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Research Paper

Multi-Component Phytopharmaceutical Development: Formulation, Characterization, and Clinical Evaluation of a Synergistic Antifungal Emulgel Utilizing *Allium sativum*, *Zingiber officinale*, and *Plumbago zeylanica* Oils

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ABSTRACT

The goal of the current study was to create and assess a polyherbal antifungal cream with ginger oil from *Zingiber officinale*, garlic oil from *Allium sativum*, and plumbagin extracted from *Plumbago zeylanica*. The physicochemical characteristics and compatibility of the medication and excipients were ascertained through preformulation experiments. Using the emulsification procedure, the cream was made. The resulting formulation's pH, viscosity, spreadability, extrudability, homogeneity, stability, and antifungal efficacy against *Candida albicans* were all assessed. Significant antifungal activity, excellent physicochemical characteristics, and high stability were all demonstrated. According to the study's findings, the created polyherbal cream is a useful topical antifungal medication

INTRODUCTION

Dermatology's therapeutic landscape has undergone a major turning point as researchers and clinicians tackle the twin problems of increasing fungal virulence and the declining effectiveness of conventional synthetic antifungal medicines. Particularly in tropical and subtropical regions where humidity and temperature maximize fungal

growth, superficial fungal infections—which include dermatophytosis, candidiasis, and different tinea manifestations—represent a significant worldwide health burden. The quick establishment of resistant strains and inadequate skin penetration are common problems with traditional topical therapy. In order to maximize the bioactivity of concentrated plant oils produced from *Allium sativum* (garlic), *Zingiber officinale*

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(ginger), and *Plumbago zeylanica* (Indian leadwort), the pharmaceutical industry has shifted its attention toward sophisticated delivery technologies like emulgels. ^[1, 2, 3]

A stabilized emulsion is integrated with a gelling matrix to create an emulgel, a dual-control delivery device. The surrounding gel matrix offers rheological characteristics for prolonged release and increased residence time, while this structure offers a special setting where lipophilic medications are solubilized within oil droplets. Targeting fungal pathogens through several pathways while maintaining superior skin permeability is achieved by combining the synergistic actions of garlic, ginger, and plumbago oils. ^[4, 5, 6, 7]

Phytochemical Profiling and Active Ingredients

The three main botanical components of the suggested emulgel have complicated chemical signatures that contribute to its effectiveness.

Allium sativum (Garlic Oil)

The antibacterial qualities of *Allium sativum*, a member of the Amaryllidaceae family, have been used for millennia. Garlic oil's distinct composition of organosulfur compounds is the main reason for pharmacological interest. The vacuolar enzyme alliinase is released when *Allium sativum* cloves are mechanically disrupted, which helps convert alliin into allicin (diallyl thiosulfinate). The main antifungal agents in garlic oil are diallyl disulfide (DADS) and diallyl trisulfide (DATS), two oil-soluble sulfides that are derived from allicin, a highly reactive, volatile molecule. ^[8, 9]

These sulfur-containing compounds, which can penetrate the fungal cell membrane and establish disulfide bonds with the sulfhydryl groups of important enzymes, are predominant in garlic essential oil, according to GC-MS research. Membrane integrity is compromised, and vital metabolic activities are inhibited as a result of this interaction. ^[10]

TABLE NO. 1

Compound identified	Average Percentage	Pharmacological action
Diallyl Trisulfide	16.8 – 33.4	A powerful fungicidal drug that stops microtubule formation.
Diallyl Disulfide	17.2-28.99	Fungal cells' precursor to reactive oxygen species.
Allyl Methyl Trisulfide	14.5 – 29.12	Combined antibacterial component.
2-Vinyl-4H-1,3-Dithiine	2.5	Membrane stability and anti-biofilm activities.
Allyl Methyl Disulfide	2.3 – 8.3	A contributing metabolite of sulfur.

Zingiber officinale (Ginger Oil) Characterization

Both volatile oils and non-volatile, strong chemicals like gingerols and shogaols can be found in abundance in the rhizome of *Zingiber officinale* (Zingiberaceae). Sesquiterpene hydrocarbons are highly concentrated in ginger essential oil. Alpha-zingiberene, the main

component, helps provide the oil its anti-inflammatory and antibacterial qualities. ^[11,12,13]

Ginger oil's antifungal action includes interfering with fungal intracellular signaling and causing oxidative stress. It has been demonstrated that phenolic chemicals, such as zingerone and other gingerol derivatives, exhibit strong anti-Candida activity by preventing hyphal production and hindering the growth of biofilms.

TABLE NO. 2

Compound identified	Average Percentage	Pharmacological action
Zingiberene	10.5 - 18.61	principal antibacterial and aromatic carrier.
Curcumin	2.9 - 9.91	Antioxidant and anti-inflammatory assistance.
Sesquiphellandrene	5.8 - 9.25	combined antifungal properties. Improvement of penetration and antimicrobial qualities.
Eugenol	7.4 – 78.81	Enhancement of antibacterial properties and penetration.
Zingerone	9.0 - 9.5	scavenging free radicals and inhibiting metabolism.

Plumbago zeylanica (Plumbago Oil) and Anti-Biofilm Utility.

The naphthoquinone plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone) is found in the roots of *Plumbago zeylanica*, also referred to as Indian leadwort or "Chitrak," a valuable medicinal plant. A strong pro-oxidant, plumbagin causes fungal cells to produce reactive oxygen species (ROS), which damages DNA and causes apoptosis.

Plumbago zeylanica oil or concentrated extract is an effective fungicidal and fungistatic agent. It is an essential part of a synergistic polyherbal formulation since it can regulate the resistance of common medications like ketoconazole, potentially increasing their efficacy by up to 12-fold.

TABLE NO. 3

Compound identified	Average Percentage	Pharmacological action
Plumbagin	32.4 – 69.1	ROS inducer, primary naphthoquinone, and antifungal.
Phenol, 2,4-bis(1,1-dimethylethyl)	54.62	Antifungal and antioxidant properties.
Lupeol	Present	anti-inflammatory and stimulates the healing of wounds.
Hexadecanoic acid	13.79	Antimicrobial activity and saturated fatty acid.
Beta- Sitosterol	Present	stability of the dermal barrier.



Pathophysiology of Superficial Fungal Infections and Biofilm Formation

Evaluating the effectiveness of the emulgel requires a thorough understanding of the target

pathogens. Yeasts like *Candida albicans* and dermatophytes like *Trichophyton rubrum* and *Microsporum canis* are the main culprits behind superficial mycoses. [14, 15, 16]

Dermatophytosis Mechanisms

Proteolytic and keratolytic enzymes are secreted by specialized fungi called dermatophytes, which infiltrate keratinized tissues like skin, hair, and nails. Tinea pedis and tinea corporis are primarily caused by species such as *Trichophyton rubrum*. Garlic oil has proven to be very powerful against *T. rubrum*, effectively preventing its growth by rupturing the integrity of its cell walls. [17, 18]

Biofilm Resistance and Candida albicans The opportunistic pathogen *Candida albicans* can create biofilms, which are intricate cell communities enmeshed in a matrix of extracellular polymeric substances (EPS). Antifungal therapy resistance is increased by the protective habitat that biofilms offer. Plumbagin from *Plumbago zeylanica*, which has been demonstrated to prevent biofilm formation by interfering with early adhesion, is strategically added to address this issue.



FUNGAL INFECTION

PRE-FORMULATION STUDY OF ACTIVE INGREDIENTS AND EXCIPIENTS

To ensure the formulation's stability and effectiveness, preformulation tests were carried out to assess the physicochemical characteristics of the active ingredients and their compatibility with excipients. The active components were ginger oil from *Zingiber officinale*, garlic oil from *Allium sativum*, and plumbagin from *Plumbago zeylanica*.

1. Organoleptic Properties

TABLE NO. 4

Ingredient	Appearance	Odor	Nature
Plumbagin	Yellow Liquid	Characteristic	Oily
Garlic oil	Pale yellow liquid	Strong and pungent	Oily
Ginger oil	Light yellow liquid	Aromatic	Oily

2. Solubility Study

TABLE NO. 5

Oil	Water	Ethanol	Oil Phase
Plumbago oil	Insoluble	Slightly soluble	Soluble
Garlic oil	Insoluble	Slightly soluble	Soluble
Ginger oil	Insoluble	Slightly soluble	Soluble

3. pH Compatibility Study of Herbal Oils with Excipients

TABLE NO. 6

Component	Observed pH Range	Compatibility with Skin	Remark
Plumbago oil	5.8 – 6.5	Compatible	No irritation expected
Garlic oil	5.5 – 6.2	Compatible	Stable in formulation
Ginger oil	5.6 – 6.3	Compatible	Stable for topical use
Carbopol gel base	6.0 – 7.0	Compatible	Requires neutralization
Final emulgel formulation	5.5 – 6.5	Highly compatible	Ideal skin PH

4. Partition Behaviour Study of Herbal Oils

TABLE NO.7

Oil	log P Value	Nature	Interpretation
Plumbago oil	2.5 – 3.0	Lipophilic	Good skin permeation
Garlic oil	>3.0	Highly lipophilic	Strong membrane penetration
Ginger oil	2.0 – 2.8	Moderately lipophilic	Suitable for topical delivery

5. Drug–Excipient Compatibility

TABLE NO. 8

Oil	Excipients Tested	Observation	Result
Plumbago oil	Carbopol940, stearic acid, cetyl alcohol, liquid paraffin	No precipitation or color shift	Acceptable
Garlic oil	Carbopol940, Stearic acid, Cetylalcohol, liquid paraffin	Absence of phase separation	Acceptable
Ginger oil	Carbopol940, stearic acid, Cetylalcohol, Liquid paraffin	There was no evidence of instability.	Acceptable

Formulation Development and Optimized Ingredients

Three separate phases are incorporated in the formation of the antifungal emulgel: the gelling matrix, the aqueous phase, and the oil phase. The goal is to develop a system with a total active concentration of 7% that is both stable and pleasing in appearance.

Selection of Excipients and Formulation Table

The polyherbal antifungal emulgel's precise composition for 100 millilitres is described below. Stearic acid and cetyl alcohol are used in this formulation to give the emulsion phase body and stability, while Carbopol 940 serves as the structural gelling agent.

TABLE NO. 9

Sr. No	Ingredient	Quantity	Role
1	Plumbago oil	1%	Antifungal
2	Garlic oil (from <i>Allium sativum</i>)	2%	Antifungal
3	Ginger oil	1%	Antifungal
4	Stearic acid	10%	Emulsifier
5	Cetyl alcohol	2%	Emollient
6	Liquid paraffin	5%	Oil phase
7	Carbopol 940	1%	Gelling agent
8	Triethanolamine	q.s.	Neutralizer
9	Glycerin	5%	Humectant
10	Methyl paraben	0.1%	Preservative
11	Propyl paraben	0.05%	Preservative
12	Purified water	q.s. (100%)	Vehicle



Preparation Methodology: The Multi-Stage Emulsification Process

To ensure homogeneity and the stability of the thermolabile oils, the emulgel is developed in three separate steps.

Stage 1: Preparation of the Oil Phase.

Stearic acid (10%) and cetyl alcohol (2%) are melted at about 70°C to create the oil phase. Once melted, the lipophilic preservatives (propyl paraben) and liquid paraffin (2%) are added. The active oils (garlic 3%, ginger 2%, and plumbago 2%) are added to this phase right before emulsification or after the temperature has somewhat fallen to prevent thermal degradation in order to retain the volatile organosulfur compounds in garlic oil and the gingerols in ginger oil. [19, 20]

Stage 2: Gel Base Preparation and Aqueous Phase

To guarantee full swelling and uniform dispersion of the polymer chains, carbopol 940 (1%) was dissolved in filtered water with constant stirring and left to hydrate for several hours. For a stable gel network to develop and for the desired rheological qualities to be achieved, Carbopol must be properly hydrated. [21;22] The residual aqueous phase was used to dissolve methyl paraben (0.1%), a hydrophilic preservative, and glycerin (5%), a humectant and plasticizer. As is frequently advised in the development of semisolid formulations, the aqueous phase was

then heated to the same temperature as the oil phase in order to assure homogeneity and avoid phase separation during emulsification. [23]

Stage 3: Formulation of the Emulgel

An initial oil-in-water (O/W) emulsion was created by gradually incorporating the oil phase into the aqueous phase while stirring quickly. Oil droplets were uniformly dispersed throughout the aqueous medium because of consistent agitation, which is essential for the stability and homogeneity of the emulsion. [24] Triethanolamine was then added to neutralise the emulsion that had developed. This raised the pH and caused Carbopol 940 to ionize, causing swelling and the creation of a three-dimensional gel network. Through this procedure, the low-viscosity emulsion was changed into a stable, non-greasy emulgel with improved spreadability and favorable rheological characteristics. [25,26]

Physicochemical Characterization and Evaluation Parameters.

Physical Appearance of Trial Batches

The created emulgel trial batches' organoleptic properties, such as color, odor, appearance, consistency, homogeneity, phase separation, and lump presence, were assessed visually. The observations are outlined below, and the formulations were created using the factorial design. [17, 28, 29]

Table: Physical Evaluation of Emulgel Trial Batches.

Parameter	Batch F1	Batch F2	Batch F3	Batch F4 (Optimized Batch)
Color	Light yellow	Light yellow	Pale yellow	Off-white to yellowish
Odor	Characteristic	Characteristic	Characteristic	Characteristic
Appearance	Smooth	Smooth	Smooth	Smooth and glossy
Consistency	Liquid	Semi-solid	Semi-solid	Semi-solid, smooth
Homogeneity	Fair	Good	Good	Excellent
Phase separation	Yes (Creaming)	Slight	Absent	Absent
Presence of lumps	Absent	Absent	Absent	Absent



Batch F4 was chosen as the optimized batch because it had the best physical attributes of all the trial formulations. It had a smooth, glossy, uniform semi-solid consistency and an off-white to yellowish color. The excellent integration of the herbal oils was demonstrated by the formulation's distinctively strong garlic and aromatic ginger scents. Batch F4 showed no signs of phase separation or lump formation, indicating high emulsion stability and even component distribution. Batches F2 and F3 demonstrated acceptable appearance and stability but somewhat poorer homogeneity than the optimal formulation,

whereas Batch F1 showed creaming with a relatively liquid consistency.

pH Determination:

To guarantee skin compatibility and reduce the risk of irritation, the pH of the prepared emulgel batches was measured with a digital pH meter. Each formulation was made as a 1% aqueous dispersion, and the electrode was submerged in the sample to be measured. In order to mirror the natural pH of the skin, the allowable pH range for topical preparations was kept between 5.5 and 6.5. [30,31,32]

Table : PH Evaluation of Emulgel Trial Batches.

Sr. No.	Batch	pH Value
1	F1	5.7
2	F2	5.7
3	F3	5.8
4	F4 (Optimized Batch)	5.9

he created emulgels are safe for topical administration and are unlikely to cause skin irritation, as all formulation batches showed pH values within the acceptable skin-friendly range of 5.5–6.5. Out of all the batches, the optimized batch

F4 had a pH of 5.9, which is near the skin's physiological pH and promotes greater patient compatibility and acceptability.



F1 BATCH



F2 BATCH



F3 BATCH



F4 BATCH

Viscosity Determination:

A Brookfield viscometer equipped with an appropriate spindle was used to measure the viscosity of the prepared emulgel formulations at

room temperature and a set rotational speed (rpm). The spreadability, consistency, and stability of topical formulations are significantly influenced by viscosity. [33,34,35]

Table: Viscosity Evaluation of Emulgel Trial Batches.

Sr. No.	Batch	Viscosity (cps)
1	F1	64000
2	F2	65000
3	F3	66000
4	F4 (Optimized Batch)	67500

High and consistent viscosity values were shown in all formulation batches, suggesting that the generated emulgels were stable and consistent. Variations in polymer concentration and composition during factorial design optimization could be the cause of the progressive rise in

viscosity from F1 to F4. Without compromising the formulation's smooth application, the optimized batch F4 demonstrated the maximum viscosity, which increased stability, retention on the skin's surface, and patient acceptability.



F1 BATCH



F2 BATCH



F3 BATCH



F4 BATCH

Spreadability:

The glass slide method was used to assess the prepared emulgel compositions' spreadability. Two glass slides were sandwiched with a small amount of emulgel, and the upper slide was given a certain amount of weight. It was noted how long it took for the higher slide to move and detach from

the bottom slide. The following formula was used to determine spreadability. [36, 37]

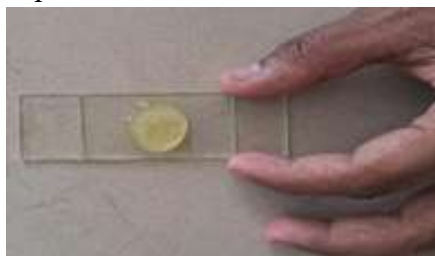
Formula:

$$S = M \times L / T$$

Sr. No.	Batch	Spreadability
1	F1	15.55
2	F2	16.00
3	F3	16.20
4	F4 (Optimized Batch)	16.50

Good spreadability was shown by all formulation batches, indicating ease of application throughout the skin's surface. Better consistency, a smoother texture, and increased patient acceptability were suggested by the optimized batch F4, which had

the highest spreadability value. The formulation's optimal viscosity and even dispersion of the gelling ingredient may be responsible for the batches' progressive improvement in spreadability.



F1 BATCH



F2 BATCH



F3 BATCH



F4 BATCH

Extrudability:

The resulting emulgel compositions were filled into a collapsible aluminum tube to assess their extrudability. To ascertain the ease of extrusion

from the container, a steady pressure was applied to the tube, and the amount of emulgel extruded was measured. Convenient application and patient compliance depend on good extrudability. [38, 39, 40]

Sr. No.	Batch	Extrudability
1	F1	88%
2	F2	90%
3	F3	92%
4	F4 (Optimized Batch)	94%

Good extrudability was shown by all formulation batches, meaning that the emulgel could be removed from the collapsible tube with little effort. Because of its smooth texture, appropriate viscosity, and enhanced homogeneity, optimized batch F4 showed the maximum extrudability.

According to the findings, the adjusted formulation has the right consistency for easy topical application and improved patient acceptability.

**F1 BATCH****F2 BATCH****F3 BATCH****F4 BATCH****Homogeneity:**

By pressing a tiny amount of emulgel between the fingers and visually inspecting the formulations for consistency, uniformity, and the presence of lumps, the homogeneity of the created emulgel

formulations was assessed. The overall quality and stability of the emulgel are enhanced by a homogenous formulation, which guarantees consistent dispersion of active components. [41, 42, 43, 44]

Sr. No.	Batch	Homogeneity	Presence of Lumps
1	F1	Uniform	Absent
2	F2	Uniform	Absent
3	F3	Uniform	Absent
4	F4 (Optimized Batch)	Highly Uniform	Absent

Every batch of the formulation exhibited good homogeneity, with a smooth texture and no lumps, suggesting that the contents were properly mixed and dispersed throughout the formulation. The emulgel's overall quality and the efficacy of the

formulation procedure were confirmed by the optimized batch F4's improved uniformity and smooth consistency when compared to the other batches.

**F1 BATCH****F2 BATCH****F3 BATCH****F4 BATCH**

Skin Irritation Test:

To assess the safety of the developed emulgel formulations for topical administration, a skin irritation study was conducted. After applying a

tiny amount of emulgel from each batch to the shaved skin region, the treated area was checked for redness, itching, swelling, or irritation for a whole day. ^[45, 46]

Sr. No.	Batch	Redness	Itching
1	F1	Absent	Absent
2	F2	Absent	Absent
3	F3	Absent	Absent
4	F4 (Optimized Batch)	Absent	Absent

uring the observation period, none of the formulation batches displayed any obvious symptoms of swelling, redness, itching, or irritation. The findings show that every created emulgel formulation was safe to apply topically

and did not cause irritation. Additionally, the optimized batch F4 showed outstanding skin compatibility, indicating that it is suitable for therapeutic use on the skin.

**F1 BATCH****F2 BATCH****F3 BATCH****F4 BATCH****Antifungal Activity:**

The agar well diffusion method was used to assess the generated emulgel formulations' antifungal efficacy against *Candida albicans*. Samples from each formulation batch were added to wells made in agar plates that had already been inoculated with

fungi culture. The zone of inhibition was determined to assess the antifungal efficacy after the plates were incubated at 37°C for 24 to 48 hours. ^[47, 48, 49]

Sr. No.	Batch	Zone of Inhibition (mm)
1	F1	11
2	F2	12
3	F3	13
4	F4 (Optimized Batch)	15

All formulation batches demonstrated appreciable antifungal activity against *Candida albicans*, indicating the effectiveness of the incorporated herbal oils. The optimized batch F4 exhibited the largest zone of inhibition, suggesting enhanced antifungal potential compared to the other trial batches. The improved activity may be attributed to better formulation uniformity, optimized composition, and synergistic action of the herbal constituents present in the emulgel.

STABILITY STUDY:

According to standard recommendations, stability studies were conducted to assess the polyherbal antifungal emulgel's chemical and physical stability under various storage circumstances. [50, 51, 52, 53]

Storage Conditions

- Room temperature: $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$
- Accelerated condition: $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$, 75% RH

Parameter	Initial	After 15 Days	After 30 Days	Observation
Appearance	Smooth and homogeneous	No significant change	No significant change	Stable
Color	Off-white to yellowish	No significant change	No significant change	Stable
Odor	Characteristic	No significant change	No significant change	Stable
pH	5.9	5.8	5.8	Within acceptable limit
Viscosity (cps)	67500	67000	66800	Slight decrease
Spreadability	16.5	16.3	16.1	Acceptable

Under both storage circumstances, the optimized emulgel formulation (F4) maintained its physical and chemical stability for the course of the trial. The look, color, odor, and homogeneity did not significantly change. Skin compatibility was indicated by the pH being within the permissible range for topical treatment. Over time, there was a minor decline in viscosity and spreadability, but these values stayed within acceptable bounds and had no effect on the formulation's overall quality. These results show that the synthesized polyherbal antifungal emulgel has adequate shelf-life qualities and high stability, making it acceptable for topical use.

RESULT

Plumbago zeylanica, *Allium sativum*, and *Zingiber officinale* oils were used in the formulation of the polyherbal antifungal emulgel, which was assessed for a number of factors.

CONCLUSION

Plumbago zeylanica, *Allium sativum*, and *Zingiber officinale* oils were used in the successful formulation and evaluation of a polyherbal antifungal emulgel in this work. The formulation demonstrated favorable physicochemical characteristics, such as homogeneity, spreadability, viscosity, and pH. Because of the synergistic impact of herbal oils, the optimized batch (F3) showed the maximum efficacy in the antifungal experiments, which showed substantial activity against *Candida albicans*. Good shelf-life was indicated by stability studies, which verified that the formulation remained stable with no notable alterations. All things considered, the created emulgel can be regarded as a secure, efficient, and promising substitute for topical antifungal therapy, particularly in overcoming drug resistance.



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