



Costus speciosus (Ketaki) – A herb with numerous medicinal properties

¹Tina W. Pandel*, ²Shailju G. Gurunani, ³Aditya R. Kaikade,

¹Research Scholar, Priyadarshini J.L College of Pharmacy,

²Assistant professor, Priyadarshini J.L College of Pharmacy

³Research Scholar, Priyadarshini J.L College of Pharmacy

ABSTRACT:

The *Costus speciosus*, often known as ketaki, is an important Ayurvedic and medicinal plant used to cure a number of diseases. *Costus speciosus* (koenex, retz.), an Indian Ayurvedic herb, has a long history of therapeutic use in Western medicine. It is being studied for its antioxidant, anticholinesterase, larvicidal, antihyperglycemic, antifungal, antibacterial, anti-inflammatory, analgesic, antipyretic, antidiuretic, estrogenic, and antistress effects, among other pharmacological traits. The rhizomes of these plants are often used to treat diabetes and are a replacement source of diosgenin. Along with examining the pharmacological and phytochemical properties of *Costus speciosus*. This study proposed that plants' medicinal and therapeutic effects should be studied, as well as their ornamental and herbal properties. As a result, the current study offers a thorough examination of the morphology, phytochemistry, and pharmacological characteristics of *Costus speciosus* in an attempt to offer guidance for future research.

Keywords: *Costus speciosus*, Ketaki, Pharmacological activities, Medicinal value of *Costus speciosus*

INTRODUCTION:

Higher plants are a key source of medicinal substances, and both traditional and modern medical systems use them. Currently, a single medicine is made from more than 2,000 species [1]. *C. speciosus*, the most well-known species in the genus, has become a significant therapeutic herb and antidiabetic decorative plant [2]. The main source of diosgenin, which has antidiabetic properties and is used to treat Diabetes mellitus, is the rhizome [3,4]. There are almost 20,000 plant species in India, of which roughly 2,500 have medical potential. India is also abundant in native herbal remedies [2]. Because *Aspergillus* sp. has anti-diabetic properties and

is used to treat diabetes mellitus, it might infect the lungs. The use of plants for medicine dates back to the ancient era. The majority of plant materials used to make herbal remedies include leaves, roots, bark, seeds, and flowers. The most well-known members of the genus *C. speciosus* are now recognised as significant antidiabetic herbs. The rhizome of *Costus speciosus* has been discovered to contain the steroidal saponin diosgenin [2]. The rhizome has been utilised in Ayurveda to cure intestinal heat, bronchitis, asthma, fever, and purgative in addition to treating smallpox. Costly plants are therefore significant in terms of tradition, medicine, and pharmacology. An essential Ayurvedic and therapeutic plant is *costus speciosus* [5,6]. Zingiberaceae is a family of about 1,300 species found in tropical Africa, Asia, and the Americas. It has fifty-two species [7]. It is popularly known as kemuka, Kushta, Kashmira, Shura, Katar in Sanskrit, pushpamoola in Kannada, kashmeeramu in Telugu, keukand, Keu in Hindi and Bengali, ChengalvaKoshta' in Telegu and Kannada, 'Kottam' or 'Koshtam' in Tamil and 'Penava' or 'Pushkarmula' in Marathi, Jomlakhuti in Assamese, Crepe ginger in English [8,9,10,11].



Fig.1: Leaves of *Costus speciosus*



Fig.2: Bulbs of *Costus speciosus*



Fig.3: Flowering plant of *Costus speciosus*



Fig.4: Rhizome of *Costus speciosus*

Classification:**Table 1: Taxonomic Classification [12]**

Kingdom	Plantae
Subkingdom	Tracheobinota
Superdivision	Supermatophyta
Division	Mangoliophyta
Class	Liliopsida
Sub class	Zingiberidae
Order	Zingiberales
Family	Coastaceae
Genus	Costus
Species	Speciosus

Table 2: Scientific Classification [12]

Kingdom	Plantae
clade	Tracheophytes
clade	Angiosperms
clade	Monocots
clade	Commelinids

Geography:

Costus speciosus may be found in the damp and wet evergreen regions of the Indo-Malayan region, as well as in Sri Lanka [13]. *Costus speciosus*, which has been utilised for medicinal purposes, is also found in Ahmednagar's Kalsubai Harishchandragad wildlife reserve [14]. *C. speciosus* is found in the Himalayan foothills from Himachal Pradesh to Assam, the Vindhya Satpura hills in Central India, the Eastern Ghats of Andhra Pradesh, and the Western Ghats of Maharashtra, Karnataka, Tamil Nadu, and Kerala [15].

Morphology:

Plant, tuberous stem rootstock, sub-wood at base, thick creep in rhizomes (120-300 cm height) [16]. It grows up to 2-2.7m tall, with long lanceolate leaves and terminal clusters of white fragrant flowers [17]. It is a striking landscape plant with huge dark green, subsessile, elliptic, or obovate leaves grouped in a spiral on the stem. It may reach a height of 3.1 m in frost-free places but often grows to around 1.8 m in colder locations where its roots harden then die back in winter [18]. The plant blooms in July and August, then the aerial portions wither away in the winter [19]. Because the blossoms of the *Costus speciosus* plant resemble crepe paper, the common name "Crepe ginger" was coined. The blooms are 5-6 cm long, with a cup-shaped labellum and golden stamens on the crest. The fruit is crimson, and the seeds are black, five in number, with a white fleshy aril [20].

Cultivation:

It is mostly grown during the wet season. It thrives in shaded areas of South India's mixed deciduous woods on rich moist soil or clayey loam soil. It thrives in shaded areas of South India's mixed deciduous woods on rich moist soil or clayey loam soil. It thrives in environments with high humidity and low temperatures. *Costus speciosus* is propagated by a variety of techniques, including vegetative methods employing rhizome species, culm division, stem cuttings, and seed dispersal by birds [21,22,23,24].

Cultivation techniques:

- A. Land preparation:** - The field is ploughed twice. The soil is fine-tilled FYM @15/hairs applied and mixed well with the soil, and furrows are created 50cm apart.
Propagation: - Although the plant may be grown from seeds, stem cuttings, and rhizomes, it is only economically propagated by rhizome cuttings. However, the selection of rhizomes for planting is critical. The rhizomes feature many buds, the majority of which are located near the stem scars and tips. During April, the rhizome's bud production is low. Rhizome cuttings for propagation should have at least two viable buds. Rhizome pieces weighing around 40 g should be chosen. One hectare of land requires around 2000-2400 kg of fresh rhizomes.
- B. Planting:** - The rhizome pieces are planted at a depth of 8-10 cm, with the eye buds pointing upwards, in rows 50 cm apart, and covered with soil. Irrigation begins shortly after planting. The thick-sized portions develop slowly, taking 40 to 45 days to sprout. This is owing to the latent eye buds on these rhizome pieces, which take longer to grow, particularly in the case of the crop seeded in April. Approximately 90-95% sprouting is attained after 70-75 days.

C. Manure and Fertilizer: - Trials indicate that the best dosage for maximising Diosgenin production is 45 kg N, 30 kg P₂O₅, and 30 kg K₂O, combined with 15 t/ha FYM. The FYM and a half dosage of P and K are administered in two split doses at 20 and 60 days after planting, with the remaining half dose of P and K given together with the second dose of N after the 60th day.

D. Weeding and Interculture: - One weeding during the crop's sprouting stage, followed by two more, keeps the crop weed-free. Most weeds are repressed during the active vegetative growth season (July to September). If the monsoon is unpredictable, at least one additional weeding will be necessary. Weeding once or twice during the dormant season aids in crop sprouting the following season. The canes cover the inter-row space between the plants in the second year of the crop, requiring just 2-3 weedings before the crop is harvested in August or September [25,26,27,28,29,30,31].

Conservation:

Plant propagation is required due to a low multiplication rate, poor seed viability, a low percentage of seed germination, and a scarcity of delayed Antibacterial roots of vegetative cuttings. Different plant biotechnological technologies like as micropropagation, germplasm preservation, and other tissue culture techniques that result in large scale production of consistent planting material can be employed for commercial multiplication and preservation of the *Costus speciosus* plant [32].

Medicinal Uses:

- a. Leaves:** - Leaves are also crushed and put to the head as a poultice. In Malaysia, the plant is cooked in water to make a decoction that is used to wash a feverish patient. A decoction of the plant is used as a smallpox lotion. Stem. The stem scrapings are administered on leprous skin.
- b. Shoot:** - For ocular Rhizome diseases, the juice of tender shoots or pith is pushed into the eye. The fresh rhizome juice is used as a purgative. The rhizome is used to treat colds, rheumatism, and pneumonia in India. It is also said to be a tonic, aphrodisiac, and a depurative. In Java, the rhizome is used to cure syphilis after confinement.
- c. Diosgenin:** - These plants are commonly employed as raw materials in the commercial manufacture of steroidal hormones. It is mostly derived from Dioscorea species, the major Indian source material being dioscoreadeltoidea. However, because to its limited distribution in a few areas in the North-West Himalaya and poor response to domestication, this source has limits in providing significant supply on an ongoing basis. It became vital to look for a different plant supply that could be easily grown under a Uses, Sanskrit poetry.

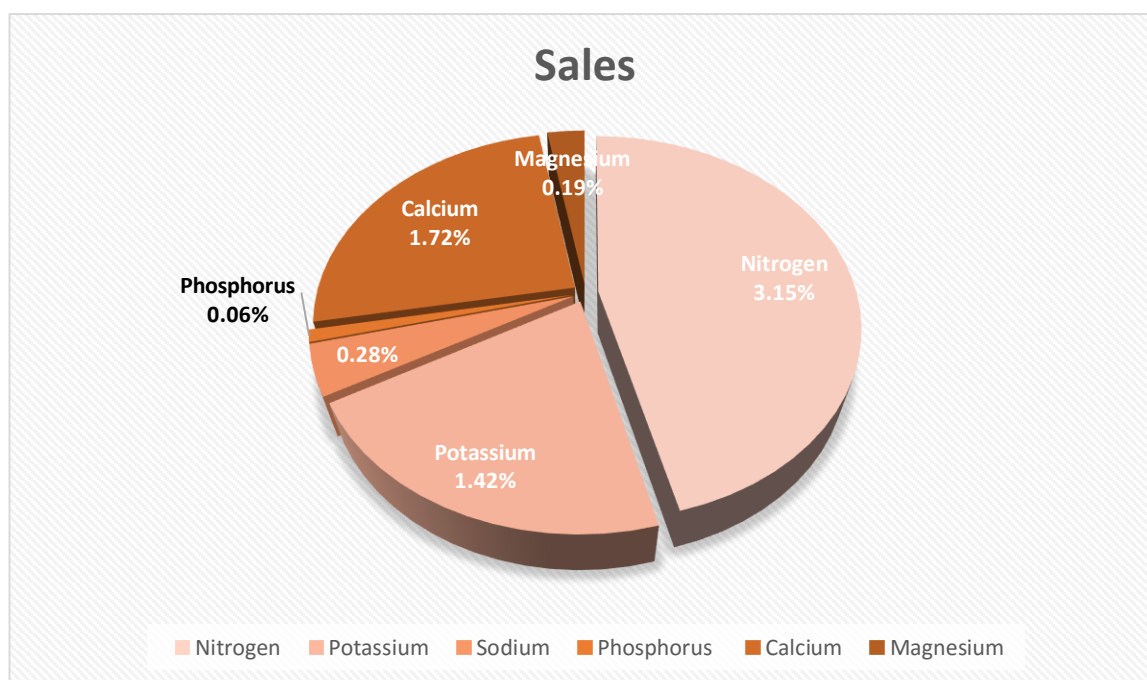
d. **Rhizomes:** - To cure cough and asthma, 3-5 g of powdered *Costus speciosus* rhizome is taken with honey. To cure dyspepsia and anorexia, a dosage of 3- 5 g of the rhizome powder is taken with hot water. The fresh juice of the rhizome of *costus speciosus* is provided to cure labour difficulties and discomfort. The paste of the leaves and rhizome is applied topically over the skin afflicted by discolouration, black patches, and itching caused by ringworm infection. at the treatment of elephantiasis, fever, and intestinal worms, a decoction of the rhizome of *Costus speciosus* is administered at a dosage of 20-25 ml. The cold-infusion of the rhizome of *Costus speciosus* functions as a blood cleanser, which is effective in patients with recurrent skin problems [33].

Ethnomedicinal Uses:

Therapeutic plants have played an important role as an alternative and supplemental therapeutic source for the majority of synthetic medications in use today. As a result, numerous nations, including India, Sri Lanka, the West Indies, China, the United States, and Africa, have recognised *C. speciosus* for its ethnomedico-botanical benefits (Maji et al. 2020) [34]. This plant has been used as a traditional medicine in India, and its therapeutic properties have been outlined in Ayurveda as well [35]. The tribal tribes of the hills of southern India have utilised this plant as both food and medicine [36]. Except for the north-eastern and southern sections of India, *C. speciosus* is still considered an unexplored species.

According to research, the leaves, stem, and, most significantly, the rhizome of *C. speciosus* have therapeutic potential. For example, the plant's roots and rhizomes have been used to treat rheumatism, anaemia, bronchitis, skin diseases, constipation, jaundice, flatulence, asthma, helminthiasis, leprosy, pneumonia, dropsy, inflammation, hiccough, fever, and some urinary diseases characterised by burning urination [37,34]. Other qualities of the rhizomes include being extremely laxative (purgative), astringent, depurative, anthelmintic, tonic, acrid, febrifuge, expectorant, and improving digestion [38,39]. *C. speciosus* rhizome juice is used to treat leprosy and also for abortion [40], and it is known to produce a cooling effect and is thus utilised in headaches [39]. Furthermore, the rhizomes, leaves, and stem have been used traditionally for their medicinal properties; for example, the infusion of leaves and stem decoction has a sudorific effect and is thus used to treat high fever patients; sometimes, they are used in bruised form and applied to the affected person suffering from fever [40,41]. Furthermore, the sap of young leaves and stems is used to treat eye and ear infections [42], catarrhal fever, colds and coughs, and snake bites [40,38]. Despite its long history as an ethnomedicinal drug and the presence of a wide range of pharmacologically active phytochemical constituents, there is very little authentic and verified information on marketed formulations and a patent on *C. speciosus* due to a lack of adequate human trials. Certain Indian ayurvedic and natural health-product companies, however, are now coming forward in this regard; for example, Dabur India Limited, one of the leading ayurvedic companies, has developed an ayurvedic formulation based on *Costus speciosus*, which is traded as Ketaki (crepe ginger/kemuka) powder and is used for the

treatment of hyperlipidemia, obesity, diabetes management, and menstrual irregularities. Furthermore, *C. speciosus* extract, together with other herbs, was employed in Khamar's (2002) patented procedure for anti-inflammatory and analgesic preparation, with patent number WO-02/085394 granted by the World Intellectual Property Organisation under the Patent Cooperation Treaty. However, additional similar formulations and advancements should be promoted for the sake of public health and the promotion of natural and safer therapies for diseases. (Fig.5).



BIOLOGICAL ACTIVITY OF *COSTUS SPECIOSUS*:

Fig. 5: *Costus speciosus* trace elements (Singh 2011) [43]

1] Anti- Cancer activity: Many modern chemotherapeutic drugs with lethal activity in vitro or in vivo block specific molecular targets required for tumour development [44]. *C. speciosus* rhizome anticancer potentials were investigated against human colon adenocarcinoma cell lines (COLO 320 DM) extracted with hexane, ethyl acetate, and methanol. According to the scientists, all studied extracts of *C. speciosus* rhizome showed significant antioxidant and antiproliferative properties in a dosage- and time-dependent manner [45]. This study demonstrated a link between *C. speciosus*' antioxidant content and its anticancer effect. Research was conducted on the *C. speciosus* leaf methanolic extract at concentrations of 1, 10, 50, 100, and 200 g/ml of Eagle's modified minimum essential medium supplemented with 10% foetal bovine serum and 1% penicillin-streptomycin. Cell viability was significantly reduced in HepG2 cells treated with 100 g/ml for 24 hours [46]. The methanolic extract disrupted cell cycle progression, as measured by increased caspase3 activity in treated cells. An examination of the effect of this extract on cellular antiapoptotic and proapoptotic molecules using molecular techniques is still required.

The authors previously studied the cytotoxicity of *C. speciosus* extracts independently of the mechanism of anticancer activity. Costunolide has caused cancer cell cycle arrest at the G2/M phase as cytometry was used to assess the phase of human breast adenocarcinoma (MDAMB231) and induced cell viability suppression with (3[4, 5dimethylthiazol2yl]2, 5diphenyltetrazolium bromide). Furthermore, costunolide inhibited the overexpression of NF- κ B subunits p65, p52, and p100 in MDAMB231 dosages of 20 and 40 μ M costunolide [47]. Furthermore, at a half-maximum inhibitory concentration (IC₅₀) of 40 μ M, costunolide-mediated anticancer effects were linked to the induction of apoptosis in MCF7. In comparison to their expressions in the normal breast cell line (MCF10A), costunolide-treated MCF7 cells displayed upregulation of cyclin D1, D3, CDK4, CDK6, p18 INK4c, p21 CIP1/Waf1, p27 KIP1, caspase3, and caspase9 [44]. Another active ingredient identified in *C. speciosus*, diosgenin, has an apoptotic effect on cancer cell growth. Diosgenin treatment of hepatocellular carcinoma HepG2 cells resulted in a cytotoxic effect with an IC₅₀ value of 32.62 μ g/ml, compared to paclitaxel treatment of HepG2 cells with an IC₅₀ value of 0.48 μ g/ml. The investigation was expanded to evaluate the IC₅₀ value of diosgenin against breast cancer MCF7 cells, and the IC₅₀ value was found to be 11.03 μ g/ml. Diosgenin enhanced the levels of death receptor 4 and caspase 3, both of which cause apoptosis in MCF7 cells [48].

The anticancer potentials of *C. speciosus*' active ingredients may be mediated through overexpression of proapoptotic and downregulation of antiapoptotic molecules, both of which reduce cancer cell proliferation and progression [49].

2] Anti- Oxidant activity: Antioxidants are a class of chemicals that inhibit oxidation by scavenging free radicals and activating cellular antioxidant enzymes [50]. Oxygen likes to take electrons one at a time, which results in the formation of reactive oxygen species (ROS) [51]. ROS molecules are critical to the oxidative stress that causes atherosclerosis, cancer, cirrhosis, and diabetes [52,53]. Oxidative stress is counteracted by enzymatic antioxidant systems that include a variety of enzymatic scavengers, such as superoxide dismutase (SOD, EC 1.15.1.1), glutathione peroxidase (GPx, EC 1.11.1.9), catalase (CAT, EC 1.11.1.6), and glutathione S-transferases (EC 2.5.1.18), in addition to the nonenzymatic molecules that include ascorbic acid (Vitamin C), tocopherol (Vitamin E), glutathione (GSH), and carotene [54,55]. Because of their redox capabilities, including free radical scavenging and strong metal ion chelation, phenols and flavonoids found in medicinal plants may protect live organisms against ROS dangers [56]. *C. speciosus* methanolic, ethanolic, and chloroform extracts of leaves, stem peel, peeled stem, and roots have been shown to have antioxidant activity in vitro. The antioxidant activity was determined using 1,1-diphenyl-2-picrylhydrazyl (DPPH), 2,2-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid, and thiobarbituric acid (TBA). The hydroxyl radical scavenging activity and free radical quenching capacity of methanolic extracts were higher [57]. This investigation confirmed the traditional applications of *C. speciosus* root and peel for various ailments and complaints. Additional research employing different solvents such as n-hexane, petroleum ether, and water should be considered. Another in vitro investigation discovered that *C. speciosus* rhizome methanolic extract showed strong free radical and nitric oxide (NO) scavenging properties when compared to ascorbic acid and quercetin standards tested using DPPH and NO scavenging techniques [58]. The inclusion of glycosides,

avonoids, triterpenoids, tannins, and steroids, according to the scientists, might explain the antioxidant effect of the methanolic extract. In the same context, the antioxidant capacity of *C. speciosus* rhizomes was evaluated in vitro using various extracts of petroleum ether, cyclohexane, benzene, ethyl acetate, chloroform, acetone, methanol, and water. Some extracts demonstrated significant DPPH radical scavenging, total antioxidant capacity (TAC), NO scavenging, ion chelation, and hydroxyl radical scavenging activities, which were attributed to *C. speciosus*'s phenolic content. Benzene extract had the highest phenolic content and antioxidant activity of all extracts, with a maximum phenolic concentration of 4.38% [20]. Furthermore, the antioxidant effect of *C. speciosus* is attributable to antioxidant compounds found in it, such as ascorbic acid, carotene, tocopherol, glutathione, phenolics, and avonoids [59].

An in vivo rat experiment was performed in which either costunolide (20 mg/kg/day) or eremanthin (20 mg/kg/day), two components of *C. speciosus*, were administered orally via an intragastric tube for two months. The findings demonstrated a significant reduction in increased TBA reactive compounds in streptozotocin (STZ) diabetic rats, as well as an increase in GSH content and SOD, CAT, and GPx activities in the brain, liver, heart, kidney, and pancreas [60]. What has to be determined is the impact of *C. speciosus* and its active components on cellular antioxidant enzymes, genes, and protein expression. *C. speciosus* ground rhizomes antioxidant capacity was investigated in 2013 by supplementing the diet of Egyptian bualo heifers with doses of 2.5 and 5 kg/tonne for one month. In comparison to the control group, which received the basic food with no treatments, *C. speciosus*-supplemented animals had better erythrocyte antioxidant capability, as evidenced by a significant decrease in MDA and an increase in TAC [61].

3] Anti- Inflammatory activity: Inflammation is a pathophysiological reaction to tissue injury that is closely linked to the aetiology of several inflammatory disorders [62]. In order to avoid the negative side effects of synthetic and chemical medications, numerous medicinal plants were employed as a substitute with minimal side effects. Anti-inflammatory properties of *Z. ocinale*, *C. longa*, and *C. speciosus* have been demonstrated [63,64]. Numerous studies have been conducted to study *C. speciosus*'s traditional usage for the treatment of inflammation, rheumatism, bronchitis, fever, and headache. In vitro research looked at the influence of costunolide on the generation of proinflammatory mediators and pathways in a murine BV2 cell culture activated with lipopolysaccharides (LPS). Through suppression of the NFB and mitogen-activated protein kinase pathways, costunolide reduced the production of tumour necrosis factor alpha (TNF), interleukin (IL), IL6, inducible NO synthase (NOS), and cyclooxygenase (COX2) in activated microglia [65]. In the same manner, the nhexanechloroform soluble fraction of methanolic *C. speciosus* rhizomes extract contained 22, 23dihydrospinaesterone, dehydrodihydrocostus lactone, dehydrocostus lactone, stigmasterol, arbusculin A, santamarine, and reynosin, which induced a prominent decrease in the levels of IL1, IL6, TNF, prostaglandin E2, lipoxgenase5, and COX2 in isolated peripheral blood mononuclear cells [66]. The anti-inflammatory properties demonstrated by *C. speciosus* above demonstrate the utility of *C. speciosus*'s use against inflammatory illnesses. Similarly, diosgenin isolated from *C. speciosus* using high-performance thin-layer chromatography had a highly significant inhibitory effect on LPS-stimulated TNF in macrophage (RAW 264.7) culture supernatant at a dose of 50 g/ml of medium, similar to methotrexate's inhibitory effect on

RAW 264.7 cells [67]. An in vivo investigation of methanolic extracts of *C. speciosus* aerial parts (400 and 800 mg/kg, orally) was conducted in 2013. The extract's anti-inflammatory effect was evaluated using a carrageenan-induced paw edoema test, which involved injecting 0.1 ml of 1% carrageenan in 0.9% saline into the subplantar area of the left hind paw. Furthermore, the analgesic impact was determined using the acetic acid-induced writhing and Eddy's hot plate models. Brewer's yeast-induced pyrexia in rats was also used to assess antipyretic efficacy. At 5 hours post medication, methanol extract dosages of 400 and 800 mg/kg demonstrated significant anti-inflammatory efficacy, with inhibition percentages of 19.36 and 40.05%, respectively. Furthermore, acetic acid reduced writhings by 14.24 and 31.90%, respectively, and extended latency duration at both high and low dosages, with the mean reaction time at 16.600.355 s and 14.120.355 s, respectively, when compared to the control in the hotplate test. In the case of Brewer's yeast-induced pyrexia, 400 and 800 mg/kg dosages significantly lowered the animals' rectal temperatures (37.03°C 0.108°C and 36.63°C 0.098°C , respectively) [64]. This conclusion was consistent with *C. speciosus*'s historic usage in fever management. As a result, the anti-inflammatory effects of *C. speciosus* isolated substances provide a promising and increasing technique for the treatment of numerous inflammatory illnesses and their accompanying symptoms. Furthermore, we urge that *C. speciosus* be studied in relation to additional inflammatory pathways such as the tolllike receptor, B-cell receptor, T-cell receptor, and receptor for advanced glycation end products (RAGE) signalling.

Between May and December 2014, 15 patients with acute pharyngitis and tonsillitis were included in a pilot cohort study at King Abdulaziz University in Saudi Arabia. *C. speciosus* aqueous solution was supplied as nasal drops at a dosage of 0.75 ml (15 drops containing 210 mg of extract) for kids aged 2–6 years and 1.5 ml (30 drops containing 420mg of extract) for individuals older than 6 years, every 8 hours for 3 days. Treatment with *C. speciosus* resulted in an improvement in acute symptoms in 60% of patients treated during the first 24 hours and a remission rate of 93% by day 5 [68].

4] Anti-Diabetic activity: Diabetes mellitus is a metabolic disorder that affects around 4% of the world's population [69]. Aside from medications typically used to treat diabetes, such as insulin, sulfonylureas, biguanides, or thiazolidinediones, various species of medicinal plants have been characterised as normoglycemic treatments with greater efficacy, fewer side effects, and lower prices [70,71].

Mosihuzzaman et al. [72] investigated the impact of *C. speciosus* rhizome juice on blood glucose levels in a noninsulindependent diabetic rat model. When given alongside glucose, *C. speciosus* exhibited no significant influence on fasting or postprandial conditions in nondiabetic rats. *C. speciosus*, on the other hand, had a hypoglycemic impact when eaten 30 minutes before the glucose injection. To fully comprehend this discovery, we must explore the influence of *C. speciosus* on intestinal glucose absorption by measuring the expression of the glucose transporter gene. Furthermore, understanding the effect of *C. speciosus* on glucose levels in fasting and feeding stages requires information on serum insulin and glucagon levels.

Another study looked at the effects of *C. speciosus* rhizome extracts on hyperglycemia in STZ-induced male diabetic Wistar rats (50 mg/kg, intraperitoneal [i.p.]), with glibenclamide (0.6 mg/kg BW, orally) serving as a control. Hexane, ethyl acetate, and methanol crude extracts were given orally to diabetic and nondiabetic rats at dosages of 250, 400, and 400 mg/kg for 60 days. Compared to the control, all three extracts significantly reduced plasma glucose levels. Hexane extract also significantly reduced glycosylated haemoglobin, total cholesterol, and triacylglycerol (TAG) [73].

This impact was attributed by the authors to the increased blood insulin levels associated with *C. speciosus* therapy. In 2008, researchers investigated the antihyperglycemic, antihyperlipidemic, and antioxidant potentials of an ethanol extract of *C. speciosus* root on alloxan-induced diabetes in male rats using a single i.p. injection of alloxan monohydrate (120 mg/kg BW) dissolved in normal saline. For four weeks, four groups of six alloxandiabetic rats were given *C. speciosus* ethanolic extract at dosages of 150, 300, and 450 mg/kg BW and a standard medication, glibenclamide (0.6 mg/kg BW) orally. The administration of 300 and 450 mg/kg dosages of *C. speciosus* ethanolic extract resulted in significantly reduced blood glucose concentrations (26.76% and 34.68%, respectively), enhanced glycogenesis, and decreased gluconeogenesis, restoring glucose levels to normal. Furthermore, these dosages considerably lowered total plasma lipids (12.87% and 178.24%, respectively), cholesterol (21.92% and 30.77%, respectively), and TAG (25.32% and 33.99%, respectively), and enhanced the activities of liver antioxidant enzymes [74]. The antidiabetic effects of *C. speciosus* may be attributed to its presence of costunolide, which stimulates cell secretion of insulin by inhibiting NOS expression and leading to cell regeneration [75]. The same authors produced hexane, ethyl acetate, methanol, and aqueous crude extracts of *C. speciosus* and administered them individually to STZ-induced diabetic rats for two months at dosages of 250, 400, 400, and 600 mg/kg BW, respectively. They discovered a significant reduction in high plasma glucose levels in diabetic rats treated with those extracts as compared to controls. Furthermore, hexane crude extract repaired the altered tissue proteins and pancreatic DNA while also restoring plasma insulin and Cpeptide levels [76]. Furthermore, when oral administration of 400 and 600 mg *C. speciosus*/kg BW to STZ-diabetic rats for 4 weeks was compared to the glibenclamide-treated group, the expression levels of insulin, insulin receptor A, glucokinase (GK), pyruvate kinase (PK), succinate dehydrogenase (SDH), and glucose transporting protein were elevated [77]. *C. speciosus* enhanced blood insulin levels as well as hepatic GK (EC 2.7.1.2), aldolase (EC 4.1.2.13), PK (EC 2.7.1.40), SDH (EC 1.3.5.1), and glycogen synthase (EC 2.4.1.11) activities.

Another recent study looked into how diabetic patients may be protected from glycation problems. Methanolic extracts of *C. speciosus* leaves from Moratuwa, Sri Lanka, were tested for their inhibitory action on porcine pancreatic amylase and glucosidase prepared from *Saccharomyces cerevisiae*. The authors confirmed the in vitro inhibitory impact of *C. speciosus* extract on the activities of amylase (EC 3.2.1.1) and glucosidase (EC 3.2.1.20). Amylase and glucosidase inhibition delayed carbohydrate digestion and lowered glucose absorption, minimising postprandial blood glucose increases and decreasing glycation plasma proteins [78]. Further research into the effect of *C. speciosus* and its active components on the expression of

intestinal monosaccharide transporter genes, gluconeogenic enzymes, and their capacity to regenerate cells is required to complete our understanding of *C. speciosus*'s normoglycemic effect.

5] Hypolipidemic Activity: Diabetes patients have excessively high blood lipid content because insulin inhibits hormone-sensitive lipase (EC 3.1.1.79). As a result of insulin deficiency, fatty acids are freed from adipose tissue, resulting in hyperlipidemia [79]. In addition, insulin inhibits 3-hydroxymethylglutaryl coenzyme A reductase (EC 1.1.1.88), a major rate-limiting enzyme in the metabolism of cholesterol-rich low-density lipoprotein (LDL) particles. This increases the synthesis of cholesterol-rich LDL particles [80]. Costunolide's potential normoglycemic and hypolipidemic effects in STZ-diabetic male Wistar rats were studied after oral administration of dosages of 5, 10, and 20 mg of costunolide/kg BW for 30 days. It was discovered that taking 20 mg of costunolide/kg BW significantly reduced total serum cholesterol, TAG, and LDL cholesterol. Simultaneously, plasma insulin, glycogen (liver and muscles), and high-density lipoprotein (HDL) cholesterol levels increased dramatically. The authors hypothesized that costunolide would enhance cell secretion of insulin by decreasing NOS expression [60]. Similarly, for 60 days, eremanthin at the same dosages was tested for its hypolipidemic impact in STZ-diabetic rats. They discovered that an oral dose of 20 mg eremanthin/kg BW significantly reduced total blood cholesterol, TAG, and LDL cholesterol while significantly increasing plasma insulin, tissue glycogen, and HDL cholesterol [73]. We propose that future studies look into the effects of *C. speciosus* on lipid digestion and absorption in terms of gene expression of intestinal fatty acid transporters, as well as the effects of *C. speciosus* on pancreatic lipases and adipose tissue hormone-sensitive lipase.

6] Hepatoprotective activity: Hepatic biomarkers include aspartate aminotransferase (AST, EC 2.6.1.1), alanine aminotransferase (ALT, EC 2.6.1.2), lactate dehydrogenase (LDH, EC 1.1.1.27), alkaline phosphatase (ALP, EC 3.1.3.1), and acid phosphatase (ACP, EC 3.1.3.2). Increased AST, ALT, LDH, ALP, and ACP activity in plasma or serum may be due to leakage from liver cells into the circulation [81]. Carbon tetrachloride (CCl₄) intoxication (at a dose of 0.1 ml/100 g BW, twice a week, i.p.) caused alterations in liver function profiles in Swiss albino mice, which were alleviated by a methanolic extract of *C. speciosus* rhizomes (100 mg/kg body BW for 14 consecutive days) in a hepatotoxicity study. In contrast to silymarin, as a reference hepatoprotective medication, the extract restores blood levels of AST, ALT, ALP, bilirubin, and total protein to normal levels. The same results were obtained after oral administration of *C. speciosus* ethanolic extract at a dosage of 500 mg/kg BW in Wistar albino rats when compared to silymarin, a typical hepatoprotective medication. This section requires further research into *C. speciosus*'s hepatoprotective activity against pharmaceuticals and chemicals that cause liver damage, such as paracetamol, nonsteroidal anti-inflammatory drugs, glucocorticoids, isoniazid, aatoxins, arsenic, vinyl chloride, and others [82].

7] Adaptogenic activity: A number of pressures generate major changes in numerous neurotransmitters in the central nervous system (CNS) and peripheral nervous system, resulting in a decrease in norepinephrine and dopamine levels in the brain [83]. Norepinephrine appears to be used in reaction to stress, resulting in an increase in dopamine concentrations [84]. Monoamine oxidase (MAO, EC 1.4.3.4) is primarily

responsible for maintaining proper levels of biogenic amines in the brain. The executive function of MAO is thought to be to inhibit the release of 5-hydroxytryptamine (5HT) [83]. *C. speciosus* extracts significantly decreased the stress-induced rise in 5HT and 5HIAA levels in brain tissues by suppressing the alarm response, which causes a significant spike in 5HT and 5HIAA levels [85]. The authors tested *C. speciosus* on MAO, although catecholomethyltransferase (EC 2.1.1.6), an enzyme that works with MAO in catecholamine catabolism, should be considered. This study demonstrated the antidepressant effect of *C. speciosus*, which might be employed in a novel medication formulation to treat CNS illnesses. As a future research advice, the impact of *C. speciosus* against a headache requires examination to examine the conventional therapy of *C. speciosus* against a headache.

8] Anti-Microbial activity: Oral administration of antibiotic substances may have undesirable side effects; for example, oral administration of penicillin may cause heartburn, nausea, vomiting, and diarrhoea. As a result, various experiments on herbs and spices as antibiotic alternatives have been done [86]. In comparison to silver sulfadiazine cream, hexane and methanol extracts of *C. speciosus* leaf and rhizomes displayed a lysis zone against *Shigella* spp., *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas* spp., *Bacillus subtilis*, and *Salmonella* spp [87]. The antifungal activity of costunolide was demonstrated by significant minimal inhibitory concentration values of 62.5 g/ml against *Trichophyton mentagrophytes*, 62.0 g/ml against *Trichophyton simii*, 125 g/ml against *Epidermophyton occosum*, 31.25 g/ml against *Trichophyton rubrum*, 125 g/ml against *Curvularia lunata*, and 62.5 g/ml against *T. There is an urgent need to research C. speciosus' antiviral potential, particularly against more prevalent illnesses such as avian influenza, infectious viral hepatitis, and human immunodeficiency viruses.*

9] Anti – cholinesterase activity: According to Bhattacharya et al. (1972, total alkaloids extracted from the rhizome of *Costus speciosus* potentiated the pharmacological activities of acetylcholine both in vitro and in vivo. Anticholinesterase action was demonstrated using frog rectus muscles and dog blood pressure. The plant's anticholinesterase effect may explain why it's used to treat eye problems and as a depurative [88].

10] Anthelmintic activity: Srivastava et al. (2011) assessed and compared the anthelmintic activity of methanolic and aqueous extracts of *Costus speciosus* aerial parts in Indian adult earthworms (*Pheretima posthuma*). When compared to standard medicines, aqueous and methanolic extracts of *C. speciosus* showed outstanding anthelmintic action at all doses. Helminthiasis, or worm infestation, is one of the world's most common and dangerous public health issues. *Costus speciosus* demonstrated high anthelmintic activity in the experimental investigation, making it a promising anthelmintic agent [89].

11] Anti-hyperglycemic activity: Diabetes mellitus is a chronic condition characterised by elevated blood glucose levels due to circulating insulin insufficiency. Diabetes mellitus is a chronic metabolic illness that affects people all over the world. Hyperglycemia is the primary cause of problems such as coronary artery disease, cerebrovascular illness, renal failure, blindness, limb amputation, neurological disorders, and early mortality, according to epidemiologic research and clinical trials [89].

M.S. Rajesh et al. (2009) investigated the antihyperglycemic efficacy of petroleum ether, chloroform, methanolic, and aqueous extracts of *C. speciosus* rhizomes in overnight fasted, STZ-induced diabetic rats. Blood glucose levels (BGL) were measured at regular intervals of 0, 30, 60, 120, and 240 minutes, indicating that all extracts of *C. speciosus* reduced BGL considerably except petroleum ether. Aqueous and methanolic extracts were considerably superior to other extracts in lowering BGL from extremely high levels to tolerable levels in 240 minutes, and this was confirmed in extended-term repeated dosage experiments [90].

12] Anti- stress activity: Every human is subjected to stress on a regular basis, and optimal amounts of stress are required for normal functioning. Stress alters the metabolism and action of neurotransmitters in the central and peripheral nervous systems. Cold immobilisation stress reduces norepinephrine and dopamine levels in the brain [91]. As a result, there is a need to manage stress so that regular functioning is not impaired.

Nitin Verma et al. (2009) investigated the effect of an alcoholic extract of *Costus speciosus* rhizomes on stress-induced alterations in neurotransmitters and the enzyme monoamine oxidase levels in albino rats. The extracts were discovered to have normalising activity against cold immobilisation stress-induced changes in norepinephrine (NE), dopamine (DA), 5-hydroxytryptamine (5-HT), 5-hydroxy indole acetic acid (5-HIAA), and the enzyme monoamine oxidase (MAO), providing biochemical evidence for the tested extracts' antistress activity [92].

13] Larvicidal activity: Mosquito-borne infections are one of the world's most dangerous health issues, producing a variety of ailments. Mosquitoes are the primary vectors of disease transmission for malaria, dengue fever, yellow fever, filariasis, schistosomiasis, and Japanese encephalitis.

Surendra Kumar Muniyandi et al. (2013) investigated the larvicidal efficacy of aqueous extracts of *Costus speciosus* Koen. Aqueous extracts of *Costus speciosus* stem, leaf, and rhizomes were tested against third- and fourth-instar larvae (*Aedes aegypti*). Leaf extracts had the highest larvicidal potential or percentage mortality when compared to rhizomes and stem extracts [93]. Larviciding is an effective method of lowering mosquito numbers in breeding areas before they mature into adults [93,94].

14] Diuretic activity: Diuretics, which are used to modify the amount and composition of bodily fluid in a range of disorders such as hypertension, nephritic syndrome, cirrhosis, renal failure, heart failure, and pregnancy toxemia, are drugs that cause increased urine flow [95]. The use of diuretics causes several negative side effects. As a result, a novel diuretic drug with therapeutic effectiveness is required.

Dubey S. et al. (2010) investigated the diuretic effectiveness of aqueous and alcoholic extracts of *Costus speciosus* rhizomes in albino rats and compared them to furosemide as a reference medication. He discovered that both extracts considerably increased urine production as well as urinary electrolyte content, suggesting that *Costus speciosus* had a diuretic effect [96].

15] Estrogenic activity: Assamese ladies are heavily researching this herb for fertility control. Choudhury Najma et al. (2012) studied the effect of methanolic rhizome extract on the ovaries and uterus of female adult mice with intact gonadotropins. Compared to the normal control, the extract resulted in a considerable drop in ovarian weight and an increase in uterine weight. This might be due to a negative feedback mechanism inhibiting the production of tropic pituitary gonadotropins, and it is also suggested that the plant has endocrine-active estrogenic activity, which leads to an increase in uterine weight. Many beneficial qualities of the plant have been identified for human health, including enzyme inhibition, antiallergic, vascular, cytotoxic, anticancer action, antifertility, and hepatoprotective activity [97].

16] Anti- spasmotic activity: Any compound's antispasmodic or spasmolytic action refers to its capacity to prevent spasms or offer relief from spasms induced by involuntary muscles. Banerji et al. (1982) tried a different extract of *C. speciosus* on the ileum of a guinea pig. The findings demonstrated that the plant had modest levels of spasmolytic action. When the activity of *C. speciosus* extract and the commonly used antispasmodic medication papaverine were evaluated, the former was shown to have lesser antispasmodic characteristics [98].

CONCLUSION:

India is home to a wide variety of herbal and medicinal plants that can be used to cure a wide range of illnesses. One of these that serves as a significant source of numerous therapeutically effective chemicals with a variety of traditional and pharmacological actions is *Costus speciosus*. Due to its poor progeny and overuse, this plant is in danger of going extinct. Therefore, other means of propagation, such as tissue culture techniques (micropropagation), and many biotechnological features are required to produce these plants on a large scale and at low costs for farmers, nurseries, and the pharmaceutical industry. Therefore, additional research may be done to demonstrate the plant's potential.

REFERENCES

1. Rajasekharan, S., Pushpangadan, P., and Biju, S.D., 1996. Jain, S.K. (ed), Deep Publications, New Delhi, India, & quot;Folk Medicines of Kerala: A Study on Native Traditional Folk Healing Art and its Practitioners," pp. 167–172.
2. Bavara G.H., Narasimhacharya A. V. R. L. (2008) *Phytotherapy Research*, 22(5), 620–626 *African Journal of Pharmacy and Pharmacology*, 7(42), pp. 2774–2779, 2013. [3] A. H. EL-far and I. I. Abou-Ghanem, & quot;Biochemical and haematological evaluation of *Costus speciosus* as a dietary supplement to Egyptian buffaloes.

3. M.M. Roy and S.C. Datta's 1977 study Indian Drugs, 15:14–16. Investigation of *Costus speciosus* (Koen) sm. as a source of diosgenin: Part-I
4. B. Dasgupta and V.B. Pandey, 1970 Diosgenin (*Costus speciosus*) has a new Indian source, according to Experiment 26:475.
5. "Anthelmintic Activity of" by S. Srivastava, P. Singh, K. K. Jha, G. Mishra, S. Srivastava, and R. L. Khosa & Aerial portions of *Costus speciosus*, International Journal of Green Pharmacy, vol. 5, no. 5, 2011, pp. 325–328.
6. "Micropropagation of *Costus speciosus* (Koem, ex. Retz) Sm., an antidiabetic plant, by using explants of pseudostems," Botany Research International, 2(3), pp. 182-185, 2009.
7. African Journal of Pharmacy and Pharmacology, 7(42), pp. 2774–2779, 2013. H. EL-far and I. I. Abou-Ghanema, "Biochemical and haematological evaluation of *Costus speciosus* as a dietary supplement to Egyptian buffaloes.
8. B. K. Kirchoff and R. Rutishauser, "The Phyllotaxy of *Costus* (Costaceae)," Bot. Gaz, 151, pp. 88–105, 19V. Devi D. and A. Urooj, "Nutrient Profile and Antioxidant Components of *Costus speciosus* Sm. and *Costus igneus* Nak.," Indian Journal of Natural Products and Resources, 1(1), pp. 116–118, 2010.
9. M. S. Rajesh, M. S. Harish, R. J. Sathyaprakash, A. R. Shetty, and T. N. Shivananda, "Antihyperglycemic Activity of the various Extracts of *Costus speciosus* Rhizomes," Journal of Natural Remedies, 9(2), pp. 235-241, 2009.
10. G.V. Satyavathi, "Medicinal Plants of India," ICMR, New Delhi, Vol. 1, 1976.
11. N. Choudhury, K. J. Chandra, and H. Ansarul, "Effect of *Costus speciosus* Koen on reproductive organs of female albino mice," International Research Journal.
12. S. Srivastava, P. Singh, G. Mishra, K. K. Jha, and R. L. Khosa, "Costus speciosus (Keukand): A Review Der Pharmacia Sinica, 2 (1), pp. 118–128, 2011.
13. A.H. El-Far and I. I. Abou-GGhanema, Biochemical and haematological evaluation of *Costus speciosus* dietary supplement to Egyptian buffaloes," African Journal of Pharmacy and Pharmacology, 7(42), pp. 2774–2779, 2013.

14. Y. K. Sarin, K. L. Bedi, and C. K. Atal, "Costus A. H. EL- far and I. I. Abou-GGhanema, Biochemical and haematological evaluation of Costus speciosus dietary supplement to Egyptian buffaloes," African Journal of Pharmacy and Pharmacology, 7(42), pp.2774–2779, 2013; "Costus speciosus rhizome as a source of Diosgenin," Current Science,43(18), pp. 569–570, 1974.
15. A. S. Wabale, M. N. Kharde, K. J. Salunke, and A. S. Petkar, "Costus speciosus (Koeing) J. E. Sm., Lobelia nicotianaefolia Roth, and Urginea indica Kunth: The Important Ethnomedicinal Plants from the Western Ghats," Asian J. Exp. Biol. Sci., 2(1), 169–170,2011.
16. J. Karthikeyan, V. Reka, and R. V. Giftson, Characterization of bioactive compounds in *Costus speciosus* (Koen.) by reverse-phase HPLC," International Journal of Pharmaceutical Sciences and Research, 3(5), pp. 1461–1465, 2012.
17. N. Choudhury, K. J. Chandra, and H. Ansarul, "Effect of Costus speciosus Koen on reproductive organs of female albino mice," International Research Journal of Pharmacy,3(4), pp. 200–202, 2012.
18. V. Devi D. and A. Urooj, "Nutrient Profile and Antioxidant Components of *Costus speciosus* Sm. and *Costus igneus* Nak.," Indian Journal of Natural Products and Resources, 1(1), pp. 116–118, 2010.
19. Eti, A. Narayanan, and B. Ganesan, "Studies on Costus speciosus Koen Alcoholic Extract for Larvicidal Activity, "International Journal of Pharmacognosy and PhytochemicalmResearch, 5(4), pp. 328–329, 2013.
20. Nehete J., M. Bhatia, and M. Narkhede, "In-vitro Evaluation of Antioxidant Activity and Phenolic Content of Costus speciosus (Koen) J. E. Sm.," Iranian Journal of Pharmaceutical Research, 9(3), pp. 271-277, 2010.
21. S. K. Muniyandi, A. T. Nandan, S. C. Veeti, A. Narayanan, and B. Ganesan, "Studies on Costus speciosus Koen Alcoholic Extract for Larvicidal Activity, "International Journal of Pharmacognosy and Phytochemical Research, 5(4), pp. 328–329, 2013.
22. P. N. Prasad, "Studies on Costus speciosus (Koen) sm. and *C. malortieanus* H. Wendl. Ph.D. Thesis, University of Madras, Tamil Nadu, India, 1982.
23. S. Srivastava, P. Singh, K. K. Jha, G. Mishra, S. Srivastava, and R. L. Khosa, "Anthelmintic activity of aerial parts of Costus speciosus," International Journal of Green Pharmacy, 5, pp. 325–328, 2011.
24. A. S. Rani, G. Sulakshana, and S. Patnaik, "Costus speciosus, an antidiabetic plant review," FS J Pharma Res, 1(3), pp. 52–53, 2012.

25. Chunekar, K.C. 1982 Bhavaprakashanighantu of Sri Bhavamishra. Commentary, Varanasi (in Hindi).
26. Dasgupta, B., and V.B. Pandey (1970) A new Indian source of diosgenin (*Costus speciosus*). Cell. Molec. Life. Sci. 26:475–476.
27. Gamble J.S. 1987. Flora of the presidency of Madras. VolIII. BishenSingh Mahendra Pal Singh, Dehra Dun, India. Pp. 1478-1493.
28. Gideon, O. 1991. Costoideae or Costaceae: A taxonomic bank controversy. Zingiberaceae Workshop, Songkla University, HatYai, Thailand. p20.
29. Khanna, P., G.L.Sharma. A.L. Rathore and S.K Manot (1977). Effect of cholesterol on in vitro suspension tissue cultures of *Costus speciosus* (Keon.) *Dioscorea floribunda*, *Solanum aviculare*, and *Solanum xanthocarpum*. Ind.J. Exptl.Biol.15:1025-1027.
30. Kirtikar, K.R. and Basu, B.D. 1987. Indian Medicinal Plants. Book Distributors, Dehra Dun. p.2444-2449.
31. Moosad, T.C.P. 1983. Amarakosam- Commentary. Kottayam (in Malayalam). P.361. Moos, N.S. 1984b. Identification of kebuka. Anc. Sci. Life., 4(2): 100-102.
32. Prakash, V., and B.N. Mehrotra (1996). Zingiberaceae of India & Biological screening and ethnobotanical diversity: In proceeding of the Biological symposium on the family Zingiberaceae, South China Institute of Botany 229-237.
33. J. P. Robinson, S. J. Britto, and V. Balakrishnan “Micropropagation of *Costus speciosus* (Koem, ex., Retz) Sm., an Antidiabetic plant by using Explants of Pseudostems,” Botany Research International, 2(3), pp.
34. Maji P, Dhar DG, Misra P, and Dhar P (2020) *Costus speciosus* (Koen. ex. Retz.) Sm.: current status and future industrial prospects. Ind Crops Prod. 152:11257
35. Thambi M., Shafi MP (2015) Rhizome essential oil composition of *Costus speciosus* and its antimicrobial properties Int J Pharm Res Allied Sci 4(1):28–32.
36. VA Pawar and PR Pawar (2014) *Costus speciosus* is a valuable medicinal plant. International Journal of Scientific Research 3(7):28–32.
37. Nair SV, Hettihewa M, and Rupasinghe HP (2014). Apoptotic and inhibitory effects on cell proliferation of hepatocellular carcinoma HepG2 cells by methanol leaf extract of *Costus speciosus*. Biomed Res Int., <https://doi.org/10.1155/2014/637098>
38. Nadkarni KM (2009), Indian materia medica. Bombay Popular Prakashan 1:385–386
39. Gupta RK (2010), Medicinal and Aromatic Plants. " CBS Publ Distrib 234:499.
40. Anonymous (2007), The Wealth of India: First Supplement Series " (raw materials). National Institute of Science Communication and Information Resources, CSIR 2:211–213.

41. Malabadi RB (2005): Antibacterial activity in the rhizome extracts of *Costus speciosus* (Koen.) J Phytol Res. 18(1):83–85.
42. Shrivastava S, Singh P, Mishra G, Jha KK, and Khosa RL (2011). *Costus speciosus* (Keukand): a review. *Der Pharmacia Sinica* 2(1):118–128.
43. Singh N. (2011). Wild edible plants: a potential source of nutraceuticals. *Int J Pharma Sci Res* 2 (12):216–225.
44. Roy A, Manikkam R. Cytotoxic impact costunolide isolated from *Costus speciosus* on breast cancer via differential regulation of cell cycle an in-vitro and in silico approach. *Phytother Res* 2015;29:1532–9.
45. Baskar AA, Al Numair KS, Alsaif MA, and 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.
46. Nair SV, Hettihewa M, and Rupasinghe HP. Apoptotic and inhibitory effects on cell proliferation of hepatocellular carcinoma HepG2 cells by methanol leaf extract of *Costus speciosus*. *Biomed Res Int*. 2014;2014:637098.
47. Pitchai D, Roy A, and Banu S. In vitro and in silico evaluation of NF- κ B-targeted costunolide action on oestrogen receptor-negative breast cancer cells: a comparison with normal breast cells *Phytother Res* 2014;28:1499505.
48. Koyuturk M, Ozsoy Sacan O, Bolkent S, and 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. El Far AH, Badria FA, and Shaheen HM Possible anticancer mechanisms of some *Costus speciosus* active ingredients concerning drug discovery *Curr Drug Discov Technol* 2016;13:123–43
50. Daisy P, Eliza J, and Ignacimuthu S. Influence of *Costus speciosus* (Koen.) Sm. rhizome extracts on biochemical parameters in streptozotocin-induced diabetic rats *Health Sci*. 2008;54:675–81. Available from: <http://www.joi.jlc.jst.go.jp/JST.JSTAGE/jhs/54.675> from=CrossRef. [Last accessed on 2016 Nov 24].

51. Navrot N, Rouhier N, Gelhaye E, and 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.13993054.2006.00777.x> [Last accessed on 2016 Nov 24].
52. Halliwell B. Antioxidants and human disease: a general introduction. *Nutr Rev* 1997;55:S44-9.
53. Nehete J, Bhatia M, Narkhede M. In vitro evaluation of antioxidant activity and phenolic content of *Costus speciosus* (Koen) J.E. Sm., *Iran J Pharm Res* 2010;9:271–7.
54. Gottfredsen RH, Larsen UG, Enghild JJ, and Petersen SV Hydrogen peroxide induces modulations of human extracellular superoxide dismutase that result in enzyme inhibition. *Redox Biol* 2013;1:24–31.
55. Kharrazi H, Vaisi Raygani A, Rahimi Z, Tavilani H, Aminian M, Pourmotabbed T, et al. Association between enzymatic and non-enzymatic antioxidant defence mechanisms with apolipoprotein E genotypes in Alzheimer disease. *Clin Biochem* 2008;41:9326.
56. Govindarajan R, Vijayakumar M, and Pushpangadan P. Antioxidant Approach to Disease Management and the Role of ‘Rasayana’ Herbs of Ayurveda. *J Ethnopharmacol* 2005;99:165–78.
57. Vijayalakshmi MA, Sarada NC. Screening of *Costus speciosus* extracts for antioxidant activity *Fitoterapia* 2008;79:197–8.
58. Jha MK, Alam MB, Hossain MS, and Islam A. In vitro antioxidant and cytotoxic potential of *Costus speciosus* (Koen.) Smith rhizome *Int J Pharm Sci Res* 2010;1:138–44.
59. Devi DV, Urooj A. Nutritive properties and antioxidant compounds of *Costus speciosus* (Koen.) Sm. and *Costus igneus* Nak. *Indian J Natl Prod Resour* 2010;1:1168.
60. Eliza J., Daisy P., and Ignacimuthu S. Antioxidant activity of costunolide and eremanthin isolated from *Costus speciosus* (Koen ex. Retz) sm. *Chem Biol Interact* 2010;188:467–72
61. El Far AH, Abou Ghanema II. Biochemical and haematological evaluation of *Costus speciosus* as a dietary supplement for Egyptian buffaloes *Afr J Pharm Pharmacol* 2013;7:27749.
62. Vazquez A, Sanchez C, Delgado N, Alfonso A, Ortega Y, and Sanchez H. Anti-inflammatory and analgesic activities of red seaweed *Dichotomaria obtusata* *Braz J Pharm Sci* 2011;47:1118.
63. Gomase PV, Shire PS, Nazim S, and Choudhari AB. Development and evaluation of polyherbal formulations for anti-inflammatory activity. *J Natl Prod Plant Resour* 2011;1:85–90.
64. Srivastava S, Singh P, Jha KK, Mishra G, Srivastava S, Khosa RL, et al. Anti-inflammatory, analgesic, and antipyretic activities of the aerial parts of *Costus speciosus* Koen *Indian J Pharm Sci* 2013;75:83–8.
65. 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.

66. Al-Attas AA, El-Shaer NS, Mohamed GA, Ibrahim SR, and Esmat A. Anti-inflammatory sesquiterpenes from *Costus speciosus* Rhizomes J Ethnopharmacol 2015;176:365–74.
67. Selim S, Al Jaouni S. Anti-inflammatory, antioxidant, and antiangiogenic activities of diosgenin isolated from the traditional medicinal plant, *Costus speciosus* (Koen ex. Retz.) Sm. Nat Prod Res 2016;30:18303.
68. Bakhsh ZA, Al Khatib TA, Al Muhayawi SM, El Assouli SM, Elky IA, Mourad SA, et al. 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 2015;36:997–1000.
69. Koyuturk M, Ozsoy Sacan O, Bolkent S, and 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.
70. Colca JR. Insulin sensitizers may prevent metabolic inflammation. Biochem Pharmacol 2006;72:125–31.
71. Medagama AB, Bandara R, Abeysekera RA, Imbulpitiya B, and 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.
72. Mosihuzzaman M, Nahar N, Ali L, Rokeya B, Khan AK, Nur E Alam M, et al. Hypoglycemic effects of three plants from the Eastern Himalayan belt Diabetes Res 1994;26:127–38.
73. Daisy P, Eliza J, and Ignacimuthu S. Influence of *Costus speciosus* (Koen.) Sm. rhizome extracts on biochemical parameters in streptozotocin-induced diabetic rats Health Sci. 2008;54:675–81. Available from : <http://www.joi.jlc.jst.go.jp/JST.JSTAGE/jhs/54.675?from=CrossRef>.
74. Bavarva JH, Narasimhacharya AV. Antihyperglycemic and hypolipidemic effects of *Costus speciosus* in alloxan-induced diabetic rats. Phytother Res 2008;22:620–6.
75. Eliza J, Daisy P, Ignacimuthu S, and Duraipandiyan V. Normoglycemic and hypolipidemic effects of costunolide isolated from *Costus speciosus* (Koen ex. Retz.) Sm. in streptozotocin-induced diabetic rats Chem Biol Interact 2009;179:329–34.
76. Eliza J, Rajalakshmi M, Ignacimuthu SJ, and Daisy P. Normalising effects of *Costus speciosus* rhizome crude extracts and their fractions on diabetic complications in STZ-induced diabetic rats MedChem Res 2011;20:11118. Available from: <http://www.link.springer.com/10.1007>.
77. Ali HA, Almaghrabi OA, and AME. Molecular mechanisms of the antihyperglycemic effects of *Costus speciosus* extract in streptozotocin-induced diabetic rats. Saudi Med J 2014;35:1501–6.
78. Perera HK, Premadasa WK, and Poongunran J. glucosidase and glycation inhibitory effects of *Costus speciosus* leaves BMC Complement Altern Med 2016;16:2.
79. Kraemer FB, Shen WJ. Hormone-sensitive lipase: Control of intracellular tri(di) acylglycerol and cholesteryl ester hydrolysis J Lipid Res 2002;43:158594

80. ChogtuB, MagazineR, BairyKL. Statin use and the risk of diabetes mellitus World J Diabetes 2015;6:352–7.
81. Contreras-Zentella ML, Hernández-Muoz R. Is liver enzyme release really associated with cell necrosis induced by oxidant stress? Oxid Med Cell Longev 2016;2016:3529149
82. Verma N, Khosa RL. Evaluation of protective effects of an ethanolic extract of *Costus speciosus* (Koenig) Sm. rhizomes on carbon tetrachloride-induced hepatotoxicity in rats. Natl Prod Radiance 2009;8:123–6.
83. Padma P, Chansauria JP, Khosa RL, and Ray AK Effect of *Annooa muricata* and *Polyalthia cerasoides* on brain neurotransmitters and the enzyme monoamine oxidase following cold immobilisation stress J Natl Remedies 2001;1:144–6.
84. Verma N, Khosa RL. Effect of *Costus speciosus* and *Wedelia chinensis* on brain neurotransmitters and the enzyme monoamine oxidase following cold immobilisation stress. Pharm Sci Res 2009;1:22.
85. 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;270:2517.
86. Lai PK, Roy J. Antimicrobial and chemopreventive properties of herbs and spices. Curr Med Chem 2004;11:145160.
87. Malabadi RB. Antibacterial activity in the rhizome extracts of *Costus speciosus* (Koen.) J Phytol Res 2005;18:835.
88. S. K. Bhattacharya, A. K. Parikh, P. K. Debnath, V. B. Pandey, and N. C. Neogy, "Anticholinesterase activity of *Costus speciosus* alkaloids," Ind. J. Pharmac, 4 (3), pp. 178–179, 1972.
89. S. Srivastava, P. Singh, K. K. Jha, G. Mishra, S. Srivastava, and R. L. Khosa, "Anthelmintic activity of aerial parts of *Costus speciosus*," International Journal of Green Pharmacy, 5, pp. 325–328, 2011.
90. M. S. Rajesh, M. S. Harish, R. J. Sathyaprakash, A. R. Shetty, and T. N. Shivananda, "Antihyperglycemic activity of the various extracts of *Costus speciosus* rhizomes," Journal of Natural Remedies, 9(2), pp. 235-241, 2009.
91. J. Tache, H. Selye, J.G. Spielberger, and Sarason (Eds.), "Stress and Anxiety," John Wiley and Sons, New York, pp. 2–3, 1978.
92. N. Verma and R. L. Khosa, "Effect of *Costus speciosus* and *Wedelia chinensis* on Brain Neurotransmitters and Enzyme Monoamine Oxidase Following Cold Immobilisation Stress," Journal of Pharmaceutical Sciences and Research, 1(2), pp. 22–25, 2009.
93. S. K. Muniyandi, A. T. Nandan, S. C. Veeti, A. Narayanan, and B. Ganesan, "Studies on *Costus*

speciosus Koen Alcoholic Extract for Larvicidal Activity," International Journal of Pharmacognosy and Phytochemical Research, 5(4), pp. 328–329, 2013.

94. S. Kanakkanath, A. Narayanan, and B. Ganesan, "Evaluation of *Costus speciosus* Koen aqueous extract for larvicidal activity," Der Pharmacia Lettre 5(4), pp. 283-285, 2013.

95. A. Agunu, E. M. Abdurahman, G. O. Andrew, and Z. Muhammed, "Diuretic activity of the stem bark extracts of *Steganotaenia araliaceahoechst*," J. Ethnopharmacol, 96, pp. 471–5, 2005.

96. S. Dubey, V. K. Verma, A. K. Sahu, A. K. Jain, and A. Tiwari, "Evaluation of Diuretic Activity of Aqueous and Alcoholic Rhizome Extracts of *Costus speciosus* Linn in Wister Albino Mice," IJRAP, 1(2), pp. 648–652, 2010.

97. J. Karthikeyan, V. Reka, and R. V. Giftson, Characterization of bioactive compounds in *Costus speciosus* (Koen.) by reverse phase HPLC," International Journal of Pharmaceutical Sciences and Research, 3(5), pp. 1461–1465, 2012.

98. Shrivastava S, Singh P, Mishra G, Jha KK, and Khosa RL (2011). *Costus speciosus* (Keukand): a review. Der Pharmacia Sinica 2(1):118–128.

