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Review Article

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Excoecaria agallocha Linn (Euphrobiaceae) : An overview

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ABSTRACT

The review is conducted on Excoccaria. Different parts plants like wood, root, leaves, stem and leaves, stem, stem and twigs, twigs and bark, bark, twigs and leaves are studied in this review. The study of this review revealed that the parts of plants like wood, root, leaves, stem and leaves; stem, stem and twigs, twigs and bark, bark, twigs and leaves are isolated by 91 compounds. The following biological activities, which are from the crude extract, are observed as follow anti cancer, antimicrobial, anti bacterial, anti-inflammatory, anti micro fouling, antioxidant, anti-histamine. They release invitro anti bacterial, anti-tumour-promoting and cytotoxicity, anti-reverse transcriptase, human cancer cell and anti HIV. This observation finally found that there are many compounds in wood and more number of biological activities in Leaves. Bark, twigs and leaves are observed as anti HIV.

Key words: *Excoecaria*, Isolated Compounds, Study of Biological Activity, Anti HIV.

INTRODUCTION

The plants of the genus *Excoecaria* (family: Euphrobiaceae) comprise nearly different 42 species spreading all over tropical Asia, Africa, and northwest Australia [9]. It is the most widely reported species. The leaves and latex of this tree has been used as a purgative and abortfacient. The recent analysis of assorted disease showed that it is used in a dart poison and fish poison in India, Malaysia and New Caledonia. The experiment analysed the diseases such as Ulcers, Rheumatism, Leprosy, and paralysis. The bark and wood of Excoecaria plants have been applied in Thailand medicine as a remedy against flatulence [3]. Recently much attention is paid to Excoecaria species due to its Anti Reverse Transcriptase and anti-HIV activities [30] [33]. In this review, we will expand the photochemical development and try to list all the compounds isolated from the genus Excoecaria over the past few decades. We include the biological activities of compound reported in recent years.

Chemical Constituents

The Chemical Constituents of *E.agallocha* Include Terpenes, Terpenoids, Alkaloid, Polyphenols, Flavanosids and Some other Compounds(1-91). Their Structures from (1-91) are showing Figure-1 along with their names and the Corresponding plant sources.

WOOD

Labdane Diterpenes

Most Labdane Diterpenes, Compounds (1-3) (7-9) (19-23) (30-35) were isolated from the wood of *E.agallocha*. (1-3) Konishi et al, were having reported for first time from the wood of *E.agallocha* [1]. And (7-9) (19-23) (30-35) also isolated from the wood of *E.agallocha* [3] [9] [12].

Seco Labdane Diterpenes

Excoecarin H (10) & Excoearin S-T₂ (15-17) were reported from the wood of *E.agallocha* [4] [7].

Isopimarane Diterpene

One of the isopimarane diterpene (18) was isolated from the wood of *E.agallocha* [8].

Diterpenes

Excoecarin M-N (11-12) was reported from the wood of E.agallocha [5].

Labdane Diterpenoids

Ponnapalli et al, three new ent-labdane type diterpenoids Agallochaexcoerin A-C (27-29) were isolated from the wood of *E.agallocha* [11].

Bis-Seco labdane Diterpenoids & Isopimarane Diterpenoids

In 2000, Konishi et al, isolated three new diterpenoids (4-6) and two new Bis-Secolabdane diterpenoids, Excoecarins **R1& R2** (13-14) and two Isopimarane diterpenoids, Agallochin J-L (24-26) and Agallochaexcorin D-F (36-38) were reported from the wood of *E.agallocha* [2] [6] [10] [13].

Alkaloid

In 1982, Prakash et al, a new piperidine alkaloid (39) was isolated from the wood stem of *E.agallocha* [14].

ROOT

Seco diterpenoids

In 2000, Anjaneyulu et al, isolated five new diterpenoids (40-44), Seco diterpenoids Agallochin M-O (49-51) were isolated from the root of *E.agallocha* [15] [17].

Ent-kaurane & beyerane diterpenoids

In 2002, Anjaneyulu et al, four new ent-kaurane and beyerane diterpenoids Agallochin **F-I** (**45-48**) were isolated from the root of *E.agallocha* [16].

Leaves

In 2006, Jain-Hua Zou et al, A new Oleanane pentacyclic type triterpenoid (52) was isolated from the leaves of *E.agallocha* [18].

Polyphenols

Four new polyphenols namely Excoecariphenols A-D (53-56) was isolated from the leaves of *E.Agallocha* [19].

Flavonoids

Two new flavonoid glycosides Excoglycoside A-B (57-58) were isolated from the leaves of *E.agallocha* [20].

Stems & Leaves

Diterpenoids

Four new diterpenoids namely Excogallochaol **A-D** (**59-62**) was isolated from the stems and leaves of *E.agallocha* [21].

In both diterpene and diterpenoids namely Agallochaol (A-J) (63-72) in diterpenoids together with seco atisans & isopimarane were reported from the stems and leaves of *E.agallocha* [22] [23] [24].

Stems & Twigs

Diterpenoids

Together ent kaurane & atisane diterpenoids named Agallochaol K-Q (73-79) were isolated from the stems & twigs of *E.agallocha* [25].

Stem

Diterpenoids

In 2000, Konishi et al, isolated three new diterpenoids, Excoecarins V_1 - V_3 (80-82) from the stem of *E.agallocha* [26].

Glycoside

A new flavanone glycoside (83) was reported from the stem of *E.agallocha*[26].

Secolabdanoids

In 2015 Annam et al, four new secolabdanoids Excolides **A-B** (84-87) were reported from the stem of *E.agallocha* [27].

Twigs & Bark

In 1974 two new piscicidal constituents (88-89) were isolated from the twigs & bark of E.agallocha [28].

Bark

One of the new atisane diterpene (90) was reported from the bark of *E.agallocha* [29].

Bark, Twigs and Leaves

In 1995 Erickson et al, a novel phorbol ester 12-deoxy phorbol-13-[(3E, 5E)-deca 3, 5-dienoate] (91) was isolated bark, twigs and leaves as the Anti-HIV principal of the E.agallocha [30].

Study of Biological Activities Leaves

Human Cancer Cell

A new Oleanane triterpenoid (52) were isolated from the leaves of *E.agallocha* the compound was found inactive in vitro against several human cancer cell lines [18].

Hepatitis C Virus (HCV)

The Leaves of *E.agallocha* isolation of polyphenol named Excoecariphenol D (**56**) showed potential inhibition toward HCV NS3-4A protesse with IC_{50} values in a range of 3.45-9.03µm.while the compound inhibited HCV RNA in huh 7.5 cells Significantely[19].

Anti-Cancer

Two new flavonoid glycoside (**57-58**) were isolated from the leaves of *E.agallocha* as Hedgehog/GLI1-mediated transcriptional inhibitors and presented cytotoxicity adjacent human pancreatic (PANC 1) and prostate (DU145) cancer cells [20].

In this case leaf crude extract as anti cancer agent. The cell viability of 85.32 and 81.96 were inaugurated to appear at 1:128 dilution of Methanol and Chloroform extracts appropriately [37].

Anti microbial

The anti microbial activities across the important of microorganisms using agar well diffusion scheme. Chloroform and Methanolic extracts were found to be powerful facing these organisms, where as hexane extracts were inoperative [35].

E.*agallocha Leaves* were obtained via extraction with 100 ml of Methanol. The antimicrobial susceptibility test show that the bacteria possessed the capacity to overcome to Nitrofurantion Gentamycin and Neomycin, and were sensitive to Flu equine. The minimum inhibitory conventration (MIC) of E.agallocha was 3.12mg/ml and minimum bactericidal concentration (MBC) was 6.25mg/ml. Inhibition zones were significantly different (p<0.05) depending on concentrations (100, 300 and 500 mg/ml) of the crude extraction of E.*agallocha* [40].

The crude extract obtained was evaluated for antimicrobial property against bacteria & fungi by Agar well diffusion mode and the zone of inhibition diameters were calculated. It acts as a concentration of 1500 μ g/ml presented antibacterial and antifungal activity against test micro-organisms with degree of variation [41].

Antibacterial

It was found that the extracts were very effective in controlling the growth of all the organisms' tested. The fragmentation process of petroleum ether, chloroform, ethyl acetate and n-butanol extracts of *E.agallocha* were determined adjacent 24 bounded and familiar bacterial pathogens. The assay was achieved by agar diffusion process [39].

Stems, Twigs

Anti-Inflammatory

The stems and twigs of the mangrove plant *E.agallocha* isolation of six ent-kaurane diterpenoids named agallochaols K-P (**69-74**), an atisane-type diterpenoid agallochaol Q (**75**) These Compounds exhibit antiinflammatory capability to suppress extraction of NF-KB and AP-1 targeted genes adding TNF- α and IL-6 induced by lipopolysaccharide (LPS) in mouse macrophages Raw 264.7 cells[24].

Bark

Anti microfouling

A new Atisane-type diterpene, ent-16 α -hydroxy –atisane-3,4-lactone(**90**) was isolated from the bark of *E.agallocha*. The compound exhibited importent anti-microfouling activity against the adherence of Pseudomonas Pseudoalcaligenes, with an EC₅₀ value of 0.54±0.01ppm [29].

Antioxident

The activity of the field and micropagated Bark and Adult trees of *E.agallocha* was determined using the DPPH Scavenging assay. The radical Scavenging activity of the extracts ($250\mu g/ml$) is expressed as percentage inhibition and IC₅₀ values of 179.16, 120.24 and 134.29 $\mu g/ml$ [36].

Antioxidative and Anti-Histamine-Release

Using DPPH Freeradical scavenging, reducingpower, measurement of total antioxidant activity and ionphore A23187-induced histamine-release assays, it was found that DW and Eth had high ant oxidative and anti-histamine-release activities compare to other fractions. However, our results showed that bark of E.*agallocha*, especially DW and Eth fractions would be considered a potential source of antioxidative and anti-histamine-release property [43].

In Vitro Anti-Bacterial

The totality of these effects showed that the extract possesses intoxicant action on the central nervous system (CNS). The extract of E.*agallocha* exhibited powerful in vitro antibacterial action against Staphylococcus aureus, Shigella dysenteriae, Shigella Sonnei and Enterococci with the zones of inhibition ranging from 11 to 15mm. While the extract showed considerable brine shrimp toxicity ($LD_{50}=20mg/ml$), it displayed only low level of toxicity in mice [44].

Wood

Antitumor-promoting and Cytotoxic

In 1998, four diterpenes (**30-35**), isolated from the resinous wood of *E.agallocha*. Promoter 12-O-tetradecanoyl phorbol-13-acetate (TPA) [31].

In 2001, Konashima et al, eight diterpenoids (**4-12**), isolated from the resinous wood of *E.agallocha*. And their inhibitory estate on the choosing of Epstein - Barr virus early antigen (EBV-EA) in Raji cells were determined [32].

STEM

Anti -Reverse Transcriptase

In this activity the enzyme based direct binding assay which was as that of the established synthetic inhibitor. Anti cancer activity of the similarly fraction was resolved applying MTS in vitro survey. It has been showed potent cytotoxicity adjacent panegyric cancer cell lines Capan-1 and Miapaca-2 with IC_{50} values of $4\mu g/ml$ and $74\mu g/ml$ [33].

Human Cancer Cell

E.Agallocha exhibited the strongest potency of cytotoxicity in A549 at a dose of 100 ml.At the highest concentration (100 µg/ml), mean reduction of 81% cell viability was observed in A549 correlated with a mean reduction of 58% cell viability in H1299. Hence inhibition of the cancer cell lines H358 and H1299 only occurred at higher concentration of the extract [45].

Bark, twigs and Leaves

Anti-HIV

In 1995, Erikson et al, a novel phorbol ester (91) as a potent in vitro inhibition of HIV replication as measured by inhibition of super anent reverse transcriptase and P24 levels (IC_{50} 6nm) [30].

Adult Trees

Antioxident and Anti-Bacterial

The activity of the field and micropagated Bark and Adult trees of *E.agallocha* was determined using the DPPH Scavenging assay. The radical Scavenging activity of the extracts ($250\mu g/ml$) is expressed as percentage inhibition and IC₅₀ values of 179.16, 120.24 and 134.29 $\mu g/ml$ [34].

Root, Stem and Leaf

In Vitro Anti-Bactrial

So far the organisms were Bacillus Subtillis, Escherichia Coli, Klebsiella Pneumoniae, Salmonella Spp., Shigella Sonnei and Staphylococcus aureus tested by the extracts (root, stem, leaf) of Eagallocha. It was demonstrated by both disc diffusion and agar well diffusion methods [38].

Stem, Bark

Antioxident

The ethanolic extract of E.*agallocha* stem bark was evaluated for antioxidant effects and evaluation of bioactive polyphenols by HPLC-DAD. It suggests that high concentration of Catchin hydrate in the extract of E.*agallocha* [42].

SNO	Name of the plant	Part of the plant	Type of Compound	Name of the Compound	
1	Excoecariaagallocha		Labdane Diterpenes	Excoecarin A(1) Excoecarin B(2) Excoecarin C(3)	[1]
2	Excoecariaagallocha		Diterpenoids	Excoecarin D(4) Excoecarin E(5) Excoecarin K(6)	[2]
3	Excoecariaagallocha		Labdane Diterpenes	Excoecarin F(7) Excoecarin $G_{1[8]}(8)$ Excoecarin $G_{2}(9)$	[3]
4	Excoecariaagallocha		Seco Labdane Diterpene	Excoecarin H(10)	[4]
5	Excoecariaagallocha		Diterpenes	Excoecarin M(11) Excoecarin N(12)	[5]
6	Excoecariaagallocha	Wood	Bis-Seco labdane Diterpenoids	Excoecarin R1(13) Excoecarin R2(14)	[6]
7	Excoecariaagallocha	wood	Seco Labdane Diterpenes	Excoecarin S(15) Excoecarin T1(16) Excoecarin T2(17)	[7]
8	Excoecariaagallocha		Isopimarane Diterpene	3α,11β-dihydroxy-ent-isopimara-8(14),15-dien-2-one(18)	[8]
9	Excoecariaagallocha		Labdane Diterpenes	Ent-13-epi-8,13-epoxy-2-hydroxy labda-1,14-dien-3-one(19) Ent-13-epi-8,13-epoxy-14S,15-dihydroxy labdan-3-one(20) Ent-13-epi-8,13-epoxy-2,3-Seco labd-14-enc-2,3-dioic acid(21) Ent-13-epi-8,13-epoxy-2,3-Seco labd-14-enc-2,3-dioic acid 3- methyl ester(22) Ent-13-epi-8,13-epoxy-2-oxa-3-oxolabd-14-ene-1R-Carboxylic acid.(23)	[9]
10	Excoecariaagallocha		Isopimarane Diterpenoids	Agallochin J(24) Agallochin K(25) Agallochin L(26)	[10]
11	Excoecariaagallocha		Ent-labdane Diterpenoids	Agallochaexcoerin A(27) Agallochaexcoerin B(28) Agallochaexcoerin C(29)	[11]

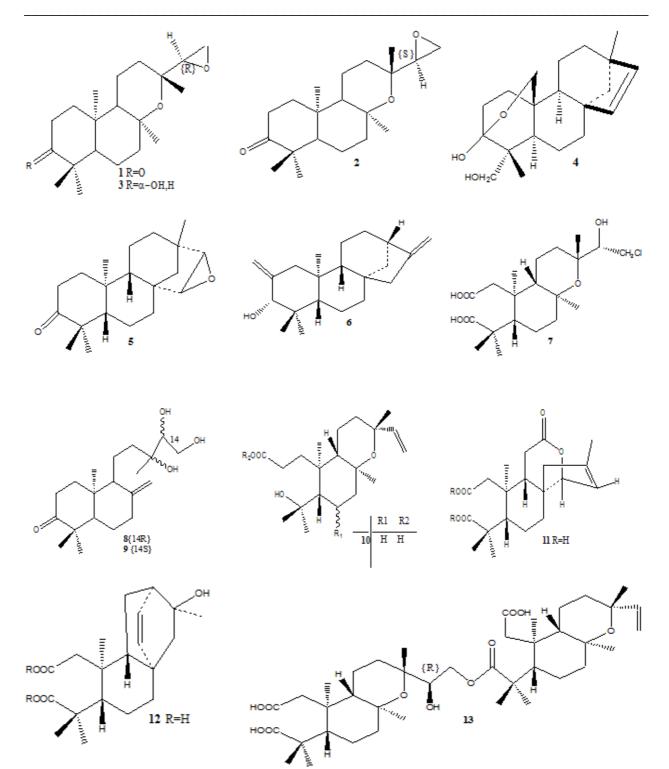
CLASSIFICATION OF COMPOUNDS IN Excoecaria agallocha

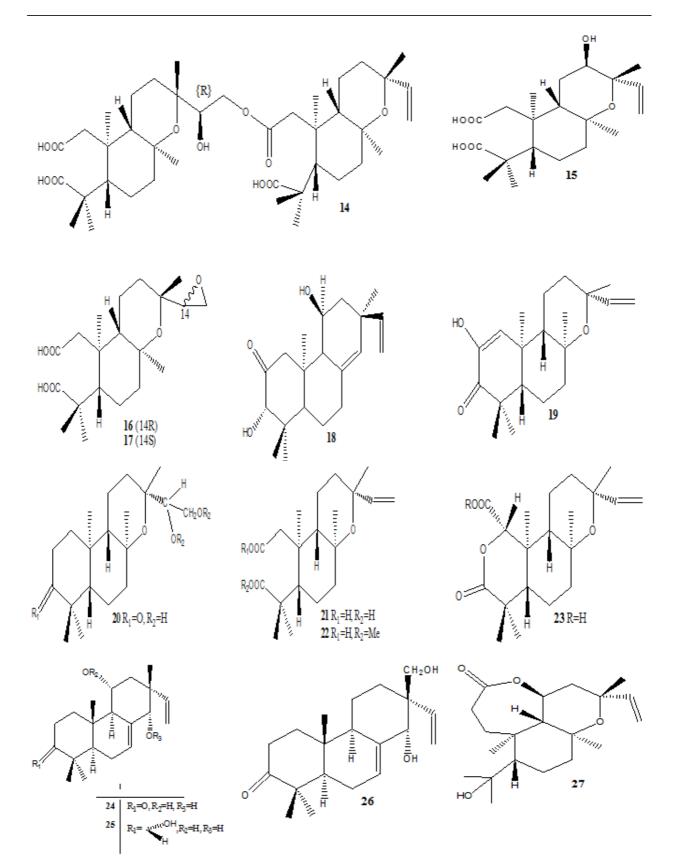
				Ribenone(30)		
12	Excoecaria agallocha			Ribenol(31)		
			Labdane Diterpenes	Ent-13-epi-Manoyl Oxide(32)		
				Ent-11a-Hydroxy-3-oxo-13-epi-manoyl oxide(33)	[12]	
				Ent-16-Hydroxy-3-oxo-13-epi-manoyl		
		Wood		Oxide(34)		
		wood		Ent-15-hydroxy-labda-8(17),13E-diene-3-one(35)		
13	Excoecaria agallocha		Ent-isopimarane Diterpenoids	Agallochaexcorin D(36)		
				Agallochaexcorin E(37)	[13]	
				Agallochaexcorin F(38)		
14	Excoecaria		Alkaloid	2,4-dimethoxy-3- ψ , ψ -dimethylallyl-trans-cinamoyl	[14]	
14	agallocha		Aikaloid	piperidine(39)	[14]	
				Agallochin A(40)	[15]	
	Excoecaria			Agallochin B(41)		
15	agallocha		Diterpenoids	Agallochin C(42)		
				Agallochin D(43)		
				Agallochin E(44)		
	Excoecaria agallocha	Root	Ent-kaurane and Beyerane Diterpenoids	Agallochin F(45)	[16]	
16				Agallochin G(46)		
10				Agallochin H(47)		
				Agallochin I(48)		
	Excoecaria			Agallochin M (49)		
17			Seco Diterpenoids	Agallochin N(50)	[17]	
	agallocha		_	Agallochin O(51)		
18	Excoecaria		Pentacyclic Triterpenoid	3β-[(2E,4E)-5-oxo-deca dienoyl oxy]-olean-12-ene(52)	[18]	
10	agallocha			3p-[(2E, 4E)-3-0x0-deca dienoyi 0xy]-olean-12-elle(32)	[10]	
	Excoecaria agallocha	Leaves		Excoecariphenol A(53)	[19]	
19			Polyphenols	Excoecariphenol B(54)		
19			Polyphenois	Excoecariphenol C(55)		
				Excoecariphenol D(56)		
20	Excoecaria		T1 '1 1 '1	Excoglycoside A(57)	[20]	
20	agallocha		Flavonoid glycosides	Excoglycoside B(58)	[20]	
21	Excoecaria agallocha	Stems and Leaves		Excogallochaol A(59)	[21]	
			Diterpenoids	Excogallochaol B(60)		
			Diterpendius	Excogallochaol C(61)	[21]	
				Excogallochaol D(62)		
				Excogallochaol D(62)		

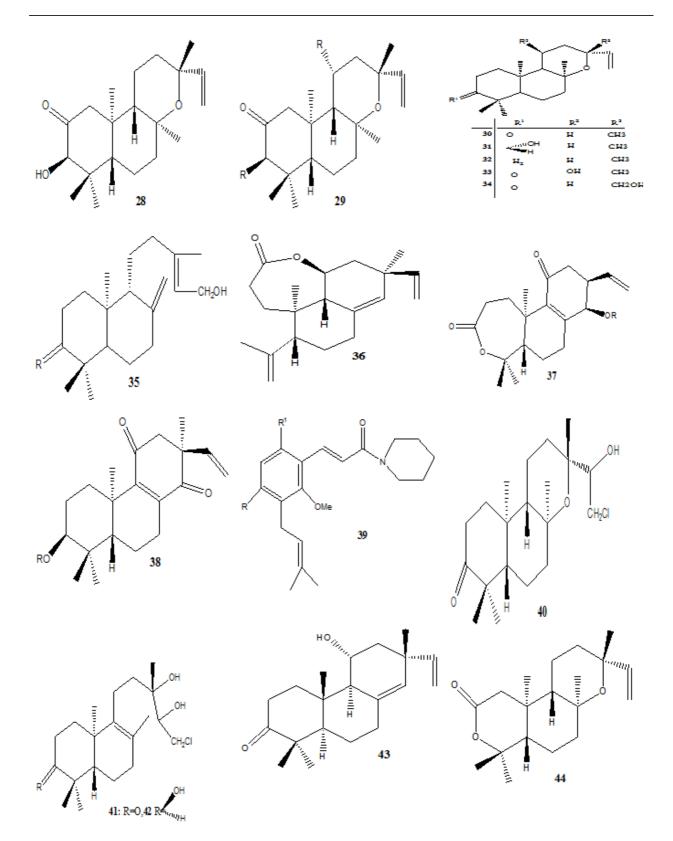
22	Excoecaria agallocha		Diterpenes	Agallochaol A(63) Agallochaol B(64)	[22]	
23	Excoecaria agallocha	Stems and Leaves	Seco atisane Diterpenoid Isopimarane Diterpenoids	Agallochaol C(65) Agallochaol D(66) Agallochaol E(67) Agallochaol F(68)		
24	Excoecaria agallocha	Leaves	Seco atisane Diterpenoid	Agailochaol F(08) Agailochaol G(69) Agailochaol H(70) Agailochaol I(71) Agailochaol J(72)	[24]	
25	Excoecaria agallocha	Stems and Twigs	Ent-kaurane Diterpenoids	Agallochaol K(73) Agallochaol L(74) Agallochaol M(75) Agallochaol N(76) Agallochaol O(77) Agallochaol P(78)	[25]	
26	Excoecaria agallocha	<u>.</u>	Atisane Diterpenoid Diterpenoids Flavanone Glycoside	Agallochaol Q(79) Excoecarin V1(80) Excoecarin V2(81) Excoecarin V3(82) 3,5,7,3,5'-pentahydroxy-2R,3R-flavanonol 3-o-α-L-	[26]	
27	Eagallocha		Secolabdanoids	rhamnopyranoside(83) ExcolideA(84) 11-epi-excolide A(85) 11,13-di-epi-excolide A(86) Excolide B(87)	[27]	
28	Excoecaria agallocha	Twigs and Bark	Piscicidal Constituent	Piscicidal Constituent(88) Huratoxin(89)	[28]	
29	Excoecaria agallocha	Bark	Atisane Diterpene	Ent-16α-hydroxy-atisane-3,4-lactone(90)	[29]	
30	Excoecaria agallocha	Bark, Twigs and Leaves	Tigline diterpene	12-Deoxyphorbal 13-(3E,5E-decadienoate)(91)	[30]	

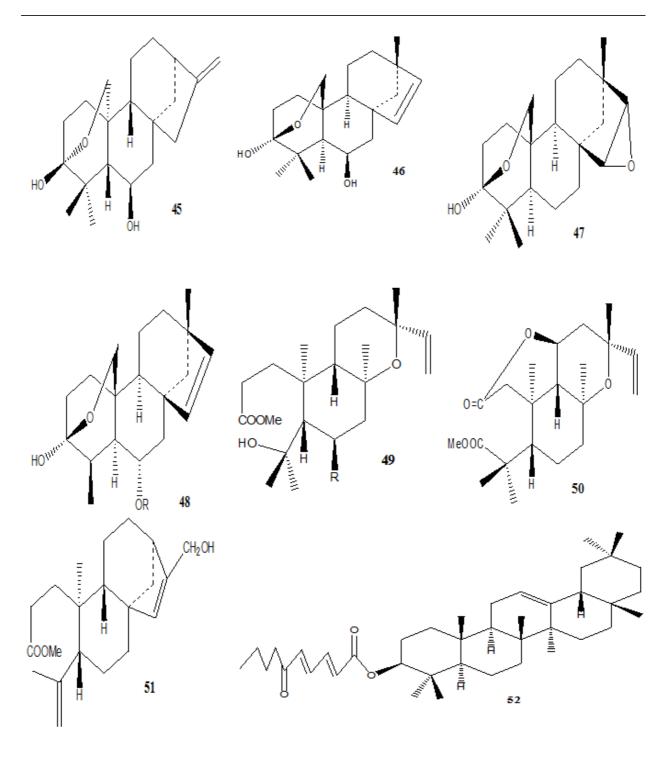
BIOLOGICAL ACTIVITY OF Excoecaria agallocha

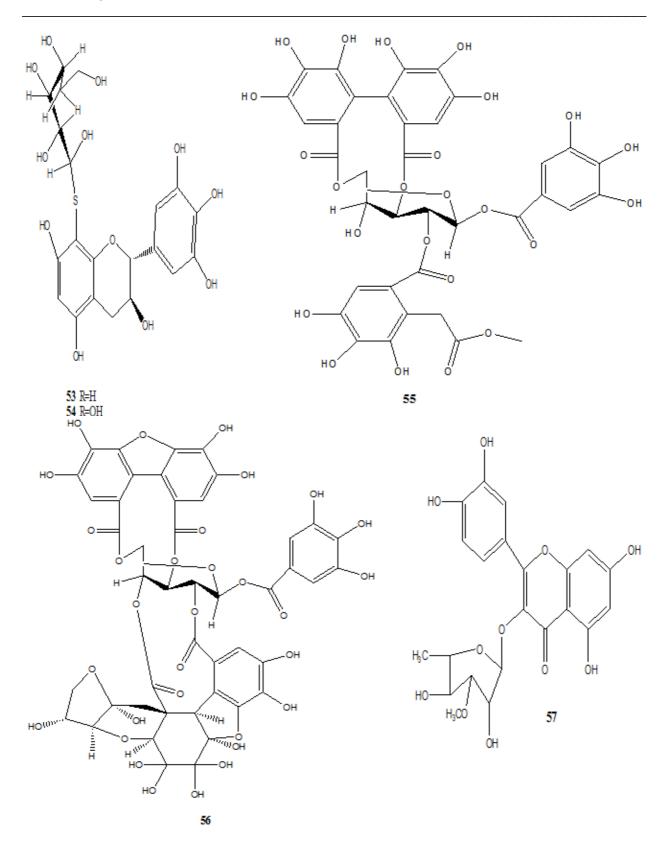
SNO	NAME OF THE PLANT	PART OF THE PLANT	EXTRACT	TYPE OF COM- POUND	NAME OF THE COMPOUND	ACTIVITY	REF
1	E.agallocha		Acetone	Triterpenoid	3β -[(2E,4E)-5-oxo-deca dienoyl oxy]-olean-12- ene(52)	Human Cancer cell	[18]
2	E.agallocha		Butanol	Polyphenol	Excoecariphenol D(56)	Hepatitis C Virus[HCV]	[19]
3	E.agallocha	Leaves	Methanol	Flavonoid glycosides	Excoglycoside A(57) Excoglycoside B(58)	Anti-Cancer	[20]
4	E.agallocha		Hexane, Chloroform, Methanol	NIL	NIL	Anti-Microbial	[35]
5	E.agallocha		Methanol, Chloroform	NIL	NIL	Anti-Cancer	[37]
6	E.agallocha		n-hexane, benzene, chloroform, acetone, ethanol and water extracts	NIL	NIL	Anti-Bacterial	[39]
7	E.agallocha		Methanol	NIL	NIL	Anti-Microbial	[40]
8	E.agallocha		chloroform, Petroleum Ether, Methanol, Ethanol	NIL	NIL	Anti-Microbial	[41]
9	E.agallocha	Stems And Twigs	Ethanol- Water	Ent-kaurane Diterpenoids Atisane	Agallochaol K(69) Agallochaol L(70) Agallochaol M(71) Agallochaol N(72) Agallochaol O(73) Agallochaol P(74)	Anti-Inflammatory	[24]
				Diterpenoid	Agallochaol Q(75)		<u> </u>
10	E.agallocha		Ethanol	Atisane Diterpene	Ent-16α-hydroxy-atisane-3,4- lactone(90)	Anti Micro fouling	[29]
11	E.agallocha	rk	Ethanol	NIL	NIL	Anti- Oxidant	[36]
12	E.agallocha	IK	Ethanol	NIL	NIL	Anti-Oxidant, Anti-Histamine- Release	[43]
13	E.agallocha		Ethanol	NIL	NIL	In vitro antibacterial	[44]
14	E.agallocha		Ether	Labdane Diterpenes	Ribenone(30) Ribenol(31) Ent-16-hydroxy-3-oxo-13- epi-manoyloxide(33) Ent-15-hydroxy-labda- 8(17),13E-diene-3-one(35)	Anti-Tumour Promoting	[31]
15	E.agallocha	Wood	Acetone	Diterpenoids	Excoecarin D(4) Excoecarin E(5) Excoecarin F(7) Excoecarin G ₁ (8) Excoecarin G ₂ (9) Excoecarin K(6) Excoecarin M(11) Excoecarin N(12)	Anti-Tumour- Promoting	[32]
16	E.agallocha	Stem	Ethanol	NIL	NIL	Anti-Reverse Transcriptase & Anti- Cancer	[33]
17	E.agallocha		Ethanol	NIL	NIL	Human Lung Cancer Cell	[45]
18	E.agallocha	Bark, Twigs and Leaves	Dichloromethane, Methanol	Phorbol Ester	12-Deoxyphorbal 13-(3E,5E- decadienoate)(91)	Anti HIV	[30]
19	E.agallocha	Adult Trees	Methanol	NIL	NIL	Anti-Bacterial & Anti- Oxidant	[34]
20	E.agallocha	Root, Stem and Leaf	Chloroform, Ethyl acetate, Butanol	NIL	NIL	Anti-Bacterial	[38]
21	E.agallocha	Stem Bark	Ethanol	NIL	NIL	Anti- Oxidant	[42]

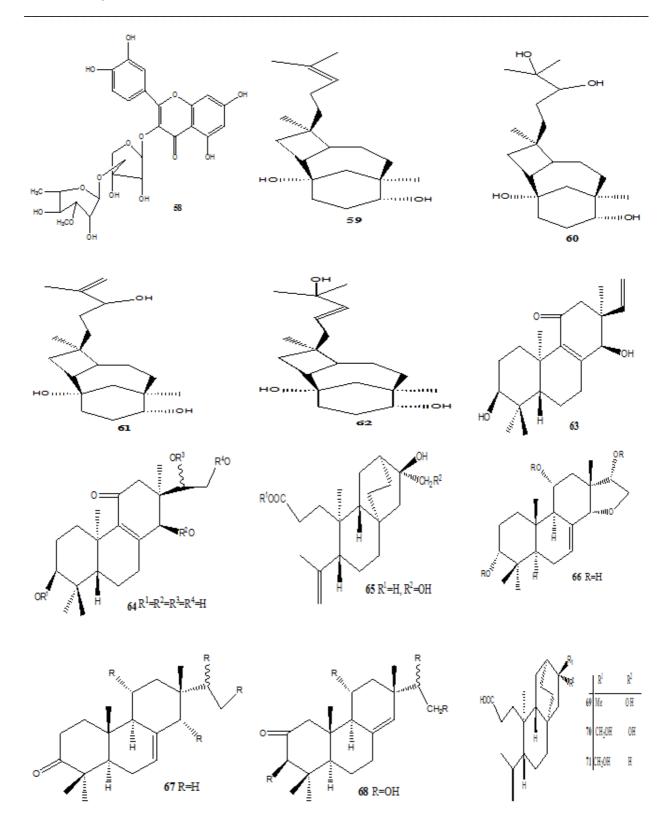


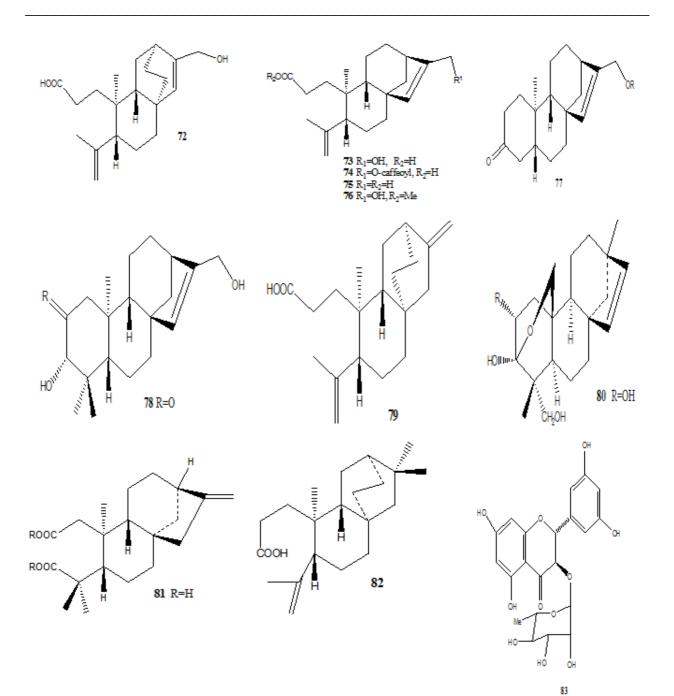


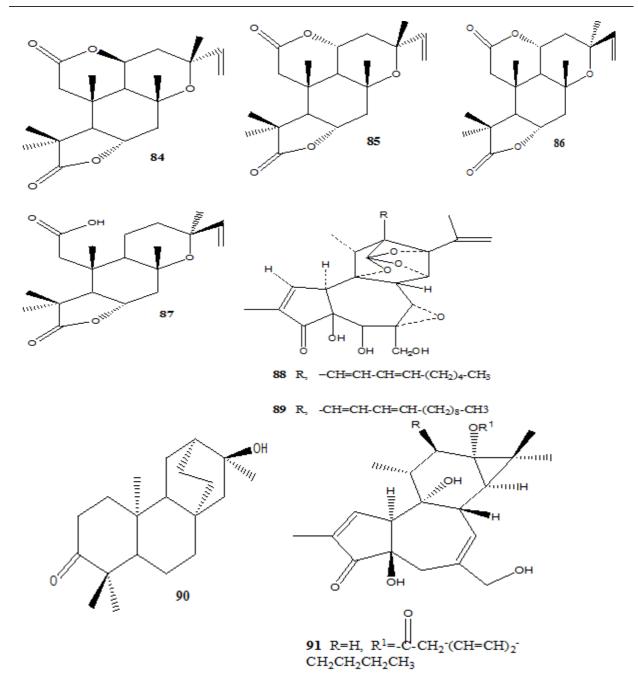












CONCLUSION

This review article focus as on the potential of *Excoecaria agallocha* to be indulged in new therapeutic drugs. It provides the basis for future research to explore the potential of herbs for the cure and management of health care. The diversity in chemical structure helpful to discover new drugs for Anti-inflammatory, Anti-microbial, Anti-reverse transcriptase, Anti cancer, Anti HIV, Anti oxidant.

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