Phytochemical and Pharmacological Insights into Hernandia nymphaeifolia: A Comprehensive Review

Durgesh Ranjan Kar[1], Moulik Bhattacharyya[1*], Saikat Polley[1], Payel Mukherjee[1], Sudeshna Halder[1], Anshuman Bhattacharya[1], , Shubhadip Bera[1], Sneha Das[1].

[1]B.C.D.A. College of Pharmacy and Technology, Campus- 2, Ghosh Para, Kolkata - 700129, West Bengal, India.

Corresponding author- Moulik Bhattacharyya

Abstract

Medicinal plants have served as the primary source of therapeutic agents since ancient times. Even today, many modern drugs are derived either directly from plant extracts or through the modification of natural compounds. Plants produce bioactive substances known as phytoconstituents, which play essential roles in their biological functions and defense mechanisms against pathogens such as viruses, fungi, and other microorganisms. Interestingly, these compounds also exhibit significant therapeutic benefits for humans. *Hernandia nymphaeifolia* is an important traditional medicinal plant widely used in various indigenous systems of medicine to manage different health conditions. Extracts obtained from different parts of the plant have shown notable therapeutic efficacy. Several pharmacological studies have reported its diverse biological activities, including anti-cytotoxic, anti-inflammatory, anti-platelet aggregation, vasodilatory, antioxidant, antimicrobial, and calcium-signaling effects. This review provides a comprehensive overview of the plant's taxonomical classification, phytochemical composition, pharmacological properties, and its potential therapeutic applications.

Keywords: Hernandia nymphaeifolia , Phytochemistry, Pharmacological activities, Antioxidant, Medicinal pl

1. Introduction

In recent years, there has been a growing scientific interest in therapeutic plants derived from natural sources, largely due to their wide-ranging pharmacological potential and relatively lower incidence of adverse effects compared to synthetic drugs [1]. Natural products have long served as a cornerstone in drug discovery and development, offering a diverse array of bioactive compounds with significant therapeutic value. This renewed focus is also driven by the

increasing global demand for safer, cost-effective, and accessible healthcare solutions. It is estimated that nearly 80% of the global population, especially those residing in developing and underdeveloped countries, depend heavily on traditional medicine for their primary healthcare needs. In many such regions, modern healthcare infrastructure remains limited or inaccessible, prompting individuals to rely on indigenous systems of medicine, including herbal remedies and plant-based formulations. Furthermore, a substantial proportion of patients in low-income countries often integrate conventional medical treatments with traditional healing practices, creating a complementary approach to disease management [2–4]. One of the major advantages of traditional medicines is their affordability. Compared to modern pharmaceuticals, herbal remedies are generally less expensive and more readily available, making them a practical option for economically disadvantaged populations. In remote and rural areas, where access to healthcare facilities and synthetic drugs is minimal, medicinal plants often serve as the only viable source of treatment. These natural remedies are deeply rooted in cultural traditions and are typically passed down through generations, contributing to their continued use and acceptance [5]. Among the various medicinal plants, *Hernandia nymphaeifolia*, belonging to the family Hernandiaceae, has attracted attention due to its ethnopharmacological significance and diverse biological activities. This plant is commonly found in coastal regions and thrives in tropical and subtropical climates, particularly along sandy beaches and seashores [6]. Despite its recognized identity, *H. nymphaeifolia* has historically been subject to taxonomic confusion and has occasionally been misidentified as *Hernandia ovigera* or *Hernandia sonora* in regions such as Taiwan and Japan [7, 8]. Such misidentifications highlight the importance of accurate botanical classification for proper scientific investigation and medicinal use. Traditionally, *Hernandia nymphaeifolia* has been utilized for a variety of therapeutic purposes. It has been employed as a hemostatic agent to control bleeding, as a depilatory for hair removal, and as a cathartic to relieve constipation [9]. In addition to these uses, different parts of the plant have been incorporated into traditional remedies for treating stomach pain, particularly in regions like Western Samoa, where indigenous knowledge systems play a crucial role in healthcare practices [17]. Phytochemical investigations of *H. nymphaeifolia* have revealed the presence of numerous bioactive constituents responsible for its diverse pharmacological properties. These compounds have demonstrated a wide spectrum of biological activities in various experimental studies. Notably, the plant exhibits significant cytotoxic effects, suggesting its potential role in anticancer

research [10, 11]. It also possesses anti-plasmodial activity, indicating possible applications in the treatment of malaria [11, 12]. Furthermore, the plant has shown anti-platelet aggregation properties, which may contribute to cardiovascular health by preventing abnormal blood clot formation [13]. In addition, *H. nymphaeifolia* exhibits strong antioxidant activity, helping to neutralize free radicals and reduce oxidative stress, which is implicated in numerous chronic diseases [14]. Its anti-inflammatory properties further support its potential use in managing inflammatory conditions [15]. The plant also demonstrates vasorelaxant activity, which may aid in regulating blood pressure, as well as antibacterial effects that enhance its usefulness in combating microbial infections [14, 16].

Overall, the increasing recognition of *Hernandia nymphaeifolia* as a valuable medicinal plant underscores the importance of exploring natural resources for drug development. Its diverse traditional applications, coupled with scientifically validated pharmacological activities, highlight its potential as a promising candidate for future therapeutic innovations.

Table 1: Plant Taxonomy: (USDA plants database)

Synonyms	***Lantern tree***	***References***
Kingdom	Plantae	[18]
Subkingdom	Tracheobionta	[18]
Super division	spermatophyta	[18]
Division	Magnoliophyta – a flowering plant	[18]
Class	Magnoliopsida- Dicotylendon	[18]
Subclass	Magnolidae	[18]
Order	Lauraies	[18]
Family	Hernandiaceae	[18]
Genus	Hernandia	[18]
Species	Hernandianymphaeifolia (Kubitzki)	[18]

2. Morphology of plant:

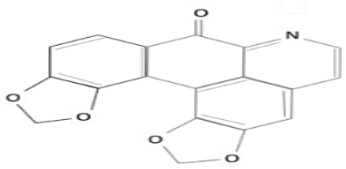
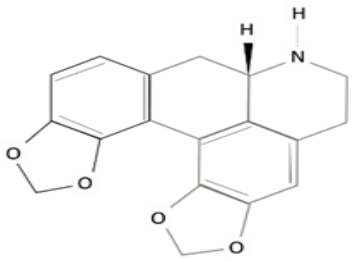
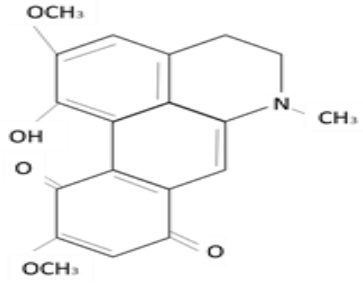
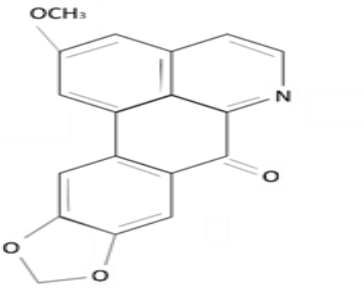
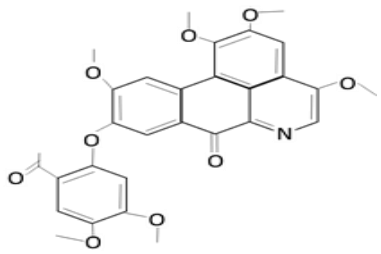
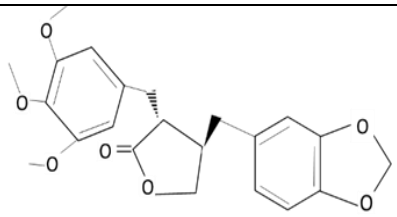
The soft-wooded trees of this species vary in height, ranging from 5 to 40 feet. They are characterized by alternating, broad, and glossy green leaves that transition in form from oblong to a shield-like, peltate shape. The inflorescences consist of small white flower clusters arranged in panicles located within the leaf axils. Its fruit is distinctively hard and black, encased in a transparent, circular, and firm layer that varies in color from whitish to reddish. The current study was undertaken to investigate the medicinal attributes and various pharmacological activities of Hernandia nymphaeifolia [17].

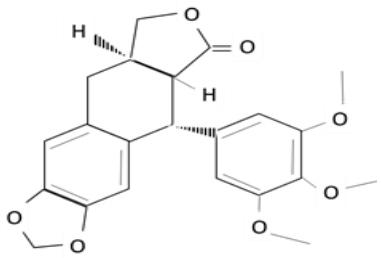
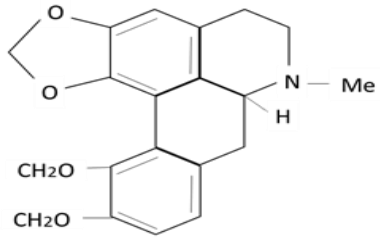
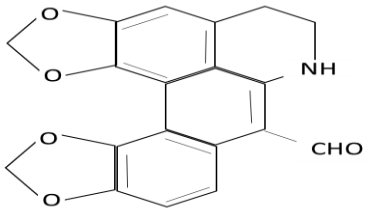
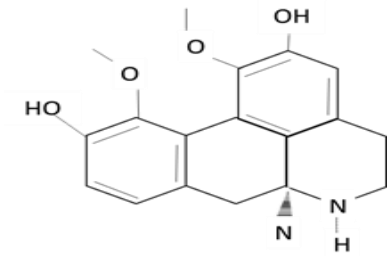
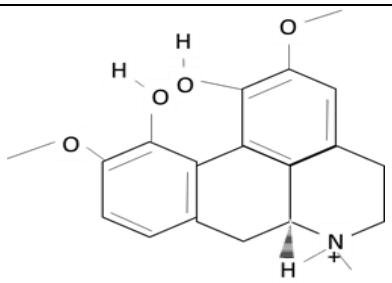
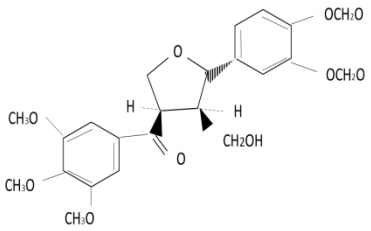
3. Phytochemistry

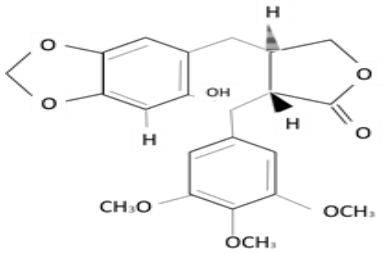
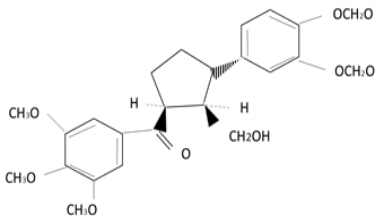
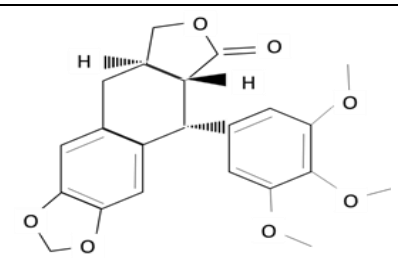
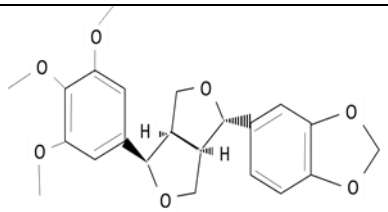
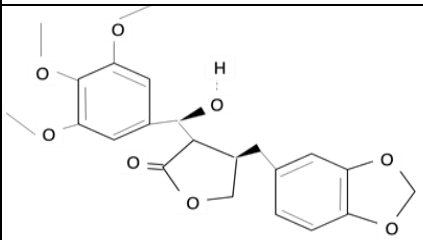
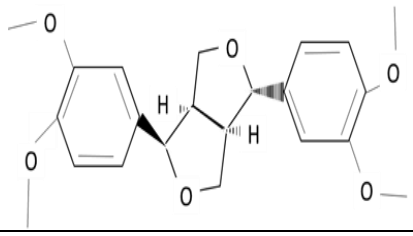
Hernandia nymphaeifolia is recognized for its rich and diverse phytochemical composition, which contributes significantly to its wide range of biological activities. Various classes of secondary metabolites have been isolated from this plant, particularly alkaloids and lignans, which are known for their pharmacological importance. Among these, oxoaporphine alkaloids and p-quinonoid aporphine alkaloids have been extensively reported, highlighting the plant's potential in bioactive compound research [7, 10]. Additionally, noraporphine alkaloids have also been identified, further expanding the diversity of its alkaloidal profile [13]. Apart from alkaloids, *H. nymphaeifolia* contains different types of lignans, including furanoid lignans and dibenzylbutyrolactone lignans, which are often associated with antioxidant and anticancer properties [13, 20]. The presence of amides adds to its chemical complexity and may contribute to its therapeutic effects [19]. Furthermore, the plant is a source of steroids, which are known for their role in anti-inflammatory and hormonal activities [13, 15]. Other notable constituents include isoquinolones and benzylisoquinoline derivatives, both of which are recognized for their diverse pharmacological actions [20]. This broad spectrum of phytochemicals underscores the medicinal significance of H. nymphaeifolia.

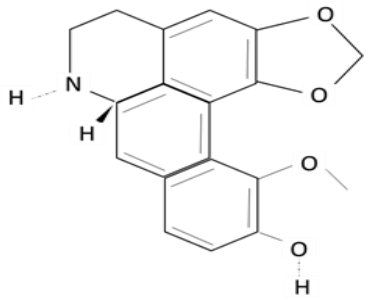
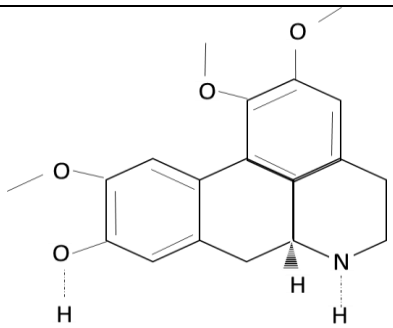
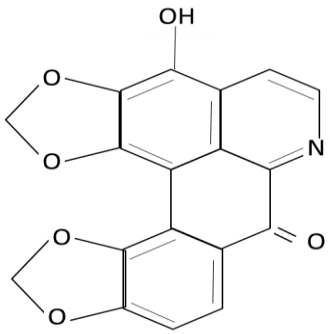
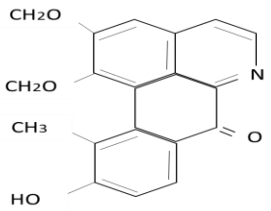
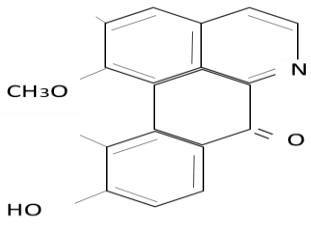
Table 2: Physical-chemical characteristics of *H. nymphaeifolia's* phytochemicals, including their pharmacological effects:

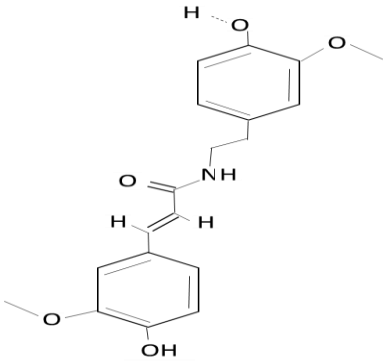
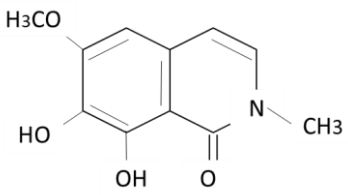
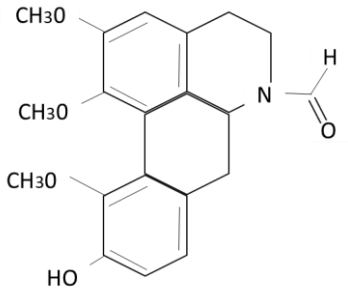
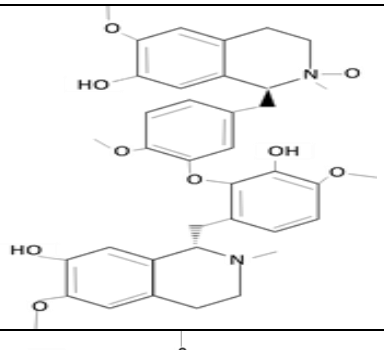
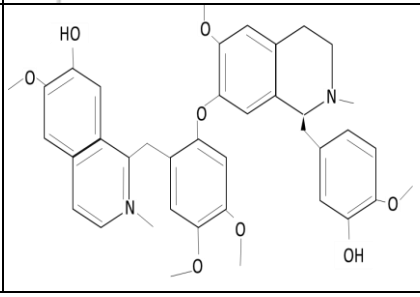
Sl No	*Name Of Compound*	*Molecular Formula*	*Chemical Structure*	*Molecular Weight*	*Nature Of Compound*	*Pharmacological Activities*	*Ref*

1	Hernandonine	$C_{18}H_9NO_5$		319.3	Oxoaporphine alkaloid	Antineoplastic activity	[7]
2	(+)-ovigerine	$C_{18}H_{15}NO_4$		309.3	Oxoaporphine alkaloid	Antineoplastic activity, Antiplatelet activity, Vasorelaxing activity,	[10, 20, 14]
3	Demethylsonodione	$C_{19}H_{17}NO_5$		339.11	P-quinonoid aporphine alkaloids	Antineoplastic activity	[10]
4	Hernanymphine	$C_{18}H_{11}NO_4$		305.29	Oxoaporphine Alkaloids	Antineoplastic activity	[10]
5	Methoxyoxohernandaline	$C_{29}H_{25}NO_9$		531.5	Alkaloid	Antineoplastic activity	[10]
6	(-)-yatein	$C_{22}H_{24}O_7$		400.4	Lignan	Antineoplastic activity	[10]

7	(-)-deoxypodophyllotoxin	$C_{22}H_{22}O_7$		398.4	Lignan	Antineoplastic activity	[10]
8	(+)-N-methylovigerine	$C_6H_5NH(CH_3)$		107.15	Alkaloid	Antineoplastic activity	[10]
9	N-formyldehydroovigerine	$C_{19}H_{13}NO_5$		335.3	Alkaloid	Antineoplastic activity	[10]
10	(+)-hernovine	$C_{18}H_{19}NO_4$		313.3	Alkaloid	Antineoplastic activity	[20]
11	(+)-magnoflorine	$C_{20}H_{24}NO_4^+$		342.4	Alkaloid	Antineoplastic activity	[20]
12	(-) hernone	$C_{23}H_{28}O_8$		432.17	Furanoid lignan	Antineoplastic activity ,Less Antiplatelet activity	[20, 13]

13	(-) hydroxyyatein	$C_{22}H_{24}O_8$		416.42	Dibenzylbutyrolactone lignan	Antineoplastic activity	[20]
14	(-) nymphone	$C_{22}H_{24}O_8$		416.42	Furanoid lignan	Antineoplastic activity	[20]
15	Deoxypodophyllotoxin	$C_{22}H_{22}O_7$		398.4	Lignan	Antineoplastic activity, Antimicrobial activity	[16]
16	(+) epiaschantin	$C_{22}H_{24}O_7$		400.4	Lignan	Antineoplastic activity, Antiplatelet activity	[16, 13]
17	Podorhizol	$C_{22}H_{24}O_8$		416.4	Lignan	Antineoplastic activity	[16]
18	(+)-epieudesmin	$C_{22}H_{26}O_6$		386.4	Lignan	Antineoplastic activity	[16]

19	Hernangerine	$C_{18}H_{17}NO_4$		311.332	Norapophines alkaloid	Antiplatelet activity, Vasorelaxing activity	[13, 14]
20	Laurotetanine	$C_{19}H_{21}NO_4$		327.4	Norapophines alkaloid	Antiplatelet activity	[13, 14]
21	3-hydroxyhernandonine	$C_{18}H_9NO_6Na$		358	Aporphine alkaloid	Anti-inflammatory activity	[15]
22	Oxohernangerine	$C_{18}H_{11}NO_5$		321.3	Oxoapophines alkaloid	Anti-inflammatory activity	[15]
23	Oxohernagine	$C_{19}H_{15}NO_5$		337.3	Oxoapophines alkaloid	Anti-inflammatory activity	[19]

24	N-trans-Feruloylmethoxytyramine	$C_{19}H_{21}NO_5$		343.4	Amide	Anti-inflammatory activity	[19]
25	7,8-dihydroxy-6-methoxy-2-methylisoquinolin-1(2H)-one	$C_{11}H_{11}NO_3$		205.21	Alkaliod	Anti-inflammatory activity	[19]
26	N-formylhernagine	$C_{20}H_{21}NO_5$		378.131	Alkaloid	Anti-inflammatory activity	[19]
27	(+)-vateamine 2'-β-N-oxide	$C_{38}H_{44}N_2O_9$		672.8	isoquinoline N-oxide alkaloids	Antioxidant activity	[14]
28	(+)-malekulatine	$C_{39}H_{46}N_2O_8$		670.8	Alkaloid	Antioxidant activity, Antimicrobial activity	[14, 16]

4. PHARMACOLOGICAL ACTIVITIES

4.1. Antineoplastic activity:

Chloroform-soluble extracts obtained from the trunk bark of *Hernandia nymphaeifolia* have been reported to possess significant anticancer potential, as demonstrated through bioassay-guided fractionation studies. Out of 44 isolated constituents, nine compounds—namely hernandonine, (+)-ovigerine, demethylsonodione, hernanymphine, methoxyoxohernandaline, (−)-yatein, (−)-deoxypodophyllotoxin, (+)-N-methylovigerine, and N-formyldehydroovigerine—exhibited pronounced cytotoxic activity against various cancer cell lines, including KB-16, P-388, HT-29, and A549 [10]. Additionally, (+)-hernovine and (+)-magnoflorine demonstrated selective cytotoxicity against the P-388 leukemia cell line in vitro, with ED_{50} values of 0.214 µg/mL and 0.229 µg/mL, respectively [20]. Further investigations have identified lignans from chloroform extracts of the trunk as key contributors to the plant's anticancer activity. These include two furanoid lignans, (−)-nymphone and (−)-hernone, along with a dibenzylbutyrolactone lignan, (−)-hydroxyyatein. These compounds exhibited notable in vitro efficacy against human lung adenocarcinoma (A549), nasopharyngeal carcinoma (KB-16), mouse lymphocytic leukemia (P-388), and human colon carcinoma (HT-29) cell lines [20]. Among the bioactive constituents, deoxypodophyllotoxin, isolated from the seeds, has emerged as a potent anticancer agent, demonstrating cytotoxic effects across a wide range of cancer cell lines, including cholangiocarcinoma, KB-16, K562, HT-29, A549, PC-3, LNCaP, and Colo-205 [21–25]. In contrast, certain compounds such as (+)-epiaschantin, podorhizol, (+)-epiedesmin, and isostegane, isolated from the bark, exhibited only limited inhibitory activity against cancer cell lines. Podorhizol showed activity against only two cell lines, while (+)-epiaschantin was selectively active against the P-388 leukemia cell line [16]. Structural modification of deoxypodophyllotoxin has led to the synthesis of several derivatives, among which four compounds—methyl acetoxydeoxypodophyllate, 2′-bromodeoxypodophyllotoxin, 2,2′-dibromodeoxypodophyllotoxin, and 2,2′,6′-tribromodeoxypicropodophyllotoxin—demonstrated enhanced cytotoxic activity compared to the parent compound. Notably, 2,2′-dibromodeoxypodophyllotoxin exhibited significant potency, with IC_{50} values of 0.75 µM and 0.46 µM against KKU-100 and HepG2 cell lines, respectively, and has been proposed as a promising lead molecule for anticancer drug development [26].Moreover, fruit extracts prepared

using a methanol:methylene chloride (1:1) solvent system showed considerable antiproliferative activity against human tumor cell lines. Compounds such as epiaschantin and epieudesmin demonstrated effectiveness against chemosensitive carcinoma cell lines, including A549 and MCF-7. Interestingly, despite reduced activity against the parental chemosensitive KB cell line, both compounds exhibited notable cytotoxicity against the multidrug-resistant KB-VIN cell line, which overexpresses P-glycoprotein, with IC_{50} values around 5 μM [27]. These findings collectively highlight the significant anticancer potential of *H. nymphaeifolia* and its bioactive constituents.

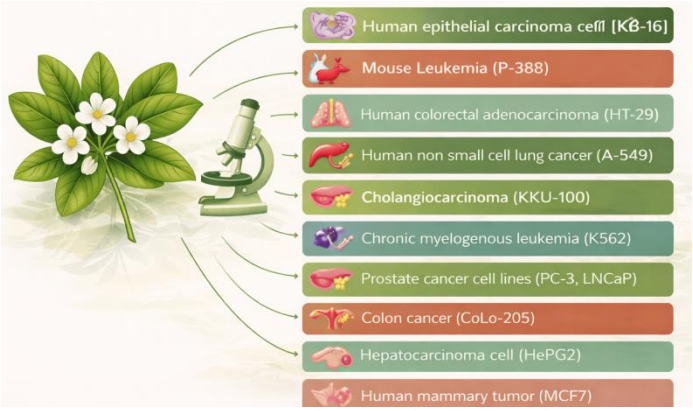


Fig. 1: Cytotoxic Cell lines inhibited by the *H. nymphaeifolia*

4.2. Antiplatelet aggregation:

Noraporphine alkaloids, including hernangerine, ovigerine, and laurotetanine, have been reported to exhibit comparatively stronger antiplatelet activity than oxoaporphine derivatives such as oxohernangerine, hernandonine, and atheroline. This enhanced activity is primarily attributed to their interaction with key platelet activation pathways involving collagen, platelet-activating factor (PAF), and arachidonic acid (AA). Among the oxoaporphines, oxohernagine demonstrated notable antiplatelet effects, particularly when substituted with 10-hydroxy-12,11-trimethoxy groups, suggesting the importance of structural modifications in modulating biological activity. Ovigerine also showed significant inhibitory effects on platelet aggregation induced by collagen, PAF, and arachidonic acid, although certain assay parameters did not reflect strong activity. In addition to alkaloids, several furanoid lignans have exhibited considerable antiplatelet properties. The activity trend among these compounds was observed in the following order: (−)-hernone (a

chevage-type lignan with a bis-tetrahydrofuran ring) < (+)-epimagnolin (bearing 3′,4′-dimethoxy substitution) < (+)-epiyangambin (with 3′,4′,5′-trimethoxy groups) < (+)-epiaschantin (containing a 3′,4′-methylenedioxy moiety) [13]. These findings indicate that both alkaloids and lignans from *Hernandia nymphaeifolia* contribute significantly to its antiplatelet potential, with structural features playing a crucial role in their activity.

4.3. Vasorelaxing activity:

A total of sixteen compounds have been isolated from *Hernandia nymphaeifolia*, several of which exhibit notable vasorelaxant properties. Experimental studies indicate that oxoaporphine alkaloids, including hernandonine, atheroline, and oxohernangerine, demonstrate comparatively weaker vasorelaxant effects. In contrast, noraporphine alkaloids such as ovigerine, laurotetanine, and hernangerine show significant inhibition of aortic contractions induced by high potassium (80 mM) and norepinephrine (3 mM). Among these, ovigerine has been identified as particularly effective in suppressing contractile responses; however, its dimeric counterpart, ovigeridimerine, does not exhibit any appreciable vasorelaxing activity. Furthermore, certain oxoaporphines, specifically oxohernagine and oxohernangerine possessing a 10-hydroxy substitution, display marked vasorelaxant effects, suggesting the importance of structural modifications in enhancing biological activity. Nevertheless, when compared with standard pharmacological agents such as prazosin, an α_1-adrenoceptor antagonist, and nifedipine, a calcium channel blocker, the vasorelaxant potency of these natural compounds is relatively lower [14].

4.4. Anti-inflammatory activity:

Inflammatory responses are often mediated by the release of granule-associated proteases from activated human neutrophils, including cathepsin G and elastase, along with the generation of reactive oxygen species (ROS) such as hydrogen peroxide and superoxide anion ($O_2^{\bullet -}$). These mediators play a crucial role in the progression of various inflammatory disorders. The anti-inflammatory potential of compounds is commonly assessed by evaluating their ability to inhibit elastase release and suppress superoxide anion production in fMLP/CB-stimulated neutrophils. In this context, methylene chloride-soluble methanolic extracts obtained from the root wood of

Hernandia nymphaeifolia have demonstrated significant anti-inflammatory activity. Phytochemical investigations led to the isolation of eight bioactive compounds, namely 3-hydroxyhernandonine, 7-oxonorisocorydine, hernandonine, oxohernangerine, oxohernagine, 4′-O-demethyl-7-O-methyldehydro-podophyllotoxin, 2-O-methyl-7-oxolaetine, and N-trans-feruloylmethoxytyramine, all of which exhibited notable inhibitory effects on inflammatory mediators. Among these, 3-hydroxyhernandonine and oxohernangerine were identified as the most potent agents, effectively suppressing fMLP-induced superoxide anion generation and elastase release [15]. Further studies revealed that additional compounds, including N-trans-feruloyl methoxy-tyramine, 7,8-dihydroxy-6-methoxy-2-methylisoquinolin-1(2H)-one, hernandonine, oxohernagine, 5,6-dihydroxy-N-methylphthalimide, and N-formylhernagine, also significantly inhibited neutrophil activation markers such as superoxide anion production and elastase release. Notably, oxohernagine exhibited remarkable efficacy, with IC_{50} values of 4.88 ± 0.29 µg/mL for elastase inhibition and 2.84 ± 0.78 µg/mL for superoxide anion suppression. Moreover, several compounds, including oxohernagine, N-formylhernagine, 7,8-dihydroxy-6-methoxy-2-methylisoquinolin-1(2H)-one, and N-trans-feruloylmethoxytyramine, showed strong inhibitory effects on lipopolysaccharide (LPS)-induced nitric oxide (NO) production, further supporting their anti-inflammatory potential [19].

4.5. Antioxidant activity:

The ethanolic extract of *Hernandia nymphaeifolia* demonstrated notable antioxidant potential, as evidenced by its activity in the DPPH radical scavenging assay. Among the isolated constituents, (+)-malekulatine ($IC_{0.200}$ = 3 mM), reticuline ($IC_{0.200}$ = 2.1 mM), and (+)-vateamine 2-β-N-oxide ($IC_{0.200}$ = 3 mM) exhibited the most pronounced free radical scavenging effects. Notably, these compounds showed superior antioxidant activity when compared to the standard reference compound, α-tocopherol [14].

4.6. Antimicrobial activity:

The growth of the Gram-negative bacterium *Neisseria gonorrhoeae* was effectively inhibited by several bioactive compounds isolated from *Hernandia nymphaeifolia*, including hernanol, kusunokinol, (−)-deoxypodophyllotoxin, deoxypicropodophyllin, (−)-maculatin, clusin, and podorhizol. These phytoconstituents demonstrated significant antibacterial potential, with

minimum inhibitory concentration (MIC) values ranging from 32 to 64 µg/mL [16]. The observed antimicrobial activity may be attributed to the ability of these compounds to disrupt bacterial cell wall integrity, interfere with essential metabolic pathways, or inhibit nucleic acid synthesis. Such findings highlight the therapeutic relevance of *H. nymphaeifolia* as a promising natural source of antimicrobial agents, particularly against drug-resistant Gram-negative pathogens.

4.7. Ca^{2+} signalling:

Several bioactive constituents isolated from *Hernandia nymphaeifolia*, including hernanol, kusunokinol, (−)-deoxypodophyllotoxin, deoxypicropodophyllin, (−)-maculatin, clusin, and podorhizol, have been reported to exhibit potent antibacterial activity against the Gram-negative pathogen *Neisseria gonorrhoeae*. These compounds demonstrated considerable efficacy, with minimum inhibitory concentration (MIC) values ranging between 32 and 64 µg/mL [16]. The antibacterial effect of these phytoconstituents may be associated with multiple mechanisms of action, such as disruption of bacterial cell membrane integrity, inhibition of key metabolic processes, and interference with nucleic acid synthesis. Collectively, these findings underscore the significant antimicrobial potential of *H. nymphaeifolia*, suggesting its promise as a valuable natural source for the development of novel therapeutic agents, particularly in combating infections caused by drug-resistant Gram-negative bacteria.

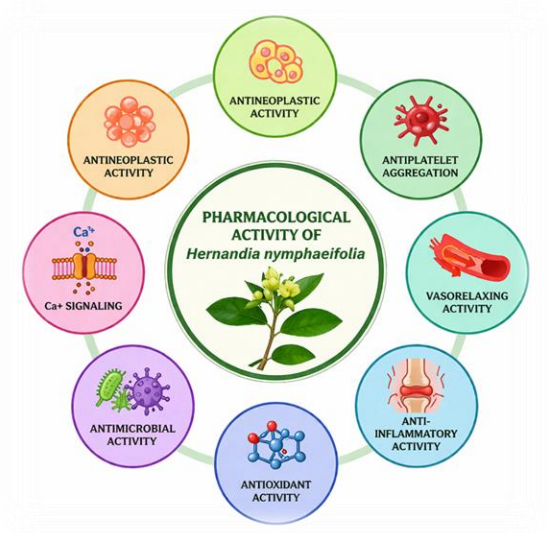


Fig 2: Pharmacological activity of *Hernandianymphaeifolia*

5. CONCLUSIONS:

In conclusion, *Hernandia nymphaeifolia* emerges as a plant of considerable pharmacological importance, supported by its rich phytochemical composition and diverse biological activities. The presence of bioactive constituents such as lignans, flavonoids, alkaloids, and phenolic compounds underpins its wide range of therapeutic potentials. These phytoconstituents have demonstrated significant cytotoxic, antimicrobial, antioxidant, and anti-inflammatory properties in various experimental studies, validating its traditional medicinal uses. Particularly noteworthy is its cytotoxic activity against multiple human cancer cell lines, indicating its promise as a potential source of anticancer agents. The ability of its compounds to induce apoptosis, inhibit cell proliferation, and interfere with key cellular pathways highlights its relevance in cancer research. Additionally, the antimicrobial activity exhibited against both Gram-positive and Gram-negative pathogens suggests its utility in combating infectious diseases, especially in the context of rising antimicrobial resistance. The antioxidant potential of *H. nymphaeifolia* further contributes to its therapeutic value by neutralizing free radicals and reducing oxidative stress, which is implicated in the pathogenesis of various chronic diseases. Moreover, its anti-inflammatory effects support its role in managing inflammatory conditions. Despite these promising findings, further research is essential to fully explore its pharmacological potential. Detailed studies on mechanism of action, toxicity, pharmacokinetics, and clinical efficacy are required to ensure safe and effective therapeutic application. Standardization of extracts and identification of lead compounds will also be crucial for drug development.

Overall, *Hernandia nymphaeifolia* represents a valuable natural resource with significant potential for the development of novel therapeutic agents, warranting continued scientific investigation and validation.

REFERENCES:

1. Shukla V, Joshi GP, Rawat MS. Lichens as a potential natural source of bioactive compounds: a review. Phytochemistry reviews. 2010 Jun;9:303-14.

2. Kisangau DP, Musila W, Muema J. Conservation status and use of medicinal plants by traditional medical practitioners in Machakos District, Kenya.

3. Mahwasane ST, Middleton L, Boaduo N. An ethnobotanical survey of indigenous knowledge on medicinal plants used by the traditional healers of the Lwamondo area, Limpopo province, South Africa. South African Journal of Botany. 2013 Sep 1;88:69-75.

4. Kinyanjui MJ, Latva-Käyrä P, Bhuwneshwar PS, Kariuki P, Gichu A, Wamichwe K. An inventory of the above ground biomass in the Mau Forest ecosystem, Kenya. Open Journal of Ecology. 2014 Jul 8;2014.

5. Popović Z, Matić R, Bojović S, Stefanović M, Vidaković V. Ethnobotany and herbal medicine in modern complementary and alternative medicine: An overview of publications in the field of I&C medicine 2001–2013. Journal of ethnopharmacology. 2016 Apr 2;181:182-92.

6. Yang, YP., Lu, SY. Flora of Taiwan. Hernandiaceae Editorial Committee of the Flora of Taiwan, Second Edition. Taipei, Taiwan, 1996.2,500-501.

7. Chen JJ, Tsai IL, Chen IS. New oxoaporphine alkaloids from Hernandianymphaeifolia. Journal of Natural Products. 1996 Feb 22;59(2):156-8.

8. Topographical distribution of Hernandianymphaeifolia (source: https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:430812-1, last accessed 21/04/2023)

9. Kan, WS., Manual of Medicinal Plants in Taiwan, vol. 1. National Research Institute of Chinese Medicine.1990 Taiwan.178–179.

10. Chen JJ, Ishikawa T, Duh CY, Tsai IL, Chen IS. New dimeric aporphine alkaloids and cytotoxic constituents of Hernandianymphaeifolia. Planta medica. 1996 Dec;62(06):528-33.

11. Angerhofer CK, Guinaudeau H, Wongpanich V, Pezzuto JM, Cordell GA. Antiplasmodial and cytotoxic activity of natural bisbenzylisoquinoline alkaloids. Journal of Natural Products. 1999 Jan 22;62(1):59-66.

12. Rasoanaivo P, Ratsimamanga-Urverg S, Rafatro H, Ramanitrahasimbola D, Palazzino G, Galeffi C, Nicoletti M. Alkaloids of Hernandiavoyronii: chloroquine-potentiating activity and structure elucidation of herveline D. Planta medica. 1998 Feb;64(01):58-62.

13. Chen JJ, Chang YL, Teng CM, Chen IS. Anti-platelet aggregation alkaloids and lignans from Hernandianymphaeifolia. Planta medica. 2000 Apr;66(03):251-6.

14. Chen JJ, Chang YL, Teng CM, Chen IS. Vasorelaxing and antioxidant constituents from Hernandianymphaeifolia. Planta medica. 2001;67(07):593-8.

15. Wei CY, Wang SW, Ye JW, Hwang TL, Cheng MJ, Sung PJ, Chang TH, Chen JJ. New anti-inflammatory aporphine and lignan derivatives from the root wood of Hernandianymphaeifolia. Molecules. 2018 Sep 7;23(9):2286.

16. Pettit GR, Meng Y, Gearing RP, Herald DL, Pettit RK, Doubek DL, Chapuis JC, Tackett LP. Antineoplastic Agents. 522. Hernandia p eltata (Malaysia) and Hernandia n ymphaeifolia (Republic of Maldives), 1. Journal of natural products. 2004 Feb 27;67(2):214-20.

17. Dittmar A. The effectiveness of Hernandiaspp.(Hernandiaceae) in traditional Samoan medicine and according to scientific analyses. Journal of ethnopharmacology. 1991 Jul 1;33(3):243-51.

18. USDA plants database. Accessed July 2, 2023. https://plants.usda.gov/home/classification/71342.

19. Lai YW, Wang SW, Hu YY, Hwang TL, Cheng MJ, Chen IS, Sung PJ, Chen JJ. Anti-inflammatory alkaloids from the root bark of Hernandianymphaeifolia. Phytochemistry. 2020 May 1;173:112326.

20. Chen IS, Chen JJ, Duh CY, Tsai IL. Cytotoxic lignans from formosanHernandianymphaeifolia. Phytochemistry. 1997 Jul 1;45(5):991-6.

21. MORIMOTO T, CHIBA M, ACHIWA K. Asymmetric Reactions Catalyzed by Chiral Metal Complexes. Part 37. Asymmetric Total Synthesis of (-)-Deoxypodophyllotoxin (I). ChemInform. 1990 Sep 4;21(36).

22. Bogucki DE, Charlton JL. An asymmetric synthesis of (-)-deoxypodophyllotoxin. The Journal of Organic Chemistry. 1995 Feb;60(3):588-93.

23. Wickramaratne DB, Mar W, Chai H, Castillo JJ, Farnsworth NR, Soejarto DD, Cordell GA, Pezzuto JM, Kinghorn AD. Cytotoxic constituents of Bursera permollis. Planta medica. 1995 Feb;61(01):80-1.

24. Lim YH, Leem MJ, Shin DH, Chang HB, Hong SW, Moon EY, Lee DK, Yoon SJ, Woo WS. Cytotoxic constituents from the roots of Anthriscus sylvestris. Archives of pharmacal research. 1999 Apr;22:208-12.

25. Jiang RW, Zhou JR, Hon PM, Li SL, Zhou Y, Li LL, Ye WC, Xu HX, Shaw PC, But PP. Lignans from Dysosmaversipellis with inhibitory effects on prostate cancer cell lines. Journal of natural products. 2007 Feb 23;70(2):283-6.

26. Suthiwong J, Wandee J, Pitchuanchom S, Sojikul P, Kukongviriyapan V, Yenjai C. Cytotoxicity against cholangiocarcinoma and HepG2 cell lines of lignan derivatives from Hernandianymphaeifolia. Medicinal Chemistry Research. 2018 Aug;27:2042-9.

27. Aimaiti S, Saito Y, Fukuyoshi S, Goto M, Miyake K, Newman DJ, O'Keefe BR, Lee KH, Nakagawa-Goto K. Isolation, structure elucidation, and antiproliferative activity of butanolides and lignan glycosides from the fruit of Hernandianymphaeifolia. Molecules. 2019 Nov 5;24(21):4005.

28. Chao YY, Jan CR, Ko YC, Chen JJ, Jiann BP, Lu YC, Chen WC, Su W, Chen IS. Effect of lignans isolated from Hernandianymphaeifolia on estrogenic compounds-induced calcium mobilization in human neutrophils. Life sciences. 2002 May 17;70(26):3109-21.