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Xylocarpous

Xylocarpus moluccensis Familia: Meliaceae Subfamilia: Cedreloideae Genus: Xylocarpus Species: X. granatum – X. moluccensis – X. rumphii Xylocarpus J.Koenig (1784) Type species: Xylocarpus granatum J.Koenig, 1784 Homotypic Granatum Kuntze, Rev. Gen. 1: 110. 1891, nom. illeg. non Saint-Lager (1880). Heterotypic Monosoma Griff. in Not. Pl. Asiat. 4: 502 (1854) Native distribution areas: Continental: Eastern Africa & W.Pacific Aldabra, Andaman Is., Bangladesh, Bismarck Archipelago, Borneo, Cambodia, Caroline Is., Comoros, Fiji, Hainan, India, Jawa, Kenya, KwaZulu-Natal, Laos, Lesser Sunda Is., Madagascar, Malaya, Maluku, Marianas, Mozambique, Myanmar, New Caledonia, New Guinea, Nicobar Is., Philippines, Queensland, Samoa, Seychelles, Solomon Is., Somalia, Sri Lanka, Sulawesi, Sumatera, Tanzania, Thailand, Tonga, Vanuatu, Vietnam References: Brummitt, R.K. 2001. TDWG – World Geographical Scheme for Recording Plant Distributions, 2nd Edition König, J.G. 1784: Naturforscher (Halle) 20: 2. 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Global Biodiversity Information Facility. 13233740. GBIF Backbone Taxonomy. Checklist dataset. Taxon: Xylocarpus. Accessed: 13233740 {{{3}}} {{{4}}}.. For more multimedia, look at Xylocarpus on Wikimedia Commons. a.1.(Bot.) Bearing fruit which becomes hard or woody.Webster's Revised Unabridged Dictionary, published 1913 by G. & C. Merriam Co. Want to thank TFD for its existence? Tell a friend about us, add a link to this page, or visit the webmaster's page for free fun content. Link to this page: Aldabra, Andaman Is., Bangladesh, Bismarck Archipelago, Borneo, Cambodia, Caroline Is., Comoros, Fiji, Hainan, India, Jawa, Kenya, KwaZulu-Natal, Lesser Sunda Is., Madagascar, Malaya, Maluku, Mozambique, Myanmar, New Caledonia, New Guinea, Nicobar Is., Philippines, Seychelles, Solomon Is., Somalia, Sri Lanka, Sulawesi, Sumatera, Tanzania, Thailand, Tonga, Vanuatu, Vietnam As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn more: PMC Disclaimer | PMC Copyright Notice The mangrove plants are the potential sources of foods and remedies for people living in the forests and nearby communities. Xylocarpus granatum J. Koenig is traditionally used to treat various diseases including diarrhea, cholera, dysentery, fever, malaria, and viral infections, among others. To summarize critically the taxonomy, ethnomedicinal, phytochemistry, and pharmacological activities of X. granatum, information was collected from different databases. An up-to-date search (till June 2020) was carried out with the help of various scientific web resources from databases such as PubMed, Science Direct, Google Scholar, and various patent offices (e.g., WIPO, CIPO, and USPTO) using the keywords "Xylocarpus granatum" and then paired with ethnomedicinal use and phytochemical, phytochemistry, and pharmacological activity (in vitro, ex vivo, and in vivo studies). Findings revealed that seeds, fruits, stem bark, leaf, and twigs of X. granatum exhibited a wide range of key phytochemicals including limonoids, phragmalin, limonoid-based alkaloids, mexicanolides, protolimonoids, flavonols, and lactones. The plant possessed potent antioxidant, anticancer, antidiabetic, antimicrobial, antimalarial, antifeedant, and neuroprotective activities. No clinical studies have been reported in the databases. Ethnomedicinal assessment indicated the application of X. granatum in various fields of medical science specially to treat various human ailments, and this was attributed to the presence of enormous alkaloids as confirmed by pharmacological studies. However, to understand the mechanism of action in-depth studies are required. In view of these findings, more research is necessary to explore and characterize the chemical compounds and toxicological aspects of this medicinal mangrove plant. Overall, it can be stated that X. granatum may be one of the hopeful medicinal herbs for the treatment of various diseases in human beings. Traditional medicines like Chinese traditional medicine, Ayurveda, Unani, and Korean traditional medicine have been used extensively ever since the ancient times. These medicines are based on using natural products for treating various human ailments [1]. Use of new medicines with no doubt helps treat different diseases, but it also poses a risk of side effects. Increased demands for reducing these side effects of the current drugs are driving researchers and pharmacologist towards formulating natural plant-based drugs, thereby exploring different traditionally used medicinal plants/herbs [1]. Xylocarpus granatum J. Koenig is a good example of a medicative plant that is used as a traditional herbal drug [2]. X. granatum is a species of the mahogany family and is widely distributed in the coastal forests of Bengal, Burma, Malay Peninsula, Andaman, and Africa. In Bangladesh, this plant is found in low lying, a swampy locality in the Sundarbans mangrove forest [3]. It is spread across the coastal areas of tropical and subtropical zones and river delta. Typically, this plant's different parts are used for different purposes, most popularly used for the treatment of diarrhea, dyslipidemia, fever, inflammation, malaria, cholera, dysentery, and so on [4, 5]. Various types of chemical compounds are extracted from the different parts of the plant such as limonoids, phragmalin, limonoids based alkaloids, mexicanolides, protolimonoids, flavonol-like compound, lactone, ethanol extract, methanol extract, and alkaloids, among others [6, 7]. Limonoids are the most vital chemical component that is isolated from the different parts of the X. granatum plant [8]. Numerous limonoids are isolated from different parts of X. granatum such as fruit peel, seed kernels, seed, fruit, and seed coat [9]. Limonoids possess diverse pharmacological activities, such as antimicrobial, antimalarial, antiviral, anticancer, antidiabetic, antioxidant, antifeedant [10], and neuroprotective effects [11]. Other potential activities X. granatum extracts include antifilarial, antidepressant, antimalarial [12], and antisecretory effects [13]. So, the limonoids are important pharmacologically active constituents of X. granatum fruit that need to be exploited further [9]. A more detailed investigation need to be done on the toxicological effects and clinical trials on humans. This review offers up-to-date information on the phytochemical profile and biopharmacological effects of X. granatum on the basis of scientific reports found in the databases. The literature on X. granatum botanical description, ethnomedicinal uses, secondary metabolites, and biological properties was collected, analyzed, and summarized in this review. Scientific search engines, such as PubMed, ScienceDirect, SpringerLink, Web of Science, Scopus, Wiley Online, SciFinder, and Google Scholar, and various patent offices (e.g., WIPO, CIPO, and USPTO), were used to collect all published articles about this species. Several terms were used as keywords like Xylocarpus granatum, chemical compounds and Xylocarpus granatum, taxonomical classification, antidiabetic and Xylocarpus granatum, and limonoids and their pharmacological activity. All published work on X. granatum in different languages (English) was cited in this study. The identification and examination of the collected manuscripts were based on their titles and abstracts. Reference lists of the retrieved papers were also examined to identify further relevant papers. Chemical structures were drawn using ChemSketch version 12.01 software. The word Xylocarpus means woody fruit (in Latin) and refers to the large and distinctly woody fruit and seeds of this genus. X. granatum taxonomical classification is given as follows [14]. The maximum height of the X. granatum is 12 m (39 ft); it is a small to medium-sized evergreen tree. The evergreen leaves of the tree have special characteristics; the leaves are pinnate and arranged spirally on the twigs (Figure 1). The trunk has buttresses and above-ground roots, which extend for long distances to either side. X. granatum flowers are white or pinkish-yellow; each flower is 8 mm wide with four parts. The flowers are produced spherical, large, woody capsules, 9–12 cm in diameter. If the capsules are split, this brings out a dozen seeds. Different parts of Xylocarpus granatum J Koenig. (a) Leaves, (b) flowers, (c) unripe fruit, (d) ripe fruit, (e) stem and bark, and (f) roots. The taxonomical classification of X. granatum [14] is as follows: Kingdom: Plantae Phylum: Magnoliophyta Class: Eudicots Order: Sapindales Family: Meliaceae Genus: Xylocarpus Species: Xylocarpus granatum J. Koenig X. granatum, a species of mangrove in the mahogany family (Meliaceae), is commonly known as "cannonball mangrove, cedar mangrove [15], dhundul [16], or puzzle nut tree" [17]. Asia, Africa, Australia [18], and the Pacific Islands are the main inhabitant of this plant [15]. This plant is found in low lying, swampy locality in the Sundarbans mangrove forests in Bangladesh [3]. This forest covers 6017 km2 in Bangladesh and mangroves are salt-tolerant forest ecosystems of tropical and subtropical intertidal regions of the world [3]. This plant extends from Tanzania, Kenya, and Mozambique to Malaysia, Indonesia, Thailand, Papua New Guinea, India, Bangladesh, and northern Australia [3]. This species is native to the tropical and subtropical western Indo-Pacific region [19]. X. granatum, a puzzle nut tree, is a mangrove species belonging to mahogany family [20, 21]. It is commonly known as "pussur" in Hindi and "dhundul" in Bengali. It is an evergreen tree having moderate-sized grey bark, usually growing in coastal forests of Bengal, Burma, the Malaya peninsula, Andaman Islands, and island of Australia and Africa [12]. It is a medicinal plant and used by different ethnic communities all over the world [22]. Several reports suggested that from past to present this plant has significant medicinal properties [23]. X. granatum plants have several bioactive compounds, including gedunin and limonoids [6, 24]. All of these compounds possess significant inhibitory activity against cancer [16, 25] and malarial, viral, feedant, diabetes, filarial activity, and fungicidal activity from ancient times [10, 26]. All of these compounds extracted from the twigs and leaves, fruits, seeds, barks, seed kernels, and stem bark. In the previous studies, researchers present various traditional uses of X. granatum extract. In southeast Asia, it is used as a treatment of diarrhea, fevers such as malaria, viral diseases like influenza, and cholera and also as an antifeedant or insecticide throughout ancient times [8, 25]. In folklore, the X. granatum plant has been applied to treat malaria, fever, cholera, dysentery, and diarrhea in many countries including India. The extraction of leaves, fruits, and barks of X. granatum possesses potential free radical scavenging activities [4]. Besides, Uddin et al. [16] proposed that this plant extract chemicals have a variety of medicinal properties and in Bangladesh, and it was employed for the treatment of fever, malaria, cholera, diarrhea, and dysentery. Also, antioxidant and antifilarial activities have been reported from ancient times [16]. The X. granatum plant contains several bioactive constituents (Table 1 and Figure 2). Limonoids are the most vital chemical component that are isolated from the different parts of the X. granatum plant [8]. Moreover, X. granatum's seeds consist of sundarbanxylogranins A–E [27]; krishnagranatins A–I [28]; thaixylogranins A–H [29]; granaxylocarpins A–E [30]; xylocarpanoids A and B [31]; xylomexicanins A–D, I, and J [32–34]; xyloccensins I, K, L, O–S, V, W, and Y [10, 12, 35, 36]; hainangranatumins A–J [37]; xylogranatins F–R [38]; thaigranatins A–E [39]; xylocartin C [40]; andhraxylocarpins A–E [41]; protoxylogranatin A-B [42, 43]; protoxylocarpins F–H [25]. Phytochemistry of Xylocarpus granatum J. Koenig. Parts Compounds References Seeds Sundarbanxylogranins A–E; krishnagranatins A–I; thaixylogranins A–H; granaxylocarpins A–E; xylocarpanoids A and B; xylomexicanins A–D, I, and J; xyloccensin I, K, L, O–S, V, W, and Y; hainangranatumins A–J; xylogranatins F–R; thaigranatins A–E; xylocartin C; andhraxylocarpins A–E; protoxylogranatin A-B; protoxylocarpins F–H [10, 12, 25, 27–43] Stem bark Xyloccensin M and N; xyloccensins Q–U; xyloccensin L; xyloccensin I, J; xyloccensins O and P [10, 44–47] Fruits Gedunin; andirobin; mexicanolide; phragmalin; cipadesin A; xylocarpins A–I; photogedunin, xylocarpin L, xyloccensin I, Y, X1, and X2; xylogranatin E; xylogranatinin [2, 8, 16, 35, 40, 48–51] Leaf and twigs Lactone; xyloccensins O–S and V; xylogranin B; xylogranatopyridines A and B; xylogranatumines A–G; xylogranatin E [22, 26, 36, 50, 52, 53] Root bark N-Methylflindersine [54] Chemical constituents of Xylocarpus granatum J. Koenig.The plant fruit contains gedunin [16, 40], andirobin, mexicanolide, and phragmalin [40]; cipadesin A [2]; xylocarpins A-I [8]; photogedunin [48]; xylocarpin L [35]; xyloccensin I, Y, X1, X2 [49]; xylogranatin E [50]; xylogranatinin [51]. Furthermore, stem bark of X. granatum consists of xyloccensin M and N [44]; xyloccensins Q–U [10]; xyloccensin L [45]; xyloccensin I and J [46]; xyloccensins O and P [47]. Leaf and twigs contain lactone [22]; xyloccensins O–S and V [36]; xylogranin B [26]; xylogranatopyridines A and B [52]; xylogranatumines A–G [53]; xylogranatin E [50], and root bark contains N-methylflindersine [54]. It is evident that X. granatum is rich in various compounds, but limonoids, which is an oxidized tetranortriterpenoid derivative, is most dominant and widely studied secondary metabolite. This group of compounds is gaining more and more interest of scientific community due to its various health promoting effects. There are as many as 100 limonoids that are extracted and characterized. Limonoids have important biological activities such as anticancer, antioxidant, antiulcer, antimicrobial, and antiviral actions [55]. Traditionally, these mangroves are also used to treat the troubles caused by dysentery, diarrhea, and abdominal pains [48]. In a recent study, 25 new limonoids have been detected using high resolution electrospray ionization mass spectroscopy (HRESIMS) in X. granatum of Hainan mangrove region. The structures of these compounds were also established using single-crystal X-ray diffraction analyses, nuclear magnetic resonance spectroscopy, and electronic circular dichroism spectra. Limonoids showed typical bridges of C3-O-C8 and C1-O-C8 in mexicanolides, whereas few compounds, which are derivatives of azadirone, showed C1-O-C29 bridges (Zahang et al., 2020). The pharmacological activities of Xylocarpus granatum J. Koenig are summarized in Table 2. Pharmacological activities. Activity Isolated compounds Cell lines/test system IC50 values References Anticancer activity Gedunin Colon cancer cell lines 16.83 µM [16] Xylogranatumines A–G A549 (human lung adenocarcinoma) tumor cell lines 10 µM per specimen [53] Protoxylocarpins F–H Five human tumor cell lines [25] Xylomexicanin A Human breast carcinoma cells (KT) 7.43 µM [32] Granaxylocarpins A-E Cytotoxicity against the P-388 and A-549 tumor cell lines 9.3 and 4.9 µM [30] Xylomexicanins F Six human tumor cell lines A549 and RERF 18.83 and 15.83 µM [44] Thaixyloogranis A–H MDA-MB-231 cell line 49.4 mM [29] Xylogranin B 48.9 nM [26] Antimalarial activity Gedunin and xyloccensin I In vitro model of Plasmodium falciparum 50 µg m/L, and (MIC) 10 µg m/L. [12] Antiviral activity Sundarbanxylogranis B Human immunodeficiency virus (HIV) 78.45 ± 1.69 µM. [27] Granatumin L and their moderate derivatives HIV-1 and influenza A virus (IAV) HIV-1 with an 15.98 ± 6.87 µM; IAV with a 14.02 ± 3.54 µM [39] Antifeedant activity Xylogranatins G The third instar larvae of Mythimna separata (walker) 1 mg m/L [38] Xyloccensins P and Q 500 ppm [10] Antidiabetic activity Xylogranin B IC50 48.9 nM or inhibited TCF/β-catenin transcriptional activity with IC50 values of 270 and 330 nM [26] Xyloccensin I α-amylase and α-glucosidase inhibition study 0.25 and 0.16 mg/mL [4] Xyloccensin S Protein tyrosine phosphatase 1B 8.72 µg/mL [52] Antidepressant- and anxiolytic-like activities Cipadesin A Mice model 5, 15, and 50 mg/kg [2] Antifilarial activity Gedunin and photogedunn Human lymphatic filarial parasite 100 mg/kg [56] Fungicidal activity Lactone Wheat powdery mildew 20 mg/mL [22] Possess different inhibitory effect Xylogranatopyridins A and B Protein tyrosinephosphatase 1B (PTP1B) 22.9 µM [52] Krishnagranatins G, H, and I Inhibit NF-κB pathway 100 ng/mL [28] Xyloccensin S Protein tyrosine phosphatase 1B 8.72 µg/mL [36] Antioxidant activity Xyloccensin I DPPH, ABTS, superoxide and hydrogen peroxide scavenging 0.041, 0.039, 0.096, and 0.235 mg/mL [4] Cancer is the abnormal proliferation of the human body's cells. The uncontrolled development of normal cells can initiate cancer. In recent studies, the anticancer properties have been found in some plant extracts and their isolated compounds developed by the researchers. Amongst them is X. granatum, a well-known mangrove plant, a rich source of bioactive compounds, such as protolimonoids (apotirucallanes) [57, 58], gedunin [16], xylogranatumines A–G [53], protoxylocarpins F–H [25], and so on, which showed anticancer activity. Besides, protolimonoids exhibited a wide range of bioactivities, including insecticidal [59], and CDC25B (M-phase inducer phosphatase 2) inhibitory properties [60]. The cytotoxic activity of gedunin extracted from bark of X. granatum demonstrated moderate levels of anticancer activity in colon cancer cell lines with IC50 value of 16.83 µM concentration. In this study, gedunin moderately inhibited CaCo2 (human colorectal adenocarcinoma) and had growth inhibitory activity [16]. Moreover, xylogranatumines A–G (apotirucallane protolimonoids) had the potential to cytotoxic activities against human A549 (lung adenocarcinoma) tumor cell line. However, at 10 µM concentration, only xylogranatumine F showed weak cytotoxic activity against A549 alveolar tumor cell with inhibition of 54.2% at the concentration of 10 µM, while others were inactive (10 µM). In addition, granaxylocarpins C, D, and E were inactive against both the P-388 and A-549 cell lines [30]. Besides, antitumor activities of thaixylogranins A–H exhibited weak cytotoxicity against the breast MDA-MB-231 cell line [61], with the concentration of IC50 values of 49.4, 58.3, 53.6, 61.1, 57.9, 44.6, 40.6, and 38.5 mM, respectively, whereas thaixylogranin E showed weak cytotoxicity against the HCT-8/T cell with an IC50 value of 36.4 mM. Compound thaixylogranins C and D exhibited weak cytotoxicity against the melanoma A375 cell with IC50 values of 47.1 and 41.9 mM, respectively; and in gastric cancer AGS cell line, thaixylogranins C and D showed same cytotoxic effect with IC50 values of 41.7 and 35.0 mM, respectively [29]. Xylogranin B was isolated from X. granatum leaves, could inhibit T cell factor (TCF)/β-catenin transcriptional activity at IC50 48.9 nM, and exhibited strong cytotoxicity against colon cancer cell lines. Xylogranin B drastically attenuated β-catenin protein; these results indicated that Wnt signal inhibitory effects [26]. All of these compounds were isolated from different parts of X. granatum. Xylocarpus granatum leaf extracts (ethyl acetate and its 1–7 fractions) had anticancer activity against HeLa (human cervical adenocarcinoma), T47D (breast cancer), and HT-29 cell (human colorectal adenocarcinoma cell line), with fraction 5 having the most powerful activity of 23.12 ppm IC50 value. However, it was concluded that, to understand the mechanism, further studies are essential [62]. Mosquitoes are the key vectors for ruining parasites and pathogens including malaria, dengue, filariasis, yellow fever, chikungunya, encephalitis, and so on [63]. Malaria is a global health problem, and about 300–500 million people are infected, while almost 1 million people die annually. Natural products may be a choice for the treatment of malaria [64]. The isolated compounds from X. granatum plant had potential antimalarial activity [65]. The compounds gedunin and xyloccensin I, isolated from X. granatum, had antimalarial activity at the concentration of 50 µg m/L only and showed a minimum inhibitory concentration (MIC) of 10 µg m/L. This antimalarial activity was exhibited by killing the parasites in in vitro model of Plasmodium falciparum [12]. A virus is a particle that replicates within the living cells of an organism. Viruses can infect all types of life forms, including animals, plants, and microorganisms (like bacteria and archaea). The medicinal plant should be a good source of antiviral agents. X. granatum plant extract contains a variety of bioactive compounds that act against virus including sundarbanxylogranins B and granatumin L [27, 39]. Hence, sundarbanxylogranins B showed moderate effect against human immunodeficiency virus (HIV) with the concentration of 20 µM; it showed a moderate inhibitory rate of 58.14 ± 3.67% and the values of IC50 and CC50 for sundarbanxylogranin B were 23.14 ± 1.29 and 78.45 ± 1.69 µM, respectively [27]. Besides, in vitro antiviral activities of granatumin L and its derivatives against HIV-1 and influenza A virus (IAV) were evaluated. Granatumin L and their derivatives exhibit activities against the HIV-1 with an IC50 value of 15.98 ± 6.87 µM and a CC50 value greater than 100.0 µM, whereas its derivative showed significant inhibitory activity against IAV with an IC50 value of 14.02 ± 3.54 µM and CC50 value greater than 100.0 µM. Thus, it was inferred by the authors that alkyl groups at the C-3 position helped in exhibiting the antiviral activity against HIV [39]. Some plants are used to treat several diseases and disorders. Antifeedant agents are natural substance, which stops or inhibits feeding by a pest, especially an insect [66]. Natural compounds should be the trusted source to control pests. X. granatum plant contains a number of isolated compounds, like secondary metabolites, and has the defense capability [67]. Several phytoconstituents and xylogranatins F, G, and R are isolated from seeds of the Chinese mangrove, X. granatum plant. These compounds exhibit good antifeedant activity against third instar larvae of Mythimna separata (Walker) at 1 mg/mL concentration [38]. Among of them, xylogranatin G was the most potent compound at 0.31 and 0.30 mg/mL concentration and 24 and 48 h; it showed 50% antifeedant activity median antifeedant concentration (AFC50), respectively [38]. Furthermore, both xyloccensins P and Q, isolated from X. granatum plant, showed potent antifeedant activity at 500 ppm concentration against third instar larvae of M. separata, whereas other compounds xyloccensins O and R–V showed weak activity [10]. Diabetes is a condition, in which the body's blood glucose is higher than the normal level [68]. Blood glucose is controlled by a vital hormone called insulin and depending on insulin the diabetes is divided into two major categories: types 1 and 2 diabetes [68, 69]. The isolated compounds from the X. granatum have antidiabetic activity. Xylogranin B, xyloccensin I, and xyloccensin S [70] exhibited antidiabetic activity by inhibiting α-amylase, α-glucosidase, and protein tyrosine phosphatase 1B (PTP1B), respectively [4, 52]. Xylogranin B acts with the concentration of the IC50 48.9 nM or inhibited TCF/β-catenin transcriptional activity with IC50 values of 270 and 330 nM [4, 26]. Besides this other compound, xyloccensin S can control blood glucose levels with the IC50 value of 8.72 µg/mL in PTP1B in vitro study [52]. In addition, xyloccensin I exhibited a hypoglycemic effect on α-amylase and α-glucosidase inhibition study at the concentrations of 0.25 and 0.16 mg/mL, respectively [4]. Hence, compounds present in the X. granatum have inhibitory effect on the enzymes (α-amylase and α-glucosidase) that increase the level of blood glucose in body. Inhibition of α-amylase and α-glucosidase plant extracts lead to reduction in the level of blood sugar and helps in management of diabetic condition [71–73]. Anxiety and depression are generally a normal reaction to stress and there will always be situations that create stress and discomfort in humans for several reasons [74]. These disorders are currently considered the most common psychiatric illnesses affecting humans [75]. It is one of the most common psychiatric disorders. Information collected from the WHO states that depression is expected to become the second leading cause of disease-related disability by the year 2020, following heart disease [76]. Current pharmacological interventions suggest that the drugs used to manage these disorders, often have a number of side effects, including drug interactions, delayed response, and even nonresponse to the treatment [77]. Natural compounds have potential antidepressant- and anxiolytic-like activities. Recent studies exhibited that cipadesin A extracted from the fruits of the X. granatum plant assert potential antidepressant- and anxiolytic-like activities [2]. In the forced swimming test (FST), cipadesin A treatment significantly decreased the floating time in in vitro testing model. Cipadesin A treatment (15 and 50 mg/kg doses) drastically reduced the floating time [2]. Moreover, in the tail suspension test, administering 15 and 50 mg/kg doses cipadesin A significantly decreased the immobility time. Furthermore, at 5, 15, and 50 mg/kg doses significantly increased the time spent in the central zone of mice. Additionally, cipadesin A at 15 and 50 mg/kg doses significantly decreased serum corticosterone and adrenocorticotropic hormone levels [2]. The study found that after seven days, cipadesin A administered orally exhibited significant antidepressant-like effect in the tail suspension and forced swimming tests in mice [2]. Filariasis is a parasitic disease caused by an infection with roundworms of the Filarioidea type [78]. These are spread by blood-feeding insects such as black flies and mosquitoes [79]. They belong to the group of diseases called helminthiases. Plants may be an effective source of antifilarial agents. Research findings proposed that photogedunin isolated from the fruits of the X. granatum plant administered by a subcutaneous route at IC50 of 0.239 and 0.213 µg/mL and CC50 of 212.5 and 262.3 µg/mL, respectively, at 5 × 100 mg/kg revealed excellent antifilarial efficacy, resulting in the death of 80% and 70% transplanted adult Brugia malayi in the peritoneal cavity of jirds, respectively [56]. Fungus infection is a major global health problem, and these life-threatening causative agents create approximately 1.5 billion deaths annually [80]. To prevent this infection, we found out some phytochemicals from natural plants. Lactone isolated from leaves of X. granatum plant showed 67.4% inhibition rate, and a strong fungicidal activity was proved against wheat powdery mildew with the 20 mg/mL concentration [22]. The petroleum ether and ethyl acetate extracts of X. granatum showed the presence of tricontanol, kaempferol, and sitosterol, which can easily penetrate the cellular barrier of powdery mildew fungus and creates pore, ultimately leading to the leakage of electrolyte causing cell death. The inhibitory activity was shown against PTP1B by xylogranatopyridines A and B isolated from the twigs and leaves of X. granatum plant. The inhibitory concentration of the chemical was an IC50 value of 22.9 µM [52]. At the concentration of 10.0 µM, krishnagranatins G, H, and I drastically inhibited the activation of nuclear factor- (NF-) κB, induced by lipopolysaccharides (LPS) at the concentration of 100 ng/mL [28]. However, these compounds implied that the previously mentione NF-κB inhibitory activity was not related to cell death. In conclusion, krishnagranatins G, H, and I displayed a significant inhibitory effect against the activation of NF-κB signaling pathways [28]. Furthermore, xyloccensin S followed inhibitory activity against PTP1B at the amount of IC50 value of 8.72 µg/mL [36]. The antioxidant constituents from ethanol bark extract of a medicinally important mangrove plant X. granatum [4]. Limonoid derivative xyloccensin I showed antioxidant activity in 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), superoxide, and hydrogen peroxide scavenging studies at IC50 values of 0.041, 0.039, 0.096 and 0.235 mg/mL, respectively [4]. In a recent study by Das and coworkers [81], demonstrated that bark ethanolic extract reflected highest ABTS scavenging activity with IC50 value of 41.50 g/mL, whereas butylated hydroxyl toluene (standard antioxidant) demonstrated antioxidant activity of 76.34 g/mL. In vivo antioxidant analysis showed that enzymatic antioxidants such as superoxide dismutase, catalase, and glutathione reductase in liver and brain tissue of diabetic mice increased when supplemented with 200 mg/kg of X. granatum. Hence, it was concluded that increase in the antioxidant defense system helped the diabetic mice in overcoming the oxidative stress. Stem bark extracts (ethanol extract, pet-ether fraction, CCl4 fraction, and CHCl3 fraction) from Xylocarpus granatum depicted antimicrobial activity against Staphylococcus epidermis (20–25 mm), Staphylococcus aureus (20–25 mm), Shigella boydii (20–25 mm), Proteus spp. (20–25 mm), Escherichia coli (20–25 mm), and Streptococcus pyogenes (20–25 mm) in terms of disc inhibition zone (diameter in mm) at concentration of 400 g/disc. However, the exact mechanism is not known [82]. Xylocarpus granatum bark extracts (methanol extracts) when supplemented in mice induced with diarrhea (induced using castor oil and magnesium sulphate) revealed that, at oral dosage of 250 and 500 mg/kg, it exhibited antidiarrheal properties by reducing the wet faeces discharge. Castor oil is known to cause diarrhea due to its hypersecretory activity caused by active component ricinoleic acid, and the antidiarrheal activity of the Xylocarpus granatum bark extracts could be due to its antisecretory effect [83]. These studies, highlighted in the present review on the different pharmacological activities exhibited by parts of Xylocarpus granatum, its extracts, and bioactive compounds, indicate the health promoting effects of Xylocarpus granatum, which thus justifies their application as indigenous medicine in different traditional medicinal system used across the globe. It also paves way for further research to translate these natural plant-based bioactive compounds as advanced pharmaceutical drugs for treating various disorders, thus allowing researchers to explore the best of both scientific as well as traditional knowledge systems. Limited research is available on the toxicity of X. granatum and its extracts. However, a study depicted that oral dosage of ethanolic bark extract of X. granatum at 1000 mg/kg body weight per day when given to healthy Balb/c mice showed no signs of toxic effects or death up to four days [81]. Another study indicated that ethyl acetate extract of X. granatum leaves had no toxicity when tested using brine shrimp lethality test (BSLT) even above 1500 ppm concentration [62]. In conclusion, though few studies indicate no toxicity, detailed experiments are necessary to further establish the toxicity or upper tolerable limits. X. granatum may be one of the hopeful medicinal herbs for the treatment of various diseases in humans. Traditionally, this plant was widely used in treating several diseases, because of its chemical constituents. Several studies have shown that X. granatum has anticancer, antiviral, antidepressant, antifeedant, and antimalarial activities ascribed to its chemical constituents such as limonoids, phragmalin, limonoid-based alkaloids, mexicanolides, protolimonoids, flavonol-like compounds, and alkaloids, among others. These chemical compounds are essential to treat many diseases and should be established as standard drugs for several known physiological disorders and diseases in medicinal chemistry and pharmacology. Still there is a lack of clinical trials on utilization of X. granatum and its bioactive compounds or extracts, and fewer studies are conducted on exploiting the development of plant-based drugs using X. granatum. Thus, more research is necessary to understand its chemical compounds and utilization as novel drugs in human studies and investigate the mechanism of action in treating various ailments. Also, the toxicological aspects of this medicinal mangrove plant need to be investigated thoroughly before developing any novel drug as limited studies are available.

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Muhammad Torequl Islam, Email: dmt.islam@bsmrstu.edu.bd. Miquel Martorell, Email: mmartorell@udec.cl. Javad Sharifi-Rad, Email: javad.sharifirad@gmail.com.

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Species of mangrove in the mahogany family Xylocarpus granatum Conservation status Least Concern (IUCN 3.1)[1] Scientific classification Kingdom: Plantae Clade: Tracheophytes Clade: Angiosperms Clade: Eudicots Clade: Rosids Order: Sapindales Family: Meliaceae Genus: Xylocarpus Species: X. granatum Binomial name Xylocarpus granatumK.D.Koenig Xylocarpus granatum, commonly known as the cannonball mangrove, cedar mangrove,[2] or puzzlenut tree,[3] is a species of mangrove in the mahogany family Meliaceae. It is found in Africa, Asia, Australasia and the Pacific Islands.[4][5][6] It is a common species of mangrove, and the International Union for Conservation of Nature has assessed its conservation status as being of "least concern". Xylocarpus granatum is a small to medium-sized evergreen tree, growing to a maximum height of 12 m (39 ft). The trunk has buttresses and above-ground roots which extend for long distances to either side. The bark is brown and smooth, and comes away in flakes. The leaves are pinnate and arranged spirally on the twigs; they have two to four pairs of leaflets and are pale green when young and darken with age. The inflorescence grows in a short panicle in the axil of a leaf or at the end of the shoot. The individual flowers are 8 mm (0.3 in) wide, with parts in fours, and are white or pinkish-yellow. They are followed by large, spherical, woody capsules, 9 to 12 cm (4 to 5 in) in diameter, which split open to reveal up to a dozen seeds.[2][7] The common name "puzzlenut tree" derives from the irregular shape of the seeds: a puzzle can be made of shuffling the seeds and attempting to reassemble them into the original spherical arrangement.[8] This species is native to the tropical and sub-tropical Western Indo-Pacific region. Its range extends from Kenya, Tanzania and Mozambique (in which it is one of ten mangrove species[9]) to India, Malaysia, Thailand, Indonesia, the Philippines, northern Australia and Papua New Guinea; it grows in the higher intertidal zone and is found in estuaries and lining the banks of creeks.[1] The wood is hard and durable and can be used for boat-building, construction and making furniture, however the trees are twisted and often hollow so large pieces of timber may not be available; the wood is also used for tool handles and other small items, and can be used as firewood but burns rather quickly. The bark is rich in tannins and has been used for strengthening rope and dying cloth. The bark, fruits and seeds have also been used in traditional medicine.[10] Mangroves in general are under threat from coastal development and from harvesting, and another threat is global warming and the consequent rise in sea levels. Xylocarpus granatum is a common species of mangrove with a very wide range, and it is probably not declining at a sufficient fast rate to be included in any threatened category. For these reasons, the International Union for Conservation of Nature has listed it as being of "least concern".[1] Wikimedia Commons has media related to Xylocarpus granatum. Wikispecies has information related to Xylocarpus granatum.

^ a b c Ellison, J.; Koedam, N. E.; Wang, Y.; Primavera, J.; Jin Eong, O.; Wan-Hong Yong, J.; Ngoc Nam, V. (2010). "Xylocarpus granatum". IUCN Red List of Threatened Species. 2010: e.T178845A7624881. doi:10.2305/IUCN.UK.2010-2.RLTS.T178845A7624881.en. Retrieved 12 November 2021. ^ a b "Cannonball mangrove". Flowers of India. Retrieved 12 July 2019. ^ Ross, Malcolm. Concluding notes, 427–436. In Ross, Malcolm; Pawley, Andrew; Osmond, Meredith (eds). The lexicon of Proto Oceanic: The culture and environment of ancestral Oceanic society. Volume 3: Plants. 2008. Pacific Linguistics 599. ^ J. S. Bunt, W. T. Williams & N. C. Duke (March 1982). "Mangrove distributions in north-east Australia". Journal of Biogeography. 9 (2): 111–120. doi:10.2307/2844696. JSTOR 2844696. ^ "Xylocarpus granatum". Germplasm Resources Information Network. Agricultural Research Service, United States Department of Agriculture. Retrieved 27 March 2011. ^ "Xylocarpus granatum". FloraBase. Western Australian Government Department of Biodiversity, Conservation and Attractions. ^ "Xylocarpus granatum J. Koenig, 1784". Lee Kong Chian Natural History Museum. Retrieved 12 July 2019. ^ Wise, Rosemary (1998). A Fragile Eden: Portraits of the Endemic Plants of the Granitic Seychelles. Princeton, NJ, U.S.A.: Princeton University Press. ISBN 0691048177. ^ The World's Mangroves, 1980–2005: A Thematic Study in the Framework of the Global Forest Resources Assessment 2005. Food and Agriculture Organization of the United Nations. 2007. pp. 15–17. ISBN 978-92-5-105856-5. ^ Fern, Ken (13 June 2019). "Xylocarpus granatum". Useful Tropical Plants Database. Retrieved 12 July 2019.

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