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FORMULATION AND EVALUATION OF ANTI-ACNE PREPARATION USING AEGLE MARMELOS.

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Abstract

Acne could even be a multifactorial chronic disease of pilosebaceous units. Propionibacterium acnes and staphylococcus epidermidis are considered because of the foremost skin bacteria that cause the formation of acne. Acne is that the most typical reasonably skin condition. It's most widespread among older, children, teenagers, and adults. Around 80% of 11 to 30-year-olds are ill with acne. Most acne cases in girls occur between the ages of 14 to 17 and in boys, the condition is commonest in 16 to 19 years old. Herbal Anti-acne cream was prepared using extracts of the plants Aegle marmelos. The plant has been reported within the literature having good anti-microbial, anti-oxidant, anti-bacterial, and anti-inflammatory activity. Acne is believed to be caused by changes in hormones that are triggered during puberty.

Acne can cause great distress and harm a person's quality of life and self-esteem.

Acne is additionally called acne could even be a protracted run disease of the skin that happens when hair follicles are blocked with dead skin cells and oil from the skin. it's characterized by blackheads or whiteheads, pimples, oily skin, and possible scarring. If primarily affect the world of the skin with a comparatively high number of oil glands including the face, upper part of the chest, and back. The resulting appearance may find yourself in anxiety, reduced self-esteem.

Keyword: Anti-acne, Anti-microbial, Coumarins, Marmelosin

1.INTRODUCTION

1.1. Clinical features

1.1.1. The lesions

The first feature of the disorder is an increased rate of sebum secretion at puberty, making the skin look greasy (seborrhea). Blackheads or comedones usually accompany the oiliness. they regularly occur over the perimeters of the nose
and the forehead (but can occur anywhere. Comedones are follicular plugs composed of follicular debris, desquamated corneocytes, and compacted sebum. they need pigmented tips from the melanin pigment deposited by the follicular epithelium at this level Accompanying the visible comedones are numerous invisible comedones, many of which don't have pigmented tips.

Fig-1 Multiple comedones and seborrhea in acne.

Fig-2 Multiple comedons in acne Note the blackened tips From Melanin

Inflamed, reddened papules develop from blocked follicles. These are a shade of bright red, often irregular in shape and quite tender to the touch and maybe set quite deep within the skin. Sometimes they develop us at their tips (pustules), but these may additionally arise independently. in an exceedingly only a few patients, variety of the papules become quite large and persist for long periods – they're then observed as nodules in severely affected patients, the nodules liquefy centrally so fluctuant cysts are formed. In reality, the lesions are pseudocysts, as they have no epithelial lining. These lesions are seen within the foremost severely affected patients, which they cause the worst scarring. this kind of severe acne is believed of as cystic or nodule cystic acne and should be very disabling and disfiguring. When the massive nodules and cysts eventually subside, they leave in their wake firm, fibrotic, nodular scars, which sometimes become hypertrophic or perhaps keloidal. The scars are often quite irregular and have an inclination to create 'bridges' Even the smaller inflamed papules can cause scars and these tend to be pock-like or are triangular indentations there is a really rare and severe quite cystic acne named as acne fulminant during which the acne lesions quite suddenly become very inflamed. At the identical time, the affected individual is unwell and develops fever and arthralgia. Laboratory investigation often reveals a polymorph nuclear leukocytosis and odd osteolytic lesions within the bony skeleton. the rationale for this disorder isn't clear, although it has been suggested that it's due to the presence of a vasculitis that's somehow precipitated as a results of the underlying acne.

Fig-3 Acne Papules

1.2. Epidemiology

About 70 percent of the population develops a degree of clinically evident acne at some point during adolescence and early adult life, but perhaps only 10–20 percent request medical attention for the matter. This proportion varies in numerous parts of the world, staring at the racial mixture, affluence, and also sophistication of medical services. The variations in incidence in numerous ethnic groups haven't been well characterized, although it does appear that Eskimos and Japanese experience less acne than do Western Caucasians. Onset is often at puberty or slightly later, although many patients don't appear troubled until the age of 16 or 17 years. Men appear to be affected earlier and more severely than women. Older age groups aren't immune and it certainly isn't rare to develop acne within the sixth, seventh, or perhaps the eighth decade.
Acne lesions sometimes appear on the cheeks and chin of infants some weeks or months old and even slightly later than that this infantile acne is often trivial and short-lived, but can occasionally be troublesome.

2. A SPECIAL VARIETY OF ACNE

A) Acne from drugs and chemical agents:

Androgens provide the foremost normal 'drive' to the sebaceous glands. It's the increased secretion of these hormones that's in command of the increased sebum secretion at puberty. When given therapeutically for any reason, they'll also cause an eruption of acne spots. Glucocorticoids, like prednisolone, when given to suppress the signs of arthritis or another chronic inflammation, can even induce troublesome acne why this might so are adequately explained. Glucocorticoids don't seem to increase the speed of sebum secretion, and also the acne that results is curiously monomorphic therein sheets of acne lesions appear (unlike ordinary acne) all at the identical stage of development. Interestingly, corticosteroid creams can, uncommonly, also cause acne spots at the situation of the applying. Paradoxically, corticosteroids are occasionally used for his or her anti-inflammatory action within the treatment of acne.

Fig-4 Infantile Acne

Fig-5 Steroid Acne

B) Oil acne

Workers who inherit contact with lubricating and cutting oils develop an acne-like eruption at the sites of contact, consisting of small papules, pustules, and comedones. This is often observed on the fronts of the thighs and forearms, where oil-soaked overalls are available in contact with the skin. an analogous 'acne form folliculitis' sometimes arises at sites of application of tar-containing ointments during the treatment of skin diseases some cosmetics seem to aggravate or perhaps cause acne. this is often because they generally contain comedo-inducing (comedogenic) agents, like cocoa butter, isopropyl myristate and derivatives, and a few mineral oils, which may induce acne. This cosmetic acne is far less of controversy now that cosmetic manufacturers are conscious of it, as they avoid those constituents that they know can cause the matter and test new products on human volunteers if there's any doubt.

C) Chloracne

Chloracne is a very severe type of industrial acne thanks to exposure to complex chlorinated naphthalenic compounds and dioxin. Epidemics have occurred after industrial accidents like occurred in Bhopal in India, within which the population round the factory was affected. The compounds responsible are extremely potent, and lesions still develop for months after exposure. Typically, numerous large, cystic-type lesions occur during this type of industrial acne-causing massive cosmetic disability. it's worth noting that it's thought that the Ukrainian President (Viktor Yushchenko) was poisoned by dioxin, causing a dramatic change in appearance.

Fig-6 Chloracne

D) Excoriated acne

This disorder is most frequently seen in young women. Small acne spots around the chin, forehead, and on the jawline are picked, squeezed, and otherwise altered by manual interference. The resulting papules are crusted and infrequently more inflamed than routine acne spots. Often, the patients have little true acne and therefore the main cosmetic problem is that the results of the labor of their fingers! Mostly this can be a minor problem that may be improved by counseling but there are some more seriously affected patients whose problem is persistent.

2.1 Pathology, etiology, and pathogenesis:

Histologically, the essential features are those of folliculitis with considerable inflammation. the precise histological picture depends on the stage reached at the time of biopsy. Usually, it's possible to create out the remnants of a ruptured follicle. within the earliest stages, a follicular plug of the horn (comedone) is identified. Later, fragments of horn appear to possess provoked a violent mixed inflammatory reaction with many polymorphs and, in places, a granulomatous reaction with many huge cells and histiocytes In older lesions, plant tissue is deposited, indicating scar formation. What will we believe is that the sequence of events? within the first place, patients with acne have a better sebum secretion rate (SER) compared with matched.
Control subjects and there's some correlation between the extent of the rise within the SER and also the severity of the acne.
Acne first appears at puberty, at which era there's an eruption within the extent of circulating androgens. Eunuchs aren't getting acne, and also the administration of testosterone provokes the looks of acne lesions. Sebaceous glands are predominantly 'androgen driven' and few other influences are as important. Follicular obstruction also plays a vital role within the development of acne lesions. Comedones are early lesions and microscopically it's commonplace to look out horny plugs within the follicular canals. Changes are described within the follicular, epithelium suggesting that there is abnormal keratinization at the mouth of the follicle. Pathogenic bacteria aren't found in acne lesions and are not involved within the pathogenesis. it's possible, nonetheless, that the standard flora incorporates a task to play within the explanation for the disease. The flora consists of Gram-positive cocci – the micrococci (also called Staphylococcus epidermidis) – and Gram-positive bacteria – Propionibacterium acnes. Also, there are yeast-like microorganisms called Pityrosporum ovale. The propionibacteria are microaerophilic and lipophilic so they're ideally suited to living within the depths of the follicle in an oily milieu, and it isn't surprising that they massively increase in numbers during puberty when their food supply, within the type of sebum, increases. the standard follicular flora is additionally in charge of hydrolyzing the lipid esters of sebum, liberating potentially irritating fatty acids that damage the follicles. The constituents of sebum and skin surface lipid (after bacterial hydrolysis) are given in how can these observations be linked? an acceptable hypothesis is about out, during which it's suggested that the important inflammatory lesions of acne are the results of follicular leakage and eventually rupture.

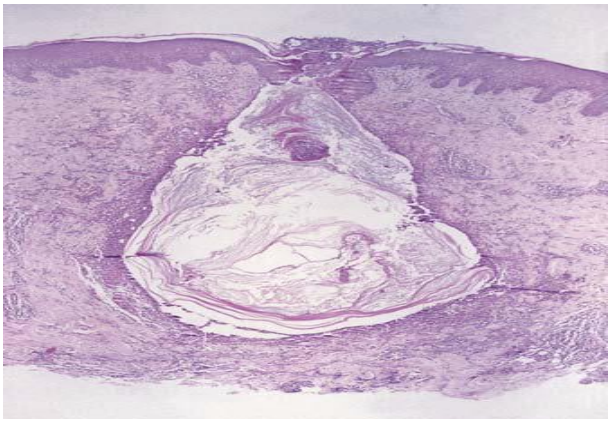

Fig-7 Pathology of inflamed acne papules showing ruptured follicle and a dense inflammatory cell.

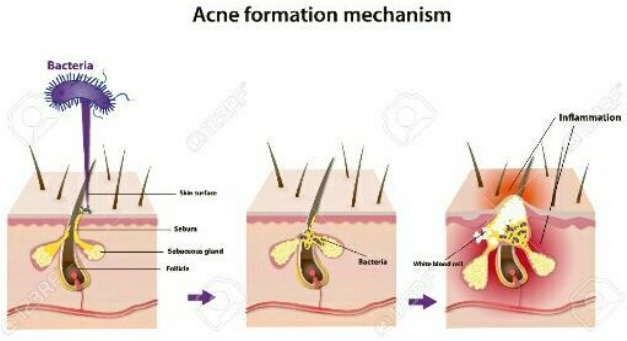

Fig:-8 Mechanism action of acne

2.2 Basic principles

Treatment may be aimed at:

- Reducing the bacterial population of the hair follicles to cut down the hydrolysis of lipids (antimicrobial agents).
- Encouraging the shedding of the follicular horny plugs to free the obstruction (comedolytic agents).
- Reducing the rate of sebum production, either directly by acting on the sebaceous glands (sebotrophic agents) or indirectly by inhibiting the effects of androgens on the sebaceous glands (anti-androgens).
- Reducing the damaging effects of acne inflammation on the skin with anti-inflammatory agents.

Table: 01 Antimicrobial Agent

Topical	Oral
Benzoyl Peroxide	Erythromycin
Clindamycin	Minocycline
Adapalene	Doxycycline
Azelaic Acid	Tetracycline
Tretonin	Cyproterone
Isotretinoin	Spironolactone
Nicotinamide	Isotretinoin

3. ACTIVE PROFILE

- Kingdom- Plantae.
- Order- Sapindales.
- Family- Rutaceae.
- Subfamily- Aurantioideae.
- Genus- Aegle. Species- Aegle Marmelos.
- Botanical name- Aegle marmelos.

3.1. Vernacular names

- English: Bengal quince, Beal fruit, Golden apple, Indian quince, Stone apple.
- Tamil: Aluvigam, Iyalbudi, Kuvilam, Mavilangai,Vilwam, Villuvam.
- Telugu: Bilvamu, Maluramu, Maredu, Sailushamu,Sandiliyamu, Sriphalamu.
- Hindi: Bel, Bili, Sirphal, and Bela, Sanskrit: Adhararutha, Asholam, Atimangaliya, Bilva.
- Bengal: Bael, Bel,
- Gujarat: Billi, Kannada: Bela, Bilva
- Malayalam: Koovalam, Vilwam.
- Orissa: Belo.

Fig-9 Aegle Marmelos Fruit

Fig-10 Aegle marmelos flower

3.2. Botanical Description

Aegle marmelos could be a slow-growing, medium-sized tree, up to 12-15 m tall with short trunk, thick, soft, flaking bark, and spreading, sometimes spiny branches, the lower ones drooping. Young suckers bear many stiff, straight spines. The deciduous, alternate leaves, borne singly or within the group, are composed of three to five oval, pointed and shallowly toothed leaflets, 4-10 cm long, 2-5cm wide, the terminal one with a protracted petiole.

Soil type: Bael is claimed to try and do best on rich, well-drained soil, but it's grown well and fruited on the oolitic limestone of southern Florida. It also grows well in swampy, alkaline, or stony soils having pH range from 5 to eight. In India, it's the reputation of thriving where other fruit trees cannot survive

Tree management: The tree has no exacting cultural requirements, doing well with a minimum of fertilizer and irrigation. The spacing in orchards 6-9 m between trees. Seedlings begin in touch in 6 to 7 years, vegetatively propagated trees in 5 years. Full production is reached in 15 years. Normally, the fruit is harvested when yellowish-green and kept for 8 days while it loses its green tint. Then the stem readily separates from the fruit.

Origin and distribution: The bael tree has its origin from the Eastern Ghats and Central India. It native to India and is found growing wild in Sub-Himalayan tracts from Jhelum eastwards to state, in central and south India. Bael is found growing along foothills of Himalayas, Bihar, Chhattisgarh, Uttaranchal, Jharkhand, and Madhya Pradesh. it's also grown in some Egyptian gardens in Surinam and Trinidad.

3.3. Documented species distribution:

Native range: India
Exotic range: Bangladesh, Egypt, Malaysia, Myanmar, Pakistan, Sri Lanka, Thailand.

3.4 Chemical constituents

Alkaloids: The alkaloids comprise the largest single class of secondary plant substances. New alkaloids from the leaves of Aegle marmelos were reported viz., ethyl cinnamamide, O- 3,3-(dimethylallyl) halfordinol, N-2-methoxy-2-[4-(3',3'- dimethylallyloxy) phenyl] ethyl cinnamamide, etc.

Terpenoids: The essential oil of Aegle marmelos (L.) Correa leaves were studied very much extensively in India by various workers since 1950. α-Phellandrene was found to be the common constituent of the essential oil from leaves, twigs, and fruits.α-Phellandrene (56%) and p-cymene (17%) were reported from leaf oil. Later, a similar report was published on leaf essential oil by many workers. P-Menth-1-en-3,5-diol was isolated and characterized from Aegle marmelos leaves. Limonene (82.4%) was reported as the main constituent from Aegle marmelos leaves and it was shown that limonene is a characteristic marker for the identification of Aegle marmelos oil samples.

Coumarins: Marmelosin, marmesin, imperatorin, marmin, alloimperatorin, methyl ether, xanthotoxol, scopoletin, scoparone, umbelliferone, psoralen, and marmelide have also been reported.

Phenylpropanoids: These are naturally occurring phenolic compounds, which have an aromatic ring to which the three-carbon side chain is attached. Among the phenylpropanoids are included hydroxycoumarins, phenylpropenes, and lignans. The most widespread plant coumarin is the parent compound, coumarin itself, which occurs in over twenty-seven plant families. Marmesin was established as a new compound from leaves, which is also a constituent of heartwood and root.

Tannins: The extreme tannin content in bael fruit was recorded in January. There is as much as 9% tannin in the pulp of wild fruits, less in cultivated type. Tannin is also present in leaves as skimmianine, it is also named as 4, 7, 8 - trimethoxyfuro- quinoline.

Polysaccharides: Galactose, arabinose, uronic acid, and L- rhamanose are obtained on hydrolysis.

Flavonoids: Mainly includes Rutin, Flavone, flavan-3-ols, flavone glycosides.

4. METHODOLOGY

A proper method has to be carried out while formulating the Anti-acne Cream,

1. Selection of active
2. Collection of Aegle marmelos
3. Extraction Method
4. Formulation
5. Preparation
6. Evaluation

4.1. Selection of active

Various extracts of bael leaves, roots, and fruits have been reported to be active against many bacterial strains. Leaf extracts have shown activity against Escherichia coli. The essential oil obtained from the leaves exhibited activity against Aeromonas sp., Escherichia coli, Pseudomonas salanacearum, and Xanthomonas vesicatoria the ethanolic extract of the root has shown activity against Vibrio cholerae, Salmonella typhimurium, Klebsiella pneumoniae, Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, and Staphylococcus aureus.

4.2. Collection

Aegle marmelos fruit was procured from the medicinal garden of RCPIPER, Shirpur.

4.3. Extraction Method of Fruit using Maceration Process

The collected fruits were washed thoroughly in H2O to get rid of the contaminants. The fruits were chopped into small pieces and dried under shade for 1 week; the dried materials were coarsely powdered using the mechanical blender. The powdered fruits of Aegle marmelos with a complete weight of 200 g were extracted by maceration method using 2.5 L of 70% ethanol as a solvent for about 1 week with occasional shaking. The ethanolic extract of Aegle marmelos fruits was filtered and concentrated to dryness under reduced pressure and controlled temperature employing a rotary evaporator. The extract was stored in a veryir-tight containers in a refrigerator at 4°C until further use.

Figure: Maceration process

Formulation Table

Ingredients	Parts Used	Category	Quantity 20 %
Aegle Marmelos 	Fruit Extract	Anti-bacterial Anti-oxidant	2
Stearic acid	-	Emulsifier	4
Cetyl alcohol	-	Stabilizer	1.6
Liquid paraffin	-	Lubricant	1.6
Glycerin	-	Humectant	2
Triethanolamine	-	Neutralizer	2
Distilled water	-	Vehicle	6.65
Methyl Paraben	-	Preservative	0.15

Table: 02. Formulation table of the anti-acne cream containing Aegle Marmelos Extract

5. EXPERIMENTAL WORK

5.1. Preparation of Anti-Acne Cream

The composition of anti-acne cream was shown in Table 2l. The oil phase consists of octadecanoic acid and other oil-soluble components like cetyl alcohol and liquid paraffin were dissolved within the oil phase. The oil phase was placed inside the beaker within the water bath. The temperature of the water bath was set to 75°C during the heating time. The water-soluble components and preservatives (glycerine, methylparaben, and triethanolamine) were dissolved within the aqueous phase and heated within the same water bath at temperature 75°C. After heating, the aqueous phase was added in portions to the oil phase with continuous stirring until the cooling of the emulsifier happened. Different proportion of Aegle marmelos fruits extract (5% and 10%) was mixed with the bottom together with fragrance.

Fig-11 Formulated Anti-acne cream.

6. EVALUATION OF ANTI-ACNE CREAM

6.1. Ph

The pH meter was calibrated employing a customary solution. About 0.5 g of the cream was weighed and dissolved in 50 ml of water and its pH was measured.

6.2. Homogeneity

The formulation was tested for homogeneity by visual appearance and touch.

6.3. Appearance

the looks of the cream was judged by its color, pearlescence, and roughness, and graded.

6.4. After feel:

Emolliency, slipperiness, and also the quantity of residue left after the appliance of a collection amount of cream was checked.

6.5. Type of smear

After the appliance of the cream, the kind of film or smear formed on the skin was checked.

6.6. Washability

The ease of removal of the cream applied was examined by washing the applied dispense with water.

6.7. Stability study

The stability study was administrated by storing the anti-acne cream at three different temperatures which are 8°C, 27°C and 40°C for 2 months.

7. EVALUATION PARAMETERS

Sr.no	Parameters	Observation
1	**Color**	White
2	**Odor**	Pleasant
3	**Consistency**	Good
4	**pH**	7.4±0.8
6	**Spreadability**	Good
7	**Washability**	Easily washeble
9	**After feel**	Emollient and slipperiness
10	**Type of Smear**	Non-greasy

Table: 03. Evaluation Parameters of anti-acne cream

8. DISCUSSION

The formulated anti-acne cream was evaluated for several physicochemical tests and the results were shown in Table 3. The type of smear formed on the skin was not greasy after the application of both creams. The creams were easy to remove after application by washing with water. The formulations were able to produce a uniform distribution of extracts from the cream. This was confirmed by visual examination and by evaluating the texture of the skin. Even though there is no change in a color reaction is observed when it was

kept for a longer time in a room temperature which indicates the stability of the product.

9. CONCLUSION

From the above observation as well as all evaluating parameters the formulations showed maximum antibacterial action against the bacterial infection. It may be due to the presence of active constituents like the ethnologic extract of Aegle marmelos. The antibacterial activity was significantly increased & retained constant at an extended period when it was converted into cream formulation comparatively to other formulation available in the market. This was a good sign for further studies to make this product into commercial standards. After the discussion, we conclude that the formulated cream of Aegle marmelos can be novel & approachable therapy for skin infections like acne vulgaris in the future where the confirmation of clinical and toxicological study was needed for further evaluation efficacy & safety of formulations.

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