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The Potential of Jamblang Bark Plants (*Syzygium cumini* (L) Skeels) as Anticancer: A Literature Review

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A B S T R A C T

Jamblang plant (*Syzygium cumini*) is one of the local fruits of Indonesia. All parts of this plant can be used for treatment, one of which is jamblang bark as an anticancer agent. Genus *Syzygium* family *myrtaceae* is one of the largest genera in Indonesia. The purpose of this literature review is to provide an overview of the active compounds contained in jamblang plants that work as anti-cancer. Based on the results of the research that has been done, the jamun plant contains the compounds β-sitosterol, friedelin, betulinic acid, flavonoids, terpenes, alkaloids, phenolics, ellagic acid, glucoside, anthocyanins, kaempferol, quercetin, isoquercetin, myricetin, tannins, carbohydrates, albumin, and so on which can be used as antiviral, cardioprotective, anti-inflammatory, anticancer, antidiabetic, carminative, antihypertensive, anti-atherosclerotic, antifungal, antioxidant and hepatoprotector. It can be concluded that the active compound that works as an anticancer is a chemical compound of flavonoids located in jamblang bark (*Syzygium cumini* (L) Skeels).

1. Introduction

Cancer is a disease that causes a high death rate in Indonesia and around the world. Cancer is the uncontrolled growth and development of cells that occur in the body. The incidence of various types of cancer has increased in developing countries. Breast cancer and cervical cancer are the two most common types of cancer in women in Indonesia. The development of cancer is often found at an advanced stage (metastatic) and involves complex molecular mechanisms that cause problems in its therapy. Indonesia, as a country in the tropics, has enormous biodiversity and is rich in medicinal raw materials, so phytopharmaca is an attractive treatment option and can be continuously developed. Indonesia has approximately 30,000 plant species and 7,000 species, including medicinal plants that have been researched scientifically. The abundance of species diversity and sources of native Indonesian fruit germplasm have not been used optimally until now. This can be seen, among others, by the large number of imported fruits circulating in various cities in Indonesia. Therefore, the wealth of abundant biological resources in Indonesia needs to be utilized as much as possible.[1-4]

One of the plants that is often used for treatment is jamblang. Jamblang is the fruit and tree name for a plant with the scientific name *Syzygium cumini.* This fruit-producing tree is still classified in the guava tribe (*Myrtaceae*). Jamblang has enormous benefits not only as a food ingredient and, in some countries, jamblang is used as herbal medicine. The methanol extract of *Syzygium cumini* (L.) Skeel leaves contain secondary metabolites in the form of flavonoids, alkaloids, tannins, and terpenoids, which are used in medicine,

among others, for anti-inflammatories, pain relievers, and antifungals. Jambolan is a large, evergreen, densely leafy tree with thick, grayish-brown bark exfoliated in woody scales. The wood is whitish, densely grained, and durable, giving chocolate coloring and some kind of Kino gum. The leaves are leathery, oval-ovate to elliptical or oblong-elliptical 6 to 12 centimeters long (variable in shape, smooth and shiny with many nerves fused at the edges), broad and less sharp at the tips. Panicles are borne mostly from the lower branches, often axillary or terminal, and 4 to 6 centimeters in length. Flowers are scented, greenish-white, in clusters of just a few or 10 to 40, and are round or oval in shape. The fruit is a berry and often oblong, 1.5 to 3.5 centimeters long, dark purple or almost black, delicious, fleshy, and edible; it contains one large seed.[5-8]

Jamblang fruit contains high levels of flavonoids, alkaloids, resins, tannins, and essential oils that have health benefits. Flavonoids are secondary metabolites that can be used as antibacterial, antimicrobial, antiviral, antifungal, anticancer, antihypertensive, cytotoxic, and hypoallergenic. Jamblang bark is known to contain flavonoids, tannins, bellic acid, ellagic acid, gallic acid, friedelin, epi-friedelanol, β-sitosterol, eugenin, epi friedelanol fatty acid esters, β-sitosterol, quercetin kaempferol, myricetin, and genin, flavonoids and tannins have also been reported from Jamblang stems. Jamblang bark, dry seeds, and a decoction of the root bark are used to treat diarrhea, dysentery, and dyspepsia and can also act as an enema. Powdered bark mixed with yogurt is given to treat menorrhagia, and when mixed with jamblang fruit juice, it cures coughs and colds. In addition, one glass of jamblang fruit juice with half a teaspoon of bark powder given daily can overcome the problem of urinary tract disorders and urinary tract infections. In India, the powdered jamun seeds are used as an antidote to strychnine poisoning. A decoction of jamun bark is used to treat asthma and bronchitis. oral ulceration, spongy gums, and stomatitis. The ashes of jamun bark can be mixed with water and used as a general anti-inflammatory agent or mixed with oil and used to treat burns. A decoction of jamun seeds relieves fatigue and tension.[9-11]

2. Methods

The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the potential of jamblang bark (*Syzygium cumini* (L) Skeels) as an anticancer agent. The search was performed using the terms: (1) "jamblang" OR "java plum" OR "*Syzygium cumini"* OR" *Syzygium cumini* in medicinal uses" AND (2) "*Syzygium cumini"* OR "anticancer." The literature is limited to preclinical studies and published in English. The literature selection criteria are articles published in the form of original articles, an experimental study about the potential of jamblang in medicinal uses as an anticancer, the control group only received liquid without therapeutic effect or no treatment, studies were conducted in a timeframe from 2013-2023, and the main outcome was potential of jamblang bark (*Syzygium cumini* (L) Skeels) as an anticancer agent. Meanwhile, the exclusion criteria were animal models that were not related to medicinal uses, the absence of a control group, and duplication of publications. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations.

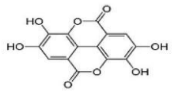
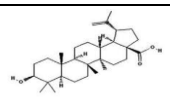
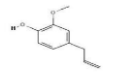
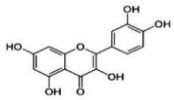
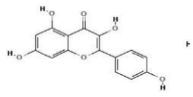
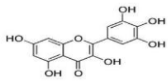
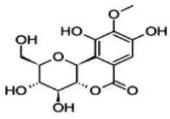
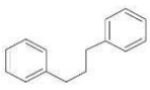
3. Results and Discussion

Studies literature on the potential of the Jamblang bark plant (*Syzygium cumin* (L) Skeels) as anticancer based on the content of active compounds from several journals, of course, produces very different information about the Jamblang plant. alkaloids, tannins, flavonoids, cardiac glycosides, ellagic acid, malic acid, citric acid, gallic acid, phenolic acids, terpenoids, saponins, phenols, polyphenols, quercetin, diphenic acid, isoquercetin, myricetin, glycosides, cyanidin compounds or chemicals, vitamin C, vitamin E, kaempferol.

Table 1. The potential of the jamblang bark plant (*Syzygium cumin*i (L) Skeels).

No	Article title	Compound content	Pharmacological activity	Reference
1.	Phytochemical composition and pleiotropic pharmacological properties of jamun, *Syzygium cumini* Skeels	Alkaloid, glycoside anthroquinone, flavonoid, tannin, saponin, phenol, cardiac glycosides, terpenoid, phytosterol, steroid, and amino.	Anticancer, antioxidant, anti-inflammatory, hypoallergenic, antibacterial, hepatoprotective, gastroprotective, cardioprotective, antidiabetic, antihyperlipidemic	Jagetia, et al (2017).
2.	Recent advances in pharmacological potential of *Syzygium cumini*: A review	Ellagic acid, glucoside, anthocyanins, kaempferol, isoquercetin, myricetin	Anti-allergic, antibacterial, anticancer, antifungal, anti-hyperlipidemic, antioxidant, hepatoprotective, hypothermic, diuretic and antihypertensive	Katiyar et al., (2016)
3.	Antioxidant activity, phenolic flavonoid content and high-performance liquid chromatography profiling of three different variants of *Syzygium cumini* seeds: A comparative study	Flavonoid, alkaloid, tannin, terpenoid	Antibacterial, antiviral, anticancer, hypoallergenic	Maryati et al.,
4.	*Syzygium cumini* inhibits growth and induces apoptosis in cervical cancer cell lines: a primary study.	Resveratrol, emodin, retinoic acid, lycopene, EGCG, and indole-3-carbinol	Anticancer, antiproliferative, and apoptotic	Barh et al (2008)
5.	Phytochemical composition and pleiotropic pharmacological properties of jamun, *Syzygium cumini* Skeels	Betulinic acid, friede lin, epi-friedelanol, ÿ-sitosterol, eugenin and epi friedelanol fatty acid esters. 36 ÿ-sitosterol, quercetin kaempferol, myricetin, gallic acid and ellagic acid, genins, flavonoids and tannins	Anticancer	Jagetia et al (2017)
6.	Acylated flavonol glycosides from Eugenia jambolana leaves	Flavonoid	Anticancer, Antidiabetic	Mahmoud et al (2001)
7.	Effect of drying on total flavonoid content and antioxidant activity of 70% ethanol extract of jamblang leaves (*Syzygium cumini*)	Flavonoid, tanin dan steroid	Anticancer, Antioxidant	Desi et al. (2020)
8.	Isolation and identification of flavonoid compounds from jamblang leaves (*Syzygium cumini*)	Flavonoid	Anti-microbial medicine for wound infections, anti-fungal, anti-viral, anti-cancer, and anti-tumor	Maryati et al (2011)
9.	Flavonoids as anticancer agents	Flavonoid	Anti-cancer	Dalia M et al (2020)
10.	Jamblang plant pharmacological activity (*Syzygium cumini* L): Literature review article	Ellagic acid	Cervical anticancer	Himyatul et al (2021)

Table 2. Secondary metabolites in *Syzygium cumini* (L.) Skeels bark.

Compound	Structure	Benefits	Mechanism	Reference
Ellagic acid	 Ellagic acid	Anticancer	Ellagic acid stimulates apoptosis via inhibition of the prosurvival transcription factor NF-κB	
Betulinic acid	 Betulinic acid	Anticancer	Triggers the mitochondrial pathway of apoptosis in cancer cells	Fulda (2008).
Eugenol	 Eugenol	Anticancer	Eugenol inhibits the growth and development of tumors, improves reactive oxygen species (ROS), induces apoptosis, and has a genotoxic effect on many cancer cells	Fenoria (2022)
Quercetin	 Quercetin	Anticancer	At low concentrations, it induces mitochondria-mediated apoptosis in HeLa cells by activating the p53 gene and reducing the cytotoxic side effects of doxorubicin, a common anti-cancer drug, in non-tumor cells.	Vidya (2021)
Kaempferol	 Kaempferol	Anticancer	Kaempferol reduces ROS metabolism and anti-inflammatory membrane cleavage and disrupts their molecular mechanisms as a mechanistic matter to overcome cancer-associated expression (KMF: Kaempferol; Nrf2: Erythroid-associated factor 2 nuclear factor 2; Keap1: Kelch-like ECH-associated protein 1; RO: Reactive oxygen species).	Imran (2019)
Myricetin	 Myricetin	Anticancer	To reduce cell proliferation, angiogenesis, metastasis, and induce apoptosis.	Afroze (2020)
Bergenin	 Bergenin	Anticancer	Bergenin also increases Bax expression and decreases Bcl-2 expression. The effect of bergenin on the distribution of cell cycle phases of HeLa cells was also investigated, and it was found that bergenin can induce G0/G1 cell cycle arrest. In addition, bergenin can also inhibit HeLa cancer cell migration and STAT3 phosphorylation.	Shi et al (2009)
Flavonoid		Anticancer	Flavonoids are able to modulate the activity of reactive oxygen species (ROS) enzymes, play a role in modulating the cell cycle, induce apoptosis and autophagy, and suppress cancer cell proliferation and invasion. Flavonoids have a dual action in regulating ROS homeostasis. They act as antioxidants under normal conditions and are strong pro-oxidants in cancer cells that trigger apoptotic pathways and decrease proinflammatory signaling pathways.	Dalia et al (2020)

Cancer is a non-communicable killer disease, which ranks second after cardiovascular disease in terms of causes of death in humans. Cancer is treated with surgery, radiotherapy, chemotherapy, or a combination of each (or all). In advanced stages, chemotherapy is the only drug to treat cancer and, therefore, has emerged as one of the most important cancer treatment modalities. Free radicals and reactive oxygen species (ROS) cause diseases such as cancer, diabetes, heart disease, and inflammation. The amount of free radicals and their production increases. Excess ROS in the body can cause this imbalance in the immune system. Therefore, there is a need for more antioxidants outside the body. Flavonoids have been shown to have various anticancer effects: they are able to modulate the activity of reactive oxygen species (ROS) enzymes, play a role in modulating the cell cycle, induce apoptosis and autophagy, and suppress cancer cell proliferation and invasion. Flavonoids have a dual action in regulating ROS homeostasis. They act as antioxidants under normal conditions and are strong pro-oxidants in cancer cells that trigger apoptotic pathways and decrease proinflammatory signaling pathways.[12-16]

Syzygium cumini fruit peel extract, together with the berry outer layer, inhibited growth and induced apoptosis in HeLa and SiHa cervical cancer cell lines in a dose- and time-dependent manner. While the crude extract respectively showed 33.7% and 24.4% growth inhibition in HeLa and SiHa cells at the highest concentration (100%) in the MTT assay, the methanol extract (80% v/v) showed an apoptotic index of 20.5% and 16.1%, respectively, for these cell lines as determined by Hoechst 33342 staining. It has also been found that the crude extract is more effective in inhibition of growth and apoptosis than the methanol extract at the most effective concentration (80%). Annexin-V binding and TUNEL assays also confirmed the apoptotic effect of the extract. Most of the cancer treatment drugs (47%) have been derived from natural resources or their semi-synthetic derivatives. Various parts of jamblang have been investigated for their cytotoxic action in vitro using a variety of different cell lines. The cytotoxic effect of the crude extract of jamun rind was studied on HeLa cells (positive HPV-18) and SiHa cells (positive HPV-16) by MTT test, and the crude extract was found to induce a cytotoxic effect on both cell types. The effect was more pronounced in HeLa cells than in SiHa cells. Likewise, the effect of 50% methanol extract showed greater apoptosis in HeLa cells than SiHa cells.[17-21]

4. Conclusion

The active compound contained in jamblang plants works as an anticancer jamblang *(Syzygium cumin)* family-owned *Myrtaceae.* It has been used in traditional medicine for the treatment of various ailments, including diabetes. The phytochemical evaluation showed that jamun contains alkaloids, anthraquinone glycosides, flavonoids, tannins, saponins, phenols, cardiac glycosides, terpenoids, phytosterols, steroids, and amino acids. The preclinical evaluation showed that jamun has several medicinal activities, including antioxidant, antibacterial, antifungal, hypoallergenic, anti-inflammatory, antidiabetic, antihyperlipidemic, gastroprotective, cardioprotective, hepatoprotective, anticancer, and radioprotective.

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