

REVIEW

Open Access



Nauclea officinalis: A Chinese medicinal herb with phytochemical, biological, and pharmacological effects

Bin Liu[†], Qi Geng[†], Zhiwen Cao, Li Li, Peipei Lu, Lin Lin, Lan Yan and Cheng Lu^{*†}

Abstract

Nauclea officinalis (*N. officinalis*), a medicinal plant of the genus *Nauclea* in the family Rubiaceae, is used in the treatment of fever, pneumonia, pharyngolaryngitis, and enteritis in China. Extracts of *N. officinalis* include alkaloids, phenolic acids, pentacyclic triterpenoids, and flavonoids, which exert all kinds of pharmacological effects, for instance anti-inflammatory, anti-tumor, antibacterial, and antiviral and therefore show good effectiveness. To gain a comprehensive and deep understanding, the medicinal chemistry and chemical biology of *N. officinalis* are summarized in this review to provide a theoretical basis. The pharmacological effects were reviewed to provide evidence or insights into potential opportunities for further studies and medicinal exploitation of *N. officinalis*.

Keywords: *Nauclea officinalis*, Phytochemistry, Biological activity, Pharmacological effect

Introduction

Nauclea officinalis (*N. officinalis*), also known as Dan Mu, is a traditional herbal medicine distributed in Hainan, Yunnan, and Guangxi in China [1]. *N. officinalis* belong to the genus *Nauclea* in the family Rubiaceae [2, 3]. A large majority of these are woody trees and shrubs that are primarily found in tropical regions [4]. In Li folk medicine, *N. officinalis* has been used to treat inflammatory and infectious diseases including diarrhea, pneumonia, and enteritis [5–7].

N. officinalis exhibits various potential bioactivities such as anti-inflammatory [8], suppression of tumor cell growth [9], antibacterial [10], antiviral [11], and antimalarial [12]. As a result, *N. officinalis* extracts were used in traditional herbal medicine for many years to treat acute tonsillitis and upper respiratory tract infection [13]. In addition, various chemical components, including

alkaloids, pentacyclic triterpenoids, and phenolic acids, were isolated and identified by different researchers from *N. officinalis* [6, 7, 12]. According to studies, *N. officinalis*' chemical components have several beneficial properties with anti-inflammatory, anti-tumor, antibacterial, and antiviral activities [14–16].

Alkaloids are the main secondary metabolites found in *N. officinalis*, which are heterocyclic molecules containing at least one nitrogen atom in their structure [17]. As the main classification of alkaloids, indole alkaloids, which have antibacterial, antimalarial, antifungal, antiparasitic, anti-inflammatory, antiviral, antineoplastic, anti-acetylcholinesterase, and anti-buthyrylcholinesterase properties [18, 19], are chemical components of *N. officinalis*. For example, strictosamide (STR) and vincosamide are the main active components of *N. officinalis* indole alkaloids [20]. STR is the most abundant constituent of indole alkaloids and has a variety of pharmacological effects, such as anti-inflammatory properties, antipyretic properties, and antiviral properties [21]. Vincosamide is an isomer of STR that exhibits anti-tumor [22], anti-inflammatory [23], and other properties. According to

[†]Bin Liu and Qi Geng contributed equally to this work

*Correspondence: lv_cheng0816@163.com

Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, Dongcheng District, Beijing 100700, China



© The Author(s) 2022. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

pharmacokinetic studies, these two compounds are readily absorbed into the plasma and exhibit good pharmacological effects.

The compounds of quinoline alkaloids have N-based heterocyclic aromatic and have a broad range of biological activities including anti-tumor, antiparasitic, antibacterial, cardioprotective, antiviral, anti-inflammatory, antioxidant, and antitussive activities [24, 25]. Triterpenoids make up this diverse class of natural plant products, which contain three terpene units and are effective against tumors, inflammation, and viruses [26]. Phenolic acids are phenolic compounds that are resonance stabilized and possess a phenol moiety. As a result, antioxidant properties are achieved through radical scavenging mechanisms that lead to H-atom donation. Furthermore, phenolic acids have health protective effects, for instance anti-microbial, anti-tumor, anti-inflammatory, and anti-mutagenic effects [27]. These findings indicate the potential medicinal value of *N. officinalis* as a Chinese herbal medicine.

Our review summarizes phytochemical, bioactive, and pharmacological effects of *N. officinalis*, providing useful information for its development and utilization.

Phytochemistry and biological activity of *N. officinalis*

Numerous types of chemical constituents have been identified in *N. officinalis*, including alkaloids, pentacyclic triterpenoids, and phenolic acids, according to phytochemical analysis (Table 1). Alkaloids are the characteristic components of *N. officinalis* and its main active ingredients.

Alkaloids

Alkaloids are the most widely reported class of compounds found in *N. officinalis*. The alkaloids in *N. officinalis* are mainly indole alkaloids; however, a few quinoline alkaloids are also present. Studies have shown that certain indole alkaloids exhibit anti-inflammatory, antibacterial, and antiplasmodial activity.

Indole alkaloids

The indole alkaloids in *N. officinalis* have the following characteristics: the structural skeleton generally consists of five six-membered rings; indoles (A/B ring) and tetrahydropyridines (C ring) form the tetrahydro- β -carboline parent ring, the D ring is a saturated or unsaturated lactam ring, the E ring can be an azapyridine or oxatetrahydrofuran ring, and some compounds have an open or non-existent E ring [12].

Chemical constituents extracted from the stems of *N. officinalis* are STR [14, 28, 29], vincosamide [14, 28, 29], nauclefine [30], nauclefidine [30],

nauclefoline [30], naucleofficine H [11, 31], naucleamide A-10-O- β -D-glucopyranoside [28, 29], and 3 α ,5 α -tetrahydrodeoxycordifoline lactam [29]. STR is a representative component of indole alkaloids, which are present in all plants of the genus *Nauclea*, at high concentrations, and is also the main active ingredient extracted from *N. officinalis*. Therefore, STR is mostly used in studies as a standardized assay for the quality of extracts from plants of the genus *Nauclea* with various biological activities, for instance anti-inflammatory, antibacterial, antiviral, analgesic, anti-tumor, and antimalarial [32–34]. Alternatively, vincosamide, an isomer of STR, assists in reducing inflammation, bacteria proliferation, and malaria transmission [35, 36]. Naucleofficine H, a colorless crystal, can stimulate the proliferation of human umbilical vein endothelial cells (HUVECs) [11] and has anti-inflammatory activity [31]. nauclefidine [30], 3 α ,5 α -tetrahydrodeoxycordifoline lactam [29], and naucleamide A-10-O- β -D-glucopyranoside [29] also have anti-inflammatory activities.

As natural extracts of *N. officinalis* stems and leaves, naucleaofficine A and naucleaofficine B, as well as 3,14-Dihydroangustine and 3,14,18,19-Tetrahydroangustine [37], are yellowish amorphous powders inhibiting inflammation and HIV-1 replication. Naucleamide G is an orange amorphous powder [28, 38], and 17-O-methyl-19-(Z)-naucleine is a yellowish amorphous powder with anti-inflammatory activity [31, 39]. Nauclealomide B, nauclealomide C, paratunamide A, paratunamide C, and paratunamide D is extracted from the leaves of *N. officinalis* [38].

Angustine, nauclefine, harmine, angustidine and nauclefine, and indole alkaloids from the bark of *N. officinalis* have anticholinesterase bioactivities [40]. Angustine, nauclefine, and nauclefine also have anti-inflammatory, antiviral, and vasorelaxant activities [41]. Angustoline, naucleofficine III, naucleidinal, (E)-2-(1- β -D-glucopyranosyloxybut-2-en-2-yl)-3-(hydroxymethyl)-6,7-dihydro-indolo[2,3-a]quinolizin-4(12H)-one, (E)-1-propenyl-12- β -D-glucopyranosyloxy-2,7,8-trihydro-indolo[2,3-a]pyran[3,4-g]quinolizin-4,5(13H)-dione, (E)-2-(1-hydroxybut-2-en-2-yl)-11- β -D-glucopyranosyloxy-6,7-dihydro-indolo[2,3-a]quinolizin-4(12H)-one, and 1-(1-hydroxyethyl)-10-hydroxy-7,8-dihydro-indolo[2,3-a]pyridine[3,4-g]quinolizin-5(13H)-one(10-hydroxyangustoline), extracts of *N. officinalis* stems and bark are weak to moderately effective against *Plasmodium falciparum* [12]. Angustoline also exhibits significant cytotoxic [12] and anti-inflammatory activities [42].

Phytochemicals such as nucleactonin A and B are synthesized from *N. officinalis* bark and wood [2]. Only nucleactonin A has been shown to exhibit anti-inflammatory activity [37].

Table 1 The phytochemistry and biological activity of *N. officinalis*

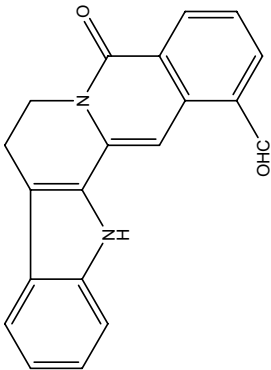
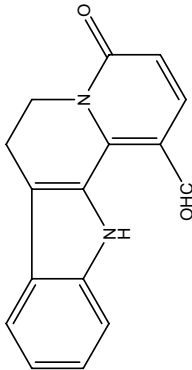
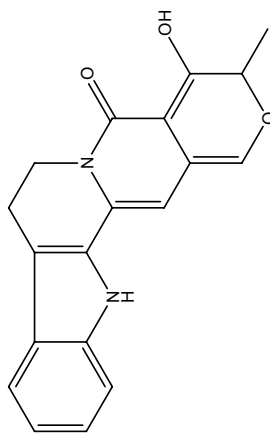
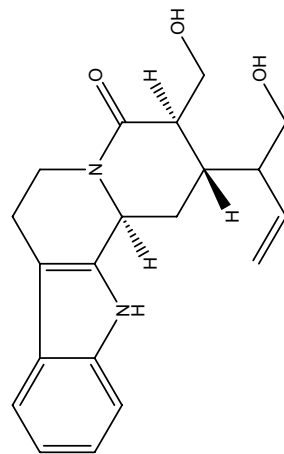
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
1	Naucleifine [30]	Stems	Indole alkaloid	$C_{20}H_{14}N_2O_2$		N/A
2	Naucleidine [30, 36, 37]	Stems	Indole alkaloid	$C_{16}H_{12}N_2O_2$		Anti-inflammatory antiviral
3	Naucleofoline [30]	Stems	Indole alkaloid	$C_{19}H_{16}N_2O_3$		N/A
4	Naucleaoiffines A [37]	Stems leaves	Indole alkaloid	$C_{20}H_{24}N_2O_3$		Anti-inflammatory antiviral

Table 1 (continued)

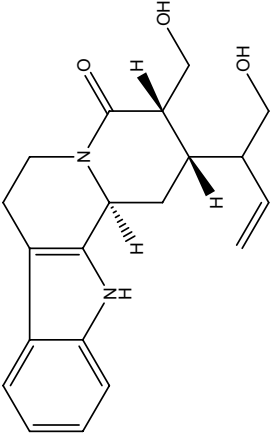
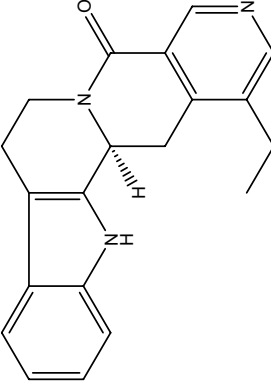
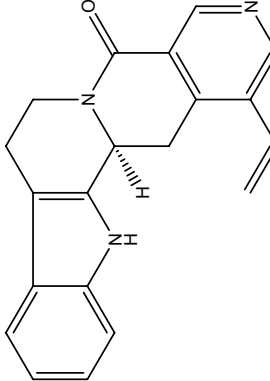
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
5	Nucleoaffines B [37]	Stems leaves	Indole alkaloid	$C_{20}H_{24}N_2O_3$		Anti-inflammatory antiviral
6	3,14-Dihydroangustine [37, 47]	Stems Leaves	Indole alkaloid	$C_{20}H_{17}N_3O$		Anti-inflammatory Antiviral
7	3,14,18,19-Tetrahydroangustine [37]	Stems Leaves	Indole alkaloid	$C_{20}H_{17}N_3O$		Anti-inflammatory Antiviral

Table 1 (continued)

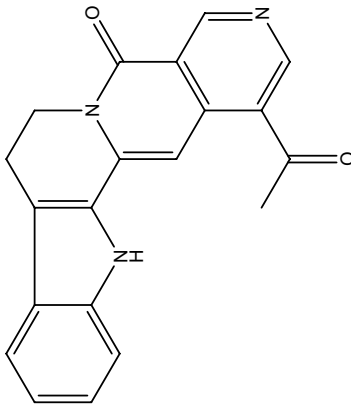
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
8	Angustoline [12, 40, 42, 47, 48]	Stems Bark	Indole alkaloid	$C_{20}H_{17}N_3O_2$		Anti-inflammatory Anti-tumor Anticholinesterase
9	Angustine [37, 40–42, 47, 48]	Bark	Indole alkaloid	$C_{20}H_{15}N_3O$		Anti-inflammatory Antiviral Vasorelaxant Anticholinesterase
10	Naucletine [37, 40, 41]	Bark	Indole alkaloid	$C_{20}H_{15}N_3O_2$		Anti-inflammatory Antiviral Vasorelaxant Anticholinesterase

Table 1 (continued)

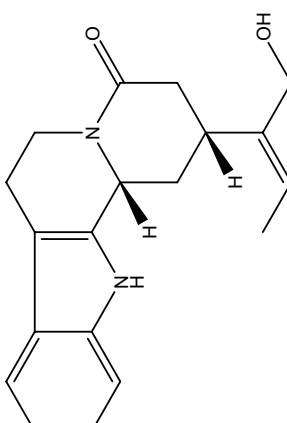
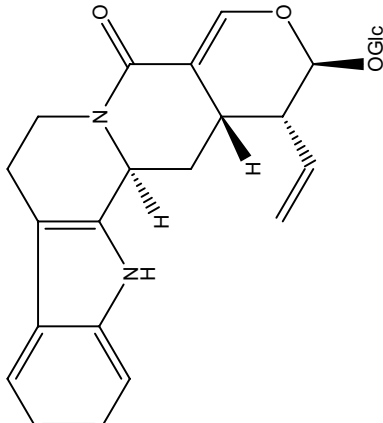
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
11	Naucleoficine H [11]	Stems	Indole alkaloid	$C_{20}H_{22}N_2O_2$		Anti-inflammatory Antiviral Antiviral
12	Strictosamide [11, 14, 28, 29, 31, 35, 36, 47–52]	Stems	Indole alkaloid	$C_{26}H_{30}N_2O_8$		Anti-inflammatory Antiviral Anti-microbial Antimalarial Analgesic Anticholinesterase

Table 1 (continued)

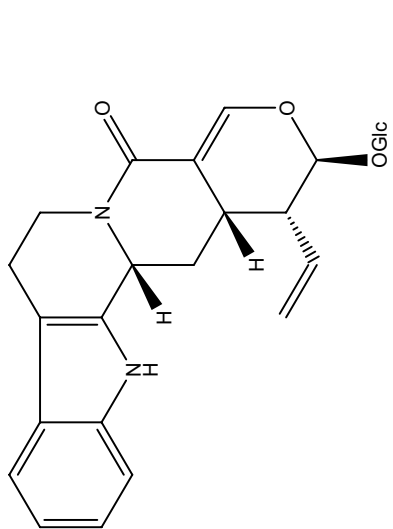
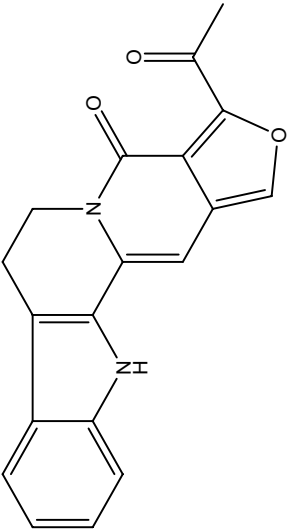
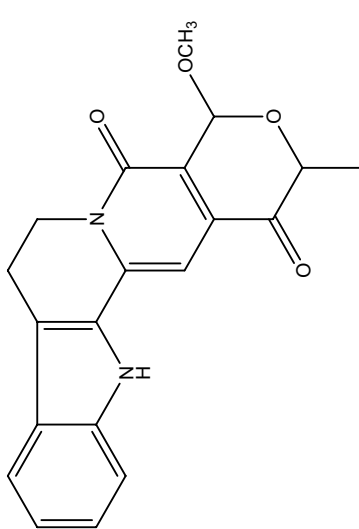
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
13	Vincosamide [14, 28, 29, 35, 36, 48, 50]	Stems	Indole alkaloid	$C_{26}H_{30}N_2O_8$		Anti-tumor Anti-inflammatory Anti-microbial Antimalarial
14	Naucleactonin A [2, 37]	Bark Wood	Indole alkaloid	$C_{19}H_{14}N_2O_3$		Anti-inflammatory Antiviral
15	Naucleactonin B [2]	Bark Wood	Indole alkaloid	$C_{20}H_{18}N_2O_4$		N/A

Table 1 (continued)

No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
16	(E)-2-(1-β-D-glucopyranosyloxybut-2-en-2-yl)-3-(hydroxymethyl)-6,7-dihydro-indolo[2,3-a]quinolizin-4(12H)-one [12]	Stems Bark	Indole alkaloid	C ₂₆ H ₂₉ N ₂ O ₈		Antimalarial
17	(E)-1-propenyl-12-β-D-glucopyranosyloxy-2,7,8-trihydro-indolo[2,3-a]pyran[3,4-g]quinolizin-4,5(13H)-dione [12]	Stems Bark	Indole alkaloid	C ₂₆ H ₂₈ N ₂ O ₉		Antimalarial
18	(E)-2-(1-hydroxybut-2-en-2-yl)-11-β-D-glucopyranosyloxy-6,7-di-hydro-indolo[2,3-a]quinolizin-4(12H)-one [12]	Stems Bark	Indole alkaloid	C ₂₅ H ₂₈ N ₂ O ₈		Antimalarial

Table 1 (continued)

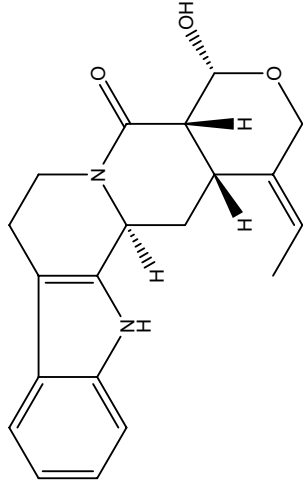
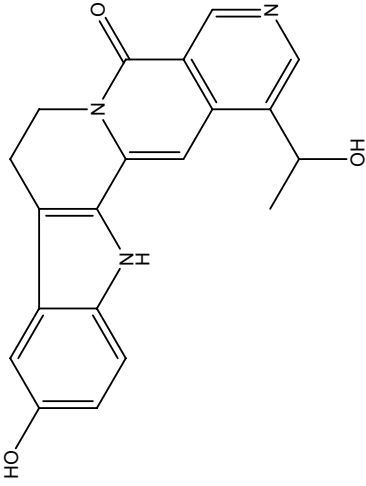
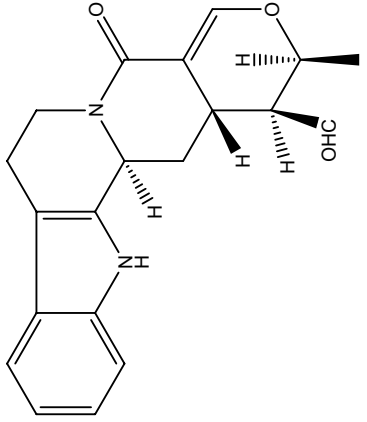
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
19	Naucleoficine III [7, 53]	Stems Bark	Indole alkaloid	$C_{20}H_{27}N_3O_3$		Anti-tumor
20	1-(1-hydroxyethyl)-10-hydroxy-7,8-dihydro-indolo[2,3-a]pyridine[3,4-g]quinolizin-5(13H)-one(10-hydroxyangustoline [12]	Stems Bark	Indole alkaloid	$C_{20}H_{17}N_3O_3$		Antimalarial
21	Naucleidinal [7, 12, 36]	Stems Bark	Indole alkaloid	$C_{20}H_{27}N_3O_3$		Anti-tumor

Table 1 (continued)

No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
22	Naucline [7, 41, 54]	Bark Stems Leaves	Indole alkaloid	$C_{20}H_{18}N_2O_2$		Vasorelaxant Anticholinesterase
23	Angustidine [40, 41]	Bark	Indole alkaloid	$C_{19}H_{15}N_3O$		Anticholinesterase
24	Nauclefine [40–42, 47]	Bark	Indole alkaloid	$C_{18}H_{13}N_3O$		Anti-inflammatory Vasorelaxant Anticholinesterase

Table 1 (continued)

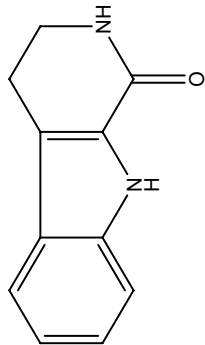
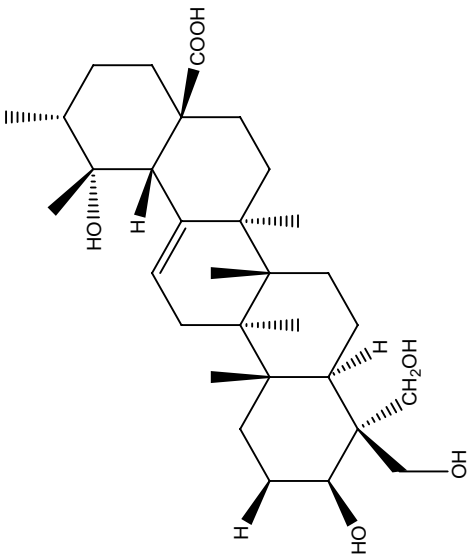
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
25	1,2,3,4-tetrahydro-1-oxo- β -carboline [42]	Twigs	Indole alkaloid	$C_{11}H_{12}N_2$		Anti-inflam-matory
26	3 β ,19 α ,23,24-tetrahydroxyis-12-en-28-oic acid [46]	Stems	Pentacyclic triterpenoid	$C_{30}H_{48}O_6$		Anti-inflam-matory

Table 1 (continued)

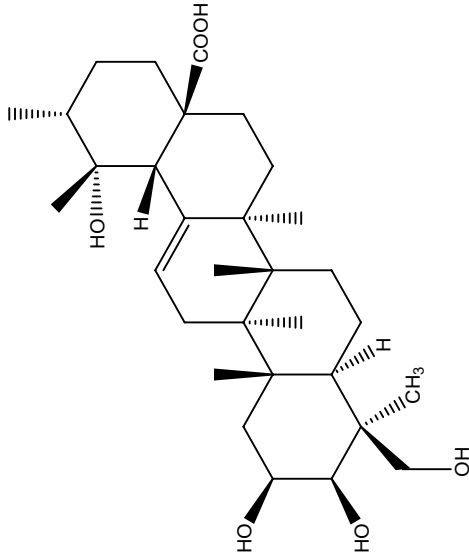
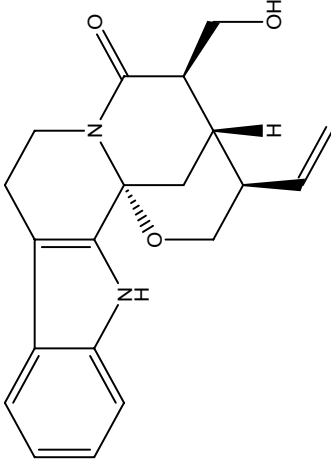
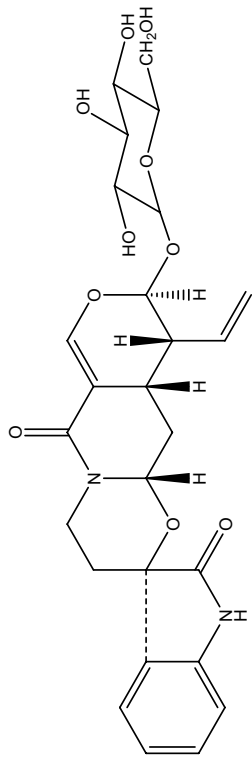
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
27	2β,3β,19α,24-tetrahydroxyurs-12-en-28-oic acid [46]	Stems	Pentacyclic triterpenoid	C ₃₀ H ₄₈ O ₆		Anti-inflammatory
28	Naucleamide G [7, 28, 38]	Stems Leaves	Indole alkaloid	C ₂₅ H ₃₇ N ₂ O ₈		Anti-inflammatory
29	Nauclealomide B [38]	Leaves	Indole alkaloid	C ₂₆ H ₃₀ N ₂ O ₁₀		N/A

Table 1 (continued)

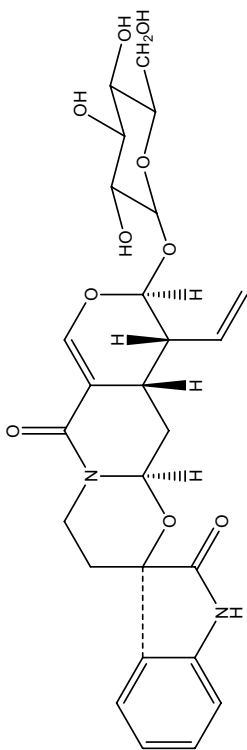
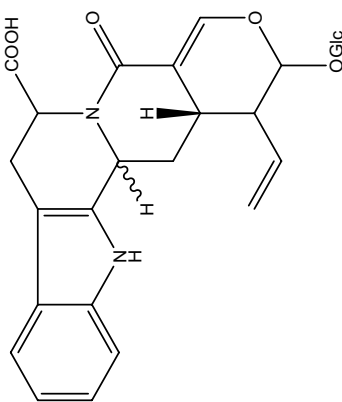
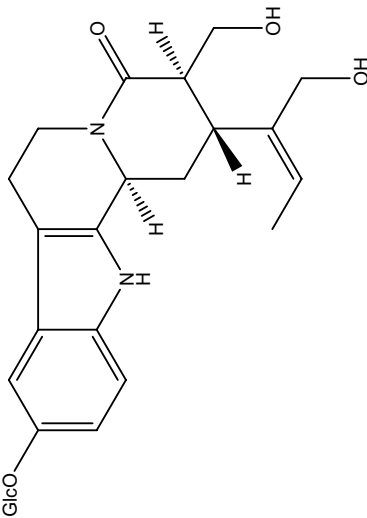
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
30	Nauclealomide C [38]	Leaves	Indole alkaloid	$C_{26}H_{30}N_2O_{10}$		N/A
31	3 <i>α</i> ,5 <i>α</i> -tetrahydrodeoxycordifoline lactam [29]	Stems	Indole alkaloid	$C_{27}H_{30}N_2O_{10}$		Anti-inflammatory
32	Naucleamide A-10-O-β-D-glucopyranoside [28, 29, 36, 47, 55]	Stems	Indole alkaloid	$C_{26}H_{34}N_2O_9$		Anti-inflammatory

Table 1 (continued)

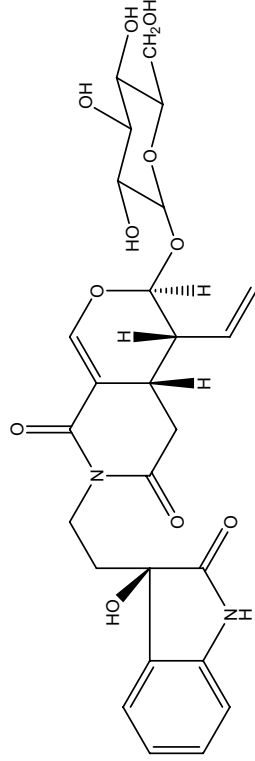
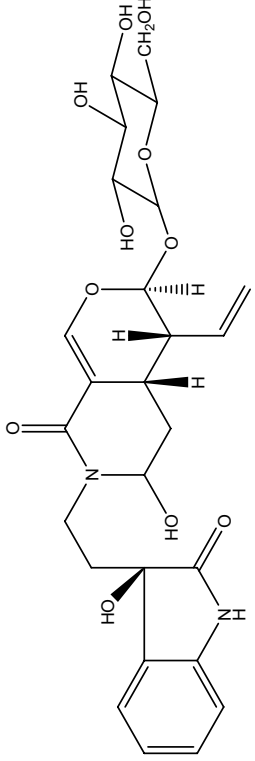
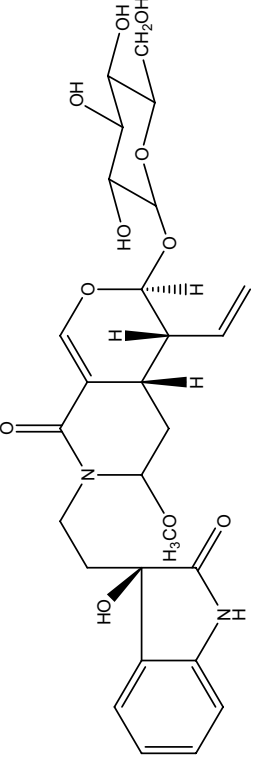
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
33	Paratunamide C [38]	Leaves	Indole alkaloid	$C_{26}H_{30}N_2O_{11}$		N/A
34	Paratunamide D [38]	Leaves	Indole alkaloid	$C_{26}H_{30}N_2O_{11}$		N/A
35	Paratunamide A [38]	Leaves	Indole alkaloid	$C_{26}H_{30}N_2O_{11}$		N/A

Table 1 (continued)

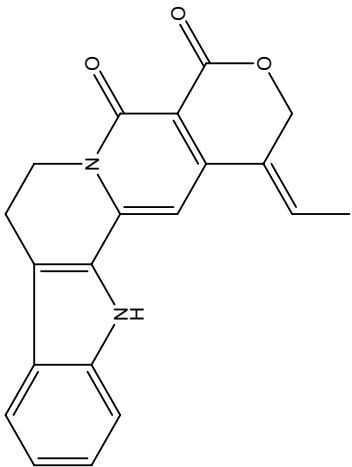
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
36	17-O-methyl-19-(Z)-naucline [31, 39]	Stems Leaves	Indole alkaloid	$C_{21}H_{29}N_2O_3$		Anti-inflam- matory
37	17-oxo-19-(Z)-naucline [42]	Bark Twigs	Indole alkaloid	$C_{20}H_{18}N_2O_3$		Anti-inflam- matory
38	Naucleofleine H [31]	Stems Bark	Indole alkaloid	$C_{20}H_{27}N_2O_3$		Anti-inflam- matory

Table 1 (continued)

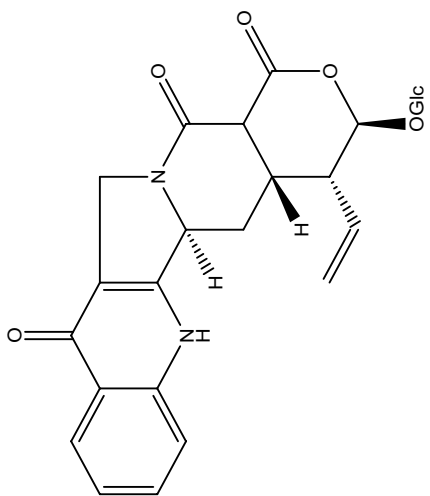
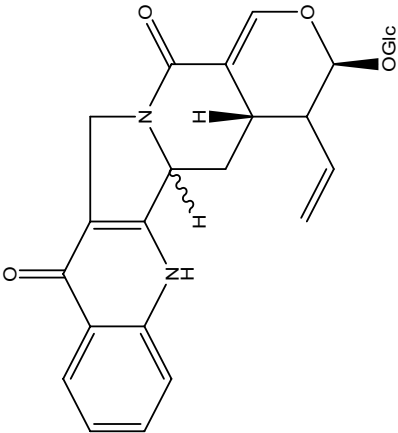
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
39	Pumiloside [11, 28, 29, 36, 47, 48, 50, 56]	Stems	Quinoline alkaloid	$C_{26}H_{28}N_2O_9$		Anti-inflammatory Anti-microbial Antivirus
40	3-epi-pumiloside [14, 29, 36, 50]	Stems	Quinoline alkaloid	$C_{26}H_{28}N_2O_9$		Anti-inflammatory Anti-microbial

Table 1 (continued)

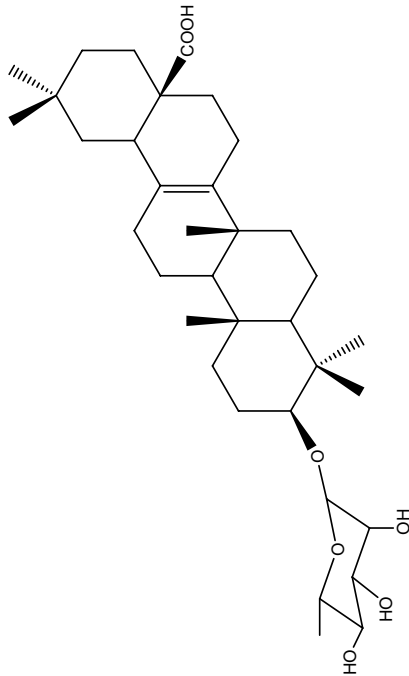
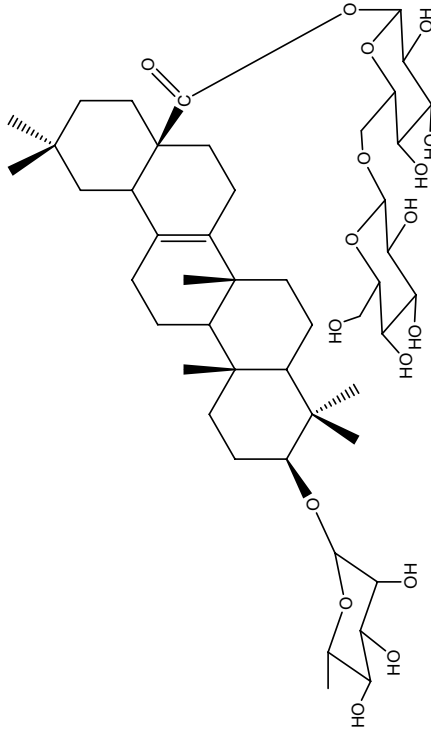
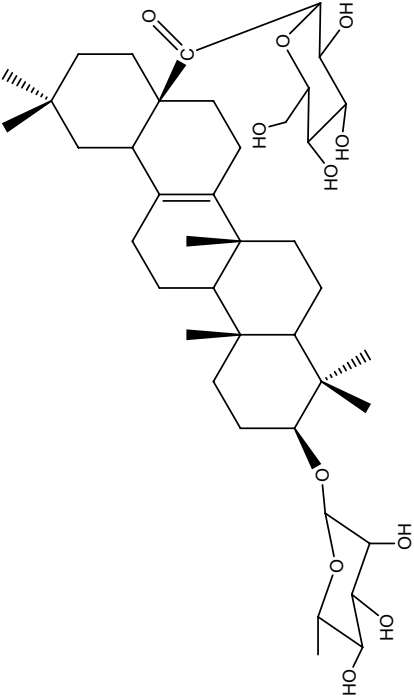
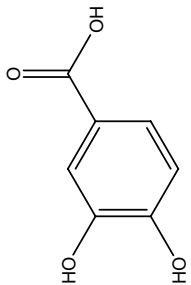
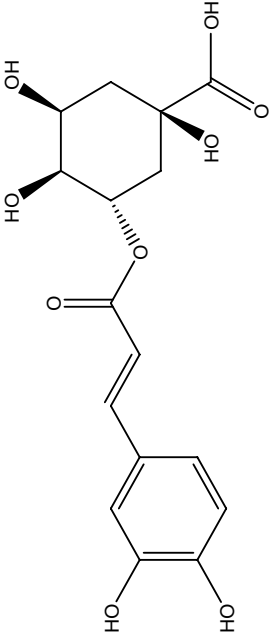
No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
41	Pyrocnicinic acid 3β-O-α-L-rhamnopyranoside [9]	Stems	Pentacyclic triterpenoid	C ₃₅ H ₅₆ O ₇		Anti-tumor
42	Pyrocnicinic acid 3β-O-α-L-rhamnopyranosyl-28-O-β-D-glucopyranosyl-(1-6)-β-D-glucopyranosyl ester [9]	Stems	Pentacyclic triterpenoid	C ₄₇ H ₇₆ O ₁₇		Anti-tumor

Table 1 (continued)

No	Identification compound	Source	Category	Molecular formula	Structural formula	biological activity
43	Pyrocincholic acid 3β-O-α-L-rhamnopyranosyl-28-O-β-D-glucopyranosyl ester [9]	Stems	Pentacyclic triterpenoid	C ₄₁ H ₆₆ O ₁₂		Anti-tumor
44	Protocatechuic acid [35, 36]	Stems	Phenolic acid	C ₇ H ₅ O ₄		Antioxidation Anti-inflammatory Anti-microbial
45	Chlorogenic acid [35, 36]	Stems	Phenolic acid	C ₁₆ H ₁₇ O ₉		Antioxidation Anti-inflammatory Anti-microbial

1,2,3,4-tetrahydro-1-oxo- β -carboline and 17-oxo-19-(Z)-naucline are isolated from twigs of *N. officinalis*. They show weak anti-tumor activity and significant anti-inflammatory activity [42]. Naucline is isolated as a brownish amorphous solid from the bark, stems, and leaves of *N. officinalis*, and exhibit potent vasorelaxant activity [41].

Quinoline alkaloids

Another class of N-based heterocyclic compounds is quinazoline alkaloids. There are about 150 quinazoline alkaloids found in plants, animals, and microorganisms that occur naturally. Several them are genetically descended from anthranilic acid [24]. The quinolone alkaloids pumiloside and 3-epi-pumiloside, extracted from the stems, are among the main active components of *N. officinalis* [43], are present in high amounts, and exhibit various effects, such as anti-inflammatory, anti-bacterial, and anti-tumor activities [7, 44, 45].

Pentacyclic triterpenoids

Pentacyclic triterpenes are also important components of *N. officinalis*. Structurally, five or six members are present in ring E of pentacyclic triterpenoids, while A, B, C, and D are six-membered rings. There are six subgroups of carbon skeletons: hopane, ursane, friedelane, gammacerane, lupane, and oleanane [26]. The stems of *N. officinalis* were extracted, 3 β ,19 α ,23,24-tetrahydroyurs-12-en-28-oic acid and 2 β ,3 β ,19 α ,24-tetrahydroyurs-12-en-28-oic acid are colorless orthorhombic crystals with significant and weak anti-inflammatory activities [46]. Pyrocincholic acid 3 β -O- α -L-rhamnopyranoside, pyrocincholic acid 3 β -O- α -L-rhamnopyranosyl-1-28-O- β -D-glucopyranosyl-(1-6)- β -D-glucopyranosyl ester, and pyrocincholic acid 3 β -O- α -L-rhamnopyranosyl-1-28-O- β -D-glucopyranosyl ester are white amorphous powders and show promising anti-tumor activity [9].

Phenolic acids

Two main subgroups of phenolic acids with one carboxylic acid group can be distinguished: hydroxybenzoic and hydroxycinnamic acids [27]. Extracted from the stems of *N. officinalis*, protocatechuic acid [35, 36], chlorogenic acid [35, 36], 3,4-dimethoxyphenol- β -D-apiofuranosyl (1-6)- β -D-glucopyranoside [14], and kelampayoside A [14, 36] exhibit excellent antioxidant, anti-inflammatory, and anti-microbial activities, and these factors are likely to contribute to *N. officinalis*' clinical effectiveness [14, 35, 36].

Pharmacological effect of *N. officinalis*

Anti-inflammatory effect

In vitro experiment

Experiments on *N. officinalis* leaf extract have shown anti-inflammatory activity in vitro, which may inhibit the cellular inflammatory response by inhibiting prostaglandin E2 production and release and inhibiting cyclic adenosine monophosphate-specific phosphodiesterase 4 activity [57, 58]. Inflammatory protein (nitric oxide [NO]) and TNF- α overproduction have been down-regulated by Naucleoffeine H through induction of lipopolysaccharide (LPS)-induced RAW 264.7 by blocking inducible nitric oxide synthase (iNOS) [31]. Naucleaffines A and B, naucleactonin A, nauclefidine, 3,14-dihydroangustine, 3,14,18,19-tetrahydroangustine, angustine, and nauclefine exhibited significant inhibitory activities against inflammation in RAW 264.7 in vitro [37]. 17-O-methyl-19-(Z)-naucline significantly inhibited NO production in RAW 264.7. No cytotoxicity was observed in 17-O-methyl-19-(Z)-naucline-treated cells [39]. 17-oxo-19-(Z)-naucline, angustoline, angustine, nauclefine and 1,2,3,4-tetrahydro-1-oxob-carboline showed that it inhibited LPS-stimulated NO production in RAW264.7 in vitro [42]. Tao et al. [46] examined the inhibitory effects of 3 β , 19 α , 23, 24-tetrahydroyurs-12-en-28-oic acid and 2 β , 3 β , 19 α , 24-tetrahydroyurs-12-en-28-oic acid on the production of NO induced by LPS in RAW 264.7 to test their anti-inflammatory effects. They exhibited inhibitory activity on the production of NO with the IC₅₀ values of 4.8 and 26.2 mM, respectively. Angustuline, an indole alkaloid found in *N. officinalis*, has anti-inflammatory effects on LPS-induced RAW 264.7 by downregulating the expression of iNOS inflammatory protein, thus inhibiting the production of NO by macrophages [59].

Moreover, STR, pumiloside, 3-epi-pumiloside, vincosamide, 3 α ,5 α -tetrahydrodeoxycordifoline lactam and naucleamide A-10-O- β -D-glucopyranoside exhibited significant inhibitory activity on inflammation [29, 50]. STR, the major compound in *N. officinalis* extract, significantly reduced pro-inflammatory mediator production including NO and cytokines. Additionally, it suppressed iNOS and phosphorylation of I κ B α and NF- κ B p65 in the NF- κ B and mitogen-activated protein kinase (MAPK) signaling pathways [29, 50].

In vivo experiment

N. officinalis is a strong modulator of inflammatory immune responses and suppresses infection and

development during the initial stages of infection and inflammation. Asthma mice can be regulated by *N. officinalis* affecting the secretion of cytokines, such as interferon gamma (IFN- γ), interleukin (IL) -10, IL-5, IL-4, and IL-2, and the infiltration of inflammatory cells in the airway [60]. *N. officinalis* leaves purified by alcohol extraction-macroporous resin inhibited systemic and local inflammatory responses in rats with acute pharyngitis [61]. Acute inflammation occurs at the beginning, *N. officinalis* extract tablets inhibited exudation, swelling, and late granulation tissue formation in animals with an inflammatory response model. In addition, *N. officinalis* injection inhibited inflammatory cell infiltration in asthmatic mice, thereby improving bronchial asthma [62]. STR is the main representative constituent of *N. officinalis* and contributes significantly to ameliorate inflammation by downregulating the expression of pro-inflammatory cytokines, including tumor necrosis factor (TNF- α), IL-1 β , and IL-6, and inhibiting the NF- κ B signaling pathway [63]. A significant reduction in the edema caused by terephthalic acid (TPA) was observed at 20 and 40 mg/kg of STR, and a significant reduction in mouse peritoneal vascular permeability in response to acetic acid. Furthermore, STR significantly reduced leukocyte numbers within the mouse peritoneum induced by sodium carboxymethyl cellulose (CMC-Na). In 20 mg and 40 mg/kg doses of STR, pain latency was markedly prolonged, and the number of writhes was decreased when 40 mg/kg was used [14].

Anticancer effect

Pyrocinncholic acid 3 β -O- α -L-rhamnopyranoside, pyrocinncholic acid 3 β -O- α -L-rhamnopyranosyl-28-O- β -D-glucopyranosyl-(1-6)- β -D-glucopyranosyl ester, and pyrocinncholic acid 3 β -O- α -L-rhamnopyranosyl-28-O- β -D-glucopyranosyl ester was presented a promising cytotoxic effect against A549 cells [9]. The cytotoxic effects of nautiloids and angustoline have been shown against several human cancer lines, including the breast prostate PC3, leukemic K562, leukemic HL-60, lung A549, as well as the gastro SGC 7901 [12]. In a study with cells of human colon cancer, human gastric cancer, and human hepatoma, nuclear antibiotic III was found to be active against them [53]. In the presence of five human cancer cell lines: HepG2, A549, KB, MCF-7, and K562, STR exhibited moderate antiproliferative properties [15]. In Nauclea roots, two new indole alkaloids, naucleaorals A and B, were isolated. Testing their cytotoxicity for human cervical cancer (HeLa) and human oral epidermoid carcinoma (KB) revealed that with an IC₅₀ value of 4.0 g/L,

Naucleaorals A exhibited significant cytotoxicity to HeLa cells, whereas a modest cytotoxicity was found for naucleaorals B against both cell lines with IC₅₀ values of 7.8 and 9.5 μ g/L, respectively [64].

Anti-microbial effect

He et al. [10] observed the sensitivity of *Escherichia coli* to *N. officinalis* decoction through an in vitro antibacterial test. The results showed that *N. officinalis* has a bacteriostatic effect on clinically isolated urinary *Escherichia coli*. Xu et al. [65] found that the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of *N. officinalis* extract against *Staphylococcus aureus* ranged 1.56–3.13% and 1.56–25%, respectively. *Staphylococcus aureus* has good antibacterial and bactericidal activities against both clinically resistant and sensitive strains, and its MIC to bacteria is close to MBC, suggesting that its antibacterial activity may be related to its direct bactericidal activity. Su et al. [66] detected the antibacterial activity of volatile components using the method of paper-disk diffusion. Results revealed that the volatile components of *N. officinalis* leaves and stems had strong antibacterial effects in Methicillin-resistant *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, and *Proteus*. It has also been reported that *N. officinalis* has significant bactericidal and antibacterial effects on bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Streptococcus haemolyticus*, and *Shigella dysenteriae*. Jiang et al. [67] showed that the combined antibacterial effect of *N. officinalis* extract and penicillin showed synergistic action and had an efficient inhibitory effect on *S. aureus*.

Antiviral effect

Children were treated with *N. officinalis* and ribavirin injections for acute upper respiratory tract infections. The results showed that *N. officinalis* injection inhibited bacterial and viral protein synthesis, and metabolism of folic acid is blocked. The clinical effect of *N. officinalis* is more significant than that of ribavirin injection and has the advantages of broad-spectrum antibacterial, anti-virus, and less susceptibility to drug resistance [61]. *N. officinalis* stems and leaves are rich in monoterpene indole alkaloids, which exhibit significant anti-HIV-1 activities, with IC₅₀s ranging from 0.06–2.08 μ M. *N. officinalis* may be a valuable source of indole alkaloids with significant anti-HIV-1 activities that could be developed into new anti-HIV agents. [37]. The anti-HIV-1 activities of Naucleaoffines A and B, naucleactonin A, nauclefidine, 3,14-dihydroangustine,

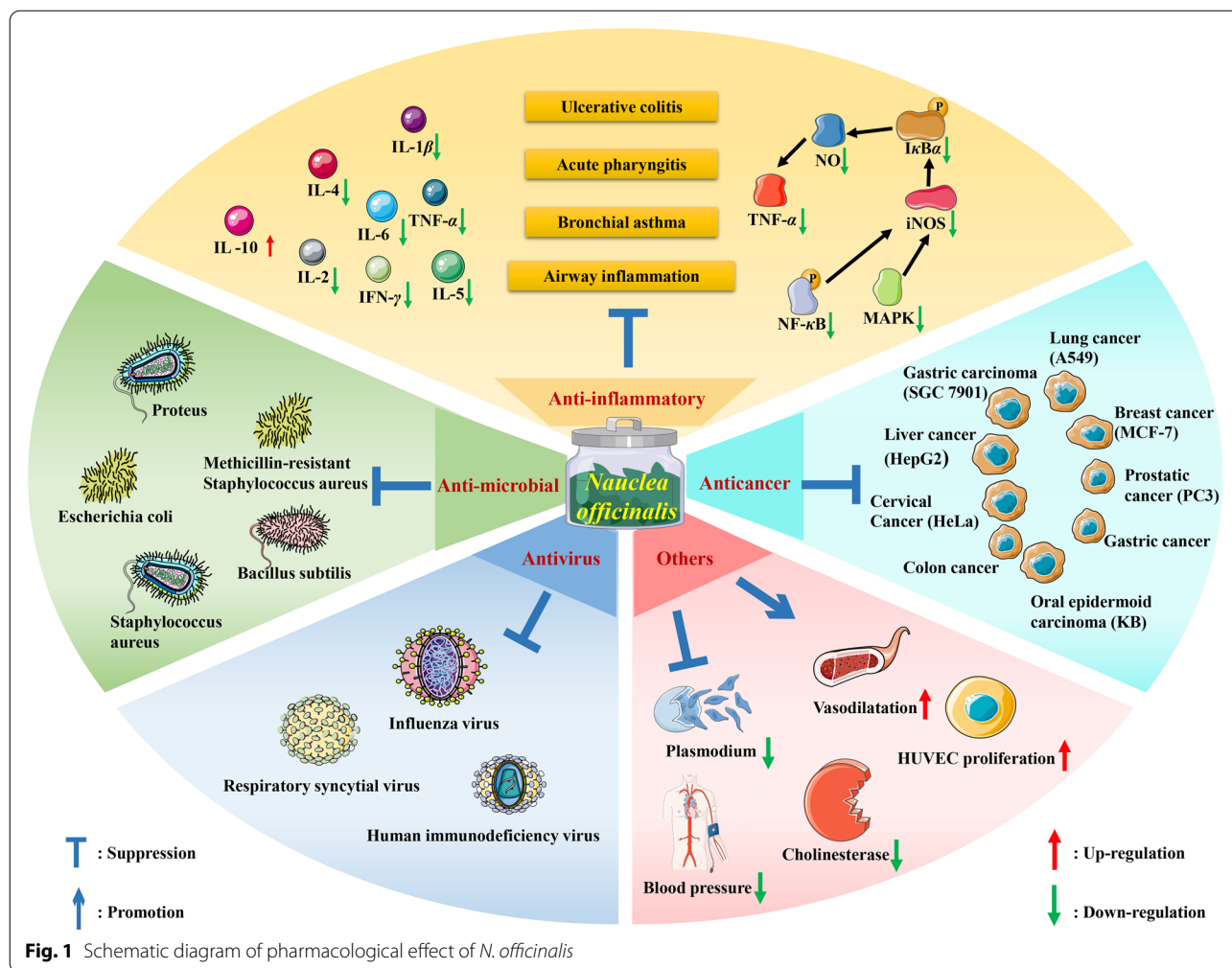
Table 2 Pharmacological effect of *Nauclea officinalis* and its different extracts in vivo and in vitro

NO	Compound Name	Cells/ Virus/Bacterials	Animal model	Dose/concentration	Results
1	Naucleoffeine H [31]	RAW264.7	/	3, 10, 30 μ M	Reduced productions of NO, iNOS and TNF- α
2	Monoterpene indole alkaloids [37]	RAW264.7, HIV-1	/	0.0625, 0.32, 1.6, 8, 40 μ M	Reduced productions of NO, inhibited the activity of HIV-1
3	Nauclea officinalis [50]	RAW264.7	/	10, 20, 50, 100 μ g/mL	Reduced mRNA expressions and productions of NO, TNF- α , IL-6 and IL-1 β ; Suppressed p-IkBa and p-p65
4	Strictosamide [29]	RAW264.7	/	0, 25, 50, 100, 200 μ M	Suppressed productions of NO, iNOS, TNF- α and IL-1 β ; Reduced expressions of p-p65, p-IkBa, p-IKkA, p-p38, p-ERK and p-JNK
5	Strictosamide [14]	/	ICR mice	20, 40 mg/kg	Reduced ear edema in mice induced by TPA; Reduced peritoneal vascular permeability in mice stimulated by acetic acid; Reduced leukocyte count in the peritoneal cavity of mice after CMC-Na treatment; Prolonged the pain latency and decreased the writhing counts
6	Extracts of <i>Nauclea officinalis</i> Pierre ex Pitard [60]	/	Balb/c mice, ovalbumin induced asthma model	1, 2, 4 mg/kg	Reduced the number of inflammatory cells in mouse BALF; Affected the secretion of cytokines in mouse BALF
7	Extracts of <i>Nauclea officinalis</i> Pierre ex Pitard leaf [57]	/	ICR mice	0.390, 0.195, 0.098 g/kg/ days	Prolonged pain latency; Reduced the number of twisting reactions and antagonized the increased intra-abdominal capillary permeability in mice caused by acetic acid; Reduced xylene-induced swelling of the pinna in mice
8	Strictosamide [63]	IEC6/HT-29 /	/ Male Balb/c mice, dextran sulfate sodium (DSS) induced ulcerative colitis model	100, 200 μ M 20, 40 mg/kg	Reduced disease activity index and reduced H&E damage in DSS model mice; Reduced the expression of p-IkBa, p-p65; Downregulated expressions of TNF- α , IL-1 β , IL-6, MPO and iNOS
9	Extracts of <i>Nauclea officinalis</i> Pierre ex Pitard [67]	Staphylococcus aureus	/	0.3125, 0.625, 1.25, 2.5, 5, 10, 20, 40, 80, 160, 320 mg/kg	Had an efficient inhibitory effect on <i>Staphylococcus aureus</i>

3,14,18,19-tetrahydroangustine, angustine, and nauclefine were, with EC_{50} ranged between 0.06 and 2.08 μ M [37]. Biological studies confirmed this activity, by measuring the IC_{50} values of 25.68 g/mL for influenza A virus and 12.50 g/mL for respiratory syncytial virus [15].

Other pharmacological effects

The ingredients of *N. officinalis* also have antimalarial, vasorelaxant, and anticholinesterase effects, promoting the proliferation of HUVEC and antihypertensive pharmacological effects. In vitro, (E)-2-(1-b-D-glucopyranosyloxybut-2-en-2-yl)-3-(hydroxymethyl)-6,



7-dihydro-indolo [2, 3-a] quinolizin-4 (12H)-one exhibited potential antimalarial activity against *P. falciparum*, [12]. STR displayed moderate antiplasmodial activity against *P. falciparum* [68].

The vasorelaxant effects of naucline, angustine, nauclifine, and nauclatine were demonstrated in rat aorta experiments, it may be facilitated by an increase in NO release by endothelial cells [41]. In addition, there was a relaxation induced by naucline independent of endothelial relaxation [54].

In the anticholinesterase activity test, angustidine, nauclifine, angustine, angustoline, and andharmane showed higher butyrylcholinesterase inhibitory potency. Angustidine is known to be one of the greatest inhibitors of acetylcholinesterase and butyrylcholinesterase, which forms hydrogen bonds with Ser198 and His438 [40].

Inflammation can be repaired by proliferating and migrating cells. A previous study found that Naucleofficine H, STR, and pumiloside (0–200 µg/mL) promoted HUVEC proliferation by upregulating vascular

endothelial growth factor (VEGF) and phosphorylation-extracellular regulated protein kinases (ERK) in HUVEC [11].

In addition, different concentrations of STR decreased Mg²⁺-ATPase activity in the brain and kidneys in vivo and in vitro. STR also increased Na⁺/K⁺-ATPase activity in the brain in vivo. These results may account for the effect of *N. officinalis* infusions on hypertension [69]. Although there are many studies to explore the pharmacological effects of *N. officinalis* (Table 2), there is still a lack of in-depth research on its mechanism of action, which also indicates that *N. officinalis* and its active ingredients have great research and development potential.

Conclusions

As one of the rare wild plant species under key protection in China, *N. officinalis* is also an important medicinal plant. The dry trunk, branches, bark, leaves, and roots

of *N. officinalis* can be medicated, and has the effect of clearing heat and detoxification, reducing swelling and relieving pain. The chemical composition of *N. officinalis* mainly includes alkaloids, pentacyclic triterpenes and their saponin compounds, phenolic acids, flavonoids, amino acids, and various trace elements. In recent years, from the consideration of expanding the source of drugs, people have paid more and more attention to composition and biological activity of *N. officinalis*. The content of total flavonoids, total flavone glycosides and alkaloids in *N. officinalis* is high, especially the content of alkaloids is as high as 3.46%, which has high medicinal value and good development potential [70].

A variety of pharmacological effects are associated with *N. officinalis*, including anti-inflammatory, anticancer, anti-microbial, and antiviral (Fig. 1). In clinic, *N. officinalis* extract syrup was used to treat acute tonsillitis, pediatric viral influenza, and lower respiratory tract infection with good results [71–73], but more rigorous researches need to be conducted. In some basic research, although a series of anti-inflammatory, anti-tumor, and anti-microbial studies have been conducted for *N. officinalis* and its extracts, these studies only briefly showed their pharmacological effects. In addition, several studies have used extracts of *N. officinalis*, but the specific active ingredient is unclear, which is not conducive to the study of the mechanism of *N. officinalis*. Therefore, exploring the in-depth mechanisms of *N. officinalis*, its extracts, and active ingredients is urgent and may help identify new drugs and targets of drug action. In recent years, with the development and utilization of *N. officinalis* herbs, resources have become increasingly important and the full and rational exploitation of *N. officinalis* resources has become the focus of future research. Meanwhile, developing new preparations or discovering more medicinal value is also an important issue for the development of *N. officinalis*.

Abbreviations

N. officinalis: *Nauclea officinalis*; STR: Strictosamide; IFN- γ : Interferon gamma; IL: Interleukin; TPA: Terephthalic acid; CMC-Na: Sodium carboxymethyl cellulose; NO: Nitric oxide; TNF: Tumor necrosis factor; iNOS: Inducible nitric oxide synthase; LPS: Lipopolysaccharide; MAPK: Mitogen-activated protein kinase; MIC: Minimum inhibitory concentration; MBC: Minimum bactericidal concentration; HUVEC: Human umbilical vein endothelial cells; VEGF: Vascular endothelial growth factor; ERK: Extracellular regulated protein kinases.

Acknowledgements

Not applicable.

Author contributions

BL and QG contributed to the data collection and manuscript drafting. ZC, LL, PL, LL, and LY were involved in the data collection and visualization. CL was involved in conception, supervision, manuscript review, and editing. It has been approved by all authors to submit the manuscript. All authors read and approved the final manuscript.

Funding

This study was supported by the Scientific and Technological Innovation Project of the China Academy of Chinese Medical Sciences (CI2021B003), National Key R&D Program of China (2020YFE0205100), Innovation Team and Talents Cultivation Program of the National Administration of Traditional Chinese Medicine (ZYXCXD-D-202005), and The Fundamental Research Funds for the Central Public Welfare Research Institutes (Z0653).

Availability of data and materials

The situation does not apply.

Declarations

Ethics approval and consent to participate

The situation does not apply.

Consent for publication

There is no current consideration or publication of this manuscript in any other journal. This manuscript has been approved by all authors to be submitted to *Chinese Medicine*.

Competing interests

This paper does not contain any conflicts of interest according to the authors.

Received: 28 September 2022 Accepted: 22 November 2022

Published online: 20 December 2022

References

- Wang J, Jiang J, Zhu F, Li X, Jia X. Simultaneous determination of phenolic acids and three alkaloids in *Nauclea officinalis* and its preparation by HPLC. *Chin Tradit Patent Med*. 2012;34(12):2326–30.
- Xuan WD, Chen HS, Du JL, Liang S, Li TZ, Cai DG. Two new indole alkaloids from *Nauclea officinalis*. *J Asian Nat Prod Res*. 2006;8(8):719–22.
- Rova JH, Delprete PG, Andersson L, Albert VA. A trnL-F cpDNA sequence study of the Condamineae-Rondeletieae-Sipaneeae complex with implications on the phylogeny of the Rubiaceae. *Am J Bot*. 2002;89(1):145–59.
- Mongrand S, Badoc A, Patouille B, Lacomblez C, Chavent M, Bessoule JJ. Chemotaxonomy of the Rubiaceae family based on leaf fatty acid composition. *Phytochemistry*. 2005;66(5):549–59.
- Xuan WD, Bian J, Chen HS. Alkaloidal constituents of *Nauclea officinalis*. *Chin Tradit Herbal Drugs*. 2007;02:170–3.
- Qi W, Wang D, Feng J, Lai Q. Research Progress on *Nauclea officinalis*, a south traditional medicine. *J Anhui Agri Sci*. 2016;44(16):111–3.
- Zhu F, Wang J, Song J, Ding S, Jia X. Chemical constituents of *Nauclea officinalis*. *Acta Pharmaceutica Sinica*. 2013;48(02):276–80.
- Wang Y, Liao J, Sun L. Review of *Nauclea officinalis* and its preparations. *Asia-Pacific Tradit Med*. 2018;14(08):80–4.
- Wang H, Liu K, Wang R, Qin S, Wang F, Sun J. Two new triterpenoids from *Nauclea officinalis*. *Nat Prod Res*. 2014;29(7):644–9.
- He Y, Huang J, Wu R. Study on antibacterial effect of the decoction of *Nauclea officinalis* in vitro. *West China J Pharma Sci*. 2012;27(5):604–5.
- Mai SY, Li YH, Zhang XG, Wang YR, Zhang JQ, Jia A. A new indole alkaloid with HUVEC proliferation activities from *Nauclea officinalis*. *Nat Prod Res*. 2021;35(18):3049–55.
- Sun J, Lou H, Dai S, Xu H, Zhao F, Liu K. Indole alkaloids from *Nauclea officinalis* with weak antimicrobial activity. *Phytochemistry*. 2008;69(6):1405–10.
- Xuan WD, Chen HS, Yuan ZX, Zhu P. Chemical constituents of *Nauclea officinalis*. *Chin J Nat Med*. 2005;03:181–3.
- Li N, Cao L, Cheng Y, Meng Z, Tang Z, Liu W, Wang Z, Ding G, Xiao W. In vivo anti-inflammatory and analgesic activities of strictosamide from *Nauclea officinalis*. *Pharm Biol*. 2014;52(11):1445–50.
- Li Z, Li Z, Lin Y, Meng Z, Ding G, Cao L, Li N, Liu W, Xiao W, Wu X, Xu J. Synthesis and biological evaluation of strictosamide derivatives with improved antiviral and antiproliferative activities. *Chem Biol Drug Des*. 2015;86(4):523–30.

16. Kuete V, Sandjo LP, Mbaveng AT, Seuokep JA, Ngadjui BT, Efferth T. Cytotoxicity of selected Cameroonian medicinal plants and *Nauclea pobequinii* towards multi-factorial drug-resistant cancer cells. *Bmc Complement Altern Med*. 2015;15(1):309.
17. Rosales PF, Bordin GS, Gower AE, Moura S. Indole alkaloids: 2012 until now, highlighting the new chemical structures and biological activities. *Fitoterapia*. 2020;143: 104558.
18. Liu C, Yang S, Wang K, Bao X, Liu Y, Zhou S, Liu H, Qiu Y, Wang T, Yu H. Alkaloids from Traditional Chinese Medicine against hepatocellular carcinoma. *Biomed Pharmacother*. 2019;120: 109543.
19. Li JY, Sun XF, Li JJ, Yu F, Zhang Y, Huang XJ, Jiang FX. The antimalarial activity of indole alkaloids and hybrids. *Arch Pharm (Weinheim)*. 2020;353(11): e2000131.
20. Wang G, Wang H, Lin Z, Hou L, Wang JY, Sun L. Simultaneous determination of 11 alkaloids in rat plasma by LC-ESI-MS/MS and a pharmacokinetic study after oral administration of total alkaloids extracted from *Nauclea officinalis*. *J Ethnopharmacol*. 2022;282: 114560.
21. Meng ZQ, Liu WJ, Li Z, Lin YW, Li MX, An SY, Ding G, Wang ZZ, Xiao W, Xu JY. Transformation of strictosamide to vincoside lactam by acid catalysis. *Chin J Nat Med*. 2013;11(2):188–92.
22. Huang XW, Bai L, Zhang L. HPLC determination of camptothecin and 10-Hydroxycamptothecin in common camptotheca fruit. *Sci Technol Eng*. 2005;12:809–10.
23. Yuan D, Ma B, Wu C, Yang J, Zhang L, Liu S, Wu L, Kano Y. Alkaloids from the leaves of *Uncaria rhynchophylla* and their inhibitory activity on no production in lipopolysaccharide-activated microglia. *J Nat Prod*. 2008;71(7):1271–4.
24. Shang XF, Morris-Natschke SL, Liu YQ, Guo X, Xu XS, Goto M, Li JC, Yang GZ, Lee KH. Biologically active quinoline and quinazoline alkaloids part I. *Med Res Rev*. 2018;38(3):775–828.
25. Shang XF, Morris-Natschke SL, Yang GZ, Liu YQ, Guo X, Xu XS, Goto M, Li JC, Zhang JY, Lee KH. Biologically active quinoline and quinazoline alkaloids part II. *Med Res Rev*. 2018;38(5):1614–60.
26. Xiao S, Tian Z, Wang Y, Si L, Zhang L, Zhou D. Recent progress in the antiviral activity and mechanism study of pentacyclic triterpenoids and their derivatives. *Med Res Rev*. 2018;38(3):951–76.
27. Kumar N, Goel N. Phenolic acids: Natural versatile molecules with promising therapeutic applications. *Biotechnol Rep (Amst)*. 2019;24: e370.
28. Yin R, Chen J, Zhao Y, Jia X, Zhang Z, Feng L, Wang H, Wang J, Zhu F. Simultaneous determination of six alkaloid components in rat plasma and its application to pharmacokinetic study of Danmu preparations by an ultra fast liquid chromatography–electrospray ionization–tandem mass spectrometry. *J Chromatogr B*. 2015;983–984:10–7.
29. Li D, Chen J, Ye J, Zhai X, Song J, Jiang C, Wang J, Zhang H, Jia X, Zhu F. Anti-inflammatory effect of the six compounds isolated from *Nauclea officinalis* Pierre ex Pitard, and molecular mechanism of strictosamide via suppressing the NF- κ B and MAPK signaling pathway in LPS-induced RAW 2647 macrophages. *J Ethnopharmacol*. 2017;196:66–74.
30. Mao L, Xin L, Dequan Y. Alkaloids of *Nauclea officinalis*. *Planta Med*. 1984;50(06):459–61.
31. Song S, Liu P, Wang L, Li D, Fan H, Chen D, Zhao F. In vitro anti-inflammatory activities of naucleofeine H as a natural alkaloid from *Nauclea officinalis* Pierre ex Pitard, through inhibition of the iNOS pathway in LPS-activated RAW 2647 macrophages. *Nat Prod Res*. 2020;34(18):2694–7.
32. Mesia K, Cimanga RK, Dhooche L, Cos P, Apers S, Totté J, Tona GL, Pieters L, Vlietinck AJ, Maes L. Antimalarial activity and toxicity evaluation of a quantified *Nauclea pobequinii* extract. *J Ethnopharmacol*. 2010;131(1):10–6.
33. Zhu F, Wang J, Yin R, Song J, Li X, Jia X. Review on chemical constituents of genus *Nauclea*. *China J Tradit Chin Med Pharm*. 2014;29(09):2877–80.
34. Li H, Tan Y, Lai W, Liu M, Fu N, Zhang J. Studies on the Fingerprint Chromatography of Hainan *Nauclea officinalis*. *Lishizhen Med Materia Medica Research*. 2009;20(11):2710–1.
35. Li N, Zhang J, Zhang Y, Ma Z, Liao J, Cao H, Wu M. Chromatographic fingerprints analysis and determination of seven components in Danmu preparations by HPLC–DAD/QTOF–MS. *Chin Med*. 2020;15:1.
36. Zhu F, Chen J, Wang H, Jia X, Wang S, Zhang Z, Zhai X, Xu J, Tan W, Ning Q, Gu J. Analysis of the chemical constituents and rats metabolites after oral administration of *Nauclea officinalis* by ultra-performance liquid chromatography quadrupole time-of-flight mass spectrometry. *J Chromatogr B*. 2015;1007:54–66.
37. Liu Y, Liu Q, Zhang X, Niu H, Guan C, Sun F, Xu W, Fu Y. Bioactive monoterpene indole alkaloids from *Nauclea officinalis*. *Bioorg Chem*. 2019;83:1–05.
38. Fan L, Liao C, Kang Q, Zheng K, Jiang Y, He Z. Indole Alkaloids from the Leaves of *Nauclea officinalis*. *Molecules*. 2016;21(8):968.
39. Liu Q, Chen A, Tang J, Ma Y, Jiang Z, Liu Y, Chen G, Fu Y, Xu W. A new indole alkaloid with anti-inflammatory activity from *Nauclea officinalis*. *Nat Prod Res*. 2017;31(18):2107–12.
40. Liew SY, Khaw KY, Murugaiyah V, Looi CY, Wong YL, Mustafa MR, Litaudon M, Awang K. Natural indole butyrylcholinesterase inhibitors from *Nauclea officinalis*. *Phytomedicine*. 2015;22(1):45–8.
41. Liew SY, Mukhtar MR, Hadi AHA, Awang K, Mustafa MR, Zaima K, Morita H, Litaudon M. Naucline, a New Indole Alkaloid from the Bark of *Nauclea officinalis*. *Molecules*. 2012;17(4):4028–36.
42. Song LL, Mu YL, Zhang HC, Wu GY, Sun JY. A new indole alkaloid with anti-inflammatory from the branches of *Nauclea officinalis*. *Nat Prod Res*. 2020;34(16):2283–8.
43. Zhang Z, Chen J, Wang H, Jia X, Zhu F, Wu Y, Huang F, Wang L. Simultaneous purification and preparation of four alkaloids from *Nauclea officinalis* by using auto purification system. *China J Tradit Chin Med Pharm*. 2016;31(02):463–6.
44. O'Connor SE, Maresh JJ. Chemistry and biology of monoterpene indole alkaloid biosynthesis. *Nat Prod Rep*. 2006;23(4):532.
45. Chen J, Xu G, Wang H, Wang J, Zhu F. Simultaneous determination of six main compounds in *Nauclea officinalis* by ultra-performance liquid chromatography. *J China Pharm Univ*. 2014;45(04):434–7.
46. Tao J, Dai S, Zhao F, Liu J, Fang W, Liu K. New ursane-type triterpene with NO production suppressing activity from *Nauclea officinalis*. *J Asian Nat Prod Res*. 2012;14(2):97–104.
47. Li Q, Zhang Y, Wu B, Qu H. Identification of indole alkaloids in *nauclea officinalis* using high-performance liquid chromatography coupled with ion trap and time-of-flight mass spectrometry. *Eur J Mass Spectrom (Chichester)*. 2011;17(3):277–86.
48. Fan L, Fan CL, Wang Y, Zhang XQ, Zhang QW, Zhang JQ, Ye WC. Alkaloids from the leaves of *Nauclea officinalis*. *Acta Pharmaceutica Sinica*. 2010;45(06):747–51.
49. Meng ZQ, Ding G, Liu YJ, Xu J, Liu WJ, Xiao W. Study on purification of strictosamide from *Nauclea officinalis* by macroporous resin. *China J Chin Materia Med*. 2011;36(8):1007–10.
50. Zhai X, Zhang Z, Jiang C, Chen J, Ye J, Jia X, Yang Y, Ni Q, Wang S, Song J, Zhu F. *Nauclea officinalis* inhibits inflammation in LPS-mediated RAW 2647 macrophages by suppressing the NF- κ B signaling pathway. *J Ethnopharmacol*. 2016;183:159–65.
51. Lian YP, Xie DW, Yuan SW, Li YJ, Ding G, Huang WZ, Xiao W. Similarity between leaves of *Nauclea officinalis* and stems of *Nauclea officinalis*. *China J Chin Materia Med*. 2015;40(22):4433–41.
52. Erdelmeier C, Wright A, Orjala J, Baumgartner B, Rali T, Sticher O. New Indole Alkaloid Glycosides from *Nauclea orientalis*. *Planta Med*. 1991;57(02):149–52.
53. Wang H, Wang R, Zhao Y, Liu K, Wang F, Sun J. Three New Isomeric Indole Alkaloids from *Nauclea officinalis*. *Chem Biodivers*. 2015;12(8):1256–62.
54. Ishizuka M, Koga I, Zaima K, Kaneda T, Hirasawa Y, Hadi AHA, Morita H. Vasorelaxant effects on rat aortic artery by two types of indole alkaloids, naucine and cadamine. *J Nat Med*. 2013;67(2):399–403.
55. Xuan WD, Chen HS, Bian J. A new indole alkaloid glycoside from stems of *Nauclea officinalis*. *Acta Pharmaceutica Sinica*. 2006;41(11):1064–7.
56. Xuan WD, Bian J, Chen HS. Studies on the Separation and Purification of Pumiloside from *Nauclea officinalis* by Macroreticular Resin. *J Chin Med Mater*. 2007;30(10):1301–4.
57. Cao L, Li N, Jiang Y, Ding G, Wang Z, Xiao W. Anti-inflammatory and analgesic effects of extracts from the leaves of *nauclea officinalis* pierre ex pitard. *China J Tradit Chin Med Pharm*. 2011;17(24):124–7.
58. Liu J. Study on chemical constituents and anti-inflammatory activity of Medicinal *Aconitum officinalis* [博士]. Shenyang: Shenyang Pharmaceutical University; 2009.
59. Huang G, Li L, Liu P, Zhang Q, Zong M, Zhao F. Effects of angustuline on NO release and iNOS expression in LPS-induced RAW2647 cells. *J Clin Med Literat*. 2019;6(28):40–2.
60. Cai X, Huang Y, Zheng Y. Effects of Danmu extract on cytokine and inflammatory cells of BALF in bronchial asthmatic mice. *China Trop Med*. 2018;18(05):427–9.

61. Meng L. Clinical observation on the treatment of acute upper respiratory tract infection in children with Biliary injection. *Hebei J Tradit Chin Med*. 2009;31(08):1213–4.
62. Huang YJ, Wu HD, Cai XJ, Mo RB, Dong W, Meng C. Effect of Danmu injection on inflammatory cells in bronchoalveolar lavage fluid of asthmatic mice. In: Chinese Medical Association Annual Meeting of Respiratory Diseases -- 2013 (the 14th National Academic Conference on Respiratory Diseases). Dalian, Liaoning, China, 2013:1.
63. Jia Q, Zhang H, Su Y, Liu X, Bai J, Lang W, Shi Q, Feng M. Strictosamide alleviates the inflammation in an acute ulcerative colitis (UC) model. *J Physiol Biochem*. 2021;77(2):283–94.
64. Sichaem J, Surapinit S, Siripong P, Khumkratok S, Jong-aramruang J, Tip-pyang S. Two new cytotoxic isomeric indole alkaloids from the roots of *Nauclea orientalis*. *Fitoterapia*. 2010;81(7):830–3.
65. Xu C, Xu X, Yin Q. Screening and pharmacodynamic evaluation of in vitro antimicrobial activities of extracts of *Nauclea officinalis*. *J Chin Res Hospitals*. 2018;5(06):59–63.
66. Su K, Gong M, Deng S, Zhou J. Study on Anti-MRS Activity of *Nauclea officinalis* Leaves. *J Anhui Agri Sci*. 2010;21(02):299–301.
67. Jiang P, Li X, Gao Q, Zhu H, Bao L, Zuo R. Inhibitory Effect of *Nauclea officinalis* Pierre ex Pitard. extract and different antibiotic combinations on *Staphylococcus aureus*. *Guizhou Agric Sci*. 2018;46(11):79–82.
68. Abreu P, Pereira A. New indole alkaloids from *Sarcocephalus latifolius*. *Nat Prod Lett*. 2001;15(1):43–8.
69. Candeias MF, Abreu P, Pereira A, Cruz-Morais J. Effects of strictosamide on mouse brain and kidney Na⁺, K⁺-ATPase and Mg²⁺-ATPase activities. *J Ethnopharmacol*. 2009;121(1):117–22.
70. Xie D, Li Y, Zhao L, Ding G, Yuan S, Xu J, Zhu H, Xiao W. Study on chemical constituents from leaves of *Nauclea officinalis*. *Zhongguo Zhong Yao Za Zhi*. 2011;36(8):1037–9.
71. Wei W, He Y, Yi Z. Clinical curative effect of danmu extract syrup in the treatment of patients with acute tonsillitis. *Chinese Community Doctors*. 2016;32(33):107–9.
72. Liao K. Clinical efficacy and safety analysis of bile extract syrup in treatment of children with viral influenza. *Chin For Med Res*. 2017;15(1):18–9.
73. Li Y. Clinical effect of Danmu Jingao Tangjiang in the treatment of lower respiratory tract infection. *Nei Mongol J Tradit Chin Med*. 2016;35(15):9.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

