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REVIEW ARTICLE

A REVIEW ARTICLE OF PHARMACOLOGICAL ACTIVITIES AND BIOLOGICAL IMPORTANCE OF CALOPHYLLUM INOPHYLLUM

Silpa Sundur*, Dr. B. Shrivastava, Dr. Pankaj Sharma, Solomon Sunder Raj, V.L. Jayasekhar

Department of pharmacology Anwar ul uloom college of pharmacy Mallepally, hyderabad

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*Corresponding Author

Silpa Sundur

Abstract

A wide variety of medicinal plants have been traditionally used for treating inflammation ulcers and different pathological conditions . Calophyllum inophyllum (Clusiaceae) is a littoral tree of the tropics, occurring above the high-tide mark along sea coasts of northern Australia and extending throughout Southeast Asia and southern India. It is used in traditional medicine against bacterial infections, inflammation, and cosmetic purposes. Phytochemical isolations of leaves, stem bark, and seed oil have confirmed the existence of several coumarins, xanthenes and triterpenes which have a wide biological activity against bacteria, protozoa. The aim of this review is to provide the general characteristics of C.inophyllum, the most common traditional uses, and its phytochemical constituents. It also gives a review mainly on the biological activities of C.inophyllum and some of their compounds isolated, pharmacological actions and medicinal applications.

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Introduction

Plants have been used since ancient times by human civilization to treat and cure diseases. They have made significant contribution to the great expansion of the pharmaceutical industry, with the isolation of bioactive substances, which owing to their complex structure, are very difficult to obtain by organic synthesis. However, its irrational use has resulted in a decline and disappearance of many tree species in the world. Therefore, a sustainable use of natural products is becoming more important . In fact, the importance of some genus as Calophyllum has increased. Calophyllum is a large group of tropical trees consisting of 180-200 different species⁶. Traditionally this species has been used in many different ways, such as wood, forages, dye extracts, making of soaps, biofuels and medicinal uses . For instance, the oil has been used for rheumatic problems, skin diseases, hemorrhages and pain. The aim of this review is to examine the different phytochemical constituents pharmacological actions of Calophyllum inophyllum including the general aspects of the species, emphasizing extracts or active individual phytochemicals which can be used as antiseptic, antiinflammation, antimicrobial, analgesic .

GENERALITIES AND TRADITIONAL USES OF Calophyllum inophyllum :

C.inophyllum (Clusiaceae) is a large evergreen tree native to southern coastal India, east Africa, Malaysia and Australia. It is a low branching and slow growing tree with a broad and irregular crown .it usually reaches 8 to 20 m in height. The tree supports a dense canopy of glossy, elliptical leaves. The very fragrant white flowers are 25 mm across and occur in racemose or panicle inflorescences consisting of 4 to 15 flowers. The fragrant flowers have been prized as an adornment and as a perfume. It is referred by various names like beauty leaf, Alexandrian laurel, ball tree, beauty leaf, Indian doomba oil tree and some other names depending on location.

For its great versatility, *C. inophyllum* is ornamental plant wood is hard and strong and has been used in construction or boat building among the medicinal uses the oil is used to treat diabetic sores, psoriasis, sun burn, heal blisters. In southern Africa and it is useful for rheumatism, arthritis and used for lesions due to herpes. It is also used for problems of scalp and hair. The leaves are used for skin care, eye inflammations.

BIOLOGICAL ACTIVITY OF PHYTOCHEMICAL COMPOUNDS

In the world there is great diversity of plants (over 300,000 species), which remains a large reservoir of phytochemicals compounds, including secondary metabolites. In contrast to primary compounds (lipids, carbohydrates, proteins, etc.), the secondary metabolites are characterized because they are stored in low concentration in plant tissues and play an important role in the survival of the plant in the environment. Secondary metabolites are a rich source of bioactive compounds that are biodegradable into nontoxic products. Phenolics, terpenes and alkaloids are considered the main groups of secondary metabolites and they are classified according to their biosynthetic pathways. It has been shown that the biological activities of *Calophyllum* genus contain a wide variety of phytochemical compounds against several infections

Table 1. Main species of genus *Calophyllum* containing compounds with biological Activity

Species	Plant portion	Compounds	Biological activity
<i>C. blancoi</i>	Seeds	Chromanones, xanthenes	Antitumor, antiviral
<i>C. calidonicum</i>	Leaves, stem bark, trunk bark	Coumarins, xanthenes	Antiviral, antifungal
<i>C. cordotoblogum</i>	Twigs, buds	Coumarins, xanthenes	antiviral
<i>C. dispar</i>	Stem bark	Coumarins	Antileukemia
<i>C. enervosum</i>	Stem bark	Xanthenes, ketones	Antibacterial, antioxidant
<i>C. inophyllum</i>	Stem bark, leaves	Coumarins, xanthenes, triterpenes	Antitumor, cytotoxic, antibacterial, analgesic
<i>C. mucigerum</i>	Stem bark	Xanthenes, coumarins	Antileukemia, insecticidal
<i>C. panciflorum</i>	Stem bark	Xanthenes, bioflavonoids	Anti tumor
<i>C. teysmannii</i>	Wood	Xanthenes	Immunomodulatory

Antimicrobial activity :

Calophyllum inophyllum has acidic phenolic groups which could be attributed to the presence of tannins. Tannins are soluble in water and the presence of alkaloid gives a bitter taste. Glycosides have been known to lower blood pressure, although some workers have attributed the cardiac action of these oils to the presence of the alkaloid, carpaine. The presence of phenolic compounds gave acidic properties and could possibly be responsible for the antimicrobial activities.

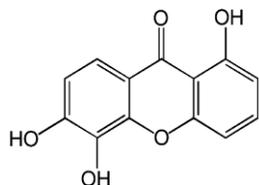
Analgesic activity:

The chemical constituents in the methanolic and chloroform extracts of *C. inophyllum* are flavonoid compound Amentoflavone^{12,13}, steroid compound campesterol^{14,15}, Arachidic acid lipid¹⁵, xanthone derivative Brasilixanthone-B and Buchanaxanthone^{16,17}, coumarin derivatives Calocoumarin-A, Calocoumarin-B, Calocoumarin-C and Apetalolide^{18,19}, and Beta Amyrin a triterpene²⁰. All these above mentioned indicate the presence of some analgesic properties of the plant

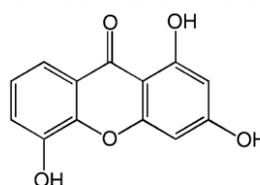
Anti inflammatory activity:

The leaves of *Calophyllum inophyllum* contain friedelin and triterpenes of the friedelin group, namely canophyllal, canophyllol and canophyllic acid, and from the heartwood xanthenes such as mesuaxanthone B and calophyllin B are obtained. All the xanthenes exhibited anti-inflammatory activity by both intraperitoneal and oral routes in rats.

Structure of Mesuazanthone-B



Structure of Mesuazanthone-A

**Anti dyslipidemic activity:**

The isolated bioactive compounds (1-5) from the leaves of *Calophyllum inophyllum* and evaluated their anti-dyslipidemic activity in triton induced hyperlipidemia model. The calophyllin acid and isocalophyllin acid mixture, canophyllin acid and amentoflavone showed dose dependent lipid lowering activity in in vivo experiments.

Anti oxidant activity:

Xanthenes and coumarins in tamanu oil demonstrate antioxidant properties, specifically inhibiting lipid peroxidation. Cell membranes are made of lipids. Lipids are organic compounds that are oily to the touch and are insoluble in water but are soluble in nonpolar organic solvents (e.g. chloroform, ether). Lipids include fats, oils, waxes, sterols, and triglycerides. The antioxidant activity of tamanu oil helps to protect skin cells from damage by reactive oxygen species (ROS) and other oxidative antagonists (Mahmud et al., 1998).

Anti cancer activity:

A search for anti-tumor-promoting agents was carried out by a primary screening of ten 4-phenylcoumarins by examining their possible inhibitory effects on Epstein—Barr virus early antigen (EBV-EA) activation induced by 12-O-tetradecanoylphorbol-13-acetate in Raji cells. All of the compounds tested in this study showed inhibitory activity against EBV, without showing any cytotoxicity. Calocoumarin-A(5) showed more potent activity than any of the other compounds tested. Furthermore, calocoumarin-A(5) exhibited a marked inhibitory effect on mouse skin tumor promotion in an in vivo two-stage carcinogenesis test. The results of the present investigation indicate that some of these 4-phenylcoumarins might be valuable as potential cancer chemopreventive agents (anti-tumor-promoters). (Itoigawa et al.,)

Antiviral activity:

The presence of the following compounds caloxanthone A, calophynic acid, brasiliensic acid, inophylloic acid, calophyllolide, inophyllum C, and E in the oil of *calophyllum inophyllum* has shown that the plant possesses antiviral activity. It is also seen that it acts against *Staphylococcus aureus*.

Anti HIV:

Ethanollic and water extracts of *Calophyllum inophyllum* (bark) were tested for their inhibitory activities against two prime enzymes of HIV which are HIV-1 protease (HIV-PR) and HIV-1 integrase (HIV-IN). The results revealed that the ethanollic and water extract of the bark extract of *Calophyllum inophyllum* exhibited potent anti-HIV-IN activity with IC_{50} values of 9.8 and 5.6 $\mu\text{g/ml}$, respectively. Whereas those for anti-HIV-1 PR effect were found to

be 63.8 and 16.3 µg/ml, respectively. This result strongly supports the basis for the use of *C. inophyllum* for AIDS treatment by local traditional practitioners of Ayurveda and Unani system of Indian medicine and it is the first report on HIV-1 Protease and HIV-1 Integrase enzyme inhibition by this plant extract.

Antifungal:

The ethanolic, chloroform and aqueous extracts of *Calophyllum inophyllum* Linn examined against different fungal cultures exerted significant growth inhibition against two species of genus *Tricophyton* simil and *mentagrophytes*. The chloroform extract exhibited an activity against human pathogens *Pseudallescheria boydii*, *Aspergillus niger*, *Candida albicans*. The isolated compounds *Freidelin*, *Canophyllool*, *Ionophynone* from these extracts have shown the antifungal activity.

Conclusions:

Calophyllum inophyllum is a species containing large amounts of phytochemicals with a wide variety of biological activities such as antimicrobial, antiviral, and against other disorders in favor of public health. This species is of great relevance due to its high potential for producing calanolides, which are highly potent phytochemical compounds against HIV-1.

Phytochemicals with new effects have been reported recently. Furthermore, there are only a few studies aimed at increasing production of high-value phytochemicals such as calanolides. This plant always promised to be interesting from a survey of the literature and folklore. The fascinating chemistry, coupled with a modern evaluation of the plant, justified that interest.

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