

## Artikel Review

# Potency of Borneo Endemic and Typical Plants as Anti-Cancer Medicines

Alhawaris<sup>1</sup>

## Abstrak

Pulau Borneo (dikenal juga dengan nama Pulau Kalimantan), Indonesia memiliki hutan yang luas yang ditumbuhi berbagai jenis tanaman. Beberapa diantaranya telah dipercaya secara turun temurun dan secara empiris memiliki khasiat sebagai obat tradisional. Diperkirakan lebih dari 200 tanaman obat tumbuh di hutan Pulau Borneo. Beberapa diantaranya telah diteliti memiliki sejumlah metabolit sekunder yang berperan sebagai antikanker, seperti Bawang Dayak/Bawang Tiwai, Tahongai, Tanaman Sarang Semut, Batang Kuning/Akar Kuning, dan Pasak Bumi/Tongkat Ali. Sementara itu, beberapa di antaranya masih perlu diteliti lebih lanjut mengenai metabolit sekunder beberapa bagian tanaman tersebut dan khasiatnya sebagai tanaman obat, terutama sebagai anti kanker, seperti Sengkubak, Kayu Bajakah, dan Jahe Balikpapan (Jahe Balikpapan). Tinjauan literatur (*literature review*) digunakan dalam studi ini untuk memperoleh informasi tentang tanaman-tanaman tersebut sebagai obat anti kanker.

**Kata kunci:** Anti-Kanker, Metabolit Sekunder, Tanaman Obat, Tanaman Endemik Borneo

## Abstract

*The Island of Borneo (it's also known as Kalimantan), Indonesia has extensive forests overgrown with various plants. Some of them have been believed for generations and empirically have efficacy as traditional medicines. It is estimated that more than 200 medicinal plants are growing in the forests of Borneo Island. Some of them had been studied to have a number of secondary metabolites that act as anticancer, such as Bawang Dayak/Bawang Tiwai (Dayak/Tiwai Onion), Tahongai, Tanaman Sarang Semut (Ant Nest Plant), Batang Kuning (Yellow Stem)/Akar Kuning (Yellow Root), and Pasak Bumi/Tongkat Ali. Meanwhile, some of them still need to be investigated further regarding the secondary metabolites of their plant parts and their properties as herbal medicines, especially as anti-cancer, such as Sengkubak, Kayu Bajakah (Bajakah Wood), and Jahe Balikpapan (Balikpapan Ginger). This study aimed to obtain information about those plants as anti-cancer medicines by literature review method.*

**Keywords:** Anti-Cancer, Secondary Metabolites, Herbal Medicines, Borneo Endemic Plants

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**Affiliasi penulis :** 1 Medical Faculty of Mulawarman University, Samarinda, East Borneo, Indonesia

**Korespondensi :** Alhawaris alhawaris@fk.unmul.ac.id

Telp: 085151440123

## INTRODUCTION

There were about 19.3 million new cases of cancer and 10 million cases of death by cancer in the world reported in 2020. Five types of cancer with the newest cases, is female breast (11.7%), lung (11.4%), prostate (7.3%), nonmelanoma of skin (6.2%), and colon (6.0%). Meanwhile, five types of cancer with the most cases of death, respectively, are lung (18.0%), liver (8.3%), stomach (7.7%), female breast (6.9%), and colon (5.8%). There are at least 36 types of cancer that have been known to date [1].

Surgery, chemotherapy, and radiotherapy are still available and commonly used for treatments of cancer these days. There are some disadvantages to using those cancer treatments. Surgery will be less effective on sensitive tissue, such as brain tissue.

Radiotherapy needs a definite position of cancer. Chemotherapy can have negative effects on healthy cells. Many types of cancer can survive from those therapies. The use of the plant as medicine for cancer is now being considered and developed. It was reported that several plants have ingredients that have anti-cancer effects [2,3]. Some secondary metabolites isolated from medicinal plants have been developed as modern drugs [4].

In estimate, there are about 233 species of Borneo endemic medicinal plants recorded that grow in tropical forests of Borneo. The plants are commonly used by local ethnic groups to treat various diseases. It can be used directly (drank or bathed) or dried beforehand for use if needed [5,6]. Parts of plants used for treatment are roots (40%), leaves (26%), stems or skins (19%), and others (15%: fruit, seeds, flowers, fruit peels, sap, tubers, water stems) [7]. Some of them are believed by Borneo natives to cure some

serious diseases such as cancer. There are even some Bornean who has proven it empirically, but research on the effects of these plants as anti-cancer has not been done much. Some of the plants described in this article are endemic to Borneo, which is widely known as medicinal plants and have been researched for their content and properties.

## OBJECTIVE

This study aimed to obtain information about potency of Borneo endemic and typical plants as anti-cancer medicines by literature review method.

## DISCUSSION

### Secondary Metabolites as Anti-Cancer

Secondary metabolites which are contained in a plant are described as organic compounds which are not involved in the normal growth, reproduction, or development of a plant. The absence of secondary metabolites does not cause sudden death of plants, but rather in a long-term impairment of the plant's survivability, aesthetics, or possibly in no significant change at all. Plant secondary metabolites have long been used for drug development to date [8]. Plant secondary metabolites have important physiological and ecological effects. Plant secondary metabolites can be classified into four major classes: terpenoids, phenolic compounds, alkaloids, and sulfur-containing compounds. These phytochemicals can be antimicrobial, act as attractants/repellents, or as deterrents against herbivores [9].

Although some natural compounds have effects as anticancer, their use in clinical practice is not possible because of their physicochemical properties (e.g., limited bioavailability) and/or their toxicity. On the other hand, secondary metabolites from plants often can be excellent leads for the development of a drug. Modifying the chemical structure of these more promising compounds is one strategic way to increase their anticancer activity and selectivity, improve their absorption, distribution,

metabolism, and excretion properties and decrease their toxicity and side effects. As the result, these are proven to have good anticancer effects through clinical trials and have even been used in therapeutic applications. [10].

Some secondary metabolite compounds that are reported to have anti-cancer activity and include: (1) Phenolic compounds (flavonoids, stilbenes, and phenolic acids), (2) Terpenoids (monoterpenoids, diterpenoids, and tetraterpenoids/carotenoids), (3) Nitrogen-containing alkaloids and sulfur-containing compounds (alkaloids and organosulfur compounds), (4) Quinones (benzoquinone, naphthoquinone, anthraquinone, and phenanthraquinone) [11,12]. Derivatives from other secondary metabolite compounds such as tannins, saponins, catechins, phytoestrogens, and mimosine showed anticancer properties against some cancer such as squamous cell, salivary gland, breast, prostate, and ovarian cancer [13].

### Borneo Endemic Plants that are Potential as Anti-Cancer Medicines

Some Borneo endemic plants have been proven through a series of studies to have anti-cancer activity and even have other nutritious effects on the health of the body. These plants contain several secondary metabolites that can inhibit the growth of cancer cells and even destroy them. These plants can be found easily and even grow wild in mainland Borneo. The following describes some of the plants in question.

#### 1. Bawang Dayak (Dayak Onion)

Dayak onion has the latin name *Eleutherine bulbosa* (Mill.) Urb. (it's also known as *Eleutherine Americana* Merr. or *Eleutherine palmifolia* (L.) Merr.). In Indonesia, especially the Island of Borneo, it is also called bawang tiwai (tiwai onion). Dayak onion (*E. bulbosa* (Mill.) Urb.) is a bulbous plant that has grass-like leaves. The bulbs have a purplish red color with a bitter taste. The Dayak people (Borneo natives)

have been using for generations the bulbs as traditional medicines [14]. Dayak people usually process it by slicing it thinly and drying it, then brewing it with boiled water.

This plant has been shown to have several pharmacological effects, including antimicrobial, anti-hypertension, anti-diabetic, anti-dermatophyte, anti-melanogenesis, anti-inflammatory, and has cytotoxic activity against cancer cells [15]. The bulb contains several compounds that are antioxidant and anticancer, such as quinones, steroids, tannins, phenols, and flavonoids [16,17]. Phenols and flavonoids in the bulb have a higher content with stronger antioxidant activity than those in the leaves and flowers [17]. Isoliquiritigenin (flavonoid group) in the bulb showed anticancer activity, induces apoptosis, antiproliferative activity against cervical cancer cells [18].

The quinone, one of the components contained in the bulb is proven to induce the process of cell death (apoptosis) of cancer cells in humans by activation of caspase-3 cleavage, DNA fragmentation, and the reactive oxygen species (ROS) generation [19]. Research using the human erythroleukemia cancer cell line K562 with IC50 shows that the quinone content (naphthoquinone and anthraquinone) in *E. bulbosa* (Mill.) Urb. can inhibit the proliferation of K562 with IC50 [20]. In silico, one of the naphthoquinone derivatives of *E. bulbosa* (Mill.) Urb. namely, eleutherinol shows inhibitory activity against human alpha estrogen receptors that play a role in the regulation of breast cancer cell proliferation [21].

## 2. Tahongai

*Kleinhovia hospita* Linn is a plant that can grow on several islands in Indonesia, including the island of Borneo. This plant is known in Indonesia by different names based on its location. On the mainland of Borneo, this plant is known as Tahongai. The local people usually process it by boiling the leaves and then drinking it as traditional medicine.

Currently, the leaves of this plant are packaged more practically and commercially in the form of teabags which are proven to be safe for consumption (based on hepatological tests on experimental animals) [22]. Phytochemical screening of ethanolic extract of *K. hospita* L. showed the presence of alkaloids, flavonoids, tannins, saponins, and steroids [23]. *K. hospita* L. leaves have been shown to have strong antioxidant activity and function as hepatoprotection. Cytotoxic effect assessment of the *K. hospita* L. leaves methanol extract showed that there was an increase in the cytotoxic effect of the *K. hospita* L. leaves on HepG2 cells (hepatocellular carcinoma cells) as the concentration increased compared to the positive control using hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) [24]. The active compounds kaempferol 3-O-β-D-glucoside and eleutherol in *K. hospita* L. did not show any cytotoxic effect on HepG2. The cytotoxic effect of this extract on HepG2 may be related to the content of the triterpenoid cycloartane in it [25]. Stem wood of *K. hospital* Linn contains secondary metabolites such as terpenoids, steroid group compounds, terpenoid-phenolic compounds, and ester derivative compounds. The ester-derived compounds have been shown to have biological activity against P-388 leukemia tumor cells, while other compounds have moderate biological activity against it [26].

Research using experimental animals shows that *K. hospita* L. extract has the potential to reduce the effects of damage to the liver and heart caused by the chemotherapy agent, such as doxorubicin (DOX) [27].

## 3. Sarang Semut (Ant Nest)

Sarang semut (ant nest) belongs to the *Rubiaceae* family and is known in Indonesia as a medicinal plant, especially for cancer treatment [28]. Some species are belonging to this plant have been identified and are part of two main genera (*Hydnophytum* and *Myrmecodia*). Many kinds of research related to this plant have

been carried out, especially those that grow in Papua. Meanwhile, information related to research on this plant in Borneo is still scant. Ant nest is also an endemic plant on the Borneo Island, although the characteristics of the ant nests in several research sites in Borneo are different species from those in Papua [6].

*Hydnophytum formicarum*, one of the species of *Hydnophytum*, its tuber contains several powerful antioxidative compounds such as flavonoid and phenolic compounds: isoliquiritigenin, protocatechualdehyde, butin and butein [29]. 7,3',5'-trihydroxyflavanone (3HFD), a flavonoid derivative obtained from *H. formicarum* has been shown to have effects of cytotoxic on MCF-7 cell line (human breast carcinoma). It was able to induce the apoptotic cell death of MCF-7 cells via up-regulation of Bax expression [30]. A study using ethanol extract of ant nest plant parts without ant residue showed inhibition against T47D cells (human mammary gland ductal carcinoma). Another effect of the extract is that it can increase the proliferation of lymphocytes [31]. *H. formicarum* leaves also have potency as a source of antioxidants and anticancer agents. The leaves contain secondary metabolites such as phenols/tannins, flavonoids, glycosides, and steroids. Methanol extract of the leaves showed moderate cytotoxic activity against the HeLa cell line (cervical carcinoma) [32].

Another ant nest plant, *Myrmecodia pendens*, its tuber has phenolic compound, especially flavonoids (kaempferol, luteolin, rutin, quercetin, and apigenin) and do not show any toxic effects on normal cells. It can be boiled and then consumed the extract as herbal medicine [33,34]. Several experimental studies have proven that *M. pendens* extracts can inhibit the proliferation of cancer cells, such as Burkitt's Lymphoma Cancer Cells (ethyl acetate extract) [35], oral cancer cells derived from the human oral cavity; HSC-3 cell line (crude extract) [36], a human oral tongue squamous cell carcinoma cell line; B88 (ethanolic extract) [37], colon cancer cell lines; Caco-2 and HCT-116 cells

(methanol extract as well as n-hexane and ethyl acetate fraction) [38,39], and HeLa cell line (ethanolic extract) [40]. Research using two types of *M. pendens* leaves extract showed that polar extracts (water) have higher anticancer activity than non-polar extracts (ethyl acetate and n-butanol) in inhibiting HeLa and MCM-B2 cells (benign mixed tumor of the canine mammary gland) [41]. Another species of *Myrmecodia*, *M. platytyrea* Becc., its methanolic extract was shown to have an anti-cancer effect on hepatocellular carcinoma (HCC) cells. Its metabolites can inhibit uPAR, STAT3, and ERK signaling pathways involved in cancer progression [42].

The effectiveness of ant nest against the progression of cancer cells may vary from region to region, depending on the conditions in which they are grown. This causes differences in their biological activity. Research using *H. formicarum* tuber extract from different locations (Setiu Wetland-Malaysia and Muara Rupit-Indonesia) showed that *H. formicarum* tuber extract from Setiu Wetland had very strong cytotoxic activity against MCF-7 (human breast cancer cell line with estrogen, progesterone, and glucocorticoid receptors) compared with *H. formicarum* from Muara Rupit. However, both of them did not show any cytotoxic activity against HeLa cells [43].

#### 4. Batang Kuning (Yellow Stem)/Akar Kuning (Yellow Root)

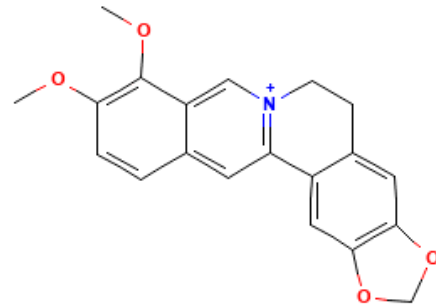
Several species that are considered as Batang Kuning (Yellow Stem) or Akar Kuning (Yellow Root) and are widely found on the Island of Borneo include *Cosciniium fenestratum*, *Arcangelisia flava*, and *Fibraurea tinctoria*. Generally, ethnic groups in Borneo recognize it from its bright yellow roots and stems. The yellow stem has long been known in Borneo Island as one of the ingredients of traditional herbal medicines to treat various diseases, especially as a treatment for malaria.

The three species of yellow stem belong to the *Menispermaceae* family and have

several secondary metabolites that are antimicrobial, antifungal, antiplasmodial, anti-diabetic, anti-hypertension, anti-hypercholesterolemic, hepatoprotective, analgesic, antioxidant, and anticancer [44,45].

A study showed that the crude extract of *C. fenestratum* stems could inhibit cell survival and increasing apoptosis in the human HN31 cell line (pharyngeal metastatic squamous cell carcinoma). It decreased the phosphorylation of p38 mitogen-activated protein kinases (responsible for regulating cell proliferation, differentiation, and apoptosis) and pAkt (a signal molecule that is key to 5-fluorouracil chemoresistance in squamous carcinoma cells). It increased tumor suppressor proteins p53 and pro-apoptotic protein Bax [46]. Ethanol extract of *C. fenestratum* showed biological activity that triggers apoptosis in HeLa cells by triggering the release of mitochondrial cytochrome-c and activation of caspases 3 and 9 [47]. Ethanol extract of *C. fenestratum* also showed the same activity against human colorectal carcinoma cell lines HCT-116 and SW480. Dichloromethane fraction induced peroxisome proliferator-activated receptor (PPAR $\gamma$ ) binding activity, which represents a pro-apoptotic activity in colorectal cancer cells [48]. The alkaloid content of *A. flava* stem extract from various regions on the island of Borneo has the potential to reduce the viability of WiDr cell line (colorectal cancer) [49]. Berberine [Figure 1], one of the major alkaloids obtained from the methanolic extract of *C. fenestratum* showed cytotoxic effects and the ability to induce apoptosis in HL-60 (human leukemia cell line) cells [50]. Berberine is also a secondary metabolite of *A. flava* and *F. tinctoria* [51]. Berberine in *A. flava* has been shown to inhibit Proto-oncogene tyrosine-protein kinase Src (one of the targets in various cancer therapies) [52] and Epidermal Growth Factor Receptor-2 (EGFR-2) [53]. Over-expression of the activity of EGFR-2 itself is common in breast cancer, especially HER2-positive breast

cancer) [53]. Meanwhile, leaves extract of *A. flava* contains alkaloids, flavonoids, terpenoids, and saponins. A study showed that the leaves extract appeared to induce necrosis rather than apoptosis in HeLa, MCF-7, and colon cancer cell line WiDr [54].



**Figure 1.** Chemical structure of berberine  
(C<sub>20</sub>H<sub>18</sub>NO<sub>4</sub><sup>+</sup>)

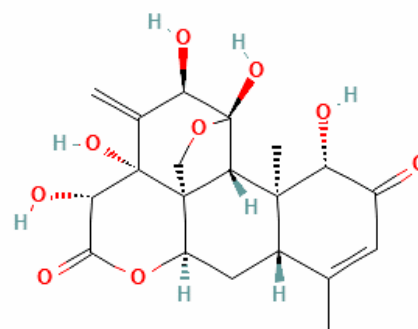
(Source: pubchem.ncbi.nlm.nih.gov)

## 5. Pasak Bumi/Tongkat Ali

Pasak Bumi or Tongkat Ali (*Eurycoma longifolia*) is one of the species from *Simaroubaceae* family which has high economic value as medicinal plant for human health and is commonly traded in several Indonesian islands, such as the island of Borneo. This plants commonly grow well in tropical rain forest areas [55].

In plant parts, especially the roots contain several metabolites that are efficacious as an aphrodisiac, anti-microbial, anti-diabetic, anti-malarial, anti-ulcer, and anti-cancer [56]. In addition to containing phenolics and flavonoids (methanol, acetone, ethyl acetate, and chloroform extracts) [57], the roots of *E. longifolia* also contain quassinoids (a nortriterpenoids class isolated exclusively from various species of the *Simaroubaceae* family) which have anticancer activity [58] against several types of cancer cells experimentally [59]. Eurycomanone [Figure 2] is the major quassinoid as a potent anticancer agent [59]. Another plant part, based on research conducted by Supartini et al. [60] using ethanol and water extracts on *E. longifolia* leaves showed the presence of flavonoids, tannins, triterpenes, kumarins, carbohydrates, and saponins (water extract

only). Meanwhile, the plant stem contains alkaloids (ethyl acetate, chloroform, and petroleum ether extracts), terpenoids (methanol, ethyl acetate, chloroform, and petroleum ether extracts), phenolic compounds, and flavonoids (methanol, acetone, ethyl acetate, and chloroform extracts) [57]. Several studies related to the anticancer activity of *E. longifolia* plant parts are summarized in **Table 1**.



**Figure 2.** Chemical structure of Eurycomanone (C<sub>20</sub>H<sub>24</sub>O<sub>9</sub>) (Source: pubchem.ncbi.nlm.nih.gov)

**Table 1.** Cytotoxic activity of *E. longifolia* Extracts Against Cancer Cell Lines

Parts	Extract	Fraction	Experimentall Cell	IC <sub>50</sub> Value (µg/mL) at 72 hours		Explanation	Ref.
Root	Aqueous	-	MCF-7 breast cancer cell line	>99.99		The methanolic (F2) extract became extra effective than the aqueous extract. F3 – F13 are fractions obtained by silica gel permeation chromatography of F2. Three fractions (F5, F6, and F7) showed strong antiproliferative activity against MCF-7 cells. F14, F15, and F16 are partitions of F7 where only F16 showed antiproliferative activity against MCF-7 cells. F5 and F6 are not partitioned because they contain eurycomanone with an IC50 value lower than F7. F16 can decrease Bcl-2 expression.	[61]
	Methanol (F2)	-		7.80 ± 0.45			
	Methanol (F2)	F3		F3	47.35 ± 0.87		
		F4		F4	34.00 ± 0.71		
		F5		F5	6.17 ± 0.38		
		F6		F6	4.40 ± 0.42		
		F7		F7	20.00 ± 0.08		
		F8		F8	46.84 ± 0.11		
		F9 – F15	>99.99				
		F16	F16	15.23 ± 0.66			
Root	Methanol	Eurycomanone	HepG2 human liver cancer cells	45 ± 0.15		The results showed that eurycomanone had the highest cytotoxic activity against HepG2 cells compared to other experimental cells. The apoptotic process triggered by eurycomanone involved the up-regulation of p53 tumor suppressor protein. The process was followed by the increasing of pro-apoptotic Bax and decreasing of anti-apoptotic Bcl-2. Apoptosis was also affected by an increase in the release of cytochrome C.	[62]
			HM3KO human skin cancer cells	60 ± 0.25			
			Hela human cervical cancer cells	60 ± 0.25			
			CaOV3 human ovarian cancer cells	79 ± 0.16			
Root	Methanol	Eurycomanone	A549 lung cancer cell line	5.1		Eurycomanone could reduce the expression of the lung cancer markers, heterogeneous nuclear ribonucleoprotein A2/B1, p53 tumor suppressor protein, and cancer-associated genes (prohibitin, annexin 1, and endoplasmic reticulum protein 28).	[63]
Root	Methanol	TAF273	K-562 leukemic cell line	TAF273	19 ± 3	TAF273 fraction shows potent anti-proliferative activity on K-562 cells. TAF273 induced apoptosis and arrested cell cycle at G1 and S phases.	[64]
		F3		F3	55 ± 2		
		F4		F4	62 ± 7		
Root	Methanol	Eurycomanone Eurycomanol	K-562 leukemic cell line	Eurycomanone	14.2	Eurycomanone and eurycomanol could inhibit Jurkat and K562 cells. Eurycomanone could prevent induction of NF-κB and mitogen-activated protein kinase signaling, but not eurycomanol.	[65]
			Jurkat (T-cell leukemia) cell line	Eurycomanone	5.89		
Root	Methanol	SQ40	LNCaP human prostate cancer cell line	5.97		SQ40 at higher concentrations can cause cell growth arrest in the G2/M phase which causes cell apoptosis.	[66]
Leave	Infusion (boiling)	-	Non-hormone-dependent MDA-	Unfermented (freeze-dried)	69.3 ± 17.2	The result showed that the unfermented freeze-dried leaf extract has the strongest cytotoxic activity	[67]

MB-231 breast cancer cell line	Unfermented (MO-dried)	84.7 ± 8.4	against MDA-MB-231 and MCF-7 cells. This extract has phenolic contents (gallic acid, chlorogenic acid, epicatechin, and epigallocatechin gallate). This extract show ability to induce apoptosis cell death which leads to DNA fragmentation on MDA-MB-231 and MCF-7. This extract caused the MDA-MB-231 cell cycle to be arrested at the S phase (failure of DNA synthesis) and caused the MCF-7 cell cycle to be arrested at the G2/M phase (DNA was damaged and unable to be duplicated). This extract caused an increase of Bax and a decrease of Bcl-2 expression in both cell lines.
	Fermented (freeze-dried)	98.3 ± 11.5	
	Fermented (MO-dried)	99.7 ± 6.8	
Hormone-dependent MCF-7 breast cancer cell line	Unfermented (freeze-dried)	45.0 ± 3.5	
	Unfermented (MO-dried)	65.7 ± 20.3	
	Fermented (freeze-dried)	66.7 ± 20.5	
	Fermented (MO-dried)	97.3 ± 13.6	

IC<sub>50</sub> Value : half inhibitory effect to cells proliferation (in a dose-dependent manner).

F1- F16 : fractions of the *E. longifolia* root methanol extract

TAF273 : a partially purified quassinoid-rich fraction of *E. longifolia* root extract.

SQ40 : a standardized quassinoids composition (SQ40) containing 40% of the total quassinoids in *E. longifolia*.

MO : microwave oven

## 6. Sengkubak

This plant (*Psycharrhena cauliflora*) is very familiar and is known by the name Sengkubak, Sansangkng, or Sensen by the natives of Borneo, especially West Borneo. The leaves [Figure 3] of this plant have been used for generations by people living in there as a natural flavor enhancer to replace synthetic flavor enhancers, such as MSG (monosodium glutamate) [68,69]. The leaves contain 58 mg/100 g of glutamic acid which contributes to the savory taste of the food. This ancestral heritage flavor enhancer is also used as a traditional treatment for headaches, flatulence, and fever (fever compresses) by residents. The antioxidant content of this plant also has the potential an anti-cancer [70].



**Figure 3.** Sengkubak leaves and dry powder of its leaves for flavor enhancer [57]

Some parts of the plant, such as leaves, roots, and stems, have been shown to have anti-cancer properties. The methanol extract of the leaves contains flavonoids and saponins [71] that can induce apoptosis and suppress the proliferation of cancer cells [72,73]. Extracts of n-hexane and dichloromethane from the leaves, branches, and roots of this plant contain steroids, terpenoids, and alkaloids. Dichloromethane extracts of roots showed the highest cytotoxic activities against HeLa cells [71]. The dichloromethane fraction of *P. cauliflora* stem crude ethanol extract at pH showed induction apoptosis on the T47D cell line [74] and so did its root alkaloid fraction extract [75].

## 7. Kayu Bajakah (Bajakah Wood)

Bajakah wood [Figure 4] grows a lot in the hinterland of the Borneo Forest and has long been used by the indigenous people there as medicine, and is also made as equipment for war or hunting. This plant began to become famous in Indonesia after its use empirically showed efficacy against breast cancer. Because of this, several high school students at the venue introduced it at the World Invention Creativity (WICO) in Seoul, South Korea (25-27 July 2019) and won a gold medal. Based on this information, people on the Island of Borneo and even some areas in Indonesia believe it is a plant with anti-cancer properties and hunt it down.



However, the type of bajakah wood used in that case has not been identified [76].

**Figure 4.** Bajakah wood and its uses as a brewed beverage [76, 77]

Not all types of bajakah wood can be used for medicinal purposes. There are at least about 200 types of it. Some of them are even poisonous and dangerous if consumed [77]. Three types of bajakah are commonly used for health, including: (1) Bajakah Lamei (treating diarrhea, curing cancer, healing wounds, and preventing heart disease, (2) Bajakah Tampala / *Spatholobus littoralis* Hassk (healing wounds), and (3) Bajakah Kalawit / *Uncaria gambir* Roxb (prevents heart disease) [78]. Experimental studies and scientific information related to the use of bajakah wood in medicine, especially as anti-cancer is still very few.

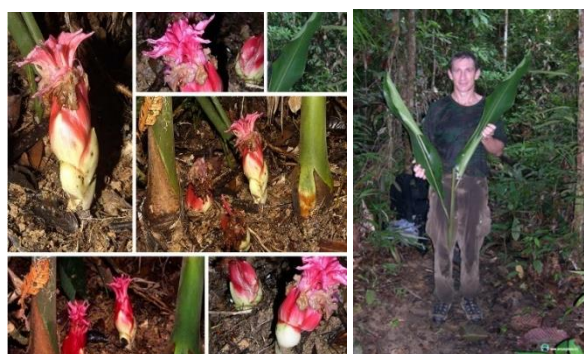
Research that has been conducted has shown that the bajakah wood (*S. littoralis* Hassk) ethanol extract contains secondary metabolites including phenolic compounds, tannins, saponins, and



flavonoids [79,80]. A study also showed that the ethanol extract of *S. littoralis* Hassk also has antioxidant activity with a very strong category [81]. It is suspected that the type of bajakah wood that is widely traded and considered as an anti-cancer drug by the people on the Island of Borneo is *S. littoralis* Hassk. However, research on bajakah wood, whether its identity, efficacy, and pharmacological effects, still needs to be investigated further.

## 8. Jahe Balikpapan (Balikpapan Ginger)

Borneo is one of the most interesting places in the world to study the richness of plants and is home to more than 300 types of ginger plants. A Danish botanist (Axel Dalberg Poulsen) had documented a new type of *Etlingera* ginger that was only found in the Protected Forest of Sungai Wain-Balikpapan, East Borneo. He named this plant *Etlingera balikpapanensis* (Balikpapan Ginger) [Figure 5]. He published this type of ginger in his book, "Etlingera of Borneo", in August 2006 [82]. Research on this species is still very little, including the content of secondary metabolites and their efficacy as herbal medicine. We have not found scientific information related to the activity of this plant as an anti-cancer.



**Figure 5.** Balikpapan ginger and its founder [82]

Research conducted by Sofia et al [83] using methanol extract of the rhizome of *E. balikpapanensis* obtained Isolate A which has a fairly good antioxidant activity which is thought to be a class of anthraquinone compounds. Meanwhile, a study conducted by Sandi et al [84] using methanol extract of the leaves of *E. balikpapanensis* showed antioxidant activity in the weak category.

Literature studies about several species of *Etlingera*, such as *E. elatior*, *E. pyramidosphaera*, *E. megaloscheilos*, *E. brevibrum*, and *E. paviana* revealed the efficacy of those species secondary metabolites (either in the rhizome, leaves, or flowers) against cancer cells experimentally (in a dose- and time-dependent manner) [85-92]. Some of those species are also found and widely grown in the forests of Borneo. Based on that information, we hypothesized that some parts of *E. balikpapanensis* also contain various secondary metabolites as well as similar plants which are efficacious against various diseases and have potential as plants with anticancer activity. Research on this still needs to be done.

## CONCLUSION

Some of the endemic and typical plants of the Borneo Island discussed in this article had been studied to contain some secondary metabolites that have anti-tumour / anti-cancer effects. Some of them still need to be identified and researched further. Besides those plants, many others thrive on the island of Borneo that needs to be investigated further regarding their efficacy as anti-cancer medicines.

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