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FORMULATION AND EVALUATION OF ACECLOFENAC SODIUM TRANSDERMAL PATCH

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ABSTRACT
The present study provides controlled constant administration of the drug Aceclofenac sodium and allows continuous input of the drugs with short biological half life and eliminates pulsed entry into systemic circulation by transdermal drug delivery system. The formulations were prepared by Solvent Casting method and evaluated for folding endurance, drug content, percentage flatness, weight uniformity and invitro release and produces satisfactory results in the evaluation test and emerge as an excellent drug delivery system.

KEYWORDS: Solvent casting, Polymer, drug delivery, Permeation.

INTRODUCTION
Transdermal medication delivers a steady infusion of the drug over prolonged period of time therefore avoiding adverse side effects and therapeutic failure frequently associated with intermittent dosing can also be avoided. Increases therapeutic value of many drugs by avoiding specific problems associated with the drug e.g., gastro-intestinal irritation, low absorption and drug interaction with food, drink and other administered drugs. Avoidance of first pass metabolism because it bypasses the liver. Self-administration is possible and they are non-invasive, avoiding the inconvenience of parenteral therapy.

Composition of Aceclofenac Sodium Transdermal Patches

Table 1: Formulation Table of Aceclofenac Sodium Transdermal Patches.

Formulation Code	Drug Aceclofenac Sodium	HPMC	Sodium Alginate	PEG	Ethanol	Water
ATF1	50mg	150mg	-	40mg	2.5ml	10ml
ATF2	50mg	200mg	50mg	40mg	2.5ml	10ml
ATF3	50mg	300mg	100mg	50mg	2.5ml	10ml
ATF4	50mg	350mg	150mg	50mg	2.5ml	10ml
ATF5	50mg	200mg	150mg	60mg	2.5ml	10ml

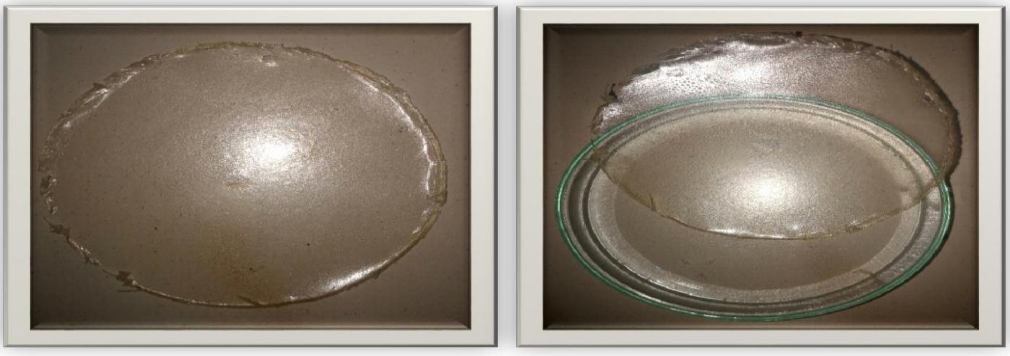


Fig 1.

The formulation of Transdermal Patches of Aceclofenac Sodium is done by Solvent casting method using HPMC and Sodium Alginate as polymeric system and then in corporating PEG as plasticizer. The Polymers and Plasticizer weighed and transferred to a beaker containing water is allowed to mix well in a magnetic stirrer. This procedure is carried out for about 20 minutes until all the ingredients are mixed well and forms a highly viscous solution. The drug being dissolved in adequate amount of ethanol is then added to the solution dropwise while rotating. Allow the solvent and drug to totally dissolve into the polymers and transfer the solution to a Petri dish that is lubricated by applying glycerine on its surface. This Petri dish is covered by an inverted funnel and allowed to dry for about 24-36 hours. The patch once formed is gently and carefully scrapped out of the Petri dish.

Evaluation of Transdermal Patches

Uniformity of thickness[10]

The thickness of patches were determined by using vernier caliper with a least count of 0.01mm.

Thickness was measured at 3 different points on the patch and average readings were taken.

Uniformity of weight

Patch of size 1×1 cm^2 was cut and weight of each patch was taken individually. The average weight was also found out.

Percentage flatness

Longitudinal strips were cut from each patch, one from the centre and two from either side. The length of each strip was measured without applying additional pressure. The variation in length because of non uniformity in flatness was measured by determining percent constitution equivalent to 100%.

Folding endurance

Folding endurance was measured manually for the prepared patches. A strip of patch of dimension 2×2 cm^2 was cut and repeatedly folded on the same place till it broke. The number of times the patch can be folded at the same place without any breakage gave the value of folding endurance.

Uniformity of drug content

Patches of size 1cm^2 was cut and placed in 100 ml volumetric flask. The contents were stirred using a magnetic bead for 24hours inorder to dissolve the patches. Subsequent dilutions were made with phosphate buffer solution of pH 7.4. The absorbance of the solution was measured against the corresponding blank solution at 225nm for Aceclofenac Sodium, using U V spectrophotometer. The experiment was repeated thrice to validate the result.

In vitro diffusion studies of transdermal patch[12]

The formulated patch was cut into 1cm^2 and placed on commercial semipermeable membrane with a pore size of 0.22mm (regenerated cellulose which was permeable to low molecular weight substances) and attached to the diffusion cell such that the cell's drug releasing surface was towards the receptor compartment filled with phosphate buffer solution of pH 7.4 at 37±0.5^{0}C. The elution medium was stirred magnetically.Aliquots(1ml) was withdrawn at predetermined time intervals and replaced with same volume of phosphate buffer of pH 7.4. The samples were analyzed for drug contents using U V spectrophotometer at 225nm.

Drug Release Kinetic Studies

Zero order

The diffusion model of Aceclofenac Sodium Transdermal Patch follows the Zero order kinetics. The graph is plotted on as Time vs Cumulative percentage drug released.

Huguchi Plot

The diffusion model of Aceclofenac Sodium Transdermal Patch is shown in a Huguchi Plot.

The graph is plotted on as Square root of Time vs Cumulative percentage drug released.

Korsmeyer – Peppas Plot

The release mechanism of Aceclofenac Sodium Transdermal Patch is represented by using a Korsmeyer - Peppas Plot. The graph is plotted on as Time vs Log Cumulative percentage drug released.

RESULTS AND DISCUSSION.

Thickness

Table 2.

SL.NO.	FORMULATION CODE	THICKNESS(mm)			Mean (mm)
		Trial 1	Trial 2	Trial 3	
1.	ATF1	0.20	0.22	0.21	0.2100
2.	ATF2	0.22	0.20	0.21	0.2100
3.	ATF3	0.18	0.19	0.19	0.1900
4.	ATF4	0.21	0.19	0.20	0.2000
5.	ATF5	0.19	0.19	0.19	0.1900

The result indicates that there was no much difference in the thickness within the formulations. The thickness of the optimized patch ATF4 was found to be 0.2000 mm. The variation in thickness may be due to difference in the concentration of the polymers.

Weight uniformity

Table 3

S. No	Formulation Code		Weight		Mean
		Trial 1	Trial 2	Trial 3	(mg)
1	ATF1	0.041	0.043	0.041	0.0416
2	ATF2	0.034	0.032	0.032	0.0326
3	ATF3	0.032	0.029	0.030	0.0303
4	ATF4	0.033	0.033	0.031	0.0323
5	ATF5	0.034	0.033	0.033	0.0333

The result indicates that the individual weight of the optimized formulation ATF4 has not deviated significantly form average weight

Percentage flatness

Table 5

S. No	Formulation Code	Initial Length (in cm)	Final Length (in cm)	% Flatness Mean
1.	ATF1	5.4	5.40	100
2.	ATF2	5.4	5.40	100
3.	ATF3	5.4	5.50	98.18
4.	ATF4	5.4	5.40	100
5.	ATF5	5.4	5.51	98

The percentage flatness is determined by percent constriction. Zero percent constriction of optimized formulation ATF4 yields 100 percent flatness.

Folding Endurance.

Table 6.

S. NO	FORMULATION CODE	FOLDING ENDURANCE			MEAN (mg)
		Trial 1	Trial 2	Trial 3	
1	ATF1	226	235	228	229.66
2	ATF2	238	247	240	241.66
3	ATF3	237	234	242	237.66
4	ATF4	258	259	257	258
5	ATF5	245	246	246	246

The folding capacity of the films subjected to extreme conditions of folding. The folding endurance value of optimised formulation is found to be 258.

Drug content uniformity

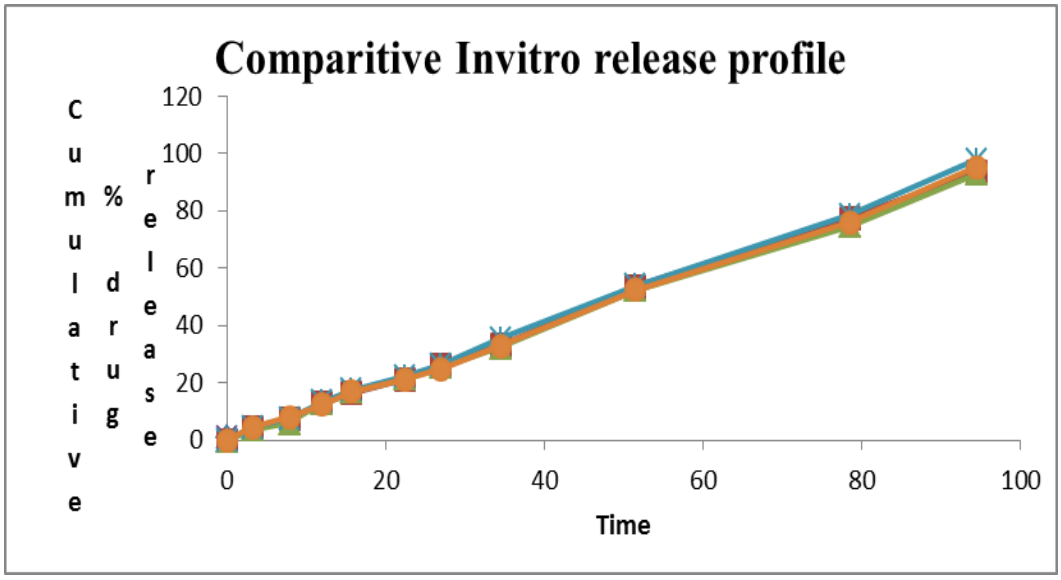
Table 7.

S. No	Formulation Code	Theoretical Value (in mg)	Practical Value (in mg)	% Drug Content
1.	ATF1	50	47.25	94.50
2.	ATF2	50	46.67	93.34
3.	ATF3	50	46.47	92.94
4.	ATF4	50	48.82	97.64
5.	ATF5	50	47.64	95.28

In vitro diffusion studies

Table 8

S.No	Time	Cumulative % drug release				
		ATF1	ATF2	ATF3	ATF4	ATF5
		0	0	0	0	0
1	1	3.25	4.21	3.89	**4.57**	4.63
2	2	7.84	7.45	6.21	**7.65**	8.01
3	3	12.02	13.01	13.21	**13.57**	12.55
4	4	15.64	16.48	16.87	**17.49**	16.87
5	5	22.47	21.25	21.52	**22.21**	21.36
6	6	26.98	26.47	25.66	**26.48**	24.88
7	8	34.51	33.21	32.48	**35.48**	32.98
8	12	51.49	53.75	52.47	**53.87**	52.46
9	18	78.54	77.48	74.64	**78.61**	76.01
10	24	94.5	93.34	92.94	**97.64**	95.28



Transdermal patches of Aceclofenac Sodium Was taken for Invitro Diffusion study.

The formulation ATF4 has a release of 97.64% at 24 Hours due to the concentration of polymers. So the formulation ATF4 is as optimized formulation for effective drug delivery.

Drug Release Kinetic Studies

Zero Order	Higuchi Plot	Korsmeyer – Peppas Plot
r^2	r^2	r^2
0.989	0.921	0.989

SUMMARY AND CONCLUSION

Formulation of Aceclofenac Sodium transdermal patch using HPMC and Sodium Alginate polymeric systems by incorporating PEG as plasticizer. The Formulations ATF1, ATF2, ATF3, ATF4, ATF5 were prepared by Solvent Casting method. ATF4 is selected as an optimized formulation because of better folding endurance, drug content, percentage flatness, weight uniformity and Invitro 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 patch was excellent and folding endurance reveals very good flexibility of patch.It follows zero order kinetics and release mechanism was Korsmeyer -Peppers model. Hence it can be concluded that Aceclofenac Sodium can be prepared in the form of transdermal patch 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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