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FORMULATION AND EVALUATION OF DOXORUBICIN TRANSDERMAL PATCHES

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ABSTRACT

Doxorubicin is a widely used anti-cancer drug which also has a comparatively good therapeutic effect against Rheumatoid Arthritis. This study shows a newer approach to treatment of Rheumatoid Arthritis with Doxorubicin using an transdermal formulation for Doxorubicin with easily available polymers like Hydroxy propyl methyl cellulose, Sodium alginate, Polyethylene Glycol etc using solvent casting technique and conduct *in-vitro* evaluation tests to prove the stability and efficacy of the same.

KEYWORDS

Doxorubicin, Transdermal Patches, Polymers, Plasticizer and Stability.

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INTRODUCTION

Transdermal delivery provides controlled, constant administration of the drug and allows continuous input of drugs with short biological half-lives and eliminates pulsed entry into systemic circulation. TDDS offers many advantages over conventional injection and oral methods. It reduces the load that the oral route commonly places on the digestive tract and liver. It enhances patient compliance and minimizes harmful side effects of a drug caused from temporary overdose. It is convenient, especially notable in patches which require only once weekly application. Such a simple dosing regimen aids in patient adherence to drug therapy. The transdermal drug delivery system has attracted considerable attention because of its many

potentials such as better patient compliance, avoidance of gastrointestinal disturbances, hepatic first-pass metabolism and sustained delivery of drugs to provide steady plasma profiles, particularly for drugs with short half-lives, reduction in systemic side effects and enhanced therapeutic efficacy.

With different types of transdermal delivery systems available, those can be used for developing formulations of drugs that are pronounced effective but not suitable for oral administration. This would help in proper use of Pharmaceutics and to lend a helping hand to patients with GIT problems and others.

MATERIAL AND METHODS

The patches were prepared with various Polymers and Enhancers. Standard solutions were prepared as per IP and used for various studies.

Doxorubicin was a gift sample from Maysa Labs Pvt. Ltd., Hyderabad, India. HPMC, Sodium alginate, Ethyl cellulose, Propylene Glycol, Ethanol were purchased from Hi-Pure Fine Chem Industries, Chennai.

Composition of Doxorubicin Transdermal Patches

Formulation Table of Doxorubicin Transdermal Patches with HPMC

METHODOLOGY

Preparation of Transdermal Patches

Transdermal patches prepared are of matrix diffusion-controlled system, prepared by solvent casting technique by using Hydroxy Propyl Methyl Cellulose, Sodium Alginate and Ethyl Cellulose as Polymer. Casting is a process in which liquid or molten form is poured into a moulds of desired shape and allowed to form a rigid object that reproduces the shape of the mould. Almost all the known polymers can be casted by this technique. The composition of the patches is shown in Table.

Accurately weighed quantities of Hydroxy Propyl Methyl Cellulose and Sodium Alginate were dissolved in 10ml of distilled water separately for each formulation. The solutions were mixed thoroughly and to this required quantity of Polyethylene Glycol was added and then mixed, required Doxorubicin was dissolved in 2.5ml of Ethanol. The drug solutions were poured into the above polymer mixture with continuous stirring with the help of a magnetic stirrer and kept aside for 10 minutes to avoid entrapment of air bubbles. The mixtures were poured into separate Petri dishes and closed with an inverted funnel and was allowed to stand for 24 hours. After drying, the transdermal films were carefully peeled off from the Petri dish, wrapped in aluminum foil and stored in desiccators.

RESULTS

Table No.1: Drug content uniformity

S.No	Formulation Code	Doxorubicin	HPMC	Sodium Alginate	PEG	Ethanol	Water
1	$DTFH_1$	50mg	150mg	-	40mg	2.5ml	10ml
2	$DTFH_2$	50mg	200mg	50mg	40mg	2.5ml	10ml
3	$DTFH_3$	50mg	300mg	100mg	50mg	2.5ml	10ml
4	$DTFH_4$	50mg	350mg	150mg	50mg	2.5ml	10ml
5	$DTFH_5$	50mg	200mg	150mg	60mg	2.5ml	10ml
6	$DTFH_6$	50mg	200mg	170mg	60mg	2.5ml	10ml
7	$DTFH_7$	50mg	250mg	150mg	70mg	2.5ml	10ml
8	$DTFH_8$	50mg	350mg	100mg	70mg	2.5ml	10ml
9	$DTFH_9$	50mg	400mg	150mg	80mg	2.5ml	10ml
10	$DTFH_{10}$	50mg	300mg	150mg	80mg	2.5ml	10ml

Table No.2: Drug content of transdermal patches

S.No	Formulation Code	Theoretical Value(in mg)	Practical Value (in mg)	% Drug Content
1	$DTFH_1$	50	47.25	94.50
2	$DTFH_2$	50	46.67	93.34
3	$DTFH_3$	50	46.47	92.94
4	$DTFH_4$	50	48.82	97.64
5	$DTFH_5$	50	47.64	95.28
6	$DTFH_6$	50	48.25	96.50
7	$DTFH_7$	50	47.85	95.70
8	$DTFH_8$	50	47.46	94.92
9	$DTFH_9$	50	46.25	92.50
10	$DTFH_{10}$	50	47.85	95.709

***In vitro* Release of $DTFH_4$**

Table No.3: *In vitro* diffusion studies data of formulation *$DTFH_4$*

S.No	Time (in hours)	Cumulative % of drug release
1	1	4.57
2	2	7.65
3	3	13.57
4	4	17.49
5	5	22.21
6	6	26.48
7	8	35.48
8	12	53.87
9	18	78.61
10	24	97.64

Table No.4: Combined data of *in-vitro* diffusion study of Transdermal patches

S.No	Time	Cumulative percentage drug release (%)									
	(Hr)	$DTFH_1$	$DTFH_2$	$DTFH_3$	$DTFH_4$	$DTFH_5$	$DTFH_6$	$DTFH_7$	$DTFH_8$	$DTFH_9$	$DTFH_{10}$
1	1	3.25	4.21	3.89	4.57	4.63	4.24	4.96	3.49	3.15	4.63
2	2	7.84	7.45	6.21	7.65	8.01	8.11	8.88	7.95	7.01	8.01
3	3	12.02	13.01	13.21	13.57	12.55	13.25	12.43	12.05	10.25	12.55
4	4	15.64	16.87	16.87	17.49	16.87	17.47	17.58	16.17	15.84	16.87
5	5	22.47	21.52	21.52	22.21	21.36	20.36	21.26	20.26	21.36	21.36
6	6	26.98	25.66	25.66	26.48	24.88	24.78	27.48	22.56	23.08	24.88
7	8	34.51	32.48	32.48	35.48	32.98	33.88	33.45	30.85	32.98	32.98
8	12	51.49	52.47	52.47	53.87	52.46	53.21	56.45	51.45	50.46	52.46
9	18	78.54	77.48	74.64	78.61	76.01	76.45	78.54	75.26	71.11	76.01
10	24	94.50	93.94	92.94	97.64	95.28	96.50	95.70	94.92	92.50	95.70

Drug Release Kinetic Studies

Zero order drug release kinetics

Table No.5: Zero order Drug Release Kinetics Data

S.No	Time (in Hours)	Cumulative % drug release
1	1	4.57
2	2	7.65
3	3	13.57
4	4	17.49
5	5	22.21
6	6	26.48
7	8	35.48
8	12	53.87
9	18	78.61
10	24	97.64

Table No.6: Higuchi Plot

S.No	Square Root of Time (in Hours)	Cumulative % drug release
1	1	0.6599
2	1.4142	0.8836
3	1.7320	1.1325
4	2	1.2427
5	2.2360	1.3465
6	2.4494	1.4229
7	2.8284	1.5499
8	3.4641	1.7313
9	4.2426	1.8954
10	4.8989	1.9896

Table No.7: Korsmeyer - Peppas plot

S.No	Time (in Hours)	Log Cumalative % drug release
1	0	0.6599
2	0.3010	0.8836
3	0.4771	1.1325
4	0.6020	1.2427
5	0.69.89	1.3465
6	0.7781	1.4229
7	0.9030	1.5499
8	1.0792	1.7313
9	1.2553	1.8954
10	1.3802	1.9896

Table No.8: Kinetic Studies

Zero Order	Higuchi Plot	Korsmeyer- Peppas Plot
r^2	r^2	r^2
0.992	0.931	0.987

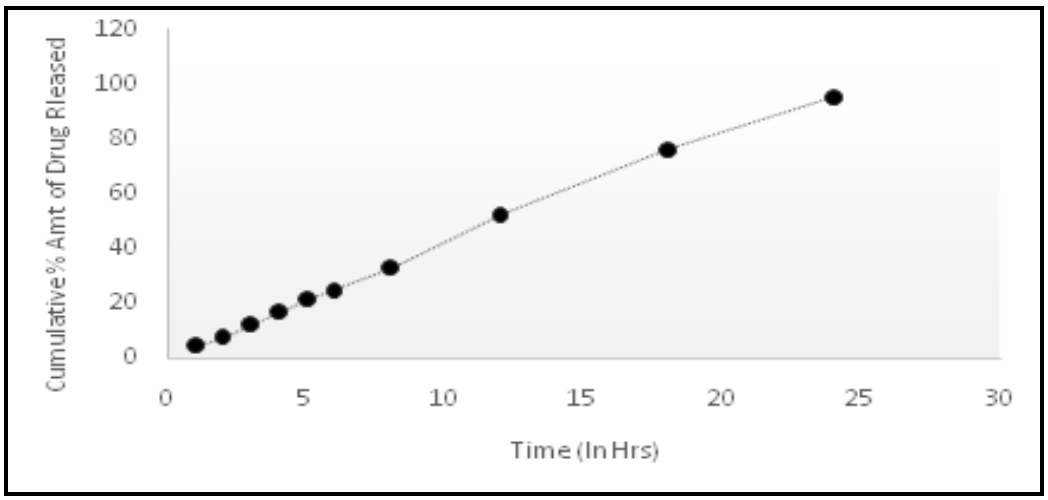
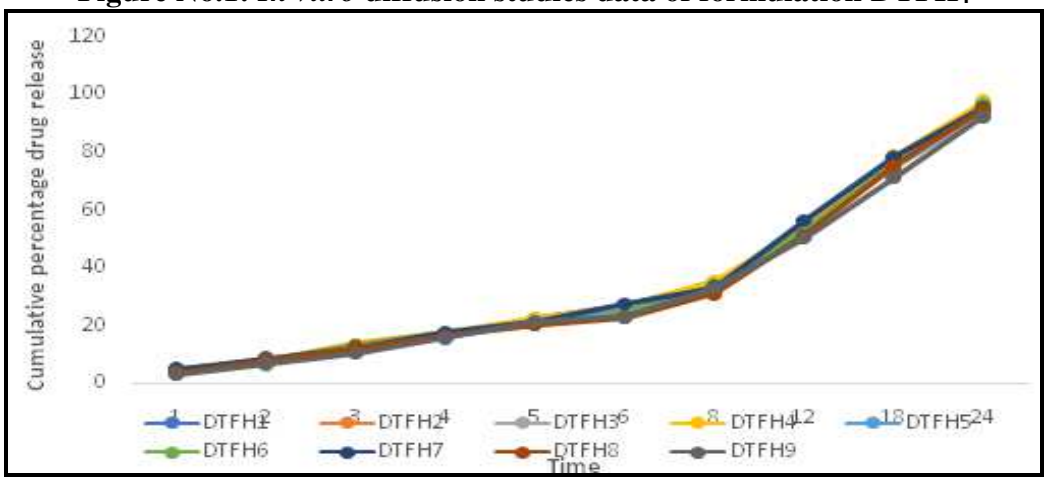


Figure No.1: *In vitro* diffusion studies data of formulation DTFH$_4$



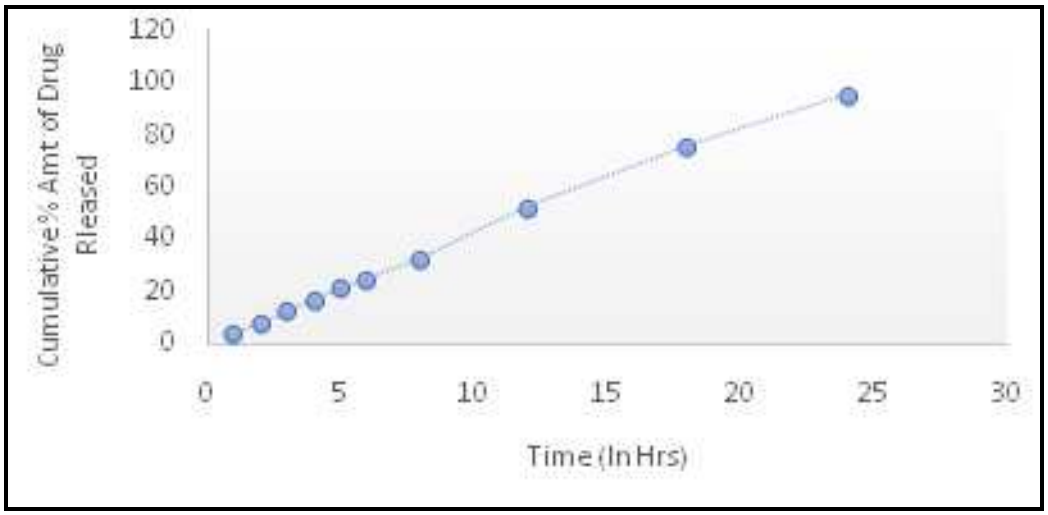


Figure No.2: Zero order Drug Release Kinetics

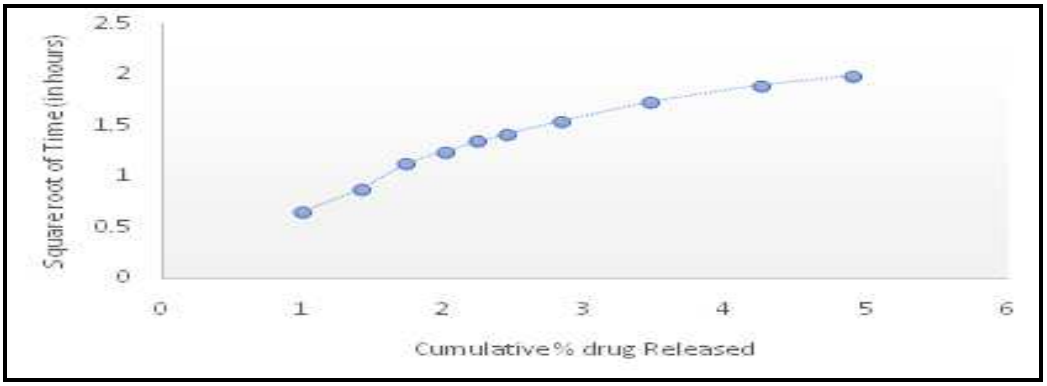


Figure No.3: Higuchi Plot

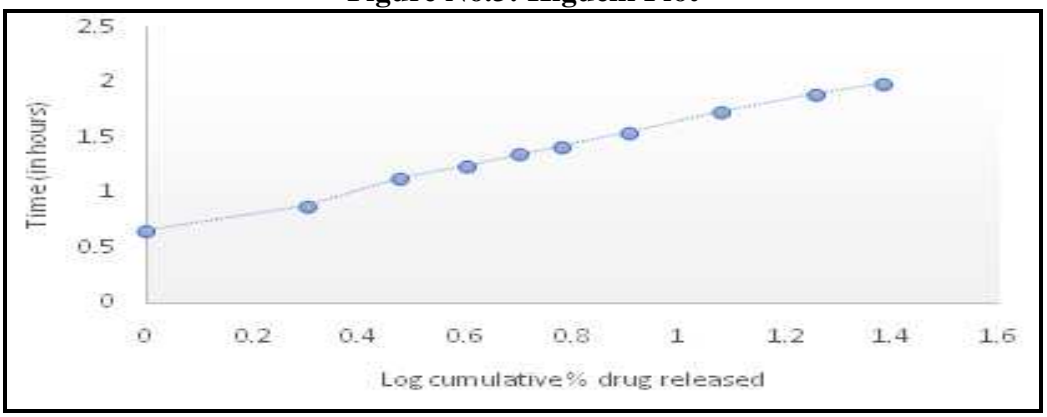


Figure No.4: Korsmeyer - Peppas plot

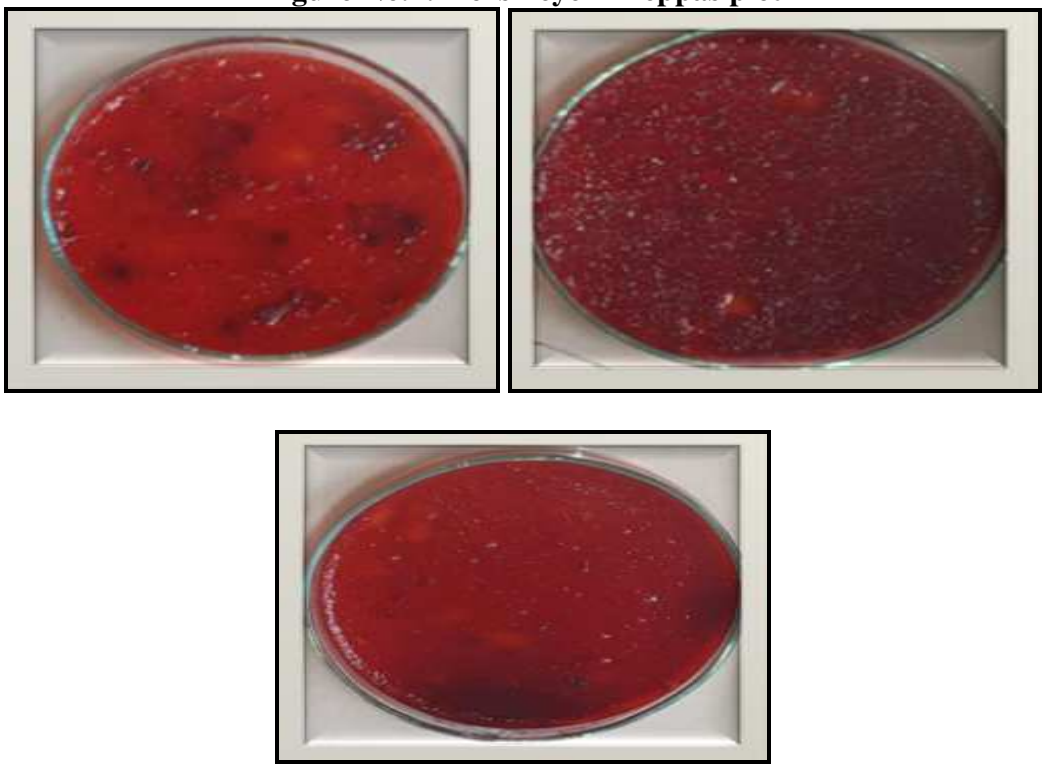


Figure No.5: Formulation of Doxorubicin Patches

SUMMARY AND CONCLUSION

The aim of present study is to formulate and evaluate Doxorubicin transdermal patches using HPMC and Sodium Alginate polymeric systems by incorporating PEG as plasticizer. The Formulations $DTFH_1$, $DTFH_2$, $DTFH_3$, $DTFH_4$, $DTFH_5$, $DTFH_6$, $DTFH_7$, $DTFH_8$, $DTFH_9$, $DTFH_{10}$ were prepared by Solvent Casting method and found to be stable formulations. Hence, the formulation with Drug + HPMC was selected for further evaluation. $DTFH_4$ is selected as an optimized formulation because of better folding endurance, drug content, percentage flatness, weight uniformity and *In vitro* diffusion release of 97.64% at the end of 24 Hours.

From the results of weight uniformity and thickness, it can be inferred that all the formulations exhibited uniform weight and thickness. This indicates that the polymeric solution of the drug is well dispersed in patches. Percentage flatness showed that the physical integrity of the patches was excellent and folding endurance reveals very good flexibility of patches. It follows zero order kinetics and release mechanism was Korsmeyer -Peppas model.

Hence it can be concluded that Doxorubicin can be prepared in the form of transdermal patches by solvent casting method using HPMC and Sodium Alginate in different ratios showed satisfactory results in the evaluation test and emerge as an excellent drug delivery system.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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