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Review Article

Unraveling The Power of Galanga in Topical Drug Delivery

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ABSTRACT

The therapeutic properties and potential of Alpinia galanga and Kaempferia galanga in the context of topical drug delivery systems are examined in this review. These plants have long been used in traditional medicine for their anti-inflammatory, antimicrobial, and antioxidant effects and contain a diverse range of phytochemicals, including 1,8-cineole, ethyl-p-methoxycinnamate, and kaempferol. The review discusses the ethnomedicinal applications, phytochemistry, pharmacological activities, and toxicological profiles of both species, focusing particularly on their ability to enhance skin penetration for transdermal formulations. Furthermore, the review explores various topical formulations such as nanoemulsions, hydrogels, and microemulsions that incorporate A. galanga and K. galanga extracts to improve skin permeability, stability, and bioavailability. The review emphasizes the potential of these plants in improving the effectiveness of plant-based topical therapies and underscores their relevance in cosmeceuticals, anti-inflammatory treatments, and antimicrobial formulations. Conclusion: The potential of Alpinia galanga and Kaempferia galanga in various topical formulations, such as nanoemulsions, hydrogels, and liposomes, is highlighted in this review. These formulations have demonstrated improved skin permeation, stability, and bioavailability, effectively delivering therapeutic compounds. The adaptability of these plants in enhancing topical drug delivery presents promising opportunities for cosmeceuticals and dermatological therapies. Further refinement and enhancement of these formulations could result in more potent plant-based treatments.

INTRODUCTION

Galanga, a tropical herb of the ginger family, is a rhizome that has been prized for its aroma and used in cooking as well as traditional medicine. Two species of galangal are of particular interest: *Alpinia galanga* (A. galanga) and *Kaempferia galanga* (K. galanga)[1,2]. A. galanga is commonly cultivated in the mid and low-country in Sri Lanka, and distributed in the Himalayas and Southern region of the Western Ghats in India. It grows in open sunny places, forests, and brushwood.1] K. galanga is native to India and distributed in China, Myanmar, Indonesia, Malaysia, and Thailand.[4] Both species have a wide range of traditional and modern medicinal

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applications.[1,2,3.] A. galanga holds significance as a medicinal plant in various traditional medicine practices and is employed for addressing microbial infections, inflammations, rheumatic pains, chest discomfort, and dyspepsia, among other health issues[1]. *Kaempferia galanga* is traditional Chinese herbal medicine , that has been used to treat various ailments such as colds, dry coughs, toothaches, rheumatism, hypertension, etc.[4] The key phyto-compounds found in A. galanga include volatile oil, phenolic compounds, phytosterols, alkaloids etc. The primary active components of A. galanga include 1,8-cineol, fenchyl acetate, bisabolene , pinene, and -1'-acetoxychavicol acetate.[3] K. galanga's rhizomes contain alkaloids, starch, gum, fatty substances, and essential soil, with its primary constituents being ethyl-p-methoxy-cinnamate, ethyl cinnamate, borneol, camphene, linoleoyl, methyl-cinnamate, and pentadecane.[2] This review article focuses on the therapeutic uses of A. galanga and K. galanga in topical drug delivery. It explores the plants' ethnomedicinal uses, phytochemistry, pharmacology, and toxicology to assess their potential as novel skin penetration enhancers for transdermal drug delivery systems.

PHYTOCHEMISTRY OF GALANGA

Both A. galanga and K. galanga possess a diverse range of phytochemicals, including essential oils, tannins, phenols, and glycosides. The rhizomes of A. galanga are particularly notable for their volatile oils, such as 1,8-cineole, β-caryophyllene, and β-selinene, which contribute to its distinctive aroma and therapeutic properties. Key active ingredients in A. galanga include phenolic compounds, p-sitosterol, and galangin, along with alpinin.[5] K. galanga also contains essential oils, terpenoids, phenolic acids, and flavonoids. The essential oil derived from K. galanga is rich in ethyl cinnamate and 2-propenoic acid, 3-(4-methoxyphenyl), ethyl ester, which are considered major compounds.[6] These phytochemicals and active ingredients contribute to the potential therapeutic and medicinal properties associated with these plants.

2.1. Phytochemical constituents

2.1.1. Volatile Oils (Essential Oils):

A. galanga and K. galanga, both known for their distinct aromas and traditional medicinal uses, possess unique volatile oil compositions. A. galanga's volatile oils are characterized by mono and sesquiterpene compounds, along with (E) - methyl cinnamate, which contribute to its characteristic odor and make it a popular choice in folk medicine and culinary applications.[7] On the other hand, K. galanga's volatile oils consist of 39 compounds, with ethyl p-methoxycinnamate, trans-ethyl cinnamate, and trans-cinnamaldehyde as the predominant components, making up a significant portion of its composition.[8] These differences in volatile oil profiles highlight the diverse chemical makeup of these plants, which likely contribute to their varied uses and effects.

a) **1,8-Cineole (Eucalyptol)[9,10]:**1,8-cineole is a monoterpene that is abundant in the essential oils of eucalyptus and rosemary. It is also found in the essential oils of *Kaempferia galanga* (K. galanga) and *Alpinia galanga* (A.galanga). It was reported that in the essential oil of K. galanga, 1,8-cineole is one of the 14 oxygen-containing monoterpenes that make up a fairly large fraction of the terpenoid composition. It is the predominant component, making up 5.7% of the oil. In the essential oil of A. galanga, 1,8-cineole is also one of the oxygen-containing monoterpenes. However, it is not the predominant component, as 6-3-carene was not detected in the oil of A. galanga. As a monoterpene, 1,8-cineole has extensively pharmacological properties, including anti-inflammatory and antioxidant effects. It is used for the treatment of respiratory diseases and cardiovascular illnesses, among other conditions.

b) **α-Pinene and β-Pinene[11,12]:** Both A.galanga and K.galanga contains α-Pinene and β-Pinene.It was reported that The essential oil of A. galanga leaves contains α-pinene at a concentration of 5.0%. The stem essential oil contains α-pinene at a concentration of 3.3%. Furthermore ,The essential oil of A. galanga leaves contains β-pinene at a concentration of 3.3%. The stem essential oil contains β-pinene at a concentration of 3.3%.In K.galanga , The essential oil was extracted and analysed using gas chromatography-mass spectrometry (GC-MS). A total of 15 chemical components were identified, including α-pinene (0.43%) and β-pinene (1.18%). However, the essential oil of K. galanga was reported to have no antibacterial activity against any of the bacteria tested. This is likely due to the small proportions of α-pinene and β-pinene present, which are known to have antibacterial properties.

c) p-Cymene[13,14]: p-Cymene was found to be a component of the essential oil found in the leaves of *Alpinia galanga*. P-Cymene is used for its antioxidant and antimicrobial activity. Conversely, The essential oil of Kaempferia galanga contains several important chemical compounds, including p-cymene. The GC/MS analysis of the essential oil extracted from the Bharamputra-1 variety of Kaempferia galanga revealed that p-cymene was present at 0.41%.

d) Camphene[15,16]: Camphene is one of the compounds identified in the rhizome essential oil of *Alpinia galanga* and *Kaempferia galanga*. It is a monoterpene compound smells like wood and acts against inflammation as well as microbes. The oil has high demand in the global market as it is used for flavoring food and in spa and perfumery. It constitutes 2.47% of the oil's composition in k.galanga.

e) Borneol and Bornyl Acetate[17,18]: Borneol and bornyl acetate, major compounds found in the essential oils of the Alpinia genus, are recognized for their wide range of medicinal properties, including antimicrobial, cytotoxic, antioxidant, anti-inflammatory, anti-asthmatic, insecticidal, and larvicidal activities, as well as their application in slimming aromatherapy. The essential oils, particularly from the leaf and rhizome of *Kaempferia galanga* (K. galanga), are noted for their high concentration of these compounds, making them potentially useful in medicines for their antinociceptive, anti-inflammatory, carminative, anticancer, antihypertensive, larvicidal, and repellent activities. Additionally, K. galanga oil, with its antimicrobial properties, has long been used in folk medicine to treat skin disorders, rheumatism, asthma, diabetes, and catarrhal conditions.

f) Ethyl-para-methoxycinnamate[19,20]: Ethyl p-methoxycinnamate (EPMC) is a prominent component found in the rhizome of *Kaempferia galanga*. It exhibits significant antimicrobial properties effective against Mycobacterium tuberculosis.Aspergillus niger was utilized to convert EPMC into ethyl p-hydroxycinnamate (EPHC). The NMR spectroscopic technique was employed to identify the EPHC metabolite. Antimicrobial research revealed that EPHC displayed activity against all tested strains, with a favorable minimum inhibitory concentration (MIC). It effectively inhibited Staphylococcus aureus and Bacillus cereus at MIC 333 µg/ml, and Pseudomonas aeruginosa, Escherichia coli, and Candida albicans at MIC 111 µg/ml.EPHC demonstrated bactericidal and fungicidal effects against all the bacteria and fungus tested, while EPMC did not exhibit the same killing potential.The isolation of the ethyl p-methoxycinnamate compound from the chloroform fraction of K. galanga ethanol

extract was performed using nuclear magnetic resonance technique to assess its skin whitening activity on B16F10 murine melanoma cells. The findings indicated that ethyl p-methoxycinnamate significantly reduced melanin synthesis in B16F10-induced murine melanoma cells stimulated by α-melanocyte excite hormone.

g) **Ethyl-cinnamate[21,22]:**

A. galanga contains ethyl cinnamate. Ethyl cinnamate has shown antifeedant effects against Spodoptera littoralis and Hylobius abietis. Whereas Ethyl-cinnamate present in K.galanga is used as an anticancer, antimicrobial, skin protector and whitening agent.

h) **Caryophyllene[23,24]:**

Trans-β-caryophyllene is one of the chemical constituents identified in *Kaempferia galanga*. It has been found to have anti-inflammatory and analgesic properties, and it contributes to the plant's overall pharmacological activities, including antimicrobial, antioxidant, and wound-healing effects

2.1.2.Phenolic Compounds[25,26]:

Phenolic compounds are found both in A.galanga and K.galanga. Phenolic compound found in A. galanga have been found to have anti-inflammatory, anti-diabetic, and antioxidant activities. They are also useful for treating allergies and inhibiting the growth of Candida albicans.

a) 1'-acetoxychavicol acetate (ACA)[83]:

The study identified 1'-acetoxychavicol acetate (ACA) as a potential antibacterial substance derived from *Alpinia galanga* (galangal), highly effective against Staphylococcus aureus strains that are resistant to multiple drugs. Out of the four main antibacterial substances extracted from galangal, ACA displayed notable efficacy, demonstrating a minimum inhibitory concentration (MIC) of 0.313 mg/mL and a minimum bactericidal concentration (MBC) of 0.625 mg/mL. ACA's mode of action involves disrupting the integrity of bacterial cell membranes, as indicated by changes in structure and leakage of cellular contents. Examination of proteins revealed that ACA inhibits the production of proteins related to the formation of cell walls and membranes while increasing the presence of proteins involved in responding to oxidative stress and generating energy, implying that ACA disrupts the function of bacterial cell membranes, leading to their impairment and eventual death. This underscores the potential of ACA as a natural preservative for food and its significance in industry.

b) Kaempferol[27]:

Kaempferol is a flavonoid found in many natural products. It has been linked to a decrease in the risk of developing some types of cancers, including skin, liver, and colon cancer. It also has antimicrobial, anti-inflammatory, antioxidant, antitumor, cardioprotective, neuroprotective, and antidiabetic activities.

c) **Quercetin[28,29]:**

Quercetin is present in both A.galanga and K.galanga. In terms of antiviral activity, quercetin exhibited the lowest binding energy when bound with the SARS-CoV-2 main protease (Mpro), indicating its potential as a viral inhibitor. This suggests that quercetin may play a crucial role in inhibiting the replication of SARS-CoV-2, making it a promising candidate for further research and analysis.

d) Phenolic Acids[30-35]:

In *Alpinia galanga*, gallic acid and ellagic acid have been discovered as phenolic acids. A study revealed that A. galanga contains 320 mg/kg of gallic acid and 518 mg/kg of ellagic acid. The characterization of these compounds was achieved using LC-MS/MS. Gallic acid is a phenolic compound that has been found to have various biological activities, including antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. It is also known to have a protective effect on the liver . Methyl gallate, also known as methyl 3,4,5-trihydroxybenzoate, is a natural compound belonging to the class of phenolic acids. It is a methyl ester derivative of gallic acid and is found in various plant sources, including A. galanga. Methyl gallate has been associated with anti-inflammatory activities .Furthermore, A. galanga exhibited potent antioxidant properties, which are linked to its elevated phenolic compound levels. Similarly, K.galanga contains a diverse range of phenolic compounds, including phenolic acids and glycosides, each with significant health benefits. Ferulic acid is known for its anti-aging and skin-protective properties, while trans-p-hydroxycinnamic acid (p-coumaric acid) offers neuroprotective and antioxidant effects, making it beneficial for cognitive health and skincare. Trans-p-methoxycinnamic acid has shown potential anticancer properties, inhibiting cancer cell growth. Other phenolic acids, such as p-hydroxybenzoic acid and methyl 3,4-dihydroxybenzoate, exhibit antioxidant, anti-inflammatory, antimicrobial, and neuroprotective effects, with the latter promoting neuronal growth. Additionally, vanillic acid offers protection against oxidative damage, further supporting its health benefits.

e) **Alpinetin[36,37]:**

Alpinetin is present in both A.galanga and K.galanga. The presence of alpinetin in A.galanga, along with other flavonoids, contributes to the biological effects such as vasodilatory and anti-inflammatory properties.

f) **Galangin[38]**

It is a flavonol, a type of flavonoid, and it is the main bioactive compound found in A. galanga. It exhibits various pharmacological properties, including anti-mutagenic, anti-inflammatory, and antioxidant activities. Galangin is also present in two other species of Alpinia, namely A. officinarum and A. calcarata, but in lower quantities compared to A. galanga

g) Alpinia Ketone[39]:

Alpinia ketone is a compound found in the rhizomes of A. galanga. It has been found to have various biological activities, including antimicrobial, antioxidant, and anti-inflammatory properties. It is also known to have insecticidal and larvicidal activities.

2.1.3. Phytosterols[40-43]:

The hypolipidemic activity of Alpinia galanga (A. galanga) is attributed to the presence of phytosterols such as β-sitosterol, cholestane, and stigmastan-3,5-diene, in addition to other compounds like dietary fibers, polyphenolics, and curcumin. β-sitosterol, which has various applications in medication, culinary uses, and cosmetics, plays a role in lowering cholesterol levels and preventing chronic inflammation associated with obesity. Stigmasterol, another important phytosterol, demonstrates anti-inflammatory properties, further enhancing the health benefits of A. galanga.

2.1.4. Tannins[44,45]:

Tannins, which are natural polyphenols known for their astringent properties, can be found in various plants, such as *Alpinia galanga* (A. galanga). It is believed that these compounds play a role in the plant's potential therapeutic effects, particularly in the inhibition of breast cancer cell proliferation and the induction of apoptosis in cancer cell lines. An analysis of the phytochemicals in *Kaempferia

galanga* L. also showed the presence of tannins. These substances are widely acknowledged for their health benefits, which include antioxidant, anti-inflammatory, and antimicrobial properties, thereby enhancing the medicinal value of different plant species.

2.1.5. Diarylheptanoids[46]:

They are one of the main compounds found in the Alpinia genus, which includes Alpinia galanga (A. galanga). It exhibits anti-inflammatory, cytotoxic, thermostabilizing, lipid-regulating, antioxidant, antiviral, and antimicrobial properties. However, diarylheptanoids have some limitations, including low oral absorption, biodistribution, and systemic bioavailability, which have hindered their success as a drug.

2.1.6 Terpenoids[47-49]:

Terpenoids, found in K.galanga is a natural plant compounds used in folk medicine, are valued for their efficacy, low side effects, and affordability. Isopimarane-type diterpenoids, known for their cytotoxic properties, can target cancer cells like HeLa cells and induce relaxation in vascular smooth muscles, aiding in hypertension management. Camphene, a bicyclic monoterpene, has been traditionally used to treat respiratory and skin conditions, as well as inflammation. Sabinene displays antimicrobial, antioxidant, and anti-inflammatory properties, making it useful in treating infections and inflammation-related ailments. β-pinene exhibits a broad spectrum of pharmacological effects, such as modulating antibiotic resistance, acting as an anticoagulant, demonstrating antitumor and antimicrobial properties, as well as showing anti-malarial, antioxidant, anti-inflammatory, and analgesic effects.

2.2.Pharmacological Activities Of Galanga:

2.2.1.Antiinflammatory Activity[50-52]:

A research study involving the extract from the rhizome of Alpinia galanga revealed its potential to reduce inflammation in mice with acetic acid-induced colitis, demonstrating that 50% to 75% of the extract had anti-inflammatory effects. Similarly, Kaempferia galanga (K. galanga) has been traditionally utilized for addressing inflammatory conditions. Its anti-inflammatory properties are linked to its ability to hinder the cyclooxygenase-2 (COX-2) enzyme, which is crucial in prostaglandin production. The ethanolic extract of K. galanga (EKG) decreased prostaglandin PGG2 production at lower concentrations. Bioactive components such as kaempferol (KAE) and ethyl-p-methoxycinnamate (EPMC) further boost its anti-inflammatory characteristics by inhibiting COX-2. Notably, K. galanga was found to be equally effective as meloxicam, a nonsteroidal anti-inflammatory drug (NSAID), in relieving pain, stiffness, and physical limitations in individuals with knee osteoarthritis.

2.2.2.Antimicrobial Activity[53-56]:

The antimicrobial effects of Alpinia galanga ethanol and water extracts have been observed against various bacterial strains, including Enterococcus faecalis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans. These extracts function by modifying bacterial cell surface hydrophobicity, membrane fluidity, and permeability. Similarly, Kaempferia galanga (K. galanga) has exhibited antibacterial activity against both Gram-positive and Gram-negative bacteria. Ethanol extracts from K. galanga rhizome, within the concentration range of 40% to 70%, effectively hindered microbial growth. The largest inhibition zone, measuring 5.88 mm, was observed against Microsporum canis, although it was smaller compared to the 10.35 mm zone produced by the standard antifungal ketoconazole.

2.2.3.Antioxidant Activity[57-59]:

Alpinia galanga(A. galanga) extracts, particularly methanol and ethyl acetate extracts, exhibit strong antioxidant activity by scavenging free radicals and inhibiting lipid peroxidation. The antioxidant potential of Kaempferia galanga(K. galanga) is mainly attributed to its flavonoid and polyphenolic compounds, such as caffeic acid and ferulic acid, which reduce oxidative stress and act as radical scavengers. In vitro studies of K. galanga essential oil (KGEO) demonstrated significant antioxidant activity with free radical scavenging effects, including DPPH, ABTS, and hydroxyl radicals. In vivo studies using a zebrafish model further confirmed KGEO's ability to alleviate oxidative stress, reduce ROS production, prevent cell death, and inhibit lipid peroxidation. It also enhanced the activities of key antioxidant enzymes like SOD, CAT, and GSH-Px, while reducing MDA levels, a marker of oxidative damage.

2.2.4. Cardioprotective Activity[60,61]:

The compounds present in Alpinia galanga, such as galangin and 1'-acetoxychavicol acetate, have demonstrated protective effects on the heart by decreasing damage to the myocardium and displaying properties that combat atherosclerosis. K. galanga is mainly employed in the treatment of long-term conditions, particularly those related to the cardiovascular and cerebrovascular systems. Furthermore, it has been recognized for its ability to widen blood vessels and lower blood pressure.

2.2.5.Anticancer Activity[62-64]:

Alpinia galanga demonstrates its ability to combat cancer by triggering cellular senescence and elevating levels of reactive oxygen species (ROS), which can impede the progression of the cell cycle. Studies on Kaempferia galanga (K. galanga) have emphasized its potential anti-cancer properties, especially in relation to human lung adenocarcinoma cell lines. Ethyl-p-methoxycinnamate (EPMC), a compound derived from K. galanga, has been found to induce dose-dependent cytotoxic and apoptotic effects in the A549 cancer cell line (which contains wild-type p53). Furthermore, EPMC has demonstrated its antioxidant properties against B16 melanoma cancer cells, with its cytotoxic effects being evaluated through the Presto Blue assay method.

2.2.6.Antidiabetic Activity[65,66]:

The potential antidiabetic activity of Alpinia galanga is demonstrated through its hypoglycemic effects, which involve increasing insulin secretion, enhancing glucose uptake, and reducing insulin resistance. These beneficial properties are mainly due to bioactive compounds such as flavonoids, phenolic acids, and terpenoids. The hydroethanolic extract of K. galanga rhizome has notably displayed significant hypoglycemic potential by effectively lowering blood glucose levels and promoting weight gain in diabetic rats treated with it, thus helping to normalize blood glucose levels, which is crucial for managing diabetes effectively.

2.2.7.Antiulcer Activity[67]:

The seeds of A. galanga are believed to have anti-ulcer properties due to the presence of 1'-acetoxychavicol acetate and 1'-acetoxyeugenol acetate. A study demonstrated that the methanolic extract of A. galanga seeds effectively inhibited Shay ulcers in rats. The anti-ulcer activity was found in the fraction containing ether-soluble neutral substances, and further separation led to the isolation of the anti-ulcer substances 1 and 2. These components displayed significant inhibitory effects when administered intraperitoneally to Shay rats at doses ranging from 2 to 10 mg per kg.

2.2.8.Antiplasmid activity[68]:

The principal bioactive compound of Alpinia galanga, 1(2)-acetoxychavicol acetate, has been identified as a promising antiplasmid agent against multi-drug resistant bacteria. The rhizomes of Alpinia galanga yielded a crude acetone extract

that demonstrated antiplasmid activity against Salmonella typhi, Escherichia coli, and vancomycin-resistant Enterococcus faecalis, showing effectiveness rates of 92%, 82%, and 8% at a concentration of 400 µg/ml SIC.

2.2.9. Anti-SARS-CoV-2 Activity[69]:

During the COVID-19 pandemic, the potential of herbal treatments increased significantly. A component found in Alpinia galanga was found to have to have antiviral effects against SARS-CoV-2.

3.Topical Formulations Of Galanga

3.1.Topical Formulations Of A.Galanga:

3.1.3. Alpinia galanga oil (AGO) As self-nanoemulsifying drug delivery system (SNEDDS) [70]:

Alpinia galanga oil [AGO], known for its anesthetic activity, faces limitations in clinical applications due to its water insolubility. A lipid-based drug delivery system, known as a self-nanoemulsifying drug delivery system (SNEDDS), has been discovered to improve the solubility and bioavailability of poorly water-soluble drugs. SNEDDS is a water-free preconcentrate system consisting of oil, surfactant, co-surfactant, and/or co-solvent, forming a nanoemulsion in aqueous media upon dilution with droplets ranging from 20–200 nm. This study aimed to develop SNEDDS for AGO and investigate its anesthetic activity and transportation pathway without using organic solvents. Three optimized formulations, SNEDDS-AGO-1, SNEDDS-AGO-2, and SNEDDS-AGO-3, with different droplet sizes of 62 ± 0.5 nm, 107 ± 2.8 nm, and 207 ± 4.3 nm, respectively, were selected. The droplet size was found to significantly impact fish anesthesia, with SNEDDS-AGO-3 showing the longest anesthetic induction time (270 sec) ($p < 0.03$). The transportation pathway and skin permeation of SNEDDS-AGO-2 were examined using nile red labelled AGO and observed under a fluorescence microscope. AGO was predominantly found in the brain, gills, and skin, indicating that the transportation pathway of AGO in zebrafish involves passing through the gills and skin to reach the brain. Additionally, SNEDDS-AGO formulations exhibited significantly higher skin permeation compared to AGO ethanolic solution. In conclusion, SNEDDS presents a promising delivery system for AGO.

3.1.2. Alpinia galanga oil (AGO) as Micro Emulsion(ME)[71]:

The aim of the study was to develop a microemulsion (ME) containing Alpinia galanga oil (AGO), 1,8-cineole (C), or methyl eugenol (M) as an active pharmaceutical ingredient (API) for enhancing their antimicrobial activities. The ME composed of 30% API, 33.4% Tween 80, 16.6% ethanol, and 20% water appeared as translucent systems with droplet size and polydispersity index of 101.1 ± 1.3 nm and 0.3 ± 0.1, 80.9 ± 1.1 nm and 0.4 ± 0.1, and 96.6 ± 2.0 nm and 0.2 ± 0.1 for ME-AGO, ME-C, and ME-M, respectively. The ME formulations demonstrated minimal bacterial concentrations ranging from 3.91 to 31.25 µg/mL and 50% fungal inhibition concentrations of 1.83 ± 0.27 to 0.46 ± 0.13 µg/mL, showing 2-4 times stronger and faster kinetic killing rates compared to their respective API alone. When stored at 4 °C, 25 °C, and 40 °C for 12 weeks, the ME formulations retained their effectiveness against fungi and Gram-negative bacteria, but their activity against Gram-positive bacteria decreased at the higher temperature of 40 °C. In conclusion, ME serves as a promising delivery system for AGO and its major compounds, enhancing their water miscibility and antimicrobial activities.

3.1.3. Galangal essential oil liposomes (GEO liposomes)[72]:

Galangal essential oil (GEO) liposomes were prepared by the ethanol injection method and characterised by size, polydispersity index (PDI) and zeta potential. The galangal rhizome contains galangal essential oil as one of its secondary metabolites, and this oil is a volatile and aromatic liquid. It has antimicrobial activity and an antioxidant effect, but its maintenance phase of antimicrobial activity is short due to its instability and effumability. Spherical colloidal particles called liposomes have an internal aqueous cavity surrounded by a self-assembled lipid membrane. They have many excellent properties, such as biocompatibility, targeting and slow-releasing potential. They represent an efficient approach for incorporating natural compounds, such as essential oil components, by improving their solubility and chemical stability.The GEO liposomes were prepared using the ethanol injection method, and the particle size, zeta potential and polydispersity index of the GEO liposomes were characterised respectively. The liposomal particles displayed the shape of spherical or ellipsoidal by AFM and TEM exposure. They were highly stable during their storage at 4°C under dark conditions.Galangal essential oil liposomes (GEO liposomes) have many potential uses.It is of great practical significance to prepare GEO liposomes, as they offer theoretical instruction for regulating antibacterial activities in natural food antiseptics.

3.1.4. **Hydrogel-based topical formulation[73]:**

The report explores the formulation of a hydrogel enriched with *Alpinia galanga* extract, known for its antibacterial and anti-inflammatory properties, aimed at providing a controlled-release topical treatment. Three distinct hydrogel formulations (F1, F2, F3) were developed using varying concentrations of polymers, cross-linking agents, and *A. galanga* extract. F1 used polyvinyl alcohol (PVA), glutaraldehyde, and glycerol, F2 used hydroxyethyl cellulose (HEC), calcium chloride, and propylene glycol, while F3 incorporated sodium alginate, calcium carbonate, and sorbitol, with gelation processes ranging from freeze-drying to UV light exposure. Evaluation parameters such as pH, spreadability, viscosity, and in vitro drug release were assessed, with all formulations demonstrating skin-compatible pH levels (5.2-5.6) and sustained drug release profiles over a 12-hour period. F3 showed the highest spreadability and drug release (99.4%), making it the most efficient formulation for delivering *A. galanga* extract. The study concludes that these hydrogels, particularly F3, are promising candidates for antibacterial therapeutic applications, combining sustained release, skin compatibility, and ease of application, paving the way for future clinical studies.

3.1.5. Emugel[74]

The emulgel formulation prepared with Alpinia galanga extract (AGEA) was characterized in a comprehensive study. The formulation involved creating an oil-in-water emulsion by heating the oil and water phases to 75°C, followed by homogenization and cooling. Carbopol-940 served as the gelling agent, and 4% phenolic-rich hydro-alcoholic Alpinia galanga extract was incorporated. Physicochemical properties, such as pH (6.12) and viscosity, were measured, showing stable behavior over time and at varying storage conditions. The emulgel exhibited strong antioxidant activity**,** with 85% DPPH scavenging capacity and 75% tyrosinase inhibition**,** indicating its potential for depigmentation. Over 90 days of stability testing, no significant changes in globule size or organoleptic characteristics were observed. In vivo tests on 13 volunteers over 12 weeks showed significant improvements in skin hydration (up to 50%), elasticity (10% increase), and reductions in sebum (20-fold decrease), erythema, and pore size. The study concluded that this AGEA-loaded emulgel holds great potential for cosmeceutical applications due to its powerful antioxidant effects and skin benefits.

3.1.6. **W/O (Water-in-Oil) emulsion[75]:**

The water-in-oil (W/O) emulsion of *Alpinia galanga* was formulated to explore its potent antioxidant and anti-aging properties. The rhizome extracts were obtained through both hot water extraction at 85°C and 70% ethanol extraction. These extracts were then incorporated into the W/O emulsions, which demonstrated high antioxidant retention over time. The emulsion provided excellent stability, preserving over 94.8% of its DPPH radical scavenging activity after 60 days, even under varying concentrations. The W/O emulsion showed, sustained release of the bioactive compounds, providing an effective shield for the water-soluble antioxidants. This formulation also enhanced skin moisture by forming a protective layer on the skin surface, which reduced water evaporation. Furthermore, the oil phase facilitated deeper absorption of the active ingredients due to its lipophilic nature, contributing to its anti-aging efficacy. This emulsion was considered ideal for use in cosmetic applications due to its dual function of antioxidant protection and deep skin penetration, offering long-term benefits for skin health.

3.1.7. A.galanga based lotion[76]:

An effective mosquito repellent could be made in a form of topical lotion with the extract of Alpinia galanga. In this formulation, microencapsulation was used to include rhizome essential oil from Alpinia galanga into it to enhance stability and release of active ingredients. Also, the moisturizing components of the lotion consisted emulsifying wax, stearic acid, shea butter; cocoa butter and plant oils that nourish skin. Aedes aegypti mosquitoes were deterred by Alpinia galanga lotion. It gave high protection at 20% concentration with up to 98.91% reduction in mosquito bites for four hours after use. This performance compared favorably with DEET-based repellents and surpassed other plant-based as well as commercial products available in the market today. Volunteers who used it did not experience any adverse skin conditions. The research received approval from Ethics Committee Faculty of Medicine University of Malaya and adhered to ethical and safety guidelines. Further testing would be necessary for commercial use including evaluations under different field conditions and against different mosquito species; Regulatory approval for market release would require additional safety assessments, stability tests, and efficacy evaluations tailored specifically to regional requirements.

3.2.Topical Formulations of K.galanga:

3.2.1. Hydrogel containing a K. galanga rhizome oil microemulsion[77]

The development of a new hydrogel with possible sunscreen and anti-inflammatory properties through incorporation of Kaempferia galanga rhizome oil into a microemulsion formulation. The gel was formed by using sodium carboxymethyl cellulose as the gelling agent, targeting moderate level of sun protection. By optimizing the concentration of oil and gelling agent, a stable and effective formulation was achieved with 85% w/w microemulsion and 1% w/w sodium carboxymethyl cellulose. This hydrogel showed pseudoplastic flow behavior which makes it suitable for topical application. The in vitro SPF (sun protection factor) of this microemulsion was about 19, revealing its ability to offer moderate sun protection. Also, the formulation showed anti-inflammatory activities. In terms of regulation, the pH and stability were found within acceptable ranges for topical products but long-term storage at 4 °C is recommended to keep it cool. This research demonstrates that K. galanga rhizome oil-based hydrogels are potential candidates for topical preparations of suntan lotion or anti-inflammatory drugs.

3.2.2. Topical ethanol extract of K. galanga rhizome (EEKG)[77]

EEKG was made into a semi-solid gel for topical application employing 2%

carboxymethylcellulose sodium salt as the gelling agent. The concentration of EEKG in gels was checked at 0.5%, 1%, 2%, and 4%. EEKG was extracted by cold-maceration using 70% ethanol while the solvent was evaporated through rotary evaporation. Wistar rats were induced oral mucosal ulcers through daily application of EEKG gel for six days in the initiation phase. Rats were divided into seven groups; normal control, negative control, triamcinolone acetonide group and four groups with different concentrations of EKKG. The most effective gel of EEKG for accelerating ulcer recovery rate and reducing inflammation compared to conventional triamcinolone acetonide treatment (a conventional treatment) is found to be the one containing only 0.5% of it after the study ended. Histopathological scores also improved with gels containing between 0.5% and 2% EEKK. In this research, EKGG displayed great inflammatory reduction properties and this made it to be a faster healer especially when you are looking at chemically induced mouth ulcers in rats given that those animals which received this substance healed within the shortest time possible compared to others that got other treatments such as Triamcinolone Acetonide which on its own is a conventional medicine. The study complied with ethical guidelines for animal experimentation while rats' number were calculated according to Federer formula used here.The extraction of EKGG from K.galanga plants which fresh rhizomes are obtained from Subang West Java Indonesia took place and detailed extraction processes was provided.

3.2.3. Mucoadhesive oral care gel containing an ethanol extract of K. galanga (EKG)[78]

The current research was aimed at fabricating a mucoadhesive oral gel containing ethanol extraction of K. galanga (EKG) for the management of oral mucosal ulcers. Three different formulations of gels (F1, F2 and F3) were made with different EKG concentration (5% and 10%) and gelling agents such as Carbopol 934 and Na-CMC. Stabilities test was done on the organoleptic, pH, viscosity, spreadability and homogeneity studies among others. The resultant products were designed to be used topically on the oral mucosal ulcers to reduce inflammation and promote healing. It should be noted that the physical stability of Carbopol 934-based gels (F1 and F2) was excellent in comparison to that of Na-CMC based gel (F3), which became unstable after fourteen days. Also a hedonic test which incorporated evaluation criteria including; overall preference, aroma , texture as well as color revealed that users preferred the 5% EKG gel over others. It was found out through this study that Carbopol 934 is the best mucoadhesive polymer to use when formulating EKG gel. Based on its physical stability and consumer acceptance, it can be concluded that the 5% EKG gel holds potential for further development as a topical treatment for oral mucosal ulcers. On top of this, presence of polyphenols in the gel as well as EPMC suggested its possible clinical application.

3.2.4. Kaempferia galanga rhizome oil-loaded microemulsions [79]

A micro-emulsion of K. galanga rhizome oil was made with 27.27%, 63.64% Tween® 80, and 9.09% water in specific ratios. It is formulated to be used topically; as a sunscreen or to reduce inflammation. Comparing it with pure K. galanga rhizome oil, this microemulsion showed improved anti-inflammatory properties as it needed lower concentration for achieving 50% reduction in NO [nitric oxide] secretion rates. The microemulsion also demonstrated moderate in-vitro sun-protection property. To make sure that this remains safe and effective for consumer use, regulatory issues would involve safety assessments like skin irritation tests and stability investigation studies on the product's shelf life parameters.

3.2.5.Herbal anti-dandruff gel [80]

The gel with antifungal properties against dandruff was made from K. galanga extract in combination with polymers like Sodium CMC, HEC, and Carbopol 934. The formulation of the gel involved two basic stages, which included dispersion of the polymers in an aqueous medium and dissolving the K. galanga extract in ethanol. These solutions were merged while triethanolamine was added dropwise to achieve gel formation for Carbopol 934. Final formulation was adjusted to 25 grams using distilled water. Scalp topical use was indicated by this gel for addressing dandruff that is attributed to Malassezia furfur fungus. Its main purpose is reducing flaking, itching and inflammation. The K. galanga extract showed effective anti-dandruff activities against Malassezia furfur with zone of inhibition measuring 22.33±0.4 mm.The optimized gel had good physical aspects like smoothness, homogeneity and elegance when applied on skin thus contained 5 % k.galanga extract and 4% Sodium CMC. A three month stability study according to ICH guidelines followed by testing gels at different temperatures (25°C and 40°C) and humidity levels (60% and 75%). Changes in appearance, pH, viscosity, spreadability, ethyl cinnamate content and antidandruff efficacy were evaluated in this investigation. These attributes were found to remain stable during the entire period of investigation which implied unchanged antidandruff activity of these gels upon ageing.The optimized gel formulation demonstrated strong potential for further development as a topical anti-dandruff treatment.

3.2.6. Formulation of a sunscreen cream incorporating K. galanga[81]

The sunscreen cream was made using a combination of k. galanga and eucheuma cottonii at a ratio of 1:1 with concentrations of 10%, 20% and 30%. Cream Two-phase system had oil phase with stearic acid, liquid paraffin, emulgide and cetyl alcohol while the water phase had glycerin, triethanolamine and aquades. The additives included methylparaben, butylated hydroxytoluene (BHT), fragrance and seaweed extract. For antioxidant activity, sun protection factor (SPF), viscosity, pH, homogeneity, microbial safety were evaluated on the cream. The cream was meant to protect the skin from harmful UV radiation including UVA, UVB and UVC rays when applied topically. The highest concentration of K.galanga and E.cottonii(30%) in the cream yielded better results as it showed an SPF of 16.7 which is indicative of high UV protection efficacy.The IC50 value for this product's antioxidant activity was found to be 20.32 µg/mL that clearly demonstrates its ability to neutralize free radicals The viscosity range of the cream was between 15,600 cps – 39,000cps to facilitate easy application whereas pH range from 6.52 –7.42 was good for skin application. This shows that the preservative could be responsible for no growth as there have been no visible signs of microbial contamination.The pH level fell within acceptable range for sunscreens ensuring none detrimental effect on skin Overall formulation containing K.galanga and E.Cottonii at 30%(Cream D) proved most effective because it displayed synergistic interplay among these components.

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