

# Insight on *Excoecaria agallocha*: An Overview

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## Abstract

*Excoecaria agallocha* is a milky mangrove widely distributed in Indian coastal regions. This review article explains chemical composition, pharmaceutical and environmental applications of *E. agallocha*. There are 20 different polyphenols, 15 terpenoids and more than 50 volatile derivatives were identified from leaves, stem, latex and root extract. Enormous number of compounds isolated from ethanolic extract of leaves. In conclusion, *E. agallocha* has huge amount of polyphenols and terpenoids, which was reported to have endocrine, epidemic and endemic disease control as anti-microbial, anti-cancer and anti-diabetic agent.

**Keywords:** Mangroves; Thillai; Terpenoids; Rutin; Antidiabetic

## Background

A mangrove is a tree, shrub, palm or ground fern, generally exceeding one half meter in height, that normally grows above mean sea level in the intertidal zone of marine coastal environments and estuarine margins. The term "Mangroves", plants which exist in muddy, wet soil in tropical or subtropical tidal waters. *Excoecaria agallocha* L. (Euphorbiaceae) is an ancient mangrove species specified in "Thillai Lord Nataraja" temple, Chidambaram as "Tala virucham" in tamil. Common name of *Excoecaria agallocha*: Agallocha, blinding tree (General name); Thillai, Kampetti (in Tamil); Tilla, Tella and Chilla (in Telugu); Thelakiriya, Thalia (in Singhalese) It is widely distributed abundant in Pichavaram mangrove forest, Indian coastal regions, Australia from northern New South Wales, along the northern coastline around to Western Australia. According to Red list criteria it is a least concern position [1] (Systematic classification) (Figure 1).

## Morphological characters identification

Habit - A dioecious tree to 15 m high with abundant white latex; Habitat - An evergreen shrub common along with higher estuarine banks, canals, tidal forest and mangrove swamps; Stem-bark grayish, lenticellate; Roots- Lateral roots spreading and intermingled with each other, supraterranean bands produce elbow-shaped pegs instead of pneumatophores; Leaves - leaves alternate, ovate-elliptic or orbicular, apex shortly acuminate, base narrowed, margin entire or sinuate-crenate, 3-8 × 1.5-3 cm, glabrous, petiolate; Flowers - Unisexual, Male flowers in catkin spikes, fragrant, yellow, 2-3 mm across; stamens 3, filaments free. Female flowers in axillary raceme, pale green, 2.5-3.5 mm across, pedicellate; calyx 3-lobed; ovary 3-celled, trilocular style; Fruit - Capsule, globose 3-lobed, seeds sub-globose; Reproductive - Flowers are pollinated by insects; Regeneration - Epigeal or modified epigeal germination [2]. This evergreen mangrove species has traditionally been used to treat sores and stings from marine creatures, and ulcers, as a purgative and an emetic, and the smoke from the bark to treat leprosy [3]. They are well-known as extreme skin irritants and tumor promoter [4]. Recent ethanobotanical survey on Kodiyampalayam coastal village, Nagapattinam district, Tamil Nadu, India depicted the presence and traditional usage of *E. agallocha* to blood glucose level reduction and fish poison [5].

## Therapeutic Applications

### Impact of *Excoecaria agallocha* on diabetes mellitus

Type 2 diabetes mellitus (T2DM), is a prototype multi-factorial complex diseases that considered as one as one of the leading causes of morbidity and mortality around the world [6]. The pancreas plays a primary role in the metabolism of glucose by secreting the hormones

insulin and glucagon. The islets of Langerhans secrete insulin and glucagon directly into the blood [7]. When the blood glucose level falls, glucagon secreted and increases blood glucose concentration partly by breaking down stored glycogen in the liver by a glycogenolysis pathway. Also, Gluconeogenesis is the production of glucose in the liver from non-carbohydrate precursors such as glycogenic amino acids [8]. Several studies were elaborated the risk factors responsible for Type 2 DM including obesity, hypertension, smoking, physical inactivity, low education, dietary patterns, family history and specific gene [9]. Recent years, researchers focused their interest to find out the potential anti-diabetic molecules from the medicinal plants to reduce the side effects caused by commercial drugs. Different type of alpha-glucosidase enzyme involved in the absorption of carbohydrate molecules such as glucose, sucrose and maltose in the small intestine, which leads to postprandial hyperglycemia. In previous studies we reported the alpha-glucosidase inhibitory effect of coastal sand dunes and salt marshes from the southeast coast of India [10]. Alloxan and Streptozotocin is widely used in inducing hyperglycemia than compared to other toxins viz., vacor, 8-hydroxyquinolone dithione and ferric nitrilotriacetate. The agents can be administered using various methods such as intra-peritoneal, intravenous, or subcutaneous; however, the first route is the most popular in rodents [11]. The 500 mg/kg body weight of ethanolic extract of *E. agallocha* exhibited most significant anti-hyperglycemic ( $P < 0.001$ ) activity in alloxan induced wistar albino mice [12]. Also the 400 mg/kg body weight of methanolic stem extracts of *E. agallocha* orally administered in experimental mice showed significant reduction in serum glucose level (23 mg/dl) was observed [13]. Overall the anti-hyperglycemic effect of *E. agallocha* reflected in a dose dependent manner. The matrix metallo-proteinase activity of different extract of *E. agallocha* confirmed with collagenase and elastase inhibitory action [14].

### Impact of *Excoecaria agallocha* on cancer chemotherapy

One of the major health issues all around the world is cancer. The major risk factors responsible causes of cancer are tobacco/alcohol consumption, preserved food products, family heredity, environmental

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Figure 1: *Excoecaria agallocha*.

pollution, sexual behaviour, medicines and its treatment procedures. Then compared to other factors, alcohol consumption increases the occurrence of cancer at oral, oesophagus, pharynx, stomach and liver region respectively. In India, the breast and cervical cancer are predominantly identified in women [15]. Cancer is the second leading disease factor cause more death in United states of America. Siegel et al. [16] estimated the death rate and various cancer sites (Oral cavity and pharynx, Digestive system, Respiratory system, Bones and joint, skin, breast, urinary system, eye, brain, endocrine system, lymphoma, myeloma) in both male and female subjects in United states of America.

Ethanollic stem extract of *E. agallocha* has a significant cytotoxic effect of different cell lines Miapaca-2, BxPC-3, PANC-1 and Capan-1, IC50 values were higher (0.11 µg/ml) compared with the positive control flavopiridol by MTS assay. It might be action of cardiac glycosides and saponin in the bioactive fraction of *E. agallocha* confirmed by chromatographic finger printing [17]. The higher concentration of methanolic and chloroform extracts of *E. agallocha* leaves showed lowest Hep-2 cells viability of 22 and 8% under *in vitro* conditions. Konoshima et al. [18] reported the diterpenoids isolated from *E. agallocha* wood showed their inhibitory action against induction of Epstein-Barr virus early antigen (EBV-EA) in Raji cells under *in vitro* conditions. Among these, the secolabdane-type diterpenoid showed anti-tumour promoting effect which analysed by *in vivo* Two-Stage Mouse Skin Carcinogenesis Test with promoter (12-O-tetradecanoylphorbol13-acetate) and an initiator 7,12-dimethylbenz[a]anthracene. The Flavonol glycosides of *E. agallocha* blocked the action of GLI-related protein is a transcriptional effector involved in tumour development which results inhibits the translocation of GLI1 in to nucleus. Therefore, it act as effective Hedgehog signaling inhibitor in cancer therapy [19,20]. Norhanom and Yadav [21] reported the long term continuous usage of the Euphorbiaceae family species like *E. agallocha* among rural Malays cause Epstein barr virus associated non-Hodgkin malignant

lymphoma. Biototoxicity of *E. agallocha* reported by Kathiresan and Thangam [22].

#### Impact of *Excoecaria agallocha* on pathogenic microbial strains

Mangrove floral species plays vital role in prevention of soil erosion, act as a sink for enormous amount of active metabolites. Apart from that, the mangroves serve as a host for many endophytes which include parasitic, facultative saprobic, actinomycetes and majority of bacterial and fungal species. Especially in *E. agallocha*, ascomycete genus *Phomopsis* species belongs to diaportheaceae family and endophytic bacteria was identified [23]. The endophytes secreted Bacteriocins are act as promising antimicrobial agent [24]. The methanol, hexane and chloroform leaf extracts of *E. agallocha* were subjected to antimicrobial assay followed the standard agar well diffusion method. Nearly 50 µl of the samples with 100 mg/ml concentration was allowing to diffusion under *in vitro* conditions for 45 min. Among those strains, the ethanolic extract of *E. agallocha* exhibited potential antibacterial activity against *Acremonium strictum*, and *Penicillium expansum* then compared to others [25]. The chloroform and water extracts from leaves of *E. agallocha* showed potential activity against urinary tract pathogens, antibiotic sensitive ophthalmic bacterial pathogens, antibiotic resistant bacterial strains and fish pathogen [26]. *Staphylococcus aureus* is a multidrug resistant pathogenic bacterial strain. It showed resistant to commercially available antibiotics such as ceftazidime, gentamicin and kanamycin. Abeysinghe [27] reported the active ethyl acetate fractions from *E. agallocha* leaves showed highest inhibition to *Staphylococcus aureus* than *Proteus* sp. in the mean time the ethanolic extracts of *E. agallocha* pronounced for significant anti-bacterial activity against *Staphylococcus aureus*, *Shigella dysenteriae*, *Shigella sonnei* and *Enterococci* bacterial strains [28]. Also the methanolic, chloroform and DMSO extract of *E. agallocha* showed higher zone of inhibition

against the soil born *Fusarium udum* fungal strains which cause wilt diseases on plants. The minimum zone of inhibition was observed in *Rhizactonia solani* and *Sclerotium roysii* strains on potato dextrose agar medium [29]. *Chryseobacterium* spp. is a fish pathogen which resistant to commercial antibiotics such as erythromycin, tetracyclines and chloramphenicol [30]. Those antibiotics used in the fisheries sectors to control the infectious diseases caused by the fish pathogens. The 500 mg/ml of methanolic extracts of *E. agallocha* showed the highest inhibition zone to *Chryseobacterium gleum* by disc diffusion and agar well diffusion assay. It also showed minimum values of minimum bactericidal concentrations and the minimum inhibitory concentration against the *Flavobacterium indicum*, *Chryseobacterium indologenes*, *Chryseobacterium gleum* and *Elizabeth kingiameningoseptica* [31]. Additionally, the ethanolic extract of *E. agallocha* showed higher inhibition to the fish pathogen *Aeromonas hydrophila*, which is a gram negative free living ubiquitous bacterial strain causes motile aeromonad septicaemia diseases [32]. Agoramoorthy et al. [33] reported the Fatty acid methyl esters extracts (FAME) from leaves of *E. agallocha* showed significant anti-bacterial and anti-fungal activity against *Bacillus subtilis*, *Bacillus pumilus*, *Candida albicans*, *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Micrococcus luteus* and *Staphylococcus aureus*.

#### Impact of *Excoecaria agallocha* on mosquito borne diseases

Mosquitoes borne diseases are dangerous which causes endangered disease like malaria, dengue, filariasis and chikungunya were caused by the mosquito arthropods [34]. Guha-Spair and Schimme [35] reported the mosquito borne diseases causes two million infections, hemorrhagic fever, shock syndrome, impaired action of central nervous system and approximately 12,000 death rate per year. *Aedes aegypti* is an endemic viral species occurrence in the Southeast Asia, Africa including West Africa, America and Pacific islands causes dengue fever [36]. Group of researchers evaluated the larvicidal activity of methanol, ethanol, chloroform and aqueous extracts of *E. agallocha* aerial parts. However the methanol extract exhibited significant inhibitory concentration against *Aedes aegypti* and *Culex quinquefasciatus* mosquito larvae [37,38]. Secondary metabolites such as chrysoeriol and 4', 5', 7- trihydroxy 3',5- dimethoxy flavones reported the highest LD50 values and mortality against Mosquito Larvae [39]. Interestingly, the methanolic extracts of *E. agallocha* showed inhibition to developmental stages of female filarial worm *Setaria digitata* which is estimated by trypan blue dye and tunnel staining for evaluating the fragmentation of chromosomal DNA [40].

#### Impact of *Excoecaria agallocha* on pandemic diseases

Acquired immunodeficiency syndrome is one of the epidemic diseases caused by the human immunodeficiency virus. Earlier, the phorbol ester bioactive compound isolated from the leaves and stem of *E. agallocha* from Northwest Australia reported to have anti-HIV potential [4]. Recently, Patil et al. [17] and his co-workers reported the reverse transcriptase (RT) enzyme inhibited by active stem ethanolic fraction of *E. agallocha* which is necessary for the synthesis of proviral DNA. The extract of *E. agallocha* showed 33% of inhibition than compared with the standard drug azidothymidine (35%).

#### Impact of *Excoecaria agallocha* on anti-oxidant and free radical scavenging efficiency

Cellular damage by free radicals causes a change of the net charge of cells, thus modifying their osmotic pressure and inducing their

swelling and their death. The free radicals act also on the mediators of the inflammatory diseases and accelerate the tissue damage. Moreover, cells lesions lead to an increase in the production of the ROS which induces the consumption and depletion of the endogenous chelating agents. The hydroalcoholic extract of *E. agallocha* exhibited significant 2,2-diphenyl-1-picrylhydrazyl (IC50 179.16 µg/ml), hydrogen peroxide (IC50 120.24 µg/ml) and nitric oxide (IC50 134.29 µg/ml) free radical scavenging activity respectively [28]. Additionally the lower concentration of alkaloid rich fractions (10 ppm) of *E. agallocha* exhibited significant 88% of DPPH free radical scavenging activity [41].

#### Impact of *Excoecaria agallocha* on anti-nociceptive effect

The drug or compounds have the capacity to reduce the sensation of pain is called anti-nociceptive agents. Somatic/visceral and acute/chronical is the major classification of pain. Also it has been called as neuropathic or inflammatory pain. However the clinical veterinarians and researchers first understand the nociceptive and antinociceptive pathways which involved in the pathophysiology process of pain [42]. Commercially available non-steroidal anti-inflammatory or anti-nociceptive drugs causes few side effects includes gastric lesions induction in patients. The alkaline chloroform fraction of *E. agallocha* at 10, 15, 20 or 25 mg/kg was orally administered into mice to evaluate its anti-nociceptive effect. The central and peripheral analgesic activity was determined using acetic acid-induced writhing and hot plate test. Alkaline chloroform fractions significantly reduced the writhing of mice in a dose dependent manner. Further HPLC-MS of Alk-CF confirmed the Rutin, Quercetin, Myricetin, Kaempferol, Luteolin, and Isorhamnetin might be responsible for its anti-nociceptive activity. *In silico* computational studies proved the higher binding affinity of rutin to COX-1 and 2 analgesic marker protein receptors [43]. Sodium thiopental-induced sleeping time, Open field, Hole cross and Hole-board test were used to determine the test samples potential on mice/rat behaviour changes such as sleeping time, number of squares visited, number of entries through the hole and head dips time by using experimental animals. Oral administration of 200 mg/kg bw of ethanolic extract of EA revealed significant decline in sleeping time and gross behaviour of mice [28].

#### Potential of *E. agallocha* in nanoparticles biosynthesis

Nanobiotechnology and bionanotechnology are essentially synonyms refer to study materials and manipulated at nanometer scale (10<sup>-9</sup> m scale) for various applications [44]. Advantages of silver nanoparticles has been increased every year in the field of optoelectronics, bimolecular detection, diagnostics, antimicrobial, cancer treatment and environmental application [45-47]. Monodisperse spherical shaped silver nanoparticles synthesized from the leaf sample of *E. agallocha*. Transmission electron microscopy determined the nanoparticles were 15 to 45 nm in size. Phenol and functional group of proteins present in the leaf extracts provide stability to the biosynthesized silver nanoparticles [48]. Crystalline nature of silver nanoparticles observed by X-ray diffraction peak pattern at (111), (200), and (220). 100 µl of biologically synthesized nanoparticles has the potential to inhibit the nitrite formation in the reaction mixture compared with catechin standard [49]. Nanoencapsulated rutin from *Excoecaria agallocha* reported to have significant anti-diabetic and diabetic wound healing activity in streptozotocin induced diabetic rats [50,51].

#### Impact of *Excoecaria agallocha* as a heavy metal bioindicator

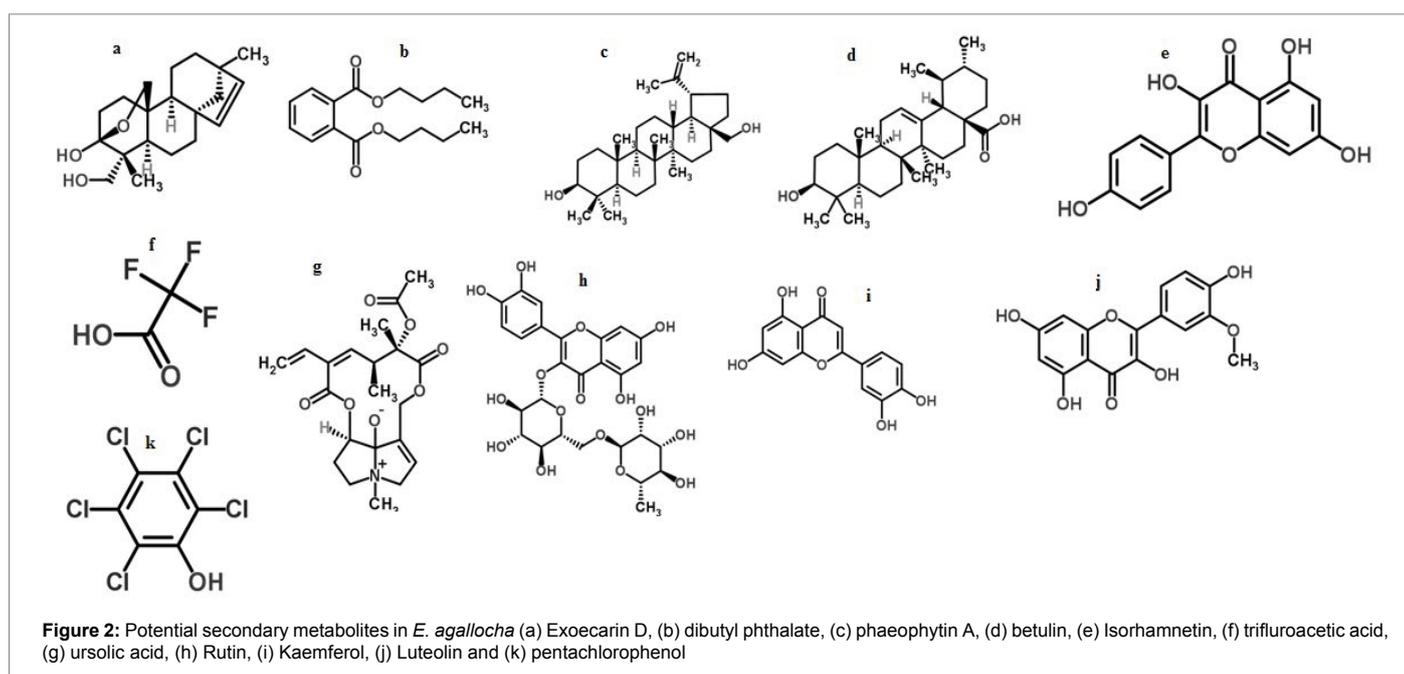
Due to industrialization, the ground water and soil content are highly polluted by the heavy metals like Zinc, copper, cadmium etc. A

huge number of studies are in progress how to scavenge or remove the heavy metals from the polluted areas such as chemical and mechanical related industries, tourist area, fish landing and harbour respectively. In plant species, the zinc and copper metals played vital role in respiratory enzyme system activation phytohormones biosynthesis, photosynthetic process especially in photo system II and some protein, carbohydrates metabolites biosynthesis [52,53]. However those metals are required in minimal quantity for plant metabolism and biosynthesis process, but few mangrove species have the capacity to accumulate huge amount of heavy metals from the affect areas. Recently, Chakraborty et al. [54] examined the bioaccumulation of zinc, copper and lead heavy metals in the various part of *E. agallocha* including leaf, stem and root. They selected the 12 major stations such as Canning, Gosaba, Diamond harbour, nayachar island, kakkwip, chemaguri, sagar south, jambu island, fraser gunge, digha, bali an dbagmara in the north east coast of bay of Bengal and sunderbans indain mangrove ecosystem. As a result of this study, in the root and stem part of *E. agallocha* showed significant level of dissolved heavy metals and it proved its bioindicator potential.

### Chemical composition of *E. agallocha*

Mangroves are rich sources of primary and secondary metabolites which are involved in many pharmaceutical and environmental applications. Numerous studies has been undertaken by various group of researchers to find out the pre liminary phytoconstituents and phenolic compounds present in different parts of *E. agallocha*. Previous phytochemical investigation studies of *E. agallocha* leaves revealed that the presence of diterpenoids, triterpenoids, flavonoids, alkaloids, anthraquinone, phytosterol, fixed oil, tannin, phorbol esters, free amino acids, mucilage, glycosides, carbohydrates, and lignin [55,56]. Novel Exoecarin D, E and F diterpenoid from Leaves of *E. agallocha* and their structure depicted as 3 $\alpha$ ,18-dihydroxy-3 $\beta$ ,20-epoxybeyer-15-ene, (15R,16S)-ent-15,16-epoxybeyeran-3-one and ent-3 $\beta$ -hydroxykaur-16-en-2-one using NMR and X-ray analytical techniques [57]. Additionally, 14-taraxeren-3-one, dibutyl phthalate, phaeophytin A, betulin, beta rosasterol, betulinic acid oleanolic and

ursolic acid also identified from EA [58]. Fresh leaves of *E. agallocha* was extracted with mixture of petroleum ether, diethyl ether and ethanol by Likens-Nickerson distillation method up to 120 min. The concentrated fractions was analysed by GC-MS, it showed the presence of dodecanediol, L-alanine-4-nitroanilide, benzene methanol, 1,1-diethoxyundecane, hexadecane, Metaraminol, 1,2-benzenediol, tetradecane, hexadecane, benzyl alcohol, benzenemethanol, 4-trifluoroacet benzyl alcohol, L-alanine -4-nitroanilide, alanine, 2,6-Octadiene-4, undecane, Pentanoic acid, hydroxybenzenepropanoic acid, diethyl methylphosphonate, acridine, trifluoroacetic acid, triethyl (pentafluorophenyl)silane, Ngainone, N-1-Adanantyl-p-methylbenzylimine, pentachlorophenol, Isohumulone, Octadecanoic acid, decane, diethylphthalate, benzamide, pentanenitrile, diacetate, clivorine and 1,2,5-trimethylphylyole by comparing the spectral data with NBS and IDENT dada base [59]. Latex contains alcohols - exocarol, agalocol, isoagalocol and mannitol;  $\beta$ -amyryn and its 3-epimer,  $\beta$ -amyrenone and cycloartenol. Twigs and bark contain a piscicidal compound which is toxic to *Cryzias latipes*. The leaf extract of *E. agallocha* used for rheumatism, paralysis, cutaneous infection and abortificant. Several Preclinical trials carried out on Secondary metabolites of *E. agallocha* showed its potential as anti-HIV, anticancer, antibacterial, antidiabetic activities and antiviral agent. Alkaloids, carboxylic acid, Flavonoids, phenol, saponin, resins, steroids, tannin and sugars from seeds of *E. agallocha* exhibited anti-inflammatory and analgesic activity [60]. The crude hexane extraction of dried root of *E. agallocha* showed the presence of acyclic hydrocarbon and n-triacontane with mosquito larvicidal and insecticidal activity [61]. Other group of researchers found that the phytoconstituents in *E. agallocha* has been increased or decresed in their content with respect to salt availability conditions. The potential chemical structures of *E. agallocha* shown in Figure 2. Jenci and Natarajan [62] observed there was a increasing change in their starch and chlorophyll content of *E. agallocha* with respect to 300 mM sodium chloride and 200 mM of potassium chloride. Dioecious nature of *E. agallocha*, the male trees are dominant then compared to female. Rao et al. [63] micro propagated the shoots and roots of *E. agallocha* under *in vitro* conditions using Murashige and Skoog, Woody Plant and a modified medium medium.



Source	Active chemical constituents	Nature of extract	Bio activity
Leaves	Benzoate, Flavonoid glycosides, Rutin, afzelin, Quercitrin, kaempferol-3-O-(2-O-acetyl- $\alpha$ -L-rhamnopyranoside, kaempferol 3-O- $\alpha$ -L-rhamnopyranoside, 2,3-secoatisane type diterpene, 3,4,5-trihydroxy methyl benzoate, Phorbol ester 12-deoxyphorbol 13-(3E,5E-decadienoate), dodecanediol, L-alanine-4-nitroanilide, benzene methanol, 1,1-diethoxyundecane, hexadecane, Metaraminol, 1,2-benzenediol, tetradecane, hexadecane, benzyl alcohol, benzenemethanol, 4-trifluoroacet benzyl alcohol, L-alanine-4-nitroanilide, alanine, 2,6-Octadiene-4,undecane,Pentanoic acid, hydroxybenzenepropanoic acid, diethyl methylphosphonate, acridine, trifluoroacetic acid, triethyl (pentafluorophenyl)silane, Ngainone, N-1-Adanantyl-p-methylbenzalimine, pentachlorophenol, Isohumulone, Octadecanoic acid, decane, diethylphthalate, benzamide, pentanenitrile, diacetate, clivorine and 1,2,5-trimethylphytyole, phenol, saponin, tannin, sugars, alkaloids, Excoecarin D, E and F diterpenoids, Mycetin, Luteolin, and Isorhamnetin	Alkaline chloroform fraction, alkaloid rich fractions, chloroform extract, DMSO extract, Ethanolic extract, Ethyl acetate fractions, Fatty acid methyl esters, methanolic extract, methanolic extracts, water fractions	Analgesic activity, anti-bacterial, anti-cancer, anti-diabetic, anti-filarial activity, anti-fungal activity against fish pathogen, urinary tract infections bacteria and antibiotic sensitive ophthalmic bacterial pathogens, anti-HIV activity, anti-inflammatory, anti-nociceptive effect, anti-tumour, bio accumulation of heavy metal, cytotoxicity, Diabetic wound healing properties, DPPH free radical scavenging activity, Nitric oxide free radical scavenging activity, mosquito larvicidal activity, silver nanoparticles production
Bark	Stachenone, stachenol, excoecariotoxin, daphnane, diterpene esters, excoecarin	Aqueous extract, ethanolic extract, hydro alcoholic extract methanolic extract	Anti-bacterial, mosquito larvicidal activity, pesticidal and piscicide activity and Neuropharmacological activity
Twigs	Stachenol, Stachenone, Excoecariotoxin, daphnane, diterpene esters		Pesticidal and piscicide activity
Stem	Phorbol ester 12-deoxyphorbol 13-(3E,5E-decadienoate)	Ethanolic extract	Anti-HIV, Reverse transcriptase viral enzyme inhibition, free radical scavenging activity, Bio accumulation of heavy metal, insecticidal activity
Root	Acyclic hydrocarbon, n-triacontane	Chloroform extracts, hexane extract	Bio accumulation of heavy metal, anti-bacterial activity, mosquito larvicidal activity, insecticidal activity
Latex	Agalocol, isoagalocol and mannitol Exocarol, excoecariotoxin, daphnane diterpene esters, $\beta$ -amyirin, stachenol, stachenone 3-epimer, $\beta$ -amyrenone, cycloartenol, alkaloids, carboxylic acid, saponin, xanthoproteins, steroids	Ethanol with water latex extracts	Causes skin irritation and eye injury, anti-inflammatory, analgesic activity, Fish poisonous chemical substance (piscicide).
Seeds	Alkaloids, carboxylic acid, Flavonoids, phenol, saponin, resins, steroids, tannin and sugars	Ethanol with water latex extracts	Anti-inflammatory, analgesic activity

Table 1: Chemical constituents and biological activities of *Excoecaria agallocha* L.

Table 1 indicates the chemical composition and biological activities of *E. agallocha*. In conclusion, this literature collections provide huge information about the traditional value, therapeutic impacts and phytoconstituents of *E. agallocha*. However few articles also examined the some toxic effects of *E. agallocha* latex part. Apart from that, the review shows the promising potential of *E. agallocha* to develop a drug molecules for epidemic, pandemic and chronic diseases like diabetes mellitus.

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#### References

- Aleman MS, Bourgeois C, Appeltans W, Vanhoorne B, De Hauwere N, et al. (2010) The Mangrove Reference Database and Herbarium. Plant Ecology and Evolution 143: 225-232.
- Kathiresan K, Ramanathan T (1997) Monograph: Medicinal plants of Parangipettai Coast. Annamalai University, Tamil Nadu, India. p: 76.
- Ghani A (2003) Medicinal Plants of Bangladesh. 2nd edn. The Asiatic Society of Bangladesh 7: 228-229.
- Erickson KL, Beutler JA, Cardellina JH 2nd, McMahon JB, Newman DJ, et al. (1995) A novel phorbol ester from *Excoecaria agallocha*. J Nat Prod 58: 769-772.
- Kaliyamurthi S, Selvaraj G, Thirugnanasambandam R (2014) Documentation of hypoglycemic and wound healing plants in Kodyampalayam coastal village (Southeast coast of India). Journal of Coastal Life Medicine 2: 642-647.
- Seghrouchni I, Drai J, Bannier E, Rivière J, Calmard P, et al. (2002) Oxidative stress parameters in type I, type II and insulin-treated type 2 diabetes mellitus: insulin treatment efficiency. Clin Chim Acta 321: 89-96.
- Worthley LIG (2003) The Australian short course on intensive care medicine. Handbook, Gillingham printers, South Australia. pp: 31-55.
- Sowka JW, Gurwood AS, Kabat AG (2009) Handbook of ocular disease management diabetes mellitus. Review of Optometry. p: 63.
- Chan JC, Malik V, Jia W, Kadowaki T, Yajnik CS, et al. (2009) Diabetes in Asia: epidemiology, risk factors, and pathophysiology. JAMA 301: 2129-2140.
- Gurudeeban S, Satyavani K, Ramanathan T (2012) Alpha glucosidase inhibitory effect and enzyme kinetics of coastal medicinal plants. Bangladesh Journal of Pharmacology 7: 186-191.
- Rees DA, Alcolado JC (2005) Animal models of diabetes mellitus. Diabet Med 22: 359-370.
- Thirumurugan G, Vijayakumar TM, Poovi G, Senthilkumar K, Sivaraman K, et al. (2009) Evaluation of antidiabetic activity of *Excoecaria agallocha* L. in alloxan induced diabetic mice. Journal of Natural Products: 1-5.
- Rahman M, Siddika A, Bhadra B, Rahman S, Agarwala B, et al. (2010) Antihyperglycemic activity studies on methanol extract of *Petrea volubilis* L. (Verbenaceae) leaves and *Excoecaria agallocha* L. (Euphorbiaceae) stems. Advances in Natural and Applied Sciences 4: 361-364.
- Satyavani K, Gurudeeban S, Ramanathan T (2016) Effect of *Excoecaria agallocha* L. extracts on elastase and collagenase inhibitory action and identification of metabolites using HPLC-UV-MS. Pharmaceutical Chemistry Journal (In press).
- Nair MK, Varghese C, Swaminathan R (2005) Cancer: Current scenario, intervention strategies and projections for 2015. Burden of Disease in India. p: 219.
- Siegel RL, Miller KD, Jemal A (2015) Cancer statistics, 2015. CA: A cancer journal for clinicians 65: 5-29.
- Patil RC, Manohar S, Upadhye M, Katchi VI, Rao A, et al. (2012) Anti Reverse Transcriptase and Anticancer activity of stem ethanol extracts of *Excoecaria agallocha* (Euphorbiaceae). Ceylon Journal of Science (Biological Sciences) 40: 147-155.
- Konoshima T, Konishi T, Takasaki M, Yamazoe K, Tokuda H (2001) Anti-tumor-promoting activity of the diterpene from *Excoecaria agallocha*. II. Biol Pharm Bull 24: 1440-1442.
- Kinzier KW, Vogelstein B (1990) The GLI gene encodes a nuclear protein which binds specific sequences in the human genome. Mol Cell Biol 10: 634-642.

20. Rifai Y, Arai MA, Sadhu SK, Ahmed F, Ishibashi M (2011) New Hedgehog/GLI signaling inhibitors from *Excoecaria agallocha*. *Bioorg Med Chem Lett* 21: 718-722.
21. Norhanom AW, Yadav M (1995) Tumour promoter activity in Malaysian Euphorbiaceae. *Br J Cancer* 71: 776-779.
22. Kathiresan K, Thangam TS (1987) Biototoxicity of *Excoecaria agallocha* L. latex on marine organisms. *Current Science* 56: 314-315.
23. Huang Z, Cai X, Shao C, She Z, Xia X, et al. (2008) Chemistry and weak antimicrobial activities of phomopsins produced by mangrove endophytic fungus *Phomopsis* sp. ZSU-H76. *Phytochemistry* 69: 1604-1608.
24. Eldeen IM, Effendy MA (2013) Antimicrobial agents from mangrove plants and their endophytes. *Microbial pathogens and Strategies for Combating them: Science, Technology and Education. FORMATEX Microbiology Book Series. Formatex Research Centre: Badajoz, Spain. pp: 872-882.*
25. Vadlapudi V, Bobbarala V, Penumajji S, Naidu KC (2009) *Excoecaria agallocha* L. antimicrobial properties against important pathogenic microorganisms. *International Journal of PharmTech Research* 1: 865-867.
26. Raja M, Ravikumar S, Gnanadesigan M, Vijayakumar V (2010) In vitro antibacterial activity of diterpene and benzoxazole derivatives from *Excoecaria agallocha* L. *International Journal of Biological and Chemical Sciences* 4: 692-701.
27. Abeysinghe PD (2010) Antibacterial Activity of some Medicinal Mangroves against Antibiotic Resistant Pathogenic Bacteria. *Indian J Pharm Sci* 72: 167-172.
28. Subhan N, Alam MA, Ahmed F, Shahid IJ, Nahar L, et al. (2008) Bioactivity of *Excoecaria agallocha*. *Revista Brasileira de Farmacognosia* 18: 521-526.
29. Kumar P, Ahmed John S (2013) Invitro anti- fungal activity of *excoecaria agallocha*. I. from pichavaram mangrove forest. *International Journal of Plant, Animal and Environmental Sciences* 3: 32-34.
30. Hsueh PR, Teng LJ, Yang PC, Ho SW, Hsieh WC, et al. (1997) Increasing incidence of nosocomial *Chryseobacterium indologenes* infections in Taiwan. *Eur J Clin Microbiol Infect Dis* 16: 568-574.
31. Laith AA, Najiah M (2014) Antimicrobial activities of blinding tree *Excoecaria agallocha* against selected bacterial pathogens. *Journal of Microbiology and Antimicrobials* 6: 29-36.
32. Dhayanithi NB, Ajith Kumar TT, Balasubramanian T (2012) Effect of *Excoecaria agallocha* leaves against *Aeromonas hydrophila* in marine ornamental fish, *Amphiprion sebae*. *Indian Journal of Marine Sciences* 41: 76.
33. Agoramoorthy G, Chandrasekaran M, Venkatesalu V, Hsu MJ (2007) Antibacterial and antifungal activities of fatty acid methyl esters of the blind-your-eye mangrove from India. *Brazilian Journal of Microbiology* 38: 739-742.
34. Kamaraj C, Bagavan A, Rahuman AA, Zahir AA, Elango G, et al. (2009) Larvicidal potential of medicinal plant extracts against *Anopheles subpictus* Grassi and *Culex tritaeniorhynchus* Giles (Diptera: Culicidae). *Parasitol Res* 104: 1163-1171.
35. Guha-Sapir D, Schimmer B (2005) Dengue fever: new paradigms for a changing epidemiology. *Emerg Themes Epidemiol* 2: 1.
36. Pancharoen C, Kulwichit W, Tantawichien T, Thisyakorn U, Thisyakorn C (2002) Dengue infection: a global concern. *J Med Assoc Thai* 85 Suppl 1: S25-33.
37. Thirunavukkarasu P, Ramanathan T, Renugadevi G, Jayalakshmi S (2011) Studies on larvicidal potential of *Excoecaria agallocha* L. bark extract. *Journal of Pharmacy Research* 4: 3480.
38. Pradeepa P, Subalakshmi K, Saranya A, Dinesh P, Raj VA, et al. (2015) Milky Mangrove *Excoecaria agallocha* L. Plant as a source for potential mosquito larvicides. *Journal of Applied Pharmaceutical Science* 5: 102-105.
39. Raihan SA (2014) Effect of Plant Flavonoids on Mosquito Larvae. *Journal of Science* 1: 27-30.
40. Patra JK, Mohapatra AD, Rath SK, Dhal NK, Thatoi H (2009) Screening of antioxidant and antifilarial activity of leaf extracts of *Excoecaria agallocha* L. *International Journal of Integrative Biology* 7: 9-15.
41. Satyavani K, Gurudeeban S, Ramanathan T, Balasubramanian T (2013) Radical scavenging effect and GCMS identification of alkaloid fractions from *Excoecaria agallocha* L. *Inventi Rapid: Ethnopharmacology* 1: 1-4.
42. Lemke KA (2004) Understanding the pathophysiology of perioperative pain. *Can Vet J* 45: 405-413.
43. Selvaraj G, Kaliampurthi S, Thirungnasambandam R, Vivekanandan L, Balasubramanian T (2014) Anti-nociceptive effect in mice of thillai flavonoid rutin. *Biomed Environ Sci* 27: 295-299.
44. Khademhosseini A, Toner M, Borenstein J, Takayama S (2008) *Micro and Nanoengineering of the cellular microenvironment: Applications and Technologies. Artech House Publishing, USA.*
45. Schultz S, Smith D, Mock JJ, Schultz DA (2000) Single-target molecule detection with nonbleaching multicolor optical immunolabels. *Proceedings of the National Academy of Sciences* 97: 996-1001.
46. Satyavani K, Gurudeeban S, Ramanathan T, Balasubramanian T (2011) Biomedical potential of silver nanoparticles synthesized from calli cells of *Citrullus colocynthis* (L.) Schrad. *Journal of Nanobiotechnology* 9: 2-8
47. Satyavani K, Gurudeeban S, Deepak V, Ramanathan T (2013) *Heliotropium Curassavicum* mediated Silver Nanoparticles for Environmental Application. *Research Journal of Chemistry and Environmen* 17: 27-33.
48. Satyavani K, Gurudeeban S, Ramanathan T (2014) Influence of leaf broth concentration of *Excoecaria agallocha* as a process variable in silver nanoparticles synthesis. *Journal of Nanomedicine Research* 1: 1-5.
49. Sangeetha A, Saraswathi U, Singaravelu (2014) Green synthesis of silver nanoparticles using a mangrove *Excoecaria agallocha*. *International Journal of Pharmaceutical Science Invention* 3: 54-57.
50. Satyavani K (2013) Nanoencapsulation, Characterization and Ointment Formulation of Rutin from *Excoecaria agallocha* L. on control of Type II Diabetes Mellitus and Diabetic Foot Ulcer using Wistar albino rats. PhD Thesis, Annamalai University, India. p: 284.
51. Satyavani K, Ramanathan T, Gurudeeban S, Balasubramanian T (2013) Drug for Treatment of Diabetes and Diabetic Foot Ulcer Using Rutin Loaded Solid Lipid Nanoparticles. *Official Journal of Patent Office (India)*. p: 326.
52. Ernst WHO, Verkleij JAC, Schat H (1992) Metal tolerance in plants. *Acta Botanica Neerlandica* 41: 229-248.
53. Shaw AJ (1990) Heavy Metal Tolerance in Plants: Evolutionary Aspects. *Nordic Journal of Botany* 13: 330.
54. Chakraborty S, Zaman S, Mitra A (2014) *Excoecaria agallocha*: a potential bioindicator of heavy metal pollution. *International Journal of Engineering Research and General Science* 2: 289-298.
55. Zou JH, Dai J, Chen X, Yuan JQ (2006) Pentacyclic triterpenoids from leaves of *Excoecaria agallocha*. *Chem Pharm Bull (Tokyo)* 54: 920-921.
56. Deepa M, Padmaja CK (2014) Preliminary phytochemical analysis and thin layer chromatography of the extracts of *Excoecaria agallocha* L. *International Journal of Pharmaceutical Sciences and Research* 5: 4535-4542.
57. Konishi T, Konoshima T, Fujiwara Y, Kiyosawa S (2000) *Excoecarins* D, E, and K from *excoecaria agallocha*. *J Nat Prod* 63: 344-346.
58. Xu J, Deng ZW, Lin WH (2009) Chemical constituents of mangrove plant *Excoecaria agallocha* in Hainan Province. *Chinese Traditional Herb Drugs* 411: 1704-1707.
59. Satyavani K, Gurudeeban S, Manigandan V, Rajamanickam E, Ramanathan T (2015) Chemical Compositions of Medicinal Mangrove Species *Acanthus ilicifolius*, *Excoecaria agallocha*, *Rhizophora apiculata* and *Rhizophora mucronata*. *Current Research in Chemistry* 7: 1.
60. Babuselvam M, Ravikumar S, Farook KM, Abideen S, Mohamed MP, et al. (2012) Evaluation of anti-inflammatory and analgesic effects on the extracts of different parts of *Excoecaria agallocha* L. *Journal of Applied Pharmaceutical Science* 2: 108-112.
61. Satyan RS, Sakthivadivel M, Shankar S, Dinesh MG (2012) Mosquito larvicidal activity of linear alkane hydrocarbons from *Excoecaria agallocha* L. against *Culex quinquefasciatus* Say. *Nat Prod Res* 26: 2232-2234.
62. Jenci M, Natarajan S (2009) Growth and organic constituent variations with salinity in *Excoecaria agallocha* L. an important halophyte. *Botany Research International* 2: 50-54.
63. Rao CS, Eganathan P, Anand A, Balakrishna P, Reddy TP (1998) Protocol for in vitro propagation of *Excoecaria agallocha* L. a medicinally important mangrove species. *Plant Cell Reports* 17: 861-865.