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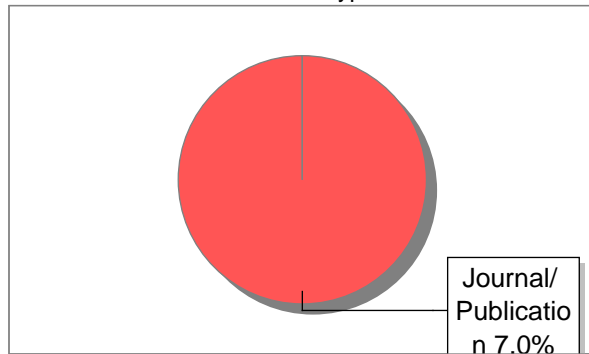
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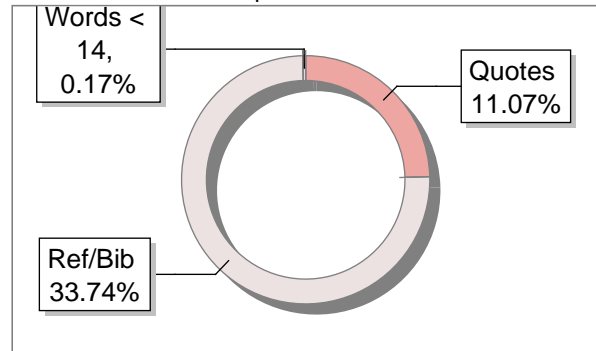
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Variability and pharmacological potential of bajakah (*Spatholobus* sp.) as an indigenous medicinal plant: a review

Nurkhasanah Mahfudh¹, Dwi Utami¹, Siti Nashihah², Mustofa Ahda¹, Andika Andika³,
Giriani Ayu Sabilla¹

¹Department of Analytical Pharmacy and Medicinal Chemistry, Faculty of Pharmacy, Universitas Ahmad Dahlan, Yogyakarta, Indonesia

²Department of Biological Pharmacy, Faculty of Pharmacy, Universitas Muhammadiyah Banjarmasin, Banjarmasin, Indonesia

³Department of Analytical Pharmacy and Medicinal Chemistry, Faculty of Pharmacy, Universitas Muhammadiyah Banjarmasin, Banjarmasin, Indonesia

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ABSTRACT

Bajakah (*Spatholobus* sp.) is an indigenous Indonesian plant that has been traditionally used as medicine, especially in Kalimantan Island, Indonesia. The variability and potential of bajakah as a traditional Indonesian medicinal plant have attracted research attention. This review article describes the traditional use, distribution, and pharmacological activity of bajakah. An integrative review method was employed, following procedures such as literature search, data analysis, and result presentation. Understanding the variations is important to understand the therapeutic potential and differences in active compound content among different types of bajakah. Furthermore, the chemical composition of bajakah has been identified, including alkaloids, flavonoids, tannins, saponins, and triterpenoids, which can potentially exhibit pharmacological effects and mechanisms of action associated with its traditional use. This review provided additional insights into the potential of bajakah as an herbal medicinal in the future. Therefore, this review article provides an overview of the traditional use distribution, and pharmacological activity of bajakah as a promising traditional medicine. Further research, including clinical studies, is needed to scientifically validate the therapeutic potential of bajakah and further understand the mechanisms of action and potential side effects associated with it.

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Corresponding Author:

Nurkhasanah Mahfudh

Faculty of Pharmacy, Universitas Ahmad Dahlan

Jl. Prof Soepomo, Janturan, Yogyakarta, Indonesia, 55164

Email: nurkhasanah@pharm.uad.ac.id

1. INTRODUCTION

Indonesia has a rich heritage in the use of medicinal plants as an important part of health care. Indonesia is a mega-biodiversity country [1], [2] because it has the second-largest tropical rainforest in the world. People in Indonesia have a habit of using traditional medicine as an alternative medicine to treat various diseases. However, bajakah contains secondary metabolites supporting traditional medicine use as a derived-plant natural ingredient. Therefore, Bajakah has been used by local people for many years for various medicinal purposes. It is a native Indonesian plant from Kalimantan that has been consumed traditionally as medicine for a long time. In Indonesia, there are three types of bajakah wood, namely bajakah tampala [1], bajakah kalawit, and bajakah lamei. These bajakah types contain differences of responsible metabolites which will ultimately affect their pharmacological properties. Therefore, the importance of herbal

use ensures its consistency and efficacy through determination of the active ingredients that reflect the intrinsic qualities of medicinal plants [3]. Bajakah plants have stems that stretch out, vines, and are known to grow in limited numbers in the forests of Central Kalimantan, Indonesia. It has been used traditionally (Bajakah decoction) by the Dayak people to treat various diseases including diarrhea, dysentery, rheumatic pain, wounds, and so on. In fact, bajakah wood is believed to have the ability to cure cancer. Besides, it is also used as a hand sanitizer material because it contains metabolites that are proven to have antibacterial activity against *E.coli* [4], [5]. Therefore, the variability and potential of bajakah as a native Indonesian traditional medicine have attracted the attention of researchers in recent years.

Knowledge of the variety of bajakah is very important to understand its therapeutic potential and the differences in the active substance content between the different types of bajakah [6]. A previous study reported that phenolic compounds were the dominant component of more than 50% in the 1-butanol stem fraction of 70% ethanol and water extract from bajakah (*S. littoralis* Hassk.) [7]. Other studies also declared that bajakah can be applied as anticancer agents [8], antidiabetic, antibacterial, antioxidant, antiinflammation [9], [10]. By combining traditional knowledge, pharmacological research, and an in-silico approach, this review article provides a comprehensive overview of traditional variability, active substances, pharmacological activity of bajakah as a promising traditional medicine. It is a very important part to understand scientifically of bajakah potency and to support its mechanism of action associated side effects in the further research.

2. METHOD

The integrative review method by Sianipar [11], [12] was used in reviewing all evidence related to the variables and potency of bajakah as a native Indonesian traditional medicine. Some related data source was used for find the evidence including online and offline source. The process includes literature search, data analysis, and results presentation.

2.1. Literature search

The time limit for articles reviewed was not set because the research related to bajakah is still relatively rare. The article used is in full text format. Google Scholar, Research Gate, and Science Direct were used to search literature with the keywords used were "Bajakah" and "Spatholobus". The inclusion criteria for this study were any research method (systematic review or literature review, experimental studies, and observational studies) and fully accessible (full text).

2.2. Data analysis

The results of the literature search were then extracted and recorded using tables consisting of traditional use, variability, potency, active substances, studies/approaches used, pharmacological activity, research methods, and research results. The data analysis was carried out descriptively. The result of analysis was presented in table to give a comprehensive understanding.

3. RESULTS AND DISCUSSION

3.1. Biodiversity, morphological, and traditional use of bajakah

Bajakah has wide variability in its use as a traditional medicine in Indonesia. The bajakah plants is an empirically used by the people of the interior of Kalimantan as a traditional medicine. The geographic spread of bajakah throughout the diverse landscapes of Kalimantan presented in Figure 1. Tropical rain forests have a high diversity of around 40,000 scattered plants which shows various variations in the form of body structure, number and other characteristics. Dayak is one of ethnic in Kalimantan which has rich of ethnomedicines [13]. Bajakah is one of medicinal plant used by Dayak people for long lime.

In Kalimantan, there are three known types of bajakah wood as shown in Figure 2 namely bajakah kalawit Figure 2(a), bajakah akar kuning Figure 2(b) and bajakah tampala Figure 2(c). This difference in the types of bajakah allows for differences or variations in the content of active compounds which will ultimately affect their pharmacological properties. The bajakah tampala tree is one of the plants used as medicine by the Dayak people. This plant thrives in peat soils. Many bajakah tampala plants can be found in the inland areas of Kalimantan, including East Kutai. In the inland areas of Kalimantan forests, including the Central Kalimantan region with an approximate area of 2,697,165.00 ha in 2013, one can find bajakah kalawit or red bajakah root. This plant shows significant growth potential in the forests of Central Kalimantan, the propagation of this plant were still developed [14]. Additionally, bajakah is not limited to the Central Kalimantan province, it also thrives in various other areas of Kalimantan such as East Kalimantan, West Kalimantan, North Kalimantan, and South Kalimantan. The tropical environment of Kalimantan's forests provides a suitable habitat for these plants. On the other hand, as mentioned on the Institut Pertanian Bogor (IPB), the bajakah lamei plant is a tropical rainforest vine that flourishes in damp regions. Locals in Central

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Kalimantan often gather the liquid from the bajakah lamei tree for consumption [15]. Currently, the bajakah plant is popular among Indonesian people because it is considered capable of curing cancer. Bajakah grows naturally and lives wild vines in the forest. Bajakah plants can be found in the forests of Central Kalimantan. The morphology of three types of bajakah were presented in Figure 2. The different colour of stem bark including red for bajakah tampala and kalawit, while yellow for bajakah lamei could be caused by different chemical content [16].

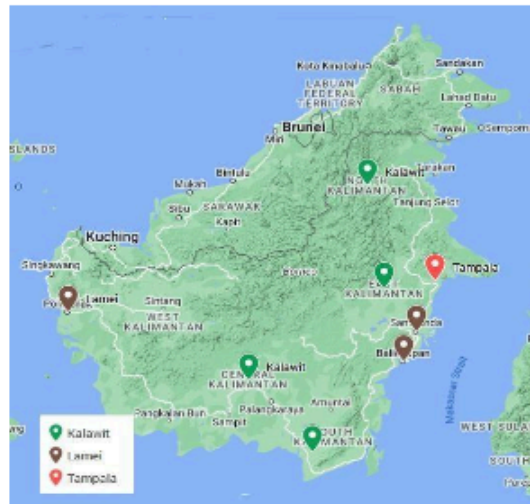


Figure 1. Distribution map of bajakah in Kalimantan

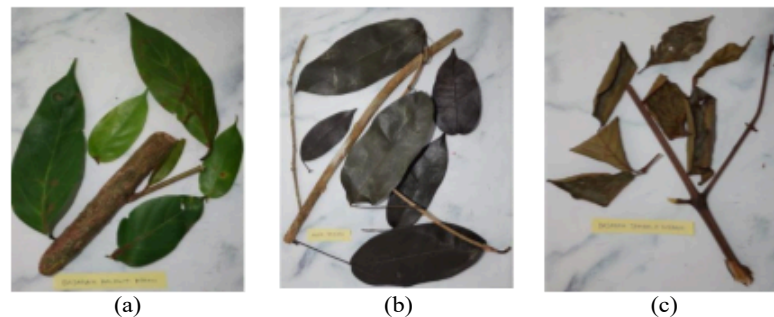


Figure 2. The morphology of bajakah types: a) bajakah kalawit; b) bajakah akar kuning; c) bajakah tampala which are distributed in Kalimantan

Kalimantan Island is an area with the largest tropical rainforest in Southeast Asia. Its plant diversity is the richest in Sunda Plains, competing with the Amazon Forest. With an area of about 7.93% of the total area of Indonesia, Central Kalimantan has a lot of diversity of medicinal plant biological resources which are widely spread in inland areas and forest areas of Central Kalimantan and are the natural habitat of these plants. In pharmaceutical development, medicinal plants are a source of bioactive compounds which are efficacious in treating various diseases. Bajakah was first discovered in 1842 by a botanist from Germany, namely Justus Karl Hasskarl [17]. Before becoming as popular as it is now, the bajakah plant was known to the people of Kalimantan as a natural medicinal plant. The Dayak people have long used the root of the plant as a medicine to restore stamina when doing activities in the forest and have used all parts of the plants as a cancer cure for

generations by the ancestors of the Dayak tribe. Meanwhile, on Pulau Pisau, Central Kalimantan, this plant is used as a medicine for dysentery and body aches, apart from wound medicine.

Other species from *Spatholobus* genus has long been utilized in Traditional Chinese Medicine (TCM) in China. *Spatholobus suberectus* (JiXueTeng) has been used as herbal medicine in China for around 100 years [18]. In several Asian countries, a few species of the genus *Spatholobus* are used as medicinal and food plants to treat menstrual discomfort, anemia, arthritis, and other ailments [19]. Previous study has evaluated 2 genus of *Spatholobus suberectus* and *Spatholobus pulcher* with genomes identifier which is 152173 bp (base pair) and 151099 bp, respectively. *Spatholobus suberectus* was also used as an anti-cancer treatment [20], [21]. A previous study has successfully identified four new isoflavones from the *Spatholobus suberectus* plant as anticancer agents. Therefore, there is a good chance that bajakah will be used to treat a variety of ailments including anticancer [22].

Traditionally, bajakah has been used to treat various health conditions such as diarrhea, dysentery, rheumatic pain, wounds, and cancer [23]. Local people use various parts of this plant, such as the bark, leaves and roots for treatment. Although there are limitations to thorough scientific research on bajakah, some early research points to the potential of this plant in traditional medicine. One study showed that bajakah was also found to have potential as a topical herbal remedy that can reduce the severity of psoriasis, a skin condition characterized by red, itchy, and scaly skin [24]. Bajakah extract has shown anti-inflammatory activity and inhibited the excessive proliferation of skin cells in psoriasis. This shows the potential of bajakah in relieving inflammation and reducing the severity of psoriasis symptoms.

Another study found that bajakah have strong antibacterial properties. The active compounds in Bajakah can fight various types of pathogenic bacteria, including those that are resistant to antibiotics. These antibacterial properties suggest that bajakah could potentially be an effective treatment that can help fight infection. Apart from that, bajakah also has an antipyretic effect and potential as an inflammation drug, helping to reduce fever [13]. This herb has also shown positive effects in the treatment of breast cancer [4]. The active compounds in bajakah have shown anticancer activity, which can inhibit cancer cell growth and stimulate apoptosis (cell death) in cancer cells. Several compounds in bajakah, such as medicarpin, maackiain, lupinalbin A, medioresinol, 8-methylretusin, biochanin A, isoliquiritigenin, cuomestrol, and trigacum, have potential as anticancer agents for breast cancer. Caspase-3 and Bcl-3 activity in the apoptotic pathway and p53 signaling by these nine chemicals show that these materials have the ability to fight against breast cancer based on the in silico approach [25]. Another in silico study reported that some flavonoids from *Spatholobus* including licochalcone A, afrormosin, 5,4',7'-trihydroxy flavone, formononetin, cajanin and dihydrokaempferol showed good binding energy values in inhibiting of Mpro SARS-COV-2 virus, and good pharmacokinetic properties according to Lipinsky Rules of Five and absorption, distribution and metabolism (ADMET), suggested to good for oral administration [26].

In addition, bajakah also contains antioxidant compounds that can protect the body from damage caused by free radicals. These compounds are important in the prevention and treatment of oxidative-related conditions, such as heart disease, diabetes, and some types of cancer. A study showed that bajakah has anticancer, antioxidant [27], and antibacterial [28] properties which are important in future traditional medicine development. Some early research also shows the potential of bajakah as an anti-diabetic drug, with its ability to regulate blood glucose levels. Although research on bajakah as an indigenous medicinal plant from Indonesia is still limited. Therefore, more exploration is needed to justify scientifically its potency as traditional medicines [29]. This preliminary evidence suggests that this plant has a variety of pharmacological properties that support the development of traditional medicine in the future. By deepening the knowledge of bajakah, it is hoped that we can better appreciate and utilize this traditional heritage for sustainable health care.

3.2. Phytochemical of bajakah

The secondary metabolites of bajakah have a considerable impact on the potency and applicability of bajakah for illness treatment. As a result, identifying and quantifying the most important active components of the herbs is required to inform the certification of the proposed herb. Another bajakah (*Uncaria nervosa* Elmer) includes alkaloids, flavonoids, and terpenoids in the form of rynchophylline and isorynchophylline, flavanol and flavonol, and ursan, respectively [30]. The thin layer chromatography (TLC) analysis of bajakah tampala (*Spatholobus littoralis*) reported the These compounds are proposed and useful for cancer and oxidative stress prevention. Other compounds of bajakah such as gentisic acid, 3,4,7-trihydroxyflavone, 6-methoxyeriodictyol, butin, plathymenin, dihydrokaempferol, liquiritigenin, calycosin, dihydroquercetin, eriodictyol, formononetin, neoisoliquiritigenin, daidzein dan saponin are active for treating several diseases including antioxidant, antiinflammation, immunosuppressor dan antipruritics based on in silico approach [31]. The phenolic and flavonoid groups are reported to possess many pharmacological activities [32].

This study reported 14 chemical components in *Spatholobus littoralis* Hassk. have potential as antioxidants, anti-inflammatory, antipruritic and immunosuppressive are predicted computationally. The laboratory tests were needed to further evidence. The highest antioxidant activity potential of *Spatholobus*

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littoralis Hassk. is dihydrokaemferol. The different varieties of bajakah have different chemical content. Bajakah akar kuning (*Uncaria gambir*) showed the highest flavonoids content among other bajakah from West Kalimantan [33].

The comprehensive review study on genus of *Spatholobus* have reported 175 phytochemicals, and flavonoids are the predominant constituents. Moreover, 141 compounds show the ideal characteristic behavior of a drug-like molecule [19]. The promising chemical content of the *Spatholobus* support the potency of this plant to develop as source of drug. The development of extraction method have been carried out to find out the flavonoid rich extract including the optimization of eutectic solven [34] and using of macroporous adsorption to increase the flavonoid content in the extract [35].

3.3. Pharmacological activity of bajakah

The active substance in bajakah has become the focus of in-depth research to understand its potential and benefits in traditional medicine. Before entering into a further discussion of the active ingredients of bajakah, it is important to acknowledge the importance of research in revealing the richness of Indonesia's traditional medicinal plants as a whole. Bajakah, as one of the well-known plants in traditional medicine, has attracted the attention of researchers to identify the active compounds contained in it.

Based on the information obtained, the active substances in Bajakah include flavonoids, tannins, phenols, saponins, alkaloids, and terpenoids. Several studies have been conducted to study the activity and potency of active substances in bajakah. For example, in silico studies were conducted to investigate the anti-cancer and therapeutic activity of psoriasis as anti-inflammatory, antifungal, antibacterial, antioxidant, and hepatoprotector. Several other studies have explored cytotoxic effects on breast cancer cells, phenolic analysis and antioxidant activity, as well as the behavior and mobility of experimental animals after administration of bajakah extracts. Thus, this study concluded that compounds from the *Spatholobus* genus have potential as candidates for breast cancer treatment and can be a focus for further research in the development of breast cancer therapy [28].

Bajakah have pharmacological activities that have been studied in depth. One of the activities observed is anti-inflammatory activity, which has the potential to reduce inflammation in the body [36]. In addition, bajakah has also shown promising anticancer activity, with several active compounds in bajakah that have the potential to inhibit the growth of cancer cells [4], [37]. Antipsoriatic activity has also been observed in bajakah, which means it can help reduce psoriasis symptoms on the skin. The in-silico method was also used to analyze the active compounds extracted from bajakah wood (*Spatholobus littoralis* Hassk.) as a psoriasis therapy. This shows the potential of bajakah as an effective traditional medicine for the treatment of skin diseases [38]. Based on the results of this in silico analysis, the study concluded that bajakah wood (*Spatholobus littoralis* Hassk.) is a good choice for psoriasis therapy. Bajakah wood has antioxidant, anti-inflammatory, antipruritic, and immunosuppressor effects. In addition, the use of bajakah wood is also beneficial in terms of availability [15] and safety [19].

Overall, in silico studies have provided valuable insight into the potency of bajakah in traditional medicine. By using various tools and computing servers, this study has identified active compounds that have potential as therapeutic agents in the treatment of breast cancer and psoriasis therapy [38]. Although these findings are promising, it is important to carry out further research in the laboratory to validate the effects and safety of using bajakah in this treatment. By combining in silico approaches and experimental research, we can develop knowledge and insights about bajakah active substances and make optimal use of them in health care.

In addition, it has also been observed that bajakah has significant antibacterial [39] and antifungal activity [40]. Bajakah extract could inhibit the eradication of formation of *S. aureus* biofilm, suggested this extract for curing and inhibiting of infection in wound. This property shows the potential of bajakah in fighting bacterial and fungal infections that are detrimental to human health. Bajakah has also been studied to have anti-inflammatory and antipyretic effects, which means it can help reduce inflammation and reduce fever [36]. Bajakah also has an antidiabetic effect with its ability to regulate blood glucose levels [9]. Anticancer [41] and immunostimulatory [42] activities have also been studied. This shows the possibility of bajakah in boosting the immune system and helping to fight cancer cell growth. The in silico study also support the strong antibacterial activity of bajakah [25].

A study also indicated that bajakah has significant antibacterial activity against harmful bacterial infections [15], [28] and antioxidant properties that can protect the body from damage caused by free radicals [9], [10]. In addition, there is potential as a Leydig cell enhancer and an increase in testosterone levels [43]. This shows the possibility of bajakah in improving reproductive function in men. The antioxidant activity of bajakah extract also could protect from the smoke and affect the morfometri of ovarium, suggested the using of bajakah for woman reproduction [44].

Several studies highlighting that bajakah also shows potential as a candidate for breast cancer treatment, with active compounds in bajakah that have an effect that inhibits the growth of cancer cells. In addition, bajakah has also been studied to have significant antibacterial activity. All of these studies provide

in-depth insight into the various pharmacological activities associated with bajakah and support its potential as a valuable traditional medicine. The list of active components and pharmacological activity of the bajakah plant (*Spatholobus* sp.) can be seen in Table 1. The in vivo study of bajakah water extract showed the capability of bajakah for antihyperlipidemia by reducing the cholesterol and triglyceride level and increase the high density lipoprotein (HDL) level in hyperlipidemic rats [45]. The extract in a dose of 200 mg/kg BW also showed the hepatoprotective against izoniasid induced rat which is showed by reducing of SGOT and SGPT [46].

Table 1. List of components of the active substance and pharmacological activity of the bajakah plant (*Spatholobus* sp.)

No.	Pharmacological activity	Active substance components	Findings	References
1.	Anti-inflammation	Flavonoids	Inflammatory power 87.65% The ethanol extract of bajakah wood has activity as an anti-inflammatory agent.	[47]
		Flavonoids, Tannins, Saponins, Phenolic, Terpenoids	Bajakah stem extract has good anti-inflammatory effects with the most effective dose of 25 mg/kg.	[36]
		-	The ethanol extract of bajakah can inhibit inflammation process is up to 19.21% at 2.5 mg/kg.	[48]
		-	The water extract of 20 gram/100 ml of bajakah tampala could reduce the udem significantly and similar with sodium diclofenac.	[48]
2.	Antifungal	Flavonoids, Tannins, Phenol, Saponins	The antifungal activity of methanol extract showed a minimum inhibitory concentration (MIC) of 35% and a minimum kill concentration (MKC) of 47.5%, as measured by its concentration density. Flavonoids are present in bajakah tampala methanol extract, which inhibits and kills the growth of <i>Candida albicans</i> but not ethanol.	[40]
3.	Antipyretic	Flavonoids, Tannins, Saponins, Phenolic, Terpenoids	Bajakah stem extract has good antipyretic effects with the most effective dose of 25 mg/kg.	[36]
4.	Antioxidants	Phenols, Flavonoids, Saponins, Tannins Alkaloids, Flavonoids, Steroids	The provision of bajakah extract had antioxidant activity and was able to reduce serum malondialdehyde in wistar rats with hyperglycemia. It exhibited strong antioxidant against α , α -difenil- β -pikrilhidrazil (DPPH) radical with an IC ₅₀ value of 8.25 μ g/mL for ethanol bajakah tampala root extract.	[9] [27]
5.	Antidiabetic	Phenols, Flavonoids, Saponins, Tannins	The provision of bajakah extract had antidiabetic activity and was able to reduce serum malondialdehyde in wistar rats with hyperglycemia.	[9]
6.	Anti cancer	Phenolic, Flavonoids, Tannins, Saponins Phenols	Their anticancer activity is weak against breast cancer and uterine cervical cancer, medium categories against liver cancer and lung cancer, and is not toxic to normal cells. Breast anticancer assay with cell line 4T1 showed that the IC50 values of the hexane fraction and fraction of ethyl acetate in sequence were 20.0 mcg/mL and 7.4 mcg/mL.	[41] [10]
		alkaloid, flavonoid, terpenoid, and phenolic	Ethanol extract of bajakah (<i>Uncaria</i> sp) has cytotoxic activity with LC50 of 23.84 using method of Brine shrimp letality test (BSLT).	[37]
7.	Immunostimulator	Flavonoids, Saponins, Tannins	Treatment of the stem extract of bajakah tampala (<i>Spatholobus littoralis</i> Hassk.) in mice induced by fever with <i>Salmonella typhimurium</i> bacteria can increase the immune system (immunostimulator) thereby reducing fever and changes in behavior and mobility of mice.	[42]
8.	Antibacterial	Flavonoids, Alkaloids	Has antibacterial activity against <i>S. aureus</i> and antifungal against <i>C. albicans</i> .	[29]
		Fenol, Flavonoid, Alkaloid, Terpenoid, and Tanin Steroids, Flavonoids, Saponins, and Alkaloids	Extract of bajakah tampala has antibacterial activity against <i>P. aeruginosa</i> . <i>Propionibacterium acne</i> . Bajakah from West Kalimantan has antibacterial activities against <i>Micrococcus luteus</i> .	[28], [49] [50]
9	Antihyperlipidemia		Extract of bajakah with dose of 9 mg/200 gBW could reduce the cholesterol and Triglyceride level and increase the HDL level	[46]

The correlation between the active substance components of *Spatholobus* sp. would likely involve understanding how these different compounds interact with each other and how their combined presence contributes to the overall medicinal or therapeutic properties of the plant. Synergistic effects between various compounds may enhance their biological activity, making the plant more effective in treating certain health conditions. Based on data active substance components of *Spatholobus* sp., then we can describe the relationship between the two as in Figure 3.

Figure 3 showed that the active compounds of the herbal medicine support to ensure its biological activities. Therefore, the identification and determination of the contained metabolites should be conducted before the evaluation of biological activity will be evaluated. The active chemical contents were also needed to standardized the quality of raw materials and extracts to give the consistent efficacy, safety and quality.

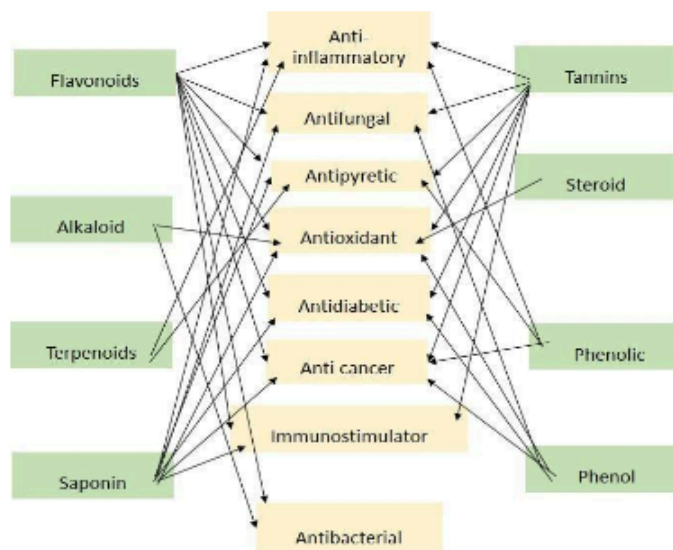


Figure 3. The relationships between active substance components of *Spatholobus* sp.

4. CONCLUSION

Bajakah is a traditional medicinal plant that has the potential as a valuable traditional medicine. Bajakah are indigenous plant from Kalimantan, and distributed in the tropical forest of Kalimantan, including Central Kalimantan, East Kalimantan and West Kalimantan. Bajakah has a wide variability in its use and has been used to treat various health conditions such as diarrhea, wounds, and cancer. Bajakah contains active compounds such as flavonoids, tannins, phenols, saponins, alkaloids, and terpenoids which have been studied to have pharmacological effects such as antioxidants, anti-inflammatory, antimicrobial, and anticancer. This review provides a deeper understanding of the potential of Bajakah as a native Indonesian traditional medicine and indicates the possibility of developing research in this field.

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
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BIOGRAPHIES OF AUTHORS







Nurkhasanah Mahfudh     is a professor in pharmaceutical science with specialist in herbal medicine at Faculty of Pharmacy Universitas Ahmad Dahlan, Yogyakarta. She has a research project for herbal medicine originated from Kalimantan with research grant from Ministry of Education, Culture, Research and Technology. She can be contacted at email: nurkhasanah@pharm.uad.ac.id.







Dwi Utami     is a lecturer in pharmaceutical science with specialist in medicinal and computational chemistry at Faculty of Pharmacy Universitas Ahmad Dahlan, Yogyakarta. She has particular research project in molecular docking of secondary metabolite of herbal medicine. She can be contacted at email: dwi.utami@pharm.uad.ac.id.







Siti Nashihah     is a lecturer in the Department of Pharmacognosy and Phytochemistry, Universitas Muhammadiyah Banjarmasin, Kalimantan Selatan. She works on development of natural materials. She can be contacted at email: siti.nashihah@umbjm.ac.id.







Mustofa Ahda     is a lecturer at Faculty of Pharmacy, Universitas Ahmad Dahlan, Yogyakarta, Indonesia. My research interests are in pharmaceutical chemistry, specifically metabolomic, chemometric, halal, and food analysis. He can be contacted at email: mustofa.ahda@pharm.uad.ac.id.



Andika     is a lecturer in the Department of Medicinal Chemistry, Faculty of Pharmacy Universitas Muhammadiyah Banjarmasin, Kalimantan Selatan. He works on computational chemistry, molecular docking and molecular dynamic. He can be contacted at email: andika@umbjm.ac.id.



Giriani Ayu Sabilla     has expertise in herbal medicines. She graduated from Master Program in Biology with focus on development of herbal medicine and physiology studies. She works as researcher fellow at Faculty of Pharmacy Universitas Ahmad Dahlan. She can be contacted at email: giriani.ayu.sabilla@mail.ugm.ac.id.