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A study of genus *Zingiber*: the role of condiments in science

Anggra Paramita[a], Indra Wibowo[b], Muhamad Insanu[a,*]

[a]Department of Pharmaceutical Biology, School of Pharmacy, Bandung Institute of Technology, Indonesia
[b]Department of Physiology, Animal Development and Biomedical Sciences, School of Life Sciences and Technology, Bandung Institute of Technology, Indonesia

ABSTRACT

Zingiberaceae family has been widely used as an herbal medicine from generation to generation. The literature review of Zingiber genus, which is part of Zingiberaceae, was conducted to provide information and to determine the correlation between bioactive compounds and pharmacological properties with their empirical uses. Articles about genus *Zingiber* were collected from online databases (e.g., Directory of Open Access Journal, PubMed, ResearchGate, ScienceDirect, and Springer), they were sorted based on inclusions criteria such as related to bioactive compounds and biological activities of the samples and also articles for the last ten years. Merely articles with DOI were reviewed. The screening process resulted in 52 reports being reviewed and grouped based on each plant's bioactive contents and pharmacological properties. The major constituents in genus Zingiber are essential oils. Therefore, the dominant activities found in this genus was related to antimicrobial and antioxidant. Furthermore, the other activities of plants were related to the bioactive compounds and their current uses. The empirical uses of these rhizomes were in line with the bioactive compounds and biological activities.

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*Corresponding authors:
insanu@fa.itb.ac.id

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1. Introduction

Traditional medicines in some areas are dominated by the use of plants as the main ingredients. Medicinal properties derived from plants can come from many different parts, including leaves, roots, stems, seeds, flowers, fruits, and rhizomes. Zingiberaceae, one of the most known aromatic flowering plants belonging to the order Zingiberales, has been widely used for medical purposes. There are 53 known species belonging to the genus *Zingiber* which are distributed in India, China, Japan, southern Korea, Indo-China, Southeast Asia, and other tropical regions (The Barcode of Life Data System, 2021; The Plant List Version 1.1, 2021).

The genus *Zingiber* is also known as profitable condiment and herbal medicine. Rhizomes from this genus have characteristics with starch and essential oils. It has been widely used as a condiment, pain reliever, antiemetic, and anti-rheumatic. However, empirical uses in some countries, cities, or tribes could be different because of the variety of chemicals or bioactive compounds influenced by their demographics.

The review of genus *Zingiber* has been discussed previously in various articles, including the results showed its traditional use, phytochemical content, pharmacological property, and cultivation methods (Sharifi-Rad et al., 2017). However, the information related to further product development was limited as food preservatives. Due to its abundant availability and ease of cultivation, genus *Zingiber* can be a future investigation in various aspects, such as a natural based for preservative, repellent, and anti-dental caries (Govindarajan et al., 2016; Moreira da Silva et al., 2018; Sivasothy et al., 2013). This review aimed to report the current use of plants of the genus *Zingiber* as traditional medicines and identify the correlation between empirical uses and its bioactive compound as well as biological effects for further research and product development. In addition, the study also provides a high potential value of genus *Zingiber* that can unfold the opportunities for commercial development in various industrial sectors. Search-related articles were conducted on various databases such as Directory of Open Access Journal (DOAJ), PubMed, ResearchGate, ScienceDirect, and Springer. The literature search was limited to articles published in 2011-2021. Furthermore, the exclusion criteria were as follows; unrelated to the compound's biosynthetic pathway, only limited to bioactive compounds as well as biological effects for further research and product development. The search process used keywords related to empirical uses, bioactive compounds, and biological activities of species of the genus *Zingiber*. The articles collected were 386 articles, sorted by considering duplication and DOI, then 52 articles were elected for review. Any dissents were resolved by discussion and deliberation to reach a consensus.

2. Overview of empirical uses

Species of the genus *Zingiber* have been used throughout the world as medicinal plants and represent popular herbal remedies in various traditional healing systems (Table 1). For instance, *Zingiber barbatum* (*Z. barbatum*) is therapeutic medicinal ginger found in Myanmar and has an activity to reduce pain from joints and muscles caused by gout (Shukurova et al., 2020). Another example is *Zingiber cassumunar* (*Z. cassumunar*), known as Phlai in Thailand, which is traditionally used to treat diarrhea, fever, menstrual disorders, gout, asthma, and jaundice (Nurkhasanah et al., 2017). Moreover, it is believed that the rhizome of *Zingiber chrysanthum* (*Z. chrysanthum*) has the potential effect of relieving body pain and gastritis. The rhizome of *Z. chrysanthum* is also used by Jammu and

Kashmir people as a flavoring agent. In addition, the leaf, rhizome, and perianth of *Z. chrysanthum* could be used as dyes, condiments, and ornamental plants (Chandra et al., 2017; Devi et al., 2017; Shah et al., 2015).

The flower bud of *Zingiber mioga* (*Z. mioga*) is used medically to alleviate rheumatism in China and is practically used as a health supplement in Eastern Asia (Kim et al., 2015; Lee et al., 2016). Meanwhile, the rhizome part of *Zingiber ottensii* (*Z. ottensii*) is also empirically used to treat wound healing, relieve gastrointestinal disease, and constipation (Thitinarongwate et al., 2021). Furthermore, *Zingiber officinale* (*Z. officinale*), the most known *Zingiber* species, is medically used to treat respiratory infections and stomach disorders in Saudi Arabia and the rhizome, processed as a beverage combined with Arabic ginger called qahwa. In China, the rhizome is traditionally used to relieve poisoning, cold, and antiemetic symptoms. Since the Vedic age, this ginger has also been known as the great medicine called 'maha- aushadhi'. (Al-Dhahli et al., 2020; Liu et al., 2019; Rahman et al., 2020).

Table 1. Empirical uses of genus *Zingiber*

Species	Part	Traditional uses	References
Z. barbatum	Rhizome	Bone pain Gout Joint pain Muscle pain	Shukurova et al. (2020)
Z. cassumunar	Rhizome	Antidiarrheal Asthma Fever Gout Jaundice Stomach disorders	Nurkhasanah et al. (2017)
Z. crhysanthum	Seeds	Flavouring agent Treat human ailment	Palariya et al. (2019)
		Gastritis Relieve body pain	Devi et al. (2017)
	Leaf Rhizome Perianth Seed	Aesthetics Condiment Dyes Ornamental plants Perfumes Spices	Chandra et al. (2017)
Z. mioga	Flower bud	Health supplement Spice	Kim et al. (2015)
		Cough Eye inflammation Relieve insect bites Rheumatism	Lee et al. (2016)
Z. ottensii	Rhizome	Bruising/contusion Constipation Gastrointestinal diseases Myalgia Sprain	Thitinarongwate et al. (2021)
Z. officinale	Rhizome	Stomach disorders Treat respiratory infections	Al-Dhahli et al. (2020)
		Arresting vomiting Cold sputum cough Dissipating cold Relieving cough Resolving phlegm Stomach colds Treat fish and crab poison	Liu et al. (2019)
		Abdominal pain Dyspepsia Flatulence Nausea	Hu et al. (2011)
Z. roseum	Rhizome	Asthma Gastric ulcer Rheumatic disorder Wound disorder	Al-Amin et al. (2019)
Z. zerumbet	Rhizome	Abdominal pain Antidiarrheal	Tian et al. (2020b)
		Analgesics Antipyretic	Chien et al. (2016)

Zingiber roseum (*Z. roseum*) is usually used as folk remedies in district Gazipur and Tangail, Bangladesh, totreat gastric ulcer, wound healing, and rheumatic disorders (Al-Amin et al., 2019). Similarly, the rhizome of *Zingiber zerumbet* (*Z. zerumbet*), another species from the genus *Zingiber*, is used to relieve abdominal pain and antidiarrheal in China and analgesic antipyretic in Taiwan (Chien et al., 2016; Tian et al., 2020).

Based on these empirical uses, the genus *Zingiber* has the potential effect of treating various diseases. Further study needs to perform to know its pharmacological properties and their mechanism of action.

3. Bioactive compounds

The primary metabolites found in the genus *Zingiber* are classified into amino acid, organic acid, and enzyme (Table 2). The rhizome of *Z. officinale* was found to have protein, carbohydrate, ash, fat, and crude fibre, which increase in line with the moisture content of the rhizome (Khan et al., 2016; Shamim et al., 2015).

Zingibain, the enzyme found in *Z. officinale*, is a proteolytic enzyme widely known to increase the tenderness of meat (Khan et al., 2016).

Even though secondary metabolites do not have a direct role in plants growth, these compounds surprisingly have the most pharmacological properties (Table 3). *Z. cassumunar* has been identified as containing alkaloid, flavonoid, saponin, tannin, quinone, and steroids/triterpenoid compounds (Yuniarto et al., 2017). The *Z. cassumunar* rhizome also contains curcumin, demethoxycurcumin, and bisdemethoxycurcumin, analyzed by the thin-layer chromatography (TLC). Chang et al. (2012) reported that *Z. zerumbet* contains alkaloids, saponins, flavonoids, tannins, terpenoids, phenols, and polyphenols. Zerumbone, the most abundant compound in *Z. zerumbet*, is classified as monocyclic sesquiterpene and found in other *Zingiber* species, including *Z. ottensii* and *Z. roseum* (Al-Amin et al., 2019; Chien et al., 2016; Thitinarongwate et al., 2021).

The genus *Zingiber* is also known for its abundant essential oils. There are various studies reported about the essential oils related to this genus, such as sabinene from *Z. capitatum* (Mektrirat et al., 2020; Okonogi and Chaiyana, 2012), zerumbone from *Z. zerumbet*, *Z. ottensii*, and *Z. roseum* (Al-Amin et al., 2019; Chien et al., 2016; Thitinarongwate et al., 2021; Tian et al., 2020), gingerol from *Z. officinale* (Zordan et al., 2020), and myrcene from *Zingiber nimonii* (Nair et al., 2019). Furthermore, Chandra et al. (2017) has explicitly identified the essential oils of *Z. chrysanthum*, including geranyl linalool (Table 3).

4. Biological activities

The biological activity of the genus *Zingiber* is affected by its phytochemical constituents. Based on in vitro studies, there are two main activities in this genus, antimicrobial, and antioxidant activity (Table 4). The in vivo testing of various species from the genus *Zingiber* also reported multiple activities, including antiemetic and anti-obesity (Table 5).

4.1. Antioxidant

Antioxidant testing of *Zingiber* species was carried out by various methods, including 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH), Ferric Reducing Antioxidant Power (FRAP), Oxygen Radical Absorbance Capacity (ORAC), The 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), and Metal Chelating Activity. The antioxidant activity testing in *Z. chrysanthum* had the result as follows; Half-Maximal Inhibitory Concentration (IC_{50}) = 10.81±0.03 µg/ml (DPPH); IC_{50} = 16.84±0.46 µg/ml (Metal chelating); Half-Maximal Reducing Power (RP_{50}) = 15.55±0.02 µg/ml (FRAP) (Palariya et al., 2019). Meanwhile, another study reported the IC_{50} of 187.93±0.75 µg/ml using the DPPH method (Chandra et al., 2017). This difference in results with the same method could be caused by various factors, such as the different parts of the plant used, different genetic diversity of the same species, and the environment. Furthermore, *Z. cassumunar* was also found to have antioxidant activity identified using the DPPH method with an IC_{50} value of 28.47 µg/ml, and RP_{50} of 990.46 ± 2.46 µM/g analyzed by FRAP (Pansanit and Pripdeevech, 2018; Sukati et al., 2019). *Z. mioga* was also tested its antioxidant activity using the ORAC method and had the IC_{50} value of 0.53 ± 0.14 to 3.10 ± 0.10 µM (Jo et al., 2016). *Z. spectabile*, which contains curcumin and demethoxycurcumin, showed the highest antioxidant activity tested with β-carotene bleaching assay with 77.27% (Sivasothy et al., 2013). In addition, *Z. zerumbet* was found to have an IC_{50} value of 2884.67 ± 232.71 µg/ml performed with the ABTS method (Tian et al., 2020b). These contrasting results of antioxidant activity can be influenced by the difference mechanism of each assay as well as the diversity of chemical constituents of the plants

Table 2. Primary metabolites found in genus *Zingiber*

Species	Part	Compounds	Class	References
Z. neesanum	Rhizome	Actinomycin C2	Amino acid	Nair et al. (2019)
		Deoxyspergualin	Organic acid	
Z. officinale	Rhizome	Alanine	Amino acid	Liu et al. (2019)
		Arginine		
		Aspartic acid		
		Cystine		
		Glutamate		
		Glycine		
		Histidine		
		Isoleucine		
		Leucine		
		Lysine		
		Methionine		
		Phenylalanine		
		Proline		
		Serine		
		Threonine		
		Tryptophan		
		Tyrosine		
		Valine		
		Acetic acid	Organic acid	Liu et al. (2019)
		Citric acid		
		Formic acid		
		Lactic acid		
		Malonic acid		
		Oxalic acid		
		Succinic acid		
		Tartaric acid		
		Zingibain	Enzyme	Khan et al. (2016)

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Table 3. Secondary metabolites found in genus *Zingiber*

Species	Part	Compounds	Class	References
Z. cassumunar	Rhizome	(2Z,6*E*)-farnesol Cembrene 3*E*-cembrene A Laurenan-2-one Sclareol β-Cyclocitral β-Isocomene γ-Curcumene	Terpenoid	Pansanit and Pripdeevech (2018)
		cis-Banglene		Norikura et al. (2020)
		Bisdemethoxycurcumin Curcumin Demethoxycurcumin	Phenol	Rafi et al. (2011)
		cis-(*E*)-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-enes (c-banglenes) *trans*-(*E*)-3-(3,4-dimethoxyphenyl)-4-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-enes (t-banglenes)	Terpenoid	Kato et al. (2018)
		(*E*)-1-(3,4-dimethoxyphenyl) butadiene (*DMPBD*)		Leelarungrayub et al. (2017)
		Sabinene Terpinen-4-ol		Mektrirat et al. (2020)
		cis-Piperitol	Phenol	Okonogi and Chaiyana (2012)
		Allo-ocimene Caryophyllene oxide *cis*-Sabinenehydrate Neo-Allo-ocimene *p*-Cymen-8-ol Terpinen-4-ol α-Terpinene α-Terpinolene γ-Terpinene δ-Elemene	Terpenoid	
		Sabinene Terpinen-4-ol γ-terpinene		Leelarungrayub et al. (2017)
Z. chrysanthum	Seed	β-pinene (*E*)-caryophyllene Limonene Terpinen-4-ol α-Pinene α-Terpineol γ-Terpinene	Terpenoid	Palariya et al. (2019)
	Leaf, rhizome, perianth and seed	Geranyl linalool	Terpenoid	Chandra et al. (2017)
Z. nimonii	Rhizome	Myrcene α-Cadinol α-Humulene β-Caryophyllene	Terpenoid	Govindarajan et al. (2016)
Z. officinale	Rhizome	(-)-Globulol Alloaromadendrene Camphene Caryophyllen Eucalyptol Geranial Geranyl acetate Neral *trans*-Caryophyllene α-Curcumene α-Humulene α-Pinene α-Zingiberene β-Bisabolene β-Pinene β-Sesquiphellandrene β-Phellandrene	Terpenoid	Abdullahi et al. (2020)
		Gingerol	Phenol	Zordam et al. (2020)
		α-Curcumene α-Zingiberene β-Bisabolene β-Phellandrene β-Sesquiphellandrene	Terpenoid	Al-Dhahli et al. (2020)
		Borneol Camphene Cineole Citral Curcumene Geraniol		Osabor et al. (2015)

		Geranyl acetate Limonene Linalool Terpineol Zingiberol α-Farnesene β-Bisabolene β-Sesquiphellandrene β-Phellandrene (4*E*,6*E*)-[6]-paradoldiene (4*E*,6*E*)-[8]-paradoldiene (4*E*,6*Z*)-[4]-paradoldiene (4*E*,6*Z*)-[8]-paradoldiene (*E*)-[4]-isoshogaol (*Z*)-6-oxo-[10]-shogaol (*Z*)-6-oxo-[6]-shogaol (*Z*)-6-oxo-[8]-shogaol 6-oxo-[6]-paradol	Phenol	Li et al. (2018)
Z. ottensii	Rhizome	Zerumbone	Terpenoid	Thitinarongwate et al. (2019)
Z. roseum	Seed, rhizome and perianth	2-(4-hydroxy-3-methoxyphenyl)-3,7-dimethoxy-4h-chromen-4-one	Flavonoid	Pemram et al. (2018)
		β-Citronellal	Terpenoid	
Z. spectabile	Rhizome	Curcumin Demethoxycurcumin	Phenol	Sivasothy et al. (2012)
		Acetyl rhamnosides Kaempferol Spectaflavoside A	Flavonoid	
		Kaempferol-3-O-(4″-O-acetyl)-α-l-rhamnopyranoside		Sivasothy et al. (2012)
		Kaempferol-3-O-(4″-O-acetyl)-α-l-rhamnopyranoside-(I-6,II-8)		
	Leaf and rhizome	Caryophyllene oxide Germacrene D *trans*-β-Ocimene α-Pinene β-Caryophyllene β-Elemene β-Pinene δ-3-Carene	Terpenoid	Sivasothy et al. (2012)
Z. striolantum	Rhizome	Cryptone	Phenol	Tian et al. (2018)
		Geranyl linalool Sabinene Terpinen-4-ol α-Pinene β-Phellandrene β-Pinene	Terpenoid	
	Flowers, leaves and stems	Cryptone	Phenol	Tian et al. (2020a)
		Terpine-4-ol Hexahydrofarnesyl acetone Phytol Sandaracopimaradiene α-Humulene β-Elemene β-Phellandrene β-Pinene	Terpenoid	
Z. zerumbet	Rhizome	1,8-Cineole	Terpenoid	Tian et al. (2020b)
		Camphene Camphor Caryophyllene oxide Zerumbone α-Humulene		
		Catechin	Flavonoid	Ghasemzadeh et al. (2016)
		Kaempferol Luteolin Myricetin Quercetin Rutin		
		Zerumbone	Terpenoid	

4.2. Antibacterial and antifungal activities

Z. cassumunar was found to have antibacterial activity with an inhibition value of 31.25 μg/ml assayed with the agar disc diffusion method. It also had a time-kill antibacterial kinetic assay with vigorous antibacterial activity against *Acinetobacter baumannii* with inhibition values ranging from 7.00 x 103 to 9.24 x 103 μ g/ml (Boonyanugomol et al., 2017; Pansanit and Pripdeevech, 2018). In addition, *Z. chrysanthum*, *Z. neesanum*, *Z. officinale*, *Z. roseum*, *Z. spectabile*, and *Z. striolantum*, and *Z. zerumbet* had the Minimum Inhibitory Concentration (MIC) value of 250 μg/ml tested using the agar diffusion and the microdilution method (Al-Amin et al., 2019; Al-Dhahli et al., 2020; Moreira da Silva et al., 2018; Nair et al., 2019; Palariya et al., 2019; Rahman et al., 2020; Sivasothy et al., 2012a; Tian et al., 2018).

Table 4. *In vitro* studies of several genus *Zingiber*

Species	Part	Activity	Methods	Targets/standards	Results	References
Z. cassumunar	Rhizome	Antioxidant	DPPH	Trolox and gallic acid	IC_{50} = 28.47 µg/ml	Pansanit and Pripdeevech (2018)
			FRAP	$FeSO_4$	RP_{50} = 990.46±2.46 µM/g	Sukati et al. (2019)
		Antibacterial	Agar disc diffusion method	*Staphylococcus aureus*	IC_{50} = 31.25 µg/ml	Pansanit and Pripdeevech (2018)
				Escherichia coli	IC_{50} = 7.81 µg/ml	
			Time-kill antibacterial kinetic Assay	*Acinetobacter baumannii*	IC_{50} = 7.00x10^3 to 9.24x10^3 µg/ml	Boonyanugomol et al. (2017)
		Anti-malaria	ICAM-1 gene expression	ICAM-1 gene	Inhibit ICAM-1 gene expression in Plasmodiumberghei	Utami et al. (2017)
		Anti-obesity	Pancreatic lipase activity	Pancreatic lipase	Inhibition = 29.17%	Iswantini et al. (2011)
		Anticoagulant	PT test	0.85% w/v NaCl	18.10±0.52 s/ 1.0 mg/ml	Sukati et al. (2019)
			APTT test		50.17±1.11 s/ 1.0 mg/ml	
		Insecticidal and repellent activities	Fumigation Assay	*Tribolium castaneum* (Herbst)	LC_{50} = 3.7 mg/liter of air	Wang et al. (2018)
				Lasioderma serricorne (L.)	LC_{50} = 1.3 mg/liter of air	
			Repellent Test	*Tribolium castaneum* (Herbst)	LD_{50} = 19.7 mg per adult	
				Lasioderma serricorne (L.)	LD_{50} = 5.4 mg per adult	
		Antiinflammatory	Gelatine zymography	MMP-9 gene	Inhibition to PMA-induced MMP-9 gene	Poachanukoon et al. (2015)
			Molecular docking and molecular dynamics	Compound D	Surface binding = (-26.83 kcal/-mol)	Jitapunkul et al. (2018)
				Compound DMPBD	Surface binding = (-29.15 kcal/-mol)	
Z. chrysanthum	Seed	Antioxidant	DPPH	BHT and Catechin	IC_{50} = 10.81±0.03 µg/ml	Palariya et al. (2019)
			Metal chelating	EDTA	IC_{50} = 16.84±0.46 µg/ml	
			FRAP	Ascorbic acid	RP_{50}= 15.55±0.02 µg/ml	
	Rhizome		DPPH	BHT and Catechin	IC_{50} = 187.93±0.75 µg/ml	Chandra et al. (2017)
	Seed				IC_{50} = 252.63±0.53 µg/ml	
	Leaf				IC_{50} = 217.94±0.11 µg/ml	
	Perianth.				IC_{50} = 355.32±0.02 µg/ml	
	Seed	Antiinflammatory	Protein denaturation assay	Diclofenac sodium	IB_{50} = 16.76±0.00 µL/ml	Palariya et al. (2019)
		Antibacterial	Agar-well diffusion method	*Staphylococcus aureus*	Zone inhibition = 14.33±0.58 mm	Palariya et al. (2019)
			Agar-well diffusion method	*Escherichia coli*	Zone inhibition = 13.33±0.58 mm	
Z. mioga	Flower buds	Anti-obesity	Oil Red O Staining	3T3-L1 preadipocyte cells	Inhibition to adipogenesis in	Lee et al. (2016)
		Anti-hyperglycaemic	Porcine pancreatic α–amylase inhibition assay	Porcine pancreatic α–amylase	IC_{50} >10x10^3 µg/ml	Jo et al. (2016)
		Antioxidant	ORAC Assay	Trolox	0.53 ± 0.14 to 3.10 ± 0.10 µM of TE	Jo et al. (2016)
Z. neesanum	Rhizome	Antibacterial	Agar disc diffusion method	*Enterococcus fecalis*	Inhibition = 21.7 ± 0.6 cm	Nair et al. (2019)
		Antifungal	Agar disc diffusion method	*Mucor rouxii*	Inhibition = 9.7 ± 0.6 cm	Nair et al. (2019)
Z. nimonii	Rhizome	Anti-repellent	Repellency bioassay	*Anopheles stephensi*	Protection = 120, 150, and 180 min	Govindarajan et al., 2016
				Aedes aegypti	Protection = 90, 120, and 150 min	
				Culex quinquefasciatus	Protection = 60, 90, and 120 min	
Z. officinale	Rhizome	Antifungal	Agar disc diffusion method	*Fusarium oxysporum*	Inhibition 50.38 ± 0.5 at 1 ml/ml	Abdullahi et al. (2020)
				Ganodema boninense	Inhibition 27.46 ± 0.5 at 1 ml/ml	
		Antibacterial	Agar-well diffusion method	*Staphylococcus aureus*	Inhibition zone 9–13 mm	Al-Dhahli et al. (2020)
				Escherichia coli	Inhibition zone 7–10 mm	
			Agar disc diffusion method	*Staphylococcus aureus*	Inhibition zone 8.13 and 19 mm	Rahman et al. (2020)

		Anticancer	MTT Assay	Cervix cancer cell-line	IC_{50} = 46.2 ± 0.6 µg/ml	Lee et al. (2016)
				Breast cancer cell-line	IC_{50} = 72.0 ± 6.6 µg/ml	
				Leukemic cell-line	IC_{50} = 80.3 ± 6.6 µg/ml	
		Anti-virus	MTT Assay	Vero cell-line	MNTD = 62.5 µg/ml	Kaushik et al. (2020)
Z. roseum	Seeds	Antifungal	Agar disc diffusion method	*Fusarium accuminata*	ZRSME: IC_{50} = 634.79±19.51a µg/ml	Pemram et al. (2018)
	Rhizomes				ZRRME: IC_{50} = 1319.14±112.76b µg/ml	
	Perianth				ZRPME: IC_{50} = 2554.60±65.16c µg/ml	
	Rhizome	Antibacterial	Agar disc diffusion method	*Escherichia coli*	Inhibition up to 16 mm at a dose of 100 µg/disc	Al-Amin et al. (2019)
		Antifungal	Agar disc diffusion method	*Candida albicans*	Inhibitions up to 7 mm at a dose of 50 µg/disc	
				Aspergillus niger	Inhibitions up to 7 mm at a dose of 50 µg/disc	
Z. spectabile	Leaf and rhizome	Antibacterial	Agar disc diffusion method	*Escherichia coli*	Inhibition = 0.19–0.38 mg/ml	Sivasothy et al. (2012)
	Rhizome	Antioxidant	FRAP		RP_{50} = 56.2 x 10^4 µg/ml	Sivasothy et al. (2013)
			β-carotene bleaching assay	*β-carotene*	Inhibition = 77.27%	Sivasothy et al. (2013)
Z. striolantum	Rhizome	Antioxidant	DPPH	BHT and ascorbic acid	IC_{50} = 421.81 ± 18.32 µg/ml	Tian et al. (2018)
			ABTS	BHT and ascorbic acid	IC_{50} = 960.87 ± 16.23 µg/ml	Tian et al. (2018)
		Antibacterial	Agar disc diffusion method	*Staphylococcus aureus*	MIC= 0.78 mg/ml	Tian et al. (2018)
				Escherichia coli	MIC = 1.56 mg/ml	
				Enterococcus faecalis	MIC = 3.12 mg/ml	
				Pseudomonas aeruginosa	MIC = 3.12 mg/m	
		Antifungal	Agar disc diffusion method	*Candida albicans*	MIC = 3.12 mg/ml	
		Anticancer	MTT Assay	Human leukemic cell-line	IC_{50} = 29.67 µg/ml	Tian et al. (2018)
				Human lung cancer cell-line	IC_{50} = 48.87 µg/ml	
				Human prostatic carcinoma cell-line	IC_{50} = 86.05 µg/ml	
Z. zerumbet	Rhizome	Antioxidant	DPPH	BHT and ascorbic acid	IC_{50} = 90293.12±3529.38 µg/ml	Tian et al. (2020b)
					IC_{50} = 32385.39±5628.23 µg/ml	
					IC_{50} = 17416.04±3274.95 µg/ml	
			ABTS	BHT and ascorbic acid	IC_{50} = 10840.13±938.35 µg/ml	
					IC_{50} = 2926.68±104.28 µg/ml	
					IC_{50} = 2884.67 ± 232.71 µg/ml	
		Antibacterial	Microdilution method	*Streptococcus mutans*	MIC = 250 µg/ml MBC = 500 µg/ml	Moreira da Silva et al. (2018)
		Apoptotic	Annexin V-FITC Assay	U-87 MG cell-line	IC_{50} = 150 µM (24 h) IC_{50} = 130 µM (48 h)	Jalili-Nik et al. (2020)
		Anticancer	MTT Assay	Lung cancer cell-line	IC_{50} = 11.09±0.39 µg/ml	Tian et al. (2020b)
				Prostatic Carcinoma cell-line	IC_{50} = 7.66±0.68 µg/ml	
				Leukemic cell-line	IC_{50} = 4.21±0.84 µg/ml	

The species from the genus *Zingiber* were also found to exhibit antifungal activity. *Z. neesanum* was reported to have antifungal activity against *Mucor rouxii* with an inhibition value of 9.7 ± 0.6 cm using the agar disc diffusion method (Nair et al., 2019). Meanwhile, *Z. officinale* was also found to have antifungal activity against *Fusarium oxysporum* with the inhibition value of 50.38 ± 0.5 cm analyzed with the agar disc diffusion method (Abdullahi et al., 2020). Furthermore, *Z. roseum* had an IC_{50} value of 634.79 ± 19.51 µg/ml against *Fusarium accuminata* (Premram et al., 2018). The variation in both the inhibition results of antibacterial and antifungal activity tests on genus *Zingiber* could be due to the diversity in the essential oil contents in each species.

4.3. Anti-obesity and anti-hyperglycemic

Obesity is defined as an excessive body fat accumulation that affects body health. The study revealed that genus *Zingiber* exhibited anti-obesity activity both in *in vitro* and *in vivo* studies. For instance, *Z. cassumunar* was found to inhibit pancreatic lipase

and reduce fat absorption. The inhibitory effect was 29.17% and was reported to be higher than the control Xenical®/orlistat with 17.53% (Iswantini et al., 2011). In another example, the water extract of *Z. mioga* reduced the lipid accumulation in the cell and the body and liver weight in High Fat diet-fed mice model (Lee et al., 2016). Moreover, the ethanol extract of *Z. mioga* also reduced blood sugar in rats and mice models for 0.1 g/kg 55.61 ± 13.24 mg/dL. Furthermore, another method was used to test the anti-hyperglycemic effect in *Z. mioga* using porcine pancreatic α-amylase inhibition assay and showed that this species had moderate inhibition with IC_{50} values >10x10^3 µg/ml (Jo et al., 2016).

Table 5. *In vivo* studies of several genus *Zingiber*

Species	Activity	Animal model	References
Z. cassumunar	Antiulcer	Rats	Yuniarto et al. (2017)
Z. mioga	Antiobesity	Mice	Lee et al. (2016)
	Anti-hyperglycaemic	Rats and mice	Jo et al. (2016)
Z. officinale	Antiobesity	Mice	Zordan et al. (2020)
	Antiobesity	Rats	Nazish et al. (2016)
	Antiemetic	Pigeon	Ullah et al. (2015)

4.4. Antivirus, antimalaria, and insect repellent activity

A study by Kaushik et al. (2020) demonstrated that *Z. officinale* tested by MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) assay in Vero cell lines performed antiviral activity against chikungunya. It was observed that this species has a high cytopathic effect with a viability of 52.90% and 49.02% (Kaushik et al., 2020). Meanwhile, in vivo study of *Z. cassumunar* revealed that the extract was effective against the *Plasmodium berghei* and is potential for further study as antimalaria (Utami et al., 2017). furthermore, another study found that *Z. nimonii* exhibit repellent activities against *Anopheles stephensi*, *Aedes aegypti*, and *Culex quinquefasciatus*. The range of protection times varied from 60-180 minutes (Govindarajan et al., 2016). In addition, the terpinen-4-ol, an essential oil from *Z. cassumunar*, showed repellent activity against *Lasioderma serricorne* and *Tribolium castaneum* (Wang et al., 2015).

Table 6. Clinical studies of several genus *Zingiber*

Target	Methods	References
Safety assesment	Subjective symptoms Blood pressure Pulse rate Blood count Hemogram Biochemical test of blood Urinalysis	Kato et al. (2018)
Reduce nausea in adult cancer patients	Randomized clinical trial Double-blind clinical trial Placebo-controlled clinical trial	Ryan et al. (2012)

4.5. Antiemetic

Z. officinale is empirically used to treat nausea and vomiting (Hu et al., 2011; Liu et al., 2019). This report is in accordance with the results of in vivo tests using pigeons treated with cisplatin, a cancer drug with nausea and vomiting side effects (Ullah et al., 2015). Moreover, it also correlates with a clinical study from 576 adult cancer patients treated with ginger as a complementary supplement which reduced nausea on day 1 (Ryan et al., 2012). This information plays essential *Z. officinale* for further study as a recommended complementary in cancer patients undergoing chemotherapy. Table 6 displays several clinical studies that have been done using extracts of several *Zingiber* plants.

4.6 Apoptotic, antiasthma, and anti-inflammatory

Another study reported zerumbone from *Z. zerumbet* was able to activate the NF-κB signalling pathway which regulates wound healing, inflammation, and apoptotic. Its apoptotic effect was tested using the Annexin V-FITC assay, and the results showed that the apoptotic cells increased from 5.2% to 11.5% (Jalili-Nik et al., 2020). Furthermore, molecular docking and dynamic simulation of *Z. cassumunar* compounds such as (*E*)-1-(3,4-dimethoxyphenyl), but-3-ene-1-ol (DMPB) and (*E*)-1-(3,4-dimethoxyphenyl) butadiene (compound DMPBD) reported having binding affinity at 5-lipoxygenase which is the enzyme caused asthma (Jitapunkul et al., 2018). Another study using gelatin zymography method also showed positive results for compound DMPB as an antiasthma by inhibiting MMP-9, an asthmatic agent, with an inhibitory effect of 0.5 - 4.0 mg/ml (Poachanukoon et al., 2015). In addition, the seeds of *Z. chrysanthum* were found to have anti-inflammatory activity analyzed by protein denaturation assay with an IB_{50} value of 16.76 ± 0.006 µL/ml with diclofenac sodium positive control (Palariya et al., 2019). Some research investigated that this *Zingiber* species was known to contain essential oils such as α-pinene, γ-terpinene, (*E*)-caryophyllene, α-terpineol, and terpenin-4-ol.

5. Product developments

Several species in the genus *Zingiber* are more popular than the others, such as *Z. cassumunar*, *Z. officinale*, and *Z. zerumbet*. Due to a large amount of research conducted, the development of this species can vary from the pharmacological aspect to the cosmetic application (Tian et al., 2020b). For instance, *Z. zerumbet*, which has been assessed for its antibacterial activity in *Streptococcus mutans*, also could be formulated as a natural agent to prevent dental caries (Moreira da Silva et al., 2018). Many studies reported evidence that *Z. nimonii* has repellent activities against mosquitoes' vectors, indicating its potential for future plant-based mosquito repellent development and is considered natural and safe (Govindarajan et al., 2016). Other than that, the presence of curcuminoids in *Z. spectabile* can also be used as a natural preservative (Sivasothy et al., 2013). Another species of the genus *Zingiber*, *Z. roseum*, can be further developed as antifungal and skincare because of its antioxidant activity (Premram et al., 2018).

6. Conclusion

The genus *Zingiber* has 53 species distributed worldwide and empirically used as a condiment, ornamental plant, perfume, dyes, and traditional medicine to treat various diseases such as gout, pain relievers, nausea and vomiting, wound healing, and asthma. The pharmacological properties of this genus commonly resulted from its different phytochemical constituents, mostly from their secondary metabolites. The major essential oil constituents found in genus *Zingiber* are sabinene, gingerol, myrcene, terpinen-4-ol, germacrene D, and zerumbone. The pharmacological properties of the genus *Zingiber* have been proven by in vitro and in vivo studies, including antioxidant, antibacterial, antifungal, antivirus, anti-obesity, antihyperglycemic, antimalaria, antiemetic, antiapoptotic, antiasthma, anti-inflammatory, and repellent. From the data collected, the empirical uses of these aromatic plants are in accordance with their bioactive compounds and biological activities. These results are expected to provide a starting template for research and future development related to the genus *Zingiber*. Ultimately, this review is intended to present the scientific-based perspective of traditional remedies of genus *Zingiber*.

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Conflict of interest

The authors declare there is no conflict of interest in this study.

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