# *Cheilocostus Speciosus* Traditional Uses And Taxonomy

Rajat Kumar, Prof. (Dr) Ravinesh Mishra, Dr. Bhartendu Sharma, Laxmipriya Nayak

*Rajat Kumar, M. Pharma Pharmacology, Baddi University, Himachal Pradesh, India*
*Prof. (Dr) Ravinesh Mishra, School of Pharmacy, Baddi University, Himachal Pradesh, India*
*Dr. Bhartendu Sharma, School of Pharmacy, Baddi University, Himachal Pradesh, India*
*Laxmipriya Nayak, M. Pharma Pharmacology, Baddi University, Himachal Pradesh, India*

## ABSTRACT

*Novel drug discovery targets can be derived from medicinal plants. One significant medicinal plant that is frequently used to cure a variety of diseases is Cheilocostus speciosus. The plant has numerous active components and pharmacological activities, including hepatoprotective, steroidogenic, antibacterial, anticancer, anti-inflammatory, antidiabetic, hypolipidemic, and antioxidant properties. This review, by examining the databases of Google Scholar, PubMed, Science Direct, and Springer Link, provides an overview of distinct investigations on C. speciosus phytochemical, toxicological, and pharmacological studies and traditional uses of C. speciosus. According to earlier research, C. speciosus has pharmaceutical potential. nevertheless, more research is still required to understand the molecular underpinnings of its biological activities, particularly in vivo models and safety evaluation of its various extracts.*

**Keywords:** *Cheilocostus speciosus, Islamic traditional medicine, therapeutic potentials*

---

1. **Introduction:** Bioactive compounds with the potential to be incorporated into new medications can be obtained from plant-active principles.[1] Compared to synthetics, herbal products are comparatively safer.[2] In An antibiotic, The *Zingiberaceae* plant family includes approximately 52 genera and more. Over 1300 species are found in tropical Africa, Asia, and the Americas. It contains cardamom, torch ginger (*Etlingera elatior*), summer tulip (*Curcuma alismatifolia*), ginger lily (*Hedychium*), shell gingers (*Alpinia*), and turmeric (*Curcuma longa*). (Maximum Elettaria).[3] The *Zingiberaceae* member *Cheilocostus speciosus*, is a vertical, roughly 2.7-meter-tall, tuberous rootstock plant that stem subwoody.[4] The taxonomic categorization and colloquial terms for Table 1 contains specifics on *C. speciosus. C. speciosus* is one of the most potent traditional medicinal plants used in Islam.[5] The truthful Hadith found in Sunan Abi Dawud and the Book of Medicine (Kitab Al-Tibb), where Umm Qasis, Says Mihsan's daughter: "I brought my son to the Messenger of Allah." when I applied pressure on his uvula to reduce its swelling. He uttered, "Why do you Hurt your kids by applying pressure to cause swelling in the uvula? Utilize this Indian aloeswood (*costus*), since it has seven different kinds of medicinal properties, one of which is a pleurisy remedy. In the field of predictive medicine, it was particularly advised to utilize *C. speciosus* as a treatment for children's tonsillitis and pharyngitis, pleurisy, and snake venom countermeasures.[6] The rhizomes and roots of *C. speciosus* are said to possess anthelmintic, anti-inflammatory, antidiabetic, hepatoprotective, antihyperlipidemic, antispasmodic, and antibacterial properties in Indian traditional medicine. actions. [7,8]

Additionally, patients with *C. speciosus* leaf baths elevated temperatures. Traditionally, rhizome juice is administered with sugar to treat leprosy. as well as to relieve headaches. [10,9] Moreover, its extract of alkaloids is utilized as an antispasmodic muscle relaxant.[11] Also employed is *C. speciosus* a meal made of plants in Southeast Asia.[12]

**2. Phytochemistry:** Crepe ginger is a common name for *C. speciosus.* According to *(Warrier et al. 1995)*, the plant's rhizomes are aphrodisiac, bitter, astringent, anthelmintic, expectorant, and tonic. *C. speciosus* phytochemical screening found that steroids, phenolic compounds, glycosides, alkaloids, and [13,14] flavonoids, tannins, polyphenols, and β-carotene.[15] Diosgenin, β-sitosterol, β-D-glucoside, furostanol saponins-costusosides, dioscin, gracillin, dihydrophytylplastoquinone, prosapogenins, and From *C. speciosus*, α-tocopherolquinone was extracted and has broad several biological actions, some of which are listed below [16, 17]. Additionally, anticancer properties of β-amyrin, camphene, costunolide, diosgenin, α-Humulene, zerumbone, and lupeol were identified. [18–22]

**Table 1: Taxonomic classification and vernacular names of *Cheilocostus speciosus***

| **Taxonomic classification** | **Name** |
|---|---|
| Kingdom | *Plantae* |
| Subkingdom | *Tracheobionta* |
| Super division | *Spermatophyta* |
| Division | *Magnoliophyta* |
| Class | *Liliopsida* |
| Subclass | *Zingiberidae* |
| Order | *Zingiberales* |
| Family | Costaceae |
| Genus | *Cheilocostus* |
| Species | *Speciosus* |
| **Vernacular names** | |
| Assam | Tara |
| Bengali | Keu, Keumut |
| Kannada | Changalvakostu, Chikke |
| Malayalam | Channakoova |
| Marathi | Penva, Pinnha, Kobee, Peva |
| Tamil | Kostam |
| Sanskrit | Kembuka, Kebuka, Kembu |
| Telegu | Kashmeeramu, Cengalvakostu |
| Classical name | Kebuka |

| | |
|---|---|
| English | Crepe ginger |
| Guajarati | Paskarmula, Valakdi |
| Hindi | Keu, Keukand, Kemuka, Kemua |
| Latin name | Costus speciosus |

**3. Biological activity of *Cheilocostus speciosus:*** Many *C. speciosus* extracts have a wide range of biological and pharmacological potentials, as demonstrated by the traditional uses of *C. speciosus* in a variety of complaints, which are covered and summarized here.

- **Antioxidant activity:** Antioxidants are a class of compounds that scavenge free radicals and stimulate the production of antioxidant enzymes within cells to effectively counteract oxidation processes.[23] Oxygen would rather take in its electrons one at a time. resulting in the production of reactive oxygen species over time (ROS).[24] ROS molecules are crucial components of the oxidative stress that is involved in diabetes, cirrhosis, cancer, and atherosclerosis. [25, 26] Enzymatic antioxidant systems combat oxidative damage by utilizing a range of enzyme scavengers, like EC 1.15.1.1's superoxide dismutase (SOD), catalase (CAT, EC 1.11.1.6), glutathione peroxidase (GPx, EC 1.11.1.9), and besides the nonenzymatic glutathione S-transferases (EC 2.5.1.18) components such as α-tocopherol, ascorbic acid (Vitamin C), and β-carotene, glutathione (GSH), and vitamin E. [27, 28] The redox characteristics of phenolics and flavonoids, found in medicinal plants, have the potential to shield living organisms against reactive oxygen species (ROS) risks. chelation of metal ions.[29] According to in vitro experiments, the antioxidant Chloroform, ethanol, and methanolic activities of *C. speciosus* were extracted from the peel of leaves, roots, and peeled stems. The protective agent the enzyme 1,1-diphenyl-2-picrylhydrazyl (DPPH) was used to measure activity. In addition, 2,2'-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid techniques using thiobarbituric acid (TBA). The extracts with methanol revealed an increased capacity to scavenge hydroxyl radicals and quench free radicals' aptitude.[30]

- **Anticancer activity:** Many of the chemotherapeutic drugs available today block particular molecular targets necessary for tumor growth and have lethal potential in vitro or in vivo. [31,32] Hexane, ethyl acetate, and methanol-extracted *C. speciosus* rhizome anticancer potentials were assessed against human colon adenocarcinoma cell lines (COLO 320 DM). According to the authors, every extract of *C. speciosus* rhizome that was examined had noteworthy antiproliferative and antioxidant properties in a manner that was dependent on both time and dose. [33,34] This study demonstrated the connection between *C. speciosus's* anticancer properties and its antioxidant concentration. A study using 1, 10, 50, 100, and 200 µg/ml of Eagle's modified minimum essential medium supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin was conducted on the methanolic extract of *C. speciosus* leaves. HepG2 cells showed a notable decrease in cell viability after being treated with 100 µg/ml for 24 hours.[35] The methanolic extract disrupted the course of the cell cycle, as evidenced by elevated caspase-3 activity in the treated cells. Further research is required to determine how this extract affects pro- and anti-apoptotic molecules in cells using molecular methods.

- **Anti-inflammatory activity:** As a pathophysiological reaction to tissue damage, inflammation is closely linked to the etiology of several inflammatory illnesses. [36,37] In light of the negative side effects of synthetic and chemical medications, several medicinal plants were employed as a less risky alternative. It has been demonstrated that Z. officinale, C. longa, and *C. speciosus* possess strong anti-inflammatory properties. [38,39] The traditional applications of *C. speciosus* for the treatment of fever, rheumatism, bronchitis, headache, and inflammation have been the subject of numerous investigations. An in vitro investigation focused on costunolide's impact on lipopolysaccharide (LPS)-stimulated generation of pro-inflammatory mediators and pathways in a murine BV-2 cell culture. By inhibiting the NF-κB and mitogen-activated protein kinase pathways, costunolide reduced the production of tumor necrosis factor-alpha (TNF-α), interleukin (IL), IL-6, inducible NO synthase (NOS), and cyclooxygenase (COX-2).[40] Similarly, in isolated peripheral blood mononuclear cells, the n-hexane-chloroform soluble fraction of

methanolic *C. speciosus* rhizomes extract contained 22, 23-dihydrospinasterone, dehydrodihydrocostus lactone, dehydrocostus lactone, stigmasterol, arbusculin A, santamarine, and reynosin, which significantly reduced the levels of IL-1β, IL-6, TNF-α, prostaglandin E2, lipoxygenase-5, and COX-2.[41]

- **Antidiabetic activity:** Globally, diabetes mellitus is a metabolic disorder that affects 4% of people.[42] In addition to medications that are frequently used to treat diabetes, including insulin, sulfonylureas, biguanides, or thiazolidinediones, several species of medicinal plants have also been identified as normoglycemic medicines with improved efficacy, fewer side effects, and affordable prices.[43,44] The impact of *C. speciosus* rhizome juice on serum glucose levels in a noninsulin-dependent diabetic rat model was investigated by *Mosihuzzaman et al.* [45]. The findings demonstrated that when *C. speciosus* was fed simultaneously with glucose, it had no discernible impact on the postprandial or fasting states in non-diabetic rats. However, when *C. speciosus* was given 30 minutes before the glucose injection, the animals experienced a hypoglycemic response. To make sense of this discovery, we must examine how *C. speciosus* affects intestinal glucose absorption by measuring the expression of the glucose transporter gene. Furthermore, understanding the impact of *C. speciosus* on glucose levels in the fasting and feeding phases requires an understanding of the blood levels of glucagon and insulin. [46,47]

- **Hypolipidemic activity:** Patients with diabetes have excessively high serum lipid concentrations because insulin inhibits hormone-sensitive lipase (EC 3.1.1.79). As a result, fatty acids are released from adipose tissue in insulin insufficiency, which also causes hyperlipidemia.[48] Moreover, 3-hydroxy- methylglutaryl coenzyme A reductase (EC 1.1.1.88), a critical rate-limiting enzyme involved in the metabolism of cholesterol-rich low-density lipoprotein (LDL) particles, is inhibited by insulin. We assessed the potential normoglycemic and hypolipidemic effects of costunolide in male Wistar rats with STZ-diabetes after oral dosages of 5, 10, and 20 mg/kg BW were given for 30 days. The results indicated a substantial reduction in total serum cholesterol, TAG, and LDL-cholesterol at 20 mg costunolide/kg BW. Concurrently, there was a notable rise in plasma insulin, muscle and liver glycogen, and high-density lipoprotein (HDL) cholesterol levels. The authors postulated that costunolide could potentially induce insulin secretion in β cells by preventing the expression of NOS. [49,50] Likewise, eremanthin's hypolipidemic impact at equivalent dosages was assessed in a study using STZ-diabetic rats for 60 days. Researchers discovered that oral administration of 20 mg eremanthin/kg BW considerably increased plasma insulin, tissue glycogen, and HDL cholesterol while dramatically lowering total blood cholesterol, TAG, and LDL cholesterol.[51] In addition to the effects of *C. speciosus* on pancreatic lipases and adipose tissue hormone-sensitive lipase, we recommend future research to examine the effects of *C. speciosus* on lipid digestion and absorption concerning the gene expression of intestinal fatty acid transporters.

- **Hepatoprotective activity:** Serum enzymes, such as lactate dehydrogenase (LDH, EC 1.1.1.27), aspartate aminotransferase (AST, EC 2.6.1.1), alanine aminotransferase (ALT, EC 2.6.1.2), alkaline phosphatase (ALP, EC 3.1.3.1), and acid phosphatase (ACP, EC 3.1.3.2), are used as biomarkers for liver function. Increased activities of AST, ALT, LDH, ALP, and ACP in plasma/serum may be caused by liver cell leakage into the bloodstream.[52] Carbon tetrachloride ($CCl_4$)-induced changes in the liver function profiles of Swiss albino mice were observed in a hepatotoxicity study. The changes were caused by $CCl_4$ intoxication, which was treated with a methanolic extract of *C. speciosus* rhizomes (100 mg/kg body BW for 14 consecutive days) twice a week. As a reference hepatoprotective medication, the extract restores serum levels of bilirubin, AST, ALT, ALP, and total protein to normal levels as compared to rats treated with silymarin.[53] The same findings were noted when *C. speciosus* ethanolic extract was given orally to Wister albino rats at a dose of 500 mg/kg BW. Additionally, silymarin, a common medication with hepatoprotective properties, was compared to the extract. [54,55] This component needs further studies about the hepatoprotective activity of *C. speciosus* against medications and chemicals that generate liver damage, that is, paracetamol, nonsteroidal anti-inflammatory, glucocorticoids, isoniazid, aflatoxins, arsenic, vinyl chloride, and other substances.

- **Adaptogenic activity:** Numerous stressors result in a substantial change in the different neurotransmitters in the central nervous system (CNS) and peripheral nervous system, which lowers norepinephrine and dopamine levels in the brain. [56,57] It seems that norepinephrine is used in stress response, which raises dopamine concentrations.[58] Monoamine oxidase (MAO, EC 1.4.3.4) is primarily involved in maintaining the normal levels of biogenic amines in the brain; it is hypothesized that the executive function of MAO is

to prevent the release of 5-hydroxytryptamine (5-HT). [59,60] By inhibiting the alarm reaction, which causes a considerable increase in 5HT and 5HIAA levels, *C. speciosus* extracts dramatically decreased the stress-induced rise in these levels in brain tissues.[61] The authors examined the effects of *C. speciosus* on MAO; however, it is important to take into account the role of catechol-O-methyltransferase (EC 2.1.1.6), an enzyme that collaborates with MAO in the catabolism of catecholamines. According to this study, *C. speciosus* has an antidepressant effect and could be utilized in a new medication formulation to treat CNS diseases. As a suggestion for further research, the effectiveness of *C. speciosus* against a headache requires a study of the plant's historic use as a headache remedy.

- **Antimicrobial activity:** When taking antibiotics orally, adverse side effects can happen. For example, taking penicillin orally can result in heartburn, nausea, vomiting, and diarrhea. As a result, a lot of research was done on using spices and herbs in place of antibiotics.[62] In contrast to silver sulfadiazine cream, hexane and methanol extracts of *C. speciosus* leaf and rhizomes demonstrated a lysis zone against Salmonella spp., Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas spp., Bacillus subtilis, and Shigella spp.[63] Costunolide's antifungal effect demonstrated significant minimal inhibitory concentration values: 62.5 µg/ml against Trichophyton mentagrophytes, 62.0 µg/ml against Trichophyton simii, 125 µg/ml against Epidermophyton floccosum, 31.25 µg/ml against Trichophyton rubrum, 125 µg/ml against Curvulari lunata, 62.5 µg/ml against T. rubrum, 250 µg/ml against Scoulariopsis sp, 250 µg/ml against Aspergillus niger, and 250 µg/ml against Magnaporthe grisea.[64] Research into *C. speciosus's* potential as an antiviral is crucial, especially for prevalent illnesses like avian influenza, infectious viral hepatitis, and human immunodeficiency viruses.

**4. Toxicological study:** The stem, leaves, and flowers were shade-dried and ground into a coarse powder using a grinder. Using maceration equipment, 50% ethanol was recovered from the 5000 g of powdered plant material. A viscous dark green extract was produced by evaporating the aqueous extract. Using Indonesian herbal pharmacopes as a guide, the ethanolic extract was examined as a standardized extract. There were no bacterial or fungal pollutants (E. Coli, Pseudomonas aeruginosa, Salmonella typhi, S. aureus, and Candida albicans), nor were there any contamination of arsenic (As), cadmium (Cd), mercury (Hg), or lead (Pb). To assess the subacute toxicity test of *C. speciosus*, one study trial has been conducted. Male mice were given *C. speciosus* at 275–1100 mg/kg/day for 90 days. Daily measurements of food and drink intake were made, and daily observations were made of toxic symptoms. After the investigation, the animals were slaughtered, and the weights of the important organs were measured and histologically analyzed. The administration of *C. speciosus* ethanolic extract at 275–1100 mg/kg/day for 90 days did not significantly alter any of the parameters, except the test animals' blood glucose and cholesterol levels decreased. [65,66] To ascertain the safety of *C. speciosus*, various extracts derived from each component of the plant were analyzed independently to calculate the extracts' LD50 and safety thresholds.

**5. Conclusion:** *Cheilocostus speciosus*, a notable member of the Zingiberaceae family, is rich in bioactive compounds with diverse medicinal properties. It shows promising antioxidant, anticancer, anti-inflammatory, antidiabetic, and antimicrobial effects. Traditional uses and preclinical studies highlight its therapeutic potential. Rich in steroids, phenolic compounds, glycosides, alkaloids, and flavonoids, C. speciosus has demonstrated significant therapeutic benefits. This plant stands as a promising candidate for developing new, safer medications derived from natural sources, offering an alternative to synthetic drugs. Further research and clinical trials could pave the way for its incorporation into modern medicine.

## 6. References:

1. Rates SM. Plants as source of drugs. Toxicon 2001;39:603-13.
2. Rajashree R, Gangolli D, Patil S, Ingawale K. Amla, ashwagandha and shatavari formulations as herbal medicines and nutraceuticals. Res J Pharm Sci 2012;1:10-5.
3. Jiang K, Delin W, Larsen K. Zingiberaceae. Flora China 2000;24:322-77.
4. Dutta AC, Dutta TC. Botany. Kolkata: Oxford University Press, Salt Lake Electronics Complex; 1998.
5. Emami SA, Sahebkar A, Javadi B. Paresthesia: A Review of its definition, etiology and treatments in view of the traditional medicine. Curr Pharm Des 2016;22:321-7.

6. Khalifa SA, Al-Elyani RA. Histological and ultrastructural studies on the effect of Costus plant and amphotericin B on male lung rats infected by Aspergillus niger – semantic scholar. Life Sci J 2012;9:5321-38. Available from: https://www.semanticscholar.org/paper/ Histological-and-ultrastructural-studies-on-the-A-khalifa/e22e0a49a98a199e57eee2df6fc43b 4112c4e46b#citingPapers. [Last accessed on 2017 Mar 28].
7. Warrier PK, Nambiar VP, Ramankutty C. Indian Medical Plants: A Compendium of 500 Species. 3rd ed. Madras, India: Orient Longman; 1995.
8. Saraf A. Phytochemical and antimicrobial studies of medicinal plant C. Speciosus (Koen.). Chem 2010;7:S405-13. Available from: http://www.hindawi.com/journals/ jchem/2010/605735/. [Last accessed on 2016 Nov 24].
9. Khare CP. Indian Medicinal Plants. New York: Springer New York; 2007. Available from: http:// www.link.springer.com/10.1007/978-0-387-70638-2. [Last accessed on 2016 Nov 24].
10. Gupta RK. Medicinal and Aromatic Plants. New Delhi, India: CBS Publishers and Distributors; 2010.
11. Bhattacharya SK, Parikh AK, Debnath PK, Pandey VB, Neogy N. Pharmacological studies with the alkaloids of C. speciosus (kemuka). J Res Indian Med 1973;8:10-9.
12. Swati S, Agarwal P. Kebuka (C. Speciosus): A critical review. World J Pharm Pharm Sci 2015;4:421-31.
13. Srivastava S, Singh P, Mishra G, Jha KK, Khosa RL. C. speciosus (Keukand): A review. Der Pharm Sin 2011;2:118-28.
14. Singh P, Khosa RL, Srivastava S, Mishra G, Jha KK, Srivastava S, et al. Pharmacognostical study and establishment of quality parameters of aerial parts of C. speciosus-a well known tropical folklore medicine. Asian Pac J Trop Biomed 2014;4:486-91.
15. Pai Kotebagilu N, Reddy Palvai V, Urooj A. Protective effect of selected medicinal plants against hydrogen peroxide induced oxidative damage on biological substrates. Int J Med Chem 2014;2014:861084.
16. Lijuan W, Kupittayanant P, Chudapongse N, Wray S, Kupittayanant S. The effects of wild ginger (C. speciosus (Koen) Smith) rhizome extract and diosgenin on rat uterine contractions. Reprod Sci 2011;18:516-24.
17. Duraipandiyan V, Al-Harbi NA, Ignacimuthu S, Muthukumar C. Antimicrobial activity of sesquiterpene lactones isolated from traditional medicinal plant, C. speciosus (Koen ex.Retz.) sm. BMC Complement Altern Med 2012;12:13.
18. Santos FA, Frota JT, Arruda BR, de Melo TS, da Silva AA, Brito GA, et al. Antihyperglycemic and hypolipidemic effects of α, β-amyrin, a triterpenoid mixture from protium heptaphyllum in mice. Lipids Health Dis 2012;11:98.
19. Rasul A, Bao R, Malhi M, Zhao B, Tsuji I, Li J, et al. Induction of apoptosis by costunolide in bladder cancer cells is mediated through ROS generation and mitochondrial dysfunction. Molecules 2013;18:1418-33.
20. Shin JW, Ohnishi K, Murakami A, Lee JS, Kundu JK, Na HK, et al. Zerumbone induces heme oxygenase-1 expression in mouse skin and cultured murine epidermal cells through activation of Nrf2. Cancer Prev Res (Phila) 2011;4:860-70.
21. Saleem M. Lupeol, a novel anti-inflammatory and anti-cancer dietary triterpene. Cancer Lett 2009;285:109-15.
22. Zhang S, Liu Q, Liu Y, Qiao H, Liu Y. Zerumbone, a Southeast Asian ginger sesquiterpene, induced apoptosis of pancreatic carcinoma cells through p53 signaling pathway. Evid Based Complement Alternat Med 2012;2012:936030.
23. Daisy P, Eliza J, Ignacimuthu S. Influence of C. speciosus (Koen.) Sm. Rhizome extracts on biochemical parameters in streptozotocin-induced diabetic rats. Health Sci 2008;54:675-81.http://www.joi.jlc.jst.go.jp/JST.JSTAGE/jhs/54.675?from=CrossRef. [Last accessed on 2016 Nov 24].
24. Navrot N, Rouhier N, Gelhaye E, Jacquot JP. Reactive oxygen species generation and antioxidant systems in plant mitochondria. Physiol Plant 2007;129:185-95. Available from: http://www.doi.wiley.com/10.1111/j. 1399-3054.2006.00777.x [Last accessed on 2016 Nov 24].
25. Halliwell B. Antioxidants and human disease: A general introduction. Nutr Rev 1997;55:S44-9.
26. Nehete J, Bhatia M, Narkhede M. In vitro evaluation of antioxidant activity and phenolic content of C speciosus (Koen) J.E. Sm. Iran J Pharm Res 2010;9:271-7.
27. Gottfredsen RH, Larsen UG, Enghild JJ, Petersen SV. Hydrogen peroxide induce modifications of human extracellular superoxide dismutase that results in enzyme inhibition. Redox Biol 2013;1:24-31.

28. Kharrazi H, Vaisi-Raygani A, Rahimi Z, Tavilani H, Aminian M, Pourmotabbed T, et al. Association between enzymatic and non-enzymatic antioxidant defense mechanism with apolipoprotein E genotypes in Alzheimer disease. Clin Biochem 2008;41:932-6.
29. Govindarajan R, Vijayakumar M, Pushpangadan P. Antioxidant approach to disease management and the role of 'rasayana' herbs of ayurveda. J Ethnopharmacol 2005;99:165-78.
30. Vijayalakshmi MA, Sarada NC. Screening of C. speciosus extracts for antioxidant activity. Fitoterapia 2008;79:197-8.
31. Jha MK, Alam MB, Hossain MS, Islam A. In vitro antioxidant and cytotoxic potential of C. speciosus (Koen.) Smith rhizome. Int J Pharm Sci Res 2010;1:138-44.
32. Devi DV, Urooj A. Nutritive profile and antioxidant componants of C. speciosus (Koen.) Sm. and Costus igneus Nak. Indian J Natl Prod Resour 2010;1:116-8.
33. Eliza J, Daisy P, Ignacimuthu S. Antioxidant activity of costunolide and eremanthin isolated from C. speciosus (Koen ex. Retz) sm. Chem Biol Interact 2010;188:467-72.
34. El-Far AH, Abou-Ghanema II. Biochemical and hematological evaluation of C. speciosus as a dietary supplement to Egyptian buffaloes. Afr J Pharm Pharmacol 2013;7:2774-9.
35. Roy A, Manikkam R. Cytotoxic impact of costunolide isolated from C. speciosus on breast cancer via differential regulation of cell cycle-an in vitro and in silico approach. Phytother Res 2015;29:1532-9.
36. Baskar AA, Al Numair KS, Alsaif MA, Ignacimuthu S. In vitro antioxidant and antiproliferative potential of medicinal plants used in traditional Indian medicine to treat cancer. Redox Rep 2012;17:145-56.
37. Nair SV, Hettihewa M, Rupasinghe HP. Apoptotic and inhibitory effects on cell proliferation of hepatocellular carcinoma HepG2 cells by methanol leaf extract of C. speciosus. Biomed Res Int 2014;2014:637098.
38. Pitchai D, Roy A, Banu S. In vitro and in silico evaluation of NF-κB targeted costunolide action on estrogen receptor-negative breast cancer cells – A comparison with normal breast cells. Phytother Res 2014;28:1499-505.
39. Selim S, Al Jaouni S. Anticancer and apoptotic effects on cell proliferation of diosgenin isolated from C. speciosus (Koen.) sm. BMC Complement Altern Med 2015;15:301.
40. El-Far AH, Badria FA, Shaheen HM. Possible anticancer mechanisms of some C. speciosus active ingredients concerning drug discovery. Curr Drug Discov Technol 2016;13:123-43
41. Vazquez A, Sanchez C, Delgado N, Alfonso A, Ortega Y, Sanchez H. Antiinflammatory and analgesic activities of red seaweed Dichotomaria obtusata. Braz J Pharm Sci 2011;47:111-8.
42. Gomase PV, Shire PS, Nazim S, Choudhari AB. Development and evaluation of polyherbal formulation for antiinflammatory activity. J Natl Prod Plant Resour 2011;1:85-90.
43. Srivastava S, Singh P, Jha KK, Mishra G, Srivastava S, Khosa RL, et al. Antiinflammatory, analgesic and antipyretic activities of aerial parts of C. speciosus Koen. Indian J Pharm Sci 2013;75:83-8.
44. Rayan NA, Baby N, Pitchai D, Indraswari F, Ling EA, Lu J, et al. Costunolide inhibits proinflammatory cytokines and iNOS in activated murine BV2 microglia. Front Biosci (Elite Ed) 2011;3:1079-91.
45. Al-Attas AA, El-Shaer NS, Mohamed GA, Ibrahim SR, Esmat A. Anti-inflammatory sesquiterpenes from C. speciosus Rhizomes. J Ethnopharmacol 2015;176:365-74.
46. Selim S, Al Jaouni S. Anti-inflammatory, antioxidant and antiangiogenic activities of diosgenin isolated from traditional medicinal plant, C. speciosus (Koen ex.Retz.) sm. Nat Prod Res 2016;30:1830-3.
47. Bakhsh ZA, Al-Khatib TA, Al-Muhayawi SM, ElAssouli SM, Elfiky IA, Mourad SA, et al. Evaluating the therapeutic efficacy, tolerability, and safety of an aqueous extract of C. speciosus Rhizome in acute pharyngitis and acute tonsillitis. A pilot study. Saudi Med J 2015;36:997-1000.
48. Koyuturk M, Ozsoy-Sacan O, Bolkent S, Yanardag R. Effect of glurenorm on immunohistochemical changes in pancreatic beta cells of rats in experimental diabetes. Indian J Exp Biol 2005;43:268-71.
49. Colca JR. Insulin sensitizers may prevent metabolic inflammation. Biochem Pharmacol 2006;72:125-31.
50. Medagama AB, Bandara R. The use of complementary and alternative medicines (CAMs) in the treatment of diabetes mellitus: Is continued use safe and effective? Nutr J 2014;13:102.
51. Medagama AB, Bandara R, Abeysekera RA, Imbulpitiya B, Pushpakumari T. Use of complementary and alternative medicines (CAMs) among type 2 diabetes patients in Sri Lanka: A cross sectional survey. BMC Complement Altern Med 2014;14:374.
52. Mosihuzzaman M, Nahar N, Ali L, Rokeya B, Khan AK, Nur-E-Alam M, et al. Hypoglycemic effects of three plants from Eastern Himalayan belt. Diabetes Res 1994;26:127-38.
53. Bavarva JH, Narasimhacharya AV. Antihyperglycemic and hypolipidemic effects of costus speciosus in alloxan induced diabetic rats. Phytother Res 2008;22:620-6.

54. Eliza J, Daisy P, Ignacimuthu S, Duraipandiyan V. Normo-glycemic and hypolipidemic effect of costunolide isolated from C. speciosus (Koen ex. Retz.) Sm. in streptozotocin-induced diabetic rats. Chem Biol Interact 2009;179:329-34.
55. Eliza J, Rajalakshmi M, Ignacimuthu SJ, Daisy P. Normalizing effects of C. speciosus rhizome crude extracts and its fractions on diabetic complications in STZ-induced diabetic rats. Med Chem Res 2011;20:1111-8. Available from: http://www.link.springer.com/10.1007/ s00044-010-9448-5. [Last accessed on 2016 Nov 26].
56. Ali HA, Almaghrabi OA, Afifi ME. Molecular mechanisms of anti-hyperglycemic effects of C. speciosus extract in streptozotocin-induced diabetic rats. Saudi Med J 2014;35:1501-6.
57. Perera HK, Premadasa WK, Poongunran J. A-glucosidase and glycation inhibitory effects of C. speciosus leaves. BMC Complement Altern Med 2016;16:2.
58. Kraemer FB, Shen WJ. Hormone-sensitive lipase: Control of intracellular tri-(di-) acylglycerol and cholesteryl ester hydrolysis. J Lipid Res 2002;43:1585-94.
59. Chogtu B, Magazine R, Bairy KL. Statin use and risk of diabetes mellitus. World J Diabetes 2015;6:352-7.
60. Eliza J, Daisy P, Ignacimuthu S, Duraipandiyan V. Antidiabetic and antilipidemic effect of eremanthin from C. speciosus (Koen.) Sm. in STZ-induced diabetic rats. Chem Biol Interact 2009;182:67-72.
61. Contreras-Zentella ML, Hernández-Muñoz R. Is liver enzyme release really associated with cell necrosis induced by oxidant stress? Oxid Med Cell Longev 2016;2016:3529149.
62. Biman B, Kamaruz Z. Evaluation of hepatoprotective activity of rhizomes of C. speciosus (J. Kanji) Smith. Pharmacologyonline 2008;3:119-26.
63. Verma N, Khosa RL. Evaluation of protective effects of ethanolic extract of C. speciosus (Koenig) Sm. Rhizomes on carbon tetrachloride induced hepatotoxicity in rats. Natl Prod Radiance 2009;8:123-6.
64. Padma P, Chansauria JP, Khosa RL, Ray AK. Effect of Annooa muricata and Polyalthia cerasoides on brain neurotransimitters and enzyme monoamine oxidase following cold immobilization stress. J Natl Remedies 2001;1:144-6.
65. Verma N, Khosa RL. Effect of C. speciosus and Wedelia chinensis on brain neurotransmitters and enzyme monoamine oxidase following cold immobilization stress. Pharm Sci Res 2009;1:22.
66. Joseph M, Kenneth GA. Stress-induced release of 5HT in the hippocampus and its dependence on increased tryptophan availability: An in vivo electrochemical study. Brain Res 1983;270:251-7.