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DEVELOPMENT AND EVALUATION OF A HERBAL HYDROGEL PATCH OF NEEM AND TURMERIC FOR TOPICAL ANTI-INFLAMMATORY ACTIVITY

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2. ABSTRACT

Transdermal patches offer a non-invasive and patient-friendly alternative to traditional drug delivery routes, by delivering a controlled dose of medication through the skin into the bloodstream. Major innovations include dissolvable and biodegradable patches, systems with enhanced drug loading and release, microneedle-based platforms, and 3D- printed patches capable of delivering a wider range of therapeutics such as biologics. The paper highlights how these emerging technologies aim to overcome limitations such as poor skin barrier permeability, first-pass metabolism, and the need for frequent dosing. The review concludes with a discussion of future challenges and opportunities in designing next-generation transdermal patches that are smarter, more adaptable and capable of delivering complex therapies.

KEYWORD: Microneedle technology, Biodegradable patches, Dissolvable patches, 3D printed patches, Skin permeability, First-pass metabolism, Smart drug delivery systems.

3. INTRODUCTION

Transdermal drug delivery is a non-invasive method in which drugs pass through the skin into systemic circulation. It provides controlled and sustained drug release, bypasses the gastrointestinal tract, and avoids first-pass hepatic metabolism. Compared with oral,

injectable, and inhalation routes, it improves patient compliance and reduces dose fluctuations.

Transdermal patches are simple dosage forms that deliver drugs at a predetermined rate for prolonged periods and can be stopped easily by removing the patch. They are widely used for smoking cessation, pain management, motion sickness, and hormone therapy. Common drugs formulated as patches include nitroglycerin, estradiol, clonidine, fentanyl, nicotine, and scopolamine.

Hydrogels help maintain skin hydration, enhance drug permeation, and provide controlled and sustained drug release. Their soft and elastic structure improves adhesion and comfort on the skin, making them promising carriers for effective transdermal drug delivery systems.

3.1 AIM

Aim:- To explore and analyze the growing significance of transdermal patch-based drug delivery systems in modern healthcare, highlighting their ability to enhance therapeutic efficacy, improve patient compliance, enable controlled drug release, and serve as a platform for advanced pharmaceutical innovations.

3.2 Objective of Work

1. To study the principles, mechanisms, and pathways of transdermal drug delivery systems and factors affecting drug permeation through the skin.
2. To review different types of transdermal patches, formulation strategies, and the role of polymers in controlled drug release.
3. To evaluate the advantages, clinical applications, and patient benefits of transdermal patches in various diseases.
4. To analyse quality control parameters, limitations, challenges, and recent advancements in transdermal drug delivery systems.

3.3 Rationale of Work

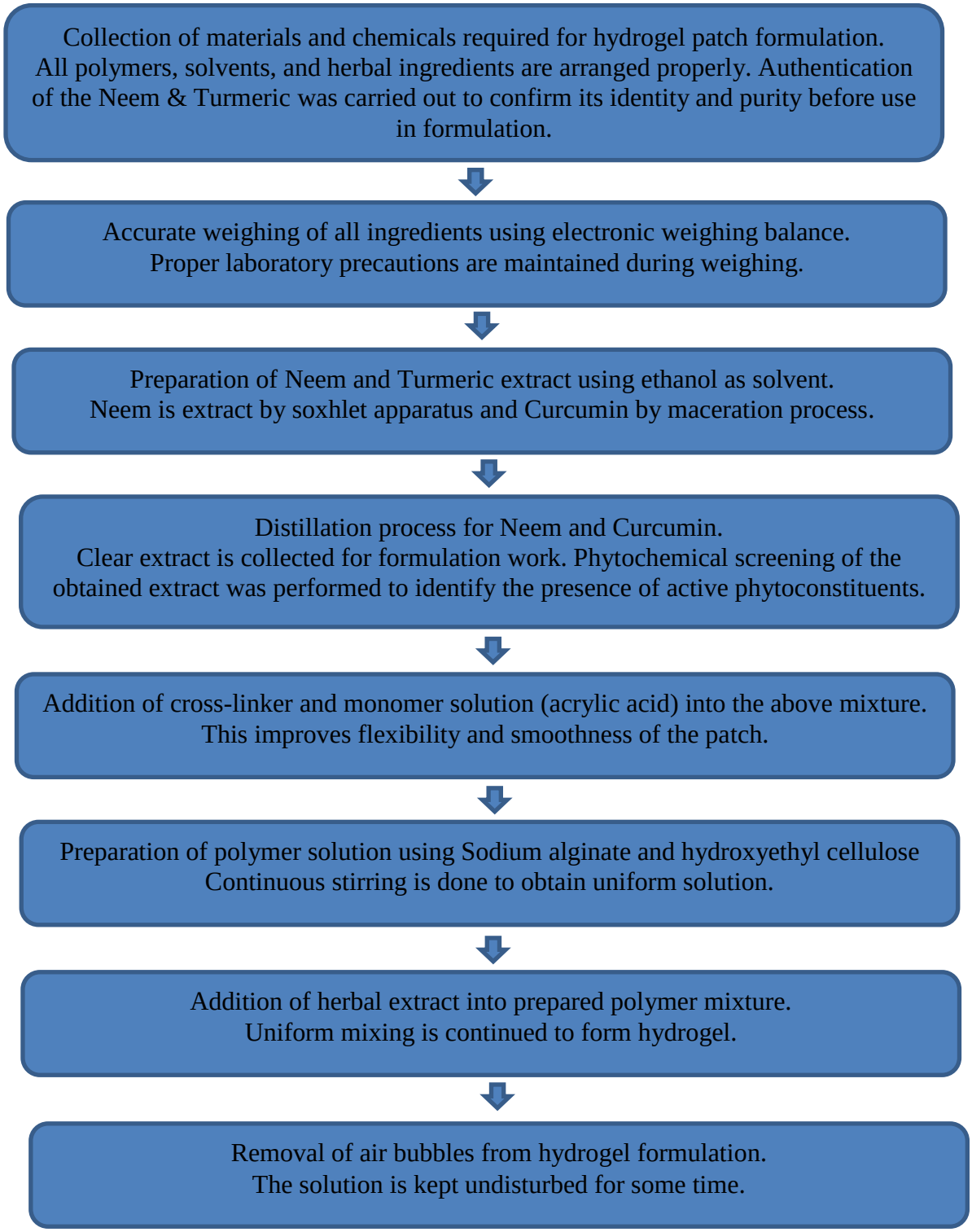
Transdermal drug delivery systems are used to avoid first-pass metabolism, improve drug absorption, and provide controlled and prolonged drug release. They are painless, easy to use, and improve patient compliance.

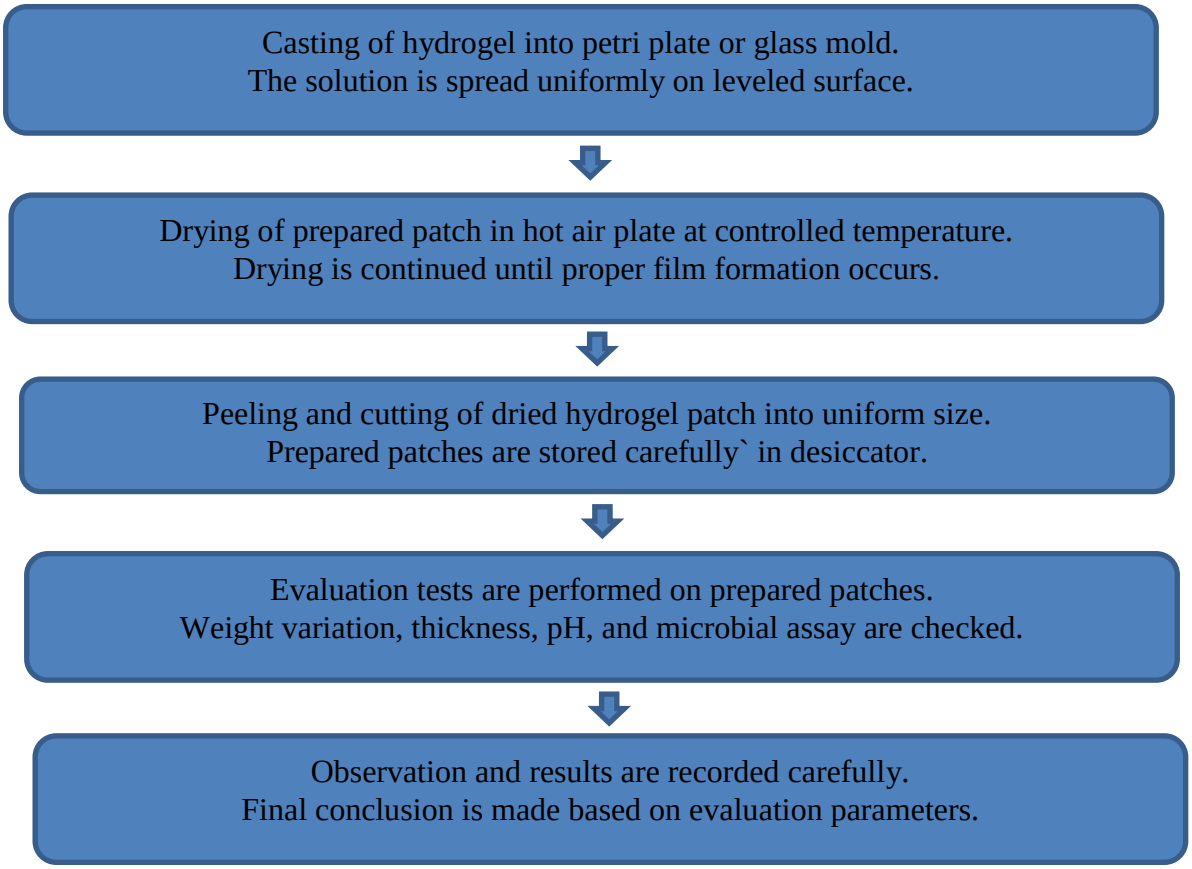
Hydrogels are suitable for transdermal applications because they retain large amounts of water, maintain skin hydration, and enhance drug permeation. Their polymeric network

enables controlled and sustained drug release.

Additionally, hydrogels are non-toxic, skin-friendly, soft, and flexible, providing better adhesion and comfort on the skin. Therefore, the present work aims to develop a hydrogel-based transdermal patch for effective and sustained drug delivery.

3.4 Plan Of Work





4. EXPERIMENTAL PROCEDURE

4.1 Sample collection and pre-treatment

The samples of turmeric was collected from local grocery shop and leaves of neem were collected from local market.

4.2 Authentication

Authentication of Neem and Turmeric plant materials was carried out to confirm their identity purity, and authenticity before extraction and formulation**.**

4.3 Extraction of Turmeric

4.3.1 Cold Maceration

Cold maceration is a simple technique, though it requires more time compared to Soxhlet extraction. In this method, the plant material is soaked in a suitable solvent at room temperature without the application of heat, allowing gradual extraction of curcumin.

Materials Required:

- Dried turmeric powder
- Organic solvent (95% ethanol)

- Glass container with a tight lid
- Filter paper

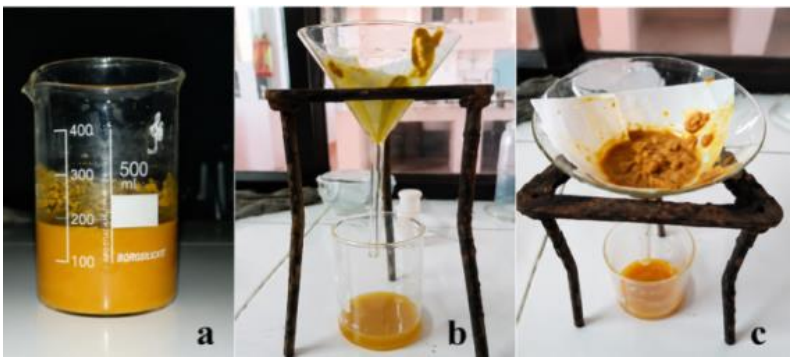


Fig. No. 4.1: Cold maceration.

Procedure

A measured quantity (30 g) of turmeric powder was placed in a glass container, and 100 ml of ethanol was added. The mixture was thoroughly stirred and the container was covered with aluminium foil to prevent contamination. It was then kept in a dark place at room temperature for 24 hours. After the maceration period, the solution was filtered and the solvent was evaporated using a water bath at 50–70°C to obtain the extract.

4.4 Extraction of Neem

4.4.1 Soxhlet Extraction (Neem)

All procedures were carried out under sterile conditions. To ensure sterility, conical flasks were autoclaved at 121°C for 15 minutes. The neem samples were accurately weighed using an electronic balance and wrapped in muslin cloth, which was then placed in the Soxhlet apparatus. For extraction, approximately 30 g of dried neem leaf powder was used along with 150 ml of ethanol as the solvent. The setup was heated using a reflux system at around 60°C. The extraction was continued for about 8–9 hours. After completion, the solvent was evaporated using a water bath maintained at 50–70°C to obtain the concentrated neem extract.

Fig. No. 4.2: Soxhlet apparatus.

4.5 Phytochemical Screening- Turmeric[4]

4.5.1 Alkaline reagent test[4]

Take 1 mL of curcumin extract in a test tube and add 2–3 drops of alcoholic sodium hydroxide solution (NaOH). Observe the formation of a deep yellow colour. Then add 1–2 drops of dilute hydrochloric acid (HCl) dropwise.

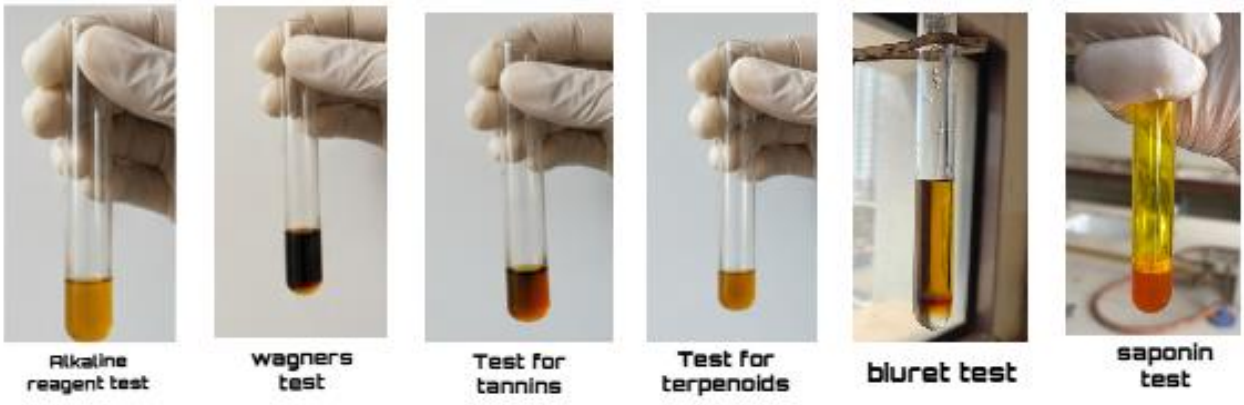


Fig. No. 4.3: Phytochemical test for Curcumin.

4.5.2 Test for Alkaloids[4]

- The extract was mixed with 3 ml of dilute hydrochloric acid and then filtered thoroughly. The filtrate was tested carefully with Wagner's test.
- **Wagner Test:** 1 ml of the filtrate extract was treated with Wagner's reagent;

4.5.3 Test for Tannins[4]

Add 1ml extract then Add 2ml chloroform after this Add concentrated sulphuric acid and observe colour change.

4.5.4 Test for Terpenoids[4]

Take 1 mL of the curcumin extract in a test tube and add 2–3 drops of chloroform, followed by 1–2 mL of concentrated sulfuric acid (H_2 SO_4) carefully along the sides of the test tube.

4.5.5 Test for Proteins[4]

Biuret's Test

Add 2 ml of Biuret reagent to 2 ml of extract. Shake well and warm it on water bath.

4.5.6 Test for Saponins[4]

1 mL of extract was taken and an appropriate amount of water was added, then the mixture was shaken vigorously and observed in a test tube for any visible changes.

4.6 Phytochemical Screening- Neem[4]

Fig. No. 4.4: Phytochemical test for Neem.

4.6.1 Steroid test[4]

Take 1 mL of neem extract in a test tube and add 2 mL of chloroform. Then carefully add 1–2 mL of concentrated sulfuric acid along the sides of the test tube without shaking.

4.6.2 Saponin test[4]

Neem leaf extract was dissolved in hot distilled water and shaken vigorously. After keeping it for 10 minutes, 2N HCl was added.

4.6.3 Ferric chloride test[4]

5 mL of neem extract was treated with ferric chloride ($FeCl_3$). A blue-black or green colour indicated the presence of tannins.

4.6.4 Biuret test[4]

Take 1 mL of neem extract in a test tube and add 1 mL of 10% sodium hydroxide (NaOH) solution. Then add 2–3 drops of 1% copper sulfate ($CuSO_4$) solution and mix gently.

4.6.5 Alkaline reagent test[4]

Take 1 mL of Neem extract in a test tube and add 2–3 drops of alcoholic sodium hydroxide solution (NaOH). Observe the formation of a deep yellow colour. Then add 1–2 drops of dilute hydrochloric acid (HCl) dropwise.

4.7 Protein denaturation test[5]

1. Preparation of Phosphate Buffer (100 mL)

The phosphate buffer was prepared by dissolving NaCl (0.8 g), KCl (0.02 g), Na_2 HPO_4 (0.14 g), and KH_2 PO_4 (0.02 g) in 100 mL of distilled water. The pH was adjusted to the range of 6.8–7.2.

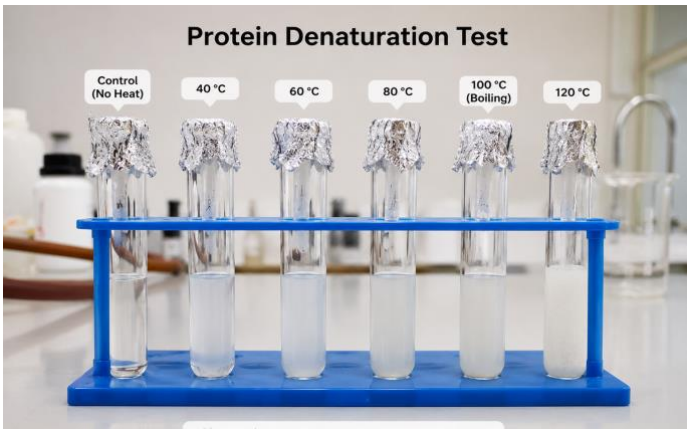


Fig. No. 4.5: protein denaturation.

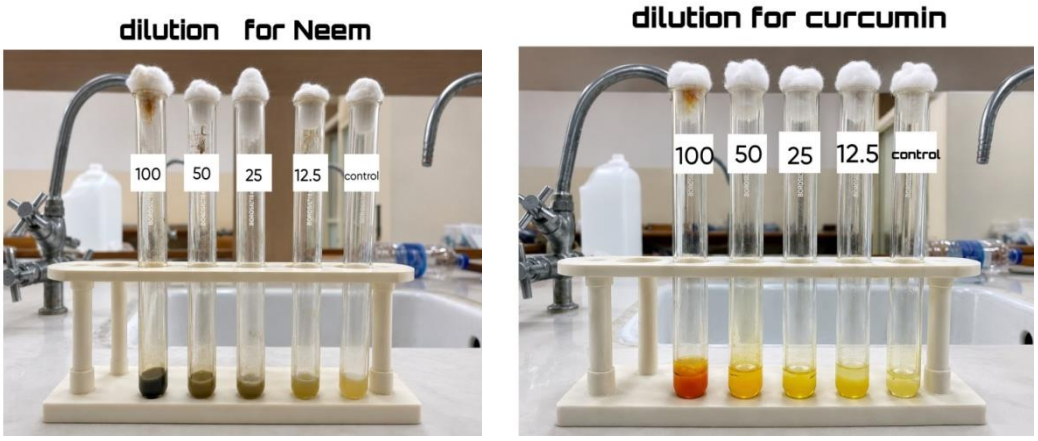
2. Procedure

For the standard solution, 2 mL of diclofenac sodium solution, 0.2 mL of egg albumin, and 2.8 mL of phosphate buffer were mixed. For the test solution, 2 mL of extract solution, 0.2 mL of egg albumin, and 2.8 mL of phosphate buffer were added. For the control, 2 mL of distilled water, 0.2 mL of egg albumin, and 2.8 mL of phosphate buffer were mixed.

3. Experimental Steps

Different concentrations of standard and test solutions (0.1–0.4 mg/mL) were prepared and incubated at 37°C for 30 minutes. The mixtures were then heated at 70°C for 15 minutes in a water bath, followed by cooling. Finally, the absorbance was measured at 280 nm using a UV spectrophotometer.

4.8 MIC (Minimum Inhibitory Concentration) Determination[6]



A **B**

Fig. No. 4.6: MIC determination A) curcumin & B) Neem.

Procedure

1. Take 5 test tubes + 1 control tube.
2. Add 1 mL broth to all tubes.
3. Add 1 mL antifungal solution to Tube 1 and mix well.
4. Transfer 1 mL from Tube 1 to Tube 2 and mix.
5. Repeat the transfer of 1 mL from tube to tube until the last tube (serial dilution).
6. Discard 1 mL from the last tube after dilution.
7. The control tube contains only broth (no antifungal agent).
8. Add an equal amount of microbial inoculum to all tubes.
9. Usually add 0.1 mL inoculum to each tube and mix properly.
10. Incubate and observe for growth inhibition. The lowest concentration showing no visible growth is the MIC.

➢ **Flow of MIC determination**

Antifungal in Tube 1 → Serial dilution (Tube 2 → Tube 3 → Tube 4 → Tube 5) → Add inoculum → Incubation → Observe growth → Determine MIC.

4.9Antimicrobial assay (zone of inhibition)[3]

Procedure

1. Prepare sterile nutrient agar plates and allow them to solidify under aseptic conditions.
2. Spread 0.1 mL bacterial inoculum (Staphylococcus aureus) uniformly on the agar surface using a sterile spreader.

3. Make wells of 6 mm diameter in the agar using a sterile cork borer.
4. Add 0.1 mL of neem extract, 0.1 mL of control, and 0.1 mL of ciprofloxacin in plate A. In the plate B, maintain the same setup, but add 0.1 mL of curcumin extract instead of neem extract.
5. Incubate the plates at 37°C for 24 hours.
6. After incubation, observe and measure the zone of inhibition (mm) around each well.

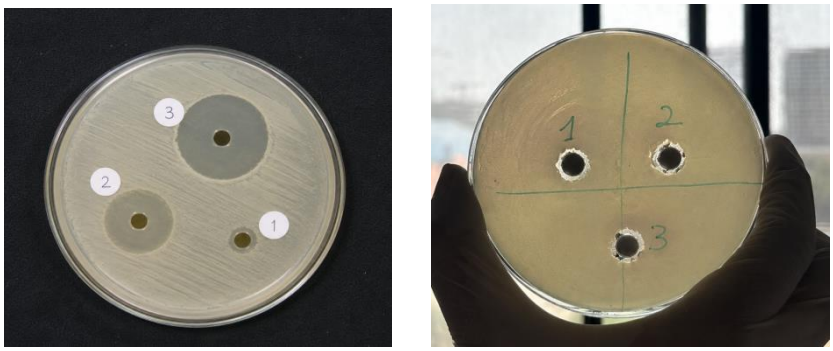


Fig. No. 4.7: Antimicrobial assay of active ingredient A)Neem & B) Curcumin.

4.10 Preparation of dosage form (Hydrogel Patch)[1]

Sr. No.	Chemical Materials	Apparatus
1	Sodium alginate (SA)	Hot plate with magnetic stirrer
2	Hydroxyethyl cellulose (HEC)	Beakers
3	Acrylic acid (AA)	Measuring cylinder
4	Ammonium persulfate (APS)	Petri dishes
5	N,N′-methylene bisacrylamide (MBA)	Aluminium foil
6	Distilled water	Electronic water bath
7	Ethanol	Vacuum oven

Sr. No.	Active Ingredient	Biological Source	Major Active Constituents
1	Neem	*Azadirachta indica*	Nimbin, Nimbidin, Azadirachtin
2	Turmeric	*Curcuma longa*	Curcumin

Formulation table[1]

Formulation Code	SA (g)	HEC (g)	AA (g)	APS (g)	MBA (g)	Observation
HECA-1	0.10	0.01	4	0.10	0.10	Very thin
HECA-2	0.10	0.02	4	0.10	0.10	Very thin
HECA-3	0.10	0.03	4	0.10	0.10	Slightly improper
HECA-4	0.10	0.03	4	0.10	0.10	Thick gel
HECA-5	0.15	0.03	4	0.10	0.10	Very thick
HECA-6	0.20	0.03	4	0.10	0.10	Thick
HECA-7	0.10	0.03	4	0.10	0.10	Thick
HECA-8	0.10	0.03	5	0.10	0.10	Highly swollen
HECA-9	**0.10**	**0.03**	**6**	**0.10**	**0.10**	**Perfect**
HECA-10	0.10	0.03	4	0.10	0.10	Improper

HECA-11	0.10	0.03	4	0.10	0.15	Hard gel
HECA-12	0.10	0.03	4	0.10	0.20	Bubbling issue

Best selected fromultion[1]

Ingredient	Quantity (HECA-9)	Use
Sodium alginate (SA)	0.10 g	Gelling
Hydroxyethyl cellulose (HEC)	0.03 g	Thickening
Acrylic acid (AA)	6 g	Swelling
Ammonium persulfate (APS)	0.10 g	Initiation
N,N′-methylene bisacrylamide (MBA)	0.10 g	Crosslinking
Distilled water	q.s.	Solvent
Ethanol	q.s.	Purification

Procedure[1]

1. Preparation of polymer solutions

Accurately weighed (SA) was dissolved in 5 mL of distilled water and stirred on a hot-plate magnetic stirrer at 37 °C for 20 minutes until a homogeneous solution was obtained.

(HEC) was dissolved separately in 5 mL of distilled water and stirred at 90 °C until a clear solution was formed.

2. Preparation of initiator and cross-linker solution

Required quantities of (APS) and N,N′-methylene (MBA) were dissolved together in 5 mL of distilled water and stirred at 37 °C to obtain a clear solution.

3. Monomer preparation

(AA) was taken separately in a clean beaker.

4. Mixing of reaction components

The prepared SA and HEC solutions were allowed to cool to room temperature. The APS–MBA solution and AA were added drop-wise to the polymer mixture with continuous stirring to obtain a uniform reaction mixture. After obtaining a uniform mixture, 1 mL of neem (Azadirachta indica) extract and 1 mL of curcumin (Curcuma longa) extract were added slowly with continuous stirring to ensure proper incorporation into the formulation.

5. Casting

The final reaction mixture was poured carefully into labelled Petri dishes. Petri dishes were covered with aluminium foil to prevent contamination.

6. Polymerization

The Petri dishes were placed in a preheated electronic water bath and subjected to the following heating cycle:

50 °C for 2 hours

60 °C for 2 hours

7. Washing

After 24 hours, the formed hydrogel patches were removed from the Petri dishes.

Patches were gently washed with a water:ethanol mixture (70:30) to remove unreacted chemicals and impurities.

8. Drying

The washed patches were dried at RT (room temperature).

9. Storage

The dried hydrogel patches were stored in polythene bags.

4.11 Evaluation of Hydrogel Patch[2]

4.11.1 Physical Appearance[2]

The prepared hydrogel patch was visually inspected for its colour, clarity, smoothness, transparency, uniformity, and presence of any air bubbles or cracks**.** The patch was observed under normal light and examined manually to ensure uniform texture and proper appearance.

Fig. No. 4.8: Physical appearance.

4.11.2 Thickness Measurement[2]

The thickness of the hydrogel patch was measured using a digital vernier calliper/micrometre screw gauge**.** Measurements were taken at three to five different points of the patch, and the average thickness was calculated to determine uniformity.

Fig. No. 4.9: Thickness.

4.11.3 Weight Variation Test[2]

For weight variation, five patches of equal size were selected and weighed individually using a digital weighing balance. The average weight was calculated, and individual weights were compared with the mean value to determine variation within the acceptable limit (±5%).

Fig. No. 4.10: Weight Variation.

4.11.4 Folding Endurance[2]

Folding endurance was determined by repeatedly folding the hydrogel patch at the same place manually until it showed signs of breaking or cracking. The number of folds required to break the patch was recorded to evaluate the flexibility and mechanical strength of the patch.

Fig. No. 4.11: Folding Endurance.

4.11.5 Surface pH Determination[2]

The hydrogel patch was allowed to swell in a small quantity of distilled water or phosphate buffer (pH 7.4**)** for about 30 minutes**.** The pH meter electrode was then brought into contact with the surface of the swollen patch, and the pH was recorded to assess skin compatibility.

4.11.6 Moisture Content Determination[2]

The prepared hydrogel patch was initially weighed **(**initial weight**)** and then placed in a desiccator containing anhydrous calcium chloride/silica gel for 24 hours. After drying, the patch was reweighed **(**final weight**).** The percentage moisture content was calculated using the formula.

4.12 Franz Diffusion Procedure for Neem + Curcumin Hydrogel Patch[2]

1. **Prepare membrane**

Soak egg membrane in phosphate buffer pH 7.4 for 30 min.

2. **Fill receptor compartment**

Add 15–20 mL phosphate buffer (pH 7.4) and maintain 37 ± 0.5°C with stirring.

3. **Mount membrane**

Fix membrane between donor and receptor compartments without air bubbles.

4. **Apply patch**

Place hydrogel patch on membrane in donor compartment.

5. **Collect samples**

Withdraw 1 mL receptor fluid at 0.5, 1, 2, 4, 6, 8 hr, replacing with fresh buffer.

6. **Analyse sample**

Measure absorbance by UV: Curcumin**:** 425 nm, Neem: 270–280 nm

7. **Calculate**

Plot cumulative drug permeated vs time to determine permeation rate.

Fig. No. 4.12: Franz diffusion.

5. RESULT AND DISCUSSION

5.1 % yield (Neem and Turmeric extract)

The crude extract of Neem was obtained by Soxhlet extraction using ethanol as solvent from 25 g of powdered sample, and the percentage yield was found to be **20%**.The crude extract of Turmeric was obtained by maceration using ethanol as solvent from 30 g of powdered drug, and the percentage yield was found to be **20%**

Percentage Yield Calculation

Formula

Percentage yield = (Weight of extract / Weight of crude drug) × 100

1. *Azadirachta indica* (Neem)

Weight of powdered sample = 30 g

Weight of extract = (20 × 30) / 100 = 6 g

So,

Percentage yield = (6 / 30) × 100 = 20%

2. *Curcuma longa* (Turmeric)

Weight of powdered drug = 30 g

Weight of extract = (20 × 30) / 100 = 6 g

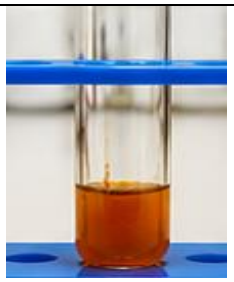
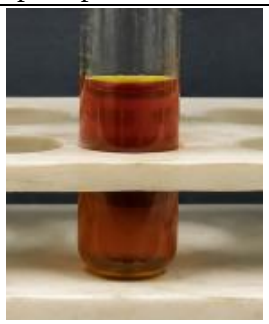
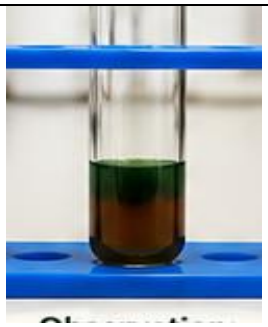
So,

Percentage yield = (6 / 30) × 100 = 20%

Final Result

- Neem extract yield = 6 g (20%)
- Turmeric extract yield = 6 g (20%

5.2 Phytochemical Analysis

S.No	Phytochemical	Curcuma longa (Turmeric) – Test & Observation	Azadirachta indica (Neem) – Test & Observation
1	Alkaloids	 Wagner's Test: Brownish-red precipitate formed	 Wagner/Dragendorff Test: Orange-reddish precipitate formed
2	Terpenoids / Steroids	 Salkowski Test: Reddish-brown colour formed	 Salkowski Test: Reddish-brown ring formed
3	Tannins	 Ferric Chloride Test: No Blue-black/green colour observed	 Ferric Chloride Test: Blue-black/green colour observed
4	Proteins	 Biuret Test: Violet/red colour developed	 Biuret Test: Violet colour developed

5	Saponins	 Foam Test: Negative	 Foam Test: Positive

5.3 MIC (Minimum Inhibitory Concentration) Determination

The Minimum Inhibitory Concentration (MIC) of curcumin was found to be 12.5 µg/mL, while neem extract showed an MIC of 25 µg/mL against the test microorganism, indicating good antimicrobial activity."

5.4 Antimicrobial assay (zone of inhibition)

Sample	Zone of Inhibition (mm)	Antimicrobial Activity
Curcumin Extract	12 mm	Moderate
Neem Extract	10 mm	Moderate
Standard Drug	17 mm	Highest

Curcumin extract showed a zone of inhibition of 12 mm, neem extract showed 10 mm, while the standard drug exhibited the highest antimicrobial activity with a 17 mm zone of inhibition.

5.5 Evaluation Test of patch

Sr no	Evaluation Parameter	Standard	Results Obtained
1.	Physical Appearance	Clear, smooth, flexible, uniform patch	Clear, smooth, flexible and uniform patch obtained
2.	Thickness	0.2–0.6 mm (uniform across patch)	0.3 mm ± 0.5 mm and found uniform throughout the patch
3.	Weight Variation	±5% acceptable variation	Within acceptable limit (±5%)
4.	Folding Endurance	>300 folds without breaking	Withstood more than 300 folds without breaking
5.	Surface pH	5.5–7.5	Found to be 6, suitable for skin application

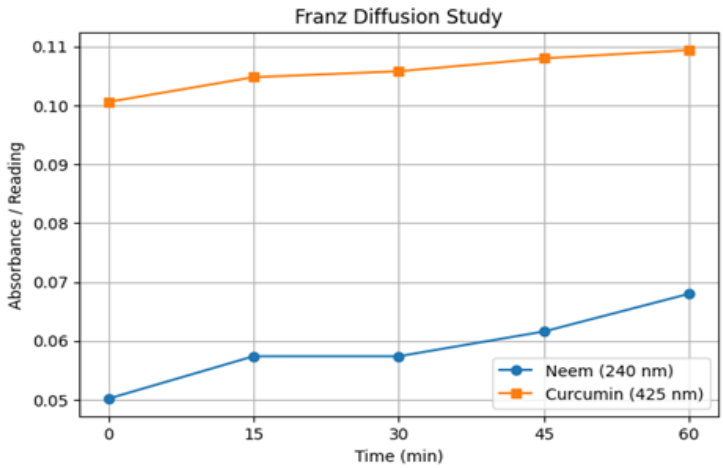
5.6 Protein Denaturation Test

- The Diclofenac standard showed maximum inhibition of protein denaturation of 99.80% at 0.2 mg/mL concentration.
- The Azadirachta indica extract showed 70.90% inhibition at 0.1 mg/mL concentration.

- The Curcuma longa extract showed 79.76% inhibition at 0.4 mg/mL concentration.
- The results indicate that both plant extracts possess significant anti-inflammatory activity compared to the standard drug.

Sample	Best Concentration	% Inhibition
Diclofenac	0.2	99.80%
Neem	0.1	70.90%
Curcumin	0.4	79.76%

5.7 Franz Diffusion



Time (min)	NEEM(240nm)	CURCUMIN(425NM)
0 min	0.0502	0.1006
15min	0.0574	0.1048
30min	0.0574	0.1058
45min	0.0616	0.1080
60min	0.0680	0.1094

The Franz diffusion study of the neem and curcumin hydrogel patch showed a gradual increase in drug permeation over time. The absorbance of Azadirachta indica increased from **0.0502 at 0 min** to **0.0680 at 60 min**, while Curcuma longa showed an increase from **0.1006 at 0 min** to **0.1094 at 60 min**. The results indicated sustained and controlled drug release from the hydrogel patch through the membrane.

6. SCOPE AND FUTURE PROSPECTIVE

The herbal hydrogel patch using neem (*Azadirachta indica*) and turmeric (*Curcuma longa*) shows strong potential in pharmaceutical and biomedical applications due to its anti-inflammatory, antimicrobial, and antioxidant properties. The hydrogel system enables controlled drug release, enhanced skin hydration, and improved therapeutic effectiveness.

It provides targeted topical delivery, reducing systemic side effects and increasing efficacy. The synergistic effect of neem and curcumin further enhances its activity. The formulation is suitable for wound healing, burns, acne, and inflammation, with future scope in nanohydrogels, smart delivery systems, and chronic wound management**.**

CONCLUSION

This study successfully developed a herbal hydrogel patch containing neem and curcumin with potential for topical application. The formulation showed wound healing, anti-inflammatory, and skin protective properties with controlled drug release and fewer side effects. Further research may help develop it into an effective pharmaceutical and skincare product.

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