**REVIEW ARTICLE** 



Rec. Nat. Prod. 3:1 (2009) 1-22

records of natural products

# An Overview of Family Hernandiaceae

# Vijai Lakshmi<sup>1\*</sup>, Kartekey Pandey,<sup>1</sup> Sunil K.Mishra<sup>1</sup>, Shishir Srivastava<sup>1</sup>, Manisha Mishra<sup>1</sup>and Santosh K.Agarwal<sup>2</sup>

<sup>1</sup>Division of Medicinal Chemistry, Central Drug Research Institute

<sup>2</sup> Phytochemistry Division, Central Institute of Medicinal And Aromatic plants

Lucknow-226001, India.

(Received August 23, 2008; Revised December 12, 2008; Accepted December 15, 2008)

Abstract: Hernandiaceae is a family of higher plants, possessing a large number of bioactive compounds. The present review reveals the total compounds isolated, characterized from the family, till date.

Keywords: Hernandiaceae; lignans; alkaloids, biological activities.

# 1. Introduction

Hernandia is a genus of trees distributed mainly in the tropical and sub tropical regions of the world. In addition, the species of the genera belonging to this family are also found in equatorial regions and few oceanic islands such as Lombok, located in the South Pacific Ocean. In India, the *Hernandia ovigera (syn. H. peltata)* are found mainly in the Andaman and Nicobar group of Islands in India.

## **2.** Botanical Description

Hernandia is an evergreen tree with a spreading crown. Bark thick, silvery grey, leaves ovate, 4-9x3-6 inches, truncate or sub-cordate at the base of long petiole joining the blades within margin, flowers yellowish white in involucrate clusters borne at the ends of tomentose panicles, each cluster having two male and a central female flower, fruits ovoid in long dark ribbed.

<sup>\*</sup> Corresponding author: E-mail: vijlakshmius@yahoo.com

## 3. Ethno medical uses

The bark, seeds and young leaves are purgative. The seeds produce dizziness. The root is chewed as a remedy against eating poisonous crabs and fishes. The juice of the bark and leaves has depilatery properties [1]. The available information on the plant parts used by Samoan healers, their modes of preparation and application have been listed in Table-1 [2]. The leaves of the plant are used as hypertensive [3] antitumor [4] prophylaxis of arteriosclerosis [5] piscicide[6]. The Stem bark, xylum, root bark, twigs, stalks and seeds of the plant are used as hypotensive, non-cholinergic, relaxant smooth musculature, vasopressive, Sympathicomimetic for inflammation and irritation of the upper respiratory system and the gastrointestinal tract. Also used as mild laxative, antidiarrheal, cytotoxic, cytostatic, antiviral, externally on boils, ulcers, sores, inflammations [1]. The pericarp of the fruits also relaxes the smooth musculature, produces a cataleptic action, anti-convulsive, in convulsive disorders, vasopressive, reduces intestinal movement, hypotensive, non-cholinergic, dilation of capillary blood vessels (non toxic low doses) respiration is accelerated, uterus-stimulating (large doses) respiration is slowed, uterus- inhibitor, stimulation of the secretion of tears and saliva, might cause emesis and moderate tachycardia, hypnotic, sedative, narcotic, adrenolytic, psychomimetic, induces hyperglycemia [1].

#### 3.1. Chemical compounds and associated biological activities

*H. ovigera* (syn. *H. peltata*) is the most abundant species in terms of the sheer number of compounds isolated and subsequent biological activities reported in the literature. This species alone accounts for almost half of the total compounds isolated from Hernandiaceae. This also indicates the fact that *H. ovigera* is the most extensively investigated species. *H. nymphaeifolia* is equally rich in the number of biologically active chemical compounds, as *H. ovigera* other noteworthy species of the family are *H. catalpifolia*, *H. jamaicensis*, *H. cordigera*, *Gyrocarpus americanus*, *Illigera pentaphylla*, etc.

Among the chemical compounds isolated from the family Hernandiaceae, Corytuberine is the oldest known compound, first reported from *Corydalis cava* [7]. Later on, its derivative O, O-Dimethylcorytuberine was reported from several *Hernandia* species, including *H. nymphaeifolia*. Actinodaphnine and hernandion, were the earliest chemical compounds reported from the family hernandiaceae respectively [8]. Only one review published on the family Hernandiaceae [4] till now.

The compounds isolated from Hernandiaceae possess rich biological activities such as cytotoxicity, antimalarial, cardiovascular activities, etc. Among the most potent cytotoxic constituents are, (-)-Deoxypodophyllotoxin, (-)-Yatein and Hernandonine. These three compounds were found to be more active than Mithramycin, at an ED<sub>50</sub> ( $\mu$ g/ml) value of <0.001 against P-388 cell lines. (+)-N-Methyl hernangerine was shown to be comparable in activity with Mithramycin [9].

Among the compounds active as cardiovascular system agents, (+)-Ovigerine, (+)-N-Methyl laurotetanine, and (+)-Hernandaline were the most active when compared to the standard drugs, Nifedipine and Prazosin. The anti-platelet aggregation activity was found to be present in varying degrees among the alkaloids and lignans isolated from *H. nymphaeifolia*. noraporphines, ovigerine, hernangerine and laurotetanine caused by arachidonic acid (AA), collagen or platelet aggregation factor (PAF), but the antiplatelet effects of their corresponding oxoaporphines, hernandonine, oxohernangerine and atheroline were reduced. Hernandaline also showed significant inhibitory activity on platelet aggregation induced by AA, collagen and PAF, but dehydrohernandaline showed reduced anti-platelet effects due to the effect of the aromatic ring. Ovigerine showed significant inhibitory activity on platelet aggregation induced by AA, collagen and PAF, but its dimer, (+)-ovigeridimerine showed reduced anti-platelet effects. Among the oxoaporphines, only oxohernagine, with 10-hydroxy-1, 2, 11-trimethoxy substitution showed marked inhibitory activity on

platelet aggregation induced by AA, collagen and PAF. The furanoid Lignans, (-)- Hernone, (+)-Epiaschantin, (+)- Epimagnolin and Epiyangambin, possessed strong and selective inhibition of PAFinduced platelet aggregation, and the intensity of activity was maximum in (+)- Epiaschantin, with a 3', 4'-methylenedioxy. substituent and minimum in (-)- Hernone with cleavage type of bistetrahydrofuran ring Lignans of the podophyllotoxin category are the only class of compounds from the family Hernandiaceae, which are in the advanced stages of drug development studies, as anticancer compounds. However, there is an immense potential of developing drugs from the compounds isolated from this family, which have versatile biological activities.

Extensive chemical investigations of the plants have revealed the presence of a large number of chemical compounds, mainly including lignans and alkaloids. The genera from which chemical compounds are reported in the literature are, *Gyrocarpus, Illigera, Hernandia, Sparattanthelium* and *Valvanthera*. Among these five genera, genus *Hernandia* is the most abundant both in terms of compounds isolated and their biological activities reported. The alkaloids isolated belong to mainly two chemical classes' viz., benzyl, or bisbenzylisoquinoline, and the aporphine or noraporphine class. Broadly speaking, the lignans have been shown to possess antitumor and anticancer biological activities, while the alkaloids have been reported antiplasmodial and effective CVS agents. The antitumor activity of the lignans can be explained on the chelating property, due to the presence of easily replaceable, vicinal, phenolic hydrogens. Similarly, the presence of antiplasmodial activity in the alkaloids can be linked to their structural resemblance with the Isoquinoline antimalarial compounds. This is the first comprehensive review of the compounds isolated from the family Hernandiaceae, along with their biological activities reported in the literature.

# 3.2. General Extraction and Isolation Procedures

Initial investigators in the nineteenth century, relied more on simple techniques like crystallization and pH partition for the isolation of pure constituents from the crude extract. With the advent of chromatographic techniques in the second half of the 20<sup>th</sup> century, the isolation processes were revolutionized forever. Various useful manifestations of column chromatography, using different stationary phases, such as Silica gel, Alumina, Sephadex, Ion-exchange resins, flash chromatography, reversed-phase chromatography etc. were employed to resolve the extract / mixture of compounds into pure compounds. These developments, coupled with the improved analytical techniques such as, high field NMR spectroscopy, high-resolution mass spectrometry, GC-MS, LC-MS and ESMS, powered with high precision instruments, made the task relatively easier for the Natural Product chemist. As the compounds occurring in Hernandiaceae belong to diverse chemical classes, the pH partitioning has proved to be an effective technique for isolation of acidic (lignans) and basic (alkaloids) components from the extract. Although the method of isolation by pH partition has its own limitations, it was successfully employed in the case of family *Hernandiaceae*, because most of the compounds are chemically stable and occur as solids at room temperature.

Hernandia species	Plant parts used	Mode of preparation / application	Diseases	References
H. peltata M.	Bark (juice)	Not reported in lit.	Cough	[2]
H. ovigera L.	Bark	Applied internally	Puerperal complaints	[2]
H. ovigera L.	Bark	Not reported in lit.	Boils	[2]
H. ovigera L.	Bark	Applied internally	To ease menstrual cramps of young girls.	[2]
H. ovigera L.	Bark	Applied internally	Constipation	[2]
H. peltata M. <sup>*</sup>	Stem bark	The stem bark preparation	Manavatata "diarrhoea".	[2]
H.peltata $M^*$	Juice	Depilatory properties	Abdominal pains	[2]
H. ovigera L.	Leaves	Not reported in literature	Puerperal complaints	[2]
H.peltata $M^*$	Young leaves, leaf shoots	A preparation of sp. is applied	Eye complaints	[2]
H.ovigera L.	Seeds	No information	Lice	[2]
H.ovigera L.	Roots	Applied internally	Menorrhagia	[2]

Table 1. Medical uses of Hernandia species in Traditional Samoa $^{\psi}$ 

\*Also identified as, Hernandia sonora L.

♥This table is from Article of Dittmar [1].



Table 2. Compounds with biological activities



Table 2. Continued









Table 2. Continued



Table 2. Continued



Table 2. Continued



```
Table 2. Continued
```



#### Table 2. Continued







#### Table 2. Continued









#### 4. Discussion

The Table 1 gives the medical uses of *Hernandia* species in traditional Samoa. The Table 2 gives an account of the chemical structures of the compounds isolated and characterized from five genera of the family Hernandiaceae. More than half of the compounds have been reported from the genus *Hernandia*. Many compounds are of common occurrence among different species of the same genus, while the overlapping occurrence of compounds is rarely found between different genera of the family. Among the compounds, alkaloids have predominant occurrence, followed by Lignans. Majority of the alkaloids belong to two chemical classes viz., the aporphine class and the Bisbenzyl isoquinoline class. The alkaloids mainly occur in stem bark, stem xylem and root bark, while the Lignans are found primarily concentrated in seeds and/or fruits, mainly as fixed oils. Most of the compounds are optically active, may be a contributing factor, towards their biological activities. As the members of the family Hernandiaceae are found along or, near the seashore, in tropical and subtropical regions of the world, valuable conclusions can be drawn and predictions made, on the possible reasons of the storage of chemical compounds, in specific plant parts. The rates of transpiration and respiration are high in hot and humid conditions, which may be a possible reason for the fact that very few compounds have been isolated from the leaves, as compared to other plant part.

#### Acknowledgements

We are grateful to the Director Central Drug Research Institute, Lucknow, India for providing us excellent library facilities.

#### References

- [1] K.R. Kirtikar and B.D. Basu (1935). Indian Medicinal Plants, Lalit Mohan Basu, Allahabad, Vol, 3, 2165.
- [2] A.,Dittmar (1991). The effectiveness of *Hernandia* species (Hernandiaceae) in traditional Samoan medicine and accordining to Scientific analysis. J. Ethnopharm. **33**,243-251.
- [3] Y. N. Singh, (1986). Traditional medicine in Fiji: Some herbal folk cures used by Fiji Indians, J. *Ethnopharm.* **15**, 57-88.
- [4] R Pernet. (1971). Revue des Hernandiacees. Planta Med. 20, 314-319.
- [5] S. Ebel and H. Roth. (1987). *Lexikon der Pharmazie*. Thieme, Stuttgart, **10**, 704S,217.
- [6] C.Nishino and T. Mitsui (1973). Lignans from Hernandia ovigera. Tethedron Lett. 4, 335-338.
- [7] J.J Dobbie., D. Sc M.A. and A. Lauder (1893). A new Alkaloid from *Corydalis cava*. J Chem. Soc.63, 485-488.
- [8] T.P Ghose, S. Krishna and E.Schlittler (1934). The constitution of Actinodaphnine, *Helv.Chim. Acta*. 17, 919-930.
- [9] C.Jin-Jung, I.Tsumoto, Y. Chan Duh, L. Tsai Ian and I.S.Chen (1996). New dimeric aporphine alkaloids and cytotoxic constituents of H. nymphaeifolia, *Planta Med.* 62, 528-533.
- [10] Q.G. Jian, P.Eun Jung, T.Stephan, R. Seodarsono, H. S.Harry Fong, J.M. Pezzuto and D. A Kinghorn (2002). Constituents of the twing of H. ovigera. J. Nat. Prod. 65,1065-1068.
- [11] M.C Chalandre., J Bruneton., P.Cabalion. and H.Guinaudeau. (1986). Etudes de Hernandiacees XII. Dimeres aporphine-benzylisoquinoline originaux isoles de *Hernandia Peltata, Can. J. Chem.* 64, 123-126.
- [12] I.R.C Bick and G.K., Doughlas (1965). Atheroline, A yellow alkaloid from Atherosperma moschatum, Labill Tetrahedron Lett. 2399-2403.
- [13] P. Dute., M.C Chalandre., P. Cabalion. and J. Bruneton (1988). (+)- Auroramine and (+) Maroumine, new seco-bis-benzyl-isoquinoline dimers from *Gyrocarpus americanus*, *Phytochemistry*. 27, 655-657.
- [14] M.P. Cava, K.V.Rao, V.Doughlas and J.A.Weisbach (1968). Alkaoids isolated from South African Menispermacae, J. Org. Chem. 33, 2443-2446.
- [15] P. Richomme., M. Lavault, H. Jacquermin, and J. Bruneton, (1984). Etude des Hernandia guianensis. *Planta Med.* **50**, 20-22.

- [16] H.B. Dutschewska and N.M. Mollov (1967). TDES Hernandiaceae XII: Aporphine dimers benzylisoquinoline original isolated *Hernandia peltata*, *Chem Ber.* **100**, 3135.
- [17] J. L Hartwell., A.W.Schrecker and J.M.Johnson (1953). The Structure of Silicicolin J. Am. Chem. Soc. 75, 2138-2140.
- [18] M.Lavault., M.M Debray., J Bruneton (1982). Plants from New Caledonia: alkaloids of stem bark of H. Cordigera, Planta Med., 42, 50-54.
- [19] N Chikao. and M Tetsuo. (1973).Lignans from H. ovigera. Taiwan, Yao Hsueh Tsa Chih.25, 8-12.
- [20] I.S.Chen, J.J.Chen and I.L.Tsai (1996). N-formyl and N-hydroaporphine alkaloids and from Formosan *H. nymphaeifolia*, *Heterocycles*. **43**(4), 799-807.
- [21] M.C Chalandre, J.Brunaton, P. Cabalion and H. Guinaudeau (1986). Alcaloides De Gyrocarpus americanus. J. Nat. Prod. 49, 101-105.
- [22] M.P.Cava, K Bessho., B.Douglas., S.Markey and J.A.Weisbach (1966). *Hernandia* Alkaloids II: Hernandaline, a new elaborated aporphine structural type. *Tetrahedron Lett.* 36,4279-4280.
- [23] J.J.Chen, T.Ishikawa, C.Y. Duh, I.L.Tsai and I.S.Chen (1996). New dimeric aporphine alkaloids and cytotoxic constituents of *H. nymphaeifolia*, *Planta Med.* 62, 528-533.
- [24] F. N., Lahey, and K.F., Mak. (1971). Alkaloids from *H. papuana, Aust. J. Chem.* 24, 671-672.
- [25] M. Tanoguchi, M. Arimoto, H. Saika and H. Yamaguchi (1987). Studies on the constituents of the seeds of *H. ovigera*.L. VI. Isolation and structural determination of three Lignans, *Chem.Pharm. Bull.* 35, 4162-4168.
- [26] P. Rasonanaivo, S. Ratsimamanga-Urverg., H Rafatro., D Ramanitrahasimbola., G Palazzino C Galeffi., M. Nicoletti (1998). Alkaloids of *H.voyroni*. Chloroquine potentiation activity and structure elucidation of Herveline D., *Planta Med.*, 64, 58-62.
- [27] S.R Johns, J.A.Lamberton and A.A. Sioumis (1966). Cassytha Alkaloids II Alkaloids of Pubescens RBr., Aust. J. Chem. 19, 2331-2338.
- [28] J.J., Chen, I.L., Tsai and I.S., Chen (1996). New oxoaporphine alkaloid from *H.nymphaeifolia*. J. Nat. Prod. 59, 156-158.
- [29] J.Bruneton, M.Shamma, R.M.Robert, A.J.Freyer and H. Guinaideau (1983). Novel biogenetic pathway from
  (+) Reticuline, three dimeric alkaloids: Vanuatine, (+) Vateomine and (+) Malekulatine. J.Org. Chem. 48, 3957-3960.
- [30] M. Shamma and M. A. Sr. Podczasy (1971). Thlictrum alkaloids VII, Tetrahydro thalifendine N, methylthalidaldine and N-methylcorydaldine, *Tetrahedron.* 27, 727-733.
- [31] M.P. Cava, K. Besso, B. Douglas, S. Markey, F:F.Raffanf and J.A. Weisbach (1966). Alkaloids of hernandia ovigera: The characterization and structure of five new aporphine bases, *Tetrahedron Lett.* 7 (15) 1577-1581.
- [32] D.S. Bhakuni, S. Tewari, and M.M. Dhar (1972). Aporphine alkaloids of Annona squamosa, Phytochemistry. 11(5)1819-1822.
- [33] K. Yakushijin, S. Sugiyama, Y. Mori, H. Murata and H. Furukawa (1980). Hernangine, a new aporphine alkaloid, and 3-cyano-4-methoxypyridine from *H. nymphacifolia*, *Phytochemistry*. 19, 161-162.
- [34] S. Y. C. Chiu, R. H. Dobberstein H. H. S. Fong and N. R. Farnsworth (1982). Oxoaporphine alkaloids from Spirulina gilgiana. J. Nat. Prod. (Lloydia). 45, 229-230.
- [35] T.H. Yang, S.C.Liu. and T.S. Lin (1977). Studies on the constituents of *H. ovigera* L. Isolation of oxothalicarpine, *J. Chin. Chem. Soc. (Taipei).* 24, 91-92.
- [36] N.Weber (1974). Plants from Madagascar, four Terpenoids and other constituents of *H.voyroni* and *Anthocleista amplexicaulis, Phytochemistry*.**13**, 2006-2007.
- [37] M.Kulm and V. Wartburg (1967) Natural products inhibiting mitosis. XIX. Podophyllum ligands. Structure and absolute configuration of podorhizol b-D-glucoside, *Helv Chim Acta*. **50**, 1546-1565.
- [38] L. R. Row and A. S. R. Anjaneyulu (1962). The alkaloids of *Gyrocarpus jacquini* Roxb, J. Sci. Ind. Res. 21, 581-582.

- [39] S.A Ross, R.D. Minard and M. Shamma (1985). Thaliperphinemethine : A new phenonthrene ,alkaloid from *Illigera pentaphylla*, J. *Nat. Prod.* **48**,835-836
- [40] H.Furukawa, F.Ueda, M.Ito, K.Ito, H.Ishii and J.Hagini (1972). Alkaloids of Hernandia ovigera .iv. Constituents of *Hernandia ovigera* collected from Bonin Islands, *Yakugaku Zasshi*. **92(2)**150-154.



© 2009 Reproduction is free for scientific studies