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Review article

An Insight into the Traditional Uses, Phytoconstituents and Pharmacological Activities of the Genus *Tylophora*

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Abstract

Traditional plants have huge demand as medicines to treat a wide range of illnesses. *Tylophora* is an important genus of medicinal plant in India, used to treat asthma and other ailments. The plants of this genus have been studied in vivo and in vitro for various pharmacological properties. In this article, we have given information regarding ethnomedicinal importance, phytochemistry and pharmacological uses of 18 species of *Tylophora*. Comprehensive information regarding different species of *Tylophora* were collected using different keywords in various electronic databases such as ACS, Google Scholar, PubMed, Science Direct, SciFinder, Web of Science, Springer Link, library search, J gate, Wiley, Semantic Scholar and ResearchGate since 1960 to 2023. Additionally, data was collected from some textbooks and chapters like Flora of India and Indian medicinal plants. This article highlights the traditional uses, phytochemistry, and pharmacological activities of the few studied taxa of *Tylophora* that would serve as a reference for pharmaceutical research. More than 100 compounds have been isolated from selected species of the genus *Tylophora*. Among them, phenanthroindolizidine alkaloids have received the most attention and are the most abundant active constituents of the plant. Other types of active components of genus *Tylophora* include C21 glycosides, secoiridoids, triterpenes, and furano alkaloids. These compounds have shown a variety of therapeutic activities like antiasthmatic, antitumour, antimicrobial, antidiabetic and antiallergic properties. This review can be an important scientific resource for further research.

Keywords: antiasthmatic; antitumour; phenanthroindolizidine alkaloids; *Tylophora*; xanthone glycosides

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Introduction

Since many centuries, natural products act as a foremost source of drugs and have enormous benefit to mankind. Natural products are extensively explored for ethnomedicinal purposes in most of the regions in the world. Though a good number of plant secondary metabolites are available commercially, exhaustive research is in progress to isolate and evaluate the potential compounds and to bring out new compounds with suitable therapeutic efficacies and low toxicities.

The genus *Tylophora* comprises 60 species,

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distributed mainly in tropical and subtropical regions of Asia, Africa, and Australia [1]. It belongs to Asclepidaceae family [2], which has now changed into Apocyanaceae [3]. Twenty-one species and two varieties are found in India [4]. The most widely used and extensively researched species in India is *Tylophora indica.* (Burm.f.) Merr. About this species, several review articles have been written [5,6]. A recent article on its ethnopharmacology, phytochemistry, and pharmacological features was published by Ritika Gurunani et al. and S Nazar et al. in the year 2020. Therefore, we have given data for this species from 2020 to present.

Despite diverse uses of the plants of the *Tylophora* genus in treating various diseases, to the best of our knowledge, no comprehensive review has before been published before, we collected and compiled the progress of the work on phytochemical and pharmacological studies along with ethnopharmacological aspects of about sixteen species of the genus *Tylophora* that are widely scattered in Asian countries, with the elucidate structures listed and drawn. The folklore uses, phytochemistry and pharmacological activities of the extracts or compounds isolated from *Tylophora* are also summarized. This paper aims to present precise data from the research on the *Tylophora* genus and to lay the groundwork for future research and development.

Methods

A detailed literature search was conducted on the sixteen plants of the genus *Tylophora* to collect all significant information about folklore uses, phytoconstituents and pharmacological activities. PubMed, PubMed Central, SciFinder, Google Scholar, J-gate, Library Search, Science Direct, Elsevier, Semantic Scholar, PubMed Central, ResearchGate and primary sources were searched since 1960 to 2023. Searching information regarding the genus *Tylophora* was carried out using Latin names of the eighteen species, covering *Tylophora asthmatica* (L.f.) Wight & Arn., *Tylophora atrofolliculata* F.P.Metcalf, *Tylophora conspicua* N.E.Br., *Tylophora cordifolia* Thwaites, *Tylophora crebiflora*, *Tylophora dalzellii* Hook.f, *Tylophora fasciculata* Thwaites, *Tylophora flava* Trimen, *Tylophora hirsuta* Wight, *Tylophora indica* (Burm.f.) Merr, *Tylophora mollissima* Wall, *Tylophora ovata* (Lindl.) Hook. ex Steud., *Tylophora pauciflora Wight & Arn*, *Tylophora secamonoides* Tsiang, *Tylophora sylvatica* Decne., *Tylophora tanakae* Maxim., and *Tylophora villosa* Blume, *Tylophora yunnanensis Schltr*. The plant names, traditional uses, isolated constituents, and pharmacological activities were extracted from the collected data. The Plant List (www.theplantlist.org) was used to validate the species names. ChemDraw 10.0 software was used to draw chemical structures.

Results and Discussion

Traditional uses

According to the scientific literature, the species of the genus *Tylophora* are widely used in local and traditional medicine to treat a variety of disorders imcluding indigestion, bronchial asthma, bronchitis, cough, liver diseases, wounds, and ulcers and as expectorant, [7-23]. Table 1 summarises the scientific names, common names, geographical distribution, and traditional uses of the *Tylophora* species. The species with traditional value are shown in Figure 1.

Phytochemistry

From the last seven decades, extensive research is going on the genus *Tylophora* for its active constituents. The genus has a variety of compounds, majorly phenanthroindolizidine alkaloids 1-90 shown in Figure 2. Others include fluroquinoline alkaloids in Figure 3, phenanthroindolizidine glycosides in Figure 4, C21 steroidal glycosides in Figure 5, secoiridoids in Figure 6, xanthones in Figure 7, and triterpenoid in Figure 8. Fatty alcohol and purine alkaloid were shown in Figure 9 and polyphenols were shown in Figure 10. The structures were elucidated by spectral and chemical means like Nuclear Magnetic Resonance (NMR), Mass, Infrared (IR), biosynthetic studies, degradation studies, including Correlated Spectroscopy (COSY), Nuclear Overhauser Effect Spectroscopy (NOESY), Heteronuclear Single Quantum Coherence spectroscopy (HSQC), and Heteronuclear Multiple Bond Correlation (HMBC) experiments, supported by High-resolution Mass Spectrometry (HRMS) and optical rotation data. These were isolated and identified from various parts of the plants like roots, leaves, stems, and aerial parts.

Alkaloids isolated from *Tylophora* species are broadly studied for different pharmacological activities and few of them were considered as

therapeutically useful compounds. More than 100 compounds were isolated from selected *Tylophora* species [24-56]. The details regarding phytochemistry are given in the Table 2. Category of the active constituents, number of isolated compounds in each category and list of species which contain those compounds are summarised in Figure 11.

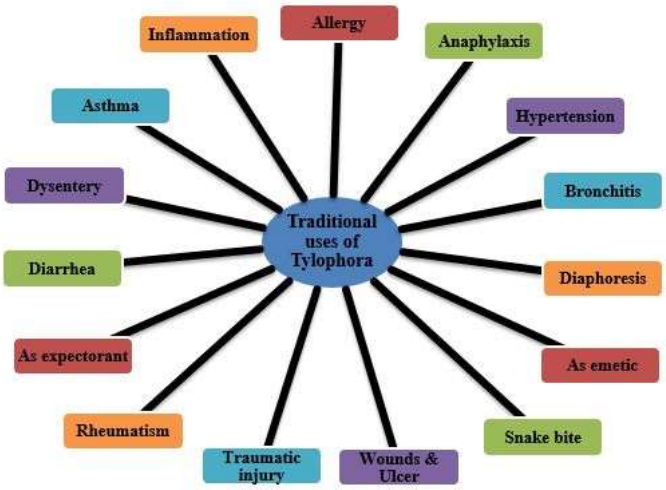


Figure 1. Traditional uses of *Tylophora* genus

Table 1. Traditional uses of *Tylophora* genus

Scientific name	Common name	Distribution	Parts used	Traditional uses	Ref.
Tylophora asthmatica	Ananthamul	Western Ghats of India, Assam, Burma and Sri Lanka	Leaves	As antiinflammatory, anti anaphylactic, emetic, expectorant agent, for asthma, dysentry and snake bite	[7-10]
Tylophora atrofolliculata	N/A	China	N/A	Rheumatism	[11]
Tylophora conspicua	N/A	Liberia east to Burundi, Tanzania and south to Angola and Zimbabwe	Leaves	Wounds and ulcers	[12]
Tylophora dalzelli	Dalzell Ipecac	Western Ghats, India	Herb	Dysentery, asthma, as emetic, expectorant, diaphoretic	[13,14]
Tylophora fasciculata	Brown Flowered Ipecac	India &Srilanka	Leaves	Wounds	[15]
Tylophora hirsute	Hairy Ipecac	Paleotropical regions of Pakistan	N/A	Asthma, high blood pressure, diarrhea, rheumatism and allergic conditions	[16]
Tylophora indica	Indian ipecac	India and Srilanka	Herb	Dysentery, asthma, as emetic, expectorant, diaphoretic	[13,14]
Tylophora ovata	Hairy Ipecac	China and Taiwan	Whole plant	Rheumatism, asthma, traumatic injury	[17]
Tylophora pauciflora	N/A	India and Southeast Asia	Whole plant	Bronchitis and bronchial asthma	[18]
Tylophora secamonoides	N/A	China	Roots	Cough	[19]
Tylophora sylvatica	N/A	Ivory coast, humid tropical Africa, including Madagascar	N/A	As purgative	[20,21]
Tylophora villosa	N/A	N/A	N/A	Liver diseases	[22]
Tylophora yunnanensis	N/A	Yunnan, Guizhou, and other places in China	N/A	Hepatitis and other liver-related diseases	[23]

N/A: not available

Table 2. List of chemical compounds of selected species of the *Tylophora* genus

No.	Compound	Species	Parts used	Type of extract	Ref.
	Phenanthroindolizidine alkaloids				
1	O-methyl tylophorinidine	*Tylophora asthmatica*	Leaves	Ethanol	[24]
		Tylophora atrofolliculata	Whole plant	Methanol	[11]
		Tylophora indica	Roots and aerial parts	Methanol	[25]
2	Desoxytylophorinine	*Tylophora asthmatica*	Leaves	Ethanol	[24]
		Tylophora atrofolliculata	Whole plant	Methanol	[11]
3	Acetyl-O-methyltylophorinidine	*Tylophora asthmatica*	Leaves	Ethanol	[24]
4	Tylophorinidine di acetate	*Tylophora asthmatica*	Leaves	Ethanol	[24]
5	Tylophorinidine	*Tylophora asthmatica*	Aerial parts	N/A	[27]
		Tylophora asthmatica	Rroots, stem and leaves	Chloroform	[9]
		Tylophora asthmatica	Leaves	Ethanol	[24]
		Tylophora atrofolliculata	Whole plant	Methanol	[11]
		Tylophora indica	Leaves	Methanol	[26]
		Tylophora ovata	Roots	Ethanol	[41]
6	Tylophorinicine	*Tylophora asthmatica*	Roots	N/A	[28]
		Tylophora indica	Leaves	Methanol	[26]
7	Tylophoridicine C	*Tylophora atrofolliculata*	Roots	Ethanol	[29]
		Tylophora atrofolliculata	Whole plant	Methanol	[11]
8	3-Demethyl anhydrodehydrotylophorinidine	*Tylophora atrofolliculata*	Whole plant	n-Butanol	[29]
9	(13aR,14S)-3,6,7-Trimethoxy-14-hydrophenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
10	(13aS,14S)-3,14-Dihydroxy-6,7-dimethoxyphenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
11	(13aS,14S)-3,14-Dimethoxy-6,7-dimethoxyphenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
12	3,6,7-Trimethoxy-phenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
13	3,7-Dimethoxy-6-hydroxyphenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
14	3,6,7-Trimethoxy-14-hydroxy-10-oxyphenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
15	3,7-Dimethoxy-6,14-dihydroxy-10-oxyphenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
		Tylophora indica	Leaves	Methanol	[26]
16	3,6,7-Trimethoxy-9(10),13a(14)-dehydrophenanthroindolizidinium chloride	*Tylophora atrofolliculata*	Whole plant	Ethanol	[30]
17	Tylophoridicine D	*Tylophora atrofolliculata*	Whole plant	n-Butanol	[31]
		Tylophora atrofolliculata	Whole plant	Methanol	[11]
		Tylophora atrofolliculata	Roots	Ethanol	[29]
		Tylophora atrofolliculata	Roots	N/A	[33]
18	2-Demethyl dehydrotylophorine	*Tylophora atrofolliculata*	Whole plant	n-Butanol	[31]

Table 2. Continued.

No.	Compound	Species	Parts used	Type of extract	Ref.
19	2-H ydroxyl anhydrodehydrotylophorinidine	*Tylophora atrofolliculata*	Whole plant	n-Butanol	[31]
20	6-Demethyl dehyrotylophorine	*Tylophora atrofolliculata*	Whole plant	n-Butanol	[31]
21	Dehydrotylophorine	*Tylophora atrofolliculata*	Whole plant	n-Butanol	[31]
22	Anhydrodehydrotylophorinidine	*Tylophora atrofolliculata*	Whole plant	n-Butanol	[31]
23	(+)-(13aS)-Deoxytylophorinine	*Tylophora atrofolliculata*	Roots	N/A	[32]
24	Tylophoridicine E	*Tylophora atrofolliculata*	Roots	Ethanol	[29]
		Tylophora atrofolliculata	N/A	N/A	[33]
25	Tylophorine	*Tylophora asthmatica*	Roots, stem, and leaves	Chloroform	[9]
		Tylophora atrofolliculata	Whole plant	Methanol	[11]
		Tylophora crebiflora	Whole plant	Methanol	[34]
		Tylophora crebiflora	Whole plant	Chloroform	[35]
		Tylophora dalzelli	Aerial parts	N/A	[36]
		Tylophora flava	Aerial parts	N/A	[9]
		Tylophora hirsuta	Aerial parts	Ethyl acetate soluble and insoluble fractions	[38]
		Tylophora indica	Leaves	Methanol	[26]
		Tylophora mollissima	Whole plant	Ethanol	[40]
		Tylophora ovata	Roots	Ethanol	[41]
		Tylophora ovata	Whole plant	Methanol	[41]
		Tylophora tanakae	Leaves and stem	Fractions of methanol extract	[46]
		Tylophora tanakae	Roots	Methanol	[48]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs	N/A	[49]
26	Desmethyltylophorine	*Tylophora dalzelli*	Aerial parts	N/A	[36]
27	Desmethyltylophorinine	*Tylophora dalzelli*	Aerial parts	N/A	[36]
28	13α-Hydroxytylophorine	*Tylophora hirsuta*	Aerial parts	Ethyl acetate	[37]
29	14-Desoxy-13a-methyltylohirsutinidine	*Tylophora hirsuta*	Aerial parts	Ethyl acetate soluble and insoluble fractions	[38]
30	5-Hydroxy-O-methyltylophorinidine	*Tylophora hirsuta*	Aerial parts	Ethyl acetate soluble and insoluble fractions	[38]
31	Tylohirsuticine	*Tylophora hirsuta*	Aerial parts	Ethyl acetate soluble and insoluble fractions	[38]
32	14-Hydroxyisotylocrebrine	*Tylophora hirsuta*	Aerial parts	Ethyl acetate soluble and insoluble fractions	[38]
33	4-Desmethylisotylocrebrine	*Tylophora hirsuta*	Aerial parts	Ethyl acetate soluble and insoluble fractions	[38]
34	Tylohirsutinine	*Tylophora hirsuta*	Aerial parts	Ethylacetate soluble mixture	[39]
35	13a-Methyltylohirsutine	*Tylophora hirsuta*	Aerial parts	Ethylacetate soluble mixture	[39]
36	13a-Methyltylohirsutinidine	*Tylophora*	Aerial	Ethylacetate soluble mixture	[39]

Table 2. Continued.

No.	Compound	Species	Parts used	Type of extract	Ref.
		hirsuta	parts		
37	Tylohirsutinidine	*Tylophora hirsuta*	Aerial parts	Ethylacetate soluble mixture	[39]
38	13a-Hydroxysepticine	*Tylophora hirsuta*	Aerial parts	Ethylacetate soluble mixture	[39]
39	Tylophorinine	*Tylophora asthmatica*	Roots, stem, and leaves	Chloroform	[9]
		Tylophora atrofolliculata	Whole plant	Methanol	[11]
		Tylophora cordifolia	Aerial parts	N/A	[9]
		Tylophora flava	Aerial parts	N/A	[9]
		Tylophora indica	Leaves	Methanol	[26]
		Tylophora mollissima	Whole plant	Ethanol	[40]
		Tylophora ovata	Whole plant	Methanol	[41]
40	Tylophoridicine A	*Tylophora ovata*	Roots	Ethanol	[41]
41	S-(+)-Deoxytylophorinidine (CAT)	*Tylophora atrofolliculata*	Roots	N/A	[42]
		Tylophora ovata	Roots	N/A	[42]
42	Septicine	*Tylophora ovata*	Leaves and stems	N/A	[43]
		Tylophora ovata	Stems and leaves	Methanol	[17]
43	3,14a-Dihydroxy-4,6,7-trimethoxy phennanthroindolizidine	*Tylophora ovata*	Whole plant	Methanol	[41]
44	3,14a-Dihydroxy- 6,7-dimethoxy phennanthroindolizidine	*Tylophora ovata*	Whole plant	Methanol	[41]
45	Tylophorinine N-oxide	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
		Tylophora indica	Leaves	Methanol	[26]
		Tylophora tanakae	Aerial parts	Methanol	[44]
		Tylophora tanakae	Leaves and caules	Polar fraction	[45]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs	N/A	[49]
46	(+)-Isotylocrebrine	*Tylophora hirsuta*	Aerial parts	Ethyl acetate soluble and insoluble fractions	[38]
		Tylophora tanakae	Leaves and stem	Fractions of A-C of Methanol extract	[46]
		Tylophora tanakae	Roots	Methanol	[48]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs	N/A	[49]
47	(-)-(R)-13aα-7-O-Desmethyltylophorine	*Tylophora tanakae*	Leaves and stems	Methanol	[47]
48	(+)-(S)-13aβ-Isotylocrebrine	*Tylophora tanakae*	Leaves and stems	Methanol	[47]
49	(-)-(R)-13a-Secoantofine	*Tylophora tanakae*	Leaves and stems	Methanol	[47]
50	(-)-(R)-13a-6-O-Desmethyl secoantofine	*Tylophora tanakae*	Leaves and stems	Methanol	[47]
51	(-)-(R)-13a-Antofine	*Tylophora tanakae*	Leaves and stems	Methanol	[47]

Table 2. Continued.

No.	Compound	Species	Parts used	Type of extract	Ref.
52	14b-Hydroxytylophorine N-oxide	*Tylophora tanakae*	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs	N/A	[49]
53	7-Demethyltylophorine	*Tylophora ovata*	Leaves and twigs	N/A	[49]
		Tylophora tanakae	Leaves and stem	Fractions of methanol extract	[46]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
54	Tylocrebrine	*Tylophora crebiflora*	Whole plant	Methanol	[34]
		Tylophora crebiflora	Whole plant	Chloroform fraction	[35]
55	Tylophoridicine F	*Tylophora atrofolliculata*	Roots	Ethanol	[29]
56	11-Keto tylophorinidine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
57	12S,14αR,15R-11-oxa-12-(2-oxopropyl)-Hydroxylboehmeriasin A	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
58	13aS-2,6-Didemethyl tylophorine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
59	2-Hydroxyl tylophornidine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
60	10R,14R-3-O-Demethyltylophorinidine N-oxide	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
61	10S-2-Hydroxyl-6-demethyltylophorinine N-oxide	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
62	10R-2-Hydroxyltylophorinine N-oxide	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
63	10R-Deoxytylophorinine N-oxide	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
64	13aR-2-Hydroxyltylophorinine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
65	10R,13aS-Tylophorine N-oxide	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
66	10R-2-Methyl O-Methyltylophorinidine N-oxide	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
67	11-Keto-O-Methyltylophorinidine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
68	3-O-Demethyltylophorinidine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
69	Trans-(+)-3,14a-dihydroxy-6,7-dimethoxyl-phenanthroindolizidine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
70	13aS-Tylophorine	*Tylophora atrofolliculata*	Whole plant	Methanol	[11]
		Tylophora atrofolliculata	Whole plant	N-butanol	[31]
		Tylophora ovata	Stems and leaves	Methanol	[17]
		Tylophora tanakae	Leaves and stems	Methanol	[47]
		Tylophora ovata	Roots	Ethanol	[41]
		Tylophora ovata	Stems and leaves	Methanol	[17]
71	Tylophovatine A	*Tylophora ovata*	Stems and leaves	Methanol	[17]
72	Tylophovatine B	*Tylophora ovata*	Stems and leaves	Methanol	[17]
73	Tylophovatine C	*Tylophora ovata*	Stems and leaves	Methanol	[17]
74	(S)-(+)-Hispidine	*Tylophora ovata*	Stems and leaves	Methanol	[17]
75	13a(S)-(+)-6-Desmethyltylophorine	*Tylophora ovata*	Stems and	Methanol	[17]

Table 2. Continued.

No.	Compound	Species	Parts used	Type of extract	Ref.
			leaves		
76	13a(S)-(+)-3-Demethyl-isotylocrebrine	*Tylophora ovata*	Stems and leaves	Methanol	[17]
77	13a(S),14(S)-(+)-3,14-Dihydroxy-6,7-dimethoxyphenanthroindolizidine	*Tylophora ovata*	Stems and leaves	Methanol	[17]
78	13a(S),14(S)-(+)-3,14-Dihydroxy-4,6,7-trimethoxy-phenanthroindolizidine	*Tylophora ovata*	Stems and leaves	Methanol	[17]
79	14β- Tylophorinine N-oxide	*Tylophora tanakae*	Aerial parts	Methanol	[44]
80	3-Demethyl-14α-hydroxyisotylocrebrine N-oxide	*Tylophora tanakae*	Aerial parts	Methanol	[44]
		Tylophora tanakae	Leaves and stem	Fractions of methanol extract	[46]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs	N/A	[49]
81	Tylophorine N-oxide	*Tylophora tanakae*	Aerial parts	Methanol	[44]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs		[49]
82	Isotylocrebrine N-oxide	*Tylophora tanakae*	Aerial parts	Methanol	[44]
		Tylophora tanakae	Leaves and stem	Fractions of methanol extract	[46]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs	N/A	[49]
83	3-Demethyl-14β-hydroxyisotylocrebrine	*Tylophora tanakae*	Aerial parts	Methanol	[44]
		Tylophora tanakae	Leaves and stem	Fractions of methanol extract	[46]
		Tylophora tanakae	Aerial parts, and roots	N/A	[49]
		Tylophora ovata	Leaves and twigs	N/A	[49]
84	(-)-7-Demethyl tylophorine N-oxide	*Tylophora tanakae*	Leaves and caules	Polar fraction	[45]
85	3,6-Didemethyl isotylocrebrine	*Tylophora tanakae*	Leaves and caules	Polar fraction	[45]
86	14α-Hydroxy-3,6-didemethyl isotylocrebrine	*Tylophora tanakae*	Leaves and caules	Polar fraction	[45]
87	3-Demethyl isotylocrebrine	*Tylophora tanakae*	Leaves and stem	Fractions of methanol extract	[46]
88	3-Demethyl-14a-hydroxy isotylocrebrine	*Tylophora tanakae*	Leaves and stem	Fractions of methanol extract	[46]
89	6-Demethyltylocrebrine	*Tylophora tanakae*	Leaves and stem	Fractions of methanol extract	[46]
90	14α-Hydroxy isotylocrebrine N-oxide	*Tylophora tanakae*	Leaves and stem	Fractions of methanol extract	[46]
	Furoquinoline alkaloids				
91	Gamma fagarine	*Tylophora asthmatica*	Roots and aerial parts	N/A	[50]
92	Skimmianine	*Tylophora asthmatica*	Roots and aerial parts	N/A	[50]
	Phenanthroindolizidine glycoside				
93	6-O-β-D-glucopynanosyl-tylophorinidine	*Tylophora atrofolliculata*	Whole plant	Methanol	[51]

Table 2. Continued.

No.	Compound	Species	Parts used	Type of extract	Ref.
	Steroidal glycosides				
94	Tylophoriside A	*Tylophora atrofolliculata*	Roots	Ethanol	[52]
		Tylophora sylvatica	Whole plant	N/A	[54]
		Tylophora sylvatica	Whole plant	Methanol	[21]
		Tylophora tanakae	Roots	Methanol	[48]
95	Atrofollicosides A	*Tylophora atrofolliculata*	Whole plant	Fraction of chloroform-methanol eluent of ethyl acetate soluble part of methanol extract	[53]
96	Atrofollicosides B	*Tylophora atrofolliculata*	Whole plant	Fraction of chloroform-methanol eluent of ethyl acetate soluble part of methanol extract	[53]
97	Atrofollicosides C	*Tylophora atrofolliculata*	Whole plant	Fraction of chloroform-methanol eluent of ethyl acetate soluble part of methanol extract	[53]
98	Cynatratoside A	*Tylophora atrofolliculata*	Whole plant	Fraction of chloroform-methanol eluent of ethyl acetate soluble part of methanol extract	[53]
99	Amplexicoside A	*Tylophora atrofolliculata*	Whole plant	Fraction of chloroform-methanol eluent of ethyl acetate soluble part of methanol extract	[53]
100	Atratcynoside B	*Tylophora atrofolliculata*	Whole plant	Fraction of chloroform-methanol eluent of ethyl acetate soluble part of methanol extract	[53]
101	Glaucogenin A 3-O-β-D-oleandropyranoside	*Tylophora atrofolliculata*	Whole plant	Fraction of chloroform-methanol eluent of ethyl acetate soluble part of methanol extract	[53]
102	Tylophoroside	*Tylophora sylvatica*	Whole plant	N/A	[54]
103	Acetyltylophoroside	*Tylophora sylvatica*	Whole plant	N/A	[54]
		Tylophora sylvatica	N/A	N/A	[55]
		Tylophora sylvatica	Whole plant	Methanol	[21]
104	Tylogenin	*Tylophora sylvatica*	Whole plant	Methanol	[21]
105	Tylophoroside B	*Tylophora tanakae*	Roots	Methanol	[48]
106	Tylophoroside C	*Tylophora tanakae*	Roots	Methanol	[48]
107	Tylophoroside D	*Tylophora tanakae*	Roots	Methanol	[48]
108	Tylophoroside E	*Tylophora tanakae*	Roots	Methanol	[48]
109	Cynatratoside B	*Tylophora tanakae*	Roots	Methanol	[48]
	Secoiridoid				
110	Secamonoide A	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
	Xanthone glycosides				
111	Secamonoide B	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
112	Desacelylcentapicrin	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
113	1,3,6-Trihydroxyxanthone	*Tylophora*	Aerial	Ethanol	[19]

Table 2. Continued.

No.	Compound	Species	Parts used	Type of extract	Ref.
		secamonoides	parts		
114	Bellidifolin	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
115	3,8-Dimethoxy-1,7-dihydroxyxanthone	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
116	Demethylbellidifolin	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
117	Isobellidifolin	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
118	1-Hydroxy-3,5,8-trimethoxyxanthone	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
119	1,3,5,6-Tetrahydroxyxanthone	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
120	Gentisin	*Tylophora secamonoides*	Aerial parts	Ethanol	[19]
	Triterpenoid				
121	α-Amyrin acetate	*Tylophora hirsuta*	Aerial parts	Methanol	[56]
	Fatty alcohol				
122	Heptaeicosanol	*Tylophora hirsuta*	Aerial parts	Methanol	[56]
	Purine alkaloid				
123	Caffeine	*Tylophora mollissima*	Whole plant	Ethanol	[40]
	Polyphenols				
124	Chlorogenic acid	*Tylophora indica*	Leaves	Methanol	[26]
125	Chlorogenic acid methyl ester	*Tylophora indica*	Leaves	Methanol	[26]

N/A: not available

Pharmacology

Table 3 summarizes the scientific names, parts of the plant, active constituent/type of extract, model and animals used in study. Various pharmacological activities and the species showing these activities are represented in Figure 12.

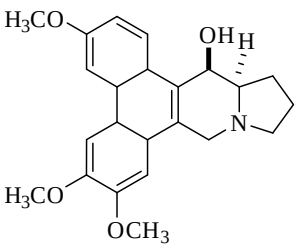
Antiasthmatic activity

On unilaterally adrenalectomized, dexamethasone treated, and stereotaxically hypophysectomized male albino rats, the effects of alcoholic extract, petroleum ether fraction, and aqueous fraction of the alcoholic extract of *Tylophora asthmatica* was studied by Udupa et al. They have calculated weight of adrenal gland, functional activities, and pituitary adrenal axis. Their study has shown that different fractions of the extract produced significant increase in weight of adrenal gland and functional activities. Increase in adrenal activity indicates increase in endogenous adrenocorticotropic hormone (ACTH). The dexamethasone suppression test showed reduction in the size of adrenal gland which was antagonized by the extract. It increased the weight of adrenal gland to normal. They say that stimulant action of the plant extract was due to direct action on adrenal gland but not by ACTH [57]. Haranath et al. examined the mode of action of *T. asthmatica* in bronchial asthama on dogs. When the aqueous extract was given intravenous (IV) in dogs, there was initial leukocytosis followed by leucopenia. The lymphyocytes and eosinophils were distinctly reduced. In isolated tissues, the aqueous extract showed a brief nonspecific antispasmodic effect. It produced a fall in blood pressure followed by a rise. The prolonged relief provided by *T. asthmatica* extract in bronchial asthma may be attributed to its effect on cell-mediated immunity [58]. *Tylophora asthmatica* extract was tested for various biological activities like interaction with lysozyme and bovine serum albumin, acute toxicity study, organ body weight ratio, various biochemical studies like concentration of serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT), haematological changes, biochemical studies, bio distribution studies, metabolism studies and anticancinogenic and antiasthmatic activity by Mulchandani. He isolated seven compounds from the ethanol extract. He did clinical study for antiasthmatic activity concluded that *T. asthmatica* alkaloids have antiasthmatic activity

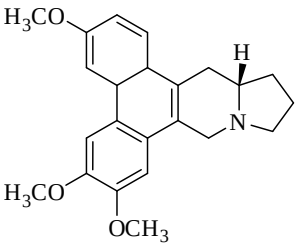
as they cure many symptoms related to asthma. Anticancinogenic activity was investigated by studying microsome mediated binding of ^{3}H-benzpyrene to DNA (deoxyribonucleic acid) at 100 microgram levels. It was found that ethanol extract did inhibit the adduct formation between ^{3}H-BP and DNA which is very characteristic of an anti carcinogenic substance [24].

Antitumor activity

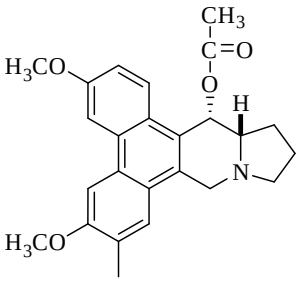
Jancy Stephen et al. studied in vitro cytotoxicity of petroleum ether extract of *Tylophora asthmatica* on tumour cell lines i.e Ehrlich Ascites Cells (EAC) and Dalton's Lymphoma Ascites (DLA) cells. In vivo study was carried out only on DLA cells. In vitro cytotoxicity study was done by Tryptan blue exclusion method, 1×10^{6} DLA and EAC cells were incubated at 37 °C for 3 h. Then, the percentage of dead cells was determined. For in vivo cytotoxicity study, 1×10^{6} cells were introduced intraperitoneally to develop ascites tumour in rats. After 24 h, five doses of drug were injected intraperitoneally on alternative days. The mortality of animals was noted and a percentage of increase in life span was calculated. Cytotoxicity determination by in vitro method showed good results. In vivo study showed significant reduction in tumour volume and increase in life span of tumour bearing animals [59]. Phytochemical exploration of *Tylophora atrofolliculata* by Cheng-Yu Chen et al. resulted in the isolation of a phenanthroindolizidine glycoside "6-o-beta-D-glycopyranosyl-Tylophorinidine" (93). Biological testing revealed that this glycoside showed stronger hypoxia inducible factor (HIF-1) inhibitory activity than digoxin. Structure activity relationship (SAR) analyses revealed that glycolyzingthis compound at c-6 reduced cytotoxicity against normal cells while increasing selectivity in tumour cell inhibition. As a result, it was regarded as a pioneer compound in the production and development of anticancer agents [51]. Xuechi Huang et al. isolated seven compounds from *T. atrofolliculata* [29]. They were tylophoridicine-C (7), tylophoridicine D (17), tylophoridicine-E (24), tylophoridicine-F (55), deoxy tylophorinidine (41), tylophorine (25), tylophorinidine (5). Cytotoxicity of these compounds was evaluated by in vitro technique on human ileocecal adenocarcinoma (HCT-8) cells and keratin-forming tumor cell line HeLa (KB) cells using Adriamycin as the positive control. All the compounds showed cytotoxicity. Compounds 24 & 55 exhibited more cytotoxic activity on cells compared to Adriamycin [29]. Cheng-Yu Chen et al. isolated 11 new alkaloids (56-66) from *T. atrofolliculata* as well as 11 known phenanthroindolizidine alkaloids (1, 2, 5, 7, 17, 39, 45, 67-69). The inhibitory effects of isolated alkaloids on HIF-1 activation were assessed using an HIF-1 mediated reporter gene assay in human breast cancer cell line (T47D) cells. Most of the alkaloids had extremely strong inhibitory effects. SAR analyses revealed the following requirements for high activity: nonpolarity at the indolizidine moiety, substitution types, and patterns on the phenanthrene and indolizidine moiety. This provided a new insight into the underlying anticancer mechanism [11]. Zhenjia Liu et al. isolated [+]-[13as]-deoxy Tylophorinine (23), a new phenanthroindolizidine alkaloid from the roots of *Tylophora artrofolliculata* and *Tylophora ovata.* In mice, the anticancer effect was studied in vivo. The interactions of this compound with double helical DNA sequences were thoroughly investigated using circular dichroic and fluroscence spectroscopy. The interactive mode between this compound and DNA was investigated using viscosity measurements. This compound appeared to interact in a sequence-specific manner with Adenine Thymine (AT) - repeated double-helical sequences, resulting in a potent anti-cancer effect and concentration-dependent interactions. Viscosity measurements confirmed that such interactions were intercalating. The compound 23 may intercalate with DNA in a sequence specific manner [32]. Cheng Yu Chen et al. have isolated four new compounds (8, 18-20) along with four known compounds (17, 21, 22&70) by column chromatography of n-butanol extracts of *T. atrofolliculata*. These alkaloids were evaluated for antitumour activity by DNA binding activity with human telomerase G-quadruplex DNA. These studies were done by G-Quadruplex binding assay with Electrospray Ionization Time-of-Flight (ESI-TOF) Mass Spectroscopy, Fluorescent intercalator displacement assay, Circular Dichorism (CD) spectroscopy. Compound 17 showed the strongest binding capacity. SAR analysis revealed that binding activity could be due to quaternary ammonium cation, molecular planarity, substitution of hydroxyl/methoxy group at C-2, methylation of hydroxyl group [31].



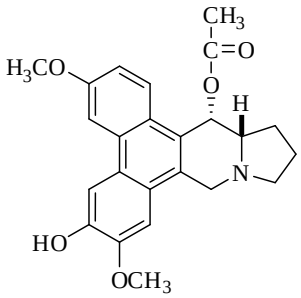
O-Methyl tylophorinidine (1)



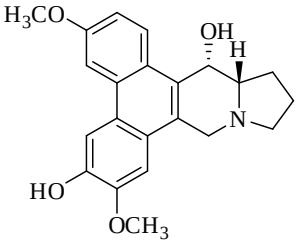
Desoxytylophorinine (2)



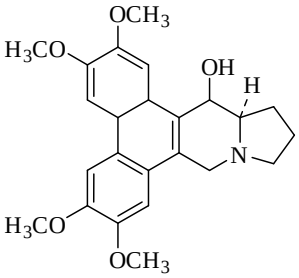
Acetyl-O-Methyl tylophorinidine (3)



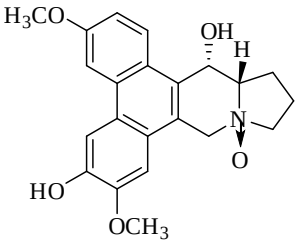
Tylophoridine diacetate (4)



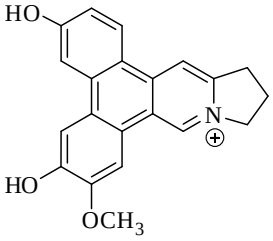
Tylophorinidine (5)



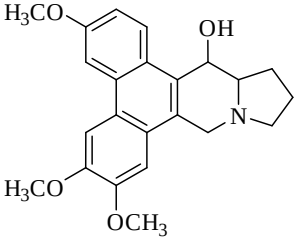
Tylophorinicine (6)



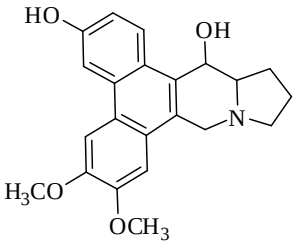
Tylophoridicine C (7)



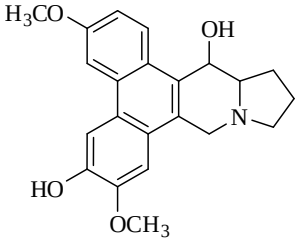
3-Demethyl anhydro dehydrotylophorinidine (8)



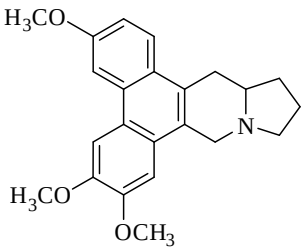
(13aR,14S)-3,6,7-Tirmethoxy-14-hydroxy phenanthroindolizidine (9)



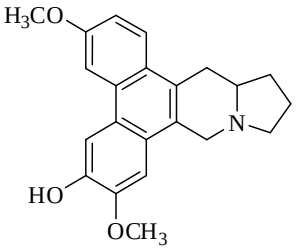
(13aS,14S)-3,14-Dihydroxy-6,7-dimethoxy phenanthroindolizidine (10)



(13aS,14S)-3,7-Dimethoxy-6,14-dihydroxy phenanthroindolizidine (11)

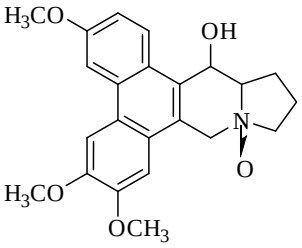


3,6,7-Trimethoxy-phenanthroindolizidine (12)

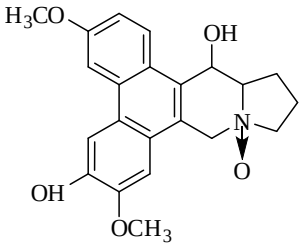


3,7-Dimethoxy-6-hydroxy phenanthroindolizidine (13)

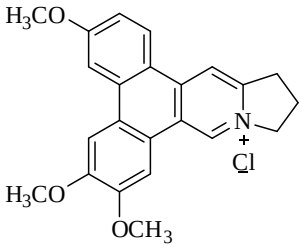
Figure 2. Chemical structures of phenanthroindolizidine alkaloids (1-90) isolated from the genus *Tylophora*



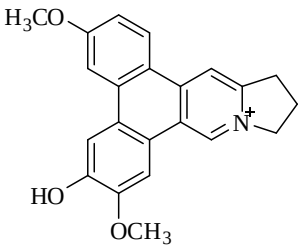
3,6,7-Trimethoxy-14-hydroxy-10-oxyphenanthroindolizidine (14)



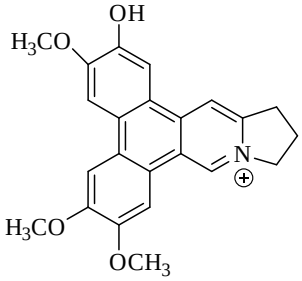
3,7-Dimethoxy-6,14-dihydroxy-10-oxyphenanthroindolizidine (15)



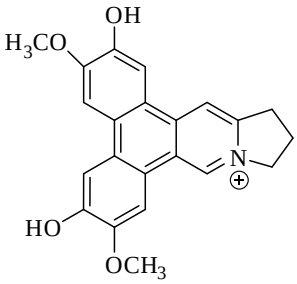
3,6,7-Trimethoxy-9(10),13a(14)-dehydrophenanthro indolizidinium Chloride (16)



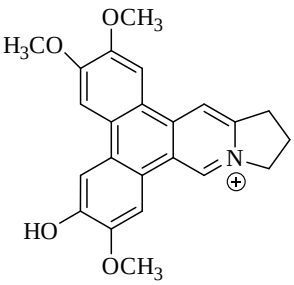
Tylophoridicine D (17)



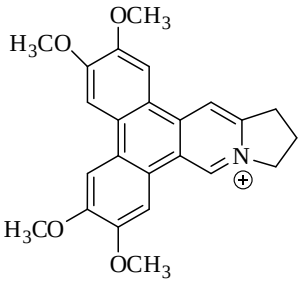
2-Demethyl dehydro tylophorine (18)



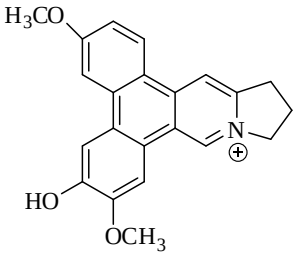
2-Hydroxyl dehydroanhydro tylophorinine (19)



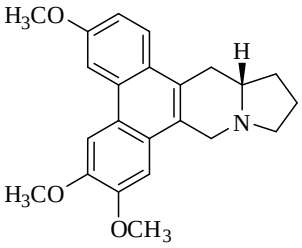
6-Demethyl dehydro tylophorine (20)



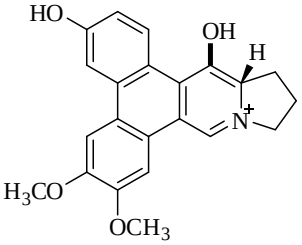
Dehydro tylophorine (21)



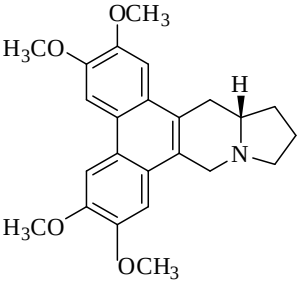
Anhyro dehydro tylophorinidine (22)



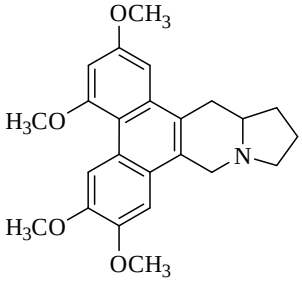
(+)-(13aS)-deoxytylophorinine (23)



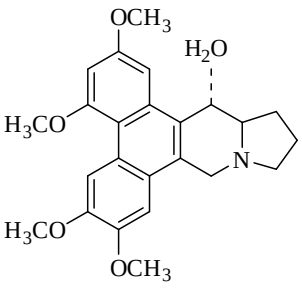
Tylophoridicine E (24)



Tylophorine (25)

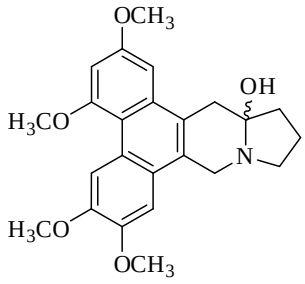


Desmethyl tylophorine (26)

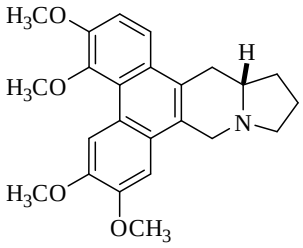


Desmethyl tylophorinine (27)

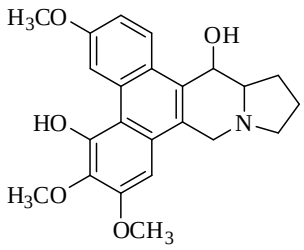
Figure 2. Continued.



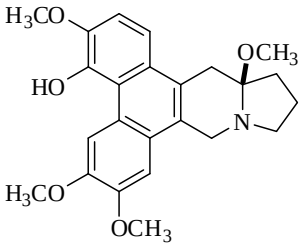
13a-Hydroxy tylophorine (28)



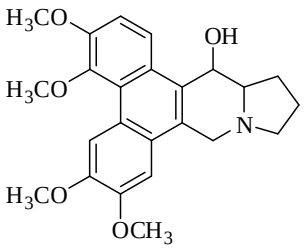
14-Desoxy-13-a-methyl hirsutidine (29)



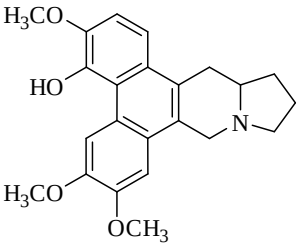
5-Hydroxy O-methyl tylophorinidine (30)



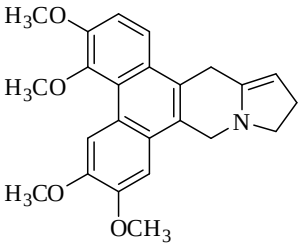
Tylohirsuticine (31)



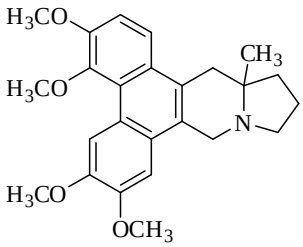
14-Hydroxy isotylocrebine (32)



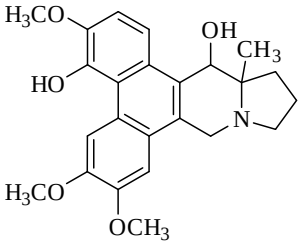
4-Desmethyl isotylocrebine (33)



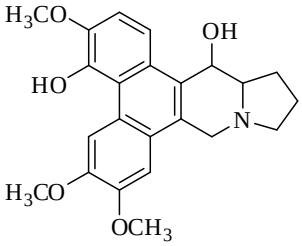
Tylohirsutinine (34)



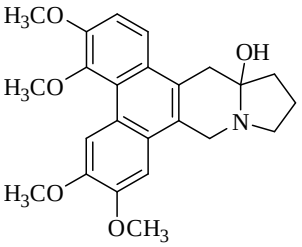
13a- Methyl hirsutine (35)



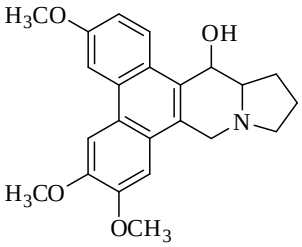
13a- Methyl tylohirsutinidine (36)



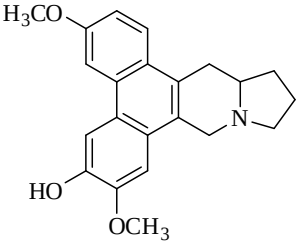
Tylohirsutinidine (37)



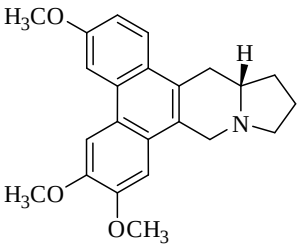
13a-Hydroxy Septicine (38)



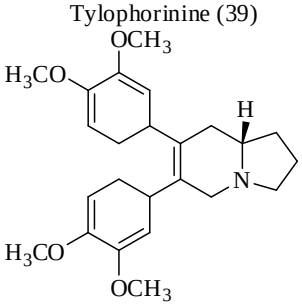
Tylophorinine (39)



Tylophoridicine A (40)

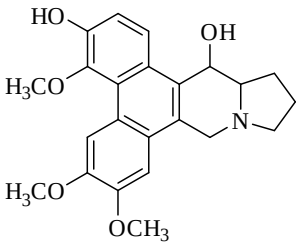


S-(+)-Deoxy tylophorinidine (41)

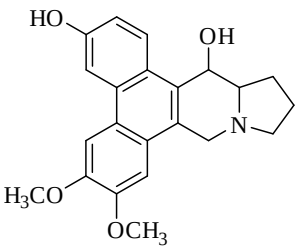


S-(+)- Septicine (42)

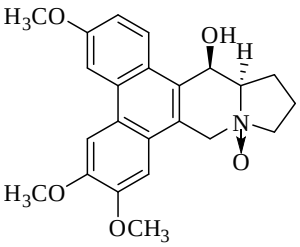
Figure 2. Continued.



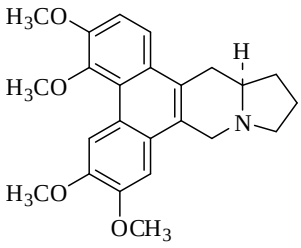
3,14α-Dihydroxy 4,6,7-trimethoxy Phenanthroindolizidine (43)



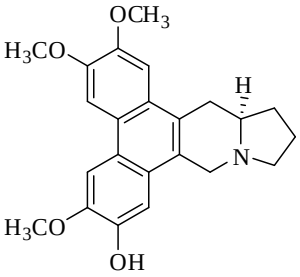
3,14α-Dihydroxy 6,7-dimethoxy Phenanthroindolizidine (44)



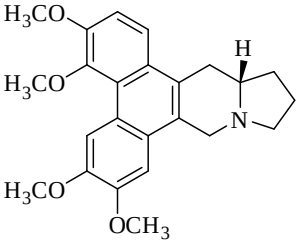
Tylophorinine N-oxide (45)



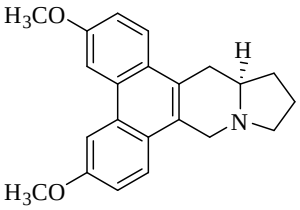
(+)-Isotylcrebine (46)



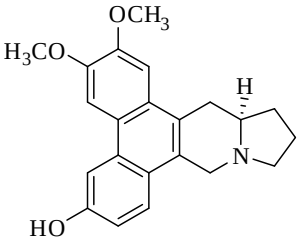
(-)-(R)-13α-7-O-Desmethyl tylophorine (47)



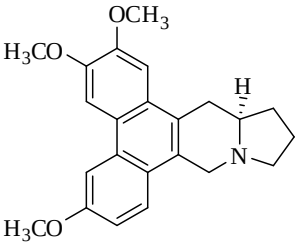
(+)-(S)-13 β Isotylocrebine (48)



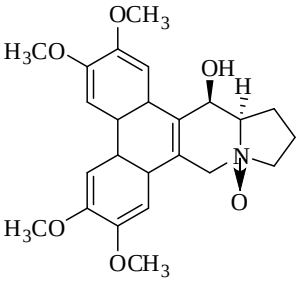
(-)-(R)-13α-Secoantofine (49)



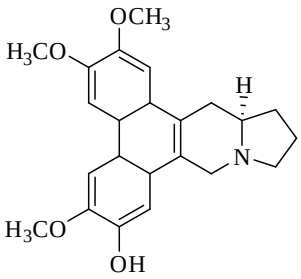
(-)-(R)-13α-6-O-Desmethyl secoantofine (50)



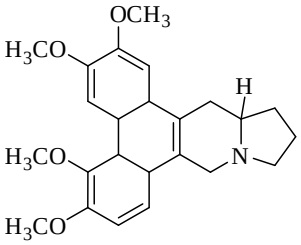
(-)-(R)-13α-Antofine (51)



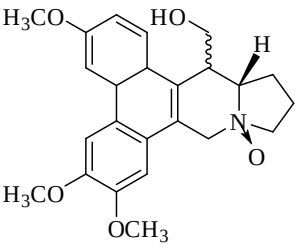
14β-Hydroxytylophorine N-oxide (52)



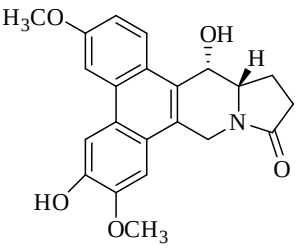
7-Demethyltylophorine (53)



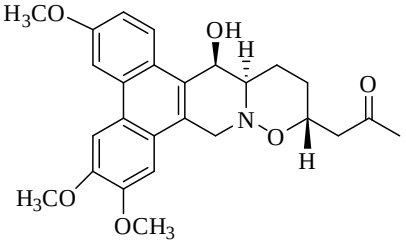
Tylocrebine (54)



Tylophoridicine F (55)

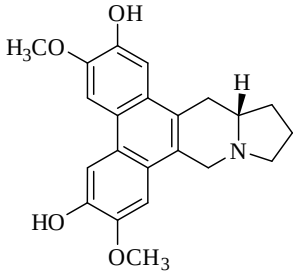


11-Ketotylophorinidine (56)

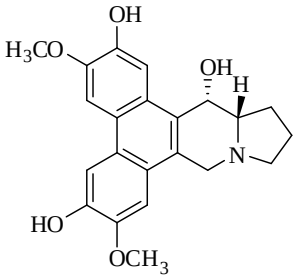


12S,14αR,15R-11-Oxa-12-(2-oxopropyl)-hydroxyl boehmeriasin A (57)

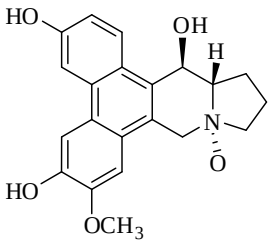
Figure 2. Continued.



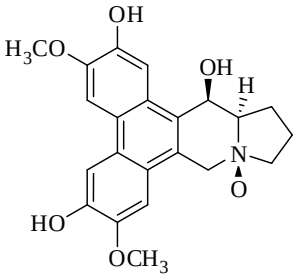
13αS-2,6-Didemethyl tylophorine (58)



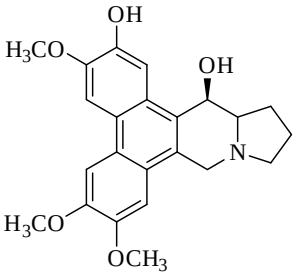
2-Hydroxyl Tylopohrinidine (59)



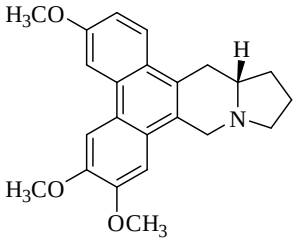
10R,14R-3-O-Demethyl tylophorinidine N-Oxide (60)



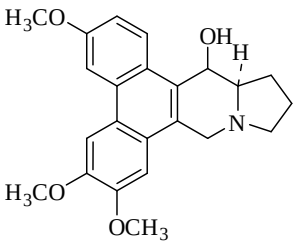
10S-2-Hydroxyl-6-demethyl tylophorinine N-oxide (61)



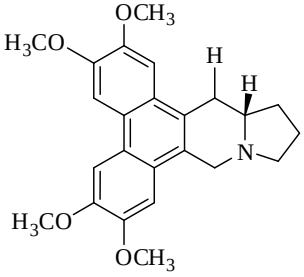
10R-2-Hydroxy tylophorinine N-oxide (62)



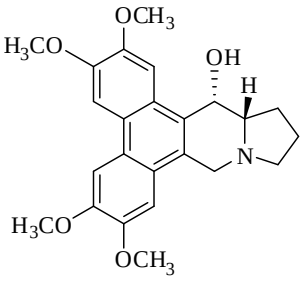
10R-Deoxy tylophorinine N-Oxide (63)



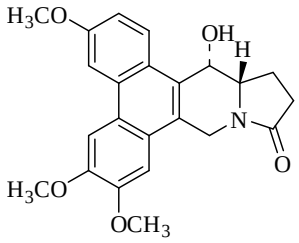
13αR-2-Hydroxy tylophorinine (64)



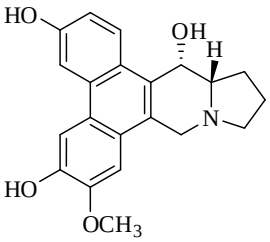
10R,13αS-Tylophorine N-oxide (65)



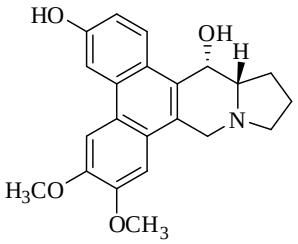
10R-2-Methyl O-methyl tylophorinidine N-oxide (66)



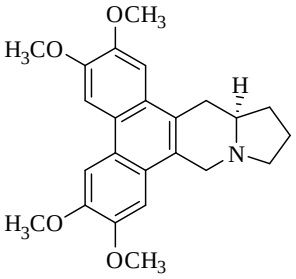
11-Keto-O-methyl tylophorinidine (67)



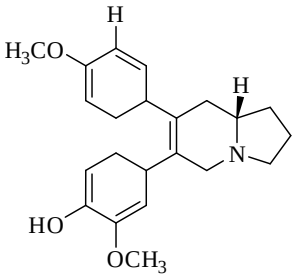
3-O-Demethyltylophorinidine (68)



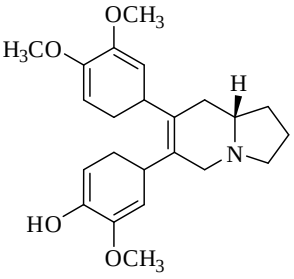
Trans-(+)-3,14α-dihydroxy-6,7-dimethoxyl-phenanthroindolizidine (69)



13αS-Tylophorine (70)

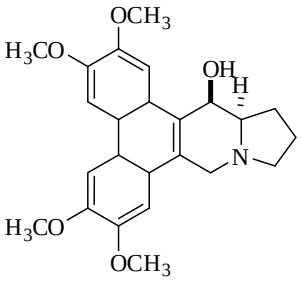


Tylophovatine A (71)

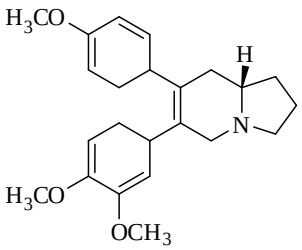


Tylophovatine B (72)

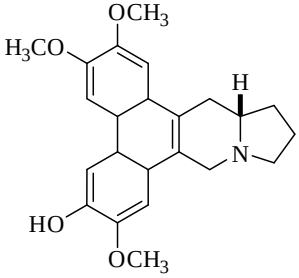
Figure 2. Continued.



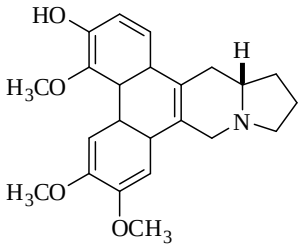
Tylophovatine C (73)



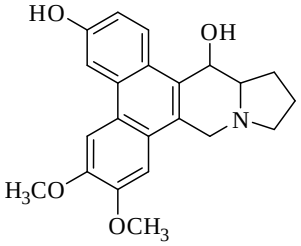
S-(+)-Hispidine (74)



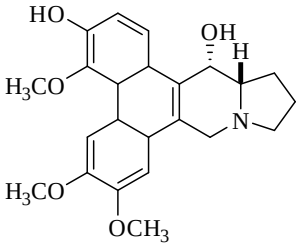
13α-(σ)-(+)-6-Δεθυλτψλοπηορινε (75)



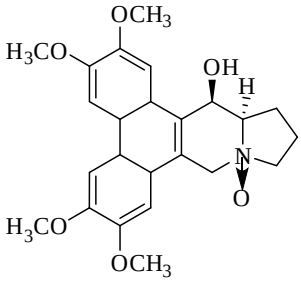
13α-(s)-(+)-3-Desmethyl isotylocrebine (76)



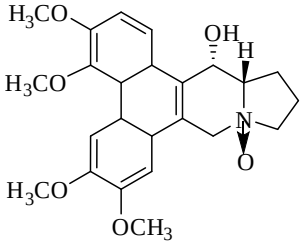
(13αS,14S)-3,14-Dihydroxy-6,7-dimethoxy phenanthroindolizidine (77)



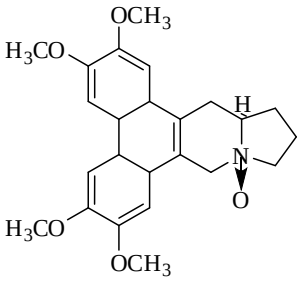
13α(s),14(s)-(+)-3,14-Dihydroxy-4,6,7trimethoxy-phenanthroindolizidine (78)



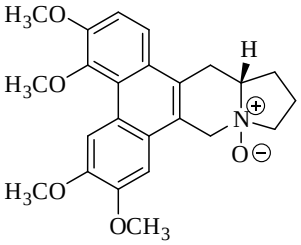
14β-Ηψδροξψτψλοπηορινε N-oxide (79)



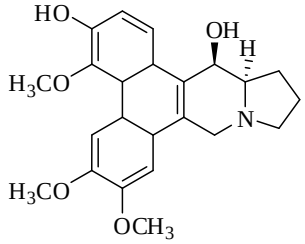
3-Demethyl-14α-hydroxy isotylocrebine N-oxide (80)



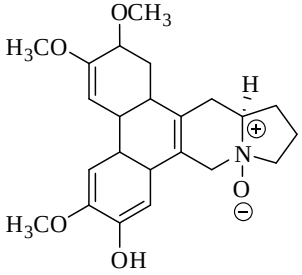
Tylophorine N-oxide (81)



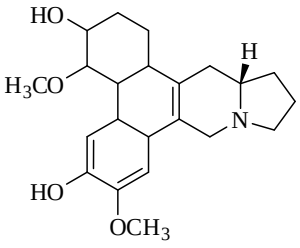
Isotylocrebine N-Oxide (82)



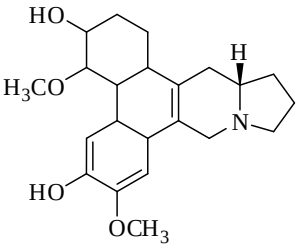
3-Demethyl-14β--hydroxy isotylocrebine (83)



(-)-7-Demethyl tylophorine N-oxide (84)

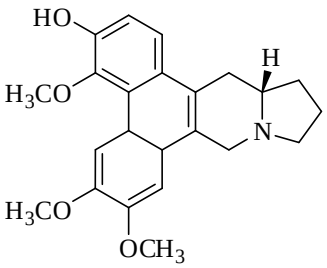


3,6-Didemethyl isotylocrebine (85)

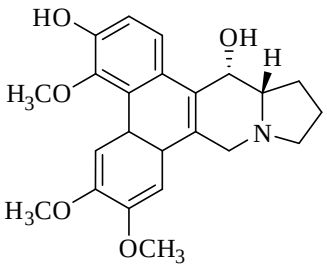


14α-Hydroxy-3,6-didemethyl isotylocrebine (86)

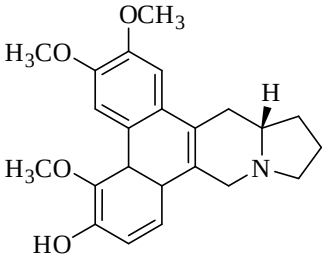
Figure 2. Continued.



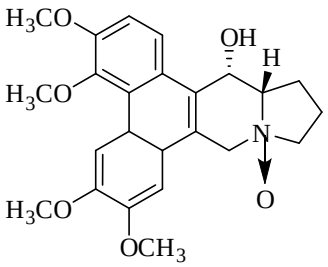
3-Demethylisotylocrebine (87)



3-Demethyl-14a-hydroxy isotylocrebine (88)

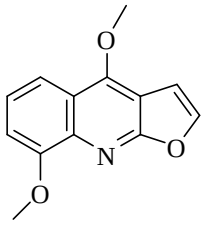


6-Demethyltylocrebine (89)

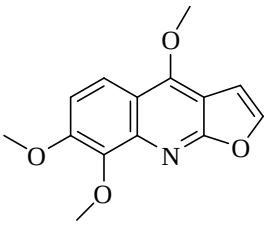


14α-Hydroxyisotylocrebine N-oxide (90)

Figure 2. Continued.

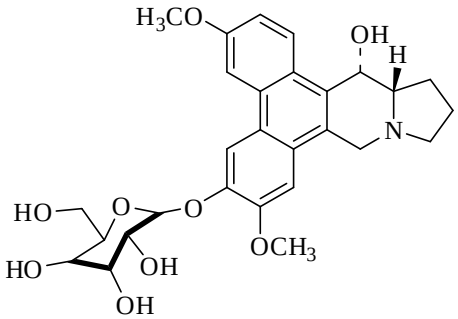


ϒ-Fagarine (91)



Skimmianine (92)

Figure 3. Chemical structures of furoquinoline alkaloids (91-92) isolated from the genus *Tylophora*



6-O-β-D-Glucopyranosyl-tylophorinidine (93)

Figure 4. Chemical structures of phenanthroindolizidine glycosides (93) isolated from the genus *Tylophora*

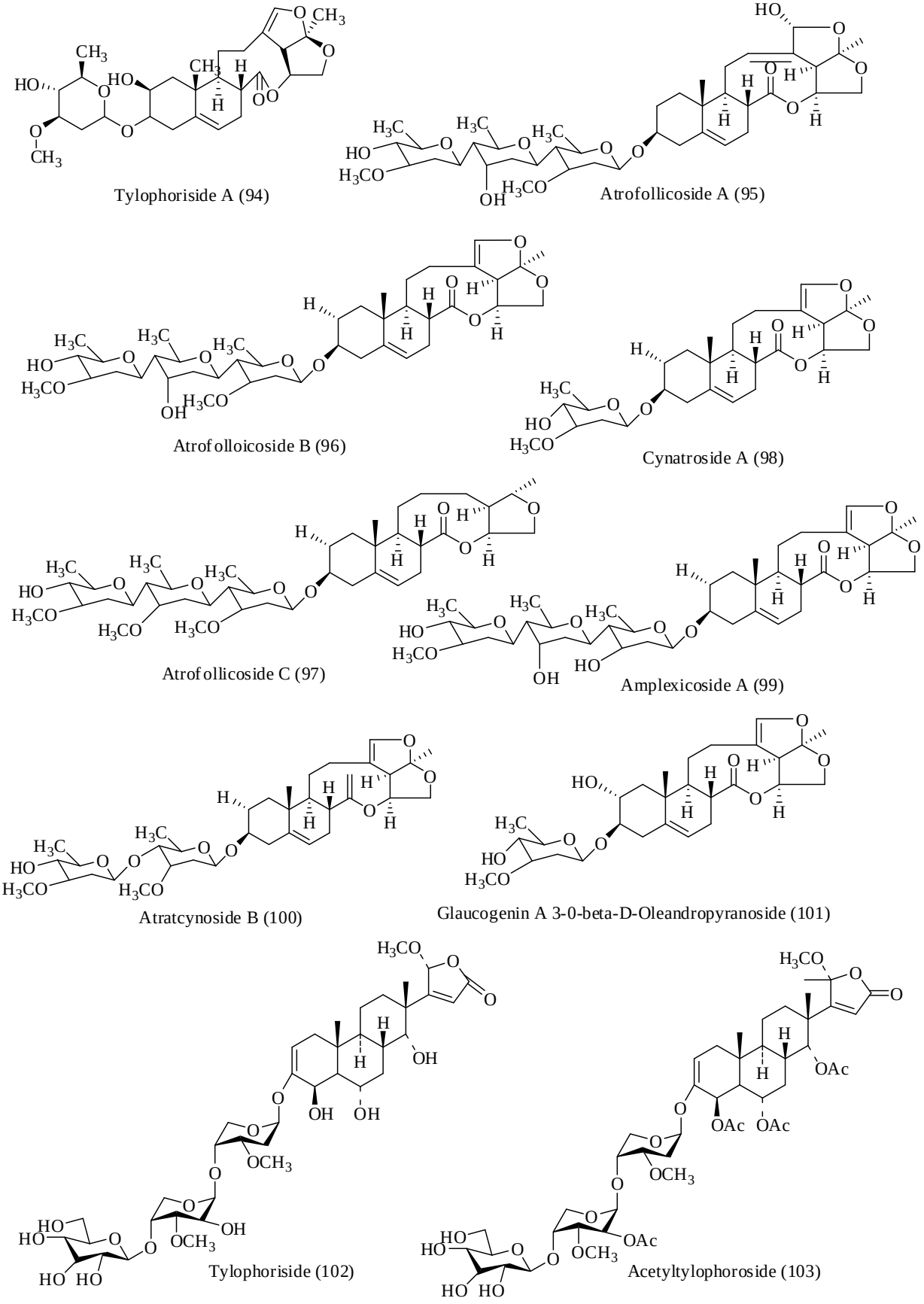


Figure 5. Chemical structures of steroidal glycosides (94-109) isolated from the genus *Tylophora*

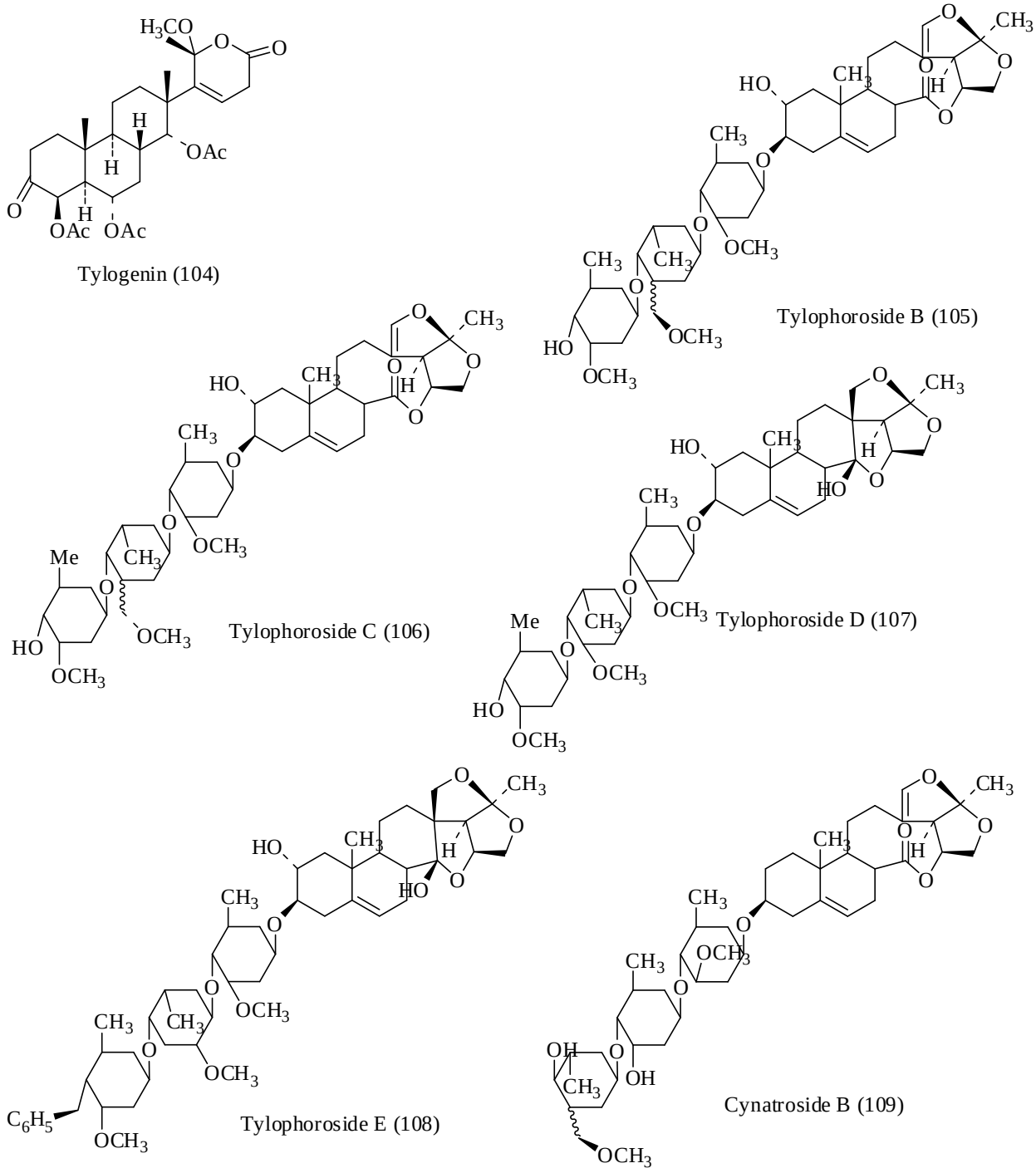
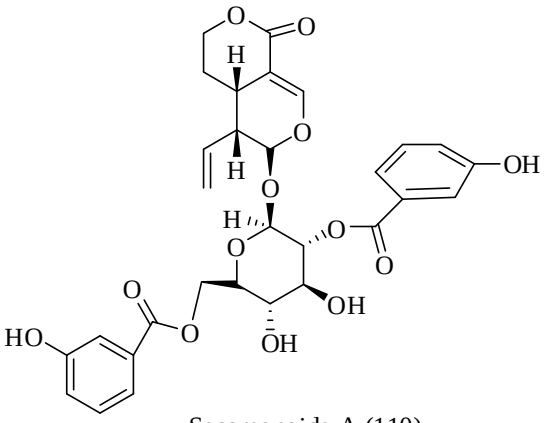
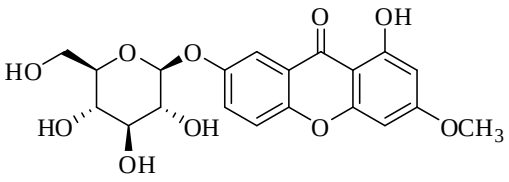


Figure 5. Continued.

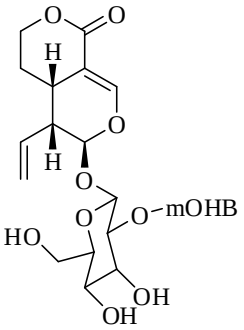


Secamonoide A (110)

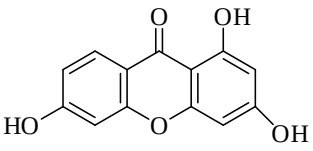
Figure 6. Chemical structures of Secoiridoid (110) isolated from the genus *Tylophora*



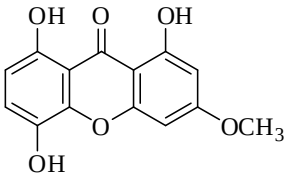
Secamonoide B (111)



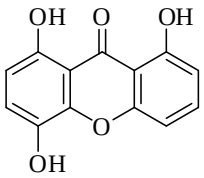
Desacetyl centapicrin (112)



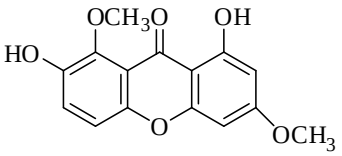
1,3,6-Trihydroxy xanthone (113)



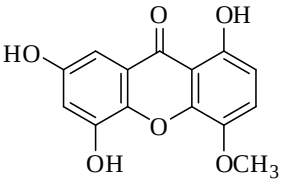
Bellidifolin (114)



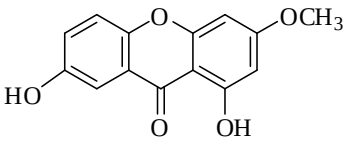
Demethyl Bellidifolin (116)



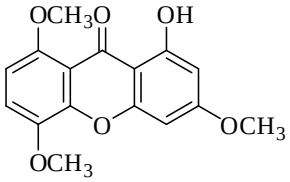
3,8-Dimethoxy 1,7-dihydroxy xanthone (115)



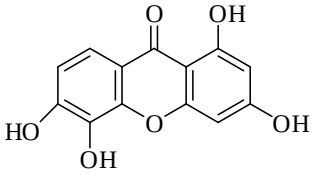
Isobellidifolin (117)



Gentisin (120)

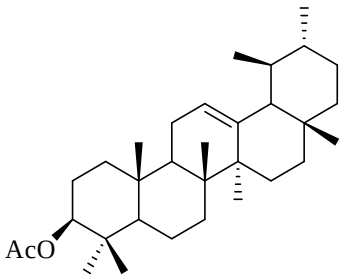


1-Hydroxy-3,5,8-trimethoxy xanthone (118)



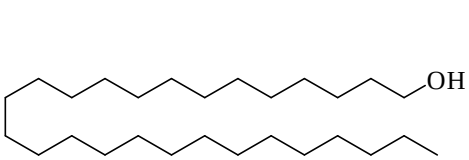
1,3,5,6-Tetrahydroxy xanthone (119)

Figure 7. Chemical structures of xanthones (111-120) isolated from the genus *Tylophora*

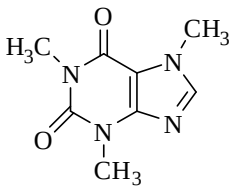


α-Amyrin acetate (121)

Figure 8. Chemical structures of triterpenoid (121) isolated from the genus *Tylophora*

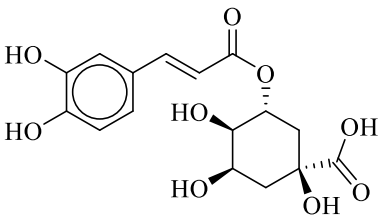


Heptaeicosanol (122)

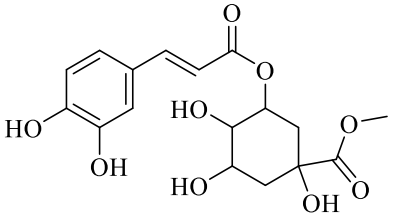


Caffeine (123)

Figure 9. Chemical structures of fatty alcohol (122) and purine alkaloid (123) isolated from the genus *Tylophora*



Chlorogenic acid (124)



Chlorogenic acid methly ester (125)

Figure 10. Chemical structures of polyphenols (124-125) isolated from the genus *Tylophora*

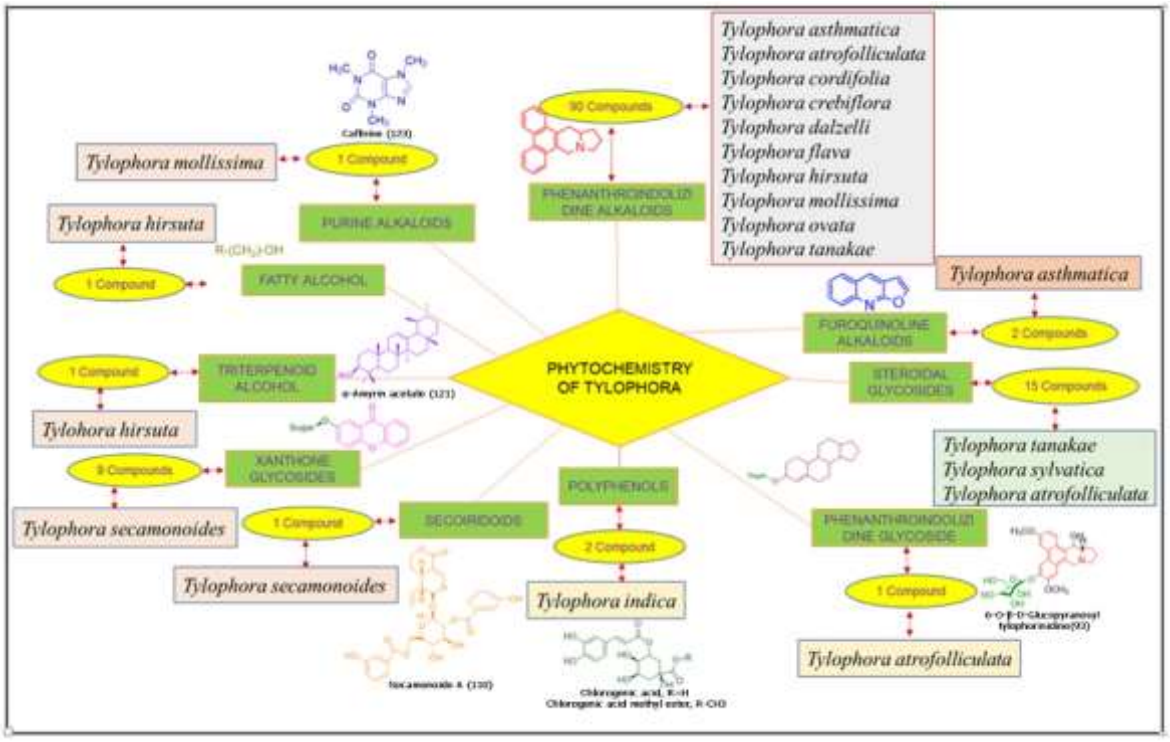


Figure 11. Phytoconstituents present in *Tylophora* genus

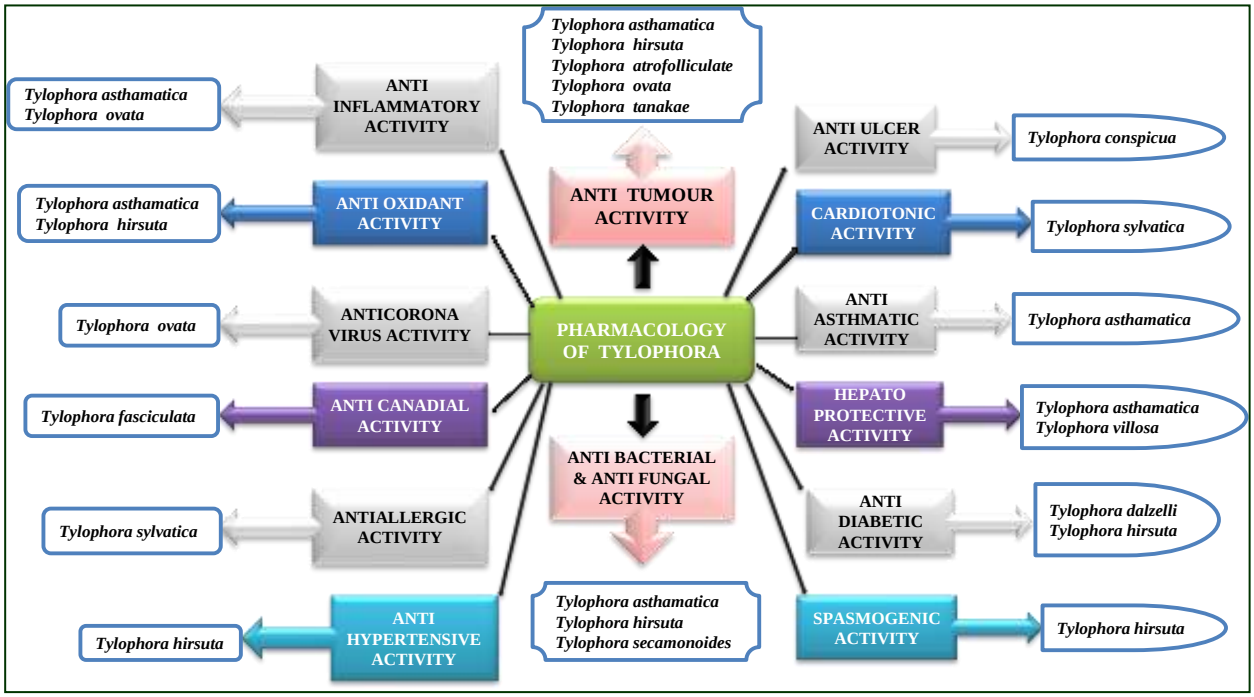


Figure 12. Pharmacological activities of *Tylophora* genus

Table 3. Pharmacological activities of the selected species of *Tylophora* genus

Activity	Species	Part used	Type of extract/compound number	Model & animal used	Ref.
Antiasthmatic activity	*Tylophora asthmatica*	Leaves	Alcohol extract, aqueous fraction, petroleum ether fraction	Normal unilaterally adrenalectomized dexamethasone treated and stereotaxicallyhyposectomized male albino rats	[57]
		Leaves	Aqueous extract	Intraperitoneally guinea pigs tested for chultz-Dale reaction, tissue sensitivity to histamine, adrenal gland weight and leucocyte count to study bronchial asthmatic activity. For anti spasmodic action, histamine and barium chloride induced anti spasmodic activity was studied on isolated tissues, rabbit duodenum or frog rectus.	[58]
		Leaves	Alcohol extract	Anti asthmatic activity, preclinical study on asthma patients. anti carcinogenic activity - microsome mediated binding of H-benzpyrene to DNA	[23]
Antitumour activity	*Tylophora asthmatica*	Entire plant	Petroleum ether	Trypan blue exclusion method on cell lines DLA and EAC on inbred strains of swiss albino mice	[59]
	Tylophora atrofolliculata	Whole plant	93	HIF-1-mediated reporter gene assay in T47D cells	[48]
		Roots	5,7,17,24,25,41 & 55	In vitro test on HCT-8 cells and KB cells	[26]
		Whole plant	1,2,5,7,17,39,45 & 56-70	HIF-1-mediated reporter gene assay in T47D cells	[11]
		Roots	23	Interaction studies with double helical DNA sequences in mice	[29]
		Whole plant	8,17-22 & 70	G-quadruplex DNA-binding activities with human telomeric DNA d[(TTAGGG)4TTA]	[28]
	Tylophora hirsuta	Aerial parts	121 & 122	Brine shrimp cytotoxicity on brine shrimp eggs	[57]
	Tylophora indica	Leaves	5,6,15,25,39,45	In vitro model on on MCF-7, HepG2, HCT-116 cell lines	[26]
		Leaves	Ethanol extract	In vivo model on mice with 7,12 dimethyl benza(a) anthracene (DMBA) as skin tumor inducer	[60]
	Tylophora ovata	Roots	1,5,39 & 40	In vitro studies on KB and A549 cells by MTT assay method	[38]
		Roots	41	Antitumour activity - *In vitro* on human cancer cell lines by MTT assay and by in vivo on Kunming (KM) mice with H22 mouse murine hepatoma xenografts Neurotoxicity – PC12 neurite outgrowth assay	[39]
			Alkaloidal extract	Proliferation was determined by MTT assay. and cell apoptosis was determined by cell morphology, Annexin V/PI, and Giemsa labeling method	[61]
		Stems and leaves	1,42 & 70-78	In vitro antiinflammatory activity, suppression of nitric oxide production in RAW264.7 cells stimulated by lipopolysaccharide and interferon-γ. In vivo anti inflammatory activity, carrageenan induced hind paw edema model in rats. Anti cancer activity, growth inhibition in HONE-1 NUGC-3, HepG2, SF-268, MCF-7, and NCI-H460 cancer cell lines	[17]
		Roots and aerial parts	1	In vitro model, TNBC (Triple Negative Breast Cancer)	[25]
	Tylophora tanakae	Aerial parts	45,52 & 79-83	Against MT-1 and MT-2 cells and HTLV-1 infected T cells	[41]

Table 3. Continued.

Activity	Species	Part used	Type of extract/compound number	Model & animal used	Ref.
	Tylophora tanakae	Leaves and caules	81 & 8 4-86	Cellular growth of PC-9, MCF-7, SW620, NUGC-3 and P388 cells were studied by MTT assay	[42]
		Leaves and stems	47-51 & 70	Drug sensitive KB-3-1 and a multidrug-resistant KB-V1 cancer cell lines.	[44]
Hepatoprotective activity	*Tylophora asthmatica*	Leaves	Methanol extract	Paracetamol induced liver toxicity in wistar strain rats	[62]
		Leaves	Methanol extract	Acetaminophen induced hepatotoxicity in rats	[63]
		Whole plant	Aqueous extract	Antitubercular drugs, INH and rifampicin were used to induce hepatotoxicity in albino rats	[64]
	Tylophora villosa	Leaves	Ethanol extract	Paracetamol induced model in mice	[22]
	Tylophora yunnanensis	N/A	N/A	HFD induced rat in vivo model	[23]
Toxicity study	*Tylophora asthmatica*	Leaves	Methanol extract	By measuring liver function parameters and relative organ weight on rats	[7]
Antibacterial and Antifungal activity	*Tylophora asthmatica*	Aerial parts	Methylene chloride and methanol extract	Disk diffusion method on *Escherichia coli, Staphylococcus aureus, Xanthomonas campestris, Bacillus subtilis, Candida albicans, Pythium ultimum, Rhizoctonia solani, Sclerotium rolfsii, Aspergillus fumigatus, Phytophthora parasitica*	[65]
	Tylophora hirsuta	Aerial parts	Methanol extract	Antileishmanial activity against *Leishmania major* Insecticidal activity against *L. minor L.* Anti bacterial activity against *Shigella flexenari* and *Bacillus substilis* Anti fungal activity against *Fusarium solani* General toxicity, brine shrimp lethality assay	[66]
	Tylophora indica	Leaves	Acetone, ethyl acetate and ethanol extracts	In vitro disk diffusion method on *Bacillus subtitlis, Staphylococcus aureus, E. coli, Pseudomonas aeruginosa, Salmonella typhi* and *Streptococcus pyogens*	[67]
		Leaf explants	Acetone and methanol extract	In vitro agar well diffusion model on *Staphylococcus aureus*, *Escherichia coli* and fungal strains *Aspergillius niger, Penicillium chrysogenum*	[68]
		Leaves	Methanol, ethanol, aqueous and ethyl acetate extracts	In vitro model on food pathogens, *E. coli, P. aeruginosa, S. aureus, B. subtilis* and *L. monocytogenes*	[69]
		N/A	N/A	In vitro model on *Enterococcus faecalis* biofilms	[70]
	Tylophora secamonoides	Aerial parts	110-120	MIC on hospital bacteria by invitro method on *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Bacillus pumilus, Bacillus cereus, Bacillus subtilis, Staphylococcus aureus, Cryptococcus neoformans, Candida albicans, Torlopsis glabrata, Candida sake*	[19]
Antiulcer activity	*Tylophora conspicua*	Leaf	Crude and alkaloidal fraction	Indomethacin induced gastric ulceration model and histamine induced gastric acid secretion in male albino rats	[71]
Spasmogenic activity	*Tylophora hirsuta*	Aerial parts	Methanol extract	Inhibition of K+ induced contractions for calcium channel blocking activity Treatement of extract on atropinised rabbit jejunum preparations	[72]
Antidiabetic activity	*Tylophora dalzelli*	Leaves and stem	Methanol extract	Streptozotocin induced hypoglycemic model on mice	[73]
Antidiabetic activity	*Tylophora hirsuta*	Leaves	Methanol and ethyl acetate extracts	Antidiabetic activity, alloxan induced antidiabetic activity in mice	[74]
		Aerial parts	Aqueous extract	Alloxan-induced diabetic model and OGTT was conducted on normal rats	[75]

Table 3. Continued.

Activity	Species	Part used	Type of extract/compound number	Model & animal used	Ref.
	Tylophora indica	Leaves	Ethanol extract	Streptozotocin (STZ)-induced diabetes in rats as in vivo model	[76]
Antihypertensive activity	*Tylophora hirsuta*	Aerial parts	Hydromethanol extract	Invasive model, spontaneous hypertensive Wistar rats	[16]
Cardiotonic activity	*Tylophora sylvatica*	Whole plant	102 & 103	Na^+/K^+ -ATPase inhibition	[51]
		N/A	103	Na^+/K^+ -ATPase inhibition	[52]
Antiallergic activity	*Tylophora sylvatica*	N/A	102-104	Inhibition of IgE induced basophil mediator release	[21]
Antioxidant activity	*Tylophora asthmatica*	Leaves	Methanol extract	DPPH Model	[77]
	Tylophora hirsuta	Leaves	Methanol and ethyl acetate extracts	Antioxidant activity, DPPH and H_2O_2 scavenging activity.	[74]
		Aerial parts	Aqueous extract	Anti oxidant activity, DPPH assay	[75]
	Tylophora pauciflora	Whole plant	Ethanol extract	Enzymatic and non enzymatic antioxidants by in vitro models	[78]
Anticanadial activity	*Tylophora fasciculata*	Leaves	Petroleum ether, ethyl acetate and ethanol extracts	Zone of inhibition and MIC against *Candida albicans*	[15]
Antiinflammatory activity	*Tylophora asthmatica*	Leaves	Petroleum ether, chloroform and methanol extracts	Carrageenan induced and formalin induced paw edema model on wistar rats	[79]
	Tylophora indica	Leaf explants	Water and hydro alcohol extract	In vitro model, BV-2 microglia cells activated with lipopolysaccharide	[80]
	Tylophora ovata	Leaves and stems	42	Lipopolysaccharide-stimulated (LPS) murine macrophages and RAW2647 cells	[40]
Anti corona virus activity	*Tylophora ovata*	N/A	Tylophorine compounds	Immunofluorescent assay of TGEV N and S protein expression and real time quantitative PCR analysis of viral yields	[81]
Anti helminthic activity	*Tylophora indica*	Leaves	Methanol extract	In vitro activity on the test organism was *Haemonchus contortus*	[82]

N/A: not available

Preliminary phytochemical screening of methanolic extract of *Tylophora hirsuta* tested positive for saponins, tannins, flavonoids, terpenoids, glycosides, phenols, sterols, carbohydrates. Alpha-amyrin acetate (121) and Heptaeicosanol (122) were isolated from *T. hirsuta* through column chromatography by Niaz Ali [56]. Structures of the compounds were confirmed by ^{1}H-NMR and ^{13}C-NMR studies. Methanol extract tested positive for brine shrimp cytotoxicity with LC_{50} of 492.33± 8.08 mg/mL. Major compound 120 showed relaxing effect/spasmolytic activity on rabbit jejunum preparations and KCl induced contractions [57]. Ehab M. Mostafa et al. evaluated antiproliferative effect of six phenanthroindolizidine alkaloids, 5, 6, 15, 25, 39, 45 obtained from methanol extract of leaves of *T. indica* through different biomechanistic pathways. Activity was tested on MCF-7, HepG-2, HCT-116 cell lines. Along with six alkaloids, septicine (42), chlorogenic acid (124) and chlorogenic acid methyl ester (125) were isolated from *T. indica* using vacuum liquid chromatography and preparative HPLC. Structures were determined by ^{1}H-NMR, ^{13}C-NMR and mass spectrometry. Geometries were determined using chiroptical techniques. Among all compounds five was proved to be potent cytotoxic agent. Bioactivities were validated by in vitro kinase receptors inhibition assay. Molecular docking studies on two receptors Aurora- A & B were determined. These studies confirmed bioactivity with receptor ligand interaction [26]. Ayesha Rabiya et al. evaluated anti neoplastic activity of *T. indica* using ethanolic leaves extract. In vivo study was done with 7, 12 dimethyl benza (a) anthracene (DMBA) as skin tumor inducer in mice. Five groups of six Swiss Albino mice in each group were used. First group was treated with carcinogen, second with carcinogen & standard drug cyclophosphamide, third, fourth, and fifth groups were treated with

100 mg/kg, 200mg/kg and 400mg/kg ethanolic extract of *T. indica*. Results showed a significant suppression in tumor incidence, yield, burden which was compared to 7, 12-dimethylbenz (a) anthracene croton oil-treated control group [60]. Four phenanthroindolizidine alkaloidal compounds, tylophoridicine A (40), tylophorinine (39), O-methyl tylophorinidine (1) and tylophorinidine (5) were isolated from roots of *T. ovata* by ZHEN Yue-Ying et al. Their structures were elucidated by NMR, NOESY, H-NMR, CD spectra, mass spectroscopy (MS) analysis as well as chemical methods. Antitumour activity was checked by MTT method (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) using KB and A549 cells. Compounds 1, 5 & 40 showed potent antitumour activities [41]. S-(+)-Deoxy tylophorinide (41) was isolated from roots of *T.ovata* and *T. atrofolliculata*. Zhen Jia L et al. have tested this alkaloid for neurotoxicity and anticancer activity by in vitro and in vivo methods. In vitro anticancer activity of the compound was evaluated by MTT assay using human cancer cell lines (gastric BGC823, human liver cancer Be17402, colon cancer HCT-8, ovarian cancer A2780 etc). Dose dependant growth inhibition was observed. IC_{50} was found to be 10^{-7} mol/L. In vivo anticancer activity was tested on Kunming mice with H22 murine hepatomaxeno grafts. Neurotoxicity was evaluated in vitro by using PC12 (rat pheochromocytoma cell line). Neurotoxicity was compared with vinblastine and vincristine. For compound 41, neurotoxicity resulted in less serious effects compared to vinblastine. The compound 41 showed high anticancer activity both in vitro and in vivo. It interacted with DNA as well as RNA. Interaction between the compound and RNA was concentration dependent which was determined by CD and fluorescence emission spectra [42]. Alkaloidal extract of *T. ovata* were tested in vitro for human cervical cancer cell line (HeLa cells) proliferation and apoptosis by the Wang Yuan-xing et al. At various time intervals, different concentrations of alkaloids were used to treat HeLa cells in vitro. Cell proliferation was determined using the MTT assay, whereas cell apoptosis was determined using the cell morphology method using Annexin V/PI and Giemsa labelling. The extract was found to inhibit the proliferation and activity of Hela cells, with the inhibition effects dependent on reaction time and alkaloid dose. The expression of Annexin V+/PI- in Hela cells increased, and the characteristics of apoptosis varied according to the results of Giemsa staining. These alkaloids could inhibit HeLa cells by inducing apoptosis [61]. Yue-Zhi Lee et al. isolated 11 alkaloids (1, 42 & 70-78) from *T. ovata* and all the alkaloids were tested for anti-inflammatory activity in vitro and in vivo, as well as anticancer activity in vitro on cancer cell lines Nagoya University - Gastric Cancer - 3 (NUGC3), epithelial tumor cell line (HONE -1), Hepatoblastoma cell line (HepG2), human glioblastoma cell line (SP - 268), Michigan Cancer Foundation (MCF - 7), and human non-small cell lung carcinoma cell line (NCT - H460). These 11 alkaloids demonstrated in vitro anti-inflammatory activity with IC_{50} values ranging from 84 nM to 20.6 µM through their suppression of nitric oxide production in RAW264.7 (monocyte/macrophage cell line) cells stimulated by lipopolysaccharide and interferon. Furthermore, these substances inhibited growth in cancer cell lines with GI_{50} (50% cell growth inhibition) values ranging from 4 nM to 24.2 µM. Compounds 70 & 73 were discovered to have strong anti-inflammatory activity, which was measured in rats using the carrageen induced hind paw edema test. Compounds 77 & 78 showed antiinflammatory activity based anticancer activity [17]. Six naturally occurring phenanthroindolizidine alkaloids from the plant *Tylophora ovata* were examined by Remiche et al. for their potential therapeutic effects on triple negative breast cancer (TNBC), a more severe type of breast cancer. They extracted six chemicals from a methanol extract of the plant's roots and aerial parts, including compound 1 and its derivatives 2, 5, 17, 22, and 24. Comparing blockage of NFKB and cell survival with synthetic compound 1, they conducted their research. SAR tests were studied using derivatives of compound 1. Both natural and synthetic compound 1 showed good results. Compound 1 performed well when compared with the gold standard in medicine, paclitaxel, by reducing spheroid development by 40% at 100 nM. They determined that Phenanthroindolizidine alkaloids were effective in fighting inflammatory and hypoxic cancer with a variety of target sites, including TNBC [25]. One new (52) and five known alkaloids (45, 80-83) were isolated from methanolic extract of

aerial parts of *Tylophora tanakae* by Nakano el al. These compounds were tested for antiproliferative activity against T-cell line derived from adult T-cell leukemia (MT-1) and T-cell line derived from normal human cord leukocytes (MT-2) cells. Some of the alkaloids had EC_{50} values in the low nanomolar range, which was comparable to the clinically used anticancer drug doxorubicin. Structure–activity relationships were examined, and it was revealed that a 14b-hydroxy moiety was required for activity against human T-lymphotropic virus type 1 infected T cells (HTLV-1). In contrast, the presence of a 2-methoxy moiety, a 7-methoxy moiety, or an N-oxide moiety, appeared to reduce the potency of antiproliferative activity against HTLV-1-infected T cells [44]. Methanol extract of fresh leaves of *T. tanakae* was subjected to column chromatography. Along with 10 known compounds, two new alkaloids (85, 86) and N-oxides (81, 84) of two known alkaloids were isolated from chloroform soluble fraction by Fumiko et al. These four compounds were tested for *in vitro* cytotoxic activity by MTT assay. All the compounds showed cytotoxic activity in nanomolar range [45]. One known phenanthroindolizidine alkaloid **(**51) and two new alkaloids (49, 50) were isolated from *Tylophora. tanakae* by DanStaerk et al. The cytotoxic activity of the isolated alkaloids, as well as three other alkaloids (47, 48 & 70**)** isolated from *T. tanakae* previously, were tested in vitro using the drug sensitive KB-3-1 and multidrug-resistant KB-V1 cancer cell lines. The structure-activity relationships of this alkaloid series were discussed. Some of the alkaloids showed IC_{50} values in the low nanomolar range, which was comparable to the activity of clinically used cytotoxic drugs [47].

Hepatoprotective activity

Malathi et al. obtained the methanolic extract of leaves of *Tylophora asthmatica* and studied the hepatoprotective and antioxidant activity on paracetmol induced hepatotoxicity in Wistar rats. The extract produced significant hepatoprotective effects as evidenced by decreased serum enzyme activities, alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) and serum bilirubin compared with the control group. The extract also produced significant antioxidant activity by increasing superoxide dismutases (SOD), catalase (CAT), glutathione peroxidase (GPx) and decreasing lactoperoxidase (LPO) levels. The obtained results indicated that the extract may have hepatoprotective potential; mostly due to its antioxidant properties on hepatocytes [62]. Anti lipidperoxidation effect of methanolic extract of leaves from *T. asthmatica* were studied by Malathi et al. on acetaminophen induced hepatotoxicity in rats. A few parameters like levels of lipid peroxide, iron, ferritin, total cholesterol, total lipid, and phospholipids were measured in both experiment and control group of rats. Methanolic extract showed significant results when compared with control rats [63]. Ajay et al. studied hepatoprotective activity of *T. asthmatica* by inducing toxicity with antitubercular drugs (rifampicin and isoniazid 50 mg/kg) in albino rats. Administration of antitubercular drugs along with co-administration of *T. asthmatica* was done for 14 days. After this time, they observed levels of serum ALT, AST, and bilirubin. *Tylophora asthmatica* treated group had no remarkable rise in values of serum ALT, AST, bilirubin (total and direct) and there were no notable histopathological changes in this group, indicating hepatoprotective effect of *Tylophora asthmatica* [64]. Aceng Ruyani et al. studied the therapeutic effect of ethanolic extract of *Tylophora villosa* leaves on paracetamol induced hepatotoxicity in mice. Paracetamol induced hepatotoxicity (PCIH) was induced by gavage administration of 250 mg/kg body weight paracetomol daily for seven days. After seven days, the ethanol extract was administered in various doses for seven to fourteen days. On days 15, 22, and 30, blood glucose, mortality, liver condition (colour, weight and volume), serum glutamic pyruvic transaminase (SGPT) and serum glutamic-oxaloacetic transaminase (SGOT) levels, and malondialdehyde (MDA) levels were measured. According to the findings, phytoconstituents of ethanolic extract had a therapeutic effect on Mus musculus. PCIH by inhibiting radicals and lipid peroxidation [22]. The goal of Yu-ping Lin et al. was to ascertain how *Tylophora yunnanensis* affected gut microbiota and its metabolites in non-alcoholic steatohepatitis (NASH) rats by preventing Nod-like receptor protein3 (NLRP3) activation. For this investigation, a rat model induced by high fat diet was used. Body weight, lipid levels, histology, and inflammatory factor levels in the rat models were measured to evaluate the therapeutic benefits of *Tylophora yunnanensis*

(TYS) on NASH animals. Using enzyme-linked immunosorbent assay (ELISA), which measured the levels of NLRP3-related components, and real-time quantitative reverse transcription polymerase chain reaction (RT-qPCR), which measured the regulatory effects of *T. yunnanensis* on NLRP3 in the NASH rats, the impacts of *T. yunnanensis* were examined. Using 16S rRNA gene sequencing technologies, changes in the gut microbiota of NASH rats were observed. For the untargeted study of metabolites in the cecum contents, ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) was employed. The findings suggested that by lowering the values of the aforementioned factors, *T. yunnanensis* could enhance NASH. They concluded that during NASH modelling, *T. yunnanensis* could considerably suppress the activation of NLRP3, control the makeup of the gut microbiota, and manage the dysregulation of metabolites [23].

Preliminary toxicity study

Malathi et al. investigated the toxicological and biochemical effects of methanolic extract of *T. asthmatica* leaves on rats. The LD_{50} value was calculated to be 223.6 mg/kg body weight. In an acute toxicity study, male rats were given a single dose (50, 100, 200, 500 and 1000 mg/kg body weight) of the extract. Lower doses produced no poisonous symptoms or death in animals, whereas 500 mg/kg body weight killed two animals and 1000 mg/kg killed four animals within 72 h. The degree of protection (assessment of liver function) was also determined by measuring biochemical indices like serum aspartate aminotransferase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) using the King's method, total protein, albumin, globulin, and bilirubin. Subchronic administration for 15 days resulted in a significant increase in serum ALT and ALP, as well as a decrease in serum total protein, albumin, and globulin [7].

Antibacterial and antifungal activity

Methylene chloride and Methanol extracts of dried aerial parts of 20 Indonesian plants with ethnomedical uses were assessed for in vitro antibacterial and antifungal properties by Disk diffusion method by Goun et al. Activity was tested on *Escherichia coli, Staphylococcus aureus, Xanthomonas campestris, Bacillus subtilis, Candida albicans, Pythium ultimum, Rhizoctonia solani, Sclerotium rofsii, aspergillus fumigatus* and *Phytophthora parasitica.* Extracts of *Tylophora asthmatica* demonstrated high activity in this bioassay system [65]. Methanolic extract of *Tylophora hirsuta* was screened for various biological activities like anti leishmanial activity by culturing, insecticidal activity examined by direct contact application using filter paper, phytotoxic activity, antibacterial activity by inoculation method, antifungal activity by agar tube dilution method, brine shrimp cytotoxicity by Bashir et al. Results showed that the plant possessed potent antileishmanial activity, non significant antibacterial action against *Shigella flexenaria* and *Bacillus subtilis* and moderate antifungal activity against *Fusarium solani* [66]. Maheshwari et al. investigated antibacterial effect & phytochemical analysis of acetone, ethyl acetate and ethanol extracts of leaves of *T. indica.* The study revealed presence of alkaloids, flavonoids, saponins, phenols, steroids, tannins, terpenoids, carbohydrates, glycosides, and amino acids. Antimicrobial activity was tested for all three extracts on six pathogens. The extracts showed more susceptibility to *Bacillus subtitlis* than other five organisms, *Staphylococcus aureus, E. coli, Pseudomonas aeruginosa, Salmonella typhi* and *Streptococcus pyogens* [67]. Manju et al. established an in vitro method for production of de novo adventious shoot formation from leaf explant by plant tissue culture technique. Acetone and methanol extracts were prepared from callus and by conventional extraction from leaves. Antimicrobial and antioxidant activity of both extracts were tested. Methanol extract showed suitable results when compared with acetone extract produced from callus [68]. The antibacterial efficacy of *T. indica* leaf extract against specific food pathogens was reported by Charu Khanna et al. to create safe natural food formulations in conjunction with antimicrobial medications. The antibacterial activity of various extracts from the leaves of *T. indica*, including methanol, ethanol, aqueous, and ethyl acetate extracts, was investigated against several food pathogens, including *E. coli, P. aeruginosa, S. aureus, B. subtilis* and *L. monocytogenes.* Methanol showed to be the most efficient antibacterial extract, followed by aqueous, ethyl acetate, and ethanol extract in terms of effectiveness [69]. *Tylophora indica* was investigated for their antibacterial activity on

Enterococcus faecalis biofilms produced on the tooth substrate by Shan Sainudeen et al. Sodium hypochlorite was used as positive control and DMSO as negative control. Human teeth were extracted, biomechanically prepared, and exposed to *E. faecalis* to create a biofilm on the root canal surface. They were kept for three weeks and given 15 minutes of treatment with the test and control solutions. Both a quantitative and qualitative analysis of the results was performed. *Tylophora indica* showed statistically significant antibacterial activity when compared with 5% sodium hypochlorite against 3 week biofilm [70]. Sheng Y et al. isolated new secoiridoid, secamonoide A (110), and a new xanthone glycoside, secamonoide B (111) from the aerial parts of *Tylophora secamonoides*, along with nine known compounds (112-120). Spectroscopic methods were used to deduce their structures. Both the new compounds showed weak antimicrobial activities (minimum inhibitory concentration (MIC) values greater than 100 mg/mL) against some hospital bacteria in vitro, according to the antimicrobial bioassay [19].

Antiulcer activity

Raji et al. investigated the effect of crude (TC) and an alkaloid fraction (TA) of *Tylophora conspicua* leaf extracts on indomethacin induced gastric ulceration and gastric acid secretion in male albino rats. Both extracts inhibited gastric ulceration in a dose-dependent manner. At a dose of 40 mg/kg, crude (TC) and alkaloidal fraction (TA) were more effective than propranolol in inhibiting gastric ulceration (TA being more potent). The extracts' highest dose (80 mg/kg) completely prevented gastric ulceration. Intravenous administration of the TC and TA reduced acid output in a dose-dependent manner. Histamine (1 mg/kg) induced gastric acid secretion was significantly reduced by 80 mg/kg of TC and TA. The findings suggested that *Tylophora conspicua*'s antiulcer activity may be mediated by gastric acid inhibition [71].

Spasmogenic activity

Cholinomimetic and Ca^{++} channel blocking activity of methanol extract of *Tylophora hirsuta* at different concentration was studied by Bashir Ahmad et al. using rabbit's jejunum. Maximum spasmogenic response was shown at a dose of 1 mg/mL. Calcium channel blocking activity was confirmed by Ca^{++} dose response curve. The results were comparable with that of verapamil, standard calcium channel blocker [72].

Antidiabetic activity

Antidiabetic potential of *Tylophora dalzelli* was studied by Shahla Najafi et al. in diabetic Balb/c mice by inducing diabetes with streptozotocin. Methanol extracts of leaves and stems were prepared and used for sthe tudy. The results were compared with gymnemic acid, which is the indigenous medicine used by tribes of Western Ghats for treating diabetes. The results were comparable with standard in terms of lowering glucose level [73]. Muhammad Furqan Akhtar et al. investigated the in vivo antidiabetic potential of methanol and ethyl acetate leaf extracts of *Tylophora hirsuta*. Antidiabetic power was assessed in alloxan-induced diabetic mice by determining serum amylase, lipid profile, body weight, oral glucose tolerance, glycated haemoglobin and also histopathological studies. Methanol extract of *T. hirsuta* showed potent antidiabetic activity in mice by reduction of oxidative stress markers [74]. Various extracts of *T. hirsuta* were tested for in vivo antidiabetic activity by Faisal R et al. using alloxan induced model. The extracts were also tested for total phenolic content by Folin-Ciocalteau method, pro inflammatory cytokinines by ELISA (enzyme-linked immunoassay) method and polyphenolic content by HPLC analysis. The aqueous extract showed remarkable antidiabetic activity when compared with standard, glibenclaimide. A significant reduction in pro inflammatory cytokinines was demonstrated. HPLC anaylsis confirmed the presence of quercetin, gallic acid, cinnamic acid and p-coumaricacid [75]. The effects of streptozotocin (STZ)-induced diabetes in rats were studied by Swathi Putta et al. using the ethanolic leaf extract of *Tylophora indica* (ETLI) for pancreatic and hepatic oxidative stress. Serum blood glucose levels were determined in each group, along with liver enzymes like AST, aspartate ALT, and ALP, antioxidant enzymes like SOD, CAT, GPx, glutathione-S-transferase (GST), reduced glautathione (GSH) and blood glucose levels were measured. Studies on histopathology were also carried out. In diabetic rats, levels of liver enzymes and antioxidant enzymes were decreased, whereas levels of thiobarbituric acid reactive substances (TBARS) increased. Histopathology research revealed that ELTI had a protective effect against the oxidative damage that streptozotocin caused to the liver and pancreas. They concluded that ELTI had

more potential antioxidant benefits on oxidative stress brought on by diabetes [76].

Antihypertensive activity

Antihypertensive activity of *T. hirstua* was studied on spontaneous hypertensive Wistar rats by Bashir Ahmad et al. In absence of atropine, fall in heart rate was 218±8 beats per minute (BPM) and in presence of atropine, BPM was 110±5.6. As atropine is an anticholinergic drug, the action is via cholinergic muscarinic receptors. The percentage drop in blood pressure and heart rate was compared to acetylcholine, a standard cholinergic drug. The findings confirmed the presence of acetylcholine-like substances in *T. hirsuta*, were responsible for fall in blood pressure and heart rate providing support for its traditional use in hypertension treatment [16].

Cardiotonic acitivity

Tylophoriside (102) and its monoacetate, acetyl tylophoriside [AcT] (103**)** are two new steroidal glycosides isolated from *Tylophora sylvatica* by Gnabre et al. Aglycone tylogenin is obtained by mild acid hydrolysis. Characterization was done by NMR methods. Fast atom bombardment mass spectrometry [FAB MS] was used to calculate their molecular weights. Both glycosides were Na/k+ATPase inhibitors hence they showed cardiotonic activity and the aglycone showed potent anti-allergic activity when compared with widely used dexamethasone and prednisolone [54]. Acetyl tylophoriside [AcT] (103) and tylogenin, were tested for Na+/K+ ATPase enzyme inhibition along with two more standard cardenolide glycosides, ouabain and ouabagenin and a non cardenolide, chlormadinone acetate. Gnabre et al. confirmed that all five compounds inhibited the enzyme in a dose response manner. Ouabain showed greater activity than the other three compounds, but at less than 250 micro molar, tylogenin appeared to have greater activity than AcT. Molecular modelling studies suggest that AcT and tylogenin fit into the receptor with the steroid nucleus flipped over from the complete gridshells orientation. Comparisons with chlormadinone acetate (CMA) suggest that this molecule is similarly flipped over in the receptor [55].

Antiallergic activity

Tylogenin (104), an aglycone of two glycosides (102 & 103) of *Tylophora sylvatica*, inhibits IgE induced basophil mediator release for allergic reactions. Inhibition of basophil dependent serotonin release [BDSR] by compound 104 was measured by BDSR assay on rabbit leukocytes. Gnabre et al. found that the inhibitory action was more significant than that of parent glycosides, 102 & 103 and the standard, dexamethasone. The activity of tylogenin was found to increase with the incubation time. Inhibition of human leukocyte dependent histamine release [LDHR] by tylogenin was measured by LDHR model test [N methyl transferase assay]. Inhibition of histamine activity was more potent by tylogenin when compared to that of dexamethasone, which is widely used [21].

Antioxidant activity

Muhammad Furqan Akhtar et al. investigated for in vitro antioxidant activity of methanol and ethyl acetate leaf extracts of *Tylophora hirsuta*. Antioxidant power was assessed in alloxan-induced diabetic mice by determining serum amylase, lipid profile, body weight, glycated haemoglobin and also histopathological studies. Methanolextract of *T. hirsuta* showed potent antioxidnat activity in mice by reduction of oxidative stress markers [74]. Faisal et al. tested for in vitro antioxidant activity by DPPH (2, 2-diphenyl-1-picrylhydrazyl) scavenging activity in alloxan induced rat model of various extracts of *T. hirsuta*. The extracts were also tested for total phenolic content by Folin-Ciocalteau method, pro inflammatory cytokinines by ELISA (enzyme-linked immunoassay) method and polyphenolic content by HPLC analysis. The aqueous extract showed the highest antioxidant activity. HPLC anaylsis confirmed the presence of quercetin, gallic acid, cinnamic acid and p-coumaricacid [75]. Swathi Putta et al. studied the antioxidant activity using an ethanolic leaf extract of *Tylophora indica* for pancreatic and hepatic oxidative stress in streptozotocin (STZ)-induced rat model. Antioxidant enzymes like SOD, CAT, GPx, glutathione-s-transferase (GST) and reduced glautathione (GSH) were estimated. Studies on histopathology were also carried out. In diabetic rats, levels of antioxidant enzymes decreased, whereas levels of thiobarbituric acid reactive substances (TBARS) increased. Histopathology research revealed that ELTI had a protective effect against the oxidative damage that streptozotocin caused to the liver and pancreas. They concluded that ELTI had more

potential antioxidant benefits on oxidative stress brought on by diabetes [76]. Malathi et al. investigated methanol extract of the leaves of *Tylophora asthmatica* for antioxidant activity by the method of Mensor et al. and reductive potential by the method of Oyaizu et al. using ascorbic acid and gallic acid as the standard. Methanol extract showed dose dependant antioxidant activity when compared with standard, which may be due to its high phytochemical content [77]. Starlin et al. investigated the antioxidant activity of *Tylophora pauciflora* ethanlo extract against enzymatic antioxidants (superoxide dismutase, catalase, glutathione-s-transferase, glutathione peroxidase, peroxidase, ascorbate oxidase, and polyphenoloxidase) and non-enzymatic antioxidants (total reduced glutathione and vitamin C). Based on the findings, they concluded that the plant could scavenge free radicals and protect against oxidative stress, which causes diseases such as cancer and other problems [78].

Anticandidial activity

It has been reported that extracts of 23 medicinal plants significantly inhibited the growth of test pathogen (*Candida albicans*). *Tylophora fasciculata* was one of the 23 medicinal plants which showed significant inhibitory activity against *Candida albicans.* MIC values of those extracts were observed by Bhakshu LM et al. The results showed that *T. fasciculata* also showed anticanadial activity. In phytochemical screening, it was found that *T. fasciculata* tested positive for presence of alkaloids, flavonoids, glycosides, saponins and volatile oils [15].

Antiinflammatory activity

Shaveta Bhardwaj et al. studied the antiinflammatory activity of petroleum ether, chloroform and methanol extracts of *Tylophora asthmatica* leaves by using carrageenan induced and formalin induced paw edema models on Wistar rats. Plethysmometer was used to measure percentage inhibition of paw edema. The results were compared with standard drug, ibuprofen. The methanol extract showed significant results when compared with petroleum and chloroform extracts [79]. Antiinflammatory activity of septicine (42), a natural alkaloid of *Tylophora ovata* was evaluated by Geun-Mook P et al. in lipopolysaccharide-stimulated (LPS) murine macrophages and RAW264.7 cells (macrophase cell line). Treating with compound 42 inhibited LPS induced NO, tumor necrosis factor (TNF - alpha), inflammatory cytokinesis l, interleukins 6 (IL - 6) production in concentration dependent manner. It also suppressed the expression of inducible NO synthase [43]. Vasuda Gupta et al. evaluated the anti neuroinflammaotry effect of aqueous and hydroalcoholic extracts of *T. indica* leaf explants micropropagated on Murashige and Skoog (MS) media supplemented with benzyl amino purine. An in vitro model, BV-2 microglia cells activated with lipopolysaccharide was used for the study. Alpha-Tubulin, lba-1, NFKB, API expression was studied, following antimigratory activity. Extracts suppressed lipopolysaccharide induced microglia activation and migration and production of nitrite. The study concluded that *T. indica* may be used as a potential anti neuroinflammatory drug [80].

Anti corona virus activity

Yang et al. have found that tylophorine compounds, including naturally occurring and synthetic phenanthroindolizidines, were effective inhibitors of transmissible gastroenteritis virus (TGEV) and enteropathogenic coronavirus transmissible gastroenteritis virus (SARS CoV). By immunofluorescent assay of TGEV N and S protein expression and real time quantitative polymerase chain reaction (PCR) analysis of viral yields, these compounds demonstrated 50 percent maximal effective concentration (EC_{50}) ranging from 8-1468 nM. They prevented TGEV-induced apoptosis. In addition, human severe acute respiratory syndrome coronavirus reduced the cytopathic effect in Vero76 cells (cell lines showing epithelial morphology). The EC_{50} values ranged from less than 5 to 340 nm. According to the findings, tylophorine compounds isolated from *Tylophora ovata* were potent anti-coronavirus agents that could be developed into therapeutic agents for treating TGEV or SARS CoVinfection [81].

Antihelminthic activity

Dhadde Gurunath et al. reported anti helminthic activity of methanol extract of *T. indica* leaves against *Haemonchus* contortus. At 50 mg/mL concentration, it showed 100 % mortality in 6 h, at 25 mg/mL concentration, it showed 90% motality in 6 h and at 12.5 mg/mL concentration, it showed 80 % mortality in 6 h which was compared with albendazole [82].

Important Findings

The Plant List (www.theplantlist.org) was used to validate the species names. According to this website, around 60 species of *Tylophora* are available in Asian countries. A huge number of species were identified in the *Tylophora* genus, but little work was done on a few species. Twenty-one species and two varieties are found in India [4].

In this article we have given information regarding ethnomedicinal importance, phytochemistry and pharmacological uses of 18 species of *Tylophora*.

Traditionally, the species of this genus were used in local and traditional medicine to treat a variety of disorders such as indigestion, bronchial asthma, bronchitis, cough, liver diseases, wounds and ulcers and as expectorant. Most of the species have the common use in treating bronchial asthma.

More than 100 compounds were isolated from selected species of the genus *Tylophora*. It has a number of phenanthroindolizidine alkaloids which are the major secondary metabolites present in almost all the plants of this genus. Other types of active components of genus *Tylophora* include C_{21} steroidal glycosides, secoiridoids, triterpenes, furano alkaloids, etc. The structures have been elucidated by spectral and chemical means like NMR, IR, COSY, NOESY, HSQC, HRMS and degradation studies. Steroidal glycosides are distributed mainly in three species, *Tylophora atrofolliculata, T. sylvatica* and *T. tanakae.* Secoiridoid and xanthone glycosides are distributed mainly in *T. secamonoides.* In most of the plants of the genus tylophorine is the major alkaloid in phenanthroindolizidine category [83]. It is an organic heteropentacyclic compound that can be extracted easily from the plant or produced by hairy root culture method or can be synthesized in the laboratory [84]. Purine alkaloid caffeine has been isolated from *Tylophora mollissima* along with phenanthroindolizidine alkaloids [40]. Triterpenoid, α-amyrin acetate and fatty alcohol, heptaeicosanol have been isolated from *Tylophora hirsuta* [56].

Fourteen different therapeutic activities have been shown by *Tylophora* species. It is regarded as one of the genera with high economic and medicinal value since these plants have excellent therapeutic activities like anticancer [11,26,28,29,38,39,48,49,57,59], antiasthmatic [23,57,58], cardiotonic [51], antimicrobial [65-70], antiinflammatory [40,79,80], and antioxidant activity [77,78]; they are also active against corona virus [81]. Active constituents isolated from five species *Tylophora asthmatica, T. atrofolliculata, T. hirsuta, T. ovata* and *T. tanakae*, mainly phenanthroindolizidine alkaloids, have shown anti tumour activity. Steroidal glycosides isolated from *T. sylvatica* have shown cardiotonic activity [51,52]. Aglycone of steroidal glycosides, tylogenin, has shown anti allergic activity [21]. Secoiridoid and xanthone glycosides isolated from *T. secamonoides* have shown antimicrobial activity [19]. This genus might play a unique role in the chemical and pharmaceutical industries. Its industrialization and application prospects are extensive [83].

More research is currently being conducted on commonly available species such as *Tylophora hirsuta, T. atrofolliculata, T. sylvatica* and *T. tanakae.* In terms of the studies on biological activities, except for a few species, compounds were isolated from all the species which were selected and in most of the cases pharmacological studies were done for the isolated compounds. For other species, pharmacological studies were done with the extracts. Both in vitro and in vivo research methods were used for the studies. Few attempts were made to identify the molecular mechanisms. As a result, future research on the biological activity of various types of monomer compounds needs to be strengthened to benefit the plants of this genus, to provide better health uses to humans. Furthermore, well developed methods for ensuring the consistency, safety, and efficacy of *Tylophora* herbs should be established.

Conclusions

To summarize, research on the genus *Tylophora* has critical economic and theoretical implications, and it needs to be studied more systematically and thoroughly based on existing research to promote the modernization process of traditional medicine. Safety and efficacy of *Tylophora* species are not fully evaluated in humans; also, clinical trials are required to confirm preclinical findings.

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Author contributions

Satyavarapu Veera Venkata Naga Satya Mahalakshmi contributed in collecting literature of the *Tylophora* genus; Marepally Chandrika, Rebbaniboni Nandini and Mannava Naga Pavithra contributed in summarsing the information; Ramadevi Korni was involved in reviewing and writing the manuscript and Mohamed Jawed Ahsan took part in drawing the structures, aligning and editing the manuscript.

Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

References

[1] Tseng YH, Chao CT. *Tylophora lui* (Apocynaceae), a new species from Taiwan. *Ann Bot Fenn.* 2011; 48(6): 515–518.

[2] Forster PI. A taxonomic revision of *Tylophora* R.Br. (Asclepidaceae: Marsdenieae) in Australia. *Aust Syst Bot.* 1992; 5(1): 29–51.

[3] Mary EE, Peter VB. A revised classification of the Apocyanaceaes.l. *Bot Rev*. 2000; 66(1): 1–56.

[4] Jagtap AP, Singh NP. Fascicles of flora of India fascicle 24. Calcutta: Botanical Survey of India, 1999.

[5] Ritika G, Saraswati P, Neetu Y, Jaya D, Sarvesh P, Swapnil S. *Tylophora indica* (Burm. f.) merr: an insight into phytochemistry and pharmacology. *J Ethnopharmacol.* 2020; 262: 1–18.

[6] Nazar S, Hussain MA, Khan A, Muhammad G, Bukhari SNA. Alkaloid-rich plant *Tylophora indica* current trends in isolation strategies, chemical profiling and medicinal applications. *Arab J Chem.* 2020; 13(8): 6348–6365.

[7] Malathi R, Patric G. Evaluation of preliminary toxicity studies on methanolic leaves of *Tylophora asthmatica* in experimental rats. *J Pharmacol Toxicol.* 2008; 3(1): 34–40.

[8] Rajendran S, Jeyalatchagan S, Jayaraj K, Singamoorthy A, Muniappan A. Traditional herbal medicines practiced by the ethnic people in Sathyamangalam forests of Western Ghats, India. *Eur J Integr Med.* 2017; 16: 61–72.

[9] Phillipson JD, Tezcan I, Hylands PJ. Alkaloids of *Tylophora* species from Sri Lanka. *Planta Med.* 1974; 25(4): 301–309.

[10] Bhavya J, Vineetha MS, Veena SM, Farhan Z, Uday M, Sunil SM, Govindappa M. Ethnomedicinal plants and isolated compounds against snake venom activity: a review. *Indian J Nat Prod Resour.* 2021; 12(4): 491–505.

[11] Cheng-Yu C, Guo-Yuan Z, Jing-Rong W, Zhi-Hong J. Phenanthroindolizidine alkaloids from *Tylophora atrofolliculata* with hypoxia-inducible factor-1 (HIF-1) inhibitory activity. *RSC Adv.* 2016; 6(83): 79958–79967.

[12] Hostettmann K, Chinyanganya F, Maillard M, Wolfender JL. Chemistry, biological and pharmacological properties of African medicinal plants. Zimbabwe: University of Zimbabwe publications, 1996.

[13] Prathamesh K, Saif K. Ethnomedicinal plants used in the treatment of respiratory diseases around Western Ghats region of Maharashtra, India. *J Global Biosci.* 2021; 10(3): 8447–8457.

[14] Masur UA, Ferrao DM, Naik DD, Rodrigues MJ, Rodrigues VS. Phytochemical studies of *Tylophora* species of Goa. *J Nat Prod*. 2015; 8: 100–105.

[15] Bhakshu LM, Venkata Ratnam K, Venkata Raju RR. Anticandidal activity and phytochemical analysis of certain medicinal plants from Eastern Ghats, India. *Indian J Nat Prod Resour.* 2016; 7(1): 25–31.

[16] Bashir A, Niaz A, Saziq A, Shumila B. Blood pressure lowering effect of *Tylophora hirsute* wall. *Afr J Biotechnol.* 2012; 11(12): 3009–3013.

[17] Yue-Zhi L, Chun-Wei H, Chenh-Wei Y, Hsing-Yu H, Iou-Jun K, Yu-Sheng C, Ih-Sheng C, Hwan-You C, Shiou-Ju L. Isolation and biological activities of phenanthroindolizidine and septicine alkaloids from the Formosan *Tylophora ovata. Planta Med.* 2011; 77(17): 1932–1938.

[18] Thangarajan S, Poochi SP, Basanth Kumar AT, Velliyur KG. Screening and GC-MS profiling of ethanolic extract of *Tylophora pauciflora. Bioinformation.* 2019; 15(6): 425–429.

[19] Sheng Y, Chun-Ping T, Yang Y. Secoiridoids and xanthones from *Tylophora secamonoides* Tsiang. *J Asian Nat Prod Res.* 2008; 10(5): 591–596.

[20] Pate MB, Rowson JM. Investigations of

certain Nigerian medicinal plants, Part I. Preliminary pharmacological and phytochemical screenings for cardiac activity. *Planta Med*. 1964; 12(1): 33–42.

[21] John NG, Marilyn JH, David GM, Jacob LP. Antiallergic activity of tylogenin, a novel steroidal compound from *Tylophora sylvatica. Int J lmmunopharmacol.* 1994; 16(8): 641–650.

[22] Ruyani A, Sinta BD, Emilia, Zulfikar, Anansyah F, Putri SR, Sundaryono A. Preliminary studies on therapeutic effect of ethanolic extract of *Tylophora villosa* leaves against paracetamol-induced hepatotoxicity in mice. *J Tradit Complement Med*. 2018; 9(4): 285–296.

[23] Lin YP, Fang QL, Xue YM, Fu SN, Hu CY, Huang F, Wang MM, Qiao X, Yin XQ, Zeng YC, Du CH, Zhao XJ, Li XP, Hua Y. Effects of *Tylophora yunnanensis* Schltr on regulating the gut microbiota and its metabolites in non-alcoholic steatohepatitis rats by inhibiting the activation of NOD-like receptor protein 3. *J Ethnopharmacol*. 2023; Article ID 116145.

[24] Mulchandani NB. Isolation, biosynthesis and biological activity of alkaloids of *Tylophora asthmatica*, a versatile medicinal plant. Bombay: Bhabha Atomic Research Centre, 1987.

[25] Reimche I, Haiqian YU, Ariantari NP, Liu Z, Merkens K, Rotfuß S, Peter K, Jungwirth U, Bauer N, Kiefer F, Jorg Martin N, Hans Gunther S, Peter P, Nicole T. Phenanthroindolizidine alkaloids isolated from *Tylophora ovata* as potent inhibitors of inflammation, spheroid growth, and invasion of triple-negative breast cancer. *Int J Mol Sci.* 2022; 23(18): 1–32.

[26] Ehab MM, Hamdoon AM, Arafa M, Mohamed AA, Mohammad MA, Suliman AA, Mohammed MG, Hesham AMG, Fatema ESAR, Khaled S, Samy S, Riaz AK. In vitro anti-proliferative, and kinase inhibitory activity of phenanthroindolizidine alkaloids isolated from *Tylophora indica*. *Plants (Basel).* 2022; 11(10): 1–19.

[27] Wadhawan VK, Sikka SK, Mulchandani NB. Minor alkaloids of *Tylophora asthmatica* X-ray analysis of tylophorinidine. *Tetrahedron Lett.* 1973; 14(51): 5091–5094.

[28] Mulchandani NB, Venkatachalam SR. Tylophorinicine: a phenanthroindolizidine alkaloid from *Tylophora asthmatica* and *Pergularia pallida. Phytochemistry*. 1984; 23(5): 1206.

[29] Xuehi H, Song G, Lihua F, Shishan Y, Xiaotian L. Cytotoxic alkaloids from the roots of *Tylophora atrofolliculata*. *Planta Med.* 2004; 70(5): 441–445.

[30] Lijie C, Zeper A, Min X, Liyan Z, Song G, Wenyi H, Yun X, Feng L, Shisan Y. On-line identification of phenanthroindolizidine alkaloids in a crude extract from *Tylophora atrofolliculata*by liquid chromatography combined with tandem mass spectrometry. *Rapid Commun Mass Spectrom.* 2004; 18(2): 184–190.

[31] Cheng-Yu C, Li-Ping B, Zhuo-Feng K, Yan L, Jing-Rong W, Zhi-Hong J. G-Quadruplex DNA-binding quaternary alkaloidsfrom *Tylophora atrofolliculata*. *RSC Adv.* 2016; 6(115): 114135–114142.

[32] Zhenjia L, Haining L, Hongyan L, Yi Z, Haijing Z, Fuqin S, Song X, Yong L, Yikang S, Shishan Y, Xiaoguang C. Interaction studies of an anticancer alkaloid, (+)-(13as)-deoxytylophorinine, with calf thymus DNA and four repeated double-helical DNAs. *Chemotherapy.* 2011; 57(4): 310–320.

[33] Xue SH, Shi SY, Xiao TL. Two phenanthroindolizidine alkaloids from *Tylophora atrofolliculata*. *Chin Chem Lett.* 2002; 13(1): 61–64.

[34] Gellertt E, Govindachari R, Lakshmikantham V, Ragade IS, Rudzatsa R, Viswanathan N. The alkaloids of *Tylophora crebriflora*: structure and synthesis of tylocrebrine, a new phenanthroindolixidine alkaloid. *Blake Proc Roy Soc Queensl.* 1948; 59(168): 1008–1014.

[35] Koppaka VR, Richard W, Bernice C. Alkaloids of *Tylophora* I: Isolationof six new alkaloids. *J Pharm Sci*. 1970; 59(10): 1501–1502.

[36] Koppaka VR, Richard AW, Bernice C. Alkaloids of *Tylophora* 111: new alkaloids of *Tylophora indica* (Burm) Merrill and *Tylophora dalzellii* Hook. f. *J Pharm Sci.* 1971; 60(11): 1725–1726.

[37] Bhutani KK, Mohammed A, Atal CK. 13a-Hydroxytylophorine from *Tylophora hirsuta*. *Phytochemistry.* 1985; 24(11): 2778–2780.

[38] Mohammed A, Bhutani KK. Minor alkaloids of *Tylophora hirsuta. Phytochemistry.* 1987; 26(7): 2089–2092.

[39] Bhutani KK, Mohammed A, Atal CK. Alkaloids from *Tylophora hirsuta*. *Phytochemistry*. 1984; 23(8): 1765–1769.
[40] Viswanathan N. Alkaloids of *Tylophora mollissima*. *J Nat Prod.* 1985; 48(6): 997–998.
[41] Zhen YY, Huang XS, Yu DQ, Yu SS. Antitumor alkaloids isolated from *Tylophora ovata*. *Acta Bot Sin.* 2002; 44(3): 349–353.
[42] Zhen-Jia L, Hai-Ning L, Hong-Yan L, Yi Z, Hai-Jing Z, Fu-Qin S, Yi-Kang Si, Shi-Shan Y, Xiao-Guang C. Anticancer effect and neurotoxicity of S-(+)-deoxytylophorinidine, a new phenanthroindolizidine alkaloid that interacts with nucleic acids. *J Asian Nat Prod Res.* 2011; 13(5): 400–408.
[43] Geun-Mook P, Jin-Kyung K. Septicine inhibits the production of inflammatory mediators in lipopolysaccharide-stimulated murine macrophages. *J Life Sci.* 2011; 21(9): 1310–1314.
[44] Nakano D, Ishitsuka K, Ikeza M, Tsuchihashi R, Okawa M, Okabe H, Tamura K, Kinjo J. Screening of promising chemotherapeutic candidates from plantsagainst human adult T-cell leukemia/lymphoma (IV): phenanthroindolizidine alkaloids from *Tylophora tanakae* leaves. *J Nat Med.* 2015; 69(3): 397–401.
[45] Fumiko A, Mio H, Tatsuo Y, Keiichi H, Nanao H, Mineko I, Setsuko I, Michio I. Further investigation of phenanthroindolizidine alkaloids from *Tylophora tanakae*. *Chem Pharm Bull.* 1998; 46(5): 767–769.
[46] Fumiko A, Yukiko I, Tatsuo Y, Keiichi H, Nanao H. Phenanthroindolizidine alkaloids from *Tylophora tanakae*. *Phytochemistry*. 1995; 39(3): 695–699.
[47] Dan S, Anne KL, Jette C, Bogdan AB, Fumiko A, Jerzy WJ. *In vitro* cytotoxicactivity of phenanthroindolizidine alkaloids from *Cynanchum vincetoxicum* and *Tylophora tanakae* against drug-sensitive and multidrug-resistant cancer cells. *J Nat Prod.* 2002; 65(9): 1299–1302.
[48] Fumiko A, Mio H, Tatsuo Y, Keiichi H, Nanao H, Ritsuo N. Glycosides of 14,15-seco-and 13,14:14,15-disecopregnanes from the roots of *Tylophora tanakae*. *Chem Pharm Bull*. 1999; 47(10): 1384–1387.
[49] Junei K, Daisuke N, Toshihiro F, Hikaru O. Screening of promising chemotherapeutic candidates from plants extracts. *J Nat Med.* 2016; 70(3): 335–360.
[50] Etherington T, Herbert RB, Jackson FB. Furoquinoline alkaloids from *Tylophora asthmatica*. *Phytochemistry*. 1977; 16(7): 1125–1126.
[51] Cheng-Yu C, Guo-Yuan Z, Tang-Gui X, Ping-Chuan J, Jing-Rong W, Zhi-Hong J. A phenanthroindolizidine glycoside with HIF-1 inhibitory activity from *Tylophora atrofolliculata*. *Phytochem Lett.* 2019; 31: 39–42.
[52] Xue-Shi H, Shi-Shan Y, Xiao-Tian L, Nan L. A novel steroid from *Tylophora atrofolliculata*. *J Asian Nat Prod Res.* 2002; 4(3): 197–200.
[53] Huang AC, Chen CY, Wang JR, Jiang ZH. Three new C_{21} steroidal glycosides *from Tylophora atrofolliculata*. *Phytochem Lett.* 2020; 36: 111–114.
[54] Gnabre JN, Pinnas JL, Martin DG, Mizsak DA, Kloosterman DA, Baczynskyj L, Nielsen JW, Bates RB, Hoffmann JJ, Kane VV. Characterization of steroidal glycosides from *Tylophora sylvatica*. *Tetrahedron.* 1991; 47(22): 3545–3554.
[55] Gnabre JN, Pinnas JL, Bates RB, Dolata DP, Gangwar S. *Tylophora* compounds as Na+/K+-ATPase Inhibitors. *Gen Pharmacol.* 1993; 24(5): 1107–1113.
[56] Niaz A. Brine shrimp cytotoxicity of crude methanol extract and antispasmodic activity of α-amyrin acetate from *Tylophora hirsuta* Wall. *BMC Complement Med.* 2013; 13(135): 1–7.
[57] Udupa AL, Udupa SL, Guruswamy MN. The possible site of anti-asthmatic action of *Tylophora asthmatica* on pituitary-adrenal axis in albino rata. *Planta Med.* 1991; 57(5): 409–413.
[58] Haranath PS, Shyamalakumari S. Experimental study on mode of action of *Tylophora asthmatica* in bronchial asthma. *Indian J Med Res.* 1975; 63(5): 661–670.
[59] Stephen J, Vijayammal PL. Antitumor activity of *Tylophora asthmatica. Anc Sci Life.* 2000; 20(1-2): 88–91.
[60] Rabiya A, Paithankar VV, Vyas JK, Wankhade A, Kochar AC. Evaluation of antineoplastic activity of ethanolic extract of *Tylophora indica. World J Pharm Med.* 2020;

9(7): 1823–1830.
[61] Wang YX, Jia SH, Zeng WY, Liu ZX, Fang ZJ. Effects of *Tylophora ovata* (Lindl) Hook. ExSteud alkaloids (TOHa) on proliferation and apoptosis of HeLa cells in vitro. *Food Sci.* 2008; 29(11): 609–611.
[62] Malathi R, Patrick GM. Hepatoprotective activity of methanolic leaves extract of *Tylophora asthmatica* against paracetamol induced liver damage in rats. *J Pharmacol Toxicol.* 2007; 2(8): 737–742.
[63] Malathi R, John SA, Cholarajan A. *Tylophora asthmatica* L. prevents lipid peroxidation in acetaminophen induced hepato toxicity in rats. *Asian J Res Pharm Sci.* 2011; 1(3): 71–73.
[64] Ajay RC, Vijay MM, Sudhir LP, Avinash VT, Vinod SD. Effect of *Tylophora asthmatica* on hepatotoxicity induced by antitubercular drugs in albino rats. *Int J Basic Clin Pharmacol.* 2016; 5(4): 1402–1407.
[65] Goun E, Cunningham G, Chu D, Nguyen C, Miles D. Antibacterial and antifungal activity of Indonesian ethnomedical plants. *Fitoterapia.* 2003; 74(6): 592–596.
[66] Bashir A, Ali N, Bashir S, Choudhary M. Biological activities of aerial parts of *Tylophora hirsute* Wall. *Afr J Biotechnol.* 2009; 8(18): 4627–4631.
[67] Maheshwari M, Vijayarengan P. Phytochemical analysis and antibacterial activities of *Tylophora indica. Int J Botany Stud*. 2020; 5(2): 110–114.
[68] Anand M, Sharma S, Preetika M. Antimicrobial and antioxidant potential of *Tylophora indica* (Burm. f.) Merrill and development of an efficient micropropagation system for its therapeautic use. *Med Plants Int J Phytomed*. 2020; 12(1): 82–89.
[69] Khanna C, Singh S, Vyas M, Das S. Evaluation of antimicrobial behaviour of *Tylophora indica* leaf extracts against selected food microbial pathogens. *Res J Pharm Technol.* 2020; 13(11): 5224–5228.
[70] Sainudeen S, Nair VS, Zarbah M, Abdulla AM, Najeeb CM, Ganapathy S. Can herbal extracts serve as antibacterial root canal irrigating solutions? Antimicrobial efficacy of *Tylophora indica, Curcumin longa, Phyllanthus amarus*, and sodium hypochlorite on *Enterococcus faecalis* biofilms formed on tooth substrate: in vitro study. *J Pharm Bioallied Sci.* 2020; 12(1): S423–S429.
[71] Raji Y, Hammed AI, Adesanwo JK, Ogunwande IA. Antiulcerogenic effects of *Tylophora conspicua* in male rats. *Phytother Res.* 2000; 14(5): 378–380.
[72] Bashir A, Niaz A, Shumaila B, Jamshaid A, Sadiq A, Ibrar K. Cholinomimetic and calcium channel blocking activities of the aerial parts of *Tylophora hirsuta* (Wall.). *J Chem Soc Pak.* 2009; 31(4): 647–651.
[73] Shahla N. Studies on hypoglycemic activity of *Tylophora dalzellii. Pharmacologyonline.* 2010; 3: 280–284.
[74] Muhammad FA, Arsalan S, Ammara S, Mirza MFAB, Ali S, Azhar R, Mohammed MAD. *Tylophora hirsuta* L. leaf extract attenuates alloxan-induced diabetes in mice by suppressing oxidative stress and α-amylase. *Asian Pac J Trop Biomed.* 2021; 11(9): 394–404.
[75] Faisal R, Ali S, Bushra A, Humaira MK, Muhammed FA, Maryam Z, Abdullah M, Kashif S, Irfan H, Naeem Q. *Tylophora hirsuta* (Wall.) extracts ameliorate diabetes associated with inflammation in alloxan-induced diabetic rats. *Endocr Metab Immune Disord Drug Targets.* 2021; 21(6): 1031–1042.
[76] Swathi P, Kotaiah S, Jagadeesh Kumar T. Protective effect of *Tylophora indica* against streptozotocin induced pancreatic and liver dysfunction in wistar rats. *Biomed Pharmacol J.* 2020; 13(4): 1755–1763.
[77] Malathi R, Ahamed JS, Cholarajan A. Antioxidant activity of extract from the leaves of *Tylophora asthmatica. J Microbiol Antimicrob.* 2012; 4(4): 70–73.
[78] Starlin T, Velliyur KG. Enzymatic and non-enzymatic antioxidant properties of *Tylophora pauciflora* Wight and Arn. an in vitro study. *Asian J Pharm Clin Res.* 2013; 6(4): 68–71.
[79] Shaveta B, Atinderpal K, Manpreet K, Jatinder PS, Jobanpreet K, Srinivas N. Evaluation of anti-inflammatory activity of *Tylophora asthmatica. Curr Trends Biotechnol Pharm.* 2021; 15(6): 90–95.
[80] Gupta V, Guleri R, Gupta M, Kaur N, Kaur K, Kumar P, Anand M, Gurcharan K, Pratap Kumar P. Anti-neuroinflammatory potential of *Tylophora indica* (Burm. f) Merrill and development of an efficient in vitro

propagation system for its clinical use. *PLoS One*. 2020; 15(3): 1–20.

[81] Cheng-Wei Y, Yue-Zhi L, Iou-Jiun K, Dale LB, Jia-Tsrong J, Du L, Chun-Wei H, Teng-Kuang Y, Yu-Sheng C, Shiow-Ju L. Identification of phenanthroindolizines and phenanthroquinolizidines as novel potent anti-corona viral agents for porcine enteropathogenic coronavirus transmissible gastroenteritis virus and human severe acute respiratory syndrome corona virus. *Antiviral Res.* 2010; 88(2): 160–168.

[82] Dhadde Gurunath S, Mali Hanmant S, Sapate Rohit B, Vakhariya Rohan R, Raut Indrayani D, Nitalikar Manoj M. Investigation of in vitro anthelmintic activity of methanolic extract of *Tylophora indica* leaves against *Haemonchus contortus*. *J Univ Shanghai Sci Technol.* 2021; 23(2): 37–42.

[83] Kumara Swamy M. Plant-derived bioactives: production, properties and therapeutic applications. 1st ed. Singapore: Springer, 2020.

[84] Junmin Z, Susan LM, Di M, Xiao-Fei S, Chen-Jie Y, Ying-Qian L, Kuo-Hsiung L. Biologically active indolizidine alkaloids. *Med Res Rev*. 2021; 41(2): 928–960.

Abbreviations

ACTH: adrenocoticotropic hormone; ALP: alkaline phosphatase; ALT: alanine transaminase; AT: adenine thymine; BPM: beats per minute; CAT: catalase; CD: circular dichorism; COSY: correlated spectroscopy; DLA: Dalton's lymphoma ascites; DPPH: 2,2-diphenyl-1-picrylhydrazyl; EAC: Ehrlich ascites Cells; ELISA: enzyme-linked immunosorbent assay; ESI TOF MS: electrospray ionization time-of-flight mass spectrometer; FAB MS: Fast-atom bombardment mass spectrometry; GPx: glutathione peroxidise; HCT-8: human colon carcinoma; HeLa cells: human cervical cancer cell line; HepG-2: hepatoblastoma cell line; HIF-1: hypoxia inducible factor; HMBC: heteronuclear multiple bond correlation; HONE-1: epithelial tumor cell line; HRMS: high-resolution mass spectrometry; HSQC: heteronuclear single quantum coherence spectroscopy; HTLV-1-infected T cells: human T-lymphotropic virus type1; LDHR: human leukocyte dependent histamine release; IV: intravenous; IL-6: interleukins 6; IR: infrared; KB cells: KERATIN-forming tumor cell line HeLa; LDH: lactate dehydrogenase; LPO: lactoperoxidase; MCF-7: Michigan cancer foundation; MDA: malondialdehyde; MIC: minimum inhibitory concentration; MT-1: T-cell line derived from adult T-cell leukemia; MT-2: T-cell line derived from normal human cord leukocytes; MTT: 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; NCT-H460: human non-small cell lung carcinoma cell line; NMR: nuclear magnetic resonance; NOESY: nuclear overhauser effect spectroscopy; NUGC3: Nagoya University gastric cancer-3; SAR: structure activity relationship; SGOT: serum glutamic-oxaloacetic transaminase; SGPT: serum glutamic pyruvic transaminase; SOD: superoxide dismutases; SP-268: human glioblastoma cell line