

FORMULATION AND EVALUATION OF HERBAL ANTIACNE GEL

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Abstract- Acne vulgaris is a long-term inflammatory disorder of the pilosebaceous unit that leads to the formation of inflammatory lesions, seborrhea, comedowns, etc. Natural remedies are more acceptable in the belief that they are suffering from fewer side effects than the synthetic ones. Herbal formulations have a growing demand in the global market. This present research work aims to formulate and evaluate herbal anti acne gel containing ethanolic extract of Neem (Azadirachta Indica) and Garlic (Allium Sativum). The formulation was evaluated for various parameters like physical appearance, PH, spreadability, extrudability, anti-acne activity assay against S.aureus was successfully studied. Ethanolic extract of Azadirachta Indica & Allium Sativum on combination show potential effect against acne vulgaris and also exert a synergistic effect on the bacteria.

Keywords- Herbal drug, Anti acne, Gel, Azadirachta Indica, Allium Sativum, Sebaceous gland.

INTRODUCTION SKIN:

Skin is the largest organ of the body, making up 16 % of body weight, with a surface area of 1.8m³. There are three structural layers of the skin: the epidermis, the dermis and subcutis. Hair, nails, sebaceous, sweat and apocrine glands are regarded as derivatives of skin. The epidermis the outer layer serving as the physical and chemical barrier between the interior body and exterior environment. The dermis is the deeper layer providing the structural support of the skin, below which is a loose connective tissue layer, the subcutis or hypodermis which is an important of fat. The Ph of the skin varies from 4 to 5.6. Sweat and fatty acids secreted from sebum influence the ph of the skin surface. It is suggested that acidity of the skin helps in preventing the growth of pathogens and other organism. The most topical preparation are meant to be applied to the skin and hence basic knowledge of skin and its physiological function and biochemistry is very important for designing topical formulations.

ANATOMY OF SKIN:

The skin is multilayered organ and anatomically has many histological layers. Skin is an anatomic barrier between the body and its environment and contributes to about 16 to 18 % of normal body weight. The over laying outer layer is called epidermis, the layer below epidermis is called dermis. Beneath the dermis are subcutaneous fatty tissues.

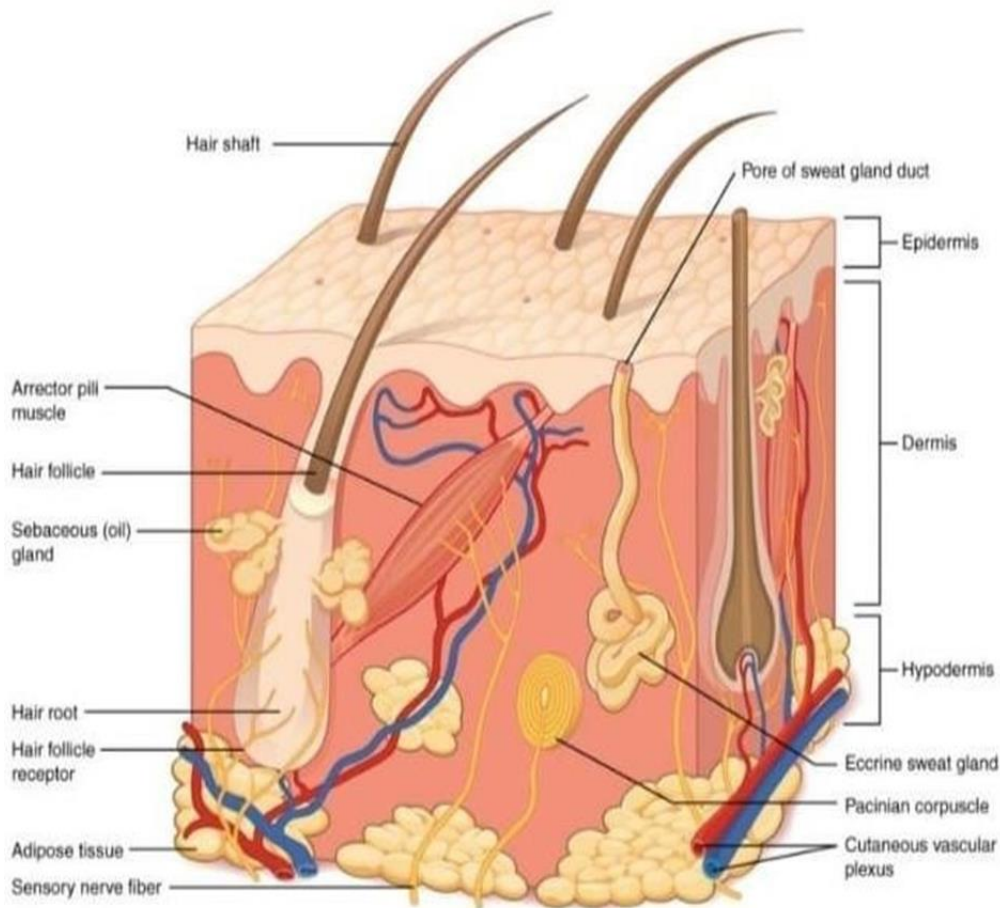


Fig. 1. Structure of skin

ACNE-

Acne vulgaris is also known as acne. Acne, from the Greek word "Akme", means peak or apex, is genetic or acquired affections of the pilosebaceous units. It is a common chronic disease caused by abnormal sebaceous production within skin follicles. Acne is the most common disorder found among youngsters usually 18-25 years of age. Acne vulgaris, which is skin disorder of the pilosebaceous gland which is characterized by formation of seborrhea, comedones, inflammatory lesions and presence of bacteria *Propionibacterium acnes*, *Staphylococcus epidermidis* and *Staphylococcus aureus* in the follicular canal and sebum production. It is almost a universal disease occurring in all races affecting 95% of boys and 83% of girls.

In male patients, acne generally clears by early adulthood. Five percent of men still have acne at age 25 years. Female patients frequently have adult acne. Twelve percent of women still have acne at age 25 years. Five percent of women still have acne at age 45 years. Acne vulgaris has a multifactorial pathogenesis, of which the key factors is genetics. Acne develops as a result of an interplay of the following four factors:

- 1) Follicular epidermal hyperproliferation with subsequent plugging of the follicle.
- 2) Excess sebum production.
- 3) The presence and activity of the commensal bacteria *Propionibacterium acnes*.
- 4) Inflammation.

Various types of Acne:

1) Acne Rosacea:

- A condition that causes a redness and often small, red, pus filled bumps on the face.
- Rosacea is most commonly affect mid aged women.
- It can be mistaken for acne or other skin conditions. In this condition blood vessel of the face enlarge indicating the flushed appearance.
- Rosacea is a chronic incurable, adult acne like skin condition that is easily controllable and curable medically.
- Rosacea inclined to develop in certain stages and causes to create inflammation of the skin of the face is specially the foreheads, cheeks, nose as well as chin.
- Sign and symptoms of Rosacea are redness of the face, tiny red pimples and fine red lines on the facial skin. And enlarge, bulbous red nose, eye problems like swollen, red eyelids and conjunctivitis.



Fig 2. Acne rosacea

2) Acne Vulgaris:

-It's the most common form of acne. Acne vulgaris is a general condition that is characterized by the development of seborrhea, comedones, nodules, pustules, papules and cysts.

- It occurs in the areas of the skin with plentiful growth such as in the upper chest, back, legs and face, sebaceous gland get infected and clogged. Usually affects people from puberty to young adulthood.

Acne Vulgaris

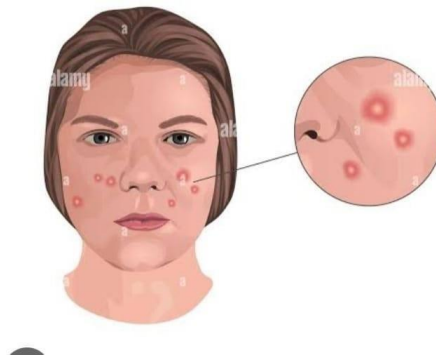


Fig 3. Acne Vulgaris

Acne Symptoms:

- Acne can be found anywhere on your body. It commonly developed on the face, neck, chest, shoulder and back in appearance.
- If you have acne it can be seen as white and red bumps or pimples with red skin.
- Generally, acne can be categorized into six major types:

1) White heads (Non-inflammatory):

This type of acne forms when you have closed pores with bacteria or oil or dead skin cells stuck. These are not painful in nature.

2) Black heads (Non-inflammatory):

- It is a non-painful acne type appearance within open pores, which are clogged with impurities like dirt or extra sebum from sebaceous gland.

3) Papules (Inflammatory):

- It develops when the impurities clogged into the pores inflame the hair follicles, It does not have visible pus.

4) Pustules (Inflammatory):

- It is a next stage of papules here the acne develops visible blobs of pus. It can cause pain in affected area.

5) Nodules (Inflammatory):

- This type of acne is painful with acne lesions deep under the skin it appears as a red bump on your skin and may take few weeks to heal.

6) Cystic lesions (Inflammatory):

Cystic acne is the stubborn form of nodular acne. It is deep rooted under the skin damaging the layers. It is the most painful among all type of acne

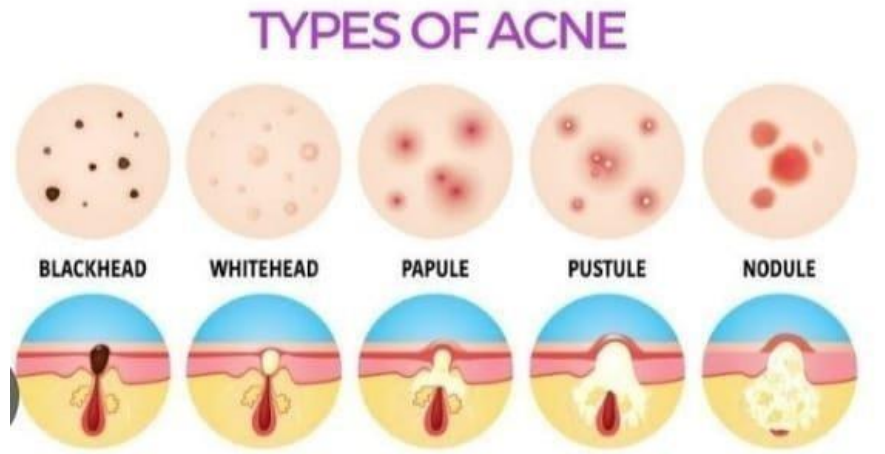


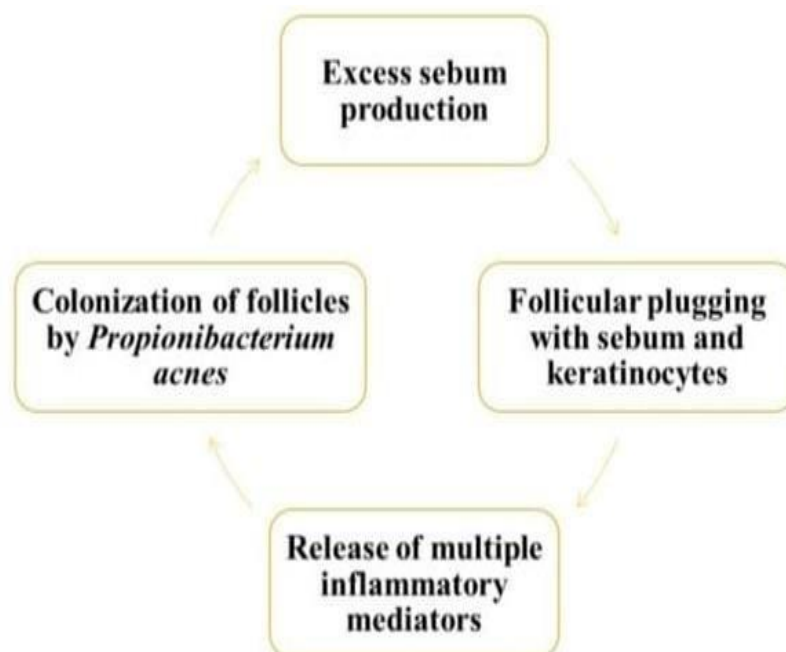
Fig.4 Types of Acne

Causes of Acne:

- Normally, extra oily skin is identified as one of the major factor inducing acne.
- Hormonal fluctuation can be blamed for acne.
- Emotional and mental stress is another significant aspect influencing changes in hormones which further produces acne on the skin.
- Impurities clogging your skin pores can give you acne.
- Cyclic hormonal levels in women.
- Occupational hazards such as chronic exposure to chemicals and air contaminants, high humidity.
- Activity of bacteria promoting comedone genesis.

SEQUENTS OF EVENTS IN ACNE:

Hormones, environmental factors as well as genetic susceptibility may be the cause for acne. Acne happens when hair follicles becomes clogged with dead skin cells and a sticky substance called sebum is produced by the sebaceous gland. This excess sebum causes skin cells to stick together inside the follicle, causing an obstruction. This leads to comedone. Once bacteria nestle in to the clogged pore or comedone, they release factors that case inflammation. This causes comedones to turn in to the pimples and pustules. Some acne lesion become so inflamed that they rupture, which forms nodules. Due to confluence of affected glands nodules form cysts which may result in to scar formation after healing.



TOPIAL DRUG DELIVERY SYSTEM:

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to promptly achieve and then maintain the desired drug concentrations. The route of administration has a significant impact on the therapeutic outcome of a drug. Skin is one of the most readily accessible organ on human body for topical administration and is main route of topical drug delivery system. Topical delivery can be defined as the application of drug containing formulation to the skin to directly treat cutaneous disorders (eg.Acne) or the cutaneous manifestation of a general disease (eg.Psoriasis) with the intend of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin. Semisolid formulation in all their diversity dominate the system for topical delivery, but foams, spray, medicated powder, solutions as well as medicated adhesive system are also in use.

- External topical that are sprayed, sprayed or otherwise dispersed on tocutaneous tissue to cover the affected area.
- Internal topical that are applied to the cutaneous membrane orally,vaginally or on ano-rectal tissues for local activities.

ADVANTAGES OF TOPICAL DRUG DELIVERY SYSTEM:

- Avoidance of first pass metabolism.
- Ability to easily terminate the medications, when needed.
- A relatively large area of application in comparison with buccal or nasal cavity.
- Ability to deliver drug more selectively to a specific site.
- Improve patient compliance.
- Improving physiological and pharmacological respons
- Provide suitability for self medication.
- Providing utilization of drugs with short biological half life.

GEL:

A gel is a solid or semisolid system of at least two constituents, consisting of condensed mass inclosing and interpenetrated by a liquid. Gels and gellies are composed of small number of solids dispersed in relatively large amount of liquid, yet they possess more soolid like than liquid like character. The characteristic of gel and gelly is the presence of some form of cutaneous structure, which provide solid like properties.

TREATMENT OF ACNE:

Treatment of acne depends on its condition and degree of severity which may vary from a mild non-inflammatory comedones to an inflammatory papule or pustules. This usually signifies the presence of propionibacterium acnes.

Topical as well as systemic therapy is available for the treatment of acne. While traditional treatment in the inflammatory phase are topical and systemic antibiotics acting as both antimicrobial and anti-inflammatory agents, modern acne therapy has been designed to interrupt the pathogenic pathway at one or more points. The excessive use of antibiotics for long periods has led to the increase resistance in acne causing bacteria i.e staphylococcus epidermis, propionibacterium acne against a number of antibiotics used to treat acne. WHO noted that majority of the worlds population depends on traditional medicine for primary health care.

Neem and Garlic is very important component of cosmetics which is used to treat pigmentation, acne and other skin problems.

PLANT PROFILE:**Neem**

Synonyms: Nira, Nimb, Vespa, Limba, Nimba.

Biological Source: Neem consist of fresh or dried leaves and seed oil of Azadirachta Indica belonging to family Meliaceae.



Fig.5 -Neem

Chemical Constituents:

Nimbin, 6- desacetylnimbinene, Nimbiene, nimbandiol, nimbolide, quercetin, Ascorbic acid, n-hexacosanol, amino acid, nimbin and nimbidinin.

Geographical Source:

It is found in India, Pakistan, shrilanka, Malaya, Indonesia, japan, tropical region of Australia and Africa. In india, it is found in uttarpradesh, Maharashtra, tamil nadu, rajasthan and Madhya Pradesh.

Uses:

- Poultice, applied to boils.
- In worms, jaundice.
- Ulceration of cowpox.
- Antiviral and antifungal.
- Antiacne

Pharmacological Uses:

Antiulcer, antifertility, antifungal, antiviral ,antipyretic.

1) Garlic:

Synonym: Garlic, Allium, Lasun.

Biological Source: It consist of the bulb part of the plant known asAllium Sativum Linn. belonging to family Liliaceae.



Fig. 6- Garlic

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:

- Carminative.
- Expectorant.
- Stimulant.
- Disinfectant.
- Antiacne.

Pharmacological Uses:

Antibacterial, Anthelmintics, Rubafacient.

AIM & OBJECTIVES:

The aim of this study was to formulate and evaluate herbal anti-acne gel containing extracts of Neem and Garlic.

The **objective** of the study:

- To prepare ethanolic extract from Neem leaves.
- To prepare ethanolic extract from Garlic.
- To formulate herbal gel containing extract of Neem and Garlic.
- To perform physical characterization, stability study, and antimicrobial activities against various bacterial and fungal strains.
- To evaluate the safety of prepared herbal gel by skin irritation study.

PLAN OF WORK**Phase I**

- COLLECTION AND AUTHENTICATION OF THE PLANT:
- EXTRACTION OF Neem.
- EXTRACTION OF Garlic.

Phase II

- FORMULATION AND OPTIMIZATION OF GELLING AGENT

- 1) Formulation of gel base
- 2) Formulation of herbal anti acne gel containing extract of Neem and Garlic.

Phase III

➤ EVALUATION OF HERBAL ANTIACNE GEL

- 1) Physical appearance
- 2) Measurement of PH
- 3) Washability
- 4) Spreadability
- 5) Extrudability
- 6) Percentage of drug content
- 7) Anti acne activity

MATERIALS & METHODS**Material:****Ingredients of formulation-**

Sr. No.	Name of ingredients	Role of ingredients
1.	Ethanolic extract of Neem.	Heal Acne Scars, Coolant, Soothing, Moistening.
2.	Ethanolic extract of Garlic.	Anti-inflammatory, Anti-fungal.
3.	Carbapol 940	Gelling agent
4.	Propylene glycol 400	Humectant, Solvent.
5.	Methyl paraben	Preservative
6.	Triethanolamine	Stabilizer or Neutralizer.
7.	Distilled water	Vehicle.

Table No. 1



Fig.6- Ingredients of formulation

Ingredients of formulation-

Sr. No.	Name of ingredients	Quantity
1.	Ethanollic extract ofNeem	0.5%
2.	Ethanollic extract ofGarlic	0.5%
3.	Carbapol 940	2%
4.	Propylene glycol 400	2%
5.	Methyl paraben	0.1%
6.	Triethanolamine	2%
7.	Distilled Water	q. s.

Table No. 2

METHODS:**Procurement of plant material:**

The fresh leaves of Neem (*Azadirachta indica*) were collected from the medicinal plant of S.P.C.O.Pharmacy , Pachegaon .District- Ahemdagar, and the bulb part of Garlic (*Allium sativum*) were purchased from the local market of pachegaon.

Extraction procedure:

Fig .8 - Extraction procedure

- Weight accurately the quantity of Neem and Garlic powder.
- Place each powder in the separate chamber of the soxhlet apparatus.
- This soxhlet extractor placed into RBF containing the extraction solvent i.e. Alcohol and Water in a ratio of 1:1.
- Take the extraction solvent i.e. Water+Alcohol in the ratio of 1:1 and pass at least the three cycles from thimble containing the drug.
- Place the reflux condenser on top of the soxhlet apparatus which closed with cotton plug from the top and allow to pass water from top to the bottom of the condenser.
- Then switch ON the assembly and pass the 5-6 cycles into the apparatus.
- After complete, the extraction removes the soxhlet apparatus and collect the extract from RBF.
- After collecting the extract it allows to evaporate on the water bath to get the concentrated extract.

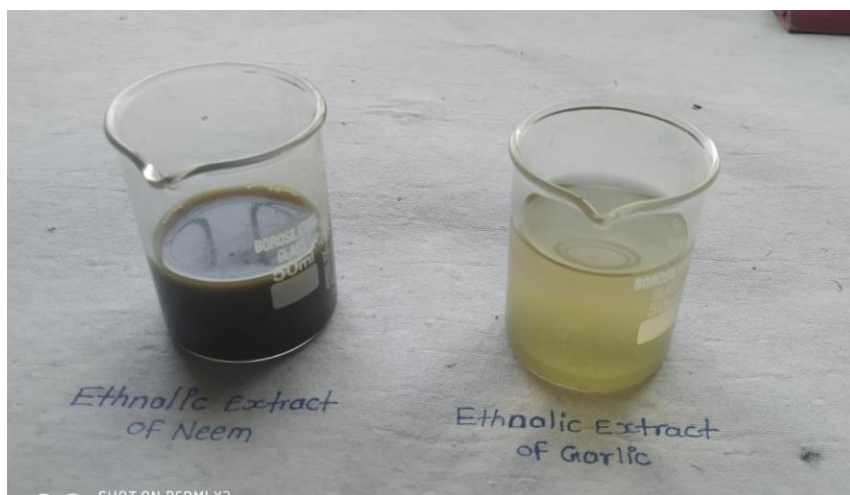


Fig.9 Ethanolic extract of Neem & Garlic

Formulation of gel:

The gel is prepared by using a 1% concentration of the extracts. In separate beaker, Carbapol 940 was dispersed uniformly in distilled water with continuous stirring, avoiding air entrapment and allowed to soak overnight. In another beaker, methyl paraben was dissolved in the remaining amount of distilled water by gently heating. To this solution, the herbal extract were added and triturate well. The above mixture was then added to the carbapol mixture and stirred well. Finally, propylene glycol and triethanolamine were added and the pH was adjusted to 6.8-7. The prepared formulation was filled in a suitable container and labeled.



Fig.10- Formulation of gel

EVALUATION OF GEL

1) Physical appearance:

Physical appearance such as Colour, Odor, and consistency were checked visually.

2) pH:

The pH of 1% aqueous solution of the formulation was measured by using a calibrated digital pH meter at a constant temperature. pH is 9.

3) Washability :

Formulation were applied on the skin and then easy and the extent of washing with water was checked manually.

4) Spreadability :

Spreadability denotes the extent of area to which the gel readily spreads on application to skin or the affected part. Two sets of glass slides of standard dimensions were taken. The gel formulation was placed over one of the slides. The other slides was placed on the top of the gel, such that the gel was sandwiched between the two slides in an area occupied by a distance of 6.0 cm along the slide. 100gm weight was placed upon the upper slides so that the gel between the two slides was pressed uniformly to form a thin layer. The weight was removed and the excess of gel adhering to the slides was scrapped off. The slides in position were fixed to a stand without slightest disturbance and in such a way that upper slides slip off freely by the force of weight tried to it. A 20gm weight was tried to the upper slide carefully. The time taken for the upper slide to travel the distance of 6.0 cm and separated away from the lower slide under the influence of the weight was noted. The experiment was repeated three times and the mean taken for calculation. Spreadability was calculated by using the following formula:

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

Where,

S= spreadability.

M= Weight in the pan (tied to the upper slide) L= Length of the glass slide

T= Time (in sec) taken to separate the slides.

5) Stability study :

Stability of the gel formulation were studied at different storage condition (8 and 40 degree celcius) Sample were withdrawn at 7, 15 and 30 days checked for their physical characteristics like appearance, Homogeneity, Ph, Viscosity and Spreadability.

6) Extrudability :

The gels were incubated at room temperature for 2 hrs before measuring their extrudability using an HDP/FE forward extrusion cell of the TA-XT2 Texture Analyzer equipped with a 5 kg load cell. Prior to measurement, the gel was measured at the following condition: Pre-test speed 1mm/s, test speed 1mm/s, trigger force 10 g, post-test speed 10 mm/s, compression distance 20mm, and outlet diameter of extrusion cell 3mm.

7) Anti-Acne activity :

The antiacne and antibacterial activities of different formulation were determined by a modified agar well diffusion method. In this method, nutrient agar plates were seeded with 0.2 ml of 24 hour broth culture of S.aureus. the agar plates were allowed to solidify. A sterile 8 mm borer was used to cut wells of equidistance in each of the plates. 0.5 ml of formulations, the herbal gel was introduced into the wells at randomly. The plates were incubated at 37 degree celcius for 24 hours. The anti acne activities were evaluated by measuring the zones of inhibitions (In mm).

RESULTS AND DISCUSSION:

The results of the evaluation are shown in below: the gels were slight yellowish to brownish with a specific odor. All formulations were found homogenous easily washable. All the formulation has slightly alkaline Ph. Amongst all the formulation F3 showed very optimum spreadability. All formulation shows better drug content.

Table no. 3: Evaluation of Gels

Sr. no.	Evaluation test	Formulation
1.	Colour	Brownish Yellow
2.	Consistency	Semisolid
3.	pH	9

4.	Spreadability gm.cm/sec	12.03
5..	Extrudability	Good



CONCLUSION:

Natural remedies are boon to any disease. In the world market, herbal formulations are in great demand. Herbal medicines are believed to be safer than allopathic medicines. All the formulations were optimized based on evaluation parameters such as physical appearance, washability, PH, spreadability, anti acne-activity.

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