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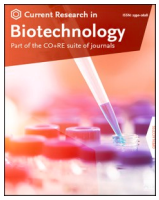

Health-promoting and medicinal properties of Zingiberaceae family plants: A minireview with a special focus on galangal, turmeric, cardamom, and ginger

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ABSTRACT

The Zingiberaceae family, including among others, galangal (*Alpinia galanga*), turmeric (*Curcuma longa*), cardamom (*Elettaria cardamomum*), and ginger (*Zingiber officinale*), has been widely used in traditional medicine and culinary practices worldwide due to its diverse health-promoting properties. This mini-review aims to provide a concise overview of Zingiberaceae species' medicinal potential and identify key areas for further research to facilitate their integration into modern medicine. Herein we summarize the existing research on the pharmacological activities of these species, with a focus on their antioxidant, anti-inflammatory, antimicrobial, anticancer, cardiovascular, digestive, and metabolic effects. Aside from the reported biological effects of traditional formulations and phytopharmaceutical preparations, emphasis is given to the primary bioactive compounds identified in these plants including diverse phenolics, terpenes, and various other secondary metabolites. Mechanisms contributing to therapeutic benefits. Moreover, highlighted is the promise of these plants for future development of drugs and nutraceuticals despite current challenges, particularly bioavailability issues and the need for more clinical studies.

1. An overview of key medicinal plants in the Zingiberaceae family and their use in traditional medicine

In traditional medicine, herbs and other plants have long been used as a source of therapeutic compounds for treating diverse acute and

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chronic diseases. Both the global herbal and pharmaceutical markets, as well as conventional healthcare systems, rely heavily on medicinal plants due to their therapeutic usefulness. Their therapeutic significance is derived from some pharmacologically active chemical compounds that exert specific and beneficial physiological effects on humans (Atanasov et al., 2015). These plants are not only rich in bioactive phytochemicals, but also contain valuable nutrients such as essential minerals and trace elements that contribute to their traditional use and modern therapeutic potential (Aberoumand and Deokule, 2008). The prospects for discovery of novel drugs and therapeutic alternatives are greatly improved by the application of approaches based on ethnopharmacological expertise which is increasingly supported and validated by cutting edge phytochemical and biomedical research on medicinal plants (Gurib-Fakim, 2006). This process benefits from a multidisciplinary approach that involves the collaboration of traditional healers, chemists, pharmacologists, botanists, and plant biotechnologists. The antioxidant properties of phenolic constituents from various medicinal plants, including those of Zingiberaceae, have been linked to their hydroxyl group content and free radical scavenging capacity, as previously described in biochemical analyses (Aberoumand, 2009; Mutakin et al., 2023). Such multidisciplinary research effort is essential given the range of secondary metabolites produced by the wide-ranging spectrum of flora (Dauletkhan et al., 2024; Gonfa et al., 2023; Matin, M. et al., 2024a; Wolfender et al., 2013).

The Zingiberaceae family includes many therapeutic plants, which are important in ethnomedicine and play a crucial role in the Ayurvedic system of medicine in India (Kumar et al., 2013). These fragrant, evergreen plants grow in tropical parts of Asia, Africa, and the Americas and have creeping, horizontal, or tuberous rhizomes (Xu and Chang, 2017). With over 200 species and 20 genera, India is especially rich in this annual or perennial Zingiberaceae family (Nair, 2019), along with South- and Southeast-Asian countries such as China, Thailand, and Indonesia, among others. It is the largest family in the Zingiberales order, with 53 genera and more than 1200 species found across tropical regions (Kress et al., 2002). Several broadly known and medicinally used species from the Zingiberaceae family are depicted in Fig. 1. The Zingiberaceae family was first divided into four tribes – Hedychieae, Globbeae, Zingibereae, and Alpinieae in 1889, and it still captures the interest of botanists and researchers due to its unique features. These features include the development of staminodia, the arrangement and varying number of ovary chambers (locules), changes to the fertile anther, and distinct orientations of the plant's rhizome, shoot, and leaves (Kress et al., 2002).

The Zingiberaceae family encompasses a diverse array of medicinally important species which are known for their health and nutritional benefits. Key species such as *Alpinia galanga* (L.) Willd. (galangal), *Curcuma longa* L. (turmeric), *Elettaria cardamomum* (L.) Maton (cardamom), and *Zingiber officinale* Roscoe (ginger) have been traditionally used across cultures for both therapeutic and culinary purposes. This narrative mini-review aims to provide a concise overview of the overall disease-preventing and healing properties of Zingiberaceae family plants, with a special focus on these four most well-established species (*A. galanga*, *C. longa*, *E. cardamomum*, and *Z. officinale*). These four species were selected due to their longstanding global prominence as both culinary spices and therapeutic agents in traditional medicine systems, and because they represent the major phytochemical classes and health-related properties observed across the broader Zingiberaceae family. The author team of the present work was assembled through networking within the experts of the Zingiberaceae Collaborative Research Group (ZCRG), formed under the auspices of the International Natural Product Sciences Taskforce (INPST) (Atanasov et al., 2021; Singla et al., 2023). To proiritise the covered literature, we specifically surveyed peer-reviewed articles from the last 10 years using databases such as PubMed and Web of Science, focusing on studies of galangal, turmeric, cardamom, and ginger.

Alpinia galanga is a medicinal plant widely distributed in Southeast Asia, including India, China, Thailand, Indonesia, Malaysia, and Sri Lanka (Hanish Singh et al., 2011). In India, particularly in the south, it is commonly used as a home remedy for various ailments (Kirtikar and Basu, 1996). Ayurveda classifies *A. galanga* rhizome as a *Vatashamana* drug that regulates body movements and flows. The rhizome is traditionally used to treat diseases, such as rheumatism, heart disease, hypertension, kidney stone, diabetes, ulcer, asthma, inflammation, bronchitis, chronic enteritis, and microbial infections (Ghosh and Rangan, 2013; Kaushik et al., 2011). Local healers (*vaidyas*) in South India use the rhizomes of *A. galanga* in combination with other herbs to treat diabetes (Wali et al., 2022). It is an ingredient of many Ayurvedic formulations, including *Rasnadhi choornam* (for cough, cold, and runny nose), *Rasnaerandadi kashayam* (for musculoskeletal disorders), and *Maharasnadi kashayam* (for arthritis, infertility, gout, and hernia) (Chitra and Thoppil, 2008; Duke et al., 2002). The rhizome is valued for its nerve-tonic and stimulant properties, and is used as a carminative,

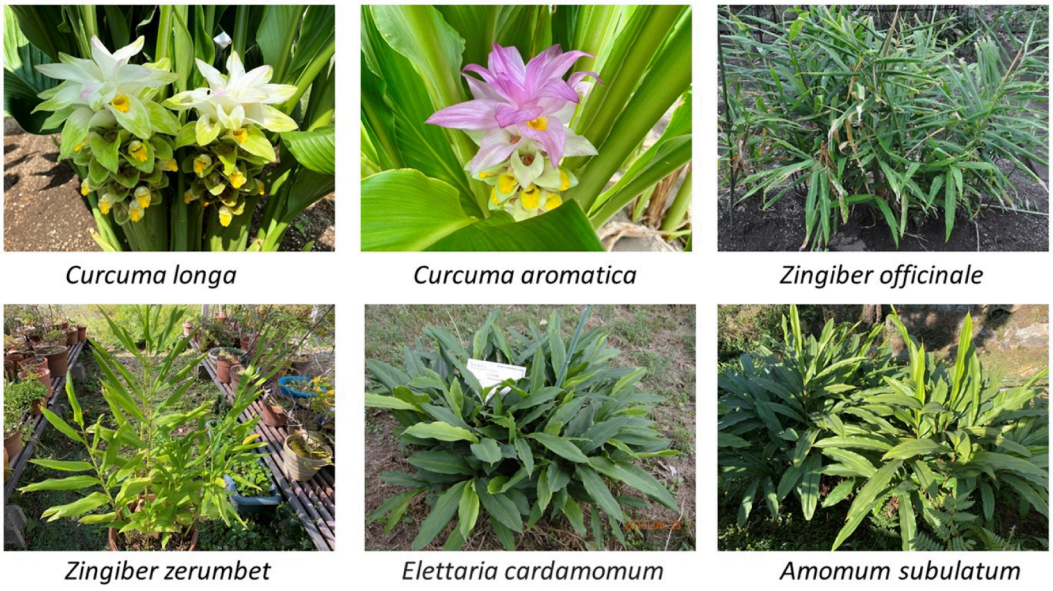

Fig. 1. Some of the medicinally important species of Zingiberaceae family (photos taken by the authors).

stomachic, disinfectant, and aphrodisiac. It is also used to treat local inflammation and skin allergies caused by insect bites and microbial infections (Namsa et al., 2009; Puri, 1971; Warrier, 1994). The Palliyar tribes of Kerala, India, use a formulation of *A. galanga* rhizome combined with *Piper nigrum* and *Z. officinale* to treat fevers and apply the leaf extract topically to relieve itching and allergic skin conditions (Pushpangadan and Atal, 1986). Similarly, the Malapandaram tribe in Kerala, India, applies a paste made from fresh rhizomes, pepper leaves, and lemongrass on the neck to relieve cough and fever (Thomas et al., 2020). The Kani tribe uses rhizome juice for dandruff, pimples, and toothaches (Dan and Thomas, 2024). Another study reported the use of rhizomes to induce abortions in traditional practices (Tushar et al., 2010). In China and Thailand, *A. galanga* has traditionally been used to promote digestive health because of its antiseptic properties, which also serve as a carminative and digestive stimulant (Farnsworth and Bunyaprapraphatsara, 1992). In Malaysia, it is used to treat constipation, piles, bilharzia (Neamsuvan et al., 2016), cough, asthma, bronchitis, headache, inflammation, rheumatoid arthritis, and colic (Burkill, 1966). For centuries, the rhizomes have been used to treat respiratory infections in Algeria (Bendjeddou et al., 2003), as well as digestive disorders and relieve bronchitis, measles, rubella, and cholera in various other countries (Bremness, 1953; Brown, 1995; Grieve, 1989; Xia, 1989). The Sudanese community in West Java, Indonesia, utilises *A. galanga* rhizomes to treat muscle pain (Roosita et al., 2008). While in Bali, it is combined with *Spondias pinnata* leaves to treat heartburn (Sujarwo et al., 2015). In Serbia, the rhizomes were employed to treat headaches and stomach pain, as an antispasmodic, and as a carminative (Jaric et al., 2011). Lev and Amar documented its use in cleansing the digestive system and addressing reproductive issues, sexual diseases, stomach problems, respiratory health, and dental care (Lev and Amar, 2000, 2008). Another study referred the use of *A. galanga* for the treatment of anorexia (Subehan et al., 2006). Beyond the medicinal uses, the flowers and young stems of this plant are also used to enrich the flavour and aroma of various dishes (Arambewela and Wijesinghe, 2006).

The rhizome of *C. longa* is one of the most popular dietary supplements globally, and is extensively used as a spice, colouring agent, food additive, cosmetic, and herbal medicine (Ammon and Wahl, 1991; Hall, 2013). Turmeric is used as a bitter, pungent, laxative, tonic, anthelmintic, emollient, astringent, and alexiteric agent (Velayudhan et al., 2012). *Curcuma longa* has been used for centuries in Ayurveda and Unani medicines to treat skin diseases, wounds, and inflammatory disorders such as arthritis and hepatitis (Ravindran, 2007). Known in Ayurveda as *Haridra*, meaning 'excellent cure for jaundice', *Curcuma longa* is also recorded as *Kusthagna* (anti-dermatosis), *Dashemani lekhaniya* (emaciating), and *Visaghna* (anti-poisonous). *Charaka Samhita*, an ancient Ayurvedic text, describes turmeric as beneficial for improving digestion, reducing obesity, and alleviating digestive tract inflammation (Sharma, 2000). Other traditional uses of *C. longa* include treatment of anorexia, cough, jaundice, biliary disorders, diabetic wounds, rheumatism, sinusitis, sprains, swelling, conjunctivitis, skin infections, haemorrhoids, arthritis, and eczema (Kurup, 1977). In Unani medicine, *C. longa* has been used to treat jaundice, bruises, and scabies (Velayudhan et al., 2012). Turmeric has been extensively described in the Indian Materia Medica as a traditional cosmeceutical with aromatic, hair growth-reducing, stimulant, and carminative properties, used either individually or in combination with other plants (Shrishail et al., 2013). In the Bihar state of India, indigenous healers employ flowers to counteract fertility and leaves to alleviate the symptoms of cold and fever (Dan, 2001). Folk remedies also involve the application of a healing paste made from fresh rhizomes to alleviate insect bite-induced irritation and pain (Dan and Thomas, 2024). The curative properties of turmeric are also widely recognized by Chinese, Korean, and Japanese Pharmacopoeias. In traditional Chinese medicine, turmeric is used to alleviate abdominal pain, jaundice (icterus), dermatitis, hepatitis, wounds, sore throat, inflammatory joints, and to provide relief from urticaria (Porkert, 1978). Turmeric is used as an effective immunomodulator in traditional medicine in Columbia (Bussmann et al., 2018). Thai traditional medicine employs it to treat skin diseases, haemorrhoids, gastrointestinal ulcers, insect bites, and gonorrhoea (Prasad, 2011). In traditional Islamic medicine, turmeric is commonly used for the treatment of inflammatory disorders, pimples, wounds, cataracts, eye health, and the relief of joint aches, scabies, and herpes. Moreover, traditional healers recommended it for obstructive jaundice, tachycardia, paralysis, and epilepsy (Ayati et al., 2019; Bahmānyar, 1967; Ghasāni, 1985; Ibn Beyṭār, 2001; Khan, 1968). The natives of Delta State, Nigeria, use an herbal infusion made of turmeric rhizome, consumed with 'Ogogoro', a local gin distilled from fermented palm wine, to treat various ailments (Fuloria et al., 2022). In Bhutan traditional medicine, turmeric is known as 'Yung-ba' and functions as an effective antidote, anti-inflammatory, and antiseptic agent (Ayati et al., 2019). Turmeric rhizomes and leaves are also utilised by the people of the Philippines and the Kurdish community of Iraq to treat arthritis (Abe and Ohtani, 2013; Ahmed, 2016). In Rifian traditional medicine of Morocco, turmeric is considered tonic, calefacient, and digestive aid (Merzouki et al., 2000). It is also used in traditional Korean medicine to treat gastroenteric diseases (Kim and Song, 2011).

Elettaria cardamomum, commonly known as cardamom, is an ancient spice used for both culinary and medicinal purposes for thousands of years in Greek, Roman, and Indian civilisations (Ashokkumar et al., 2020). Often called the "Queen of spices" in India, it has been referenced in ancient Indian literature as *Ela* in Sanskrit (Mahindru, 1982). Cardamom has been employed in Ayurvedic medicine to reduce fat, treat urinary and skin ailments, bronchitis, asthma, and constipation (al-Zuhair et al., 1996; Hamzaa and Osman, 2012; Jafri et al., 2001; Kunnumakkara et al., 2009; Nair and Unnikrishnan, 1997; Saeed et al., 2014). It has also been traditionally used to treat cataracts, nausea, diarrhoea, cardiac disorders (Gilani et al., 2008; Khan et al., 2011), anorexia, dyspepsia, haemorrhoids, renal and vesical calculi, halitosis (Sharma et al., 2011), and to improve eyesight (Singh and Singh, 1996). In Ayurveda, cardamom is often used as an additive or *Prakshepa dravyas* in formulations like *Chyawanaprasha*, *Eladi vati*, and *Sitopaladi churna* (Sarvade et al., 2016). The cardamom mixture *Eladigana churna* is commonly used to treat arthritis, congestion, and itching, whereas *Ariyaru kashayam* is used to treat skin disorders in children (Vijayan et al., 2002). Other Ayurvedic medicines using cardamom as the major component include *Elakanadi kashayam* (chronic respiratory problem and asthma), *Eladi ghrita* (abdominal bloating, weakness, anemia, and diabetes), *Eladi thailam* (dermatitis, urticaria, and scabies), and *Chaturjata churna* (anorexia and skin disorder). Various formulations of cardamom are also commonly used in the Unani system of medicine. For instance, *Arq elaichi* serves as a carminative, fortifies the stomach and gastrointestinal function, and is administered for nausea, vomiting, flatulence, and indigestion. Similarly, *Jawarish anarain* and *Jawarish shahi* protect the digestive system and liver (Anwar et al., 2016; Jamal et al., 2006; Mobeen and Moazzam, 2022). Ancient Greek botanists have recorded it as a traditional remedy for coughs, abdominal discomfort, spasms, and sciatica (Davis, 2005). Some tribes in the Kasaragod District of Kerala, India use powdered dried seeds with milk to treat digestive issues while the Kanikkaran tribe combines seed powder with coconut water to treat urinary disorders (Dan and Thomas, 2024; Thomas et al., 2017; Thomas et al., 2020). Cardamom is widely used as a flavouring agent in baked goods, sweets, tea, and coffee, particularly in Asian and Arab countries (Menon, 2000; Sengottuvelu, 2011). The cardamom seeds are aromatic, acrid, sweet, cooling, carminative, alexiteric, cardiac tonic, digestive, diuretic, expectorant, and stimulant. Cardamom reduces caffeine content in coffee. The mixing of cardamom with coffee is known as *Qahwa* in Arabic culture, and is renowned for alleviating headaches and stress (Verma et al., 2009). In the Indian states of Kerala and Tamil Nadu, crushed cardamom capsules are boiled with tea and water to infuse a pleasant aroma known as *elakkai* tea, which has traditionally been used to alleviate fatigue and depression (Ashokkumar

et al., 2019). Daily consumption of cardamom with a tablespoon of honey in conventional medicine is believed to enhance eyesight (Singh and Singh, 1996). On the other hand, some reports have pointed out that excessive cardamom capsule use may lead to impotence (Nair, 2011). Other reports note that, cardamom combined with *Syzygium aromaticum* (clove), has been used as an anti-fertility treatment (Sethi et al., 1987). In traditional Tibetan medicine, cardamom capsules are combined with cinnamon and long pepper to address health issues such as obesity, blood sugar imbalance, and diseases affecting the liver, kidneys, and heart (Ashokkumar et al., 2019). It is valued for its diuretic, carminative, and aromatic-stimulant properties (Islam and Sarwar, 2020; Waghmare, 2020). Additionally, cardamom powder can be used to manage bronchial asthma by reducing excessive mucus in the respiratory system, acting as a cough suppressant, and easing cold symptoms (Nair and Unnikrishnan, 1997). Furthermore, cardamom is used to prevent food poisoning and is considered as an antidote for snake and scorpion venom, providing relief from inflammation and headache (Govil, 1998).

Zingiber officinale rhizomes, widely used as a dietary condiment, possess carminative, digestive, diaphoretic, antispasmodic, expectorant, astringent, stimulant, and diuretic properties (Warrier, 1989). It is extensively utilised as an essential ingredient in Ayurveda, Chinese, African, Greek, Roman, Unani, Tibetan, Arabic, and Korean traditional medicines (Ali et al., 2008; Chrubasik et al., 2005; Govindarajan, 1982; Vasala, 2004). In Ayurvedic texts, *Z. officinale* is referred to as *Maha aushadhi*, signifying 'great medicine' for the treatment of various diseases and is recommended for enhancing digestion (Warrier, 1989). It is used traditionally to treat common cold, rheumatism, neuralgia, colic, motion sickness, and gastrointestinal problems such as loss of appetite, disturbed stomach, morning sickness, nausea, diarrhoea, pyrosis, and dyspepsia (Ali et al., 2008; Surh, 1999). The *Bhavprakash Nighantu*, one of the oldest Ayurvedic texts, describes dried ginger (*shunthi*), alone or with other medicines, as effective for fever, vomiting, cough, respiratory diseases, diarrhoea, heart diseases, rheumatoid arthritis, piles, jaundice, and gastrointestinal disorders. It is also mentioned in the treatise that taking fresh ginger (*ardraka*) alone or along with other drugs is effective against fever, asthma, cough, diarrhoea, indigestion, oedema, anorexia, urticaria, and arthritis. Slices of fresh ginger with salt used before meals are beneficial for dyspepsia and indigestion (Bhavprakash, 2012). The indigenous groups of Kasaragod District in Kerala, India, use fresh rhizome extract for gastrointestinal issues and flatulence, and incorporate it into medicinal formulations for snake bites (Dan and Thomas, 2024; Thomas et al., 2017). In traditional Chinese medicine, ginger is also used to treat various conditions, such as nausea, stomach pain, cholera, diarrhoea, haemorrhage, rheumatism, and toothaches. It is a major ingredient in various Chinese and Japanese traditional medicines for treating gastrointestinal and hepatic disorders and hypertension, and is used as an antiemetic, antitussive, expectorant, and diaphoretic (Afzal et al., 2001). Traditional healers in Arab countries use *Z. officinale* as an aphrodisiac agent to provide warmth to the body. It is combined with other plants to treat colds, catarrh, bronchitis, and gastrointestinal disorders, such as constipation and acidity. Ginger is used for promotion of eye health, and ginger tea is highly popular as a general tonic for treating cataracts (Ghazanfar, 1994; Higashikawa et al., 2024). Ginger is highly valued in African folk medicine as an antiemetic, diuretic, and carminative (Iwu, 1993). While in Greek and Roman traditional medicine, ginger is employed as a digestive aid, antiemetic agent and for rheumatological problems and motion sickness. The Greek physician Galen reported *Z. officinale* for purification of the body and for restoring body balance (Langner et al., 1998). The uses and therapeutic actions of ginger are described in detail in the Unani Pharmacopoeia of India (The Unani pharmacopoeia of India, 2007). Ginger decoction or juice mixed with honey is used to treat coryza, headache, cough, and asthma, and fresh ginger paste is used to treat gout, sciatica, rheumatoid arthritis, and other inflammatory conditions. In Unani medicine, ginger is combined with other ingredients and used for ankylosing spondylitis, lack of appetite, flatulence, hoarseness of voice, haemorrhoids, ascites, rectal prolapse, anorexia, dyspepsia, hemiplegia, and facial palsy. In Tibetan traditional medicine, ginger is recommended as an appetite stimulant, digestive aid, diuretic, astringent, diaphoretic, antispasmodic, expectorant, peripheral circulatory stimulant, and anti-inflammatory agent (Govindarajan, 1982). In the United States, ginger is commonly recommended as a folk remedy for nausea related to morning and motion sickness (Glover, 2007; Rockville, 1998).

Numerous bioactive compounds, such as terpenes, ketones, flavonoids, carotenoids, alcohols, and phytoestrogens, are found in plants belonging to the Zingiberaceae family, known for their medicinal properties. The rhizomes of these plants, whether tuberous or non-tuberous, are distinctive and possess potent aromatic and therapeutic qualities (Chen et al., 2008). Ginger represents a prominent and broadly-used prototypical member of the Zingiberaceae family, containing numerous bioactive compounds, contributing to its use in traditional medicine and culinary practices (Ali et al., 2008; Matin, Maima et al., 2024). Research has shown considerable interest in the Zingiberaceae family for its potential as dietary anti-inflammatory agents, and pre-clinical research as well as accumulating human studies suggest that these plants may provide benefits in diverse chronic conditions such as osteoarthritis, rheumatoid arthritis, metabolic disorders, hypertension and major depressive disorder (Lakhan et al., 2015; Matin, M. et al., 2024b; Matin, M. et al., 2024c). Along this line, traditional remedies have long utilized ginger for the treatment of numerous ailments, such as gingivitis, asthma, nausea, toothaches, stomachaches, vomiting, diarrhea, and respiratory disorders (Grzanna et al., 2005). Some of the common crude drugs derived from Zingiberaceae plants that are broadly used in traditional medicine systems are depicted in Fig. 2.

In traditional Thai medicine in particular, several plants from the Zingiberaceae family are used due to their anti-allergic and other medicinal properties. *Curcuma longa* and *C. zedoaria* are traditionally used for itching and skin conditions, with the latter having notable anti-allergic effects, while *Kaempferia galanga* alleviates allergies, *K. parviflora* treats allergies and digestive issues and is considered an aphrodisiac; and *Z. cassumunar*, *Z. officinale*, and *Z. zerumbet* are utilized for inflammation and skin ailments, as an anti-asthmatic, and for reduction of gas and inflammation, respectively (Tewtrakul and Subhadhirasakul, 2007).

The most common medicinally used products of the Zingiberaceae family plants with their biological sources and selected key phytoconstituents are presented in Table 1.

The World Health Organization (WHO) defines traditional medicine as "the total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement, or treatment of physical and mental illness" (WHO, 2019). Different populations have created distinctive traditional medical practices that are ingrained in their respective historical and cultural contexts. Ayurveda, Unani medicine, and traditional Chinese medicine (TCM) are a few well-known traditional medical practices that have gained acceptance both locally and globally(Ansari et al., 2021; Jaiswal et al., 2016; Yuan et al., 2016). One of the oldest medical systems is TCM. It includes a variety of techniques such as moxibustion, massage, acupuncture, herbal treatments, cupping therapy, and physical activity (Matos et al., 2021). Globally, traditional medicine systems rely on plants, animals, and minerals resources to treat a range of human and animal health conditions. Moreover, traditional medicine continues to be a primary healthcare option in many developing countries because it is accessible, affordable, and culturally relevant (Ekor, 2014; Moeta et al., 2023; Mokgobi, 2014). Along the same line, recently there has been a significant rise in popularity of plant-based medicines in developed countries (Barnes et al., 2016; Egan et al., 2011).

Ginger represents a prominent and broadly-used plants from the Zingiberaceae family within the Ayurvedic system. Table 2 provides detailing about scientific names, Ayurvedic names, common names, and

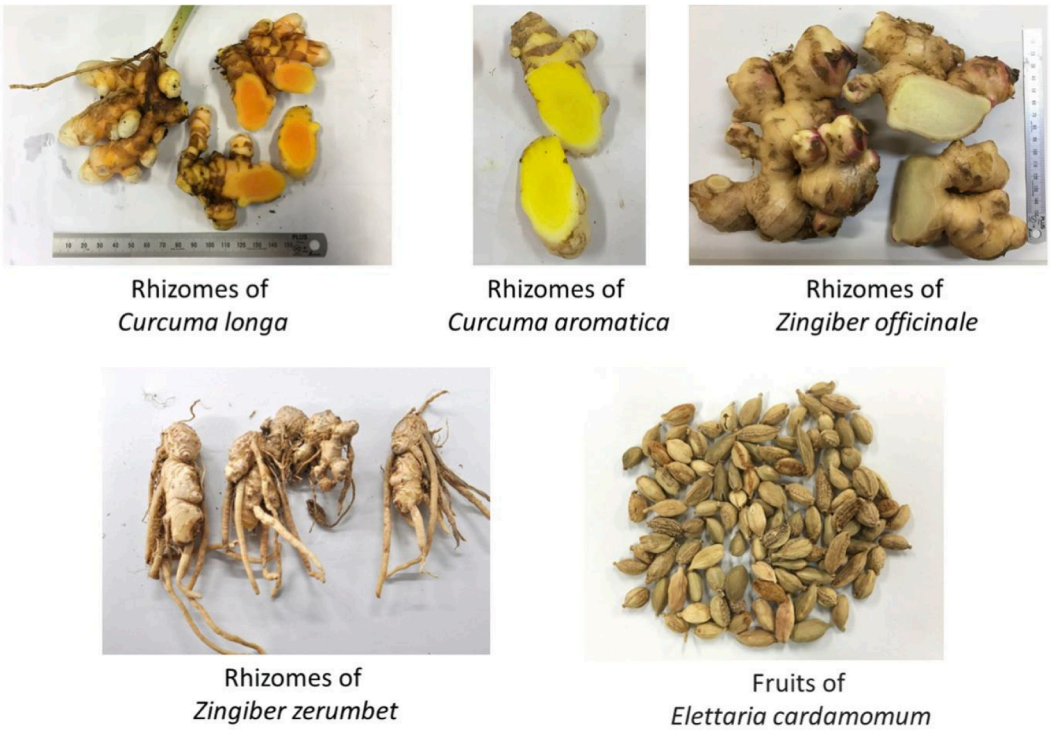

Fig. 2. Some of the common crude drugs used in traditional medicine systems belonging to the Zingiberaceae family: *Curcuma longa; Curcuma aromatica; Zingiber officinale, Zingiber zerumbet, Elettaria cardamomum* (photos taken by the authors).

traditional applications of commonly used plants from Zingiberaceae family. Notable examples include Shunthi (*Z. officinale*), Haridra (*C. longa*), Rasna (*A. galanga*), Ela (*E. cardamomum*), Kra chai (*B. rotunda*), and Kapur kachri (*H. spicatum*), among others. These species are frequently employed in the treatment of digestive and respiratory disorders. Specifically, Shunthi, Haridra, Kra chai, aromatic ginger, white turmeric, and Vanaharidra exhibit notable anti-inflammatory properties. Additionally, Haridra, Kapur kachri, White turmeric, Tavakshira, and Vanaharidra are helpful for skin ailments. Furthermore, Kali haldi is recognized as an antiseptic, while Rasna serves as a general tonic.

Detailed overview of traditional Chinese medicinal plants of the Zingiberaceae family along with their Chinese names, common names, and therapeutic uses are described in Table 3**.** Jiāng (*Z. officinale*), Yü-chin (*C. longa*), Gaoliangjiang (*A. officinarum*), Shan nai (*K. galanga*), Yu jin (*C. aromatica*), E zhu (*C. phaeocaulis*), Wen yu jin (*C. wenyujin*), and Guangxi e-zhu (*C. kwangsiensis*) plants are noted for their anti-inflammatory properties. They also promote blood circulation, with Jiāng, Yü-chin, Yu-jin, E zhu, Wen yu jin, and Guangxi e-zhu being particularly effective in this regard. Additionally, Jiāng, Yü-chin, Shan nai, Wen e zhu, Yu-jin, and Guangxi e-zhu are used as pain relievers, while Gaoliangjiang serve as appetite stimulants.

The Zingiberaceae family of plants also play an important role in the Greek (Unani) system of medicine, where they are known by various names with specific therapeutic uses (Table 4). For instance, Zanjabeel (*Zingiber officinale*), Zard chob (*Curcuma longa*), Kulanjan (*Alpinia galanga*), Heel kalan (*Amomum subulatum*), Kencur (*Kaempferia galanga*), Zaranbad (*Curcuma zedoaria*), Kaali haldi (*Curcuma caesia*), Kapoor kachri (*Hedychium spicatum*), Khulanjan (*Alpinia officinarum*), and Heel khurd (*Elettaria cardamomum*) are particularly noted for their potential in treating digestive disorders. These plants are also widely used for their anti-inflammatory properties, with Zanjabeel, Zard chob, and Kencur being especially effective. Additionally, Zanjabeel, Kencur, Heel khurd, and Zard chob are commonly used in managing respiratory conditions. Beyond these uses, Tavakshira is known for its benefits in liver ailments, while Zaranbad is often utilized to address menstrual issues.

Next to standalone uses, Zingiberaceae plants are also broadly used in diverse traditional medicine formulations. Thus, diverse formulations from the Ayurvedic medicine are shown in Table 5. For instance, ginger is a key ingredient in several Ayurvedic formulations such as Trikatu Churna, Chitrakadi Vati, Hingwashtak Churna, Talisadi Churna, and Mahayogaraja Guggulu. Additionally, cardamom is used in Sitopaladi Churna and Talisadi Churna. Ginger is particularly noted for its ability to balance all three doshas – Vata, Pitta, and Kapha – making it a versatile ingredient in the Ayurvedic medicine.

Zingiberaceae plants are also used in diverse TCM formulations. Table 6 represents the traditional Chinese formulations Si-Ni-San, Xiao Yao San, Ping Wei San in which ginger in particular is used as main constituents, and which are commonly used in the treatment of digestive and neural problems.

Various Greek (Unani) formulations also use Zingiberaceae plants**,** and Table 7 outlines selected Unani formulations that specifically feature ginger and cardamom as their key ingredients. These formulations serve distinct therapeutic purposes: Jawarish Jalinoos is effective for digestive system issues, Majoon Suranjan addresses pain and inflammation, Habb-E-Jiryan supports reproductive health, Sharbat Amla acts as a rejuvenating tonic, and Roghan Zanjabeel is used to manage joint pain.

In the following sections, we first discuss the bioactive compounds of Zingiberaceae plants, then review their health-promoting effects (antioxidant and anti-inflammatory, among others), and finally address current challenges and future perspectives.

2. Bioactive compounds in Zingiberaceae plants

The Zingiberaceae family is well-known for its abundance in bioactive compounds which have been extensively investigated for their potential therapeutic properties. Numerous scientific investigations have emphasized the significance of phenolic compounds, terpenes, and terpenoids, as well as some alkaloids present in these botanical species.

The genus *Alpinia* is the largest within the Zingiberaceae family,

Table 1
The most common medicinally used products of the Zingiberaceae family plants and some of their key phytoconstituents.

Product categories	Biological sources and specific product variety	Characteristic phytoconstituents	References
Gingers	*Zingiber officinale* (ginger) *Zingiber zerumbet* (bitter ginger)	6-, 8-, 10- and 12-gingerol, 6-, 10-, and 8-shogaol, zingerone, zingiberene, paradols, α-farnesene, α-curcumene, β-bisabolene, and β-sesquiphellandrene	(Li, X. et al., 2021)
Turmeric variations	*Curcuma longa* (turmeric) *Curcuma zedoaria* (white turmeric) *Curcuma aromatica* (wild turmeric) *Curcuma xanthorrhiza* (Javanese turmeric)	Curcuminoids (curcumin, demethoxy curcumin, and bisdemethoxycurcumin) and volatile oils (β-curcumene, *ar*-curcumene, camphor, germacrone, curzerenone, xanthorrhizol, 1,8-cineole, β-elemene and linalol)	(Ahmad et al., 2011; Shabana et al., 2015)
Cardamoms	*Elettaria cardamomum* (green cardamom, true cardamom) *Amomum subulatum* (black cardamom, large cardamom, Nepal cardamom)	1,8-cineole, α-pinene, α-terpineol, linalool, limonene, myrcene, menthone, β-phellandrene, sabinene, linalyl acetate, nerolidol and α-terpinyl acetate	(Ashokkumar et al., 2020; Noumi et al., 2018)
Galangals	*Alpinia officinarum* (lesser galangal) *Alpinia galanga* (greater galangal, Thai galangal) *Kaempferia galanga* (sand ginger, aromatic ginger, kenchur)	3,5,7-trihydroxy flavone (galangin), limonene, α-terpineol, 1,8-cineole, α-pinene, apigenin, camphor, kaempferol, chrysin, luteolin, α-fenchyl acetate, β-ocimene, β-myrcene, vanillic acid, ferulic acid and *p*-hydroxybenzoic acid	(Basri et al., 2017; Das et al., 2020)
Fingerroot	*Boesenbergia rotunda* (fingerroot)	Alpinetin, boesenbergin, cardamonin, panduratin, pinocembrin, pinostrobin, rotundaflavone	(Ongwisespaiboon and Jiraungkoorskul, 2017)

encompassing the highest number of species, totalling 230 (Cruz et al., 2020). Other notable genera in the family include *Etlingera*, *Curcuma*, *Globba*, *Zingiber*, *Renealmia*, *Riedelia*, *Amomum*, *Aframomum*, *Boesenbergia*, *Hedychium*, *Hornstedia*, and *Meisteria* (Britannica, 2020). While *Riedelia*, *Globba*, and *Meisteria* are primarily valued for their ornamental qualities and are not widely recognized for culinary or medicinal applications, certain species of *Renealmia*, *Hedychium*, and *Hornstedia* are utilized locally for medicinal purposes and occasionally in cooking. In contrast, genera such as *Alpinia, Etlingera, Curcuma, Zingiber, Amomum,* and *Boesenbergia* hold significant importance in both cooking and traditional medicine (Aronson, 2016). Consequently, this section will focus primarily on these latter genera and their bioactive compounds.

2.1. Phenolics

The Zingiberaceae family plants contain diverse bioactive compounds, including phenolic acids, flavonoids, and tannins, which contribute to their rich phenolic profile and strong antioxidant properties. The main flavonoid components isolated from the *Alpinia* genus include flavones, flavonols, flavanones, and chalcones, with predominant compounds such as prunetin, rhamnetin, and luteolin 7-O-glucuronide 5-O-rhamnoside in the fruits; delphinidin 3-O-(6′′-O-p-coumaroyl) glucoside, hyperin, and quercetin 7-O-(6′′-malonyl) glucoside in the roots; and pinostrobin, epicatechin glucoside in the leaves, alongside significant amounts of phenolic acids and tannins, particularly in the roots and leaves (Ying et al., 2021). The roots of *A. officinarum* are especially rich in phenolic acids such as chlorogenic acid, ellagic acid, and syringic acid, with notably higher concentrations of ellagic acid, syringic acid, chlorogenic acid, and flavonoids including hesperetin, apigenin, and kaempferol compared to *Z. officinale*, and the absence of compounds like rutin, pyrocatechol, catechin, and caffeic acid in its extract (Abdel-Hady et al., 2024). Flavanones such as pinocembrin and alpinetin, alongside chalcones like flavokavin B and cardamomin, are notable, as are flavanols like (+)-catechin and epicatechin, with important glycosides including quercetin 3-O-robinobioside and rutin (Cruz et al., 2020; Ma et al., 2017).

Eleven phenolic compounds were isolated from *A. galanga* fruits, including four newly identified compounds – (*R*)-4-(1-methoxypropyl) phenol, (*S*)-3-(4-hydroxy-3-methoxyphenyl)propane-1,2-diyldiacetate, (*R*)-3-(4-hydroxy-3-methoxyphenyl)propane-1,2-diyldiacetate, and 3′-demethoxycrataegusanoid E. In the same study, the other seven known compounds were l′-acetoxychavicol acetate, 4-(1-ethoxypropyl)phenol, vanillin, acetovanillone, cinnamaldehyde, 3-buten-2-one, and 4-hydroxy-3-methoxycinnamaldehyde (Liu, P. et al., 2023). The methanolic extracts of *A. galanga* rhizomes were observed to contain *p*-hydroxybenzoic acid, vanillin, vanillic acid, syringaldehyde, and ferulic acid (Wang, H. et al., 2023). In the same extracts, the predominant phenolic compounds were identified to be ellagic acid, gallic acid, (+)-catechin, quercetin, catechol, isorhamnetin, t-cinnamic acid, and protocatechuic acid (Aljobair, 2022; Nampoothiri et al., 2014). Notable flavones include tectochrysin and chrysin, while prominent flavonols are kaempferol 3,4′-dimethylether, galangin, and kaempferide (Erusappan et al., 2022; Kazemi et al., 2022; Ma et al., 2017). (Zhang et al., 2015) analyzed 17 key phytochemicals in *A. officinarum*, finding that the rhizomes contained higher concentrations of most compounds, with kaempferide, izalpinin, diarylheptanoid, hexahydrocurcumin, nootkatone, and galangin showing the greatest differences, and galangin being the most abundant in both the rhizomes and aerial parts. Additionally, eight flavonoids were identified, including kaempferol 3-O-methyl ether, kaempferol 3,4′-O-dimethyl ether, various acetylated forms of kaempferol 3-O-rhamnoside, and their respective derivatives (Wang, S.J. et al., 2023).

The study by Allabaksh (Allabaksh, 2024) identified the presence of several phenolic compounds in *C. angustifolia* rhizome extracts, particularly highlighting gallic acid in the ethanol extract, which had the highest concentration, followed by berberine, rutin, and quercetin. In contrast, phenolic acids in ginger were found in lower concentrations, influenced by factors such as cultivation methods, climate, and storage conditions. Nur Diyana (Nur Diyana, 2024) observed that enzyme-assisted extraction from fertigated ginger yielded higher concentrations of ferulic acid compared to slope-grown ginger, and also detected higher levels of syringic, gallic, *p*-coumaric, and vanillic acids in fertigated ginger. Water extracts, however, only contained gallic and vanillic acids, underscoring the impact of extraction methods on phenolic content. Abdel-Hady and the team (Abdel-Hady et al., 2024) reported prominent levels of ellagic acid (31.89 μg/mL), hesperetin (22.91 μg/mL), quercetin (19.56 μg/mL), daidzein (18.49 μg/mL), and syringic acid (11.33 μg/mL) in the *Z. officinale* ethyl acetate extract, though pyrocatechol and rutin were either trace or absent. Similarly, Al-Areer

Table 2
Commonly used Zingiberaceae plants in the Ayurvedic traditional medicine system.

Botanical Name	Ayurvedic Name	Common Name	Traditional Uses	References
Zingiber officinale	Shunthi	Ginger	Improves digestion, and treats nausea, colds, coughs, arthritis, and inflammatory conditions	(Imtiyaz et al., 2013; Sharma and Singh, 2020)
Curcuma longa	Haridra	Turmeric	Anti-inflammatory, and antioxidant, treats wounds, skin conditions, joint disorders, and digestive disorders, and enhances complexion	(Bhowmik et al., 2009; Fuloria et al., 2022)
Alpinia galanga	Rasna	Greater galangal	Treats rheumatism, chest pain, arthritis, digestive disorders, respiratory ailments, and as a general tonic	(Verma and Sharma, 2022)
Elettaria cardamomum	Ela	Cardamom	Digestive aid, treats respiratory disorders, detoxifies, and is a flavoring agent	(Ashokkumar et al., 2020; Sengupta and Bhattacharjee, 2009)
Boesenbergia rotunda	Kra chai	Fingerroot	Digestive disorders, cough, asthma, and as an anti-inflammatory agent	(Eng-Chong et al., 2012)
Alpinia officinarum	Kulanjana	Lesser galangal	Digestive disorders, cold, inflammation, homeostasis	(Abubakar et al., 2018)
Kaempferia galanga	Kachur	Aromatic ginger	Treats cough, asthma, bronchitis, diabetic hypertension, digestive disorders, and as an anti-inflammatory	(Kumar, 2020)
Curcuma zedoaria	Kachora	White turmeric	Anti-inflammatory, anti-microbial, treats digestive disorders, and skin diseases, and is effective against flatulent colic	(Kanase and Khan, 2018; Lobo et al., 2009)
Hedychium spicatum	Kapur kachri	Spiked ginger lily	Treats respiratory and digestive disorders, dropsy headache, hair falling, and skin diseases	(Singh and Thakur, 2014)
Curcuma angustifolia	Tavakshira	East Indian arrowroot	Improves strength and immunity, liver diseases, skin/blood disorders, and works as an antibacterial agent	(Sharma et al., 2019)
Curcuma aromatica	Vanaharidra	Wild turmeric	Anti-inflammatory, treats skin disorders, wound healing, and respiratory ailments	(Sikha et al., 2015)
Curcuma caesia	Kali haldi	Black turmeric	Used in treating asthma, fever, locomotor depressant, and as an antibacterial	(Behar et al., 2014; Pandey and Chowdhury, 2003)

Table 3
Commonly used Zingiberaceae plants in traditional Chinese medicine (TCM).

Botanical Name	Chinese Name	Common Name	Traditional Uses	References
Zingiber officinale	Jiāng	Ginger	Treats nausea, improves digestion, relieves colds and coughs, alleviates pain and inflammation, warms the body, and enhances circulation	(Yang et al., 2013)
Curcuma longa	Yü-chin	Turmeric	Antiangiogenic, reduces inflammation, treats diabetes, improves blood circulation, and relieves pain	(Li et al., 2010; Li, Y. et al., 2021)
Alpinia officinarum	Gaoliangjiang	Lesser galangal	Treats digestive disorders, relieves nausea, reduces inflammation, and improves appetite	(Ding et al., 2019)
Amomum villosum	Sharen	Villous amomum	Treats digestive disorders, vomiting, improves appetite, and enhances digestion	(Xu et al., 2022; Zeng et al., 2022)
Kaempferia galanga	Shan nai	Aromatic ginger	Treats digestive disorders, relieves muscle pain, and acts as an anti-inflammatory, diuretic agent	(Wang et al., 2021)
Curcuma zedoaria	Wen e zhu	White turmeric	Treats digestive disorders, relieves pain and inflammation, and acts as a tonic for the digestive system	(Wilson et al., 2016)
Curcuma aromatica	Yu jin	Wild turmeric	Reduces inflammation, alleviates pain, and enhances blood circulation	(Fei et al., 2022; Liu, M. et al., 2018)
Curcuma phaeocaulis	E zhu	Dark stemmed curcuma	Treats dysmenorrhea, some digestive disorder symptoms, relieves pain and inflammation, and improves blood circulation	(Chen, Z. et al., 2018)
Curcuma wenyujin	Wen yu jin	Wenyujin turmeric	Treats cardiovascular disorders, reduces inflammation, improves blood circulation, and enhances liver health	(Li, Y. et al., 2021)
Curcuma kwangsiensis	Guangxi e-zhu	Guangxi turmeric	Treats jaundice, relieves pain and inflammation, and improves blood circulation	(Yuan et al., 2020; Yue et al., 2022)

and the team (Al-Areer et al., 2023) reported that quercetin consistently showed the highest concentration across both fresh and powdered ginger, with particularly high levels in Soxhlet-extracted samples. On the other hand, gallic acid, caffeic acid, rutin, and naringin were also detected but only in certain extraction solvents such as ethanol, water or ethyl acetate. The ethanolic extract of *Etlingera rubroloba* was analyzed by Jabbar and the team (Jabbar et al., 2024), who identified 2-methoxyanofinic acid and *p*-coumaric acid among the phenolic compounds. Other notable phenolics included sinapyl alcohol acetate, first reported in *E. rubroloba* and also found in *Etlingera alba*. Additionally, Koch and the team (Koch et al., 2024) reviewed the diverse array of phenolic compounds in the *Etlingera* genus, noting that various species contribute to a broad spectrum of phenolic profiles. *E. elatior* was reported to contain the flavonoids rutin, quercetin, quercetin 7-*O*-glucoside, and kaempferol, as well as the phenolic acid including 5-*O*-caffeoylquinic acid and chlorogenic acid (Ge et al., 2020; Sinsuebpol et al., 2023). Lastly, essential oils from *E. pavieana* were dominated by phenylpropanoids, with *trans*-anethole (78.54 %) and methyl chavicol (19.36 %) as major components, and minor amounts of monoterpenes (1.55 %), oxygenated monoterpenes (0.40 %), and sesquiterpenes (0.09 %) (Naksang et al., 2020).

Boesenbergia rotunda, also known as fingerroot or Krachai, is a member of the Zingiberaceae family (Kongsui et al., 2023). The studies on *B. rotunda* revealed a rich distribution of flavonoids, especially flavanones across different plant parts. Tan and the team (Tan et al., 2015) found that the nonaerial organs, such as rootlets and rhizomes, contained higher levels of flavonoids, with pinostrobin being the most abundant in both propagated and field-grown plants. Additionally, pinocembrin was concentrated in the rhizomes of field-grown plants and the shoot bases of propagated ones. This indicates that pinostrobin plays a central role in the flavonoid biosynthesis pathway. Rhizomes of *B. rotunda* were also rich in both pinostrobin and panduratin A (Kongsui et al., 2023; Thomya et al., 2023). Furthermore, Nguyen and the team (Nguyen et al., 2022) isolated several compounds, including,

Table 4
Zingiberaceae plants used in the Greek (Unani) traditional medicine system.

Botanical Name	Arabic Name	Common Name	Traditional Uses	References
Zingiber officinale	Zanjabeel	Ginger	Treats indigestion, stomach discomfort, diarrhea, alleviates nausea, colds, coughs, and acts as an anti-inflammatory	(Khan et al., 2021)
Curcuma longa	Zard chob	Turmeric	Anti-inflammatory, antioxidant, treat digestive disorders, liver ailments, and skin conditions, and enhances wound healing	(Zaidi, 2019)
Alpinia galanga	Kulanjan	Greater galangal	Treats rheumatism, arthritis, dyspepsia, and digestive disorders, and acts as a cardio tonic and nervous stimulant	(Shiffa et al., 2016)
Amomum subulatum	Heel kalan	Large cardamom	Treats digestive disorders, and acts as a carminative, desiccant, resolvent	(Jamal et al., 2005)
Kaempferia galanga	Kencur	Aromatic ginger	Treats menstrual stimulation, alleviates coughs, colds, and acts as an anti-inflammatory	(Singh, A. et al., 2023)
Curcuma zedoaria	Zaranbad	White turmeric	Anti-inflammatory, treats respiratory diseases, menstrual disorders, and acts as a liver tonic	(Kayum et al., 2021)
Curcuma aromatica	Zard chob	Wild turmeric	Treats respiratory disorders, fever, digestive disorders, and acts as an antibacterial agent	(Agyare et al., 2016; Sikha et al., 2015)
Curcuma angustifolia	Tavaksheera	East Indian arrowroot	Promotes bile production in the liver, helpful for skin, and acts as an antibacterial, antimicrobial, and anti-fungal agent	(Nath et al., 2022)
Curcuma caesia	Kaali haldi	Black turmeric	Treats respiratory disorders, fever, digestive disorders, and acts as an antibacterial	(Behar et al., 2014; Ibrahim et al., 2023)
Hedychium spicatum	Kapoor kachri	Spiked ginger lily	Treats digestive disorders, respiratory disorders, and acts as a treatment for baldness	(Singh, M. et al., 2023)
Alpinia officinarum	Khulanjan	Lesser galangal	Treats gastrointestinal disorders, improves appetite, and acts as a carminative	(Dixit et al., 2012)
Elettaria cardamomum	Heel khurd	Cardamom	Digestive agent, antispasmodic, cardiotonic, and enhances flavor in culinary uses	(Jamal et al., 2006; Singhal et al., 2022)

Table 5
Ayurvedic formulations utilizing Zingiberaceae family plants.

Name of Ayurvedic Formulation	Zingiberaceae plants used	Uses of the Formulation	References
Trikatu Churna	Ginger rhizome (*Zingiber officinale*)	Improves digestion, helps in bronchitis and asthma, possesses antibacterial activity	(Dahikar et al., 2010)
Mahasudarshan Churna	Haridra (*Curcuma longa*), Karcura (*Curcuma zedoaria*), Shunthi (*Zingiber officinale*)	Used in treating fever, malaria, useful in rejuvenating the body	(Chauhan et al., 2013)
Sitopaladi Churna	Cardamom seeds (*Elettaria cardamomum*)	Treats cough, cold, asthma, bronchitis, and improves respiratory health	(Meena et al., 2011)
Chitrakadi Vati	Shunthi dried rhizome (*Zingiber officinale*)	Improves digestion, provides anti-nauseant effect, and enhances appetite	(Kumar et al., 2016)
Hingwashtak Churna	Ginger rhizome (*Zingiber officinale*)	Relieves bloating, gas, and abdominal distension	(Maurya et al., 2020)
Talisadi Churna	Ginger rhizome (*Zingiber officinalis*), Ela (*Elettaria cardamomum*)	Treats asthma, allergic bronchitis, and respiratory disorders	(Mishra et al., 2015)
Ashwagandharishta	Turmeric rhizome (*Curcuma longa*)	Rejuvenates, strengthens the nervous system, and improves immunity	(Kotteswari et al., 2018)
Mahayogaraja Guggulu	Ginger rhizome (*Zingiber officinale*)	Treats various neurological disorders	(Lavekar et al., 2010)

pinostrobin, pinocembrin, alpinetin, and a new flavanone derivative (7,4′-dihydroxy-5-methoxyflavanone) from *B. pandurata*. Chatsumpun and the team (Chatsumpun et al., 2017) also identified three new biflavonoids—rotundaflavanochalcone, *iso*-rotundaflavanochalcone,

Table 6
Selected traditional Chinese formulations utilizing ginger.

Name of Chinese Formulation	Zingiberaceae Plant Used	Uses of Formulation	References
Si-Ni-San	*Zingiber officinale* (Ginger rhizome)	Used for treating nausea, vomiting, and digestive disorders	(Zhang et al., 2006)
Xiao Yao San	*Zingiber officinale* (Ginger rhizome)	Traditionally used for liver ailments and mental disorders	(Zhang et al., 2012)
Ping Wei San	*Zingiber officinale* (Ginger rhizome)	Used for treating Parkinson's disease	(Li, D. et al., 2023)

and de-O-methyl rotundaflavanochalcone—from the methanolic extract of *B. rotunda* roots, along with 12 known compounds. Similarly, Mohammed and the team (Mohammed et al., 2019) reported the isolation of six key chemical constituents from *B. rotunda* rhizomes, including pinostrobin, pinostrobin chalcone, cardamonin, 4,5-dihydrokavain, pinocembrin, and alpinetin.

Emmanuel and the team (Uche Emmanuel et al., 2023) analyzed bioactive compounds from *Aframomum melengueta* seeds, identifying key flavonoids such as kaempferol (15.68 μg/mL), flavanones (18.41 μg/mL), and rutin (11.75 μg/mL). Other phenolic compounds, including anthocyanins, flavan-3-ol, cyanogenic glycosides, ribalinidine, catechins, and resveratrol, were also quantified. The highest concentration of 23.10 μg/mL was assigned for sapogernin while naringenin was the lowest at 1.06 μg/mL. Luca and the team (Luca et al., 2022) further identified diarylheptanoids as the most abundant compounds, along with phenolic and organic acids (nine derivatives), and hydroxyphenylalkanes, including gingerol-related compounds like 6-gingerol.

2.2. Terpenes and terpenoids

Terpenes and terpenoids are a major class of secondary metabolites in the Zingiberaceae family, with significant diversity across species. Terpenes are simple hydrocarbons found in essential oils with structures based on isoprene units (C5). They include hemiterpenes (C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), triterpenes (C30), and tetraterpenes (C40). Terpenoids are modified terpenes with added oxygen and functional groups. They include various classes like alcohols, aldehydes, esters, ethers, epoxides, ketones, and phenols (Masyita et al., 2022). Fig. 3 illustrates the most notable bioactive compounds from the Zingiberaceae family.

Table 7
Selected Greek (Unani) medicine formulations involving Zingiberaceae medicinal plants.

Name of Unani Formulation	Zingiberaceae Plants Used	Uses of Formulation	References
Jawarish Jalinoos	*Zingiber officinale* (Ginger rhizome) *Elettaria cardamomum* (Cardamom fruits) *Alpinia galanga* (Greater galangal rhizome)	Used in the weakness of brain, heart, liver, cures flatulence in stomach, helps in palpitation	(Meena et al., 2013)
Majoon Suranjan	*Zingiber officinale* (Ginger rhizome)	Used for joint pain and inflammation	(Verma et al., 2023)
Roghan Zanjabeel	*Zingiber officinale* (Ginger rhizome)	Ginger oil used topically for joint pain relief and muscle relaxation	(Khan et al., 2021)

Generally, essential oils from *Alpinia* species primarily consist of monoterpenes, with monoterpene hydrocarbons being the most abundant (Ghosh et al., 2014). Significant compounds include 1,8-cineole (eucalyptol), *α*-pinene, *β*-pinene, and *β*-caryophyllene (Van et al., 2021). 1,8-Cineole is particularly prevalent in *A. galanga*, *A. calcarata*, and *A. officinarum* (Chandrakanthan et al., 2020; Hamad, 2016; Ivanovic et al., 2021; Nampoothiri et al., 2016; Zhang et al., 2020; Zhou et al., 2024). Regional differences affect composition, with North Indian varieties are richer in *α*-fenchyl acetate while South Indian varieties containing more 1,8-cineole (Nampoothiri et al., 2016; Raina and Abraham, 2015). Recent studies have identified new monoterpene esters in *A. zerumbet* (Youn et al., 2024) and monoterpene-chalcone conjugates (Cruz et al., 2020; Ma et al., 2017). Analysis by Chandrakanthan and the team (Chandrakanthan et al., 2020) found that the essential oils from *A. calcarata* rhizomes are mainly composed of oxygenated monoterpenes, with significant amounts of 1,8-cineole, α-terpineol (11.62 %), and fenchyl acetate. Additionally, newly discovered monoterpene esters in *A. zerumbet* include (2′E)-2′-methoxy-4′-oxo-6′-phenylhexenoic acid 4-hydroxy-2-isopropyl-5-methylphenyl ester and (2′E)-2′-methoxy-4′-oxo-6′-phenylhexenoic acid 4-hydroxy-5-isopropyl-2-methylphenyl ester (Youn et al., 2024). (Ma et al., 2017) reviewed monoterpene-chalcone conjugates such as rubraine and isorubraine, alongside notable monoterpenoids like 1-terpinen-4-ol, which were also presented prominently in the report of (Cruz et al., 2020).

Monoterpenes in the *Curcuma* genus were reported in several studies, with varying concentrations and profiles. For instance, 1,8-cineole was identified in *C. aeruginosa* and *C. longa* essential oil (Aarthi et al., 2024; Jani et al., 2024). Additionally, minor monoterpenes in *C. longa* such as *α*-phellandrene, *α*-terpinolene, *α*-bergamotene, *α*-pinene, and camphor showed considerable variation across different regions (Aarthi et al., 2024; Jani et al., 2024).

Zingiber pellitum leaves contain significant amounts of monoterpene hydrocarbons, including *β*-pinene (12.0 %) and *α*-pinene (10.0 %) (Omar, 2015). In contrast, *Z. officinale* (ginger) essential oil is characterized by high levels of 1,8-cineole (23.9 %) and 2,2-dimethyl-3-methylenenorbornane (12.2 %) (Hamad, 2016). While *β*-pinene and *β*-caryophyllene are commonly found, compounds such as terpinen-4-ol and *p*-cymene are present in lower concentrations or are absent in *Z. pellitum* oils (Hanh et al., 2023).

Moreover, other notable terpenes also reported include camphene, isoborneol, and d-(+)-camphor, *β*-ocimene, 1,8-cineole, *β*-pinene in the *Etlingera* genus (Koch et al., 2024). Specifically, *E. elatior* essential oils are rich in various monoterpenes, prominently featuring β-pinene, α-pinene, and camphene (Sangthong et al., 2022). Additionally, high

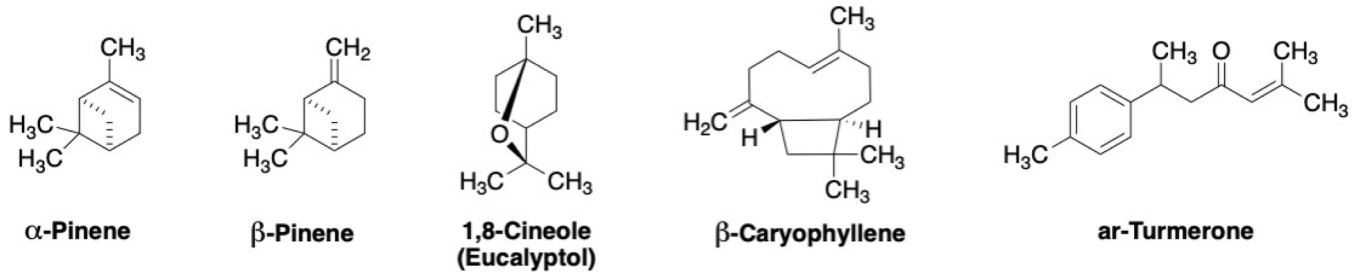

Fig. 3. Selected common terpene and terpenoid compounds found in *Zingiberaceae* family plants.

levels of α-pinene and 1,8-cineole have been observed in other *Etlingera* species, such as *E. sayapensis* and *E. coccinea* (Jems et al., 2021; Li, M. et al., 2020; Pimentel et al., 2023).

Amomum tsao-ko had high levels of 1,8-cineole, along with other monoterpenes like geranial and geraniol with notable amounts of *α*-terpineol, limonene, and *β*-pinene (Li et al., 2022; Sim et al., 2019). *β*-pinene was a key compound present in *Alpinia xanthioides* rhizomes, and terpinen-4-ol in roots (Thinh, 2021). Similarly, *Alpinia rubidium* oil is primarily made up of monoterpene hydrocarbons such as *β*-phellandrene, limonene, and *δ*-3-carene, which constitute 83.3 % of its composition, while *Amomum repoense* also has a high content of monoterpene hydrocarbons (75.7 %), with *β*-pinene as the major component (33.5 %) and notable amounts of (*E*)-*β*-ocimene (9.6 %) and *γ*-terpinene (9.1 %) (Huong et al., 2018).

In *B. armeniaca*, the essential oil comprises key monoterpenoids including *β*-pinene (4.83 %), and linalool (11.63 %). Similarly, the essential oil from *B. stenophylla* is notably high in methyl cinnamate (83.17 %), with *β*-pinene (4.84 %) and linalool (1.18 %) (Nor, 2018). In contrast, *B. rotunda* essential oil showed a lower proportion of monoterpenes (4.2 %), including *β*-pinene (11.4 %) and *α*-pinene (2.9 %), compared to its higher levels of sesquiterpenes and non-terpenes (Omar, 2015).

Hedychium spicatum leaf oil is rich in *β*-pinene (33.4 %) and *α*-pinene (10.4 %), while its stem oil contains *β*-pinene (17.2 %) and 1,8-cineole (9.7 %) (Ding et al., 2024). 1,8-cineole and linalool were identified as key components in various *Hedychium* species (Rawat et al., 2022). In *H. flavum*, *β*-pinene (16.8 %) and (*E*)-nerolidol (11.8 %) are prominent, with coronarin E (20.3 %) as the most abundant compound (Tian et al., 2020). On the other hand, *H. puerense* rhizome oil exhibits linalool (26.5 %), *β*-pinene (18.6 %), *γ*-terpinene (12.1 %), and terpinen-4-ol (7.7 %) (Hong et al., 2021).

Sesquiterpenes are the most commonly identified terpenes in the essential oils of Zingiberaceae family after monoterpenes (Youn et al., 2024). Unique sesquiterpenoids such as 4-isopropyl-6-methyl-1-naphthalenemethanol have been found in *A. oxyphylla* and *A. officinarum*. (Youn et al., 2024). Studies have identified *β*-caryophyllene (47.7–49.0 %) as a major sesquiterpenoids in *A. nigra* essential oils, alongside *α*-humulene (7.5–7.8 %) and caryophyllene oxide (4.3–4.5 %) (Ghosh et al., 2014). Additionally, *A. galanga* also contains zerumbone, zerumbone epoxide, and α-humulene (Wang, S.J. et al., 2023) and *α*-farnesene and *α*-curcumene (Hamad, 2016). *A. officinarum* essential oils are rich in *β*-caryophyllene, *γ*-cadinene, and *α*-farnesene, with sesquiterpenes forming a large part of their chemical composition (Zhang et al., 2020). Various *Alpinia* species also contain sesquiterpenoids like trans, *trans*-farnesol and nootkatone (Ma et al., 2017).

Significant sesquiterpenes identified in *C. longa* essential oils included curlone (*β*-turmerone), and *ar*-turmerone, which were prominent in various studies (Aarthi et al., 2024; Fahmy et al., 2023; Ivanovic et al., 2021; Jani et al., 2024; Kirmani et al., 2024; Zhang, J. et al., 2023). *β*-Sesquiphellandrene (Aarthi et al., 2024; Kirmani et al., 2024), *β*-curcumene and xanthorrhizol (Jani et al., 2024), and a minor amount of α-santalene, caryophyllene, *α*-humulene, *β*-farnesene, *β*-santalene, *α*-curcumene, *β*-bisabolene (Aarthi et al., 2024; Kirmani et al., 2024) were found in *C. longa*, with notable concentrations in specific cultivars. Additionally, in *Curcuma caesia*, curzerenone and epi-curzerenone are notable, with the plant's composition predominantly consisting of oxygenated sesquiterpenes, followed by sesquiterpene hydrocarbons (Jani et al., 2024; Khuntia et al., 2023). (Zhang, J. et al., 2023) isolated two new sesquiterpenes from *C. longa* rhizomes: (*1S,2R,5R,7S,8R*)-2,8-epoxy-5-hydroxybisabola-3,10-dien-9-one and (*1R,2R,5R,7S,8R*)-2,8-epoxy-5-hydroxybisabola-3,10-dien-9-one, along with 6-(4-hydroxymethylphenyl)-2-methyl-hept-2-ene-4-one.

In *Etlingera velutina*, sesquiterpene hydrocarbons accounted for 62.5 % of the composition, with *α*-cubebene and 2-undecanone being the major components (Luo et al., 2022). Similarly, sesquiterpenes, including *β*-cubebene, have been identified in *E. rubroloba* and other *Etlingera* species, though their concentrations vary depending on the plant part and the extraction method employed (Andila and Nugroho, 2022).

Zingiber genus also contains high concentrations of sesquiterpene hydrocarbons and oxygenated sesquiterpenes (Hanh et al., 2023; Rawat et al., 2023). The major compounds in *Z. pellitum* roots were *β*-caryophyllene, 9-epi-(*E*)-caryophyllene, humulene epoxide II in *Z. pellitum* (Hanh et al., 2023). Zerumbone was a major component in *Z. zerumbet* roots and rhizomes, while (*E*)-nerolidol, and *β*-caryophyllene in its leaves and cones (Rawat et al., 2023). *α*-Zingiberene, *β*-sesquiphellandrene, *ar*-curcumene, and *α*-curcumene were also prominent in *Z. officinale* (Hamad, 2016; Ivanovic et al., 2021).

In *Amomum gagnepainii*, sesquiterpene hydrocarbons, and oxygenated sesquiterpenes are major components, with farnesyl acetate, zerumbone, and *β*-caryophyllene being particularly notable (Huong et al., 2018). The essential oil of *A. unifolium* rhizome contains *β*-phellandrene (monoterpene, 18.5 %), with sesquiterpenes such as torulosol (16.1 %), germacrene D (5.7 %), *α*-cadinol (5.5 %), and (*6S, 7R*)-bisabolene (5.1 %) (Doan et al., 2023).

In *B. albosanguinea*, sesquiterpenes constitute 39.0 % of the oil, with notable compounds including *α*-gurjunene (9.3 %), *β*-caryophyllene (4.5 %), germacrene D (3.6 %), bicyclogermacrene (3.4 %), and *α*-elemene (3.3 %) (Ngalang et al., 2024). Similarly, *B. longiflora* showcased a rich sesquiterpenoid profile, longipinocarvone (81.69 %) including *β*-caryophyllene (3.41 %), *t*-caryophyllene (1.54 %), and patchoulene (2.97 %) of the essential oil (Kar, 2015). In contrast, *Boesenbergia* extracts revealed a lower sesquiterpene content, making up 24.5 % of the profile, where (*E*)-nerolidol (15.7 %) and *α*-selinene (9.2 %) are prominent (Omar, 2015). Moreover, *B. armeniaca*'s essential oil contains a substantial proportion of sesquiterpenes, including nerolidol (42.55 %) and *β*-caryophyllene (6.25 %) (Nor, 2018).

The essential oil from *H. coccineum* rhizomes contains unique sesquiterpenes like (*E*)-nerolidol (15.9 %) and 7-hydroxyfarnesen (15.5 %) in its aerial parts (Arya et al., 2022). *H. spicatum* oils also contains sesquiterpenes such as *(E)*-nerolidol (7.8 %) (Ding et al., 2024). The variety of sesquiterpenes in *Hedychium* species can vary significantly due to environmental factors (Rawat et al., 2022).

Diterpenoids in *Alpinia* species include both known and newly discovered compounds. Notably, *A. galanga* seeds contain a recently identified labdane diterpene, Galangalditerpene D, which adds to the class of cyclic terpenoids. Alongside this novel compound, other diterpenoids such as galangalditerpene C and (*E*)-labda-8(17),12-dien-15,16-olide have also been identified (Zhou et al., 2024). Additionally, *Alpinia* species such as *A. galanga* and *A. officinarum* have been reported to contain diterpenoids like coronarin E and zerumin A (Ma et al., 2017). In *A.* oxyphylla and *A. officinarum*, labdane-type diterpenoids are predominant, including intermedin A and B, and the bis-labdanic pahangensin A. Moreover, *A. katsumadae* has yielded seven acyclic triterpenoids with complex substitutions (Youn et al., 2024). Similarly, in *Amomum villosum*, a study identified several diterpenoids, including avxanthin D, 12(S)-hydroxy-15ξ-methoxy-labdan-8(17),13(14)-dien-15,16-olide, and isocoronarin D, among others (Xu et al., 2024). Additionally, *Amomum uliginosum* rhizomes have yielded triterpenoid compounds such as stigmast-4-en-3-one (Chate and Nuntawong, 2015).

2.3. Other bioactives

The Zingiberaceae family contains several other notable bioactive compounds, each with unique key structures, as illustrated in Fig. 4. For instance, kavalactones, which are key components of *Alpinia zerumbet*, are distinguished by their arylethylene-pyrone skeleton (Youn et al., 2024). Notably, kavalactones such as dihydro-5,6-dehydrokavain and 5,6-dehydrokavain were also prominent in *A. zerumbet* (Chan et al., 2023; Chate and Nuntawong, 2015; Cruz et al., 2020; Ma et al., 2017; You et al., 2022). A novel kavalactone, 4′-hydroxy dihydro-5,6-dehydrokavain, was recently isolated from the leaves of *A. zerumbet*.

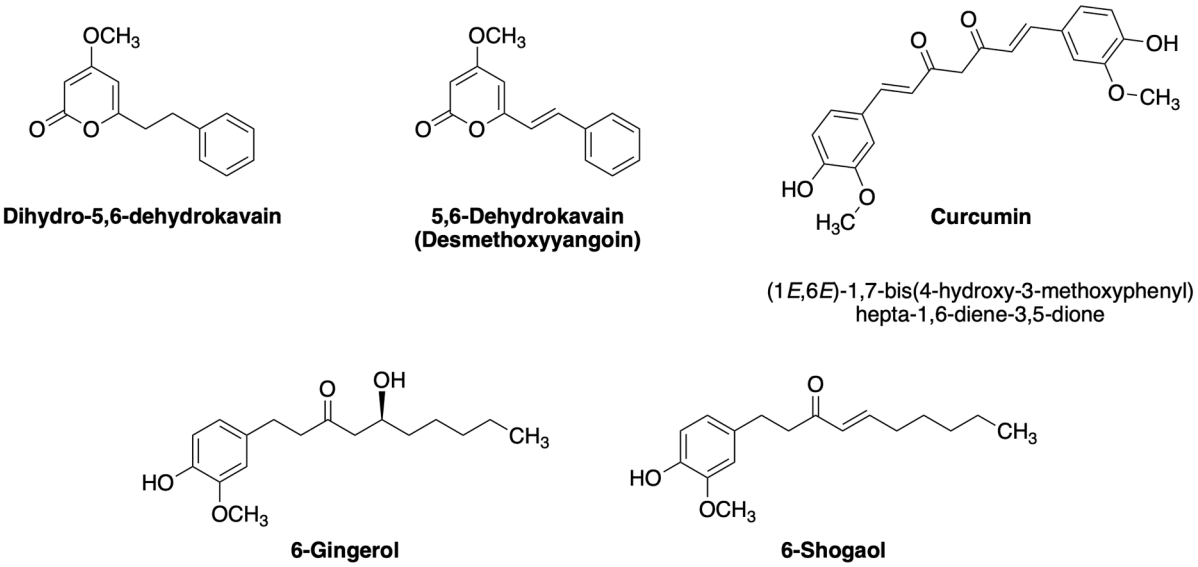

Fig. 4. Selected key bioactive compounds found in *Zingiberaceae* family plants.

In addition, four known kavalactone dimers were discovered, including *rel*-1,*trans*-3-bis-(4-methoxy-2-oxopyran-6-yl)-*cis*-2,*trans*-4-diphenyl cyclobutene, asymmetrical cyclobutane dimers (aniba dimer A and aniba dimer C), and 6,6′-(3,4-diphenylcyclobutane-1,2-diyl)bis(4-methoxy-2H-pyran-2-one) (You et al., 2022). Moreover, 5,6-dehydrokavain has also been reported in the rhizomes of *Amomum uliginosum* (Chate and Nuntawong, 2015).

Diarylheptanoids, or diphenylheptanoids, are categorized as linear or cyclic, and can also form hybrids with flavonoids, sesquiterpenes, or chalcones. In *Aframomum officinarum*, most isolated diarylheptanoids are linear (Sun et al., 2016). (Youn et al., 2024) reviewed 133 diarylheptanoids in the *Alpinia* genus, including 74 monomeric compounds like trans-(4R,5S)-epoxy-1,7-diphenyl-3-heptanone from *Alpinia officinarum* and oxyphyllacinol derivatives from *Alpinia katsumadae*. Newly identified dimeric diarylheptanoids, such as katsumadainols C1–C10 and alpinidinoids A–C, feature complex structures with C–C bonds and oxygen bridges. Hybrid diarylheptanoids, including diarylheptanoid–monoterpene and diarylheptanoid–flavone conjugates, further enhance the structural diversity of this group. (Ma et al., 2017) reported that the main diarylheptanoids isolated from *Alpinia* species include oxyphyllacinol, yakuchinones A and B, alnustone, bisdemethoxycurcumin, calyxin J, calyxin K, calyxin L, calyxin Q, calyxin R, epicalyxin B, epicalyxin H, epicalyxin J, alpinnanin B, deoxycalyxin A, officinin A, alpinin C, blepharocalyxins A–E, neocalyxin A, neocalyxin B, and katsumadains A and B. (Luca et al., 2022) also identified that diarylheptanoids were the most abundant in *Aframomum melegueta*.

The diarylheptanoids in *Curcuma* species are mainly curcumin, demethoxycurcumin, and bisdemethoxycurcumin, with curcumin being the most studied curcuminoid for its anti-inflammatory, antioxidant, and anticancer activities. The study by (Bhardwaj et al., 2023) found that *Curcuma caesia* rhizomes contain various phenolic compounds but reported a lower total phenolic content compared to other Curcuma species, with significant amounts of curcumin, phenol, and coumarin present. Additionally, (Barbosa and Minguillan, 2021) observed a notable increase in curcumin content in *C. longa* rhizomes when cured (residue after ethanol extraction), though this finding focused primarily on curcumin without extensive detail on other phenolic acids. (Song et al., 2023) focused on curcuminoids rather than flavonoids in *C. longa* rhizomes and tuberous roots, but it is important to note that the presence of curcumin and its analogs might influence overall flavonoid content indirectly. The rhizomes had higher average levels of curcumin (36.70 mg/g), demethoxycurcumin (7.37 mg/g), and bisdemethoxycurcumin (6.72 mg/g), while tuberous roots showed lower and more variable contents, with curcumin averaging 14.46 mg/g and the other curcuminoids significantly lower, reflecting unstable quality. In the study by (Do Chau Minh Vinh et al., 2024), curcumin was the most common compound, ranging from 0.77 % to 10.30 %, demethoxycurcumin, ranged from 0.33 % to 6.92 %, and bisdemethoxycurcumin had the lowest levels, from 0.03 % to 3.23 %.

Phenolic ketones consist of a ketone group attached to a phenol side chain. Particularly 6-gingerol, a β-hydroxy ketone, and its dehydrated derivative, 6-shogaol, are significant bioactive compounds in *Z. officinale,* with 6-gingerol being considered the primary contributor to ginger's pharmacological activity, especially for its antioxidant and anti-inflammatory effects. Ghosh et al. (Ghosh et al., 2023) revealed that the 6-gingerol content varied significantly among ginger varieties, ranging from 2.88 % to 6.17 %, and showed a strong correlation with total phenolic content values. (Jorge-Montalvo et al., 2023) conducted a comparative analysis of extraction methods for total phenols (9.422–10.037 mg GAE/g dm), 6-gingerol (4.072–4.838 mg/g dm), and 6-shogaol (0.194–0.263 mg/g dm) from GFD samples, revealing notable differences in extraction efficiency. (Foudah et al., 2020) stated that extracts prepared with ultrasonication-assistance had the highest levels of these compounds, with 6-shogaol ranging from 10.7 to 19.7 mg/g and 6-gingerol from 6.9 to 17.8 mg/g. Similarly, Gonzalez-Gonzalez and the team (Gonzalez-Gonzalez et al., 2023) optimized a microwave-assisted extraction method for gingerols and shogaols, demonstrating high efficiency with a short extraction time and precise results. Nevertheless, (Abdou et al., 2021) focused on the extraction optimization, specifically targeting three major phenolic compounds: 6-gingerol, 6-shogaol, and 6-paradol, from *A. melegueta* using ultrasound-assisted extraction. It should be noted that zingerone, a ketone resulting from the degradation of gingerol, is the least pungent compound in ginger. It is not present in fresh ginger but is formed from gingerol during cooking or heating processes (Ahmad et al., 2015).

3. Health-promoting properties

This section explores key health benefits associated with these species, including their antioxidant capabilities, which combat oxidative stress; anti-inflammatory effects, offering relief from chronic inflammation; and antimicrobial properties that support immunity against pathogens. Furthermore, emerging research highlights their potential anticancer potential, as well as cardiovascular benefits that enhance

Table 8
Key antioxidant compounds of selected broadly studied Zingiberaceae plants.

Zingiberaceae species	Antioxidant content
Ginger (*Zingiber officinale* Roscoe)	*Phenolic Compounds*: gingerol, shogaol, and paradol *Flavonoids*: quercetin and kaempferol. *Gingerols and Shogaols*: primary bioactive compounds in fresh ginger and dried or heated ginger, respectively
Turmeric (*Curcuma longa*)	*Curcuminoids:* curcumin, demethoxycurcumin, and bisdemethoxycurcumin *Essential Oils:* Turmeric essential oils also contain antioxidants like turmerone, atlantone, and zingiberone
Galangal (*Alpinia galanga*)	*Phenolic Acids*: galangin, a flavonoid
Lesser Galangal (*Alpinia officinarum*)	*Essential oil*: methyl eugenol, chavicol, and eugenol
Black Ginger (*Kaempferia parviflora*)	Methoxyflavones, 6-shogaol, 6-gingerol, and oleoresin
Cardamom (*Elettaria cardamomum*)	Phenolic compounds, flavonoids, and essential oils (cineole and limonene)

both cardiac and vascular health. Finally, these plants are known to support the digestive system and positively influence metabolic functions. The following subsections delve into the scientific studies associated with each of these bioeffects, detailing the underlying mechanisms and research supporting their use in health maintenance and disease prevention.

3.1. Antioxidant properties

The Zingiberaceae family plants are notable for their high antioxidant content, which contributes to their health-promoting properties (Boyina et al., 2025). The Table 8 presents a comparison of antioxidant levels among well-known species, including ginger (*Z. officinale* Roscoe), turmeric (*C. longa*), galangal (*A. galanga*), and others, reveals that they exert their beneficial effects through diverse mechanisms (Table 8) (Alolga et al., 2022; Chen, T.V. et al., 2022; Hamidi et al., 2022). The awareness of the involved pathways and mechanisms helps understanding the health benefits associated with these plants (Semwal et al., 2015).

The diverse antioxidant actions of the compounds of Zingiberacea plants (Table 8) contribute to their health benefits and their potential to counteract oxidative stress.

Free radicals are molecules that contain unpaired electrons and can cause cellular damage. They can be scavenged by antioxidants neutralizing radicals by electron or hydrogen atom donation, maintaining the reactive species to prevent additional damage (Phaniendra, 2015; Tvrdá and Benko, 2020). Phenolic compounds found in Zingiberaceae plants, such as those in ginger, turmeric, and galangal, including gingerol-shogaol and curcumin, among others, neutralize various free radicals. These free radicals that are neutralized include superoxide anions ($O_2^{\bullet-}$), hydroxyl radicals ($HO^{\bullet}$), peroxyl radicals ($ROO^{\bullet}$), as well as reactive oxygen and nitrogen species (ROS and RNS) (Lushchak and Lushchak, 2021). Free radical play major roles in the development of age-related diseases (cardiovascular diseases, eye diseases, neurodegenerative diseases and sarcopenia) as they contribute to the formation of cholesterol oxide derivatives which have pro-oxidant, pro-inflammatory and cytotoxic properties(Ghzaiel et al., 2022). Therefore, the identification of antioxidants molecules is crucial, especially for the prevention of age-related diseases which have important economic and social impacts.

Fenton reaction ($(H_2O_2 + Me^{n+} \rightarrow HO^{\bullet} + OH^{-} + Me^{(n+1)+})$ where Me is a transition metal such as copper, iron, or aluminum) and Haber-Weiss reaction (in the presence of Fe^{2+}) ($O_2^{\bullet-} + H_2O_2 \rightarrow O_2 + HO^{\bullet} + OH^{-}$) can stimulate the formation of the extremely reactive hydroxyl radical ($HO^{\bullet}$). Antioxidants inactivate ROS and RNS and some of them can also bind to the metal ions, chelating them from participating in such reactions (Jomova et al., 2012; Kehrer, 2000). Various phenolic compounds play a role in chelating iron and copper ions, thereby inhibiting the formation of hydroxyl radicals and enzymes like xanthine oxidase (XO) (Limon-Pacheco and Gonsebatt, 2009).

Antioxidants can also modify gene expression associated with various signaling pathways. The Nuclear factor erythroid 2-related factor 2 (Nrf2) pathway is a significant part of cellular antioxidant mechanism. When activated, Nrf2 translocates to the nucleus and binds to antioxidant response elements (ARE) in DNA, enhancing the expression of genes coding for antioxidant enzymes and other protective molecules (He et al., 2020; Raghunath et al., 2018). As an illustration, ginger and turmeric enhance the activation of antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT), elevate reduced gluthathione (GSH) levels, interfere with pathways leading to lipid peroxidation, reduce nitric oxide production, and neutralize hydroxyl radicals. Additionally, ginger significantly interrupts the expression of nitric oxide synthase (*i*NOS), reduces the number of caspase-3 positive cells, diminishes tumour necrosis factor-α (TNF-α) expression, and through this action, directly scavenges the production of ROS (Ballester et al., 2023). Moreover, ginger extract increases the levels of specific antioxidant components due to the activation of Nrf2. Ginger is a key suppressant of the pro-apoptotic protein Bax and inhibitor of hydrogen peroxide (H_2O_2), malondialdehyde (MDA), and myeloperoxidase (MPO), while also activating phosphatidylinositol-3-kinase (PI3K) and protein kinase B (Akt) in B cells, thus protects cells against oxidative stress and inflammation-induced cell damage (Ozkur et al., 2022).

Ginger's anticancer and antioxidant properties are attributed to its antioxidant compounds, which include gingerols, flavonoids, and phenolic acids (Alolga et al., 2022). The phosphatidylinositol 3-kinase (PI3K)/AKT pathway plays a crucial role in regulating numerous important cellular processes. Activation of the PI3K/AKT signaling pathway is fundamental to the pathophysiology of various human cancers (Faes and Dormond, 2015). Ginger extract prevents the phosphorylation of AKT in human liver cell cultures, thereby protecting hepatocytes from damage caused by hydrogen peroxide (Romero et al., 2018). 6-gingerol effectively reduces the activity of XO, an enzyme involved in the production of uric acid. This inhibition helps to decrease the generation of harmful ROS (Koh et al., 2009).

Ginger extract is a potent bioactive agent against chronic inflammatory complications in the cells. It decreases the levels of pro-inflammatory markers such as the mammalian target of rapamycin (mTOR), NF-kB, interleukin (IL)-6, total antioxidant capacity (TAC), c-reactive protein (CRP), and tumor necrosis factor alpha (TNF-α) (Jalali et al., 2020). Certain research studies also demonstrates that gingerols can cause cell cycle arrest, leading to growth inhibition and a reduction in tumor size and load by upregulating CKDIs p21 (Cyclin-Dependent Kinase Inhibitors) involved in regulating cell cycle progression from G1 to S phase (Zadorozhna and Mangieri, 2021). Thus, ginger extract's properties in human cells resemble the action of anticancer drugs.

Lipid peroxidation is a harmful process of free radicals' attack against phospholipids in cell membranes, leading to cell disintegration. Antioxidants protect against lipid peroxidation by neutralizing harmful radicals and minimizing the size of invasion (Halliwell and Chirico, 1993; Valgimigli, 2023; Yin et al., 2011). The active antioxidative compounds of Zingiberaceae family plants prevent cells lipid peroxidation through multiple mechanisms. Curcumin's actions in the cellular metabolism are for example proven to reduce ROS concentration, and neutralize advanced glycation end products and lipid peroxidation (Alizadeh and Kheirouri, 2019). Curcumin action is known for activation of sirtuin (SIRT)1 and SIRT3, but at the same acting against SIRT2 activation. It is curcumin's indirect antioxidant effect, because of SIRT1 and SIRT3 preventive features, whereas SIRT 2 enhances pro-oxidative actions (Alizadeh and Kheirouri, 2019). SIRT1 is a protein that reduces the levels of ROS by inhibiting protein 65, which suppresses the NF-κB signaling pathway. SIRT1′s location in the nucleus enables it to activate the FOXO3a transcription factors, leading to increased production of the antioxidant genes such as CAT and SOD (Ballester et al., 2023). Mitochondrial SIRT3 plays a crucial role in maintaining cellular

redox balance by activating various key enzymes (Lai et al., 2013).

Curcumin also acts by inhibiting enzymes involved in inflammation, such as cyclooxygenase-2 (COX-2) (Vasanthkumar et al., 2019) and leukotrienes (LTs), adhesion molecules and matrix metalloproteinases (MMPs). Curcumin has a broad range of anti-inflammatory effects, including reducing inflammation caused by ROS(Vaiserman et al., 2020). It decreases the expression of toll-like receptor 4 (TLR4) and inhibits the activation of mitogen-activated protein kinase (MAPK) and NF-κB pathways, as demonstrated in rat vascular smooth muscle cells (Vasanthkumar et al., 2019).

The primary bioactive compounds in cardamom are 1,8-cineole and α-terpinyl acetate. These componds have multiple applications in food and medicine, and their yields are influenced by multiple factors, including processing techniques, essential oil extraction methods, and various agronomic conditions (Hamdy et al., 2025). The antioxidant properties of cardamom lead to decreased levels of malondialdehyde (MDA), advanced protein oxidation products (APOP), and nitric oxide (NO) in the liver and plasma. Additionally, the presence of cellular antioxidants such as CAT, SOD, and GSH help in mitigating oxidative stress. In rat supplementation experiments, the cardamom supplied group showed a notable increase in CAT, SOD, and GSH activity (Rahman et al., 2017).

In vitro studies are crucial for understanding the antioxidant activities of compounds found in Zingiberaceae plants such as ginger, turmeric, and galangal. These studies typically involve various assays and experimental setups to evaluate the antioxidant potential of plant extracts, isolated compounds, and essential oils. Table 9 broadly explains different *in vitro* studies on antioxidant activiy in Zingiberaceae plants.

Accumulated evidence has shown that a handful of Zingiberaceae plants can help provide ionizing radiation protection in different ways. Specifically, *Amomum subulatum* extracts may help mitigate radiation-induced lung injury, suggesting its potential as a nutraceutical for preventing radiation toxicity(Drishya et al., 2023).

In vivo research works employing animal models also significantly aid in understanding how extracts of plants and chemicals function within living animals, including their bioavailability, metabolism, and overall impact on oxidative stress-related disorders including liver injury, diabetes, neurodegenerative disorders, colitis, arthritis, and hypertension (Tao et al., 2020; Yeung et al., 2024). For example in a work involving ginger supplementation, ginger extract (100 mg/kg body weight) was given to rats once daily for four weeks and carbon tetrachloride (CCl_4) was used to produce liver injury in rats. The ginger suplementation showed a dramatic decrease in oxidative stress indicators, including MDA, while increasing the quantified antioxidant enzyme (SOD and CAT) activities (Amran et al., 2015). In another work, ginger extract (200 mg/kg body weight) was administered to diabetic rats for 8 weeks in streptozotocin-induced diabetic rat model, and the supplementation dramatically lowered oxidative stress indicators and lipid peroxidation levels in cardiac tissues, increasing the activity of

Table 9
In vitro studies on the antioxidant potential of selected Zingiberaceae plants.

***In vitro* assay**	**Principle**	**Procedure**	**Potency of selected Zingiberaceae plants**	**References**
DPPH (2,2-diphenyl-1-picrylhydrazyl)Radical Scavenging	DPPH: the ability of antioxidants to scavenge the stable DPPH radical, resulting in colour change from purple to yellow.	Plant extracts + DPPH solution. A decrease in absorbance measured spectrophotometrically. More the colour change better the scavenging activity.	Turmeric & Black ginger: High; IC_{50} (1 to 5 μg/mL) Ginger: Moderate to high; IC_{50} (10 to 50 μg/mL) Galangal: Moderate; IC_{50} (20 to 60 μg/mL) Cardamom: Moderate; IC_{50} (50 to 100 μg/mL)	(Aloliqi, 2022; Fedorova et al., 2014)
FRAP Assay (Fe^{2+} equivalents)	FRAP (Ferric Reducing Antioxidant Power) assay measures the ability of antioxidants to reduce ferric ions (Fe^{3+}) to ferrous ions (Fe^{2+}), resulting in a colour change.	Plant extracts are mixed with a ferric-tripyridyltriazine complex, and the increase in absorbance is measured. A higher absorbance indicates a stronger reducing power.	Turmeric & Black Ginger: High, >2mM Fe^{2+} eq Ginger, Cardamom & Galangal: Moderate, 1–1.5 mM Fe^{2+} eq	(Selmeci et al., 2005; Shamsabadi et al., 2023)
ABTS (2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) Radical Cation Decolorization [Trolox equivalent antioxidant capacity (TEAC) values]	ABTS assay: generate the blue-green ABTS + radical cation, which is reduced by antioxidants to a colorless form	Plant extracts are added to the ABTS + solution. Reduction in absorbance is measured. The higher the reduction, the greater the antioxidant activity.	Turmeric & Black Ginger: High, TEAC > 2 mM. Ginger, Cardamom & Galangal: Moderate, TEAC 1–1.5 mM	(Chakotiya et al., 2017; Mao et al., 2019)
Oxygen Radical Absorbance Capacity (ORAC Values)	ORAC assay evaluates the ability of antioxidants to scavenge peroxyl radicals generated by the thermal decomposition of AAPH (2,2′-azobis(2-methylpropionamidine) dihydrochloride).	Plant extracts are mixed with a fluorescent probe and AAPH, and the fluorescence decay is measured over time. The antioxidant capacity is quantified based on the inhibition of fluorescence decay.	Turmeric & Black Ginger: High, ORAC > 10,000 μmol TEAC/gm Ginger, Cardamom & Galangal: Moderate, ORAC 5000–8000 μmol TEAC/gm	(Huh et al., 2018)
Total Phenolic Content (TPC) [GAE (gallic acid equivalents)/gm]	TPC assay measures the TPC in plant extracts using the Folin-Ciocalteu reagent, which reacts with phenolics to produce a blue colour.	Plant extracts + Folin-Ciocalteu reagent + sodium carbonate, and the absorbance is measured.	Turmeric & Black Ginger: High, 200–400 GAE/gm Ginger, Cardamom & Galangal: Moderate, 150–250 GAE/mg	(Babaahmadi-Rezaei et al., 2020; Danciu et al., 2015)
Total Flavonoid Content [QE (quercetin equivalents)/gm]	TFC assay measures the total flavonoid content in plant extracts using colorimetric methods, typically involving aluminum chloride.	Plant extracts are mixed with aluminum chloride, and the absorbance is measured. The results are expressed as quercetin equivalents (QE).	Turmeric & Black Ginger: High, >500 mg QE/gm Ginger, Cardamom & Galangal: Moderate, >100 mg QE/gm	(Foshati et al., 2023; Lakhan et al., 2015)

glutathione peroxidase (GPx) and decreasing heart fibrosis and inflammation (Li, Y. et al., 2012). Similarly, recent findings show that dietary ginger supplementation modulates liver antioxidant enzyme systems in mice in a dose- and age-dependent manner, further supporting its role in systemic oxidative stress regulation (Matin, M. et al., 2025).

In respect of *in vivo* tests with curcumin, mice with Parkinson's were given curcumin (50 mg/kg body weight) for 4 weeks after being treated with 6-hydroxydopamine (6-OHDA), which resulted in dramatically reducedoxidative stress indicators in brain tissues while increasing the amounts of antioxidant enzymes, and also decreasing neuronal loss and enhancing motor skills (Li, Y. et al., 2012). In another work, mice with dextran sulfate sodium (DSS)-induced colitis were given curcumin (100 mg/kg body weight) for 10 days, resulting in lowering oxidative stress indicators while increasing the activity of antioxidant enzymes in colon tissues (Guo et al., 2022).

To explore the hepatoprotective properties of galangal extract in a rat model of alcohol-induced liver injury, rats were given galangal extract (200 mg/kg body weight) for 6 weeks while also consuming chronic alcohol, whereby the galangal extract effectively decreased oxidative stress indicators such as MDA while increasing antioxidant enzyme activity in liver tissues (Hemabarath et al., 2008). In another work, rats with collagen-induced arthritis (CIA) were treated with galangal extract (100 mg/kg body weight) for 4 weeks and showed a dramatic decrease in oxidative stress indicators while increasing the activity of antioxidant enzymes in joints (Raut and Shaji, 2022).

In respect of *in vivo* tests with black ginger, in a mice experiment, the animals were administered black ginger extract (100 mg/kg body weight) for 8 weeks following amyloid-beta peptide treatment, successfully reducing oxidative stress markers but raising antioxidant enzyme levels in cerebral tissues and improving cognitive performance and reducing amyloid β plaque deposition (Temviriyanukul et al., 2023).

Cardamom also showed effectiveness *in vivo*, with cardamom extract (100 mg/kg body weight) administered to spontaneously hypertensive rats (SHR) for a period of 12 weeks, resulting in lowered oxidative stress indicators in blood and cardiac tissues (Yahyazadeh et al., 2021).

Ginger contains gingerol and zingerone, which have established valuable bioactivity, including anti-inflammatory, antioxidant and immunomodulatory effects. The results of an experiment on mice animal models showed that oral supplementation of 6-gingerol in a dose ranging from 50 to 75 mg/kg body weight over three weeks led to decreased blood glucose and oxidative stress levels, and better insulin sensitivity (Ali et al., 2018).

Biomarkers for oxidative stress provide a crucial understanding of how antioxidant therapies from Zingiberaceae plants such as ginger, turmeric, and galangal influence cells and biomolecules. Thus, several studies have shown that ginger, galangal, black ginger, cardamom and curcumin extracts significantly reduce MDA and thiobarbituric acid reactive substances (TBARS) levels in various animal models, indicating a reduction in lipid peroxidation and oxidative stress (Aloliqi, 2022; Razak et al., 2023).

Protein carbonyls formed by the oxidation of protein side chains indicate oxidative damage to proteins (Fedorova et al., 2014). Advanced oxidation protein products (AOPP), byproducts of protein oxidation are also used as markers of oxidative stress (Fedorova et al., 2014). Treatment with ginger, black ginger, curcumin, cardamom and galangal extract has been reported to decrease protein carbonyl levels, suggesting protection against protein oxidation (Selmeci et al., 2005). Zingiberaceae supplementation has been found to reduce levels of 8-OHdG (Shamsabadi et al., 2023) and DNA strand breaks, indicating additional protective effects on DNA integrity.

3.2. Anti-inflammatory effects

In addition to their antioxidant capacity, Zingiberaceae plants have been widely studied for their anti-inflammatory effects, which are closely linked through overlapping molecular pathways and phytochemical mediators. Multiple research works indicated significant anti-inflammatory potential for *Z. officinale*, *C. longa*, *A. galanga*, and *E. cardamomum*, as well as single compounds isolated from these plants.

Many studies demonstrated versatile anti-inflammatory action for turmeric obtained from *C. longa* rhizomes as well as for its major bioactive constituent curcumin (Iweala et al., 2023). A study by Das *et al.* reported that turmeric inhibits COX and LO enzymes, which produce ROS and are implicated in the inflammatory response, and further examined the potential of silver nanoparticles derived from turmeric oil that may be promising anti-inflammatory agents (Das et al., 2019). Another study found that fermented turmeric exhibits anti-inflammatory effects by reducing the levels of nitric oxide (NO), prostaglandin E2 (PGE-2), COX-2, inducible nitric oxide synthase (iNOS), NF-κB, tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6) in LPS-treated RAW 264.7 cells (Kim et al., 2017). This finding is also supported by Asanga *et al.*, who showed that *C. longa* rhizomes inhibit both acute and sub-acute inflammation by targeting COX-1, COX-2, phosphodiesterase-4B, and antioxidant enzymes (Asanga et al., 2024). Additionally, Lee et al. demonstrated that a combination of turmeric and *Allium hookeri* effectively suppresses inflammatory cytokines (IFN-γ, IL-1β, IL-6, IL-13, and IL-17) by inhibiting the NF-κB/COX-2 pathway and iNOS (Lee et al., 2020). Furthermore, Yong *et al.* reported that turmeric fermented with *Lactobacillus fermentum* exhibits stronger anti-inflammatory properties than unfermented by suppressing the expression of the c-Jun N-terminal kinase (JNK) signal pathway (Yong et al., 2019). A study by Meizarini *et al.* explored the anti-inflammatory effects of turmeric on COX-2 receptors using a wound dressing assay model, and the results demonstrated that turmeric combined with zinc oxide significantly reduced TNFα expression levels, showing greater anti-inflammatory activity compared to turmeric combined with eugenol (Meizarini et al., 2018). To further highlight turmeric's anti-inflammatory potential, Toden *et al.* examined turmeric oil and found that it protected against dextran sulphate sodium (DSS)-induced colitis by upregulating anti-inflammatory cytokines such as IL-10 and IL-11, as well as FOXP3 (Toden et al., 2017). Similarly, modified pectic polysaccharide from turmeric significantly reduces inflammation and induced anti-ulcer effects by inhibiting IL-8, TNFα, and NF-κB, while increasing IL-10 and reducing Galectin-3 and H^+ K^+-ATPase expression (Rajagopal et al., 2018). A study by Akinyemi and Adeniyi also found that turmeric oil inhibited acetylcholinesterase and adenosine deaminase activity and suppressed cytokine and inflammatory biomarker production (such as IL-6, IL-10, and TNF-α) in cadmium-treated rats, suggesting its potential as an anti-inflammatory agent against cadmium-induced neurotoxicity (Akinyemi and Adeniyi, 2018). Similarly, another study reported that turmeric effectively lowered levels of inflammatory markers IL-6 and TNF-α by LPS-stimulated polymorphonuclear cells, highlighting its anti-inflammatory properties (Qabaha et al., 2017). Furthermore, research on bisabolane-type sesquiterpenoids from turmeric rhizomes showed that these compounds inhibit inflammatory cytokine expression by modulating the NF-κB/MAPK and RIG-1/STAT-1/2 signaling pathways *in vitro*, reinforcing turmeric's role in anti-inflammatory activity (Ti et al., 2021). In line with these findings, another study reported that turmeric significantly reduces IL-6 and TNF-α gene expression and decreases NO production in peritoneal macrophages, further underscoring its potent anti-inflammatory effects (Cardenas Garza et al., 2021). Further, a hot water extract of *C. longa* has been shown to protect against liver damage and reduce hepatic oxidation and inflammatory cytokines, indicating its potential use in treating ethanol-induced liver damage (Uchio, R. et al., 2017). Additionally, nanoparticles formulations have been found to enhance bioavailability and absorption of turmeric, demonstrating notable anti-inflammatory activity (Pareek et al., 2019). In respect of bioactive constituents of turmeric, diarylheptanoids (Sun et al., 2020), a compound group including curcuminoids, are demonstrated to be responsible for numerous pharmacological effects, including anti-inflammatory action

(Anand et al., 2008; Evans, 2002; Li, H. et al., 2020; Prasad et al., 2014). Thus, recent research further supports the benefits of oral *C. longa* curcuminoids (curcumin, demethoxycurcumin, and bisdemethoxycurcumin) application in reducing carrageenan-induced acute paw inflammation in rats (Islam et al., 2024). Additionally, an ethanolic extract of *C. longa* offers dose-dependent protection against aspirin-induced gastric ulcers, highlighting its therapeutic versatility (Savaringal and B, 2018). Similarly, turmeric-derived bisacurone at a concentration of 50 μg in high-fat diet-fed BALB/c mice decreased pro-inflammatory cytokines and modulated inflammation by inhibiting NF-κB-mediated pathways (He et al., 2023). Furthermore, nano-encapsulated curcuminoid preparations with poly(vinyl pyrrolidone) effectively inhibited inflammatory and oxidative responses in Croton oil-induced cutaneous inflammation in male Swiss mice, demonstrating improved bioavailability and anti-inflammatory effects at a dose of 200 μg in 70 % acetone (Lima et al., 2021).

Z. officinale has a long history of use in treating several inflammatory disorders (Shahrajabian et al., 2019). These disorders, though diverse, share chronic inflammation as a primary underlying cause. Among these conditions associated with chronic inflammation are rheumatic diseases such as rheumatoid arthritis, respiratory diseases like asthma, neurodegenerative diseases, and periodontal disease (Furman et al., 2019). Scientific evidence suggests that ginger extracts and their active compounds, including gingerols, shogaols, and zingerone, among others, possess potent and versatile anti-inflammatory properties (Ballester et al., 2022). Neuroinflammation is a well-established contributor to the progression of neurodegenerative diseases. Several studies have highlighted ginger and its compounds as potential anti-inflammatory agents for preventing conditions such as Alzheimer's and Parkinson's (Arcusa et al., 2022). Specifically, 6-shogaol has exhibited neuroprotective properties in both *in vitro* and *in vivo* models (Ha et al., 2012; Na et al., 2016). This compound exerts its neuroprotective action by reducing levels of inflammatory markers (e.g., PGE2, TNF-α, IL-1β, IL-6, iNOS, and COX-2), inhibiting the NF-κB and MAPK/ERK signaling pathways, and activating the PPAR-γ transcription factor (Ha et al., 2012; Han et al., 2017). Other ginger compounds, like zerumbone, promoted an anti-inflammatory microglial phenotype by modulating the MAPK/NF-κB signalling pathways in LPS or Aβ1-42 stimulated primary microglial cells. These findings were confirmed in *in vivo* using transgenic APP/PSEN1 mice (Li, L. et al., 2020). Regarding respiratory diseases, several studies have demonstrated the anti-inflammatory effects of ginger and its active compounds in murine asthma models. Thus, ginger extracts suppressed the Th2-mediated immune response in ovalbumin-induced allergic asthma (Khan et al., 2015). Furthermore, in a house dust mite-induced asthma model, ginger extract and 6-shogaol reduced inflammation by promoting airway smooth muscle relaxation and inhibiting chronic inflammation pathways (Yocum et al., 2020). Additionally, 6-gingerol enhanced dexamethasone's effects by reducing immune cell levels and pro-inflammatory markers (Ajayi et al., 2022). Moreover, zingerone has exhibited anti-inflammatory actions in both *in vitro* and *in vivo* models of asthma through the upregulation of the AMPK/Nrf2/HO-1 signaling pathway (Zhu et al., 2021). Ginger has also been studied for its anti-arthritic properties. *In vitro* studies have shown that ginger extract, as well as 6-shogaol and zingerone, decrease the levels of pro-inflammatory cytokines and reduce the expression of matrix metalloproteinase-2 (MMP-2), MMP-9, and MMP-13, representing markers of severity in rheumatoid arthritis, in fibroblast-like synoviocytes (Frondoza et al., 2004; Li, N. et al., 2023; Ribel-Madsen et al., 2012; Ruangsuriya et al., 2017; Xue et al., 2014). Additionally, *in vivo* models of the streptococcal cell wall (SCW)-induced arthritis and collagen-induced arthritis (CIA) in mice; and adjuvant-induced arthritic (AIA) in rats, have demonstrated that ginger extracts and its compounds (6-shogaol, 8-shogaol or cedrol) also reduce paw edema volume, joint inflammation, cartilage deterioration, and bone loss (Funk et al., 2009; Hwang et al., 2017; Zhang et al., 2021). Randomized clinical trials have been conducted on rheumatoid arthritis and osteoarthritis, also showing a reduction in joint inflammation in humans (Aryaeian et al., 2019; Jo et al., 2022; Naderi et al., 2015). Similarly, clinical trials have been conducted using ginger extract to treat gingival pain and inflammation, showing no significant differences compared to ibuprofen (Menon et al., 2021). Studies using an *in vivo* Wistar rat model also suggested that 6-shogaol reduces periodontal inflammation and bone loss by modulating RANKL/OPG balance (Bezirci et al., 2024).

While the genus *Alpinia* comprises more than 500 species, of which only about 35 are known to have pharmacological properties, *Alpinia officinarum* and *Alpinia galanga* are particularly notable for their anti-inflammatory properties (Youn et al., 2024). Several *in vitro* studies have been carried out to determine the anti-inflammatory activity of *Alpinia* species. A study using a hydroalcoholic extract of *A. galanga* rhizomes showed that it down-regulates the release of pro-inflammatory mediators (IL-6, TNF-α, NO, and ROS) and stimulates the release of the anti-inflammatory mediator IL-10 in RAW 264.7 cells stimulated with LPS, with the anti-inflammatory effect occurring through the modulation of TLR4 and the JAK/STAT pathway (George et al., 2021). Similarly, other studies showed that an extract of *A. officinarum* rhizomes inhibited NO in LPS-induced RAW 264.7 cells (Lee et al., 2009) and in LPS-activated mouse peritoneal macrophages (Abubakar et al., 2018; Matsuda et al., 2006). This effect is of importance, since excessive NO produced by iNOS is implicated in several inflammatory conditions, including arthritis, asthma, and inflammatory bowel disease (Cinelli et al., 2020). The anti-inflammatory properties of *Alpinia* species have also been demonstrated in various animal models. Thus, Lee et al. showed that an ethanolic extract of *A. officinarum* rhizomes has anti-inflammatory effects on acute and chronic arthritis in rats (Lee et al., 2009). The extract showed an acute anti-inflammatory effect by reducing edema volume in rats with carrageenan-induced arthritis. Additionally, it exhibited anti-inflammatory, anti-rheumatic, and anti-nociceptive activities in Freund's complete adjuvant-stimulated chronic arthritis in rats (Lee et al., 2009). Furthermore, not only the anti-inflammatory activity of the extract has been demonstrated, but many studies have focused on the activity of the isolated constituent galangin. Galangin (3,5,7-trihydroxyflavone), a flavonoid with diverse anti-inflammatory properties, is found in the leaves, aerial parts, and rhizomes of *A. officinarum*, and in the rhizomes of *A. galanga*, along with other bioactive compounds like galangol, kaempferide, and alpinin (Basri et al., 2017; George et al., 2021). Biological activity and phytochemical studies have also shown that other *Alpinia* species share similarities with *A. officinarum*. As previously mentioned, chronic inflammation is seen as a key factor contributing to various human diseases, including neurodegenerative disorders, type II diabetes, arthritis, and more (George et al., 2021). Galangin in particular, exhibits an anti-inflammatory effect under neuroinflammatory conditions both *in vitro* and *in vivo* by inhibiting the expression of iNOS, TNF-α, IL-6, IL-1β, and COX-2 in LPS-stimulated BV-2 microglial cells (Al-Abd et al., 2017; Choi et al., 2017; Zhang, F. et al., 2023). The anti-inflammatory effects of galangin are proposed to involve the inhibition of MAPK, PI3K/Akt, and JNK1/2 phosphorylation, the activation of Nrf2/CREB and PPAR-γ signaling pathways, and the inactivation of the NF-κB pathway (Choi et al., 2017; Kim et al., 2019; Zhang, F. et al., 2023). In diabetes, chronic hyperglycemia leads to inflammation by activating pro-inflammatory pathways and increased oxidative stress. In this context, galangin reduced liver oxidative stress and inflammation in fructose-fed rats by downregulating the TNF-α, IL-6, and NF-κβ pathways (Sivakumar and Anuradha, 2011). Similarly, in a streptozotocin-induced diabetic model, galangin reduced ROS, IL-6, IL-1β, and TNF-α levels, while enhancing antioxidant defence mechanisms (GSH, SOD, and CAT) and inhibiting NF-κB pathway in the kidney (Aladaileh et al., 2021). These studies support the anti-inflammatory effects of galangin, which could be a direct consequence of the inhibitory effect against the overproduction of ROS caused by diabetes (Honmore et al., 2016).

Multiple studies also have shown that *E. cardamomum* exerts an anti-inflammatory effect due to its richness in biologically active compounds,

including 1,8-cineole and its esters, limonene, α-terpinyl acetates and polyphenols (Abdullah et al., 2022). Studies on LPS-stimulated cells have shown that both aqueous and alcoholic extracts of *E. cardamomum* increase the expression of anti-inflammatory cytokines and receptors (IL-4 and IL-10, LXRa and PPARγ) and decrease proinflammatory cytokines (IL-6, TNF-α, IL-1β, and IL-8) and NO production (Cardenas Garza et al., 2021; Mueller et al., 2010; Souissi et al., 2020; Sreedharan et al., 2023). These inflammation-modulating effects are dose-dependent (Majdalawieh and Carr, 2010). The key bioactive cardamoṁs compound 1,8-cineole has also shown the ability to inhibit the activity of both COX-1 and COX-2 (Beer et al., 2017). *E. cardamomum* extract has shown analgesic and anti-inflammatory effects in experimental models of acute inflammatory pain (Arpitha et al., 2019; Mehjabeen et al., 2015; Sermugapandian et al., 2018). These effects are attributed to its dose-dependent ability to decrease the levels of TNF-α, IL1β and IL6, COX-2 expression, and are similar in efficacy to standard analgesics like diclofenac (10 mg/kg) (Sermugapandian et al., 2018). Cardamom extracts have also been able to prevent acute liver damage caused by acetaminophen in rats by modulating inflammation (Alkhalifah et al., 2022). Bioactive components of cardamom (1,8-cineole, cardamonin) have also been effective in modulating acute inflammation in experimental models of lung injury (Zhao et al., 2014), colitis (Santos et al., 2004), pancreatitis (Lima et al., 2013), shock liver damage (Santos et al., 2001) or atopic dermatitis (Yoo et al., 2020), improving tissue injury and decreasing inflammatory cell infiltration, TNF-α, IL-6, IL-1β levels, NF-κB, p65, and TLR4 expression, as well as MMP-9 activity and tissue production of Th2-derived cytokines. The consumption of 3 g of cardamom per day for at least 10 weeks has been shown to reduce inflammatory markers, such as TNF-α, IL-6, and hs-CRP, in various diseases characterized by chronic inflammation which are documented in conditions such as type 2 diabetes (Azimi et al., 2014; Azimi et al., 2016; Ghazi Zahedi et al., 2021; Zahedi et al., 2022), overweight, hyperlipidemia and pre-diabetes (Fatemeh et al., 2017; Kazemi et al., 2017), non-alcoholic fatty liver disease (Daneshi-Maskooni et al., 2018) or polycystic ovary syndrome (Cheshmeh et al., 2022b). Additionally, a drink rich in cardamom rhizome consumed for 2 months demonstrated similar anti-inflammatory effects in women with atherosclerosis (Winarsi and Susilowati, 2018). Moreover, a standardized cardamom extract supplement has been found effective in managing cytokine storms in COVID-19 patients by reducing IL-6, TNF-α, and IL-10 gene expression after just 5 days of consumption (500 mg, three times daily for 10 days) (Shakeeb et al., 2022). Furthermore, the bioactive component of cardamom, 1,8-cineole, administered at a dose of 200 mg three times daily as a concomitant therapy for 6 months during winter, has been effective in reducing airway inflammation in chronic obstructive pulmonary disease (COPD) (Worth et al., 2009). Experimental studies also indicate that cardamom can prevent lung injury caused by pan masala, showing a direct link between its effects and inflammation modulation at the pulmonary level, including reductions in edema, fibrin, and erythrocyte extravasation, and epithelial degeneration and necrosis in terminal bronchioles and alveoli (Kumari and Dutta, 2013). *E. cardamomum* has also been shown to be effective in situations of neuroinflammation (Gomaa et al., 2019). Thus, in an experimental model of dementia associated with type 2 diabetes, daily administration of cardamom extract, which is high in terpenoid compounds, for 8 weeks led to a dose-dependent reduction in neuroinflammation. This was evidenced by lower hippocampal levels of proinflammatory cytokines, including TNF-α, IL-1β, and IL-6, and was accompanied by improvements in cognitive functions such as learning and memory in the treated animals (Gomaa et al., 2019). Similarly, in an experimental stroke model, 14 days of treatment with varying doses of *E. cardamomum* essential oil and its primary component, 1,8-cineole, resulted in a dose-dependent reduction of plasma MDA and NO levels, as well as a significant decrease in the expression of Caspase 3, IL-1β, TNF-α, and iNOS in the cerebral cortex, with more pronounced effects for 1,8-cineole (Farivar et al., 2020). Furthermore, pretreatment with 1,8-cineole in inflammation induced by Aβ (25–35) in differentiated PC12 cells led to reduced mitochondrial membrane potential, lower levels of ROS and NO, decreased proinflammatory cytokines, and reduced expression of NOS-2, COX-2, and NF-κB (Khan et al., 2014). Finally, cardamom may also be beneficial in treating other chronic painful conditions associated with inflammation. Cardamonin has been shown to inhibit chondrocyte ferroptosis, a process involved in the development of osteoarthritis. Additionally, it helps prevent cartilage damage and reduces the levels of inflammatory mediators such as MMP13, iNOS, and COX-2 (Gong et al., 2023). Furthermore, in a culture model of chronic dermal inflammation, cardamom essential oil significantly inhibited skin cell proliferation and the expression of vascular cell adhesion molecule 1 (VCAM-1) and macrophage colony-stimulating factor (M−CSF) (Han and Parker, 2017).

Overall, the evidence consistently highlights the anti-inflammatory efficacy of Zingiberaceae plants across *in vitro*, *in vivo*, and even human studies, supporting their potential as natural therapeutic agents for managing chronic inflammatory conditions.

3.3. Antimicrobial properties

Beyond inflammation, Zingiberaceae species also exhibit broad-spectrum antimicrobial activity, supporting their traditional use in treating infections and preserving food and herbal formulations. Antimicrobial resistance poses a significant global health challenge, driving the search for new antimicrobial agents from natural sources (Prestinaci et al., 2015). Plants from the Zingiberaceae family have long been used in traditional medicine for their antimicrobial effects (Habsah et al., 2000). This section briefly discusses the scientific evidence for the antibacterial, antifungal, and antiviral properties of key Zingiberaceae species, including *A. galanga*, *Z. officinale*, *C. longa*, and *E. cardamomum*. *In vitro* and *in vivo* studies evaluating the antimicrobial activity of various extracts and compounds isolated from these plants against a range of pathogenic microorganisms are shortly concisely presented, discussing along with their potential plausible mechanisms of action and potential therapeutic applications.

Many published studies reported that *A. galanga* extracts and its essential oils demonstrate significant antibacterial activity. The essential oil, rich in piperitenone and limonene, was active against Gram-negative bacteria by virtue of its ability to disrupts membrane permeability (MIC and MBC values of 2.0 mg/mL for *Shigella sonnei* and *Salmonella typhi*, 4.0 mg/mL for *Escherichia coli*, 8.0 mg/mL for *Staphylococcus aureus*) (Prakatthagomol et al., 2011). Antibacterial activity of plant extracts was shown to decrease with decreasing solvent polarity, with the polar solvent methanol reveling to be optimal (Rao et al., 2010). Furthermore, most studies showed that rhizome has the highest antibacterial activity, especially against Gram-positive bacteria. *Bacillus. subtilis* was the most sensitive to methanol rhizome extract, whereas *Pseudomonas aeruginosa* was the most resistant (methanol extract's MIC values 0.040–0.640 mg/mL; MBC values 0.080–2.56 mg/mL) (Rao et al., 2010). Another study demonstrated that rhizome extracts (25 μg/mL) inhibited *Mycobacterium tuberculosis* growth (>80 %) upon the use of either acetone or ethanol as solvents for extraction (Gupta et al., 2014). Nevertheless, while most studies attribute higher antibacterial activity to rhizome, Tang et al. (2018) demonstrated that flower methanolic extract had even higher polyphenol content than the respective rhizome extract, and enriched fraction of the methanolic extract exhibited higher inhibitory activity against *S. aureus* (MIC_{50} value 79 μg/mL) than against *Listeria monocytogenes* (MIC_{50} value 158 μg/mL) (Tang et al., 2018). 1′-acetoxy eugenol acetate was identified as primary phytochemical responsible for the antibacterial activity in the latter study.

A. galanga rhizome extracts has also been shown to exhibit antifungal properties in several studies. The n-hexane extract and its fraction V, both rich in (2,6-dimethylphenyl)borate, displayed activity against *Malassezia furfur* (MIC values 0.04–0.08 mg/mL and 0.313–2.5 % (v/v), respectively) (Laokor and Juntachai, 2021). Moreover, in another study

ethanol extracts of *A. galanga* rhizome was active against three yeast-like and seven filamentous pathogenic fungi (Ficker et al., 2003). Additionally, chloroform extract of the rhizome demonstrated activity against *Cryptococcus neoformans* and *Microsporum gypseum* (MIC value 128 and 16 μg/mL, respectively) (Phongpaichit et al., 2005). Furthermore, several terpenoid compounds isolated from the plant demonstrated anti-*Candida* spp. activity (Haraguchi et al., 1996; Morita and Itokawa, 1988).

In addition to antibacterial and antifungal activities, interstingly 1′S-1′-acetoxychavicol acetate from *A. galanga* rhizome inhibited HIV-1 replication (Tamura et al., 2009; Ye and Li, 2006).

Z. officinale rhizome is well-documented for its antimicrobial properties (Aleem et al., 2020; Harun and Mohamad, 2023). From a total of 40 *in vitro* studies on antibacterial activities of ginger rhizome, 38 showed noticeable activity (Abdalla and Abdallah, 2018). However, most positive results were not as effective as the reference antibiotics. These findings exhibited significant variations and inconsistencies, suggesting that factors such as extraction procedures and the geographical locations from where the plants were collected greatly influenced the results (Abdalla and Abdallah, 2018). The 50 % hydroethanolic extract showed good antibacterial activity against seven different bacterial strains, with MIC values ranging between 31.25 and 62.50 μg/mL (Abd-Alrahman et al., 2013). Among the chloroform, methanol, and aqueous extracts of *Z. officinale* tested against different bacterial and fungal strains, the methanol extract exhibited the highest activity, while the aqueous extract showed weak or no activity (Bashir et al., 2015), suggesting that the antimicrobial agents could be polar and semi-polar compounds. Moreover, the crude extract and methanolic fraction demonstrated antibiofilm formation, significant MIC values, a rapid decrease in bacterial viable counts *in vitro*, and reduced pathogenicity of *Streptococcus mutans* (Hasan et al., 2015). The *Z. officinale* essential oil inhibited the proliferation of 15 bacterial strains, 3 yeasts, and 4 mycelial fungi, with MICs ranging from 0.125 to 2.0 mg/mL, demonstrating both bactericidal and fungicidal actions (López et al., 2017). Essential oil in both *in vitro* and *in vivo* studies exhibited high antibacterial activity, but one of the *in vitro* studies particularly revealed activity against 18 multi-drug resistant Gram-negative bacteria (Vaz et al., 2022). Furthermore, significant antifungal activity of *Z. officinale* essential oil against several phytopathogenic fungi was reported (MIC value of 1 μL/mL) (Abdullahi et al., 2020). Several studies also suggest the potential antiviral activity of *Z. officinale* against various viruses including enterovirus, rhinovirus, hepatitis C and SARS-CoV-2 (José-Rita et al., 2022; Mbadiko et al., 2020).

Various *Curcuma* species have been also studied for their antibacterial properties (Adamczak et al., 2020). For example, *C. longa* has been reported by many researchers to exhibit significant antibacterial activity (Mun et al., 2013; Odo et al., 2023; Rattanasuk et al., 2023; Suwal et al., 2021). Similarly, *C. aromatica* (Al-Reza et al., 2011; Xiang et al., 2017) and *C. caesia* (Borah et al., 2019; Thomas and Jose, 2014) have demonstrated notable antibacterial effects. Both aqueous and ethanolic extracts of *Curcuma* species are effective against common pathogens, multidrug-resistant bacteria, and biofilms. In addition to the extracts, oil byproducts and purified curcumin from *Curcuma* species displayed significant antibacterial properties. *C. longa* extract inhibits the growth of several bacteria including *S. aureus*, *E. coli*, and *Bacillus* species (Odo et al., 2023). In a recently published study, a purified product from *C. longa*, curcumin, was demonstrated to be active against *Salmonella Typhimurium*, a bacterium causing salmonellosis (Gulel et al., 2024). Moreover, curcumin also demonstrated antimicrobial activity against drug-resistant bacteria like methicillin-resistant *S. aureus* (MRSA) (Mun et al., 2013) and multidrug-resistant *K. pneumoniae* (MDR-K) with MIC and minimum bactericidal concentration (MBC) of 0.195 and 6.25 mg/ml, respectively (Rattanasuk et al., 2023). Additionally, an ethanolic extract of *C. longa* disrupted the biofilms of *P. aeruginosa* and *S. aureus* isolates at concentrations of 0.5–2 mg/ml (Suwal et al., 2021). *Curcuma* extracts have also been shown to possess antifungal properties. The ethanolic extract of *C. longa* in particular was active against pathogenic fungi such as *Cryptococcus neoformans* (MIC 128 μg/mL) and *Candida albicans* (MIC 256 μg/mL) (Ungphaiboon et al., 2005). Furthermore, it exhibited antifungal activity against pathogenic fungi including *Alternaria alternate* (EC_{50} 0.188 mg/mL), *Fusarium chlamydosporum* (EC_{50} 0.1742 mg/mL), *Fusarium graminearum* (EC_{50} 0.1088 mg/mL), *Fusarium tricinctum* (EC_{50} 0.2547 mg/mL) and *Sclerotinia sclerotiorum* (EC_{50} 0.3135 mg/mL) (Chen, C. et al., 2018). In line with these findings, Mugahi et al. (2022) demonstrated that appling blend of extracts, including turmeric (*C. longa*) extract, when applied as a natural preservative, significantly improved microbial stability and extended the shelf-life of fish fillets, specifically underscoring the antimicrobial effectiveness of Zingiberaceae-derived compounds in food systems (Mugahi et al., 2022).

E. cardamomum has been reported to exhibit both antibacterial and antifungal effects (Abdullah et al., 2021; Abdullah et al., 2017; El Malti et al., 2007; Noumi et al., 2018; Tarfaoui et al., 2022). Extracts and essential oils of *E. cardamomum* inhibit the growth of pathogenic bacteria, disrupt biofilms, and affect pathogenic fungi (Abdullah et al., 2021; Abdullah et al., 2017; El Malti et al., 2007; Noumi et al., 2018). Cardamom extract has shown efficacy against a wide range of bacteria, including *S. aureus* (MIC 9.4 mg/mL), *E. coli* (MIC $<$ 2.34 mg/mL), *Salmonella enteridis* (MIC 9.4 mg/mL), *Klebsiella pneumoniae* (MIC 9.4 mg/mL), *Proteus penneri* (MIC 9.4 mg/mL), *Enterobacter cloacae* (MIC $<$ 2.34 mg/mL), *Shigella sonnei* (MIC 18.75 mg/mL), and *Listeria monocytogenes* (MIC 18.75 mg/mL) (El Malti et al., 2007).

E. cardamomum fruit and seed extracts also demonstrated antibacterial activity against bacteria that cause chronic periodontitis, e.g., *Aggregatibacter actinomycetemcomitans* (MIC 0.5 % (v/v)), *Fusobacterium nucleatum* (MIC 0.25 % (v/v)), *Porphyromonas gingivalis* (MIC 0.062 % (v/v)), and *Prevotella intermedia* (MIC 0.125 % (v/v)) (Souissi et al., 2020). Other studies have also shown that cardamom leaves essential oil exhibited antibacterial action (MIC 2000 μg/mL) as well as biofilm-degrading activity (IC_{50} 243.3 μg/mL) against the major dental carries contributor *Streptococcus mutans* (Batubara et al., 2016). According to Abdullah et al. (2017), cardamom essential oil mixed in ethanol was effective against strains of *S. mutans* (MIC 5 mg/mL), *S. aureus* (MIC 10 mg/mL), *S. Typhimurium* (MIC 10 mg/mL), and *C. albicans* (MIC 5 mg/mL) (Abdullah et al., 2017). In another study, the essential oil of green cardamom had effective antimicrobial activity against *E. coli* O157:H7 (MIC 1 % v/v) and *P. aeruginosa* ATCC 14213 (MIC 1 % v/v) (Abdullah et al., 2021). Ethiopian cardamom essential oil showed fungal growth inhibition zones ranging from 12.67 to 34.33 mm, with MIC values from 0.048 to 0.19 mg/mL and MBC values ranging from 0.19 to 1.75 mg/mL (Noumi et al., 2018). The anti-biofilm efficacy of *E. cardamomum* ethanolic and acetonic extracts against multidrug-resistant *Candida* species showed inhibition zones of 10–15 mm (Vijayalakshmi et al., 2016).

Taken together, these findings affirm the antimicrobial potential of Zingiberaceae extracts, particularly from ginger, turmeric, galangal, and cardamom, though further mechanistic studies and clinical validations are warranted.

3.4. Anticancer potential

A growing body of evidence has also revealed the anticancer potential of Zingiberaceae phytochemicals, highlighting their ability to interfere with tumorigenic pathways and cellular proliferation. *Z. officinale, C. longa, A. galanga,* and *E. cardamomum* have been recognized for their potent anticancer properties against cancers such as lung, breast, colon, pancreas, and liver. The bioactive compounds in these plants have been shown to inhibit oncogenic signaling pathways, promote processes like apoptosis and autophagy, and suppress cancer progression by reducing proliferation, invasion, cancer stemness, and metastasis (Soumya et al., 2023).

In ethionine-induced liver cancer rats, *Z. officinale* extracts inhibited the expression levels of NFκB and TNF-α at 100 mg/kg body weight

concentration, thus inhibiting NFκB activation (Habib et al., 2008). Similarly, in a BALB/c xenograft pancreatic cancer mouse model, 6-shogaol, a key compound of *Z. officinale*, not only downregulated NF-κB signaling but also enhanced gemcitabine-induced apoptosis in pancreatic cancer cells (Zhou et al., 2014). Diverse notable phytoconstituents of *Z. officinale*, including 6-gingerol, 6-paradol, 6-shogaol, and zingerone, exhibit potent anticancer properties and provide synergistic effects when combined with standard anticancer drugs. For instance, 6-gingerol inhibits invasion, cancer stemness, iron transport, and PD-L1 while promoting p53-mediated apoptosis in non-small cell lung cancer (NSCLC) (Kang et al., 2023). Additionally, in A549 lung cancer cells, 6-gingerol suppresses USP14 expression, inhibits proliferation, and enhances ROS levels, iron accumulation, and autophagosome formation (Tsai et al., 2020). In breast cancer, the 6-gingerol with paclitaxel combination promotes the Caspase 7 as well as Bax activation and exhibits significant inhibition of proliferation and of tumor growth (Wala et al., 2022). Similarly, in ovarian cancer, 6-gingerol combined with cisplatin upregulates p53, Caspase-8, Bax, and Apaf1, enhancing the therapeutic effect (Salari et al., 2023). Moreover, a formulation of 6-gingerol with doxorubicin and alginate hydroxyapatite showed significant inhibition of proliferation in liver cancer cells (Manatunga et al., 2018). 6-Shogaol, induces apoptosis in colon cancer by upregulating p53, Bax, and Caspase-3,8,9 while downregulating bcl-2 levels. It also induces cell cycle arrest by downregulating cdc2 and cdc25A in female athymic nude mice (Qi et al., 2015). In female BALB/c cervical cancer mice, the compound induced apoptosis via downregulation of p-PI3K, p-Akt, as well as p-mTOR, and also induced cell cycle arrest at the G2/M phase (Pei et al., 2021). Similarly, in oral cancer cells 6-shogaol downregulates p-PI3K, p-Akt as well as p-mTOR levels and upregulated Bax levels (Huang et al., 2021). In breast cancer as well as NSCLC, it also downregulates p-JNK, decreses p–c-jun, as well as p65 levels and upregulates LC3 I and LC3 II expression levels, and further inhibits 26S proteasome and promotes caspase-independent pyroptosis (Nedungadi et al., 2018). Additionally, in breast cancer cells it downregulates Notch signalling via γ-secretase activation, induces cell cycle arrest at the G2/M phase, and promotes autophagic cell death (Ray et al., 2015). 6-paradol, another phytoconstituent of ginger, inhibits proliferation, invasion and metastasis of pancreatic cancer cells by inhibiting the epidermal growth factor receptor (EGFR) protein levels (however without inducing change in mRNA levels) via ubiquitination-mediated proteasomal degradation and thus hinders the PI3K/AKT pathway. In addition, with the EGFR inhibitor Erlotinib, it further exhibited significant activity on the PI3K/AKT pathway and EGFR inhibition (Jiang et al., 2021). Notably, 6-paradol is in general less explored for its anticancer potential and further research could enhance it as a potential scaffold for anticancer drug discovery. Zingerone, another active phenolic phytoconstituent of ginger, inhibits tumor growth and promotes ROS levels as well as apoptotic-mediated cell death via Bid upregulation and Bcl-2 downregulation in DMBA-induced breast cancer-bearing Sprague Dawley rats (Gan et al., 2019). Similarly, in colon cancer cells, zingerone enhances Bax, caspase-3, and −9 and downregulates Bcl-2 levels and exhibits significant inhibition potential (Su et al., 2019). In neuroblastoma, the compound also inhibited tumor growth via inducing cell cycle arrest at the mitosis state, caspase-3 and PARP-1 cleavage, cyclin D1 downregulation, and phosphorylation of Ser10 at histone H3 protein (Choi et al., 2018). Interestingly, zingerone also inhibits cancer cell proliferation and angiogenesis via downregulation of matrix metalloproteinases MMP-2,9 and further inhibits the JAK/STAT pathway (Bae et al., 2016). In liver cell cancer, the phytochemical-derived carbon dots-zingerone nanoparticles significantly reduced the expression levels of VEGF and VEGFR and further inhibited the EGFR-mediated PI3K/Akt/mTOR and Akt/eNOS signalling pathways and also inhibited angiogenesis (Kung et al., 2023). In addition, in oral cancer, phytochemical-derived zingerone nanoparticles downregulate N-cadherin as well as vimentin levels, inhibit MMP-2,and −9, hinder the protein involved in epithelial–mesenchymal transition, and inhibit proliferation, invasion and metastasis (Yang et al., 2022).

C. longa is well-studied for its diverse pharmacological activities in the context of cancer, and particularly its primary bioactive phytoconstituent, curcumin, is known for its significant anticancer properties. An ethanolic extract of *C. longa* has been shown to inhibit cancer cell growth and induce apoptosis by upregulating Bax and caspase-3 while downregulating Bcl-2, leading to cell cycle arrest at the G1 phase (Widyananda et al., 2022). Curcumin specifically inhibits proliferation and promotes apoptosis in breast cancer cells through the downregulation of Bcl-2, Akt, mTOR, CDC25, and CDC2, alongside caspase-3 cleavage and G2/M phase cell cycle arrest (Hu et al., 2018). It also induces ferroptosis in cancer cells by modulating SLC1A5, increasing ROS and Fe^{2+} levels, and promoting lipid peroxidation (Cao et al., 2022). In NSCLC, curcumin inhibits tumor growth by downregulating circ-PRKCA, which acts on miR-384 to regulate ITGB1 protein expression, establishing the circ-PRKCA/miR-384/ITGB1 axis as a potential therapeutic target (Xu et al., 2021). Furthermore, in liver cancer stem cells, curcumin inhibits PI3K, Akt, and mTOR, and induces apoptosis via cytochrome *c* release (Wang, J. et al., 2018), and in colon cancer, it upregulates miR-34a and miR-34b/c independently of p53, promoting apoptosis and inhibiting invasion and migration through the KEAP1/NRF2/miR-34a/b/c pathway (Liu, C. et al., 2023). Additionally, curcumin inhibits the Wnt/β-catenin pathway and miR-130a expression in colorectal cancer, promoting apoptosis (Dou et al., 2017), and downregulates PD-L1 by blocking the JAK/STAT pathway and upregulating miR-206, leading to apoptosis in colon cancer cells (Tong and Wu, 2024). Combination strategies using nanotechnology approaches have been used to enhance the anticancer potential of curcumin and also have been reported in the context of counteracting various cancers. Notably, in cisplatin and paclitaxel resistant lung cancer cells, curcumin induces apoptosis via modulating proteins involved in apoptosis, downregulates the Axl receptor tyrosine kinase at both mRNA and protein levels, which has implications in resistance mechanisms, and enhances the activity of cisplatin and paclitaxel (Kim et al., 2015). Similarly, ultrasound-responsive doxorubicin/curcumin co-loaded alginate-shelled nanodroplets have been shown to promote apoptosis and inhibit proliferation in oral cancer cells (Baghbani and Moztarzadeh, 2017). In NSCLC, curcumin exhibits a synergistic effect with cisplatin by inhibiting XRCC1 protein, inducing apoptosis, and reducing cellular proliferation (Tung et al., 2016). Additionally, curcumin, in combination with erlotinib, reduces cell viability, inhibits proliferation, promotes apoptosis, and suppresses NFκB activation in lung cancer cells, demonstrating its potential to overcome erlotinib resistance (Yamauchi et al., 2014). Furthermore, nanoparticle-based formulations of curcumin, such as liposomal curcumin, curcumin-loaded micelles, solid lipid nanoparticles, carbon nanotubes, nanosuspensions, nanoemulsions, and exosomes, have all shown promising anticancer properties (Wu et al., 2021).

Variety of anti-cancer activities have been also reported for *A. galanga* and compounds derived from it. The aqueous extract of *A. galanga* was reported to reduce the cell viability and cellular proliferation of gastric cancer cells in a time and dosage-dependent manner (Hadjzadeh et al., 2014). Likewise, the ethanolic extract of *A. galanga* in combination with doxorubicin exhibited cell cycle arrest at the G2/M phase, and interestingly it also inhibited the MMP-9 expression levels that are elevated by doxorubicin (alone) in metastatic breast cancer cells (Ahlina et al., 2020). In human epidermal growth factor receptor 2 −overexpressing breast cancer the ethanolic extract of *A. galanga* promotes cell cycle arrest at the G2/M phase, elevates intracellular ROS levels, induces cellular senescence, and in combination with doxorubicin, it exhibited synergistic effect (Jenie et al., 2021). Furthermore, in MCF-7/HER2 + breast cancer cells, the methanolic extract of *A. galanga* inhibits proliferation and induces apoptosis (Ibrahim, 2021). A similar activity is observed in in another work with MCF-7 breast cancer cells, where the ethanolic extract also inhibits proliferation and promotes apoptosis (Samarghandian et al., 2014). Additionally, in metastatic

triple-negative breast cancer, the ethanolic extract of *A. galanga* in combination with lymphocyte T-cells exhibited antiproliferative activity and showed affinity towards PD-1 as well as PD-L1 which supports its immune-potentiation potential (Alif et al., 2021). Notably, 1′-acetoxychavicol acetate isolated from *A. galanga* inhibits proliferation as well as invasion of Endocrine-Resistant breast cancer cells by downregulation of EGFR2, pERK1/2, pAKT, cyclin D1, MYC, C-X-C chemokine receptor type 4, urokinase plasminogen activator, and VEGF, respectively (Pradubyat et al., 2022). Among the isolated phytoconstituents of the plant, galangin, a predominant flavonoid of *A. galanga,* has demonstrated significant anticancer potential against various cancers. In breast cancer, it promotes apoptosis and inhibits cellular proliferation and tumor growth through caspase-3, −8, and −9 cleavage, upregulation of Bid, Bad, p21, and p53, and downregulation of p-PI3K, p-Akt, cyclin-B1, cyclin-D3, and CDKs (Liu, D. et al., 2018). Likewise, in ovarian cancer, it promotes caspase-3,and −7 cleavage, p21 and Bax upregulation, p-Akt, and p-p70S6K downregulation and induces p53-dependent apoptotic cell death (Huang et al., 2020). In gastric cancer, galangin increases intracellular ROS levels, reduces Nrf2 and NQO-1 expression, and downregulates p-JAK2, p-STAT3, and Bcl-2 while upregulating PARP and caspase-3 cleavage, thereby inhibiting the JAK/STAT pathway (Liang et al., 2021). Additionally, in renal cancer cells, when combined with TNF-related apoptosis-inducing ligand (TRAIL), galangin acts as a sensitizer for TRAIL-resistant cells by inhibiting NF-κB activation and downregulating Bcl-2, cFLIP, Mcl-1, and survivin (Han et al., 2016). In nasopharyngeal carcinoma, it induces cell cycle arrest at S-phase via a p53-independent apoptosis induction and hinders the PI3K/AKT pathway (Lee et al., 2018). Furthermore, in glioblastoma, galangin inhibits proliferation, invasion, and metastasis and prevents Skp2-induced EMT by downregulating Zeb1, N-cadherin, snail, and vimentin (Xiong et al., 2020a). Notably, it also induces apoptosis, pyroptosis, and autophagy simultaneously in glioblastoma cells (Kong, Y. et al., 2019).

In respect to *E. cardamomum*, the methanolic extract of the plant, when combined with cyclophosphamide, has been shown to inhibit tumor growth in Ehrlich solid tumor-bearing mice by downregulating oxidative stress biomarkers and upregulating glutathione, antioxidants, and pro-apoptotic proteins (Almeer et al., 2021). In liver cancer induced by diethylnitrosamine in Sprague Dawley male rats, the extract similarly inhibited tumor growth through downregulation of TNF, IL-1, hepatic MDA, and NF-κB expression while upregulating ornithine decarboxylase, alanine transaminase, aspartate transaminase, glutathione, alkaline phosphatase, and γ-glutamyl transferase levels (Elguindy et al., 2016). Cardamonin, a key alkaloid of *E. cardamomum*, has also demonstrated significant anticancer effects against various cancers such as breast, colon, and lung (Ramchandani et al., 2020). In breast cancer, cardamonin promotes apoptosis by upregulation of p21, p27, as well as Bim, promotes cell cycle arrest at the G2/M phase, downregulates cyclin D1, and also elevates caspase-3 cleavage together with intracellular ROS levels and thus inhibits proliferation via JNK-FOXO3a pathway (Kong, W. et al., 2019). It also works synergistically with doxorubicin to reduce tumor growth and reverse drug resistance by targeting IL-6, IL-8, MCP-1, and NF-κB in chemotherapy-resistant breast cancer stem cells (Jia et al., 2016). However, in triple-negative breast cancer, it was reported that the cardamonin induces Nrf2 activation which has to be carefully addressed (Jin et al., 2019). In cervical cancer cells resistant to mTOR inhibitors, cardamonin inhibits proliferation by reducing mTOR, raptor, and S6K1 phosphorylation (Niu et al., 2020). In colon cancer, it prevents tumor development, promotes apoptosis via β-catenin nuclear translocation, and induces cell cycle arrest at the S phase (James et al., 2017). Furthermore, in 5-fluorouracil-resistant colon cancer cells, cardamonin elevated the apoptosis by Bax upregulation, promoted caspase-3/-9 cleavage, and downregulated the expression levels of c-MYC, octamer-binding transcription factor 4, cyclin E, and NF-κB and thus inhibited proliferation through TSP50/NF-κB pathway (Lu et al., 2018). In glioblastoma stem cells, cardamonin also induces apoptosis by downregulating STAT3 and associated proteins, thereby hindering the JAK/STAT pathway (Wu et al., 2015). In lung cancer, it inhibits invasion as well as migration, promotes cell cycle arrest at the G2/M phase, promotes apoptosis via Bax upregulation together with Bcl-2 downregulation, and also downregulates the expression of cyclin D1, CDK4, PI3K, Akt, and mTOR respectively, and hinders the PI3K/Akt/mTOR pathway (Zhou et al., 2019). Similarly, cardamonin also promotes apoptosis and inhibits the proliferation via the downregulation of mTOR as well as p70S6K levels in lung cancer cells (Tang et al., 2014).

These findings support the anticancer promise of Zingiberaceae phytochemicals, though the field would benefit from more rigorous clinical research to translate preclinical efficacy into therapeutic outcomes.

3.5. Cardiovascular health benefits

In parallel with their anticancer effects, members of the Zingiberaceae family contribute to cardiovascular health, offering both cardioprotective and vasorelaxant benefits. Cardiovascular diseases remain the leading cause of global mortality, highlighting the urgent need for effective preventive strategies based on safe and accessible interventions (Banach et al., 2025). Diverse plants of the Zingiberaceae family show cardiovascular benefits, particularly cardioprotective effects and vasorelaxant activity.

3.5.1. Cardiac effects

There is much evidence concerning the beneficial cardiac activity of various extracts or single compounds isolated from Zingiberaceae family plants. Besides much *in vitro* evidence, several studies have been performed *in vivo* in either isoproterenol- or doxorubicin-induced cardiac damage. Some of the plants used in traditional medicine or endowed with cardioprotective effects include *Z. officinale* (containing 6-shogaol and zingerone) (Amran et al., 2015; Hemalatha and Mainzen Prince, 2016; Kawase et al., 2023; Liu et al., 2019), *K. parviflora* (black ginger) (Weerateerangkul et al., 2012; Weerateerangkul et al., 2013), *C. amada* (zerumin A) (Jatoi et al., 2007), and *C. longa* rhizomes (Mohamad et al., 2009; Mohanty et al., 2006) (Fig. 5).

In myocardial infarction induced by isoproterenol in Wistar rats, *Z. officinale* extract markedly reduced the levels of cardiac troponin, alanine transaminase, creatine kinase MB isoenzyme (CK-MB), aspartate transaminase, and lactate dehydrogenase (LDH) and increased those of the antioxidant enzymes GPx and SOD (Amran et al., 2015).

K. parviflora is traditionally used to treat different ailments including hypertension (Hashiguchi et al., 2022; Weerateerangkul et al., 2013). *In vitro*, high concentrations of the extract attenuate swine heart fibrillation with, however, a yet unknown mechanism (Weerateerangkul et al., 2013). *In vivo*, this plant extract reduces ventricular myocyte Ca^{2+} transient, probably *via* cardiac cGMP level elevation induced by NO signaling (Weerateerangkul et al., 2012).

In vitro, 6-shogaol, a constituent of *Z. officinale*, inhibits cultured cardiomyocyte hypertrophy induced by phenylephrine, cardiac fibrosis, and cultured cardiac fibroblasts differentiation to myofibroblasts induced by TGF-β, likely through the inhibition of p300-histone acetyltransferase (p300-HAT) activity. In *in vivo* mice, 6-shogaol attenuates pressure overload-induced (by transverse aortic constriction) left ventricular hypertrophy as well as its progression leading to systolic dysfunction, and cardiac fibrosis, thus highlighting its potential for the treatment of heart failure (Kawase et al., 2023).

In isoproterenol-induced myocardial infarcted rats, the phenolic alkenone zingerone, isolated from *Z. officinale*, restricts myocardium troponin-T leakage. Furthermore, at the cardiomyocyte mitochondria level, favours ROS scavenging by GPx, improves cytochrome-c oxidase- and nicotinamide adenine dinucleotide (NAD) dehydrogenase-induced dysfunction, reduces Ca^{2+} overload (thus leading to a negative inotropic effect), and preserves morphology *via* an increase in the ATP concentration, thereby preventing ionic gradient loss and swelling. Therefore, zingerone daily intake might reduce the risk of myocardial

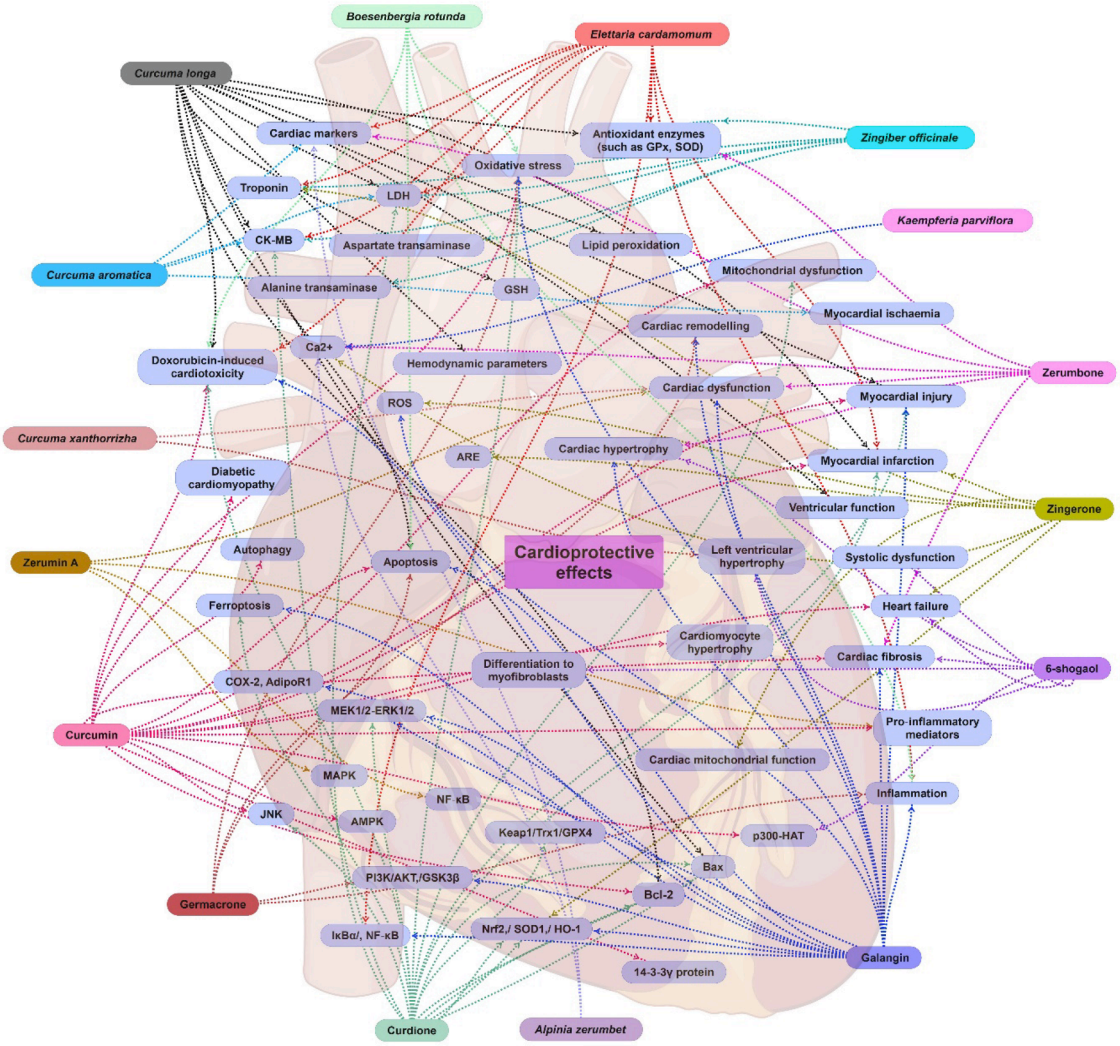

Fig. 5. Main pathways underpinning the cardiac effects of Zingiberaceae family plants and constituents (visualised with SimpleMind, with modifications through Adobe Illustrator and BioRender.com). Zingiberaceae extracts and isolated constituents have been shown to modulate these pathways, leading to improved cardiac function and reduced damage.

infarction (Hemalatha and Mainzen Prince, 2016). Moreover, as zingerone triggers the phosphorylation of endothelial nitric oxide synthase (eNOS), thus activating Nrf2 as well as antioxidant response element (ARE), it represents a promising agent for the management of heart failure (Liu et al., 2019).

Zerumbone is the main and most extensively studied phytoconstituent of *Z. zerumbet*, also known as shampoo ginger (Munir et al., 2021; Yob et al., 2011). Apart from its potent anti-inflammatory and analgesic properties (Chan et al., 2024), several *in vitro* and *in vivo* studies have demonstrated its cardioprotective effects due to the regulation of cardiac marker and endogenous antioxidant levels, as well as suppression of cardiac fibrosis and hypertrophy, thereby reducing cardiac dysfunction following pressure overload (Munir et al., 2021; Sari et al., 2021; Tojima et al., 2021).

One of the most studied Zingiberaceae species is, no doubt, *C. longa*. In Wistar rats, one-month administration of this species before ischemia–reperfusion injury significantly reduced myocardial infarction size compared to the untreated group: the antioxidant status was restored, and the lipid peroxidation was also inhibited, resulting in an improvement in ventricular function (Mohanty et al., 2004). It has been hypothesised that an anti-apoptotic action *via* the modulation of Bax and Bcl-2 underpins its cardioprotective activity (Mohamad et al., 2009; Mohanty et al., 2006).

Similar results have been obtained in an *in vivo* rat model of myocardial infarction induced by isoproterenol: pre-treatment for one month with *C. longa* improved the antioxidant status and restored the hemodynamic parameters to control values (Mohanty, 2009).

Interestingly, pre-treatment with a water or ethanolic extract of *C. longa* protected rats from doxorubicin-induced cardiotoxicity: mortality, as well as the levels of LDH and CK-MB, were significantly reduced, whereas GSH increased along with a marked decrease in serum NO (El-Sayed, 2011).

Hypertension is a risk factor leading to cardiovascular complications such as left ventricular hypertrophy and increased heart muscle mass. In hypertensive mice, administration of *C. xanthorrizha* extract with captopril reduced the heart muscle mass and left ventricle thickness compared to the captopril alone group, highlighting its adjuvant effect (Hijriani et al., 2020).

In a rat model of acute myocardial ischemia induced by isoproterenol, pre-treatment with hydroalcoholic extracts of *C. aromatica* decreased the levels of cardiac injury biomarkers, including CK-MB and LDH, along with those of serum MDA. Furthermore, elevation in the ST-segment and T-wave was also prevented: the strongest activity was shown by *C. aromatica* extract consisting of 70 % hydroalcoholic solvent (Li et al., 2016).

Curcuma amada rhizomes, commonly called mango ginger and

resembling *Z. officinale* in morphology and *Mangifera indica* in taste, contain zerumin A (Jatoi et al., 2007) that shows cardioprotective effects mediated by MAPK and NF-κB activation, as well as pro-inflammatory mediators inhibition (Policegoudra et al., 2011; Shyni et al., 2021).

Curcumin shows excellent cardioprotective effects. It limits cardiomyocyte hypertrophy, thus preventing the development of heart failure, *via* the inhibition of p300-HAT (Wongcharoen and Phrommintikul, 2009). Furthermore, curcumin improves cardiac function and prevents cardiac fibrosis following myocardial infarction. *In vivo*, down-regulation of pro-inflammatory cytokine in macrophages, of IL18 in cardiac fibroblasts, and modulation of the downstream TGF-β1-p-SMAD2/3 pathway seems to underpin its cardioprotective activity (Zhao et al., 2021).

In streptozocin- and high-fat diet-induced diabetic mice, curcumin ameliorates cardiomyopathy inhibiting apoptosis and promoting autophagy, likely activating JNK1 and AMPK pathways (Pourbagher-Shahri et al., 2021; Yao et al., 2018). Noticeably, it protects from doxorubicin-induced cardiotoxicity and myocardial injury by reducing oxidative stress and mitochondrial dysfunction. The latter effect is linked to curcumin up-regulation of 14–3-3γ protein and mitochondrial Bcl-2 (He et al., 2018).

Both *in vitro* and *in vivo* studies have demonstrated that the sesquiterpenoid germacrone, found in Curcuma species including *C. zedoaria* (Lobo et al., 2009), shows cardioprotective effects. In isoproterenol-induced cardiac injury, it attenuates oxidative stress, apoptosis, inflammation and cardiac remodeling, the latter *via* inhibition of the phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT) pathway (Fang, Z. et al., 2023).

In vitro (H9c2 cells) and *in vivo* (mice) evidence points to the sesquiterpenoid curdione, a constituent of *Curcumae Radix*, as a valuable protective agent against myocardial infarction induced by isoprenaline. Several mechanisms seem to underpin this beneficial activity. Curdione modulates the Keap1/Trx1/GPX4 pathway, inhibits ferroptosis, reduces MDA levels, and increases those of ferritin heavy chain 1, GSH peroxidase 4, and GSH (Wang, H. et al., 2023). Furthermore, it inhibits apoptosis, oxidative stress and, in H9c2 cell limits proliferation and morphological damage, and decreases the levels of CK-MB and LDH. Finally, curdione activates the Nrf2/SOD1/HO-1 pathway, modulates Bax and Bcl-2, and ameliorates mitochondrial dysfunction (Ma et al., 2023).

Similar results have been observed in a model of doxorubicin-induced cardiotoxicity, where curdione inhibits oxidative stress, extracellular signal-regulated kinase1/2 (Erk1/2) and c-Jun-N-terminal kinase, limits Nrf2/HO-1 activation, decreases the levels of elevated CK-MB and LDH release, activates the Nrf2/HO-1 pathway, modulates Bax, and Bcl-2, and ameliorates mitochondrial dysfunction (Wu et al., 2019).

A. zerumbet is used as a remedy for atherosclerosis (Cruz et al., 2023). In addition to vasorelaxant and hypotensive effects, pre-treatment of rats for 30 days with the hydroalcoholic extract of the leaves before isoproterenol-induced myocardial infarction, limits the leakage of cardiac marker enzymes, i.e., creatine kinase-NAC (CK-NAC) and CK-MB, the size of the infarct areas, as well as the increase in heart rate. The latter effect was ascribed to the blockade of voltage-dependent L-type Ca^{2+} channels (Paulino et al., 2019).

A. officinarum, commonly known as lesser galangal (Castaneda et al., 2019), contains the flavonoid galangin, which has shown cardioprotective properties in *in vitro* and *in vivo* studies. Galangin: *i*) relieves ischemia–reperfusion myocardial injury stimulating the Nrf2/Gpx4 pathway, thus inhibiting lipid ROS-induced ferroptosis; *ii*) limits cardiac remodelling and myocardial fibrosis induced by pressure overload; *iii*) inhibits MEK1/2-ERK1/2 and PI3K-Akt-GSK3β activation, responsible for GATA4-induced cardiac hypertrophy; *iv*) inhibits pressure overload-induced IκBα and NF-κB activation, cardiomyocyte apoptosis, collagen synthesis, and cardiac fibrosis (Thangaiyan et al., 2020; Wang et al., 2019; Yang et al., 2023). Furthermore, the flavonoid ameliorates cardiometabolic disorders and cardiovascular complications affecting the expression of COX-2, cardiac adiponectin/adiponectin receptor 1 (AdipoR1), NF-κB, and restoring the physiological levels of antioxidant enzymes. This mitigates inflammation, oxidative stress, and caspase-3-induced apoptosis (Abukhalil et al., 2021; Prasatthong et al., 2021). Finally, galangin counteracts doxorubicin-induced cardiotoxicity in mice *via* Nrf2/HO-1 activation (Fang, G. et al., 2023).

E. cardamomum extracts contain effective cardioprotective agents. In rat models of either doxorubicin-induced cardiotoxicity or isoproterenol-induced myocardial infarction, cardamom extract supplementation prevents myocardial damage (as assessed by histopathology and ultrastructural analysis) and loss of function, oxidative stress, apoptosis, inflammation, and increased VEGF immunoreactivity (Abu Gazia and El-Magd, 2018; Goyal et al., 2015).

B. rotunda, commonly called fingerroot, has shown beneficial effects against a rat model of doxorubicin-induced cardiotoxicity, where it ameliorated inflammation, oxidative stress, and apoptosis. The phytoconstituents and the mechanisms involved in the cardioprotective effect, however, remain to be elucidated (Zhang, L. et al., 2023).

Altogether, Zingiberaceae-derived compounds demonstrate cardioprotective effects through diverse mechanisms, suggesting their potential role in preventing or mitigating cardiovascular diseases.

3.5.2. Vascular effects

The first research evidence consistent with the beneficial vascular activity of extracts or single components isolated from a Zingiberaceae family plant dates back to the beginning of the new millennium. Once again, the precious cultural heritage of traditional medicine, using natural herbs to treat vascular ailments, allowed the identification of the agents responsible for these beneficial activities. More than 20 years of pharmacological *in vitro* investigation, performed mainly in coronary, conduit, and resistance vessels, also supported by *in silico* analysis, has provided a plethora of interesting agents isolated from the natural remedies used in different countries. The results obtained in the last five years demonstrated the vasorelaxant effects of the essential oil of *A. zerumbet* (containing 19 substances, with the predominance of 1,8-cineole, terpinen-4-ol, and p-cymene (Rocha et al., 2023)), *A. officinarum* extract and its compounds eucalyptol, coniferyl alcohol, and 3-(3,4-dihydroxyphenyl)-7-hydroxy-4H-chromen-4-one (Haam et al., 2022), curcubisabolanin A, a seco-cadinane sesquiterpenoid (curcumane C), and two nor-bisabolene enantiomers [(+)- and (−)-curcumane D] isolated from the rhizomes of *C. longa* L. (Chen, J.F. et al., 2022; Qiao et al., 2019), ethyl-p-methoxycinnamate and the enantiomeric sesquiterpenoids (+)/(−)-phaeocauline 3–5 isolated from the rhizomes of *K. galanga* L. (Srivastava et al., 2021) and *Curcuma phaeocaulis* (Liu et al., 2020), respectively, the extract of the rhizomes of *B. rotunda* (L.) Mansf. [*B. pandurata* (Roxb.) Schltr.] (containing the vasoactive flavonoid naringenin 5-methyl ether, pinostrobin chalcone, and 4-hydroxypanduratin A (Adhikari et al., 2020)), and different extracts obtained from *Z. officinale* var. *rubrum* (Razali et al., 2020) as summarised in Fig. 6.

Several pathways and targets were identified as responsible for this vasoactivity: *i*) inhibition of extracellular Ca^{2+} influx; *ii*) inhibition of Ca^{2+} release from the sarcoplasmic reticulum; *iii*) activation of the eNOS/sGC pathway through the PI3K/AKT signalling pathway; *iv*) activation of $K_{Ca}1.1$ and $K_{ir}6.1$ channels; *v*) stimulation of prostacyclin release; *vi*) stimulation of muscarinic receptors. Though *in vitro* and *in silico* analysis hypothesized a direct interaction between several Zingiberaceae family plant components [e.g., 1,8-cineole, terpinene-4-ol, and p-cymene (Rocha et al., 2023)] and vascular smooth muscle Ca^{2+} channels such as ryanodine receptor 1, $Ca_V1.2$, and IP3 receptor 1, patch-clamp experiments are necessary to directly prove this hypothesis.

Interestingly, the *in vitro* vasorelaxant activity was translatable to *in vivo* experimental models. For example, in two different rat models of

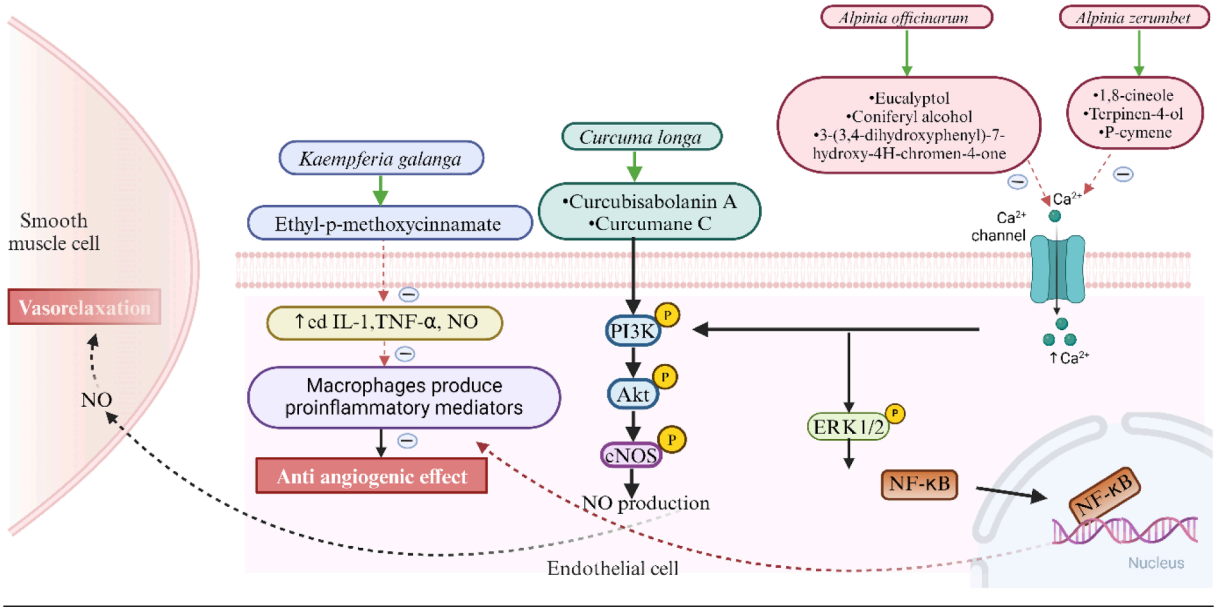

Fig. 6. Main pathways involved in the vascular effects of Zingiberaceae family plants and constituents (prepared with Biorender).

hypertension (fed by either Nω-nitro-L-arginine methyl ester or high fructose), administration of an aqueous extract of large cardamom markedly counteracted the rise in blood pressure, restored the plasma NO metabolites level reducing that of heart, kidney, and aorta MDH, alleviated vascular wall hypertrophy, and improved the vascular response to acetylcholine in phenylephrine pre-contracted aorta (Kanthlal, 2021; Kanthlal et al., 2020). These beneficial effects were ascribed mainly to the antioxidant properties of the extract. Similar results were observed in spontaneously hypertensive rats treated with different extracts obtained from *Z. officinale* var. *rubrum* (Razali et al., 2020). The authors suggested that three major constituents of the extract, namely 6-gingerol, 8-gingerol, and 6-shogaol, likely contributed to the vasorelaxant effects. More importantly, two recent systematic reviews and *meta*-analyses of clinical trials have concluded that either ginger or curcumin/turmeric supplementation has a favorable impact on several markers of human high blood pressure and endothelial function (Dehzad et al., 2024; Hasani et al., 2019), thus being proposed as a complementary method to improve critical risk factors leading to the development of cardiovascular diseases. Nonetheless, further studies are warranted before definitive conclusions may be reached.

Vascular endothelial injury is an initiating factor in the development of diabetic cardiovascular complications and a hallmark of several pathologies. In a recent study by Xu et al. (Xu et al., 2023), an *A. zerumbet* Fructus essential oil-loaded nanoemulsion, composed of bovine serum albumin-dextran sulfate conjugate and sodium deoxycholate, was developed as an effective oral drug delivery system for treating vascular endothelial injury induced by hyperglycemia. The nanoemulsion improved oral absorption and prolonged systemic circulation time of the essential oil, protected HUVECs from high glucose-induced injury, and prevented endothelial dysfunction and *tunica media* fibroelastosis caused by hyperglycemia by improving oxidative stress and inhibiting inflammation in a type 2 diabetes mellitus mouse model. Noticeably, the *A. zerumbet* fructus essential oil limited the phenotypic changes in HUVECs and the occurrence of endothelial-mesenchymal transformation, which underpin the development of cardiovascular diseases, downregulating Krüpple-like factor 4, decreasing histone H3 acetylation, and inhibiting the transduction of the Notch/Snail signalling axis (Zhang et al., 2022).

As cardiovascular diseases are the main cause of death in developed countries, the vasorelaxant effects of Zingiberaceae family plant extracts and single components might represent an alternative therapeutical approach for the development of innovative, effective natural weapons capable of preventing and treating vascular diseases. In particular, the numerous beneficial effects of Ginger (*Z. officinale* Roscoe) on the vascular system (Li, C. et al., 2021), might be exploited to reduce the hallmarks and improve the cognitive function of patients affected by vascular dementia, a common and devastating form of dementia, as recently outlined by Schepici et al. (Schepici et al., 2021), or to control high blood pressure, either in the form of functional food and nutraceutical or in the form of nanoemulsion, as demonstrated in a rat model of hypertension (Hanifah et al., 2021).

The vascular benefits observed, particularly in endothelial protection and blood pressure modulation, highlight the relevance of Zingiberaceae plants as candidates for vascular health-promoting interventions.

3.6. *Digestive system support and metabolic effects*

Complementing their cardiovascular activity, Zingiberaceae plants are also well recognized for their positive effects on digestion, metabolism, and gastrointestinal function—key domains of their traditional use.

The rhizome extract of *A. galanga* (200 mg/kg) significantly reduced ulcer scores and exhibited antioxidant activity against indomethacin-induced gastric ulcers in Wistar rats, with effects comparable to those of ranitidine (20 mg/kg) (Johnley et al., 2020). The compounds 1′*S*-1′-acetoxychavicol acetate and 1′*S*-1′-acetoxyeugenol acetate, isolated from *A. galanga* rhizomes, effectively reduced gastric mucosal damage, with ED_{50} values of 0.61 and approximately 0.90 mg/kg, respectively, against gastric lesions induced by ethanol in rats (Matsuda et al., 2003). 1′*S*-1′-Acetoxychavicol acetate also protected against lesions caused by 0.6 M HCl (ED_{50} = 0.73 mg/kg) and aspirin (ED_{50} = 0.69 mg/kg), but did not affect indomethacin-induced lesions or acid output in pylorus-ligated rats at doses of 0.5–5.0 mg/kg. The presence of the 1′-acetoxyl group was found to be essential for the observed gastroprotective effects. The gastroprotective activity of 1′*S*-1′-acetoxychavicol acetate was diminished by pretreatment with indomethacin and *N*-ethylmaleimide and notably increased glutathione levels in the gastric mucosa, suggesting that endogenous prostaglandins and antioxidant mechanisms are involved in its protective activity (Matsuda et al., 2003). The ethanolic extract of *A. galanga* (500 mg/kg) notably reduced the gastric

mucosal damage caused by pyloric ligation and hypothermic restraint stress in rats. It significantly lowered gastric secretion and provided strong protection against damage from 80 % ethanol, 0.6 M HCl, 0.2 M NaOH, and 25 % NaCl. The extract also prevented mucus depletion due to hypothermic stress, suggesting its potential anti-ulcer properties (Al-Yahya et al., 1990). Mitsui et al. had previously reported that *dl*-1′-acetoxychavicol acetate and 1′-acetoxyeugenol acetate from *A. galanga* seeds effectively inhibited ulcer in Shay rats at dosages of 2–10 mg/kg when administered intraperitoneally (Mitsui et al., 1976).

A labdane diterpenoid, alpigalangin L, isolated from the fruits of *A. galanga*, demonstrated significant glucagon-like peptide 1 (GLP-1) promotive effects, increasing it by 413.8 % at a concentration of 50 μM in NCl-H716 cells. The compound increased the mRNA expression of proglucagon (Gcg) and proprotein convertase subtilisin/kexin type 1 (Pcsk1), and the phosphorylation of protein kinase A (PKA), cAMP response element-binding protein (CREB) and glycogen synthase kinase-3-beta (GSK3β), suggesting an antidiabetic potential (Liu et al., 2024). In a different study, the methanolic extract of *A. galanga* was administered to streptozotocin-induced diabetic rats at doses of 200 and 400 mg/kg for 21 days, resulting in significant dose-dependent reductions in fasting blood glucose levels and improvements in lipid profiles (Verma et al., 2015). Another study evaluated the effects of alcoholic extract of *A. galanga* rhizomes on diabetes-induced nephropathy in streptozotocin-treated Wistar rats (Kaushik et al., 2013). The extract was administered daily for 40 days at doses of 50, 100, and 200 mg/kg. The extract significantly reduced blood glucose, urinary albumin, blood urea nitrogen, and oxidative stress markers, and improved body weight, lipid profiles, and antioxidant enzyme levels (Kaushik et al., 2013). A study conducted to investigate the antihyperlipidaemic effects of the ethanolic extract and chloroform fraction of *A. galanga* rhizomes in Triton-induced hyperlipidaemic rats found that treatment at doses of 200 and 400 mg/kg significantly reduced total cholesterol, triglyceride, and low-density lipoprotein (LDL) levels and increased high-density lipoprotein (HDL) cholesterol levels (Iyer et al., 2013). Powdered rhizome (2–4 g/kg) and its methanol and aqueous extracts (4 g/kg) significantly reduced blood glucose levels, similar to gliclazide, in normal male New Zealand rabbits (Akhtar et al., 2002). The most significant dose-dependent glucose decrease was observed 6 h after administration of powdered rhizomes at 3 and 4 g/kg, with levels falling from 100 mg/dL (control) to 88.3 and 75.4 mg/dl, respectively. Methanolic and aqueous extracts, at the 4 g/kg dose, showed similar effects at the same post-treatment interval (Akhtar et al., 2002).

The aqueous extract of *A. galanga* rhizome, administered orally at a dose of 500 mg/kg to male Wistar rats, demonstrated preventive effects against alcohol- and CCl_4-induced liver toxicity, which closely resembled the effects of silymarin in terms of biochemical parameters, antioxidant activity, and histology (Srivastava et al., 2024). *Alpinia galanga* essential oil, at concentrations ranging from 15 to 125 μg/mL, inhibited lipid accumulation in 3 T3-L1 cells by downregulating adipogenesis-related genes, such as peroxisome proliferator-activated receptor gamma (PPARγ), sterol regulatory element binding protein 1c (SREBP-1c), CCAAT/enhancer binding protein α (C/EBPα), glucose transporter type 4 (GLUT4), lipoprotein lipase (LPL), cluster of differentiation (CD)-36, adipocyte protein 2 (aP2), acetyl-CoA carboxylase 1 (ACC1), and fatty acid synthase (FAS) (Liang et al., 2018). Furthermore, in a mouse model of obesity induced by a high-fat diet, *A. galanga* freeze-dried powder reduced body weight, fat ratio, serum triglycerides, cholesterol, and liver enzymes and ameliorated fatty liver, while upregulating lipid oxidation-related genes such as PPARα and carnitine palmitoyltransferase 1 (CPT-1) (Liang et al., 2018). 1′-Acetoxychavicol acetate significantly reduced glycerol 2-phosphate dehydrogenase (GPDH) activity and inhibited lipid accumulation in 3 T3-L1 adipocytes by downregulating PPARγ and C/EBPα without showing cytotoxicity. It also induced AMPK phosphorylation in a dose-dependent manner. In rats, a 0.05 % 1′-acetoxychavicol acetate-supplemented high-fat diet led to reduced weight gain and visceral fat mass compared to a high-fat diet alone, without causing steatohepatitis (Ohnishi et al., 2012).

Galangin demonstrated anti-fibrotic effects in hepatic fibrosis by suppressing proliferation, promoting apoptosis, and downregulating fibrotic markers and pathways in LX-2 cells, including reduction of alpha smooth muscle actin (α-SMA) and collagen I expression, inhibition of phosphoinositide 3-kinase (PI3K)/ protein kinase B (Akt) and Wnt/β-catenin signalling, and increased BCL2 Associated X (Bax)/ B-cell lymphoma 2 (Bcl-2) ratio (Xiong et al., 2020b). *In vivo*, galangin (20–80 mg/kg) reversed CCl_4-induced liver damage and oxidative stress markers, reduced hepatic malondialdehyde and hydroxyproline levels, and enhanced antioxidant enzymes. Histological analysis confirmed that it alleviated liver damage and downregulated α-SMA and transforming growth factor beta 1 (TGF-β1), indicating its potential to inhibit liver fibrosis (Wang et al., 2013). Another study demonstrated that galangin inhibited pancreatic lipase, with an IC_{50} of 48.20 mg/ml, and in a dose of 50 mg/kg galangin significantly reduced body weight, energy intake, and parametrial adipose tissue weight induced by a cafeteria diet for six weeks. Moreover, it decreased serum lipid levels, liver weight, lipid peroxidation, and hepatic triglyceride accumulation (Kumar and Alagawadi, 2013). Galangin supplementation from day 15 to 60 prevented metabolic disturbances and improved insulin sensitivity in Wistar rats fed fructose for the first 15 days, counteracted the elevated levels of TNF-α, IL-6, and TGF-β1 in the liver, and inhibited NF-κB nuclear translocation (Sivakumar and Anuradha, 2011). In another study, oral administration of *A. galanga* ethanolic extract (20 mg/day) also effectively lowered the serum and tissue levels of total cholesterol, triglycerides, and phospholipids, and significantly increased the serum levels of HDL in high-cholesterol-fed white Wistar rats over a period of 4 weeks (Achuthan and Padikkala, 1997).

In respect of the use of turmeric and its constituents, in a double-blind, placebo-controlled study lasting eight weeks, curcumin extract (500 mg, once daily) demonstrated a considerable reduction in gastrointestinal symptom scores and anxiety levels. Compared to placebo, there were no substantial changes in intestinal microbiota or small intestinal bowel overgrowth (Lopresti et al., 2021). A *meta*-analysis by Yin et al. showed a significant positive effect on the clinical remission of ulcerative colitis when curcumin was used as an adjuvant, although no significant effects were observed in terms of clinical improvement or endoscopic remission (Yin et al., 2022). The authors suggested a possible dose–response relationship and recommended that curcumin delivery should be improved to increase its bioavailability, and efficacy. In a randomised controlled trial, Lang et al. reported that the addition of curcumin to mesalamine therapy induced remission in patients with mild-to-moderate ulcerative colitis without any adverse effects (Lang et al., 2015). In rats with irinotecan-induced intestinal mucosal injury, curcumin (100 mg/kg) exhibited antidiarrheal activity by inhibiting NF-κB activation and oxidative stress, reducing stool frequency, and reversing intestinal mucosal damage (Ouyang et al., 2019). A combination of curcumin and fennel essential oil improved the symptoms and quality of life of patients with irritable bowel syndrome, resulting in a significant decrease in the symptom severity score (Portincasa et al., 2016). In a randomized clinical trial (RCT), Khonche et al. evaluated the efficacy of curcumin adjunctive therapy in patients with peptic ulcers caused by *Helicobacter pylori* and assessed the severity of dyspepsia (Khonche et al., 2016). Curcumin administration in addition to the standard anti-*Helicobacter* regimen was safe in patients with peptic ulcers, and it also improved dyspepsia symptoms. Studies with enterovirus 71 also found that curcumin inhibits viral translation and increases intestinal epithelial viability by decreasing the phosphorylation of protein kinase C delta (PKCδ) (Huang et al., 2018).

A diet supplemented with curcumin increased mice survival and eliminated tumour burden in an azoxymethane/interleukin-10 knockout (AOM/Il10$^{-/-}$) model, with limited effects on the mucosal immune response, but in association to beneficial effects in colonic microbiota (McFadden et al., 2015). Given the growing recognition of the gut microbiota as a key modulator of immune, metabolic, and

inflammatory responses, these microbial shifts may significantly contribute to curcumin's protective effects (El Boukhari et al., 2025). Curcumin (100 and 300 mg/kg) decreased the expression of the colon chemokine ligand 1 (CXCL1) and CXCL2 genes and exhibited significant antidiarrheal effects in 5-fluorouracil-injected rats (Sakai et al., 2016). It also reduced indomethacin-induced gastric injury in Wistar rats by activating the NO/cGMP/potassium channel (KATP) pathway (Diaz-Triste et al., 2014). Dietary supplementation with curcumin (200 mg/kg) enhanced growth performance and fat metabolism in broiler chicks and increased the small intestine villus absorptive area, resulting in improved nutrient absorption (Rajput et al., 2013). At the same time curcumin was demonstrated to represent promising dietary pancreatic lipase inhibitor, with potential applications for the prevention and management of obesity (He et al., 2024). Conducted research also demonstrated that curcumin prevented indomethacin-induced gastropathy in male Sprague-Dawley rats by significantly decreasing the levels of intercellular adhesion molecule-1 (ICAM-1) and TNF-α (Thong-Ngam et al., 2012). Curcumin also ameliorated aflatoxin B1-induced toxicity in male Fisher-344 rats. It significantly enhanced glutathione *S*-transferase and microsomal uridine 5′-diphospho-glucuronyl transferase activity and reduced aryl hydrocarbon hydroxylase activity in the aflatoxin-B1 intoxicated rats (Nayak and Sashidhar, 2010). Turmeric ethanol and ethyl acetate extracts blocked the binding of [3H]-tiotidine to histamine receptors in HL-60 cells, revealing their protective effect against gastric ulcers (Kim et al., 2005). The crude extract of *C. longa* showed inhibitory effects on irritable bowel disease by blocking calcium channels in hyperactive states (Gilani et al., 2005). The ethanol extract of *C. longa* (500 mg/kg) also demonstrated an anti-ulcer effect, inhibiting both gastric secretion and intestinal spasms and protecting the gastroduodenal mucosa against hypothermic-restraint stress, pyloroic ligation, indomethacin, and reserpine administration (Rafatullah et al., 1990). The powdered rhizome of *C. longa* protects the gastric mucosa against irritants by increasing the mucin content of gastric juice (Mukherjee et al., 1961), and curcumin has been found to reduce intestinal gas formation (Bhavani Shankar and Sreenivasa Murthy, 1979). *Curcuma longa* has been shown to enhance the secretion of gastric wall mucus, gastrin, secretin, and pancreatic enzymes, and has anti-inflammatory properties that protect the gastrointestinal tract (Fadhlizil Fasihi Mohd Aluwi et al., 2022).

A study was conducted on 45 patients who were administered *C. longa* supplements in conjunction with hypoglycaemic drugs for 120 days (Abbas et al., 2022). The results demonstrated a significant decrease in haemoglobin A1C levels and advanced glycation end products, as well as an enhancement in neuropathic sensation when compared to the control group that received antidiabetic medication (Abbas et al., 2022). The ethanol extract of *C. longa* rhizome (1 % of diet) exhibited hypoglycaemic effects in KK-A^{y} mice with genetic diabetes. Dose-dependent stimulation of human adipocyte differentiation and PPAR-γ ligand-binding activity was observed with the extract at concentrations of 5 and 10 μg/mL (Kuroda et al., 2005). Curcuminoids (100 mg/kg) from *C. longa* also significantly reduced blood glucose and liver alterations in streptozotocin-induced diabetic rats (Islam et al., 2024). A clinical trial demonstrated that curcumin (1000 mg/day) upregulates PPAR-γ in the peripheral blood mononuclear cells of type-2 diabetic patients with coronary heart disease (Shafabakhsh et al., 2020). Nanocurcumin capsules (80 mg/day) significantly reduced the severity of diabetic sensorimotor polyneuropathy in type-2 diabetes patients in a randomised double-blind placebo-controlled study. Notable reductions in fasting blood sugar, HbA1C, neuropathy score, and total reflex score have been observed (Asadi et al., 2019). In a randomized, double-blind, placebo-controlled trial involving diabetic patients, nanocurcumin (nano-micelle, 80 mg/day) also significantly reduced HbA1c, fasting blood glucose, and body mass index after the treatment period (Rahimi et al., 2016). Oral administration of a combination of *C. longa* and *Boswellia serrata* (phytosome) was effective in treating non-proliferative diabetic retinopathy and treatment-naïve diabetic macular oedema, as measured by best-corrected visual activity and central macular thickness (Guarino et al., 2022). Curcumin (0.5 % in diet for 8 weeks) demonstrated hypolipidaemic effects in streptozotocin-induced diabetic rats by significantly reducing the cholesterol, triglyceride, and phospholipid levels. The treatment increased the cholesterol-7a-hydroxylase activity in the liver, suggesting an enhanced rate of cholesterol breakdown (Babu and Srinivasan, 1997). The *C. longa* leaf essential oil considerably inhibited α-amylase *in vitro* (IC_{50} 43.06 ± 1.24 μg/mL) compared to metformin (IC_{50}16.50 ± 0.66 μg/mL) (Sharma et al., 2022). In a randomised, double-blind, placebo-controlled trial, curcumin supplementation (500 mg, three times daily) reduced proteinuria in patients with overt diabetic nephropathy (Vanaie et al., 2019). Administration of 15 and 30 mg/kg doses of curcumin also ameliorated diabetic nephropathy in diabetic Sprague-Dawley rats, as demonstrated by reduced renal dysfunction and oxidative stress (Sharma et al., 2006).

Fermented *C. longa* (300 mg/kg) mitigated alcoholic fatty liver disease in C57BL/6 mice by regulating lipid metabolism (Lee, M. et al., 2022). This regulation involved cytochrome P450 2E1 (CYP2E1), sterol regulatory element-binding protein-1c (SREBP-1c), carnitine palmitoyltransferase 1 (CPT-1), and PPAR-α levels, and reduced hepatic lipid droplets induced by alcohol consumption (Lee, M. et al., 2022). Mun et al. also found that *C. longa* rhizome water extract (300 mg/kg) prevented high-fat diet-induced non-alcoholic fatty liver disease (NAFLD) in C57BL/6 mice (Mun et al., 2019). The extract significantly reduced intracellular ROS and MDA levels and suppressed cluster of differentiation 36 (CD36) and fatty acid transport proteins (FATP2 and FATP5). Moreover, it downregulated acetyl-coenzyme A carboxylase (ACC), SREBP-1c, and fatty acid synthase (FAS), while upregulating 5′ adenosine monophosphate-activated protein kinase (AMPK), PPAR-α, and CPT-1 (Mun et al., 2019). Turmeric hot water extract (0.175 %) prevented non-alcoholic steatohepatitis in mice by reducing hepatic oxidative stress and inflammation, as evidenced by the decreased mRNA expression of proinflammatory cytokines, vascular cell adhesion molecule-1 (VCAM-1), monocyte chemoattractant protein-1 (MCP-1), F4/80 (epidermal growth factor-like module-containing mucin-like hormone receptor-like 1), and CC motif chemokine receptor 2 (CCR2) (Uchio et al., 2018). The hydroalcoholic extract of *C. longa* (100 mg/kg) altered the level of some metabolites in liver samples from Sprague-Dawley rats fed a high-fat saturated fatty acid diet, apparently affecting the transmethylation pathway and choline metabolism to enhance hepatic fat export (Tranchida et al., 2017). *Curcuma longa* extract (100 and 300 mg/kg) also mitigated fatty liver disease and prevented hypercholesterolaemia by regulating cytochrome P450 7A1 (CYP7A1), LDL receptor, haeme oxygenase 1 (HO-1), and *β*-hydroxy *β*-methylglutaryl-CoA (HMG-CoA) reductase in rats fed a high-cholesterol diet (Yiu et al., 2011). Curcumin alleviated steatohepatitis in high-fat diet-fed rabbits by modulating the respiratory chain, oxidative stress, and TNF-α levels. It reduced the non-alcoholic steatohepatitis grade and aminotransferase levels, enhanced mitochondrial antioxidants and function, and lowered mitochondrial ROS (Ramirez-Tortosa et al., 2009).

Curcuma longa (50, 100, and 200 mg/kg) demonstrated dose-dependent hepatoprotective effects against isotretinoin-induced toxicity in Wistar albino rats by reducing liver enzyme and MDA levels and enhancing the antioxidant enzyme status (Nuriyeva et al., 2023). Vinegar-processed *C. longa* has shown enhanced efficacy in treating dysmenorrhoea in rats with liver depression and Qi stagnation. The treatment significantly reduced elevated serum hepatic markers, writhing scores, sex hormones, pain factors, and blood rheological indicators (Wu et al., 2023). Adaramoye et al. demonstrated the hepatoprotective potential of methanolic extract of *C. longa* rhizome (100 mg/kg) against D-galactosamine-induced hepatic damage in mice, with significantly elevated antioxidant enzymes and attenuated hepatic markers compared to vitamin C (Adaramoye et al., 2010). The ethanol extract of *C. longa* (40 mg/mL; 0.187 mg/kg/day) also exhibits hepatoprotective effects against bleomycin-induced chronic hepatotoxicity

in IRC mice by decreasing plasma markers, MDA levels, and increasing superoxide dismutase activity (Karamalakova et al., 2019). Hasan evaluated the short-term chemopreventive effects of *C. longa* (100 mg/kg/day) against oxidative stress in Sprague-Dawley rats (Hasan, 2020). The study demonstrated antioxidant effects in the liver and kidney, as evidenced by normal serum levels of alanine aminotransferase (ALT) and creatinine, reduced MDA levels, and increased antioxidant enzyme levels. The ethanol extract of *C. longa* rhizomes alleviated potassium bromate-induced hepatotoxicity in Wistar rats by stabilising vimentin (Awoniran and Adeyemi, 2018). Along the same line, turmeric hot water extract (20 mg/kg) mitigated acute ethanol-induced liver damage in C57BL/6 mice by suppressing inflammatory cytokines (TNF-α and IL-6) and oxidative stress, as evidenced by the reduced levels of thiobarbituric acid-reactive substances (Uchio, Ryusei et al., 2017).

In another study demonstrating hepatoprotective potential, the ethanol extract of *C. longa* rhizomes alleviated potassium bromate-induced hepatic necrosis in Wistar rats, enhanced liver function, and decreased lipid peroxidation (Adeyemi and Awoniran, 2019). The ethanolic extract of *C. longa* rhizomes (250 and 500 mg/kg) also prevented thioacetamide-induced liver cirrhosis in Sprague Dawley rats by promoting apoptosis and inhibiting hepatocyte proliferation (Salama et al., 2013). He et al. found that specifically curcumin (20 μM) promoted apoptosis in stellate cells by altering the levels of apoptosis-related growth factors, increasing Fas and p53 levels, and significantly reducing anti-apoptotic factors (He et al., 2015). Turmeric components have been shown to combat hepatobiliary diseases through the gut-liver axis and a two-way interaction between the gut microbiota and the liver (Gao et al., 2024). Turmeric ethanolic extract pretreatment increased alcohol dehydrogenase, aldehyde dehydrogenase, and antioxidant enzyme activities in a binge rat model, while regulating CYP2E1 activity, ROS levels, B-cell lymphoma-2 (Bcl-2), Bcl-2-associated protein X (Bax), and the proinflammatory cytokines TNF-α, IL-1β, and IL-6 (Lee, H. Y. et al., 2022). Curcumin modulates the Nrf2/HO-1 and transforming growth factor beta 1 (TGF-β1)/mothers against decapentaplegic homologue 3 (Smad3) pathways, thus mitigating CCl_4-induced acute liver injury in mice. Pretreatment with curcumin (50, 100, and 200 mg/kg) reduced CCl_4-induced oxidative stress, and caspase-9 and −3 activities (Peng et al., 2018). Oral administration of turmeric ethanol extract (100 mg/kg/day) reduced oxidative stress-related liver damage in rats with carbofuran-induced hepatotoxicity (Hossen et al., 2017). In cadmium-induced hepatotoxicity model, *C. longa* inhibited rat hepatic stellate cell activation and mitigated the hepatotoxic histologic changes (El-Mansy et al., 2016). Similarly, Kim et al. found the hepatoprotective effects of fermented turmeric (30 and 300 mg/kg) against CCl_4-induced oxidative stress in Sprague–Dawley rats (Kim et al., 2014). The treatment mitigated CCl_4-induced increases in serum ALT, aspartate aminotransferase (AST), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH) activities, and enhanced antioxidant capacity. Diarylheptanoids from the ethyl acetate fraction of *C. longa* rhizomes also showed hepatoprotective effects *in vitro* in human liver-derived Hep G2 cells (Song et al., 2001).

In respect of cardamom, in a double-blind, RCT involving 120 pregnant women with gestational age under 22 weeks and mild to moderate nausea and vomiting, cardamom intake (1.5 g/day) resulted in short-term improvement in gastrointestinal discomfort (Ozgholy et al., 2015). Cardamom (2 % feed) also showed gastroprotective effects in aspirin-induced (500 mg/kg, single dose) gastric ulcers, reducing both the ulcer index and score (Hamza et al., 2019). Qiblawi et al. reported that cardamom substantially inhibited aspirin-induced gastric lesions in rats when methanolic extract (100–500 mg/kg) and essential oil (12.5–50 mg/kg) were administered (Qiblawi et al., 2020). Cardamom essential oil at 100 and 200 mg/kg P.O. provided 40 % and 80 % protection, respectively, in a castor oil-induced diarrhoea mouse model. Moreover, *in vitro*, the oil inhibited both carbachol (1 μM) and high K^+ (80 mM)-induced contractions, with an EC_{50} of 0.76 mg/mL in rat ileum preparations (Alam et al., 2021). In other work, the crude extract of cardamom exhibited antispasmodic effects with both gut-stimulatory and inhibitory actions *via* cholinomimetic and Ca^{2+} antagonist mechanisms. It stimulated isolated guinea pig ileum at 3–10 mg/ml in an atropine-sensitive manner and relaxed contractions in the rabbit jejunum, showing effect on the Ca^{2+} curves similar to verapamil (Gilani et al., 2008). Studies on rats revealed that a 500 mg/kg crude methanolic extract, its petroleum ether soluble fraction at 50 and 100 mg/kg, and its insoluble fraction at 450 mg/kg inhibited ethanol- and aspirin-induced gastric lesions but not pylorus ligation (Jamal et al., 2006). The methanolic extract reduced ethanol-induced lesions by 70 %, and the petroleum ether-soluble fraction achieved 50 % reduction at both doses. Notably, the petroleum ether soluble fraction nearly eliminated aspirin-induced lesions at a 12.5 mg/kg dose (Jamal et al., 2006).

Aqueous extracts of cardamom (10 % w/v, perfused at 0.15 mL/min) tested in pentobarbitone-anaesthetised rats increased gastric acid secretion (Vasudevan et al., 2000). The effects of aqueous and methanolic cardamom extracts on gastric secretion were also examined in rabbits, and oral administration of either extract significantly decreased both gastric secretion and pepsin output (Sakai et al., 1989). Cardamom hot water extract (10 mL/kg) demonstrated antidiarrheal activity in Swiss-Webster strain mice by increasing the latency period of diarrhoea (Rahman et al., 2008).

An *in vitro* susceptibility study showed that cardamom seed extract had a minimum inhibitory concentration of 100 μg/mL against *Helicobacter pylori*, an etiological factor associated with the development of gastritis and peptic ulcer disease (Mahady et al., 2005). In another study, cardamom essential oil was administered to microbiota-depleted IL-$10^{-/-}$ mice infected with *Campylobacter jejuni*, resulting in reduced intestinal pathogen loads, improved clinical outcomes, and decreased inflammatory responses, indicating its potential for treating acute campylobacteriosis and preventing postinfectious complications (Heimesaat et al., 2021). An *in vitro* anthelmintic study demonstrated that cardamom methanolic extract exhibited potent activity against the ovine gastrointestinal worm *Teladorsagia circumcincta*, with an EC_{50} of 0.37 mg/mL (Esteban-Ballesteros et al., 2019).

In Wistar albino rats, oral administration of nanoliposomes of 1,8-cineole-rich cardamom seed extract at 550 mg/kg b.w. for 35 days normalised the fasting blood glucose levels and serum lipid profiles, with beneficial pattern of regulation of key enzymes (Paul et al., 2019). At 1 mg/mL, the aqueous and methanol extracts of *E. cardamomum* showed α-glucosidase inhibition rates of 10.41 % and 13.73 %, respectively. For α-amylase inhibition, aqueous extracts achieved 82.99 % inhibition, and methanol extracts reached 39.93 % (Ahmed et al., 2017). Cardamom supplementation (1 % of the diet) for 8 weeks in male Wistar rats fed a high-fat diet improved glucose tolerance, reduced abdominal fat, prevented dyslipidaemia, and mitigated liver inflammation and oxidative damage, as evidenced by histological analysis (Rahman et al., 2017).

A RCT conducted on 83 overweight or obese patients with type 2 diabetes who were administered 3 g of cardamom supplementation for over 10 weeks also revealed a significant decrease in HbA1c, insulin, homeostasis model assessment-estimated insulin resistance (HOMA-IR), and triglycerides and an increase in sirtuin-1 (Sirt1) levels (Aghasi et al., 2019). A double-blind, placebo-controlled trial involving 80 pre-diabetic subjects, who were administered 3 g of cardamom daily for 8 weeks, showed significant reductions in the serum high-sensitivity C-reactive protein (hs-CRP) ratio and MDA compared to the placebo group (Kazemi et al., 2017). In another RCT, 42 patients with type 2 diabetes who received 3 g of cardamom daily for 8 weeks demonstrated significant improvements in total cholesterol, LDL, and HDL levels compared with the control group (Azimi et al., 2014). Among a cohort of 99 obese and diabetic women with polycystic ovary syndrome (PCOS), a 16-week intervention comprising a low-calorie diet and 3 g of green cardamom per day resulted in substantial reductions in anthropometric indices, glycaemic levels, and androgen hormones compared to the control group (Cheshmeh et al., 2022a). Supplementation with green cardamom

also downregulated the expression of fat mass and obesity-associated (FTO), CPT-1A, leptin receptor (LEPR), and lamin A/C (LAMIN) genes while upregulating PPARγ. These findings suggest that green cardamom may improve metabolic and hormonal parameters in women with PCOS (Cheshmeh et al., 2022a). In another study, 80 overweight or obese prediabetic women were randomly assigned to receive either 3 g of green cardamom or placebo for 2 months. Cardamom supplementation significantly reduced total and LDL cholesterol levels, and enhanced insulin sensitivity compared with the placebo group (Fatemeh et al., 2017).

In a randomised, double-blind, placebo-controlled study, supplementation with 3 g of ground green cardamom for 10 weeks significantly reduced systolic blood pressure and serum levels of hs-CRP levels together with increase in serum NO level in 83 overweight or obese patients with T2DM, suggesting improved vascular function and potential benefits for vascular health in this population (Zahedi et al., 2022). In a study of 87 overweight or obese patients with non-alcoholic fatty liver disease, 3 months of green cardamom supplementation (500 mg capsules, three times daily) significantly increased Sirt1 levels and reduced hs-CRP, TNF-α, IL-6, alanine aminotransferase, and fatty liver severity compared to placebo (Daneshi-Maskooni et al., 2018). Another study assessed the efficacy of cardamom in dexamethasone-induced hepatic steatosis, dyslipidaemia, and hyperglycaemia in 24 albino rats. Cardamom treatment (1 g/kg orally for 12 days) significantly reduced dexamethasone-induced metabolic disturbances (Nitasha Bhat et al., 2015). *In vivo* experiments demonstrated that 15-day oral pretreatment with ethanolic aqueous cardamom extract (200 mg/kg) significantly reduced acetaminophen (300 mg/kg)-induced liver damage, oxidative stress, inflammation, and apoptosis in mice. Additionally, cardamom boosted antioxidant enzyme activity and elevated Nrf2, heme oxygenase 1 (HO-1), and NAD(P)H dehydrogenase [quinone] 1 (NQO-1) levels, aiding in liver protection (Alkhalifah et al., 2022). Cardamom oil (3 g/kg) application also notably reduced total cholesterol (31 %), LDL cholesterol (44 %), and triglycerides (42 %), while also lowering cardiac and liver cholesterol, in Wistar rats fed a high-cholesterol diet for 8 weeks. It also enhanced hepatic antioxidant activity and increased serum ascorbic acid levels (Nagashree et al., 2017). The aqueous extract of *E. cardamomum* demonstrated significant inhibition of pancreatic lipase and α-amylase enzymes in a concentration-dependent manner, with IC_{50} values of 288.75 μg/mL and 220.5 μg/mL, respectively (Al-Yousef et al., 2021). Cardamom aqueous extract treatment (10 mL/kg for 20 days) effectively mitigated tamoxifen-mediated (45 mg/kg for 10 days) severe pancreatic changes, including the degeneration of pancreatic acini, increased levels of pancreatic enzymes, glucose, fatty acids, and triglycerides, and the reduced insulin levels (Attia et al., 2023).

In respect of digestive system support by *Z. officinale*, the aqueous extract of the plant (75–300 mg/kg) alleviated loperamide-induced constipation in Wistar rats by enhancing gastrointestinal-transit (53.42–85.57 %), gastric emptying (55.47–98.88 %), and stool composition, while restoring oxidative balance, with increased spontaneous intestinal contractions (EC_{50} = 10.52 μg/mL) without impacting electrogenic fluid transport (Abidi et al., 2022). In a 12-week double-blind, parallel randomised controlled trial with 52 relapsing-remitting multiple sclerosis patients, ginger supplementation (500 mg thrice daily) also significantly reduced constipation, nausea, bloating, and improved abdominal pain compared with placebo (Foshati et al., 2023). In another study, ginger rhizome extract (2 × 100 mg) significantly increased interdigestive antral motility during phase III of the migrating motor complex and enhanced the motor response to a test meal in the corpus in 12 healthy volunteers, with a trend of increased motor response in other gastro-duodenal regions (Micklefield, 1999). *Zingiber officinale* extract (0.8 g/ml) pretreatment for 7 and 14 days also significantly reduced indomethacin-induced ulceration in rats by 57.51 % and 59.90 %, respectively (Airaodion, 2019). In another relevant work, a 95 % ethanolic extract of *Z. officinale* demonstrated gastroprotective effects in rats exposed to HCl, water immersion restraint stress, and aspirin-induced gastric ulcers (Chantharangsikul et al., 2016). Doses of 0.1–1.0 g/kg significantly reduced gastric lesions by up to 81.7 % for HCl. The extract increased visible gastric mucus secretion and tended to enhance soluble gastric mucus secretion in a histamine-induced secretion model using gastric fistulae, without affecting gastric pH, acid, or pepsin levels (Chantharangsikul et al., 2016). Ginger extract-loaded gastro-retentive floating beads (200 mg/kg) also notably reduced the lesion extent and enhanced gastric mucosa recovery in cold-restraint stress-induced gastric ulcers in albino rats, surpassing free ginger extract and showing comparable or superior effects to cimetidine (10 mg/kg) (Kumar Singh and Pal Kaur, 2011). Administering ginger extract (1.5–5 g/kg) daily for three days, after inducing gastric ulcers with acetic acid in male Sprague-Dawley rats, significantly reduced ulcer size and oxidative stress in a dose-dependent manner, whereby the extract mainly increased growth factor expression, suppressed chemokines, and partially suppressed TNF-α (Ko and Leung, 2010). Administered orally at 500 mg/kg to albino rats, ginger extract also significantly reduced stomach lesions induced by 80 % ethanol, 0.6 M HCl, 0.2 M NaOH, and 25 % NaCl. It also protects ulcers from non-steroidal anti-inflammatory drugs and hypothermic restraint stress (Al-Yahya et al., 1990). In another work, acetone extract (1000 mg/kg) and zingiberene (100 mg/kg) significantly reduced HCl/ethanol-induced gastric lesions by 97.5 % and 53.6 %, respectively, when administered orally. Furthermore, 6-gingerol (100 mg/kg) inhibited the lesions by 54.5 % (Yamahara et al., 1988). The gingerol-rich fraction of the methnol extract of dried ginger rhizome demonstrated potent inhibitory activity against all *Helicobacter pylori* strains (MIC: 0.78–12.5 μg/mL), with notable inhibition of $CagA^{+}$ strains (Mahady, 2003).

A review of 41 articles revealed that ginger supplementation significantly decreased blood glucose levels in 28 studies, reduced MDA levels in nine studies, and lowered serum creatinine levels in 17 studies (Veisi et al., 2022). Moreover, 15 studies reported a reduction in total cholesterol (TC) and 14 studies noted a decrease in triglycerides (TG). Ginger also mitigated renal injuries from diabetes in 26 studies, highlighting its ameliorative effects on diabetic nephropathy (Veisi et al., 2022). A randomized, double-blind, placebo-controlled trial of 76 patients with type 2 diabetes mellitus and non-alcoholic fatty liver disease (NAFLD) found that 1000 mg ginger powder capsules taken twice daily for three months significantly reduced body mass index, waist and hip circumferences, liver transaminases, and blood pressure, and improved insulin levels, insulin resistance, and high-density lipoprotein cholesterol compared to baseline (Ghoreishi et al., 2023). Ginger supplementation (2000 mg/day for eight weeks) reduced the inflammatory marker neutrophil-to-lymphocyte ratio (NLR), high-sensitivity C-reactive protein (hs-CRP), decreased triglyceride levels, and increased serum albumin in diabetic patients with end-stage renal disease (ESRD) undergoing haemodialysis (Veisi et al., 2023). In a clinical trial that employed a randomized, double-blind, placebo-controlled methodology, 44 diabetic patients were randomly assigned to either the ginger (2000 mg/day for 8 weeks) or placebo group (Rostamkhani et al., 2023). The outcome of the study showed that ginger supplementation led to a significant decrease in blood glucose levels, improvement in insulin sensitivity, and reduction in serum urea levels in patients (Rostamkhani et al., 2023). The antidiabetic effects of ginger and cinnamon administered orally at a 1:1 ratio (500 mg/kg and 100 mg/kg, respectively) for 6 weeks were also compared to those of metformin in streptozotocin (STZ)-induced diabetic male Sprague-Dawley rats (Ayuob et al., 2021). This combination significantly improves hypoglycaemia and antioxidant levels, primarily by enhancing islet cell repair through the upregulation of pancreatic p53 expression (Ayuob et al., 2021). In another study, ginger extract administered at 200 and 400 mg/kg doses markedly reduced myocardial fibrosis and inflammation in rats with STZ-induced diabetes by modulating gene expression in the SMAD/TGF-β pathway, an effect comparable to metformin (200 mg/kg) (Abdi et al., 2021). Similarly, *Z. officinale* (500 mg/kg/day) and metformin (500 mg/kg/day) effectively mitigated testicular degeneration and maintained structural integrity in

STZ-induced diabetic rats after six weeks of treatment, as demonstrated by histopathological examination (Al-Shathly et al., 2020). An aqueous ginger extract (500 mg/kg) administered orally for six months also exhibited therapeutic effects on liver alterations in STZ-induced diabetic rats comparable to metformin (500 mg/kg) (Alshathly, 2019). Specifically, ginger treatment significantly reduced blood glucose levels, liver enzymes, and preserved total antioxidant levels, while normalizing body weight and liver index. Further histopathological analysis has revealed that ginger mitigates diabetes-induced liver damage, including degenerative changes, lipid deposition, and fibrosis, with results similar to metformin (Alshathly, 2019). In a randomized, double-blind, placebo-controlled trial, 64 participants who received either ginger (1 g/day) or a placebo twice daily, for 2 months, showed that ginger reduced the levels of pro-inflammatory cytokines (IL-6 and TNF-α) and the acute phase protein hs-CRP (Mahluji et al., 2013). Treatment with polyphenolic-rich *Z. officinale* extract (500 mg/kg) significantly lowered fasting blood glucose levels compared to the control groups in STZ-induced diabetic rats after 28-day oral administration (Kazeem et al., 2013). The extract normalized liver carbohydrate-metabolizing enzymes, enhanced antioxidant enzyme activity, and reduced liver function enzyme activity in the STZ treated animals (Kazeem et al., 2013). In another animal-based study, oral administration of 500 mg/kg aqueous ginger extract for 30 days to STZ-induced diabetic rats reduced plasma glucose levels by 38 % on day 15 and by 68 % on day 30 (Abdulrazaq et al., 2012). Aqueous ginger extract (500 mg/ml) administered for four weeks significantly reduced fasting blood glucose and MDA levels, while increasing serum insulin levels and enhancing insulin sensitivity in alloxan-induced diabetic and insulin-resistant diabetic rats compared to control and ginger-only treated rats (Iranloye et al., 2011). Methanolic (100 and 200 mg/kg b.w.) or aqueous extracts (150 and 300 mg/kg b. w.) administered orally for 65 days to male alloxan-induced diabetic rats also improved the fertility index, sexual organ weight, serum testosterone levels, sperm motility, and sperm count (Shalaby and Hamowieh, 2010). In another study, an aqueous extract of raw ginger (500 mg/kg, intraperitoneally) administered daily for 7 weeks to STZ-induced diabetic rats exhibited hypoglycaemic, hypocholesterolemic, and hypolipidaemic effects and effectively reversed the animals' diabetic proteinuria (Al-Amin et al., 2007). Similarly, oral administration of ethanolic *Z. officinale* extract (200 mg/kg) for 20 days notably decreased hyperglycaemia in STZ-induced diabetic rats, outperforming the standard anti-hyperglycaemic agent gliclazide (25 mg/kg) (Bhandari et al., 2005). *Z. officinale* (4 mL/kg per day) significantly increased insulin levels and decreased fasting glucose, serum cholesterol, TG, and blood pressure in STZ-induced type I diabetic rats over a 6-week period (Akhani et al., 2004). *In vivo* rat studies indicated that long-term (8 weeks) ginger consumption significantly increased pancreatic lipase, amylase, trypsin, and chymotrypsin activity, but a single-dose ginger treatment decreased these enzyme activities in the pancreas, while stimulating amylase and sucrase in the intestinal mucosa (Platel and Srinivasan, 2000).

In iron-loaded human hepatoma (Huh7) cells, 6-gingerol-rich ginger extract (3.125–12.5 μg/mL) exhibited significant antioxidant activity by reducing labile cellular iron, intracellular ROS, and lipid peroxidation (Chuljerm et al., 2023). In rats with diethylnitrosamine toxicity, administration of ginger essential oil (1–l0 μg/mL) for two months significantly increased serum HDL levels by 31 % and decreased LDL levels by 55 %. Moreover, serum ALT and ALP levels were reduced by 57 % and 54 %, respectively, and GPx activity was increased by 75 %. Histopathological analysis has confirmed the protective effect of ginger against liver abnormalities (Fahmi et al., 2019). Pretreatment with ginger (100 mg/kg) significantly reduced acetaminophen (APAP)-induced hepatic enzymes (ALT, AST, and ALP), bilirubin, and oxidative stress marker (MDA) levels, while restoring TG and protein levels. Histopathological analysis has revealed that ginger substantially mitigates liver damage, including necrosis and vacuolisation (Abdel-Azeem et al., 2013). Methanol extracts of ginger, chicory, and their combination (250 and 500 mg/kg) effectively restored biochemical and blood cell alterations in rats with CCl_4-induced liver damage, as well as histopathological changes (Atta et al., 2010). Similarly, pretreatment with aqueous *Z. officinale* extract (200 and 400 mg/kg) significantly reduced serum ALT and ALP activities and enhanced the hepatic antioxidant status in rats with APAP-induced acute hepatotoxicity (Ajith et al., 2007). Ginger extract containing 4-gingerol, 6-gingediol, 6-gingerol, lemon extract containing eriodyctiol, rutin, hesperidin, and isorhamnetin and their combination also prevented CCl_4-induced liver damage in Wistar rats, as confirmed by histological analysis (Bekkouch et al., 2022). Along the same line, oral administration of graded doses of *Z. officinale* methanol extract for 4 weeks following a 1-week CCl_4 treatment in female rats significantly ameliorated liver damage, as evidenced by histopathological analysis, improved liver function biomarkers (AST, ALT, and ALP), reduced total protein, and increased antioxidant levels (GSH and CAT) in a dose-dependent manner (Oke et al., 2019).

In male golden Syrian hamsters fed standard chow supplemented with 3 % cholesterol and 15 % butter for 21 weeks, administration of ginger extract (800 μg/kg body weight/day) for 5 weeks significantly reduced liver stearoyl-CoA desaturase 1 (SCD1) expression, plasma non-esterified fatty acids (NEFA), and oxidative stress markers (MPO and TBARS), and enhanced cholesterol efflux in the liver (Carnuta et al., 2018). In hepatic tissue, the extract decreased cholesterol, triglyceride, NEFA, MPO, and TBARS levels and elevated paraoxonase 1 (PON1), thereby enhancing lipid metabolism markers (ABCG5/G8, CYP7A1, LXRα/β, and PPARγ) (Carnuta et al., 2018). Ginger extract (400 mg/kg/day) treatment reversed ferrous sulfate-induced liver and kidney damage in rats, improved serum markers and renal function, and reduced lipid peroxidation. Histological analysis confirmed the protective effects of the ginger extract (Gholampour et al., 2017). *Zingiber officinale* extract (125 mg/kg) and 6-gingerol (50 mg/kg) also significantly reduced mercuric chloride ($HgCl_2$)-induced hepatorenal toxicity and oxidative stress in male Sprague-Dawley rats, as evidenced by improved biochemical parameters and histopathological analysis (Joshi et al., 2017). Rats treated with carbendazim (CBZ) and the concurrent 6-gingerol-rich fraction (6-GRF) at doses of 50, 100, and 200 mg/kg for 14 days showed that 6-GRF normalized CBZ-induced reductions in white blood cells, neutrophils, lymphocytes, and platelets (Salihu et al., 2016). 6-GRF also enhanced antioxidant enzyme activity and glutathione levels in the liver and kidneys, while decreasing CBZ-elevated hydrogen peroxide and MDA levels. Histological analysis confirmed that 6-GRF mitigated CBZ-induced oxidative damage and improved haematological and hepatic/renal functions (Salihu et al., 2016). Twelve-week administration of ginger (400 mg/kg) also counteracted cadmium (Cd) exposure-induced alterations in rabbit kidneys and liver, including the increased mRNA expression of pro-apoptotic caspase 3, proliferation (MKI67), proto-oncogene (C-fos), and antioxidant enzyme (GST) markers, while reducing anti-apoptotic Bcl2 expression (Baiomy and Mansour, 2015). Similarly, The CCl_4-induced liver fibrosis in male Wistar rats was attenuated by daily oral administration of *Z. officinale* extract at 300 or 600 mg/kg, which significantly reduced liver enzyme levels, inflammation, and pro-inflammatory cytokines and inhibited the transforming growth factor beta 1 (TGF-β1)/ Mothers against decapentaplegic homolog 3 (Smad3) and NF-κB/ inhibitor of nuclear factor kappa B (IκB) signalling pathways compared to CCl_4 alone (Hasan et al., 2016). A standardised *Z. officinale* extract (400 mg/kg) also increased mRNA and protein levels of LDL receptors and reduced the protein expression of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase in the liver of rats fed a high-fat diet (HFD) (Nammi et al., 2010). These results indicate that *Z. officinale* can restore lipid homeostasis by altering the expression of LDL and HMG-CoA reductase (Nammi et al., 2010). Similarly, the ethanolic extract of ginger (400 mg/kg) administered concomitantly with a HFD for 6 weeks resulted in a reduction of TNF-α and IL-6 expression, in association to inhibited NF-κB activation in the liver of HFD-fed rats (Li, X.H. et al., 2012). Studies with HuH-7 cells in the same work showed that ginger extract (100 μg/ml)

pretreatment also decreased NF-κB target inflammatory genes IL-6, IL-8, and serum amyloid A1 (SAA1), and inhibited NF-κB activity, IκBα degradation, and IκB kinase (IKK) activity in IL-1β-induced inflammation (Li, X.H. et al., 2012). Ginger treatment also reduced body weight by 10 %, lipid droplet area by 66 %, and MDA levels by 41 %, while increasing glutathione *S*-transferase (GST) activity by 222 % in Wistar rats fed an unhealthy diet (Leal et al., 2019). The ethanolic extract of *Z. officinale* rhizomes (250 or 500 mg/kg) and silymarin (200 mg/kg) significantly mitigated thioacetamide-induced liver damage and fibrosis in rats, and immunohistochemical analysis revealed reduced liver proliferation in extract-treated rats compared with untreated controls (Abdulaziz Bardi et al., 2013). *Zingiber officinale* oil at 200 mg/kg for 28 days also lowered serum enzyme activities, TG and total cholesterol levels, while enhancing glutathione (GSH), GST, and SOD activities against acute ethanol-induced fatty liver in male Wistar rats (Nwozo et al., 2014). Similarly, ginger ethanol extract significantly enhanced antioxidant and liver marker enzyme levels while reducing MDA, AST, ALT, ALP, gamma-glutamyl transferase (GGT), and total bilirubin in CCl_4-induced liver fibrosis in rats (Motawi et al., 2011). Co-administration of ginger extract (400 mg/kg) with atorvastatin mitigated hepatic damage, restored enzyme levels, and improved cholesterol levels, suggesting a potential strategy for managing hypercholesterolaemia with reduced risk of liver dysfunction (Heeba and Abd-Elghany, 2010). In another study, ginger aqueous ethanol extract notably reduced lipid peroxidation in tissue preparations, achieving up to 94 % inhibition in liver homogenates and 92 % in brain homogenates and liver mitochondria during ROS-induced lipid peroxidation and DNA damage, but only partially protected against H_2O_2-induced DNA damage (Ajith, 2010). In a double-blind, placebo-controlled trial, ginger supplementation (1000 mg twice daily) for three months significantly improved blood pressure, serum insulin levels, insulin resistance (HOMA-IR), and HDL cholesterol in 76 patients with type 2 diabetes mellitus and NAFLD (Ghoreishi et al., 2023). Both groups exhibited reduced body mass index (BMI), waist and hip circumferences, and liver transaminase levels, but no significant changes were observed in inflammatory markers or FibroScan imaging indices (Ghoreishi et al., 2023). These effects were in line with the outcome of animal research study, in which ginger extract treatment reversed the effects of a HFD on endoplasmic reticulum (ER) stress in male Wistar rats with NAFLD that caused notable weight gain, higher plasma lipid levels, glucose, hepatic enzymes, and increased expression of lipogenic and ER stress genes, such as C/EBP homologous protein (CHOP), X-box binding protein 1 (XBP1), and glucose-regulated protein (GRP78) (Kandeil et al., 2019).

4. Current challenges and future perspectives for the development of new Zingiberaceae-derived drugs and nutraceuticals

The Zingiberaceae plants are rich in bioactive compounds that contribute to their broad pharmacological properties, attracting a great interest for developing novel drugs, natural remedies and plant-based nutraceuticals. Addressing these challenges encompasses multiple approaches: developing new combination therapies and plant-based products, improving delivery methods to enhance bioavailability and target treatments, and conducting rigorous clinical trials. Bioavailability and absorption issues as well as the need for more clinical trials will be presented in more detail in the following two subsections.

4.1. Bioavailability and absorption issues

Indian spices, which include ginger, turmeric, galangal, and cardamom among others, have long been used in food preparation and traditional medicine. The medicinal properties of these rhizomatous plants are attributed to their abundance of bioactive compounds, among others curcuminoids, gingerols, shogaols, and terpenes. The development of new drugs and nutraceuticals from plant-based sources has garnered significant interest due to their potential health benefits and lower side effects compared to synthetic compounds (Atanasov et al., 2021). However, the efficacy of such compounds is significantly influenced by their bioavailability.

In the context of the reviewed Zingiberaceae plants specifically, a recent patent documentation analysis highlights the growing innovation activity around ginger, reflecting increasing interest in its commercialization and therapeutic applications (Matin, Maima et al., 2025). Ginger contains multiple bioactive compounds, such as 6-gingerol and 6-shogaol, which exhibit prominent anti-inflammatory and antioxidant properties (Yeh et al., 2014). However, the clinical use of these compounds is significantly limited by their low bioavailability, primarily due to rapid metabolism and poor absorption. Current research aiming to overcome such issues has focused on gingerols in capsule form, but novel strategies are still needed that enhance their solubility and bioavailability. Advanced technologies, such as proliposomes (Wang, Q. et al., 2018), self-microemulsifying drug delivery systems (SMEDDS) (Xu et al., 2016), as well as polymeric micelles (Zhen et al., 2020), could play a key role in improving the plasma concentration of 6-gingerol.

Curcuminoids, the primary bioactive ingredient in turmeric, are a mixture of many compounds that are rapidly metabolized into various bioactive forms after ingestion, but they have poor bioavailability in the body's organs (Liu et al., 2016). In rats, the detection limit for curcumin in plasma is quite low, at 0.35 μg/ml, making it difficult to achieve detectable concentrations after oral administration (Khursheed et al., 2022). Once absorbed, curcumin is quickly metabolized in the liver to glucuronide and sulfate conjugates of curcumin, which are less bioactive than free curcumin (Tsuda, 2018). A number of methods have been developed to overcome the poor bioavailability associated with the use of *C. longa* (turmeric). These include adjuvants (Cai et al., 2021), liposomes (Sinjari et al., 2019) and nanoparticles (Jiang et al., 2023) and other nanoformulations (Lushchak et al., 2020).

Similarly, galangal is rich in compounds such as galangin and alpinin, known for their antimicrobial and anti-inflammatory properties (Aljobair, 2022). However, these compounds also face challenges with poor absorption and rapid metabolism. Thus, research is focusing on the use of permeation enhancers to improve their bioavailability (Simon et al., 2022).

Cardamom, which is rich in essential oils and compounds like cineole and α-terpinyl acetate, is prominently studied for its antioxidant and anti-inflammatory effects (Cardenas Garza et al., 2021). Yet, the stability and absorption of its volatile components are challenging. To enhance stability and absorption, methods like encapsulation in stable carriers and formulation into emulsions are being explored (Al-Ismail et al., 2014; Souza et al., 2022).

Taken together, while ginger, turmeric, galangal, and cardamom offer considerable potential health benefits, their bioavailability and absorption remain a significant challenge. Overcoming these challenges is essential to fully harnessing the therapeutic potential of these remarkable herbs. Further research is warranted on formulation, delivery systems, and factors influencing absorption to develop effective interventions.

4.2. Need for further clinical studies

Clinical studies on ginger have shown promising results in treating nausea and vomiting during pregnancy (Sharifzadeh et al., 2018). Analysis of clinical trials, including those registered on ClinicalTrials.gov, supports these findings and also suggests ginger's broader therapeutic potential (Matin, M. et al., 2024c). However, to confirm these benefits and explore additional uses such as cancer prevention, further well-designed research is needed.

Curcumin has shown potential therapeutic effects in preclinical studies and limited clinical trials (Dai et al., 2018; Ringman et al., 2012; Sandoughdaran et al., 2021). However, most studies conducted so far were of short duration and involved very few participants. Therefore,

there is a need for a larger, extended and longer period clinical studies to validate the potential health effect of curcumin on chronic diseases, including arthritis (Dai et al., 2018), Alzheimer's disease (Ringman et al., 2012), and cancer (Sandoughdaran et al., 2021).

While some clinical studies suggest that cardamom may lower inflammatory markers in obese women with PCOS (Cheshmeh et al., 2022b) and improve blood sugar levels and insulin resistance in type 2 diabetes (Aghasi et al., 2019), there remains a notable lack of robust evidence from clinical trials. More rigorous trials are needed to determine its medicinal properties and safety in various populations.

The therapeutic potential of galangal in modern medicine remains largely unexplored, with a notable lack of clinical studies assessing its efficacy and safety. This highlights the need for further research to validate its traditional uses and identify new therapeutic applications.

Taken together, the clinical evidence supporting the health benefits of ginger, turmeric, galangal, and cardamom is still in its infancy. Although preclinical studies and traditional uses offer promising insights, more well-designed clinical trials are essential to confirm their efficacy, safety, and optimal dosages. Additionally, standardized methods for extracting bioactive compounds, as well as rigorous quality control, are crucial to ensure consistent efficacy and safety of herbal products. Although widely consumed and generally well-tolerated, Zingiberaceae plants may cause mild side effects at high or prolonged doses. For instance, ginger has been associated with gastrointestinal discomfort in some individuals, while turmeric may induce gallbladder contractions and potentiate the effects of anticoagulant drugs (Kim et al., 2012; Pinsornsak, 2012; Singh et al., 2012). These safety aspects, although not commonly problematic at culinary doses, warrant consideration in clinical studies and the development of standardized supplements.

Despite the promising pharmacological profiles of Zingiberaceae-derived compounds, none have yet received regulatory approval as formal therapeutics by major health agencies such as the FDA or EMA. However, many of these plant extracts, particularly from ginger and turmeric, are widely marketed as dietary supplements and traditional medicine products with claimed health benefits. This underscores the need for rigorous scientific and regulatory pathways to transition these botanicals from traditional use to evidence-based clinical applications.

5. Conclusion

The Zingiberaceae family, including notable species like ginger, turmeric, galangal, and cardamom, exhibits a diverse range of bioactive compounds with significant therapeutic potential. Traditional medicinal systems across various cultures have long utilized these plants for treating digestive, respiratory, cardiovascular, and inflammatory ailments. These plants contain diverse phenolics, terpenes, and other bioactives that contribute to their antioxidant, anti-inflammatory, antimicrobial, anticancer, and cardioprotective properties.

Despite their widespread traditional use and substantial preclinical evidence supporting their health benefits, further rigorous clinical research is necessary to fully establish standardized therapeutic applications and dosages. Challenges such as bioavailability and absorption issues limit the efficacy of these compounds when used in clinical settings, and innovative delivery mechanisms are under development in order to enhance their therapeutic potential.

The findings of the reviewed research underscore the value of integrating Zingiberaceae family plants into modern medicine – not as replacements for conventional therapy, but as complementary agents that could enhance health and wellness. Ginger's success in clinical trials for nausea exemplifies the real-world potential of this plant family's remedies, and similar efforts for the other spices are warranted.

In summary, Zingiberaceae family plants present a promising foundation for developing natural health products and nutraceuticals. Advancing our understanding of these plants through continued research could support the development of new, accessible therapeutic agents for managing chronic diseases and promoting general health. With coordinated interdisciplinary efforts across pharmacology, biotechnology, and clinical science, the rich medicinal legacy of Zingiberaceae plants can be translated into evidence-based therapeutic and nutraceutical applications that meet modern health needs.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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