melting thin layers of medication embedded in the adhesive. The main disadvantage to transdermal delivery systems stems from the fact that the skin is a very effective barrier; as a result, only medications whose molecules are small enough to penetrate the skin can be delivered by this method. The first commercially available prescription patch was approved by the U.S. Food and Drug Administration in December 1979. These patches administer transdermal red scopolamine for motion sickness.<sup>[2,3,4,5]</sup>

### **Cancer**

“Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue”. Cancer is caused by the changes to DNA. Most of the Cancer causing DNA changes occurs in section of DNA called genes. These changes are also called genetic changes.<sup>[6]</sup>

### **MATERIALS AND METHODS**

**Methotrexate:** Methotrexate, is a chemotherapy agent and immune-system suppressant. It is used to treat cancer, autoimmune diseases, and ectopic pregnancies. It is an antimetabolite

**Polyvinylpyrrolidone:** Used as a solubilizing agent, which promotes faster dissolution and improve drug absorption. **Hydroxypropylmethylcellulose [HPMC]:** It act as a matrix forming polymer that controls drug release.

**Polyethylene glycol:** it act as a plasticizer and improving the flexibility and adhesion of the patch. **Ethanol:** Act as a penetration enhancer and increasing the skin permeability.

**Formulation Table**

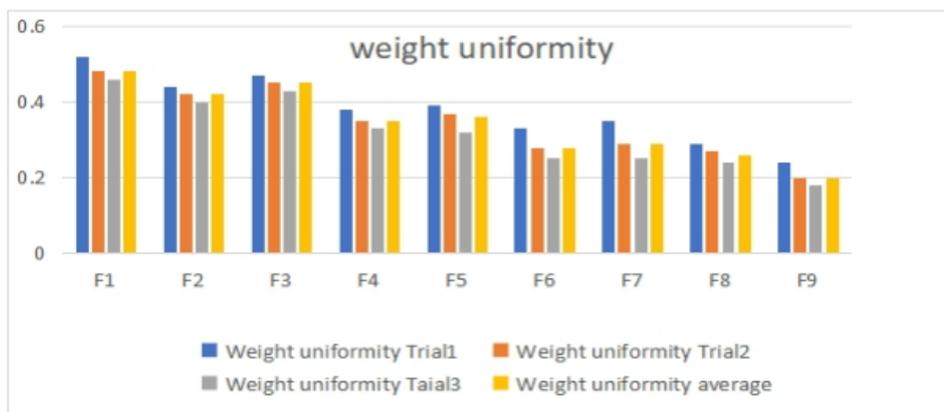
Ingredients	Batches								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Amount of MTX	5	5	5	5	5	5	5	5	5
polyvinylpyrrolidone PVP (mg)	100	100	100	100	100	200	300	400	500
HPMC(mg)	100	200	300	400	500	100	100	100	100
PEG 400	30	30	30	30	30	30	30	30	30
Ethanol	10	10	10	10	10	10	10	10	10
Distilled water v/v ml	10	10	10	10	10	10	10	10	10

**Preparation Of Transdermal Patch By Solvent Casting Method**

Transdermal patch was prepared by a solvent casting method. Precisely weigh the amount of polymer and soak in solvent 24 hrs before the preparation in a prescribed amount of solvent in a beaker. After soaking the polymer by using the glass rod gently mix the polymer solution to form thick viscous solution with less air entrapment. In case of any air bubbles are entrapped in the solution by using sonicator remove their bubbles. Weigh the approximate amount of the drug and transfer it into the mortar and made fine powder and transfer the powdered drug into polymer solution and make clear viscous solution. Transfer the solvent in a petridish which is pre applied with a lubricant. Place the petridish in a room temperature for 24 hrs to remove the moisture content and to form thin film. After forming a thin film it off from the petridish with the help of the ointment spatula and store for the further evaluation tests.

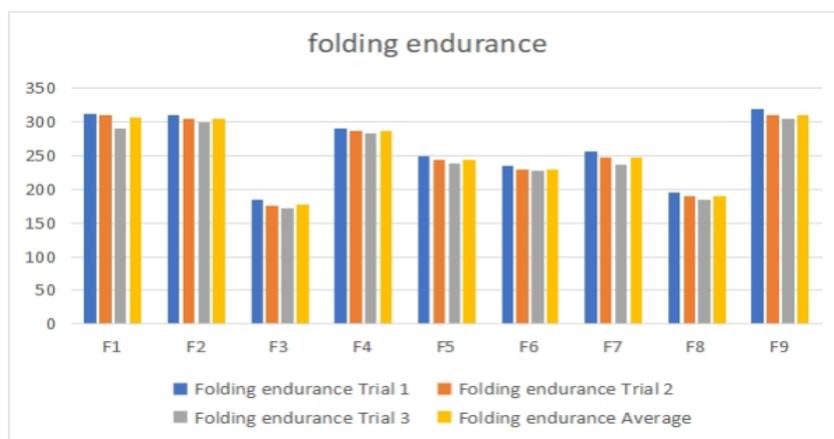
**Evaluation test****weight uniformity**

S.No	Formulation code	Weight uniformity			
		Trial1	Trial2	Trial3	average
1	F1	0.52	0.48	0.46	0.48
2	F2	0.44	0.42	0.40	0.42
3	F3	0.47	0.45	0.43	0.45
4	F4	0.38	0.35	0.33	0.35
5	F5	0.39	0.37	0.32	0.36
6	F6	0.33	0.28	0.25	0.28
7	F7	0.35	0.29	0.25	0.29
8	F8	0.29	0.27	0.24	0.26
9	F9	0.20	0.20	0.18	0.20



### Folding Endurance

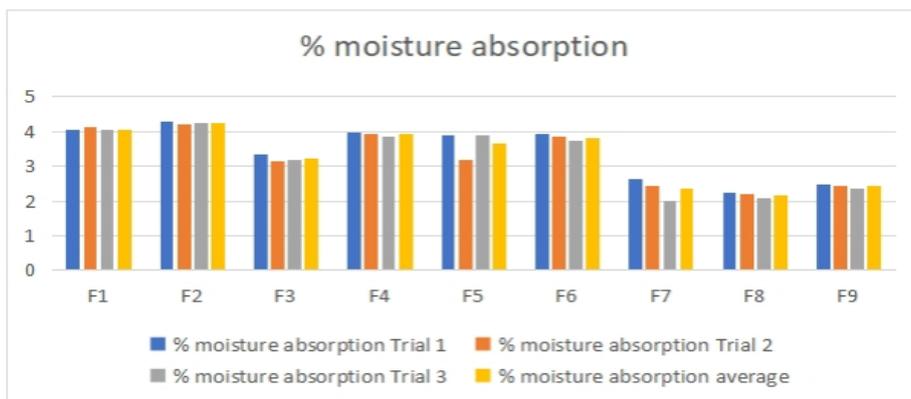
S. No	Formulation Code	Folding endurance			
		Trial 1	Trial 2	Trial 3	Average
1	F1	312	310	290	307
2	F2	310	305	300	305
3	F3	185	176	172	177
4	F4	290	287	283	286
5	F5	250	244	238	244
6	F6	234	230	228	230
7	F7	256	248	237	247
8	F8	195	190	185	190
9	F9	320	310	305	311



### Percentage Moisture Absorption

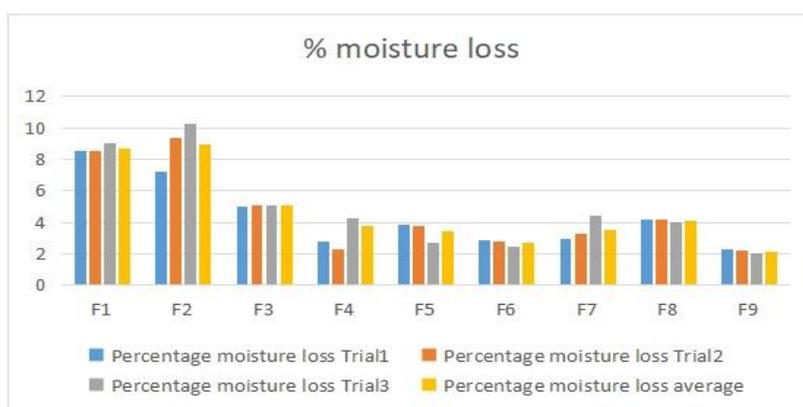
S no	Formulation Code	% moisture absorption			
		Trial 1	Trial 2	Trial 3	average
1	F1	4.03	4.13	4.03	4.06
2	F2	4.29	4.19	4.24	4.24
3	F3	3.35	3.15	3.20	3.23
4	F4	3.97	3.92	3.87	3.92
5	F5	3.88	3.19	3.89	3.65
6	F6	3.93	3.84	3.72	3.83
7	F7	2.63	2.44	2.02	2.36

8	F8	2.23	2.19	2.08	2.16
9	F9	2.46	2.43	2.37	2.42



### Percentage Moisture Loss

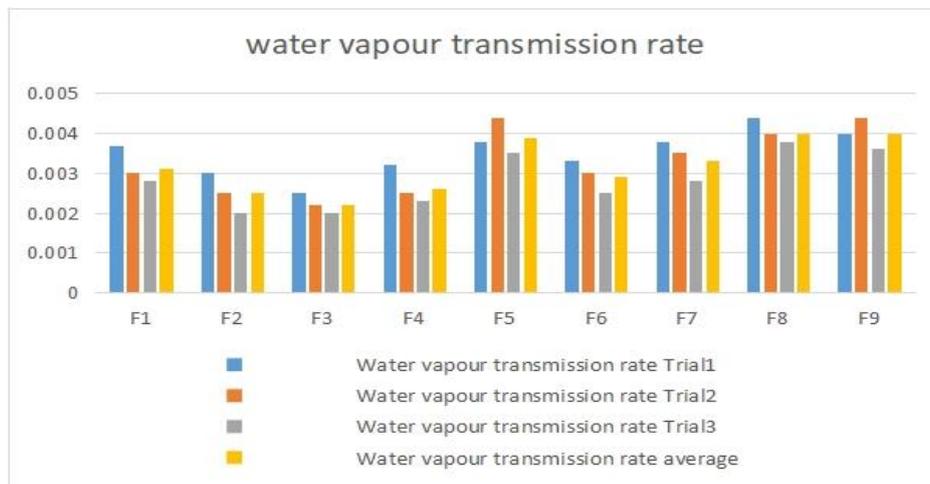
S No	Formulation code	Percentage moisture loss			
		Trial1	Trial2	Trial3	average
1	F1	8.56	8.53	9.02	8.70
2	F2	7.22	9.36	10.27	8.95
3	F3	5.04	5.07	5.05	5.05
4	F4	2.75	2.27	4.23	3.75
5	F5	3.89	3.76	2.67	3.44
6	F6	2.87	2.78	2.47	2.70
7	F7	2.98	3.25	4.46	3.56
8	F8	4.20	4.15	4.05	4.13
9	F9	2.25	2.19	2.03	2.15



### Water vapour transmission rate

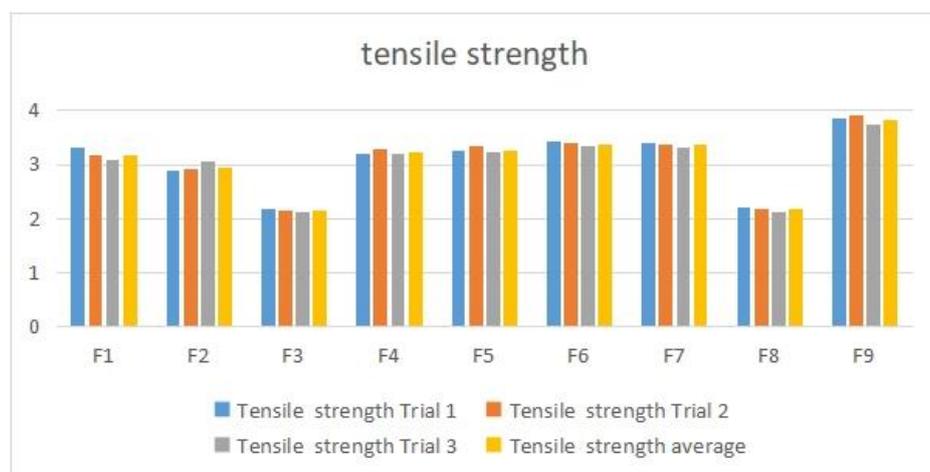
S no	Formulation code	Water vapour transmission rate			
		Trial1	Trial2	Trial3	average
1	F1	0.0037	0.0030	0.0028	0.0031
2	F2	0.0030	0.0025	0.0020	0.0025
3	F3	0.0025	0.0022	0.0020	0.0022
4	F4	0.0032	0.0025	0.0023	0.0026

5	F5	0.0038	0.0044	0.0035	0.0039
6	F6	0.0033	0.0030	0.0025	0.0029
7	F7	0.0038	0.0035	0.0028	0.0033
8	F8	0.0044	0.0040	0.0038	0.0040
9	F9	0.0040	0.0044	0.0036	0.004



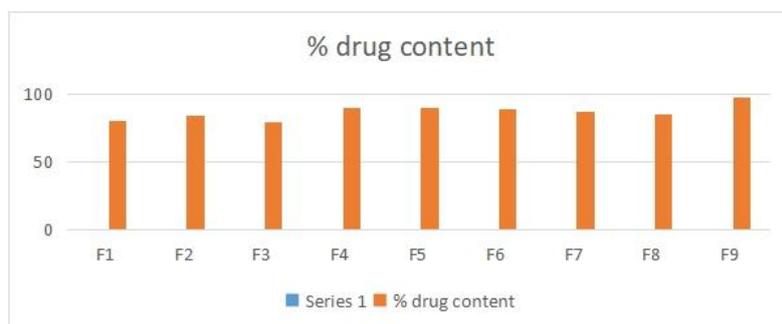
### Tensile strength

S. No	Formulation code	Tensile strength			
		Trial 1	Trial 2	Trial 3	average
1	F1	3.30	3.16	3.10	3.18
2	F2	2.89	2.91	3.05	2.95
3	F3	2.19	2.14	2.11	2.14
4	F4	3.20	3.29	3.20	3.23
5	F5	3.25	3.33	3.23	3.27
6	F6	3.44	3.39	3.33	3.38
7	F7	3.41	3.38	3.32	3.37
8	F8	2.21	2.18	2.13	2.17
9	F9	3.85	3.90	3.75	3.83



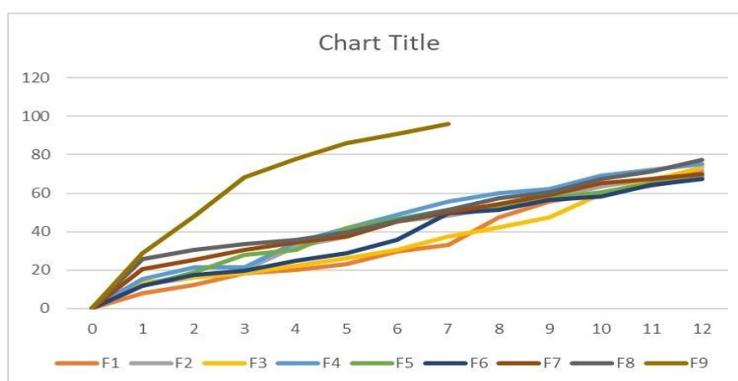
## Drug Content

S. No	Formulation Code	Concentration (mg/cm <sup>2</sup> )	% Drug Content
1	F1	1.82±0.054	81
2	F2	1.177±0.073	84
3	F3	1.028±0.012	80
4	F4	1.078±0.045	90
5	F5	1.067±0.037	90.52
6	F6	1.058±.022	89
7	F7	1.047±0.019	87.04
8	F8	1.033±0.017	85.54
9	F9	1.87±0.075	98



## In vitro drug distribution study

S. No	time [hrs]	Percentage cumulative drug release								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	1	8.057	12.147	13.586	15.49	11.754	11.718	20.452	25.586	28.574
2	2	12.162	16.056	16.292	21.52	18.748	17.711	25.446	30.570	47.721
3	3	18.247	20.253	18.302	21.58	27.752	19.670	30.389	33.567	68.281
4	4	20.123	32.302	22.375	34.63	30.650	24.674	34.286	35.556	77.712
5	5	23.154	37.348	26.382	41.72	41.623	28.654	37.263	39.543	85.816
6	6	29.562	45.370	30.421	48.76	46.604	35.523	45.246	45.537	90.886
7	7	33.325	48.412	37.404	55.88	51.520	49.519	50.223	51.529	95.890
8	8	47.462	52.423	42.435	59.92	53.590	51.500	54.219	57.513	
9	9	55.578	57.504	47.482	62.256	57.516	56.450	59.200	60.502	
10	10	60.222	63.526	59.498	69.278	60.498	58.423	65.192	67.470	
11	11	63.812	67.573	66.512	72.306	65.420	64.320	67.176	71.350	
12	12	68.421	71.589	73.533	75.330	69.300	67.290	70.163	77.420	



## CONCLUSION

The methotrexate transdermal patches showed good physical, mechanical, and stability characteristics. The tensile strength and WVTR values indicated strong and stable patches suitable for skin application. Transdermal patches was prepared by solvent casting method we prepared total 9 formulations with different ratios among all those formulations F9 contain HPMC and PVP (500mg). According to evaluation tests F9 shows best drug release profile. Therefore, we concluded F9 is the best formulation.

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