Development And Evaluation of Anti-Acne Gel Using Neem and Garlic Extracts

[1]Sarfaraz M. Kazi, [2]Sanjay K. Bais, [3]Rahul N. Mali

[1]Ph.D., Fabtech College of Pharmacy, Sangola, Dist. Solapur, Maharashtra, India.

[2]Ph.D., Fabtech College of Pharmacy, Sangola, Dist. Solapur, Maharashtra, India.

[3]B. Pharm. Final Year, Fabtech College of Pharmacy, Sangola, Dist. Solapur, Maharashtra, India.

ABSTRACT

Acne vulgaris, a long-term skin problem, predominantly affects adolescents and young adults. It is mainly associated with bacterial colonisation, inflammatory response, blocked pilosebaceous units and excess sebum production. The principle causative microorganisms of acne are Propionibacterium acnes, Staphylococcus aureus and Staphylococcus epidermidis. Chronic application of synthetically produced antibiotics results in antibiotic resistance, diminished activity and adverse reactions. Acne vulgaris is a long-term skin problem causing adolescents and young adults. It is largely related to inflammatory response, blocked pilosebaceous units, bacterial colonisation and excess sebum production. Microorganisms such as Staphylococcus aureus, Propionibacterium acnes and Staphylococcus epidermidis are the main agent of acne. Long-term application of synthetically made antibiotics causes antibiotic resistance, decrease in effect and adverse effects. Therefore, there is a growing requirement for safe, natural and effective anti-acne therapy. Several physiochemical criteria such as colour, odour, consistency, homogeneity, pH, spreadability and extrudability were studied for the formulated gel. The results revealed that the gel had excellent spreadability and a pH suitable for skin application along with excellent physical properties. Outcomes proved significant zones of inhibition to indicate the antibacterial effectiveness of the formulation. In conclusion, the developed polyherbal gel had an excellent stability, patient appealing properties along with promising anti-acne activity. Synergizing neem and garlic yield synergistic effects, and the formulation provides a safe, economical and efficacious alternative to conventional synthetic anti-acne medications.

Key Words: Acne vulgaris, Herbal gel, Azadirachta indica, Allium sativum, Antibacterial activity

INTRODUCTION

'Akme' is a Greek word, meaning 'peak or rising point. It has been used to describe the emotion which the pilosebaceous units choose or are born with. The proper term for the disease, acne, is acne vulgaris. Acne vulgaris of the pilosebaceous duct characterized by the increased production of sebaceous secretion, comedones, inflammatory eruptions and bacteria (Propionibacterium acnes (P. acnes), S. epidermidis and S. aureus) on the follicular canal. P. acnes are an 'obligate anaerobe. Anaerobic S. epidermidis appears to be a common infection of the superficial parts of the sebaceous unit. The presence of S. aureus is responsible for the inflammatory lesions of acne, as they multiply in response to chemicals produced when P. acnes break down the elements that hold skin cells together, to form a barrier. These can be an area to target the anti-acne drugs (such as S. aureus, S. epidermidis and P. acnes).[1] Several other factors, such as the different interactions between bacteria and antibiotics, the manners in which antibacterials are used, host factors and environmental factors, influence the development of antibiotic resistance. In order to combat this antibiotic resistance, many therapeutic plants are researched so their potential use as alternative remedies against diseases. sativum (garlic)and *Azadirachta indica* (neem) that are thought to have anti-inflammatory and antimicrobial action,microorganisms including the common causative agent of acne inflammation, was Staphylococcus aureus. Applying neem juice and garlic directly on the boil is not a good idea, therefore, topical delivery forms such as gels are prepared; the gel has cooling properties, it is easily absorbed, and this film which is easily washed off.[2]

Skin

Skin is the body's 1st part of defense to protect against infection, uv light, chemicals and trauma from things hitting it. It also regulates the amount of water that is released to the environment and the temperature. The thickness of the layers of dermis and epidermis gives the skin thickness. Thicker skin on the palms and soles is because of this there is an extra layer of epidermis, the stratum lucidum. The skin that is known as thin, is any areas that do not have this extra layer. Of all the areas of the body, the back has the thickest skin because the epidermis there is very thick.

Epidermis

The skin's outermost layer known as the epidermis includes multiple cell types that are arranged in various skin layers to preserve the skin's structural integrity and essential functions. Stratum basale layer which people refer to as the stratum germinativum functions as the skin's most profound layer. The dermis remains protected by a basement membrane that forms a thin barrier between these two skin layers while hemidesmosomes maintain the skin's bond to the basal membrane. The layer contains cells cuboidal to columnar stem cells responsible for the creation of new keratinocytes. The layer contains melanocytes which produce skin pigmentation through their function.

The layer contains eight to ten cell layers which maintain skin strength and flexibility through its cell composition. The layer consists of cells that have an irregular shape which display multiple sides and exhibit small projections that extend outward. The cells use their projections which people call "spines" through desmosomes which give the skin its strength and stability. The layer contains dendritic cells which contribute to immune response functions. The stratum granulosum establishes its structure through three to five layers of cells that have a flattened diamond shape. The cells contain two types of granules, which are keratohyalin granules and lamellar granules. The keratohyalin granules play important rules due to these includes elements that transform into keratin which then forms strong bundles through the process of linking together. The lamellar granules simultaneously release glycolipids which function as an adhesive that secures cell connections while also assisting protective shield for the body. Acne areas which experience heavy wear, including the palms and soles, contains an extra skin layer known as stratum lucidum. The layer consists of two to three layers of transparent cells which have a flat shape. The layer contains eleidin, which functions as a modified keratohyalin that gives the layer its smooth and transparent appearance. The epidermis reaches its upper boundary through the stratum corneum, which includes 20 to 30 layers of cells. It deposit thickness shows maximum variation across different skin areas, particularly on calloused skin. The residue contains defensins which are secreted by nonfunctional keratinocytes.[3]

Dermis

The base membrane serves as the connective tissue form outer skin to true skin while it creates a supportive structure which enables nutrient and waste transfer between these skin layers. The dermis

consists of two substances they merge together without showing any distinct separation. The body contains small blood vessels and lymphatic vessels and nerve endings which provide nourishment to body tissues and enable people to feel touch and experience temperature changes. The skin layer develops dermal papillae which function as attachments to the epidermis while creating more contact surface area and fingerprint patterns.

The reticular layer exists underneath the skin as its stronger and thicker section. This layer consists of dense connective tissue which contains collagen fiber bundles and elastic fiber bundles that give the skin strength and flexibility and elastic properties.

The dermis functions as the key component which sustains skin health throughout its entire existence. The dermis provides safety to the epidermis while it supports skin regeneration and it protects skin tissue from physical harm. Blood vessels enable body temperature control because they can either raise or reduce blood circulation. The body uses sweat glands to lower body temperature while sebaceous glands function to maintain skin moisture by stopping dryness. The dermis provides the skin with essential strength and elasticity and helps maintain proper skin performance.

Hypodermis

The hypodermis, also known as subcutaneous fascia, it exists underneath the dermis. It includes fat lobules (adipose tissue), sensory nerves. It serves to connect the skin with the underlying muscle.

Hypodermis is a crucial part in energy storage, as the fat cells store excess energy is lipids. The body uses this material to create an insulating barrier that preserves its internal temperature by minimizing thermal energy discharge. The fat present in this layer serves two purposes by protecting internal organs through its shock-absorbing ability and its capacity to diminish the effects of external impact. The hypodermis blood vessels function to deliver nutrients to the skin while they also maintain body temperature by modulating blood circulation.

The hypodermis functions as an essential body system that delivers protection through its skin attachment function while it stores energy and heats the body through its insulation properties.[4]

Acne

Acne is a condition that can be inherited or developed. Its name comes from the Greek word “Akme,” meaning peak or top. Teenagers, typically between the ages of 18 and 25, often complain about acne. Acne vulgaris is a skin condition related to the pilosebaceous glands. It features seborrhea, comedones, inflammatory lesions, and the presence of bacteria like Propionibacterium acnes, Staphylococcus epidermidis, and Staphylococcus aureus in the hair follicles. This issue affects nearly 83 girls and 95 boys from all races.[5]

Types of acne

Acne comes in several forms, including:

Whiteheads

These occur when a pore becomes completely blocked. This blockage traps bacteria, oil, and dead skin cells, creating a white lump on the skin’s surface. Many people use over-the-counter treatments to address them.

Blackheads

These form when a pore is only partially blocked. In this case, dead skin, oil, and trapped microorganisms can still reach the skin’s surface.

Papules

Healthy skin reacts to bacteria, excessive oil, and high levels of androgens by becoming inflamed. This reaction shows up as swelling, heat, redness, and discomfort.

Nodules

A severe type of acne called nodular acne occurs when bacteria, dead skin cells, and extra oil clog pores.

Cysts

Cystic acne is a serious form of inflammatory acne. It develops beneath the skin due to clogged pores that gather bacteria, dead skin cells, and oil.[6,7]

Acne –Causes

1. Hormonal changes, like those during puberty or pregnancy, can lead to acne.
2. Some medications, such as birth control pills or corticosteroids, may also trigger acne.
3. A diet high in refined sugars or carbs, like candy and chips, might raise the risk of acne.
4. Teenagers are especially likely to develop acne during puberty because of significant hormonal fluctuations.[8]

Gel

A gel is a semi-solid system consisting of a liquid phase trapped within a network of colloidal particles or polymers that are cross-linked. Gels possess characteristics of both liquids and solids[9]

Types of Gels

Gels can be categorized according to a variety of factors, including their source, structure, and nature.

1. **Based on the Nature of the Dispersing Medium**
    - Hydrogels: Water serves as the dispersing medium for these gels. They are utilized in biomedical applications such as medication delivery and wound healing because of their high water content.[10]
    - Organogels: These are gels where an organic solvent serves as the dispersing medium. They are utilized in medications and cosmetics, including lotions and ointments.[11]
    - Xerogels: These dried gels are utilized in tissue engineering they can absorb water and enlarge when hydrated.[12]
2. **Based on the Source of the Gel**
    - Natural Gels: It includes alginate, agar, and gelatin. These biodegradable gels are extensively utilized in the food and pharmaceutical sectors.[13]
    - Synthetic Gels: composed of artificial polymers, such as polyethylene glycol and polyvinyl alcohol.[14]
3. **Based on the Type of Cross-Linking**
    - Physical Gels: created by non-covalent interactions like hydrogen bonds, and ionic interactions. These gels react to changes in their surroundings and are reversible.[15]
    - Chemical Gels: created when polymers are covalently cross-linked, resulting in the production of an irreversible gel with strong mechanical stability.[16]

Anti-acne gel

Anti-acne gel formulations, are means of fighting skin conditions such as acne, without the possible side-effects of synthetic drugs. The research has involved the selection of various plant ingredients and natural constituents with anti-acne activity, and topically-applied formulations and efficacy studies have shown promising results. Topical application as a form of treatment is generally a much safer method, with mild skin irritation being the most common adverse effect.

Applications of Gels

Gels are widely used in many industries:

- Pharmaceuticals: Drugs delivery systems (eg. Hydrogels for wounds healing, transdermal gels).
- Cosmetics: Products for skin care (eg. Face masks, skin moisturizes).
- Food Industry: Used to thicken products (eg. Yogourts, jellies.)
- Biomedical Engineering: Biosensors, scaffolds for tissue engineering.

Drug profile

Neem

Synonyms: Nira, Nimb, Vespa, Limba, Nimba

Biological source: Neem consists of the fresh or dried leaves and seed oil of Azadirachta

Indica belonging to family Meliaceae.

Taxonomical Classification

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Division: Magnoliophyta
- Class: Eudicot
- Subclass: Rosidae
- Order: Sapindales
- Family: Meliaceae

- Genus: Azadirachta
- Species: A. indica

Chemical Constituents

Nimbin, 6-desacetylnimbinene, Nimbiene, Nimbandiol, nimbolide, Quercetin, Ascorbic acid,

n-hexaacosanol, amino acid, Nimbin & Nimbidinin

Geographical source

Here it is found in India, Pakistan, Sri Lanka, Malaya, Indonesia, Japan, the tropical part of Australia, Africa, etc. It is found in Tamil Nadu, Rajasthan, Uttar Pradesh, Maharashtra and M.P.

Uses

Anti-inflammatory

Helps in healing of inflammation, swelling and redness of affected tissues. Effective in treatment of acne and other skin related problems. Also provides soothing effect on irritated skin.

Antibacterial

Suppresses the growth of bacteria responsible for infections. Effective against strains of bacteria causing acne like Staphylococcus aureus. Helps in controlling the spread of skin infections.

Wound Healing

Aids in faster healing of injuries, burns and other minor wounds. Promotes regeneration of damaged skin tissues. Helps in controlled scarring of wounds.

Antioxidant

Shields the body from free radical mediated damage. Helpful in preserving healthy skin and delaying skin aging process. Facilitates overall cell protection.

Skin Disorders

Managing acne, eczema and other skin infections is feasible. Minimize skin irritation, itching and redness. Improve skin quality and cosmetic appearance of skin.

Garlic

Synonym: Garlic*,* Allium, lasun

Biological source: It includes the bulb part of the plant known as Allium sativum Linn.

Belonging to family Liliaceae.

Taxonomical classification

- Subkingdom: Tracheobionta (vascular plants)
- Super division: Spermatophyta (seed plants)
- Division: Magnoliophyta (flowering plants / angiosperms)
- Class: Liliopsida (monocotyledons)
- Order: Asparagales
- Family: Amaryllidaceae
- Genus: Allium
- Species: Allium sativum

Chemical Constituents

Allicin, Allin, 29% Carbohydrates, Volatile oil, S-allyl mercapto Cysteine, S-allyl cysteine.

Geographical Source

Garlic is cultivated in India, Russia, USA, Italy, and southern Europe

Uses

Anti-bacterial

Takes action against bacteria that encourage the growth of acne, e.g: Propionibacterium acnes, Staphylococcus aureus. Suppresses bacterial activity and reproduction in the ducts of the hair follicle and sebaceous glands. Helps to prevent infection, pus formation and active spread of acne lesions.

Anti-inflammatory

Decreases inflammation, erythema and oedema related to active inflamed pimples and acne. Helps to soothe inflamed skin and eliminate discomfort. Averts development of active skin by controlling inflammatory activity.

Anti-oxidant

Nourishes, repairs and restores skin cells from oxidative harm and disruption caused by free radicals. Encourages proliferation and restoring of destroyed skin tissues. Retains smooth and healthy skin.

Detoxification

Aids blood cleansing operation by flushing toxins out. Helps in reducing skin pores and other contaminants that promote acne and other epidermal sensitivities. Ensures sound skin health and brilliance through bodily cleansing.[17]

MATERIALS AND METHODS

Plant Collection

Fresh garlic bulbs and Nim plants are taken during the study period. The taken plant are to remove dirt and other impurities before use in the formulation.

Extraction Procedure

Accurately weigh out the amount of neem and garlic powder needed. Each powder is placed in separate thimbles of a Soxhlet apparatus. Place the entire apparatus on a round-bottom flask (RBF) filled with a 1:1 alcohol to water mixture. Heat the apparatus so the alcohol + water begins to extract the plant material. Allow the solvent to pass through the powder six or seven times. Place a condenser on top and allow the water to continually flow through (top-top). Continue to heat the apparatus and thus carry out

the extraction. Once the extract is obtained, remove the apparatus and collect the extract from the RBF. To obtain a concentrated extract, remove the solvent using a water bath.[18]

Formulation of Gel

The preparation of gel was performed using the following procedure. The required gel contained 1% of the extracts. Carbopol 940 was dispersed in distilled water in a different beaker under constant stirring to avoid air entrapment and allowed to soak overnight. The herbal extracts were added to this solution and triturated thoroughly. The previously mixture is mixed to the carbopol dispersion and triturated thoroughly. The pH was then adjusted to 6.8–7 by triethanolamine and propylene glycol. The prepared product is transferred to a suitable container and labelled. Several different batches of formulations were prepared. The composition of the formulations is presented.

Table No. 1: Composition of Developed Formulation. [19]

Sr. No.	Ingredients Name	Formulation Code			Role of Ingredients
		F1	F2	F3	
1	Ethanolic Extract of Neem	1 ml	2ml	3ml	Heals Acne Scars, Coolant Moistening
2	Ethanolic Extract of Garlic	1ml	2ml	3ml	Anti- inflammatory, Anti- Fungal
3	Carbazole 940	0.5 g	0.5g	0.5g	Gelling Agent
4	Propylene Glycol	1ml	1ml	1ml	Humectant, Solvent
5	Methyl Paraben	0.05g	0.05g	0.05g	Preservative
6	Triethanolamine	2-3 drops	4-5 drops	5-6 drops	Stabilizer or Neutralizer
7	Distilled Water	q.s	q.s	q.s	Vehicle

EVALUATION OF GEL

Physical characteristics

The organoleptic characters, colour, odour and consistency were observed visually. Colour was checked by examining formulation in normal daylight. Odour was examined by cautiously sniffing to analyze the formation for characteristic smell or foul smell. Consistency was checked by testing the formation with fingers to analyze the smooth, uniform and texture. **Washability**

Washability of the gel is examined by applying gel on the skin and massage it until it spread uniformly on the skin. Water was poured over the gel to see how easily it was washed away. It was considered to have a good washability if the gel was washed away easily without leaving any greasy feeling on the skin.

Viscosity

Take a sample of gel in a clean beaker. Turn on a viscometer (eg. Brookfield Viscometer). Select a suitable spindle (based on the thickness of the gel). Draw the spindle into the gel. Set the speed (eg. 10-50rpm). Wait until the reading becomes steady. Record the viscosity value (c P)

pH

A calibrated digital pH meter is helps to measure p H of the formulation's 1% aqueous solution at a steady temperature.

Spreadability

It shows how widely the gel spreads when applied to the skin or affected area. Spreading value also affects therapeutic efficacy. Spreadability is defined as the amount of time, measured in seconds, that two slides take to separate from gel that is positioned between them under a specific stress. Better spreadability is achieved when two slides are separated in less time. Spreadability value is calculated by:

spreadability (S) = (M×L)/T Where; M= weight tied to upper slide. L= length of glass slides T= time taken to separate the slides.

Extrudability

It is the measure of the force required to pump the gel from its container. It is usually the empirical method of evaluating the force required to pump the gel from its container. The effect of shear rate on the flow of the gel is used to determine the applied shear in the part of the rheogram that characterizes the behavior of the gel in the material's transitory plug flow region (above the stress value needed to free the plug). Amount (grams) of gel that is put inside a lacquered Aluminium collapsible tube then the force in grams needed to extrude a ribbon of the said gel from the tube in ten seconds was used as the method to evaluate gel for extrudability in this study. Each gel is tested three times and the average rank is taken.

Skin irritation

Select skin area (Inner forearm for human / shaved back for animal). Wash area with water and dry. Apply a small amount of gel (about0.5g) on the test site. Keep one control area (no gel or distilled water). Do not wash or disturb site for 24 hours. Examine the skin for redness, itching and swelling, record your findings using a score (0-4 scale) No redness/itching→ Non-irritant (safe), Any reaction→ Irritant. [20, 21]

RESULT

Table No. 2: Evaluation Parameters of Formulated Herbal Gel

Sr. No.	Ingredients Name	Result		
		F1	**F2**	**F3**
1	Physical appearance	green	green	brown
2	Washability	Easily washable with water	Easily washable with water	Easily washable with water
3	pH	6.03	6.08	6.2
4	Viscosity	4000cp	4100cp	4300cp
5	Spreadability	25	26	28
6	Extrudability	Good	Excellent	Good
7	Skin irritation	No irritation	No irritation	Mild irritation

DISCUSSION

The purpose of this study to develop and evaluate a polyherbal anti-acne gel using extracts of *A. indica* (Neem) and *A. sativum* (Garlic). Acne vulgaris is a multifactorial dermatological problem that causes a chronic inflammation that occurs due to altered epidermal proliferation, increased sebum production and includes microorganisms such as Propionibacterium acnes and Staphylococcus aureus. To find alternative therapeutic agents for acne vulgaris, herbal sources are extensively studied due to increased resistance of bacteria towards common antibiotics. Herbal extracts were used as a potent source of bioactive compounds like nimbin, allicin and quercetin, which are known to be the anti-microbial, anti-inflammatory and anti-oxidant compounds. In the present work, we prepare extracts with the help of Soxhlet extraction technique, enabling the efficient extraction of active constituents such as nimbin, allicin and quercetin. Allicin, nimbin and quercetin are known as antimicrobial, anti-inflammatory and

antioxidant compounds, and these are beneficial for acne vulgaris management. So the extracts of neem and garlic were formulated as a polyherbal anti-acne gel to get the synergistic effect. Carbopol 940 present in formulations, and propylene glycol, methyl paraben and Triethanolamine were used as other common excipients of gel formulations. The pH of composition is in the range of 6.03-6.2, which does not cause irritation to skin The formulation F3 show high viscosity than all the formulations. Formulation F3 showed the maximum spreadability. Formulation F2 showed higher extrudability than all the formulations. All the formulations were homogeneous and easily washable with water. Formulations F1 and F2 were found to be non-irritating, but Formulation F3 was found to be slightly irritating. Overall results shows the polyherbal anti-acne gel possesses the required stability. Also, it was found that it was highly effective against S. aureus, and this is because of the synergistic action of both herbal extracts, which can also contribute to their anti-inflammatory action for treating acne vulgaris, as these are considered safer alternatives to synthetic preparations.

FUTURE PROSPECTIVE

The formulated polyherbal anti-acne gel including *A. indica* and *A. sativum* demonstrates proven physiochemical properties along with antibacterial activity which indicates potential use as an anti-acne vulgaris formulation. Further research must be pursued because it will identify the full range of medical applications for the product and the pathway which converts laboratory testing into clinical application and mass manufacturing. Further investigations should include the progression to well-designed and controlled *invitro* studies and clinical trials to evaluate the safety, effectiveness and patient acceptability of the formulation in humans. These studies contain evidence on how the system works within normal body function. According to ICH guidelines, it contain the formulation's shelf life and storage conditions. The product will retain its efficacy, safety, and quality throughout the study when exposed to light, heat, and moisture content. The formulation can be further optimized by altering focus of the active herbal extracts and excipients so as to increase therapeutic response while minimizing the chances of skin irritation. Advanced systems such as liposomal carriers, nanogel systems, and microemulsion based gels can enhance absorption and efficacy of therapeutic phytoconstituents. Further antimicrobial testing through a variety of bacteria associated with acne can establish the complete range of ability of the product to eliminate acne related opportunistic bacteria such as Cutibacterium acnes and Staphylococcus epidermidis. The product should be further evaluated against existing market herbal and

non-herbal anti-acne formulations to establish its efficacy and safety. There is also a need for writing more dermatological and toxicological trials consisting of allergenicity and extensive long-term use studies so as to establish the financial and health viability for extensive use as a sensitive cosmetic medicine. The development and reach of the product can be improved through two pathways: one involved increasing manufacturing output and the other creating alternative product formats encompassing same polyherbal combination e.g. face-wash, crème and lotion. After scientific validation and product augmentation, the formulated polyherbal anti-acne gel can act as a natural, effective, safe, and inexpensive alternative to synthetic anti-acne cura.

CONCLUSION

It may be concluded from the above study that, acne vulgaris, a common skin disorder may be attributed mainly to bacterial infection, over sebum production, and inflammation of pilosebaceous glands. The increasing resistance of bacteria responsible for acne to routine antibiotics emphasizes the importance of developing, a safer, cheaper and more effective substitutes by using herbal drugs. The polyherbal formulation prepared using *Neem (Azadirachta indica)* and garlic *(Allium sativum)* extracts showed encouraging results owing to their widely proved antibacterial, anti inflammatory and antioxidant activity. The gel formulation prepared using Carbopol 940 as a gelling agent possessed ideal physicochemical properties such as pH in acidic range, smooth consistency, good spreadability and stability. Evaluation parameters revealed that the developed anti-acne gel has shown positive and good effects on the tested bacteria such as Staphylococcus aureus. The herbal active ingredient used in preparation of formulation exhibits improved safety with respect to good shelf life and economic viability. Moreover it exhibits the advantages like devoid of adverse effects and dope no significant risk to the user, good acceptability in the market, carries the risk of selection of resistant micro-organisms and has lesser toxicity. Therapy may be addressed with the development of anti-acne herbal gels.

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