Zingiberaceae Plants: A Cornucopia of Promising Chemotherapeuticals for Cancer Cure

T. Soumya, P. R. Jayasree, and P. R. Manish Kumar

1 Introduction

Cancer, the second leading cause of human death worldwide, behind cardiovascular disease, might soon rank as the leading cause of death. It is the single most important barrier to increasing life expectancy in every country of the world in the 21st century [1]. Cancer is an abnormal growth of cells caused by multiple changes in gene expression which leads to dysregulation in balancing cell proliferation and cell death. As a consequence, a population of cells evolve at the site of origin, capable of invading into tissues at distant sites, causing significant morbidity and death of the host, if untreated [2–5]. Cancers are conventionally treated using a combination of three major modes - surgery, radiation, and chemotherapy. Chemotherapy involves treatment of cancer with one or more chemicals known to have cytotoxic, antineoplastic activity. Traditional chemotherapeutic agents, which act by killing rapidly dividing cancer cells, also harm cells that divide rapidly under normal circumstances, thereby resulting in side effects such as immunosuppression and mucositis among others. Newer anticancer drugs (targeted chemotherapy) are not indiscriminately cytotoxic, but rather target proteins that are abnormally expressed in cancer cells and are essential for their growth [6]. It is believed that anticancer effects of plants develop by suppressing pathways involved in cancer progression, DNA repair, increasing body immunity, and inducing antioxidant effects [7–9].

During the last few decades, ethnomedicinal plants have played a significant role in the development of anticancer drugs with fewer side effects in different continents of the world. Out of 121 prescription drugs that are being used today for

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cancer treatment, 90 are plant-based and 75% of them were discovered from folklore claims. Secondary metabolites from plants, including alkaloids, terpenoids, and polyphenolic compounds with promising anticancer potential, have been developed for clinical practice [10, 11]. Classical examples include Vinca alkaloids (vinblastine and vincristine), isolated from *Catharanthus roseus* G. Don. (Apocynaceae), paclitaxel and docetaxel - semisynthetic derivatives of Taxanes (diterpenoids) from the Pacific Yew tree, *Taxus brevifolia* and *T. baccata* respectively, irinotecan and topotecan - semisynthetic derivatives of Camptotheca alkaloids, isolated from *Camptotheca acuminate* and *Podophyllum lignans* from mayapple tree, *Podophyllum peltatum* and *P. hexandrum* [11–13].

Zingiberaceae is one of the largest families of the plant kingdom, distributed widely throughout the tropics, particularly in Southeast Asia [14, 15]. The family consists of a large number of economically and medicinally important plants well known for their use in ethnomedicine. The Zingiberaceae plants contain a number of volatile and essential oils including terpenoids, phenylpropanoids, flavonoids, and sesquiterpenes, which have been reported to possess anticancer activity [16–19]. Hence, these plants are considered to be excellent candidates for development of novel chemotherapeutics. Various extracts and pure compounds / secondary metabolites isolated from *Curcuma*, *Zingiber*, *Kaempferia*, *Alpinia*, *Amomum,* and *Hedychium* genera reportedly possess anticancer activity as evidenced by *in vitro* and *in vivo* studies [20–24]. Few notable examples for anticancer compound include curcumin/curcuminoids (*Curcuma longa*), zerumbone (*Zingiber zerumbet*), gingerol, and shogaol (*Zingiber officinale*) among many others [25–29]. Even though a number of review articles were available about various biological activities of different genera of Zingiberaceae family, a comprehensive scrutiny about anticancer potential of these plants was found lacking. Hence, this chapter aims to overview anticancer potential of organic solvent extracts and compounds identified therein belonging to different genera of Zingiberaceae plants.

2 Zingiberaceae

The taxonomic position of the Family Zingiberaceae is as follows:

Kingdom:	Plantae
Subkingdom:	Trachebionta
Superdivision:	Spermatophyta
Division:	Magnoliophyta
Subdivision:	Angiospermae
Class:	Monocotyledonae (Liliopsida)
Subclass:	Zingiberidae
Order:	Zingiberales
Family:	Zingiberaceae

Zingiberaceae commonly known as ginger family is a one of the largest families of flowering plants comprising 52 genera divided into more than 1300 species. These aromatic herbs, with creeping horizontal or tuberous rhizomes, are distributed throughout tropical Africa, Asia, and the America [14, 15]. India is one of the richest regions displaying high diversity of Zingiberaceae with 21 genera and around more than 200 species, confined to northeastern, southern parts of India and Andaman-Nicobar Islands [15]. The members of Zingiberaceae are perennial rhizomatous herbs. The rhizome is sympodially branched and composed of distinct segments. The rhizomes are variously colored ranging from pale yellow, orange-yellow, deep yellow, blue, greenish blue, pink, or combinations of these in different species. The young rhizomes and axillary buds are protected by scale leaves. Leafy shoots are generally unbranched and true aerial stem is present in some genera and absent in others; yet others have very short true stem or pseudostem with clasping leaf sheaths. Other general characteristics of Zingiberaceae include distichous simple leaves, presence of terminal or lateral inflorescence on the leafy shoot, highly modified - ephemeral - delicate flower and capsular fruit [15, 30]. Members of the family are usually aromatic in all plant parts, have functions as natural sources of spices, herbal medicine, natural dyes, perfumes, and as multipurpose aesthetic compounds [31, 32].

Zingiberaceae is well known for its use in ethnomedicine. It constitutes a vital group characterized by the presence of volatile oils and oleoresins. Generally, the rhizomes and fruits are aromatic, tonic, stimulant, and occasionally nutritive. Some are used as food as they contain starch in large quantities, while others yield an astringent and diaphoretic juice. Some of the medicinally and economically important genera of Zingiberaceae include *Alpinia, Amomum, Curcuma*, and *Zingiber*, followed by *Boesenbergia, Kaempferia, Elettaria, Hedychium*, *Elettariopsis,* and *Etlingera* [30, 33, 34]. Detailed literature survey reveals that many species of the family are used for treatment of various ailments due to their unique medicinal values. They are part of many herbal preparations in Chinese, Thai, African, and Indian traditional medicinal systems including Ayurveda [33, 35–38]. Zingiberaceae species *Alpinia, Amomum, Curcuma, Elettaria, Hedychium, Kaempferia,* and *Zingiber* play a major role in the preparation of many Ayurvedic drugs [33]. Various species from Zingiberaceae reported with different biological activities include antimicrobial, antifungal, anti-inflammatory, anticancer, antioxidant, antiviral, antidiabetic, antiarthiritic, larvicidal, neuroprotective, and heptoprotective activities [25, 39–52].

3 Phytochemistry of Zingiberaceae

Various pharmacological activities of Zingiberaceae plants are credited to the presence of phytochemicals / secondary metabolites therein. Phytochemical analyses of different genera of Zingiberaceae have revealed the presence of a wide range of pharmacologically active phytochemical groups which mainly include terpenoids, diarylheptanoids, phenylpropanoids, and flavanoids [16]. Interestingly, these

phytochemical groups have been considered to be potential candidates for chemotherapeutics development [17–19, 53]. Close to 100 terpenoid compounds have been identified from Zingiberaceae. Mono- and sesquiterpenoids such as α-pinene, β-pinene, 1,8-cineole, camphor, terpinen-4-ol, β-caryophyllene, and zingiberene are common chemical constituents of most of Zingiberaceae species, especially in essential oils extracted from rhizome [26, 39, 54]. Among diterpanoids, labdane-type diterpenes occur commonly in species of *Alpinia, Amomum, Hedychium, Curcuma,* and *Zingiber* [55–59] and pimarane diterpenes have been reported from *Kaempferia* species [60]. Diarylheptanoids is another pharmacologically prominent group of secondary metabolites from Zingiberaceae plants, commonly found in *Curcuma, Alpinia,* and *Zingiber* species. Curcuminoids, isolated from several *Curcuma* sp., is a good example for diarylheptanoids with remarkable biological activities [61]. Another group of bioactive phytochemicals are phenylpropanoids, mostly reported from *Alpinia, Kaempferia*, *Curcuma,* and *Zingiber* spp. [62–66]. Flavonoids and related derivatives are the constituents of plants such as *Alpinia, Amomum, Boesenbergia, Kaempferia,* and *Zingiber* genera [67–71]. Phenylbutanoids are yet another rare group in nature found only in the genus *Zingiber* [72, 73]. The molecular structures of some of the well known bioactive phytochemical compounds from Zingiberaceae plants reported with anticancer activity have been shown in Fig. 1.

4 Anticancer Activities Reported from Different Genera of Zingiberaceae Family

Anticancer activities reported from various Zingiberaceae species can be categorized according to different genera. This in itself reveals the hidden treasure trove within the Zingiberaceae plant family, which can contribute tremendously to chemotherapeutic drug development. Table 1 highlights the significant anticancer activities of different extracts, essential oils, and pure compounds from different genera of Zingiberaceae family.

4.1 Genus Alpinia *Roxb.*

The tropical and subtropical genus, *Alpinia* Roxb., with about 230 species, is mainly distributed in the Indo-Pacific region [15]. The genus is generally called as ‘shell ginger’ and several species are cultivated as ornamentals. *Alpinia* species are well known medicinal herbs with incredible biopharmaceutical potential. The presence of bioactive substances such as terpenoids, diarylheptanoids, phenylpropanoids, and flavonoids is key to their therapeutic efficiency [175]. Many *in vitro* studies carried out in diverse cancer cell lines and *in vivo* studies with animal models reflect

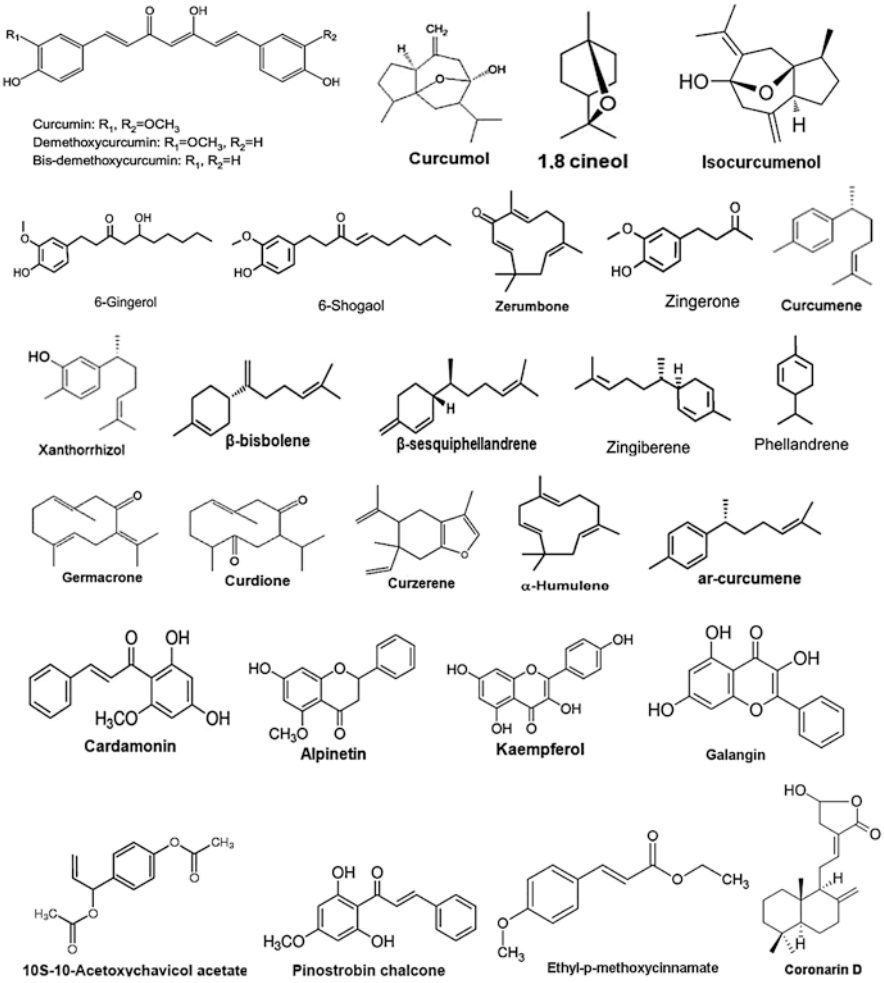

Fig. 1 Molecular structures of some phytochemicals from Zingiberaceae plants reported with anticancer activities

clearly the anticancer potential of *Alpinia* species. Antiangiogenic potential of n-hexane and ethyl acetate fractions from *A. oxyphylla* fruits has been tested against zebrafish model, human umbilical vein endothelial cells, and tumor cell lines [74]. Hexane and chloroform extract of *A. galanga* rhizome lead to the isolation of two compounds, viz. 1'(S)-1'-acetoxychavicol acetate and p-coumaryl alcohol γ-O-methyl ether, both of which were found to exhibit significant cytotoxicity against human cancer cell lines like A549, SNU638, HT1080, HL60, and HCT116 [75]. 1'S-1'-acetoxychavicol acetate (ACA) is a phenylpropanoid compound reported from various *Alpinia* spp. such as *A. galanga and A. conchigera*, and is known to induce apoptotic cell death in various cell lines [76, 176]. ACA was found to inhibit

Table 1 List of anticancer bioactive extracts, fractions, and pure compounds of various genera of Zingiberaceae family

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
Genus Alpinia Roxb.				
A. oxyphylla	Fruits	Hexane and ethyl acetate fractions	Antiangiogenic against zebrafish model, human umbilical vein endothelial cells and tumor cell lines	[74]
A. galanga	Rhizome	10S-10-Acetoxychavicol acetate and p-coumaryl alcohol c-O-methyl ether	Cytotoxicity against A549, SNU638, HT1080, HL60 and HCT116 human cancer cell lines	[75]
A. conchigera	Rhizome	10S-10-Acetoxychavicol acetate	Apoptotic induction in MCF-7, HSC-2, HSC-4, HepG2 and CaSki	[76]
A. officinarum	Rhizome	Galangin	Prevents skin cancer	[77]
		7-(3,4-Dihydroxyphenyl)-1-(4-hydroxy-3-methoxyphenyl)-4-en-3-heptanone	Cytotoxicity against HepG2, MCF-7 and SF-268 cancer cell lines	[78]
		Diarylheptanoids	Induces mitochondrial apoptosis and S-phase cell cycle arrest in neuroblastoma IMR-32 cell line	[79]
A. mutica	Rhizome	Pinostrobin	Cytotoxic against KB, MCF-7 and Caski cancer cells	[80]
A. purpurata	Leaves	Ethyl acetate extract	Cytotoxicity against OAW42 and HeLa cells	[81, 82]
A. pahangensis	Rhizome	Hexane and ethyl acetate extracts	Cytotoxic against KB, CaSki and HCT116 cancer cells	[83]
A. murdochii	Rhizome and leaves	Hexane and dichloromethane extracts	Cytotoxic effect against SKOV-3 cells	[84]
A. katsumadai	Seeds	Rubraine, isorubraine, and sumadain	Cytotoxicity against HepG2, MCF7 and MDA-MB-435 cancer cell lines	[85]

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
A. zerumbet	Flowers	Dichloromethane and methanol extracts	Antitumor activity against Ehrlich Ascites Carcinoma (EAC) cells *in vivo*	[86]
	Flowers	5,6,dehydrokawain	Cytotoxicity against MCF7, HepG2, HEP-2 cancer cell lines	
A. nantoensis	Rhizome and leaf extracts	Ethanol extract	Inhibit cell migration and invasion MCF-7 and MDA-MB-231 breast cancer cell lines	[87]
A. scabra	Leaves and rhizome	Hexane and chloroform extract	Cytotoxic against MCF7 and SKOV-3 cell lines	[88]
A. blepharocalyx	Seeds	Diarylheptanoids	Antiproliferative against HT-1080 (human) and 26-L5 (murine) carcinoma cell lines	[89]
A. pricei	Rhizome	Ethanolic extract	Induce apoptosis against KB carcinoma cell lines through mitochondria-dependent pathway	[90]
Genus Amomum Roxb.				
A. subulatum	Fruit	Cardamonin	Induce apoptosis in HCT116 cancer cell lines through extrinsic apoptotic pathway	[91]
	Seeds	Hexane and ethyl acetate extracts	Cytotoxicity against MCF7 and HeLa cancer cell lines	[92]
A. aculeatum	Leaves	Aculeatin A and B	Cytotoxic against MCF7 breast cancer cell line	[93]
A. kravanh	Fruit	Ethanol extract	Cytotoxicity against SMMC-7721 cell lines	[46]

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
A. tsao-ko	Fruit	Tsaokoarylone	Cytotoxic against A549 and SK-Mel-2 cancer cell lines	[94]
		Essential oil	Induces apoptosis against HepG2 cell line	[95]
		Isotsaokoin, hannokinol, 2,3-dihydro-2-(4′-hydroxy-phenylethyl)-6-[(3″,4″-dihydroxy-5″-methoxy) phenyl]-4-pyrone and 4-dihydro-2-(4′-hydroxy-phenylmethyl)-6-[(3″,4″-dihydroxy-5″ methoxyphenyl) methylene]-pyran-3,5-dione	Cytotoxicity against HepG-2, SMMC-7721, HeLa and A549 cancer cell lines	[96]
		Ethanol extract	Antitumor activity against ovarian cancer SKOV3 cells with antiangiogenic activity *in vivo*	[97]
A. villosum	Seeds	Polysaccharides	Cytotoxic effects against human hepatocellular carcinoma cell lines Hep G2	[98]
A. verum	Shoots	Essential oils	Cytotoxic against Human prostate DU145 cancer cell line	[99]
A. xanthioides	Seeds	Monoterpenoids, Sesquiterpenoids, Terpene Glycosides, Amoxantin A (diterpenoid)	Cytotoxicity against SK-OV-3, SK-MEL-2, A549 and HCT15 cancer cell lines	[100–103]
A. maximum	Roots and Fruits	Labdane diterpenoids	Cytotoxicity against MCF-7, SMMC-7721, MG-63 and HepG2 cancer cell lines	[104]
Genus Kaempferia L.				
K. rotunda	Rhizome	Pinostrobin	Antitumor activity against human breast cancer, T47D cell line (*in vitro*) and xenograft model (*in vivo*)	[105]
		Lectin	Induces apoptosis in Ehrlich ascites carcinoma cells, SW48 and SW480 colorectal cancer cell lines	[106, 107]

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
K. galanga	Rhizome	Alcoholic extracts and Ethyl-p-methoxycinnamate	Antitumor activity against Ehrlich ascites carcinoma cells and human cholangiocarcinoma CL-6 cell line (*in vitro*) as well as *in vivo* model	[108, 109]
		Polysaccharides	Antitumor activity on H22 solid tumor (*in vivo*)	[110]
		Ethyl-p-methoxycinnamate	Cytotoxicity against HSC-3 and Ca922 cell lines	[111]
K. parviflora	Rhizome	Ethanol extract	Apoptosis induction in leukemic HL60 and U937 cell lines	[112]
			inhibition of cell migration and invasion and induction of apoptosis in HeLa (cervical) and SKOV3 (ovarian) cells	[113, 114]
		Polymethoxyflavones	Cytotoxicity against human cervical (HeLa) and gastric adenocarcinoma (AGS) cell lines	[115]
		5,7,4-trimethoxyflavone	Cytotoxicity against human cholangiocarcinoma HuCCA-1 and RMCCA-1 cell lines	[116]
K. angustifolia	Rhizome	Abietene diterpene and kaempfolienol	Cytotoxicity against HL-60 and MCF-7 cancer cell lines	[117]
K. elegans	Rhizome	Labdane and clerodane diterpenoids	Cytotoxicity against leukemic HL60 cell line	[118]
K. pulchra	Rhizome			
Genus Curcuma L.				

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
C. longa	Rhizome	Various extracts	Cytotoxicity against U937, Molt4, A549, T98G, HeLa, MDA-MB-231 human cancer cell lines and murine melanoma cell line, B164A5	[119–122]
		Curcuminoids / Curcumin	Anticancer activity against multiple human carcinomas including melanoma, head and neck, breast, colon, pancreatic, prostate and ovarian cancers	[123–128]
C. amada	Rhizome	Supercritical CO_2 extract	Cytotoxicity against human glioblastoma (U-87MG) cell line	[129]
	Rhizome and leaves	Methanol extracts	Cytotoxicity against human MCF7 and MDA-MB-231 breast cancer cell lines	[130]
C. aromatica	Rhizome	Aqueous extract	Induces apoptosis and G2/M arrest in colon carcinoma cell lineLS-174-T	[131]
		Essential oil	Antitumor and chemoprevention against hepatoma in mice models (*in vivo*)	[132–134]
		Ethanolic extract	Antiangiogenic and proapoptotic activity in Ehrlich ascites tumor model (*in vivo*)	[135]
C. caesia	Rhizome	Methanol extract	Antitumor activity on Ehrlich's ascites carcinoma (EAC) bearing mice.	[136]
			Antitumor potential against DEN-induced hepatocellular carcinoma	[137]

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
C. zedoaria	Rhizome	Ethanolic extract	Antiproliferative and invasive activities against human esophageal squamous carcinoma TE-8 cells (*in vitro*) and suppress tumor formation in mice (*in vivo*)	[138]
		Hexane and chloroform extracts	Cytotoxicity against ovarian cancer cells SKOV3	[139]
		Essential oil	Cytotoxic effects on gastric cancer AGS cells and induce cell cycle arrest and apoptosis	[140]
			Cytotoxic and induces apoptosis in non-small cell lung carcinoma H1299 cells and antitumor activity against H1299 xenograft mice model (*in vivo*)	[141]
			Antiangiogenic activity both *in vitro* and *in vivo* -suppressing melanoma growth and lung metastasis	[142]
		Isocurcumenol	Cytotoxicity against human cancer KB, A549, K562 cell lines and mice DLA (Daltons Lymphoma Ascites) cells	[21]

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
C. xanthorrhiza	Rhizome	Xanthorrhizol	Inhibit tumor nodules in a spontaneous mouse lung metastasis model (*in vivo*)	[143]
			Induce apoptosis via activation of p53-dependent mitochondrial pathway in HCT 116 MCF 7 and MDA-MB-231 cancer cell lines	[144, 145]
			Induce caspase-independent apoptosis in oral squamous cell carcinoma SCC-15 cell line	[146]
C. purpurascens	Rhizome	Dichloromethane extract	Induces apoptosis through mitochondrial-dependent pathway in colon cancer HT-29 cells	[147]
		Essential oil	Cytotoxicity against MCF7, Ca Ski, A549, HT29, and HCT116 human carcinoma cell lines	[148]
C. mutabilis	Rhizome	Petroleum ether extract and labdane diterpenoid (Cm epoxide)	Induce apoptosis in colorectal cancer HCT116 and leukemic K562 cells	[149]
C. kwangsiensis	Rhizome	Essential oil	Cytotoxicity against B16 and LNCaP cancer cells	[150]
C. phaeocaulis	Rhizome	Ethanol extract	Antiproliferative activity and induces apoptosis in breast cancer MCF7 cell lines	[142]
Genus Zingiber Boehmer				

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
Z. officinale	Rhizome	Ethanol extract	Cytotoxicity against Human pancreatic cancer cell lines (Panc-1, AsPC-1, BxPC-3, CAPAN-2, CFPAC-1, MIAPaCa-2 and SW1990) as well as induces autophagic cell death in Panc 1 cells both *in vitro* and *in vivo* (xenograft mice model)	[151]
		6-shogaol and 6-gingerol	Induce apoptosis in against B164A5 murine melanoma cells	[48]
		6-shogaol	Induce cell cycle arrest and apoptosis against in colon cancer cell line HCT-116. Antitumor activity against colon cancer cells (*in vivo*)	[152]
			Induces endoplasmic reticulum stress and mitochondrial apoptosis induction in cervical cancer HeLa cells	[153]
		Gingerol	Induce apoptosis in SW-480 and HCT116 cancer cells	[154]
			Induce apoptosis in A549 cells *via* extrinsic pathway	[155]
	Leaves	Methanol extract	Induce apoptosis in human colorectal cancer HCT116 and SW480 cells	[156]

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
Z. zerumbet	Rhizome	Petroleum ether extract fractions	Cytotoxicity against human breast cancer MCF 7 cell lines	[157]
		Zerumbone	Induction of mitochondria-mediated apoptosis in chronic myelogenous leukemia K562cells	[158]
			Induces apoptosis in CEM-ss, H1299, HCT116, NB4, P-388D1 and Raji cancer cell lines. Antitumor activity against colorectal, liver, lung and cervical *in vivo* mice models	[159, 160]
Z. cassumunar	Rhizome	Chloroform extract Cis-3-(3', 4'-dimethoxyphenyl)-4-[(E)-3, 4 dimethoxystyryl] cyclo-hex-1-ene and 8-(13,14-dimethoxyphenyl)-2-methoxynaphto-1,4-quinone	Cytotoxicity against human T-acute lymphoblastic leukemia (CEMss) and cervical (HeLa) cancer cell lines	[161]
Genus Elettaria Maton				
E. cardamomum	Seeds	Aqueous extract	Cytotoxicity against mouse lymphoma YAC-1 cells.	[162]
Genus Hedychium J. Koenig				

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
H. coronarium	Rhizome	Ethanol extract	Induce G1 phase cell arrest, apoptosis and inhibition of migratory potential of cervical cancer HeLa cells	[163]
		Labdane diterpenes	Chemo preventive and antiproliferative activity against HepG2 cancer cells Cytotoxicity against A-549, SK-N-SH, MCF-7 and HeLa cancer cell lines	[164]
		Labdane diterpenoids (Hedycoronals A and B) and Diarylheptanoids	Antiangiogenic activity and cytotoxic activity against B16, HT-29, HepG2 and HeLa cancer cell lines	[165]
		Coronarin D	Induces G2/M arrest, apoptosis and autophagy in human nasopharyngeal carcinoma NPC-BM and NPC-039 cells	[166]
			Induce apoptotic cell death through the upregulation of JNK/MAPK pathways in human hepatocellular carcinoma (HCC) Huh7 and Sk-hep-1 cells	[167]

(continued)

Table 1 (continued)

Species name	Parts used	Bioactive extract / fractions / compounds	Anticancer activity	References
H. spicatum	Rhizome	Labdane-diterpenoids	Cytotoxic activity against Colo-205, A-431, MCF-7, A549, HL-60, THP-1, A-375 cancer cell lines and Chinese hamster ovary cells (CHO)	[168]
		Sesquiterpenes	Cytotoxicity against A549, B-16, HeLa, HT-29, NCIH460, PC-3, IEC-6 and L6 cancer cell lines	[169]
		Essential oil	Cytotoxicity against A549, DLD-1, SW 620, FaDu, HeLa MCF-7 and MDA-MB-231 cancer cell lines	[170]
Genus Boesenbergia Kuntze				
B. rotunda	Rhizome	Methanolic extract	Cytotoxicity against MCF-7, MDA-MB-231, CaOV3, HT-29 and HeLa cancer cell lines	[171]
		Panduratin A	Cytotoxicity and apoptosis induction against HT-29 and MCF-7 cancer cell lines	[172]
		Boesenbergin A	Cytotoxicity against A549, PC3, HepG2 and HT-29 cancer cell lines	[173]
		Hexane and methanol extracts, Cardamonin	Antiproliferative activity, induce cell cycle arrest and apoptosis against nasopharyngeal carcinoma, HK1 cells	[174]

inflammatory transcription factor NF-κB, growth of oral squamous cell carcinoma, and potentiate effect in combination with cisplatin by modulating pro-inflammatory microenvironment [177, 178]. Flavonoid mixture as well as galangin (3, 5, 7-trihydroxyflavone) isolated from *A. officinarum* reportedly exhibits a broad absorption band at 270–290 nm related to the UV-B area, supporting that galangin could be a potential whitening agent capable of preventing skin cancer [77].

Recently, galangin was found to induce apoptosis *via* p53-dependent pathway in ovarian cancer cells, A2780/CP70 and OVCAR-3 [179]. A compound, 7-(3,4-dihydroxyphenyl)-1-(4-hydroxy-3methoxyphenyl)-4-en-3-heptanone isolated from *A. officinarum,* was found to possess remarkable cytotoxicity against HepG2, MCF-7, and SF-268 [78]. Diarylheptanoids isolated from *A. officinarum* have been shown to wield multiple antitumor effects in neuroblastoma cell lines [79]. A novel compound, pinostrobin chalcone, has been isolated from *A. mutica* which displays notable cytotoxic potential against various human carcinoma cell lines (KB, MCF-7, and Caski) with significant IC_{50} values [80]. *A. purpurata* ethyl acetate extract exhibited antioxidant and anticancer activity against OAW42 and HeLa cells [81, 82]. Crude extracts from *A. pahangensis* and *A. murdochii*, endemic to Malaysia, have shown cytotoxic activity against different cancer cell lines [83, 84]. A novel monoterpene-chalcone conjugate, sumadain, isolated from *A. katsumadai* showed potent cytotoxicity against HepG2, MCF7, and MDA-MB-435 cancer cell lines [85]. Dichromethane and methanol extracts from *A. zerumbet* flowers exhibit potent antitumor activity against Ehrlich Ascites Carcinoma (EAC) cells *in vivo* and 5,6,dehydrokawain (DK) isolated from the extract displayed potent antiproliferative activity against various human cancer cell lines, MCF7, HepG2, HEP-2 with noteworthy IC_{50} values [86]. Ethanol extracts prepared from *A. nantoensis* rhizome and leaf were reported to inhibit cell migration, invasion, and sphere formation in breast cancer cell lines, MCF-7 and MDA-MB-231. This study also revealed the extracts' capability to inhibit signal transductions in EGFR as well as the PI3K/AKT and Ras-ERK pathways, which are crucial players of tumor cell migration and invasion [87].

4.2 Genus Amomum *Roxb.*

Amomum is the second largest genus after *Alpinia* within Zingiberaceae with about 150 -180 species, widely distributed in Southeast Asia. In India, the genus is represented by 22 species, mostly restricted to North-Eastern and southern India. A chalcone, namely, cardamonin (2′,4′-dihydroxy-6′-methoxychalcone), first isolated from *A. subulatum* (black cardamom) fruit, has been reported to affect cell growth by modulation of a variety of cell signaling pathways, including mammalian target of rapamycin (mTOR), NF-κB, cell surface receptors, and Wnt/β-catenin pathways [180, 181]. Cardamonin also potentiates TNF-related apoptosis-inducing ligand (TRAIL) for induction of apoptosis through ROS-CHOP (CCAAT/Enhancer-Binding Protein Homologous Protein)-mediated upregulation of death receptors (DRs), which makes TRAIL more effective as an anticancer therapy [91]. Hexane and ethyl acetate extracts of *A. subulatum* seeds exhibited cytotoxicity against MCF7 and HeLa cancer cell lines besides being immunosuppressive effect against peripheral blood mononuclear cells [92]. Activity-guided fractionation of hexane- and chloroform-soluble extracts of *A. aculeatum* leaves led to the isolation of aculeatin A and B, found to be cytotoxic against MCF7 breast cancer cell line (*in vitro*)

and *in vivo* hollow fiber assay [93]. *A. villosum* and *A. kravanh* have cytotoxic effects against human hepatocellular carcinoma cell lines SMMC-7721 and Hep G2, respectively [46, 96, 182]. Essential oil and various pure compounds such as tsaokoarylone, isotsaokoin, hannokinol, 2,3-dihydro-2-(4′-hydroxy-phenylethyl)-6-[(3″,4″-dihydroxy-5″-methoxy)phenyl]-4-pyrone, and 4-dihydro-2-(4′-hydroxy-phenylmethyl)-6-[(3″,4″-dihydroxy-5″-methoxyphenyl) methylene]-pyran-3,5-dione isolated from *A. tsao-ko* fruit (part of traditional Chinese medicine) have been reported with cytotoxicity against various human cancer cell lines [94–96]. Ethanol extract from this plant was found to inhibit ovarian cancer and decrease angiogenesis *in vivo*, through endoplasmic reticulum (ER) stress-mediated interruption in p-STAT3/NF-κB/IL-6 and VEGF loop of angiogenesis regulation [97].

4.3 Genus Kaempferia L.

The genus includes about 70 species, two third of which are found in Asia and remaining one third in Africa [33]. The flavanone, pinostrobin, isolated from *Kaempferia rotunda* rhizome chloroform extract, has been shown to possess anticancer activity against human breast cancer *in vitro* (T47D cell line) and *in vivo* (Xenograft model). Repair of breast tissue and suppression of c-Myc expression were evident on mice with T47D breast cancer xenograft [105]. Lectin isolated from *K. rotunda* was found to inhibit proliferation of Ehrlich ascites carcinoma cells and induce mitochondrial apoptosis in colorectal cancer cells, SW48 and SW480 [106, 107]. Alcoholic extracts of *K. galanga* rhizome were reported to possess antineoplastic activities in both *in vivo* and *in vitro* model systems [108, 109]. Interestingly, water-soluble polysaccharides purified from *K. galanga* rhizome reportedly protect thymus and spleen of solid tumor bearing mice and also capable of enhancing immunoregulatory ability of $CD4^+$ T cells, the cytotoxic effects of $CD8^+$ T cells and NK cells, thereby inhibiting tumor [110]. Additionally, major constituent of volatile oil of *K. galangal*, Ethyl-p-methoxycinnamate, has been reported with anticancer potential against oral cancer HSC-3 and Ca922 cell lines [111]. Ethanol extract of *K. parviflora* rhizome, commonly known as Thai black ginger used in traditional medicine, showed dose-dependent inhibition of cell proliferation and induction of apoptosis in leukemic HL60 and U937 cell lines [112]. The ethanol extracts of *K. Parviflora* rhizome supercritical CO_2 fluid extracts (SFEs) of *K. parviflora* have been contained in higher concentration of polymethoxyflavones (PMFs), which showed potent antiproliferative activity against both human cervical (HeLa) and gastric adenocarcinoma (AGS) cell lines [115]. It is also reported to possess anticancer properties as evidenced by suppression of growth and survival signaling pathways, inhibition of metalloproteinase 2 activity, inhibition of cell migration, and invasion and induction of apoptosis in cancer cell lines such as HeLa (cervical) and SKOV3 (ovarian) cells [113, 114]. Extracts and flavone derivatives from the rhizome of *K. parviflora* have been shown to suppress multidrug

resistance-associated proteins (MRP) in A549 (lung cancer) cells, making it useful as modulators of drug resistance in cancer cells [183]. 5,7,4-trimethoxyflavone isolated from *K. parviflora* rhizome extract reportedly possesses anticancer activity against human cholangiocarcinoma HuCCA-1 and RMCCA-1 cell lines [116]. Methoxyflavones isolated from *K. parviflora* have been demonstrated to exhibit melanogenesis inhibition in theophylline-stimulated murine B16 melanoma 4A5 cells, without notable cytotoxicity to normal cells [23, 184]. *K. angustifolia* rhizome extracts and pure compounds abietene diterpene and kaempfolienol present therein were found to be cytotoxic against Leukemic HL-60 and breast cancer MCF-7 cell lines [117]. Labdane and clerodane diterpenoids isolated from *K. elegans* and *K. pulchra* found cytotoxic against leukemic HL60 cell line [118].

4.4 Genus Curcuma *L.*

The genus *Curcuma* L., with around 120 species, is distributed mainly in tropical and subtropical Asia. *Curcuma longa*, commonly known as turmeric and a major source of curcumin, has been consumed as a dietary spice and a cure for human ailments for thousands of years in Asian countries. The potential anticancer activity of turmeric and curcumin was demonstrated by Kuttan et al. 1985 [185] in both *in vitro* and *in vivo* models. Various crude extracts of *C. longa* were reported to have antiproliferative activity against different human cancer cell lines such as, U937 (myeloid leukemia), Molt4 (acute lymphoblastic leukemia), A549 (lung carcinoma), T98G (glioblastoma), HeLa (cervical cancer), MDA-MB-231 (breast cancer), and murine melanoma cell line (B164A5) [119–122]. The immunomodulatory activities of the polar fractions of *C. longa* hot water extracts were investigated using human peripheral blood mononuclear cells (PBMC). High polarity fraction containing polysaccharides exhibited stimulatory effects on PBMC proliferation, thereby attesting to its potential use as an adjuvant supplement for cancer patients with suppressed immunity due to exposure to chemotherapeutic drugs [186].

Other *Curcuma* sp. reported with antiproliferative potential include *C. amada* (mango ginger), *C. aromatica* (wild turmeric), *C. caesia* (black turmeric), *C. zedoaria* (white turmeric), and *C. xanthorrhiza* (Java turmeric). Supercritical CO_2 extract of *C. amada* rhizome reported to have specific anticancer potential against human glioblastoma (U-87MG) cell line induces apoptosis or drug resistance in a dose-dependent manner [129]. Methanol extracts from *C. amada* leaves and rhizome also reportedly possess antiproliferative activity against breast cancer cell lines MCF7 and MDA-MB-231 [130].

Aqueous extract of *C. aromatica* inhibited LS-174-T (colon carcinoma) cell proliferation in a dose- and time-dependent manner, inducing extrinsic and intrinsic apoptosis by activation of caspase-8, -9, and -3 and G2/M phase arrest. Downregulation of cyclin B1 and CDK1 without the participation of p53 was also observed in a study by Hu et al. [131]. Treatment with *C. aromatica* oil also inhibited growth of implanted hepatoma in mice models which could be correlatable with

suppression of PCNA (Proliferating cell nuclear antigen) protein [132–134]. Alcoholic extracts of *C. aromatica* and *C. caesia* rhizome have been found to possess potent antiangiogenic and proapoptotic activity under *in vivo* conditions [121, 135–137].

C. zedoaria rhizome termed Ezhu in Chinese is extensively used in traditional Chinese medicine to treat various ovarian and cervical cancers. Ethanolic extract of *C. zedoaria* rhizome is known to exhibit strong antiproliferative and invasive activities against human esophageal squamous carcinoma TE-8 cells and suppress tumor formation in mice. Upregulation of PTEN and downregulation of phosphorylated Akt, mTOR and STAT3 expressions, attenuation of FGFR1 and MMP-2, activation of caspase-9, -3 and PARP, and suppression of Bcl-2 leading to apoptosis were observed in the same study [138]. Hexane and chloroform extracts of *C. zedoaria* were found to have moderately potent cytotoxic activity on ovarian cancer cells (SKOV3) as well as umbilical vein endothelial cells [139]. Essential oil obtained from *C. zedoaria*, known as 'zedoary', possesses efficient cytotoxic effects on H1299 (non-small cell lung carcinoma) and AGS (gastric cancer) cells and can induce cell cycle arrest and apoptosis. Potential active compounds of Zedoary oil, detected using gas chromatography and mass spectrometry (GC-MS), were 8,9-dehydro-9-formyl-cycloisolongifolene, 6-ethenyl-4,5,6,7-tetrahydro-3,6-dimethyl-5-isopropenyl-trans-benzofuran, eucalyptol, and γ-elemene [141, 142]. Zedoary oil also reportedly exhibits antiangiogenic activity both *in vitro* and *in vivo*, resulting in suppressing melanoma growth and lung metastasis, associated with downregulating MMPs [140]. Isocurcumenol isolated from *C. Zedoaria* rhizome shows antiproliferative potential in KB (nasopharyngeal carcinoma), A549 (lung carcinoma), K562 (leukemic), and DLA (Daltons Lymphoma Ascites) cells [21].

Methanol extract of *C. xanthorrhiza* rhizome possesses cancer chemopreventive potential [187]. Xanthorrhizol is the most active and abundant compound isolated from the essential oil of *C. xanthorrhiza,* rhizomes. Studies have shown that xanthorrhizol is an attractive chemopreventive agent as it inhibited tumor nodules in a spontaneous mouse lung metastasis model and TPA (12-O tetradecanoylphorbol-13-acetate) - induced skin cancer promotion in mice, by decreasing phosphorylated ERK (pERK), JNK, and p38 expression [143, 188]. This compound is known to induce apoptosis via activation of p53-dependent mitochondrial pathway in HCT 116 (colon cancer), MCF 7, and MDA-MB-231 (breast cancer) cell lines [144, 145]. Xanthorrhizol also reported to induce caspase-independent apoptosis through ROS-mediated p38, MAPK, and JNK (c-jun N-terminal kinase) activation in SCC-15 (oral squamous cell carcinoma) cells [146]. A combination of xanthorrhizol with other compound(s) like tamoxifen, astaxanthine, and α-tocopherol showed more effective antiproliferatve activity against breast and esophageal cancer cell lines [189].

Dichloromethane extract from Javanese medicinal plant *C. purpurascens* rhizome induces apoptosis through mitochondrial-dependent pathway in colon cancer HT-29 cells [147]. *C. mutabilis* is an endemic Zingiberaceae plant confined to Western Ghats of India and the petroleum ether extract of this plant rhizome as well as a novel labdane diterpenoid isolated from this extract reported to be cytotoxic to

various cancer cell lines and induce apoptosis in colorectal cancer HCT116 and leukemic K562 cells [149]. Essential oil isolated from various *Curcuma* species, such as *C. elata*, *C. kwangsiensis*, *C. yunnanensis*, *C. nankunshanensis*, *C. sichuanensis*, *C. rubescens*, C. *purpurascens,* and *C. mutabilis,* also exhibited cytotoxicity against various cell lines [148, 150, 190, 191].

Curcumin : Anticancer activity of curcumin need a special mention, as it's a most studied compound from *Curcuma* species of Zingiberaceae family. Curcuminoids represent a major component of the phytoconstituents found in various *Curcuma* species [192]. Of the various curcuminoids known, curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione), also called iferuloylmethane, deserves a special mention. It is one of the most studied curcuminoids displaying a wide spectrum of biological actions, including cholesterol-lowering, chemopreventive, antidiabetic, anti-inflammatory, antimicrobial, and antioxidant activities [193–195]. Other commonly found curcuminoids are derivatives of curcumin which are known as demethoxycurcumin and bisdemethoxycurcumin [196].

Curcumin has been studied in multiple human carcinomas including melanoma, head and neck, breast, colon, pancreatic, prostate, and ovarian cancers [123–128]. Curcumin's potent antioxidant and free-radical quenching properties play an important role in the inhibitory effects of the compound on the initial stages of carcinogenesis as demonstrated by animal models of various tumor types [197]. NF-κB and AP-1 are two transcription factors intimately involved in the cellular pathways leading to tumorigenesis. NF-κB and AP-1 expression is induced by various stressful stimuli (tumor promoters including oxidative stress, UV irradiation and infectious antigens, pro-inflammatory cytokines such as TNF-α and IL-1), resulting in expression of genes involved in inflammation and cellular proliferation [198]. Curcumin has an inhibitory effect on both NF-κB and AP-1 activation. Its effect on NF-κB, is mediated through inhibition of IκK and results in inactive NF-κB remaining bound to IκBα in the cytoplasm leading to suppression of a variety of gene products involved in carcinogenesis and tumor growth including cyclin D1, VEGF (Vascular endothelial growth factor), COX-2 (cycloxygenase-2), c-myc, Bcl-2, ICAM-1, and MMP-9 (Matrix metalloproteinase-9) [199]. Curcumin also has a stimulatory effect on the extrinsic apoptotic pathway, which is triggered by the binding of 'death activators' such as TNF-α and Fas-ligand to their corresponding cell surface receptors. In addition to proapoptotic effect, curcumin also induces autophagic cell death in chronic myelogenous leukemia, esophageal cancer, and malignant glioma cells, mediated through inhibition of the Akt/mTOR/p70S6 kinase pathway and the ERK1/2 pathway [200, 201]. Curcumin has demonstrated antiangiogenic effect *in vivo* xenograft models, by regulating a variety of proangiogenic growth factors, enzymes, and transcription factors like bFGF (basic fibroblast growth factor), VEGF, angiopoetin-1 and 2, COX-2 MMP-9 [126, 202]. Its derivative, demethoxycurcumin (DMC), has been reported to affect a number of cellular adhesion molecules involved in the processes of metastasis [203].

Curcumin is known to target mTOR, which is recognized as a key therapeutic target for the prevention and / or treatment of cancer [204]. Curcumin has been shown to have numerous cytotoxic effects on cancer stem cells (CSCs) by

suppressing the release of cytokines, particularly interleukin (IL)-6, IL-8, and IL-1, which stimulate CSCs [205]. It is an inhibitor of enzymes involved in epigenetic changes of chromatin such as DNA methyltransferase, histone acetyl transferase, and histone deacetylase (HDAC) leading to selective activation or inactivation of genes (oncogenes/tumor suppressors) implicated in cancer death and progression. Curcumin also modulates miRNAs (miR-15a, miR-16, miR-21, miR-22, miR-26, miR-101, miR-146, miR-200, miR-203, and let-7) and their multiple target genes. Altogether, curcumin is able to restore the epigenetic regulation balance and appears as an attractive preventive and/or therapeutic approach against human cancer [206, 207].

Although curcumin has long been used extensively to treat several inflammatory diseases including cancer, poor aqueous solubility and reduced bioavailability limit its efficacy as a promising therapeutic agent in cancer therapy. Various research groups have focused on increasing the bioavailability of curcumin by combining other phytochemicals as adjuvants. For instance, curcumin has often been used in combination with other phytochemicals such as resveratrol, quercetin, sulforaphane, retinoic acid, and folates in cancer treatment [208–210]. The chemosensitizing effect of curcumin has been reported in cancers of the breast, colon, pancreas, gut, liver, lung, prostate, brain, lymphoma, and leukemia [211, 212]. Various types of curcumin nanoparticles appropriate for cancer treatment have been developed, such as polymer nanoparticles, liposomes, micelles, solid lipid nanoparticles (SLNs), and polymer conjugates, with improved bioavailability, devoid of degradation and further metabolism and with enhanced targeting capacities [207, 213, 214].

4.5 Genus Zingiber *Boehmer*

The genus *Zingiber* represented by 141 species is distributed mainly in tropical Asia. *Z. officinale* rhizome extract and its major pungent components, 6-shogaol and 6-gingerol, have been reported to induce antiproliferative effects on several tumor cell lines [48]. Ginger extract significantly reduced the elevated expression of NF-κB and pro-inflammatory TNF-α in *in vivo* model with liver cancer, thereby acting as an anticancer and anti-inflammatory agent [215]. Ethanol extract of ginger is also reported to have potent anticancer activity against pancreatic cancer cells, inhibit cell cycle progression, and induce ROS-mediated apoptosis [151]. Experimental studies also showed that ginger extracts as well as the purified constituents therein such as 6-gingerol and 6-shogaol exerted anticancer activity against gastrointestinal cancer cells by modulating several signaling molecules like NF-κB, STAT3, MAPK, PI3K, ERK1/2, Akt, TNF-α, COX-2, cyclin D1, cdk, MMP-9, survivin, cIAP-1, XIAP, Bcl-2, caspases, and other cell growth regulatory proteins [22]. The remarkable increase of shogaols in steamed ginger contributed to its improved anticancer potential [216, 217]. 6-shogaol significantly inhibited cell proliferation in colon cancer cell lines HCT-116 and SW-480, with IC_{50} values of 7.5 and 10 μM, respectively, and can cause cell cycle arrest in G2/M phase by p53/

p21-mediated pathway [152]. It is known to act through endoplasmic reticulum stress and mitochondrial pathways involved in apoptosis induction in HeLa (cervical cancer) cells [153]. Gingerol was also found to sensitize A549 cells to TRAIL-induced apoptosis by inhibiting the autophagy flux [155], inhibit cell proliferation, and induce apoptosis in SW-480 cells and HCT116 (colon cancer) cells [154]. Methanol extract of ginger leaves also reportedly induce apoptosis and reduction of cell viability in human colorectal cancer cells [156].

Various organic solvent extracts and bioactivity guided column chromatography subfractions of *Z. zerumbet* rhizome displayed strong antiproliferative effects on breast cancer MCF7 cells [157]. Zerumbone, a natural cyclic sesquiterpene from *Z. zerumbet*, reported to have a diverse range of biological activities, including anticancer and antitumor activities. Studies have demonstrated that zerumbone has little or no cytotoxic effect on normal human cells but induces apoptosis in many cancer cell lines [158–160]. Chloroform extract of *Z. cassumunar* rhizome and compounds therein cis-3-(3', 4'-dimethoxyphenyl)-4-[(E)-3, 4 dimethoxystyryl] cyclo-hex-1-ene and 8-(13,14-dimethoxyphenyl)-2-methoxynaphto-1,4-quinone showed strong activity against human T-acute lymphoblastic leukemia (CEMss) and cervical (HeLa) cancer cell lines [161].

4.6 Other Zingiberaceae Plants with Anticancer Potential

Experimental evidence suggests that aqueous extracts of *Elettaria cardamomum* (cardamom) extracts exert anti-inflammatory roles (immunomodulatory). It is evident that black pepper and cardamom aqueous extracts together significantly enhance the cytotoxic activity of natural killer cells, thereby indicating their potential anticancer effects [162]. *E. cardamomum* extract also possesses potential chemopreventive effects evidenced by preventing diethylnitrosamine (DENA)-induced hepato-cellular carcinoma through blocking oxidative stress, decreasing pro-inflammatory cytokine, NF-κB, and ornithine decarboxylase (ODC) [218].

Labdane diterpenes (isocoronarin D, methoxycoronarin D, ethoxycoronarin D, and benzoyl eugenol) from *Hedychium coronarium* ethanol extract reported to possess chemopreventive effect [164]. Other labdane-type diterpenes reported from this plant showed moderate to potent cytotoxic activities against different cancer cell lines. They are reported with antiangiogenic activity, proved through inhibition of human vascular endothelial cells [165]. Coronarin D from *H. coronarium* induces significant G2/M arrest, apoptosis, and autophagy in various human cancer cell lines including nasopharyngeal carcinoma (NPC) cells [166, 219]. It is also reported to induce cell death through the upregulation of JNK/MAPK and caspase-dependent apoptosis pathways in human hepatocellular carcinoma (HCC) Huh7 and Sk-hep-1 cells [167]. *H. coronarium* rhizome ethanol extract can induce apoptosis-mediated G1 phase cell arrest, while inhibiting the migratory potential of cervical cancer HeLa cells [163].

Two novel labdane-diterpenes isolated from chloroform extract of *Hedychium spicatum* rhizomes have shown good cytotoxic activity against Colo-205 (Colon cancer), A-431 (skin cancer), MCF-7 (breast cancer), A549 (lung cancer), and Chinese hamster ovary cells (CHO) [168]. Six new sesquiterpenes, including two potent cytotoxic (against HeLa cells) compounds, have been isolated from this extract [169]. Essential oil isolated from *Hedychium spicatum* rhizome also reported cytotoxicity against various cancer cell lines [170].

5 Conclusion

To conclude, members of family Zingiberaceae continue to provide innumerable bioactive extracts and compounds reported with potent cytotoxic and anticancer activities. As a matter of fact, many of these plants are utilized either as ingredients of traditional food varieties or additives in time-tested, traditional ethnomedicinal herbal preparations, well known for their efficacious cure of a plethora of diverse ailments. Discovery of various anticancer compounds from these plants is emerging as a highly enriched, promising, and biocompatible bioresource for modern /complementary or alternative medicine systems. Compared to the notorious and undesirable side effects of chemotherapeutics used in the past decades, these compounds can be developed for effective and specific targeting of key proteins of cancer-related signaling pathways. Despite an impressive array of such compounds, the hunt needs to continue for hitherto unexplored, yet to be discovered drug candidates within the Zingiberaceae family of plants.

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