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MINI REVIEW

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Pharmacological effects of *Polyalthia cerasoides* (Roxb.) Bedd.: A brief review

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ABSTRACT

Polyalthia cerasoides (Roxb.) Bedd. is also known as *Guatteria cerasoides* or *Uvaria cerasoides* belonging to the family of Annonaceae. *Polyalthia cerasoides* is used in traditional and folklore system of medicine extensively across Asian and African countries for its various pharmacological properties as treatment of toothaches, fever, and combat stress. An exhaustive bibliographic search related to *P. cerasoides* noticed that a large number of bioactive compounds, such as aporphine alkaloids, sequiterpenes, diterpenes, Phenolics, and Isoquinolene compounds enriched the stem bark and roots. The scientific ethnopharmocological studies proved that it possesses a wide range of biological activities such as anti-inflammatory, antioxidant, antidiabetic, antimicrobial, hepatoprotective, anticancerous, analgesic studies, and antistress activities. Isolated bioactive compounds (Cerasoidine, Polyalthidin, laudanidine, codamine, bidebiline E, etc.) exhibits the antimalarial activity against Plasmodium falciparum, antimycobacterial activity against Mycobacterium tuberculosis and anticancer activities have been reported. Its efficacy on diseases proved the future usefulness of different species of *P. cerasoides*. The toxicity studies reveal its non-toxic effect even at larger doses. This review provides the scope of phytochemical, pharmacological, medicinal, and non-medicinal uses of *P. cerasoides*. Further extensive investigation on *P. cerasoides* for its therapeutic potential related to folklore claims and shed the light on its unexplored potentialities.

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KEYWORDS

Polyalthia cerasoides; bioactive compounds; pharmacological activities; folklore

Introduction

Plants are the richest repositories of diverse phytochemical compounds, which render them to serve as a potential source of bioactive components for the development of therapeutic drugs. A magnitude of change has been observed in usage of medicine, from allopathic toward natural/traditional medicine. Demand for plant-based medicines is increased, owing to its effectiveness, safeness, and restoring the natural ability of the body [1]. The main source for plant-based medicines is the countries like India, Africa, etc., which are rich in biodiversity. India is not only rich in biodiversity but also acquainted with vast knowledge of traditional medicine. Resurgence in the research areas like ethno pharmacology and pharmacology allied to traditional medicine revolutionized the elucidation of novel bioactive components [2]. In search of novel drugs from plants, based on the traditional knowledge, would be considered as a fruitful and promising approach for the development of effective therapeutic drugs than the available ones. *Polyalthia cerasoides* (Roxb.) Bedd. (Annonaceae), is a medium-sized tree (Fig. 1), growing to 10–20 m in height and 20–50 cm in diameter, and is found in mostly in Asian countries [3]. It is locally called as "Gutti dudduga or gutti palla chettu" in the Andhra Pradesh region; this is familiar for its edible fruits [4]. Andhra Pradesh and Tamil Nadu (States of India) tribal people use the fruits and stem bark of the plant used in folklore medicine, while African tribal's use the fruits, roots, and leaves of the plant

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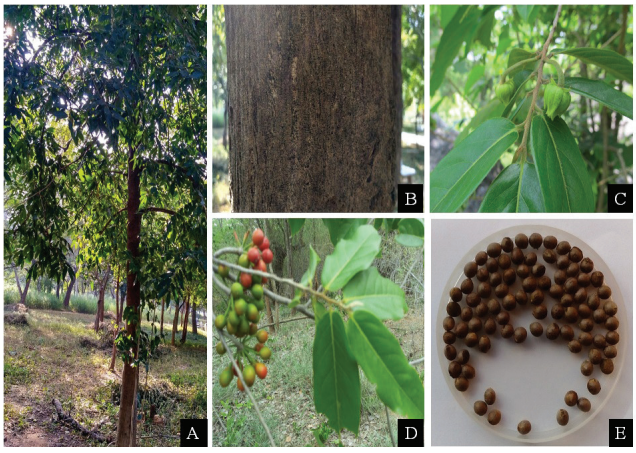


Figure 1. Photographic representation of *Polyalthia cerasoides* (Roxb.) Bedd. (A): Tree, (B): bark, (C): flower, (D): fruits, and (E): seeds.

for treatment of toothaches, fever, as an aphrodisiac, as a deparasitant, and as an anti-inflammatory. Stem bark of *P. cerasoides* reduces the brain stress [5]. The present review summarized the plant profile, phytochemistry, and ethnopharmocological scientific proven activities of *P. cerasoides*. It is also mentioned the need of clinical studies of isolated compounds to develop the novel therapeutic drugs from this natural resource.

Taxonomy and Distribution

Its taxonomy and nomenclature are as follows: Plant name: *Polyalthia cerasoides*; Kingdom: Plantae; Phylum: Tracheophyta; Class: Magnoliopsida ; Order: Magnoliales; Family: Annonaceae; Genus: *Polyalthia*; Species: *cerasoides*. It is mainly distributed in Africa, Burma, China, India, and Thailand [3,6].

Synonyms

Latin: *Polyalthia cerasoides* syn: *Guatteria cerasoides, Uvaria cerasoides*

Common names

Telugu:	Gutti palla chettu/Gutti Dudduga
Hindi:	Kudumi
Tamil:	Nedunarai
Kanada:	Habbe/Sanhesare
Malayalam:	Cherunedunar, Narela

Ethnomedicinal significance

Powder from Stem bark and seeds of *P. cerasoides* used to combat stress by the local medical practitioners of the Tirunelveli district of Tamil Nadu [7]. Stem bark used as a folk medicine by the tribal people of north Odisha to treat diabetes [8]. Root decoction used as traditionally as a tonic and febrifuge by the native people in Thailand [9].

Phytochemical Profile

Bhargavi et al. [6] reported the presence of phytochemical constituents like Alkaloids, Tannins, Terpenoids, Saponins, and Phenols from stem bark extracts. Rawani et al. [10] reported the presence of saponins, steroids, and Terpenoids from the fruit extracts (aqueous).

Bioactive constituents

A large number of bioactive constituents reported from roots and stem (Table 1).

Roots

Aporphine alkaloid-bidebiline E, octadeca-9,11,13-triynoic acid, three sesquiterpenes, α-humulene, Caryophyllene oxide, α-cadinol, four Isoquinoline alkaloids, laudanosine, laudanidine, codamine, reticuline; these nine compounds reported by Kanokmedhakul et al. [11]. Cerasoidine, a Bis-aporphine alkaloid reported by Shono et al. [12].

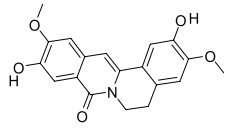
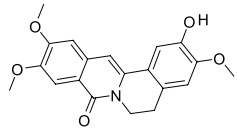
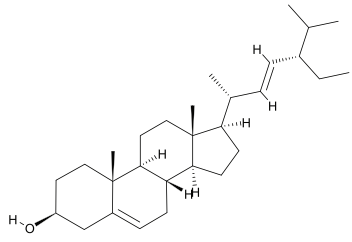
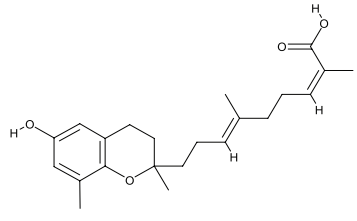
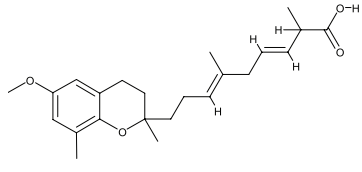
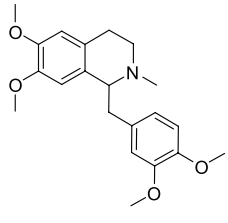
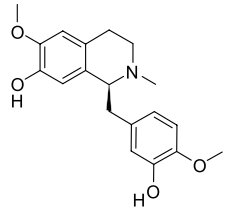
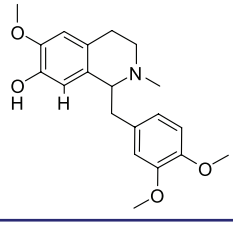
Stem

The liquid chromatography–mass spectrometry studies have been reported the 28 bioactive compounds such as, Humulene, Laudanosine, Reticuline, Maculosine, Retrorsine N-oxide, Delcosine, Ergosine, Thalicarpine, Azetidine 2-carboxylic acid, Isovaleric acid, Methyl amino alanine, Phenethylamine, Methylcytosine, Deoxyquercetin, Acetoxyvalerenic acid, methyl linolenate, Caffeoylmalic acid, Ellagic acid, Hydroxycyanthin, Benzoylmethylecgonine, Eupaformonin, Pelarginidin chloride, Indicaxanthin, Galangin TrimethylEther, Dihydroxy Stearic Acid, Myricetin, Rutacridone Epoxide, Caffeoylshikimic acid; Ethylcetatel extract yielded two oxoprotoberberine alkaloids, cerasoidine, and cerasonine [13,14]; Methanol extract yielded N-4(-hydroxy-B-Phenethyl-4-hydroxycinnamide; Hexane extract yielded stigmasterol; Dichloromethane extract yielded stigmasterol and triterpenes. Polycerasoidin, Polycerasoidol, and Polyalthidin-a benzopyran derivative [15].

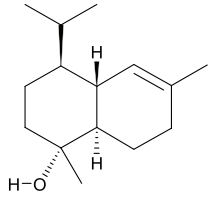
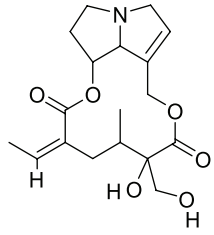
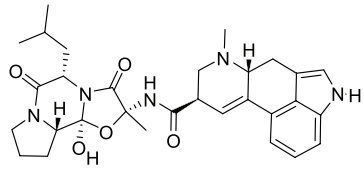
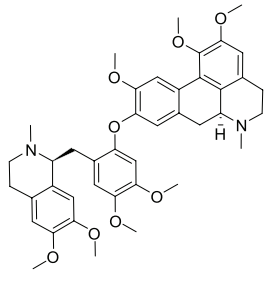
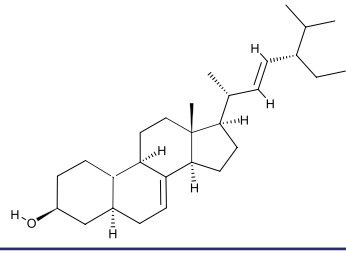
Antibacterial Activity

The extensive use of antibiotics results in the development of antibiotic resistant bacteria, and proved the insufficiency of the available antimicrobial drugs. This rising incidence of antibiotic resistant

Table 1. Phytochemicals/bioactive compounds isolated from the *P. cerasoides* (Roxb.) Bedd.

Phytochemical/compound name	Plant part	Extract medium	Structure	References
Cerasodine	Root, stem	ethylcetatel		[12–14]
Cerasonine	Stem	ehtylcetatel		[14]
Stigmasterol	Stem	Hexane, dichloromethane		[15]
Polycerasoidol	Stem	Benzopyran derivative		[15]
Polyathidin	Stem	Benzopyran derivative		[15]
Laudanosine	Root, stem	hexane, EtOAc, and MeOH		[11]
Reticuline	Root, stem	hexane, EtOAc, and MeOH		[11,13,14]
Codamine	Root	hexane, EtOAc, and MeOH		[11]

continued

Phytochemical/compound name	Plant part	Extract medium	Structure	References
ά- cadinol	Root	EtOAc		[11]
Retrorsine	Stem	Ethanol		[13]
Ergosine	Stem	Ethanol, EtOAc		[13,14]
Thalicarpine	Stem	Ethanol, EtOAc		[13,14]
α-Spinasterol	Seed	Petroleum ether		[33]

bacteria led the researchers to investigate the potent antimicrobial compounds from various medicinal plants. Ravikumar et al. [16] reported, stem bark extracts of *P. cerasoides* exhibited well marked antimicrobial potential against *Pseudomonas*, *Klebsiella*, and *Staphylococcus* (24 clinical strains, 8 of each). All the strains showed more susceptibility to the Ethyl acetate (EA) fraction than compared with Dichloromethane (DCM) fraction. Zone of inhibition for *Klebsiella pneumoniae* (EA 20.12 ± 0.29 mm, DCM 14.30 ± 0.17 mm), *Pseudomonas aeruginosa* (EA 20.00 ± 0.11 mm, 13.52 ± 0.22 mm), and *Staphylococcus aureus* (EA 18.35 ± 0.28 mm, DCM 14.47 ± 0.18 mm). The microbial strains showed that potential susceptibility with ethyl acetate fraction, because of, which consists two berberine alkaloids such as cerasoidin and cerasonine. DCM fraction exhibited less effective response because of benzopyran alkaloids [16].

Rawani et al. [10] reported fruit extracts [Aqueous (Aq) and Chloroform Methanol (CM) (1:1)] of *P. cerasoides* possess antimicrobial potential against four bacterial strains. *Staphylococcus aureus* (Aq 14.03 ± 0.008 mm, CM 30.80 ± 0.57), *Bacillus subtilis* (Aq 15.20 ± 0.15 mm, CM 26.30 ± 0.25), *Escherichia coli* (Aq 18.57 ± 0.32 mm, CM 28.27 ± 0.32 mm), and *Pseudomonas aeruginosa* (Aq 18.37 ± 0.15, CM 30.33 ± 0.24 mm). Chloroform: Methanol (1:1) extracts showed effective antimicrobial response than the aqueous extracts [10].

Minimum Inhibitory Concentration Studies

Treeratnapiboon et al. [9] reported the minimum inhibitory concentration (MIC) studies of Hexane and Dichloromethane extracts from the roots of *P. cerasoides*. Among 27 strains (18 reference strains and 9 clinical isolates), 14 strains are Gram-negative and 11 are Gram-positive bacteria and two are fungal strains. Both the extracts selectively displayed the antigrowth activity against Gram-positive bacteria. Dichloromethane extract exhibited the highest activity against *Corynebacterium diphtheriae* with MIC of 32 μg/ml and the least with *Bacillus cereus* (128 μg/ml) and *Micrococcus luteus* (256 μg/ml) [9].

Acute Toxicity Studies

Goudarshivananavar et al. [17] analyzed the toxic effect of *P. cerasoides* extracts at various concentrations 50, 100, 200, 500, 1,000, 2,000 mg/kg b.w. and reported no toxicity of plant extracts even at 2,000 mg/kg b.w.

Pharmacological Activities of *P. cerasoides*

Polyalthia cerasoides have the several pharmacological activities, proved by scientific observations of experimental works. The bark, leaves, and fruits are extensively used in traditional medicine due to the presence of several phytoconstituents like alkaloids, terpenoids, saponins, and flavonoids. Scientific evaluations of isolated bio-compounds have ethnomedicinal and novel pharmacological effects. Table 2 represents the pharmacological findings obtained from various parts of the plant in different solvent extractions.

Antidiabetic Activity

Diabetes is a metabolic disorder that occurs due to insulin imbalance production. Some of the physiological or developmental factor effects on pancreatic beta cells cause hormonal imbalance probably diabetes [18]. Current lifestyle, such as mistimed sleeping, shift work, or eating at abnormal night-time hours, have been related to type 2 diabetes, obesity, and metabolic syndrome [19]. The number of people who have diabetes has raised steeply more than 371 million persons globally, and is projected to affect 522 million people by the year 2030 [20]. In the developing countries, phytotherapy play a prominent role in the management of the disease for some decades. Identification of plant materials that can manage diabetes and its complications would save millions of people [21]. A study was conducted to test the antidiabetic activity by *P. cerasoides* stem bark. After treating streptozotocin (STZ) diabetic rats for 21 days (chronic study) with a single dose of pcEE (400 mg/kg bw) was shown an effective antidiabetic role by significantly lowering the fasting blood glucose (FBG) levels in diabetic rats. The decrease in blood glucose levels was from 349 ± 7.7 mg/dl (Diabetic rat) to 168 ± 6.4 mg/dl (control) from 0 to 21 days' time period. The decreasing glucose levels were nearly similar to the effect of standard drug glibenclamide (341.8 ± 7.8 mg/dl to 159.3 ± 6.3 mg/dl). However, acute exposure of different plant extraction in n-hexane, ethyl acetate, ethanol, and aqueous extracts of *P. cerasoides* stem bark to 12 hours fasted normal and STZ induced diabetic rats at a dose of 200, 400, and 600 mg/kg bw for acute studies. Among four extracts, PcEE and PcEAE (400 mg/kg bw) showed effects on blood glucose levels. However, PcEAE showed the least effect on the reduction of blood glucose compared with PcEE. The remaining two extracts did not show any positive effect in FBG levels. Nearly, 400 mg/kg bw of pcEE treated showed the potential increasing the body weights (179.1 ± 4.9 to 185.5 ± 8.3) but diabetic rats showed the decreased body weights when compared with control rats. Liver and kidney morphological changes were prevented by pcEE (400 mg/kg bw) administration compared with diabetic rats. It clearly reveals that *P. cerasoides* has the antidiabetic effect [6]. Bhargavi et al. [22] reported the hypolipidemic effect of the stem bark ethanolic extract at 400 mg/kg bw. Changes the lipid profile (lowered the total cholesterol, triglycerides, low-density lipids, and very low density lipids) and serum biochemical marker enzymes like, aspartate transaminase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) in STZ induced rat models [22].

Increase the levels of serum lipid profile levels, such as cholesterol, triglycerides, low density lipoprotein (LDL), very low density lipoprotein levels, and decreasing levels of high density lipoprotein (HDL) levels in the diabetic rats may be due to insulin activates lipoprotein lipase and hydrolysis of triglycerides [23]. Insulin increases uptake of fatty acids into adipose tissue and increases triglyceride synthesis. HDL is an anti-atherogenic lipoprotein [24]. The level of HDL-cholesterol slightly increased after the administration of ethanolic extract of *P. cerasoides* stem bark at 400 mg/kg bw [22]. This might be due to increase in the activity of lecithin

Table 2. Pharmacological activities of *P. cerasoides* (Roxb.) Bedd.

Activity	Plant part	Extraction medium	Against toxic factor	Animal modal/mode of study	Dosage	Administration route	Result	Reference
Anti stress activity	Stem bark	Ethanol	Cold immobilization stress	Albino rat/*in vivo*	100 mg/kg bw	Gastric Intubation.	Increase the levels of monoamine oxidase (MAO), decreasing the elevated levels of 5-HT and 5-HIAA induced by the stress.	[7]
Anticancerous/ Antipropliferative	Seeds	Petroleumether extract	Methylmethane sulfonate	Swiss albino mice/ CACO-2 cell lines	5–10 mg/kg bw	I.P (Intraperitoneal)	The compounds Clerodane diterpenoid, Spinasterol, and α-Spinasterol showed antiproliferative action on CACO-2 cell line and also showed anticancerous activity against the MMS-induced mutagencity in albino mice.	[33]
Hepatoprotective	Stem bark	Ethyl acetate	CCl_4	Albino rat/*in vivo*	250 and 500 mg/ kg bw	P.O (orally)	SOD and CAT levels increased, elevated levels of LPO reduced to normal	[17]
	Stem bark	Ethanolic extract	CCl_4	Albino rat/*in vivo*	100 mg/kg bw	Gastric intubation.	Elevated levels of serum and tissue SGPT, SGOT, and Alkaline phosphates significantly reduced, total proteins levels increased, and lipidperoxidation levels decreased	[29]
Antioxidant	Stem bark	Alcoholic		Swiss albino mice and *in-vitro* studies	100 mg/kg body weight	orally	DPPH, hydroxyl radicals, Superoxide anion scavenging, reducing power assays scavenging by P.c bark extract	[32]
Anti-inflamatory	Stem bark	Ethyl acetate/ petroleum ether	Carrageenan	Albino rat	100 and 200 mg/ kg bw	p.o	Ehtylacetate fraction inhibits the paw edema by 57.38% and 68.5% when compared with petroleum ether fraction (26.22% and 36.06%). Ethyl acetate fraction effective inhibition and similar to the effect of standard drug Diclofenac (75.4%)	[17]
Analgesic activity	Stem bark	Ethyl acetate/ petroleum ether	Acetic acid	rat	100 & 200mg/ kg bw	P.o	Ehtylacetate fraction reduces the pain by 61.73% and 63.68% compared with petroleum ether (28.2% and 48.8%), ethyl acetate fraction significantly reduced the pain as standard drug diclofenac (63.75%)	[17]
Antidiabetic	Stem bark	Methanol	STZ	Rat	200 and 400 mg/ kg bw	Oral	FBG levels significantly lowered in PcEE group compared with STZ-treated group.	[6]
	Stem bark	Ethanol	STZ	Rat	400 mg/kg bw	oral	Serum marker enzymes ALT, AST, and ALP levels lowered, and lipid profile levels [total cholesterol, TG, LDL, and (acetylated low density lipoprotein (ALDL))] retained to normal and HDL levels not changed.	[22]

cholesterol acyl transferase, which may contribute to the regulation of blood lipids. AST, ALT, and ALP are considered as a part of liver toxicity markers. In streptozotocin-induced diabetic animals, change in the serum enzymes is directly related to changes in the metabolic functions of AST, ALT, and ALP. It has been reported that the increased aminotransferase activities under insulin deficiency [25] were responsible for the increased gluconeogenesis and ketogenesis during diabetic. The mechanism, by which the serum aspartate and alanine aminotransferases are raised in diabetic untreated, may involve increased liberation of these enzymes from tissues (mainly liver), owing to oxidative stress or the formation of advanced glycosylation end product [26]. The increase in the activities of these enzymes in serum of diabetic control might be induced due to liver dysfunction.

Hepatoprotective Activity

Hepatic diseases are one of the most serious and common disease to the mankind. Pathogenesis of the hepatic diseases is due to the oxidative stress and the inflammation [27]. Despite, tremendous advances in modern medicine, the management of liver disease is still a major challenge [28]. A promising hepatoprotective activity with stem bark extracts of *P. cerasoides* was evidenced against Carbon tetrachloride (CCl_4)-induced hepatotoxicity in albino rats. Alcoholic extract of 100 mg/kg bw reduces the lipid peroxidation and serum phosphate levels in the liver. Liver marker enzymes glutamic oxaloacetic transminase [(serum glutamic oxaloacetic transaminase (SGOT)), AST], glutamic pyruvic transaminase [(serum glutamic pyruvic transaminase (SGPT)), ALT], and alkaline phosphatase levels were significantly increased in blood serum as well as liver tissue in the CCl_4-treated rats when compared with the control. The elevated levels of key marker enzymes were reduced to normal levels in the alcoholic extract *P. cerasoides* (100 mg/kg bw for 7-day treatment). Decreased total protein levels and increased (lipid peroxidation (LPO)) levels were neutralized in the plant extract administered group of rats, indicating that the plant extract may scavenges the reactive oxygen species produced by CCL_4 metabolism in which could be acted as hepatoprotective drug agent [29]. Goudarshivananavar et al. [17] reported the ethyl acetate fraction at dose 250 and 500 mg/kg bw significantly improved the levels of liver antioxidant enzymes such as Catalase (368.2 ± 1.54 and 398.4 ± 5.23), Superoxide dismutase (SOD) (15.11 ± 1.58 and 19.54 ± 3.22), and peroxides (118.78 ± 5.12 and 131.32 ± 4.30), when compared with CCl_4-induced hepatic rats (121.54 ± 1.53, 8.48 ± 0.12, and 48.43 ± 2.70 units/mg). Increased depleted antioxidant enzyme levels in the liver tissue may prove that the plant extract protecting the structural integrity of hepatic cells or reconstruction of necrotic hepatic cells. Effectiveness of the plant extract was similar to the standard drug Silymarin [17]. These findings suggest the presence of potential bioactive components to normalize the antioxidant enzymes that are involved in combating reactive oxygen species (ROS), and thus protecting the structural integrity of hepatocyte cells.

Antioxidant Activity

Oxidative stress causes the generation of free hydroxyl radicals and ROS have been implicated in degenerative/pathological process. Free radicals aroused during the stress have a broad range of effects in biological systems [30]. Plant-based medicines serve as an excellent antioxidant because of the presence of various phenolic contents. Natural Plant-based antioxidants protect from the damaging effect of oxidative stress by quenching the ROS and OH^- free radicals, and therefore, useful in the treatment of cancer, cardiovascular, and anti-inflammatory diseases [31]. Ravikumar et al. [32] analyzed the antioxidative potential of alcoholic bark extracts of *P. cerasoides* by using 2,2-diphenyl-1-picrylhydrazyl (DPPH). The hydroxyl radical, Superoxide anion scavenging, and reducing power assays were reported the dose-dependent inhibition of DPPH scavenging activity and indicates 50% inhibition rate. This concentration was designated to 0.589 µg/ml of tannic acid/mg of plant extract equivalency. The significant antioxidant potential of *P. cerasoides* extracts might be attributed to the presence of polyphenols (Hydroxycinnamic acid and Ellagic acid). This study shed the light on the potential antioxidant properties of *P. cerasoides* and supports its use to develop potent antioxidant drugs [32]. Ethylacetate fraction exhibited DPPH radical (1–100 µg/ml) scavenging activity with inhibitory concentration (IC) 50 is about 42.43 µg/ml, whereas the IC value of standard ascorbic acid (1–5 µg/ml) was 3.19 µg/ml [17].

Anti-Stress Activity

Padma et al. [7] noticed the anti-stress capability of *P. cerasoides* stem bark alcoholic extracts. Albino

rats were used as models for the study. Cold immobilization stress induced in rats after treating with plant extracts. Stress causes the rise in the level of enzymes like Nor-epinepephrine, dopamine, 5-hydroxytryptamine (5-HT), 5-hydroxy Indole acetic acid (HIAA) in control group rats. Plant extract treated group, plant extract at dose 100 mg/kg bw for a period of 16 days normalized the levels of all the enzymes. Pretreatment with plant extracts resulted in increasing the level of Monoamine oxidase and reduced the levels of other enzymes induced by stress. The elevated level of monoamine oxidase by the plant extracts indicates its adaptogenic potential. This study authenticates the use of *P. cerasoides* stem bark by the folklore (Tirunelveli district, Tamil Nadu) as a tonic to combat the condition of stress [7].

Anticancerous/Antiproliferative Studies

A number of plant-based medicines currently used as effective anticancerous agents like vinblastine, vincristidine, paclitaxol, bleomycin, cisplatin, prednisome, and procarbasome. Ravikumar et al. [33] reported antiproliferative effect of isolated compounds spinasterol and clerodane diterpenoid on CACO-2 cell lines. Clerodane diterpenoids induce apoptosis (cell death) effective at lower concentrations. Spinastrerol and α-spinasterol showed an antiproliferative effect in a dose-dependent manner. A significant activity was observed at 30, 60, and 80 nm compared with the reference standard drug paclitaxol. Clerodane diterpenoid, Spinastrerol, and α- spinasterol exhibited Antiproliferative action at various concentrations with an IC_{50} value of 28.6 + 4.54 nM/ml, 57.7 + 6.81 nM/ml, 60.0 + 7.10 nM/ml [33]. Banjerdpongchai et al. [34] recently proved the anticancer property of *P. cerasoides*. The purified compound the 6, 8-dihydroxy-7-methoxy-1-methyl-azafluorenone (DMMA) isolated from roots of the plant. The inhibitory concentrations at 20% and 50% (IC_{20} and IC_{50}) of DMMA toward Human Cancer Cells HL-60 (18.7 and 46.7 μM), U937 (11.7 and 29.2 μM), MOLT-4 (14.0 and 35.0 μM), HepG2 (7.4 and 20.1 μM), MDA-MB231 (16.7 and 55.6 μM), and PBMCs (12.4 and 31.1 μM). DMMA inhibited the five human cancer cell proliferations in a dose-dependent manner from (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT)) assay, HepG2 cells were the most sensitive to and MDA-MB231 cells were the most resistant against DMMA-induced Cytotoxicity as showed by the IC_{50} levels [34]. Clerodane diterpenoids was induced the apoptosis by interfering with topoisomerase-II inhibition, whereas phytosterols induce apoptosis by BCL2 Associated X (Bax) apoptosis regulator protein activation [35]. This study authenticates the use of diterpenoids and phytosterols from the *P. cerasoides* seeds to develop effective anticancerous drugs in near future.

Anti-Inflammatory Activity

Polyalthia cerasoides stem bark extracts possess significant anti-inflammatory activity. Carrageenan-induced paw edema in Swiss albino rats used to explore the anti-inflammatory effect of the plant extract. Ethyl acetate fraction at dose 100 and 200 mg/kg bw inhibited the paw edema by 57.38% and 68.85%, and the petroleum ether fraction was 26.22% and 36.06%. Ethyl acetate fraction exhibited effective inhibition and it is similar to the effect of standard drug diclofenac (75.4%) [17].

Analgesic Activity

Goudarshivananavar et al. [17] analyzed the analgesic property of *P. cerasoides* petroleum ether and ethyl acetate extracts against acetic acid induced writhing model and reported the effectiveness of ethyl acetate extract at dose 100 and 200 mg/kg bw reduced the pain by 61.73% and 63.68%, whereas petroleum ether reduced the pain by 28.2% and 48.8%. Ethyl acetate fraction showed significant reduction of pain, similar to standard drug diclofenac (63.75%) [17].

Antimalarial Activity/Mycobacterium Activity

Malaria is the major parasitic disease, mostly found in tropical countries and other countries. Present days, it leads to major global public health problem spread of drug resistance and limited number of effective drugs [36]. This necessitates searching the safe and effective antimalarial drugs alternative to the existing ones. Traditional medicinal knowledge yields the anti-malarial drugs like quinine and artemesin and their efficiency to control malaria, stimulated many researchers to find the similar potential anti-malarial drug from the plant sources [37]. Kanokmedhakul et al. [11] reported the antimalarial activity against the *P. falciparum* (K1, multidrug-resistant strain). The isolated compounds bidebiline E(1), octadeca-9,11,13-triynoic acid (2), caryophyllene oxide (4), codamine (7), and

laudanidine (8) from *P. cerasoides* root extraction (various solvents) exhibits the antimalarial activity. Compounds 1, 2, 4, 7, and 8 showed an inhibitory concentration of 50% reduction in parasite growth of *P. falciparum* were 4.2, 5.0, 2.8, 4.2, and 7.0 μg/ml; among these, compounds 8 and 2 showed efficient antimalarial activity and compounds 1 and 7 exhibit equal inhibitory concentration (IC_{50}) but compound 4 showed the moderate IC_{50}. Compound 3 (alpha-humulene) did not show any antimalarial activity [11].

Compounds 1, 2, and 3 possess the Antimycobacterial activity against *M. tuberculosis* H37Ra using the microplate Alamar Blue assay with reference standard drugs isoniazid and kanamycin sulfate. MIC of compound 1 showed 6.25 μg/ml, compound 2 was 6.25 μg/ml, and compound 3 represents with same MIC (6.25 μg/ml) as 1, 2 compounds, whereas compounds 4, 7, and 8 did not show any inhibitory action against the *M. tuberculosis*, they showed inactive action [11].

Conclusion

Polyalthia cerasoides stem bark and fruits are used by the folklore as a traditional medicine to combat the condition of the stress. Phytochemical screening revealed the presence of tannins, phenols, alkaloids, triterpinoids, and saponins. However, the seeds possess the sterols. Pharmacological studies revealed the significant effect of plant extracts similar to that of standard drugs. The largest number of compounds is isolated from root and stem barks but the pharmacological studies on isolated compounds are limited. However, the isolated bioactive compound like 6,8-dihydroxy-7-methoxy-1-methyl-azafluorenone showed the antiproliferative effect on human cancer cells. Codamine, laudanidine, bidebiline E, and caryophyllene oxide showed very efficient antimalarial activity against the *P. falciparum*. Even though it is used as a traditional medicine for combating stress, for a long time, only the effect of crude extract was reported. Present review highlighted the pharmacological activities reported from previous studies, and stressed the need of pharmacological and clinical studies to evaluate the effectiveness of bioactive compounds from *P. cerasoides*. This review provides the scope for further investigation of unexplored potentialities (anti-stress compounds) and the possibility to develop the novel and the most effective anti-stress medicine.

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