

REVIEW ARTICLE

Kaempferia galanga: A Multifaceted Medicinal Plant in Traditional and Modern Contexts

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ABSTRACT

Kaempferia galanga L., commonly referred to as aromatic ginger or sand ginger, is a rhizomatous herb that is a member of the Zingiberaceae family and has been highly regarded in traditional medicine throughout Asia. Historically, it has been utilized to alleviate various ailments, including headaches, colds, asthma, rheumatism, and gastrointestinal issues. Recent phytochemical research has uncovered that *Kaempferia galanga* is rich in bioactive compounds such as ethyl cinnamate, ethyl p-methoxycinnamate, kaempferol, and cineole, which play a significant role in its diverse pharmacological effects. Contemporary pharmacological research has confirmed its properties as an antioxidant, anti-inflammatory, antimicrobial, anticancer, analgesic, and neuroprotective agent, validating many of its ethnomedicinal applications. Moreover, emerging research suggests its potential in cosmeceutical and nutraceutical formulations. This review highlights the ethnobotanical significance, phytochemical diversity, and therapeutic potential of *Kaempferia galanga*, emphasizing the need for further research to elucidate its mechanisms of action, safety profile, and clinical efficacy for modern drug development.

Keywords: *Kaempferia galanga*; Zingiberaceae; Ethnomedicine; Phytochemistry; Antioxidant

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Introduction

The prevalence of chronic diseases associated with lifestyle choices is increasing at an alarming rate as the global population ages. Worldwide, human dietary habits represent the most crucial modifiable element in managing these chronic conditions. Studies show that maintaining traditional healthy eating practices and adopting a therapeutic plant-based diet can lower the risk of these diseases while boosting immunity (1). As a result, traditional medicinal botanical remedies, especially those used as food in traditional practices, are becoming more popular and in demand (2).

There are over 25,791 plant species recognized for their medicinal properties, of which 5,411 are included in the Red List of Threatened Species by the International Union for Conservation of Nature (IUCN) due to overexploitation (3). Many herbal remedies are being developed based on traditional knowledge. In anticipation of future pandemics, like the recent COVID-19 pandemic that started in early 2020, researchers have begun exploring the potential of developing new therapies from medicinal plants and their active compounds (4). It has been observed that adding botanical medicines with anti-inflammatory properties to anti-inflammatory diets can help reduce the worsening of COVID-19 symptoms associated with chronic conditions such as diabetes and obesity (5). Alongside widely known medicinal plant species, other botanical remedies traditionally used by local ethnic communities also hold

significant importance in folk medicine. As global human mobility increases, urban populations are beginning to recognize these lesser-known species. The Zingiberaceae family is one such group, including many medicinal plants valued for their ethnomedicinal importance not only in India but also in various regions worldwide (6).

These plants have been employed in traditional medicine and are essential to cultural heritage. The most prevalent members of this family consist of *Zingiber*, *Curcuma*, *Alpinia*, and *Kaempferia*, among others (Figure 1) (7).

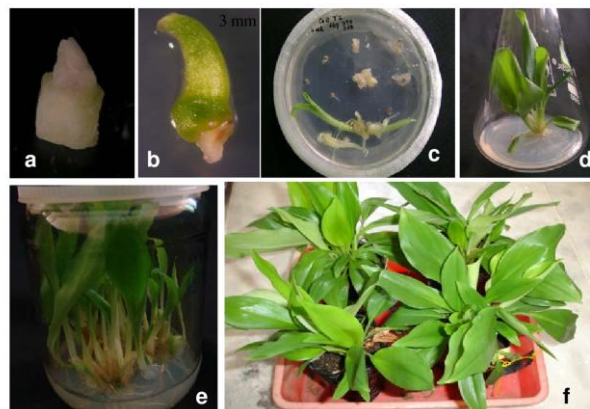


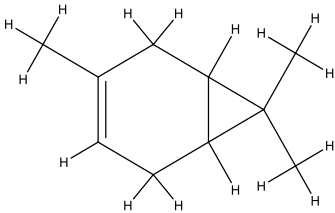
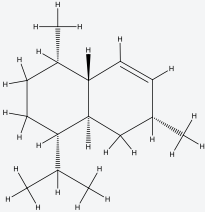
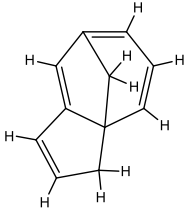
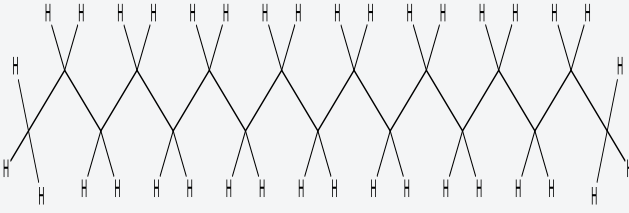
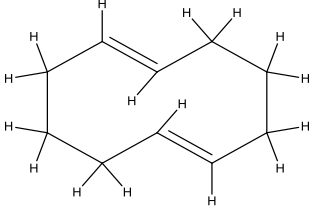
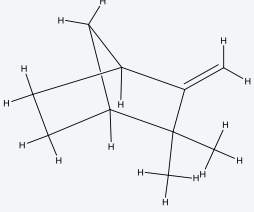
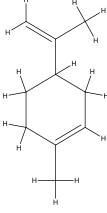
Figure 1. *In vitro* plant micropropagation and shoot regeneration stages from apical explants of *Kaempferia galanga* L. (8).

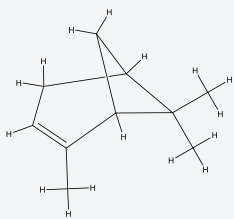
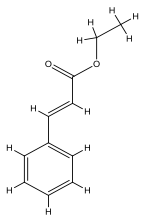
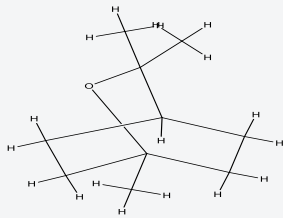
Phytochemistry

Major chemical constituents

Major chemical compounds found in *K. galanga* are phenolics, cyclic dipeptides, flavonoids, terpenoids, diarylheptanoids, essential oils and polysaccharides, which are mentioned below (**Table 1**).

Table 1. Chemical constituents of *K. galanga*.

S. No.	Chemical Constituents	Structure	CID
1	3-carene		26049
2	Cadinene		441005
3	3H-3a,7-methanoazulene		86185943
4	Heptadecane		12398
5	1,6-Cyclodecadiene		5365639
6	Camphene		6616
7	Limonene		22311

S. No.	Chemical Constituents	Structure	CID
8	Alpha pinene		6654
9	Ethyl cinnamate		637758
10	Eucalyptol or 1,8-cineole		2758

Pharmacological activities

Anti-inflammatory and analgesic properties

The major bioactive constituents found in *K. galanga* are flavonoids, terpenoids, and phenols, which exert prominent anti-inflammatory activity by blocking cyclooxygenase (COX) and lipoxygenase (LOX). Concomitant inhibition of the cyclooxygenase (COX) and lipoxygenase (LOX) pathways diminishes the downstream synthesis of inflammatory mediators like prostaglandins (PGs) and leukotrienes (LTs), thereby contributing to anti-inflammatory activity (8). Also, they suppress NF- κ B signaling and decrease the generation of nitric oxide (NO) and reactive oxygen species (ROS), leading to antioxidant and anti-inflammatory effects (9). Ridditida et al. used an experimental model to investigate anti-inflammatory and analgesic activity. The plant exhibits analgesic effects mediated both centrally and peripherally. Suppression of PGs reduces nociceptor sensitization in the peripheral region, but opioid receptor modulation and TRPV1 receptor interaction are connected to the central region (10).

Antimicrobial and antiviral effects

K. galanga exhibits antimicrobial and antiviral activities because of its essential oils and phenolic content, including terpenoids, flavonoids, and ethyl p-methoxycinnamate. It has previously been shown that this plant's rhizome has antibacterial action against a variety of Gram-positive and Gram-negative bacteria because it damages the integrity of the cell wall, which causes *K. galanga* to have antibacterial activity (11). Through membrane disruption and intracellular component leakage, the essential oils, which are abundant in cineole, camphene, and borneol, further

strengthen their antibacterial and antifungal properties. They are effective against *Candida albicans* and dermatophytes. *K. galanga* exhibits encouraging antiviral qualities; *in vitro* research has shown that it inhibits enteroviruses, herpes simplex virus, and influenza virus. Suppression of viral replication, disruption of viral entry into host cells, and alteration of host immune responses are thought to be the mechanisms behind antiviral action (12,13).

Anticancer and cytotoxic activities

Extracts of *K. galanga* have previously been shown to have anticancer properties. Major phytoconstituents include ethyl p-methoxycinnamate (EPMC), flavonoids, diarylheptanoids, and styryl pyrones. It is among the herbs that block the stage of neoplasia that promotes tumor growth. After being evaluated using an indirect immunofluorescent test and Western blot analysis, it has been shown that KG methanolic extracts stop TPA (12-O-tetradecanoylphorbol-13-acetate) from activating the early Epstein-Barr virus antigen in Raji cells, which stops tumor formation. Additionally, methanolic extracts of KG Linn have shown an inhibitory effect on human T cell leukemia (HT-29 cell line) and human cardiac fibroblast (HCF-7) only at dosages greater than 250 μ g/mL (13).

Antioxidant and immunomodulatory effects

K. galanga has strong antioxidant and immunomodulatory effects because of the flavonoids, such as luteolin and apigenin, and its total phenolic content is also primarily responsible for this antioxidant activity. Its capacity to scavenge free radicals, prevent lipid peroxidation, and strengthen inherent antioxidant defenses, such as glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD), provides it with antioxidant

potential. These benefits contribute to reducing cellular damage brought on by oxidative stress, which is linked to ageing, inflammation, and chronic illnesses. By regulating immunological responses, both innate and adaptive, *K. galanga* exhibits immunomodulatory qualities. TNF- α , IL-1 β , and IL-6 are examples of pro-inflammatory cytokines released, and macrophage activity is altered (14,15).

Toxicity studies and their potential adverse effects and contraindications

Toxicological investigations of *K. galanga* have already demonstrated a broad margin of safety. Some of the safety assessments that have already been done by some researchers are mentioned below: According to Kanjanapothi et al. (2004), an oral dose of 50,000 mg/kg of *K. galanga* rhizome ethanol extract was the highest amount that could be tolerated, and no deaths were recorded in rats. In both the male and female test groups, no variations were found in any of the parameters analyzed by hematological analysis. There is no skin irritation in pathology and histopathology. Also, no deaths were reported in 28-day subacute toxicity trials when 25, 50, or 100 mg/kg of the ethanolic *K. galanga* extract was given. Therefore, based on the above toxicological investigations, during the course of treatment, *K. galanga* is safe for the vital organs. They showed a broad margin of safety for essential organs. Potential adverse effects and contraindications were not observed at the tested doses; however, the lack of data in humans and on long-term use means caution is warranted, especially in pregnancy (16).

S. Siska et al. (2023) investigated the acute toxicity of the ethyl acetate fraction of KG (EAFKG) using measures such as liver and kidney histological morphology and blood chemistry values. In this investigation, 40 DDY strain mice weighing between 20 and 35 g were employed, including both male and female mice. For each sex, there were four groups of mice. Groups 1, 2, 3, and 4 received the EAFKG orally at dosages of 0.128, 0.64, 3.2, and 16 g/kg BW, respectively. Observations were made during the entire day. Using a clinical spectrophotometer, serum levels of AST, ALT, and creatinine were assessed. The test results showed that there were no fatalities in either the male or female mouse groups. EAFKG's rhizome is practically non-toxic (LD50 > 15 g/kg BW). There was no recorded mortality. A blood test did not reveal any notable alterations in the kidney or liver. The drug is acutely safe, and practically no acute organ toxicity is seen even at very high doses (17).

Shawkat et al. (2015) investigated the sedative potential of different rhizome and leaf extracts of *K. galanga* in Swiss albino mice. Oral administration of acetone, petroleum ether, chloroform, and methanol extracts at 100 and 200 mg/kg showed no toxicity or mortality. This indicates good tolerability. In locomotion parameter assessment, the acetone leaf extract (200 mg/kg) caused up to 95% suppression, which is higher than that of diazepam (70%). The finding suggests that *K. galanga* is safe enough to be used, but it exhibits potent sedative and CNS depressant

properties due to its traditional use for restlessness, stress and anxiety. No mortality or overt toxicity is observed at doses of 100–200 mg/kg, but a risk of sedation and CNS depression is observed if combined with alcohol, benzodiazepines or barbiturates (18). Despite *K. galanga*'s long history of use as TCHM, its comprehensive toxicity and safety assessments are still unknown, according to Amuamuta et al (2017). The acute and subacute toxicity tests of the ethanol extract from its rhizomes indicate that it exhibits no noticeable toxicity concerning morbidity or mortality, with a maximum single oral dose of up to 5,000 mg/kg (body weight) and a daily dose of 1,000 mg/kg (body weight) administered for a consecutive period of 30 days. No such contraindication is observed in animals, but extrapolation to humans still requires caution, even though systemic safety is observed even with prolonged administration (19).

In an *in vitro* investigation, Jacob et al. (2023) found that many bioactive compounds found in *K. galanga*'s rhizome support the plant's anti-inflammatory, anticancer, antibacterial, and antioxidant qualities. Therefore, additional *in vivo* research could shed light on whether *K. galanga* rhizome extracts can be employed alongside existing conventional treatments for chronic illnesses. An *in vitro* toxicity evaluation of *K. galanga* rhizome extract showed dose-dependent cytotoxicity against HeLa cancer cells. The extract had an IC50 value of 25.04 μ g/mL and induced apoptosis in 24.63% of cells. Both analyses show that the extract exhibits selective therapeutic value of anticancer activity rather than general toxicity. At higher concentrations, the extracts show cytotoxic effects even on non-cancerous cells, leading to cell death, which requires *in vivo* validation (20).

Umar et al. (2012) investigated the finding that *K. galanga* has anti-inflammatory activity. They isolated *K. galanga* extract using petroleum ether, chloroform, and methanol. Extract of the plant (2 g/kg per animal) was tested for its potency in addressing inflammation through the carrageenan-induced paw oedema model. The chloroform extract demonstrated the highest level of inhibition (42.9%) in comparison to the control ($p < 0.001$). Consequently, it underwent further fractionation through repeated washing with chloroform, hexane, and a hexane-chloroform mixture (1:1). The chloroform fraction (1 g/kg) exhibited the most significant inhibitory effect (51.9%, $p < 0.001$) on carrageenan-induced oedema. This chloroform fraction was subsequently separated using a mixture of chloroform and hexane-chloroform (1:3). The chloroform fraction (1 g/kg) exhibited the most significant inhibitory effect (51.9%, $p < 0.001$) on carrageenan-induced oedema. This chloroform fraction was subsequently separated using a combination of chloroform and hexane-chloroform (1:3). The main component of the active sub-fraction, ethyl-p-methoxycinnamate (EPMC), was identified through GC-MS analysis and subsequently recrystallized. Carrageenan-induced oedema was dose-dependently reduced by EPMC, with an effective dose (ED50) of 100 mg/kg. At higher concentrations, EPMC modulates immune function,

which particularly exacerbates immune suppression to show an anti-inflammatory response, thereby increasing susceptibility to infections. This is why this drug is contraindicated in patients taking immunosuppressants or those with chronic immune-related conditions (21).

Adulteration and identification

Issues of adulteration in the herbal market

Consumers often fail to recognize this adulteration and purchase herbs that closely resemble genuine *Kaempferia* species. Studies carried out in India have revealed that Ayurvedic medicines frequently include adulterants. In the course of an ethnomedical study conducted in Northeast (NE) India, we discovered that species in the family Marantaceae, such as *Calathea bachemiana* and *Maranta leuconeura*, are contaminating *Kaempferia* species. Elephants in Assamese woodlands mostly eat plants in the Zingiberaceae and Marantaceae families. The Marantaceae family of plants has received little taxonomic research in Asia; prior research on the family identified 55 species in the region. Species from the Zingiberaceae and Marantaceae families utilize rhizomes for clonal propagation. The aboveground biomass of the species of both families exhibits a remarkably rapid growth rate in order to multiply quickly. Additionally, during the monsoon, plants in the Zingiberaceae and Marantaceae families begin to reproduce. Herbal healers find it challenging to identify individuals belonging to both families at the species level once the blooming season ends due to the physical similarities of their leaves. The adulteration of *Kaempferia* by leaf-shaped Marantaceae species arises as a result of this identification challenge. To resolve this problem, during the monsoon season, species from both families were collected and identified by a renowned curator at Gauhati University. Two Marantaceae species and four *Kaempferia* species that were obtained from Assam made up the study's materials (21).

Application in food and industry

A variety of medicinal and culinary uses of *K. galanga* for health benefits, food, and nutritional purposes are well documented (22). Aromatic ginger is used as a therapeutic spice in Indian, Chinese, and Southeast Asian cuisines. A huge portion of the population consumes it in health-promoting pickles. Scientific studies on its specific nutritional and safety status, as well as its practical use, have not yet been conducted. Creating novel health products based on "whole foods" or specific plant bioactivity has been a hot area of study. Made from *K. galanga* tubers, "Beras Kencur" is a well-known Java beverage. The essential oil that is derived from the rhizome and leaves is used in Bangladesh to flavor food and drinks and to fragrance vinegar (23). In Indonesia and Malaysia, traditional herbal preparations known as 'Makjun' and 'Jamu' are eaten for health benefits.

Biotechnological advancement

Tissue culture

Tissue culture is an essential method for the rapid and disease-free growth of plants. It is a highly researched technique for sustainable growth and agricultural enhancement. Farmers can effectively use the *in vitro*-produced micro cox rhizomes. Plantlets produced by rhizome-induced *in vitro* propagation are easily transportable and cause little damage. The plant can be multiplied by using the rhizomes of *K. galanga* (24). It takes a year to propagate a mature rhizome. There is documentation of *K. galanga* cell suspension-based culture, *in vitro* plant regeneration, and microrhizome production (25,26). The *K. galanga* rhizome was used to establish an *in vitro* plant regeneration technique using MS media. After two weeks of adaptation in a growth room, 98% of the *K. galanga* plantlets survived. Furthermore, Park et al. asserted that using silver nanostructures instead of sodium hypochlorite to sterilize the surface of rhizome buds produced growth (27). Adenine sulphates (Ads), naphthalene acetic acid, benzyl adenine, indoleacetic acid, and indole butyric acid are among the plant growth stimulants that have been employed in studies to induce numerous shoots in *K. galanga*. After adding BA (IAA (0.5 mg/L, 1 mg/L) to MS, Parida et al. (2010) discovered that there were a lot more shoots. Additionally, they tailored the media to produce a high amount of leaf biomass, which contained 0.5 mg/L IAA and 1 mg/L BA. The micropropagated plants also showed genetic stability, according to the results of the RAPD study (28). In 2011, Mohanty et al. developed a method for *in vitro* leaf biomass propagation and rapid micropropagation by using MS agar media to inoculate explants and multiply *K. galanga in vitro* (micro). In MS medium containing 0.1 mg/L TDZ (thidiazuron) and 2.0 mg/L NAA, Vidya et al. (2022) discovered that the highest concentration of AgNPs (25 mg/L) resulted in the strongest microrhizome induction in MS medium containing 0.1 mg/L TDZ (thidiazuron) and 2.0 mg/L NAA. Another study found that when *K. galanga* pseudostem explants were grown in liquid MS media instead of MS agar, they produced more shoots. Plantlet height was positively impacted by activated charcoal (AC), but the quantity of multifaceted multifaceted plant generated was negatively impacted. However, there was no variation in the number of roots, their length, or the size and quantity of leaves (29). The effective growth of *K. galanga*'s embryogenic callus was achieved with 0.5 mg/L BAP and 2.5 mg/L 2,4-D added to an MS solid medium. Globoid or torpedo-shaped somatic embryos were successfully transplanted into the field after being taken out of callus culture and wrapped in calcium alginate beads, where they demonstrated a 50% success rate (30). Genetic stability of tissue-grown plants is necessary for the commercial use of the technique. It requires the bulk production of true-to-type plants of a specific genotype on a large scale (31). Only a few publications on tissue culture experiments in *K. galanga* have been published to date

(32), and *in vitro* production of leaf biomass for potential commercial use is not discussed by any of them.

Genetic engineering for enhanced bioactive compound production

Up to 70 different R genes that show resistance to significant plant diseases have been found, isolated, and cloned in a variety of plants during the last 15 years (33,34). These genes encode proteins with higher levels of structure and amino acid sequence conservation. Cytoplasmic receptor-like proteins are expressed by about 75% of cloned plant disease resistance (R) genes, which are characterized by an N-terminal nucleotide-binding site (NBS) and a leucine-rich repeat (LRR) domain (35). According to whole-genome sequence research, the genomes of rice and *Arabidopsis* contain roughly 600 NBS-LRR genes (36,37) and 150-175 NBS-LRR genes, respectively (20,21). Based on whether a TIR domain (Drosophila Toll and mammalian Interleukin-1 receptor homology region) is present at the protein's N-terminus, the NBS-LRR gene family is split into two classes: the TIR NBS-LRR class and the non-TIR NBS-LRR class (38). LRR and NBS are two examples of small motifs of their encoding proteins that are highly conserved, despite the fact that the sequence homology of the NBS-LRR genes shows considerable variation. These patterns allow the rapid separation of the NBS-LRR genes or resistance gene analogues (RGA) from different plant species utilizing a polymerase chain reaction-based technique using degenerate oligonucleotide primers constructed from these domains. Many plant species, including wheat (39), barley (40,41), tomato (42), rice (43), sugarcane, soybean (44,45), maize (46), ginger (47), and turmeric (48), have made extensive use of this tactic. Many RGAs are tightly linked to or co-segregate with established disease resistance loci, according to genomic mapping and phylogenetic research. Therefore, these isolated RGAs have proven useful tools for dissecting, tagging, and isolating genes that confer both qualitative and quantitative resistance to diverse illnesses. RGA clones offer crucial resources for researching the structure and the development of the NBS-LRR gene family in numerous plant species, as well as useful markers for genetically mapping the genes responsible for disease resistance. The herbaceous medicinal plant known as greater galangal (*Kaempferia galanga* L.) belongs to the Zingiberaceae family, which has more than 60 species. These are mostly grown in China, India, and Southeast Asia and are widely disseminated throughout Asia's and Africa's tropics and subtropics. The plant is widely used to make spices, perfumes, cosmetics, and ayurvedic medications (49). The plant products have excellent therapeutic qualities and are frequently used to treat headaches, peptic ulcers, fatigue, diarrhea, and migraine (50). Since *K. galanga* only reproduces vegetatively and is completely sterile, conventional crop enhancement techniques are inappropriate. Furthermore, *K. galanga* is a wild species that is on the verge of becoming an endangered one due to its low rhizome regeneration. Given the increased

demand for *K. galanga* and its higher economic and medicinal qualities, a suitable protocol is required to create disease-free stocks. Almost all *Kaempferia* species, even those in the Zingiberaceae family, are similarly susceptible to dangerous diseases like *Fusarium oxysporum*'s soft rot, leaf blotch from *Taphrina maculans*, and rhizome rot from *Pythium* spp. Therefore, disease-resistant galangal cultivars may only be produced by cloning, characterizing, and then transforming resistance genes. Since this species has not yet been found to have R genes or RGA, it offers a desired system for research on both qualitative resistance and quantitative response. The genus *Kaempferia*'s NBS-LRR genes were cloned and sequenced to (i) discover NBS-LRR RGAs; (ii) evaluate the degree of sequence variation in these genes; and (iii) use gene index and phylogenetic analysis to determine the links between the cloned plant NBS-LRR-expressing R genes and the *Kaempferia* RGA.

Conclusion

Reviewers and numerous researchers have claimed that the plant possesses a wide range of pharmacological actions. The active components of *K. galanga* rhizome extract have been shown to suppress gastric, colon, oral and multiple myeloma cancer cells through mechanisms that involve apoptosis, cytotoxicity, and the suppression of tumour cell growth. It may impact the course of the cell cycle of HepG2 cells and trigger death. Regarding anti-obesity initiatives, in a study, Tsumura Suzuki Obese Diabetes (TSOD) mice were given 1 to 3 per cent extracts of *K. galanga* for eight weeks. All problems, including body weight growth, peripheral neuropathy, glucose intolerance, hyperinsulinemia, visceral fat buildup, insulin resistance, and abnormal lipid metabolism, were inhibited in the treated mice. *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas*, *Aspergillus*, and *Candida albicans* are all susceptible to the antibacterial properties of *K. galanga* rhizome extract. Several pathogenic bacteria and fungi were suppressed in a disc diffusion study utilising a disc impregnated with 10 µL with ethanolic and methanolic extracts of *K. galanga*, with the highest inhibition zone (21.3 ± 0.08) against *Staphylococcus aureus*.

Anti-inflammatory activity: iNOS mRNA expression was significantly reduced by the chemical and plant extract, whereas COX-2 mRNA expression was not. *In vivo* experiments revealed that the most efficient fractions for lowering rat paw oedema were hexane and chloroform. Because it has generated favorable results, including increasing skin moisturization, reducing wrinkles, and improving skin, it can also be used for external applications in the cosmetics and pharmaceutical industries. As a natural acne remedy, the *Kaempferia* plant extract decreased the buildup of fat and triglycerides in sebocytes, hence lowering skin infections. Based on all of the pharmacological activities, it has been determined that the plant has promise for treating a variety of diseases in terms of formulation. Thus, from all the reported information available, the plant has various potential anticancer, anti-inflammatory, antibacterial, antifungal, and antimicrobial

properties, which help in the treatment of diseases. Keeping all this in mind, the reviewers and researchers may explore these properties in the formulation and development of a suitable formulation for their clinical importance in the near future.

Author Contributions

All the authors have equal contributions in drafting the manuscript.

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Conflict of Interest

Declared none.

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Data Availability

Not applicable.

Ethics Approval

Not applicable.

Use of Generative AI

No artificial intelligence tools were used in the preparation of this manuscript.

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