

## ICOPMAP SPECIAL EDITION

### REVIEW

# Bajakah plant (*Spatholobus littoralis* Hassk) as an anti-inflammatory

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#### Keywords

Anti-inflammatory  
Bajakah wood  
Dihydrokaempferol  
In silico  
In vitro  
In vivo

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#### Abstract

**Background:** Indonesian communities have long relied on traditional medicine, often derived from plant-based ingredients that are readily accessible throughout the region. One such plant, Bajakah (*Spatholobus littoralis* Hassk), native to Kalimantan and found in abundance in the deep forests of Borneo Island, has been used by local communities for generations. It serves as a traditional remedy for various ailments, including digestive disorders such as diarrhoea and dysentery, as well as musculoskeletal issues like muscle aches and wound healing. The wood of Bajakah Tampala contains chemical constituents such as flavonoids, alkaloids, and steroids, with flavonoids particularly noted for their ability to inhibit the expression of inflammatory mediators. **Method:** This research aims to assess the anti-inflammatory potential of Bajakah wood. The study, conducted as a narrative review, utilised scientific databases, including PubMed, ResearchGate, and Google Scholar. **Result:** In silico investigations identified dihydrokaempferol as a promising anti-inflammatory agent, while in vitro analyses confirmed the anti-inflammatory properties of Bajakah stem extract, demonstrated by its ability to prevent protein denaturation. **Conclusion:** Additionally, in vivo studies highlighted the significant anti-inflammatory efficacy of a low-dose Bajakah stem extract at 2.5 mg/kg.

#### Introduction

The body's reaction to infection includes inflammation, characterised by redness, swelling, pain, and heat. Inflammation is also known as a non-specific immune response, where the body works to protect itself from infection or tissue damage caused by microorganisms or foreign substances (Stankov, 2012). This process occurs due to the secretion of inflammatory mediators by cells. The enzyme cyclooxygenase (COX) plays a key role in inflammation, platelet aggregation, and pain. Non-steroidal Anti-Inflammatory Drugs (NSAIDs) and corticosteroid anti-inflammatories are typically used to counteract the inflammatory response. However, the use of these medications often leads to side effects on the cardiovascular system and liver, with significant impacts on the stomach and kidneys (Walker *et al.*, 2017). Therefore, there is a need for alternative medications that offer anti-inflammatory effects with minimal side effects.

In general, traditional medicine made from plant-based ingredients is commonly used in Indonesian communities and is readily available. One of the plants frequently employed in traditional medicine is Bajakah Wood (*Spatholobus littoralis* Hassk), a native Kalimantan plant. This plant is recognised for its medicinal properties by the local community and is known as "Kayu Bajakah Tampala." The Dayak community uses this plant as an alternative treatment for various diseases, a practice passed down through generations (Nastiti & Nugraha, 2022)

Bajakah Tampala wood contains chemical compounds such as flavonoids, alkaloids, and steroids (Iskandar & Warsidah, 2020). Among these, flavonoids play a more significant role in the pharmacological effects of medicinal plants. These compounds have potential wound-healing and anti-inflammatory properties (Panche *et al.*, 2016). Flavonoids can suppress the activity of enzymes (nitric oxide synthase isoforms,

cyclooxygenase, and lipoxygenase) that produce inflammatory substances like histamine, bradykinin, serotonin, leukotrienes, and prostaglandins. (Tuñón *et al.*, 2009). This study seeks to determine the mechanism of action of Bajakah Wood's anti-inflammatory effects.

## Methods

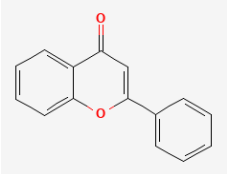
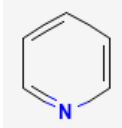
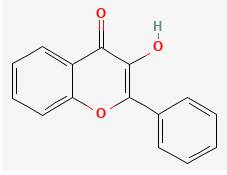
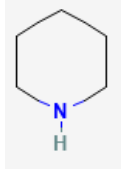
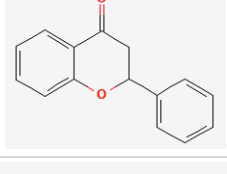
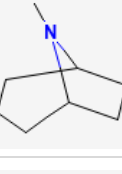
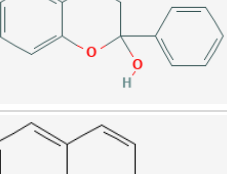
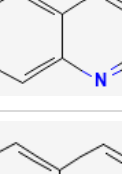
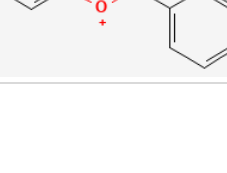
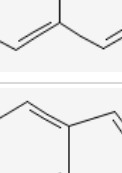
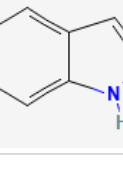
To understand the anti-inflammatory properties of Bajakah wood, the authors included studies that investigated the specific compound responsible for reducing inflammation. The study was a narrative review using the scientific electronic databases:

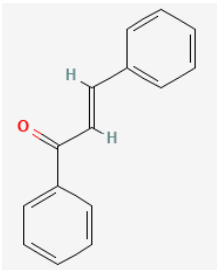
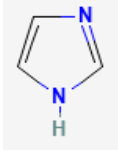
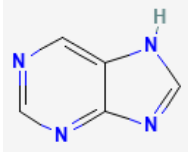
PubMed, Research Gate, and Google Scholar. Seven journals were used as the basis for comparison and discussion in this study. All related articles by keywords "Anti-inflammatory", "Bajakah Wood", "Dihydrokaempferol", "In Silico", "In Vitro", and "In Vivo" from Bajakah Wood were collected from June 29 to July 24, 2024. All authors contributed to the manuscript equally.

## Results

Table I shows the structure of derivative compounds of flavonoids and alkaloids.

**Table I: Structure of flavonoids and alkaloid derivative compounds**

Flavonoids		Alkaloids	
Compounds	Structure	Compounds	Structure
Flavone		Pyridine	
Flavonol		Piperidin	
Flavanone		Tropane	
Flavanol		Quinoline	
Anthocyanidin		Isoquinoline	
Chalcone		Indole	

Flavonoids		Alkaloids	
Compounds	Structure	Compounds	Structure
		Imidazole	
		Purine	

Based on a literature search regarding the anti-inflammatory compounds present in Bajakah wood stems (*Spatholobus littoralis* Hassk), seven highly

relevant sources were identified for analysis. These sources include one *in silico* study, two *in vitro* studies, and four *in vivo* studies, as detailed in Table II.

**Table II: Pharmacological test results of Bajakah as an anti-inflammatory**

No	Title	Methods	Parameter	Results	Researches
1	In silico analysis of active compounds in Bajakah wood stems ( <i>Spatholobus littoralis</i> Hassk) as psoriasis therapy	<b>In Silico.</b> The active compounds from Bajakah were identified using the Knapsack database. The PASS server predicted their antioxidant, anti-inflammatory, antipruritic, and immunosuppressive properties. Molecular docking studies using STITCH revealed their potential mechanisms of action in the human body, which were further analysed using Cytoscape.	Average Pz values	Bajakah's most potent bioactivity is as an antioxidant, primarily due to dihydrokaempferol, which has a high probability of activity ( $P_a = 0.691$ ). while computationally predicted to have potential testicular activity, empirical evidence remains limited or inconclusive.	(Prasetyorini et al., 2022)
2	The effect of Bajakah Tampala stem ( <i>Spatholobus littoralis</i> Hassk) extract on clotting time in vitro	<b>In Vitro.</b> One millilitre of venous blood will be collected from each group and placed into a separate test tube. Ten microliters of solution from each experimental group (excluding the normal group) will be added to the respective blood samples. Every 30 seconds, the blood surface will be gently disturbed with a lancet needle until a fibrin thread appears. The time taken for fibrin thread formation will be recorded.	Blood clotting time	Both the normal and negative control groups exhibited comparable average bleeding times. In contrast, the 5% Bajakah extract group demonstrated the shortest clotting time among all groups. This suggests that Bajakah extract contains secondary metabolites, such as tannins, saponins, and flavonoids, which accelerate blood clotting.	(Moyananda et al., 2023)
3	In vitro wound healing potential of stem extract of <i>Spatholobus littoralis</i> Hassk	<b>In Vitro.</b> A protein denaturation inhibition assay was employed to assess the anti-inflammatory activity of the test substance at seven concentration levels (250, 500, 750, 1000, 1600 ppm), including negative and positive control groups. Wound scratch assay on ten groups (1, 2.5, 5, 10, 50, 100, 500, 1000 ppm, negative and positive controls) to evaluate fibroblast migration.	Protein denaturation inhibition method	The study demonstrated that Bajakah stem extract, at concentrations ranging from 10 to 1000 ppm, stimulated fibroblast migration. However, the most pronounced effect was observed at concentrations of 500 and 1000 ppm, which led to complete wound closure within 22 hours.	(Ariesanti et al., 2021)
4	Anti-inflammatory and antipyretic effects of Bajakah Tampala stem Extract ( <i>Spatholobus littoralis</i> Hassk) in	<b>In Vivo.</b> The treatments consisted of the primary treatment (oedema induction with 1% carrageenan, fever induction with baker's yeast) and the second treatment, which was injection of Bajakah stem extract (EBB) at a dose of or NaCl (K! = negative control), 25 mg/kg (K2), 50	Oedema area, leukocyte count, and rectal temperature	The study's results showed that the administration of EBB reduced oedema and leukocyte count after induction with 1% carrageenan and the rectal temperature of mice after induction with baker's yeast. The conclusion is that EBB has sound anti-inflammatory and	(Zayani et al., 2022)

No	Title	Methods	Parameter	Results	Researches
	mice ( <i>Mus musculus</i> L.)	mg/kg (K3), and 100 mg/kg (K4) and 80 mg/kg aspirin (K5 = positive control)		antipyretic effects, with the most effective dose being 25 mg/kg.	
5	Anti-inflammatory activity of Bajakah wood ( <i>Spatholobus littoralis</i> Hassk) extract	<b>In Vivo.</b> This study used 21 male Wistar rats aged 3-4 months, weighing between 150 and 250 grams. The anti-inflammatory activity test used the 1% carrageenan induction method, administered subplantar to the soles of the rats' feet. Anti-inflammatory activity was measured with a plestimometer starting from the minute (before administration of 1% carrageenan), 60, 120, 180, and 240 minutes after induction of 1% carrageenan. Data analysis was performed using one-way ANOVA	Average percentage of oedema in rat feet and average percentage of inhibition in rat feet	The anti-inflammatory potential was determined by calculating the percentage inhibition of oedema formation in the treatment groups, which exhibited a statistically significant reduction in oedema volume ( $p < 0.05$ ). The 400 mg/kg body weight dose was the most effective, inhibiting oedema formation by 87.65%.	(Nastiti & Nugraha, 2022)
6	Anti-inflammatory activity test of ethanol extract of Bajakah stem root ( <i>Spatholobus littoralis</i> Hassk) on male white rats ( <i>Rattus novergicus</i> )	<b>In Vivo.</b> Bajakah Roots ethanol extract was prepared using the percolation method with 96% ethanol solvent. Phytochemical screening of the crude extract, positive control test (Sodium Diclofenac 25 mg), and EEKB suspension doses of 100, 200, and 300 mg/KgWB were performed. Bajakah Roots ethanol extract dose of 300 mg/KgBW had an anti-inflammatory effect with a percentage of inflammation value of 13,66%, an inflammation inhibition value of 82,05%, and a sodium diclofenac value of 25 mg. KgBW has a percentage of inflammation value of 11,6% and a percentage of inflammation inhibition value of 96,90%.	Inflammation over time for each treatment, and inflammation inhibition over time for each treatment	The decrease in percent inflammation in the Na Diclofenac 25 mg, Bajakah Roots ethanol extract 100, 200, and 300 mg/KgBW groups began at 180 minutes and continued until 360 minutes. The positive group (Natrium Diclofenac) had the lowest percent inflammation, followed by the Bajakah Roots ethanol extract 100, 200, and 300 mg/KgBW groups. It can be concluded that the higher the dose of Bajakah Roots ethanol extract given, the lower the percent inflammation in the carrageenan-induced mouse paws, approaching that of Natrium Diclofenac (positive control).	(Amalia & Dalimunthe, 2022)
7	Anti-inflammatory activity of Bajakah stem ( <i>Spatholobus littoralis</i> Hassk) ethanolic extract in carrageenan-induced paw oedema mice	<b>In Vivo.</b> A randomized controlled trial was conducted to assess the anti-inflammatory potential of Bajakah extract. Adult Wistar rats were randomly assigned to five groups: a water control, a diclofenac control, and three Bajakah extract dose groups (2.5, 250, and 1250 mg/kg). Carrageenan-induced paw oedema was used as the inflammatory model. Paw oedema was measured over a 210-minute period.	Anti-inflammatory effects of Bajakah extract and oedema reduction	The carrageenan-induced paw oedema model revealed a significant increase in paw diameter across all groups. While all Bajakah extract doses (2.5, 250, and 1250 mg/kg) showed similar AUC values from 150 to 210 minutes, diclofenac sodium (positive control) exhibited the lowest total AUC (236 mm.min). Bajakah extract at the lowest dose (2.5 mg/kg) demonstrated the highest anti-inflammatory effect (19.21% inhibition), approaching that of diclofenac sodium (21.53%).	(Rousdy et al., 2022)

Based on the data provided from in vivo studies, low-dose Bajakah stem extract (*S. littoralis* Hassk) at 2.5 mg/kg (study 4) showed promising anti-inflammatory efficacy (Table III). Bajakah stem extract administered at a dose of 2.5 mg/kg was able to provide 19.21% & inflammation inhibition, approaching the effectiveness

of the control drug (diclofenac sodium) of 21.53%. Low doses are generally associated with a better safety profile. However, further research is needed to confirm these findings and determine the optimal safe and effective dose.

Table III: Dosage from the in vivo method

Study in vivo	Part of Bajakah	Dosage	Effects
1	Stem	25, 50, 100 mg/kg	Reduced oedema, leukocytes, and temperature
2	Wood	400 mg/kg	Reduced oedema
3	Root	100, 200, 300 mg/kg	Reduced inflammation
4	Stem	2.5, 250, 1250 mg/kg	Reduced inflammation

## Discussion

### Chemical compounds of Bajakah

Bajakah wood (*Spatholobus littoralis* Hassk), also known as Bajakah tampala, is a traditional herbal medicine inherited from the Dayak people of Kalimantan (Nastiti & Nugraha, 2022). This plant is rich in bioactive compounds such as flavonoids, alkaloids, and steroids, which are believed to contribute to its efficacy in treating various diseases.

Flavonoids exert their anti-inflammatory effects by inhibiting the enzymes cyclooxygenase and lipoxygenase, which are involved in the production of arachidonic acid. This reduction in arachidonic acid leads to the suppression of the synthesis of various inflammatory mediators such as PGE<sub>2</sub>, leukotrienes, histamine, bradykinin, and thromboxane. Ultimately, this results in oedema reduction and pain relief (Verri *et al.*, 2012)

In addition to flavonoids, other compounds like alkaloids also possess anti-inflammatory properties. Alkaloids work by inhibiting the release of prostaglandins in inflamed tissues (Barbosa-Filho *et al.*, 2006). Another group of compounds with anti-inflammatory effects are steroids. The chemical structure of plant steroids makes them ideal candidates for use as anti-inflammatory agents (Patel *et al.*, 2015).

A study by Saputera and colleagues (2019) employed phytochemical screening techniques to confirm the presence of flavonoids in Bajakah root. The positive flavonoid test involved the reaction of Bajakah extract with lead acetate, resulting in a brown precipitate. This precipitation is attributed to the hydroxyl groups present in the benzene rings of flavonoids. This observation corroborates the presence of flavonoids in the Bajakah root.

Furthermore, the presence of saponins in the Bajakah root was also established. Hasanah and colleagues (2021) described a method for detecting saponins: dissolving the extract in water, heating it to boiling, vigorously shaking it vertically to form foam, and adding one drop of 1 M HCl. The persistence of foam after HCl addition indicates the presence of saponins.

The presence of tannins in the Bajakah root suggests the existence of proteins as well. Mueller-Harvey and colleagues (2006) explained that tannins can interact with proteins through three types of bonds: hydrogen bonds, ionic bonds, and covalent bonds. Hydrolysed and condensed tannins bind to proteins via hydrogen bonds between the phenolic groups of tannins and the carboxyl group of proteins.

Abdulrahman and colleagues (2021) conducted a phytochemical screening study to identify the bioactive compounds present in ethanol extracts of the Bajakah stem. Their findings revealed the presence of alkaloids, hydroquinone/tannin phenol, and flavonoid compounds. However, saponin and steroid compounds were not detected in the stem extract.

### Bajakah as an anti-inflammatory agent

Research findings from several journals reviewed indicate that the Bajakah plant (*S. littoralis* Hassk) possesses anti-inflammatory activity. In silico studies suggest that active compounds in Bajakah wood stem have potential therapeutic applications for psoriasis. The results indicate that dihydrokaempferol has the highest potential as an antioxidant, anti-inflammatory, antipruritic, and immunosuppressive agent. While computer analysis suggests the potential of these compounds, further in vitro and in vivo studies are needed to substantiate their effectiveness.

The main results of the phytochemical screening of bajakah are flavonoids, phenolics, saponins, tannins, steroids, and terpenoids. Flavonoid compounds have potential as wound healers and anti-inflammatory agents (Panche *et al.*, 2016). These compounds can block the activity of enzymes like nitric oxide synthase, cyclooxygenase, and lipoxygenase, which are responsible for producing inflammatory substances such as histamine, bradykinin, serotonin, leukotrienes, and prostaglandins (Corwin *et al.*, 2009). Flavonoid compounds also have antioxidant properties that can accelerate wound healing and inflammation (Ginwala *et al.*, 2019). In vitro studies demonstrate that Bajakah stem extract (Study 3) exhibits stronger anti-inflammatory potential by inhibiting protein denaturation, a process involved in inflammation. In

contrast, Study 2 investigates blood clotting time, which is not directly related to inflammation

### Anti-inflammatory mechanism

Inflammation is a complex tissue response to various “attacks” such as bacterial infections, burns, or wounds (Chen *et al.*, 2013). This process is characterized by several hallmarks, including redness, heat, pain, and swelling. During inflammation, the body releases a variety of systemic mediators, cytokines, and chemokines. These molecules play a crucial role in attracting cells to the injury site, triggering the inflammatory stimulus responses, and ultimately aiding tissue repair. However, if the inflammatory stimulus

persists, it can lead to chronic inflammation, a prolonged condition with detrimental effects.

As seen in Figure 1, inflammation triggers the release of prostaglandins, signalling molecules that promote inflammation. Medications like NSAIDs combat inflammation by blocking the production of prostaglandins (Brunton *et al.*, 2008). An enzyme called cyclooxygenase (COX) is responsible for converting arachidonic acid into prostaglandins. COX has two primary forms: COX-1 and COX-2. COX-1 is constantly present and helps maintain normal bodily functions and stability. Conversely, COX-2 is induced by inflammatory stimuli like cytokines, endotoxins, and growth factors (Zukhrullah *et al.*, 2012).

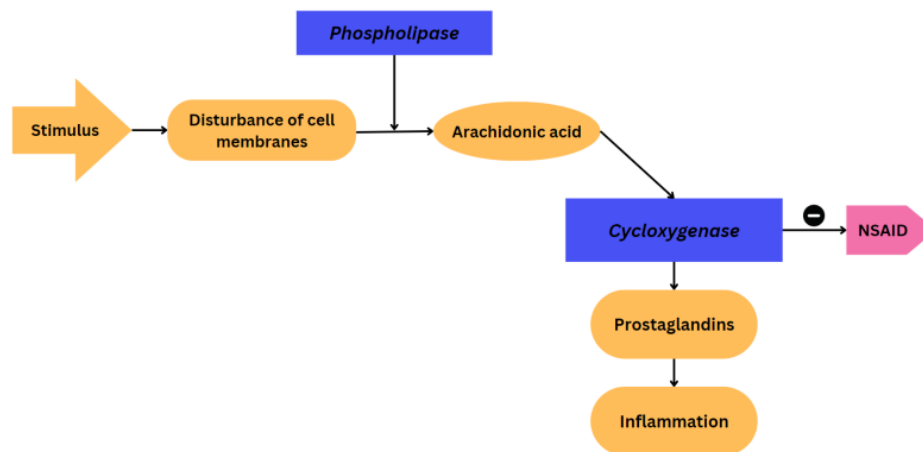


Figure 1: Anti-inflammatory mechanism

Inflammation manifests in two forms: acute and chronic. Acute inflammation is a short-term response that involves various factors to combat infection or injury. The acute inflammatory process is initiated by a range of internal and external triggers that cause damage to tissues and blood vessels. In response, the body enhances blood flow to the affected area. This occurs through the dilation of arteries and capillaries, facilitated by prostaglandins, leukotrienes, and nitric oxide. This increased blood flow causes blood to pool and flow too slowly in the injured area (Putri & Anita, 2017).

### Comparing Bajakah wood to regular anti-inflammatory

As a Nonsteroidal Anti-Inflammatory Drug (NSAID), aspirin has the ability to relieve pain, reduce fever, and decrease inflammation. It works by inhibiting the cyclooxygenase-1 (COX-1) enzyme, thus blocking the production of prostaglandins, which promote

inflammation and blood clotting (Rahmadanita & Sumarno, 2019).

The Bajakah plant (*S. littoralis Hassk*) exhibits significant anti-inflammatory properties. Phytochemical analysis of Bajakah revealed a rich profile of flavonoids, phenolics, saponins, tannins, steroids, and terpenoids. Flavonoids, in particular, have been shown to promote wound healing and exert potent anti-inflammatory effects (Panche *et al.*, 2016). These compounds achieve their anti-inflammatory effects by inhibiting the expression of nitric oxide synthase isoforms, cyclooxygenase, and lipoxygenase, thereby suppressing the release of inflammatory mediators such as histamine, bradykinin, serotonin, leukotrienes, and prostaglandins (Corwin *et al.*, 2009). Additionally, flavonoids possess antioxidant properties that contribute to accelerated wound healing and reduced inflammation (Ginwala *et al.*, 2019).

### Formulations of Bajakah as an anti-inflammatory agent

Agustin and Wibowo (2023) define encapsulation as the process of coating one material (core) with another material (coating) to achieve various objectives. The core material can be an active substance, internal phase, or filler, while the coating material can be a coating, external phase, or carrier material. Encapsulation serves as a multifaceted technique employed to safeguard sensitive substances from environmental factors, preserve organoleptic properties such as colour, flavour, and aroma, achieve controlled release of drug substances, ensure safe handling of toxic materials, enable targeted drug delivery, and mitigate adverse drug reactions (Jyothi *et al.*, 2010).

In the realm of formulations derived from natural sources, microencapsulation stands out as a prominent technique. This process is applied to a wide range of natural ingredients to enhance their stability, safeguard them from environmental influences, and preserve or augment their activity for improved effectiveness and stability. Additionally, microencapsulation serves as a solution for extending the shelf life of the core substance extracted from natural materials. This encapsulation process involves employing polymers that act as a protective shield for the core substance while simultaneously functioning as a stabiliser against external disturbances. Consequently, the core substance can be shielded and its stability maintained. The microencapsulation method emerges as an excellent choice for aiding in the preservation of the stability of core substances derived from natural sources (Pratama *et al.*, 2021).

### Conclusion

Based on the research findings reviewed from various journals, the Bajakah plant, specifically the wood stems of *Spatholobus littoralis* Hassk, exhibits significant anti-inflammatory properties. In silico studies suggest that dihydrokaempferol, a compound found in Bajakah, shows potential as an antioxidant, anti-inflammatory, antipruritic, and immunosuppressive agent. Moreover, phytochemical screening of Bajakah reveals the presence of flavonoids, phenolics, saponins, tannins, steroids, and terpenoids, with flavonoids particularly showing promise as wound healers and anti-inflammatory agents. In vitro studies further support the anti-inflammatory potential of Bajakah stem extract by inhibiting protein denaturation, a key process in inflammation. Additionally, in vivo studies indicate that low-dose Bajakah stem extract at 2.5

mg/kg demonstrates significant anti-inflammatory efficacy, nearing the effectiveness of the control drug diclofenac sodium. Nevertheless, human clinical trials are required to verify these findings and establish the safety profile of Bajakah for anti-inflammatory purposes.

### Acknowledgement

The author would like to thank the Republic of Indonesia Defence University lecturers, laboratory assistants, and friends for all the input provided.

### Source of funding

This review received no external funding.

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