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Formulation and Evaluation of Ethosomal Gel from Syzygium Cumini for Anti-Acne Activity

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Abstract: The present work was undertaken to formulate and analyze an ethosomal gel using Syzygium cumini seed extract for its potential anti-acne efficacy. Syzygium cumini (Jamun) is a well-known medicinal plant rich in bioactive elements such as anthocyanin's, phytosterols, flavonoids, and polyphenols, containing antibacterial, anti-inflammatory, and antioxidant effects. Jamun seeds were gathered, dried, ground into a powder, and then Soxhlet extracted using ethanol. The resulting extract was integrated into ethosomes, which are soft lipid vesicles made of phospholipids, ethanol, and water, known for improving skin penetration.
The ethosomal suspension was prepared by the hot method and subsequently incorporated into a Carbopol gel base to obtain a smooth topical formulation. Phytochemical screening confirmed the presence of key active constituents. The pH, viscosity, spread ability, homogeneity, and drug content of the prepared ethosomal gel were assessed. The formulation's anti-acne potential was evaluated using an in vitro protein denaturation assay. The findings showed that the ethosomal gel had high consistency and stability, as well as acceptable physicochemical characteristics appropriate for topical administration. Finally, this study demonstrates that *Syzygium cumini* seed extract can be successfully formulated into an ethosomal gel, offering a promising herbal alternative for acne management with improved dermal delivery.

Keywords: *Syzygium cumini*, Ethosomal gel, Jamun seed extract, Anti-acne activity, Herbal formulation, Soxhlet extraction, Phytochemical screening, Ethosomal gel.

1. INTRODUCTION

Acne vulgaris or Acne is a skin disorder that impacts nearly everyone. It is triggered by male hormones generated by the adrenal glands of both sexes and typically affects people in their teenage and early adult years. Mostly on the face, acne manifests as nodules, pustules, whiteheads, and blackheads. Pain, pustules, papules, discomfort, erythema, and loss of function are some of the symptoms. Because of this obstruction, dead cells cannot be removed, and bacteria typically colonize and attack the sebum,

causing whiteheads, blackheads, and irritation in the end [1]. Acne may occur when the sebaceous glands become blocked and the surface pores of the skin get obstructed. The body's defense mechanism tries to combat severe acne. Staphylococcus epidermidis and Propioni-bacterium acnes are important bacteria that cause shallow cysts and inflammatory acne by converting sebum fatty compounds into unsaturated lipids that draw neutrophils [2].

The global prevalence of acne highlights its importance as a public health concern, affecting up to 80– 90% of adolescents and a significant portion of adults, with increasing cases observed due to modern lifestyle factors such as pollution, stress, and high-glycemic diets. The pathogenesis of acne is also linked to hormonal sensitivity of sebaceous glands, increased keratinocyte proliferation, and an exaggerated immune response, which together create a persistent inflammatory cycle. Conventional topical therapies often face limitations such as skin irritation, poor penetration, and reduced patient compliance, especially in individuals with sensitive skin. Early and appropriate treatment is essential to control lesions, prevent complications, and improve overall skin health. If acne left untreated, acne may lead to post-inflammatory hyperpigmentation, permanent scarring, and significant psychological impact, including reduced self- confidence and emotional distress. Therefore, effective management of acne focuses on controlling sebum secretion, reducing microbial growth, minimizing inflammation, preventing lesion formation, and improving skin barrier function to achieve long-term therapeutic outcomes [3]

SKIN:

The skin is the largest organ of the body and forms a continuous protective covering that separates the internal environment from the external world. It not only acts as a physical barrier but also participates in thermoregulation, immune defense, sensation, and metabolic functions such as vitamin D synthesis [4].

LAYERS OF THE SKIN:

Anatomically, skin is usually described as having three main layers:

- Epidermis (outer)
- Dermis (middle)

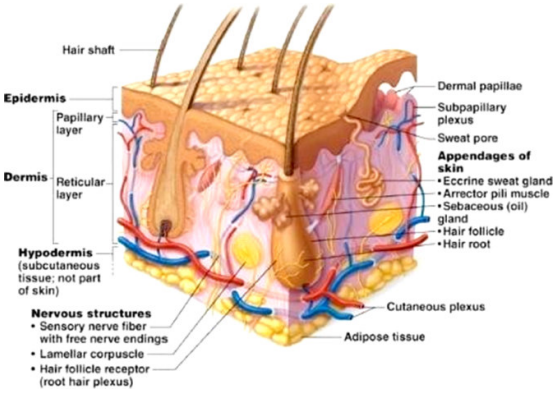

Fig 1: visual representation of human skin.

- Hypodermis or subcutaneous tissue (inner, sometimes considered supporting layer rather than true skin).

EPIDERMIS:

The stratum basale, stratum spinosum, stratum granulosum, stratum lucidum in thick skin, and stratum corneum are the five epithelial layers that make up the stratified squamous epithelium, which is avascular and fed by diffusion from the dermis. In addition to Merkel cells (which sense touch), Langerhans cells (which monitor the immune system), and keratinocytes and melanocytes (which produce pigment) [5].

STRATUM CORNEUM AND BARRIER FUNCTION:

The flattened, anucleate corneocytes that make up the outermost stratum corneum are immersed in a lipid-rich extracellular matrix; this structure is frequently referred to as "brick and mortar." This layer serves as the primary permeability barrier, limiting the entry of chemicals, microorganisms, and allergens and avoiding excessive water loss—two critical functions in topical and transdermal drug administration. In this layer, dendritic cells are also present [6].

DERMIS:

The dermis, which is made up of connective tissue rich in collagen and elastin fibers and provides strength, elasticity, and mechanical support, is located under the epidermis and is separated into two parts: the deep reticular and superficial papillary regions. The superficial dermis also contains blood arteries, lymphatics, nerve endings, hair follicles, sebaceous glands, and sweat glands and plays a critical role in

thermoregulation, sensation, and wound healing. The deep reticular dermis is the deeper layer, which is thicker, less cellular, and composed of dense connective tissue.

HYPODERMIS (SUBCUTANEOUS TISSUE):

The hypodermis, also known as the subcutaneous layer, connects the skin to the underlying muscles and bones and is primarily composed of adipose tissue and loose areolar connective tissue. It offers thermal insulation, cushioning, and mechanical protection in addition to serving as an energy storage reservoir. As we age, the hypodermis's capacity to store fat and provide cushioning diminishes.

SKIN APPENDAGES AND RELEVANCE TO ACNE:

Sweat glands, sebaceous glands, and hair follicles are all regarded as skin appendages that result from interactions between the dermis and epidermis throughout development. Sebaceous glands penetrate into hair follicles and release sebum, which lubricates skin and hair but also plays a significant role in acne when paired with follicular hyper keratinization, microbial colonization, and inflammation [(7).]

NEED FOR NOVEL TOPICAL DELIVERY:

The stratum corneum is an effective barrier composed of closely spaced corneocytes in a highly ordered lipid matrix, only a small portion of topically applied acne medications actually penetrate the viable epidermis and pilosebaceous units.[7] This "brick-and-mortar" structure, which severely restricts the diffusion of many hydrophilic and high-molecular- weight drugs, a large portion of the applied dose from conventional creams or gels remains on the surface and is easily removed by washing, rubbing, or clothing. As a result, patients may experience local irritation from concentrated drug on the surface without achieving adequate drug levels in deeper skin layers, which contributes to suboptimal clinical response and poor adherence. These limitations have driven interest in novel dermal and transdermal systems that can modulate the barrier, enhance penetration, and provide more predictable delivery profiles [(8)]

BARRIERS TO SKIN PENETRATION WITH CONVENTIONAL GELS:

The stratum corneum is the primary barrier to penetration; only relatively small, moderately lipophilic molecules can effectively pass through its crystalline lipid lamellae and densely cross- linked corneocyte envelopes, which restrict diffusion along intercellular pathways. Penetration into deeper epidermis and follicles is restricted for hydrophilic medications, plant extracts, and many anti-acne actives because simple incorporation into conventional gels or creams rarely overcomes this barrier [9]. Additionally, conventional semisolids offer little control over spatial targeting; the drug primarily distributes close to the surface, and any flux must be driven by large concentration gradients, which raises the possibility of irritation without providing a commensurate therapeutic benefit. Additionally, the absence of occlusivity or substantively in traditional vehicles may result in a variable residence time and a high degree of patient-to-patient variability in the actual absorbed dose [(10)]

RATIONALE FOR USING VESICULAR SYSTEMS:

In order to overcome these obstacles, vesicular carriers such as liposomes, ethosoms, niosomes, and related nanostructures have been created. These carriers encapsulate drugs in biocompatible, deformable bilayers that interact well with stratum corneum lipids. When compared to straightforward solutions or gels, these systems can increase drug thermodynamic activity at the skin's surface, improve partitioning into the stratum corneum, and encourage diffusion along intercellular lipid domains, leading to higher drug deposition in the epidermis and dermis. Crucially, vesicular systems can be designed to prefer dermal delivery over systemic delivery, allowing for targeted accumulation around pilosebaceous units and inflamed follicles perfect for acne while reducing systemic exposure and related side effects. Overall, such nanocarriers offer improved permeation, better localization at the site of action, and the potential for sustained release, making them a rational choice over conventional creams or gels for novel anti-acne formulations [(11)]

GEL:

Gels consist of a liquid medium interpenetrated by small inorganic particles or large organic molecules, forming a rigid colloidal system. They primarily comprise water and

gelling agents that provide firmness, spread ability, and stability. Hydrogels, a key subtype, mimic the extracellular matrix with biocompatibility and hydrophilicity for drug protection and release.

Gels enable precise drug release control, enhance bioavailability, and suit routes like oral, ocular, vaginal, and transdermal delivery. In situ gelling systems transition from sol to gel upon administration, triggered by stimuli such as temperature or pH, prolonging residence time at the target site. Common uses include wound healing, acne treatment, and sustained release for neurological or dermatological therapies. Key elements include polymer selection (e.g., carbomers, cellulose derivatives), solvents, pH adjustments, preservatives, and mixing techniques for uniform distribution. Gelling agents like tragacanth, sodium alginate, or Pluronic ensure viscosity without stiffness [12]

ADVANTAGES:

Gels bypass first-pass metabolism.

- Enhance bioavailability via sustained release.
- Provides non-invasive topical delivery with reduced systemic side effects.
- They ensure better spread ability, hydration of application sites.
- Compatibility with sensitive skin for conditions like wounds or inflammation.
- Optimal cutaneous penetration supports prolonged local action without frequent dosing.

DISADVANTAGES:

- Skin irritation from excipients or drugs.
- Potential allergic reactions.
- Poor permeability for hydrophilic.
- Manufacturing requires precise viscosity control to avoid phase separation [13]

ETHOSOMES:

Ethosomes are intended to be a non-invasive drug delivery method. According to Touitou (1996), ethosomes are lipid vesicular structures that contain a comparatively high concentration of ethanol. They are soft and pliable vesicles. High concentration of ethanol in ethosome formulation was considered to be the key explanation for their improved skin penetration ability compared to normal liposomes. The combination of phospholipids and the high concentration of ethanol in ethosomes may be the primary cause of the deeper distribution and penetration in the skin. It demonstrates higher entrapment efficiency, increased drug retention in the skin, improved permeation and enhanced therapeutic effect compared to conventional liposomes. Several studies confirm that ethosomal formulations significantly improve topical delivery of herbal and synthetic anti-acne actives. Ethosomal gels also show better stability, spread ability and transdermal delivery efficiency than simple gels or creams [14]

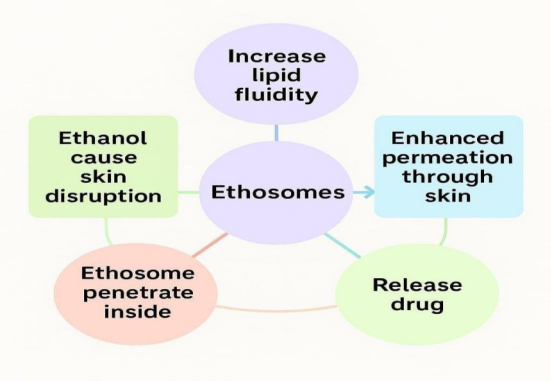

Fig 2: Benefits of ethosomes.

ADVANTAGES OF ETHOSOMES:

- It is non-toxic.
- Ethosomes can be used to deliver big substances.
- Improves medication penetration through the skin.
- Patient compliance is high.
- Easy method in contrast to phonophoresis and iontophoresis [15]

LIMITATIONS OF ETHOSOMAL DRUG DELIVERY:

- In both lipophilic and watery conditions, the medication must be sufficiently soluble to enter the systemic circulation and reach cutaneous microcirculation.
- The molecular size of the medicine should be appropriate for percutaneous absorption.
- Expensive.
- The excipients and boosters used in drug delivery systems cause dermatitis or skin irritation.
- In both lipophilic and watery situations, the medication must be sufficiently soluble to pass cutaneous microcirculation and enter the systemic circulation.

SYZYGIUM CUMINI:

Syzygium cumini, commonly known as jamun or black plum, is a tropical evergreen tree widely used in traditional medicine across India, Southeast Asia, and other tropical regions. The tree's various parts—including seeds, bark, leaves, and fruit pulp—have longstanding ethno medicinal uses for treating diabetes, digestive problems, infections, and inflammatory conditions. Its seeds, known as "Khasta-e-Jamun" in Unani medicine, are traditionally used for liver tonic, blood enrichment, and skin ailments, including wounds and rashes [16]

Syzygium cumini seeds are rich in bioactive substances such as flavonoids, tannins, phenolic acids, and other polyphenols, according to phytochemical research. These compounds are well known for their antioxidant ability, which helps counter oxidative stress associated with acne etiology. In addition to its antioxidant qualities, the seed extract has noteworthy anti-inflammatory qualities that help lessen localized skin inflammation and strong antibacterial activity against bacteria linked to acne, such as Propionibacterium acnes and Staphylococcus aureus. [17]

Wound-healing potential has also been reported, which supports the use of Syzygium cumini in skin repair and regeneration. Additionally, preliminary evidence suggests that phytoconstituents from the seed may have sebum-modulating effects, helping to regulate excess oil production, a key factor in acne development. The presence of antioxidant, antibacterial, and anti-inflammatory phytochemicals in Syzygium cumini seeds provides a strong rationale for its use as a natural anti- acne agent, especially when formulated in systems that enhance skin penetration and targeted delivery [18]

2. PLANT PROFILE

Syzygium cumini, commonly known as Jamun or Black Plum, is a tropical evergreen tree found in many parts of India and Southeast Asia. It is famous for its sweet, Jamun fruits and its many health benefits. The tree grows easily, provides good shade, and lives for many years. Almost every part of the Jamun plant—fruits, leaves, seeds, and bark—is used for food, medicine, and traditional remedies. Because of its usefulness and importance, it is widely grown in villages, cities, and forests.

TAXONOMICAL CLASSIFICATION:

- Kingdom: Plantae
- Sub-kingdom: Tracheobionta (Vascular plants)
- Super division: Spermatophyta (Seed plants)
- Division: Magnoliophyta (Angiosperms / Flowering plants)
- Class: Magnoliopsida (Dicotyledons)
- Subclass: Rosidae
- Order: Myrtales
- Family: Myrtaceae
- Genus: Syzygium
- Species: Syzygium cumini (L.) Skeels [19]

PHYTOCHEMICAL CONSTITUENTS PRESENT IN THE PLANT:

- Alkaloids
- Glycosides
- Flavonoids
- Phenolic Compounds
- Tannins
- Terpenoids
- Sterols
- Saponins
- Fixed oils and fatty acids
- Proteins
- Carbohydrates
- Resins
- Trace minerals

MORPHOLOGY

TREE:

- Height**:** 10–30 meters (can reach up to 40 m in favorable conditions)
- Lifespan**:** Over 100 years
- Trunk**:** Straight, greyish-brown bark; exfoliates in patches
- Canopy**:** Dense, spreading, evergreen

ROOT:

- The plant has a strong taproot system.
- Lateral roots spread deep and wide, helping the tree stand firmly.
- Roots are thick, woody, and capable of absorbing water even in dry conditions.

LEAVES:

- Leaves are simple, opposite, and evergreen (stay on the tree all year).
- Shape: Oval or oblong.
- Colour: Dark shiny green on the surface, lighter below.

- Texture: Smooth and leathery.
- Smell: Leaves have a slight aromatic scent when crushed.
- Size: Usually 7–15 cm long.

FRUITS:

- Fruit type: Berry. And Shape: Oval or oblong.
- Color changes from green → pink → deep purple/black when ripe.
- Taste: Sweet, slightly sour, and astringent.
- Rich in vitamins, minerals, and antioxidants.
- Ripe fruits stain the tongue purple.

SEED:

- Usually one large seed inside the fruit.
- Seed is oblong and greenish-white.
- Used in traditional medicine, especially for diabetes. [20]

MEDICINAL USES:

- Tocolytic Effect
- Antidiabetic Activity
- Antioxidant Activity
- Anti-inflammatory
- Antiseptic Property
- Wound-Healing Activity

3. MATERIALS AND METHODS

a. COLLECTION:

From October to December, syzygium cumini seeds were gathered from the regions of Hosur and Tirupattur in Tamilnadu, India. After collecting, the seeds were cleaned and separated from the pulp for additional processing.

b. DRYING:

In the drying process, water or other solvents are evaporated. The seeds were dried in a lab until they lost all of their moisture, which takes around seven days. The seeds were pounded into a powder and sieved into a fine powder after drying.

c. EXTRACTION:

The extraction process is done by separating the soluble plant metabolites, the residue is also known as insoluble portion which remains. The end product is referred as extract, which is a complex combination of metabolites that might be liquid, semisolid or dry powder after the water has been eliminated.

EXTRACT:

Extract is the substance that is left behind after extraction and includes the active ingredient.

METHODS OF EXTRACTION:

a. CONVENTIONAL METHODS

- Maceration
- Percolation
- Infusion
- Decoction
- Soxhlet Extraction / Hot Continuous Extraction
- Hydro-distillation
- Steam Distillation
- Solvent Extraction (simple solvent reflux)
- Cold Pressing / Expression
- Liquid–Liquid Extraction
- Solid–Liquid Extraction

b. NON-CONVENTIONAL METHODS

- Ultrasound-Assisted Extraction (UAE)
- Microwave-Assisted Extraction (MAE)
- Supercritical Fluid Extraction (SFE)
- Pressurized Liquid Extraction (PLE) / Accelerated Solvent Extraction (ASE)
- Enzyme-Assisted Extraction (EAE)

SOXHLET EXTRACTION:

It is one of the types of extraction techniques for removing the plant's active components in soxhlet extraction. This extraction procedure has made use of a variety of solvents, herbs, and plant and animal tissues. This approach involves packing the powdered crude medication onto a filter-paper thimble and putting it inside a Soxhlet apparatus' extraction chamber. The medication in the thimble is repeatedly washed through the condensed liquid after the solvent in the flask is heated and its vapors rise and condense. This method's main advantage is that it saves time, energy, and money by effectively extracting vast amounts of material with comparatively little solvent. Although it is typically employed as a small-scale batch process, it becomes much more cost-effective when converted into a continuous system for medium- or large-scale extraction.

APPARATUS:

- Reflux condenser
- Distillation flask
- Heating mandle

- Thimble
- Water inlet, outlet pipes.etc.

PROCEDURE:

The fully developed Syzygium cumini fruits were used to harvest the seeds, which were then air- dried for seven to ten days in a lab. Once dry, they were processed into a fine powder using a mixer grinder. After that, ethanol was used as the solvent for Soxhlet extraction of the powdered seeds. For the extraction, 30 g of seed powder was placed in the Soxhlet thimble, and 300 mL of ethanol was added to the round-bottom flask. The apparatus was built with a condenser, and the extraction was allowed to run for 6–8 hours. After completion, the ethanol extract was collected for future use [21]

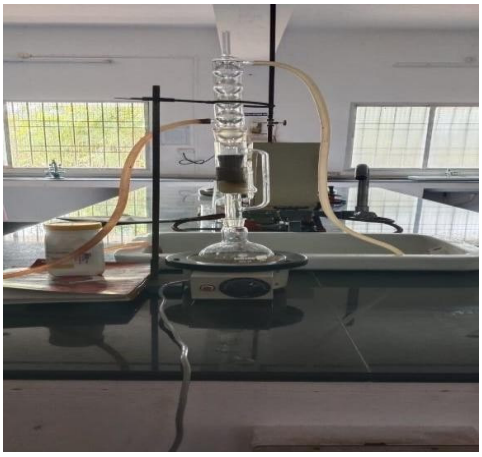

Fig.3: Soxhlet Extraction

ETHOSOMAL GELS:

Ethosomal gel is a gel formulation that contains ethosomes, which are pliable, soft lipid vesicles mostly made of ethanol, water, and phospholipids. These vesicles increase the transport of medicines via the skin by enhancing skin permeability. Ethosomes offer regulated drug release and are easier to apply when distributed in a gel.

KEY FEATURES:

- Contains lipid vesicles with high ethanol content
- Improves transdermal and dermal drug delivery
- Enhances drug penetration into the stratum corneum
- Offers better stability and easy application compared to liquid ethosomal suspensions

MATERIALS USED IN ETHOSOMAL GEL FORMULATION:

- Active pharmaceutical ingredient (API)
- Carbopol
- Water
- Ethanol
- Glycerine
- Methyl Paraben
- Lavender oil

ETHOSOME PREPARATON:

There are various methods that are used for the Ethosome preparation process. The three most common methods include;

- Cold approach
- Hot method
- Traditional mechanical dispersion approach

HOT METHOD:

1. For the hot technique of ethosome preparation, firstly, at 40°C, a colloidal solution is created by dispersing phospholipid in water and heating on a water bath. Additionally, ethanol and propylene glycol are mixed at 40 degrees Celsius to function as the organic phase. This is then introduced into the aqueous phase and stirred together at a temperature of 40°C.
2. In the next phase, the drug is solubilized by dissolving in a suitable solvent, either water or ethanol (depending on solubility), and then simultaneously added to the above mixture. To further reduce size, sonication or the extrusion technique can be applied. Illustrate the heating procedure for the preparation of ethosomes. [22]

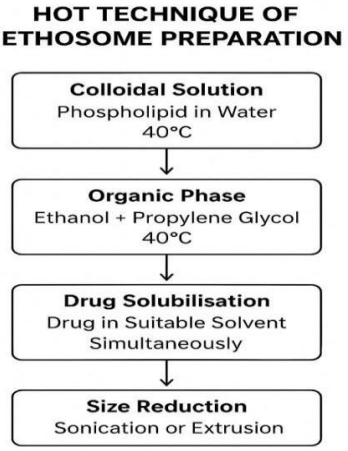

Fig.4: Ethosomal preparation

SETUP OF THE GEL BASE:

1. The name "gel base" refers to the fundamental component of a gel product, which is basically a viscous liquid that functions as a carrier for other active chemicals so that they can be suspended in a consistency similar to gel.
2. It is extensively utilized in pharmaceutical, cosmetic, and personal care products and offers a stable substrate for topical applications such as lotions, creams, and masks.
3. Herbs or powders can be added to tailor the effect. After adding the necessary quantity of the gelling agent (Carbopol) to the solvent (water), thoroughly mix the mixture until the desired gel consistency is reached.

FORMULATION OF ETHOSOMAL GEL:

Table.1: Ingredient of Ethosomal Gel

S.NO	INGREDIENTS	USES	QUANTITY NEEDED FOR 100gm	QUANTIY NEEDED FOR 10gm
1.	Syzygium cumini extract	Anti- acne Anti-inflammatory	2gm	0.2gm
2.	Carbopol	Gelling agent	8gm	0.8gm
3.	Ethanol	Penetration enhancer	30ml	3ml
4.	Glycerin	Solvent and co-solvent	5ml	0.5ml
5.	Methyl paraben	Preservative	0.5gm	0.05ml
6.	Sodium hydroxide	P^H adjuster	0.5gm	0.05ml
7.	Lavender oil	Flavoring agent	Few drops	Few drops
8.	Water	Vehicle	QS as needed	QS as needed

PROCEDURE OF ETHOSOMAL GEL FORMULATION

i). PREPARATION OF ETHOSOMES CONTAINING JAMUN SEED EXTRACT:

1. Formation of the Ethanolic Phase:

A measured quantity of phospholipid (typically 2–3%) is weighed and transferred to a clean beaker. Ethanol (20–40%) is slowly added to the phospholipid while stirring continuously. Stirring is maintained until the phospholipid dissolves completely, producing a clear ethanoic solution essential for ethosome formation.

2. Addition of Jamun Seed Extract:

Approximately 0.2 g of Jamun seed extract is carefully weighed and incorporated into the ethanoic phospholipid solution. The mixture is stirred gently to distribute the extract uniformly within the lipid–ethanol phase. This ensures proper entrapment of the herbal active in the vesicular system.

3. Hydration of the Ethosomes:

Distilled water is added dropwise to the ethanoic mixture with constant mixing. The contrast between the high ethanol content and the incoming water triggers the spontaneous formation of ethosomal vesicles. Hydration continues until a uniform dispersion is obtained.

4. Size Reduction by Sonication:

The ethosomal suspension is subjected to sonication for 3–5 minutes. Sonication reduces vesicle size, enhances stability, and improves the penetration ability of the ethosomes. A fine, milky dispersion indicates proper vesicle formation

ii) PREPARATION OF THE CARBOPOL GEL BASE:

- Dispersion of Carbopol
- Hydration of the polymer
- Incorporation of the ethosomal dispersion
- Addition of preservative
- P^H adjustment and addition of fragrance
- Adjustment of final volume
- Packaging

1. Dispersion of Carbopol:

About 0.8 g of Carbopol 940 is weighed and sprinkled gradually into 8 mL of distilled water under continuous stirring. This method prevents lump formation and ensures adequate wetting of the polymer.

2. Hydration of the Polymer:

The dispersing mixture is kept undisturbed for 2–3 hours to allow complete hydration. This step is important because fully swollen Carbopol provides the smooth and uniform structure required for the final gel.

3. Incorporation of the Ethosomal Dispersion:

The previously prepared Jamun-loaded ethosomal suspension is added slowly to the hydrated Carbopol gel. Mixing is carried out gently to avoid air entrapment and to achieve thorough blending of the active ethosomal phase with the gel base

4. Addition of Preservative:

A solution of 0.05 g methyl paraben dissolved in a small amount of warm distilled water is added to the mixture. The preservative ensures microbiological safety during storage.

5. PH Adjustment and addition of Fragrance:

Approximately 0.05 g sodium hydroxide is added dropwise to adjust the gel's pH to the range suitable for dermal application (around pH 6–7). After pH adjustment, 0.1mL of lavender oil is incorporated to improve sensory attributes.

6. Adjustment of Final volume:

Distilled water is added to bring the total weight of the formulation to 10 g. The entire mixture is stirred until it becomes uniform, smooth, and free from visible particles.

7. Packaging:

The finished ethosomal gel is transferred to a clean, airtight container to prevent contamination and evaporation. The container is labeled with the formulation details and date of preparation.

Table.2 Qualitative Analysis of Phytochemical constituents. [29]

QUALITATIVE ANALYSIS OF SYZYGIUM CUMINI EXTRACT

	TEST FOR ANTHOCYANINS		
S.NO	**EXPERIMENT**	**OBSERVATION**	**INFERENCE**
1.	**HCL TEST:** To the 2ml of extract, add 2ml of 2N HCl and few drops of ammonia	Pink red solution which turns into blue violet after addition of ammonia	Presence of Anthocyanin
	TEST FOR PHYTOSTEROLS		
1.	**SALKOWSKI TEST:** To the filtrate, add few drops of conc. H_2SO_4, shaken well and allow to stand	Red colour in lower layer	Presence of Phytosterols
2.	**HESSE RESPONSE TEST:** To the 5ml of extract, add 2ml of chloroform and 2ml of conc. H_2SO_4	Pink ring/ red colour is formed in lower chloroform layer	Presence of Phytosterols
	TEST FOR TANNINS		
1.	**BROMINE WATER TEST:** To 10 ml of bromine water, add 0.5gm of plant extract	Decolouration of bromine	Presence of Tannins
2.	**LEAD ACETATE TEST:** To 1 ml of filtrate, add 3 drops of lead acetate solution	A creamy gelatinous precipitate is produced	Presence of Tannins
	TEST FOR PHENOLIC COMPOUNDS		
1.	**FERRIC CHLORIDE TEST:** To the aqueous extract solution, add few drops of 10% $FeCl_3$ solution	Dark green/ Bluish black colour	Presence of Flavonoids
2.	**ELLAGIC ACID TEST:** To the aqueous extract solution, add	Solution turns muddy/ Niger brown precipitate is produced	Presence of Flavonoids

	few drops of 5% glacial acetic acid and 5% Sodium Nitrite solution		
	TEST FOR FLAVONOIDS		
1.	**FERRIC CHLORIDE TEST:** To the aqueous extract solution, add few drops of 10% $FeCl_3$ solution	A Green precipitate is produced	Presence of Flavonoids

EVALUATION TEST OF ETHOSOMAL GEL.

1. PHYSICOCHEMICAL EVALUATION:

This test is being performed in order to determine the basic sensory characteristics such as physical appearance, color, odor, texture and homogeneity, to ensure the quality of the formulated gel which enhances and influences the user acceptability.

PROCEDURE:

- Place ~1–2 g of gel on a clean white glass plate.
- Observe visually for color, phase separation, and presence of any particulate matter.
- Smell the sample to record odor (pleasant, faint, or pungent) and note any off-odours indicating rancidity or contamination.
- A texture by touching between thumb and forefinger: smoothness, grittiness, and spread uniformly on skin to check feel.

2. PH MEASUREMENT:

This test is performed in order to determine PH for skin compatibility and stability by using calibrated digital PH meter and magnetic stirrer. This is done to determine the acidity or alkalinity of the ethosomal gel and ensures the acceptable skin range of 5.0-7.0 in order to prevent irritation and discomfort after application on the skin.

PROCEDURE:

- Calibrate the pH meter with standard buffers (pH 4, 7 and 9) at room temperature.
- Weigh 1 g of gel and disperse in 10 mL distilled water (1:10 w/v) and stir for 10 min to equilibrate.
- Immerse electrode and record pH after stabilization (30–60 s). Record the P^H value. [23]

3. SPREADABILITY:

- This test is performed to evaluate how easily the ethosomal gel spreads on the skin after the application under a small pressure. It also ensures whether the gel has suitable consistency to improve patient comfort. It can be calculated by using the formula,

$S = (M \times L) / T$

Where

S → Spread ability
M → mass tied to upper slide (g) L → length moved (cm)
T → time (s)

PROCEDURE:

- Place the sample between two glass slides and put suitable weight on the top of the slides for 1 min to make a consistent film.
- Fasten a thread to the upper slide, suspend it from a normal weight, and time how long it takes for the slide to rise. Calculate the spread ability and record the values.

4. EXTRUDABILITY:

This test is performed to evaluate the ease of expellation of the formulated ethosomal gel from the container (collapsible tube) under low pressure. It also ensures whether the gel possess appropriate expellation during stability studies which depends on the viscosity and texture.

PROCEDURE:

- The sample is being filled in collapsible and nozzle is closed with standard cap.
- The amount of force required to extrude gel is applied and is measured by using the texture analyzer.
- It should be extruded smoothly under a mild pressure.

5. SKIN IRRITATION TEST/ PATCH TEST:

This test is performed in order to determine whether the formulated gel produces any visible effects such as irritation, swelling, adverse skin reactions after it is applied topically, which is caused by active ingredients, excipients, solvents and ethosomal components. It makes sure about the skin compatibility and safety. It should be done after getting the approval and informed consent from the Institutional Ethical Committee (IEC). Alternatively, we can use animal models for the study test.

PROCEDURE:

- Select healthy volunteers usually 5. Apply the sample on the fore arm and keep the patch for 24 hrs, then remove the patch
- Observe the changes on the skin like redness, swelling, burning, itching and rashes. Record the observations. [24]

6. WASHABILITY/ WASH- OFF TEST:

This test is performed in order to determine the ease of removal of formulated ethosomal gel from the skin surface without leaving any sticky or oily residue. It also evaluates the surface behavior of the formulation and compatibility with normal cleaning conditions.

Table 2: wash ability parameters

S.NO	PARAMETERS	RESULT
1.	If it washes off completely	Easily washable
2.	If little amount of gel remains	Partially washable
3.	If it is difficult to remove	Difficult to wash

PROCEDURE:

- Apply required amount of gel on the marked area of skin and allow it to spread evenly and stand it for 5 min
- Simulate washing under running water for 30 sec.
- Rub the area gently with fingers and observe the changes and record it.

7. STABILITY STUDIES:

This test is performed in order to check how long the formulation remains safe and effective during storage and to identify physical changes like color, phase separation and texture. This will monitor the chemical stability and chemical degradation of the drug and determines suitable storage conditions to establish the shelf- life.

PROCEDURE:

- Fill the formulated gel in suitable air tight container.
- Label each with respective batch number, date and storage condition such as room temperature, refrigerator and photo stability.
- Evaluate and perform tests with different time intervals at day 0, 1 month and 3 months.
- Compare each time interval with day 0 values and record the observation.[26]

8. ANTI-MICROBIAL STUDIES:

This test is performed to check whether the formulation can inhibit or kill the microorganisms such as bacteria and fungi and ensures the safety of the formulation to use and does not support microbial growth. This will also confirm the product therapeutic activity against pathogens.

PROCEDURE:

- Make sterile nutrient agar and pour into Petri dishes and solidify.
- Prepare a fresh microbial suspension (e.g., bacterial culture) in sterile saline.
- Dip a sterile swab into the microbial suspension and allow the plates to stand for 5- 10 min, Using a sterile cork borer (6–8 mm) make evenly spaced wells in the agar.
- Pipette a measured volume of your ethosomal gel extract or formulation into each well.
- Allow diffusion for 15–30 min at room temperature, then incubate plates inverted at suitable temperature 35–37°C for 16–24 hours and measure the inhibition zones.

9. LOSS ON DRYING:

This test is performed to determine the amount of moisture content and volatile matter present in the sample which assess the dryness and stability. It is done in order to prevent microbial growth occurred due to moisture content and maintains uniformity, shel-life and efficacy of the product. It can be calculated by using the formula;

$LOD = Initial\ weight - Final\ weight \div initial\ weight \times 100$

PROCEDURE:

- Accurately weigh 2gm of syzygium cumini seed powder on a clean, dry porcelain dish and note the initial weight.
- Set the dish to 105^0 C in a hot air oven. Dry for 2hrs and remove the dish, cool it in a dessicator and weigh again until the constant weight is achieved.
- Record the weight and perform the process again.
- Use the above formula, to determine the percentage purity of loss of drying [27,28]

RESULTS AND DISCUSSION

FORMULATION:

The formulation of herbal gel involves the utilization of seed extract of Syzygium cumini, with the ethosomal gel basis being the active ingredient. The process involves in the preparation of ethosomal suspension which is homogenized and gel base is prepared by using Carbopol and the ethosomes were incorporated with gel base to form herbal gel formulation.

EVALUATION:

Physicochemical, physical, chemical, skin safety, and microbiological experiments were used to assess the gel's efficacy and purity. For user acceptability and ease of use, physical attributes such spread ability, texture, and appearance were evaluated. The integrity of the formulation was verified by chemical tests such as pH, stability, and photosensitivity. Studies on skin irritation and antimicrobials confirmed that the gel is free of microbiological contamination and safe to apply topically.

Table 3: Composition of Ethosomal Gel

COMPOSITION OF ETHOSOMAL GEL FORMULATION:

S.NO	INDREDIENTS	QUANTITY REQUIRED
1.	Syzygium cumini extract	0.2 gm
2.	Carbopol	0.8 gm
3.	Ethanol	3 ml
4.	Glycerin	0.5 ml
5.	Methyl paraben	0.05 ml
6.	Sodium hydroxide	0.05 ml
7.	Lavender oil	Few drops
8.	Water	QS as needed

Table 4: Qualitative Analysis of Phytochemical Constituents.

QUALITATIVE ANALYSIS OF SYZYGIUM CUMINI EXTRACT:

S.NO	SECONDARY METABOLITES	RESULTS (PRESENCE/ ABSENCE)
1.	Anthocyanin's	+
2.	Alkaloids	+
3.	Glycosides	+
4.	Phytosterols	+
5.	Tannins	+
6.	Amino acids& proteins	+
7.	Phenolic compounds	+

8.	Flavonoids	+
9.	Carbohydrates	+
10.	Steroids	+

Table 5: Physiochemical Parameters

PHYSIOCHEMICAL PARAMETERS OF ETHOSOMAL GEL:

S.NO	PARAMETERS	FORMULATION RESULT
1.	Color	Light yellow
2.	Odor	Characteristic
3.	Homogeneity	Smooth & Homogeneous
4.	Wettability	Moistures skin
5.	Emolliency	Smooth & Hydrate skin
6.	Spreadability	Good & Evenly spread
7.	Wash ability	Easy to wash
8.	Physical appearance	No visible particulates
9.	Extrudability	Smooth

Table 6: Irritancy Test

TEST FOR IRRITANCY:

PARAMETER	ERYTHEMA	IRRITANT	EDEMA
Test for irritant	None	None	None

Table 7: chemical parameters

CHEMICAL PARAMETERS:

S.NO	PARAMETERS	FORMULATION RESULT
1.	pH	5.8
2.	Loss on Drying	5.62

Table 8: Microbiological parameters

MICROBIOLOGICAL EVALUATION:

S.NO	PARAMETER	FORMULATION RESULT
1.	Anti- microbial test	pass

Table 9: Stability test

STABILITY EVALUATION:

S.NO	PARAMETER	FORMULATION RESULT
1.	Stability test	pass

CONCLUSION

The anti-acne properties of an ethosomal gel containing extract from Syzygium cumini seeds were successfully developed and assessed in this work. Pharmacognostical and physicochemical analyses supported proper standardization of the crude drug, while HPLC confirmed the presence of active phytoconstituents. The ethosomal gel exhibited satisfactory pH, viscosity, spread ability,

consistency, and stability, indicating good topical acceptability. The extract demonstrated notable antioxidant, antibacterial, and anti-inflammatory properties, which are essential in controlling acne pathogenesis. In- vitro anti-acne and antimicrobial studies further validated the therapeutic potential of the formulation. The ethosomal carrier system enhanced penetration and delivery of herbal actives, improving overall efficacy. Thus, *Syzygium cumini* ethosomal gel represents a promising herbal topical system for acne management. This work provides scientific support for its traditional use and highlights its potential as a safer alternative to synthetic anti-acne therapies. To verify long-term safety and efficacy, additional in vivo and clinical research is advised.

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