



Exploring the Phytochemical Composition and Pharmacological Activities of *Cerbera manghas* and *C. odollam*: A Comprehensive Review

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ABSTRACT

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Cerbera manghas and *C. odollam*, often perceived as similar species, exhibit distinct physical characteristics and phylogenetic classifications. Despite their reputation as poisonous plants, both species have diverse benefits and are potential sources of pharmacological compounds. This report comprehensively summarizes the compounds identified within the genus *Cerbera*, coupled with reported bioactivities. Over 100 compounds, including phenolics, flavonoids, terpenoids, and steroids, have been isolated from *C. manghas* and *C. odollam*. Cardiac glycosides (steroids) are the predominant compounds in these species and demonstrate robust cytotoxic activity. Furthermore, both plants show promise as antioxidants and antimicrobial agents, and exhibit insecticidal, termiticidal, and larvicidal properties. This review consolidates the current understanding of the phytochemical and pharmacological attributes of *C. manghas* and *C. odollam*.

Keywords: *Cerbera*, *Cerbera manghas*, *Cerbera odollam*, Pharmacological activities, Phytochemicals

Introduction

Cerbera genus is a mangrove plant that belongs to the Apocynaceae family and is widespread in tropical Asia, Australia, and various islands in the Indian and western Pacific Oceans.¹ The two most common species of *Cerbera* are *C. odollam* and *C. manghas*. In Indonesia these two species are known as "bintaro", while in other countries they are known as pong-pong tree, blind rhino, mango laut, wood octopus, and babuto.²

C. manghas is a tree that can reach 20 m in height with a diameter of 70 cm. The branches of the tree are thick and succulent, while the stem contains prominent lenticels and softwood. The leaves are dark green and spirally arranged. The fruit is oval and has a single seed. When ripe, it changes colour to bright red.³ *C. odollam* is a tree measuring up to 12 m and has dark green leaves with leaf stalks measuring 2–5 cm long. The fruit is round, like an apple or a small mango, with poisonous seeds. When the fruit is ripe, it will change from green to reddish purple to brownish black and fall from the tree.⁴ Distinguishing features include the flowers of *C. odollam* with tiny yellow eyes and the oval fruits. In contrast, flowers of *C. manghas* have a prominent pink eye, and fruits are more elongated, resembling mango.⁵ In several reports, it is stated that the *C. manghas* species is the same as *C. odollam*. Based on the phylogenetic tree, *C. odollam* and *C. manghas* are different plants.⁶ Based on literature search, the two species are also reported to contain different compounds or secondary metabolites.⁵

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Almost all parts of the bintaro plant contain a toxin called "Cerberin" which is a toxin that can block human calcium ion channels, thereby disrupting the heartbeat and can cause death, therefore this plant is known as 'suicide tree.' Ingestion of the kernel can cause nausea, vomiting, hyperkalemia, thrombocytopenia, and ECG abnormalities. Exposure to high doses of *Cerbera odollam* carries the highest risk of mortality.⁷ Apart from that, there are also reports of cases of death due to ingestion *C. odollam* seeds in the US, with symptoms of vomiting and bradycardia.⁸ There are also reports of women committing suicide several hours after ingestion pong-pong seeds obtained via the internet.⁹ However, this plant is also reported to have various activities, including antioxidant,¹⁰⁻¹¹ anticancer,¹² anti-inflammatory,¹³ and antimicrobial.¹⁴ These activities are due to the secondary metabolites contained therein, such as saponins, terpenoids, and alkaloids, phenolic acids, flavonoids, cardiac glycosides, steroids, iridoids, lignans, and other compounds.³ Various reports also show its potential as a bioinsecticidal and pesticide in the agricultural field and termiticidal activity in various species.¹² This review article summarizes various compounds reported from *C. manghas* and *C. odollam*, along with their multiple bioactivities, including cytotoxic, antioxidant, antimicrobial, insecticidal, termiticidal, and larvicidal activities. Although several studies also discuss reviews of the *Cerbera* genus, in this article, the review is more comprehensive regarding compounds that have been reported in both species (*C. odollam* and *C. manghas*) as well as their activities, starting from the first report up to the latest data. This review is essential to provide more information regarding the potential of *Cerbera* plants in various bioactivities, both from extracts and isolated compounds, so that this plant is not only known as a poisonous plant but also a valuable plant.

Methodology

This review was based on a literature review. The literature used was reliable literature published from 1976 until 2023. The literature used were scientific articles, research journals, and books on both national and international levels. The literature review was carried out by searching for articles using the keywords "bintaro," "*Cerbera*,"

“*Cerbera manghas*,” “*Cerbera odollam*,” “compound of *Cerbera*,” “bioactivity of *Cerbera*,” and so on Google Scholar, ScienceDirect, Springer, MDPI, PubMed and Researchgate.

Results and Discussion

Compounds in *Cerbera manghas* and *Cerbera odollam*

More than 100 compounds, including phenolics, terpenoids, and steroids, have been isolated from *C. manghas* and *C. odollam*. The most common group of compounds among these two groups is the cardiac glycoside group, a steroid derivative. The complete data are presented in Table 1. Data were sorted by library year, from oldest to latest. The compounds previously reported in the literature have not been rewritten. The first report was published in 1976, reporting the isolation of flavonoid and steroid compounds, namely Nicotiflorin, Rutin, and (+)-Bornesitol.¹⁵ The subsequent discovery was reported in 1977, reporting the isolation of several compounds belonging to the cardiac glycoside group, including Cerberin, Nerifoliin, and Thevetin B. The compound most often found in *Cerbera* plants (*C. manghas* and *C. odollam*) is Cerberin, a group of cardiac glycosides. This compound is found in several parts of plants, namely leaves,¹⁷ fruit,¹⁸ and seeds.^{16, 19-21}

Most of the compounds were isolated from parts of plant leaves, whereas parts of plants rarely studied are fruits. Only one publication was found regarding compounds from *C. manghas* fruit parts, namely phenolic acid and terpenoid groups,¹⁸ including benzoic acid, vanillic acid, Vanillin, and Isophthalaldehydic acid.

Bioactivities

Cytotoxic Activity

The bintaro plant is known to be toxic and poisonous. Some studies on the cytotoxic activity of bintaro plants are presented in Table 2. Cytotoxic activity in the genus *Cerbera* was partly reported as the ED₅₀ value (µg/mL) and partly as the IC₅₀ value (µg/mL). Some of the literature initially said concentrations in micromolar units, but in this study, it was converted to µg/mL to be compared with other studies.

Almost all of the literature reports the activity of the isolated compounds from the genus *Cerbera*, except for one report regarding the cytotoxic activity of *Cerbera* extract.⁴⁰ The cytotoxic activity of *Cerbera* compounds and extract was tested against oral human epidermoid carcinoma (KB), breast cancer cells (BC, MCF7 & T47D), human small cell lung cancer (NCI-H187), ovarian cancer cell lines (SKOV3 & CaOV3), kidney of an African green monkey (Vero), human liver hepatocellular carcinoma cell line (HepG2), promyelocytic leukemia cell line (HL-60), cervical carcinoma cells (HeLa), human colon cancer cells (Col2), and human endometrial cancer (Ishikawa).

Most of the compounds tested for cytotoxic activity were cardiac glycosides, and most showed strong cytotoxic activity, including 17 α - and 17 β -Neriifolin, Cerberin, 7,8-Dehydrocerberin, Tanghinin, Neriifolin, and Tanghinigenin. Cerberin's cytotoxic activity against KB, BC, and NCI-H187 cells was reported twice by different literature and gave results that were not much different, showing strong activity against all three cancer cells.^{19,21} The mechanism of cell death by 17 β H-Neriifolin was further evaluated using Hoescht 33342 assay, and it was found that the compound killed the cancer cells via apoptosis. 17 β H-Neriifolin and ouabain both bound at α -subunit in Na⁺, K⁺-ATPase and their binding energy were -8.16 ± 0.74 kcal/mol and -8.18 ± 0.48 kcal/mol respectively.⁴¹

Besides of that, other literature states that the compound 2'-Epi-2'-O-Acetylthevetin B (GHSC-74) (cardiac glycoside group) isolated from *C. manghas* seed, can reduce the viability of HepG2 cells, which is influenced by time and dose.⁴⁶ Other research states that β -D-Glucosyl-(1 \rightarrow 4)- α -L-thevetosides of 17 β -digitoxigenin (GHSC-73) (cardiac glycoside group) isolated from the seed of *C. manghas* can reduce the viability of HepG2 cells which is influenced by time and dose without decreasing the viability of Chang human liver cells and Swiss albino 3T3 fibroblasts, induced efficiently stimulated apoptosis in HepG2 cells as evidenced by DNA fragmentation, annexin V/PI binding assay and DAPI staining.⁴⁷

Table 1: Compounds isolated from *C. odollam* and *C.manghas*

Compound	Group	Plant part	Species	Reference
Nicotiflorin				
Rutin	Flavonoid	Leaves	<i>C. manghas</i>	15
(+)-Bornesitol	Steroid			
Cerberin				
Neriifolin				
Thevetin B		Seed		
2'-O-Acetyl thevetin B				
Deacetyltanghinin	Steroid (Cardiac glycosides)		<i>C. manghas</i>	16
Gentiobiosyl deacetyltanghinin				
17 β H-tanghinigenin β -L-thevetoside		Root bark		
17 β H-tanghinigenin β -D-glucosyl-(1 \rightarrow 4)- β -L-thevetoside		& stem		
Digitoxigenin β -L-thevetoside				
17 β H-digitoxigenin β -L-thevetoside		Leaves		
Cerbinol				
Cerberic acid	Iridoid	Bark	<i>C. manghas</i>	22
Cerberinic acid				
Manghaslin				
Clitorin	Flavonoid	Leaves	<i>C. manghas</i>	23
3-O)-(2-Rhamnosylrutinosyl-7-O- β -glucosylquercetin	Flavonoid	Leaves	<i>C. manghas</i>	24
17 α -Neriifolin	Steroid (Cardiac glycosides)	Leaves	<i>C. manghas</i> ;	25
17 α -Deacetyltanghinin			<i>C. odollam</i>	

Compound	Group	Plant part	Species	Reference
Cerleaside A				
8 β -Hydroxydigitoxigenin- α -L-thevetoside (= Cerdollaside)				
17 α -Cerdollaside				
Digitoxigenin (α -L-acofrioside)				
(= solanoside)				
17 α -Solanoside				
Tanghinigenina α -L-Acofrioside				
17 α -Digitoxigenin β -D-allopyranosyl- α -L-thevetoside				
17 α -Tanghinigenin β -D-glucos-3-ulosyl-(1 \rightarrow 4)- α -L-thevetoside			<i>C. odollam</i>	
Oleagenin β -D-glucosyl-(1 \rightarrow 4)- α -L-thevetoside (= Cerleaside B)				
Digitoxigenin β -D-Gentiotriosyl-(1 \rightarrow 4)- α -L-thevetoside	Steroid (Cardiac glycosides)	Leaves	<i>C. manghas</i>	26
17 α -Digitoxigenin β -D-glucosyl-(1 \rightarrow 4)- α -L-thevetoside				
17 β -Digitoxigenin β -D-glucosyl-(1 \rightarrow 4)- α -L-thevetoside				
17 α -Tanghinigenin			<i>C. manghas</i> ;	
17 β -Tanghinigenin			<i>C. odollam</i>	
Digitoxigenin Gentiotriosyl-(1 \rightarrow 4)- α -L-thevetoside				
Tanghinigenin				
17 α -Digitoxigenin β -D-Apiosyl-(1 \rightarrow 6)- β -D-glucosyl-(1 \rightarrow 4)- α -L-thevetoside	Steroid (Cardiac glycosides)	Stem	<i>C. manghas</i>	27
17 α -Digitoxigenin β -D-cellobiosyl- α -L-thevetoside				
17 α -Digitoxigenin β -D-Gentiobiocyl-(1 \rightarrow 4)- α -L-thevetoside				
(-)-Olivil				
(+)-Cycloolivil				
5-5"-Bis-olivil (= Cerberalignan A)	Lignan	Stem	<i>C. manghas</i> ;	28
5'-5"-Bis-olivil (= Cerberalignan B)				
5'-5'''-Bis-olivil (= Cerberalignan C)				
Olivil 4-O- β -D-glucoside		Leaves	<i>C. manghas</i>	
Olivil 4'-O- β -D-glucoside				
Cerberalignan D-I	Lignan	Stem	<i>C. manghas</i> ;	29
			<i>C. odollam</i>	
Cerberalignan J-N	Lignan	Stem	<i>C. manghas</i>	30
Cerberidol				
Epoxyerberidol				
Cycloerberidol				
Cerberidol-3-O- β -D-allopiranosyde	Terpenoid	Leaves	<i>C. manghas</i> ;	31
Cerberidol-3,10-bis-O- β -D-allopiranosyde				
Epoxyerberidol-3-O- β -D-allopiranosyde				
Cycloerberidol-3-O- β -D-allopiranosyde				
10-O-Benzoyltheveside				
10-Dehydrogeniposide				
Loganin	Iridoid	Leaves	<i>C. manghas</i>	32
Theviridoside				

Compound	Group	Plant part	Species	Reference
Theveside				
10-Carboxyloganin	Iridoid			
Cyclocerberidol-3-O- β -D-glucoside				
Epoxyerberidol-3-O- β -D-glucoside				
3-(Hydroxyisopropyl)pentane-1,4-diol-1-O- β -D-glucoside				
3-(Hydroxyisopropyl)pentane-1-ol-1-O- β -D-glucoside	Terpenoid	Leaves	<i>C. manghas</i>	33
(3 ξ ,4 ξ)-3-Isopropyl-3,4-epoxypentane-1,5-diol-1-O- β -D-glucoside				
(Z)-3-Isopropyl-3-pentene-1,5-diol-1-O- β -D-glucoside				
(-)-14-Hydroxy-3 β -(3-O-methyl-6-deoxy- α -L-rhamnosyl)-11 α ,12 α -epoxy-(5 β ,14 β ,17 β H)-card-20(22)-enolide				
(-)-14-Hydroxy-3 β -(3-O-methyl-6-deoxy- α -L-glucopyranosyl)-11 α ,12 α -epoxy-(5 β ,14 β ,17 β H)-card-20(22)-enolide	Steroid (Cardiac glycoside)	Roots	<i>C. manghas</i>	34
(-)-17 β -Neriifolin				
(-)-Cycloolivil	Lignan			
17 β -Neriifolin				
3 β -O-(2'-O-Acetyl-L-thevetosyl)-15(14 \rightarrow 8)-abeo-5 β -(8R)-14-oxo-card-20(22)-enolide (= 2'-O-Acetyl cerleaside A)	Steroid (Cardiac glycoside)	seed	<i>C. odollam</i>	19
3 β -O-(2'-O-acetyl- α -L-thevetosyl)-14 β -hydroxy-7-en-5 β -card-20(22)-enolide	steroid (Cardiac glycoside)	seed	<i>C. manghas</i>	21
(= 7,8-Dehydrocerberin)				
1,3-Bis(<i>m</i> -carboxylphenyl)-propan-2-one	Phenolic acid	Bark	<i>C. manghas</i>	35
2-(<i>m</i> -carboxylphenyl)-3-(<i>m</i> -carboxylbenzyl) succinic acid				
Cerberic acid A & B	Iridoid	Bark	<i>C. manghas</i>	36
<i>p</i> -Hydroxybenzaldehyde	Phenol			
Benzamide	Amide			
n-Hexadecane acid monoglyceride	Fatty acid			
Loliolide	Iridoid	Leaves	<i>C. manghas</i>	17
β -Sitosterol				
Daucosterol	Steroid			
Triticusterol	Steroid			
Dihydroxy-4-methoxy benzoic acid				
2-Hydroxy-4-methoxy-6-methyl benzoic acid	Phenol	Stem bark	<i>C. odollam</i>	37
Uvaol				
(23Z)-9,19-cycloart-25-ene-3 β ,24-diol				
Euphorbol				
Ursolic acid	Terpenoid	Leaves	<i>C. manghas</i>	38
2 α -Hydroxyursolic acid				
3-O-Acetyl ursolic acid				
α -Amyrin				
Benzoic acid				
Vanillic acid	Phenolic acid	Fruit	<i>C. manghas</i>	18
Vanillin				

Compound	Group	Plant part	Species	Reference
<i>p</i> -Hydroxybenzaldehyde				
Isophthalaldehydic acid				
β -hydroxypropiovanillone				
Ficusol				
Evofofin B				
3,4'-Dihydroxypropiophenone				
<i>p</i> -Hydroxybenzoic acid				
Protocatechuic acid				
Cerbinal	Terpenoid			
β -Amyrin				
Lupeol	Steroid	Leaves	<i>C. odollam</i>	39
β -Sitostenone				
Triticasterol				

Table 2. Cytotoxic activity of extracts/compounds on *C. odollam* and *C. manghas*

Compound	Group	Cytotoxic to-	Concentration	Value	Species	Reference
3 β -O-(2'-O-acetyl-L-thevetosyl)-15(14 \rightarrow 8)-abeo-5 β -(8R)-14-oxo-card-20(22)-enolide (= 2'-O-Acetylcerleaside A)		KB		7.56		
		BC		4.62		
		NCI-H187		7.42		
		KB		Inactive		
Cerleaside A		BC		9.12		
		NCI-H187		inactive		
		KB		0.078		
17 α -Neriifolin		BC		0.049	<i>C. odollam</i>	19
		NCI-H187		0.032		
		KB		0.017		
17 β -Neriifolin		BC	ED ₅₀	0.048		
		NCI-H187	(μ g/mL)	0.076		
		KB		1.92		
	Steroid (Cardiac glycoside)	BC		1.63		
Cerberin		NCI-H187		1.24		
		KB		1.29		
		BC		0.77		
		NCI-H187		2.3		
		KB		1.75		
7,8-Dehydrocerberin		BC		0.0006	<i>C. manghas</i>	21
		NCI-H187		16.7		
		KB		0.05		
Tanghinin		BC		1.48		
		NCI-H187		0.1		
		MCF7		0.009		
		T47D	IC ₅₀	0.011		
17 β H-Neriifolin		SKOV3	(μ g/mL)	0.015	<i>C. odollam</i>	42
		CaOV3		0.017		

Compound	Group	Cytotoxic to-	Concentration	Value	Species	Reference
		Vero		0.013		
Neriifolin		HepG2		0.15		43
Tanghinigenin		HL-60		0.84		44
		HepG2		44.7		
Cerberic acid A	Iridoid	MCF-7		52.3		36
		HeLa		48.7		
(-)-14-Hydroxy-3 β -(3-O-methyl-6-deoxy- α -L-rhamnosyl)-11 α ,12 α -epoxy-(5 β ,14 β ,17 β H)-card-20(22)-enolide		Col2		0.015		
		Col2		0.0042	<i>C. manghas</i>	
	Steroid (Cardenolide)	Ishikawa				
(-)-14-Hydroxy-3 β -(3-O-methyl-6-deoxy- α -L-glucopyranosyl)-11 α ,12 α -epoxy-(5 β ,14 β ,17 β H)-card-20(22)-enolide		Col2		0.02		34
		Ishikawa		0.008		
(-)-17 β -Neriifolin	Steroid (Cardiac glycoside)	Col2		0.01		
		Ishikawa		0.09		
	Methanol extract of leaves	MCF-7		8.49		
		T47D		10.99		
	Methanol extract of fruit	MCF-7		100	<i>C. odollam</i>	40
		T47D		> 100		

Note: Activity category in ED₅₀ values (μ g/ml); Strong if <5, moderate if 5-20, weak if 20-50, and inactive if >50.¹⁹ Activity category in IC₅₀ values (μ g/ml); strong if <10, moderate if 10-50, weak if 50-100, and inactive if >100.⁴⁵

Antioxidant activity

Several studies have reported the antioxidant activity of the bintaro plant. However, the literature is limited to the activity of the plant extract or fraction (both *C. odollam* and *C. manghas*) with several different extracting solvents, and no reports have been found regarding the antioxidant activity of compounds in the bintaro plant. A summary of the antioxidant activities of the *C. odollam* and *C. manghas* extracts and their fractions is presented in Table 3. Overall antioxidant activity was stated to be very strong if IC₅₀ value is < 50 μ g/mL, strong if IC₅₀ value is 51-100 μ g/mL, moderate if IC₅₀ value is 101-150 μ g/mL, and weak if IC₅₀ value is > 150 μ g/mL.⁴⁸ From these results it can be seen that extracts that provide powerful antioxidant activity are methanol extract of the bark *C. odollam*, and fractions that provide extreme antioxidant activity are carbon tetrachloride and chloroform fraction of the methanolic extract of leaves and bark *C. odollam*.^{37,39}

Antimicrobial activity

The bintaro plants (*C. odollam* and *C. manghas*) have been reported to have antimicrobial (both antibacterial and antifungal) potential. However, the literature regarding the antifungal activity of *Cerbera* plants is less than that regarding its antibacterial activity. Several reports on the antimicrobial activities of bintaro plants are presented in Table 4.

Overall, polar solvent extracts were better antibacterial agents than nonpolar solvents. This can be seen from the antibacterial activity of butanol extract of *C. manghas* leaves against *K. pneumonia* which is better than n-hexane extract.⁵⁰ Likewise, ethyl acetate extract of *C. manghas* leaves has better antibacterial activity against *E. coli* than dichloromethane extract.⁵¹ However, water extracts do not seem to provide good antibacterial activity, such as water extracts of *C. manghas* seed and meat.⁵²

Other literature also reports that phylloplane yeast isolated from *C. manghas* leaves can inhibit growth and sporulation of *Aspergillus* sp. and *Penicillium* sp.⁵³

Insecticidal, Termiticidal and Larvicidal Activities

Several studies have reported the *Cerbera* plant's insecticidal, termiticidal, and larvicidal activities. The data are presented in Table 5. Most of the literature reports the activity of *Cerbera* leaves. Based on the data in Table 5, the seed is the part of the *Cerbera* plant that has the potential to be an insecticidal is the seed.⁵⁶ Literature related to termiticidal activity on *Cerbera* plants is still rare. Based on research by Hashim et al.⁵⁷, a part of the *Cerbera* plant that provides the highest termiticidal activity after 14 days is the flower, with a termite mortality (TM) of 100%.

The larvicidal activity reported by Komalamisra et al.⁵⁸ and Tarmadi et al.⁵⁹ yielded different results, even though they used the same samples and plant parts. This is because the origin of the plants used is different, where the *C. odollam* samples tested by Komalamisra et al.⁵⁸ came from Thailand, while those tested by Tarmadi et al.⁵⁹ came from Indonesia. Differences in the growing locations of plants can produce different secondary metabolites, thus providing other activities.

Reports of insecticidal, termiticidal, and larvicidal activities of *C. manghas* extract were lower than those of *C. odollam*. *C. manghas* leaf extract does not have a significant lethal effect on *R. linearis* insects; it also provides mortality of only 33%.^{60,65}

Apart from the data in the table, there was also termiticidal activity against *Coptotermes* sp. observed every two days during the ten days of observation. The report showed that the methanol extract of *C. odollam* leaves caused 100% termite mortality on the last observation. Whereas bark extracted with n-hexane and acetone caused 100% termite mortality on the eighth day of the treatment.⁶⁶ Termiticidal activity of the compound was carried out by Tarmadi et al.⁶⁷ where the oleic acid isolated from *C. manghas* showed low termiticidal activity as it delivered

low mortality in *Coptotermes gestroi* Wasmann and *Cryptotermes cynocephalus* Light.

Other literature also reports that leaves, rinds, and stem bark extracts of *C. odollam* showed low larvicidal activity against *Culex quinquefasciatus*. In contrast, seed kernel extract and its fractionation using n-hexane and ethyl acetate solvents showed high activity.⁶⁸

Conclusion

In conclusion, *Cerbera manghas* and *Cerbera odollam* have emerged as promising sources of pharmacologically relevant compounds, often recognized for their toxicity. The presence of diverse secondary metabolites, including phenolics, flavonoids, terpenoids, and steroids, highlights their potential medicinal significance. Notably, cardiac glycosides, identified as the dominant steroid compounds, exhibit robust cytotoxic activity, emphasizing the pharmacological potential of these plants. This investigation revealed variations in antioxidant and antimicrobial activities, with methanol extracts displaying high antioxidant potential and polar extracts demonstrating superior antimicrobial efficacy. Despite their documented insecticidal, termiticidal, and larvicidal activities, a comprehensive comparative analysis across species, plant parts, and extraction solvents remains limited because relevant reports are scarce. This study highlights the

need for further research to explore a wider range of bioactivities inherent in *Cerbera* plants that are yet to be extensively investigated. Continued exploration of their pharmacological properties is key to unlocking the full spectrum of potential applications of these intriguing botanical species.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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Table 3; Antioxidant activity of *C. odollam* and *C. manghas* extracts/fractions with DPPH method

Species	Extract/fraction	IC ₅₀	Reference
<i>C. manghas</i>	Ethanol extract of leaves	292 µg/mL	49
	Methanol extract of the bark	46.0 µg/mL	
	n-hexane soluble fraction of the methanol extract of the bark	135.0 µg/mL	
	Carbon tetrachloride soluble fraction of the methanol extract of the bark	26.0 µg/mL	37
	Chloroform soluble fraction of the methanol extract of the bark	21.0 µg/mL	
	Aqueous fraction of the methanol extract of the bark	62.5 µg/mL	
<i>C. odollam</i>	Methanol extract of leaves	75.02 µg/mL	
	Carbon tetrachloride fraction of the methanolic extract of leaves	72.01 µg/mL	
	Chloroform fraction of the methanolic extract of leaves	40.00 µg/mL	39
	Petroleum ether fraction of the methanolic extract of leaves	280.01 µg/mL	
	Aqueous fraction of the methanolic extract of leaves	265.17 µg/mL	
	Standard equivalent in methanolic extract. (IC %) at 5 µg/mL	80.029%	14
	Standard equivalent in aqueous extract. (IC %) at 5 µg/mL	88.381%	

Table 4: Antimicrobial activity of extracts/compounds on *C. odollam* and *C. manghas*

Species	extract/fraction	Mass/ Concentration extract/ fraction	Bacteria	Diameter of the inhibition zone (mm)	Reference
Antibacterial					
<i>C. manghas</i>	n-hexane extract of the leaves	250 mg/mL		17.5	
		500 mg/mL		18	
		1000 mg/mL	<i>Klebsiella pneumoniae</i>	19	50
	Butanol extract of the leaves	250 mg/mL		21	
		500 mg/mL		23.5	
		1000 mg/mL		25	
n-hexane extract of the seed	0.05 g/mL	<i>Staphylococcus aureus</i>	8.43	52	
		<i>Bacillus cereus</i>	4.88		

Species	extract/fraction	Mass/ Concentration extract/ fraction	Bacteria	Diameter of the inhibition zone (mm)	Reference
<i>C. odollam</i>	Ethyl acetate extract of the seed		<i>Escherichia coli.</i>	3.56	51
			<i>Staphylococcus aureus</i>	5.15	
			<i>Bacillus cereus</i>	2.26	
	Aquades extract of the seed		<i>Escherichia coli.</i>	0.11	
			<i>Staphylococcus aureus</i>	0.39	
			<i>Bacillus cereus</i>	0	
	Ethyl acetate extract of the meat		<i>Escherichia coli.</i>	10.95	
			<i>Bacillus cereus</i>	4.24	
			<i>Escherichia coli.</i>	8.35	
	n-hexane extract of the meat		<i>Staphylococcus aureus</i>	5.28	
			<i>Bacillus cereus</i>	1.31	
			<i>Escherichia coli.</i>	2.59	
	Aquades extract of the meat		<i>Staphylococcus aureus</i>	0.16	
			<i>Bacillus cereus;</i>	0	
			<i>Escherichia coli.</i>		
	Ethyl acetate extract of the leaves	10 mg/mL		10	
		20 mg/mL	<i>Staphylococcus aureus</i>	11.33	
		30 mg/mL		13.67	
		10 mg/mL		8.5	
		20 mg/mL	<i>Escherichia coli</i>	9.17	
		30 mg/mL		10.33	
		10 mg/mL		9.83	
	Dichloromethane extract of the leaves	20 mg/mL	<i>Staphylococcus aureus</i>	13.33	
		30 mg/mL		15.83	
		10 mg/mL		7.17	
		20 mg/mL	<i>Escherichia coli</i>	8.33	
		30 mg/mL		10.17	
Methanol extract of the seed	500 µg/hole	<i>Streptococcus saprophyticus</i>	16		
		<i>Streptococcus pyogenes</i>	11		
		<i>Salmonella typhi</i>	15		
		<i>Shigella boydii;</i>	0		
		<i>Shigella sonnie; Staphylococcus epidermis</i>			
		<i>Shigella flexneri;</i>	6		
		<i>Shigella dysenteriae;</i>			
<i>Staphylococcus aureus</i>					
Methanol extract of the leaves	400 µg/disc	<i>Bacillus megaterium;</i>	8		
		<i>Shigella flexneri</i>	39		

Species	extract/fraction	Mass/ Concentration extract/ fraction	Bacteria	Diameter of the inhibition zone (mm)	Reference
	Pet ether fraction of methanol extract of the leaves		<i>Bacillus cereus</i> ; <i>Shigella sonni</i>	7-8	
	Carbon tetrachloride fraction of methanol extract of the leaves		<i>Bacillus subtilis</i> , <i>Bacillus megaterium</i> , <i>Bacillus cereus</i> , <i>Staphylococcus aureus</i> & <i>Sarcina lutea</i>	7-9	
	Chloroform fraction of methanol extract of the leaves	400 µg/disc	<i>Bacillus subtilis</i> , <i>Bacillus polymyxa</i> , <i>kleb species</i>	7-8	
	Aqueous fraction of methanol extract of the leaves		<i>Bacillus subtilis</i>	7	
<i>C. odollam</i>	Methanol extract of the leaves	100 µL/well	<i>Bacillus subtilis</i> ; <i>Staphylococcus aureus</i> ; <i>Escherichia coli</i> <i>Salmonella typhi</i> <i>Corynebacterium diphtheria</i> ; <i>Klebsiella pneumonia</i>	2 3 0	14
Antifungal	Ethanol extract of the leaves	100 mg	<i>Aspergillus niger</i> <i>Fusarium oxysporum</i> <i>Penicilium citrum</i> <i>Aspergillus niger</i>	13.4 0 15.73 10.72	55
<i>C. odollam</i>	Ethanol extract of the fruit		<i>Fusarium oxysporum</i> <i>Penicilium citrum</i>	9.39 8.67	
	Methanol extract of the leaves	100 µL/well	<i>Saccharomyces cerevisiae</i> <i>Candida albicans</i>	26 25	14
	Aqueous extract of the leaves		<i>Saccharomyces cerevisiae</i> <i>Candida albicans</i>	16 9	

Table 5: Insecticidal, termiticidal, and larvicidal activity of extracts on *C. odollam* and *C. manghas*

Species	Part of plant	Species of larvae	Value	References
Insecticidal				
<i>C. manghas</i>	Seed	<i>Riptortus linearis</i>	Mortality = 33.33%	60
	Leaf	<i>Spodoptera litura</i>	Mortality = 16.66%	61
Fruit	Mortality = 100%			
	Leaves	<i>Spodoptera litura (instar 2)</i>	LC ₅₀ = 0.6 %	62
			LC ₉₅ = 11.88%	
	Granule extract of leaves	<i>Spodoptera litura (instar 2+3)</i>	LC ₅₀ = 0.28 %	63
			LC ₉₅ = 2.89%	
		<i>Spodoptera litura Fab</i>	LC ₅₀ = 1.41%	

Species	Part of plant	Species of larvae	Value	References
<i>C. odollam</i>	Seed	<i>Eurema sp</i>	LC ₅₀ = 0.189 %	56
			LC ₉₅ = 1.36%	
	Flesh of fruit		LC ₅₀ = 0.315 %	
	Leaves		LC ₅₀ = 0.297 %	
			LC ₉₅ = 6.453%	
<i>C. odollam</i>	Leaves	<i>Coptotermes gestroi</i>	TM = 75.76%	57
	Fruit		TM = 60.61%	
	Wood		TM = 36.36%	
	Bark		TM = 63.64%	
	Flower		TM = 100%	
	Seed		TM = 48.48%	
<i>C. manghas</i>	Leaves	<i>Aedes aegypti</i>	LC ₅₀ = 5.097%	64
			LC ₉₀ = 25.300%	
	unripe fruits		LC ₅₀ = 102.23 mg/L	58
			LC ₉₀ = 312.42 mg/L	
	Leaves		LC ₅₀ = 96.16 mg/L	
			LC ₉₀ = 229.9 mg/L	
	Rind		LC ₅₀ > 1.0 g/L	
			LC ₉₀ > 1.0 g/L	
	Bark		LC ₅₀ > 1.0 g/L	59
			LC ₉₀ > 1.0 g/L	
	Leaves		LC ₅₀ > 1.0 g/L	
			LC ₉₀ > 1.0 g/L	
seed kernel	LC ₅₀ = 0.76 g/L			
	LC ₉₀ > 1.0 g/L			

Note: TM = Termite Mortality; LC = Lethal Concentration

References

- Quigley DTG, Fenwick D.C *erbera* sp. (Apocynaceae) drift mesocarps: first record from British waters and a summary of previous records from north-western Europe. *Cah Biol Mar.* 2019; 60:419-423. Doi: 10.21411/CBM.A.A9AA3201
- Ruekert LF, Cunningham EA, Naqvi H. *Cerbera odollam*: a case report of attempted suicide by pong pong. *J. Psychiatr Pract.* 2019; 25(3):219-221. Doi: 10.1097/PRA.0000000000000391.
- Maharana PK. Ethnobotanical, phytochemical, and pharmacological properties of *Cerbera manghas* L. *J. Biosci.* 2021; 46:25-33. Doi: 10.1007/s12038-021-00146-6.
- Islam MS, Ahmed Z. A Pharmacological and phytochemical review on *Cerbera odollam* a plant with significant ethnomedicinal value. *EJPMR.* 2017; 4(12):19-21.
- Chan EWC, Wong SK, Chan HT, Baba S, Kezuka M. *Cerbera* are coastal trees with promising anticancer properties but lethal toxicity: A short review. *J. Chin Pharm Sci.* 2016; 25(3):161-169. Doi: 10.5246/jcps.2016.03.019.
- Alvarado-Cárdenas LO, Ochoterena H. A Phylogenetic Analysis of the Cascabela-Thevetia Species Complex (Plumeriaceae, Apocynaceae) Based on Morphology. *Ann Mo Bot Gard.* 2007; 94(2):298-323. Doi: 10.3417/0026-6493(2007)94[298:APAOTC]2.0.CO;2.
- Menezes RG, Usman MS, Hussain SA, Madadin M, Siddiqi TJ, Fatima H, Ram P, Pasha SB, Senthilkumaran S, Fatima TQ, et al. *Cerbera odollam* toxicity: Review. *J. Forensic Leg Med.* 2018; 58:113-116. Doi: 10.1016/j.jflm.2018.05.007.
- Wermuth ME, Vohra R, Bowman N, Furbee RB, Rusyniak DE. Cardiac toxicity from intentional ingestion of pong-pong seeds (*Cerbera odollam*). *J. Emerg Med.* 2018; 55(4):507-511. Doi: 10.1016/j.jemermed.2018.05.021.
- Fok H, Victor P, Bradberry S, Eddleston M. Novel methods of self-poisoning: repeated cardenolide poisoning after accessing *Cerbera odollam* seeds via the internet. *Clin Toxicol.* 2018; 56(4):304-306. Doi: 10.1080/15563650.2017.1369543.
- lawsipo P, Choksawangkam W, Promdan C, Nilkasam P. Antibacterial and antioxidant activities of *Cerbera manghas* and *C. odollam* leaf extracts. *Burapha Sci J.* 2017; 22:1-12.
- Iqbal Z, Iqbal MS, Mishra K. Screening of antioxidant property in medicinal plants belonging to the family Apocynaceae. *Asian J. Pharm Clin Res.* 2017; 10:415-418.
- Saxena M, Jadhav EB, Sankhla MS, Singhal M, Parihar K, Awasthi KK, Awasthi G. Bintaro (*Cerbera odollam* and *Cerbera manghas*): an overview of its eco-friendly use,

- pharmacology, and toxicology. *Environ Sci Pollut Res.* 2023; 30:71970-71983. Doi: 10.1007/s11356-022-22585-w.
13. Yi YS, Cho JY, Kim D. *Cerbera manghas* methanol extract exerts anti-inflammatory activity by targeting c-Jun N-terminal kinase in the AP-1 pathway. *J. Ethnopharmacol.* 2016; 193:387-396.
 14. Sahoo A, Marar T. Phytochemical analysis, antioxidant assay and antimicrobial activity in leaf extracts of *Cerbera odollam* Gaertn. *Pharmacogn J.* 2018; 10(2): 285-292. Doi: 10.5530/pj.2018.2.50.
 15. Sakushima A, Nishibe S, Hisada S, Noro Y, Hisada Y. Studies on the constituents of Apocynaceae plants; Isolation of flavonol glycosides and some other components from the leaves of *Cerbera manghas* L (1). *Yakugaku Zasshi.* 1976; 96(8):1046-1048. Doi: 10.1248/yakushi1947.98.10_1395.
 16. Abe F, Yamauchi T. Studies on *Cerbera* I. Cardiac glycosides in the seeds, bark, and leaves of *Cerbera manghas* L. *Chem Pharm Bull.* 1977; 25(10): 2744-2748 Doi: 10.1248/cpb.25.2744.
 17. Zhang XP, Pei YH, Liu MS, Kang SL, Zhang JQ. Chemical constituents from the leaves of *Cerbera manghas*. *Asian Pac J. Trop Med.* 2010; 3(2):109-111.
 18. Cao LL. Chemical constituents in fruits of mangrove plant *Cerbera manghas* L. *Chinese Pharm J.* 2013; 24:1052-1056.
 19. Laphookhieo S, Cheenpracha S, Karalai C, Chantrapromma S, Ratapaa Y, Ponglimanont C, Chantrapromma K. Cytotoxic cardenolide glycoside from the seeds of *Cerbera odollam*. *Phytochemistry.* 2004; 65:507-510. Doi: 10.1016/j.phytochem.2003.10.019.
 20. Carlier J, Guitton J, Bévalot F, Fanton L, Gaillard Y. The principal toxic glycosidic steroids in *Cerbera manghas* L. seeds: Identification of cerberin, neriifolin, tanghinin and deacetyltanghinin by UHPLC–HRMS/MS, quantification by UHPLC–PDA-MS. *J. Chromatogr B.* 2014; 962:1-8. Doi: 10.1016/j.jchromb.2014.05.014.
 21. Cheenpracha S, Karalai C, Rat-A-Pa Y, Ponglimanont C, Chantrapromma K. New cytotoxic cardenolide glycoside from the seeds of *Cerbera manghas*. *Chem Pharm Bull.* 2004; 52(8):1023-1025. Doi: 10.1248/cpb.52.1023.
 22. Abe F, Okabe H, Yamauchi T. Studies on *Cerbera* II. Cerberin and its derivatives, yellow pigment in the bark of *Cerbera manghas* L. *Chem Pharm Bull.* 1977; 25(12):3422-3424. Doi: 10.1248/cpb.25.3422.
 23. Sakushima A, Hisada S, Ogihara Y, Nishibe S. Studies on the constituents of Apocynaceae plants. Gas Chromatography-Mass Spectrometric determination of new flavonoid triglycosides from the leaves of *Cerbera manghas* L. *Chem Pharm Bull.* 1980; 28:1219-1223. Doi: 10.1248/cpb.28.1219.
 24. Sakushima A, Nishibe S, Hisada S. A new flavonol glycoside from *Cerbera Manghas*. *Phytochemistry.* 1980; 19:712-713. Doi: 10.1016/0031-9422(80)87052-X.
 25. Yamauchi T, Abe F, Wan ASC. Cardenolide Monoglycosides from the Leaves of *Cerbera odollam* and *Cerbera manghas* (*Cerbera*. III). *Chem Pharm Bull.* 1987; 35(7):2744-2749. Doi: 10.1248/cpb.35.2744.
 26. Yamauchi T, Abe F, Wan ASC. Studies on *Cerbera*. IV. Polar Cardenolide Glycosides from the Leaves of *Cerbera odollam* and *Cerbera manghas*. *Chem Pharm Bull.* 1987; 35(12):4813-4818. Doi: 10.1248/cpb.35.4813.
 27. Yamauchi T, Abe F, Wan ASC. Studies on *Cerbera*. V. Minor Glycosides of 17 α -Digitoxigenin from the stems of genus *Cerbera*. *Chem Pharm Bull.* 1987; 35(12):4993-4995. Doi: 10.1248/cpb.35.4993.
 28. Abe F, Yamauchi T, Wan ASC. Lignans related to olivil from genus *Cerbera* (*Cerbera* VI). *Chem Pharm Bull.* 1988; 36(2):795-799. Doi: 10.1248/cpb.36.795
 29. Abe F, Yamauchi T, Wan ASC. Sesqui-, sester- and trilignans from stems of *Cerbera manghas* and *C. odollam*. *Phytochemistry.* 1988; 27(11):3627-3631. Doi: 10.1016/0031-9422(88)80780-5.
 30. Abe F, Yamauchi T, Wan ASC. *Cerberalignans J-N, oligolignans from Cerbera manghas*. *Phytochemistry.* 1989; 28:3473-3476. Doi: 10.1016/0031-9422(89)80367-X.
 31. Abe F, Yamauchi T, Wan ASC. Normonoterpenoids and their allopyranosides from the leaves of *Cerbera* species (Studies on *Cerbera*. VIII). *Chem Pharm Bull.* 1989; 37:2639-2642. Doi: 10.1248/cpb.37.2639.
 32. Yamauchi T, Abe F, Wan ASC. 10-*O*-benzoyltheveside and 10-dehydrogeniposide from the leaves of *Cerbera manghas*. *Phytochemistry.* 1990; 29(7):2327-2328. Doi: 10.1016/0031-9422(90)83063-7.
 33. Abe F, Yamauchi T. 10-Carboxyloganin, normonoterpenoid gluosides and dinormonoterpenoid glucosides from the leaves of *Cerbera manghas* (Studies on *Cerbera*. 10). *Chem Pharm Bull.* 1996; 44(10):1797-1800. Doi: 10.1248/cpb.44.1797.
 34. Chang LC, Gills JJ, Bhat KPL, Luyengi L, Farnsworth NR, Pezzuto JM, Kinghorn AD. Activity-guided isolation of constituents of *Cerbera manghas* with antiproliferative and antiestrogenic activities. *Bioorg Med Chem Lett.* 2000; 10:2431-2434. Doi: 10.1016/S0960-894X(00)00477-7.
 35. Zhang XP, Liu MS, Zhang JQ, Kang SL, Pei YH. Chemical constituents from the bark of *Cerbera manghas*. *J. Asian Nat Prod Res.* 2009; 11(1):75-78. Doi: 10.1080/10286020802514531.
 36. Zhang XP, Liu MS, Pei YH, Zhang JQ, Kang SL. Phenylpropionic acid derivatives from the bark of *Cerbera manghas*. *Fitoterapia.* 2010; 81(7):852-854. Doi: 10.1016/j.fitote.2010.05.010.
 37. Hasan CM, Kuddus MR, Rumi F, Masud MM. Phytochemical screening and antioxidant activity studies of *Cerbera odollam* Gaertn. *Int J. Pharm Biol Sci.* 2011; 2(1):413-418.
 38. Zhang XP, Pei YH, Liu MS, Kang SL, Zhang JQ. Triterpenoids from the leaves of *Cerbera manghas*. *Nat Prod Res Develop.* 2011; 23(3):443-445.
 39. Rahman MS, Faisal A, Hasan CM, Ahsan M, Mahsud MM. Chemical and Biological Investigations of *Cerbera odollam* Gaertn. *Dhaka Univ J. Pharm Sci.* 2017; 16(2):179-186.
 40. Nurhanan MY, Asiah O, Ilham MAM, Syarifah MMS, Norhayati I, Sahira HL. Anti-proliferative activities of 32 Malaysian plant species in breast cancer cell lines. *J. Trop For Sci.* 2008; 20(2):77-81.
 41. Yunos, Nurhanan M, Osman A, Jauri MH, Sallehudin NJ, Mutalip SSM. The *In Vitro* Anti-Cancer Activities of 17 β H-Neriifolin Isolated from *Cerbera odollam* and its Binding Activity on Na⁺, K⁺-ATPase. *Curr Pharm Biotechnol.* 2020; 21(1):37-44. Doi: 10.2174/1389201020666190917154850.
 42. Syarifah MMS, Nurhanan MY, Haffiz JM, Ilham AM, Getha K, Asiah O, Norhayati I, Sahira LH, Suryani SA. Potential anticancer compound from *Cerbera*. *J. Trop For Sci.* 2011; 23(1):89-96.
 43. Zhao Q, Guo YW, Feng B, Li L, Huang CG, Jiao BH. Neriifolin from seeds of *Cerbera manghas* L. induces cell cycle arrest and apoptosis in human hepatocellular carcinoma HepG2 cells. *Fitoterapia.* 2011; 82(5): 735-741. Doi: 10.1016/j.fitote.2011.03.004.
 44. Wang GF, Guo YW, Feng B, Li L, Huang CG, Jiao BH. Tanghinigenin from seeds of *Cerbera manghas* L. induces apoptosis in human promyelocytic leukemia HL-60 cells. *Environ Toxicol Pharmacol.* 2010; 30(1):31-36. Doi: 10.1016/j.etap.2010.03.012.
 45. Indrayanto G, Putra GS, Suhud F. Chapter six-Validation of in-vitro bioassay methods: Application in herbal drug research. *Profiles Drug Subs Exci Relat Methodol.* 2021; 46:273-307. Doi: 10.1016/bs.podrm.2020.07.005
 46. Feng B, Guo YW, Huang CG, Li L, Chen RH, Jiao BH. 2'-epi-2'-O-Acetylthevetin B extracted from seeds of *Cerbera manghas* L. Induces cell cycle arrest and apoptosis in human

- hepatocellular carcinoma HepG2 cells. *Chem Biol Interact.* 2010; 183(1):142-153. Doi: 10.1016/j.cbi.2009.10.012.
47. Feng B, Guo YW, Huang CG, Li L, Chen RH, Jiao BH. β -D-Glucosyl-(1-4)- α -L-thevetosides of 17 β -digitoxigenin from seeds of *Cerbera manghas* L. induces apoptosis in human hepatocellular carcinoma HepG2 cells. *Exper Toxicol Pathol.* 2012; 64(5):403-410. Doi: 10.1016/j.etp.2010.10.005.
 48. Rozirwan R, Hamid H, Redho YN, Rezi A, Nadila NK, Fauziyah F, Wike AEP, Riris A. Antioxidant activity, total phenolic, phytochemical content, and HPLC profile of selected mangrove species from Tanjung Api-Api port area, South Sumatra, Indonesia. *Trop J Nat Prod Res.* 2023; 7(7):3482-3489.
 49. Monjur-Al-Hossain ASM, Sarkar S, Saha S, Hossain ML, Hasan MM, Biological assessment on *Cerbera manghas* (linn.). *Pharmacology online.* 2013; 1:155-160.
 50. Musdja MY, Aeni M, Djajanegara I. Comparison of antibacterial activities leaves extracts of *Cerbera manghas* and leaves extracts of *Azadirachta indica* against *Klebsiella pneumoniae*. *Asian J. Pharm Clin Res.* 2018; 11(3):51-55.
 51. Musdja MY, Chadidjah, Djajanegara I. Antibacterial activity of dichloromethane and ethyl acetate extracts of bintaro leaf (*Cerbera manghas*, linn) against *Staphylococcus aureus* and *Escherichia coli*. *Int J. Curr Res.* 2019; 11(1):398-402.
 52. Rizal S, Dewi H, Utomo TP. , Effect of solvent types on antibacterial activity of bintaro (*Cerbera mangas* L.) meat and seeds extract. *J. Tek Ind Has Pert.* 2015; 20(1):51-64.
 53. Sukmawati D. Antagonism mechanism of fungal contamination animal feed using phylloplane yeasts isolated from the bintaro plant (*Cerbera manghas*) Bekasi in Java, Indonesia. *Int J. Curr Microbiol App Sci.* 2016; 5:63-74.
 54. Ahmed F, Amin R, Shahid IZ, Sobhani MME. Antibacterial, cytotoxic and neuropharmacological activities of *Cerbera odollam* seeds. *Orient Pharm Exp Med.* 2008; 8(4):323-328. Doi: 10.3742/OPEM.2008.8.4.323.
 55. Chu SY, Singh H, Ahmad MS, Mamat AS, Lee BB. Phytochemical screening of antifungal biocompounds from fruits and leaves extract of *Cerbera odollam* Gaertn. *Malays Appl Biol.* 2015; 44(3):75-79.
 56. Utami S. Insecticide on spp. Pest in Laboratory Scale. *J. Penelit Hut Tanam.* 2010; 7(4):211 -220.
 57. Hashim R, Boon JG, Sulaiman O, Kawamura F, Lee CY. Evaluation of the decay resistance properties of *Cerbera odollam* extracts and their influence on properties of particleboard. *Int Biodeterior Biodegradation.* 2009; 63(8):1013-1017. Doi: 10.1016/j.ibiod.2009.07. 002.
 58. Komalamisra N, Trongtokit Y, Rongsriyam Y, Apiwathnasorn C. Screening for larvicidal activity in some Thai plants against four mosquito vector species. *Southeast Asian J. Trop Med Public Health.* 2005; 36(6):1412.
 59. Tarmadi D, Gunandini DJ, Yusuf S. Larvicidal activity of *Cerbera odollam* Gaertn against a dengue vector, *Aedes aegypti* (Diptera: Culicidae), J-SustaiN. 2018; 175-188. Doi: 10.1007/978-981-10-5430-3_14.
 60. Haryanta D, Susilo A, Sa'adah TT. Repelence of bintaro plant extract (*Cerbera manghas*) against pod-sucking insects (*Riptortus linearis*) (Hemiptera). *Int J. Biol Biomed Eng.* 2020; 14:229-238. Doi: 10.46300/91011.2020.14.30.
 61. Somsroi P, Chaiyong S. Effect of Suicide Tree Crude Extract (*Cerbera odollam* Gaertn.) on Common Cutworm (*Spodoptera litura* Fabricius). *Rajabhat Agric.* 2016; 15(1):16-21.
 62. Utami S, Syaufina L, Haneda NF. Toxic effect of crude extract of bintaro leaf (*Cerbera odollam* Gaertn) on larvae *Spodoptera litura* of Fabricius. *J. Ilmu Pert Ind.* 2010; 15(2): 96-100.
 63. Sholahuddin AH, Subchan W, Prihatin J. Toxicity of granules of bintaro leaf extract (*Cerbera odollam* Gaertn.) on armyworm (*Spodoptera litura* Fab.). *Bioedukasi.* 2018; 16(1):15-21. Doi: 10.19184/bioedu.v16i1.7717.
 64. Permana TI, Sasmitasari NID, Susetyarini E, Nuryady MM, Dinindra AM, Agustin JU, Lutfi MA, Ayu P, Alimatul Z. Bintaro leaves (*Cerbera manghas*): Toxicity to *Aedes aegypti* instar III larvae. *J. Kes Masy.* 2022; 17(4):509-516.
 65. Susilo A, Haryanta D, Sa'adah TT. Response of *Riptortus linearis* towards the application of Bintaro (*Cerbera manghas*) leaf extract, *Eurasia. J. Biosci.* 2019; 13:2217-2224.
 66. Tarmadi D, Prianto AH, Guswenrivo I, Kartika T, Yusuf S. Influence of bintaro (*Cerbera odollam* Gaertn) and kecubung (*Brugmansia candida* Pers) extract against subterranean termite *Coptotermes* sp. *J. Trop Wood Sci Tech.* 2007; 5(1): 38-42.
 67. Tarmadi D, Himmi SK, Yusuf S. The efficacy of the oleic acid isolated from *Cerbera manghas* L. seed against a subterranean termite, *Coptotermes gestroi* Wasmann and a drywood termite, *Cryptotermes cynocephalus* Light. *Procedia Environ Scien.* 2014; 20: 772-777. DOI 10.1016/j.proenv.2014.03.093.
 68. Meisyara D, Tarmadi D, Zulfritri A, Fajar A, Ismayati M, Himmi SK, Kartika T, Guswenrivo I, Yusuf S. Larvicidal Activity of Bintaro (*Cerbera odollam*) against *Culex quinquefasciatus*. *IOP Conf Ser Earth Environ Sci.* 2020; 591:012010.