International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

An overview on herbal plant: Polyalthia longifolia Thwaites

Kirti Rai, Harshita Mishra,Albert Alex, Dr Satyender Dr kajila Dr Sarthak Bhattacharya
HIMT College of Pharmacy, Greater Noida - 201310, Uttar Pradesh, India.

Submitted: 25-02-2022 Accepted: 02-03-2022

ABSTRACT:
Medicinal herbs are a gift from nature to help people live long, healthy lives free of illness. They are crucial for our well-being. The medicinal plant business in India has a long and illustrious history and is still highly regarded today despite India having one of the world's most diversified medical cultures. As elixirs for treating various ailments, medicinal plants are thought to be far safer than synthetic pharmaceuticals. More than 2,000 medicinal plants have been identified in our country. A native of the arid parts of India, Polyalthia longifolia is known as "Ashoka" in Pakistan and Sri Lanka, where it is widely cultivated. Indigenous medicine utilises this herb as an antipyretic. It's been found that the bark and leaves of this plant have antibacterial properties, cytotoxic effects, antiulcer properties, hypoglycemic properties, and an antihypertensive effect. P. longifolia pharmacologic properties are thoroughly examined in this study in an effort to point the way for future research.
Keywords: Polyalthia longifolia, phytochemicals, pharmacological activities

I. INTRODUCTION:

There are about 350 Polyalthia species in the Annonaceae family, with the majority of them located in Southeast Asia, Africa, and Australia/New Zealand. 'Polyalthia longifolia, often known as the "Green Champa" or the "Buddha Tree," is in fact what you're looking at.P. longifolia (sometimes known as the "street tree") is widely evaluated for its ability to reduce noise pollution. P. longifolia's symmetrical pyramidal growth and pendulous branches allow it to reach over 15.0 m. The wide spreading branches of P. angustifolia create a pyramidal crown with grey and smooth bark.

Polyalthia gets its name from Greek origins meaning "many" and "treatment." It is used to treat duodenal ulcers in Ayurvedic medicine and in traditional decoctions for a number of diseases. P. longifolian bark and leaves have also been used to treat bacterial infections, inflammation, diabetes, and various digestive ailments.

Before reviewing Polyalthia and P. longifolia, previous studies sum up the overall phytochemistry and pharmacological properties of Polyalthia extracts. A evaluation of the medicinal uses of P. longifolia chemical components has not been done to our knowledge. Consequently, in this present examination, the phytochemistry and the pharmacological investigations of this medicinal plant will be summarised in order to describe its several uses.

Scientific Classification:
Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliophyta
Subclass: Magnoliales
Order: Magnoliales
Family: Annonaceae
Genus: Polyalthia
Species: longifolia
Vernacular names of Polyalthia longifolia (Sonn.) Thwaites
Bengal: Debdaru
English: Ashoka
Hindi: Deodari
Tamil: Asogu
Malayalam: Aranamaram

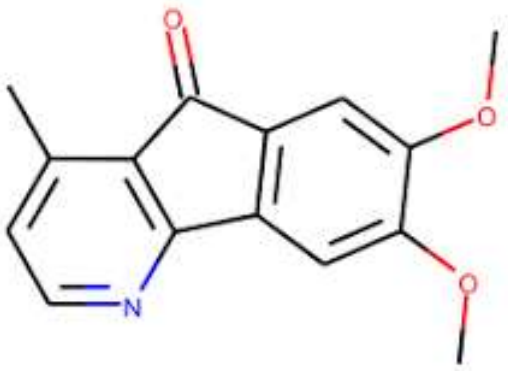
International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

Leaves of Polyalthia longifolia(Sonn.)

Distribution and habitat:
India, Pakistan, and Sri Lanka are home to a common plant known as Polyalthia longifolia Thwaites (Annonaceae).

Description: The plant thrives in India's tropical and subtropical regions up to a height of 1500 metres.Trees up to 12 metres tall, pyramid-like, evergreen and appealing with a straight, undivided main stem are called columnar trees. Intensely pendulous branches that measure between one and two metres in length. This plant has alternating, exstipulated, distichous, and moderately fragrant leaves that measure 7.5-23 by 1.5-3.8 cm. In addition to being pinnately veined, leathery or subcoriaceous, and short-petiolate, the edges are strongly undulating. About 6 mm is the length of the petiole. Bright and glossy, the leaves are narrowly lanceolate and have an acuminate tip. The flowers are 2.5-3.5 cm in diameter, yellowish to green, and have serrated petals. They occur in fascicles or short pendunculate umbels from branches below the foliage. Short, triangular sepals with reflexed ends are wide and short. Connective tissue grows truncately out of the cells. The truncated growth of the stamens. ovaries are indeterminate; style oblong; ovules 1 to 2 Ripe fruits (1.8-2 cm long, 1 seeded) on this plant have short glabrous stalks of around 1.35 cm. The seed coatings are shiny and smooth. The berries and flowers begin to develop around February.

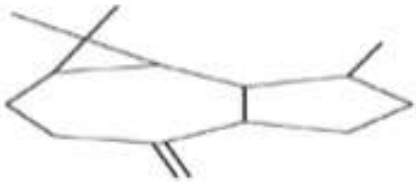
Chemical Constituents: Longifolia p. (Sonn.) diterpenoids, alkaloids, tannins, and mucilage are the primary constituents of Thwaites.The chief components of the plant are O-methylbulbocapnine-N-oxide (1),polyfothine (2), N-methylnandigerine-N-oxide (3), oliveroline-N-oxide (4), pendulamine A (5), N-pendulamine B (6), 8-oxopolyalthiane (7), 16-oxo-5 (10), 13halimadien-15-oic acid (8), 16-Oxo-3, 13-clerodadien-15-oic acid (9), 16hydroxycleroda-3, 13-dien-16, 15-olide (10), Caryophyllene (11), longifolene-(V4) (12), aromadendrene (13), viridiflorene (14).



Polyfothine

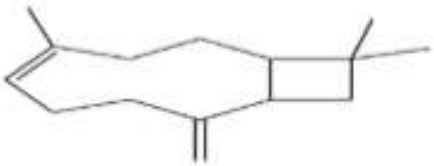
International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

Pendulamine



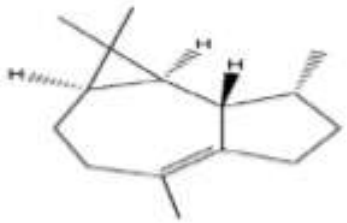
Caryophyllene

longifolene-(V4)



aromadendrene

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781



viridiflorene

THERAPEUTIC APPLICATIONS OF P. LONGIFOLIA:

Anticancer activity

P. longifolia leaves' chloroform fraction and alcoholic extract were tested for their anticancer capabilities for Annonaceae plants, as well as for the antitumor and anticancer active principles detected in them. In HL-60 cells, the chloroform fraction's mechanism of apoptotic activity was investigated further. All cancer cells have dysregulated apoptosis, therefore drugs that promote cancer cells' programmed cell death could be useful anticancer therapies. Anticancer medications work in a variety of methods, all of which lead to cancer cell cytotoxicity by activating apoptosis.

An extract of P. longifolia var. pendula included the metabolites 3-hydroxyhalimane-13(14) en-15,16-olide and (-)-8-oxypolyalthiine. It was discovered that the compounds have (–)-8-oxo–polyalthiine and 3,5,16-trihydroxyhalima-13(14)en-15,16-olide structures. To determine cytotoxicity, a modest number of human cell lines were used. P. longifolia stem and stem bark were found to contain the azafluorene alkaloids darienine, polyfothine, and isooncodine, three non-bioactive azafluorene alkaloids.

The IC_{50} for P. longifolia leaves extract and its chloroform fraction was 6.1 g/mL in human colon cancer cell line SW-620. Cell proliferation was inhibited by the extract and the chloroform fraction. It was discovered that HL-60 cells were more susceptible to cell death after being treated with chloroform fraction. DNA ladders and enhanced annexin-V-FITC cell binding were seen in HL-60 cells treated with a chloroform fraction. The mitochondrial membrane potential was also reduced in these cells. All of the apoptotic criteria outlined above were satisfied by the chloroform fraction in HL-60 cells .

An acid known as polyalthialdoic acid (also known as 16,13(14)Z-dien-15-oic acid) was identified in the stem bark of P. longifolia Thw (Annonaceae). For example, researchers found kolavenic acid and z-dien-15,16 olide in the plant during bioassays. Chemical and spectroscopic methods were used to identify these structures. The crown gall tumor-cultured brine shrimp and potato discs identified these three chemicals to be highly bioactive. Three human cancer cell lines were also shown to have antitumor activity. These habits might be beneficial in the battle against cancer. Polyalthialdoic acid showed the greatest ED50 (6 10–1 g/mL) in human tumour cell culture systems .

The antiproliferative activities of Hemidesmus indicus, Aphanamixis polystachya, P. longifolia, and Moringa oleifera extracts were investigated on a variety of human cell lines, including erythroleukemia K562, B-lymphoid (Raji), T lymphoid (Jurkat), and erythroleukemia K562 (HEL). The electrophoretic mobility shift test was sufficient to identify plant extracts that inhibit transcription factor binding. the interaction between nuclear factor and target DNA was disrupted by hibinus indicus, oleifera longifolia, and M. Hibino. Polystachyaa sequences are recognised by nuclear factor kappaB. (NF-κB). Extracts of P. foetida and C. elegans exhibited no influence on NF-κB/DNA interactions. H. sophera O. auricularis. sanctum is the scientific name given to this species in the scientific literature. Anti-inflammatory medications can use extracts that diminish NF-κB binding activity while also decreasing cell proliferation, whereas extracts that inhibit both NF-κB binding activity and tumour cell growth could be useful in the quest for anti-cancer therapy .

Antimicrobial activity:

Several P. longifolia extract metabolites have shown substantial antibacterial activity in

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

bioassay, including 1F, 2G, 3A, 4A, 5V, 5W, and 5X, among others.

Rashid and coworkers isolated clerodane diterpene (4C) from P. longifolia stem bark extract (3I). For this purpose, they tested the whole extract and its metabolites against seven gramme positive and gramme negative (and seven fungal) types of bacteria and found both to be extremely antibacterial.The most effective antibiotics against Bacillus polymyxa and Shigella shiga were kanamycin and diterpene 3I, whereas 4A was ineffective.

The metabolites 3A and 4A were found by Murthy et al., who studied seed extracts. The two-fold serial dilution method and the paper disc method were used to evaluate the antibacterial and antifungal activities of 3A and 4A. As in the previous study, MTT f 4A was found to have a significant antibacterial effect in this investigation. Candida and Saccharomyces may be killed by 4A as effectively as dithane M-45 and nystatins, the most prevalent fungicides in use today. 3A had less effect on one Gram+ve species (Bacillus) than standard gentamycin did .

Additional studies have shown that 3A and/or 4A are effective at killing bacteria. P. longifolia compounds were tested against 11 fungi and 21 bacteria using disc diffusion. 4A, 4B, 4L, and 4O. Five of the clerodanes identified have been shown to have antimicrobial properties' (3A, 4A, 3K, 3O and 3P). The most successful method was found to be 3A. Among this variation's metabolites, they discovered seven different ones: (4S). E. coli was able to be killed by the vast majority of the compounds tested. S. aureus and Sporothrix schenckii were both destroyed by the most potent compound tested, Diterpene 3A .

The MICs for reference and clinically isolated S. aureus strains were lower, although 3A could treat methicillin-resistant S. aureus at 15.625–31.25 mg/l. Within 24 hours of combining 3A with 7.5 percent sodium chloride, S. aureus' capacity to survive high salt concentrations was gone (NaCl). The use of 3A at 100 mg/kg reduced the microbial burden in the spleen, liver, lung, blood, and kidney.P. longifolia leaves have been shown to have antifungal efficacy against Cryptococcus neoformans, Candida albicans, and Neurospora crassa by Bhattacharya et al (saprophyte). Cell membrane permeability, cell wall structure, or the formation of reactive oxygen species (ROS) have been proposed as antifungal mechanisms for 3A's effect in Candida albicans. Zhang et al. investigated the antibacterial activity of P. longifolia stem bark extracts against MRSA and S. aureus. 4B had more activity than 3A, according to the reports.

P. longifolia stems were subjected to an ethanolic extraction and the resulting metabolite 1F was studied. Antibacterial, antifungal, anti-mycobacterial and anticandidal activities of this metabolite were investigated using the disc diffusion method and found to be poor. Researchers examined the antibacterial potential of a variety of P. longifolia extracts, including petroleum ether and methanolic extracts (5V, 5W, and 5X). By Jain et al., the stem bark of P. longifolia has been isolated and examined for its ability to inhibit aerobic microorganisms. In comparison to butanol, 1U had a greater antibacterial effect, but it was less potent than the industrial standards (erythromycin, vancomycin, oxacillin and ciprofloxacin).

The names of two flavonoids (F1 and F2) found in the bark of P. longifolia were concealed.One demonstrated substantial inhibition of B. subtilis, while the other showed moderate inhibitory effects on E. coli, B. thuringiensis, B. subtilis, as well as P. aeruginosa.

Antimicrobial activity was also evaluated on extracts from various sections of P. longifolia. The antibacterial activity of petroleum ether extract was shown to be superior to other solvent extracts.

Polyalthia longifolia leaf PLEAF and ampicillin were investigated for their synergistic effects against MRSA local isolates (SEM). MRSA-killing PLEAF fraction and ampicillin combo was found to be effective in a clinical trial We found extensive cell shrinkage, as well as tougher cells with fibrous matrices, in the SEM image .

Antiinflammatory activity:

Clerodane diterpenes (3A and 3K) and cleroda-oic acids (3A, 3K) have been found in P. longifolia extracts, according to a number of studies (4A, 4L, 4H). Compounds 4L and 3K of the plant were shown to have an inhibitory effect on fMLP/CB-induced generation of superoxide in neutrophils. 4H exhibits anti-inflammatory effects in human neutrophils, according to Chang et al. FMLP-activated human neutrophils produce elastases at different concentration levels. PKB/AKT, calcium, and the p38 signalling pathway all reduced degranulation and the human neutrophil respiratory burst. According to Wu et al., the IC50 values of 3A and 4A on the formation of nitric oxide in LPS-stimulated macrophage cells

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

(RAW 264.7) were 1 m Anti-inflammatory and cytoprotective enzyme gp91phox was upregulated by 3A whereas COX-2 and iNOS were downregulated. Ho-1, an anti-inflammatory and cytoprotective enzyme, was likewise enhanced by 3A, according to Shih et al. Microglial activation and neuronal cell death can be treated with 3A, which reduces LPS-induced cell death .

Our team found five anti-inflammatory diterpenes using methanolic extracts of P. longifolia seeds. A concise description of the content: 3A, 3C, and 3Q have IC50 values lower or comparable to indomethacin and allopurinol.

Hypotensive activity:

Blood pressure was decreased by a methanol extract of P. longifolia root bark containing 50% of the original amount.30 mg/kg kovanic acid reduced MAP by 22%. This extract contains clerodane, clerodane imide, lysicamine, and lysicamine. The extract decreased blood pressure in both normal and hypertensive rats.

Antiulcer activity:

HCl, ethanol, and water-induced gastric ulcers in mice and rats were all used to test the leaves' antiulcer benefits. Each and every one of the animal models demonstrated statistically substantial antiulcer effectiveness (P 0.01). All of these variables dropped considerably following pylorous ligation (P 0.01) when compared to the control group. As a result, it reduced ulcer development in HCl-ethanol-induced ulcers by 89.71% and in stress-induced ulcers by 95.3%.

Antioxidant Properties:

4H scavenging capacities were tested using the DPPH free radical assay and the cell-free xanthine oxidase system. Up to 10 m, 4H had no influence on DPPH or WST-1. This reveals that 4H inhibits O2• release by scavenging both free radicals and O2•. 4H did not activate superoxide dismutase (0.5 U/ml) to eliminate 4H's antioxidant activity. Sashidhara et al. studied the antioxidant activity of 3 substances: 2C (4.10 mM), 2G (2.38 mM), and 2D (2.4 mM) (1.91 mM). The 2G metabolite of P. longifolia leaves, with an IC50 of 14.67-0.023 mg/ml, is an extra antioxidant.

In contrast, the antioxidant activities of two flavonoids (F1 and F2) isolated from the bark of P. longifolia were studied.F1 was more antioxidant-active than F2. The acetone extract of P. longifolia leaves had DPPH, ABTS, and ferric ion reducing activities. The researchers employed 710.54 mg ascorbic acid equivalent/g dry weight to assess Fe3O4's reduction capability against DPPH and ABTS free radicals.

When tested against DPPH free radicals, the chemical 1U derived from the butanol portion of P. longifolia stem bark was found to be effective by Jain et al. At 40 g/ml, the antioxidant activity of the 1U and butanol fractions was 57.95 and 66.05 percent, respectively. Using these data, it appears that 1U is a superior antioxidant to vitamin C .

Cadmium poisoning can be prevented or treated using P. longifolia water and methanolic leaf extracts, according to this study (a prominent environmental toxin).

Cytotoxicity:

Some of the plant's isolated components, such 3A and 4A, have anti-cancer potential. On P. longifolia, Wu et al. used the KB cytotoxicity test to assess the bioassay-guided methanolic extract separation. Human alveolar basal epithelial cells (A549) and the tebu-knockdown bios (KB), as well as cell lines from various cancers and leukemias (HCT-8 and P-388) in vitro were all killed by the extract's metabolite 5F. Brine shrimp bioassays were used to investigate the cytotoxicity of three chemicals from the stem bark of P. longifolia (3A, 4A, and 4B). On potato discs, A-549, MCF-7, and HT-29 crown gall tumours were halted by these medications .

Chen and colleagues found that some of the isolated compounds (3A; 5G; 4,5-dimethylthiazol-2yl)-2,5,diphenyltetrazolium bromide) were especially effective against breast, prostate, lung, and colon cancer cell lines.Adenocarcinoma gastric cell line (AGS) and Hepatoma cell line (HA59T) were the two cell lines that 5A was most active against. 1L', 3A, 3C, 3K; 4N; 5A; 5F; 5R; 5AA; and 3AA were the other 13 metabolites discovered. Compounds 3A-3C, 3O, 4L, and 4J were tested on MCF-7 and MDA-MB-231 breast cancer cells in addition to hepatoma cells. In these experiments, 3A, 3C, and 3O were found to be effective in inhibiting Hep 3B and Hep G2. (3)Misra et al. The MTT reduction experiment indicated no cytotoxicity of 3A at 200 mg/ml on J774A.1 macrophages. Wu et al. employed 12 diterpenes from P. longifolia fruit methanolic extract to see if A influences the viability of human neuroblastoma (SKNMC) cells. Except 3AA and 4O, they influenced SKNMC cell division. 3W and 3AA had the greatest influence on SKNMC cells. TLC bioautographic studies also revealed substantial acetylcholinesterase inhibitory effects.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

Substantial anti-acne activity in TLC bioautographic tests. Moreover .

Various cell lines have been used to test the cytotoxicity of other substances. Studies were conducted on PA1, MCF-7, MCF-7, MCF-7A, and cervical cancer cells (C33A) to determine if 3P and 3Q had growth inhibitory effects.In Vero, the 3Q outperformed the 3P. (a cell line derived from an African green monkey). The ethanolic extract of P. longifolia leaf contained cytotoxic values of 2105.14, 23010.62, and 2703.001 g/ml, respectively. The extracts' CTC50 values were evaluated using MTT assays.

The MTT experiment revealed that compounds 3A, 4A, and 4B are cytotoxic to a promyelocytic cell line (HL-60). The IC50s for 3A, 4A, and 4B were 25, 11, and 6.25 m, respectively. Compound 3A may affect the viability of N18 and C6 cell lines from mouse neuroblastoma and rat brain tumours.Chemical 3A increased pro-apoptotic proteins and decreased anti-apoptotic proteins in response to treatment with this compound. Activation of pERK1/2 and p-p38 MAPK expression by 3A-induced autophagy in N18 and C6 has also been examined. 3A, an anti-cancer drug, has been found to stimulate ROS-mediated synthesis of two MAPK proteins. There were two IC50 values for P. longifolia leaves: 71.1 and 44.8 micrometres for the ethyl acetate component of the leaves. When tested on A549 and MCF-7 cancer cells, only 4A (4O-R) showed any cytotoxicity, whereas the other compounds were all inert.

ROS overproduction produced cell necrosis in two human clear-cell renal carcinoma lines, 3A and 3B, for example (786O and A498). Apoptosis in 786O and A498 cells is regulated by cell phase arrest, the breakdown of focal adhesion complexes, and the inhibition of apoptotic signalling pathways.

Triedpsin was also used to separate the two seed protein fractions, namely F1 and F2. For HeLa and A-549 cells, F2 had a substantial cytotoxic effect at 30 and 10 g/ml, respectively, according to the MTT experiment. F2 enhanced apoptosis in HeLa and A549 cells in G0 phase at 30 and 10 g/ml. This study suggests that F2 peptide can kill cancer cells.

Hypoglycemic activity:

P. longifolia var. pendula leaf extracts had hypoglycemic and antihyperglycemic effects in alloxan-induced diabetes rats. To reduce blood glucose, P. longifolia extracts and powders were used. However, none of the biochemical indicators were appreciably altered by the extracts. As a result, neither the extracts nor the crude powder show any antidiabetic characteristics, but they do have a significant glucose lowering effect.. Succrose loading causes hyperglycemia, while the existence of antihyperglycemic action prevents it. This action is now often regarded as the most critical attribute of a medication used to treat diabetes.

Miscellaneous Activities:

It was found that the acetone extract of the leaves of P. longifolia had two isolated metabolites (3A and 4A), both of which have antifeedant effect against Achara janata (the casterlooper).

Bark of P. longifolia was used to isolate the anti-plasmodial metabolites 3L, 3U, and 3V, which had IC50 values ranging from 1.51-3.37 g/ml. P. longifolia steam barks were identified as 1C, 3A, 3Q, 4A, 5J, and 5R and investigated for anti-plasmodial efficacy against P. falciparum K1. There were three compounds that had IC50 values of between 3 and 6 micrograms per millilitre, while others had a modest anti-plasmodial effect.

It was shown that the recovered components might be used to combat P.acnes, a bacterium that causes acne. P. acnes was revealed to be a significant target for the antibacterial activity of all of the extracts studied. All doses of Polyalthia longifolia methanol extract (50 to 200 mg/50L) showed a good zone of inhibition.

The antileishmanial properties of clerodane diterpene 3A from P. longifolia leaf extract were studied in the lab and on animals. 3A possesses antileishmanial activity comparable to miltefosine (5 g/ml) (IC50: 5.790.31). When 3A was taken orally, the percentages of inhibition in the liver and bone marrow were 86.881.3 and 83.71.5, respectively. P. longifolia stem bark extract isoforms have also been evaluated against Leishmania donovani axenic amastigote, amastigote, and promastigotes in THP-1 macrophage cells by Zhang's group.With only 3A showing activity, the other compounds' IC50 values varied from 1.60 to 2.34 g/l.

In a research published in the Journal of Agricultural and Food Chemistry, 4B out of seven identified compounds from P. longifolia root bark (50 percent defatted extract in methanol) reduced mean arterial blood pressure by 22%.

Hydroalcoholic extracts of 3A and 3K were shown to have antihistaminic properties when they were isolated from the CH3Cl-soluble

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

fraction. Dosage dependent IC50 values were reported for 3A (29.7 g/ml) and 3K (189.2 g/ml), respectively .

The metabolite 3A, which was proven to be the most efficient in reducing H. pylori growth, has an MMIC of 31.25 g/ml.There were no significant inhibitory effects for 3K (MIC value >125 g/ml) .

To test their ability to decrease cholesterol in the hamster model fed a high fat diet, researchers used ethanolic extracts of P. longifolia leaves to extract four distinct clerodane diterpenes (3A, 3K, 3P, and 4A). But just one of the four, compound 3A, exhibited action that was equivalent to that of lovastatin, while the other three had none. 3-hydroxy-3-methylglutaryl coenzyme inhibitor Reductase donovani, an enzyme .

Extraction 3A, 4A, and 4B from the plant's leaves were used to investigate anti-trypanosome activity against T. brucei, T. congolense, and L. mexicana promastigotes. EC50 for pathogen 3A is less than 0.38 g/ml, and the pathogen has several targets for its activity. IC50 values for 2J of P. longifolia ranged from 773.09–1.47 mg/ml, with an antioxidant and antityrosinase activity of 2J being found .

Using both in vitro and in silico screening approaches, the Nuygen group recently reported that compounds 3C and 3Q have strong inhibitory action against the xanthine oxidase enzyme compared to the conventional medication allopurinol.

In a system of traditional medicine, P. longifolia has been widely used and continues to be used. Toxicology tests on leaf extracts in Wistar albino rats have corroborated this. Antioxidant activity was elevated in the cadmium-induced tissues after treatment with P. longifolia leaf extracts. The presence of phenolic chemicals and other potent antioxidants in this plant's leaf extract may account for some of this benefit.

CLINICAL TRIAL:

Ten women over 50 experienced myocardial infarction, unstable angina, and angiographically diagnosed coronary artery disease. A matched control group of postmenopausal women with normal angiographically verified coronary arteries (N=10) was also created. Everyone in the research had a full hemogram, lipid and lipoprotein profiles, and a blood biochemistry test. A 12-lead ECG and chest X-rays were ordered. The JNC VI Criteria were used to assess blood pressure.

Serum and plasma were taken from the antecubital vein of overnight fasted people in the morning and stored in vacutainers and EDTA respectively. After that, the serum/plasma was isolated and stored at 80°C for further study.

TC, TG, and HDL-C concentrations were measured using enzyme assays that were readily accessible and well acknowledged in the industry (Accurex Biomedical Pvt. Ltd.). Friedwald's technique was used to determine LDL-C and VLDL-C.

The bark of a single tree in northern India was recognised as P. longifolia var. pendula by a botanist. A Soxhlet extraction equipment was used to extract 15 grammes of pulverised bark with 70% v/v alcohol at boiling temperature. Vacuum drying at 60°C was used to dry the alcoholic extract, Rotavapor 67. 1.92 g of powdered dry material was contained in the sample. The extract was reconstituted in RPMI 1640 medium for in vitro investigations. It was necessary to store the purified HPLC extract in amber bottles with nitrogen at 20°C (HPLC data not shown).

Boyum [68]density gradient centrifugation was used to separate PBMCs from research individuals' blood. RPMI-1640 media with 10% foetal calf serum, 2 mM L-glutamine, 20% sodium bicarbonate, 20 mM HEPES, and antibiotics was used to cultivate these cells at a temperature of 37°C and 5% CO2.

The National Center for Cell Sciences in Pune provided this cell line (THP-1). We used the previously described RPMI-1640 medium with 10% heat-inactivated calf serum to maintain the cells alive (Sigma)[69, 70].This monocytic cell line was utilised to simulate human monocytes in order to eliminate the variability and scarcity of monocytes found in peripheral human blood when they were separated. In the study of inflammation and the production of inflammatory cytokines and mediators, including MMPs, researchers frequently use THP-1 cells as a suitable surrogate for human monocytes-macrophages .

We discovered no statistically significant differences between the two groups in terms of age, BMI, and BMI in the patient group when using unpaired Student's t tests.

Findings from our study showed no significant difference in BMI and age between the two study groups we were considering, which indicates that they are similar. Postmenopausal women with CAD exhibited considerably higher lipid and lipoprotein levels than those without CAD[73,74]. This suggests that the lack of oestrogen

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

during menopause is a risk factor for heart disease because it raises levels of bad lipoproteins and lowers levels of good ones.

MOLECULAR TARGET:

Nonsteroidal anti-inflammatory, analgesic, and antipyretic medications frequently used today decrease PGE2 synthesis.P. longifolia leaves, stem bark, and root extracts (300 mg/kgw) prevent LPS-induced pyrexia better than aspirin. Polyalthia genus phytochemicals have been shown to have diverse effects, such as the anti-inflammatory properties of 36 and 40 confirmed on RAW264. LPS-treated macrophages. Human neutrophils produce superoxide anion when exposed to E-dien-15-oic acid methyl ester in vitro; 36 protects RAW264.7 macrophages from LPS-induced nitric oxide generation[75]in addition to preventing LPS-induced neurotoxicity by reducing COX-2 and NF-κB levels (p65)[34]; CD (36 or 38) therapy reduced NO and inflammatory cytokines production in a dose-dependent manner (PGE2, and TNF).

The chemicals' accessibility may need several biological and pharmacological research. 9 kg P. longifolia leaves yielded 16-hydroxycleroda, 3,13-dien, and 15,16 olide (38) good rate of yield, which enhances its drug/medicine potential. When applied to solid tumours, such as gliomas, CD (36) reduced tumour cell proliferation at doses ranging from 20–40 M , glioblastoma , urothelial, breast , colon , lung , hepatoma , and head and neck , carcinoma cell lines, and in liquid tumors (leukemia) , respectively. Polyalthia's CD is the most widely investigated chemical in anti-cancer research. On the other hand CD might be a possible drug that could target various signalling molecules, such as those involved in cancerous, inflammatory, migratory, and invasive pathways. MAKs and the PI3k/Akt signalling cascade are two of the most important oncogenic pathways in tumour formation and cell survival.Cancer cell proliferation and growth would be reduced if CD inhibited ERK1/2 and/or PI3K/Akt pathways, as has been shown in RCC in several studies and bladder cancer cell lines. In glioma and leukaemia cell lines, CD induced cell death by activating JNK, p38 MAPK, and ERK1/2. Through cell cycle arrest in the G2/M phase, CD can decrease cell growth orG0/G1 phase '. RCC patients treated with CD may have increased p53, FoxO3a, and FoxO4[50]and leukemia cancer cell lines so that cells can be killed. A positive feedback loop involving stress-activated JNKs, P38 MAPKs, and/or ERKs may control cell death and survival [86]. Increasing ROS levels enhances JNK/p38 MAPK levels, which in turn increases JNK/p38 MAPK levels .The role of NF-κB in regulating inflammation by inducing pro-inflammatory cytokines is widely acknowledged. A recent study found that NF-κB interacts with various signalling pathways such as FAK, mTOR, and PI3K/Akt, as well as NF-kB itself., in order to control inflammation, CD inhibited pNF-κB, which had an effect on colon cancer's inflammatory response cell line. In other words, CD may help treat IBD by deactivating the NF-κB pathway. In HeLa cells, polyphenol-rich P. longifolia extracts reduced carcinogenic miRNA-221-5p, according to Shanmugapriya et al (2019 and 2020). A microRNA is a non-coding RNA that acts as a base pair for a larger messenger RNA (mRNA). Repressing gene expression appears to be the primary role of miRNAs, which block translation, promote mRNA degradation, and deadenylate mRNA .Thus, a single miRNA may influence hundreds or even thousands (or perhaps hundreds or thousands) of mRNAs, which could contribute to the growth of tumour cells. More research is required to properly comprehend how Polyalthia crude extract or a single molecule interacts with miRNA and silenced genes.

Anticancer activities of a single Polyalthia component or extract have only been studied in very small amounts of study. In metastatic prostate cancer, Afolabi et al. discovered that methanol extracts of P. longifolia were anti-cancer (2020). Researchers found that P. longifolia methanol extracts triggered endoplasmic stress and activated apoptotic pathways in cells.Proteomic and biochemical studies indicated GRP78/BiP as an important initiator of ER stress and cell deat.It is possible that tetranorditerpene1-naphthaleneacetic-7-oxo-1,2,3,4,4a,7,8a-octahydro-1,2,4a,5tetra methyl acid is one of the substances that inhibits prostate cancer cell proliferation , this may potentially have an effect on the growth of human leukaemia HL-60 cells.

By infecting and altering the genetic coding of host immune cells, viruses cause cancer in those who have weak or suppressed immune systems . Three alkaloids and two terpenoids have anti-viral properties. Such prenylated benzopyrans such as suberosol and ENT kaur-16-en-19-oic acid suppress HIV reverse transcriptase function and viral syncytium. 19-(2-substitute furan) nonadeca-5,7-diynoic acid has no effect on HSV-1 at all.

II. CONCLUSION:

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 1409-1420 www.ijprajournal.com ISSN: 2249-7781

Preclinical and clinical studies have proven P. longifolia's medicinal usefulness for a variety of ailments. Bioprospecting and drug development for the treatment of many inflammatory disorders and diseases, such as cancer, might benefit from additional study on this indigenous remedy. As far as medicinal applications and research go, this plant is only beginning to blossom. This suggests that the phytochemicals in the plant can be used to treat disease. Research into P. longifolia has shown that it merits additional, more in-depth study in the hope of discovering new drugs. If you'd like to know how P. longifolia and its extracts can help cure a specific ailment, you'll need more research.

REFERENCES:

[1]. WHO. IUCN and WWF: Guidelines on the conservation of medicinal plants, IUCN Gland, Switzerland. 1993; 1: 4–6.
[2]. Bhagwati U. Utilization of medicinal plants by the rural women of Kulu, Himachal Pradesh. Indian J Trad Know. 2003; 2: 366–70.
[3]. Harsha VH, Hebbar SS, Hegde GR, Shripatti V. Ethnomedical knowledge of plants used by Kunabi tribe of Karnataka in India. Fitoterapia. 2002; 73: 281–7.
[4]. Patwardhan B, Vaidya AD, Chorghade M. Ayurveda and natural products drug discovery. Current science. 2004 Mar 25:789-99
[5]. Dahanukar SA, Kulkarni AR, Rege NN. Pharmacology of medicinal plants and natural products. Indian J Pharma. 2000;32:81–118.
[6]. Ashish G. Herbal folk remedies of Bankura and Medinipur districts, West Bengal. Indian J Trad Know. 2003; 2: 393–6
[7]. Krishnamurthi AK, Manjunath BL, Sastri BN, Deshaprabhu SB, Chadha YR. New Delhi, CSIR; 1969. The Wealth of India, Raw Materials.; 7: 295-8.
[8]. Rastogi RP, Mehrotra BN. New Delhi: Council of Scientific and Industrial Research; 1960. Compendium of Indian Medicinal Plants.
[9]. Raghunathan K, Mitra R, editors. New Delhi: Central Council for Research in Ayurveda and Siddha; 1982. Pharmacognosy of Indigenous Drugs; pp. 127–36.
[10]. Faizi S, Khan RA, Mughal NR, Malik MS, Sajjadi KE, Ahmad A. Antimicrobial activity of various parts of Polyalthia longifolia var.pendula: isolation of active principles from the leaves and the berries. Phytother Res. 2008; 22: 907–12
[11]. Chen CY, Chang FR, Shih YC, Hsieh TJ, Chia YC, Tseng HY. Cytotoxic constituents of Polyalthia longifolia var. pendula. J Nat Prod. 2000; 63: 1475–8
[12]. Wu YC, Duh CY, Wang SK, Chen KS, Yang TH. Two new natural azafluorene alkaloids and a cytotoxic aporphine alkaloid from Polyalthia longifolia. J Nat Prod. 1990; 53: 1327–31
[13]. Verma M, Singh SK, Bhushan S, Sharma VK, Datt P, Kapahi BK. In vitro cytotoxic potential of Polyalthia HL-60 cells. Chem Biol Interact. 2008; 171: 45–56.
[14]. Zhau G, Jung JH, Smit DL, Wood KV, Laughlin MC. Cytotoxic clerodane diterpenes from Polyalthia longifolia. Planta Med. 1991; 57: 380.
[15]. Lampronti I, Khan MT, Bianchi N, Ather A, Borgatti M, Vizziello L. Bangladeshi medicinal plant extracts inhibiting molecular interactions between nuclear factors and target DNA sequences mimicking NF-κB binding sites. Med Chem. 2005; 1: 327–33.
[16]. Faizi S, Mughal NR, Khan RA, Khan SA, Ahmad A, Bibi N. Evaluation of the antimicrobial property of Polyalthia longifolia var. pendula: isolation of a lactone as the active antibacterial agent from the ethanol extract of the stem. Phyther Res 2003; 17(10): 1177-81
[17]. Sampath M, Vasanthi M. Isolation, structural elucidation of flavonoids from Polyalthia longifolia (Sonn.) Thawaites and evaluation of antibacterial, antioxidant and anticancer potential. Int J Pharm Pharm Sci 2013;5(1):336-41.
[18]. Rashid MA, Hossain MA, Hasan CM, Reza MS. Antimicrobial diterpenes from Polyalthia longifolia var. pendulla (Annonaceae). Phyther Res 1996;10(1):79-81.
[19]. Faizi S, Khan RA, Mughal NR, Malik MS, Sajjadi KE, Ahmad A. Antimicrobial activity of various parts of Polyalthia longifolia var. pendula: isolation of active principles from the leaves and the berries. Phytother Res 2008;22(7):907-12
[20]. Sashidhara KV, Singh SP, Shukla PK. Antimicrobial evaluation of clerodane diterpenes from Polyalthia longifolia var.

pendula. Nat Prod Commun 2009;4(3):1934578X0900400305

[21]. Murthy MM, Subramanyam M, Bindu MH, Annapurna J. Antimicrobial activity of clerodane diterpenoids from Polyalthia longifolia seeds. Fitoterapia 2005; 76(3-4): 336-9.

[22]. Misra P, Sashidhara KV, Singh SP, Kumar A, Gupta R, Chaudhaery SS, Gupta SS, Majumder HK, Saxena AK, Dube A. 16α- Hydroxycleroda- 3, 13 (14) Z- dien- 15, 16- olide from Polyalthia longifolia: a safe and orally active antileishmanial agent. British journal of pharmacology. 2010 Mar;159(5):

[23]. Sashidhara KV, Singh SP, Srivastava A, Puri A, Chhonker YS, Bhatta RS. Discovery of a new class of HMG-CoA reductase inhibitor from Polyalthia longifolia as potential lipid lowering agent. Eur J Med Chem 2011;46(10): 5206-11

[24]. Sari DP, Ninomiya M, Efdi M, Santoni A, Ibrahim S, Tanaka K. Clerodane diterpenes isolated from Polyalthia longifolia induce apoptosis in human leukemia HL-60 cells. J Oleo Sci 2013;62(10):843-8.

[25]. Gupta VK, Verma S, Pal A, Srivastava SK, Srivastava PK, Darokar MP. In vivo efficacy and synergistic interaction of 16α-hydroxycleroda-3, 13 (14) Z-dien-15, 16-olide, a clerodane diterpene from Polyalthia longifolia against methicillin-resistant Staphylococcus aureus. Appl Microbiol Biotechnol 2013; 97(20): 9121-31. Afolabi S, Olorundare O, Ninomiya M, Babatunde A, Mukhtar H, Koketsu M. Comparative antileukemic activity of a tetranorditerpene isolated from Polyalthia longifolia leaves and the derivative against human leukemia HL-60 cells. J Oleo Sci 2017; 66: 1169-74 0/advpub_ess17042/_article/-char/ja/

[26]. Bhattacharya AK, Chand HR, John J, Deshpande MV. Clerodane type diterpene as a novel antifungal agent from Polyalthia longifolia var. pendula. Eur J Med Chem 2015; 94: 1-7

[27]. Zhang J, Jain SK, Jacob MR, Tekwani BL, Hufford CD, Muhammad I. Antileishmanial and Antimicrobial Clerodane Diterpenes from Polyalthia longifolia. Planta Med 2013; 79(05): P88

[28]. Jain PK, Patra A, Satpathy S, Jain S, Khan S. Antibacterial and Antioxidant Activities of 3-O-methyl Ellagic Acid from Stem Bark of Polyalthia longifolia Thw. Chiang Mai J Sci 2018; 45(2): 858-67.

[29]. Bose S, Byahatti VV, Souza MD, Bose A. Antioxidant and antimicrobial activities of isolated constituents from the bark of Polyalthia longifolia. Int J Green Pharm 2010; 4(2): 93.

[30]. Ghosh G, Subudhi BB, Badajena LD, Ray J, Mishra MK, Mishra SK. Antibacterial activity of Polyalthia longifolia var. angustifolia stem bark extract. Int J PharmTech Res 2011; 3(1): 256-60

[31]. Satish S, Mohana DC, Ranhavendra MP, Raveesha KA. Antifungal activity of some plant extracts against important seed borne pathogens of Aspergillus sp. J Agric Technol 2007; 3(1): 109

[32]. Kirubakari B, Chen Y, Sasidharan S. Synergistic Effect of Polyalthia longifolia Leaf and Antibiotics

[33]. Malairajan P, Gopalakrishnan G, Narasimhan S, Veni K. Evaluation of anti-ulcer activity of Polyalthia longifolia (Sonn.) Thwaites in experimental animals. Indian J Pharma. 2008; 40: 126–8.

[34]. Sashidhara KV, Singh SP, Srivastava A, Puri A. Identification of the antioxidant principles of Polyalthia longifolia var. pendula using TEAC assay. Nat Prod Res 2011; 25(9): 918-26

[35]. Chang HL, Chang FR, Chen JS, Wang HP, Wu YH, Wang CC. Inhibitory effects of 16-hydroxycleroda-3, 13 (14) E-dien-15-oic acid on superoxide anion and elastase release in human neutrophils through multiple mechanisms. Eur J Pharmacol 2008; 586(1-3): 332-9.

[36]. Wu TH, Cheng YY, Liou JR, Way TD, Chen CJ, Chen YH. Clerodane diterpenes from Polyalthia longifolia var. pendula protect SK-N-MC human neuroblastoma cells from β-amyloid insult. RSC Adv 2014; 4(45): 23707-12

[37]. Chen XX, Liang G, Chai WM, Feng HL, Zhou HT, Shi Y. Antioxidant and antityrosinase proanthocyanidins from Polyalthia longifolia leaves. J Biosci Bioeng 2014; 118(5): 583-7.

[38]. Zhao G, Jung JH, Smith DL, Wood KV, McLaughlin JL. Cytotoxic clerodane diterpenes from Polyalthia longifolia. Planta Med 1991; 57(04): 380-3

[39]. Sashidhara KV, Singh SP, Sarkar J, Sinha S. Cytotoxic clerodane diterpenoids from the leaves of Polyalthia longifolia. Nat Prod Res 2010; 24(18): 1687-94
[40]. Faizi S, Khan RA, Azher S, Khan SA, Tauseef S, Ahmad A. New antimicrobial alkaloids from the roots of Polyalthia longifolia var. pendula. Planta Med 2003; 69(04): 350-5
[41]. Thiyagarajan V, Lin SH, Chia YC, Weng CF. A novel inhibitor, 16-hydroxy-cleroda-3, 13-dien-16, 15-olide, blocks the autophosphorylation site of focal adhesion kinase (Y397) by molecular docking. Biochim Biophys Acta-Gen Subj 2013; 1830(8): 4091-101.
[42]. Thiyagarajan V, Sivalingam KS, Viswanadha VP, Weng CF. 16-hydroxy-cleroda-3, 13-dien-16, 15-olide induced glioma cell autophagy via ROS generation and activation of p38 MAPK and ERK-1/2. Environ Toxicol Pharmacol 2016; 45: 202-11 30
[43]. Afolabi SO, Olorundare OE, Babatunde A, Albrecht RM, Koketsu M, Syed DN. Polyalthia longifolia extract triggers ER stress in prostate cancer cells concomitant with induction of apoptosis: insights from in vitro and in vivo studies. Oxid Med Cell Longev 2019; 6726312 journals/omcl/2019/6726312/
[44]. Liu C, Lee WC, Huang BM, Chia YC, Chen YC, Chen YC. 16-Hydroxycleroda-3, 13-dien-15, 16-olide inhibits the proliferation and induces mitochondrial-dependent apoptosis through Akt, mTOR and MEK-ERK pathways in human renal carcinoma cells. Phytomedicine 2017; 36: 95-
[45]. Chen YC, Huang BM, Lee WC, Chen YC. 16-Hydroxycleroda-3, 13-dien-15, 16-olide induces anoikis in human renal cell carcinoma cells: involvement of focal adhesion disassembly and signaling. Onco Targets Ther 2018; 11: 7679-90
[46]. Rupachandra S, Sarada DV. Anti-proliferative and apoptotic properties of a peptide from the seeds of Polyalthia longifolia against human cancer cell lines. Indian J Biochem Biophys 2014; 51: 127-134
[47]. Nair R, Shukla V, Chanda S. Assessment of Polyalthia longifolia var.pendula for hypoglycemic and antihyperglycemic activity. J Clin Diagn Res. 2007; 3: 116–21
[48]. Phadnis AP, Patwardhan SA, Dhaneshwar NN, Tavale SS, Row TN. Clerodane diterpenoids from Polyalthia longifolia. Phytochemistry 1988; 27(9): 2899-901.
[49]. Annan K, Ekuadzi E, Asare C, Pistorius D, Oberer L, Gyan BA. Antiplasmodial clerodane diterpene alkaloids from the stem bark of Polyalthia longifolia. Planta Med 2014; 80(10): PD114
[50]. Michael A. A study on impact of medicinal plants Polyalthia longifolia and Bacopa monnieri with reference to acne treatment. Current Trends in Biotechnology and Pharmacy. 2021 Nov 1; 15(5): 401-5
[51]. Gbedema SY, Bayor MT, Annan K, Wright CW. Clerodane diterpenes from Polyalthia longifolia (Sonn) Thw. var. pendula: Potential antimalarial agents for drug resistant Plasmodium falciparum infection. J Ethnopharmacol 2015; 169: 176-82 115002652
[52]. Edmond MP, Mostafa NM, El-Shazly M, Singab AN. Two clerodane diterpenes isolated from Polyalthia longifolia leaves: comparative structural features, anti-histaminic and anti-Helicobacter pylori activities. Nat Prod Res 2020:1-5
[53]. Ebiloma GU, Katsoulis E, Igoli JO, Gray AI, De Koning HP. Multi-target mode of action of a Clerodane-type diterpenoid from Polyalthia longifolia targeting African trypanosomes. Sci Rep 2018; 8(1): 1-9