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REVIEW PAPER

Comprehensive review of medicinal plant *Nauclea orientalis* (L.)

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Summary

Due to their minimal adverse effects, approximately 21,000 plant species were employed for medicinal purposes globally. Medicinal plants are regarded as a plethora of natural constituents that can be utilized as nutraceuticals and developed into synthetic drugs to enhance health. *Nauclea orientalis* (L.) L. (*Rubiaceae* family), a plant that is indigenous to Australia, India, Sri Lanka, Thailand, the Philippines, Indonesia, and other countries, is utilized in the Indigenous Medical Sector to treat a diverse array of ailments due to its high alkaloid content. In order to provide a comprehensive overview of this multifunctional plant, the classification, habitat, medicinal applications, chemical constituents, phytochemical and physicochemical properties, and diverse pharmacological activities of its parts have been examined. Moreover, this review article establishes a scientific foundation that can be used to conduct future research in order to develop nutraceuticals from this plant.

Key words: ***medicinal plant, Nauclea orientalis, pharmacological and phytochemical review, Rubiaceae***

Słowa kluczowe: ***roślina lecznicza, Nauclea orientalis, przegląd farmakologiczny i fitochemiczny, Rubiaceae***

INTRODUCTION

According to the World Health Organization, medicinal plants are essential for the health of millions of individuals worldwide [1]. Plants possess numerous medicinal properties that are advantageous for the enhancement of human health. The treatment of human illnesses in Indigenous Medicine involves the synthesis of medications from natural sources, including plants, animals, minerals, and metals [2].

Nauclea orientalis (L.) L. is a large tree native to North Australia [3]. It is also found in Sri Lanka, India, Thailand, Indonesia, Vietnam, the Phillipines, and Laos [4]. It belongs to the *Rubiaceae* family. Alkaloids, glycosides, phenolic composites, and terpenoids are present in the leaves, stem, bark, and root of *Nauclea orientalis*. Due to presence of these phytoconstituents plant exhibit valuable medicinal properties. Various conditions have been treated with the various components of *N. orientalis* in indigenous medicine. Thus, the present comprehensive review was conducted to provide a concise summary of the phytoconstituents and medicinal properties of this plant.

Despite the fact that numerous studies have been conducted on *N. orientalis* to investigate its phytochemical and pharmacological properties, the information that is currently available is fragmented and there is a lack of a thorough scientific evaluation. While the earlier reports mostly concentrated on isolated biological activities or ethnomedicinal uses, there was insufficient discussion of the full correlations between phytoconstituents, pharmacological mechanisms, traditional applications, and therapeutic potential. Hence, this review offers a critical summary and assessment of the prevailing evidence regarding the pharmacological activities, traditional uses, future research prospects, and phytochemistry of *N. orientalis* in order to pinpoint scientific gaps and potential applications in the development of nutraceuticals and drugs.

METHODOLOGY

A wide range of electronic databases, including Google Scholar, PubMed, Scopus, Web of Science, Research Gate, Science Direct, DOAJ, Academia, and other trustworthy scientific databases from all accessible sources provided the data for this comprehensive review from December 2020 to January 2026 in Jaffna District, Sri Lanka, using the keywords.

Based on literature, researchers created a data entry form to collect comprehensive information about this medicinal plant, including its classification, distribution, morphology, habitat, therapeutic uses, biochemical contents, phytochemical properties and various pharmacological actions.

Original research articles, review articles, and conference abstracts that had been peer-reviewed were included. Duplicate records and studies that did not focus on *N. orientalis* were omitted. The emphasis on recent literature aimed to incorporate the latest scientific evidence, while earlier significant studies were also evaluated for contextual background.

RESULTS AND DISCUSSION

Taxonomical classification

Table 1 provides the details of the taxonomic classification of *N. orientalis* plant [4-8].

Distribution of *Nauclea orientalis*

The native distribution of *N. orientalis* extends from South East Asia, New Guinea to Tropical Northern Australia and in different countries such as Sri Lanka, India, Malaya, and Philippine islands. These plants are grown at the elevations up to 500 m AMSL [5, 8].

In Sri Lanka, it is distributed commonly in both dry and moist regions such as Battticaloa, Trincomalee, Kurunegala, Bibile, *etc*. [5]. In Australia, these plants are distributed in North West Australia, North East Queensland, and the Top End of the Northern Territory. *Nauclea* species are found throughout the northern, northeastern, eastern, south-western, central, southeast, and peninsular regions of Thailand. They are also found in some regions of Papua New Guinea [4].

Description of *Nauclea orientalis*

A sub-canopy, deciduous and small tree, reaching extreme tallness about 30 m (98 ft.), with a cylindrical bole around a diameter of 1 m (3.3 ft.) (Figure 1). Flowering plant, flowering season vary, May and June in Sri Lanka, September to January in Australia, and August to October in the Philippines.

This plant is shown in Figure 1, and different parts of this plant are shown in Figure 2. The *N. orientalis* plant is briefly described botanically in Table 2 [4–5, 8].

Table 1.

Scientific classification of *Nauclea orientalis* plant

Classification	Name
Domain:	Eukaryota
Kingdom:	Viridiplantae
Phylum:	Tracheophyta
Class:	Magnoliopsida
Order:	Gentianales
Family:	*Rubiaceae*
Genus:	*Nauclea*
Species:	*Nauclea orientalis* (L.) L., *Nauclea wallichiana* Br., *Nauclea cordata* Roxb., *Nauclea officinalis* Pierrc ex Pit., *Nauclea lattifolia* Sm., *Nauclea roxburghii* Don., *Nauclea parviflora* Wall., *Cephalanthus orientalis* Linn., *Cephalanthus chinensis* Lam., *Sarcocephalus cordatus* Miq., *Plantanocarpum cordatum* Korth., *Sarcocephalus orientalis* Merr., *Nauclea orientalis* L. (=*Sarcocephalus cordatus* (Roxb.) Miq.) [6]
Common/ English Names [4]:	Leichhardt Tree, Leichhardt Pine, Cape York Leichardt, Soft Leichhardt, Yellow Cheese wood, Canary Cheese wood, Cheese wood or Canary Wood, Burr Tree
Sinhala Name:	Bakini, Bakmi, Rata-bakmi
Sanskrit:	Kadamba
Tamil:	*Wellai Kadambu, Athuvangi, Vammi* [6]
Vernacular Names [4-5, 7-8]	
Australia:	gadugay (Djabugay people), kabal (Kuku Yalanji), jirrib or wowerlk (Jawoyn people), kaapi or kalpi (Pakanh), atulwanyj (Uw Oykangand), atulganyj (Uw Olkola)
Sri Lanka:	Bakmee, Attuvangi, Vammi (T), Bakmi (S), Yellow cheese wood (E), Bhantriya (Sa)
Thailand:	Kanluang
Phillipines:	balikakak, kabag, kabak, mabalot, malbog, Bangkal
Indonesia:	Kayu mas
Vietnam:	Gao Vang
Laos:	Karn Luang

Indications in Traditional medicine

According to Ayurveda, Bakmi is dominant in pungent, bitter and astringent taste, with cold potency and *tridosha* alleviating action. Its bark, leaves, roots and juice of fruits have been used in various forms for ulcers, conjunctivitis, mouth ulcers, vomiting, diarrhoea, urinary calculi, and jaundice since Vedic period in India and a time unmemorable in Sri Lankan *Deshiya Chikitsa* [6].

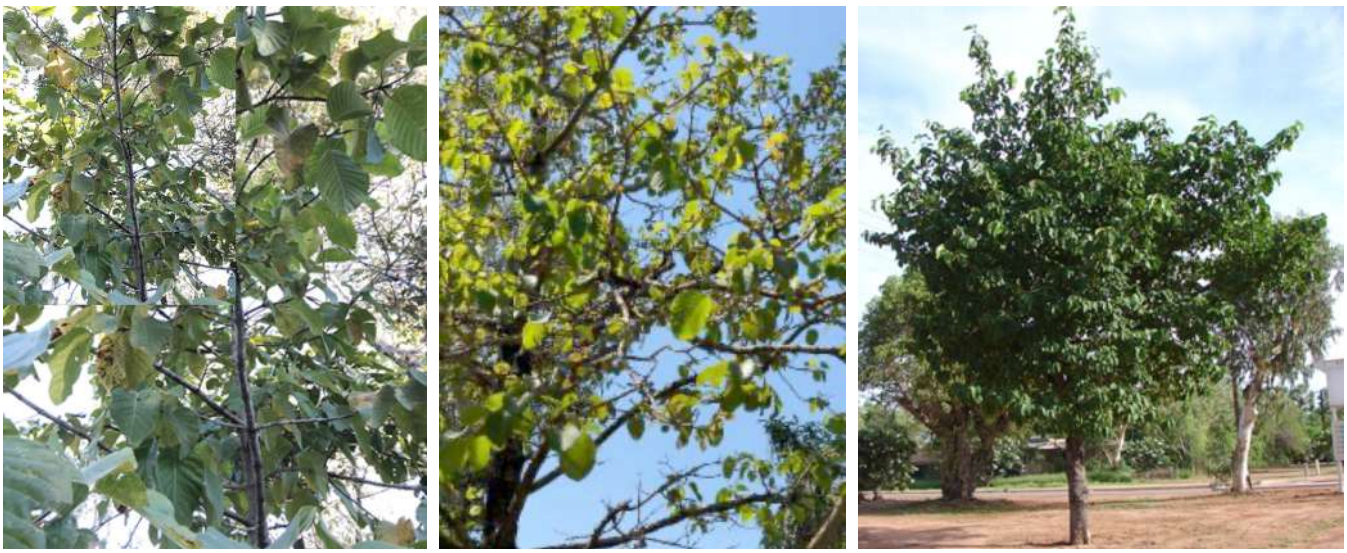

Figure 1.

Nauclea orientalis tree

N. orientalis is a natural plant to Sri Lanka, found to possess valuable medicinal properties [9] and it has been used to treat inflammation-associated conditions. In traditional Ayurvedic and folk medicine, it is mostly employed in crude aqueous formulations such as decoctions, infusions, and pastes. Leaves of *N. orientalis* have been used externally as a vulnerary for wound healing, pain relief and swelling in wounds. Also, preparations made from barks have been used in the management of skin ailments ("*Kshudra kushta*") and haemorrhoid-like symptoms. Also, both the leaves and barks were used to treat jaundice. This plant's bark has analgesic properties and is used as a natural

Figure 2.

Image of different parts of *Nauclea orientalis*, A – leaves, B, C & D – flowers, E & F – fruits

Table 2.

Morphological description of the aerial parts of *Nauclea orientalis* plant

Parts	Description
Branches	Young branches often lenticellate and minutely stellate-pubescent. With the time branches with leaf-scars become prominent.
Bark	Bark of silvery-grey or grey-creamy, having orange to yellow colour in a cut. Possess smooth or fissured and flaky texture.
Leaves	Simple opposite, broadly ovate-oval 15–30 cm by 7–15 cm entire, undulate leaves. Leaf base is slightly cordate and rounded or very obtuse at the apex, upper surface – smooth/glabrous, glossy green bottom surface – glabrous to finely pubescent, prominent yellow venation with 5–8 pairs of lateral veins.
Stipules	Interpetiolar stipules, 1.2–2.5 cm long, slightly connate and obovate-rotundate with small red glands-resembling insect eggs – on either side of surface. Vegetative buds – strongly flattened. Petioles 1.8–2.5 cm long.
Flowers	Axillary and/or terminal inflorescence, having 2.5–4 cm diameter per single flowering globose head. Small, sessile, numerous, regular, bisexual flowers with a sweet scent/fragrance. Pale yellow or yellowish to orange in colour. Calyx – 4 or 5 fleshy sepals, fused into calyx-tube originating from globose heads with 1.8–2.5 cm diameter on stout peduncles. Corolla – 4 or 5 petals, fused to corolla-tube, imbricate, yellow to orange colour. Androecium – Stame – epigynous, long, 2-locules, with numerous imbricated axile ovules Style – white, spindle shaped, prominent protrusion Stigma-white, 1.5–2 cm long, large and clavare.
Fruits	Syncarp-multiple fruit, fleshy globular , indehiscent, green turning yellow to brown when ripe, intensely aromatic, 4 to 5 cm (1.6 to 2.0 in) in diameter, with rugose (wrinkled surface), 2-locular, globose to slightly ovoid in shape.
Seeds	Small, ovoid to ellipsoid seeds around 1 to 10 mm in length, numerous, recalcitrant and showing epigeal germination.

treatment for wounds and skin disorders [10]. Also, *Parisheka Sweda* and *Yoga Vasti* treatments in Ayurveda, prepared from *N. orientalis* were admitted to be active in the management of sciatica (*Grudhrasi*) [11]. Similarly, the bark of this plant has been used traditionally as an antipyretic, vulnerary, analgesic (for toothache) and anti-diarrhoeal agent. Also leaves are used to treat boils and tumours [5].

These traditional usages are generally built on water-based preparations, notably decoctions, however, modern studies commonly employ solvent extracts (aqueous, ethanolic, methanolic, or hydro-alcoholic extracts) for phytochemical and pharmacological investigations.

Stem decoction of the plant is used for the management of fatigue in Laos [12]. Wood and bark have been used as painkiller by local people in North-Eastern Thailand and Papua New Guinea [13]. A clinical study was performed in Sri Lanka in which *Parisheka Sweda* (7 days) followed by *Yoga Vasti* using *N. orientalis* in patients. It was found that this plant can be suggested as an active treatment for sciatica [11].

Commonly, *N. orientalis* is traditionally used in gastrointestinal disorders, respiratory conditions, febrile and infectious diseases as well as intestinal worm infestations. These uses are based primarily on ethnomedicinal knowledge and have not been sufficiently corroborated by systematic pharmacological studies.

Several traditional applications of *N. orientalis*, such as for inflammatory disorders, wounds, fever, and pain have been found to be reliable with modern pharmacological findings like antioxidant, anti-inflammatory, analgesic and antibacterial activities. However, many of ethnomedicinal claims still lack scientific exploration, especially in terms of toxicity evaluation, dosage standardization, and clinical validation.

Phytochemical constituents of *N. orientalis*

Tannins and saponins were identified as chemical ingredients in the crude leaf extracts of *N. orientalis* [3]. Flavonoids, phenols, phytosterols, and tannins were detected in the ethanolic leaf extract of *N. orientalis* [14-15]. Alkaloids, flavonoids, tannin, saponin, polyphenol chemicals, reducing agents, and proteins were also present in its aqueous extract [16]. According to other research, aqueous bark extract from *N. orientalis* included notable amounts of polyphenols [17] and tannins, alkaloids, reducing sugars, and polyphenols [18].

Numerous chemical components extracted from *N. officinalis* were recognized: phenolic acids, pentacyclic triterpenoids, quinoline alkaloids, and indole alkaloids including vincosamide and strictosamide [19]. Strictosamide was the most plentiful alkaloid in all parts of this plant [20].

The chemical constituents found in the base, middle, and end of *N. orientalis* stem revealed the presence of terpenoids because of the type of triterpenoids, phenolic acids, tannins, flavonoids, and essential oils of phenol groups of simple phenol types [21]. Indoloquinolizidine alkaloids may be regarded as the major class of chemicals in the *Nauclea* genus [22].

Another phytochemical study found that Twenty-one compounds such as naucline, naucleline, naucletine, angustine, angustoline, 3,14-dihydroangustoline, angustidine, subditine, strictosamide, pumiloside, naucleficine, naucleactonin C, harmane, 1,2,3,4-tetrahydro-1-oxo-β-carboline, benzamide, cinnamide, blumenol B, blumenol A, β-sitosterol, stigmast-4-en-3-one and vanillin were successfully isolated from *N. officinalis* and decontaminated using numerous chromatography procedures [23].

N. orientalis is reported to contain a variety of secondary metabolites, primarily including alkaloids (such as strictosamide and naucline), flavonoids, phenolics, tannins, saponins, phytosterols, and terpenoids. Most of the available evidence is qualitative, and there is a lack of quantitative data (e.g., total phenolic content, total flavonoid content, and antioxidant assays). Standardization of these compounds relies on chromatographic fingerprinting methods (TLC and HPLC) and the identification of specific marker compounds. The absence of an official pharmacopoeial monograph underscores the need for validated quality control methods.

The major elements (chemical constituents) of the different parts of the *N. orientalis* were summarized in the Table 3.

Quantitative phytochemical analysis and standardization

Numerous phytochemicals such as alkaloids, flavonoids, tannins, terpenoids, phenolics, and glycosides have been qualitatively identified in *N. orientalis*. However, detailed quantitative phytochemical studies are still limited. Most of the available reports describe only the presence or absence of secondary metabolites, while information regarding the exact amounts of major bioactive compounds is scarce. Among the reported constituents, strictosamide, naucline, angustine-type alkaloids, and various phenolic compounds are considered important due to their pharmacological significance.

Major pharmacopoeias, including the Ayurvedic Pharmacopoeia of India, British Pharmacopoeia, United States Pharmacopoeia, and WHO monographs, do not have official pharmacopoeial standards for *N. orientalis*. Thus, formal requirements for minimum levels of active constituents, parameters of purity or standardized extracts have not yet been established. However, phytochemical studies have used chromatographic methods such as thin layer chromatography (TLC), high performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC-MS), and gas chromatography–mass spectrometry (GC-MS) to identify major alkaloids and phenolic constituents. Strictosamide has been proposed as a possible chemical marker compound because it is repeatedly reported as the major alkaloid in various parts of the plant.

Pharmacological activities of the *N. orientalis*

Antioxidant activity

It was discovered that *N. orientalis* stem-derived isolated composites had DPPH inhibitory action. With IC_{50} values of 6.6 μM, 12.4, and 40.3 μM, respectively, grandifloroside, methyl protocatechuate, and a lignan, (+)-pinoresinol, demonstrated very strong effects. Grandifloroside, an isolated terpenoid glycoside showed much more activity even than the positive control Trolox (IC_{50}, 7.0 μM). Antioxidants are thought to have an effect on DPPH radical scavenging because of their capacity to provide hydrogen. Further, *in vitro* thiobarbituric acid assay for lipid peroxidation inhibition exhibited comparable IC_{50} values for grandifloroside (67.9 μM), and methyl protocatechuate (813.0 μM) far beyond the Trolox (IC_{50}, 2265.2 μM). These results suggest the inhibitory potential of compounds from *N. orientalis* by preventing the formation of peroxides

Table 3.

Chemical constituents of different parts of *Nauclea orientalis*

Group of phytochemicals	Constituents	Potential anti-inflammatory / analgesic constituents
Stem and leaf		
Alkaloids – *β-carboline alkaloids* (indole derivative)	nauclorienine, antirhine, *iso*-antirhine, alangine, naucline, neonaucline, angustidine, subditine [24]	antirhine [25]; alangine [26]
	a new indole alkaloid, (nauclorienine), 17-O-methyl-19-(Z)-naucline along with seven known alkaloids [27]	naucline [27–28]
Leaf		
Alkaloids – *β-carboline alkaloids* (indole derivative)	angustine, nauclefine, 18,19-dihydroangustine, angustoline, 10-hydroxyangustine, 3,14-dihydroangustine, 3,14-dihydroangustoline, 3,14,18,19-tetrahydroangustine [29]	angustine [28, 30]; nauclefine [28]; angustoline [28, 31]; 3,14-dihydroangustine [30]
Phenolic compounds – flavonoids	vitexin, vicenin, kaempferol 3-O-rutinoside, rutin [32]	vitexin [33–37]; vicenin [38–42]; kaempferol 3-O-rutinoside [43–47]; rutin [48–53]
Glycosides – monoterpene quinolone alkaloid glucosides	kanluaengosides A, kanluaengosides B, (3*S*) – pumiloside [32]	(3*S*)-pumiloside [54–55]
monoterpene indole alkaloid glucosides	kanluaengosides C, kanluaengosides D, paratunamide B, paratunamide C [32]	
monoterpene tetrahydro-*β*-carboline alkaloid glucosides	strictosamide, vincosamide, 10-hydroxystictosamide, 6'-O-acetylstrictosamide, 10-hydroxyvincoside lactam [32, 56–57]	strictosamide [54–55]; vincosamide [54, 58]
monoterpene glycoside	eugenyl *β*-rutinoside [32]	
Stem/bark		
Alkaloids indole alkaloids	nauclealines A, nauclealines B [59] naucline, angustine, angustidine, nauclefine and naucletine [60]	
Terpenoids iridoid monoterpenoids	loganetin [61]	loganetin [62]
triterpenoid derivatives (sterols)	sitosterol [63], *β*-sitosterol [59]	sitosterol/*β*-sitosterol [64–67]
pentacyclic triterpenoids	3α-hydroxyurs-12-en-28-oic acid methyl ester, 3*α*,23-dihydroxyurs-12-en-28-oic acid, 3*α*,19*α*,23-trihydroxyurs-12-en-28-oic acid methyl ester, oleanolic acid [68]	oleanolic acid [69–71]

Phenolic compounds simple phenols	methyl protocatechuate, *trans*-p-coumaric acid, 3-(2,4- dihydroxylphenyl) propanoic acid (DPP acid), methyl 3-(2,4 dihydroxylphenyl) propanoate [61] 3,4,5-trimethoxyphenol [61]	methyl protocatechuate / protocatechuic acid [72]; *trans-p*-coumaric acid [73–76]
flavonoids	noreugenin [63]	noreugenin [77–78]
anthraquinone	aloe emodin [61]	aloe emodin [79–80]
lignin	(+)-pinoresinol [61]	(+)-pinoresinol [81]
phenolic apioglucoside	kelampayoside A [59]	
Glycosides – coumarin glucosides	skimming, adicardin [61]	skimmin [82]
tetrahydro-*β*-carboline monoterpene alkaloid glucosides	naucleosides [63], naucleosides A, naucleosides B, strictosamide, vincosamide, pumiloside [59]; strictosidine lactam, naucleaorine, epimethoxynaucleaorine [68]	strictosamide [54–55, 83–84]
monoterpenoid glycoside (*α*-pinene derivative)	naucleaorinoside A [61]	
steroidal glycosides	sitosteryl-*β*-D-glucoside [59]	
secoiridoid glucosides	sweroside, grandifloroside [61]	sweroside [84–88]
iridoid glucoside	loganin [61]	loganin [89–91]
other	palmitic acid [63]	
Root		
Alkaloids *β*-carboline alkaloids (indole derivative)	naucleficine, naucleactonin A, naucleidinal, 19-epi-naucleidinal, A novel naucleidinal derivative, naucleaoral A, naucleaoral B [92–93], two new cytotoxic isomeric indole alkaloids – naucleficine and naucleactonine [94]	naucleactonin A [30, 95] naucleidinal, 19-epi-naucleidinal, naucleaoral A, naucleaoral B [93]
Phenolic compounds –	vanillic acid [93]	vanillic acid [96–100]
Glycosides – tetrahydro-*β*-carboline monoterpene alkaloid glucosides	pumiloside, strictosamide [92–93]	pumiloside, strictosamide [54–55]
secoiridoid glucosides	aligenoside, sweroside[93]	sweroside [45, 84, 86–88]

and hydroperoxides [61]. Also, the mature fruits from the *N. orientalis* were found to exhibit an antioxidant activity with EC_{50} value less than 150 μg/ml, by DPPH scavenging assay [101].

Because the stem-derived constituents isolated from *N. orientalis* were assessed as pure compounds rather than crude extracts, there was no need for an extraction solvent or concentration. In contrast, antioxidant activity of mature fruit was reported using crude extract; however, the extraction solvent was not specified in the original study.

An *in-vitro* study has shown that the aqueous extract of *N. orientalis* has excellent antioxidant potential due to the occurrence of high flavonoid [16] and polyphenol contents [14, 102]. The aqueous bark extract of *N. orientalis* demonstrated strong antioxidant action in the DPPH and FRAP assays [17]. Other DPPH assay exhibited that ethanol extract of *N. orientalis* has high antioxidant action [15]. Another study was found that three isolates of endophytic fungi from *N. orientalis* have been isolated in a total of 12 isolates had high

antioxidant activity [103]. Its methanol bark extract exhibited concentration-dependent antioxidant activity by ferric reducing power assay and phosphomolybdenum methods [104]. Because it contains phenolic compounds, the aqueous bark extract of *N. orientalis* has higher antioxidant action [18].

Furthermore, another study reported that its leaf extract exhibited strong antioxidant activity in the DPPH assay with an IC_{50} value of 29.57±1.40 μg/ml, along with low haemolytic activity against human red blood cells, indicating minimal cytotoxicity under the tested conditions [105].

While some studies demonstrated the antioxidant properties of *N. orientalis* extracts through DPPH, FRAP, and lipid peroxidation assays, the majority of these studies were restricted to *in vitro* models and did not employ standardized extraction procedures. Further studies with standardized extracts and *in-vivo* models of oxidative stress are needed to confirm its therapeutic potential.

Anthelmintic activity

The chloroform, ethyl acetate, and ethanol extracts of *N. orientalis* leaves exhibited dose-dependent anthelmintic activity at 40, 60, and 80 mg/ml against *Pheretima posthuma*. At 80 mg/ml, the activity was at its highest, and all of the extracts significantly shortened the times it took for paralysis and death to happen. The extracts at 80 mg/ml showed similar anthelmintic effects, even though albendazole was more effective [3].

Anti-bacterial activity

A comprehensive randomized experimental study was conducted to assess the anti-staphylococcal activity of crude alcoholic leaf extract (mature leaves) of *N. orientalis*, which was included in the ointment base. Prepared ointment showed comparable activity to Erythromycin ointment. This study further concluded that leaves extract of *N. orientalis* incorporated ointment could be used in the treatment of superficial wounds [2]. The ethanolic extract, ethyl acetate fraction, and hexane fraction exhibited the strongest antibacterial activity against *E. coli* and *S. aureus* when the disk diffusion method was employed [106]. An anti-staphylococcal and pro-repairing effect was demonstrated by the crude alcoholic leaf extract (mature leaves) of *N. orientalis* [107].

Crude stem bark extract of *N. orientalis* exhibited only weak anti-bacterial effects against positive and negative bacterial strains [108]. Another study [109] demonstrated that the methanolic leaf extract of N. orientalis exhibited the most potent antibacterial efficacy against bacterial isolates, such as *E. coli*, *S. aureus*, and *P. aeruginosa*, in comparison to root extracts.

Acetylcholinesterase inhibitory activity

The crude extracts of stem bark and isolated compounds, including rotundic acid, (3β)-3,19, 23,24-tetrahydroxyurs-12-en-28-oic acid, and β-sitostenone, were evaluated for acetylcholinesterase inhibitory activity, using galanthamine as a positive control. All samples exhibited only weak inhibitory effects when compared to the standard drug [108].

Anti-cancer activity

According to the study, three of the nine angustine-type alkaloids that were separated from ammoniacal extracts of *N. orientalis* leaves confirmed *in vitro* anti-proliferative action against both epidermal growth factor-dependent mouse epidermal keratinocytes and the human bladder carcinoma T-24 cell line [29]. The two isomeric indole alkaloids (naucleaorals A and B) that were separated from the roots of *N. orientalis* displayed cytotoxic activity in the human cervical carcinoma cell line HeLa, according to another study [110–111]. With IC_{50} values of 4.0 and 7.8 μg/ml, the isomeric alkaloids (biscoclaurines) extracted from *N. orientalis* shown notable cytotoxicity against HeLa cell lines [94, 112]. Nauclorienine, a novel corynanthe-type indole alkaloid, and seven other known alkaloids that were extracted from the stems and leaves of *N. orientalis* have demonstrated strong inhibitory effects against a variety of human cancer cell lines with IC_{50} values similar to those of cisplatin [27]. Another study discovered that the plant's aqueous bark extract (2.0 g/kg) could reduce the oxidative stress, inflammation, apoptosis, and DNA fragmentation that Dox causes in Wistar rats [18].

Antimalarial activity

Plasmodium falciparum was moderately inhibited *in vitro* by the chemicals that were extracted from the dried stem of *N. orientalis* using chloroform [68]. Another *in-vitro* study found that the hexane (IC_{50} 1.93 μg/ml) and methanol (IC_{50} 3.91 μg/ml) fractions from leaf extract of *N. orientalis* showed potential antimalarial activity comparable to chloroquine phosphate against *Plasmodium falciparum* 3D7 [113].

Anti-inflammatory activity

In vivo study reported that the *N. orientalis* bark extract treated group exhibited significant reduction ($p > 0.5$) in TNF-α and caspase-3 expression and

increased Bcl-2 expression and concluded that this extract has potential to attenuate doxorubicin-induced inflammation and apoptosis in Wistar rats [18, 115].

The anti-inflammatory activity of *N. orientalis* might be primarily due to indole alkaloids like strictosamide which has been reported to inhibit NF-κB and MAPK signalling pathways in macrophages. These pathways are key players in cytokine-mediated inflammatory responses, providing a potential molecular explanation for the traditional use of the plant in inflammatory disorders.

Anti-haemolytic activity

The methanol bark extract of N. orientalis has been reported to possess both mild haemolytic and anti-haemolytic effects *in vitro*. The effects were compared to those of acetylsalicylic acid, which is the standard reference drug. This showed that the extract may have antioxidant and membrane-stabilizing properties [104].

Antidiabetic activity

The hot water extract of *N. orientalis* exhibited the most significant α-glucosidase inhibitory activity among the evaluated extracts, suggesting its potential anti-diabetic effect *via* the inhibition of carbohydrate-digesting enzymes [114].

Cardioprotective activity

In Wistar rat models, the bark extract of *N. orientalis* has demonstrated promising cardioprotective potential against doxorubicin-induced cardiotoxicity. Phytochemical studies have demonstrated the occurrence of phenolics, flavonoids, and alkaloids [115], which could be accountable for its therapeutic potentials. A recent *in vivo* study [18] showed that the extract markedly ($p < 0.05$) decreased cardiac markers, oxidative stress, inflammation and apoptosis as well as restoring antioxidant enzyme contents. Histological assessment further confirmed attenuation of myocardial injury. Reported effects were similar to the standard cardioprotective drug that is known based on negative (doxorubicin-treated) and positive (dexrazoxane-treated) controls. Nonetheless, while these results are promising, the evidence is early and further mechanistic and clinical validation is necessary.

CONCLUSION

Nauclea orientalis (L.) L. is a high alkaloid-contained plant and its different parts have been used in indigenous medicine to treat different ailments. In current comprehensive review, classification, habitat, medicinal uses, chemical constituents, phytochemical properties and various pharmacological activities of its various parts have been discussed. However, the lack of standardized specifications of extracts and clinical validation at present limits its translation into evidence-based medicine. Further interdisciplinary studies involving phytochemistry, pharmacology, toxicology and clinical studies are required to determine its therapeutic potential and to facilitate the development of evidence based herbal formulations and nutraceutical products.

Ethical approval: *The conducted research is not related to either human or animal use.*

Conflict of interest*: Authors declare no conflict of interest.*

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