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The Efficacy of Secondary Metabolit Compounds in Keledang Plant (Artocarpus lanceifolius) as Anticytoxic: Literature Review

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Abstract:*Cancer is a disease characterized by the presence of eccentric cells that can grow uncontrollably and have the competency to assail, move cells and body tissues. Indonesia as the second most sizably voluminous megabiodervisty in the world with abundant flora diversity with sundry benefits. The keledang plant is empirically kenned to be efficacious as an anticytotoxic. The purport of the literature review is to review the content of secondary metabolites and the bioactivity of the keledang plant in inhibiting cancer cell magnification. Methods utilized in article search reviewing national and international journals that have been scopus indexed, accredited by SINTA utilizing the Pubmed, Google Philomath and Researchgate platforms.Systematic Literature Review (SLR) design is a systematic literature review by identifying, assessing and interpreting all findings on one research topic.The results of the study obtained that the keledang plant yielded sundry isoprenylated flavonoid compounds containing isoprenyl side chain at C-3, 2,4-dioxygenated or 2,4,5-trioxygenated pattern in ring B of 2,3 flavone framework, exhibiting consequential cytotoxic effect on murine leukemia P-388 cells. Artobiloxanthone binds to the active site of the enzyme transglutaminase 2 (TG2), this enzyme as an anticancer target.*

Keywords:*Anticytotoxic, Artocarpus lanceifolius, Cancer, Secondary metabolites, Keledang plant.*

I. Introduction

Indonesia is an archipelagic country with abundant biodiversity. Sundry medicinal plants grow throughout the island of Indonesia. From a total of about 40,000 species of medicinal plants that have been kenned to the world, 30,000 of them are thought to subsist in Indonesia. This number represents 90% of medicinal plants found in Asia. One of the places where this biodiversity is located is in forest areas. Indonesia's forest area is 63.7% of Indonesia's land area, or about 125.9 million hectares [1]. This makes Indonesia affluent in sundry kinds of plants, including medicinal plants with sundry properties. Medicinal plants are a mundane alternative for cancer treatment in many countries, and more than 3000 plants ecumenical have been reported to have anticancer properties. Several incipient cytotoxic secondary metabolites are isolated from plants every year and are a source of incipient possibilities to be explored in the fight against cancer [2]. The natural product utilization has expanded due to their expected chemotherapy activities. Mainly, medicinal plants are broadly applied in the development of the drugs as anti-inflammatory and anticancer agents, and additionally sources of incipient valuable materials. Despite the techniques of cancer aversion and therapeutic drugs available, in additament to sundry methods for early diagnosis, herbal medicines can be recommended along with synthetic drugs. Plant medicines are utilized as one of the fundamental therapeutic agents against cancer [3].

Cancer is a chronic disease that minimizes the quality of life of the sufferer. High stressors and low coping due to disease prognosis, therapy management, and minimal convivial support, have an impact on poor psychological conditions[4].snRNA mutations have been reported in multiple types of cancer including medulloblastoma, chronic lymphocytic leukemia, B cell non-Hodgkin lymphomas, as well as hepatocellular and pancreatic carcinoma [5].

Artocarpus lanceifolius is one of the medicinal plants that has long been kenned for its anticytotoxic properties which are empirically often utilized by the public for sundry kinds of treatment. Artocarpus lanceifolius, Roxb (Moraceae), comprises 60 genera and 1400 species. The three main genera are Artocarpus, Ficus, and Morus [6]. Artocarpus lanceifolius locally kenned as "Keledang" is an evergreen tree of medium size to sizably voluminous enough to be found in evergreen lowland forests up to 1100 m high. Keledang is an endemic recherche plant with very constrained distribution, especially on the islands of Sumatra, Bangka and Kalimantan [7].

Predicated on the research of Madiyawati, et al, phytochemical tests have been carried out on the fruit, seeds and skin of keledang (Artocarpus lanceifolius Roxb) which showed that the three components contained alkaloids, flavonoids, steroids and terpenoids. One of the active compounds that can be utilized as antioxidants is flavonoid compounds, so that keledang has the potential to be a natural antioxidant. The list of plants exhibiting anticancer activity was then categorized predicated on the IC50 value (cytotoxicity designator). The CBG plant family has anticancer properties between 93, 100, 36, and 62 species having IC50 values below Class I (vigorous), Class II (moderate), Class III (dormant), and Class IV (inadequate IC50 data) each. Species that have vigorous anticancer activity include Artocarpus elasticus [8]. The capability of microorganisms and organic compounds to truncate metal ions and stabilize them into nanoparticles forms the substructure of green synthesis of these nanoparticles. The green synthesis of variants of nanoparticles utilizing a diverse array of plant extracts has been reported [9].

The results of research that has been carried out by the keledang plant are kenned to engender sundry isoprenylated flavonoids containing an isoprenyl side chain at C-3, as well as a 2,4-dioxygenated or 2,4, 5-trioxygenated pattern in ring B of the 2,3-flavone framework. Anterior phytochemical studies revealed a number of novel prenylated flavones from the bark of the keledang plant, some of which exhibited consequential cytotoxic effects on murine P-388 leukemia cells. Recent investigations isolated a prenylated flavone, 12-hydroxyartonin E, which contains alcohol functionality in the prenyl moiety [10]. Re-study of different keledang tree bark samples amassed from the same location, led to the isolation of the compound, along with incipient prenylated flavones [11].

So that the inditement of this literature review aims to provide information and an overview of the content of secondary metabolites and bioactive compounds contained in the keledang plant, as well as to determine the potential of the keledang plant as an anti-cytotoxic. The results of this literature search can additionally be utilized as the substratum for further research on the utilization of the keledang plant for the treatment of other diseases [12].

II. Research Methods

The method used is a literature study utilizing a Systematic Literature Review (SLR) design, namely a systematic literature review by identifying, assessing and interpreting all findings on one research topic. By utilizing the databases of Google Philomath, Science Direct, Neliti, Pubmed, and Wiley [13]. The process of reviewing this article was carried out by probing in the cyber world with the keywords "Keledang plant activity; Phytochemicals of the keledang plant; Artocarpus lanceifolius; Anticytotoxic; Cytotoxic activity in Artocarpus lanceifolius". Sources of primary data obtained include national and international journals that have been indexed by Scopus. The journals are then screened. Inclusion criteria are journals that discuss the keledang plant as an anticytotoxic [14].

III. Results and Discussion

The phytochemical test results for the secondary metabolites obtained from each extract are listed in Table 1. Predicated on the results obtained, it is kenned that the n-hexane extract contains triterpenoid and steroid compounds, the ethyl acetate and chloroform extracts contain flavonoids and phenols, while the methanol extract contains flavonoids, alkaloids, and phenols [15].

Table 1. Phytochemical test results from each extract solvent [16-18].

Phytochemical Test	Reagent	Extract			
		n-hexane	Chloroform	Ethyl acetate	Methanol
Flavonoids	• Mg + amyl alcohol	-	+	++	++
	• NaoH 10%	-	+	++	++
	• Liebermann-Burchard	+	-	-	-
Triterpenoids	• Salkowski	+	-	-	-
Steroids	• Liebermann-Burchard	+			
	• Dragendroff's	-	-	+	+
Alkoloid	• Wagner		-	+	+
	• Meyer	-	-	+	+
Phenol	• $FeCl_3$ + Ethanol 70%	-	+	+	++

The extract was withal tested for toxicity utilizing the Lethal Concentration (LC_{50}) value. The Lethal Concentration (LC_{50}) value was obtained from the linear regression equation determined by the probit value and the concentration log. The results of the BSLT test for each extract are listed in Table 2. The highest LC_{50} value was found in the chloroform extract and the lowest was in the nhexane extract. But all extracts showed very high toxicity. Extracts with LC values less than 100 g/mL were considered highly toxic, LC values between 100 g/mL to 500 g/mL moderately toxic, LC values 500 g/mL up to 1000 g/mL scarcely toxic, and LC values above 1000 g /ml is considered non-toxic. Predicated on the results utilizing the BSLT method, it was found that secondary metabolites derived from the bark of Artocarpus lanceifolius Roxb were proven to significantly affect the breeding rate of Artemia salina L shrimp larvae after a circadian incubation period with very high toxicity. These results can be utilized as a screening method to cull compounds as anticancer agents from plants. This postulation is predicated on the fact that the higher the secondary metabolite toxicity level of a plant utilizing the BSLT method (the more minuscule the LC_{50} value) the more preponderant the potential of the plant to be utilized in anticancer treatment [19]. These results can be utilized as a screening method to cull compounds as anticancer agents from plants. This postulation is predicated on the fact that the higher the secondary metabolite toxicity level of a plant utilizing the BSLT method (the more minuscule the LC_{50} value) the more preponderant the potential of the plant to be utilized in anticancer treatment [20].

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Table 2. BSLT results from the bark extract of Artocarpus lanceifolius Roxb [22-23].

Extract	Concentration (µg/ml)	LC_{50} (µg/ml)
n-hexane	1	1.0853
	10	
	100	
Chloroform	1	0.1635
	10	
	100	
Ethyl Acetate	1	0.3615
	10	
	100	
Methanol	1	0.2609
	10	
	100	

Keledang plant engendered sundry isoprenylated flavonoid compounds containing an isoprenyl side chain at C-3, as well as a 2,4-dioxygenated or 2,4,5-trioxygenated pattern in ring B of the 2,3-flavone framework, exhibiting a paramount cytotoxic effect on murine leukemia P-cells. 388. Artobiloxanthone can bind to the active site of the enzyme transglutaminase 2 (TG2), this enzyme is considered an anticancer target [24].

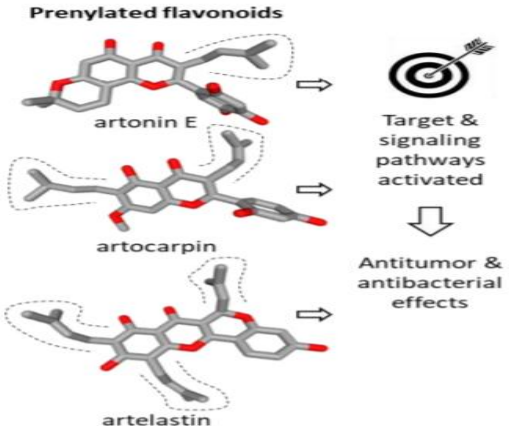

Figure 1. Active compound Anticancer agent from Artocarpus lanceifolius Roxb [25].

The cytotoxic activity test of P-388 murine leukemia cells showed that the 3-prenylflavone, pyranoihydrobenzoxanthone, cyclopentenochromone, and part of the dihydrobenzoxanthone and pyranoflavone frameworks had very active cytotoxic activity, while the furanodihydrobenzoxanthone, xantonolide, and part of the dihydrobenzoxanthone and pyranoflavone frameworks had very active cytotoxic activity. dormant cytotoxic. Cytotoxic activity is influenced by the presence of free prenyl C-3 or prenyl C-3 composing a hemiacetal ring that binds to the flavonoid framework and there is a di or tri-oxygenation system in ring B. Cytotoxic activity inclines to decrement and inclines to be dormant due to further modification of prenyl C-3, there is a prenyl that opens at C-3 and C-8 [26].

Reveal marked cytotoxic properties against different cancer cell lines in vitro. It was found to interfere with the microtubule network of MCF7 breast cancer cells and interfere with cell cycle development. Artelastin causes accumulation in the S phase due to a drug-induced delay in DNA replication [27]. It is a potent inhibitor of mitogen-induced proliferation of T and B lymphocytes and an inhibitor of the engenderment of cytokines, such as interferon-, interleukin IL-2,-4 and -10, in stimulated splenocytes. Artelastin exhibits marked antioxidant properties, inhibiting the engenderment of reactive oxygen species (ROS) and the expression of inducible nitric oxide synthase (iNOS) in lipopolysaccharide-stimulated macrophages [28].

IV.Conclusion

The keledang plant (Artocarpus lanceifolius Roxb) has a high flavonoid content which has active compounds in the form of artonin E, artocarpin, and artelastin where artelastin shows consequential antioxidant properties, inhibits the engenderment of reactive oxygen species (ROS) and the expression of induced nitric oxide synthase (iNOS) in macrophages stimulated by lipopolysaccharides capable of inhibiting cancer cells or as anticytotoxic.

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