REVIEW ON PREPARATION & PHARMACOLOGICAL EVALUATION OF HERBAL GEL

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ABSTRACT
The increasing frequency of intake of antibiotics to overcome this problem explores several side effects. Therefore it needs to focus on the herbal formulation as a topical first-line treatment. In the present study, three medicinal plants Citrus sinensis, Curcuma longa and Aloe barbadensis having significant antibacterial potential were selected to formulate a polyherbal gel for the management of several skin diseases. Extraction of Citrus sinensis, Curcuma longa and Aloe barbadensis was done and characterized. The topical gels were prepared which comprised extract of orange peel, aloevera, and turmeric with a different concentration. The prepared gel was kept at room temperature for 24 hours and evaluated. Based on this study, polyherbal anti-acne gel showed significant antibacterial activity on Staphylococcus aureus and Staphylococcus epidermis with no irritation. The physicochemical evaluation of developed formulation showed clear, uniform and free from fibre and particle. It was also observed good spreadability and consistency with pH nearer to skin. Thus the study result concluded that the polyherbal gel with extract of Citrus sinensis, Aloe barbadensis and Curcuma longa with concentration 0.2%, 1% and 0.8% respectively was an appropriate formulation for the first-line topical treatment of acne vulgaris.

KEYWORDS: Polyherbal Gel, Anti-acne, Aloevera, Citrus sinensis, Curcuma longa.

INTRODUCTION
Irritation is a complex process, which is regularly associated with pain and involves existences such as: the increase of vascular permeability, increase of protein denaturation and membrane modification. When cells in the body are injured by microbes, physical agents or chemical agents, the injury is in the form of tension. Irritation of tissue is due to response to
stress. It is self-protective response that is characterized by redness, pain, heat, and swelling and loss of function in the injured area. irritation is one of the body’s unfocused internal systems of fight, the respond of a tissue to an accidental cut is similar to response that results from other type of tissue injured caused by burn due to high temperature radiation, bacterial or viral invasion.\textsuperscript{1} A recent study on the ethanolic leaf extract of \textit{E. adenophorum} has report anti-inflammatory activity in dinitrofluorobenzene induced paw edema in mouse for the first time.\textsuperscript{2} It is fine identified that topical gels are addition accepted among all the topical preparations due to ease of applications. Current drug administration is a restricted to a small area drug release system any place in the body through ophthalmic, rectal, vaginal and skin as topical routes. Skin is one of the majority readily accessible organs on human being body for topical administration. For the topical treatment of dermatological disease as well as skin concern, a wide variety of vehicle ranging from solids to semisolids and liquid research is on hand to clinician and patients. Within the major group of semisolid preparations, the use of transdermal gels has prolonged both in cosmetics and in pharmaceutical preparations. Transdermal application of gels at pathological sites offer great advantage in a more rapidly release of drug directly to the site of action, independent of water solubility of drug as compare to creams and ointment\textsuperscript{3} judgment healing power in plants is an antique idea. It is predictable that there are 2, 50,000 to 5, 00,000 species of plants on earth.\textsuperscript{4} The concentration of the gelling agents is usually in 0.5% to 2.0% ranges with a few exceptions. External application of gel at skin offers certain advantages like quick release of drug directly to the site of action and better application property\textsuperscript{5} whereas \textit{in situ} gelling system involves use of polymers that have phase transition from solution to gel upon alterations in physico-chemical properties of drug Herbal formulations have become popular due to their natural origin and are used in variety of health ailments like liver problems, diabetes and heart problems.\textsuperscript{6}

**Collection of Plant Material**

Collection of the specimen such as Ripen pericarp of fruits \textit{Citrus} sinensis (Rutaceae), leaves of \textit{Aloe barbadensis} (Liliaceae) and Rhizomes of \textit{Curcuma longa} (Zingiberaceae). The specimens for the planned study are collected and genuine. Other chemicals are obtained from Himedia Laboratories Pvt. Ltd, and LobaChem, Mumbai.\textsuperscript{7}
Extraction of the pericarp of fruits *Citrus sinensis* (Orange peel)

*Citrus sinensis* peels were collected from an orange fruit juice producer. The peels were then wash and fully dried in an oven at 60°C for 72 hrs. Using Mortar and crusher the dried peels were powdered with particle size ranging of 0.5 mm to 0.1 mm and sock in methanol with mass to volume ratio 1:25(g/mL) for 72 hrs. It was then clean through Whatman No. 1 filter paper and collected into glass Petri dishes (Figure 1). This complete process of extraction and purification was repeated two-three times follow by evaporation of the collected extract and dry at 37°C.\(^8\)

![Figure 1: Extract of the pericarp of fruits *Citrus sinensis* (Orange peel).](image)

**Extraction of leaves of *Aloe barbadensis* (aloe vera)**

*Aloe Vera* leaves collect from the local nursery. The leaves washed through water and rind were detached (Figure 2). The inside gel scrapped and cut into small pieces and solar dried at 30-45°C for three weeks and dry gel particles were collected.\(^9\)

![Figure 2: Extract of leaves of *Aloe barbadensis* (aloe vera).](image)
Active Constitutes of Aloe Vera
The Aloe vera leaf gel contains about 98% water. The total solid content of Aloe vera gel is 0.66% and soluble solids are 0.56% with some seasonal fluctuation. On dry matter basis aloe gel consists of polysaccharides (53%), sugars (17%), minerals (16%), proteins (7%), lipids (5%) and phenolic compounds (2%) Aloe vera contains 200 potentially active constituents: vitamin, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids, which are responsible for the multifunctional activity of Aloe.\textsuperscript{[10]}

![Salicylic acid]

Extraction of Curcuma longa (Turmeric extract)
Take 20gm of Curcuma longa powder and mixed with a sufficient quantity of n-Hexane and kept away for 2 hrs. Then the solution was filtered out then precipitated powder was mixed in acetone for 10-15 minutes. Then solution was filtered another time and the filtrate was dried in air, the extract curcumin was isolated by scrapping using a spatula.\textsuperscript{[11-12]}

Figure 3: Extract of Curcuma longa (Turmeric extract).
**Evaluation and Phytochemical screening of extract**

All extract was analyzed by FTIR and for its phytoconstituents such as saponins, anthraquinone glycosides, phytosterols, tannins, flavonoids, carbohydrates, triterpenoids, polyphenol and alkaloids.[13]

**Method of Preparation of Gel Containing Extract**

The topical gels were prepared which comprised extract of orange peel, aloe vera, and turmeric with a different concentration (Table 1). The gels were prepared by using Carbapol 940, propylene glycol-400, ethanol, methylparaben, propylparaben, EDTA, triethanolamine and required amount of water in a sufficient quantity to prepare 50 g of gel. Water required for these formulations which can be divided into two same parts. In one part, an accurate amount of extracts were separately dissolved in 15 ml of water and to this calculated quantity of propylene glycol-400 and ethanol were added. In another part, Carbapol-940 was dissolved in 35 mL and to this solution methylparaben, propylparaben and EDTA (Ethylenediaminetetraacetic acid) were added.15 Both of these solutions were mixed in a beaker and triethanolamine was added drop wise to the formulation for adjustment of required skin pH (6.8—7) and to obtain the gel with required consistency. It was then stirred by using propeller for at least 2 hours at 500 (rpm). subsequent to stirring, the prepared gel appear to be uniform and devoid of any bubbles. The prepared gel was kept at room temperature for 24 hours.[14]

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ingredient</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Orange peel extract</td>
<td>0.2%</td>
</tr>
<tr>
<td>2</td>
<td>Aloe-vera extract</td>
<td>1%</td>
</tr>
<tr>
<td>3</td>
<td>Turmeric extract</td>
<td>0.8%</td>
</tr>
<tr>
<td>4</td>
<td>Propylene glycol-400</td>
<td>4%</td>
</tr>
<tr>
<td>5</td>
<td>Ethanol</td>
<td>3%</td>
</tr>
<tr>
<td>6</td>
<td>Water</td>
<td>q.s.</td>
</tr>
</tbody>
</table>

**Formula**

<table>
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<th>Sr. No</th>
<th>Ingredient</th>
<th>Formula</th>
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<tbody>
<tr>
<td>1</td>
<td>Carbopol</td>
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</tr>
<tr>
<td>2</td>
<td>Water</td>
<td>35%</td>
</tr>
<tr>
<td>3</td>
<td>Methyl paraben</td>
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</tr>
<tr>
<td>4</td>
<td>Propylparaben</td>
<td>0.02%</td>
</tr>
<tr>
<td>5</td>
<td>EDTA(Ethylenediaminetetraacetic acid)</td>
<td>0.03%</td>
</tr>
<tr>
<td>6</td>
<td>Triethanolamine</td>
<td>0.025%</td>
</tr>
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</table>
Active Constituents: The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumeron, atlantone, and zingiberone. The other constituents present in turmeric are sugars, proteins, and resins. The best-researched active constituent is curcumin, which comprise 0.3–5.4 percent of raw turmeric.

Pharmacokinetics: Pharmacokinetic studies in animals have demonstrated that 40–85 percent of an oral dose of curcumin passes through the gastrointestinal tract unchanged, with most of the absorbed flavonoid being metabolized in the intestinal mucosa and liver. Because of its low rate of absorption, curcumin is frequently formulated with bромелайн for better absorption and improved anti-inflammatory effect.

Pharmacological Screening of Curcuma Longa
Antioxidant Effects: Water- and fat-soluble extracts of turmeric and its curcumin component exhibit strong antioxidant activity, comparable to vitamins C and E. The study of ischemia in the feline heart demonstrated that curcumin pretreatment decrease ischemia-induced change in the heart. An *in vitro* study measure the effect of turmeric on endothelial heme oxygenase-1, an inducible stress protein, was conducted utilizing bovine aortic endothelial cells. Incubation (18 hours) with curcumin result in improved cellular resistance to oxidative damage.

Hepatoprotective Effects: Turmeric has been found to have hepatoprotective action is similar to silymarin. Animal studies have been demonstrated turmeric shows hepatoprotective effects from a variety of hepatotoxic insults, include carbon tetrachloride (CCI4), galactosamine, acetaminophen (paracetamol), and Aspergillus aflatoxin. Turmeric hepatoprotective effect is mainly a result of its antioxidant action, as well as its ability to reduce the formation of pro-inflammatory cytokines. Turmeric extract inhibited fungal aflatoxin production by 90 percent when given to ducklings infected with Aspergillus parasiticus. Curcumin also reversed biliary hyperplasia, fatty changes and necrosis increase by aflatoxin production. Sodium curcuminate, a salt of curcumin, also exerts choleretic effects by increasing biliary excretion of bile salts, cholesterol, bilirubin, as well as enhance bile solubility, therefore probably preventing and treating cholelithiasis.

Anti-inflammatory Effects: The volatile oils and curcumin of Curcuma longa exhibit potent anti-inflammatory effects. Oral administration of curcumin in subtances of acute
inflammation was found to be it is effective like as cortisone or phenylbutazone, and one-half as effective in cases of chronic inflammation. In rats with Freund’s adjuvant-induced arthritis, oral administration of Curcum longa significantly reduced inflammatory swelling compared to controls. Curcumin longa has anti-inflammatory properties may be recognized to its ability to inhibit both biosynthesis of inflammatory prostaglandins and neutrophil function in inflammatory states. Curcumin may also be applied topically to neutralize inflammation and irritation associated with inflammatory skin situation and allergies although think about must be used to prevent staining of clothing from the yellow pigment.

**Anticarcinogenic Effects** - Animal studies involving rats and mice, as well as *in vitro* studies utilizing human cell lines, have demonstrated curcumin’s ability to inhibit carcinogenesis at three stages: tumor promotion, angiogenesis, and tumor growth. In two studies of colon and prostate cancer, curcumin inhibited cell proliferation and tumor growth. Turmeric and curcumin are also capable of suppressing the activity of several common mutagens and carcinogens in a variety of cell types in both *in vitro* and *in vivo* studies. The anticarcinogenic effects of turmeric and curcumin are due to direct antioxidant and free-radical scavenging effects, as well as their ability to indirectly increase glutathione levels, thereby aiding in hepatic detoxification of mutagens and carcinogens, and inhibit in nitrosamine formation.

**Antimicrobial Effects** - Turmeric extract and the essential oil of Curcuma longa inhibit the growth of a variety of bacteria, parasites, and pathogenic fungi. A study of chicks infected with the caecal parasite *Eimeria maxima* demonstrated that diets supplemented with 1-percent turmeric resulted in a reduction in small intestine lesion scores and improved weight gain. Another animal study, in which guinea pigs were infected with either dermatophytes, pathogenic molds, or yeast, found that topically applied turmeric oil inhibited dermatophytes and pathogenic fungi, but neither curcumin nor turmeric oil affected the yeast isolates. Improvements in lesions were observed in the dermatophyte- and fungi-infected guinea pigs, and at seven days post-turmeric application the lesions disappeared. Curcumin has also been found to have moderate activity against Plasmodium falciparum and Leishmania major organisms.

**Cardiovascular Effects** - Turmeric shows protective effects on the cardiovascular system include reducing cholesterol and triglyceride levels, falling susceptibility of low density lipoprotein (LDL) to lipid peroxidation, and inhibit platelet aggregation. These effects has been noted that with low doses of turmeric. A study of 18 atherosclerosis rabbits given low-
dose (1.6–3.2 mg/kg bodyweight daily) turmeric extract verified decreased in susceptibility of LDL tolipid peroxidation, in addition to lower plasma cholesterol and triglyceride levels. The higher dose does not decrease lipid peroxidation of LDL, but cholesterol and triglyceride level decreases, although to a smaller degree than with the lower dose. Turmeric extract’s effect on cholesterol levels may be due to decreased cholesterol uptake in the intestines and improved conversion of cholesterol to bile acids in the liver.

**Gastrointestinal Effects**- The Constituents of *Curcuma longa* produce several protective action on the gastrointestinal tract. Sodium curcuminate inhibited by intestinal spasm and p-tolymethylcarbinol, a turmeric component, increased gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric also has been show inhibitory action on ulcer formation which is cause by stress, alcohol, indomethacin, pyloric ligation, and reserpine, extensively increasing gastric wall mucus in rats subjected to these gastrointestinal insults.

**Curcumin enhances immunity**- Curcumin can also help to body fight off cancer should some cells escape apoptosis. When researchers looked at the lining of the intestine after ingestion of curcumin, they found that CD4+ T-helper and B type immune cells were greater in number. Turmeric also produce localized immune stimulation and enhances immunity in general. Researchers in India have accepted increased antibodies and more immune action in mice given curcumin.\textsuperscript{[15-26]}

**Physiochemical evaluation of formulation**

**Antifungal activity**

The comparison of the formulated herbal gel was done with the marketed antifungal formulation (Zolef Cream) by carrying out the antifungal activity pf all developed batches and blank formulation by Cup-plate method. *Aspergillus aureus* and *Candida albicans* were the two different bacteria cultures using agar the antifungal test was performed. Petri plates with well diffusion prepared nutrients was kept for drying and cooling. With the help of micro wire loop each bacterial culture was spread. To drill holes of 4 mm a sterilized captool of 6 mm diameter it was used. In to these holes then 0.5g of gel was added form each batch. incubation of plates were then done at 270C for 48 hr. If any zone of inhibition develops (diameter in mm) it was then measured for the particular compound with each fungal strength.\textsuperscript{[27]}
Spreadability

Spreadability was determined by using apparatus which consists of a wooden block, which is provided by a pulley at one end. In this method, spreadability was determined on the basis of slip and drag characteristics of gels. An excess of gel (about 2 g) under study was placed on the ground slide then gel is sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided to hook. A 1 kg weight placed at the top of the two slides for the 5 min to eject air and to provide a homogeneous film of the gel between these slides. The top plate subjected to pull of 80 g with the help of string which is attached to the hook then the time (in seconds) which is required by the top slide to cover a distance of 7.5 cm was measured. A shorter interval indicate better spreadability of gel.

Spreadability was determined by using the following formula

\[ S = \frac{M \times L}{T} \]

Where,

- \( S \) = Spreadability
- \( M \) = Weight in the pan (tied to the upper slide)
- \( L \) = Length moved by the glass slide
- \( T \) = Time (in sec.) taken to separate the upper slide from the ground slide\(^{28}\)

Homogeneity

All prepared gel formulations were tested for homogeneity by visual inspection after the gels have been set in to the container. They were tested for their presence and appearance of any aggregates.\(^{29}\)

Determination of pH

The pH of the gel formulations was determined by using a calibrated digital pH meter (SYSTEM 361) at constant room temperature range (24± 2°C).\(^{30}\)

Rheological study

By using Cone and Plate viscometer, the viscosity of the formulated batches was determined. In a procedure, a definite quantity of gel was added to a beaker covered with a thermostatic jacket. The gel was rotated at 100 rotations per minute with spindle.\(^{31}\)
Extrudability
The gel preparation were filled in standard plugged portable aluminium tubes and sealed by pressing to the end. The weight of tubes were recorded and the tubes were placed between two glass slides and were clamped. 500gm was placed over the slides and then the cap was detached. The measure of extruded gel was collected and weighed. The percent of extruded gel was calculated as
1. When it is greater than 90% then extrudability is excellent.
2. When it is greater than 80% then extrudability is good.
3. When it is 70% then extrudability is fair.

Viscosity
Viscosities of gels were determined using Brookfield viscometer. Gels were tested for their rheological characteristics at 25°C using Brookfield viscometer (DV-III programmable Rheometer). The measurement was made over the whole range of speed settings from 10rpm to 100rpm with 30seconds between 2 successive speeds and then in a descending orders.

CONCLUSION
In recent times herbal medicines are more considered as safe with fewer side effects than synthetic drug for the treatment of acne vulgarism. Therefore In the worldwide market. Natural remedies including herbal formulation are in great demand. It is a very good attempt to formulate and evaluate the polyherbal anti-acne gel along with the constancy studies. Based on this studies, polyherbal anti-acne gel prepared from the extract of Citrus sinensis (0.2%), Aloe barbadensis (1%) and Curcuma longa (0.8%) showed significant antibacterial activity on Staphylococcus aureus and staphylococcus epidermis with no irritation. The polyherbal gel showed a synergistic effect as compared to individual extract with good stability. Thus the study result concludes that the formulated polyherbal gel with extract of Citrus sinensis, Aloe barbadensis and Curcuma longa with concentration 0.2%, 1% and 0.8% respectively can be used for the treatment of various skin diseases.

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