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Ginger (*Zingiber officinale* Roscoe): A mini-review of constituents and biological activities

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Abstract: *Zingiber officinale* Roscoe is commonly recognized worldwide as "ginger," cultivated in areas of Japan, Austria, Latin America, and China throughout Africa, South-eastern Asia. Frankly, Indians used ginger in enormous quantities. More than 100 ginger composites were already registered. Ginger, which is usually defined as healthy and used to treat different diseases, can be attributed to a variety of bioactive compounds, such as gingerols, zingiberene, and shogaols. Vital oil and oleoresin are important products that are responsible for the distinctive taste and pungency of ginger. Ginger has been widely studied for its pharmacological activities and has been reported to exhibit antibacterial activity, antifungal activity, anti-inflammatory, and anti-analgesic activity, anticoagulant activity, gastrointestinal relief, cardiovascular system effects, hypoglycemic and hyperglycemic activity, anti-cancer activity, and immune-boosting action. In the present analysis, we have compiled up-to-date data on chemistry, biological activities along with medicinal uses of ginger.

Keywords: *Zingiber officinale* Roscoe, zingiberene, gingerols, shogaols, biological activities.

1. Introduction

The Zingiberaceae tribe constitutesabout 1,300 varieties in 50 genera; plants of this family are classified by their tuberous or non-tuberous stems that provide different advantageous products for fruit, drugs, spices, perfume, coloring, and aesthetics [1]. Hedychium, Curcuma, Kaempferia, Zingiber, Amomum, Elettaria Alpinia, and Costus are a few of the financially relevant groups of this genus. Both of these are well-known for mainstream medical purposes [2]. Zingiberaceae plant rhizomes are valuable sources of essential oils containing a variety of compound terpenoid mixtures, primarily analeptic, aromatic, and stimulant. Different terpenoid complexes have been acknowledged in the essential oils of ginger plants with various physiological, anti-arthritic, anti-cancer, anti-inflammatory, anti-diabetic, anti-HIV, antioxidant, antimicrobial, and chemopreventive compounds [3]. Zingiberaceae, widely distributed in tropical and subtropical regions of Asia, particularly

Thailand, Indonesia, Malaysia, India, as well as America and Australia [4]. A particular class, *Zingiber officinale* Roscoe is widely known as "ginger" [5], grown in portions of Japan and China throughout Africa, Latin America, South-eastern Asia, and Austria [6].

After black pepper, Ginger is the world's most widely civilised and consumed spice. Morphologically, ginger is classified into gajah or elephant, red and emprit ginger [7]. In terms of form, colour, odour, and chemical constituents, these vary from each other. Specifically, there is a large rhizome, less odour and fiber in the elephant variety, while the red one has a comparatively smaller rhizome, red skin, sharp odor, and more fiber. Conversely, Emprit ginger hasasmall rhizome, beige skin color with asharp odor and more fiber [7].

Moisture Contents	8.56
Crude Fibers	5.83
Total Carbohydrate	63.55
volatile Oil	1.68
Crude Protein	8.12
Ash	6.13
Total Phenol	2.51
Total Flavonoids	1.67

Fig.1.Various constituents (%) of Ginger.

Bioactive compounds such as zingiberene, gingerols (GNs), and shogaols (SGs) can be attributed to the nutraceutical values of ginger [8]. It is known to be non-toxic in all ginger developed countries and used as a measure of the traditional treatment [9]. Previous pharmacological studies showed ginger to have different biological activities such as antibacterial activity [10], antifungal activity [11], anti-inflammatory activity and anti-analgesic [12], anticoagulant effect [13], gastrointestinal relief [14-16], effect on cardiovascular system [17], hypoglycemic and hyperglycemic activity [18-19], anticancer activity [20], and immune-boosting action [21].

2. Biological activities

Various biological activities of ginger have been complied in Fig.2.

Fig.2. Different Biological activities of Ginger.

2.1. Anti-microbial activity

Earlier research has shown that ginger and its components show a strong role in interfering with infectious development. In addition to inhibition against Salmonella typhi, a study supporting this found that ginger has antimicrobial activity, contrary to Bacillus subtilis, Salmonella typhi and E Coli was seen by ethanol extract of ginger [22]. Ginger powder has noticeable inhibitory behavior against Candida albicans (ethanolic extract) [23-25]. In comparison to anaerobic Gram-negative bacteria, the N-hexane and ethanol extracts of ginger demonstrated inhibition. The oral pathogens were also destroyed by ginger components at a minimum bactericidal concentration (MBC) range [26,]. In contrary to Sacharomyces cerevisiae, Aspergillus Niger, Lactobacillus acidophilus, and Mycoderma sp., essential ginger extract demonstrated inhibition, so ginger may be responsible for protection compared to normal parasitic and fungal antagonists [27].

There are many elements of Ginger (GN and SG) that have antibacterial and antifungal effects [28-30]. For instance, the predominant components [6] -GN and [12] -GN indicated periodontal bacteria inhibition [26]. Hiserodt et al. conducted in-vitro experiments and reported [10]-GN; as active inhibitor of M. avium and M. tuberculosis [31]. Phytochemicals are responsible for antimicrobial properties, as reported earlier. Phlobotannins, flavonoids, tannins, saponins, alkaloids, steroids and glycosides are present in *Z. officinale* extracts. The explanation for the antimicrobial activities of the officinale can be clarified [32-33]. Antimicrobial activities of methanolic extracts of ginger as well as turmeric and linseed against various Gram-negative and Gram-positive bacteria have been documented by Gur et al. The findings of their research indicate that the combined form of linseed and ginger root is found to be more efficient [34]. Another study reported that enhanced solubility of active constituents in an organic solvent is responsible for the higher inhibition of the methanol extract of ginger than the aqueous [35-37]. Water is unable to extract nonpolar constituents. These findings are similar to the results of Gomaa & Hashish, which showed that ginger methanol extracts showed greater antimicrobial activity compared to aqueous extracts [38]. Similarly, Malu et al., Gull et al. and Yalemwork et al. reported that the tested bacterial strains in their study showed poor susceptibility to the *Z. officinale* aqueous extract. The findings from this study publicized that the extracts of *Z. officinale* obtained from zone 3 displayed better antibacterial activity than those obtained from the other two zones i.e. zone 1 and 2. These differences in the antibacterial activity among *Z. officinale* obtained from different zones may be due to genetic differences, soil mineral availability, environmental and climatic factors [39-41].

Singh et al. reported complete and moderate inhibition in essential oils (EO) and CCl_4 oleoresin against Fusarium moniliforme and other tested fungi and bacteria [42]. A new study also confirmed the antimicrobial activity of CCl_4 extract by agar well diffusion method [43]. Moreover, for the EO, reasonable activity against Aspergillus flavus, Fusarium moniliforme, and Aspergillus fumigatus was interpreted [44]. The presence of protein in *Zingiber officinale* was reported by Wang and Ng, stronger antifungal activity was established against different fungi [45]. Using the water and steam distillation process, EO was separated and both samples were then placed in the refrigerator prior to further study. In both the samples positive results were obtained against antibacterial activity. Both samples repressed the growth of five bacteria, including Staphylococcus aureus, Bacillus cereus, Escherichia coli, Bacillus subtilis, and Staphylococcus aureus (MRSA) immune to methicillin, while emprit ginger prevented three species from developing i.e. Escherichia coli, Staphylococcus aureus, and MRSA [46]. Composite films of black pepper and ginger EOs integrated with polymers such as polyvinyl alcohol (PVA)/chitosan composites (CS)/gum arabic (GA) have recently been prepared in a sample using a solvent casting process. In addition, antimicrobial activity was carried out and the findings of their analysis supported the inhibition against the growth of B. cereus, S. aureus, E. coli, and S. typhimurium. The results indicated that representative for gram positive bacteria B. cereus and S. aureus more sensitive to the tested composite than the gram negative bacteria [47]. Further, Sayyad et al. and Noori et al. were also reported the similar results [48-49]. In another experiment, by using the nutrient agar system, the antimicrobial activity of ginger wine and ginger extract against four isolates of various pathogens including Escherichia coli, Staphylococcus aureus, Enterococcus, Lacto Bacillus, and Pseudomonas was determined. Streptomycin [50-51] is the product of antimicrobial susceptibility of pathogenic

bacterial isolates against widely used antibiotics. The new research carried out activities of ginger heritage ethanol and methanol oil extracts, according to bacteria accessible from infections of the intestinal region. For ethanol oil extract, among five species isolated from digestive tract, including E. coli, Salmonella spp, Shigella spp, Citrobacter and Enterobacter spp. Only Enterobacter spp showed the resistance to ginger ethanol extract. Moreover, Citrobacter spp was inhibited by the ginger, followed by Shigella spp , Salmonella spp, and E.coli and for methanol oil extract, shows that Escherichia coli, Salmonella species, Enterobacter spp, Shigella spp and Citrobacter spp. were detected from stool samples respectively [52]. Senthamil et al. concluded that ethanol extracts revealed antimicrobial potential in ginger compared to aqueous extracts [53].Another study reported that *25% of ginger flower extract has been sufficient to inhibit the growth of various tested microorganisms such as Streptococcus pneumonia, Haemophilus influenza, and Candida albicans[54*].

2.2. Immunomodulatory Activity

The alcohol extract of *Zingiber officinale*was discovered by Wilasrusmee et al. It was also documented that ginger repressed the replication of lymphocytes and inhibited the production of IL-2 and IL-10 in deadly lymphocytes [55]. In addition, ginger can inhibit the development of both alloantigen- and mitogen-stimulated lymphocytes [56]. Moreover, possibly ginger obstruct production of both alloantigen- and mitogen-stimulated lymphocyte [56]. In 2006, Zhou et al. performed *in-vitro* and *in-vivo* experiments to examine the effect of ginger's volatile oil on the immunological function [57]. In continuation to this, another study observed resistance towards T lymphocyte proliferation as well as the decrease in the numbers of the total T lymphocytes and T lymphocyte helper (Th) cells in concentration dependent manner by executing theophylline inhibition test reported by Shore et al. with minor changes [58]. Moreover, secretion of IL-1 was inhibited by the volatile oil of ginger in a concentration-dependent style [57]. Finally, the growth of both prolonged infection and autoimmune illnesses are totally interrelated with immunological function status; therefore, the exploration of immunomodulatory effects was considered for further study. And the study suggested, the volatile oil of ginger influences both cell-mediated immune response and nonspecifific proliferation of T lymphocyte [57].

In 2009, Carrasco et al. assessed the immunomodulatory function of clove and ginger EO's through humoral and cellular immune responses in mice. Results showed that the cell-mediated reaction was not altered by GEO activity and the humoral immune response was restored [21]. Sheep red blood cells (SRBCs) require the assistance of T- and B-lymphocytes in addition to macrophages for the development of antibodies to the T-dependent antigen [59].Another research recorded that cyclophosphamide induces a reflective suppressive effect on immunity and antibody manufacture facilitated by all cells [60]. The levels of the antibodies were substantially decreased since cyclophosphamide administration. The production of circulating anti-SRBC antibodies has been enhanced in a dosage-independent manner by GEO intervention. In addition, by affecting T-lymphocytes and macrophages, it can tortuously alter humoral reaction [61].Results of another study revealed that GEO is effective in restoring reduced humoral immunity in mice [21]. Studies have shown that imidothiazoles had also improved serum thymic hormone-like factor levels in humans [62].

In 2018, a review by Jafarzadeh provide a comprehensive knowledge regarding the immunomodulatory, anti-inflammatory

and anti-oxidative properties of ginger and its components [63].The results of a study concluded that [6]-Gingerol as an adjunct anti-mycobacterial and immunomodulatory drug for the treatment of drug-susceptible and drug-resistant strains of tuberculosis [64]Yang et al. isolated a neutral ginger polysaccharide fraction (NGP) from ginger. NGP also displayed a remarkable immunological activity on the RAW264.7 cells *in-vitro*. The results of their study concluded that NGP could be a potential immune agent and might provide meaningful information for further chain conformation and immune mechanism research [65].

2.3. Antioxidant activity

Zingiber officinale's antioxidant activity was isolated in 1985 by Lee and Ahn [60]. In 1992, Jltoe et al. performed antioxidant activity of acetone extract of nine tropical gingers by using thiocyanate method and thiobarbituric Acid method [66] and the results of the experiment confirmed that the extracts from three gingers (Z. cassumunar, C. aeruginosa, and A. kepulaga) have strong activity, which can replace α-tocopherol as a naturally occurring antioxidant.Additional work is being performed in order to discover elements that inhibit lipid peroxidation. Truthfully, it has been found that zingerone acts as a superoxide anion scrounger [67]. In addition, zingerone was found to inhibit lipid peroxidation at elevated concentrations [68]. Antioxidant properties in human ginger erythrocyte membranes have also been identified by other researchers. Ginger suppressed the synthesis of conjugates such as diene, triene and tetraene in human erythrocyte membranes, in addition to the inhibition of lipid peroxidation by around 72 percent [69].

Ginger is the main component of a commonly consumed health food (Amitra Bindu) in India. By working as a vulture for free radicals and anti-carcinogenic effects, this mixture prevents lipid peroxidation [70]. Tropical ginger is also reported to contain cassumunins A and B and cassumunarins, newly isolated curcuminoids that display antioxidant properties in rats with H_2O_2-induced oxidative stress [71]. Ginger extracts obtained by supercritical CO_2 extraction revealed its utmost antioxidant effect at a concentration of 0.20 percent when calculated by the process 1, 1-diphenyl-2picyrlhydrazyl (DPPH) and $Na_2S_2O_3$-I_2 titration. In addition, synergistic effects on the ginger extract of tartaric acid, citric acid, and ascorbic acid were also found [72]. The antioxidant activity between the CO2 extract and butylated hydroxy toluene (BHT) was evaluated in another study. And reported that there was a respectable scavenging behavior in ginger extract, which may be attributed to high polyphenolic content [73]. *In-vivo* analysis revealed that rats overwhelm malonaldehyde production, lipid peroxidation, and shield DNA from oxidative damage caused by lipopolysaccharide (LPS) after ingestion of ginger in their diet [74]. Based on an analysis of DPPH radical scavenging involvement, thiobarbituric acid reactive substances (TBARS), total phenols, and power reduction, antioxidant activity was determined [75]. Anti-radical activity and overall phenol content of the clove or ginger extract were not necessarily compromised following irradiation. Storage for a few months had a greater effect on antioxidant activity than irradiation therapy, resulting in increased anti-radical activity, decreased strength, and total phenols in ginger. In 2010, Swarnalatha et al. studied composite *in-vitro* behavior such as [6]-GN, [8]-GN, [10]-GN and [6]-SG for DPPH scavenging [76]. [6]-SG generates α, β-unsaturated ketone moiety, while illustrating extreme antioxidant and anti-inflammatory properties across all GNs, [10]-GN is the most effective meaningful position owing to carbon chain duration [77]. Li et al. reported [6] -Dehydroshogaol, [6]-SG and 1-dehydro-6-gingerdione are effective nitric oxide synthesis inhibitors in triggered

macrophages [78]. Another study reported major antioxidant and antimicrobial activities of *Zingiber officinale's* EO and oleoresin [79]. Total phenolic and flavonoid problems were determined by Ali et al., and the antioxidant function of elicitor-treated ginger rhizome and callus, [6]-GN and [6]-SG and callus was further determined by Ali et al. The outcomes of their analysis showed that [6]-GN and [6]-SG had comparable antioxidant activity [80].

2.4. Antitumorigenic activity

Ginger may have anticarcinogenic potential in contrast to such naturally occurring plants. One research indicates that the production of carcinogenic N-nitrosodimethylamine in sodium borohydride therapy can be prevented [81]. Ginger also has been reported as knowingly raising the activity of aryl hydrocarbon hydroxylase [82]. Katiyar et al. have confirmed that ethanolic ginger extract in a mouse skin tumorigenesis model induces anti-tumor effects. Since cyclooxygenase-induced skin cancer promoters, epidermal ornithine decarboxylase (ODC), and lipoxygenase and inflammation and hyperplasia activities are conventionally used to support skin disorders [83]. In addition to skin tumour formation and variety, Ginger offers protection when applied topically to SENCAR mice [83]. [6]- Paradol and its derivative ([6]-dehydroparadol), a non pungent compounds significantly lessened the frequency and the variety of skin tumors commenced by 7, 12-dimethylbenz [a] anthracene (DMBA) and encouraged by 12-O-tetradecanoylphorbol-13-acetate (TPA) [84]. Both composites also repressed H_2O_2 production, TPA-induced inflammation, myeloperoxidase (MPO) activity and ornithine decarboxylase (ODC) activity in mouse skin and also the formation of oxidized DNA base *in-vitro*. Which may offer the biochemical origin for antitumor promoting activities of these vanilloids in mouse skin carcinogenesis [85-86]. Ginger also acts as antitumor through modulation of hereditary pathways such as modulation of apoptosis, activation tumour suppressor gene, and inhibition of vascular endothelial growth factor (VEGF). Earlier study has shown that terpenoids, an elements of ginger prompt apoptosis in endometrial cancer cells via the activation of p53 [87].

Liu et al. determined the antitumor activity of GEO by using Dalton's Lymphoma Ascites (DLA) cell line induced solid tumor and Ehrlich Ascites Carcinoma (EAC) cell line induced ascites tumor model in mice and cyclophosphamide was used as reference drug. The treatment with GEO reduced the volume of solid tumor development [88-89]. Another observation indicates that 6-GN multi-targeting products have potent anti-tumor activities in meningioma cells by blocking the signalling mechanism of Wnt / β-catenin, but are not toxic to normal human neuron cells. Therefore, meningiomas may be putative targets for pharmacological treatment [90]. Recently, Liao et al. obtained five polysaccharides from ginger by three different extraction technologies such as hot water extraction (HWE), enzyme assisted extraction (EAE) and ultrasonic cell grinder extraction (UCGE) and further calculated their antitumor activities. The results concluded that the polysaccharide with proper molecular weight and the linkage of →6)-β-D-Galp-(1→ might have better antitumor activities [91].

2.5. Anticancer Activity

Some of the factors such as genetic transformations, heavy metal consumption, smoking, and other contamination and deficiency of accurate diet are the reasons of cancer.

2.5.1. Colon/Pancreatic Cancer

In 2005, the Manju and Nalani research showed

that the threat of pancreatic cancer decreased in wildlife because of the antioxidant properties of ginger and GN. They perceived that rat plasma and hemolysate concentrations of thiobarbituric acid reactive substances (TBARS), lipid hydroperoxides and conjugated dienes were decreased by ginger supplementation [92]. As well as the effect of [6]-GN on HPAC expressing wild-type p53, two human pancreatic cancer cell lines, and BxPC-3 expressing mutated p53 was studied. No chemoreception effect of ginger extract was found in male Wistar rats by Dias et al. on colon carcinogenesis [93]. In addition to this, multiple studies have shown that [6]-GN plays a role in the activation of apoptosis in the LnCaP prostate cancer cell line by increasing p53 and Bax expression and also decreasing Bcl-2 expression.Additionally, [6]-GN changes skin-tight proteins linked to junctions and suppresses pancreatic cancer cell invasion and metastasis. These [6]-GN functions were mediated by inhibition of the extra cellular signal-regulated kinases (ERK) pathway by NF-/ Snail inhibition. Thus, [6]-GN suppresses PANC-1 cells invasive activity [94].Another part of ginger, [6]-SG, activates Ca^{2+} signals by triggering the TRPV1 channels in the pancreatic β-cells. [6]-SG enhanced intracellular Ca^{2+} in a concentration-dependent manner[95].

Min et al. studied the effects of [6]-GN and [6]-SG on human COLO 205 colorectal cancer cells and observed that [6]-SG was capable of inhibiting the growth of COLO 205 cells and was a more powerful apoptosis cause than [6]-GN [96]. Additional Sung et al. found that chemokine receptor CXCR4 expression is limited downwards. In other words, it prevents gastric malignant cells invasion [97].Recently, in support of this research, Shamoto et al. have shown that Zerumbone inhibits the angiogenesis of pancreatic cancer cells by inhibiting proangiogenic gene products based on NF-κB and NF [98]. In vitro experiments performed by Brown et al. revealed that both ginger extract and [6]-GN directly, by blocking the transmission of angiogenic indications to the endothelial cells that provide blood to colon cancer cells, and implicitly intervening, suggesting that ginger phytochemicals have distinct potential for strategies for chemoprevention and chemotherapy [99].Ginger supplementation suppresses colon carcinogenesis in the presence of the procarcinogen 1, 2-dimethylhydrazine (DMH) [100].

2.5.2. Gastric Cancer

In some neoplastic cells, ginger extract shows in-vitro and in-vivo chemo sensitising effects. Another research in support of this found that ginger reverses the delay in gastric emptying caused by cisplatin, suggesting that ginger serves as an antiemetic for cancer chemotherapy [101]. It can also be helpful in improving the gastrointestinal side effects of chemotherapy for cancer.[6]-GN increases the TRAIL-induced reduction in the viability of gastric cancer cells by inhibiting the activation of TRAIL-induced NF-βB while [6]-SG alone decreases the capability of destroying microtubules [102]. Siddaraju and Dharmesh reported that phenolic fractions of ginger as inhibitors of both ATPase and H. Pylori growth, and also showed prohibition against ulcer.It drastically reduced the gastric ulcer region when ginger extract was given to Sprague-Dawley rats in acetic acid-induced ulcers. Ginger extract has also attenuated increased xanthine oxidase and myeloperoxidase production, as well as the amount of malondialdehyde (MDA) in the ulcerated mucosa. Thus, by serving as an antioxidant, ginger extract promotes ulcer healing and inhibits gastric mucosal damage [103].Zerumbone disrupted cell proliferation, VEGF expression, and NF- κB activation in gastric cancer cell lines.In a review, the evidences for the chemopreventive and chemotherapeutic potential of ginger extract and its active components using *in-vitro*, animal

models, and patients have been described [104]. Fu et al. concluded shogaols as novel dietary colon cancer preventive agents [105]. Another study reported that the combination of ginger and Gelam honey may be an effective chemopreventive and therapeutic strategy for inducing the death of colon cancer cells [106]. Recently, a review compiled the role of ginger and its active compound in the inhibition of cancer growth through modulating cell signalling pathways [107]. Recently, Song et al. reported achieves a satisfactory effect of ginger-isolated moxibustion on cancer-related fatigue in the patients with gastric cancer [108].

2.5.3. Ovarian Cancer

Among the five isolated compounds (4-, 6-, 8-, and 10-GN, as well as 6-SG), [6]-SG demonstrated the most powerful cytotoxicity toward tumour cells. The growth of transgenic mouse ovarian cancer cell lines was also inhibited [109]. In vitro studies show that[6]-SG is one of the better active components of ginger studied, implying that the application of nutritional means in the cure and disability of ovarian cancer , for example, will be ginger [110].

2.5.4. Breast cancer

Breast cancer in women all over the globe is the most prevalent evil. The research looks at the effects of [6]-GN on oxygenation, permeability, activity, penetration and metallopeptidase matrix (MMP) levels, i.e. MMP-2 or MMP-9 in the human breast cancer cell line MDAMB-231. The findings show that the activity of MMP-2 or MMP-9 in MDA-MB231 cells was limited after treatment with [6]-GN, accompanied by dose-dependent treatment [111].

3. Conclusion

Since ancient times, use of natural products as medicine has played a critical role in health care for several diseases. A continuous topic for further discovery is the spectrum of natural products. An overall overview of ginger constituents and biological processes was given in the present study.

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Conflict of interest

Authors have no conflict of interest.

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