IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Formulation & Evaluation Of Anti-Acne Gel

Kulkani Onkar[1], Darandale Vishal[2], Miss.Tarate S.C[3], Dr. Kolhe S.D [4]

[1,2] Student Of Bachelor Of Pharmacy, Anand Charitable Sanstha's College Of Pharmaceutical Science And Research ,Ashti, District-Beed. Maharashtra, India.

[3]Assistant Professor Dept., Of Chemistry,

[4]Professor Dept. Of Pharmaceutics, Principal Anand Charitable Sanstha's College Of Pharmaceutical Science And Research ,Ashti, District- Beed. Maharashtra, India

ABSTRACT:

Objective: The present research work deals with the development and evaluation of herbal anti-acne gel containing the fruit extract of *Cinnamomum tamala & Curcuma longa.*

Conclusion: The idea that natural medicines are safer and have fewer side effects than synthetic ones makes them more acceptable. The demand for herbal formulations is rising on the global market. Establishing the herbal anti-acne gel with *C. tamala & C. longa* extract is a trending approach. However further *in vivo* studies are highly recommended to prove the efficacy of our developed anti-acne formulation.

Keywords: *Cinnamomum tamala, Curcuma longa, Propionibacterium acne,* MIC, Carbopol 980,*in vitro* antimicrobial activity.

INTRODUCTION

1.1. SKIN [1-2]:

The skin is the human body's most enormous and easily accessible organ. The average human skin covers around 2 square metres and weighs 4.5-5 kg, or about 16% of body weight. It also receives one- third of all blood supply. Because most topical preparations are intended to be applied to the skin, understanding the skin's physiological functions and biochemistry is critical for designing topical formulations. The skin's pH ranges from 4 to 5.6. Sweat and fatty acids released by sebum have an effect on the pH of the skin's surface. It has been proposed that skin acidity helps in the prevention of pathogen and other organism growth.

1.1.1. ANATOMY-PHYSIOLOGY OF SKIN [2]

The skin is a multi-layered organ with numerous histological layers. Skin serves as an anatomic barrier between the body and its surroundings, occupying around 16-18% of typical body weight. The outer layer is called the epidermis, while the layer beneath it is called the dermis. Subcutaneous fatty tissues exist beneath the dermis[2].

1.2. ACNE [3-5]:

Acne is a chronic skin disorder that occurs when hair sacs become clogged with dead skin cells. Acne vulgaris is the medical term for acne. 70% to 80% of the people affected are between the ages of 11 and 25. It can be identified by the development of inflammatory and non- inflammatory lesions of the hair follicles and/or sebaceous glands, collectively known as the pilosebaceous unit. Acne is common during adolescence, but a severe case can cause an unattractive appearance

and, in many cases, scarring even after therapy. Acne can be classified as mild, moderate, or severe based on the severity of the symptoms.

- **Non inflammatory lesions**- It is categorized as open comedons (blackheads) and closed comedons (white heads).
- **Inflammatory lesions**- It manifests themselves as papules, pustules, cysts and nodules. Acne vulgaris is generally characterized by formation of seborrhea, comedones, inflammatory lesions and presence of bacteria in the follicular canal and sebum production.

1.2.1. ACNE – TYPES[6-10]

Acne rosacea, rosacea

It is a skin disorder that primarily affects women and causes blood vessels in the face to expand, causing the face a flushed appearance. Rosacea is a typical, persistent, incurable adult acne-like skin disorder that is medically treatable and manageable. Rosacea often affects the middle third of the face, particularly the nose, with periods of aggravation and respite. The symptoms may come and go, and the skin may be clear for weeks, months, or years before rebounding. Rosacea tends to develop in stages and results in inflammation of the skin on the face, particularly the forehead, cheeks, nose, and chin. Rosacea symptoms and indicators include: facial redness, tiny red pimples, and fine red lines. Rosacea symptoms and signs include: facial redness, tiny red pimples, and thin red lines on the skin; an enlarged, bulbous red nose; and eye problems such as swollen, red eyelids and conjunctivitis.

Acne vulgaris

The most common type of acne; typically affects persons between the ages of puberty and young adulthood. Hickey, blemish, zit A pustule or papule is a tiny inflammatory elevation of the skin that is common in acne. The distinction between a pimple and acne: Unlike typical acne, rosacea is primarily a disease of adults (ages 30-50), specifically those with pale skin. Unlike acne, rosacea normally does not have any blackheads or whiteheads. Acne is a chronic or long-term condition that affects many teens and adults. Some people have one or two spots on and off, while others suffer frequent discharges of spots with lots of pus-filled pimples. Almost every human being are develops pimples at some point in their lives. When the body begins puberty at the age of 12, hormones begin to be released and begin to work in the bodies of both men and women. Food or pollution at this point should disturb hormonal equilibrium.

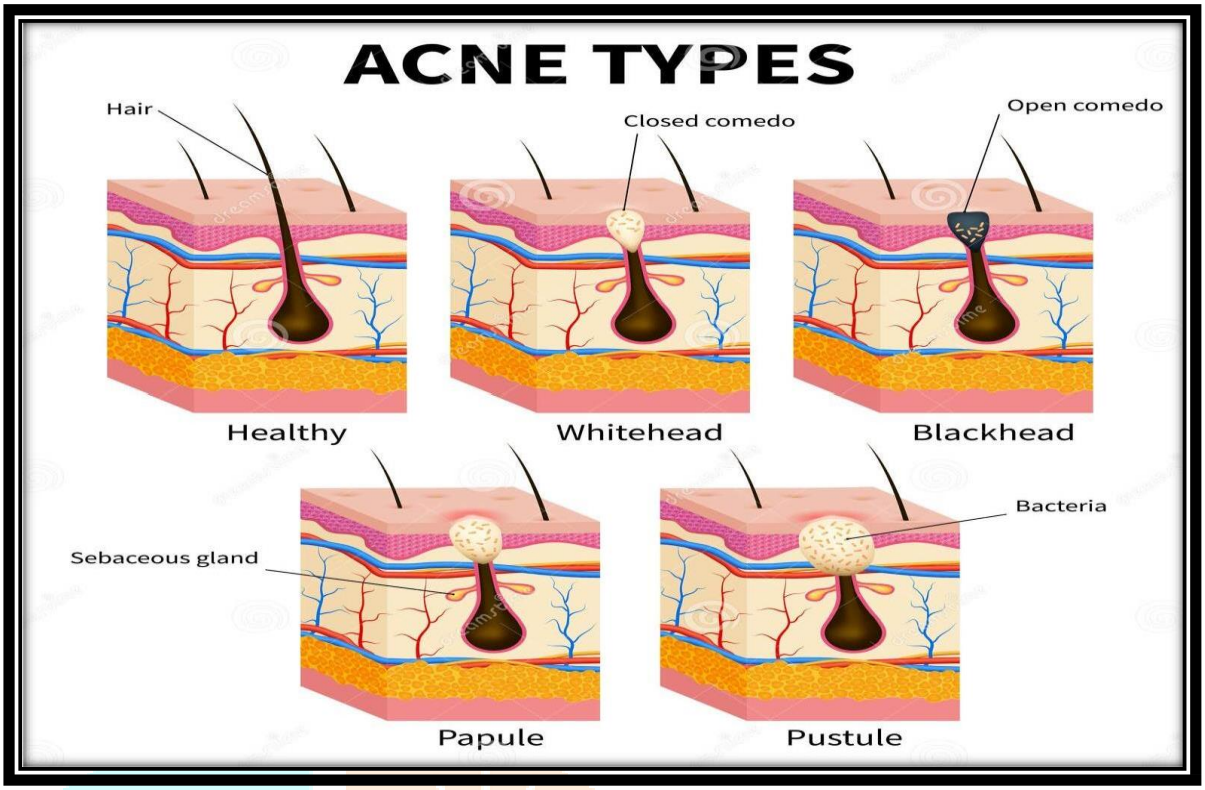
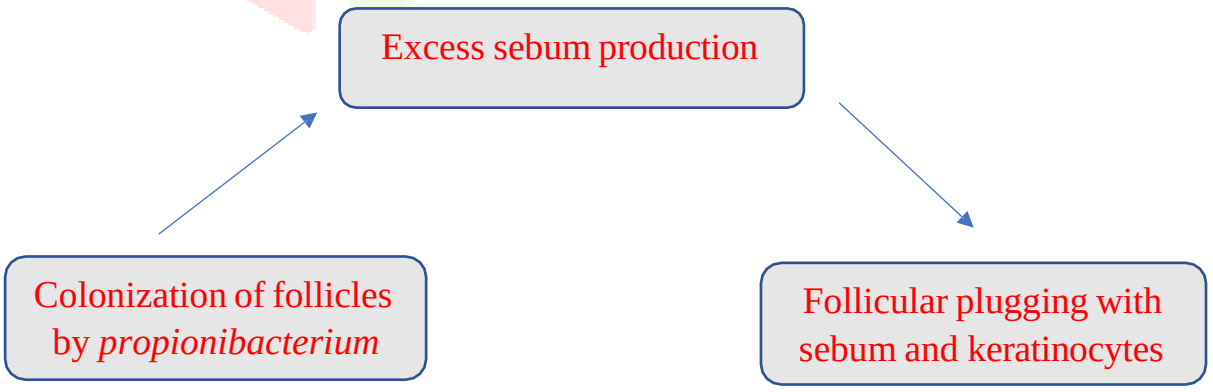


FIGURE 1: TYPES OF ACNE

1.2.2. SEQUENTS OF EVENTS IN ACNE

Acne may be triggered by hormones, environmental causes, or genetic vulnerability. Acne develops when hair follicles become clogged with dead skin cells and the sebaceous glands generate a sticky material called sebum. Excess sebum causes skin cells inside the follicles to adhere together, causing a blockage. This results in a comedone. When bacteria nestle within a plugged pore or comedone, they release inflammatory chemicals. Comedones become pimples and pustules as a result of this. Some acne lesions grow inflammatory and break, forming nodules. Nodules create cysts as a result of the confluence of affected glands, which may result in scar formation after healing.



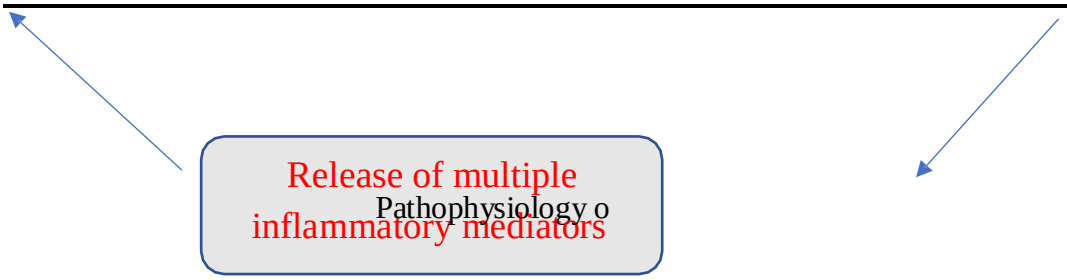


FIGURE 2: PATHOPHYSIOLOGY OF ACNE

1.3. TOPICAL DRUG DELIVERY SYSTEM [8]:

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 organs on human body for topical administration and is main route of topical drug delivery system. Topical delivery can be defined as the application of a drug containing formulation to the skin to directly treat cutaneous disorders (e.g. acne) or the cutaneous manifestations of a general disease (e.g. Psoriasis) with the intent of containing the pharmacological or other effect of the drug to the surface of the skin or within the skin. Semi-solid formulation in all their diversity dominate the system for topical delivery, but foams spray, medicated powders, solutions, as well as medicated adhesive systems are also in use.

- External topical that are spread, sprayed, or otherwise dispersed on to cutaneous tissues to cover the affected area.
- Internal topical that are applied to the mucous membrane orally, vaginally or on anorectal tissues for local activity.

1.3.1. 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.
- Providing utilization of drugs with short biological half-life,
- Improving physiological and pharmacological response
- Improve patient compliance.
- Provide suitability for self-medication

1.3.2. Disadvantages of Topical Drug Delivery System:

- Skin irritation of contact dermatitis may occur due to the drug and/or excipients.
- Poor permeability of some drugs through the skin.
- Possibility of allergenic reactions.
- Can be used only for drugs which require very small plasma concentration for action
- Enzyme in epidermis may denature the drugs
- Drugs of larger particle size not easy to absorb through the skin

1.4. GEL [9-10]:

A gel is composed of at least two constituents, typically a small amount of solids and a relatively large amount of liquid. Gels have a condensed mass that encloses and is interpenetrated by a liquid phase. This means that the solid particles are dispersed within the liquid phase. The presence of a cutaneous structure is a defining characteristic of gels and jellies. This structure provides the substance with its solid-like properties, allowing it to maintain its shape and resist flow.

Gels are indeed a unique and versatile class of dosage forms that involve the entrapping of a significant amount of aqueous or hydro- alcoholic liquids within a network of colloidal solid particles.

FIGURE 3: HERBAL GEL

1.5. NEED FOR STUDY:

- Now a day's herbal remedies are having more demand.
- To develop an ecofriendly and economically cheaper formulation.
- To overcome the problems associated with the intake of antibiotics for treating acne.
- Developing such an herbal formulation could be avoiding side effects of synthetic formulation.

1.6. STUDY PLAN:

- Review of literature
- Procurement of raw materials and other pharmaceutical ingredients
- Preparation of plant extracts and its phytochemical screening
- Determination of Antimicrobial activity of both plant extracts by MIC (Minimum Inhibitory Concentration) method
- Development of Formulation
- Characterization and *in vitro* Evaluation of Anti acne gel

2. AIM AND OBJECTIVES:

2.1. AIM: The aim of study is to develop and evaluate an anti-acne gel containing *Cinnamomum tamala* and *Curcuma longa* for antimicrobial activity against Acne vulgaris.

2.2. OBJECTIVES:

- To collect dried leaves of *Cinnamomum tamala* (Tejpat) and dried rhizomes of *Curcuma Longa* (Turmeric).
- To obtain *Cinnamomum tamala* and *Curcuma Longa* extracts.
- To assess the phytochemical screening of *Cinnamomum tamala* and *Curcuma Longa.*
- Formulation and evaluation of herbal anti-acne gel.
- To carry out *in vitro* antimicrobial activity of anti-acne gel.

3.1. EXCIPIENTS PROFILE:

3.1.1. ACTIVE INGREDIENTS PROFILE:

A. *Cinnamomum tamala* [15]:

FIGURE 4: CINNAMOMUM TAMALA

Synonym: Tejpatta, Tejpat

Scientific name: *Cinnamomum tamala*

Biological source:

Family: Lauraceae

Chemical constituent: Cinnamaldehyde, Cinnamic acid, Coumarin, Eugenol, Polyphenols, Flavonoids, Steroids, Terpenoids & Glycosides.

Part used: Dried leaves Uses:

- The chemical constituents found in tejpat leaf oil exhibit strong enzyme activity, which plays a vital role in facilitating melanin production.
- The polyphenol content and the water extract from these leaves display antioxidant activity.
- The aqueous extract of *Cinnamomum tamala* leaves shows the anti- inflammatory & antimicrobial activity.
- *Cinnamomum tamala* possesses fungicidal/fungistatic properties.

B. *Curcuma longa* [16]:

FIGURE 5: CURCUMA LONGA

Synonym: Haldi, Haridra Scientific name: *Curcuma longa*

Biological source: It is obtained from rhizomatous plant. Family: Zingiberaceae

Chemical constituent: Curcumin, Demethoxy curcumin, Bisdemethoxy curcumin, Curcumol, Zingiberene.

Part used: Dried rhizomes Uses:

- Turmeric has gained popularity in both the pharmaceutical and cosmetic industries.
- Turmeric is valued for its potential benefits in skincare, such as protecting skin from aging, wrinkles, sun damage and moisture loss.
- Turmeric is used in food preparation as a preservative which preserves the freshness and characteristic of food.
- It acts as a natural preservative due to its antioxidant and antimicrobial properties.
- Turmeric possesses a wide range of beneficial properties including anti-inflammatory, antifungal, anti-mutagenic, virucidal etc.

3.1.2. EXCIPIENT PROFILE:

A. Carbopol 980 [17]:

FIGURE 6: CARBOPOL 980

Non-proprietary name: Polyacrylate polymer

Synonym : Unipol980 N, Acrylic Acid Resin, 2-Propenic Acid Homopolymer, Acrylic Polymer

Chemical name : Carbomer Homopolymer Type C USP NF Molecular formula : $C_3H_4O_2$

Molecular weight : 102.13 gm/mol Functional category : Rheology modifier Application in pharmaceutical formulation:

- Carbopol 980 polymer is a highly efficient thickening agent and it is used in the formulation of clear aqueous and hydroalcoholic gels.
- Carbopol 980 can be found in wound care products like hydrogels and dressings, where it helps maintain a moist environment conductive to wound healing.
- It helps to achieve the desired viscosity and consistency of the product, allowing for easy application to the skin.
- In transdermal patches and topical drug delivery system, Carbopol 980 can aid in the controlled release of drug through the skin.

B. ALOEVERA [18]:

FIGURE 7: ALOVERA

Non-proprietary name: Aloe.

Synonym : Aloe, Aloe barbedensis, Ghritkumari

Biological source : Dried juice collected by incision from the leaves of various species of aloe.

Chemical constituents: Anthraquinones, Vitamin A, C, and E, Aloin, Emodin, Cholesterol, Lupeol, Campesterol, Bradykinase.

Molecular formula : $C_{16}H_{13}NO_3$

Functional category : Emollient, Anti-inflammatory, Anti-microbial, Antifungal, Antioxidant.

Application in pharmaceutical formulation:

- Aloevera juice or gel protects skin from sunburn.
- Aloevera can be used topically to accelerate wound healing. It promotes cell proliferation and tissue repair, making it valuable in creams, gels and ointment for burns, cuts and other injuries.
- Aloevera contains compounds with anti-inflammatory properties which can be beneficial in treating conditions like arthritis.
- Aloevera has natural antibacterial and antifungal properties. It can be used in creams and ointments for treating infections.

C. TRIETHANOLAMINE [19]:

Non-proprietary name: Trolamine

Synonym : Daltogen, Sterolamide Chemical name : Triethylamine Molecular formula : $C_6H_{15}NO_3$

Molecular weight : 149.188 g/mol Structure :

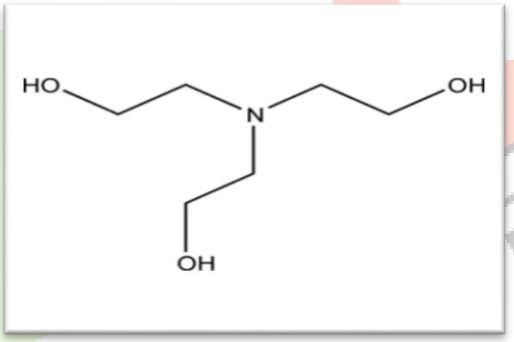


FIGURE 8: TRIETHANOLAMINE

Functional category : Emulsifier Application in pharmaceutical formulation:

- Triethanolamine can act as an emulsifier, helping to blend oil and water based ingredients in cosmetic products.
- TEA can also function as an emollient, which means it helps to soften and smooth the skin.
- TEA can be used as a buffering agent to stabilize the pH of the cosmetic formulation.
- TEA can help solubilize the certain ingredients in the cosmetic formulations, improving the even distribution of active substances in the product.

D. PROPYL PARABEN:

Non-proprietary name: Propylparaben sodium

Synonym : Propyl parahydroxybenzoate sodium Chemical name : Propyl 4-hydroxybenzoate Molecular formula : $C_{10}H_{12}0_3$

Molecular weight : 180.20 gm/mol Structure :

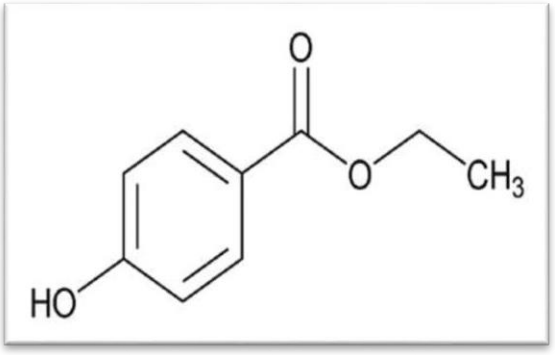


FIGURE 9: PROPYLPARABEN

Functional category : Preservative Application in pharmaceutical formulation:

- Propyl paraben helps extend the shelf life of cosmetic products by inhibiting the growth of bacteria, yeast and molds.
- It helps stabilize the formulation of cosmetic products, preventing them from degrading or separating over time.
- In some cases, it can also be used to preserve the fragrance in cosmetic products.
- By preventing the microbial contamination, propyl paraben contributes to the safety of cosmetic products, reducing the risk of skin irritation when used as intended.

E. METHYL PARABEN:

Non-proprietary name: Methyl hydroxyl benzoate

Synonym : Metyl ester, Methyl 4- hydroxybenzoate Chemical name : Methyl 4- hydroxybenzoate

Molecular formula : $CH_3(C_6H_4(OH)COO)$ Molecular weight : 152.149 g/mol Structure :

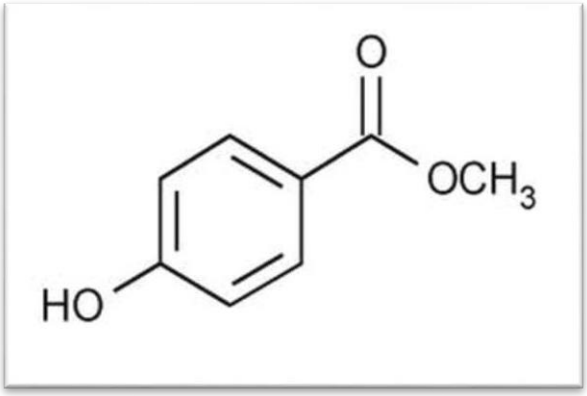


FIGURE 10: METHYL PARABEN

Functional category : Preservative Application in pharmaceutical formulation:

- Methylparaben helps prevent the growth of bacteria, yeast, and molds in cosmetic formulations.
- By inhibiting microbial growth, methylparaben extends the shelf life of cosmetics and pharmaceuticals, reducing the likelihood of spoilage or contamination.
- It is a cost-effective preservative, making it an attractive option for manufacturers.

4. METHODOLOGY

4.1. MATERIALS:

TABLE 1: LIST OF CHEMICALS

SR. NO.	MATERIAL
1	*Cinnamomum tamala*
2	*Curcuma longa*
3	Carbopol 980
4	Aloevera
5	Triethanolamine
6	Methyl paraben
7	Propyl paraben
8	Propylene glycol

4.2. EQUIPMENTS USED:

SR. NO.	INSTRUMENTS

1	Electronic balance
2	Tray dryer
3	Grinder
4	Soxhlet apparatus
5	Digital pH Tester
6	Viscometer

4.3. METHODOLOGY:

4.3.1. METHOD OF PREPARATION OF PLANT EXTRACT [20-21]:

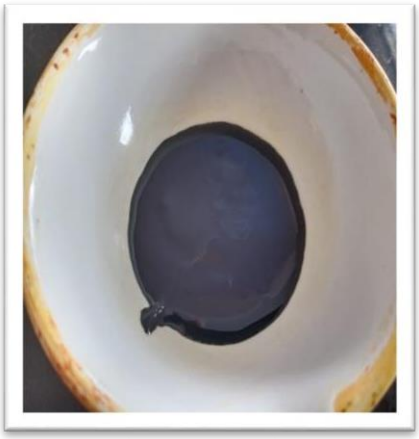
* Preparation of *Cinnamomum tamala* leaf extract:

The plant leaves were collected, dried and grounded into coarse powder. 50 gm of coarse powder was placed in a thimble of Soxhlet and run with 500 ml of (95%) of alcohol, kept for 2-3 hours at 60^0C boiling point. Collect the solvent from round bottom flask, evaporate the solvent and collect the extract.

*Preparation of *Curcuma longa* extract:

Dried rhizomes of *Curcuma longa* were collected and 50 gm of rhizomes were grounded to get a coarse powder, and soaked in 500 ml of ethanol in beaker and beaker was covered with aluminium foil, kept for 6-7 days with occasionally shaking, extract was filter through whatman filter paper No.1 and then evaporate the solvent and collect the extract.

- Extract of *Cinnamomum tamala*



Extract

FIGURE 11: EXTRACT OF C. TAMALA

- Extract of *Curcuma longa*

Extract

FIGURE 12: EXTRACT OF C. LONGA

4.3.2. PREPARATION OF ANTI ACNE GEL [24-25]:

Accurate quantity of carbopol-980 was suspended in 50 ml of distilled water with continuous stirring and soak it for 24 hours.

Solution 1: The required quantities of methyl paraben (0.2 ml), propyl paraben (0.1 ml), Propylene glycol (5 ml) and aloevera (3 gm) were dissolved in 10 ml of distilled water in a beaker

Solution 2: In another beaker weigh 1 gm of each extracts of *Cinnamomum tamala* and *Curcuma longa* were dissolved in 5 ml of alcohol.

Then mix the solution 1 in a soaked Carbopol-980 by continuous strirring and add solution 2 by continuous stirring and make up the volume upto 100 ml with distilled water. After mixing all the ingredients, add drop wise triethanolamine was made to the formulation for obtaining the desired consistency of the gel and to adjust the desired skin pH.

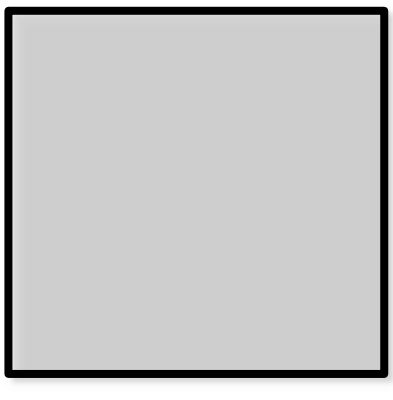


FIGURE 13: FORMULATION OF ANTI ACNE GEL

Formulation of anti-acne gel:

TABLE 3: FORMULATION OF ANTI-ACNE GEL:

SR. NO.	INGREDIENTS	F1	F2	F3
1	*Cinnamomum tamala*	1gm	1gm	1gm
2	*Curcuma longa*	1gm	1gm	1gm
3	Aloevera	3 gm	3 gm	3 gm
4	Carbopol-980	1 gm	1.5 gm	2 gm
5	Propylene glycol	5 ml	5 ml	5 ml
6	Methyl paraben	0.2 ml	0.2 ml	0.2 ml
7	Propyl paraben	0.1 ml	0.1 ml	0.1 ml
8	Triethanolamine	1 ml	1 ml	1 ml
9	Distilled water	Q.S	Q.S	Q.S

- **POST FORMULATION STUDIES:**

4.3.3. EVALUATION OF ANTI-ACNE GEL [25-27]:

1. Physical Examination: The prepared anti-acne gel formulations are inspected visually for their colour, and appearance.

2. pH Evaluation: pH evaluation is the important criteria especially for the topical formulation. The pH of the anti-acne gel should be between 5.2-7 to mimic the skin condition. If the pH of the prepared anti-acne is acidic or basic, it may cause irritation to the patient. pH of the prepared anti- acne gel was measured using digital pH tester.

1 gm of gel was dissolved in 100 ml of distilled water and it was placed for 2 hr and then dip the glass electrode into an anti-acne gel. The measurement of pH of each formulation was done in triplicate and average values were calculated.

3. Spreadability: Spreadability denotes the extent of area to which the anti- acne gel readily spreads on application to skin or the affected part. The bioavailability efficiency of an anti-acne gel formulation also depends on its spreading value.

About 1 gm of gel was placed in a circle of 1 cm diameter on a 20*20 cm glass plate, over which the second glass plate is placed. Weight of 500 gm was allowed to rest on upper glass plate for 5 min and then increase in diameter of the gel due to spreading was noted.

4. Extrudability: It is usual empirical test to measure the force required to extrude the material from tube. More quantity extruded better was Extrudability.

The formulation under study was filled in clean, lacquered aluminum collapsible tube with nozzle tube of 5 mm opening and applies pressure on tube by keeping weights. Extrudability was then determined by measuring amount of anti-acne gel extruded through the tip when the pressure was applied on tube.

Extrudability = Applied weight to extrude anti-acne from tube(g)/Area(cm^2).

5. Viscosity: Viscosity is a measure of a liquids resistance to flow. Thicker the gel has more resistance to flow and possesses a higher viscosity. Viscosity of formulated anti-acne gel was determined by Brookfield Viscometer using spindle no.63 LV at 100 rpm at a temperature of 25^0 C. The determination was carried out in triplicate and the average of three readings was recorded.

5. RESULT AND DISCUSSION

5.1. PREFORMULATION STUDIES:

5.1.1. Extraction: *Cinnamomum tamala* and *Curcuma longa* both has a good ability to extract solvent in ethanol. Soxhlet extraction process gives better yield in *C. tamala* and maceration process gives better yield in *C. longa.*

5.2 POST FORMULATION STUDIES:

5.2.1. Physical examination:

TABLE 5: PHYSICAL EXAMINATION OF ANTI-ACNE GEL.

FORMULATION	COLOUR	TEXTURE	CONSISTENCY
F1	Dark Yellow	Smooth	Good
F2	Dark Yellow	Smooth	Very good
F3	Dark Yellow	Smooth	Medium

Discussion: As compared to F1 & F3 formulations F2 formulation

meets expected texture & consistency properties.

5.2.2. **pH**: The pH of the F1, F2, and F3 gels ranged from 5.2 to 7.0, which is similar to the pH range of human skin. Therefore, none of the three gels would irritate skin.

TABLE 6: PH ANALYSIS

FORMULATION	pH
F1	6.5
F2	5.5
F3	5.2

Discussion: According to the results, the pH of all the three formulation that is F_1, F_2 and F_3 were found to be in range of 5.2 to 7.0 which is good for skin pH. All the formulation of anti-acne gels were shown pH nearer to skin.

5.2.3. **Spreadability**: The therapeutic potential of a gel formulation depends on the spreadability, which describes how far a gel spreads when applied to skin. In this investigation, all the formulations had acceptable spreadability.

TABLE 7: SPREADABILITY

FORMULATION	SPREADIBILITY(cm/sec)
F1	5.5
F2	6.3
F3	4.7

Discussion: Among the three formulations F2 formulation has good spreadibility.

5.2.4. **Extrudability**: All 3 formulations showed good extrudability.

TABLE 8: EXTRUDABILITY

FORMULATION	EXTRUDABILITY(gm/cm^2)
F1	80.2
F2	82.5
F3	78.3

5.2.5. **Viscosity**: The viscosity of a fluid serves as a proxy for its flow resistance; the higher the viscosity, the higher the flow resistance. Viscosity is a crucial factor to consider when assessing gel preparations. The F1, F2, and F3 gels used in viscosities were listed below.

TABLE 9: VISCOSITY

FORMULATION	VISCOSITY
F1	6
F2	7
F3	8

6. CONCLUSION

The idea that natural medicines are safer and have fewer side effects than synthetic ones makes them more acceptable. The demand for herbal formulations is rising on the global market. Establishing the herbal anti-acne gel with *C. tamala & C. longa* extract is a trending approach.

Based on the result and discussion, following conclusion were drawn:

- The prepared formulation were found to be yellow in colour with smooth texture.
- All the formulation were shown pH nearer to skin required that is 5.2-7 pH.
- Lesser the time taken for separation of the 2 slides better the spreadability. Hence, F_2 showed desired spreadability than F_1 & F_3.
- From the result, F_2 showed desired extrudability because when desired weight was applied to extrude the gel from the tube, F_2 showed smooth extrusion from the tube compared to F_1 and F_3.
- The combination of *Cinnamomum tamala* and *Curcuma longa* may produce an effect to minimize the acne problem.
- In vitro antimicrobial study shows that F2 formulation gives better zone of inhibition.
- Hence it can be concluded that the prepared polyherbal anti-acne gel was stable and safe in order to protect skin against antimicrobial activity.REFERENCE :

1. P.P.Sharma. Formulation, Manufacturing and Quality Control. 5th edition.Vandana publications, Delhi; 2014; 149-152.

2. Bhardwaj Suruchi, Parashar Shweta, Verma Kajal, Arora Radhika, Chhikara B.S. Evaluation of awareness about beauty products composition and proper utilization among college students. Integr. J. Soc. Sci., 2019;6(2): 57-64.

3. P. Ravisankar, O. Sai Kaushik, V. Himaja1, J. Ramesh, P. Pragna. Acne- causes and amazing remedial measures for acne. Indo American journal of pharmaceutical research, 2015;5(7): 2512-2522.

4. Leyden JJ. Current issues in antimicrobial therapy for the treatment of acne. Journal of European academy of dermatology and venereology 2001;15(3): 51-55.

5. Mishra US, Murthey PN, Mishra D, Sahu K. Formulation and Standardization of Herbal gel containing methanolic extract of calophylluminophyllum. Asian journal of pharmaceutical and clinical

research 2011;1(1): 276-289.

6. James WD. Clinical practice. Acne. N Engl J Med. 2005 Apr 7;352(14):1463-1472. doi: 10.1056/NEJMcp033487. PMID: 15814882.

7. Son BK, Yun Y, Choi IH. Efficacy of ah shi point acupuncture on acne vulgaris. Acupunct Med. 2010 Sep;28(3): 126-129. doi: 10.1136/aim.2010.003004. PMID: 20813813.

8. Enshaieh S, Jooya A, Siadat AH, Iraji F. The efficacy of 5% topical tea tree oil gel in mild to moderate acne vulgaris: a randomized, double-blind placebo-controlled study. Indian J Dermatol Venereol Leprol. 2007 Jan- Feb;73(1): 22-25. doi: 10.4103/0378-6323.30646. PMID: 17314442.

9. Mohsin J. Jamadar, Rajmahammadhusen shaikh. Preparation and Evaluation of herbal gel formulation. Journal of Pharmaceutical Research and Education 2017;1(2): 201- 224.

10. Jinu Mariya, K. Krishnakumar, Rejin Jose, Dineshkumar B, Anoop Narayanan V. Hydrogels: Recent trends in pharmaceutical formulation. Journal of pharmaceutical biology. 2016;6(2):86-88.

11. Oyal, Sharma P, Ramchandani V, Shrivastava SK, Dubey PK. Novel anti- inflammatory topical herbal gels containing withaniasomnifera and boswellia serrat. International journal of Pharmaceutical and Biological Science Archive. 2011; 2(4):1087-1094.

12. Amichai B, Shemer A, Grunwald MH, Low-dose isotretinoin in the treatment of acne vulgaris. Journal of American Academy of Dermatology 2006; 54(4); 644-646.

13. Khandewal K. Practical Pharmacognosy. 20th ed. Nirali prakashan: 2010; 25.1-25.9.

14. Gowthaman SR, Ranjith S. Extraction methods and applications of curcumin: A review. Cancer. 2015:39.

15. Thakur S, Chaudhary G. Review based upon ayurvedic and traditional uses of Cinnamomum tamala (Tejpatta). Int J Pharm Sci Rev Res. 202;68: 71-8.