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Green therapeutics: Formulating a transdermal patch with aqueous extract of Azadirachta Indica a. Juss and investigating its antimicrobial potential

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Abstract
The rising demand for eco-friendly and sustainable healthcare solutions has fueled interest in plant-based therapeutics. Azadirachta indica A. Juss (Neem), known for its broad-spectrum antimicrobial and medicinal properties, represents a promising candidate for transdermal drug delivery systems. This study focuses on the formulation of a transdermal patch incorporating the aqueous extract of A. indica and evaluating its antimicrobial efficacy. The patch was prepared using biodegradable polymers to ensure skin compatibility and controlled drug release. Antimicrobial activity was assessed against selected bacterial and fungal strains, demonstrating significant inhibitory effects compared to controls. The findings suggest that neem-based transdermal patches hold potential as a green therapeutic approach for managing microbial infections, combining sustainability, patient compliance, and effective drug delivery.

Keywords: Azadirachta Indica (Neem), transdermal patch, antimicrobial activity, green therapeutics, plant-based medicine, aqueous extract, sustainable drug delivery

Introduction

The relentless pursuit of innovative pharmaceutical formulations, aiming at heightened therapeutic efficacy with minimal side effects, remains a driving force in contemporary pharmacological research. In this dynamic landscape, the exploration of natural products with established medicinal properties emerges as a promising avenue. Among these, Azadirachta indica, colloquially known as Neem, commands attention due to its rich pharmacological profile and historical significance in traditional medicine.

Azadirachta indica, a tree indigenous to the Indian subcontinent, has been an integral part of traditional medicine for centuries. Its versatile medicinal properties have sparked keen scientific interest, compelling researchers to systematically investigate its therapeutic potential.

Within this exploration, the present study undertakes a comprehensive examination, focusing on the formulation and evaluation of a transdermal patch utilizing the aqueous extract of Azadirachta indica. The transdermal route, with its advantages such as sustained drug release and improved patient compliance, emerges as a compelling approach for drug delivery. This research aims not only to capitalize on these benefits but also to leverage the inherent medicinal properties of Azadirachta indica.

The research's significance extends beyond the mere development of a novel drug delivery system; it lies in the meticulous utilization of Azadirachta indica's aqueous extract. By concentrating on the aqueous extract, this study aligns with the escalating emphasis on green and sustainable pharmaceutical practices. Additionally, the investigation into the antimicrobial potential of the aqueous extract adds a crucial dimension, addressing the global concern of antimicrobial resistance.

The primary objectives of this research are twofold. Firstly, to formulate a transdermal patch that incorporates the aqueous extract of Azadirachta indica and rigorously assess its efficacy as a drug delivery system. Secondly, to delve into the antimicrobial potential of the aqueous extract, thereby contributing valuable insights to the ongoing discourse on natural antimicrobial agents.

In pursuit of these objectives, the study integrates advanced pharmaceutical formulation techniques, principles of drug delivery, and microbiological assays. This holistic approach provides a comprehensive evaluation of the proposed transdermal patch and the antimicrobial activity of Azadirachta indica.

This research transcends the boundaries between traditional knowledge and contemporary pharmaceutical science. It not only serves as a bridge but also holds the promise of introducing a novel, sustainable, and effective therapeutic approach.

Green Therapeutics: A Revolution in Drug Development

1. Historical Evolution of Green Therapeutics

The historical use of plants as medicinal remedies traces back to the earliest civilizations, with compelling evidence of therapeutic applications found in ancient Egyptian, Chinese, and Greek texts. Over 5000 years ago, the Sumerians meticulously documented herbal studies on clay tablets, listing hundreds of medicinal plants such as myrrh and opium [1]. In 3000 BC, ancient Chinese and Egyptian writings, notably the Ebers Papyrus, elaborated on the medicinal uses of numerous plants, including garlic, juniper, cannabis, castor bean, aloe, and mandrake [1].

Throughout the middle Ages and the Renaissance, herbalists played a pivotal role in healthcare, contributing to the continued utilization of plants in medicine. However, the landscape shifted in the 20th century with the advent of synthetic drugs. The perception of synthetic compounds as more potent and reliable led to a decline in the reliance on plant-based remedies, marking a significant transition in medical practices.

2. Significance of Utilizing Plant Extract in pharmaceutical Formulations

The World Health Organization notes that 80% of people in developing countries rely on ethnomedicines for primary

healthcare, while half of the global population still depends on plant-derived ethnomedicines [2].

In Tamil literature, neem (Azadirachta indica) is recognized as the first medicinal plant in the Siddha system, historically used for ailments like smallpox and infectious diseases [3]. Scientists found evidence on the use of A. indica on a skull having cranial surgery. These discoveries suggest the use of A. indica in both surgical and phytochemical processes in the world's most ancient and developed civilizations [3].

Neem holds significant medicinal importance in modern medicine, Unani, Ayurveda, and Homeopathy. Neem tree in Sanskrit is called as "Arishtha", which means "reliever of sickness" [4]. With chemical investigations revealing isoprenoid and non-isoprenoid compounds [5]. Isoprenoids include diterpenoids and triterpenoids [6], while non-isoprenoids consist of amino acids, polysaccharides, polyphenolic compounds, coumarin, sulphurous compounds, dihydrochalcone, aliphatic compounds, and tannins. Neem's active compounds play a crucial role in disease management, exhibiting diverse biological and pharmacological activities [7] such as antioxidant, anti-inflammatory, anti-arthritic, antipyretic, antiviral, spermicidal, hypoglycemic, anthelminthic, antigastric ulcer, and antitumor effects [8].

3. Current landscape of Natural Product-based Therapeutics

The current natural product-based therapeutics landscape involves extensive research and development, with ongoing clinical trials exploring the efficacy and safety of plant-derived compounds for diverse diseases. Notable examples include artemisinin from sweet wormwood for malaria, paclitaxel from Pacific yew bark as an anti-cancer drug, and resveratrol from grapes and red wine for its health-promoting effects like anti-inflammatory and antioxidant properties.

Pharmacological Profile of NEEM

As scientific knowledge advances, Green Therapeutics is positioned to be a pivotal player in the future of medicine, providing natural, effective, and safe alternatives to synthetic drugs. Recent research underscores neem's diverse therapeutic potential, offering compelling evidence of its pharmacological efficacy.

1. Antimicrobial Activity

Neem extracts, derived from Azadirachta indica, exhibit potent antimicrobial activity against a broad spectrum of bacteria, fungi, and viruses. The major bioactive compound, azadirachtin, is particularly effective against gram-positive bacteria such as Staphylococcus aureus and Bacillus subtilis. Additionally, neem extracts demonstrate activity against Mycobacterium tuberculosis, the causative agent of tuberculosis [9]. Various parts of the neem plant play a role in inhibiting microbial growth and breaking down cell walls. Azadirachtin, a complex tetranortriterpenoid limonoid found in neem seeds, is the key constituent responsible for both antifeedant and toxic effects in insects [14]. Neem also functions as a potent free radical scavenger due to its rich antioxidant content. Azadirachtin and nimbolide exhibit concentration-dependent antiradical scavenging activity and reductive potential, with nimbolide showing greater efficacy than azadirachtin and ascorbate [15].

2. Anti-inflammatory Properties

Neem extracts exhibit significant anti-inflammatory properties, making them valuable for treating conditions such as arthritis and rheumatism. Studies have shown that neem extracts can inhibit the production of inflammatory mediators, such as prostaglandins and leukotrienes, thereby reducing inflammation and ain [10].

3. Anti-diabetic Effects

Neem has been shown to possess antidiabetic properties, with studies demonstrating its ability to lower blood glucose levels and improve insulin sensitivity. Neem extracts have been found to inhibit the activity of α-glucosidase, an enzyme responsible for carbohydrate digestion, thereby slowing the absorption of glucose into the bloodstream [11].

4. Antineoplastic Activity

Neem extracts have shown promising antineoplastic activity, with studies demonstrating their ability to inhibit the growth and proliferation of cancer cells. Azadirachtin has been found to induce apoptosis, a programmed cell death process, in various cancer cell lines [12].

5. Immunomodulatory Effects

Neem extracts have been shown to possess immunomodulatory properties, enhancing the body's immune response to infections. Studies have demonstrated that neem extracts can stimulate the production of immune cells, such as macrophages and lymphocytes, and enhance their phagocytic and cytotoxic activities [9].

6. Gastroprotective Effects

Neem extracts have been shown to exhibit gastroprotective properties, protecting the stomach lining from damage caused by ulcers and other gastric disorders. Studies have demonstrated that neem extracts can enhance the production of gastric mucus, which acts as a protective barrier against acid and irritants [13].

Novel Drug Delivery System

The objective of the Novel Drug Delivery System (NDDS) is to efficiently deliver therapeutic drugs to specific body sites, ensuring prompt action and maintaining the desired concentration. This system should regulate drug delivery rates according to the body's needs over a specified treatment period.

The primary focus areas for NDDS research and development include:

- Liposomes
- Niosomes
- Nanoparticles
- Transdermal drug delivery
- Oral drug delivery
- Implants
- Microencapsulation
- Polymer in drug delivery

1. NDDS Categorization

- **Sustained Diffusion:** Sustained diffusion involves formulating pharmaceutical dosages to delay or prolong therapeutic effects in the systemic circulation, resulting in a sustained plasma profile.

- **Controlled Diffusion:** Controlled diffusion extends beyond sustained drug action, emphasizing predictability and reproducibility in drug diffusion kinetics. It includes Rate-Preprogrammed, Activation-Modulated, Feed-Back Regulated, and Site-Targeting systems.

2. Merits of drug delivery system

The merits of drug delivery systems include improved treatment for chronic illnesses (e.g., Cancer, Asthma, Arthritis), increased bioavailability, reduced systemic side effects related to high drug concentrations, sustained drug administration, decreased occurrence of side effects, prevention of first-pass metabolism and gastrointestinal degradation, enhanced patient compliance, targeted drug delivery to minimize toxicity, versatile and pH-dependent drug diffusion according to the body's demands, and biocompatibility.

3. Factors that limit its usage

- Physiological factors (enzymes, pH, transit rates, food, diseases) can impact drug bioavailability, affecting controlled diffusion precision.
- Intact products accumulating at sites may cause slow drug diffusion, leading to local irritation.
- Formulating sustained diffusion for short half-life drugs is challenging, requiring large doses for continuous diffusion.
- Products with substantial drug amounts risk unsafe overdose if improperly made, causing rapid diffusion.
- Ceasing therapy post-administration can be difficult due to toxicity or other reasons.
- Not suitable for potent drugs.

4. Topical Drug Delivery System [16]

Topical drug delivery, effective for local infections, administers drugs through the skin via routes like ophthalmic, rectal, vaginal, and skin. The skin, covering about $2m^2$ in adults, is crucial for drug delivery. Controlled drug delivery gains significance as the skin acts as a barrier limiting drug penetration.

The skin's lipid-rich nature and low water content hinder transport, posing absorption challenges. Hydrophilic or charged molecules face difficulties due to the lipid-rich Stratum corneum (40% lipids, 40% protein, 20% water). Lipophilic drugs are more suitable for topical delivery.

Topical delivery ensures safe and effective drug penetration to the desired area with lower doses, enhancing bioavailability and patient compliance. It addresses dermatological conditions, fueling a growing market. Advanced approaches like chemical enhancers, liposomes, bio-polymers, etc., surpass conventional methods in efficacy, tolerability, and patient compliance.

Despite the skin's barrier properties posing challenges, novel topical delivery systems using nanoscale carriers are explored for dermal and transdermal delivery.

4.1 Advantages of topical drug delivery systems [17]

- Bypasses first-pass metabolism
- Convenient and easy application
- Avoids intravenous therapy risks and absorption challenges
- Enables easy termination of medications
- Delivers drugs selectively to specific sites
- Prevents gastro-intestinal incompatibility
- Suitable for drugs with short half-life and narrow therapeutic window
- Enhances patient compliance
- Allows self-medication
- Achieves effectiveness with lower daily drug dose
- Disadvantages of topical drug delivery systems
- May cause skin irritation or dermatitis
- Some drugs have poor skin permeability
- Larger particle size drugs are not easily absorbed
- Risk of allergenic reactions
- Limited to drugs requiring very small plasma concentrations for action

5. Transdermal Drug Delivery System [18]

Transdermal drug delivery systems (TDDS) are self-contained forms applied to intact skin, delivering drugs at a controlled rate to the systemic circulation. This method is suitable for potent, low-molecular weight agents that may not endure the gastrointestinal tract or are subject to significant first-pass metabolism by the liver.

TDDS, in the form of patches, administer drugs topically for systemic effects at a predetermined rate. These devices, whether active or passive, offer an alternative route for medication administration, allowing pharmaceuticals to pass through the skin barrier. The patches work through a diffusion process, maintaining a constant drug concentration in the bloodstream over an extended wearing period.

5.1 Advantages of TDDS [19]

- Serves as an alternative to oral administration.
- Avoids gastrointestinal absorption, preventing enzymatic and pH-related deactivation.
- Allows reduced pharmacological dosages with a shorter metabolization pathway.
- Provides constant dosing, eliminating peaks and valleys in medication levels.
- Supports multi-day therapy with a single application.
- Enables rapid medication notification in emergencies and quick termination of drug effects via patch removal.

5.2 Disadvantages of TDDS

- Unsuitable for drugs requiring high blood levels, may cause skin irritation or sensitization
- Adhesives may not adhere well to all skin types, potentially uncomfortable to wear
- High product cost hinders widespread acceptance
- Influencing properties on transdermal delivery include diffusion from the vehicle
- Penetration through the skin barrier activates the pharmacological response

6. Kinetics of Transdermal Permeation

Understanding skin permeation kinetics is crucial for developing successful transdermal therapeutic systems.

Transdermal permeation of a drug involves the following steps:

- Sorption by stratum corneum.
- Penetration of drug through epidermis.
- Uptake of the drug by the capillary network in the dermal papillary layer.

7. Basic Components of Transdermal Drug Delivery Systems

- Polymer matrix or matrices control drug diffusion in transdermal devices, with potential polymers including natural ones like cellulose derivatives, zein, gelatin, waxes, and synthetic elastomers such as polybutadiene. Synthetic polymers like polyvinyl alcohol, polyethylene, and polyacrylate are also suitable for this purpose.
- The drug is a key component in transdermal devices, contributing to the controlled diffusion mechanism.
- Permeation enhancers aid in improving the penetration of drugs through the skin in transdermal applications.
- Other excipients play supporting roles in transdermal formulations, complementing the polymer matrix and enhancing drug delivery.

7. Physicochemical evaluation

- **Patch Thickness**

Measure the thickness of the prepared drug patch using a digital micrometer at various points to determine the average thickness and standard deviation, ensuring uniformity.

- **Weight Uniformity**

After drying the patches at 60°C for 4 hours, cut specified areas from different parts of the patch and weigh them on a digital balance. Calculate average weight and standard deviation values from individual weights.

- **Folding Endurance**

Cut a specific area of the strip and repeatedly fold it at the same place until it breaks. The number of folds without breaking indicates the folding endurance value.

Materials & Methods

1. List of Chemical Reagents

Sl. No.	Chemical Name	Company Name
01	Hydroxypropyl methyl cellulose (HPMC)	Himedia
02	Dichloromethane	SRL
03	Eudragit L 100	Ottokemi
04	PolyethyleneGlycol4000(PEG- 4000)	SRL
05	Poly Vinyl Alcohol (PVA)	Himedia
06	Dimethyl sulfoxide (DMSO)	MP Biomedia
07	Penicillin-G 10	SRL
08	Tween-80	SRL

All chemicals and reagents used in the present study were of analytical reagent grade (AR grade).

2. Preformulation Studies

Preformulation testing, the initial step in developing drug dosage forms, involves investigating the physical and chemical properties of a drug substance alone and with excipients. The goal is to generate information aiding formulators in creating stable, bioavailable, and manufacturable dosage forms. The studies include finding absorption maxima, examining physical appearance, determining solubility, establishing a standard curve, and conducting infrared spectroscopy studies (compatibility studies).

2.1 Finding the absorption maxima (λ max)

The drug was identified by determining its absorption maxima. Ultraviolet-Visible spectrophotometry was employed to gain specific insights into the chromophoric part of the molecules. When organic molecules in solutions are exposed to light in the Visible/Ultraviolet region, they absorb light at specific wavelengths based on the type of electronic transition associated with the absorption. For the extract solution (5, 10, 15, 20, 25 µg/ml) in distilled water, a standard cuvette was used, and it was scanned in the range of 200-800 nm in a UV spectrophotometer. The maximum absorption was observed at 382 nm. Consequently, all subsequent measurements were conducted at 382 nm.

Collection of Azadirachta indica A Juss. Leaves (Neem)

Azadirachta indica A Juss. Leaves were collected from the hostel boundary area of KIIT campus-06, KIIT University. Collected leaves were weighed and about40 gm of leaves were taken and cleaned with distilled water to remove any dirt or contaminants and pat-dried by tissue paper.

1. Extraction of leaves of Azadirachta indica A Juss.

The pat-dried leaves were then subjected to size reduction by the use of a mortar and pestle with a small amount of acetone to grind the neem leaves forming almost a paste like consistency. This increases the surface area, facilitating better extraction. Further the neem leaf-acetone mixture was placed in a beaker. Then 100ml of acetone was added to the mixture. The ratio of neem leaves to acetone may vary depending on your specific requirements. Shake it well to ensure thorough mixing.

Allow the neem leaf to soak in acetone for a specific period, such as 48 to 72 hours. This allows the acetone to extract bioactive compounds from the neem leaves. After the extraction period, filter the acetone extract using a filtration setup (filter paper and funnel) to separate the liquid extract from the solid residue. Store the filtered acetone extract in a clean, airtight container. Protect it from light and heat.

2. Screening of Antimicrobial activity of Azadirachta indica A. juss

The sample's antimicrobial activity was assessed using the disc diffusion technique (Indian Pharmacopoeia 1996, vol II A-105). Escherichia coli, sourced from KIIT School of Biotechnology Lab, served as the test microorganism and was maintained through periodic sub-culturing on nutrient agar. The sample's impact was compared to the positive control (Penicillin-5µg/disc), and after 24 hours, the plates were observed. The zone of inhibition was determined by measuring the minimum dimension of the area devoid of bacterial growth around the patch.

- **Priniciple:** Antibiotic-impregnated discs, with known concentrations, are positioned on agar plates uniformly inoculated with the test bacterium. After 18-24 hours of incubation at 37°C, the antibacterial agent diffuses through the agar, potentially inhibiting bacterial growth. The susceptibility is gauged by the diameter of the inhibition zone around the disc, with organisms reaching the disc edge considered resistant.

- **Experimental condition:** Organisms used: Escherichia coli Media used: Nutrient Agar Test Sample: Neem Extract Standard (Positive Control): Penicillin Negative Control: Acetone

- **Preparation of Nutrient Agar:** Nutrient Agar Preparation: Dissolve 8.2 gm of agar powder in 250 ml of water. Steam the medium to eliminate heat-coagulable material, filter it, and distribute 5ml portions into culture tubes. Plug the tubes with non-absorbent cotton and sterilize the medium in an autoclave for at least 15 minutes at 15 pounds per sq. inch at 121°C.

- **Preparation of Paper Disc:** By using standard punching machine what man filter paper was cut and standard paper of

6.0 mm diameter was prepared. The paper discs were sterilized in a hot air oven at 160ºC for 1hour. The paper discs were then impregnated with the test solution.

Formulation of Transdermal Patch [20]

A 2.5% w/v solution of polyvinyl alcohol (PVA) was made to create the backing membrane for the transdermal patch. For which in a beaker, 100ml of distilled water was heated to approximately 60℃, and 2.5g of weighed PVA was slowly added with continuous stirring using a magnetic stirrer. It was crucial to avoid exceeding 60℃, and if the temperature rose beyond this point, the heat was turned off.

After complete dissolution of PVA, the solution was cooled, poured into a glass petri plates covered with aluminum foil (with small holes for air passage), and placed in a water bath set at 60℃ for a minimum of 4 hours. If the solution did not set completely, excess solution could be discarded for the next step.

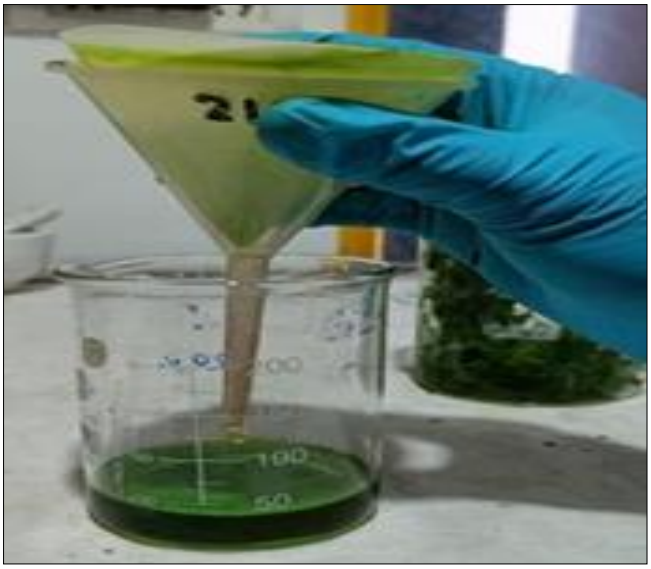
In another beaker, 100ml of Dichloromethane was utilized as the solvent system, and it was gently mixed with 5g of Eudragit L 100 over a period of 30 minutes to prevent the formation of lumps. The addition of Eudragit L 100 was carried out gradually to ensure thorough mixing, and no specific temperature was specified for the mixing process. Furthermore, the drug was gradually incorporated into the polymeric solution and stirred using a magnetic stirrer to achieve a uniform mixture. Subsequently, 5ml of a 5% PEG solution was introduced to function as a plasticizer. To enhance penetration, 2ml of DMSO and 2ml of Tween 80 were added. It's crucial to emphasize the avoidance of heat during the mixing process. Each component was added slowly with continuous stirring, emphasizing the goal of attaining a homogeneous solution.

In conclusion, 10-20ml of the prepared solution was gently applied to the pre-established backing membrane, left uncovered, and allowed to undergo comprehensive drying at room temperature for 24-48 hours. Following this, the patches were meticulously cut into 1 cm × 1 cm pieces and stored in a polyethylene bag for subsequent evaluation.

Observations

1. Extraction of leaves of Azadirachta indica A Juss.

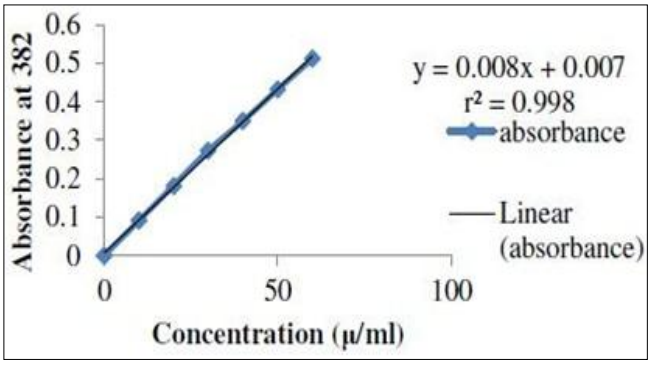
A deep green thick slurry was observed upon filtration of the neem leaf-acetone extract which was used as the drug component.



Attached below are

a. standard curve of Aqueous Extract of Azadirachta indica A Juss.and

b. Standard curve values of Aqueous Extract of Azadirachta indica A Juss.



Concentration (µg/ml)	Absorbance at 382 nm
	Average ± SD
0	0.000± 0.000
10	0.091± 0.001
20	0.182± 0.001
30	0.273± 0.001
40	0.363± 0.001
50	0.432± 0.001
60	0.512±0.008
Mean ± S.D: n = 3	

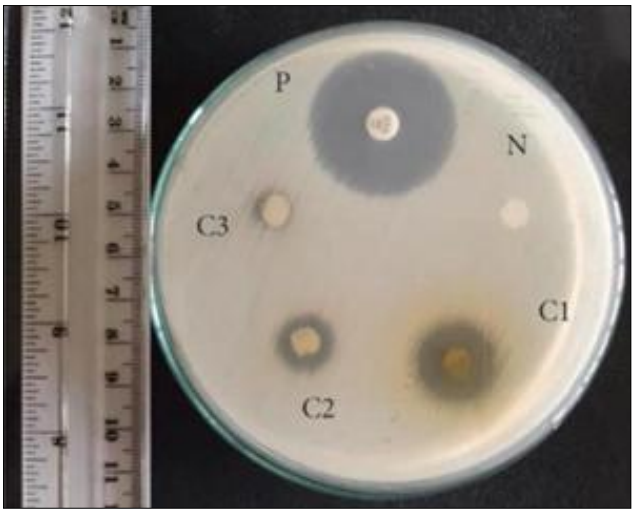
2. Screening of Antimicrobial activity of Azadirachta indica A. juss

Antimicrobial property of leaf extract of A. indica by well diffusion method -

In the agar plate images attached, a) the neem did show its inhibition zone but hypothetically t could be because of the green pigment of the neem extract that may have overlapped and b) this is how the agar plate looked with positive control, negative control & test sample.

The ideal scenario agar plate images should look like this:

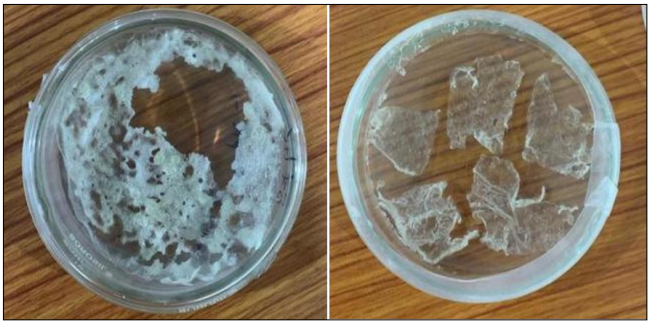
Where the positive control (P) shows the maximum zone of inhibition, (N) shows no zone of inhibition and (C1, C2, C3) shows a varied zone of inhibition with each being different extracts.



3. Formulation of Transdermal Patch

The two images attached here a) when the resulting solution is added to the backing membrane already established in the glass petri dish b) after the entire solution has dried up then a transparent sheet like structure is shown

The attached image shows a comparison that c) if the polymeric mixture isn't uniform then lumps could be seen in the patch d) if the polymeric mixture is uniform then a sheet like structure will be seen that could be cut into rectangular pieces.



Results

The following image attached under 7.2 a show the antimicrobial activity of the neem extract which means the antimicrobial activity of neem extract hasthe ability to inhibit or kill microorganisms, such as bacteria, fungi, or viruses. Neem extract holds therapeutic significance due to its diverse medicinal properties. It has been traditionally used in various cultures for its anti-inflammatory, antioxidant, antibacterial, antiviral, and antifungal properties. Neem is known to have potential benefits in treating skin conditions, boosting the immune system, promoting dental health, and managing various ailments.

The following image attached under 7.3 d shows the formation of neem extract based transdermal patch. A transdermal patch is significant for its localized and sustained delivery, offering convenient and targeted administration of therapeutic substances. This method minimizes systemic side effects, enhances patient compliance, and holds potential for various medical applications.

Neem extract transdermal patch offers significant therapeutic value by delivering localized and sustained anti-inflammatory, antibacterial, and antimicrobial effects for skin health. Its convenient application reduces side effects, promotes holistic well-being, and provides a targeted solution for various skin conditions.

Discussion

The pursuit of novel drug sources with potent antimicrobial properties is essential in the face of increasing antibiotic resistance. Selecting neem extract for antimicrobial drug development, particularly through a neem leaf-based plant extract, is grounded in its rich traditional use, broad-spectrum activity, potential to address antibiotic resistance, and sustainable nature. This choice holds promise for contributing to the development of effective and environmentally friendly therapeutic interventions.

Rationale for that is:

- **Innate Antimicrobial Properties of Neem:** Neem (Azadirachta indica) boasts a long history of traditional medicinal use, primarily due to its inherent antimicrobial properties, making it a valuable candidate for drug development.

- **Versatility in Targeting Microorganisms:** Neem demonstrates versatile antimicrobial activity against bacteria, fungi, and viruses, offering a comprehensive solution to combat a wide range of infectious agents.

- **Addressing Antibiotic Resistance:** The emergence of antibiotic-resistant strains necessitates alternative sources. Neem's natural compounds hold promise in addressing this challenge without the risk of resistance seen with conventional antibiotics.

- **Rich Bioactive Compounds in Neem Leaves:** Neem leaves are abundant in bioactive compounds, such as nimbin, nimbidin, and azadirachtin, known for their antimicrobial and immunomodulatory effects. Extracting from neem leaves ensures a thorough capture of these valuable constituents.

- **Synergistic Efficacy and Safety Profile:** Neem's complex chemical composition allows for potential synergistic effects, enhancing overall antimicrobial efficacy. Moreover, neem is generally considered safe, with minimal concerns about adverse effects.

- **Sustainable Approach:** Creating a neem leaf-based plant extract aligns with a sustainable and eco- friendly approach to drug development, tapping into the medicinal properties of a naturally occurring plant.

- **Versatility for Various Health Challenges:** Beyond its antimicrobial properties, neem demonstrates anti-inflammatory, antioxidant, and wound-healing effects, expanding its potential applications in addressing various health challenges.

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