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Formulation and Evaluation Transdermal Patch of Aqueous Extract of Azadirachta indica A. Juss using Different Polymers

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Abstract: *The goal of the Novel Drug Delivery System is to deliver a therapeutic dose of drug to an appropriate place within the body quickly so that the desired drug concentration can be maintained. Over a set treatment period, the drug-delivery system should supply the medicine at a rate controlled by the body's requirements. A transdermal patch is a medicated adhesive patch that is applied to the skin to deliver a specific amount of medication into the bloodstream through the skin. This generally aids in the recovery of a damaged bodily part. The patch provides a controlled release of medication into the patient, usually through a porous membrane covering a reservoir of medication or through thermoregulation melting thin layers of drug incorporated in the adhesive, which is a benefit of transdermal drug delivery over other types of medication delivery such as oral, topical, intravenous, intramuscular, and so on. As a result of persistent experimentation with nature, man must have known the therapeutic potential of neem since past. When used both internally and externally, it is beneficial to the skin. It cleanses the blood and treats acne, pimples, boils, and other skin problems. The flavour of neem is bitter. However, it is this bitterness that is responsible for the tree's therapeutic efficiency. Transdermal patches are presently available in a wide range of therapeutics.*

Keywords: NDDS, Transdermal Patch, Neem, Infrared Spectroscopy

I. INTRODUCTION

Transdermal drug - delivery systems are patches that are applied to the skin and distribute drugs for systemic effects at a predefined and controlled rate. A transdermal drug delivery system, which can be active or passive, is a device that allows you to administer medication via your skin. Pharmaceuticals can be given through the epidermal barrier using these technologies. Transdermal patches, in theory, are incredibly simple to use. A medication is given to the inside of a patch that is worn on the skin for an extended period of time in a reasonably high dosage. The medication enters the bloodstream immediately through the skin through a diffusion process. Because the patch has a high concentration and the blood has a low concentration, the medication will continue to diffuse into the blood for a long time, keeping a consistent drug concentration in the blood flow [1].

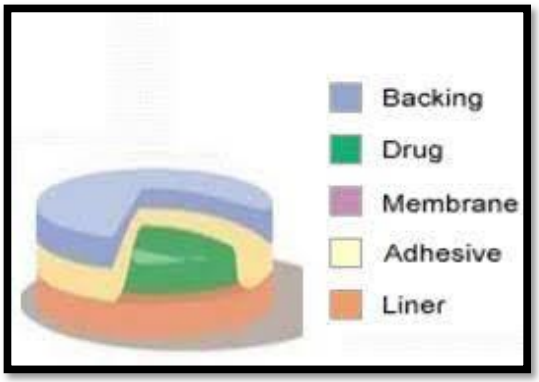

Fig 1: Structure of Transdermal Patch

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Pathway of transdermal permeation

Diffusion of pharmaceuticals via the intact epidermis and through skin appendages, such as hair follicles and sweat glands, which establish shunt channels through the intact epidermis, are examples of drug penetration through the skin. However, these skin appendages make up only 0.1 percent of the total human skin surface area, therefore their contribution is frequently overlooked (with only a few exceptions having been noted). The Stratum corneum, as previously indicated, usually limits medication absorption through the skin. The intercellular lipid route between the corneocytes and the transcellular route crossing through the corneocytes and intervening lipids are the two pathways through the intact barrier that can be identified. In both cases, the permeant must diffuse at some point through the intercellular lipid matrix, which is now recognised as the major determinant of percutaneous transport rate [2].

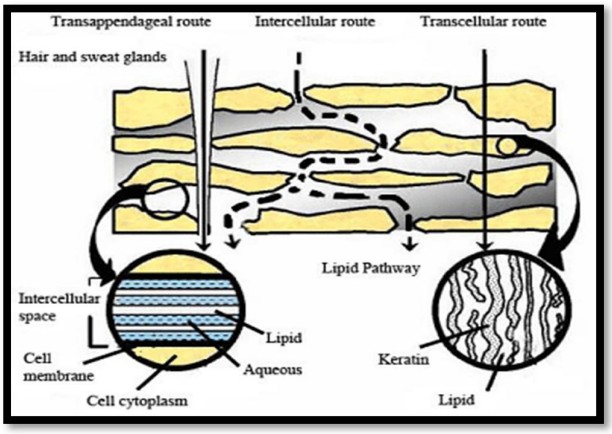

Fig 2: Drug Pathway of Skin

Desirable Features for Transdermal Patches

- The composition is relatively invariant
- The system size is appropriate;
- The application location is defined
- The application technique is highly repeatable.
- Zero-order delivery (in most cases)
- Efficient delivery

Advantages

- Transdermal drug delivery avoids gastrointestinal absorption as well as its related pitfalls of enzymatic and pH-related inactivation.
- This method also allows for reduced pharmacological dosing due to the transdermal route's shortened metabolization pathway versus the gastrointestinal pathway.
- A single application can provide multi-day therapy. In the event of an emergency, immediate communication of medicine is required, as well as the ability to quickly terminate pharmacological effects by removing the patch.

Disadvantages

- The medicine, which requires high blood levels, cannot be given and may induce skin irritation or hypersensitivity.
- The adhesives may not stick well to all skin types and may be uncomfortable to wear.
- The product's high cost is also a major deterrent to its widespread adoption.
- Characteristics that influence the medicament's transdermal delivery diffusion from the vehicle.
- Activation of the pharmacological reaction through penetration of the epidermal barrier.

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Limitations of transdermal drug delivery system –

- Higher molecular weight candidates (>500 Daltons) do not penetrate through Stratum corneum.
- Drugs with a very low or high partition coefficient do not reach systemic circulation.
- High melting drugs are not suitable due to their low solubility in both water and fat.
- Local irritation at the patch application site.
- A lag time associated with drug delivery across the skin, resulting in a delay in onset of action.
- Variation in absorption rate dependent on application location.
- Presence of skin disorders.
- Individual differences in adhesive effectiveness.

Neem

The neem tree (Azadirachta indica) is a tropical evergreen tree that is native to India and other Southeast Asian countries. Because of its restorative versatility, neem is regarded in India as "the village pharmacy," and its medicinal characteristics have been employed in Ayurvedic medicine for over 4,000 years. In Sanskrit, neem is known as "arista," which means "perfect, complete, and imperishable." Compounds found in the seeds, bark, and leaves have been shown to have antiseptic, antiviral, antipyretic, anti-inflammatory, anti-ulcer, and antifungal properties. "Nimba" is derived from the Sanskrit term "nimbitisyasthyamdadati," which means "to bring good health"[4].

Objectives of project -

- To transform the herbal extract into a new dosage form.
- To create a unique topical formulation of neem leaf aqueous extract for the treatment of skin infections.
- Antimicrobial assays were used to assess the anti-acne activity of a transdermal patch.
- To delve into the many facets of traditional Indian herbal medicine.
- To make conventional medicine more accessible and affordable.
- To encourage the rational application of traditional medicine.

II. PREFORMULATION STUDY

The initial step in the rational development of pharmacological dosage formulations is Preformulation testing. It is the study of the physical and chemical properties of a pharmacological ingredient on its own and in combination with excipients. Preformulation testing's overall goal is to provide information that will assist the formulator in producing stable and bioavailable dosage forms that can be mass manufactured. Preformulation studies are conducted out as follows:

A. Finding the Absorption Maxima
B. Physical Appearance
C. Standard Curve
D. Phytochemical Evaluation
E. Infrared spectroscopy studies (compatibility studies)

Finding the Absorption Maxima

The absorption maxima were discovered in order to identify the medication. To gain detailed information on the chromophoric portion of the molecules, ultraviolet visible spectrophotometry was used. When organic molecules in solutions are exposed to light in the visible/ultraviolet spectrum, they absorb light of a certain wavelength based on the type of electronic transition involved. The extract solution (5, 10, 15, 20, 25 µg/ml) in distilled water was placed in a standard cuvette and scanned in a UV spectrophotometer between 200 and 800 nm. Its maximum wavelength is 382 nm. As a result, all measurements were performed at 382 nm.

Physical Appearance –

Colour, Texture & Solubility determine visually.

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Standard Curve

A precisely weighed quantity of AE (100mg) was transferred to a 100ml volumetric flask and dissolved in a moderate amount of distilled water (D.W) to form the standard stock solution of 1 mg/ml. 1ml of the stock was placed in a 10ml volumetric flask and made up with buffer; 0.5ml to 3ml of the solution was transferred to a 10ml volumetric flask and made up to the needed volume with more D.W, yielding concentrations ranging from 5 to 50 µg/ml. A UV spectrophotometer was used to determine the absorbance of these solutions at 382nm. The absorbance and concentration were used to create the calibration curve.

Phytochemical study [5,6]-

Test	Observation	Inference
Test For Alkaloids		
Dragendroff"s test: The extract was treated with Dragendroff"s reagent (potassium bismuth iodide solution).	Orange brown Precipitate was formed.	Presence of alkaloids
Mayer's reagent: The extract was treated with Mayer's (potassium mercuric iodide solution) reagent.	Precipitate formed	Presence of alkaloids
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		
Brontrager's test: To the extract add dilute H_2SO_4 and filtered. Filtrate was extract with little chloroform layer was separated out and add equal volume of dilute NH_3.	Red colour observed in ammonical layer	Presence of glycosides
Test for Saponin glycosides		
Foam test: Shake the extract with water.	Foam was produced/formed	Presence of saponin Glycosides
Test for Tannins and Phenolic compounds		
Ferric chloride test: To the aqueous extract few drops of ferric chloride solution were added.	Dark black colour formed	Presence of tannins and phenolic compounds
Bromine water test: To the aqueous extract is treated with bromine water.	Discoloration of bromine Water.	Presence of tannins and phenolic compounds
$KMnO_4$ test: To the aqueous extract is treated with dilute $KMnO_4$.	Discoloration of solution	Presence of tannins and phenolic compounds
Test for Reducing sugar		
Benedict's test: 0.5ml of extract solution 1ml of water 5 to 8 drops of Fehling's solution was added.	Brick red precipitate.	Presence of reducing sugar

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Test for Amino acids		
Ninhydrin test: The aqueous extract is heated with 5%ninhydrin solution on boiling water bath for 10 min.	Purple colour formed	Presence of amino acids
The aqueous extract is treated with solution sodium hydroxide and lead acetate solution and boiled.	Black precipitate is formed	Presence of amino acids
Test for Flavonoids		
Shinoda test: To the methanol extract add potassium hydroxide solution and then 10% ammonia.	Yellow colour Precipitate formed.	Presence of flavonoids
To the ethanol extract, add few drops of Lead acetate solution.	Yellow colour Precipitate formed.	Presence of flavonoids
Test for Steroids		
Salkowski Test: To the extract add chloroform solution few drops of con. H_2SO_4 was added shaken and allowed to stand.	Greenish fluorescence was formed.	Presence of steroids

Infrared spectroscopic studies (compatibility studies) -

To produce a stable product, the medicine and excipients must be compatible with one another. The interaction between the medicine and the excipients has an impact on the drug's bioavailability and stability. Compatibility studies are vital in the formulation development of new excipients that have never been utilised in formulations containing the active ingredient. Fourier transform infrared spectroscopy (FTIR) is used to investigate interactions by comparing physicochemical features such as wave numbers[7].

III. MATERIALS & METHODS

Plant Profile[8] –

Fig 3: Leaves of *Azadirachta indica* A. Juss.

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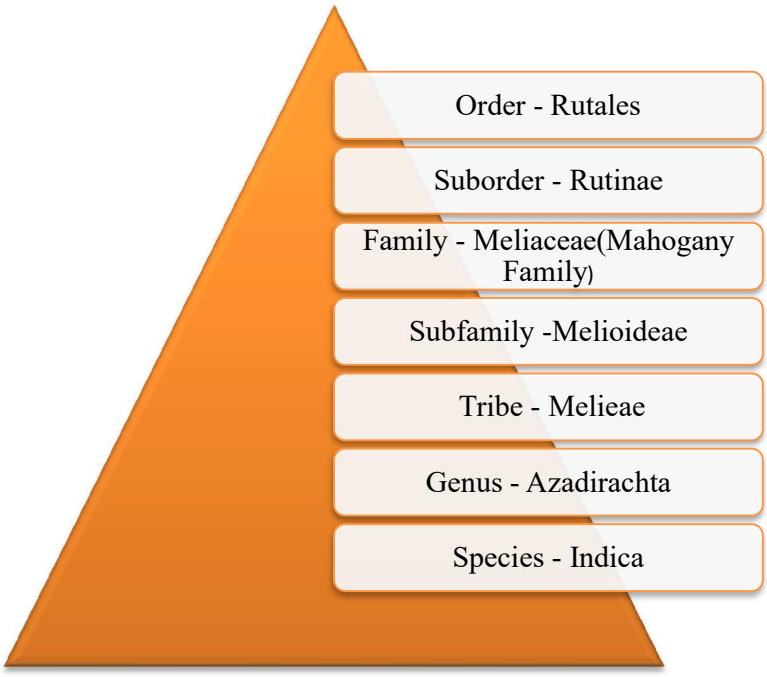

Fig 4: Taxonomy of Neem Plant

Pharmacological activity [9] -

- Analgesic agent
- Antipyretic agent
- Antimicrobial activity
- Antibacterial activity
- Antifungal activity
- Antiviral activity

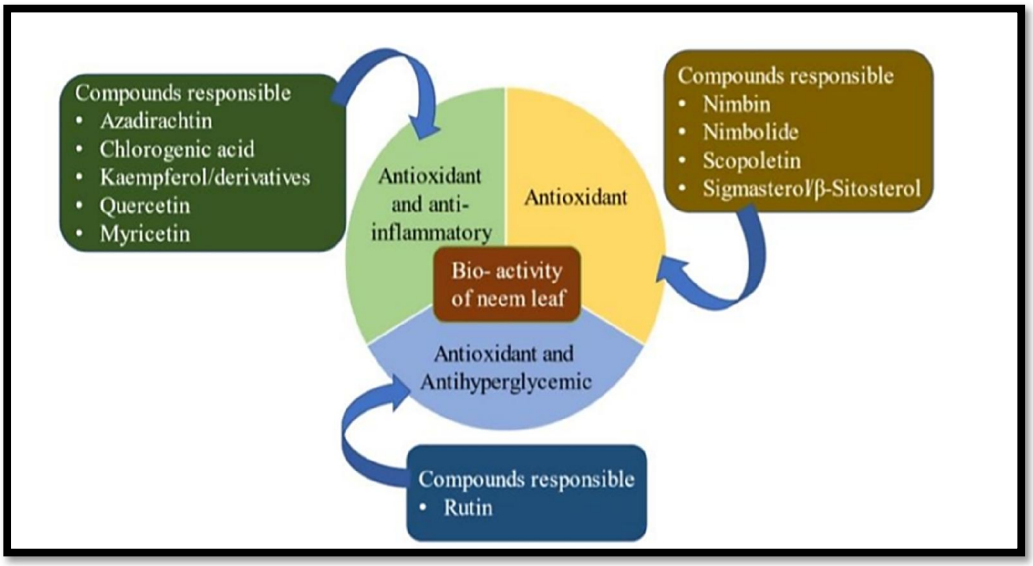

Fig 5: Bio-activity of the compounds present in neem leaf

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Excipient Profile [10, 11]-

Gelatine –

Gelatine is a protein made from animal by-products. Collagen, the most prevalent protein in the animal world, is partially hydrolysed to produce it, with significant amounts seen in connective tissues. It is made up of eighteen amino acids, with eight of them being essential. Gelatine, being a polydisperse polymer, has a variety of characteristics and functions that make it ideal for pharmaceutical and medical applications.

Properties -

Safe, Soluble, Thermoreversible, Digestible, Biocompatible, Odourless / flavourless, Low allergenic potential.

Uses -

Water-binding, Gelling, Strengthening / Stabilizing, Film forming, Adhesion, Soluble, Thermo-reversible, Foaming.

Structure -

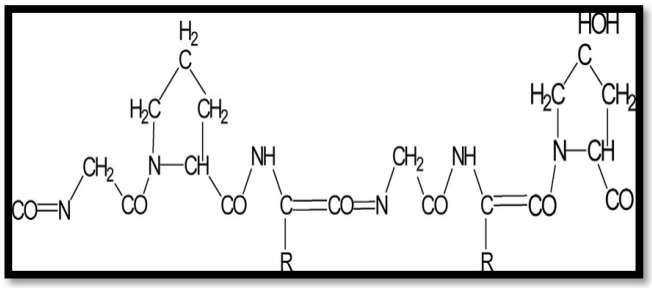

Fig 6: Structure of Gelatine

Molecular Weight of Gelatine – 15 to 400 kDa

Source -

Gelatin is manufactured from the connective tissues of calves and pigs, as well as decomposing animal hides and boiled pulverised bones. Slaughterhouses provide bones, skins, and tissues from animals.

Pharmaceutical Uses of Gelatine –

- Gelatin can be used as a binder or coating for tablets, making them a less expensive option than capsules.
- During granulation, gelatine can bind powders like starch, cellulose derivatives, and gum acacia.
- Gelatin coatings can also help to compensate for some of the tablet's flaws. These benefits include increased swallowability, reduced taste and aroma, and aiding in the protection of APIs from oxygen and light.
- Gelatin bone plugs give stability after joint surgery and do not need to be removed due of their biodegradability.

Sodium Alginate -

The sodium salt of alginic acid, a colourless or light yellow powdered or crystalline polysaccharide used as a food thickening and stabiliser, as well as in pharmaceuticals, paint, and paper coating.

Properties -

- The carboxyl groups of alginates are linked with a sodium ion in sodium alginate, which is a neutral salt.
- Alginic acid is not soluble in water, but sodium alginate is, and produces a smooth viscous solution in both cold and hot water.

Uses

Stabilizing agent, suspending agent, tablet and capsule disintegrant, tablet binder, viscosity increasing agent.

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Chemical Structure -

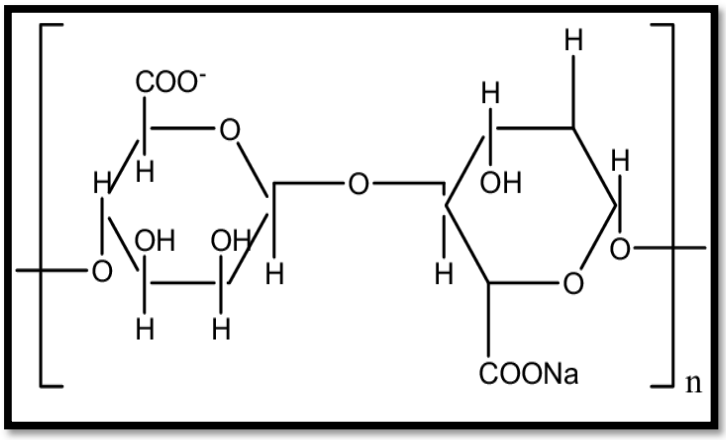

Fig 7: Structure of Sodium Alginate

Molecular Weight of Sodium Alginate – 216.12 g/mol
Source – Brown seaweeds (Phaeophyceae).

Pharmaceutical Uses of Sodium Alginate –

- Because it can delay the dissolution of a drug from tablets, capsules, and aqueous solutions, sodium alginate has also been employed in the development of sustained-diffusion oral formulations.
- Sodium alginate can be used as a binder and disintegrant in tablet formulations, and it has also been utilised as a diluent in capsule formulations.
- In the treatment of gastroesophageal reflux, sodium alginate has been used in conjunction with an H2-receptor antagonist, as well as haemostatic agent in surgical dressings.
- Sodium alginate is commonly found in alginate dressings used to treat oozing wounds because it improves the gelling qualities.

Glycerine –

Glycerine is the popular term for the chemical compound glycerol, which is known scientifically as glycerol. It is a necessary component of many lipids, which includes fats, waxes, and steroids.

Properties -

It's a clear, odourless, viscous, hygroscopic liquid with a sweet taste that's about 0.6 times sweeter than sucrose.

Uses –

Antimicrobial preservative, emollient, humectant, plasticizer, solvent.

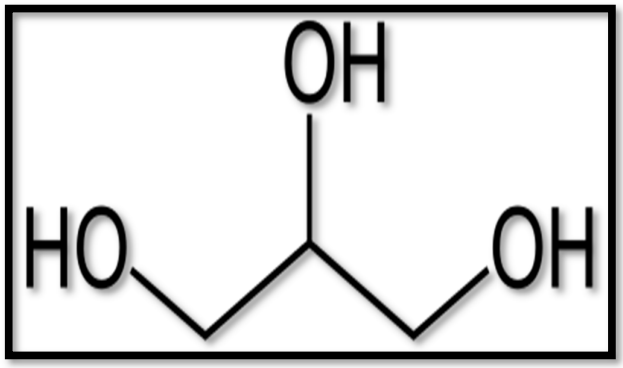

Fig 8: Structure of Glycerine

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Molecular Weight of Glycerine - 92.09 g/mol.

Pharmaceutical Uses of Glycerine –

- It is utilised in a wide range of pharmaceutical formulations such as oral, ophthalmic, topical, and parenteral medicines.
- It is largely employed in topical medicinal formulations and cosmetics for its humectant and emollient qualities.
- It is primarily utilised as a solvent in parenteral formulations.
- Glycerine is employed as a solvent, sweetening ingredient, antibacterial preservative, and viscosity raising agent in oral solutions.
- It's also utilised as a plasticizer and in the production of film coatings.

DMSO –

Dimethyl sulfoxide(DMSO) is a polar organic liquid that is usually employed as a chemical solvent and free radical scavenger. It has a variety of pharmacological effects, including analgesia and anti-inflammatory properties. It is employed as a carrier or topical application of medications due to its ability to penetrate biological membranes.

Properties –

Dimethyl sulfoxide appears as a clear liquid, essentially odourless, colourless and hygroscopic.

Uses –

Penetration enhancer, solvent.

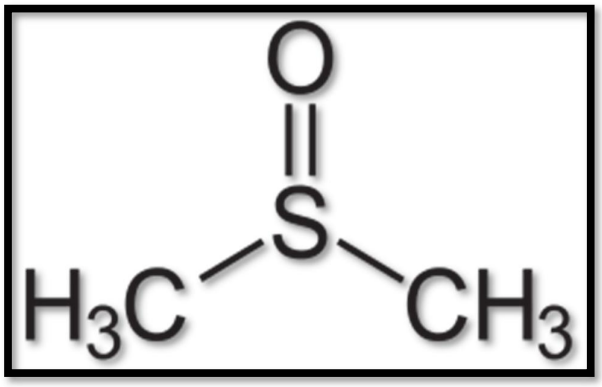

Fig 9 : Structure of Dimethyl Sulfoxide

Molecular Weight of Dimethyl Sulfoxide - 73.13 g/mol

Pharmaceutical Uses of DMSO –

- For cyclosporin, timolol, and a variety of other medicines, dimethyl sulfoxide has been used to boost transdermal distribution.
- It has also been studied for its potential application in an experimental parenteral formulation for the treatment of liver cancers.
- Dimethyl sulfoxide is used in idoxuridine paint formulations as a solvent to promote medication solubility and as a means of allowing the antiviral agent to penetrate deeper into the epidermis.

Formula for transdermal patches of *azadirachta indica* a. Juss –

Table 1: Formula for Transdermal Patches of *Azadirachta Indica* A. Juss

Sr no.	Ingredients	Quantity	Pharmacological Property
1	Aqueous Extract	40 mg	Antibacterial activity, Antifungal activity
2	I.Gelatine	240 mg	Gelling agent, Thickening agent

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	I.Sodium Alginate	240 mg	Stabilizing agent, Suspending agent
3	DMSO	0.3 ml	Penetration enhancer
4	Glycerine	0.3 ml	Antimicrobial preservative, emollient, Plasticizer
5	Water	q. s	Solvent

Procedure for extraction of leaves of *azadirachta indica* (by Soxhlet apparatus) [12] –

1. The shade dried leaves were subjected to size reduction.
2. About 100g of the dried powder was extracted continuously in Soxhlet apparatus with petroleum ether for 24 hrs to remove the waxy materials.
3. Then it was extracted with distilled for 72h. After 72h, the water substance was evaporated to obtain the crude extract.
4. The extract was dried under vacuum oven.

Fig 10: Procedure for Extraction of leaves of *Azadirachta indica* (By Soxhlet Apparatus)

Fig 11: Extraction of *Azadirachta Indica* A. Juss by Soxhlet Apparatus

Fig 12: Aqueous Extract of *Azadirachta Indica* A. Juss

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Procedure for preparation of transdermal patches [13]–

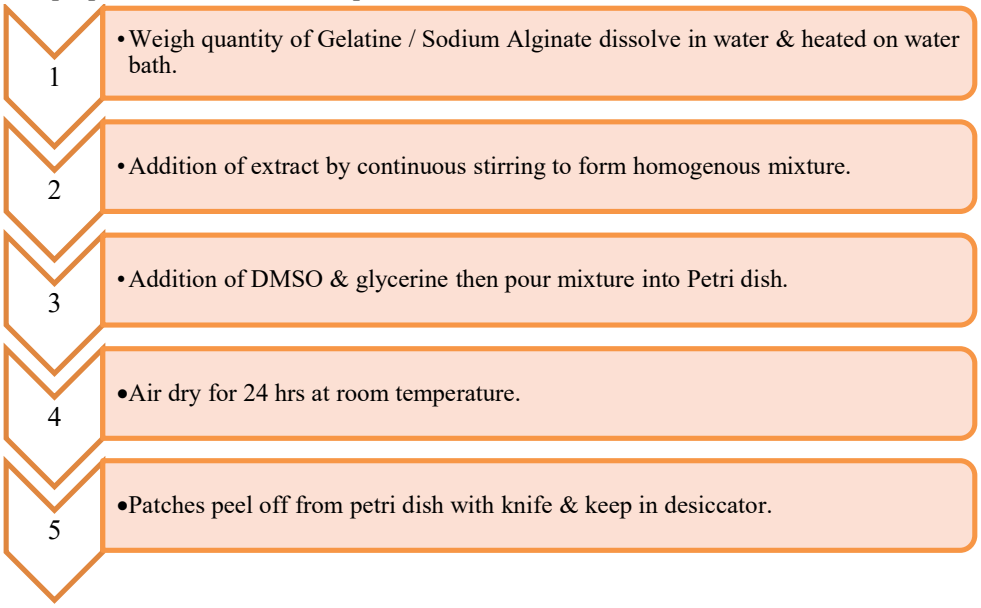

Fig 13: Procedure for Preparation of Transdermal Patches

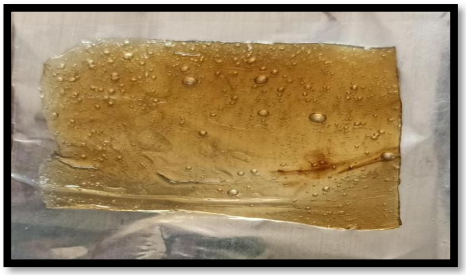

Fig 22: Transdermal Patch of *Azadirachta Indica* By using Polymer Gelatine

Fig 23: Transdermal Patch of *Azadirachta Indica* By using Polymer Sodium Alginate

IV. EVALUATION OF TRANSDERMAL PATCHES OF *AZADIRACHTA INDICA* A. JUSS

Physico-chemical evaluation of *azadirachta indica* A.Juss Transdermal patch [14,15] –

Uniformity of Weight

This was accomplished by weighing five distinct patches from each batch at random and calculating the average weight of three. The tests were carried out on a patch that had been dried at 60°C for 4 hours before being tested.

Thickness of Patch

At several spots on the patch, the thickness was measured with a digital vernier calliper. Three patches were chosen at random from each formulation. The thickness of a single patch was measured and the average value was found.

Drug Content

The patches were taken and placed in a beaker with 100 ml D.W. For 5 hours, the mixture was agitated with a magnetic bead. The solution was then filtered and spectrophotometrically evaluated for drug concentration using suitable dilution at 382 nm.

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Folding endurance -

This was established by folding one patch in the same spot over and over until it broke. The value of folding endurance was determined by the number of times the patch could be folded in the same area without breaking.

$$\text{Percent moisture content} = \frac{\text{Final Weight} - \text{Initial Weight}}{\text{Initial Weight}} \times 100$$

Percentage Moisture content–

The patch was precisely weighed and placed in aluminium chloride-based desiccators. The patch was removed and weighed after 24 hours. The difference between the end and beginning weight was used to calculate the % moisture uptake. In terms of original weight. It is calculated using the formula below.

Surface pH -

The patches were allowed to swell for 2 hours at room temperature after being in place in 1 ml of distilled water, and the pH was measured by placing the electrode on the patch's surface and allowing it to equilibrate for 1 minute.

Percent Elongation –

When a patch sample is stressed, it stretches, which is referred to as strain. Strain is defined as the distortion of a patch divided by the sample's initial dimension. Patch elongation rises in general as the plasticizer content increases. It is calculated using the formula below.

$$\text{Percentage elongation} = \frac{\text{Increase in length of patch} - \text{Final Length of Patch}}{\text{Initial length of patch}} \times 100$$

Stability Study [16,17]-

Physical parameters like color, consistency and pH were determined at room temperature and 40^0C.

Anti-microbial Assay [18,19,20]–

Principle –

Antibiotic-impregnated discs with a known concentration Discs are placed on an agar plate that has been uniformly infected (or seeded) with a culture of the microorganism to be examined. At 370°C, the plate is incubated for 18-24 hours. During this time, the antimicrobial drug diffuses into the agar, potentially inhibiting organism development. The diameter of the inhibitory zone surrounding the disc is proportional to the effectiveness of susceptibility. Organisms that grow to the disc's edge are resistant.

Procedure –

Using a modified agar well diffusion method, the antibacterial activity of several formulations was assessed. In this procedure, nutrient agar plates were seeded with 0.2 mL of Staphylococcus aureus/Candida albicans 24-hour broth culture. The agar plates were left to solidify. In each plate, a sterile 8 mm borer was used to cut two equidistance wells. Each petriplate had a test solution in the first well and a standard solution in the second well, which were inserted at random. The plates were incubated for 24 hours at 37°C. The antibacterial activity was assessed by measuring the zones of inhibition (in mm).

Experimental condition for anti-bacterial activity –

- **Organisms used**: *Staphylococcus aureus*
- **Media used**: Nutrient Agar.
- **Test used**: AE patch.
- **Standard**: Ciprofloxacin.
- **Experimental condition for anti-fungal activity –**
- **Organisms used:** *Candida albican.*

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- **Media used:** Nutrient Agar.
- **Test used:** AE patch.
- **Standard:** Fluconazole.

V. RESULT & DISCUSSION

Preformulation Study

Finding Absorption Maxima –

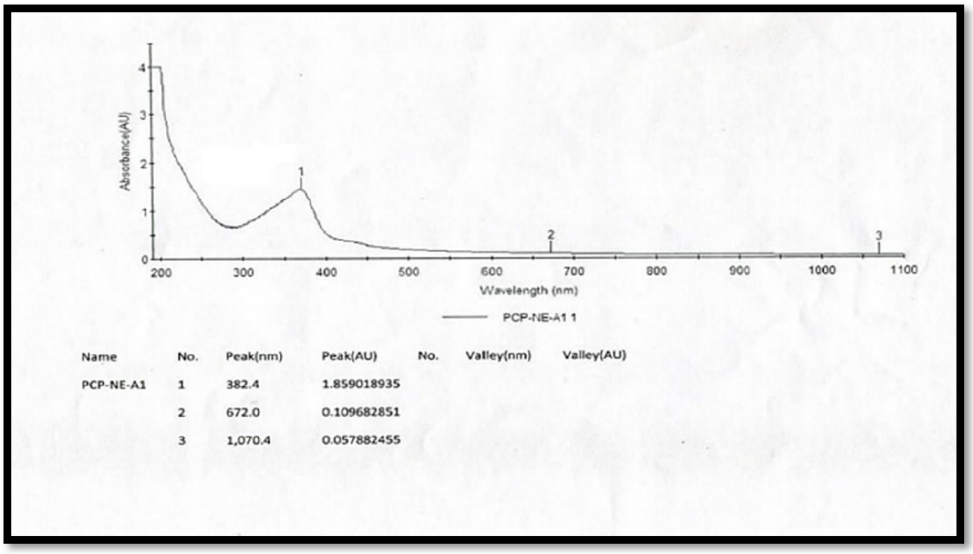

Fig 24: Absorption maxima (ƛ max) of Aqueous Extract of *Azadirachta indica* A Juss.

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

Physical appearance –

- Colour: Pale Yellow
- Texture: Fine
- Solubility: Freely soluble in Distilled Water

Standard Curve

Table 5: Standard values of Aqueous Extract of *Azadirachta indica* A. Juss

Concentration (µg/ml)	Absorbance at 382 nm
10	0.008
20	0.152
30	0.257
40	0.354
50	0.405
60	0.500

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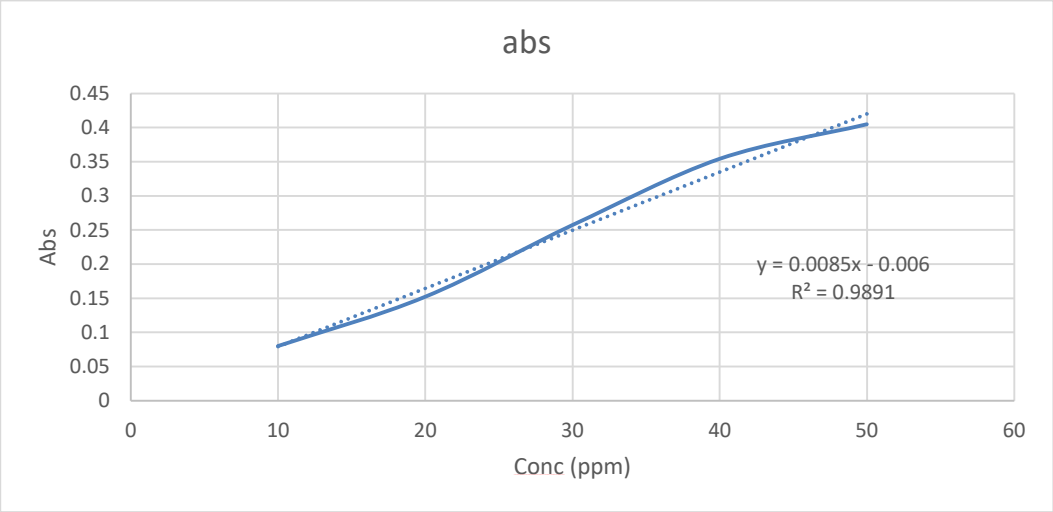

Fig 25: Standard Curve of Aqueous Extract of *Azadirachta indica* A. Juss

Phytochemicals Studies –

Table 6: Phytochemical constituents

Sr No.	Chemical Constituents	Aqueous Extract
1	Alkaloids	++
2	Saponins	++
3	Tannins	++
4	Phenolic Compounds	++
5	Reducing Sugar	--
6	Amino Acid	--
7	Flavonoids	++
8	Steroids	++

Fig 26: Phytochemical Evaluation

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Infrared spectroscopy studies –

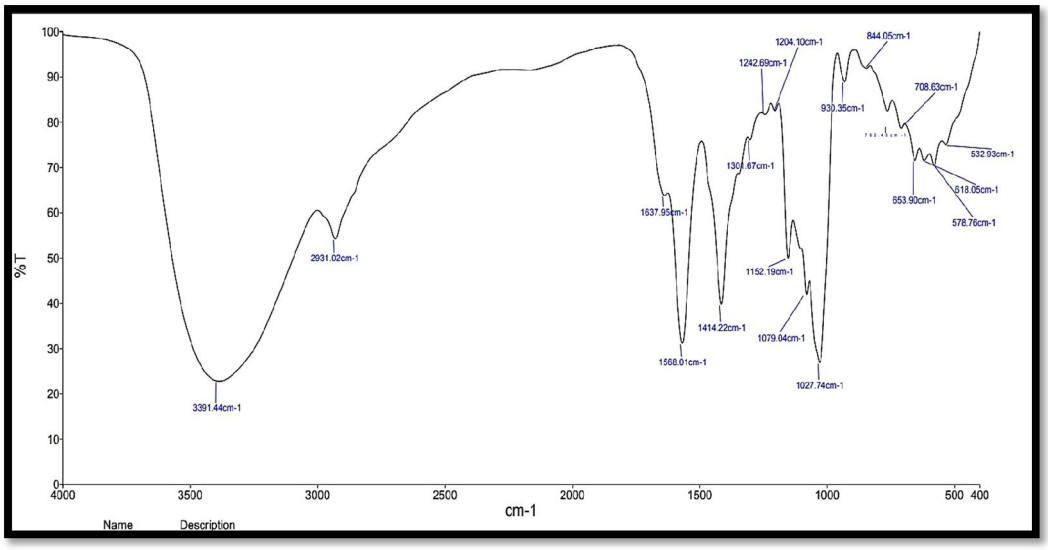

Fig 27: FTIR Spectrum of Aqueous Extract of *Azadirachta indica* A. Juss

Table 7: FTIR Interpretation of Aqueous Extract of *Azadirachta indica* A. Juss

Wave Number(cm^{-1})	Functional Group
3391.44	C=O stretching
2931.02	C-H Stretching
1637.95	C-C Stretching
921.39	C-O Stretching
1414.22	OH Bending
763.74, 653.03	C-H Rocking

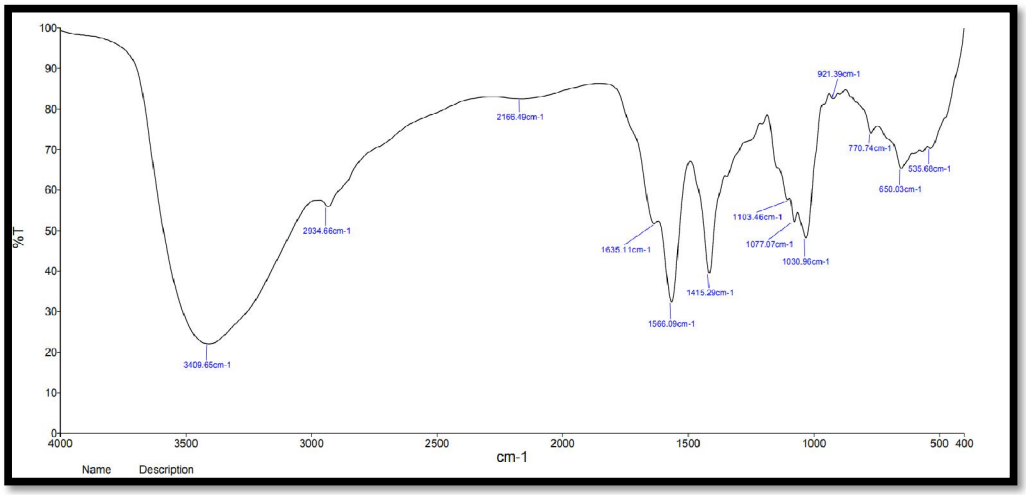

Fig 28: FTIR spectrum of Gelatin

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Table 8 – FTIR Interpretation of Gelatin

Wave Number (cm^{-1})	Functional Group
3409.65	C=O Stretching
2934.66	C-C Stretching
1635.11	C-C Stretching
1415.29	OH Bending
921.39	C-O Stretching
770.76	CH Rocking

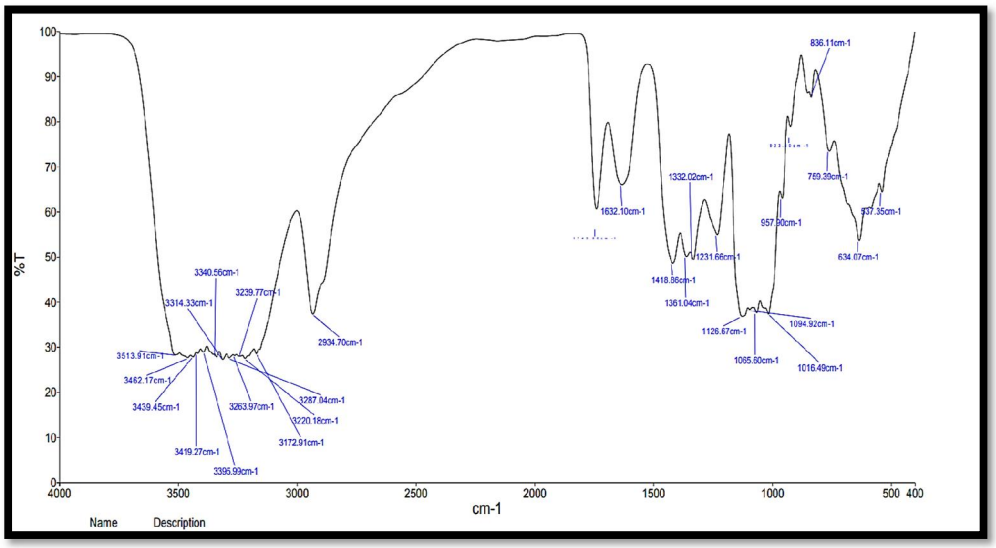

Fig 29: FTIR spectrum of Gelatin formulation

Table 9: FTIR Interpretation of Gelatin formulation

Wave Number (cm^{-1})	Functional Group
3462.17	C=O Stretching
1740.66	C-C Stretching
1632.11	C-C Stretching
1126	OH Bending
923.100	C-O Stretching
759.39	CH Rocking

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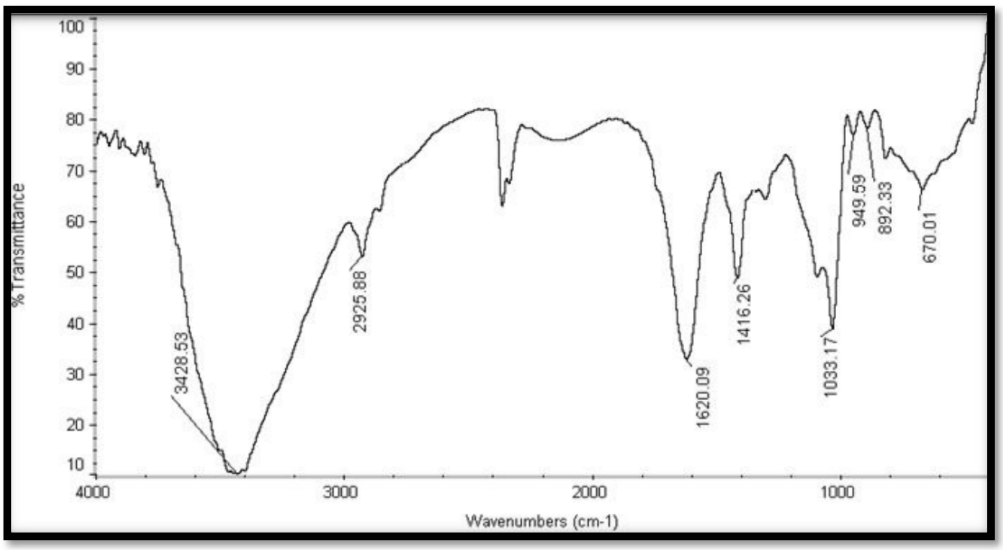

Fig 30: FTIR Spectrum of Sodium alginate

Table 10: FTIR Interpretation of Sodium Alginate

Wave Number(cm^{-1})	Functional Group
3248.58	C-H Stretching
2925.88	C-H Stretching
1620.09,1416.26	C-C Multiple bonds Stretching
1416.26	O-H Stretching

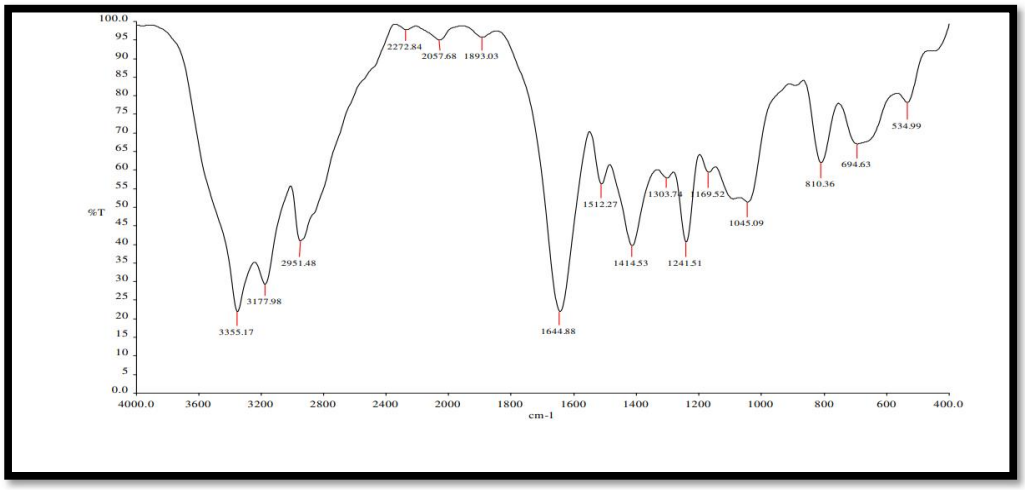

Fig 31: FTIR Spectrum of Sodium alginate formulation

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Table 11: FTIR Interpretation of Sodium Alginate Formulation

Wave Number (cm^{-1})	Functional Group
3355.17	O-H Stretching
1414.53	O-H Bending
1045.91	C-O Stretching
1115.29	C-O Stretching
1045.09	C-O Stretching
810.36	C-H (Out Plane Bending)
694.63	C-H (Out Plane Bending)

There was no extra peak (or) broadening of peaks detected in the FTIR graphs of drug, excipients, and formulations, indicating that there is no incompatibility between drug and excipients.

EVALUATIONS PARAMETERS

Table 12: Physico chemical evaluation of Aqueous Extract of *Azadirachta indica* A. Juss Transdermal patches

Evaluation Parameters	Transdermal Patch of Gelatine (G)	Transdermal Patch of Sodium Alginate (S)
Uniformity of Weight (g)	0.45 ± 0.05	0.42 ± 0.05
Thickness (mm)	0.35 ± 0.20	0.30 ± 0.10
Drug Content (%)	85.69 ± 0.56	83.35±0.94
Folding Endurance (No.)	20 ± 0.75	10 ± 0.35
Moisture Uptake (%)	2.74 ± 1.03	2.093 ± 0.44
Moisture Content (%)	3.50 ± 0.22	1.80 ± 0.03
Surface pH	7.3 ± 0.20	7.2 ± 0.36
Percent Elongation (% mm)	86 ± 1.08	82 ± 0.23

STABILITY STUDY –

Table 13: Stability Study of Aqueous Extract of *Azadirachta indica* A. Juss Transdermal patches

Parameters	At room Temperature	At 40^0C
Colour	No Change	No Change
Texture	No Change	No Change
pH	G - 7.3 ± 0.20 S - 7.2 ± 0.36	G – 7.0 ± 0.45 S - 6.9 ± 0.33

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ANTIMICROBIAL ASSAY –

Table 14: Antimicrobial Assay of Aqueous Extract of *Azadirachta indica* A. Juss Transdermal patches

Antimicrobial Agent	Formulation Code	Zone of Inhibition (in mm)
Staphylococcus aureus	For Gelatine Patch	20 mm
	For Sodium Alginate Patch	22 mm
Candida albicans	For Gelatine Patch	32 mm
	For Sodium Alginate Patch	28 mm

Anti-bacterial Activity -

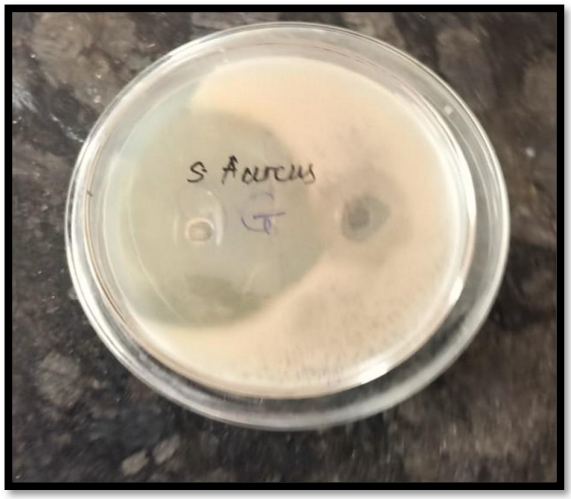

Fig 32: Zone of inhibition Shown by Sodium Alginate Patch

Fig 33: Zone of inhibition Shown by Gelatine Patch

Anti-fungal Activity –

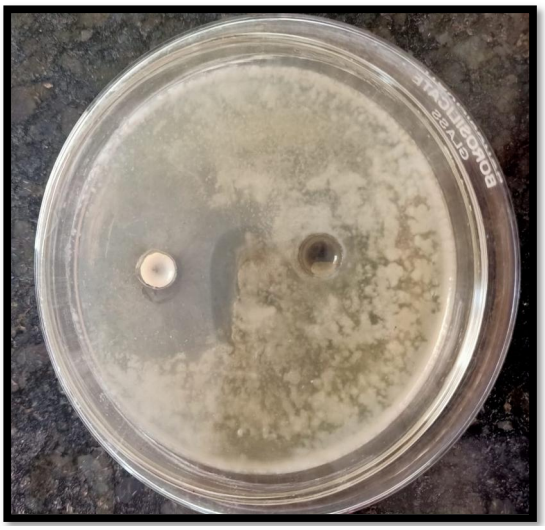

Fig 34: Zone of inhibition Shown by Sodium Alginate Patch

Fig 35: Zone of inhibition Shown by Gelatine Patch

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VI. CONCLUSION

Solvent casting technique was used to make an aqueous extract of Azadirachta indica transdermal patch. To achieve thin, clear, smooth, stable, and high permeable transdermal patches, various formulation parameters, Drug-Polymer ratios, and permeation enhancers were evaluated. There was no extra peak (or) broadening of peaks detected in the FTIR graphs of drug, excipients, and formulations, revealing that there is no incompatibility between drug and excipients. To make a flexible patch, 0.3ml of glycerin was added as a plasticizer without changing its diffusion properties. If the amount is exceeded, the film becomes rigid and loses its flexibility. The plasticizer softens the polymer particles as it diffuses through the patch. Latex coalescence and patch formation are accelerated by this softening.

Percentage Moisture uptake, Percentage Moisture content, Thickness, Folding Endurance, Percentage Drug content, and Percent Elongation were all assessed on the patches. There was no noticeable change in medication content between the patch formulations. This implies that the medicine was dispensed in a uniform manner during the patch production. The findings of the stability tests revealed that there is no substantial change from its initial state after three weeks at 40°C. The antimicrobial screening revealed that the Gelatine patch effectively inhibited bacteria growth in the patch's surroundings. Using various polymers, the current work has achieved the goals of producing a transdermal patch containing Azadirachta indica aqueous extract.

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CONFLICT OF INTEREST

The author declared no conflict of interest.

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