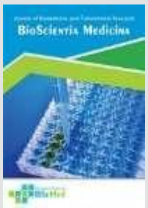

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Botanical and Chemical Overview, Traditional Uses and Potential of Anticancer Activity from Several Costus Plants: A Narrative Review

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ABSTRACT

Plants in the Costus genus are known to have various activities, starting from an antibacterial agent, anti-inflammatory, antioxidant, anticancer, antidiabetic, and so on. From some previous studies that have been conducted, it is stated that some Costus plants have a high potential to be a prospective anticancer candidate in the future. This review will discuss botanical and chemical overview, traditional uses, and potential anticancer activity of several Costus plants, namely *C.speciosus*, *C.igneus*, *C.spiralis,* and *C.pictus*. In conclusion, anticancer activity assay was carried out by several methods using various cell cultures resulting in an IC_{50} value ranging from strong and very strong, with the strongest potency belonging to *C.speciosus* with an IC_{50} value of 13.87 μg/ml. In addition, the active phytoconstituent, mainly diosgenin, contributes to the anticancer activity, which also strengthens the potential of Costus plants.

1. Introduction

Currently, the development of traditional medicine systems has been widely carried out. The principle of herbal medicine is important in developing therapeutic agents. Traditional medicine systems are carried out by using various types of plants. From those plants, often used plant species are classified as rare and endemic and only found in certain areas that are difficult to access. The use of these rare and endemic plant species has several limitations, and the main problem is that data or information on biological activities is inadequate, but these plant species may have various biological activities that are important in the world of health that has not been fully explored.

Many plant species that have been used by several tribes in the Asian continent are pharmacognostic, equivalent to phytopharmacology, but these plant species are still very rare and rarely found. Some of these plants belong to the Costus genus, which is not widely known but has various important activities in the medical world.

Diverse extracts of costus plant elements were studied and mentioned to have numerous pharmacological activities that are antioxidant activity[1,2], antimicrobial, antibacterial[3,4], antidiabetic[5], antihyperlipidemic, hepatoprotective[6], anti-inflammatory[7], anti-arthritis[8], and antipyretic has also been reported.[9]

Sources of *C.speciosus* that inhibit the growth of diverse kinds of cancer cells, such as liver, colon, and prostate cancer cells, in a dose-dependent manner stated from research consisting of ethanolic, water, ethyl acetate, and methanolic.[10]

C.speciosus

C.speciosus has a taxonomic order of kingdom Plantae, division Magnoliophyta, Order Zingiberales, Family Costaceae, Genus Costus, and Species *Cheilocostus speciosus.* (J. Koenig) Sm. *Cheilocostus speciosus* has synonyms *Cheilocostus speciosus*, *Banksea speciosa* J.Koenig, *Hellenia speciosa* (Koenig .J) Dutta S.R. *Planera speciosa* (Koenig .J) Giseke, and others.[11]

C.speciosus is an ornamental, herbaceous succulent plant with a height of up to 2.7 meters. The rhizome is sheathed at the bottom and leafy upwards. The leaves are elliptical to oblong or oblong-lanceolate, thick, spirally arranged, smooth surface at the bottom with a stem clamping sheath up to 4 cm, large flowers, white, pointed tip like a cone, and bright red.[12]

Figure 1. Leaf and flower of *C.speciosus*

The widely distributed plant is located in India with humid or subtropical climates from sea level to the Himalayas. Found throughout countries with tropical evergreen forests, up to 1200 meters in height.[13]

The constituents that have been found leading far from numerous parts of *C.speciosus* include diosgenin which, according to Dasgupta[14] believed to be the largest constituent secluded from *C.speciosus*. The documented levels of diosgenin in stems were 0.65%, 0.37% in leaves, and flowers 1.21%.[12] Added constituents that have been secluded comprise tigogenin, dioscin, gracilin, and -sitosterol glucoside.[13] The seeds contain 6% fatty oil, pale yellow with a sweet smell, with a composition of 55.97% palmitic acid, 8.3% stearic acid, 22.75% oleic acid, 6.8% linoleic acid, and 1.7% arachidic acid.[12]

The key genin is the diosgenin product of saponins from seeds, three genins, and glucose on acid hydrolysis. Two new furostanol saponins, costusoside I and J, were considered the following derivatives 3-O-[β-D-glucopyranosyl(1→4)-β-D-glucopyranosyl]-26-O-(β-D-glucopyranosyl-22α-methoxy (25R) furost-5-en-3β,26-diol and it is 22 hydroxy.[15,16] Sitosterol-β-D-glucoside, prosapogenins A and B dioscin, dioscin, gracilin, 3-O-[α-L-rhamnopiranosil(1→2)-β-D-glucopyranosyl]-26-O-[β-D-glucopyranosyl]-22α-methoxy-(25R) furost-5-en-3β,26-diol, protodioscin, and methyl protodioscin have been isolated from seeds.[15,17]

Two new quinone compounds, namely dihydrophylylplastoquinone and its 6-methyl derivative [18], together with tocopherol quinone and 5α-stigmast-9(11) en-3β-ol, were insulated from seed, and their structures were clarified, in addition to methylhexadecanoate, methyloctadecanoate, and tetracosanyloctadecanoate secluded from seeds.[17]

Meanwhile, some constituents insulated from roots consist of 24-hydroxytriacontane-26-one and 24-hydroxytricontane-27-one[19] along with methyltriacontanoate, diosgenin, sitosterol[12,20], 8-

hydroxy triacontane-25-one and methyltriacontanoate.[20] 5α-stigmast-9(11)-en-3β-ol has also been categorized.[12,15,19] The radicle of *C.speciosus* also encompass sitosterol-β-D-glucoside, prosapogenins A and B dioscin, dioscin, gracilin[21], 3-O-[α-L-rhamnopiranosil(1→2)-D-glucopyranosyl]-26-O-[β-D-glucopyranosyl]-22α-methoxy-(25R)furost-5-en-3β,26-diol, protodioscin and methylprotodioscin. Other components identified include 31-norcycloartanone, siloartanol, cycloartenol, and cycloalaudenol.[12,15]

In addition, five new compounds were isolated (oxoacids and branched fatty acid esters), including 13-methylpentadecanoic tetradecyl, 11-methyltriadecanoic acid, 4-oxotriaconsanoic acid, 14-oxoheptacosanoic acid, and 15-oxooctacosnoic acid from the rhizomes.[22] The rhizome also produced methyl 3-(4-hydroxyphenyl)-2E-propenoate.[12,15] Saponins diosgenin[23], dioscin, gracilin, and beta-sitosterol-beta-D-glucoside are also incorporated in rhizome[24,25], as well as essential oils containing pinocarveol, kadinene, cineol, p-methoxybenzophenone, and carvacrol 6.[12]

The content of the steroid glycosides prosapogenin B dioscin, dioscin, gracilin, methyl protodioscin, methylprotogracillin, protogracilin, 26-O-β-D-glucopyranosyl-(25R)-furost-5-ene-3β,22ζ,26- triol, diosgenin 3-O-β-Dglucopyranosyl(1→3)-β-D-glucopyranoside is a subversive fragment of the methanol source.[26,27]

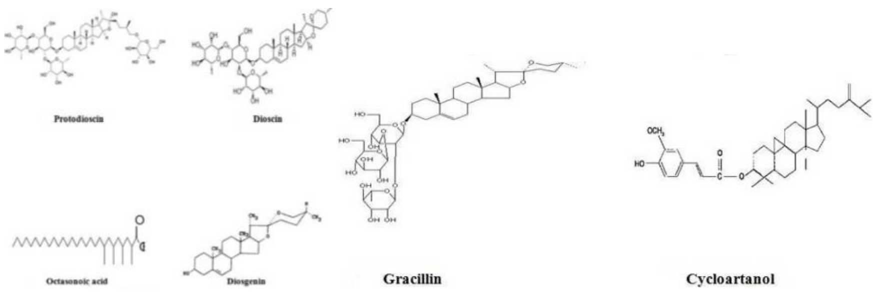

Figure 2. Structure of several isolated phytoconstituents from *C.speciosus*

C.igneus

C.igneus has a taxonomic order, namely kingdom Plantae, division Tracheophyta, order Zingiberales, family Costaceae, genus Costus, and species *C.igneus* N.E.Br. *C.igneus* has synonyms *Chamaecostus cuspidatus*, *Costus cuspidatus*, and *Globba cuspidata* Nees & Mart.[11]

C.igneus is a tropical evergreen perennial plant that has simple, alternate, whole, and oval leaf shapes with a length of 4-8 inches with equivalent venation. The light purple has black, enormous, smooth leaves underside and is organized spirally nearby the stem, establishing a striking, curved clump that emerges from the underground stem. *C.igneus* plants can reach a height of up to 60 cm, with the falling tallest stems lying on the ground. Warm months produce Flowers and have a diameter of 2.5-12.5 cm, appearing on the head like a cone at the end of the branch.[28]

Figure 3. *C.igneus* plant

C.igneus leaves show that in phytochemical screening, they are rich in protein, iron, and antioxidant integrants such as ascorbic acid, tocopherol, carotene, terpenoids, steroids, and flavonoids.[28,29] Carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, and flavonoids demonstrated that in a different study, the source of methanol contains the largest quantity of phytochemicals.[30] The content of *C.igneus* incorporating bis(2'-Ethylhexyl)-1,2-benzene-dicarboxylate (59.04%) compounds whole from tocopherol and steroid ergosterol to the ether fraction.[31]

The presence of the terpenoid lupeol and steroid stigmasterol was demonstrated in the stem [32]. the rhizome of *C.igneus* was secluded from the bioactive composites of quercetin and diosgenin.[33]

C.pictus

C.pictus has a taxonomic order, namely kingdom Plantae, division Tracheophyta, order Zingiberales, family Costaceae, genus Costus, and species Chrysolophus *pictus* Don.[11] *C.pictus* has synonyms, including *Ceratina hieroglyphica*, *Cremastocheilus mexicanus,* and *C.congestus*.[34]

C.pictus is a monocot perennial herb that has bright green leaves when immature and dark green when ripe with a large smooth surface. *C.pictus* is a tropical evergreen plant, and the undersurface is bright purple. The largest leaves are located at the base, and the smaller leaves reach the apex and collect spirally on the stem. The leaves have parallel pinnate veins, the base is red, and the sheath is fused to the margins, piling up at the apex. The leaves have a minty character and smell with a sour taste. The flowers are yellow with linear red stripes appearing on the head like a cone occupying the apex.[35]

Figure 4. *C.pictus* plant

Its rhizomes, stems, and flowers are rich in essential and auxiliary metabolites. Auxiliary metabolites incorporate alkaloids, flavonoids, phenols, saponins, terpenoids, tannins, and steroids. The content of *C.pictus* leaf incorporates calcium oxalate crystals together with carbohydrates, triterpenoids, proteins, alkaloids, tannins, saponins, flavonoids, and volatile oils. Analysis of the saponified leaves extract with the GC-MS instrument revealed 18 main chemical compounds of *C.pictus*. The fundamental constituent in ether segment is bis(2'-Ethylhexyl)-1,2-benzene-dicarboxylate. The appearance of tocopherol is known to be the cause of the antioxidant properties of leaf extracts [31]. Extracts of leaves, stems, and rhizomes with different solvents are known to contain L-Arabinopyranose methyl glycosides as reference compounds.[36]

C.spiralis

C.spiralis has a taxonomic order, namely kingdom Plantae, division Tracheophyta, order Zingiberales, family Costaceae, genus Costus, and species *Costus spiralis* (Jacq.) Roscoe. *C.spiralis* has synonyms *Alpinia spiralis* Jacq., *Amomum spirale* (Jacq.) Steud., and *Gissanthe spiralis* (Jacq.) Salisb.[37]

Figure 5. *C.spiralis* plant

C.spiralis is a perpetual plant broadly dispersed in humid and subtropical South America, specifically in the Amazon basin. The leaves are large and are on a spiral stem. This plant grows on leaves that are arranged in a spiral and also has flowers with striking colors. The flowers are produced at the tips of the heads that are close together, with three petals resembling a tube and the overall shape of a pine cone.[38]

Phytochemical analysis proved the presence of several secondary metabolites contained in *C.spiralis*, including saponins[39], flavonoids[40], sterols, and furostanol glycosides.[41] Furthermore, the presence of inulin, oxalic acid, tannins, sitosterol, sapogenins, mucilage, and pectin was also found.[42–44] In the methanol fraction, there are several compounds, namely flavonoids, steroids, and alkaloids.[45]

The structures of four different types of flavonoids, including Kaempferol 3-O-neohesperidoside, Kaempferide 3-O-neohesperidoside, Quercetin 3-O-neohesperidoside, and Tamarixetin 3-O-neohesperidoside have been secluded from *C.spiralis* leaf, and the structures have been acknowledged.[4647] In addition, Antunes et al.,[40] succeeded in isolating a new flavonol glycoside compound from *C.spiralis* leaves, namely 3,5-dihydroxy-7,4'-dimethoxyflavone 3-O-neohesperidoside whose aglycone part is known to have antitumor activity[48] and has been presented to be active against the trypomastigote form of *Trypanosoma cruzi.*[49] Meanwhile, de Oliveira et al.,[50] isolated two new flavone compounds from *C.spiralis* leaves, namely schaftoside and isoschaftoside, both of which are isomeric pairs.

Traditional uses

Genus Costus plants are widely known for their traditional uses. *C.speciosus*, also known as Thebu is an herb that is widely found in south and southeast

Asian countries and has been broadly used in traditional Ayurvedic medicine to manage countless infirmities. The use of astringent, aphrodisiac, purgative, anthelmintic, and expectorant is from sources Root and rhizome[51], constipation, burns, skin diseases, bronchitis, and asthma[2], while the aerial parts are used to reduce fever and treat mental illness.[52]

A native Brazilian plant known as *C.spiralis*, also known as cana-de-macaco or cana-de-brejo, can be found in the Amazon and Atlantic forests.[53] Urinary tract infections and kidney stones are commonly treated with *C.spiralis*.[54] The decoction of the leaf is used to cure diarrhea, while the infusion of the leaf is used to treat hypertension and is a diuretic. Hepatitis and stomach discomfort are treated with stem infusion. In addition to being taken orally, *C.spiralis* is applied topically to treat tumors and sores caused by syphilis.[55]

C.igneus, also known as fire costus, is a plant native to south and central America that is broadly utilized in India to manage diabetes, especially the leaves. People suffering from diabetes are recommended for a month to use one leaf in the morning and night.[56,57] Meanwhile, aerial parts of *C.igneus* are believed to treat kidney disease in traditional Mexican medicine.

C.pictus, which is known as insulin plant, fire Costus, and spiral ginger, is a plant with various biomolecular functions. *C.pictus* is a perennial herb native to Central and South America.[58] In India, *C.pictus* is utilized to manage diabetes so, which is frequently known as an insulin plant.[59,60] The leaves and rhizomes are known to have antidiuretic, anthelmintic, antibacterial, and antitumor activity.[61] In addition, *C.pictus* has also been reported to have anti-inflammatory and antihyperglycemic activity, and its plant parts are used in the treatment of kidney disease.[62]

Anticancer activity

Based on research, several Costus plants have been shown to have anticancer activity. The activity is divided into several mechanisms, including antiproliferative, cytotoxic, and apoptotic. Some of the Costus plants that will be discussed regarding their anticancer activity are *C.speciosus*, *C.igneus*, *C.pictus,* and *C.spiralis*.

In 2014 a study of apoptotic activity and inhibition of cell proliferation was conducted on methanol, and n-hexane extracts of *C.speciosus* leave using HEPG2 hepatocellular carcinoma cells and the MTS assay method. The methanol extract showed the best inhibition of HEPG2 cell growth with an IC_{50} value of 93.3 μg/ml, and the percentage of apoptotic and necrotic cells were 14.7 and 61% analyzed by flow cytometry, respectively.[51] Another study using the roots showed that extracts of 70% methanol, 70% ethanol, and water from the roots of *C.speciosus* had good cytotoxic activity against HEPG2 cells with IC_{50} values of 13.87, 24.06, and 53.69 μg/ml, respectively [63]. Similar results were shown by the cytotoxicity of the rhizome methanol extract using the BSLT (Brine Shrimp Lethality Test) method with an LC_{50} value of 31.55 μg/ml[2].

The choice of extraction solvent affects the strength of cytotoxic activity, apoptosis, and inhibition of proliferation. Methanol extract produces a very strong IC_{50} value because methanol is a solvent with a medium polarization of index that can remove important and effective ingredients from the leaves of *C.speciosus* maximally compared to n-hexane with a lower polarity index so that its ability to attract important compounds in lower plants.[51]

Another thing that is important and greatly affects the anticancer activity of *C.speciosus* is the presence of certain bioactive compounds such as diosgenin, curcumin, and curcuminoids.[64] The content of rhizome and root incorporate saponins, 5α-stigmasten-3b-ol, sitosterol-β-D-glucoside, dioscin, dioscin prosapogenins A and B, gracilin, and quinine.[64] Diosgenin knows for the induction of apoptosis in human leukemia cells. Chemotherapeutic properties in solid cancers and leukemias are known to occur due to curcumin and curcuminoids. In addition, it is also known that the methanolic extract of *C.speciosus* root contains vanillin, quercetin, and cinnamic acid, which have anticancer activity.[18]

Meanwhile, the cytotoxic activity of *C.pictus* was carried out on HT-1080 fibrosarcoma cells using the MTT assay. The ethanolic extract of *C.pictus* leaves showed an IC_{50} value of 120 µg/ml with a 50% decrease in cell viability, and the methanol extract showed cytotoxicity at 80 and 120 µg/ml concentrations [68]. Meanwhile, the removal of aqueous showed merely a small amount of cytotoxic activity and was not significant at concentrations of 40 and 80 µg/ml. The higher the concentration of the given extract, the higher the decrease in cell viability.[68] Hemocytometer help to determine the possibility of the cell and concentration of cell by using the trypan blue dye exclusion method. Ethanol extract is known to be safe against normal human lymphocytes but exhibits cytotoxic activity against cancer cells. This indicates that the ethanolic extract of *C.pictus* has selective toxicity. The ethanolic extract of *C.pictus* has anticancer activity and has not been fully elucidated. The most likely is the involvement of mitochondria.[49-51]

Then another study used chloroform fraction, methanol soluble fraction, and methanol insoluble fraction. These fractions were tested for cytotoxic activity against HT29 (colon cancer) and A549 (lung carcinoma) cells by MTT assay. The results obtained IC_{50} values for HT29 cells were 125, 150, and 200 µg/ml for the chloroform fraction, soluble in methanol and insoluble in methanol. Meanwhile, in cell A549, the IC_{50} values were 125, 150, and 175 µg/ml with the same order of fractions with 24-hour treatment.[50-56]

In contrast to testing the anticancer activity of other Costus plants against human cancer cells, testing the cytotoxic/genotoxic activity of aqueous extracts of *C.spiralis* leaves and stems was carried out using meristematic root cells of *Allium cepa* (shallots). The cytotoxic activity of the extract was expressed by the percentage of the mitotic index (MI). The concentration of aqueous extract of the leaves and stems of *C.spiralis* with the highest percentage of the mitotic index was 18 µg/ml.[57,59]

Testing of anticancer activity against *C.igneus* was carried out using ethanolic extract of leaves against HEPG2 hepatocellular carcinoma cells. Cytotoxic activity was measured by MTT assay and yielded an IC_{50} value of 62.5 µg/ml with cell viability of 52.23%.[58]

The inhibitory activity shown by the extract or fractions is the result of the bioactive constituents extracted by the solvent, efficiency, and polarity index of each extraction solvent. The methanol extract efficiently induces apoptosis in HEPG2 cells and caspase-3 activation. The methanol extract decreased the mitochondrial membrane potential indicating that the mitochondrial apoptotic pathway occurs by opening the mitochondrial permeability transition pore. Methanol extract has significant reticence of ceproliferation with a proapoptotic influence along with cell cycle arrest in S and G2/M phases [52]. Molecular docking analysis proves that diosgenin which is a steroidal saponin compound, is an effective blocker of the STAT3 actuation pathway and has anticancer activity in hepatocellular carcinoma.[53] Diosgenin converses multidrug resistance in cancer cells and strengthens the effectiveness of trendy chemotherapy.[59,60]

The presence of polyphenolic compounds and several other bioactive compounds, including diosgenin which is known to have the function of upregulating COX-2 and 5-LOX enzymes, costunolide, which induces intracellular thiol depletion [61], and lupeol, which acts to upregulate FADD and down-regulate p13-kinase/Akt.[62]

Various phytoconstituents exhibit antitumor activity by modulating cellular and signaling pathways intricate in several phases of cancer. Polyphenols exhibit anticancer roles through the induction of apoptosis, antioxidant mechanisms, modulation of cell growth factors, inhibition of angiogenesis, and their selective action on rapidly dividing cells.[63]One of the in vitro methods to evaluate the anticancer activity of *C.pictus* in various cells was carried out by testing the inhibitory activity of HDAC (Histone Deacetylase) on HEPG2 cells. HDAC inhibitors inhibit cell proliferation and apoptosis in tumor cells.[64] Upregulation of apoptotic molecules p21, p27, p53, caspases, Reactive Oxygen Species (ROS), and down-regulation of anti-apoptotic agents such as Akt, Bcl 2, NFkB, JAK, STAT3, MMPs, actin, and vimentin are aimed at the anticancer mechanism of *C.speciosus.*[10] *In vitro* cytotoxicity assays on ascites Ehrlich carcinoma cells, Dalton's lymphoma ascites, and MCF-7 showed the antiproliferative potential of *C.igneus*.[65-66]

It is interesting that besides the high potential for cytotoxic activity of methanol extract, it should be noted that the methanol extract showed the strongest cytotoxic activity after 48 hours. This phenomenon was caused by the incubation of phenolic compounds with different cells for 24 hours which was considered too short to produce significant activity on cell viability. On the other hand, longer time also causes low cytotoxicity of polyphenolic compounds which are thought to be unstable and highly susceptible to degradation and/or reactions with other factors such as oxygen and metal ions.[66]

Plant	Part	Extraction solvent	Methods	Cell	IC_{50} (µg/ml)	Reference
C.speciosus	Root	Water	MTT assay	HEPG2	53.69	43
		Methanol 70%			13.87	
		Ethanol 70%			24.06	
	Rhizome	Methanol	BSLT	*Artemia salina* nauplii Ocean 90	31.55[1]	2
	Leaf	Methanol	MTS assay	HEPG2	93.3[2]	31
				THP-1	58.1[2]	
				Normal human lung cell	>100	
C.igneus	Leaf	Ethanol	MTT assay	HEPG2	62.5	52
C.pictus	Leaf	Ethanol	MTT assay	Fibrosarcoma HT-1080	120	48
	Cortex	Methanol		HT-29 cell line	150[3], 200[4]	50
				A549 cell line	125	
		Chloroform		HT-29 cell line	150[3], 175[4]	
				A549 cell line	125	
C.spiralis	Leaf	Water	*A.cepa* test	Root meristematic cell	18	53
	Stem				18	

[1]LC_{50}; [2]24-hours incubation; 48-hours 77.3 & 42.2 µg/ml; [3]methanol soluble fraction; [4]methanol-insoluble fraction

The reduction in mitotic activity of *A.cepa* meristematic cells in the presence of the aqueous extract of *C.spiralis* was due to inhibition of DNA synthesis or cell block in the G2 phase as a result of DNA damage.[66] The delay in DNA checkpoint damage gives the damaged DNA time to repair, after which the cell cycle brake is released, and progress is resumed.[67]

Flavonoids are known to contribute and be involved in anticancer activity. Flavonoid modulates key elements involved in apoptotic signal transduction pathways and has chemopreventive potential. Flavonoid-protein interactions with their antioxidant properties mediate protective effects and suppress carcinogenic development.[68]

Autophagy, apoptosis, and necrosis are the most varieties of cell death[69]. Among the three major pathways of cell death, apoptosis is the most well-planned and most ordered mode of cell death.[70,71] Costunolide, which is known to be a key compound in plants of the genus Costus, has been extensively studied for its antiproliferative-cytotoxic, apoptosis induction, and cell cycle regulator of cancer cells either in vitro or in silico. Costunolide induced cell death in MCF-7, and MDA-MB-231 cells in a dose-dependent behavior and 50% cell viability at a concentration of 40 M. This concentration becomes an effective dose with a 50% reduction in breast cancer cell viability and is nontoxic to normal breast cells.[71] Costunolide is also known to inhibit the development of T24 cells (bladder cancer) through the induction of apoptosis with apoptotic rates of 21.43 and 52.87%, with cells exposed to costunolide concentrations of 25 and 50 M.[71,72] The role of costunolide in the development of breast cancer cell cycle MCF-7 and MDA-MB-231 showed significant accumulation in the G2/M phase.[72] While this was going on, in silico research revealed stable connections between caspases and cell cycle regulators and costunolide. Positive cell cycle regulators (cyclin D1, D3, CDK-4, and CDK-6) and costunolide interact well, and caspases 3 and 9 adopt various postures throughout each contact. Hydrogen bonds with bond lengths under 3Å are present in all interaction.[72]

2. Conclusion

Several plants of the Costus genus, including *C. speciosus*, *C.igneus*, *C.pictus,* and *C.spiralis*, have been shown to have potential as prospective anticancer candidates, as reported from various research studies. The anticancer activity was tested using several test methods such as MTT assay, MTS assay, *Allium cepa* test, and BSLT using cell cultures for liver cancer, fibrosarcoma, colon, lung, and monocytic leukemia. The anticancer potential of the plant genus Costus is determined by several factors, one of which is the choice of extraction solvent, where the methanol extract shows excellent cytotoxic and apoptotic activity with a very strong IC_{50} value.

In addition, there are active phytoconstituents that contribute to the anticancer activity of plants of the genus Costus including diosgenin and costunolide, where costunolide has been extensively studied to work by inducing cell death in several cancer cell cultures and has also been shown to be able to stop the cancer cell cycle, especially in the G2/M phase. Meanwhile, diosgenin is known to function to upregulate COX-2 and 5-LOX enzymes.

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