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Review Article

A comprehensive review of pharmacological and toxicological properties of *Cheilocostus speciosus* (J.Koenig) C.D.Specht

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ABSTRACT

Cheilocostus speciosus (J.Koenig) C.D.Specht has been commonly used in many indigenous clinical complications to healing various ailments. A list of phytochemicals has been extracted and identified with multiple pharmacological and therapeutic properties from the different parts of *C. speciosus* (J.Koenig): sterioidal and furostanol saponins, sterioidal and furostanol glycosides, triterpene, phytoserol, sesquiterpenes, benziquinone, and fatty acid esters. Compared with other parts of the *C. speciosus* (J.Koenig), rhizomes are most extensively studied for their anthelmintic, aphrodisiac, astringent, depurative, expectorant, febrifuge, purgative, and toxin neutralizing properties. Generally, this plant has been reported to have a range of pharmacological activities, including antibacterial, anti-hyperglycemic, anti-inflammatory, anti-pyretic and anti-diuretic, anti-larvicidal, anti-stress, and estrogenic. These findings are highly promising and indicate that the plant needs to be carefully investigated for its diverse therapeutic benefit and associated toxicities and tolerance level. The present review will discuss geographical mapping, morphology, traditional, phytochemistry, and pharmacological prospects of *C. speciosus* (J.Koenig).

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1. Introduction

The biological evaluation of plants and their extract develops a basic platform for the traditional herbal system of medicine. Medicinal plants contribute remarkably to the development and discovery of recent and newer drugs (Bindu et al., 2016). Herbal preparations derived from medicinal plants are widely used in developing countries and already get their remarks worldwide because of their safety and effectiveness over large varieties of clinical and medical cases (Indrayanto et al., 1999). According to WHO, about 80% of the world population depends on traditional herbal medicine in case of major and minor ailments (Pawar and Pawar, 2014). Currently, approx. 420,000 plants are known to exist and around 10,000 to 15,000 plants in the world have medicinal value (Ashraf et al., 2014). With a steadily growing global tenderness to herbal medicines, the demand for raw materials of medicinal plants becomes increasing day by day (Chaturvedi et al., 2007). Nowadays, medicinal herbs move from very marginal to general use with the modern medical science demands of the safest alternatives of current synthetic drugs with multiple adverse and health-hazardous effects. Considerable attention has been paid recently to the development of environmentally friendly and bio-friendly plant-based products for the prevention and mitigation of various human diseases (Dubey et al., 2004). A major part of Ayurvedic therapy seeks to promote good wellness, which means maximum physical, mental and social well-being. Despite the considerable substantial scientific advantage, modern orthodox health care currently has big issues with toxic medications, chronic conditions, disease resistance, autoimmune disorders, and old age disorders (Devasagayam, 2007). *Cheilocostus speciosus* (J.Koenig) C.D.Specht is historically known as crape ginger. It is an essential medicinal plant grown in tropical India and belongs to

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the *Costaceae* family. Within the *Zingiberales*, *Costaceae* species are readily recognized and differentiated by well-formed and often ramified aerial shots that have a distinctive monostichous (one-sided) spiral phyllotaxy (Kirchoff and Rutishauser, 1990). *C. speciosus* (J.Koenig) is an erect, succulent, perennial herb, which grows from a horizontal rhizome up to 2.7 meters in height. From the medical point of view, the rhizome is the most important part of the *C. speciosus* (J.Koenig) and is characterized by its hadrocentric vascular bundles inside. Several medicinal properties, particularly asthma, fungal diseases, rheumatism, diabetes, hepatoprotective disorders, are attributed to it (Srivastava et al., 2011a-b).

2. Botanical and geographical identity of *Cheilocostus speciosus* (J.Koenig) and its traditional use

2.1. Taxonomical classification of *Cheilocostus speciosus* (J.Koenig) C.D.Specht

Table 1 represents the taxonomical classification of *Cheilocostus speciosus* (J.Koenig) C.D.Specht (Srivastava et al., 2011a-b).

2.2. Vernacular names

Though *Cheilocostus speciosus* (J.Koenig) C.D.Specht is the main identity for this plant. However, various countries recognize this plant in their local names. Table 2 represents the different vernacular names attributed to *C. speciosus* (J.Koenig) (Srivastava et al., 2011a-b, Swati, and Agarwal, 2015).

2.3. Geographical distribution

C. speciosus (J.Koenig) is native to all countries of Southeast Asia but mostly found in the hill tract areas of India, Indonesia, Malaysia, and Sri Lanka. However, in some tropical regions, including Hawaii, it is also naturalized (Swati and Agarwal, 2015). This plant loves to grow in humid and wet evergreen conditions thus for the geographical and environmental suitability *C. speciosus* (J.Koenig) native to the areas of the Indo-Malayan region and Sri Lanka (El-Far and Abou-Ghanema, 2013). The plant is also distributed in hill track areas of Chittagong, Bangladesh (Pawar and Pawar, 2014).

2.4. Cultivation

The rainy season is suitable for the cultivation of *C. speciosus* (J.Koenig) (Muniyandi et al., 2013). It is grown in fertile, organic, moist, well-drained soils in shade (Rani et al., 2012). The high humidity and low-temperature tropical climate (13 °C are the best place for growing) is suitable for growth. Crepe ginger grows from rhizomes, and in the second year, a single rhizome can produce new shoots under ideal growing conditions and increase to a 3 ft. wide clump. This plant is propagated vegetatively by rhizomes, division of the culms, cutting off stems. It can be grown by seeds, too, whereas 62 percent of germination of seeds has been done by birds (Pawar and Pawar, 2014).

2.5. Morphology

C. speciosus (J.Koenig) is a perennial, erect, succulent herbaceous plant, up to 2.7 m in height, arising from a horizontal rhizome (Srivastava et al., 2011b). From the rhizome of the *C. speciosus* (J.Koenig) red stems have emerged which bears large, soft, and variegated leaves. Rhizomes wrapped in sheaths on the lower side, leafy upward, elliptically arranged to oblong, or oblong-lanceolate tops. The leaves are tall, white with a diameter of approximately 1.5 Inches, cones like end spikes, brighter red bracts and lip white with the yellowish middle, small, concave discs, and a base of hair turf. Leaves of *C. speciosus* (J.Koenig) are sub-sessile, spirally arranged, and form a tube-shaped structure around the steam. Flowers (white) is 5-6 cm long and have a cup-shaped mark and yellow crests. The fruit is red colored capsule-shaped. Seeds are black, mounted in a white fleshy aril (Stone, 1970). Flowers are juicy, multicellular, and turning to deep crimson red during fruiting while also have identical eye-shaped nectarines on bracts. The flowers look like crepe paper and are therefore generally referred to as crepe ginger. The plant flowers in July and August, and after the flowers die, the red conical bracts remain attractive. The stems usually germinate in April. From December to March or even April the rhizome remains dormant (Nehete et al., 2010, Rani et al., 2012). The properties such as yellow-colored trichrome on the petaloid stamen and the 5.58% upper and 10.5% lower stromal index make *C. speciosus* (J.Koenig) unique to the species. The root of *C. speciosus* (J.Koenig) is cylindrical and has a fleshy mass inside.

2.6. Traditional uses

C. speciosus (J.Koenig) has been found to have a diverse number of pharmacological activities which include antibacterial, antidiuretic, anti-choline ester, antioxidant, anti-inflammatory, antipyretic, larvicidal, anti-stress, antifungal, anti-hyperglycemic, and estrogenic activities (Shobana and Naidu, 2000). The rhizome of *C. speciosus* (J.Koenig) has been reported to contain up to 3.37% of diosgenin (Singh et al., 2013), which is a steroidal sapogenin used for the synthesis of sex hormones, cortisone, and oral contraceptives, and traditionally given for their antidiabetic properties (Kumar et al., 1984). Rhizome extract of *C. speciosus* (J.Koenig) is traditionally used as a tonic for treating constipation, inflammation, leprosy, anemia, and other skin disorders (Sivarajan and Balachandran, 1994). Rhizome juice is applied to the head for cooling and headaches relief, bruised leaves are applied in fever, the boiled stem is applied in fever, dysentery, pneumonia, rheumatism, dropsy, urinary diseases, jaundice. For high fever patients, leaf infusion or decoction is used as a sudorific or in a bath. Rhizome juice is also used as an anti-vermin to treat leprosy internally and is supplied with sugar while also have anabolic, antifertility, antibacterial, CNS depressant, and uterine contraction properties (Bhattacharya and Nagaich, 2010). Young stems are used to treat diarrhea, cough, cuts, bruises, scabies, snake bite antidote, jaundice, contains papaverine alkaloids and is responsible

Table 1
Taxonomical classification of *C. speciosus* (J.Koenig).

Kingdom	**Plantae**
Subkingdom	Tracheophytes
Super division	Spermatophyta
Division	Angiosperms
Class	Monocots
Subclass	Commelinids
Order	Zingiberales
Family	Coastaceae
Genus	Cheilocostus
Species	*C. speciosus*

Table 2
Vernacular names of *C. speciosus* (J.Koenig).

Name	**Reference**
Palauan	Isebsab
Bengali	keu, kemuk or keumul
Sinhala	Thebu
English	Spiral flag
Guajarati	Paskarmula
Hindi	Keukand
Kannada	Kosta
Manipur	Okchak Khombi
Marathi	Pushkarmula
Sanskrit	Pushkarmula
Tamil	Kostam
Mizo	Sumbul
Malay	Setawar
Telegu	Kostamu
Assamese	Jom lakhuti
Latin name	*Cheilocostus speciosus*

for smooth muscle relaxation and antispasmodic activities arthritis (Ariharan et al., 2012). The rhizome extract in their traditional applications. Because of the potent anxiolytic properties, leaves of *C. speciosus* (J.Koenig) are traditionally given in mental disorders. *C. speciosus* (J.Koenig) rhizomes extract stimulates the uterine contraction due to non-estrogenic effects (Lijuan et al., 2011). The leaves and rhizomes are an important source of diosgenin which has anti-diabetic properties. The leaves have hypoglycemic properties and insulin potentiating action in addition to decreasing blood glucose (Daisy et al., 2008). It is one of the important constituents of the indigenous drug "amber mezhugu" which is useful in rheumatism. In Ayurveda, it is used to subdue vata and kapha and promotes complexion (Chopra et al., 1956). The rhizome is a source of essential oil that possesses antibacterial activity (Asolkar and Chopra, 1992) and its antifungal activity is due to the presence of steroid saponins and sapogenins. The plant is also used for eye and ear infections (Rani et al., 2012). Pharmacological studies also reveal that rhizomes have been seen to exhibit cardiotonic, hydrochloretic, diuretic, and CNS depressant activities (Srivastava et al., 2011a).

2.7. Other uses

C. speciosus (J.Koenig) is usually used as an ornamental plant in many countries across the globe. In South-East Asia they are being used as a food plant. Young tender shoots are used as a vegetable. It can be used as a cosmetic product for

sexual attraction on eyelashes (Najma et al., 2012).

3. Phytochemistry

Different parts (seeds, leaves, stem, rhizomes, and for flowers) have been used and a variety of natural compounds have been identified from a different fraction or extract of different plant parts (Table 3, Fig. 1).

4. Pharmacological activities

4.1. Antimicrobial activity

The antibacterial activity of *C. speciosus* (J.Koenig) rhizome was studied by Ariharan et al. (2012). Based on the observation antimicrobial activity of the aqueous extract of the rhizome of *C. speciosus* (J.Koenig) has been found significantly effective against gram-positive (*Staphylococcus aureus* and *Staphylococcus epidermis*) and gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*) bacteria where the zone of inhibition depends on the applied dose of the extract (Ariharan et al., 2012). In details, for gram-positive *S. aureus* and *S. epidermis,* the aqueous extract of the rhizome of *C. speciosus* (J.Koenig) showed 74 and 72% of inhibition with a zone of inhibition value of 15.5 and 12.9 respectively. Meanwhile for gram-negative *E. coli*, *P. aeruginosa*, *S. typhimurium* this value becomes 8.3, 15.4, and 18 with a percentage of inhibition value of 55, 57, and 58 respectively (Ariharan et al., 2012). While their activity correlates with their phytochemical index, the abundance of total orthodihydric phenols have been identified and claimed for the microbial resistance properties of *C. speciosus* (J.Koenig). However, while antimicrobial properties of different parts *C. speciosus* (J.Koenig) were compared, different solvent extracts of rhizome had the maximum effect and the presence of alkaloid diosgenin could be responsible for these dose-dependent effects to different microbial species (Ariharan et al., 2012). Two sesquiterpenes lactones: costunolide and eremanthin, have been identified from hexane, chloroform, ethyl acetate, and methanol extracts of *C. speciosus* (J.Koenig) with antifungal activity even effective at the lowest concentration (Duraipandiyan et al., 2012). But compared to other extracts the hexane extract showed the maximum inhibition against different pathogenic fungi with the following order: *Trichophyton mentagrophytes* and *T. rubrum* (MIC: 62.5 µg/mL)*; Epidermophyton floccosum* and *Curvulari lunata* (MIC: 125 µg/mL)*,* while showed lowest inhibition (MIC: 250 µg/mL) for *Magnaporthe grisea, Scopulariopsis sp and Aspergillus niger* (Duraipandiyan et al., 2012).

4.2. Anti-diabetic and anti-lipidemic activity

Type-2 diabetes (diabetes mellitus) has been recognized as a metabolic disorder leading to considerable morbidity and death. It is regarded as one of the world's top five causes of death (Ahmed et al., 2010). An exhaustive list of current hypoglycemic agents for diabetes, such as insulin, sulfonylurea, biguanides, and thiazolidinedione are available together with insulin therapy (Ahmed et al., 2010). These anti-diabetic medications, however, showed many adverse effects. Nowadays, herbal medicines get preference over current oral hypoglycemic drugs because of their easy accessibility, low cost, bio-friendly, least effect to human and environment, perceived efficacy with least incidence of adverse events, even if their compounds are unknown (Ahmed et al., 2010). A novel sesquiterpenes, i.e. eremantine has been isolated from *C. speciosus* (J.Koenig) (Fig. 2) and evaluated by Eliza et al. (2009)*,* in the STZ-induced diabetic rat model to determine whether the plant has anti-diabetic and anti-lipidemic effects. This study suggests, increased glucose levels in STZ-treated diabetic rats were significantly lowered by the administration of eremanthin at a dose of 20 mg/kg body weight compared to normal rats. The possible mechanism to understand the anti-diabetes effect of eremanthin could be drugs inhibition of hepatic gluconeogenesis or stimulation of glucose absorbance in the muscle and adipose tissues with an upregulated regeneration process by revitalizing the beta cells for the secretion of insulin and their anabolic effects to get the insulin available for the cellular glucose metabolism (Eliza et al., 2009). Mosihuzzaman et al. reported that anti-diabetic effects of *C. speciosus* (J.Koenig) are glucose diet-dependent, *C. speciosus* (J.Koenig) rhizome-prepared juice showed a significant hypoglycemic effect only when administered 30 minutes before the glucose administration but had no significant effect on fasting or postprandial conditions (Mosihuzzaman et al., 1994). To investigate the antioxidant and lipid-lowering activity of *C. speciosus* (J.Koenig) Shediwah *et al.,* employed atherogenic diet-induced hyperlipidemia in rabbit's model. During this treatment setup, *C. speciosus* (J.Koenig) extract (0.8g/kg BW/day) was given to rabbits for 30 days to understand the effects of crude extract of *C. speciosus* (J.Koenig) to total lipid index (Shediwah et al., 2019). The obtained results showed that *C. speciosus* (J.Koenig) at 0.8g/kg BW/day dose significantly reduce the serum level total triacylglycerol (TG), cholesterol (TC), low-density lipoprotein (LDL), and aspartate aminotransferase compared to the control group, while histopathological imaging of organs also validates these effects with low lipid deposition around the liver, heart, aorta, and other vital organs of the human by the Shediwah et al. (2019).

4.3. Anthelmintic activity

Helminthiasis or worm infestation is one of the most common and one of the world's most serious health issues. However, in many developing countries, this problem is more severe and becomes a severe threat for children and geriatric (Bihari et al., 2010). The anthelmintic activity of the methanol and aqueous extracts of aerial parts of *C. speciosus* (J.Koenig) in adult Indian Earthworms (*Pheretima posthuma*) has been measured and compared by Srivastava et al. (2011). The findings of this report explicitly showed that this plant has a significant effect on paralyzed the earthworm and is capable of killing them in dose-dependent (25-100 mg/mL) and time-dependent manner compared to the conventionally used anti-helminthic drug. The anti-helminthic property of

Table 3
List of the phytochemicals identified from *C. speciosus* (J.Koenig).

Name of the phytochemicals	Identification method	Chemical group	Plant part	Reference
Diosgenin	TLC, NMR (1H, 13C), MS, IR	Phytosteroid sapogenin	Leaves, stem, rhizomes, and seeds	(Binny et al., 2010)
Costusosides I and J	CC, TLC, NMR (1H, 13C), MS, IR	Furostanol saponins	Seeds	(Singh and Thakur, 1982a)
β-Sitosterol-β-D-glucoside	CC, TLC, NMR (1H, 13C), MS, IR	Steroid glycoside	Seeds	(Singh and Thakur, 1982b)
Prosapogenins A and B	CC, TLC, NMR (1H, 13C), MS, IR	Steroidal saponins	Seeds	(Singh and Thakur, 1982b)
Dioscin	CC, TLC, NMR (1H, 13C), MS, IR	Spirostanyl glycoside	Seeds	(Singh and Thakur, 1982b)
Gracillin	CC, TLC, NMR (1H, 13C), MS, IR	Steroidal saponins	Seeds	(Singh and Thakur, 1982b)
Protodioscin	CC, TLC, NMR (1H, 13C), MS, IR	Steroidal saponins	Seeds	(Singh and Thakur, 1982b)
Methyl protodioscin	CC, TLC, NMR (1H, 13C), MS, IR	Furostanol bisglycoside	Seeds	(Singh and Thakur, 1982b)
α-Amyrinsterate	NMR (1H, 13C, DEPT, HMQC, and HMBC), MS, HPLC, TLC	Triterpene	Leaves	(Rani et al., 2012)
β-Amyrin	MPS, IR, NMR (1H), TLC	Triterpene	Leaves	(Rani et al., 2012)
Lupeol Palmitates	MPS, IR, NMR (1H), TLC	Esters of palmitic acid	Leaves	(Rani et al., 2012)
6-methyl-dihydrophytylplastoquinone	MPS, IR, NMR (1H), TLC	Benzoquinones	Seeds	(Mahmood et al., 1984)
Dihydrophytylplastoquinone	MPS, IR, NMR (1H), TLC	Benzoquinones	Seeds	(Mahmood et al., 1984)
α-Tocopherolquinone	MPS, IR, NMR (1H), TLC	Benzoquinones	Seeds	(Mahmood et al., 1984)
5α-Stigmast-9(11)-en-3β-ol	MPS, IR, NMR (1H), TLC	β-sitosterol	Seeds	(Mahmood et al., 1984)
13-Methylpentadecanoate	MPS, IR, NMR (1H), TLC	Fatty acid ester	Rhizomes	(Mahmood et al., 1984)
11-methylpentadecanoate	MPS, IR, NMR (1H), TLC	Fatty acid ester	Rhizomes	(Mahmood et al., 1984)
Tri-acontanol	MPS, IR, NMR (1H), TLC	Phytosterol	Rhizomes	(Mahmood et al., 1984)
Tetradecyl-5α-stigmast-9(11)-en-3β-ol	MPS, IR, NMR (1H), TLC	Phytosterol	Rhizomes	(Mahmood et al., 1984)
Triacontanoic acid	TLC, NMR (1H, 13C), IR	Fatty acid	Rhizomes	(Gupta et al., 1986)
14 oxoheptacosanoic acid	TLC, NMR (1H, 13C), IR	Fatty acid	Rhizomes	(Gupta et al., 1986)
14 oxo-octacosanoic acid	TLC, NMR (1H, 13C), IR	Fatty acid	Rhizomes	(Gupta et al., 1986)
Sitosterol	TLC, NMR (1H, 13C), IR	Phytosterol	Rhizomes	(Gupta et al., 1986)
Methyl protogracillin	TLC, NMR (1H, 13C), HPLC	Furostanol bisglycoside	Rhizomes	(Inoue et al., 1995)
Cavacrol	TLC, NMR (1H, 13C), IR	Monoterpenoids (essential oil)	Rhizome	(Chakre, 2010)
Pinocarveol	TLC, NMR (1H, 13C), IR	Allyl alcohol	Rhizome	(Chakre, 2010)

Table 3
Continued.

Name of the phytochemicals	Identification method	Chemical group	Plant part	Reference
Pinocarveol	TLC, NMR (1H, 13C), IR	Allyl alcohol	Rhizome	(Chakre, 2010)
Cadinene	TLC, NMR (1H, 13C), IR	Bicyclic sesquiterpenes (essential oil)	Rhizome	(Chakre, 2010)
Eremanthin	CC, X-ray crystallography, GC-MS	Sesquiterpenes	Rhizome	(Duraipandiyan et al., 2012)
Costunolide	CC, X-ray crystallography, GC-MS	Sesquiterpenes	Rhizome	(Duraipandiyan et al., 2012)
Cineol	TLC, NMR (1H, 13C), IR	Monoterpene cyclic ether (essential oil)	Rhizome	(Chakre, 2010)

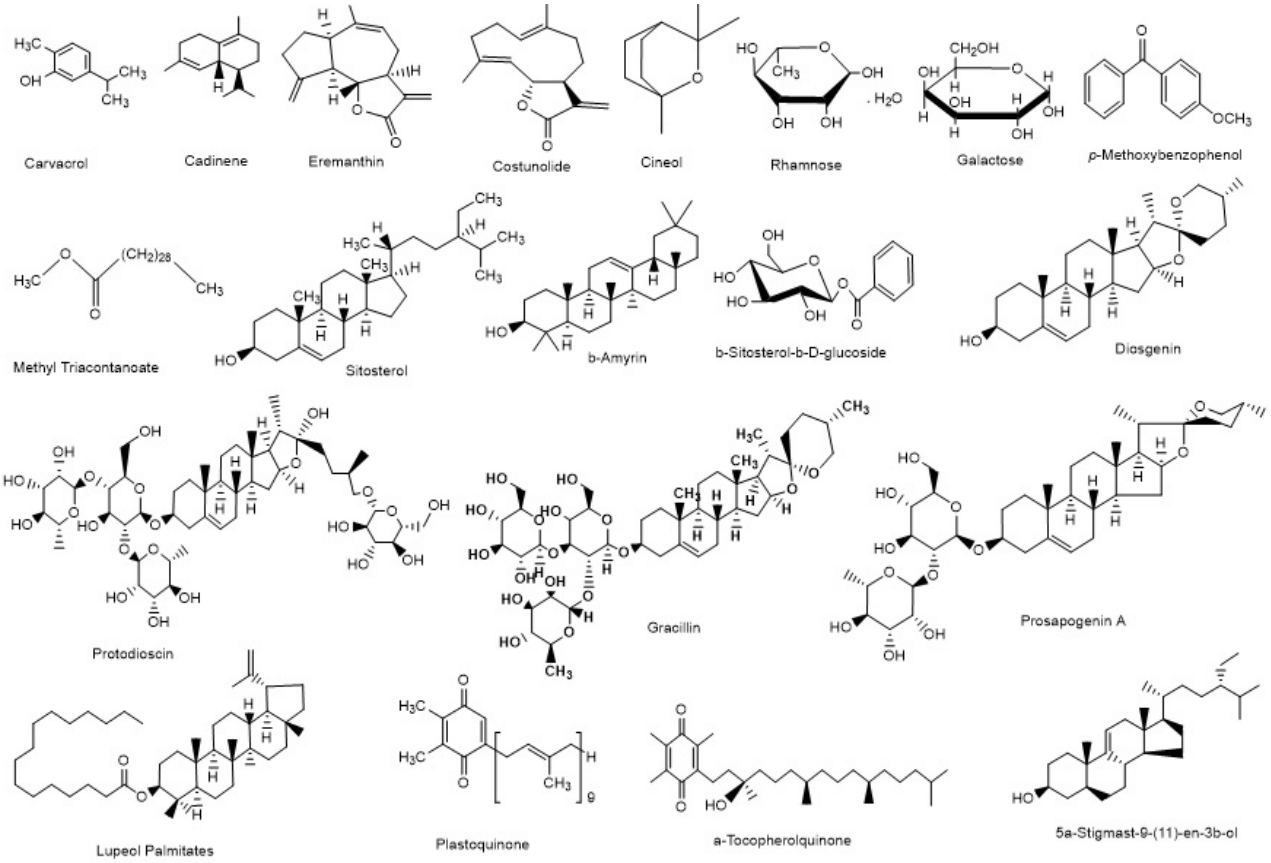

Fig. 1. Structures of some important compounds extracted from *Cheilocostus speciosus* (J.Koenig) C.D.Specht.

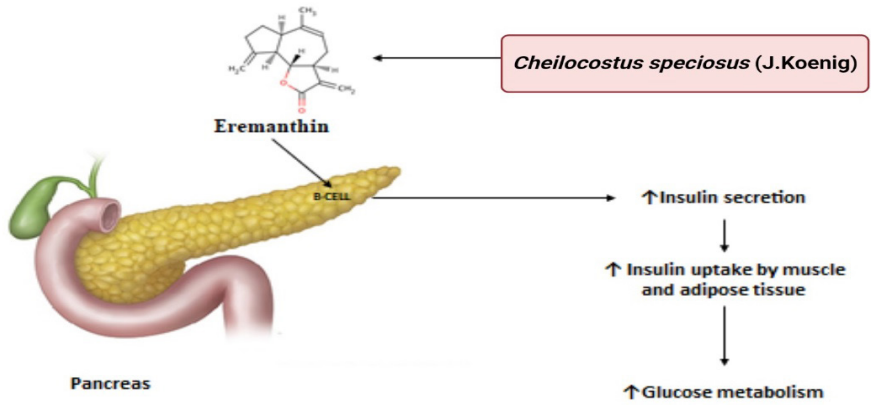

Fig. 2. Anti-diabetic effect of eremanthin from *C. speciosus* (J.Koenig).

C. speciosus (J.Koenig) is most probably due to the presence of different secondary metabolites, for example, alkaloids, flavonoids, glycosides, phenols, saponins, sterols, and so on (Srivastava et al., 2011b).

4.4. Antioxidant activity

To evaluate the antioxidant properties of *C. speciosus* (J.Koenig) in the *in-vitro* model, Nehete et al. (2010) employed eight different extracts of *C. speciosus* (J.Koenig), namely acetone, aqueous, benzene, chloroform, cyclohexane, ethyl acetate, methanol, and petroleum ether extracts, and assessed their reactive oxygen species (ROS) and reactive nitrogen species (RNS) properties in a different analytical laboratory set up involving DPPH, hydroxyl and nitric oxide radical scavenging, antioxidant capacity, and ion chelating activity treatment set up to indexing the total phenolic content of *C. speciosus* (J.Koenig) (Nehete et al., 2010). While comparing the findings of different extracts, the *C. speciosus* (J.Koenig) benzene extract showed the maximum antioxidant capacity as it has 4.38 percent of the total phenol content of its overall phytochemicals content (Nehete et al., 2010). However, when another group re-evaluated the antioxidant properties of *C. speciosus* (J.Koenig), the results showed that methanol extract had the highest hydroxyl radical scavenging and free-radical quenching properties (Vijayalakshmi and Sarada, 2008). It has been well-documented that *C. speciosus* (J.Koenig) has remarkable antioxidant properties that may be due to the presence of large number of valuable phytochemicals such as anthocyanins, catechins, coumarins, flavones, flavonols, lignans, phenolic acids, proanthocyanins, quinones, stilbenes, tannins, and xanthones which keep living organisms from protein and deoxyriboneuclic acid (DNA) damage caused by uncontrolled production of reactive oxygen species (ROS) and concurrent lipid peroxide (Jha et al., 2010).

4.5. Anti-inflammatory, analgesic and antipyretic activity

C. speciosus (J.Koenig) possess potent anti-inflammatory, analgesic, and antipyretic properties. A previous *in-vivo* study was conducted by Srivastava et al. (2013) to investigate the anti-inflammatory, analgesic, and antipyretic properties of methanolic extract of aerial parts of *C. speciosus* (J.Koenig). The methanolic extract showed its maximum effects at 400 and 800 mg/kg body weight doses level (Srivastava et al., 2013). A previous research group induced pro-inflammatory mediators in murine BV-2 cell line by treating cells with lipopolysaccharides (LPS) then applied costunolide, a major phytoconstituents of *C. speciosus* (J.Koenig), to assess its effect in the generation of pro-inflammatory. Results showed costunolide attenuated the expression of different inflammatory cytokines: cyclooxygenase-2 (COX-2), interleukin-1 (IL-1), interleukin-6 (IL-6), monocyte chemotactic protein 1 (MCP-1), nitric oxide synthase (NOSs), and tumor necrosis factor-alpha (TNF-α) (Rayan et al., 2011). The study suggested that the possible mechanism for anti-inflammatory properties of costunolide maybe because of the inhibition of the nuclear factor-κB (NF-κB) and mitogen-activated protein kinase (MAPK) signaling pathways (Rayan et al., 2011). Similar findings were also replicated by a previous pilot cohort trial on patients with acute pharyngitis and tonsillitis in Saudi Arabia (Bakhsh et al., 2015).

4.6. Anticancer activity

C. speciosus showed potent anticancer activity to different cancer cell lines (Table 4).

4.7. Hepatoprotective activity

Liver diseases are commonly caused by the toxic effect of chemicals such as carbon tetrachloride and chemical therapeutic agents and the major cause of mortality and morbidity worldwide (Samal et al., 2011). Liver functions and their pathological complications are generally diagnosed by mapping the serum level of different biomarkers namely glutathione (GSH), alanine aminotransferase (ALT), bilirubin, lactate dehydrogenase (LDH), serum glutamic pyruvic transaminase (SGPT), and acid phosphatase (ACP) (Samal et al., 2011), while some other markers can also be affected by liver functions such as total cholesterol (TC), total triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) (Contreras-Zentella and Hernández-Muñoz, 2016). To evaluate the hepatoprotective effect of methanolic extract of rhizome of *C. speciosus* (J.Koenig), liver injury was induced in the mice model with high dose paracetamol (750 mg/kg) intra-peritoneally. Administration of the methanolic extract (200 mg/kg) showed their actions against paracetamol-induced liver injury by suppressing the markers enzymes of liver damage: aspartate aminotransferase (AST), alkaline phosphatase (ALP), and alanine aminotransferase (ALT), as well as tumor necrosis factor-α (TNF-α), compared to standard drug silymarin. At the same time, the histopathological profiling of liver of experimental mice also demonstrated that paracetamol toxicity was significantly reduced by *C. speciosus* (J.Koenig) extract and that the histoarchitecture of the liver tissues was the same that those of control and silymarin treated mice. The presence of phytochemicals such as; different glycosides, polyphenols, steroids, and saponins in *C. speciosus* (J.Koenig) could be the possible reasons for its hepato-protective activity (AlSaadi et al., 2018). Meanwhile, other groups test the ethanolic extract of the rhizomes of *C. speciosus* (J.Koenig) to assess the hepatoprotective effect in carbon tetrachloride-induced liver damage in mice model, and the results showed the extract significantly suppressed the serum level of glutamic oxaloacetic transaminase (SGOT) (Verma and Khosa, 2009b).

4.8. Adaptogenic activity

Stresses depleted the norepinephrine and dopamine levels in the brain thus induce a major change in the central and peripheral nervous system (Padma et al., 2001). Nowadays, norepinephrine is clinically utilized to treat stress by controlling the monoamine oxidase (MAO) activity in the brain whilst restoring the biogenic amines

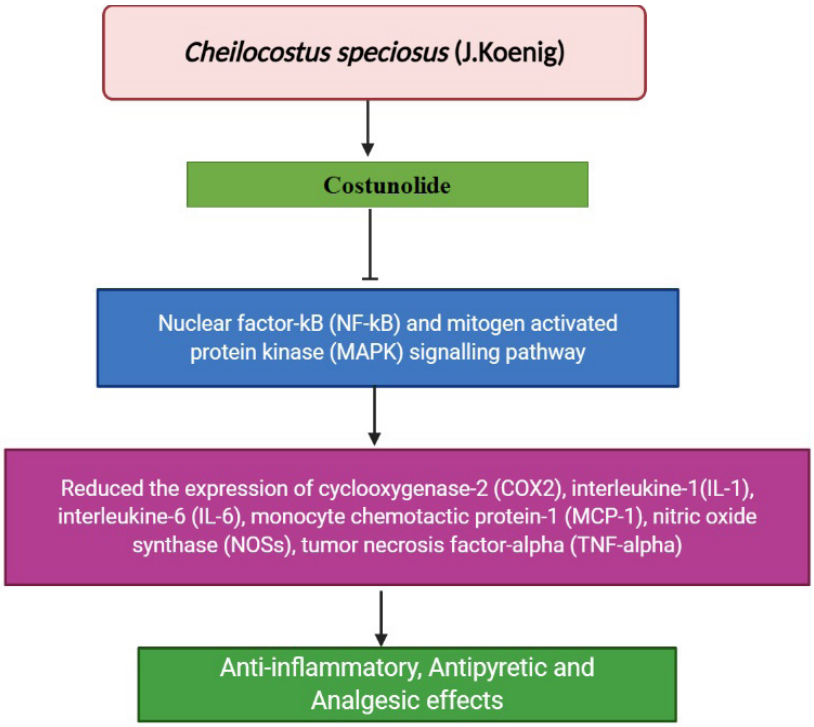

Fig. 3. Anti-inflammatory, anti-pyretic, and analgesic properties of *C. speciosus* (J.Koenig).

Table 4
Anticancer activity of *C. speciosus* (J.Koenig).

Name of the cell line	IC50 value	Name of the compound or extracts used	Mechanisms	Reference
Human colon adenocarcinoma cell lines (COLO 320 DM)	41.88 µg/mL (ethyl acetate), 41.88 µg/mL (methanol)	Hexane, ethyl acetate, methanol	↑Apoptosis, ↓Proliferation	(Baskar et al., 2012)
Human hepatocellular carcinoma (HepG2)	93.3 µg/mL (24h) 77.3 µg/mL (48h)	Methanol	↑Cell cycle arrest, ↑Apoptosi, ↓Cell viability	(Nair et al., 2014)
Human acute monocytic leukemia cells (THP-1)	58.1 µg/mL (24h) 42.2 µg/mL (48h)	Methanol	↑Cell cycle arrest, ↑Apoptosi, ↓Cell viability	(Nair et al., 2014)
Human breast adenocarcinoma (MDA-MB-231)	40 µM (24h)	Costunolide from *C. speciosus*	↑Arrest the cell cycle at the G2/M phase, ↓Cell viability, ↓NF-κB	(Roy and Manikkam, 2015)
Breast cancer cell line (MCF-7 and MCF-10A)	40 µM (24h)	Costunolide from *C. speciosus*	↑Cyclin D1, D3, CDK-4, CDK-6 (cell cycle arrest) ↑Caspase-3, and caspase-9 (apoptosis)	(Roy and Manikkam, 2015)
Hepatocellular carcinoma (HepG2)	32.62 µg/mL (24h)	Diosgenin from *C. speciosus*	↑Apoptosis	(Selim and Al Jaouni, 2015)
Breast cancer cell line (MCF-7)	11.03 µg/mL (24h)	Diosgenin from *C. speciosus*	↑Death receptor, caspase-3 (apoptosis)	(Selim and Al Jaouni, 2015)

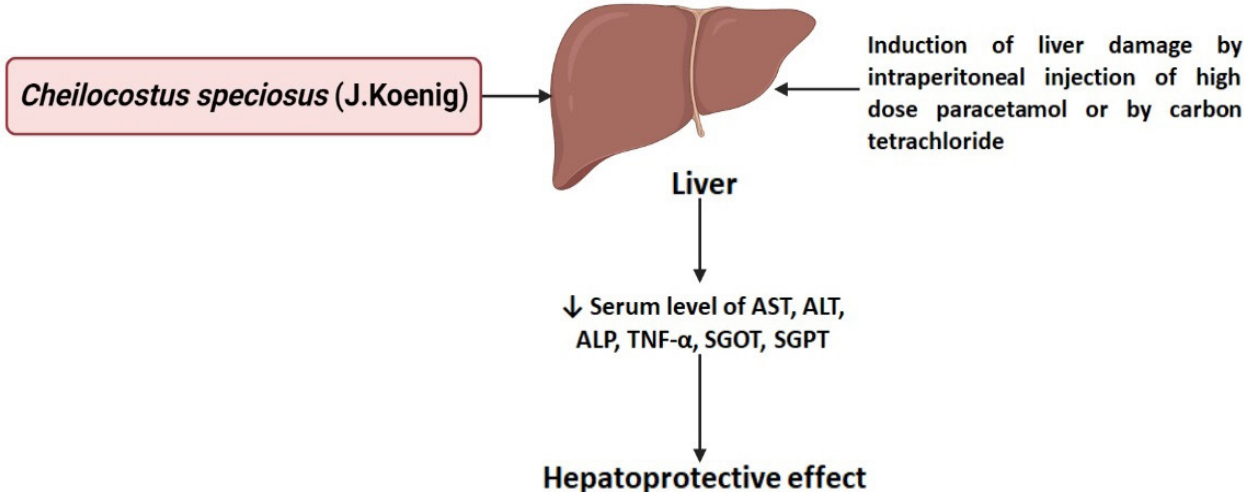

Fig. 4. Hepatoprotective effect of *C. speciosus* (J.Koenig). [ALP: alanine amino transferase; **TNF-α:** tumor necrosis factor- α; **AST:** aspartate aminotransferase; **ALP:** alkaline phosphatase; **SGOT:** glutamic oxaloacetic transaminase, and **SGPT:** serum glutamate-pyruvate transaminase].

in the brain at a normal level (Verma and Khosa, 2009a). A previous research group studied the adaptogenic activity of alcoholic extracts of rhizomes of *C. speciosus* (J.Koenig) on stress-induced albino rat model by assessing their effects in brain neurotransmitter's: dopamine (DA), norepinephrine (NE), 5-hydroxy indole acetic acid (5-HIAA), 5-hydroxy tryptamine (5-HT), and enzyme monoamine oxidase (MAO). This study data provide significant biochemical evidence of the anti-stress activity of C. speciosus (J.Koenig) (Verma and Khosa, 2009a).

4.9. Neuropharmacological evaluation

For the very first time, methanolic extract of *C. speciosus* (J.Koenig) rhizome was employed at a dose of 200 and 400 mg/kg in Swiss albino mice model to determine the extent of the anxiolytic and depressant effect on the central nervous system (CNS). During this experiment, neuropharmacological effects of methanolic extract of *C. speciosus* (J.Koenig) was investigated on different laboratory setup: hole-board, elevated plus maze, forced swimming, thiopental induced sleep, and tail suspension and light/dark, were 400 mg/kg dose of *C. speciosus* (J.Koenig) had produced significant CNS depressant effect while compared to standard diazepam (Chen et al., 2019).

4.10. Larvicidal activity

One of the most hazardous health issues in the world is mosquito-borne diseases. Several diseases including malaria, yellow fever, dengue fever, schistosomiasis, filariasis, *Japanese encephalitis* are transmitted by mosquitoes (Muniyandi et al., 2013). Thus, the discovery of any plant and plant-derived constituents could be the safest alternative to the use of synthetic larvicides, as these compounds can pollute water and soil (Muniyandi et al., 2013). With this objective, the larvicidal activity of alcoholic leaf, rhizome, and stem extract of *C. speciosus* (J.Koenig) has been evaluated against third and fourth instar larvae (*Aedes aegypti*). All of the extracts had shown the maximum larvicidal potential at 2000 µg/mL, while all extracts at all doses level confirmed their dose-dependent larvicidal properties (Muniyandi et al., 2013).

4.11. Endocrine activity

The main female sex hormone is estrogen. It is responsible for developing and regulating the sexual characteristics of the female and also one of the major regulators for the development of the reproductive system (Fig. 5). Any abnormalities in the release or function of estrogen can therefore change the women's reproductive systems and their behavior (Lombardi, 2001). A previous study investigated the effect of the methanolic rhizome extract of *C. speciosus* (J.Koenig) on the ovary and uterus of adult female mice. At 250 and 500 mg/kg dose, the extract had a considerable reduction in ovarian weight whilst increased the uterine weight compared to normal control. The change of uterine and ovarian weights could be associated with the inhibition of the release of the pituitary gonadotropin hormone thus proven and replicate the endocrine properties of *C. speciosus* (J.Koenig) (Najma et al., 2012).

4.12. Diuretic activity

Diuretic agents are inhibitors of ion transport that decrease Na's reabsorption at various sites in nephrons, resulting in urinary urine induction by sodium (Na) and other ions like chloride (Cl) greater than normal with water. Adjustment of the body fluid and composition is explicit in their roles in a range of disorders, including high blood pressure, nephritis, cirrhosis, renal failure, heart failure, and pregnancy toxemia (Agunu et al., 2005). The diuretic effect of aqueous and alcoholic extract of *C. speciosus* (J.Koenig) rhizomes was evaluated by Dubey et al. (2010) at a dosage of 250 mg/kg in albino

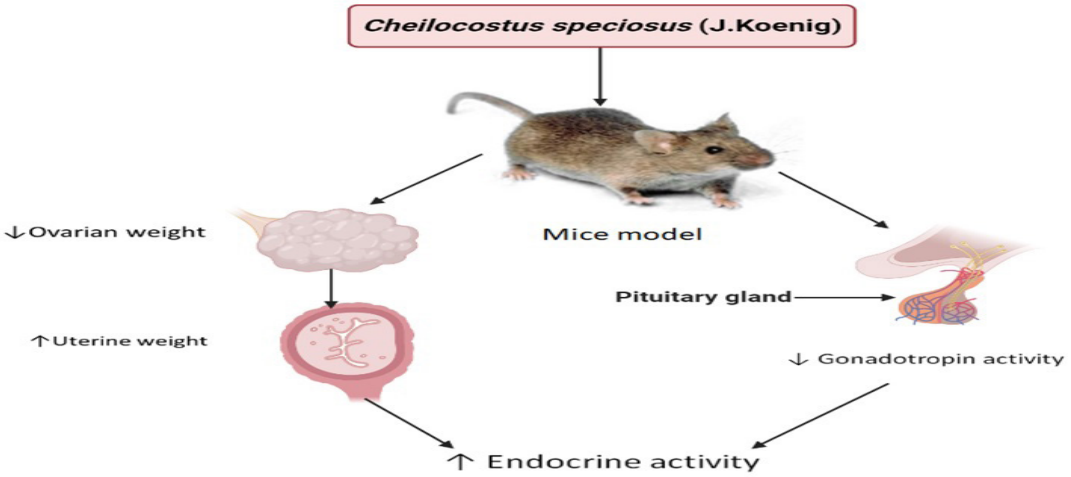

Fig. 5. Endocrine activity of *C. speciosus* (J.Koenig).

rats and the result was compared with furosemide (100 mg/kg BW) as the standard diuretic drug. The study concluded that urine and urinary electrolyte concentration considerably increased by both extracts of *C. speciosus* (J.Koenig) (Dubey et al., 2010).

5. Toxicological studies

The collected stem, leaves, and flowers were shade-dried and powdered in a grinder to get a coarse powder. The powdered plant material (5000 g) was extracted with 50% ethanol with a maceration afterward to have the desired amount of the plant extract (Sari and Nurrochmad, 2016). The aqueous part of the extract was then evaporated to obtain a viscous dark green extract. The ethanolic extract was analyzed as a standardized extract following Indonesian herbal pharmacopeia. There were no contaminants of arsenic (As), cadmium (Cd), mercury (Hg), and lead (Pb) and no bacterial and fungus contaminants (*E. coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *S. aureus*, and *Candida albicans*) (Sari and Nurrochmad, 2016). There is only one research trial that has been done to evaluate the subacute toxicity test of *C. speciosus (*J.Koenig*). C. speciosus* (J.Koenig) at 275-1100 mg/kg/day was administered to male mice for 90 days. Food and drink intakes were measured every day, and toxic symptoms were observed every day. The animals were sacrificed at the end of the study and the weights of vital organs were examined and subjected to histological examination (Sari and Nurrochmad, 2016). The results showed that the administration of *C. speciosus* (J.Koenig) ethanolic extract at 275-1100 mg/kg/day for 90 days did not show any significant disturbance in all parameters, except for reductions of cholesterol and blood glucose levels of test animals (Sari and Nurrochmad, 2016).

6. Concluding remarks

This review supports the different therapeutic potentials of *C. speciosus* (J.Koenig) and its role in various diseases. This review opens a new way to explore the compounds responsible for these therapeutic effects and also concludes with a scientific need to study the possible mechanism of action for their therapeutic actions. So far, many activities have not been studied, so that anyone can consider these plants to explore the rest medicinal properties of *C. speciosus* (J.Koenig).

List of abbreviations

WHO: world health organisation; **CNS**: central nervous system; **STZ**: streptozotocin; **TG**: total triacylglycerol; **TC**: cholesterol; **LDL**: low-density lipoprotein; **ROS**: reactive oxygen species; **RNS**: reactive nitrogen species; **DNA**: deoxyriboneuclic acid; **LPS**: lipopolysaccharides; **MAPK**: mitogen-activated protein kinase; **HepG2**: human hepatocellular carcinoma; **MDA-MB-231**: human breast adenocarcinoma; **MIC**: minimum inhibitory concentration; **IC_{50}**: inhibitory concentration for 50% populations; **GSH**: glutathione; **ALT**: alanine amino transferase; **LDH**: lactate dehydrogenase; **SGPT**: serum glutamic pyruvic transaminase; **ACP**: acid phosphatase **AST**: aminotransferase; **ALP**: alkaline phosphatase; **TNF-α**: well as tumor necrosis factor-α; **MAO**: monoamine oxidase; **DA**: dopamine: **NE**: norepinephrine; **5HIAA**: 5-hydroxy indole acetic acid; **5-HT**: 5-hydroxy tryptamine; **NF-κB**: nuclear factor-Kb; **MAPK**: mitogen-activated protein kinase;**BW**: body weight; **CC**: column chromatography; **GC**: gas chromatography; **TLC**: thin layer chromatography; **NMR**: nuclear magnetic resonance spectroscopy; **MS**: mass spectroscopy; **IR**: infrared spectroscopy; **HPLC**: high performance liquid chromatography; **MPS**: moving particle semi-implicit; **DEPT**: distortion less enhancement by polarization transfer; **HMBC**: heteronuclear multiple bond correlation spectroscopy; **HMQC**: heteronuclear multiple quantum coherence.

Conflict of interest

The authors declare that there is no conflict of interest.

References

Agunu, A., Abdurahman, E.M., Andrew, G.O.,

Muhammed, Z., 2005. Diuretic activity of the stem-bark extracts of *Steganotaenia araliacea* hochst [Apiaceae]. J. Ethnopharmacol. 96(3), 471-475.
Ahmed, M.F., Kazim, S.M., Ghori, S.S., Mehjabeen, S.S., Ahmed, S.R., Ali, S.M., Ibrahim, M., 2010. Antidiabetic activity of *Vinca rosea* extracts in alloxan-induced diabetic rats. Int. J. Endocrinol. 2010, 841090.
AlSaadi, B.H., AlHarbi, S.H., Ibrahim, S.R., El-Kholy, A.A., El-Agamy, D.S., Mohamed, G.A., 2018. Hepatoprotective activity of *Costus speciosus* (Koen. Ex. Retz.) against paracetamol induced liver injury in mice. Afr. J. Tradit. Complement. Altern. Med. 15, 35-41.
Ariharan, V.N., Devi, V.N.M., Rajakokhila, M., Prasad, P.N., 2012. Antibacterial activity of *Costus speciosus* rhizome extract on some pathogenic bacteria. Int. J. Adv. Lif. Sci. 4, 24-27.
Ashraf, M.A., Khatun, A., Sharmin, T., Mobin, F., Tanu, A.R., Morshed, T., Fakir, T.A., Begum, R.A., Nabi, A.N., 2014. MPDB 1.0: A medicinal plant database of Bangladesh. Bioinformation 10, 384-386.
Asolkar, L., Chopra, R., 1992. Second Supplement to Glossary of Indian Medicinal Plants With Active Principles. Publications & Information Directorate.
Bakhsh, Z.A., Al-Khatib, T.A., Al-Muhayawi, S.M., ElAssouli, S.M., Elfiky, I.A., Mourad, S.A., 2015. Evaluating the therapeutic efficacy, tolerability, and safety of an aqueous extract of *Costus speciosus* rhizome in acute pharyngitis and acute tonsillitis. A pilot study. Saudi. Med. J. 36(8), 997-1000.
Baskar, A.A., Al. Numair, K.S., Alsaif, M.A., Ignacimuthu, S., Ignacimuthu, S., 2012. *In vitro* antioxidant and antiproliferative potential of medicinal plants used in traditional Indian medicine to treat cancer. Redox Report. 17(4), 145-156.
Bhattacharya, S., Nagaich, U., 2010. Assessment of anti-nociceptive efficacy of *Costus speciosus* rhizome in swiss albino mice. J. Adv. Pharm. Technol. Res. 1(1), 34-40.
Bihari, C.G., Shankar, N.B., Kumar, J.P., Keshari, P., Ellaiah, P., 2010. Phytochemical investigation and screening for anthelmintic activity of leafy extracts of various *Ocimum* (Tulsi) species. J. Pharm. Res. 3(9), 2140-2141.
Bindu, C., Bhat, P.R., Prasad, G.K., Girish, B.C., 2016. Relative potency of antidiabetic effect of *Costus speciosus* (koen. Ex retz.) Smith plant extract in mouse fibroblast cell line. IJRG 4(3), 99-106.
Binny, K., Kumar, S.G., Dennis, T., 2010. Anti-inflammatory and antipyretic properties of the rhizome of *Costus speciosus* (koen.) sm. J. Basic Clin. Pharm. 1(3), 177-181.
Chakre, O.J., 2010. The wealth of India-a CSIR's encyclopaedia of information resource on economic plants, animals and minerals. Cur. Sci. 99(7), 969-971.
Chaturvedi, H., Jain, M., Kidwai, N., 2007. Cloning of medicinal plants through tissue culture—a review. Indian J. Exp. Biol. 45, 937-948.
Chen, U., Hussain, M.S., Mazumder, T., Uddin, S.N., Banik, S., 2019. Neuropharmacological evaluation of methanolic extract of *Costus speciosus* Linn. rhizome in Swiss albino mice. Asian Pac. J. Trop. Biomed. 9(5), 217-221.
Chopra, R., Nayar, S., Chopra, I., Asolkar, L., Kakkar, K., 1956. Glossary of Indian Medicinal Plants, New Delhi. Council of Scientific Industrial Research.
Contreras-Zentella, M.L., Hernández-Muñoz, R., 2016. Is liver enzyme release really associated with cell necrosis induced by oxidant stress?. Oxid. Med. Cell. Longev. 2016(12), 3529149.
Daisy, P., Eliza, J., Ignacimuthu, S., 2008. Influence of *Costus speciosus* (Koen.) Sm. Rhizome extracts on biochemical parameters in streptozotocin induced diabetic rats. J. Health Sci. 54(6), 675-681.
Devasagayam, T.P., 2007. Introduction to serial reviews: recent advances in Indian herbal drug research. J. Clin. Biochem. Nutr. 40(2), 73.
Dubey, N., Kumar, R., Tripathi, P., 2004. Global promotion of herbal medicine: India's opportunity. Cur. Sci. 86(1), 37-41.
Dubey, S., Vijendra, K., Amit, K., Amit, K., Tiwari, A., 2010. Evaluation of diuretic activity of aqueous and alcoholic rhizomes extracts of *Costus speciosus* Linn in wister Albino rats. Int. J. Res. Ayurveda Pharm. 1(2), 648-652.
Duraipandiyan, V., Al-Harbi, N.A., Ignacimuthu, S., Muthukumar, C., 2012. Antimicrobial activity of sesquiterpene lactones isolated from traditional medicinal plant, *Costus speciosus* (Koen ex.Retz.) Sm. BMC Complement. Altern. Med. 12(1), 13.
El-Far, A., Abou-Ghanema, I., 2013. Biochemical and hematological evaluation of *Costus speciosus* as a dietary supplement to Egyptian buffaloes. Afr. J. Pharm. Pharmacol. 7(42), 2774-2779.
Eliza, J., Daisy, P., Ignacimuthu, S., Duraipandiyan, V., 2009. Antidiabetic and antilipidemic effect of eremanthin from *Costus speciosus* (Koen.) Sm., in STZ-induced diabetic rats. Chem. Biol. Interact. 182(1), 67-72.
Gupta, M.M., Lal, R.N., Shukla, Y.N., 1981. Aliphatic hydroxyketones and diosgenin from *Costus speciosus* roots. Phytochemistry. 20(11), 2553-2555.
Gupta, M.M., Verma, R.K., Akhila, A., 1986. Oxo acids and branched fatty acid esters from rhizomes of *Costus speciosus*. Phytochemistry 25(8), 1899-1902.
Indrayanto, G., Utami, W., Syahrani, A., 1999. *Costus speciosus* (Koenig) J.E. Smith: *In vitro* cultures, micropropagation, and the production of diosgenin and other phytosteroids. In: Bajaj Y.P.S. (Ed.) Medicinal and Aromatic Plants XI. Biotechnol. Agric. For. 43, 57-77.
Inoue, K., Kobayashi, S., Noguchi, H., Sankawa, U., Ebizuka, Y., 1995. Spirostanol and furostanol glycosides of *Costus speciosus* (Koenig.) Sm. Nat. Med. 49(3), 336-339.
Jha, M., Alam, M., Hossain, M., Islam, A., 2010. *In vitro* antioxidant and cytotoxic potential of *Costus speciosus* (Koen.) Smith rhizome. Int. J. Pharm. Sci. Res. 1(10), 138-144.
Kirchoff, B.K., Rutishauser, R., 1990. The phyllotaxy of costus (Costaceae). Bot. Gaz. 151(1), 88-105.
Kumar, S., Shukla, R., Singh, K., Paxton, J., Husain, A., 1984. Glyceollin: A phytoalexin in leaf blight of *Costus speciosus*. Phytopathology 74(11), 1349-1352.
Lijuan, W., Kupittayanant, P., Chudapongse, N., Wray, S., Kupittayanant, S., 2011. The effects of wild ginger (*Costus speciosus* (Koen) Smith) rhizome extract and diosgenin on rat uterine contractions. Reprod. Sci. 18, 516-524.
Lombardi, G., 2001. Estrogens health in males. Mol. Cell. Endocrinol. 178, 51-55.

Mahmood, U., Shukla, Y.N., Thakur, R.S., 1984. Benzoquinones from *Costus speciosus* seeds. Phytochemistry 23(8), 1725-1727.
Mosihuzzaman, M., Nahar, N., Ali, L., Rokeya, B., Khan, A.K., Nur, E.A.M., Nandi, R.P., 1994. Hypoglycemic effects of three plants from eastern Himalayan belt. Diabetes Res. 26(3), 127-138.
Muniyandi, S., Nandanan, A., Veeti, S., Narayanan, A., Ganesan, B., 2013. Studies on *Costus speciosus* Koen alcoholic extract for larvicidal activity. Int. J. Pharmacogn. Phytochem. Res. 5, 328-329.
Nair, S.V., Hettihewa, M., Rupasinghe, H.P., 2014. Apoptotic and inhibitory effects on cell proliferation of hepatocellular carcinoma HepG2 cells by methanol leaf extract of *Costus speciosus*. Biomed. Res. Int. 2014, 637098.
Najma, C., Chandra, K., Ansarul, H., 2012. Effect of *Costus speciosus* Koen on reproductive organs of female albino mice. Int. Res. J. Pharm. 3, 200-202.
Nehete, J., Bhatia, M., Narkhede, M., 2010. *In vitro* evaluation of antioxidant activity and phenolic content of *Costus speciosus* (Koen) JE Sm. Iran J. Pharm. Res. 9(3), 271-277.
Padma, P., Chansauria, J., Khosa, R., Ray, A., 2001. Effect of *Annooa muricata* and *Polyalthia cerasoides* on brain neurotransimitters and enzyme monoamine oxidase following cold immobilization stress. J. Nat. Remedies. 1, 144-146.
Pawar, V., Pawar, P., 2014. *Costus speciosus*: an important medicinal plant. IJSR 3(7), 28-33.
Rani, A.S., Sulakshana, G., Patnaik, S., 2012. *Costus speciosus*, an antidiabetic plant-review. FS J. Pharm. Res. 1(3), 51-53.
Rastogi, R.P., Mehrotra, B., 1990. Compendium of Indian Medicinal Plants. Central Drug Research Institute.
Rayan, N.A., Baby, N., Pitchai, D., Indraswari, F., Ling, E.A., Lu, J., Dheen, T., 2011. Costunolide inhibits proinflammatory cytokines and iNOS in activated murine BV2 microglia. Front. Biosci. (Elite Ed). 3, 1079-1091.
Roy, A., Manikkam, R., 2015. Cytotoxic impact of costunolide isolated from *Costus speciosus* on breast cancer via differential regulation of cell cycle—an *in vitro* and *in silico* approach. Phytother. Res. 29, 1532-1539.
Samal, P.K., Dangi, J., Meena, K.P., Beck, N., Maheshwari, G., Patel, A., 2011. Hepatoprotective activity of *Butea monosperma* bark on liver damage caused by paracetamol in rats. Research J. Pharm. Tech. 4(5), 771-774.
Sari, I., Nurrochmad, A., 2016. Sub-acute toxicity study of ethanolic extract of pacing (*Costus speciosus*) in male mice. IJPCR 8, 440-444.
Selim, S., Al Jaouni, S., 2015. Anticancer and apoptotic effects on cell proliferation of diosgenin isolated from *Costus speciosus* (Koen.) Sm. BMC Complement. Altern. Med. 15, 301.
Shediwah, F.M.H., Naji, K.M., Gumaih, H.S., Alhadi, F.A., Al-Hammami, A.L., D'Souza, M.R., 2019. Antioxidant and antihyperlipidemic activity of *Costus speciosus* against atherogenic diet-induced hyperlipidemia in rabbits. J. Integr. Med. 17(3), 181-191.
Shobana, S., Naidu, K.A., 2000. Antioxidant activity of selected Indian spices. Prostaglandins Leukot. Essent. Fatty Acids. 62(2), 107-110.
Singh, I., Gautam, Y., Vimala, Y., 2013. Detection and isolation of diosgenin from *Costus speciosus* callus raised from non-germinal seeds. Int. J. Chem. Life Sci. 2, 1240-1242.
Singh, S.B., Thakur, R.S., 1982a. Costusoside-I and costusoside-J, two new furostanol saponins from the seeds of *Costus speciosus*. Phytochemistry 21(4), 911-915.
Singh, S.B., Thakur, R.S., 1982b. Saponins from the seeds of *Costus speciosus*. J. Nat. Prod. 45, 667-671.
Sivarajan, V., Balachandran, I., 1994. Ayurvedic Drugs and Their Plant Sources, Oxford and IBH Publishing.
Srivastava, S., Singh, P., Mishra, G., Jha, K., Khosa, R., 2011a. *Costus speciosus* (Keukand): A review. Der Pharm. Sin. 2, 118-128.
Srivastava, S., Singh, P., Mishra, G., Jha, K.K., Khosa, R.L., 2011b. Anthelmintic activity of aerial parts of *Costus speciosus*. Int. J. Green Pharm. 5(4), 325-328.
Srivastava, S., Singh, P., Jha, K.K., Mishra, G., Srivastava, S., Khosa, R.L., 2013. Antiinflammatory, analgesic and antipyretic activities of aerial parts of *Costus speciosus* Koen. Indian J. Pharm. Sci. 75(1), 83-88.
Stone, B.C., 1970. The Flora of Guam. A manual for the identification of the vascular plants of the island. Micronesica 6, 1-659.
Swati, S., Agarwal, P.K., 2015. A critical review. World J. Pharm. Sci. 4, 421-429.
Verma, N., Khosa, R., 2009a. Effect of *Costus speciosus* and *Wedelia chinensis* on brain neurotransmitters and enzyme monoamine oxidase following cold immobilization stress. J. Pharm. Sci. Res. 1(2), 22-25.
Verma, N., Khosa, R., 2009b. Evaluation of protective effects of ethanolic extract of *Costus speciosus* (Koenig) Sm. rhizomes on carbon tetrachloride induced hepatotoxicity in rats. Nat. Prod. Radiance. 8, 123-126.
Vijayalakshmi, M.A., Sarada, N.C., 2008. Screening of *Costus speciosus* extracts for antioxidant activity. Fitoterapia 79(3), 197-198.