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Bintaro (*Cerbera odollam* and *Cerbera manghas)*: an overview of its eco-friendly use, pharmacology, and toxicology

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Abstract

Bintaro is a tropical mangrove plant often used as a shade tree found in Asia, Australia, Madagascar, and the Islands of the Western Pacific Ocean. The word Bintaro is also often pinned to its closest relative species, the *Cerbera odollam*. Flower color is one of the distinguishing features between these two species. Human poisoning with the cardiotoxic plant Bintaro is common in Southeast Asia because it bears a fruit that yields a powerful poison that has been used for suicide and homicide, hence it is also called the "Indian suicide tree". The seeds of Bintaro contain Cerberin, a cardiac glycoside toxin of the heart that blocks the calcium ion channels in heart muscles, resulting in disruption of the heartbeat most often fatally. The bio-active compound in the kernels of Bintaro varies due to which plant possesses other properties as well. The plant may also be used for medicinal purposes as it shows many pharmaceutical properties. The seeds of the plant have auspicious anticancer properties through apoptotic activity and the leaf extract of the plant was screened for its antioxidant activities. In addition, it is also used as an insecticide, pesticide, or antifungal agent. This review highlights the Pharmaceutical, toxicological, and environmentally friendly approaches of Bintaro.

Keywords Bintaro · Toxicity · *Cerbera Odollam* · *Cerbera manghas* · Anti-Microbial Activity · Pharmaceuticals

Introduction

Bintaro (*Cerbera odollam* and *Cerbera manghas*) is a dicotyledonous Angiosperm, a plant species, belonging to the poisonous Apocynaceae family (Wermuth et al. 2018). The plant is known by several names such as a pong-pong tree, Mango Laut, Blind rhino, Babuto, and Wood octopus (Ruekert et al. 2019; Sukmawati 2016). It occupies coastal and marshy areas (wet areas) along the seashores and rivers of the tropic including Southern India, Southeast Asia, Madagascar, and Australia (Shankar and Rai 2009). Due to its deadly toxic seeds, the genus name is derived from Cerberus, the hell dog from Greek mythology hence indicating the toxicity of the seeds. It is extensively unknown to the western world. Bintaro tree has a resilient nature and speedy growing so generally

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used to shadow the road. Typically, this tree has a height of up to 12–15 m tall, has shiny dark green leaves, is ovoid with delicate white and yellow flowers, and has a fragrance of Jasmine (Gaillard et al. 2004). It is a non-meal plant as it contains toxins in almost all parts inclusive of the trunk, flower, seed, and fruit. The plant has an extended history, In Madagascar, the seeds were utilized in sentence rituals to punish Kings and Queens (Sukmawati 2016). The plant bears a fruit, softball-sized, similar to that of the green mango called Othalanga, which turns into bright red at maturity (Maharana 2021). Each fruit contains one poisonous seed, these seeds are comprised of an alkaloid (cerberine, nitritolin, and theven) steroids, terpenoids, and saponins which are toxic and cause heart attack and sudden death (Musdja and Djajanegara 2019). The difficulty of finding cerberin in autopsies and the ability of strong spices to hide its flavor make it an ideal lethal weapon. In the South Indian state of Kerala, India, it accounts for half of all cases of plant poisoning, a condition that is the cause of a significant number of deaths, hence, it acts as a suicide and homicide agent (Sahoo and Marar 2018). The scientific exploitation of plans revealed due to the presence of the natural bio-active compound in a plant shows multiple biological effects including anticancer, anti-inflammatory, analgesic, antibacterial properties, etc. The plant's leaves have been shown cytotoxic activity against various types of cancer. It is well-known that the prevention of cancer and chemotherapy, which are based on natural ingredients, is less harmful than any other treatments (Harlev et al. 2012). Botanists, microbiologists, and chemist are trying their best to find a cure for various diseases, where, plant like Bintaro comprises numerous phytochemicals which includes alkaloids, terpenoids, and tannin that have been reported to have antimicrobial and analgesic properties (Aziz et al. 2021). Therefore, Bintaro as a medical herb can be introduced into medication therapy to achieve better outcomes. Various studies have also highlighted its potential aspects as bioinsecticide and pesticide in the agricultural field. It has a unique agent that drives away or kills insect pests and inhibits pest feeding activity. The leaf and fruit extract of the plant has antifungal properties that have the potential to kill or inhibit the growth of any fungus. Thus, this clearly indicates that it has the potential of being a bio fungicide that could be employed as an alternative to synthetic fungicide. Organic plant-based pesticides and fungicides against insects and fungus respectively, not only be effective but also safer and eco-friendly. Bintaro has non-edible vegetable oil in its seeds, therefore it can also act as a raw material for the production of biodiesel (Zikri et al. 2020). As this plant has tremendous benefits, thus it has various applications and therefore can be utilized in adverse fields.

Significant phytochemical constituents

Phytochemicals are the chemicals produced through the plant via primary and secondary metabolism (Table 1). They are most often involved in the biological activity of the plants, and may also play a role in plant growth and defense against a pathogen, or predator (Chu et al. 2015). Some phytochemical has been used as poisons and others as conventional remedy. They typically help the plant to withstand bacteria, fungi and plant virus infections as well as the consumption by insects and other animals. Various essential phytochemicals have been reported to be found in Bintaro, such as steroids, tannins, terpenoids, flavonoids, phenol, saponins, cardiac glycosides, lignans, and iridoids in different parts of the plants such as leaves, stem, and root (Maharana 2021). Steroids, tannins, and terpenoids are believed to have antifungal and antimicrobial properties in a plant (Chu et al. 2015). Phenolic acids are accountable for antioxidant activities (Piazzon et al. 2012). Besides these, cardiac glycoside exhibits cytotoxic activity against carcinogenic cell that acts as an anticancer agent (Cheenpracha et al. 2004).

Toxicology of Bintaro

One complete Ingestion of a single seed of Bintaro can lead to a fatal heart attack (Wermuth et al. 2018). In the plant, the seed is the most toxic part and belongs to several Cardiac glycosides, including Cerberin, the most poisonous ingredient among other components (Tsai et al. 2008). Apart from Cerberin, there is a mixture of other bioactive components such as Odollin, Neriifolin, and Cerberoside (Misek et al. 2018). Due to its violent cardiotoxic nature, it is used for the purpose of suicide and as a Homicidal agent. According to various studies, the bioactive compound in Bintaro can lead to the death of insects. The higher the concentration of the chemical compound, the higher the mortality rate of the insects (Sholahuddin et al. 2018); thus, it may also be used as a natural pesticide for pest management by inhibiting the feeding activity of the pest on the plant. Animal Studies have shown that the consumption of a very small amount of kernel could lead to death. The minimum fatal dose is found in half of the kernel. It can be 1.8 mg/kg and 3.8 mg/kg in dogs and cats respectively. So, ingesting half or a whole kernel would be enough to cause death. The lethal period after the ingestion can occur either in 3–6 h or within 1–2 days (Menezes et al. 2018). Cardiac glycosides like Cerberin and Neriifolin cause heart failure by binding and blocking with

Table 1 Significant phytochemicals in different parts of the Bintaro (*Cerbera odollam* and *Cerbera manghas*)

Plant part	Class of chemical compounds	Significant phytochemicals	References
Leaf	Terpenoids	Uvaol, Euphorbol, Blumenol A, Cerberidol, Cerbinal, Euscaphins, Ursolic acid	(Xiao-po et al. 2011; CAO et al. 2013; Chan et al. 2015)
Leaf	Phenolic Acids	Succinic acid, isopthalic acid, p-hydroxycinnamic acid	(CAO et al. 2013; Chan et al. 2015; Zhang et al. 2010a, b)
Leaf	Flavonoids	Clitorin, Manghaslin, Nicotiflorin, Rutin	(Chan et al. 2015)
Leaf	Cardiac glycosides	Neriifolin, Cerleaside A,	(Chan et al. 2015; Zhang et al. 2010a, b)
Leaf	Steroids	Bornesitol, Daucosterol	(Chan et al. 2015; Zhang et al. 2010a, b)
Leaf	Iridoids	Loganin, Theveside, Theviridoside	(Chan et al. 2015)
Bark	Terpenoids	Cerbinal	(CAO et al. 2013; Chan et al. 2015)
Bark	Iridoids	Cerberic acid A,B Succinic acid	(Piazzon et al. 2012; Zhang et al. 2009; Chan et al. 2015)
Stem	Terpenoids	Cerbinal	(Xiao-po et al. 2011; Chan et al. 2015)
Stem	Phenolic acid	Vanillic acid	(CAO et al. 2013; Chan et al. 2015)
Stem	Iridoids	Coniferaldehyde	(Maharana 2021)
Stem	Lignans	Cerbers ligninA-1, Cerbera ligninJ-N Cycloolivil	(Chan et al. 2015)
Stem	Flavonoids	Aromamadedrin, Naringenine	(Chan et al. 2015)
Stem	Iridoids	Lthevetoside, 8-Hydroxypinoresinol	(Maharana 2021)
Stem	Cardiac glycosides	Neriifolin	(CAO et al. 2013; Chan et al. 2015)
Root	Terpenoids	Cerbinal	(CAO et al. 2013; Chan et al. 2015)
Root	Cardiac glycosides	Lthevetoside	(Maharana 2021)
Root	Iridoids	Coniferaldehyde	(Maharana 2021)
Fruit	Terpenoids	Ursolic acid, Cerbinal	(CAO et al. 2013; Chan et al. 2015)
Fruit	Phenolic acids	Benzoic acid, Vanillin, Ficusol, Evofolin,	(CAO et al. 2013; Chan et al. 2015)
Fruit	Cardiac glycosides	Cerberin	(CAO et al. 2013; Harlev et al. 2012)
Seeds	Cardiac glycosides	Tanghiiegnin, Digitoxigenin, Cerberin, Neriifolin, Thevetin B	(Abe and Yamauchi 1977)

Na + K + ATPase pump (Hossan et al. 2019). This will leads to the accumulation or increase in the concentration of Na + inside the cell and prevent K + influx which will lead to a decrease in the concentration of K + outside

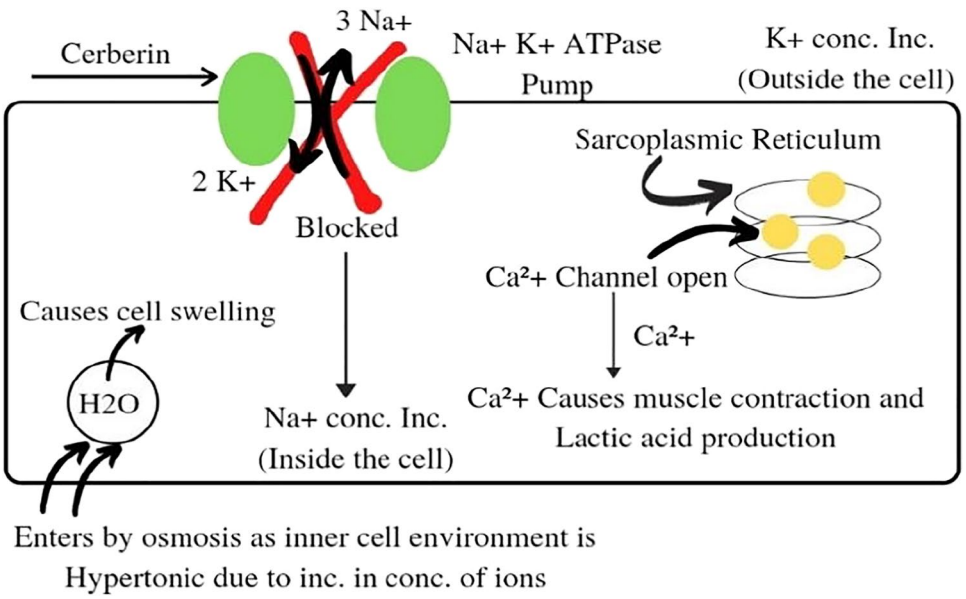

Fig. 1 Mechanism of the active component (Cerberin) of Bintaro Blocking the Na + K + pump and causing an electrolytic imbalance

the cell and causes an electrolyte imbalance as shown in Fig. 1.

It stimulates the sarcoplasmic reticulum to open its Ca2 + channels, leading to Ca2 + accumulation in the cells causing the production of lactic acid, which in turn leads to academia, myocardial contractility, and, ultimately, death. Ingestion of a single seed from the plant in the biological systems of the human body causes different biological effects. The most common effects of toxicity that are observed in the human body are nausea, vomiting, irregular heartbeat, dysfunction of organelles, myocardial infarction, thrombocytopenia, dilated pupils, and bradycardia (Bernshteyn et al. 2020). The route of administration of Bintaro in the human body and its biological effects are represented in Fig. 2.

Pharmaceuticals applications

Pharmaceutical is the term that is used for the substances that are used in the diagnosis, treatment, or prevention of diseases. Bintaro is one of the plants that have many pharmaceutical properties like anti-cancer, anti-bacterial, analgesic, anti-inflammatory, and many more. The plant's anticancer capabilities have been examined extensively in terms of its preventative, protective, tumor-suppressing, immunomodulatory, and apoptotic actions against a variety of cancers. Similarly, some specific secondary metabolites of the plant show analgesic effect and are able to lower the pain. Due to the presence of its therapeutic potential diseases such as rheumatism, dysuria and ringworm may be treated (Fig. 3).

Anti-cancer properties

In this century, cancer has become one of the leading causes of death and disease. In the medical field of cancer treatment, several types of new drugs and synthetic therapies have emerged, including radiation therapy, chemotherapy, and immunotherapy. However, they are still subject to negative side effects (Das et al. 2015). Researchers and botanists recommend paying special attention to plants as the primary source for safe and effective cancer treatment. Plants like Bintaro, which are compared to artificial drugs are an amazing source for the development and manufacture of effective, well tolerated, and safe anti-cancer drugs. The phytochemicals contained in a Bintaro can inhibit the growth, colony formation, and migration of cancer cells. Numerous subsequent in vitro and in vivo studies confirmed that few cardiac glycosides appear to be selective in killing cancer cells, including human lung, pancreatic, and skin cancer cells (Mutalip et al. 2014). The new findings showed that digoxin, digitoxin, and ouabin are known to be involved in a complex cellular signaling mechanism that leads to selective tumor

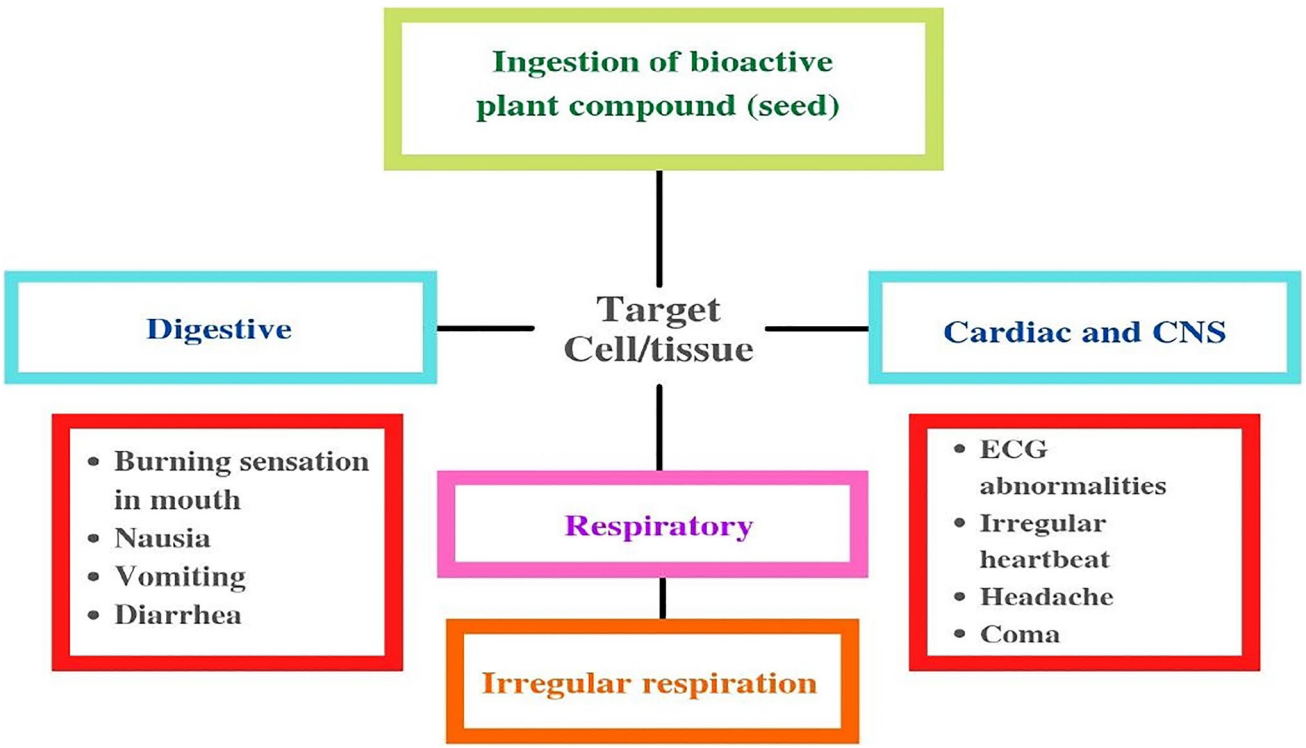

Fig. 2 The Biological effects of Bintaro's seed targeting various bodily biological systems

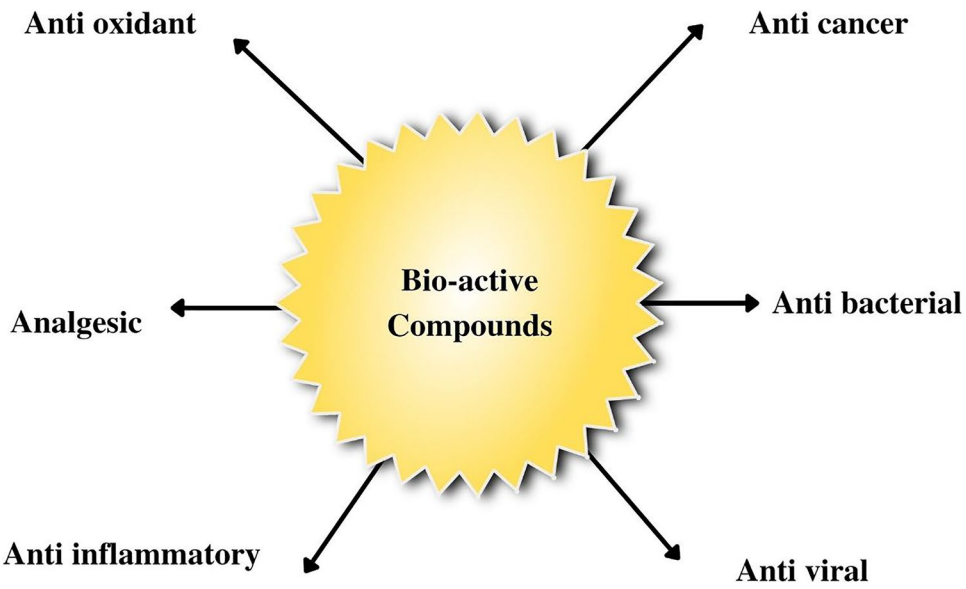

Fig. 3 Illustration of pharmaceuticals applications of Bintaro

control but not normal cell proliferation (Syarifah et al. 2011). It is typically believed that the formation of growth-promoting oxidants (reactive oxygen species ROS) is a prime catalyst in the stages of neoplasm promotion and progression. The prooxidant enzymes are evoked or activated by varied tumor promoters for example cyclooxygenases (COX) and lipoxygenases (LOX). flavonoids are significantly effective at inhibiting COX and LOX and thus inhibit tumor cell proliferation (Ren et al. 2003). Bintaro leaf extract has been investigated to be able to strongly suppress MCF7 and T47D cells. The leaf extract was also tested against breast cancer (MCF7 and T47D), and ovarian cancer (SKOV3 and CAOV3) (Syarifah et al. 2011). Cardenolide and 17β-Neriifolin from Bintaro roots have an antiproliferative effect against human CO12 colon cancer cells (Chang et al. 2000). Cardenolide glycoside of 2′-o-acetylacerlasid A, 17α Neriifolin, 17β-Neriifolin, Cerberin, 7,8—Dehydrocerberin, Deacetyltanghinin, and Tanghinin isolated from Bintaro are cytotoxic to human oral cancer cells (KB), human breast cancer cells (BC) and the human lung NCI-H187 Carcinogenic cells (Cheenpracha et al. 2004; Laphookhieo et al. 2004). Tanghiiegnin reduces the activity of HL-60 promyelocytic leukemia cells with an IC50 in a time and dose-based manner (Wang et al. 2010). Neriifolin from the leaf and fruit of the plant is effective against stomach cancer as it reduces the viability of HepG2 cells of human hepatocellular carcinoma and also induces the arrest of the S and G2/M phases of the cell cycle (Zhao et al. 2011).

Figure 4 shows that the flavonoids that have been isolated from the leaf of the plant using scientific techniques are an efficient treatment for carcinoma cells because they induce cell death and inhibit the further proliferation of the cell.

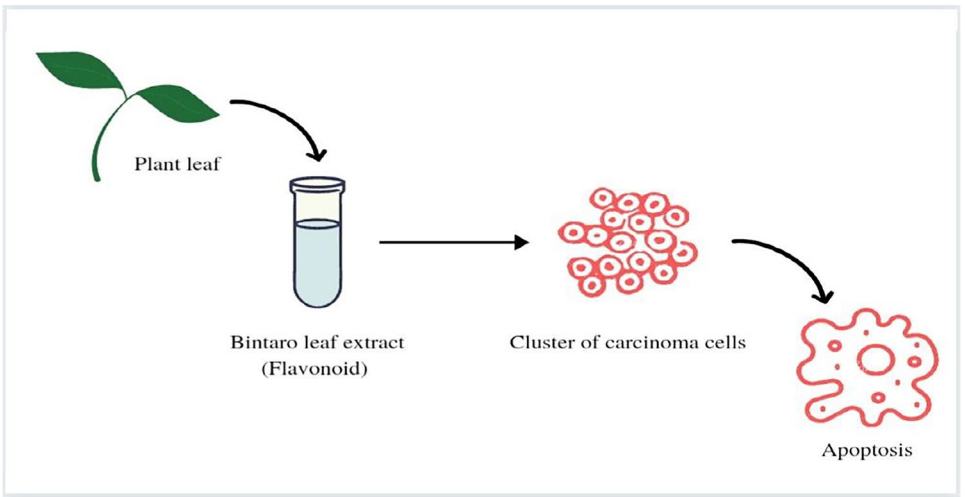

Fig. 4 Illustration of leaf extract of Bintaro (flavonoids) on carcinoma cells

Antioxidant and Analgesic Properties

Bintaro, from a family of Apocynaceae, could be a robust supply of antioxidants and analgesic, mainly, flavonoids, tannins, and phenolic compounds, indicating its potential use in pharmacological products designed to improve individual standards (Iqbal et al. 2017). The chloroform and carbon tetrachloride fractions from the trunk bark of the plant showed the strongest antioxidant activity (Wong et al. 2013). To predict the antioxidant activity of the plant, A DPPH assay was performed in which the ethanol extract converted the free radical DPPH into a stable form of DPPHH by donating electrons or hydrogen radicals (Monjur-Al-Hossain et al. 2013). The extract showed a concentration-dependent DPPH radical scavenger activity due to the presence of phenols, and flavonoids which were comparable to that of the standard antioxidant ascorbic acid (Iqbal et al. 2017; Monjur-Al-Hossain et al. 2013).

Bintaro's methanolic extract was found to reduce sleepiness and potentiate pentobarbital-induced sleep time in mice, suggesting its central depressant activity, thus indicating a probable sedative action (Ahmed et al. 2006). Also, the leaf extract contains cerberin, which decreases the duration of action of pentylenetetrazole-induced tonic seizures and mortality and creates a hypnotic effect (Tripathi 2021). The extract may have the ability to inhibit the release of prostaglandins to relieve pain (Monjur-Al-Hossain et al. 2013). The peripheral analgesic effects of the plant extract can be linked to the inhibition of cyclooxygenases and/or lipoxygenases, while the central analgesic effect of the extract can be interfered with by the inhibition of central pain receptors (Hossain et al. 2013). Quercetin (a flavonoid) showed an analgesic effect and was able to lower the pain threshold in the hot plate test (the application of heat stimulates the mice to pain) at a dose of 3.5 mg/kg (Xiao et al. 2016). The effective doses of quercetin (60–200 mg/kg) in various models of animals have an analgesic effect equivalent to that of aspirin (100 mg/kg) or morphine (2 mg/kg) (Xiao et al. 2016). The extract yields mild writhing inhibition similar to the conventional drug Diclofenac sodium which suggests large analgesic activity (Hossain et al. 2013).

Anti-bacterial and anti-viral properties

The combination of Bintaro's antibacterial and antiviral properties due to the presence of significant Phytochemicals represents a doubtless path-breaking interference to lessen the spread of disease-causing pathogens. Tests/experiments were carried out to determine the antibacterial activity of the ethanolic extract of the Bintaro flower using a in vitro well diffusion technique. The researchers observed that the ethanolic extract from Bintaro flowers indicates an antibacterial effect against *Staphylococcus aureus* (Lestari et al. 2017). This approach is extensively applicable and suitable for the initial screening of substances for their antibacterial properties (Lestari et al. 2017; Ahmed et al. 2008). The results of the tests of antibacterial activity showed that the zone of inhibition value 21 already had an antibacterial activity of 30.53 mm at a concentration of 10%. It also shows an increase in concentration also increases the zone of inhibition of *Streptococcus aureus* (Lestari et al. 2017). A similar test was performed against *Streptococcus pyogenes*, *Salmonella typhi*, *Shigella flexneri*, and *Shigella dysenteriae*. The Bintaros seed extract was found to have moderate antibacterial activity against *Staphylococcus pyogenes* and *Salmonella typhi*, while it had mild antibacterial activity against *Shigella flexneri* and *Shigella dysenteriae* (Ahmed et al. 2008). According to studies, butanol and hexane extract from Bintaro leaves have a sufficiently strong antibacterial effect on *K. pneumonia*, while butanol extract from Bintaro leaves has a greater effect than Bintaro hexane extract (Musdja et al. 2018). Bintaro leaf ethyl acetate and dichloromethane extract also have an antibacterial effect against gram-positive (*S. aureus*) and gram-negative (*E. coli*) bacteria (Musdja and Djajanegara 2019). Antiviral and cytotoxic activity was also observed in Bintaro, showing selective antiviral activity towards Viruses of vesicular stomatitis (VSV) (Kemal et al. 2015). Bintaro fruit ethanol extract was evaluated for antiviral properties, 0.0050.1 mg/ml against herpes simplex virus (HSV). A crude extract from the fruit of Bintaro can inhibit the growth of HSV (Manoharan and Kaur 2013). According to these studies, it can be concluded that Bintaro can be used as a medicinal plant to deal with fever, malaria, diabetes and gastrointestinal problems, and other infectious diseases (Musdja and Djajanegara 2019). Bintaro cardiac glycoside antiviral activities can effectively suppress viral protein translation, interrupt previous viral mRNA splicing, to inhibit various viral diseases such as HIV, HMV, Ebola, Chikungunya, and coronavirus (Reddy et al. 2020).

Anti-inflammatory properties

Inflammation occurs with any form of physical injury. Under ordinary situations it is auto-limited however can turn into persistent and chronic inflammatory disorder would possibly develop. Symptoms of inflammation include redness, swelling from heat, and pain (Ferrero Miliani et al. 2007). There are two forms of inflammation acute and chronic. Acute inflammation is speedy and transient while chronic inflammation is constant and has an extended healing time (Byeon et al. 2012). Bintaro is a medicative herb historically used to improve the clinical symptoms of inflammation or inflammatory disorders due to the presence of flavonoids that act as anti-inflammatory agents (Yi et al. 2016). In-vitro research of anti-inflammatory impact on mouse model through methanol extract of Bintaro towards LPS stimulated

macrophages inducing hepatitis and peritonitis shows the anti-inflammatory properties of Bintaro (Yi et al. 2016). The activated inflammatory cells keep their inflammatory impact by generating histamines, prostaglandins, reactive oxygen species (ROS), and nitrogen reactive species which include Nitric oxide (NO) (Massarotti, 2008). Other inflammatory mediators like Src play a vital role in sustaining this cellular response. It is a tyrosine-protein kinase that is involved in the functional activation of the macrophage-mediated inflammatory response (Byeon et al. 2012). Kaempferol is an active flavonoid found in Bintaro methanol extract and plays a crucial role in its auspicious anti-inflammatory properties by inhibiting the route of Syk/Src and exerting an anti-inflammatory response (Jeong et al. 2014). In recent studies, it has been found that the administration of kaempferol also shows anti-inflammatory effects against HCl-induced gastric lesions and LPS-induced pancreatitis. The efficiency of kaempferol evaluating with the performance of well-known capsules which include ranitidine and indomethacin appears to signify its capacity and possible use as anti-inflammatory remedy or agent (Kim et al. 2015). Likewise, Quercetin, another surprising flavonoid, has been reported to have potent and persistent anti-inflammatory effects. It inhibits the production and blocks the pathway of inflammation-producing enzymes namely, COX and LOX (Li et al. 2016). Therefore, Bintaro can be used as a medication remedy for treating various diseases such as Alzheimer's, Rheumatoid arthritis, Diabetes, Osteoporosis, etc. (Kaur et al. 2013).

Figure 5 shows the enzymes COX and LOX cause inflammation by releasing archednoic acid, which is a precursor to prostaglandins that cause an inflammatory response. The inhibition of these enzymes by quercetin reduces the release of archednoic acid and prevents inflammation.

Neuropharmacological Properties

Neuroprotection means the mechanism which is capable of battling down the nervous system towards neural harm due to numerous neurodegenerative issues which include Alzheimer's disorder, Anxiety, Parkinson's disorder, etc. Bintaro has been stated for its herbal neuroprotective activities (Kumar et al. 2015). Bintaro's phytochemicals, including triterpenoids, alkaloids, flavonoids, saponins, etc., are found in a wide variety of plant components that can alter the neurotransmitters and can change one's behavior, mood, and mental state in living organisms (Kumar et al. 2015; Yunilla 2016). Various neuropharmacological properties of Bintaro are summarized in Fig. 5.

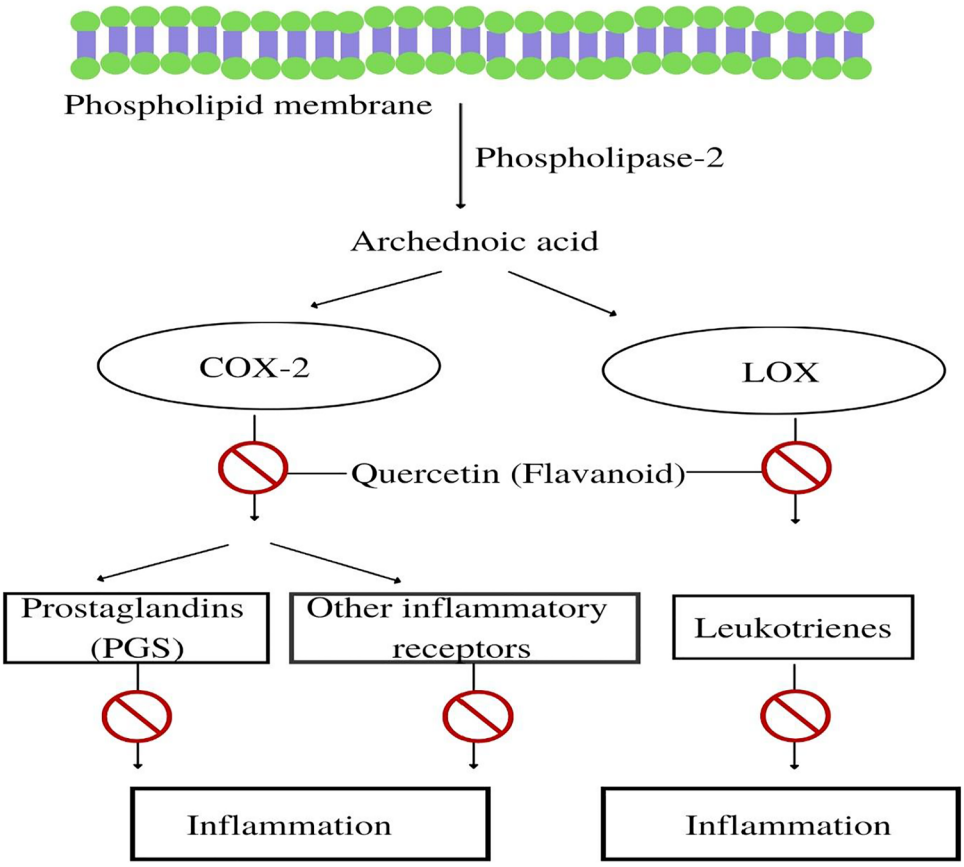

Fig. 5 Illustration of the anti-inflammatory mechanism of Quercetin

Anxiety

Anxiety disorders are major problems of mental health that may have a negative impact on a person's day-to-day existence. It was reported that intake of Betulinic acid produces anti-anxiety activity in animals. Prescription drugs containing betulinic acid have been emphasized as a means of remedy for preventing or treating anxiety (Gangwal 2013). Sedation and hypnotics researchers have studied that the administration of beta-amyrin potentiates the anesthetic effect in test animals (mice), so α/β-amyrin (triterpenoid) was known for its sedative effect (Otimenyin 2022) (Fig. 6).

Memory

Studies have discovered that the combination of triterpenoid and saponins (Escin) extracted from the plant that has been confirmed to enhance learning and memory recovery and decrease hippocampal injury in cerberal ischemic mice (Zhang et al. 2010a, b).

Neuroprotective activities

Asiatic acid has been studied for its neuroprotective effects by neutralizing reactive species of elements. Various efforts have been made to get anti-Alzheimer agents from herbal resources. Cannabinoids found to act as anti-Alzheimer agents (Gangwal 2013).

Pain and Nociception

Studies stated that triterpenoids perform a crucial function in the remedy of pain (Gangwal 2013). Researchers have investigated the anti-nociceptive effect of euphol towards nociceptive reaction caused by ligature of the sciatic nerve (Scott et al. 2004). In animal models, oleanolic acid has inhibitory effects on the acute nociception induced by capsaicin (Maia et al. 2006).

Depression

A condition that affects mental health and is defined by an ongoing sad mood or a lack of enthusiasm in tasks, both of which cause severe damage in day-to-day living. There are many first-line medications available for the therapy of such mental disorders; however, these medications may also have some undesirable side effects. The discovery of anxiolytic or depressive pharmaceuticals derived from plants offers a number of advantages over more conventional treatments. β amyrin and norepinephrine are additionally determined to act as an antidepressant (Otimenyin 2022). Flavonoids are also reported as an antidepressant (Kumar et al. 2015).

Eco-friendly applications

To be earth-friendly or not detrimental to the ecosystem is the precise meaning of the term "eco-friendly." The applications which support the ecosystem and environment and do not harm are called eco-friendly applications. A tropical

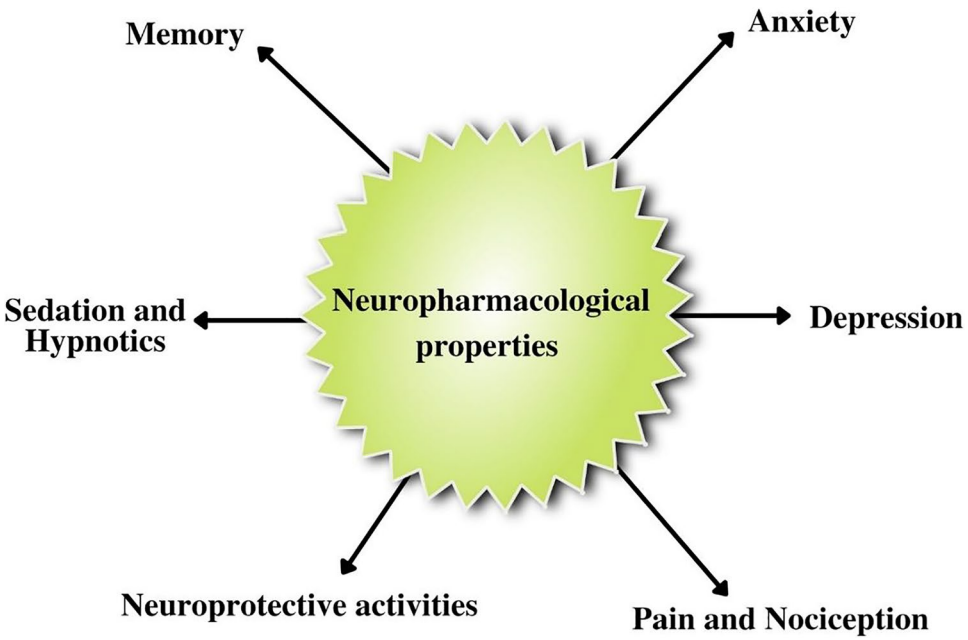

Fig. 6 Illustration of various neuropharmacological properties

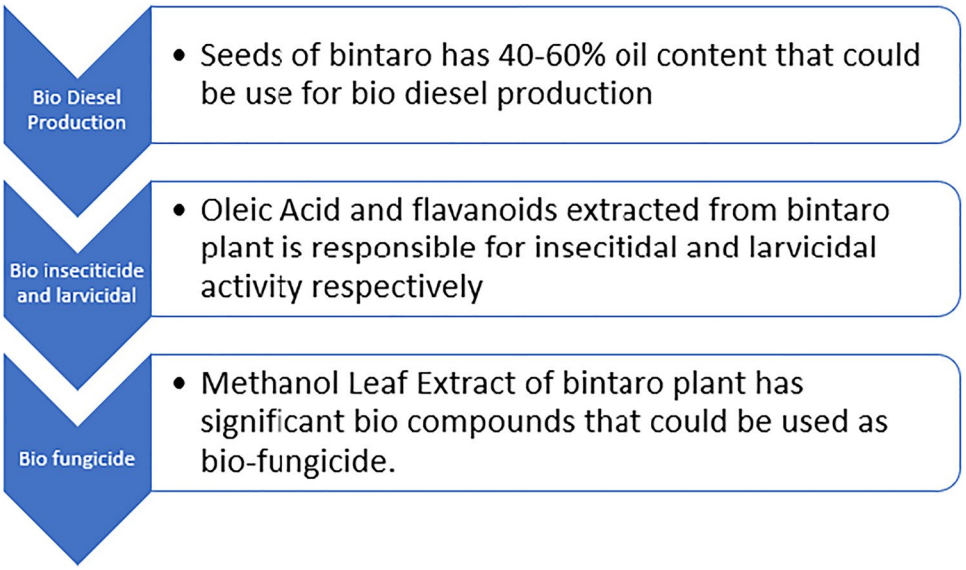

Fig. 7 Illustration of eco-friendly applications of Bintaro

mangrove plant Bintaro is considered as an eco-friendly plant as it has three major eco-friendly applications as shown in Fig. 7 below. The below applications can be considered as an innovative approach towards sustainable development as it has great economic and cultural importance and potential.

Biodiesel production

Environmental issues arising from the continuous consumption and depletion of energy fuels, stimulate studies into alternative energy sources (Husin et al. 2018). Many scientists are researching for new alternative energy sources where Bintaro oil is one of the alternative energy sources for future biodiesel Production (Bhikuning and Hafnan 2019; Rizki et al. 2018). It is the non-edible vegetable oil that can surely replace fossil diesel (Rizki et al. 2018; Marlinda et al. 2016). It is defined as the long chain of mono-alkyl esters of fatty acids derived from vegetable oil with or without a catalyst (Rizki et al. 2018). Various studies and strategies have been followed for the production of biodiesel, the most preferred process for biodiesel production is two-step esterification and transesterification to reduce impurities and the acid value of the oil in order to convert it into biodiesel (Rizki et al. 2018) that can be made on a huge scale and also the mentioned process of the manufacturing process is extremely simple and quick. According to studies, Bintaro seeds contain a large proportion of 46–64% of oil thus, they can be utilized as a raw material for the production of biodiesel (Sutapa and Ropa 2019). Biofuel can be mixed with conventional fuel in any percentage. Biodiesel mixed with diesel contributes many valuable properties to the diesel engine (Noor et al. 2018). The combination of Diesel fuel and biodiesel emits fewer harmful gases than diesel fuel (Patel and Sankhavara 2017). The best thing about Bintaro biodiesel is that its physical and chemical properties such as density, viscosity, flash point, etc. meet the standard values of ASTM, D6751, and EN14214 (Ong et al. 2014; Lie et al. 2018). The other advantages of using biodiesel over petroleum diesel are biodegradable, highly energy-efficient, non-toxic, low-combustion, easily available, renewable, and environmentally friendly fuel (Noor et al. 2018). These efforts can reduce reliance on petroleum-derived fuels and provide a more environmentally friendly fuel (Ong et al. 2014).

Bio-insecticide and larvicidal activities

The Bintaro plant comprises of active phytochemicals that can be used as organic bioinsecticidal, pesticides, and for larvicidal effects, and thus, the use of natural insecticides and pesticides in agricultural fields can suppress the growth of insects, reduce damage to crops and increase crop production (Haryanta et al. 2020). It was found that the extract from the Bintaro plant possesses an inhibitory and lethal effect on the development of *Riptortus linearis*, a pod-sucking pest that infects soybean plants and can affect plant production both qualitatively and quantitatively (Haryanta et al. 2020; Krisnawati and Adie 2018). Bintaro is also reported to have biological activity against insects as a growth inhibitor, food deterrent, etc. Oleic acid extracted from Bintaro seeds indicates insecticidal activity against the Subterranean termite *Coptotermmes gestroi* and the drywood termite *Cryptotermes cynocephalus* (Tarmadi et al. 2014). Another active biocompound called flavonoid (quercetin), which is widely distributed in Bintaro, could be useful as a termite control agent. Flavonoids are said to be associated with resistance to insect infestation and also to have an anti-feedant effect against *C. formosanus* (Ohmura et al. 2000). The Bintaro fruit extract has been shown to have anti-termite and

larvicidal effects. In the bioassay test of a sample of Bintaro fruit and subsequent extraction with the maceration method using methanol, it was found that the hexane fraction of the Bintaro fruit has the highest mortality rate against *S. oryzae* (Guswenrivo et al. 2013). The methanol flower extract also showed high potential in terms of termite mortality, termite decay, and soil burial decay against *C. Optotermes gestroi* (Hashim et al. 2009). Mosquitoes act as vectors of dangerous human diseases and are one of the major public health problems. *Aedes aegypti* is a vector of dengue. Chemical treatment is an effective however unsafe method for the environment, so it is important to develop and increase plant-based treatment to eliminate these problems (Tarmadi et al. 2018). Various studies and experiments have been carried out to eliminate mosquito larvae naturally. It was found that the crude extract from Bintaro seeds and leaves has a significant impact on larval mortality and inhibited the development of larvae in pupae. The higher the concentration of Bintaro seed and leaf extract, the faster it kills the insects (Tarmadi et al. 2018; Wahyuni et al. 2018). Another pathogenic vector is *Culex quinquefasciatus*, which is responsible for the spread of the Arbovirus. Bintaro seed extract using ethyl acetate and n-hexane shows high larvicidal activity against *Culex quinquefasciatus*, indicating that Bintaro could be used for larval control (Meisyara et al. 2020).

Biofungicides

The intensive use of fungicides in the agriculture field has resulted in environmental pollution that poses a significant risk to human health, so there is a need to develop natural plant-based biofungicides (Chu et al. 2015). The antifungal bioassay of the ethanolic extract from leaves and fruits was done through Kirby-Bauer disk diffusion test method, it was found that the extract from Bintaro leaves shows an antifungal effect of killing fungi like *Aspergillus niger*, *Fusarium oxysporum* and *Penicillium citrum* (Chu et al. 2015). Methanol leaf extract of Bintaro shows the presence of antifungal effect higher than the preferred standard antifungal drug fluconazole, as the leaf extract possesses a fantastic ability to apply as an antifungal agent against fungus like *Saccharomyces cerevisiae* and *C. Albicans* (Sahoo and Marar 2018). Studies have also shown that phytochemicals from Bintaro seeds also have an antifungal effect against *C. Albicans* (Sukmawati 2016). In antifungal paper disk assay, methanol wood extract of Bintaro was reported to have an antifungal effect against *Trametes Versicolor*, *Pcynoporus sanguineus*, and *Schizophyllum commune* (Hashim et al. 2009). *Penicillium digitatum* is one of the most common pathogens causing post-harvest rot in fruits (Singh et al. 2015). Tannins, a significant secondary plant metabolite in Bintaro, acted against *Penicillium digitatum* by inhibiting mycelial growth and reproductive structure (spore) germination (Zhu et al. 2019). Flavonoids have also been tested as antifungal agents against the genus Aspergillus (Gizaw et al. 2022). The antifungal activity of triterpenoid and saponins with oleanolic acid has been studied in vitro using the Agar dilution method and has been found to have a high rate of performance against yeast and dermatophyte species (Heng et al. 2014). Similarly, Phenols also show strong antifungal activity against a broad range of fungi, including *Pseudomonas aeruginosa*, and *Staphylococcus aureus* (Rao et al. 2010).

Bintaro: current progress and future perspective

The phytochemical, pharmacological, and eco-friendly characteristics of the Bintaro plant are addressed in this article. The use of this plant in traditional folk medicine includes that of an analgesic, an anticonvulsant, a cardiotonic, and for action that lowers blood pressure. Secondary metabolites found in this plant include saponins, terpenoids, and alkaloids. Additionally, this plant contains phenolic acids, flavonoids, cardiac glycosides, steroids, iridoids, lignans, and other chemicals (Maharana 2021). In terms of importance, cardiac glycosides are the most important phytochemical substances, followed by phenolic and terpenoid acids. Again, the leaf contains a wider variety of phytochemicals as well as a bigger amount of them, followed either by fruit, the seed, the stem, and the root. The plant has a wide range of pharmacological properties, including antioxidant, antitumor, anti-inflammatory, and antibacterial properties. This study may be of use to researchers who want to pursue future researches along similar lines (Maharana 2021).

The barks, leaves, fruits, and seeds of Bintaro trees all include components that may be used in the production of organic insecticides. It has been shown that the use of natural pesticides in agricultural settings may lower the populations, lessen the amount of damage done to crops, and raise the amount of food produced from such crops. An investigation on the effects of Grayak caterpillar feeding on Bintaro fruit is being carried out from the Research Institute of Rawa Land (Balittra) in Banjar Baru, in the province of South Kalimantan. The findings of a study that was carried out in 2008 revealed that as many as thirty percent of the grayak caterpillar's colony perished within twenty-four hours after ingesting dips in Bintaro. After sixty to seventy-two hours after receiving this medication, the death rate increased to ninety to ninety-five percent (Purwanti et al. 2021).

According to the findings of a study conducted by Faperta IPB, bintaro fruit has the potential to be utilized as an alternative fuel. Even taking into account the findings of toxicity tests conducted on the secretion of the fruits, it can be concluded that Bintaro oil is appropriate for utilization as

a fuel since it has an odor, smoke, as well as other remnants which are considered to be harmless (Hendra et al. 2016).

In Madagascar, heart problems are traditionally treated using seeds as part of the country's traditional medicine. Bark has a number of medicinal applications, including laxative, antipyretic, and therapy for dysuria and ringworm. Rheumatism may be treated by rubbing fresh red fruit on affected areas of the legs. Oil, when massaged onto the skin, may relieve itching. Thus, focus of the researchers should be more towards medical field, economic field, and agricultural field that can help the different sectors worldwide.

Conclusion

Bintaro (*Cerbera odollam, Cerbera manghas*) is a widely distributed plant. The geographic range of Bintaro is in tropical, subtropical Southeast Asia. Although Bintaro is generally known to be extremely toxic, but the other constituents of plants have been described with various biological and pharmaceutical properties of medicinal importance due to the presence of significant secondary metabolites. Most types of phytochemicals are found in stems, leaves, fruit, seeds, etc. Several in vitro and in vivo studies and experiments have reported that Bintaro has amazing therapeutic potential that includes anti-cancer, antimicrobial, antioxidant, analgesic, and neuropharmacological activities that could improve an individual's standard of living, so it could be a new way to alleviate human suffering. Various studies have also highlighted its potential as a bio- insecticide and bio fungicide in the agricultural sector as it has unique agents that could repel or kill insects and fungi respectively, clearly suggesting its potential to be a future bio-insecticide and fungicide that could be used as an alternative to synthetic ones. Also, Bintaro oil is one of the potential inedible oil that could be used as an alternative to petroleum for future biodiesel production. This is not only effective, but also safe and Environmental-friendly.

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