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REVIEW ARTICLE

A Review of the Phytochemical and Pharmacological Characteristics of *Hernandia nymphaeifolia*

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Abstract

Since ancient times, medicinal plants have been the primary source of most medications. In actuality, a large number of the medications that are now on the market may be obtained either directly in extract form or in modified synthetic form. As phytoconstituents, which are employed by plants to carry out biological processes and defend us from predators like viruses, fungi, and other microbes, they are naturally able to produce goods that are helpful for humans. *Hernandia nymphaeifolia* is a traditional medicinal plant that is used in several traditional remedies to treat several ailments. The extracts from various portions of the plant have excellent therapeutic effectiveness. Numerous pharmacological investigations have demonstrated this plant's capacity to display anti-cytotoxic, anti-inflammatory, anti-platelet aggregation, vasodilator, antioxidant, anti-microbial, and Ca^{2+} signalling properties. The current study covers a thorough examination of the plant's systematic botanical position, phytochemical analysis, investigations into the plant's pharmacological activity, and therapeutic uses.

Keywords: Aporphine Alkaloid, *Hernandia nymphaeifolia*, Lantern Tree, Pharmacological Activity

1. Introduction

Researchers have recently concentrated on therapeutic plants made from natural ingredients due to their extensive pharmacological relevance[1]. Nearly 80% of the world's population, particularly in developing nations, frequently relies on traditional medicines and goods for their healthcare requirements. A large number of sick persons in poor countries mix conventional care with traditional medicine[2-4]. Traditional medicines are frequently less expensive than contemporary medications, and they are likely the only natural cures that are accessible and available in distant rural areas of underdeveloped nations[5].

H. nymphaeifolia, a member of the Hernandiaceae family, is a popular beach plant that may be found in tropical and subtropical climates[6]. In Taiwan and Japan for several periods, this plant has occasionally been misidentified as *Hernandia ovigera* or *Hernandia sonora*[7]. In general, Hernandiaceae sp. is common in the place of seaside Melanesia, Micronesia, and Polynesia (Figure 1). The taxonomical hierarchy is shown in Table 1.

In traditional medicine, this plant has been employed as a haemostatic, depilatory, and cathartic agent[9]. The chemical constituents display a range of biological behaviours, including notable cytotoxic[10,11], anti-plasmodial[11,12], anti-platelet aggregation[13], antioxidant[14],

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source: https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:430812-1[8]

Figure 1. Topographical distribution of *H. nymphaeifolia*.

Table 1. Taxonomical hierarchy: (USDA plants database)[17]

Synonyms	Lantern tree
Kingdom	Plantae
Subkingdom	Tracheobionta
Super division	spermatophyta
Division	Magnoliophyta – a flowering plant
Class	Magnoliopsida- Dicotylendon
Subclass	Magnolidae
Order	Lauraies
Family	Hernandiaceae
Genus	*Hernandia*
Species	*Hernandia nymphaeifolia* (Kubitzki)

anti-inflammatory[15], vasorelaxant[14] and antibacterial[16] behaviours. Western Samoa stomach pain has also been treated with this plant[9].

2. Plant Taxonomy

2.1 Morphology of Plant

Trees are in height scale from 40 ft to 5 ft with soft wooded. The leaves are alternating, broad, peltate, and oblong to shield-shaped with a shiny greenish colour. Flowers are resembling panicles with tiny white clusters in the axilla. Whitish to the reddish coloured transparent circular firm is covered the hard black coloured fruit. The fruit was a hard, black appearance, and was covered by a translucent, whitish to reddish-coloured round firm[9].

The present work was carried out to explore the chemical properties of *H. nymphaeifolia* with some pharmacological activities.

2.2 Chemical Constituents Present in Various Parts of the Plant

Hernandia nymphaeifolia has different types of Oxoaporphine alkaloids[7], P-quinonoid aporphine alkaloids[18], Norapophines Alkaloid, Furanoid lignan[13], amides[19], Dibenzylbutyrolactone lignan[20], steroids[13,15]. isoquinolones, benzylisoquinolines[20] and their derivatives. The details of some of the physical chemical characteristics of *H. nymphaeifolia's* phytochemicals, including their pharmacological effects in Table 2.

3. Pharmacological Activities of the *H. nymphaeifolia*

3.1 Antineoplastic Activity

Chloroform-soluble extracts of this plant's trunk bark have been shown to exhibit carcinogenic activities through bioassay-guided analysis. Among all 44 of the isolated compounds, 9 compounds which include Hernandonine, (+)-ovigerine, demethylsonodione, hernanymphine, methoxyoxohernandaline, (—)-yatein, (—)-deoxypodophyllotoxin, (+)-N-methylovigerine, and N-formyldehydroovigerine revealed remarkable anticancer effects against KB16, P-388, HT-29, and A549 cell lines[10]. Both (+)-hernovine and (+)-magnoflorine showed specific cytotoxicities against

Table 2. Physical-chemical characteristics of *H. nymphaeifolia*'s phytochemicals, including their pharmacological effects

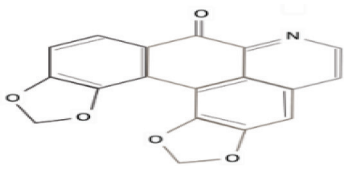
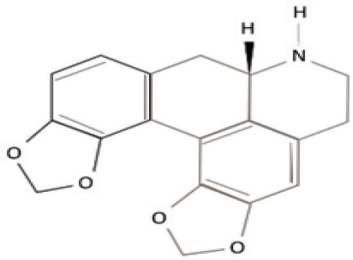
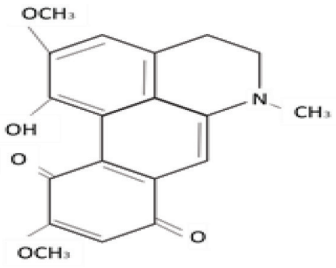
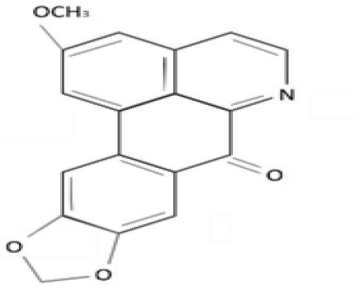
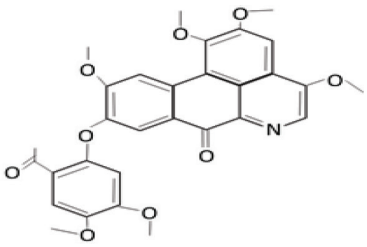
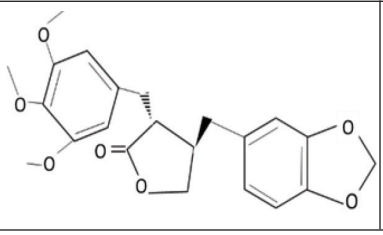
Sl. No.	Name of Compound	Molecular Formula with molecular weight (m/z)	Chemical Structure	Parts of plant	Nature of Compound	Pharmacological Activities	References
1	Hernandonine	$C_{18}H_9NO_5$ 319.3		Root	Oxoaporphine alkaloid	Antineoplastic activity	7
2	(+)-ovigerine	$C_{18}H_{15}NO_4$ 309.3		Trunk bark	Oxoaporphine alkaloid	Antineoplastic activity, Antiplatelet activity, Vasorelaxing activity,	10,14,20
3	Demethylsonodione	$C_{19}H_{17}NO_5$ 339.11		Trunk bark	P-quinonoid aporphine alkaloids	Antineoplastic activity	10
4	Hernanymphine	$C_{18}H_{11}NO_4$ 305.29		Stem bark	Oxoaporphine Alkaloids	Antineoplastic activity	10
5	Methoxyoxohernandaline	$C_{29}H_{25}NO_9$ 531.5		Trunk bark	Alkaloid	Antineoplastic activity	10
6	(-)-yatein	$C_{22}H_{24}O_7$ 400.4		Trunk bark	Lignan	Antineoplastic activity	10

Table 2. Continued...

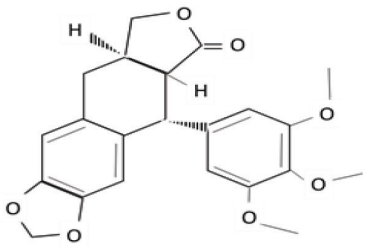
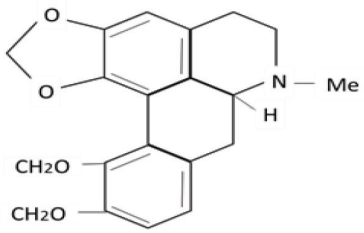
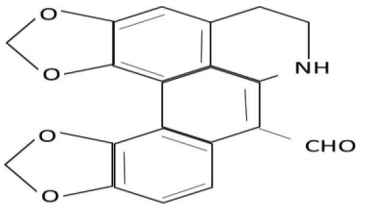
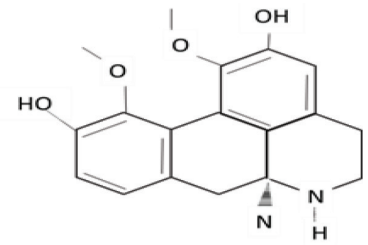
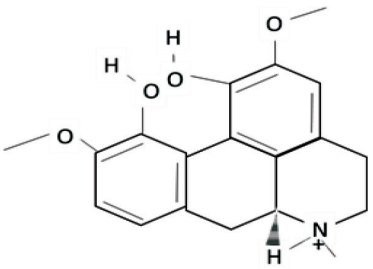
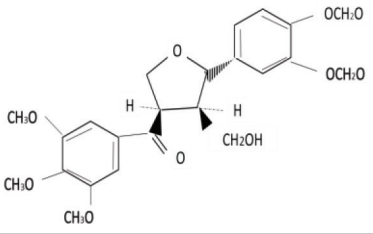
Sl. No.	Name of Compound	Molecular Formula with molecular weight (m/z)	Chemical Structure	Parts of plant	Nature of Compound	Pharmacological Activities	References
7	(-)-deoxy-podophyllo-toxin	$C_{22}H_{22}O_7$ 398.4		Trunk bark	Lignan	Antineo-plastic activity	10
8	(+)-N-methy-lovigerine	$C_6H_5NH(CH_3)$ 107.15		Trunk bark	Alkaloid	Antineo-plastic activity	10
9	N-formylde-hydrooviger-ine	$C_{19}H_{13}NO_5$ 335.3		Trunk bark	Alkaloid	Antineo-plastic activity	10
10	(+)-hernovine	$C_{18}H_{19}NO_4$ 313.3		Trunk bark	Alkaloid	Antineo-plastic activity	20
11	(+)-magno-florine	$C_{20}H_{24}NO_4^+$ 342.4		Trunk bark	Alkaloid	Antineo-plastic activity	20
12	(-) hernone	$C_{23}H_{28}O_8$ 432.17		Trunk bark	Furanoid lignan	Antineo-plastic activity, Less antiplatelet activity	20,13

Table 2. Continued...

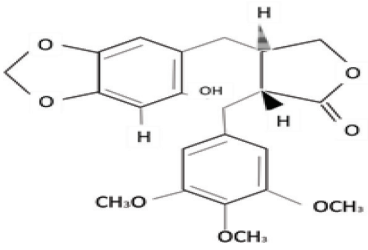
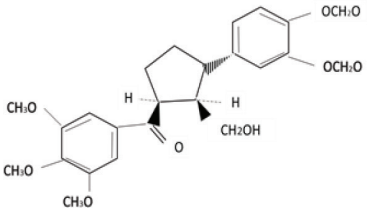
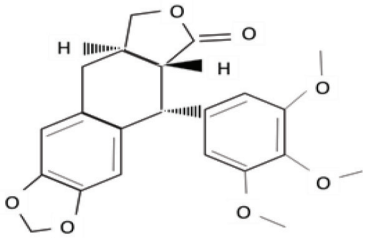
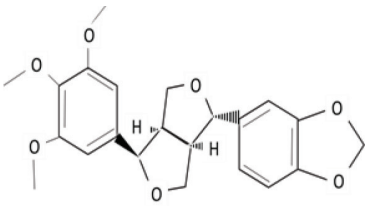
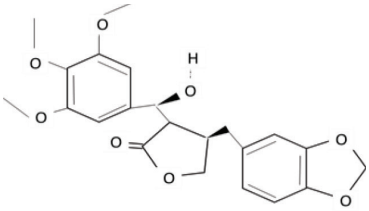
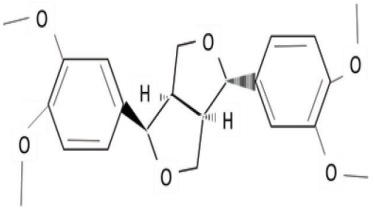
Sl. No.	Name of Compound	Molecular Formula with molecular weight (m/z)	Chemical Structure	Parts of plant	Nature of Compound	Pharmacological Activities	References
13	(-) hydroxyyatein	$C_{22}H_{24}O_8$ 416.42		Trunk bark	Dibenzylbutyrolactone lignan	Antineoplastic activity	20
14	(-) nymphone	$C_{22}H_{24}O_8$ 416.42		Trunk bark	Furanoid lignan	Antineoplastic activity	20
15	Deoxypodophyllotoxin	$C_{22}H_{22}O_7$ 398.4		Root wood	Lignan	Antineoplastic activity, Antimicrobial activity	16
16	(+) epiaschantin	$C_{22}H_{24}O_7$ 400.4		Trunk bark	Lignan	Antineoplastic activity, Antiplatelet activity	13,16
17	Podorhizol	$C_{22}H_{24}O_8$ 416.4		Fruit	Lignan	Antineoplastic activity	16
18	(+)-epieudesmin	$C_{22}H_{26}O_6$ 386.4		Fruit	Lignan	Antineoplastic activity	16

Table 2. Continued...

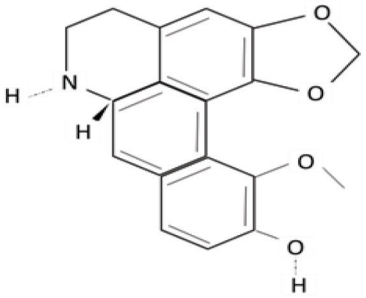
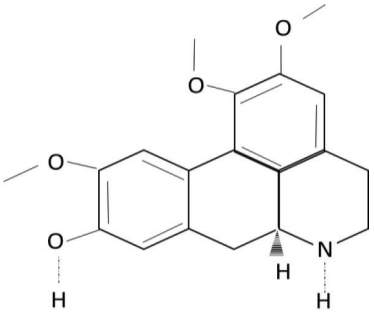
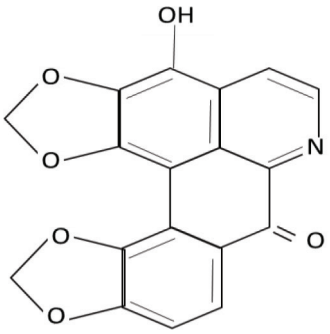
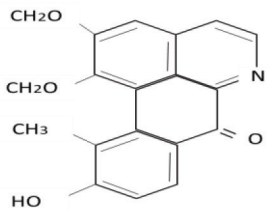
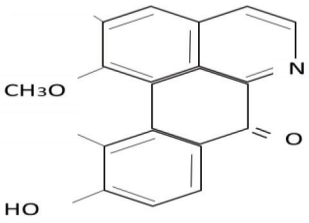
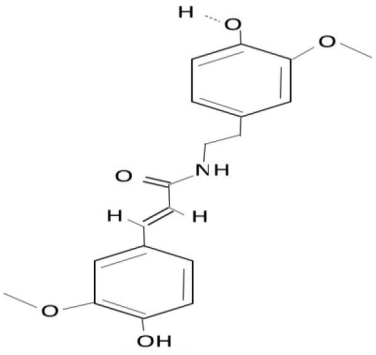
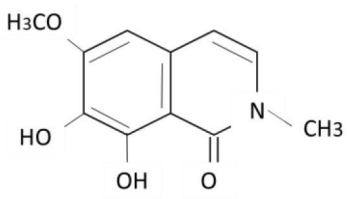
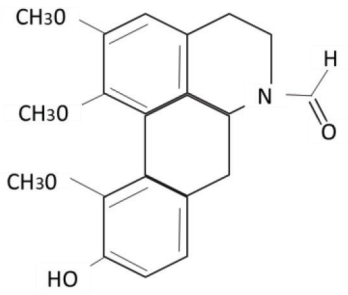
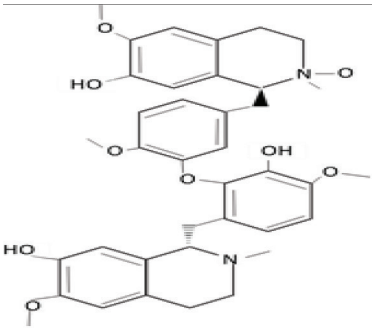
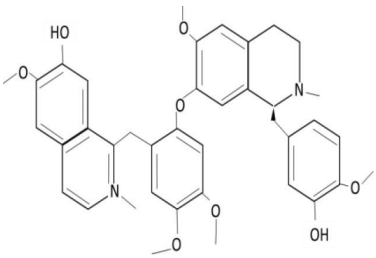
Sl. No.	Name of Compound	Molecular Formula with molecular weight (m/z)	Chemical Structure	Parts of plant	Nature of Compound	Pharmacological Activities	References
19	Hernangerine	$C_{18}H_{17}NO_4$ 311.332		Trunk bark	Norapophines alkaloid	Antiplatelet activity, Vasorelaxing activity	13,14
20	Lauroteta-nine	$C_{19}H_{21}NO_4$ 327.4		Trunk bark	Norapophines alkaloid	Antiplatelet activity	13,14
21	3-hydroxy-hernando-nine	$C_{18}H_9NO_6Na$ 358		Root bark	Aporphine alkaloid	Anti-inflammatory activity	15
22	Oxohernan-gerine	$C_{18}H_{11}NO_5$ 321.3		Root bark	Oxoapophines alkaloid	Anti-inflammatory activity	15
23	Oxohernag-ine	$C_{19}H_{15}NO_5$ 337.3		Root bark	Oxoapophines alkaloid	Anti-inflammatory activity	19

Table 2. Continued...

Sl. No.	Name of Compound	Molecular Formula with molecular weight (m/z)	Chemical Structure	Parts of plant	Nature of Compound	Pharmacological Activities	References
24	N-trans-Feruloylmethoxy-tyramine	$C_{19}H_{21}NO_5$ 343.4		Root bark	Amide	Anti-inflammatory activity	[19]
25	7,8-dihydroxy-6-methoxy-2-methylisoquinolin-1(2H)-one	$C_{11}H_{11}NO_3$ 205.21		Root bark	Alkaliod	Anti-inflammatory activity	[19]
26	N-formylhernagine	$C_{20}H_{21}NO_5$ 378.131		Root	Alkaloid	Anti-inflammatory activity	[19]
27	(+)-vateamine 2′-β-N-oxide	$C_{38}H_{44}N_2O_9$ 672.8		Trunk bark	isoquinoline N-oxide alkaloids	Antioxidant activity	[14]
28	(+)-malekulatine	$C_{39}H_{46}N_2O_8$ 670.8		Trunk bark	Alkaloid	Antioxidant activity, Antimicrobial activity	[14,16]

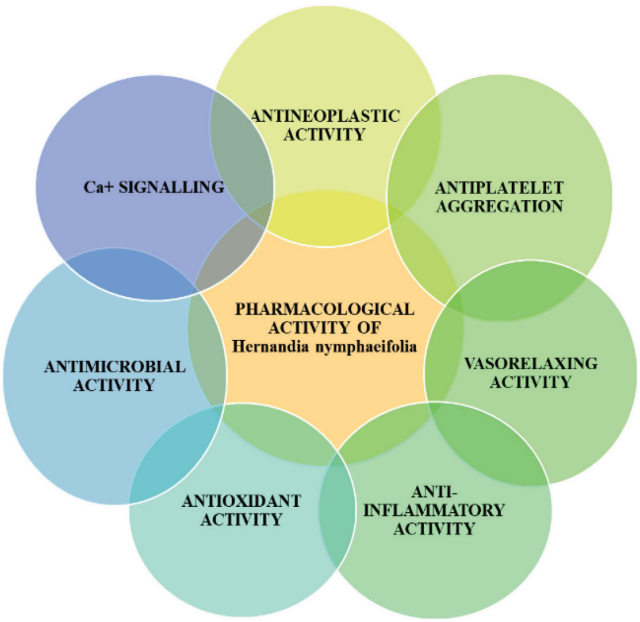


Figure 2. Pharmacological activity of *H. nymphaeifolia*.

the P-388 cell line *in vitro* (ED50 = 0.214pg/ml and 0.229pg/ml, respectively)[20]. In other research, lignan from chloroform extracts of the *H. nymphaeifolia* trunk showed anticancer properties. Two furanoid lignans, (-) nymphone and (-) hernone, as well as one dibenylbutyrolactone, (-) hydroxyyatein, are present in these chloroform extracts. *In vitro* analysis revealed that these molecules were efficient towards human lung adenocarcinoma (A549), human nasopharyngeal cancer (KB16), mouse lymphocytic leukemia (P-388), and human colon carcinoma (HT-29)[20]. Deoxypodophyllotoxin, which is a potent anticancer agent obtained from the seed of H.nymphaeifolia[21]. It is exhibiting a cytotoxic impact on several distinct cell lines, especially cholangiocarcinoma, KB16, k562, HT-29, A549, PC-3, LNCaP, and Colo205[22-25]. Moreover, (+)-epiaschantin, podorhizol, (+)-epiedesmin, and isostegane isolated from bark, had only minor inhibitory effects on cancer cell lines. Just two types of cell lines are responsive to podorhizol, and only the P388 leukaemia cell line was responsive to (+)-epiaschantin[16]. With Deoxypodophyllotoxin's restructuring, 12 compounds were synthesized, 4 of which exhibited more strong cytotoxic effects than Deoxypodophyllotoxin. These 4 compounds are Methyl acetoxydeoxypodophyllate, 2′-Bromodeoxypodophyllotoxin, 2,2′-Dibromodeoxypodophyllotoxin, and 2,2′,6′-Tribromodeoxypicropodophyllotoxin. By displaying IC50 values of 0.75 and 0.46 M against the KKU-100 and HepG2 cell lines, respectively, 2, 2′-Dibromodeoxypodophyllotoxin demonstrated significant activity. 2,2′-Dibromodeoxypodophyllotoxin is used as the lead compound for anticancer activity[26]. Fruits of *H. nymphaeifolia* exhibited ant-proliferative action against human tumour cell lines when extracted using a 1:1 mixture of methanol and methylene chloride. According to the study, the chemosensitive carcinoma cell lines A549 and MCF-7 were relatively sensitive to the effects of epiashantin and epieudesmin. Surprisingly, although being less active against the parent chemosensitive cell line of KB-VIN, which overexpresses P-glycoprotein, both drugs showed considerable action with an IC50 value of 5 M against this tumour cell line (KB)[27] (Figure 3).

3.2 Antiplatelet Aggregation

The species of the Hernandia showed potent Antiplatelet aggregation activities[28]. Noraporphines, such as Hernangerine, Oviigerine, and laurotetanine, are said to

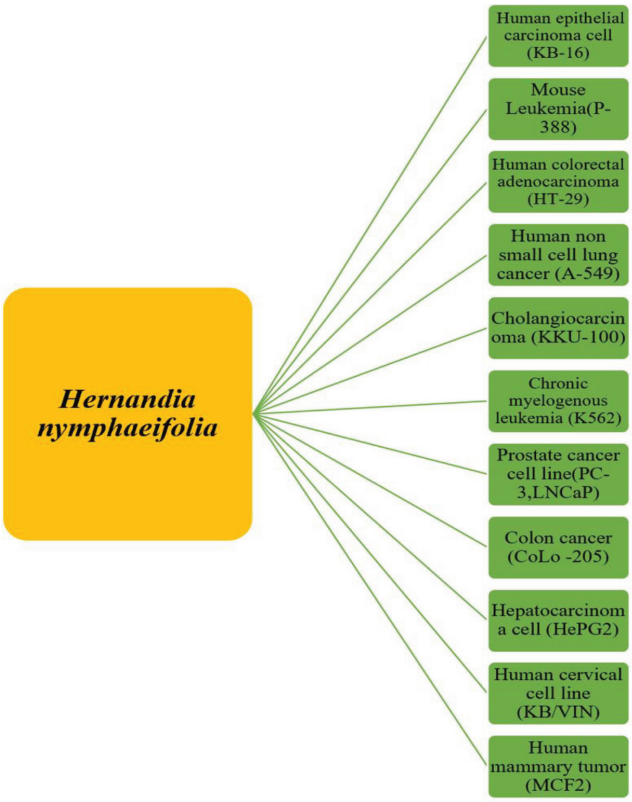


Figure 3. Cytotoxic cell lines inhibited by the *H. nymphaeifolia*.

have greater antiplatelet activities than oxoaporphines, such as Oxohernangerine, Hernandonine, and atheroline, because they interact with collagen or PAF, Arachidonic acid (AA)[29]. Oxohernagine demonstrated a strong antiplatelet effect amongst oxoaporphines if 10-hydroxy-12,11trimethoxy had been substituted. Ovigerine exhibits considerable antiplatelet action because of collagen, platelet-activating factor, and arachidonic acid, although its diameter was not exhibiting significant activity. Several furanoid lignans showed considerable antiplatelet action, with levels of activity (-) hernone (chevage type with bis-tetrahydrofuran ring)< (+) epimagnolin (containing 3',4' -dimethoxy)< (+) epiyangambin (with 3',4',5' -trimethoxy) <(+) epiaschantin (with 3',4' -methylenedioy)[13,30].

3.3 Vasorelaxing Activity

Sixteen chemicals have been isolated from this plant so far that have potent vasorelaxing abilities. Based on the research, the vasorelaxant effects of their related oxoaporphines - hernandonine, atheroline, and oxohernangerine were decreased. However, the norapophines - ovigerine, laurotetanine, and hernangerine showed considerable reduction of aortic contractions generated by high K^+ (80 mM) with norepinephrine 3 mM. Ovigerine significantly inhibits aortic contraction generated by high k+ and norepinephrine, however, its dimer ovigeridimerine has no vasorelaxing effects. Amongst oxoaporphines, oxohernagine and oxohernangerine, both having a 10-hydroxy modification, exhibited remarkable vasorelaxant action. Even though the reported prazosin (a1-adrenoceptor inhibitor) and nifedipine (calcium-channel blocker) are far stronger than all these natural substances› vasorelaxant effects[14].

3.4 Anti-inflammatory Activity

Numerous inflammatory conditions are brought on by the granule proteases produced by human neutrophils, such as cathepsin G and elastase, in addition to Reactive Oxygen Species (ROS), such as hydrogen peroxide and superoxide anion ($O_2^{\bullet}$)[31,32]. The proinflammatory effect has been evaluated by preventing elastase release from fMLP/CB-induced neutrophil $O_2^{\bullet}$ production. Methylene chloride soluble methanol extracts of root woods of *H. nymphaeifolia* showed significant anti-inflammatory activity. Isolated eight molecules comprising, 3-Hydroxyhernandonine, 7-Oxonorisocorydine, Hernandonine, Oxohernangerine, Oxohernagine, 4'-O-Demethyl-7-O-methyldehydro-podophyllotoxin, 2-O-Methyl-7-oxolaetine, and N-trans-Feruloylmethoxytyramine were displayed effective anti-inflammatory action. 3-hydroxyhernandonine and Oxohernangerine were the most efficacious of eight isolated compounds in suppressing fMLP-induced $O_2^{\bullet-}$ production and elastase release[15]. Further study showed that N-trans-feruloylmethoxytyramine, 7,8-Dihydroxy-6-methoxy-2-methylisoquinolin-1(2H)-one, hernandonine, oxohernagine, 5,6-dihydroxy-N-methylphthalimide, and N-formylhernagine might indeed clearly suppress fMLP-induced superoxide anion formation and/or elastase release. With IC_{50} values of 4.88±0.29µg/ml in elastase release and 2.84±0.78µg/ml for superoxide anion production, respectively, oxyhernagine was extremely effective. Additionally, compounds such as Oxohernagine, N-formylhernagine, 7,8-dihydroxy-6-methoxy-2-methylisoquinolin-1(2H)-one, and N-trans-Feruloylmethoxytyramine demonstrated strong suppression against lipopolysaccharide (LPS)-induced Nitric Oxide (NO) production[19].

3.5 Antioxidant Activity

The plant *H. nymphaeifolia*'s ethanolic extracts exhibited significant antioxidant efficacy in the DPPH study. The three substances with the highest antioxidant activity in scavenging the free radical DPPH were (+)-malekulatine (IC0.200 = 3 mM), reticuline ($IC_{0.200}$ = 2.1 mM), and (+)-vateamine 2-b-N-oxide ($IC_{0.200}$ = 3 mM). These compounds also outperformed the well-known antioxidant α-tocopherol[14,33].

3.6 Antimicrobial Activity

The gram-negative bacteria Neisseria gonorrhoeae was observed to be inhibited by the substances hernanol, kusunokinol, (-)-deoxypodophyllotoxin, deoxypicropodophyllin, (-)-maculatin, clusin, and podorhizol (minimal inhibitory concentration 32-64 g/mL)[16]. Another experiment demonstrates that the phytochemical deoxypodophyllotoxin, a derivative of dibenzyl butyrolactone lignan, exhibits potent anti-herps simplex virus action[34,35]. Berbeerine (-) showed *in vitro* efficacy against Trypanosoma cruzi at a 50 mg/

ml concentration in another study conducted on this plant[36].

3.7 Ca^{2+} Signalling Pathway

It was examined that lignans isolated from *H. nymphaeifolia* including epi-magnolin, epi-aschantin, epi-yangambin, yatein, and deoxypodophyllotoxin exert several different effects on Ca^{2+} signalling. The lignans enhanced Ca^{2+} concentration independently but inhibited thapsigargin-induced capacitative Ca^{2+} entry and intracellular Ca^{2+} release. According to the findings, these lignans affect Ca^{2+} signalling in renal tubular cells in several ways, increasing Ca^{2+} inflow while decreasing ATP- and thapsigargin-induced Ca^{2+} release and capacitative Ca^{2+} entry[37]. Another study found that these five lignans from *H. nymphaeifolia* affected estrogenic compound-induced Ca^{2+} mobilization in human neutrophils. The lignans reduced intracellular free Ca^{2+} levels without affecting clomiphene-induced increases. However, epi-aschantin inhibited tamoxifen-induced Ca^{2+} influx, demonstrating that the lignans affected estrogenic compounds-induced Ca^{2+} signalling in numerous ways[38]. The study investigated to determine how these five lignans from *H. nymphaeifolia* affected the production of Reactive Oxygen Species (ROS) and the mobilization of Ca^{2+} in human neutrophils. Without affecting ROS creation caused by arachidonic acid, the lignans, which include epi-yangambin, epi-magnolin, epi-aschantin, deoxypodophyllotoxin, and yatein, inhibited ROS generation generated by N-formyl-methionyl-leucyl-phenylalanine and phorbol myristate acetate. Additionally, they reduced the amounts of intracellular free Ca^{2+} in both Ca^{2+}-containing and Ca^{2+}-free media. The findings reveal the many modifications that lignans make to Ca^{2+} signalling and ROS production in human neutrophils[39].

4. Conclusion

According to the World Health Organization, more than 80% of people worldwide who live in underdeveloped nations rely mostly on herbal remedies for their essential medical needs. Traditional and ethnobotanical uses of natural substances, particularly those derived from plants, have drawn a lot of attention in recent years due to their well-known efficacy and largely accepted safety for use by humans. The traditional method is the one to employ when looking for novel compounds to treat various diseases. The main goal of this review was to describe and investigate the pharmacological and therapeutic benefits of *H. nymphaeifolia*. Preclinical research showed that this plant has anti-cytotoxic, anti-inflammatory, anti-platelet aggregation, vasodilator, antioxidant, anti-microbial, and Ca^{2+} signalling characteristics. Since there may be more therapeutic benefits to this plant than are now understood, researchers are looking into its therapeutic potential.

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