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Phytochemical Constituents and Pharmacological Activities of *Picrasma javanica*

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Abstract

Picrasma javanica Blume or also known as *Picrasma nepalensis* or *Picrasma philippinensis* is a plant belongs to the Simaroubaceae family, which is known for its secondary metabolites namely quassinoids with various pharmacological properties including antitumor, antimalarial and antiviral. The plant traditionally used as medicine for different diseases in Myanmar, Thailand and Indonesia.

The purpose of this study is to discern the phytochemical constituents and pharmacological activities of *Picrasma javanica.*

The background, phytochemical constituents and pharmacological benefits of *Picrasma javanica* were reviewed and supported from previous studies, including in vivo and in vitro studies. The literature used in the review comprises of published books, journals, reviews and articles published from the year of 1969 to 2018, which are available in ScienceDirect, PubMed, Scopus and GoogleScholar. Chemical structures presented in this paper are either drawn with ACD/ChemSketch.

Picrasma javanica possesses several phytochemical constituents, including quassinoids, alkaloids and triterpenoids. Compounds of the plant were isolated and studied for their pharmacological activities such as antimalarial, antiproliferative, antiviral, antimicrobial and membrane stabilising activity. Most importantly, these studies showed that the key players for the pharmacological benefits are quassinoids and alkaloids present in the plant.*Picrasma javanica* indeed has therapeutic potentials which may be beneficial for people. However, further extensive studies must be done on the plant as the detailed information on its pharmacological activities are still lacking.

Keywords: Simaroubaceae, *Picrasma javanica*, quassionoids, phytochemicals, pharmacological properties.

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1. Introduction

The use of natural products as lead compounds for the research and development of new drugs is nothing new. In fact, it has been a practice throughout history, especially with new diseases and illnesses emerging due to the increase in world's population and changing environments. Natural products such as plants and marine organisms are being utilised as they comprise of vast chemical and structural diversity with various biological activities. These activities, when studied extensively with recent technological advances may guide the new drug discoveries. In light of this, this paper will be highlighting the phytochemistry and pharmacological activities of a plant species, namely *Picrasma javanica*.

Picrasma javanica Blume or also known as *Picrasma nepalensis* or *Picrasma philippinensis* is a plant belongs to the Simaroubaceae family. Simaroubaceae family consists of 32 genera with more than 170 species of plants and is distributed throughout the tropical areas of America,west Africa, Madagascar, regions of Asia and Australia. The family is known for its secondary metabolites namely quassinoids which possess a broad range of pharmacological properties including antitumor, antimalarial and antiviral [1].

*P. javanica*is a medium-sized tree which may grow up to 20m high, commonly found in north eastern India and throughout south east Asia. The plant is often characterised by its bitterness, attributed to the presence of quassinoids, as any other plants in the Simaroubaceae family [2]. The plant was traditionally used in countries like Myanmar, Thailand and Indonesia as a medication for malaria, cancer, acquired immune deficiency syndrome (AIDS) [3] and to reduce fever as well as a replacement of quinine [2, 3].

The tradition of using *P. javanica* as medicine in treating diseases provide the means for researchers to initiate studies on the activities on the plant. Besides, Simaroubaceae family was already known for their potential as a source of bioactive molecules with curative properties that are of benefits to the people. Nonetheless, the plant and the other members of the family have yet to be extensively studied by the researchers. With this in mind, the present paper intended to focus on the phytochemical and pharmacological properties of *P. javanica* to direct future studies and exploitations of the values attributed to the plant.

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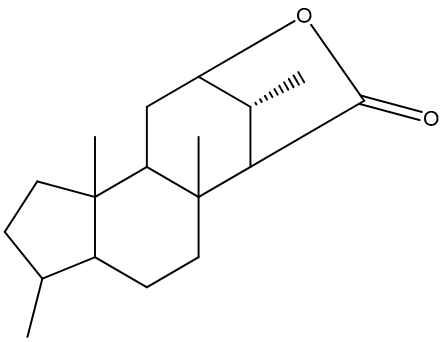
2. Methodology

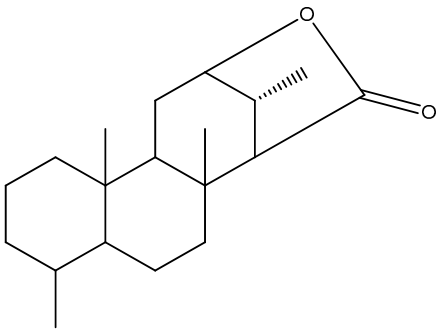
This paper highlighted the phytochemical constituents and pharmacological activities as well as the mechanisms of *P. javanica* that were previously studied including both *in-vivo* and *in-vitro* studies. The literature used in the review comprises of published books, journals, reviews and articles published from the year of 1969 to 2018, which are available in ScienceDirect, PubMed, Scopus and GoogleScholar. Chemical structures presented in this paper are either drawn with ACD/ChemSketch or obtained from the literature. The keywords used in searching the references are Simaroubaceae; Picrasma javanica; Quassionoids; phytochemical; pharmacological properties; antimalarial; anti-proliferative activity; antiviral; antibacterial; membrane stabilizing activity.

3. Phytochemical Constituents

As described above, Simaroubaceae family consists of plants with dozens of individual compounds which have been recognised; some of which are quassinoids, alkaloids, triterpenes, steroids and other different classes. Furthermore, the researchers have deduced that quassinoids are the most abundant group of compounds in this particular family [1]. These group of compounds may be in the free state or in the form of esters and they all chemically related [4]. In fact, the bitterness attributed to the plants in Simaroubaceae family is due to the presence of quassinoids [5, 6]. This group of compounds can be classified into 5 distinct groups according to their basic skeletons. The 5 groups are, C-18 **(1)**, C-19 **(2)**, C-20 **(3)**, C-22 **(4)** and C-25 **(5)**[1, 4, 6]. Compound **1-5** in **Figure 1** demonstrate the carbon skeleton structure of quassinoids.



C-18 **(1)** carbon skeleton



C-19 **(2)** carbon skeleton

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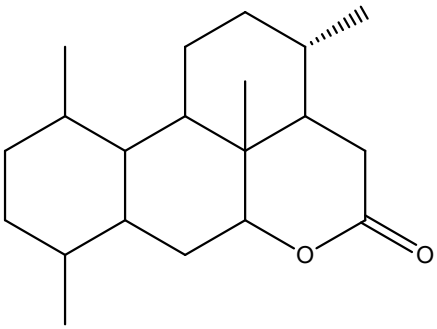
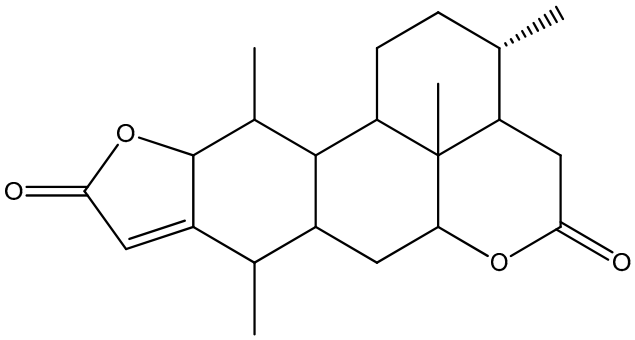
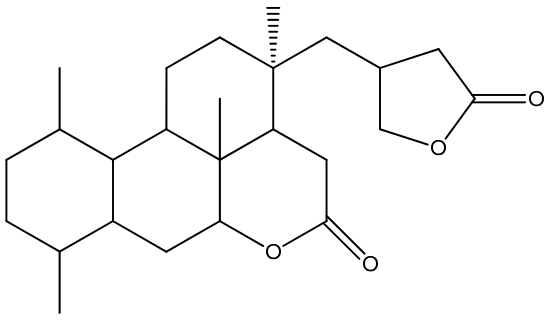
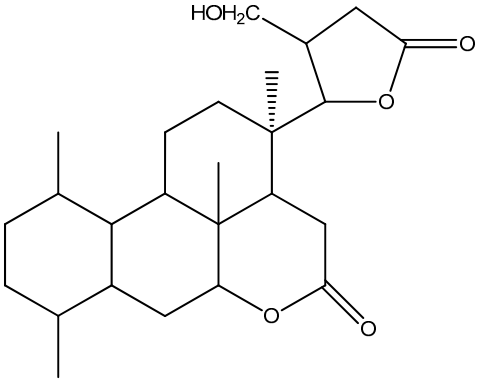


C-20 **(3)** carbon skeleton



C-22 **(4)** carbon skeleton





C-25 **(5)** carbon skeleton (a, b)

Figure 1. Basic skeletons of quassinoids.

*P. javanica*was found to have many phytochemical constituents that were isolated from many different parts of the trees. This includes the stem, leaves, bark and fruits. These compounds were obtained and identified by numerous analytical methods such as Nuclear Magnetic Resonance (NMR) Spectroscopy, Infrared (IR) Spectroscopy, High Performance Liquid Chromatography (HPLC) and Ultraviolet (UV) Spectroscopy [7, 8].**Table 1** elucidated the current findings on the compounds of *P. javanica.* Other than quassinoids, quassinoid glycosides, alkaloids and triterpenoids were also extracted from the plants.From the table, it can be concluded that the majority compounds found in P. *javanica* are quassinoids, which is in line with the statement that "quassinoids can be considered a taxonomic marker of the Simaroubaceae family" [1].

Table 1 Chemical constituents of *Picrasma javanica.*

Compound Class	Chemical Constituents	Part of Plants	Reference
Quassinoids	Javanicin B **(6)**	Bark	[7]
	Javanicins E **(7)**, F **(8)**, G **(9)**, M **(10)**	Bark	[8]
	Javanicins H **(11)**, I **(12)**, J **(13)**	Leaves	[9]
	Javanicins K **(14)**, L **(15)**, O **(16)**, R **(17)**, S **(18)**	Leaves	[10]
	Javanicin T **(19)**	Stem	[10]
	Javanicin N **(20)**	Wood	[11]
	Javanicins P **(21)**, Q **(22)**	Leaves	[11]
	Javanicins U **(23)**, V **(24)**, W **(25)**	Stem	[12]
	Javanicins X **(26)**, Y **(27)**	Bark	[12]
	Javanicin Z **(28)**	Bark	[13]

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	Dihydrojavanicin Z **(29)**	Bark	[13]
	Picrajavanins A **(30)**, B **(31)**	Not described	[5]
		Bark	[3]
	Picrajavanins C **(32)**, D **(33)**, E **(34)**, F **(35)**, G **(36)**	Bark	[3]
	Picrajavanins H **(37)**, I **(38)**, J **(39)**, K **(40)**, L **(41)**, M **(42)**	Bark	[14]
	Neoquassin **(43)**	Stem	[15]
	Picrasin A **(44)**	Stem	[15]
		Bark	[14]
	Nigakilactones B **(45)**, F **(46)**	Leaves, stem	[10]
Quassinoid Glycosides	Javanicinosides B **(47)**, C **(48)**	Bark	[7]
	Javanicinosides D **(49)**, F **(50)**, H **(51)**	Bark	[15]
	Javanicinoside E **(52)**, G **(53)**	Stem	[15]
	Javanicinosides I **(54)**, J **(55)**, K **(56)**, L **(57)**	Stem	[16]
Alkaloids	5-hydroxydehydrocrenatine **(58)**	Not described	[17]

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	5-hydroxycrenatine **(59)**	Not described	[17]
	4-methoxy-1-vinyl-β-carboline **(60)**	Bark	[18]
	6-hydroxy-4-methoxy-1-vinyl-β-carboline **(61)**	Not described	[19]
	Javacarboline **(62)**	Stem	[20]
Triterpenoids	Hispidol A **(63)**	Stem	[15]
	Lanosta-7,24-dien-3-one **(64)**	Stem	[15]

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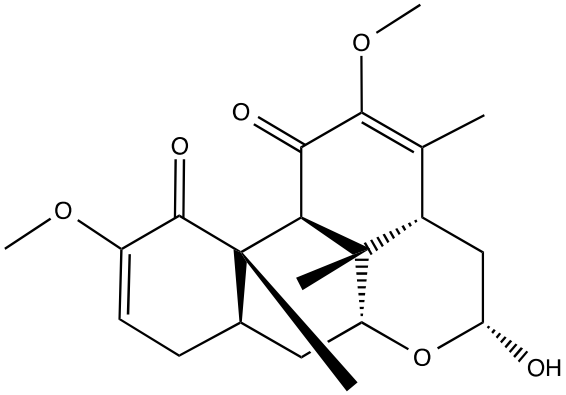
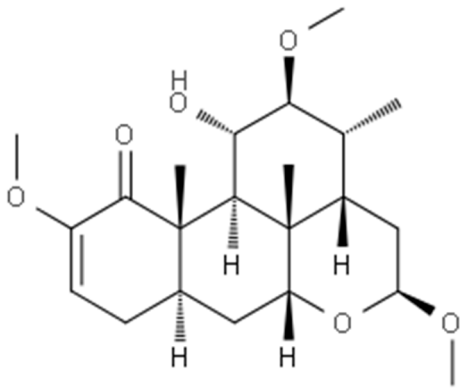
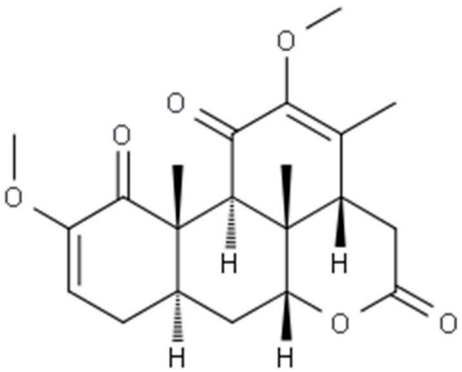


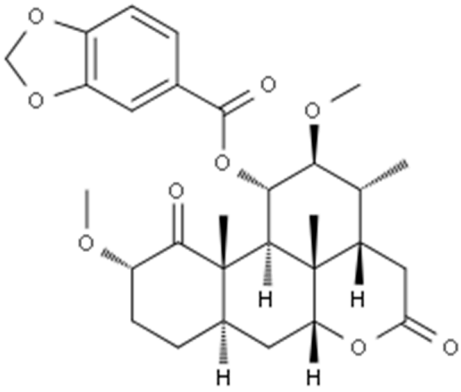
Javanicin B **(6)**



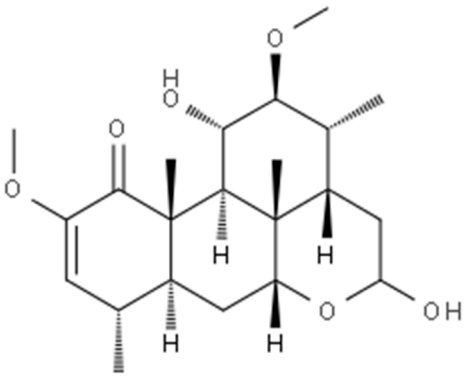
Javanicin E **(7)**



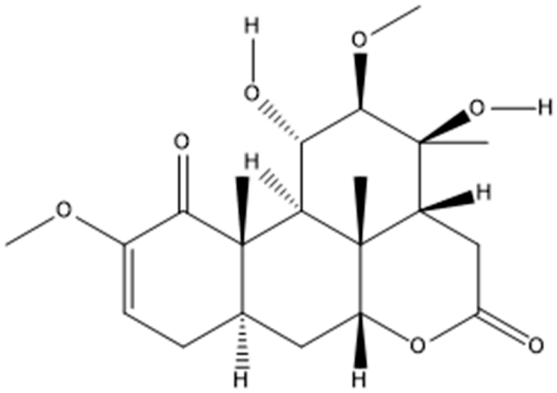
Javanicin F **(8)**



Javanicin G **(9)**



Javanicin M **(10)**



Javanicin H **(11)**

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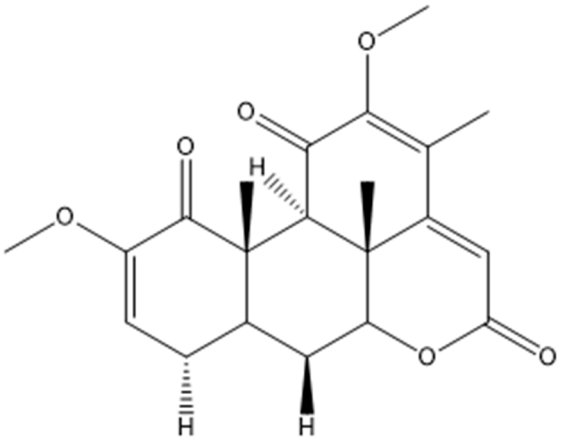
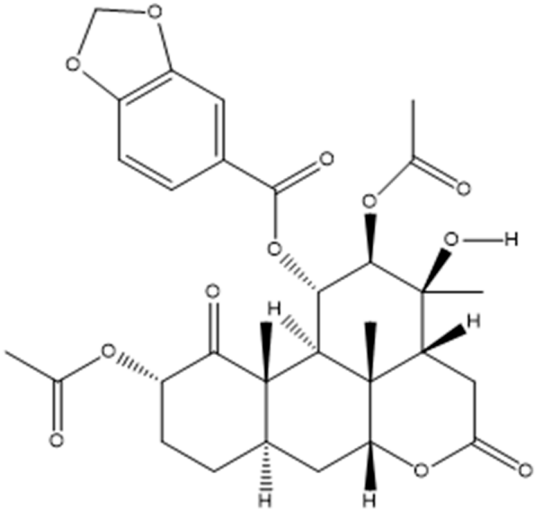
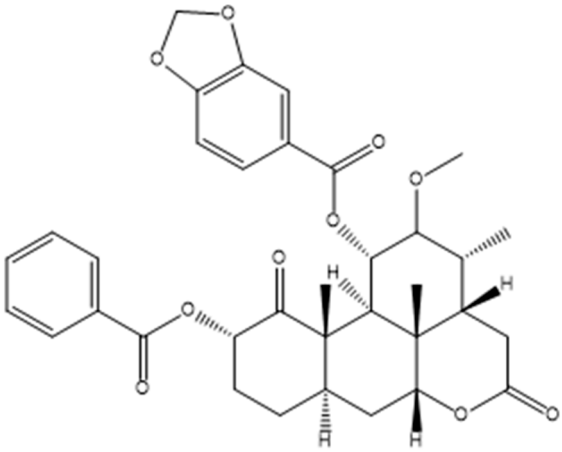


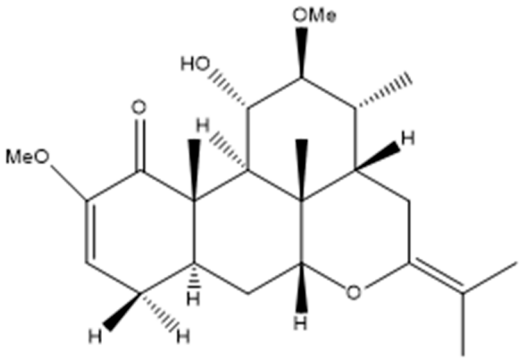
Javanicin I **(12)**



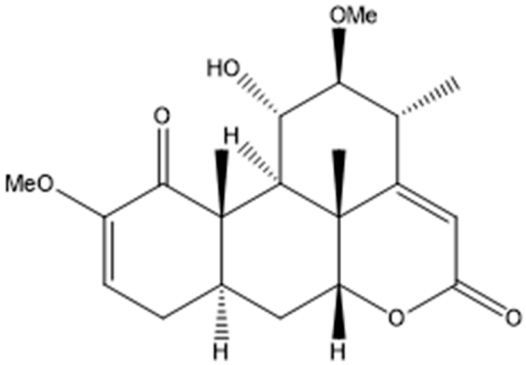
Javanicin J **(13)**



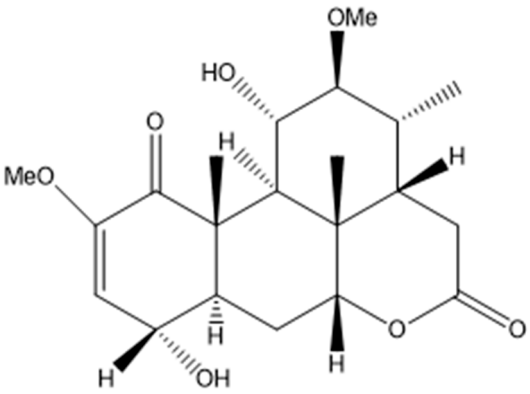
Javanicin K **(14)**



Javanicin L **(15)**



Javanicin O **(16)**



Javanicin R **(17)**

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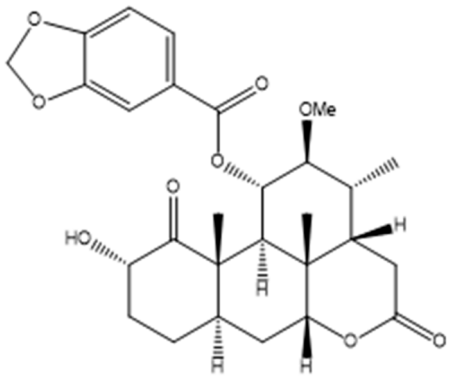
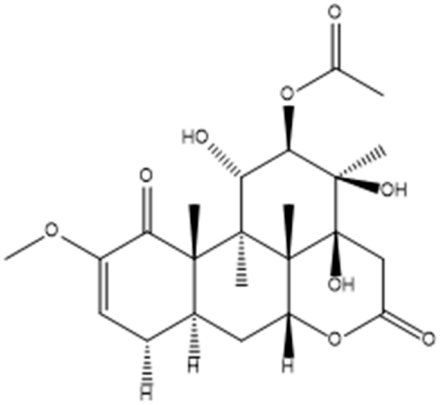
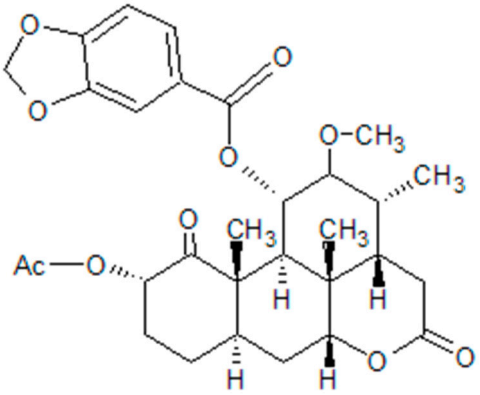


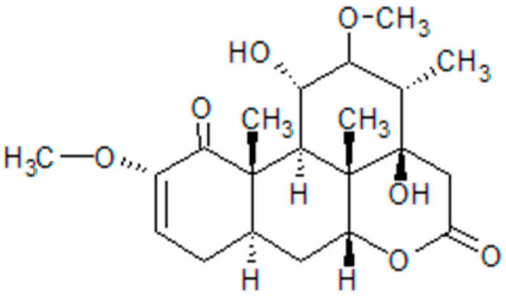
Javanicin S **(18)**



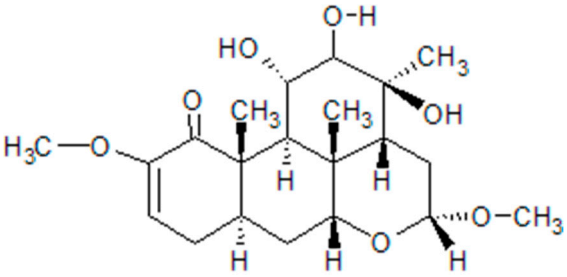
Javanicin T **(19)**



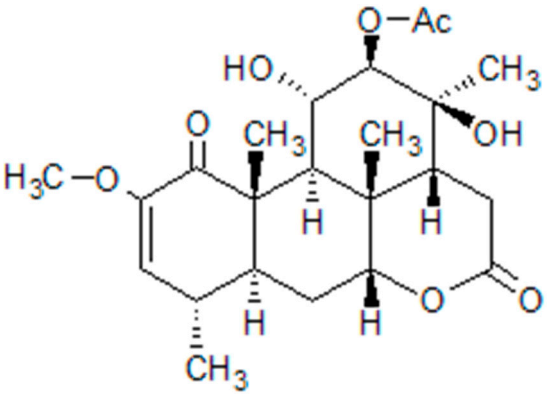
Javanicin N **(20)**



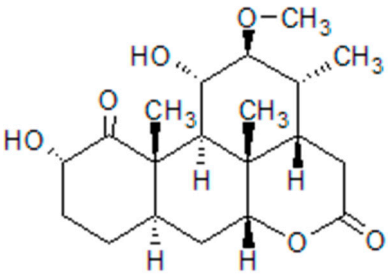
Javanicin P **(21)**



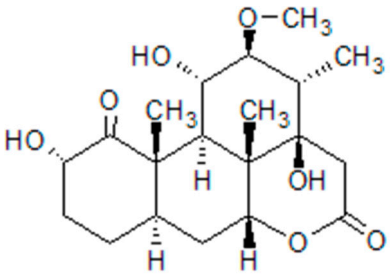
Javanicin Q **(22)**



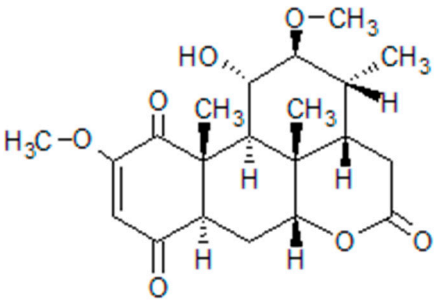
Javanicin U **(23)**



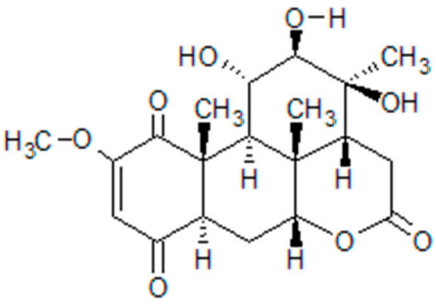
Javanicin V **(24)**



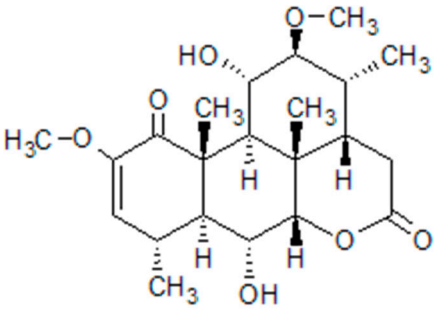
Javanicin W **(25)**



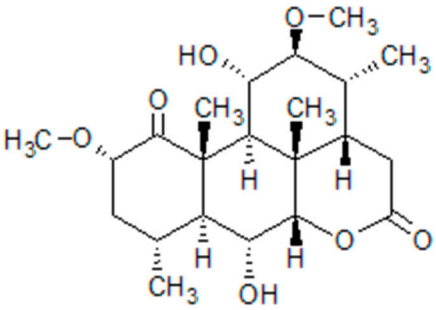
Javanicin X **(26)**



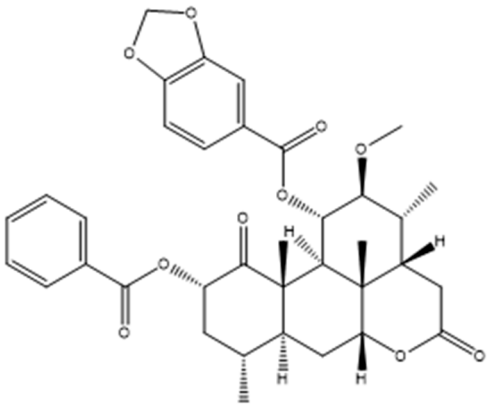
Javanicin Y **(27)**



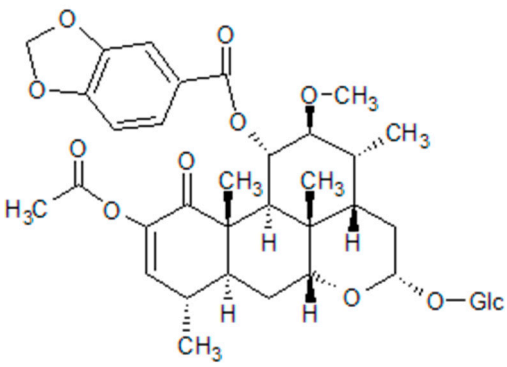
Javanicin Z **(28)**



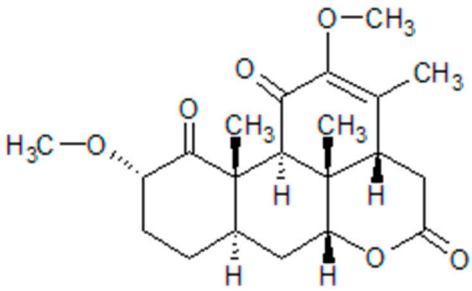
Dihydrojavanicin Z **(29)**



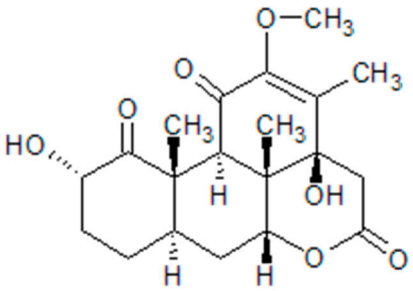
Picrajavanin A **(30)**



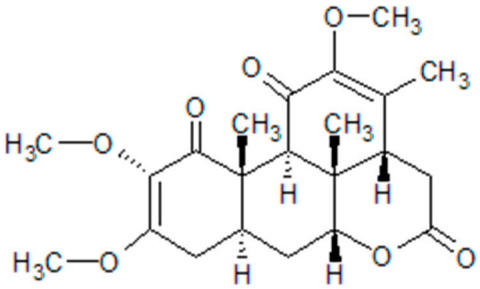
Picrajavanin B **(31)**



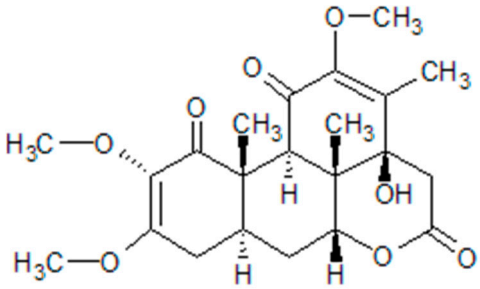
Picrajavanin C **(32)**



Picrajavanin D **(33)**



Picrajavanin E **(34)**



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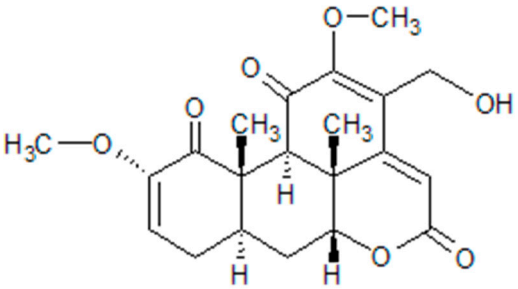
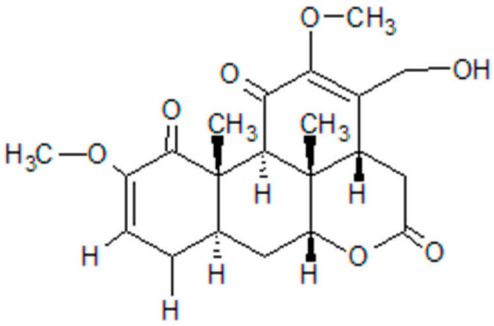


Picrajavanin G **(36)**



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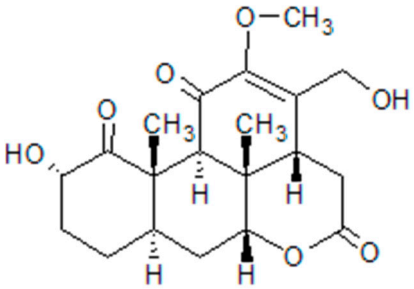
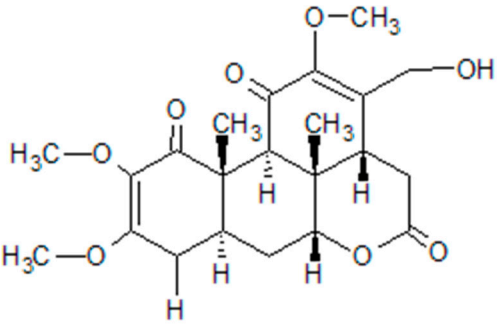


Picrajavanin I **(38)**



Picrajavanin J **(39)**

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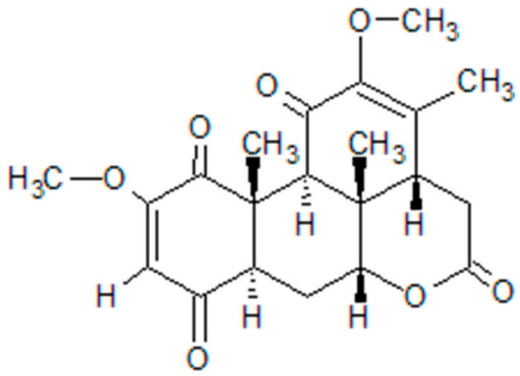
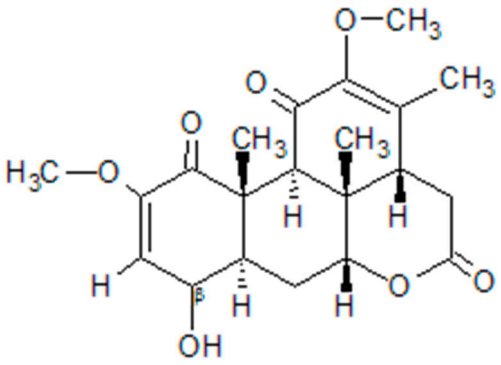
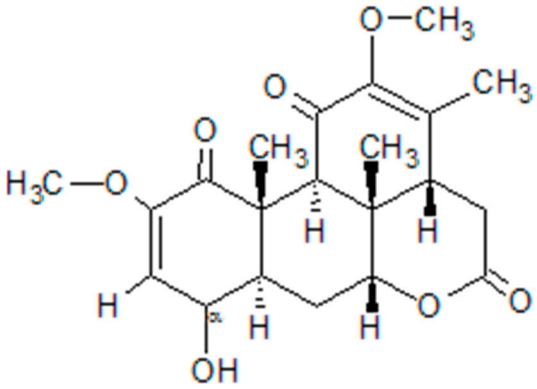


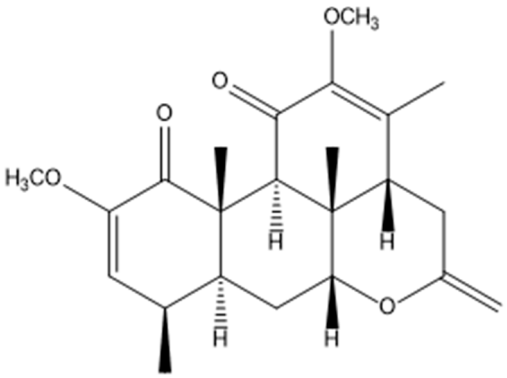
Picrajavanin K **(40)**



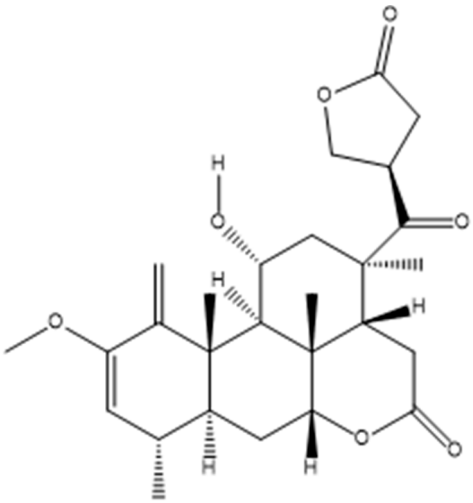
Picrajavanin L **(41)**



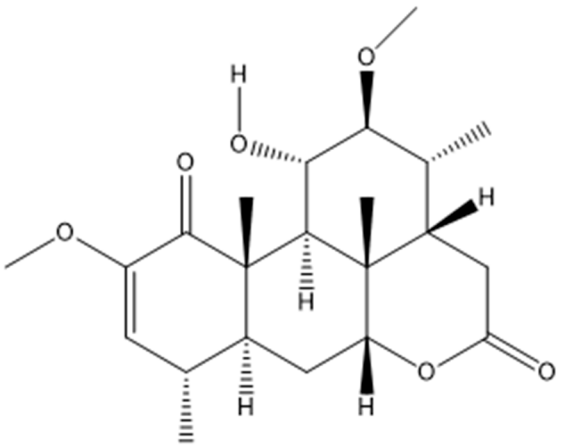
Picrajavanin M **(42)**



Neoquassin **(43)**



Picrasin A **(44)**



Nigakilactone B **(45)**

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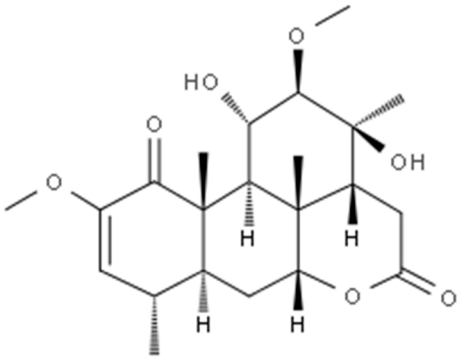
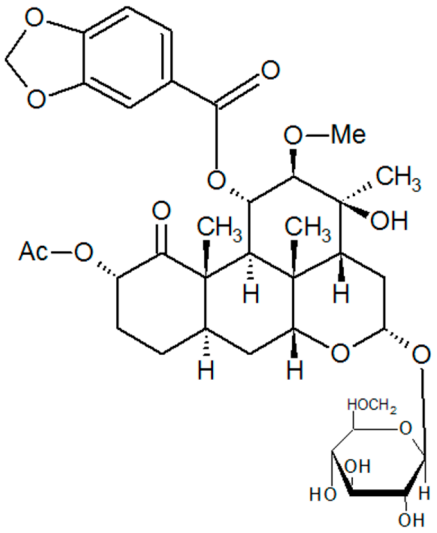
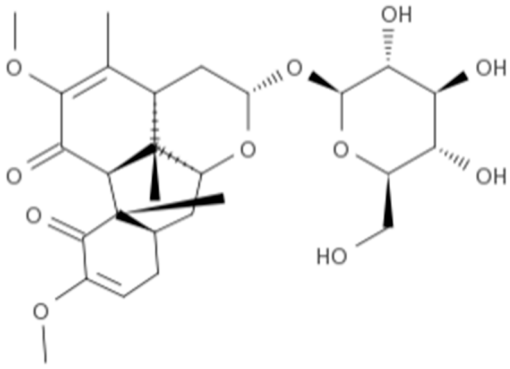


Nigakilactone F **(46)**

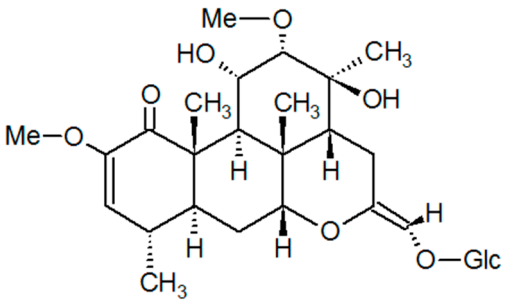
Figure 2 shows quassinoid constituents of *Picrasma javanica.*



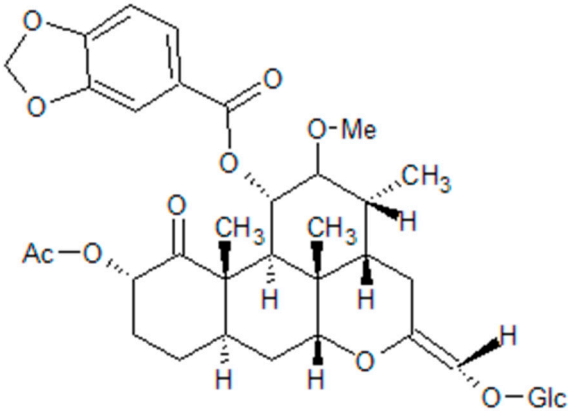
Javanicinoside B **(47)**



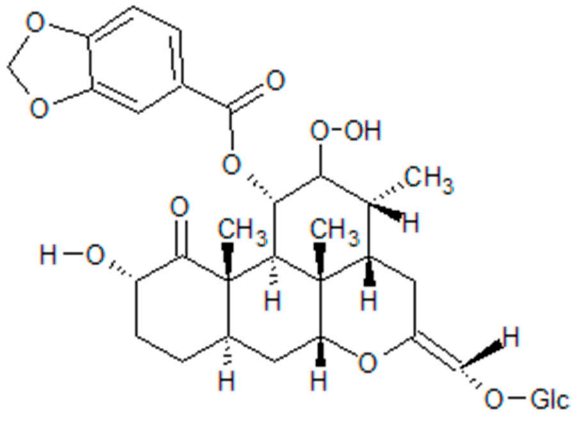
Javanicinoside C **(48)**



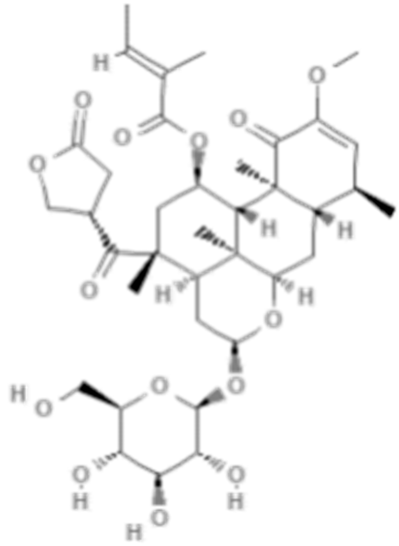
Javanicinoside D **(49)**



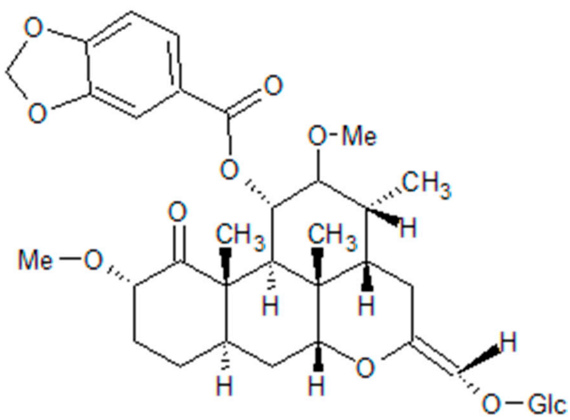
Javanicinoside F **(50)**



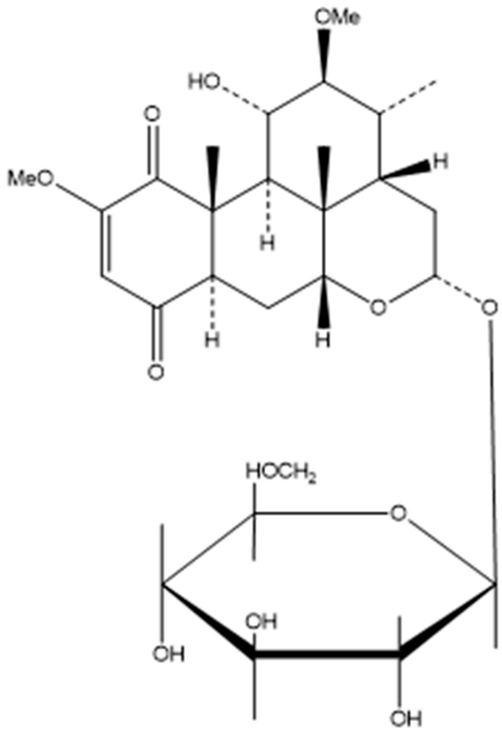
Javanicinoside H **(51)**



Javanicinoside E **(52)**



Javanicinoside G **(53)**



Javanicinoside I **(54)**

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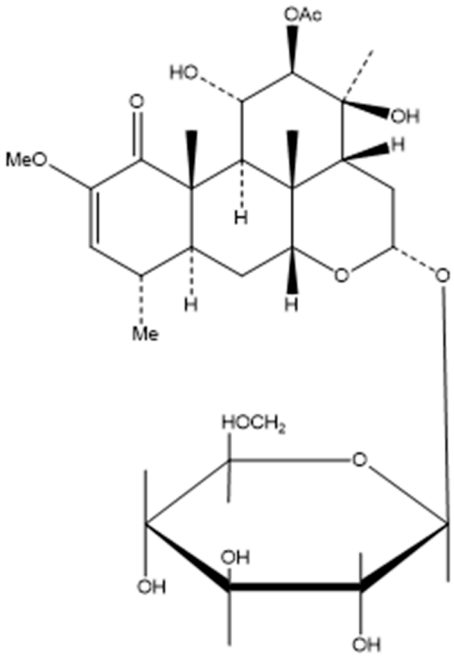
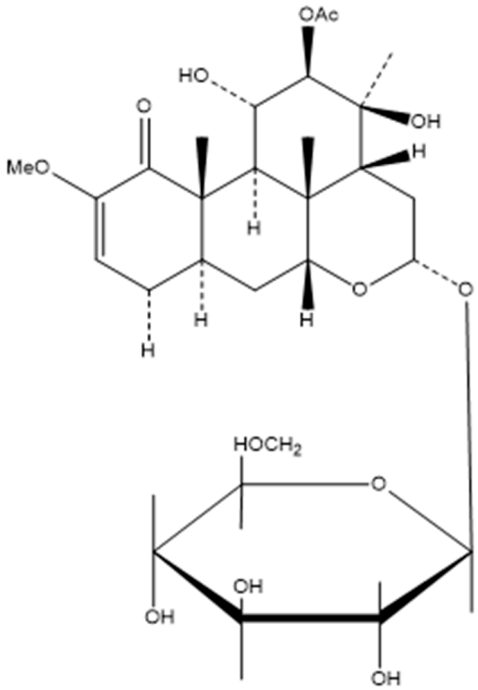
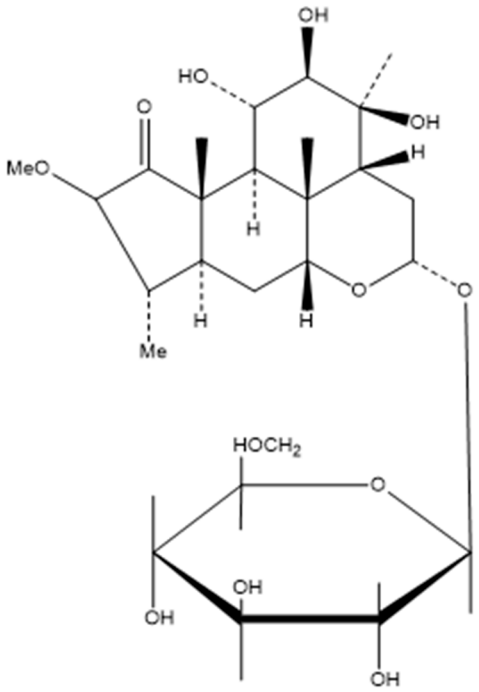


Javanicinoside J **(55)**



Javanicinoside K **(56)**



Javanicinoside L **(57)**

Figure 3 Quassinoid glycosides of *Picrasma javanica.*

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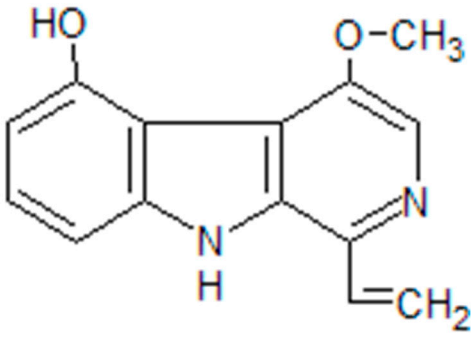
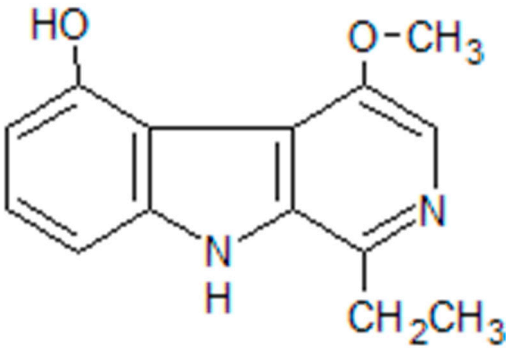
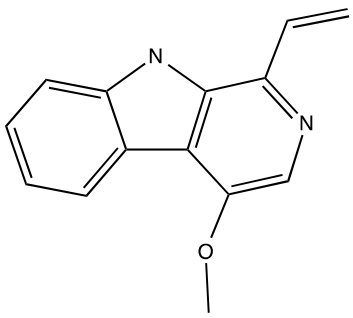


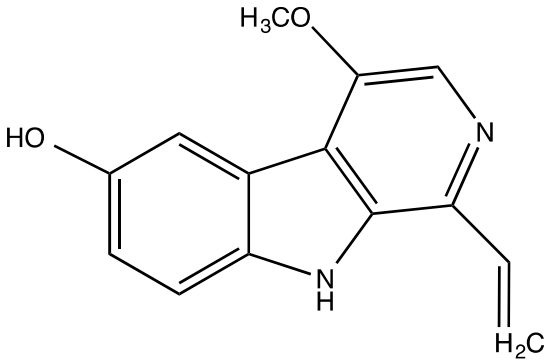
5-hydroxydehydrocrenatine **(58)**



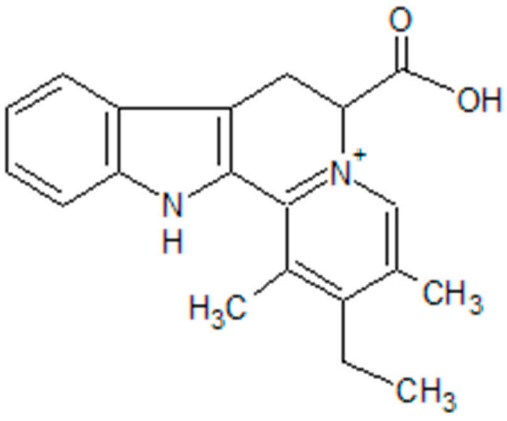
5-hydroxycrenatine **(59)**



4-methoxy-1-vinyl-β-carboline **(60)**



6-hydroxy-4-methoxy-1-vinyl-β-carboline **(61)**



Javacarboline **(62)**

Figure 4 Alkaloids of *Picrasma javanica.*

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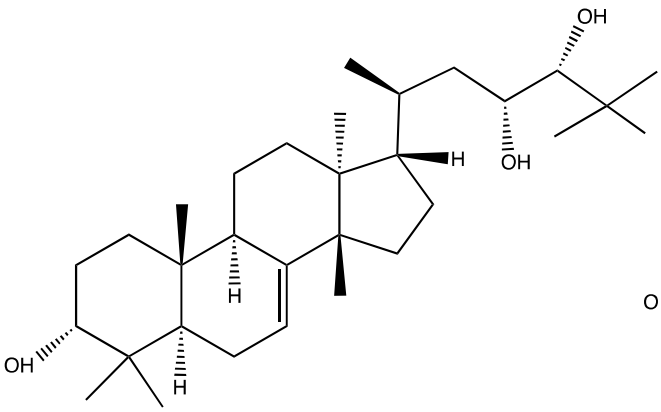
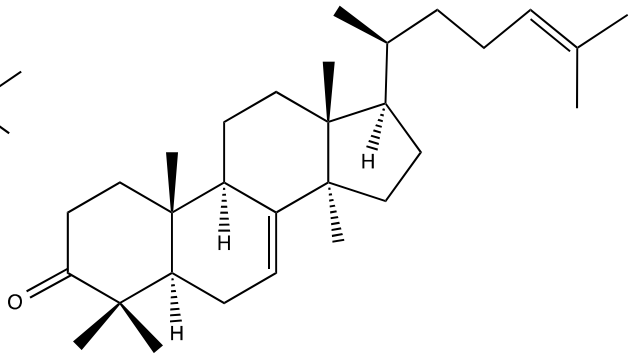


Hispidol A **(63)**



Lanosta-7,24-dien-3-one **(64)**

Figure 5 Triterpenoids of *Picrasma javanica.*

4. Pharmacological Properties

4.1. *Anti-malarial activity*

The latest World Malaria report which was released in November 2017 revealed that malaria cases increased in a very large amount from in 2016, compared to the previous year. These cases proved that malaria prevalence is high throughout the world. According to World Health Organization [21], malaria is "a life-threatening disease caused by parasites that are transmitted to people through the bites of infected female Anopheles mosquitoes". Malaria is one of the deadliest parasitic infections, but it is curable and preventable. despite having effective treatment and prophylaxis methods, there is a growing resistance of malarial parasites to antimalaria agents. The resistance towards antimalarials boosts many researchers to continuously find potential natural compounds to be developed as antimalarials.

Traditionally, *Picrasma javanica* is one of the plants commonly used as antimalaria in countries like Myanmar, Thailand, Indonesia [22] and northern India[23, 24].The plant is used to treat malaria in the form of decoction[23, 25]. The record of use of this plant species as antimalarial went as far as the year 1942 during World War 2, where soldiers infected by Plasmodium spp. were treated with *P. javanica*[22]. Despite the abundant information on the utilisation of *P. javanica* to fight malarial parasites, studies on the exact compounds responsible for the antimalarial property of the plant are still lacking.

Among the earlier studies on *P. javanica* activity against malarial parasites is an in-vitro test done by Pavanand*et al.*[19] where they investigated on the inhibition of *P. javanica*

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against *Plasmodium falciparum* isolates. The results of the study showed that the isolated alkaloids, specifically 4-methoxy-1-vinyl-β-carboline and 6-hydroxy-4-methoxy-1-vinyl-β-carboline, possess some antimalarial activity, though they are much lesser than the antimalarial agent, mefloquine. Furthermore, the researchers brought upon the possibility of in vivo metabolism converting these compounds to active metabolites which was not detected in the vitro test. In a similar study done by Saiin *et al*. [26], different crude extracts from *P. javanica* stembark were scrutinized and they discovered that hexane extract had the highest in vitro antimalarial activity against *P. falciparum*. Afterwards, they did further fractionations to identify which compound provided more activity against malarial parasites. The results showed that β-sitosterol is a major compound in the fraction with the highest inhibitory activity but its poor solubility in DMSO did not permit further antimalarial investigation. Meanwhile, other isolated fractions from the same fraction as β-sitosterol showed inhibition against P. falciparum. These fractions however, need to be further fractionated to establish the precise compounds exhibiting antimalarial activity.

Saiin & Sirithunyalug [22] reviewed on indole alkaloids extracted from *Picrasma javanica*. Based on the review, they found out that currently there are fourteen purified indole compounds from *P. javanica* but only two compounds, 4-methoxy-1-vinyl-β-carboline and 6-hydroxy-4-methoxy-1-vinyl-β-carboline were assessed on their antimalarial activity. This review demonstrated that studies on indole alkaloids extracted from *P. javanica* are scarce. Additionally, Takasu *et al*. [27] had synthesized several β-carbolines and their corresponding salts which have a pi-delocalized lipophilic cationic structure for the purpose of evaluating both in-vivo and in-vitro activity of these compounds against malaria. These compounds as well as their quaternary carbolinium cations were found to have positive antimalarial action. Additionally, these researchers discovered that these cations provide more selective toxicity against malarial parasites. This finding gives a perspective for new research on the potential of *P. javanica* as new source for antimalarial agent.

Previously, only indole alkaloids of *P. javanica* were mentioned to have antimalarial activity. However, quassinoids, another group of compounds which can be found in *P. javanica* also have activity against malarial parasites. For instance, Praptiwi*et al*.[28] corroborated that extracts from stembark and leaves of *P. javanica* had the ability to reduce parasitaemia induced in mice better than chloroquine. These researchers assumed that such effect is expected due to the presence of alkaloids and quassinoids in *P. javanica*, which can also be found in the other members of Simaroubaceae family that exhibit similar inhibition

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activity against malarial parasites. In fact, the antimalarial activity of quassinoids from the Simaroubaceae family has been extensively studied. For example, several studies have suggested that quassinoids act as antimalarial by disrupting protein synthesis followed by nucleic acid inhibition. Such mechanism is fundamentally different than the mechanism of action of chloroquine [29], demonstrating the possibility of plants from Simaroubaceae family as sources of antimalarial drugs. Even more, researchers found out that the ester moiety of quassinoids contributed to higher antimalarial activity compared to those without it [30, 31]. These types of studies may give us a head start on how compounds from *P. javanica* work against malarial parasites.

Through these findings, it can be inferred that there are not many studies done on the antimalarial activity of *P. javanica* although the plant was proven to have some activity against malaria and was used traditionally in some countries to treat malaria. These reasonings should be advocated to initiate more research on the antimalarial properties of *P. javanica*.

4.2. *Antiproliferative activity*

Cancer is a group of diseases where there is an abnormal cell growth that can spread to neighbouring areas and worse, invading other organs. World Health Organization [32] proclaimed that cancer has the ability to kill one in six people annually, although recently, the organization highlighted that cancer can be managed when there are early diagnosis, immediate treatment and palliative care for cancer patients. This means, cancer treatment plays a major role in preventing deaths due to cancer. For this reason, researchers are encouraged to find novel anti-tumour compounds sourced from natural products to widen the choices for therapeutic agents for cancer. These new compounds may be studied extensively and designed to have more specificity towards cancer cells. Especially since most available anticancer agents are known to not only target the cancer cells but also the normal, healthy cells.

Studies have shown that *P. javanica* has some degree of antiproliferative and cytotoxic activity, which are among the characteristics of anticancer agents. These studies however, employed different methodology to assess the anticancer property of *P. javanica*. In the initial researches of *P. javanica* activity against cancer, Koike*et al.*[20] first discovered the cytotoxicity activity of *P. javanica* when they were isolating a β-carboline alkaloid,

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namely javacarboline from the stem of the plant. The cytotoxic property found was attributed to this compound since it exhibited cytotoxicity in-vitro against human tumor PC-6 cells as well as murin lymphocytic leukaemia P-388 cells at GI_{50} values of 35.9 µg/ml and 32.5 µg/ml, respectively. In a more recent study, Sharmin *et al.*[33] utilised the brine shrimp lethality bioassay to assess the anticancer activity of *P. javanica*. This particular bioassay was used as an indication of cytotoxicity as well as other pharmacological properties such as anticancer, antiviral and pesticidal effect. Through this method, it was found that the crude extracts contained potent bioactive compounds as the lowest LC_{50} value obtained was 1.04±0.31 µg/ml. Based on the result, it is suggested that further fractionation of the crude extracts is done to identify the exact compounds exerting the cytotoxicity effect.

Furthermore, Win *et al.*[3] revealed that chloroform extract of *P. javanica* has antiproliferative activity against five human cancer cell lines (A549, HeLa, PANC-1, PSN-1 and MDA-MB-231). The in-vitro antiproliferative evaluation was executed with 5-fluorouracil as a positive control to compare with the activity of the extract against the five cancer cell lines. The extract showed its antiproliferative activity with IC_{50} values between 1.6 to 22.1 µg/mL. The same extract was then separated via chromatographic method and ten quassinoids were characterised, named picrajavanicins A, B, C, D, E, F, G, as well as javanicins B, F and I. However, each of these isolates did not show any antiproliferative activity, which led the researchers to postulate that the antiproliferative property found in the chloroform extract may be accredited to the other quassinoids and β-carboline alkaloids in *P. javanica*. These studies showed that *P. javanica* does have anticancer activity, though more in-depth investigations are needed to recognize which compounds contributed to the activity.

Another study on *P. javanica* where eight tetracyclic quassinoids were isolated from the chloroform extract of *P. javanica* bark (picrajavanicins H, I, J, K, L, M, picrasin A and 2'-isopicrasin A) and evaluated for antiproliferative activity has revealed that these quassinoids were active against human pancreatic cancer PANC- 1 cell line. Moreover, picrasin A and 2' isopicrasin A were found to have additional antiproliferative activity in human cervical cancer HeLa cell lines. In contrast to the prior mentioned studies, this study has additional analysis on the structure-activity relationships (SAR) of the discovered quassinoids which led the researchers to learn that substituents at C-4 and C-13 have significance on the activity against the pancreatic cancer PANC-1 cell lines [14]. Such finding provided supplementary information on the anticancer activity of *P. javanica* which may be helpful in the future development of anticancer agent sourced from this plant species.

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Having said that, a study revealed that bark extracts of *P. javanica* has no anticancer activity [34], which is conflicting with previous findings. This study utilised the mechanism-based yeast bioassay to check the antiproliferative effect of several Indonesian plants from Apocynaceae, Simaroubaceae and Magnoliaceae. The bioassay is a panel of yeast strains that is used to see if there is any inhibition zone produced when yeast growth is prohibited. The activity was assessed by calculating the required concentration of sample to produce inhibition zone of 12mm around a well. Generally, compounds which give positive results are topoisomerase inhibitors, which is a common DNA damaging agent used in anticancer treatment. Based on the results, Zuhrotun *et al*. [14] affirmed that *P. javanica* is inactive as anticancer agent. Then again, this study might signify that the mechanism of *P. javanica* as anticancer is unlike the topomerase inhibitors, which indicates that more studies are indeed needed to not only discern the active compounds in *P. javanica*, but also to establish the mechanism of anticancer activity of the plant.

4.3. *Antiviral activity*

Infection by human immunodeficiency virus type 1 (HIV-1) induces host cells to activate innate and cellular immune responses for the purpose of limiting viral invasion. In contrast, HIV uses many strategies to counteract the host cell responses. One example of the strategy is through a virion-associated accessory protein called viral protein 1 (Vpr), with 96 amino acids and molecular weight of a basic protein which is 14kDa. This protein is involved in the pathogenesis and viral replication of HIV, resulting in the promotion of viral infection [35],. For this reason, inhibition of Vpr may help the infected patient by halting viral replication; opening the opportunities for the development of anti-HIV therapy. Not to mention, Vpr is said to be a good drug target for acquired immunodeficiency syndrome (AIDS) therapy [36]. Consequently, such opportunity may be used to foster the findings of natural compounds as new anti-HIV agents.

The potential of *P. javanica* as a source for antiviral protein R was discovered based on a study where isolated quassinoids from the plant were evaluated on their inhibition of Vpr expression [37]. The study demonstrated that this newly discovered property of *P. javanica* is quite different from other plant species exhibiting similar inhibition, in terms of its structure-activity relationships (SARs). Overall, quassinoids with methyl group at C-13 and hydroxy group at C-16 are the compounds with the most Vpr inhibitory activity. Other

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than that, the presence of hydroxy at C-14, carbonyl at C-4 and the absence of methoxy at C-3 also increase the inhibition, albeit being less significant considerations than the substitutions in C-13 and C-16. Such comprehensive study provided some information which can be utilised by the researchers in the synthesis of antiviral agents.

In actuality, the previously mentioned study is the only reported data of *P. javanica* activity against virus, showing that investigations of *P. javanica* are rarely done. As for the other plant species in Simaroubaceae family, several investigations were carried out to discover the antiviral property of the plants [38, 39, 40] . These studies may be helpful to some degree, especially since the plants in the family have similar compound characteristics. For instance, Nawawi *et al*. [38] affirmed that *Eurycoma longifolia* has inhibitory activity against herpes simplex virus type 1 (HSV-1) and it exhibited strong toxicity both in-vivo and in-vitro, which means that extra precautionary steps are needed if the plant is developed as antivirals. In another study where a quassinoid compound named simalikalactone D was isolated from chloroform crude extract of *Quassia Africana*, the researchers discovered that this quassinoid is responsible for the pronounced antiviral activity of the plant against several viruses [39]. They then postulated that ester group at C-15 and epoxymethano bridge between C-8 and C-13 might be the compound features contributing to the activity against viruses. Additionally, *Ailanthus excelsa*, another plant from Simaroubaceae family also showed antiviral activity in the form of chloroform extract, rather than methanol extract [40].

In short, although not many studies were done on the antiviral activity of *P. javanica* and the other plants in Simaroubaceae family, the available studies are significant in a way that they provided some knowledge on the possibility of developing antiviral agents from these natural sources.

4.4. *Antimicrobial activity*

In present days, exposure to microbes such as bacteria, virus and fungi may cause diseases, some of which are infectious and incurable. These organisms cannot be seen with naked eyes hence most people are more prone to taking lightly the protection steps against microbes. This is why, scientists are always in the search of new antimicrobial agents to counter these arising diseases. Khan*et al*. [41] reported that all extracts and fractions of *P. javanica* exhibited broad spectrum of antibacterial activity but none worked against tested moulds. The bacteria and protozoa used in the experiment included Bacillus species,

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Micrococcus species, Staphylococcus species as well as Pseudomonas aeruginosa and Salmonella typhi. This sole report on antibacterial activity of *P. javanica* may be very helpful in future researches concerning the particular activity of the plant.

Other members of Simaroubaceae have been reported to possess antibacterial activity as well. *Ailanthus altissima* extracts was found to have antibacterial activity against different bacteria and fungi [42, 43]. Other plants in similar family showing antibacterial activity in different extracts includes *Simaba ferruginea*[44], *Quassia indica*[45] , *Ailanthus excelsa*[46] and *Samadera indica*[47].

4.5. *Membrane stabilising activity*

Membrane stabilising action of natural products is investigated to assess their anti-inflammatory activities [48, 49]. Various disorders arise from the release of lysosomal enzymes during inflammation. Common anti-inflammatory agents used, non-steroidal drugs (NSAIDs) work by impeding these lysosomal enzymes or by stabilising lysosomal membranes [49]. With this in mind, natural compounds are continuously being assessed for their anti-inflammatory activity, regardless of their mechanism of action.

P. javanica was found to have membrane stabilising activity through a method where hypotonic solution and heat-induced haemolysis of human red blood cells were used. Extracts of *P. javanica* have protected human red blood cells membrane from lysis induced by hypotonic solution and heat [50]. Although this is the only study found on the membrane stabilising activity of *P. javanica*, it equipped the researchers to further investigate the compounds in *P. javanica* with this particular activity.

Plants in similar family also exhibited similar activity, such as *Eurycoma longifolia*, *Ailanthus excelsa*[51] and *Samadera indica* [52]. The studies employed the same method as above to assess the membrane stabilising activity of the plants. These researches, however, must be further evaluated to identify and isolate the active chemical constituents responsible for the activity, which will then lead to the discovery of new and natural anti-inflammatory agents.

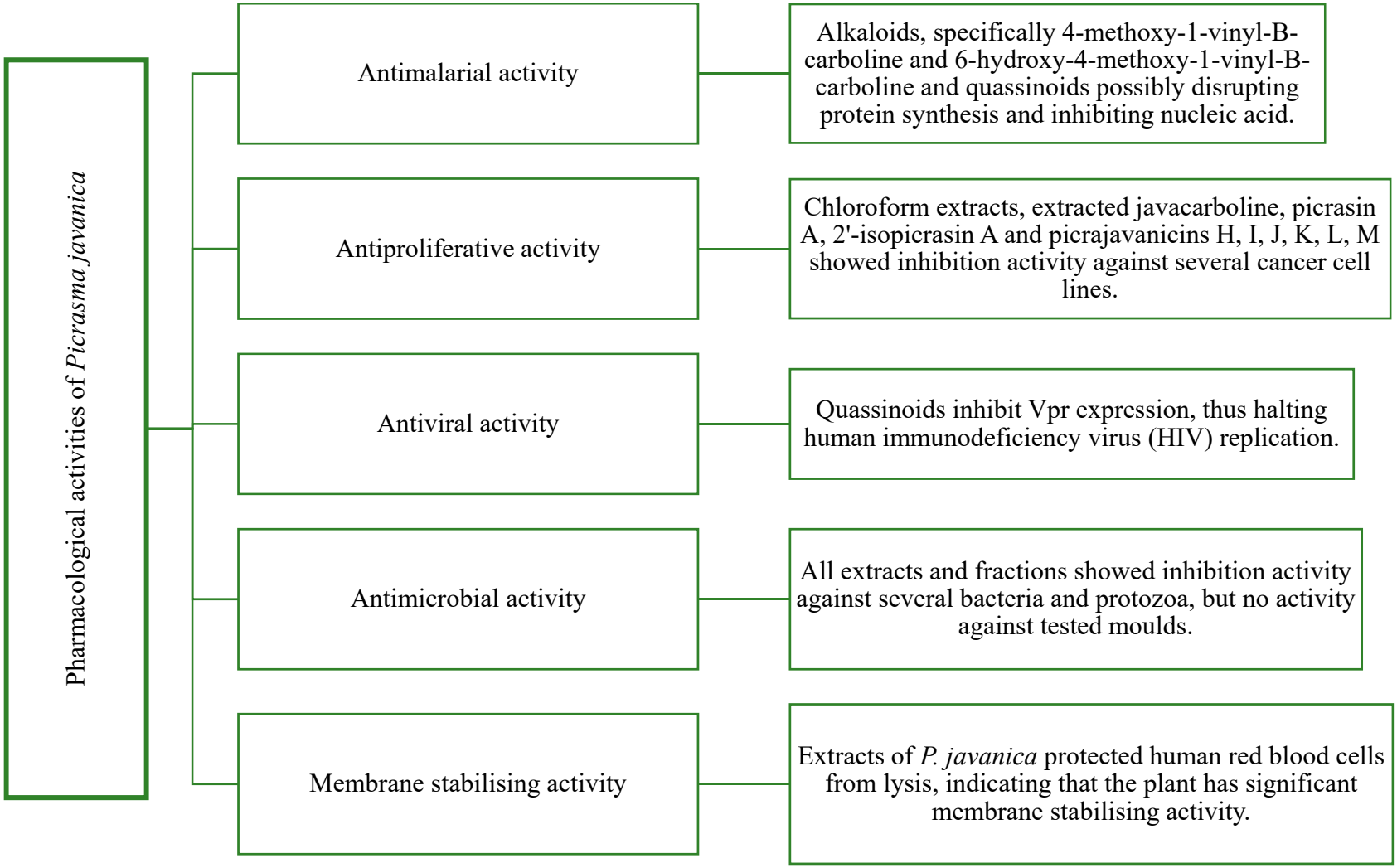

Figure 6 Summary of pharmacological activities exhibited by *Picrasma javanica*.

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5.Conclusion

Picrasma javanica, also known as *Picrasma nepalensis* or *Picrasma philippinensis,* is a plant among Simaroubaceae family. The family is recognized for the presence of their bitter group of compounds called quassinoids. As such, the constituents of *Picrasma javanica* that have been isolated from different parts of the plant as of today include quassinoids, alkaloids and triterpenoids. These phytochemical compounds may exhibit pharmacological activities that are beneficial to men. Some of the activities which have been studied are antimalarial, antiproliferative, antiviral, antimicrobial and membrane stabilising activity. It is clearly evident that most of these studies discovered that extracts of *P. javanica* exhibit these activities and the key players are quassinoids and alkaloids in the plant. Although the mechanism of actions are unclear and details such as the specific compounds inducing these activities are lacking, it is clear that *P. javanica* does have therapeutic benefits for the mankind. Thus, it is hoped that further studies are done to discover the potential therapeutic effects of *Picrasma javanica* in details, so that it can become a source of new medicinal agents with therapeutic benefits and fewer side effects to the people.

Conflict of interest

The authors declared that there is no conflict of interest.

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