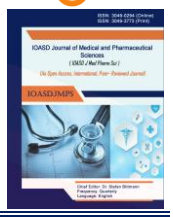
OPEN ACCESS

IOASD Journal of Medical and Pharmaceutical Sciences

IOASD J Med Pharm Sci, Vol-3, Iss-3, Jul-Sept., 2026
Frequency: Quarterly
ISSN: 3049-0294 (Online)
ISSN: 3049-3773 (Print)
Homepage: https://ioasdpublisher.com/ioasdjmps



The Pharmacological Potential and Pharmacognosy of *Costus pictus*; A Comprehensive Review

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DOI: 10.67224/ioasdjmps.2026.v03i03.017

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ABSTRACT

One of the indigenous Mexican plants that has recently been imported in India is Costus pictus D. Don. It is sometimes referred to as "Insulin plant" or "Spiral Ginger" and has been well-known off-late as a result of its anti-diabetic effects. This plant's leaves have been said to have anti-diabetic qualities. The high value secondary metabolites, bioactive chemicals, and exceptional blooming characteristics of this diabetes plant (Costus pictus D. Don) make it a commercially immense medicinal herb. Due to its wide range of distribution in India, this plant has been proven to posses' anticancer, anti-inflammatory and so on. Pharmacological activities of this plant are based on the modulation of many signaling pathways, and targeting these pathways may lead to the creation of effective medicines for the treatment of several illnesses. With the application of several experimental animal methods, ethnopharmacological work has been refined continuously to look for novel, powerful therapeutic compounds from plant sources for the treatment of several illnesses in general and neurological disorders in particular. Therefore, increased attention has been made to focus *Costus pictus* plants in this review. Moreover, this review paper also describes and analyzes the currently available information on morphological and molecular identification, phytochemicals, and other pharmacological research that have been reported till date.

Keywords: Indigenous, Insulin plant, Anti-diabetic, Ethnopharmacological, Neurological ailments.

Review Article

Article History

Received: 01-07-2026

Accepted: 25-08-2026

Published: 31-08-2026

INTRODUCTION

Any plant that can be utilized therapeutically or that can be served as building block for the production of effective pharmaceutical is considered to be a medicinal plant. This definition enables the distinction between plants that are considered to be medicinal but have not yet gone through a complete investigation and plants whose therapeutic capacities and ingredients have been portrayed scientifically. Conventional based medical systems are still widely practiced due to a variety of reasons. Population growth, insufficient drug supply, expensive treatment costs, side effects of several synthetic drugs, and the growth of drug resistance have all contributed to a greater extent in utilizing plant materials as a source of medicine for an extensive range of human diseases. Long before during the prehistoric period, people recommended plants for medical purposes. Chinese texts, Egyptian papyrus, and ancient Unani scrolls all had conversed about the usage of plants. There was evidence that around 4000 years ago, Unani Hakims, Indian Vaids, and cultures from the Mediterranean and Europe have used herbs as medicine. Herbs were employed to heal rituals by indigenous societies in Rome, Egypt, Iran, Africa, and America, while other cultures followed traditional medical systems (Unani, Ayurveda, and Chinese medicine) that systematically utilized herbal remedies [1].

Table 1: Classification and Systematic Position of the *Costus pictus* D. Don

S. No	Classification	Plant
1	Domain	Eukaryota
2	Kingdom	Plantae
3	Subkingdom	Viridaeplantae
4	Phylum	Tracheophyta
5	Subphylum	Euphyllophytina
6	Infraphylum	Radiatopses
7	Class	Liliopsida

S. No	Classification	Plant
8	Subclass	Commelinidae
9	Superorder	Zingiberanae
10	Order	Zingiberales
11	Family	Costaceae
12	Subfamily	Asteroideae
13	Tribe	Coreopsideae
14	Genus	*Costus L.*
15	Species	*Costus pictus* D.Don

Costus pictus

Costus pictus D. Don is a member of the *Costaceae* family and is frequently referred to as spiral ginger and generally recognized as fiery *costus*, step ladder or spiral flag or insulin plant (Table-3). It is one of the best proved plants to treat diabetes. The leaf of this plant aids in the body's development of insulin. As a result, it is also known as insulin plant. *Costus* species are widely dispersed throughout tropical regions of the world. It has also been observed in parts of central India, the sub-Himalayan range, and the Western Ghats of India. It is commonly grown as an ornamental plant in south India. Local people use the leaves to reduce their blood sugar level. Several studies have been conducted to examine this plant's anti-diabetic potential. Furthermore, (Fig.1) this plant has been demonstrated to have a variety of pharmacological actions viz., hypolipidemic, diuretic, antioxidant, antimicrobial, and anticancer effect [2].

Table 2: Major constituents of essential oil from various *Costus* plants

Various species of *Costus*	Stem oil (%)	Leaf oil (%)	Rhizome oil (%)	Reference
Costus afer Ker		sesquilavandulyl acetate (17.0%), β-caryophyllene (12.3%) and Z, E-farnesol (9.9%)		Taiwo & Bolanle (2003)
Costus speciosus			α-Humulene (20.55) and Zerumbone (55.11)	Shafi, (2015)
Costus (Saussurea lappa Clarke)			Eudesma-5,11(13)-dien-8,12-olide (52.01	Abdelwahab et al., (2019)
Saussurea costus)			aldehydes (7Z, 10Z, 13Z)-7, 10, 13-hexadecatriena (25.5%)	Gwari et al (2013)
Costus lucanusianus J. Braun & K. Schum	4-(1,3,3-trimethyl-bicyclo [4.1.0] hept-2-yl)-but-3-en-2-one (28.10%), 3',8,8'-trimethoxy-3-piperidyl-2,2'-binaphthalene-1,1',4,4'-tetrone (22.06%)	11-Octadecenoic acid, methyl ester (41.00%), squalene (16.40%) and hexadecanoic acid, methyl ester (10.19%)	octadecane, 3-ethyl-5-(2-ethylbutyl) – (18.23%)	Onanuga,., & Oloyede (2022),
Costus pictus	hexadecanoic acid (28.3%), 9,12-octadecadienoic acid (18.33%), linalyl propanoate (6.03%), dodecanoic acid (5.62%),	hexadecanoic acid (24.51%), 2-pentanol (22.48%), β-ionone (8.69%), α-ionone (8.01%),	Hexadecanoic acid (25.26%), dodecanoic acid (16.56%), tetradecanoic acid (10.20%),	Jose B, Reddy (2010)

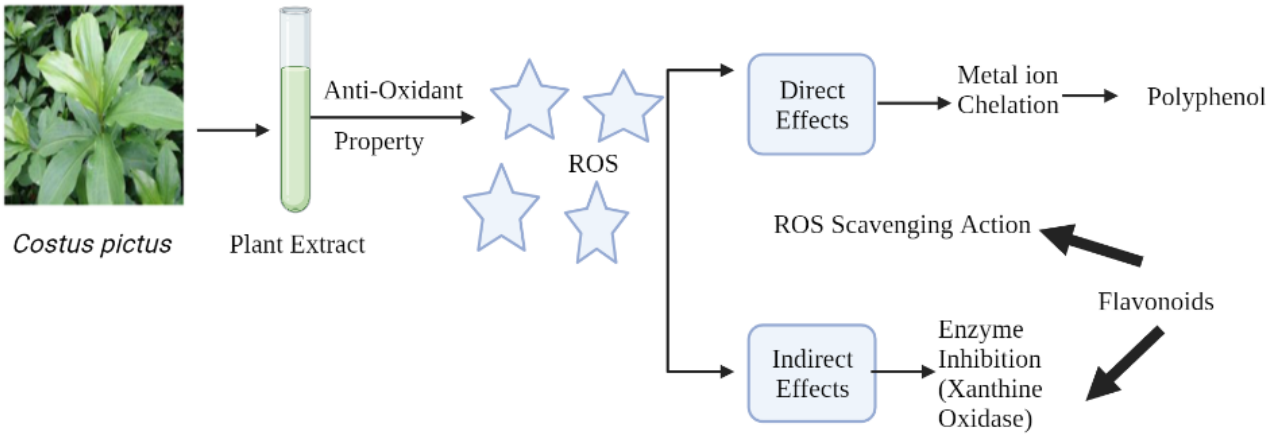

Figure 1: Summary of the molecular mechanism of Anti-Oxidant Property of *Costus pictus*

Molecular Identification

Despite, rising demand from pharmaceutical industries, this species has not been much concentrated at the molecular level**.** Hence effort was made by different researchers to characterize *Costus pictus* collected from various regions of India to understand genetic variation within the *C.pictus* complex. Understanding the genetic diversity of a plant is mandatory for improving plant breeding and production [3].

Breeders could benefit from the rapid advancements pertaining to molecular marker systems, which have proven to be effective tools for assessing and evaluating genetic diversity and for understanding genetic relationships within and among species [Table-2]. Thus, identification of specific plant accessions/genotypes through molecular techniques could be successful in contrast to conventional set of morphological markers. Numerous medicinal and aromatic plants have been studied and the genetic difference at the molecular level in *Costus pictus* has been determined using the random amplified polymorphic DNA (RAPD) marker method [4].

Table 2: Medicinal properties of different parts of *Costus* species

Portion of the plant (*Costus species)*	**Bioactive chemical compounds**	**Activity**
Whole plant	Disogenin	Astringent, anthelmintic, depurative, expectorant, aphrodisiac and purgative.
Roots	Diosgenin, sitosterol, dioscin, gracillin, cycloartanol, cycloartenol and cycloalaudenol.	Antifungal, tonic, antibacterial, Expectorant and stimulant.
Rhizomes	Diosgenin, dioscin, gracillin and Beta-sitosterol.	Antiinflammatory, antispasmodic, antiarthritic, antidiabetic, hydrochloretic, diuretic, CNS depressant, antivermin and cardiotonic,
Leaves	Diosgenin	Diabetes, eye and ear infections, fever, dysentery, mental disorders and diarrhorea.

Authentication should not be permitted for AFLP, RAPD, SAMPL, until these markers are turned into LAMP or SCAR [5]. These markers are effective for identifying genetic variation among plant species. Apart from morphological, anatomical, and chemical markers, LAMP, SCAR, and DNA bar-coding has been proved to be excellent methods for authenticating medicinal plants. In order to completely eliminate adulterants and false components that have degraded traditional medicine, DNA markers can be employed in future to construct reference records of conventional medicines (such as DNA sequences and fingerprints). As these can be processed, DNA-based technologies can offer an effective, reliable, and less expensive method of simultaneously evaluating the integrity of hundreds of samples. The medical potential and economic success of herbal products will be greatly increased by DNA-based authentication of medicinal plants, which can be useful

as a device for quality control and protective observation of herbal pharmaceuticals and nutraceuticals.

A strong, dependable, stable and quick assay is AFLP that was potentially used in marker-assisted breeding, genome mapping, as well as DNA fingerprinting [6]. The use of restriction site-specific adaptors and particular primers, with a numerous number of selected nucleotides under rigorous amplification conditions, confirms the reproducibility of AFLP. The phylogenetic connections, biogeographic history and pollination background of *Costus* (Costaceae) were determined by the utilization of genetic data from the internal and external transcribed spacer (ITS and ETS) portions of 18S-26S nuclear ribosomal DNA.They had modified and sequenced both strands. *C. pictus* exhibited numerous alleles for both ITS and ETS, while *C. dubius, C. malortieanus,* and *C. pulverulentus* from the Barro Colorado Island in Panama had several ITS alleles. Cloning was done on the PCR products. From each PCR mixture, six to ten positive clones had been applied for sequencing. Further, they have determined evolutionary relationships among *Costus* species and found that the ITS and ETS rDNA sequences had been proven to be an effective method [7].

The reported that using next-generation sequencing it would be possible to find molecular markers in the transcriptome of plant tissues that are connected to their physiological functions. By mixing bioinformatics techniques, they sequenced the leaf transcriptome of *C. pictus* using Illumina's reversible dye terminator sequencing technology in order to discover transcripts relevant to the plant's anti-diabetic characteristics. Further, conserved miRNAs in *C. pictus* were detected by Transcribed Sequence Assemblies (TSA) using a computer-based homology method [8]. The results of this study provided the framework for further investigation in miRNAs and miRNA-mediated gene regulation in future.

Anti-diabetic activity

Diabetes mellitus is nothing but a chronic hyperglycemia carried on by relative insulin shortage which has a variety of etiological factors. Diabetes is linked to problematic issues with protein, lipid, and glucose metabolism. Owing to the negative effects of oral hypoglycemic medications, much interest has been shown in herbal treatments for type 1 diabetes mellitus. New oral hypoglycemic substances derived from therapeutic plants may be a valuable source for the production of pharmacological entities or as a dietary supplement to already approved therapies [Table-4]. In contrast to synthetic pharmaceuticals, herbal drugs are considered to be less toxic and have no side effects [9]. A biguanide compound called metformin is prescribed to diabetics as an antihyperglycemic drug. In addition to treating type II diabetes, the drug metformin also improves liver function to those peoples with non-alcoholic fatty liver ailment [10]. Enhanced insulin receptor tyrosine kinase action, as well as increased activity and translocation of glucose transporters towards the serum membrane mediate the main metformin transporters. The ability of metformin to repair the enzymatic pathways involved in insulin signaling as well as elevated insulin receptor expression have also been connected to it. This reduction in fasting glucose and glucosidase inhibitory levels in the diabetic group administered metformin is the primary cause in this treatment [11]. Biguanides, sulphonylureas, and thiazolidinediones were found to be effective hypoglycemic agents. However, they have certain undesirable consequences. As a result of this, various laboratories all across the world were seeking new medications with low side effects.

In comparison to monotherapy, the use of synthetic therapies combining with medicinal plants could be more effective and ubiquitous. Drug-herb interactions, however, can have both positive and negative outcomes [12]. A novel and highly effective therapeutic approach to treat hyperglycemia is by adopting combination therapy. Combining, pharmaceuticals with phytochemicals may minimize the negative side effects caused by synthetic drugs. Due to their natural origin and long-standing use, herbal products have been believed to be intrinsically safe rather than being supported by systematic investigations. To match the bioavailability of the medicine and the phytochemical, new formulations and co crystallization procedures need to be employed [13].

Numerous plant species are being utilized by various Asian tribes due to their pharmacognostic properties, even though they are still extremely rare and infrequently encountered. Some of these plants are members of the *Costus* genus, which is still not well-known but performs a number of vital functions in the field of medicine. Numerous extracts from *Costus* plant have been investigated and reported to have a variety of pharmacological effects, especially antidiabetic activity [15].

Antidiabetic properties of *Costus pictus* may involve enhanced glucose homeostasis such as elevation of peripheral glucose utilization, rise in hepatic glycogen production or decline in glycolysis due to enzymes, reduced intestinal absorption of glucose and decline in the carbohydrates glycemic index. Previous studies have revealed that methyl tetracosanate and beta-amyrin are the main bioactive phytoconstituents that showed improved glucose absorption in 3T3-L1 adipocytes. A further investigation indicated that the b-L-arabinopyranose methyl glycoside on *C. pictus* plants tends to possess antidiabetic properties [16].

Table 4: Anti-diabetic effect of various *Costus* plants with recent studies

Plants	Model	Part/extract/drug used	Results	Reference
Costus pictus	Male wistar rats	Two groups- methanolic extract of *Costus pictus* (200 & 400 mg/kg p.o.), 3rd groups- metformin (225 mg/kg) & enalapril (3.2 mg/kg), 4th groups - metformin, enalapril and MECP (200 mg/kg) and 5th groups - metformin, enalapril and MECP (400 mg/kg)	Combination treatment of synthetic drugs and herbs (metformin, enalapril, and MECP) lowers blood glucose levels and have positive effects in managing diabetic nephropathy.	Sanaye et al., (2022)
Costus pictus D. Don	Alloxan-induced diabetic rats	Aqueous (CPAQ) and methanolic (CPME) extract of plant and/or in combination with metformin	Metformin and methanolic extract (co-administration) - heals tissue injury improve all metrics; increase effectiveness, and lowers blood glucose levels.	Naik et al., (2022)
Costus Speciosus	Male adults albino rats (Sprague strain)	1st group – control, 2nd group (hexane extract of rhizome - 250 mg/ kg B. W), third group (metformin -500 mg/ kg B. W), other 3 groups (STZ (45 mg/ kg B.W. /i.p.).	2nd and 3rd group showed enhancement and improvement of disruption of liver functions, renal functions, immunological and antioxidant properties, and pancreatic histology.	Kilany et al., (2022)
Costus spicatus	Albino wistar male rats	Oral administration rhizome extract of *Costus spicatus* to diabetic induced rats (500 mg/kg body weight)	500mg/kg of *C. spicatus* rhizome extract was found to have potential anti-diabetic effects	
Costus spicatus jacq	Albino wistar male rats	Streptozotocin (45mg/kgb.w.) and aqueous rhizome extract of *Costus spicatus* (500 mg/kg b.w)	Aqueous rhizome extract of *Costus spicatus* showed anti-diabetic effectiveness without causing liver damage when compared to Glibenclamide.	Azhagumad havan et al., (2018).
Costus igneus	Male albino rats	Crude extract of leaves of *Costus igneus*	*Costus igneus* (250mg/kg and 500mg/kg) shows potential anti-diabetic properties.	Chimurkar et al., (2018)
Costus igneus	wistar albino rats	Group I - Non-diabetic, Group II - streptozotocin induced, Group III Diabetic rats, Group IV to IX – different extract of *C. igneus* leaf	hexane extract of *C. igneus* leaves (200mg) decrease in level of blood sugar (114.8± 7.08) and 400mg extract reduces sugar at 91.6± 6.12.	Khanday et al., (2019)

Anti-cancer activity

Cancer or malignant disease is the major ailment that is commonly affecting people at different ages and genders throughout the world. It is a group of abnormal cells represented by uncontrolled cellular proliferation capable of invading or spreading towards further parts of the body. Apoptosis stated to be irregular or defective, plays a significant role in the pathological condition of cancer. This causes proliferation to continue uncontrolled growth, which creates cancerous cells that are resistant to natural death. To combat this, researchers concentrated on anticancer tactics that specifically target the uncontrollable growth of cancerous cells and the disorder of apoptosis. A collaborate approach of cell biology, *in vitro* and *in vivo* research and structural chemistry is the need of the hour to produce new anticancer drugs [17].

According to the [18], effective therapeutic treatment includes interventions like surgery,

chemotherapy, psychosocial support and radiotherapy. Due to the rising rate of cancer-related mortality and undesirable side effects, these therapies dropped short of the criteria for a successful cancer treatment. Hence, nontoxic therapeutic and preventive agents derived from plants should be proposed as an alternative. For the purpose of creating new anticancer agents, it is imperative to find new bioactive compounds. Plants are the most important sources of these compounds but the chemical constituent is still poorly understood.

The leaves of insulin plant, *Costus pictus D. Don*, are used as a nutritional supplement to treat diabetes. Although the antidiabetic effects of this plant are well established, the mode of action and impact on various cell types are still unknown. On investigation of anti-cancer potential in leaf extracts of *Costus pictus D. Don* through breast cancer cell lines (MCF-7), active ingredients like alkaloids, terpenoids, steroids, glycosides and proteins were found [18]. Treatment with different solvents of *Costus pictus* leaf extracts showed that there was decrease in growth and survival of breast cancer cell lines. Since, the most popular *in vitro* models used in cancer cell lines are derived from tumors, characterization of MCF-7 cell lines demonstrated that they are good models for studying the biological pathways involved in cancer and also proved to be an effective tool in genetic studies of breast cancer. It was evident in their study that the selected leaf extracts of the *Costus pictus* showed inhibition against MCF-7 cell lines. The same author studied about the aqueous leaf extract of *Costus pictus* in order to detect antitumor activity against Dalton's Ascites Lymphoma (DAL) induced cancer in mice. The study revealed that treatment at doses of 200 mg/kg and 400 mg/kg body weight inhibited the tumor activity by reinstating various parameters (tumor, hematological and serum biochemical) and the histoarchitecture of the tissues in the liver (Fig.2).

A study on anticancer activity of *C. pictus* methanolic extract (CPME) against several cancer and normal cells revealed that CPME showed significant cytotoxic activity on Liver hepatocellular carcinoma cells (Hep G2) and also specified that HDAC enzymes have negative effects [19]. Hence, HDAC inhibition was performed on Hep G2 cells to determine whether *C. pictus'* anticancer activity is due to HDAC regulation. The result attributed that there was a significant decrease in HDAC inhibition (55%). Several studies have suggested that HDAC inhibitors may inhibit cell proliferation and induce apoptosis in tumor cells. Besides leaf extracts, a study conducted on bark extracts of the *Costus pictus* D. Don significantly reduced the viability of the A549 lung carcinoma cell line through a dose-dependent manner [20].

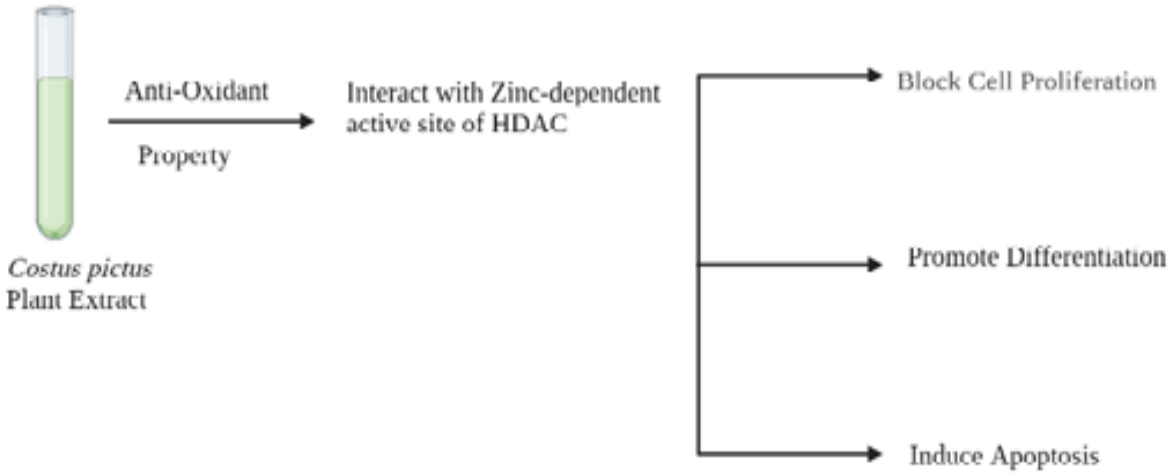

Figure 2: Summary of the molecular mechanism of Anti-Cancer Property of *Costus pictus*

Anti-inflammatory properties

Numerous diseases (chronic inflammatory diseases, hyperglycemia, cancer and rheumatoid arthritis) are caused due to inflammation, which is a serious complication and causative agent for the development [21]. Inflammatory mediators usually involve eicosanoids such as leukotrienes and prostaglandins. They are closely attributed to inflammatory disorders that are synthesized by enzymes called cyclooxygenases (COX) and lipoxygenases (LOX) within many cells in the body. COX enzymes are vital in response to systemic inflammation that regulates downstream of immune cell stimulation and inflammatory cytokine formation (Fig.3). LOX are a family of non-heme dioxygenases that are essential for the production of leukotrienes, which have been linked to the pathophysiology of a number of inflammatory ailments [22].

Reduced exercise, dormant lifestyle behavior and decreased physical activity are all associated with elevated signs of chronic inflammatory process of type 2

diabetes mellitus. Molecules that promote inflammation are interleukin, C - reactive protein and pro-inflammatory Interleukin-1 and alpha-tumor necrosis factor. These inflammation promoting molecules discharged into the blood stream and then inside particular organs might be responsible for the cause of metabolic inflammation. IL-1 is the most effective molecule of the innate immune system that inhibits cell function and induce death by stimulating the nuclear factor kappa-light-chain-enhancer of activate B cells (NF-B) [23].

β-amyrin a pentacyclic triterpene that exhibit anti-inflammatory properties was identified from the leaves of *Costus* plants by an *in-vitro* model through LPS-induced human peripheral blood mononuclear cells and a carrageenan-induced rat model. Numerous findings affirmed the methods involved in the basis of mechanism of the anti–inflammatory activity of β-amyrin. α, β-amyrin improved periodon in rat model that was attributed to reduction in the production of inflammatory causing cytokine TNF- α [24]. They express anti-inflammatory properties by reducing the cytokines production and expression due to NF-κB and cyclooxygenase. It can therefore be concluded that α, β-amyrin improves dyslipidemia and hyperglycemia by recovering glucose tolerance in mice and weakens atherogenic health risks, possibly through anti-inflammatory and antioxidant effects [25].

The rhizomes of *C. speciosus* contained 8 bioactive chemical compounds that showed marked reduction in the levels of PGE2, cytokines, lipoxgenase-5 and COX-2. [26]. The bioactive components primarily flavonoids and related polyphenols extracted from methanolic leaf extracts of *Costus pictus* were found to possess powerful anti-inflammatory activity against various kinds of ailments [27]. The methanolic extract of *Costus pictus* was also shown to significantly inhibit the formation of reactive oxygen species, which blocked the connection of nitric oxide at some stage in the inflammatory process [28].

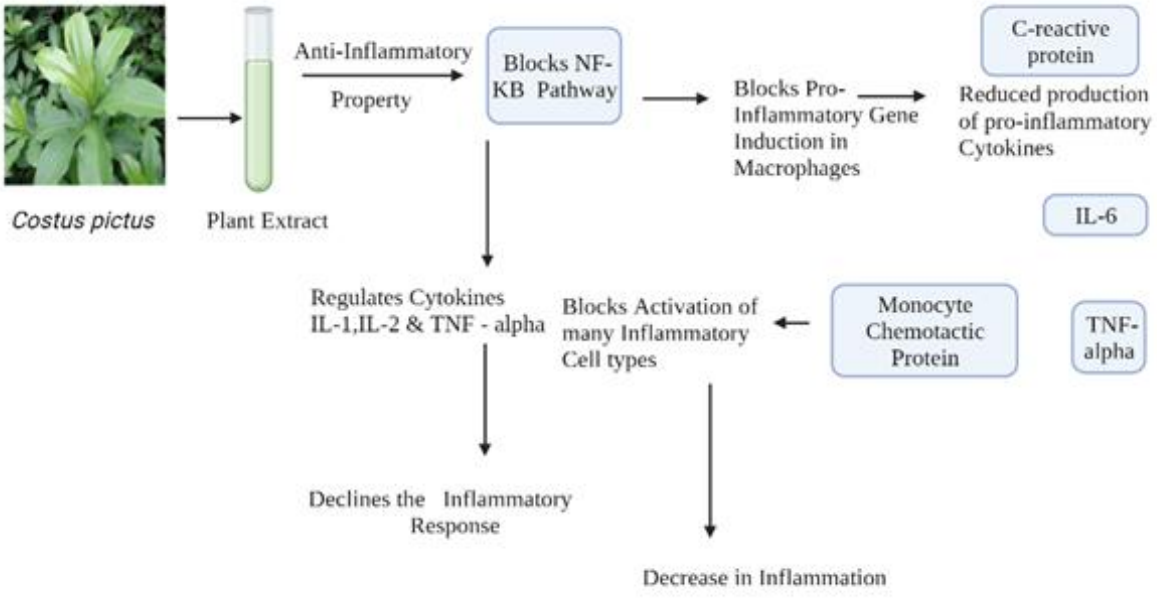

Figure 3: Summary of the molecular mechanism of Anti-Inflammatory Property of *Costus pictus*

Hepatoprotective property

The treatment of liver disorder is still a difficulty for contemporary medicine and liver ailments continue to cause severe health issues (Fig.4). The liver is engaged in various key activities, including metabolism, secretion and storage and it plays a crucial role in controlling physiological functions. It also detoxifies a range of medications and foreign substances and plays a crucial part in converting and removing the chemicals that are vulnerable to cause toxicity [29]. Because of the extensive and illogical over-the-counter medication in recent years, drug-induced liver disorders have been a significant source of worry. The most widely prescribed non-steroidal anti-inflammatory medicine is paracetamol/acetaminophen (NSAIDS). Although it is regarded to be safe at therapeutic doses, an overdose could result in deadly complications such as centrilobular liver necrosis. Antioxidant additives are a promising therapeutic approach for the controlling and treatment of liver ailments. Clinically approved treatments for liver disorders include polyherbal remedies and synthetic medicines which were used to treat liver damage [30]. The harmful consequences of highly reactive chemicals taking place on membrane phospholipids include lipid peroxidation, protein thiol oxidation, fragmentation of DNA, cell lysis and cell death [31]. Numerous investigations established that oxidative stress was a key pathophysiologic mechanism

found behind paracetamol-induced liver injury. Most common signs associated with liver damage was often represented by necrosis of hepatocytes and raised levels of various enzymes and proteins such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), bilirubin and albumin [32].

A recent study concluded that synthetic medication, silymarin was found to be equivalent to methanolic leaf extract of *Costus pictus* D which exhibits therapeutic potential against acute liver failure produced by paracetamol toxicity [33]. Flavonoids and phenolic acids found in the *Costus pictus* leaves not only scavenge free radicals, but also blocks free radicals production thereby restraining cellular damage [34].

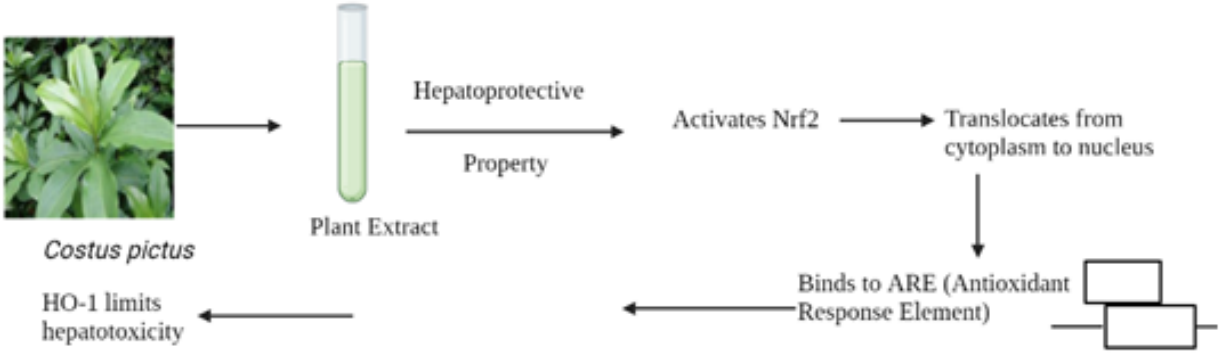

Figure 4: Summary of the molecular mechanism of hepatoprotective of *Costus pictus*

Analgesic activity

An undesirable feeling called pain is associated with real or potential tissue injury. Initially on, direct activation of the sensory nerve fibers is responsible for the cause of pain to be experienced. On the other end, inflammatory mediators are responsible for the discomfort at the delayed stage. Current pain killers and anti-inflammatory drugs have worked well, but they can have serious side effects like ulcers, osteoporosis, endocrine disruption and anaemia [35]. Opioids and non-opioids (NSAIDs and antipyretic analgesics) are two types of analgesics that are often practiced. Opioids still remains the cornerstone of pain treatment and it is the most effective and dependable centrally acting painkillers. Their usage is restricted because of the risk of addiction and negative effects. The negative side effects of NSAIDs' which are often used for mild-to-moderate pain includes gastrointestinal, renal and cardiac effects [36].

Studies on the analgesic potential of phytoconstituents in conventional medicinal plants are receiving more interest. They frequently exhibit adequate biological activity with smaller amount of side effects than manufactured medications. Essence of fresh leaves and stems from *Costus pictus* demonstrated a substantial and dosage dependent suppression of central and peripheral pain sensitivity in rats [37]. A recent study conducted by [38] in Wistar albino rats showed that the percentage of pain reduction by hydroalcoholic extract from *C.pictus* was 70% (68.23%) at 200 mg/kg, whereas it was higher than 70% (82.87%) at 400 mg/kg BW. This outcome was similar to that of the widely prescribed medications viz., morphine (87.85%) and diclofenac sodium (85.36) and proved that a dosage of 400 mg/kg could be appropriate for use in future research to determine analgesic effects. Long term usage of synthetic analgesic drugs may develop drug resistance and survival risk medication response. But, due to vast therapeutic range in herbal drugs long term usage will not produce any significant change.

Nephroprotective effects

Kidney ailments will be ranked as the sixth greatest cause of mortality near 2040. Several physiological malfunctions that are categorized as pre-, intra- and post-renal result in kidney impairment. Pre-renal factors include intestinal microbiota, rhabdomyolysis, and diabetes and liver disorders. Post-renal factors include prostate extension, prostate cancer, urethral blockages and bladder infections. Due to negative side-affects with synthetic drugs, the alternate option is the use of nephroprotective drugs synthesized from plants. There are several nephroprotective compounds available in plants that cure kidney ailments [39]. Many researchers had investigated about the possible mechanism behind the plant extracts or individual compounds interfering with molecular pathways to ameliorate kidney disorders using plants and phytochemicals as nephroprotective agents [40].

Experiments on lead induced kidney damage in albino rat model proved that *Costus* considerably restored the decreased superoxide dismutase (SOD), glutathione peroxidase (GSH-PX), glutathione-S-trasferase activity (GST) and catalase (CAT) levels thereby proving to have a nephroprotective activity [41]. Doxorubicin toxicity is linked with excessive free radical production and oxidative stress. Doxorubicin conversion to semiquinone radicals and iron anthracycline complex

synthesis are very reactive with proteins, DNA and membrane lipids that leads to severe nephrotoxicity [42]. Additionally, doxorubicins alter the equilibrium of endogenous antioxidants and free radicals, harming cellular and membrane components [43]. The *Costus pictus* extract treatment showed to inhibit lipid oxidation, which was accompanied by a return to normal levels of reduced glutathione and antioxidant enzymes. This mechanism demonstrated that the C*ostus* plants possessed potent anti-peroxidation and antioxidant properties. Hence the author came to a conclusion that the studied plant extracts confirmed nephroprotective effect against the doxorubicin-caused renal damage due to rich phytochemicals, notably antioxidant components [44].

Hypolipidemic activity

Hyperlipidemia is an important predisposing factor responsible for the occurrence and aggravation of cardiovascular illnesses such as coronary heart disease. A high concentration of total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) present in plasma is associated with an elevated risk of atherosclerotic diseases (Keys, 1975). High plasma cholesterol levels, as well as the production of reactive oxygen species (ROS) are responsible for the development of coronary artery disease (CAD) and atherosclerosis. The mechanism behind hypercholesterolemia is due to oxidative damage. Despite significant breakthroughs in illness detection, the efforts attempted to improve human life quality and proper disease treatment methods have still been remaining unfinished [45]. There is currently no effective treatment for many of these ailments besides significant negative or dangerous health risks. The alternate option is to use medicinal plants for hypolipidemic study. These plants serve as vital raw materials for the manufacture of drugs since they are a rich source of bioactive chemicals. It has been known that plants produce and store a variety of secondary metabolites, including glycosides, tannins, volatile oils and alkaloids [46].

The methanolic and aqueous leaf extracts (200 mg/kg) from the plant *Costus pictus* have showed to reduce diabetes-induced hyperlipidemia in rats [47]. In comparison to conventional drug-treated groups, methanolic extract (200 mg/kg) treatment significantly decreased total triglycerides, LDL, cholesterol and VLDL while increasing HDL. Thus, they have confirmed that methanolic extract had the most significant hypoglycemic and hypolipidemic action and it is a key antihyperglycemic for phytoconstituents research.

The pentacyclic triterpenes present in the *C. pictus* extract (α and β amyrins) may be responsible for hypolipidemic activity. These amyrins could have significant antihyperglycemic and antihyperlipidemic activities according to research stated by [48]. The reduced expression of lipogenic genes due to pentacyclic triterpenes showed its hypolipidemic impact. The same hypothesis applied to *C. pictus* extract that reduced hypercholesterolemia in PTU-induced thyroid dysfunction rats [49].

Neuroprotective activity

Any detrimental effect on the nervous system brought due to chemical, physical or biological substance that restricts an organism to survive, responding to environment is referred to as neurotoxicity [50]. The brain may be able to counteract the negative effects of short-term exposure caused due to neurotoxicants, but prolonged exposure, even at low concentrations, may result in damage to the brain [51]. Heavy metals like Cd, Pb, Hg and As exhibit neurotoxic effects [52] via typical pathways through oxidative reactions (ROS) and association with micronutrients [53]. Certain medicinal plants and their phytochemical compounds have attracted attention for their potential as medicinal herbs. However, due to several factors that include separation, nano-manufacturing technology, pathway methods and toxic effects, the use of such natural chemicals and their derivatives in the nanoscale size range appeared to be desirable for the treatment of neurodegenerative illnesses [54].

The *Costus afer* leaf extract (CALE) in combination with zinc proved to be helpful in reducing the neurotoxicity caused by a low dosage heavy metal cocktail in rats by reverting the pro-inflammatory, anti-inflammatory and histopathological alterations considerably [55]. The anti-alzheimer activity of *Costus pictus* extract was confirmed due to elevation in the levels of catalase, acetylcholine and glutathione peroxidase. The extracts of *Costus pictus* significantly (0.01) increased the level of glutathione in a dose dependent manner, which act as a remover for different electrophiles, singlet oxygen and chemical group radicals.

CONCLUSION

Costus pictus is rich in flavonoids and terpenoids, as well as other phytochemicals that function as an inducer of the mechanism in the treatment of several ailments. This plant has a significant antioxidant impact, followed by antihyperlipidemic, anti-inflammatory, antimicrobial, anticancer and antidiabetic property all of which are associated to the resolution of cardiovascular disorders such as coronary heart disease (CHD) and neurological disorders. In view of this, future attempts should be focused on evaluating *Costus pictus* plant in the long-term effects of bioactive compound and/or its constituents to cure diseases and the treatment of associated symptoms. Additionally, a thorough exploration is required into the risk analysis and safety evaluation of the pharmaceutical use of bioactive compound or its derivatives in the treatment of several illnesses. Concentrating on single compound or its

components might not be sufficient for treatment of certain diseases. Combining single compound with substances containing numerous modes of actions is expected to be more successful than single compound medications. Further, a multi target drug against various risk factors is a crucial approach and a contemporary method for treating several diseases particularly neurological disorders. Since, *Costus pictus* are blessed with multifaceted properties, we should not waste these plants by just allowing them to grow naturally and expire, instead harness them for future neurological research.

Conflict of interest statement

The authors declare that they have no conflicts of interest.

Acknowledgments

This work was supported financially and technically by Central Council for Research in Ayurvedic Sciences (CCRAS), Ministry of AYUSH. Govt. of India (CCRAS Sanction No:F.No.12-13/2021-CCRAS/Estt./Rectt/2541., Dated:17.08.2022) New Delhi and Department of Animal Nutrition, Veterinary College and Research Institute (TANUVAS), Theni-625 602, Tamil Nadu, India.

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