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FORMULATION AND EVALUATION OF HERBALTRANSDERMAL PATCH FOR SKIN ALLERGIES

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Abstract

Traditional system of medicine is one of the centuries old practice and long serving companion to humankind in the fight against disease and in leading a healthy life. Indigenous people have been using the unique approach of their traditional system of medicine for centuries and among the most renowned are the Chinese, Indian, African systems of medicine. Traditional medicine refers to any ancient and culturally based healthcare practice differing from scientific medicine and is largely transmitted orally by communities of different cultures.[1] The World Health Organization (WHO) observes that it is difficult to assign one definition to the broad range of characteristics and elements of traditional medicine, but that a working definition is essential. It thus concludes that the traditional medicines ‘‘[include] diverse health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain wellbeing, as well as to treat, diagnose or prevent illness.[2]

Keywords: Traditional system, Ayurveda, herbal transdermal Patch, Azadiracta Indica

Introduction

TRANSDERMAL DRUG DELIVERY SYSTEM

The (TDDS) are defined as self-contained, discrete dosage forms which, when applied to the intact skin, deliver the drug(s), through the skin, at a controlled rate to the systemic circulation. Transdermal drug delivery is a viable administration route for potent, low-molecular weight therapeutic agents which cannot withstand the hostile environment of gastrointestinal tract and/or subject to considerable first-pass metabolism by the liver.

Transdermal drug delivery systems are topically administered medicaments in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate. A transdermal drug delivery device, which may be of an active or a passive design, is a device which provides an alternative route for administering medication. These devices allow for pharmaceuticals to be delivered across the skin barrier.

Advantages of TDDS [15]

This approach to drug delivery offers many advantages over traditional methods:

 As a substitute for the oral route

 Transdermal drug delivery enables the avoidance of gastrointestinal absorption, with its associated pitfalls of enzymatic and pH associated deactivation

 This method also allows for reduced pharmacological dosaging due to the shortened metabolization pathway of the transdermal route versus the gastrointestinal pathway

 The patch also permits constant dosing rather than the peaks and valleys in medication level associated with orally administered medications. Multi-day therapy with a single application. Rapid notification of medication in the event of emergency, as well as the capacity to terminate drug effects rapidly via patch

removal

Disadvantages of TDDS

 The drug that requires high blood levels cannot be administered and may even cause irritation or sensitization of the skin

 The adhesives may not adhere well to all types of skin and may be uncomfortable to wear

 High cost of the product is also a major drawback for the wide acceptance of this product

 Properties that influence transdermal delivery diffusion of the medicament from the vehicle

 Penetration through the skin barrier activation of the pharmacological response

Basic Components of Transdermal Drug Delivery Systems

1. Polymer matrix or matrices

2. The drug

3. Permeation enhancers

4. Other excipients

1. Polymer Matrix

The Polymer controls the diffusion of the drug from the device. Possible useful polymers for transdermal devices are:

a. Natural Polymers: e.g., cellulose derivatives, Zein, Gelatin, Shellac, Waxes, Proteins, Gums and their derivatives, Natural rubber, Starch etc.

b. Synthetic Elastomers: e.g., polybutadieine, Hydrin rubber, Polysiloxane, Silicone rubber, Nitrile, Acrylonitrile, Butyl rubber, Styrene butadieine rubber, Neoprene etc.

c. Synthetic Polymers: e.g., polyvinyl alcohol, Polyvinyl chloride, Polyethylene, Polypropylene, Polyacrylate,Polyamide ,Polyurea, Polyvinyl pyrrolidone, Polymethyl methacrylate, Epoxy etc.

2. Drug

For successfully developing a transdermal drug delivery system, the drug should be chosen with great care. The following are some of the desirable properties of a drug for transdermal delivery.

Physicochemical properties

 The drug should have a molecular weight less than approximately 1000 Daltons

 The drug should have affinity for both lipophilic and hydrophilic phases. Extreme partitioning characteristics are not conducive to successful drug delivery via the skin

 The drug should have low melting point

 Along with these properties the drug should be potent, having short half life and be non- irritating

3. Permeation Enhancers

These are compounds which promote skin permeability by altering the skin as a barrier to the flux of a desired penetrant. These may conveniently be classified under the following main headings:

A. Solvents

These compounds increase penetration possibly by swallowing the polar pathway and/or by fluidizing lipids. Examples include water alcohols – methanol and ethanol; alkyl methyl sulfoxides – dimethyl sulfoxide, alkyl homologs of methyl sulfoxide dimethyl acetamide and dimethyl formamide; pyrrolid- ones- 2 pyrrolidone, N-methyl, 2-purrolidone; laurocapram (Azone), miscellaneous solvents- propylene glycol, glycerol, silicone fluids, isopropyl palmitate.

B. Surfactants

These compounds are proposed to enhance polar pathway transport, especially of hydrophilic drugs. The ability of a surfactant to alter penetration is a function of the polar head group and the hydrocarbon chain length.

 Anionic Surfactants: e.g. Dioctylsulpho - succinate, Sodium lauryl sulphate, Decodecyl- methyl sulphoxide etc. Nonionic Surfactants: e.g. Pluronic F127, Pluronic F68, etc

 Bile Salts: e.g. Sodium mstaurocholate, Sodium deoxycholate, Sodium tauroglycocholate

 Binary system: These systems apparently open up the heterogeneous multilaminate pathway as well as the continuous pathways.e.g. Propylene glycol-oleic acid and 1, 4-butane diollinoleic acid

C. Miscellaneous Chemicals

These include urea, a hydrating and keratolytic agent, N, N-dimethylmtoluamide, calcium thioglycolate, anticholin- ergic agents.

Some potential permeation enhancers have recently been described but the available data on their effectiveness sparse. These include eucalyptol, di-omethyl- ßcyclodextrin and soyabean casein

4. Other Excipients

A. Adhesives: The fastening of all transdermal devices to the skin has so far been done by using a pressure sensitive adhesive which can be positioned on the face of the device and in the back of the device and extending peripherally.

Both adhesive systems should fulfill the following criteria

 Should adhere to the skin aggressively, should be easily removed

 Should not leave an un washable residue on the skin

 Should not irritate or sensitize the skin

The face adhesive system should also fulfill the following criteria

 Physical and chemical compatibility with the drug, excipients and enhancers of the device of which it is a part

 Permeation of drug should not be affected

 The delivery of simple or blended permeation enhancers should not be affected

B. Backing membrane: Backing membranes are flexible and they provide a good bond to the drug reservoir, prevent drug from leaving the dosage form through the top, and accept printing.

It is impermeable substance that protects the product during use on the skin e.g. metallic plastic laminate, plastic backing with absorbent pad and occlusive base plate (aluminium foil), adhesive foam pad (flexible polyurethane) with occlusive base plate (aluminium foil disc) etc.

design is characterized by the inclusion of a liquid compartment containing a drug solution or suspension separated from the diffusion liner by a semi-permeable membrane and adhesive. The adhesive component of the product responsible for skin adhesion can either be incorporated as a continuous layer between the membrane and the diffusion liner or in a concentric configuration around the membrane.

Material and Methods

Preformulation Studies

Preformulation testing is the first step in the rational development of dosage forms of drugs substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavailable dosage forms that can be man produced. The following Preformulation studies are carried out

- Finding the absorption maxima
- Physical appearance
- Solubility
- Standard curve
- Infrared spectroscopy studies (compatibility studies)

Finding the absorption maxima (λ max)

The absorption maxima was found for identification of drug. Ultraviolet Visible spectrophotometry has been used to obtain specific information on the chromophoric part of the molecules. Organic molecules in solutions when exposed to light in the Visible/ Ultraviolet region of the spectrum absorb light of particular wavelength depending on the type of electronic transition associated with the absorption.

The extract solution (5, 10, 15, 20, 25 µg/ml) in distilled water was taken in a standard cuvette and scanned in the range of 200-800 nm in UV spectrophotometer. It exhibits maxima at 382 nm. Therefore, further all measurements were taken at 382 nm.

Collection of *Azadirachta indica* A Juss. leaves

Azadirachta indica A Juss. leaves were collected from Periyar College of Pharmaceutical Sciences campus, Tiruchppalli, Tamilnadu. Collected leaves were authenticated by Botanist, Dept. of Botany, National College, Trichy. Leaves were cleaned and shade dried at room temperature.

Extraction of leaves of *Azadirachta indica* A Juss.[37]

The shade dried leaves were subjected to size reduction and passed in to sieve no 20 and then 40. About 500g of the dried powder was extracted continuously in Soxhlet apparatus with petroleum ether for 24 hrs to remove the waxy materials. Then it was extracted with distilled for 72h. After 72h, the water substance was evaporated to obtain the crude extract (7.4%w/v). The extract was dried under vacuum oven.

Phytochemical Studies [38,39]

The AE (Aqueous Extract) was subjected to phytochemical studies to find out the presence and absence of constituents.

Table No.3: Phytochemical Tests

EXPERIMENT	OBSERVATION	INFERENCE
Test for Alkaloids		

1.Dragendroff's test: The extract was treated withDragendroff's reagent (potassium bismuth iodide solution)	Orange brown Precipitate was formed	Presence of alkaloids
2.Mayers' reagent's: The extract was treated with Mayer's (potassium mercuric iodide solution) reagent	Precipitate formed	Presence of alkaloids
3.Wagner's reagent: The extract was treated with wagner's reagent (iodide and potassium triiodide solution)	Reddish brown Precipitate was formed	Presence of alkaloids
Test for Glycosides		
1.Brontragers test: To the extract add dilute H2SO4 and filtered. Filtrate was extract with little chloroform layer was separated out and add equal volume of dilute NH3.	Red colour observed in ammonical layer	Presence of glycosides
Test for Saponin glycosides		
1.Foam test: Shake the extract with water.	Foam was produced/formed	Presence of saponin Glycosides
Test for Tannins and Phenolic compounds		
1.Ferric chloride test: To the aqueous extract few rops of ferric chloride solution were added	Dark black colour formed	Presence of tannins and phenolic compounds
2.Bromine water test: To the aqueous extract is treated with bromine water	Discoloration of bromine Water	Presence of tannins and phenolic compounds
3.KMnO4test: To the aqueous extract is treated with dilute KMnO4.	Discoloration of solution	Presence of tannins and phenolic compounds.
Test for Reducing sugar		
1.Benedict's test: .5ml of extract solution 1ml of water 5 to 8 drops of fehlings solution was added.	No brick red precipitate	Absence of reducing sugar
Test for Amino acids		

1.Ninhydrin test: The aqueous extract is heated with 5%ninhydrin solution on boiling water bath for 10 min.	No purple colour formed	Presence of amino acids
.The aqueous extract is treated ith solution sodium hydroxide and lead acetate solution and boiled	No black precipitate is formed	Presence of amino acids
Test for Flavonoids		
1.Shinoda test: To the methanol extract add potassium hydroxide solution and then 10% ammonia.	Yellow colour Precipitate formed.	Presence of flavonoids
2.To the ethanol extract, add few drops of Lead acetate solution.	Yellow colour Precipitate formed.	Presence of flavonoids.
Test for Terpenoids		
1.4gm of extract was treated ith 0.5ml of acetic anyhydride and 0.5ml of chloroform and dded concentrated solution of sulphuric acid	No Red violet colour was obtained	Absence of terpenoids
Test for Steroids		
. Libermann- Buchard Test: To extract add chloroform solution a few drops of acetic anhydride and 1ml of con. I2SO4 were added through the side of the test ube and set aside for a while.	Brown ring was formed at the junction.	Presence of steroids
. Salkowski Test: o the extract add chloroform olution few drops of con. I2SO4 was added shaken and llowed o stand.	reenish fluorescence was ormed.	resence of steroids
. Libermann's Reaction: Mix ml of extract with 3ml of acetic nhydride, heat and cool. Add ew drops of Con. H2SO4.	lue colour was formed	resence of steroids

Preparation of Transdermal Patch [40]

Six batches of Aqueous Extract of leaves of *Azadirachta indica* A. Juss. transdermal patches were prepared using drug with two different polymer in three different ratio (1:4,1:6 &1:8). Weighed quantity of polymer was dissolved in calculated quantity of water and heated on a water bath. Calculated amount of extract was added to the above mixture and stirred well until a homogenous mixture was formed. Then calculated amount of permeation enhancer and glycerin were added. In all the six batches the quantity of extract was same.

The resultant mixture was poured into a Petridish and air dried at room temperature for 24h.The patches were then peeled off from the Petridish with the help of a knife and kept in desiccator.

Table No.4: Formula for TDDS

Ingredients	Formulation Code					
	TP1	TP2	TP3	TS4	TS5	TS6
Aqueous Extract (mg)	40	40	40	40	40	40
Pectin (mg)	150	230	310	-	-	
S.Alginate (mg)	-	-	-	150	230	310
DMSO (ml)	0.3	0.3	0.3	0.3	0.3	0.3
Glycerin (ml)	0.3	0.3	0.3	0.3	0.3	0.3
Water	q.s	q.s	q.s	q.s	q.s	q.s

Preparation of Calibration curve of *Azadirachta indica* A. Juss. Extract

Accurately weighed quantity (100mg) of AE was transferred into a 100ml volumetric flask and dissolved in small amount of distilled water (D.W) and made up to the volume to make the standard stock solution of 1 mg/ml.

From the stock, 1ml was taken in 10ml volumetric flask and made up the volume with the buffer; from this solution 0.5ml to 3ml solution was transferred to 10ml volumetric flask and made up to required volume with more D.W and the resulting concentration ranges from 5 to 50 µg/ml. The absorbance of these solutions was determined at 382nm using UV spectrophotometer. The calibration curve was constructed between the absorbance and concentration.

Preparation of phosphate buffer pH 7.4

Phosphate buffer pH 7.4 was prepared as per the method described in I.P 1996 using disodium hydrogen phosphate and sodium hydroxide. The pH was adjusted to 7.4 prior to quantitative estimation.

Physico chemical evaluation of *Azadirachta indica* A.Juss. Transdermal Patch [41,42]

Formulated patches were subjected to the preliminary evaluation tests. Patches with any imperfections, entrapped air, or differing in thickness, weight (or) content uniformity were excluded from further studies.

1. **Uniformity of weight**This was done by weighing five different patches of individual batch taking the uniform size at random and calculating the average weight of three. The tests were performed on patch which was dried at 60˚C for 4 h prior to testing.

2. **Thickness of the Patch**

The thickness of the patch was assessed by using digital vernier caliper at different points of the patch. From each formulation three randomly selected patches were used. The average value for thickness of a single patch was determined.

3. **Drug content determination**

The patches were taken and added to a beaker containing 100 ml of D.W. The medium was stirred magnetic bead for 5 h. The solution was later filtered and analyzed for drug content with proper dilution at 382 nm spectrophotometrically.

4. Folding Endurance

This was determined by repeatedly folding one patch at the same place till it broke. The number of times the patch could be folded at the same place without breaking gave the value of folding endurance.

5. Percentage Moisture uptake

The patch were weighed accurately and placed in desiccators containing aluminium chloride. After 24 h, the patch were taken out and weighed. The percentage moisture uptake was calculated as the difference between final and initial weight. With respect to initial weight. It is calculated by using following formula.

Final weight – Initial weight

Percentage moisture content =

X 100 Initial weight

6. Percentage Moisture content The patch were weighed and kept in desiccators containing calcium chloride. After 24h the patch were taken out and weighed. The percentage moisture content was calculated using the following formula.

Initial weight –Final weight

Percentage moisture content = X 100 Initial weight

7. Determination of surface pH

The patches were allowed to swell by keeping them in contact with 1 ml of distilled water for 2 h at room temperature and pH was noted down by bringing the electrode in contact with the surface of the patch, allowing it to equilibrate for 1 min.

8. Percent Elongation

When stress is applied, a patch sample stretches and this is referred to as strain. Strain is basically the deformation of patch divided by original dimension of the sample. Generally elongation of patch increases as the plasticizer content increases. It is calculated by using following formula.

Increase in length of patch

Percentage elongation = X 100

Initial length of patch

9. Tensile strength

Tensile strength is the maximum stress applied to a point at which the patch specimen breaks. It is calculated by the applied load at rupture divided by the cross- sectional area of the strip as given in the equation below

Load at failure

Percentage elongation = X 100

Patch thickness x Patch width The results of Physico chemical parameters are shown in Table:14

Cellophane Membrane Treatment

Cellophane membrane was boiled in the D.W for 1 h and washed with fresh D.W for three times and kept in ethanol for 24 h. It was washed with D.W and treated with 0.3% sodium sulphite and soaked in distilled water for 2 min at 60°C followed by acidified with 0.2% sulphuric acid. Finally the membrane was dipped in boric buffer (pH 9) till it is used for permeation study.

Drug Permeation Studies [43]

The *in vitro* diffusion rate of *Azadirachta indica* A. Juss. transdermal patches were evaluated by open ended tube through using distilled water as diffusion medium up to 8 h studies. The cellophane membrane was tide in one end of the tube and then immersed in the receptor compartment containing 200ml of 7.4 buffer solution. Which was stirred at medium speed and maintained at 37°C±2°C. Samples were withdrawn at regular time intervals and the same volume was replaced by fresh diffusion medium. The samples were analyzed using UV – visible spectrophotometer (Shimadzu UV1700) set at 382 nm.

6.10. Stability studies [46,47]

a) Stability

Stability is official defined as the time lapse during which the drug product retains the same property and characteristics that it possessed at the time of manufacture. This process being early development phases.

Instability in modern formulation is often undetectable only after considerable storage period under normal conditions. To assess the stability of a formulated product it is usual to expose it to high stress conditions to enhance deterioration and therefore the time required for testing is reduced. Common high stresses are temperature and humidity. This will eliminate unsatisfactory formulation.

b) Strategy of stability testing

- The study of drug decomposition kinetics
- The development of stable dosage form
- Establishment of expiry date for commercially available drug product is some of the needs of stability testing
- Data from which study should be provided on at least 3 primary batches of the drug product
- The batches should be manufactured to a minimum of pilot scale
- Important point of view of the safety of the patient, patient relieves a uniform dose of drug throughout the shelf life of the product

Table No.5: Stability condition chart

Intended Storage Condition	StabilityTest Method	ICH Test Temperature and Humidity (period in months)	WHO Test Temperature and Humidity(period in Months)
Room Temperature	Long term	25±20C/60±5%RH	25±20C/60±5%RH or 30±20C/65±5%RH 30±20C/75±5%RH
	Intermediate	30±20C/65±5%RH	30±20C/65±5%RH
	Accelerated	40±20C/75±5%RH	40±20C/75±5%RH
Refrigerated	Long term Accelerated	50C/ambient 25±20C/60±5%RH	5±30C 25±20C/60±5%RH or 30±20C/65±5%RH
Freezer	Long term	-200C/ambient	-200C±50C

Results and Discussion

Absorption maxima (λ max) of Aqueous Extract of *Azadirachta indica* A. Juss

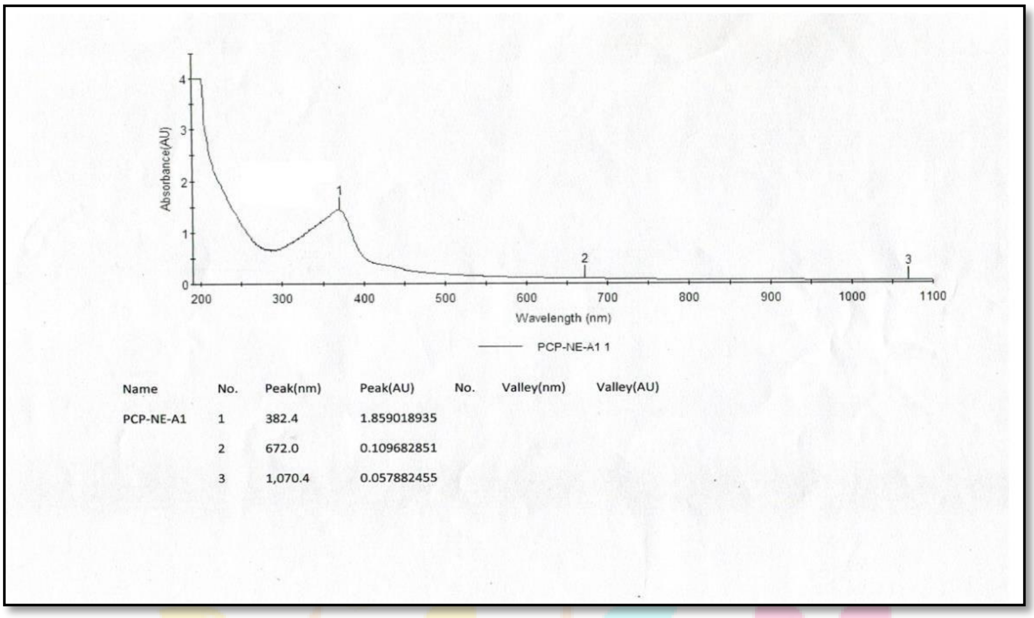

Fig No.20: Absorption maxima (λ max) of Aqueous Extract of *Azadiractha indica* A Juss.

The sharp peak observed at 382 nm, further measurements were taken at 382nm.

Physical appearance

Colour : Green

Taste : Bitter taste

Solubility Freely soluble in Distilled Water

Phytochemical Studies

Table No.7: Phytochemical constituents

S.No.	Chemical constituents	Aqueous Extract
1.	Alkaloids	+
2.	Saponins	+
3.	Tannins	+
4.	Phenolic	+
5.	compounds	+
6.	Flavonoids	+
7.	Steroids	+
8.	Glycosides	+
9.	Amino acids	-
10.	Reducing sugar	-
	erpenoids	

(+) Presence of constituents (-) Absence of constituents

The phytochemical studies revealed that the presence of alkaloids, saponins, tannins, phenolic compounds, flavonoids and sterol.

7.1. Hygroscopic Nature

Table No. 8. Hygroscopic Nature determination

t Room Temperature	5%RH at 40^{0}C
ample No-1	ample No-1
Veight gain observed (0.41±2.1)	Veight gain observed (0.38±0.6)

The results, it is observed that the prepared Transdermal patch is hygroscopic in nature.

7.2. Compatibility study FTIR studies

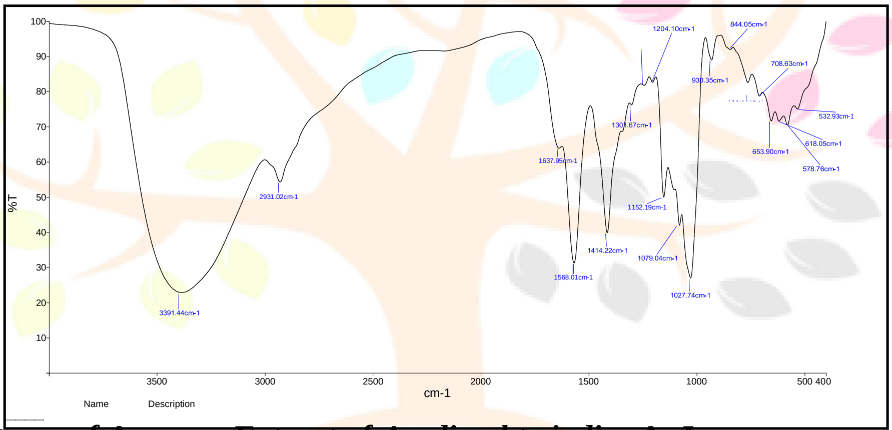

Fig No. 22: FTIR Spectrum of Aqueous Extract of *Azadirachta indica* A. Juss

7.3. Physico chemical evaluation of Aqueous Extract of *Azadirachta indica* A. Juss Transdermal patch

Table No.14: Physico chemical evaluation of Aqueous Extract of *Azadirachta indica* A. Juss Transdermal patches

ormulation code		niformity f weight (g)	hickness (mm)	Drug content (%)	Folding ndurance e(no's)	Moisture Uptake (%)	Moisture Content (%)	Surface pH	Percent longation (% mm)	Tensile Strength (Kg/mm^2)
ransdermal Patch of Pectin (P)	P1	0.38±0.14	.43±0.73	5.23±0.92	235±0.76	.14±0.08	.866±0.07	.1±0.10	85±0.32	5.300±0.55
	P2	**0.46±0.85**	**.49±0.23**	**5.69±0.56**	**249±0.23**	**.85±1.03**	**.422±0.22**	**.3±0.72**	**91±1.11**	**6.361±0.87**
	P3	0.49±0.10	.50±1.13	8.98±0.16	254±0.36	.79±1.03	.940±0.36	.2±0.72	86±1.08	.7031±0.87
ransdermal Patch of Sodium alginate (S)	S4	0.39±0.43	.36±0.33	2.03±0.22	241±0.72	.75±0.65	.736±0.46	.0±0.33	82±0.23	5.513±0.86
	S5	**0.41±0.65**	**.45±0.76**	**3.35±0.94**	**265±0.44**	**.97±0.44**	**.657±0.03**	**.1±0.12**	**87±0.92**	**6.253±0.62**
	S6	0.48±0.50	.47±0.16	0.13±0.40	247±0.42	.79±0.35	.457±0.03	.2±0.12	89±0.86	6.432±0.74

Mean ± S.D: n = 3

7.4. Optimized formula of *Azadirachta indica* A Juss. Transdermal patch

Table No.15: Optimized formula of *Azadirachta indica* A Juss. Transdermal patch

S.NO.	Ingredients	P (Pectin)	S (Sodium alginate)
1.	Extract (mg) *Azadirachta indica*	40	40
2.	Polymer (mg)	240	240
3.	DMSO/SLS(ml)	0.3	0.3
4.	Glycerin (ml)	0.3	0.3
5.	Water (ml)	q.s	q.s

Pictures of Prepared Patches

Physicochemical Evaluation of Selected formulations

Table No. 16: Uniformity of weight

. No.	**ormulation code**	**Veight(g)**
.	**ectin (P2)**	**.46±0.85**
.	odium alginate (S5)	.41±0.65

Mean ± S.D: n= 3

Table No. 17: Thickness of the patch

S. No.	**Formulation code**	**Thickness (mm)**
1.	**Pectin (P2)**	**0.49±0.23**
2.	Sodium alginate (S5)	0.45±0.76

Mean± S.D:n=3

Table No. 18: Determination of Drug content

S. No.	**Formulation code**	**% Drug content**
1.	**Pectin (P2)**	**85.69±0.56**
2.	Sodium alginate (S5)	83.35±0.94

Mean ± S.D: n=3

Table No. 19: Folding Endurance

S. No.	Formulation code	Folding Endurance
1.	**Pectin (P2)**	**249±0.23**
2.	Sodium alginate (S5)	245±0.44

Mean ± S.D: n =3

Table No. 20: Percentage Moisture Uptake

S. No.	Formulation code	% Moisture uptake
1.	**Pectin (P2)**	**2.85±1.03**
2.	Sodium alginate (S5)	1.97±0.44

Table No. 21: Percentage Moisture Content

S. No.	Formulation code	% Moisture content
1.	**Pectin (P2)**	**3.422±0.22**
2.	Sodium alginate (S5)	1.657±0.03

Mean ± S.D: n=3

Table No. 22: Surface pH

S. No.	Formulation code	urface pH of patches
1.	**Pectin(P2)**	**7.3±0.72**
2.	Sodium alginate(S5)	7.1±0.12

Mean ± S.D: n=3

Table No. 23: Percent Elongation

S. No.	Formulation code	% Elongation (%mm)
1.	**Pectin(P2)**	**91±1.11**
2.	Sodium alginate(S5)	87±0.92

Mean ± S.D: n=3

Table No.24: Tensile Strength

S. No.	Formulation code	Tensile strength (kg/mm^2)
1.	**Pectin(P2)**	**6.361±0.65**
2.	Sodium alginate(S5)	6.253±0.25

Mean ± S.D: n=3

***In vitro* drug difuusion study**

Table No.25: *In vitro* drug diffusion study

Time in (min)	% drug diffusion					
	Pectin (P)			Sodium Alginate(S)		
	P1	P2	P3	S4	S5	S6
0	0	**0**	0	0	**0**	0
30	6.78	**5.2**	2.98	7.15	**4.86**	3.46
60	10.30	**8.6**	4.78	12.36	**9.5**	5.72
90	13.65	**11.21**	5.64	16.19	**11.98**	9.34
120	17.89	**15.96**	7.15	20.72	**16.28**	12.20
150	23.10	**18.54**	9.45	24.37	**20.41**	17.40
180	29.54	**22.34**	14.82	30.97	**25.01**	22.19
210	33.68	**27.45**	19.38	34.65	**32.21**	25.30
240	39.70	**31.23**	25.48	38.98	**36.43**	29.68
270	45.58	**38.42**	30.98	43.12	**42.11**	33.76
300	48.77	**43.58**	38.73	48.94	**46.36**	36.15
330	53.22	**49.86**	42.54	54.30	**52.21**	42.56
360	57.10	**55.25**	45.24	59.61	**55.34**	47.26
390	62.41	**60.46**	49.64	65.73	**59.43**	53.90
420	67.38	**65.46**	53.28	68.60	**64.22**	58.76
450	72.34	**69.46**	59.74	70.12	**68.18**	63.12
480	77.10	**73.04**	64.10	74.62	**71.46**	67.92

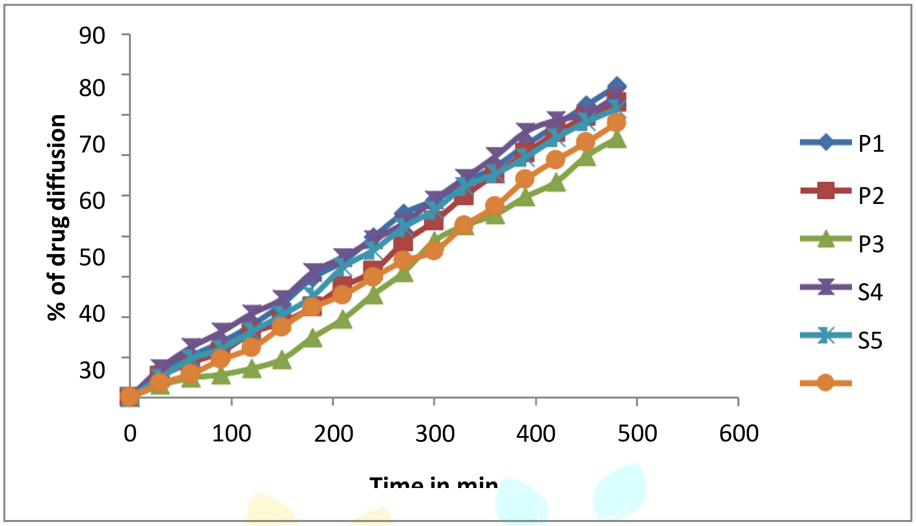

Fig No.33:*In vitro* drug diffusion study

% of drug release

Fig No.34: *In vitro* drug diffusion profile of P2

Table No. 27 : *In vitro* drug diffusion profile of S5

.No	ime (min)	% Drug diffusion of 5
	0	.86± 0.23
	0	.95± 0.45
	0	1.98± 0.44
	20	6.28± 0.76
	50	0.41± 1.78
	80	5.01± 0.59
	10	2.21± 1.23
	40	1.23 ± 0.61
0	70	2.11±1.24
1	00	6.36± 1.90
2	30	2.21±1.54
3	60	5.34± 0.23
4	90	9.43± 1.34
5	20	4.22± 0.91
6	50	8.18± 0.72
7	80	1.46± 0.61

Mean S.D:n=3

Stability study of Aqueous Extract of *Azadirachta indica* A Juss. Transdermal Patch

Table No: 33. Stability study of P2

Parameter	Room temperature	40 ± 2^0C& RH 70±5%
Visual Appearance	Brown colour	Brown colour
Initial	No change	No change
At the end of 1st month	No change	No change
At the end of 2nd month	No change	No change
At the end of 3rd month	No change	No change
Colour	Brown	Brown
Initial	No change	No change
At the end of 1st month	No change	No change

At the end of 2nd month	No change	No change
At the end of 3rd month	No change	No change
Texture	Smooth	Smooth
Initial	No change	No change
At the end of 1st month	No change	No change
At the end of 2nd month	No change	No change
At the end of 3rd month	No change	No change
Drug content	No change	No change
Initial	**85.69%**	**85..69%**
At the end of 1st month	85.22%	85.14%
At the end of 2nd month	84.95%	84.81%
sAt the end of 3rd month	84.21%	84.06%

The stability studies of formulation of aqueous extract of *Azadirachta indica* A Juss. transdermal patch was carried out for 3 months as per the procedure described in the table

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SUMMARY AND CONCLUSION

Six batches of (P1, P2, P3, S4, S5 & S6) Aqueous extract of *Azadirachta indica* transdermal patches were prepared by solvent casting technique.

The various formulation parameters, Drug-Polymer ratios and permeation enhancers were optimized to get thin, transparent, smooth, stable and high permeable transdermal patches.

The FTIR graphs of drug, excipients and formulations showed that there is no extra peak (or) broadening of peaks were observed and thus it indicates that there is no incompatibility between drug and excipients.

From the optimization, best 2 formulations P2 & S5 were selected based on physico chemical evaluation and *in vitro* drug diffusion study 0.3ml of glycerin was added as plasticizer to produce a flexible patch without having major influence on their diffusion property. If the amount exceeds, the film loses its flexibility and become stiff.

The plasticizer diffuses through the patch and softens the polymer particles. This softening promotes latex coalescence and patch formation. All the six batches were evaluated for Percentage Moisture uptake, Percentage Moisture content, Thickness, Folding Endurance, Percentage Drug content, Percent Elongation, Tensile strength and Adhesive strength.

The formulations P2 & S5 showed maximum % Moisture uptake, Moisture content, Thickness, folding endurance, % Drug content, Percent elongation, Tensile strength No significant difference in drug content was observed between the patches among the six formulations. This indicates the homogenous dispensing of drug during the patch preparation.

The data obtained from *in vitro* diffusion profile of selected formulations were fitted with various kinetic equations to determine the mechanism of drug diffusion and diffusion rate as indicated by higher correlation coefficients (r^2). The drug diffusion from P2 & S5 follows zero order and non-fickian diffusion.

. The stability studies results showed that there is no significant change from its initial nature till the period of three months at 40˚C ±2˚C/75 5% RH.

The present work has achieved the objectives of formulation of transdermal patch of Aqueous extract of *Azadirachta indica* by using different polymers. The diffusion kinetics confirms that the formulation followed zero order, non-fickian diffusion model.

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