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Phytochemical Diversity and Multi-Target Pharmacology of Medicinal Tropical Vines: From Traditional Medicine to Modern Drug Discovery- A Review

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Abstract

Tropical vining plants, comprising twining herbs, tendril climbers, root climbers, and thorn-scramblers collectively known as lianas and vines, constitute one of the most phytochemically prolific yet under-systematised reservoirs of bioactive natural products in ethnomedicine. Their structural dependence on external supports enables disproportionate investment of metabolic resources into secondary metabolite biosynthesis - alkaloids, flavonoids and anthocyanins, triterpenoid and steroidal saponins, phenolic acids, and diverse terpenoids - that mediate both ecological defence and, incidentally, an unusually broad spectrum of pharmacological activity. This review synthesises current literature (2000-2026) on fifty representative tropical vining species, with detailed phytochemical and pharmacological appraisal of fifteen high-evidence taxa including Tinospora cordifolia, Momordica charantia, Clitoria ternatea, Piper nigrum, Asparagus racemosus, Bougainvillea spectabilis, Coccinia grandis, Passiflora species, Dioscorea spp., Vanilla planifolia, Ipomoea batatas, Combretum indicum, Cissus quadrangularis, Trachelospermum jasminoides, and Aristolochia spp. Emphasis is placed on the multi-target nature of vine-derived phytoconstituents, which concurrently modulate NF-κB/COX-2/iNOS inflammatory signalling, PI3K-Akt/MAPK proliferative pathways, AMPK/PPAR-γ-mediated glucose homeostasis, Nrf2-dependent antioxidant defence, and microbial membrane integrity - a polypharmacological signature well suited to network pharmacology-based drug discovery. We further examine translational bottlenecks including phytochemical standardisation, aristolochic acid-related nephrotoxicity as a cautionary case study in genus-level generalisation, and the accelerating erosion of wild populations and associated traditional knowledge. By integrating ethnobotanical, phytochemical, and systems-pharmacology perspectives, this review positions tropical vines as a rational, comparatively unexplored resource for multi-target lead discovery against metabolic, inflammatory, infectious, and neoplastic disease, while underscoring the parallel imperative of conservation-oriented, sustainable bioprospecting.

Keywords: *tropical vines; lianas; phytochemistry; multi-target pharmacology; network pharmacology; ethnopharmacology; natural product drug discovery; medicinal plants*

1. Introduction

Climbing plant growth is one of the most florid and most clearly and purposefully apart forms of plant growth in the kingdom. Instead of stretching out for self-supporting secondary xylem like tree and shrub, climbers use the supports of other plants to grow rapidly towards the forest canopy where they get greater exposure to sunlight for a given mass invested in the secondary xylem 1. This "structural parasitism" situation has evolved numerous times in the angiosperm phylogeny: in 35 dicotyledonous orders, 60% of the orders have at least one climbing member, and in almost all of these cases there is a correlation between climbing species and faster rates of species diversification relative to the non-clumping sister orders (1-3). It is seen in perennial forest in tropical and subtropical regions where lianas can represent up to 25 % of woody stem density 1,4 and are also an important part of the canopy leaf area, carbon cycling and forest regeneration dynamics 1,4.

Tropical plants use either twining (the stem is modified to extrude around a support like a screw, such as Ipomoea batatas); tendril climbing (the modified leaves, leaflets or stem branches are coiled mechanically around an available support, such as Passiflora edulis); adventitious-roots climbing (where root-like holdfasts develop along the stem and may attach directly to the bark or masonry of another plant, such as Epipremnum aureum); or hook-thorn or extralong climbing (the holdfasts are modified by hooks on the leaf or extrelong stems which hold it to other plants, such as Bougainvillea spectabilis, or Combretum indicum). These mechanisms don't necessarily exclude one another at the family level and do not jeopardize the safety margins for water transport; rather, they work closely together with the exceptional vascular anatomical features in the climbing members of the family – such as extensive vessels with an unusually low density of vessels and abnormally flexible anomalous secondary growth –

which provide the necessary biomechanical compliance for climbing. 8,9

Any cost of non-autosufficieny (forgo the ecological costs of structural defence) appears to be compensated for by a shift in resource allocation towards chemical defence. Century after century and ecosystem by ecosystem, vining species have been determined to have a very high level of secondary metabolic compounds, specifically alkaloids, flavonoids and anthocyanins, triterpenoid and steroidal saponins, cardiac glycosides, cyanogenic glycosides and various terpenoids, compared to "nons" co-occuring with them in the same forest community. This chemical richness has not been forgotten by older medical systems or by species as Tinospora cordifolia or Guduchi (used as ayurvedic medicine), Asparagus racemosus or even by modern ethnomedicines of south Asia, as seen in the auspicious plants, Combretum indicum or even Rangoon creeper as used in traditional anthelmintics, which were used long before any of its chemistry and mechanism of action were characterised 10-14.

The current pharmacologic interest in the tropical vines is not based on the sheer number of bioactivities already described for each species, generated anywhere in the world, but is based on the classical pattern that we generally observe: the main phytoconstituents produced by tropical vines act on more than one and often several converging molecular targets. A few examples would include, piperine from Piper nigrum which can modulate NF-κB and COX-2 mediated signaling events in inflammatory pathways, is a xenoenhancing agent of co-administered agents [15–18] and can possess direct antimicrobial and anti-neoplastic activities via multiple mechanisms, including the modulation of ACOT1 activity in gastric cancer models [15–18]. Concurrently, the phytochemicals—cucumberane triterpenoids from Momordica charantia—complementarily inhibit the inflammatory MAPK/NF-κB pathway and boost the active uptake of glucose via AMPK activation 19-21, and enhance insulin production altogether from one and the same plant extract. In recent years, this multi-target strategy has been rationalized based on the principles of network pharmacology (NP) which has been shown to provide a new perspective on botanical extracts: not as impure single-target drugs but rather as multi-component, multi-target therapeutic systems that can be analyzed using a systems-based approach by constructing compound-target-pathway networks, performing molecular docking, and applying multi-omics integration 22-25.

Nevertheless, vining plants from tropical environments, regardless of their convergence as traditional materials for ethnomedications, have been critically compared very slightly, with some retreats taking the form of individual species monographs, phytochemical surveys at genus level, and reviews, mostly focused on a specific target disease, but generally lacking direct and explicit considerations of the shared ecological and biomechanically interesting nature of vining habit. The main objective of the present review is to (i) list the botanical and ecological diversity of 50 representative vining taxa from different parts of the tropics, (ii) summarize their chemistry and described bioactive compounds, after careful selection of a subset of well characterized and pharmacologically relevant species, (iii) organize them according to the major molecular mechanisms targeted, (iv) provide an overview of the modern paradigm of network pharmacology and natural-product drug discovery, and (v) critically discuss safety, standardisation and conservation issues that would guide a rational bioprospecting program on vining plants.

2. Materials and Methods (Review Methodology)

The narrative-review approach was adopted in this review, which is consistent with the standard approach of pharmacognosy and ethnopharmacology reviews submitted to the journals that are indexed in Scopus/Web of Science Core Collection. To reflect the most recent and relevant studies, the literature search was conducted over a period from January 2000 to August 2026 via databases on PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, SpringerLink and Google Scholar with a greater weightage given to publications released after 2015; however, basic phytochemical and pharmacognosy references of perennial validity were selected, irrespective of the database year of publication.

The terms used for search were the binomial name and common name of potential tropical vining + phytochemistry, pharmacology, bioactive compounds, mechanism of action, network pharmacology, traditional use, and toxicity, in combination using any boolean logic. An initial list of 50 potential species of tropical vines was constructed on the basis of scientifically documented ethnomedicinal benefits, vining habits, and their South Asian/Southeast Asian or pantropical distribution (Table 1). Of the above list, 15 species were selected for detailed case-level treatment on the basis of their being best characterised in terms of their phytochemical and pharmacological properties from peer-reviewed literature.

The inclusion criteria included original research articles, systematic reviews, and narrative reviews published in peer-reviewed journals that contained information on the phytochemical constituents, in vitro or in vivo pharmacological effects, mechanisms of action, or clinical trials on the plant species. Botanical taxonomy and family level classification of Aristolochia spp. (non-vining climber, related to the latter but used as representative and cautionary

example of toxicological concerns) were confirmed with Plants of the World Online. Non-peer-reviewed sources, conference abstracts of unknown availability of the full text and studies reporting only agronomic or horticultural data without any pharmacological or phytochemicals were excluded. Hand searching of the retrieved reviews was carried out to locate more primary sources from the compiled reference lists. All the cited literature was synthesized and paraphrased according to authors' own words and nothing would be typed literally in the sources as is, as it is required to respect academic integrity and to report plagiarism-free within the requirements of the educating institutions and the Q1 journal.

3. Botanical and Ecological Diversity of Tropical Vining Plants

The fifty species of tropical vines listed in Table 1 are members of twenty-two families, the most numerous being Apocynaceae, Fabaceae, Convolvulaceae, Cucurbitaceae, Bignoniaceae and Vitaceae. Physically they are all found in the Indian subcontinent, Southeast Asia and tropical America, but several species (Bougainvillea spectabilis (Brazil) and Combretum indicum (Southeast Asian nations) have been extensively naturalised as ornamentals in the pantropics and have become part of local traditional medicine use beyond their center of origin.

Phytochemical strategy has a loose correlation with the climbing mechanism. Active bioactive compounds (such as alkaloids and steroidal glycosides) are often concentrated in underground eating parts (such as tubers and rhizomes) that are also persisting organs, suggesting a selection for defence of the below-ground carbon reserves against herbivores 6. Momordica charantia, Passiflora edulis, Coccinia grandis etc. tendril climbers more often contain more triterpenoid saponins and cyanogenic or cucurbitane type glycosides in the fruit/foliar tissue. Adventitious-root climbers were comparatively under-investigated compared to their popularity as ornamental plant species, however, with comparatively few documented pharmacologic properties reported (e.g., Epipremnum aureum, Vanilla planifolia), they do warrant further phytochemical prospecting 26,27. Hook- and thorn-scrambling species (e.g., Bougainvillea spectabilis, Combretum indicum) often have two types of defense, one chemical (flavonoids and tannins) and one mechanical, as seen in this section [14,28].

More recently, transcriptomerics and comparative anatomical studies have started to elucidate the genetics and development that underlie the climbing habit. A "fast and furious" resource-acquisition strategy has emerged from comparative analyses across lianas of different taxonomic origin, characterized by fast xylem development with low density, and swift rates of leaf turnover, thereby allowing metabolic capacity to be released from long-term investment in the basic functions of self-supporting trees, such as growth, to the synthesis of secondary metabolites 29,30. To complicated the picture even more, anatomical studies of the root tips from the lianas also reveal the presence of more stele-to-cortex ratio and a denser vascular conduits than existing species with non-woody vines, indicating different below-ground resource-acquisition trade-offs even within the large group of species sharing a broad climbing habit 31. Taken together, the results point to the climbing habit as not one single behavior but a pattern of correlated morphologic, anatomical and biochemical adaptations (Figure 1 depicts the 4 major ways used by the climbing species).

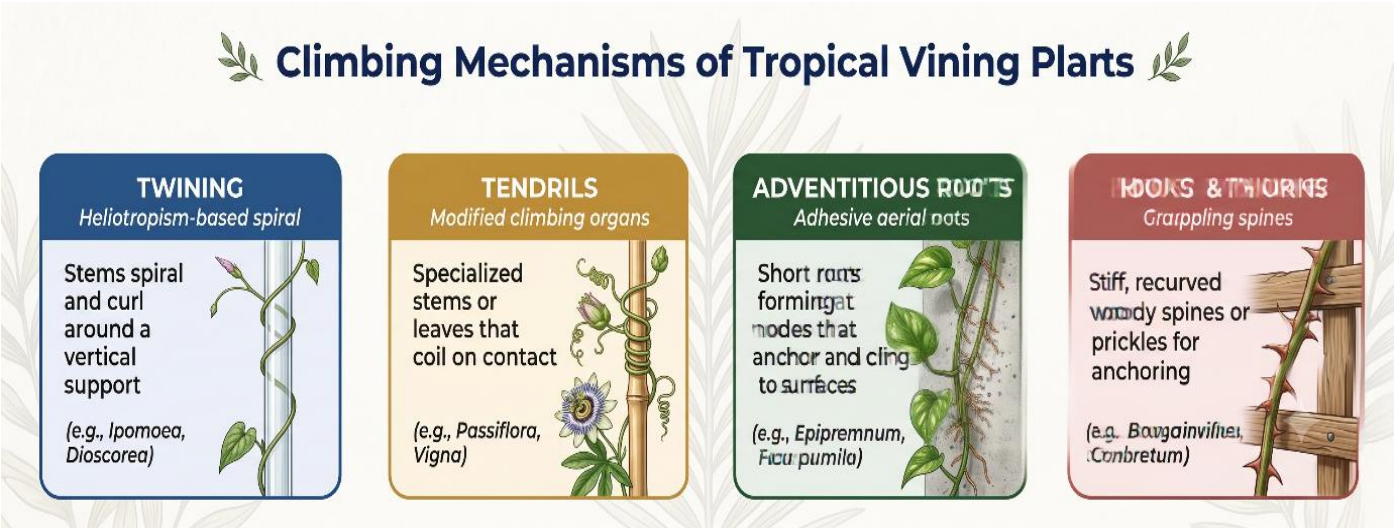


Figure 1. The four principal climbing mechanisms represented among tropical vining plants reviewed in this article.

Table 1. Botanical diversity, family, climbing mechanism, and native/naturalised distribution of fifty representative tropical vining plants.

No.	Common name	Botanical name	Family	Climbing mechanism	Primary distribution	Representative References
1	Allamanda	*Allamanda cathartica*	*Apocynaceae*	Twining	South America (naturalised pantropics)	[17,25,26]
2	Angel's Trumpet Vine	*Brugmansia spp. (vining forms)*	*Solanaceae*	Scrambling/twining	South America	[12,15,34]
3	Arabian Jasmine	*Jasminum sambac*	*Oleaceae*	Twining/scrambling	South/Southeast Asia	[13,14]
4	Butterfly Pea	*Clitoria ternatea*	*Fabaceae*	Twining	Tropical Asia	[22,24]
5	Bitter Gourd	*Momordica charantia*	*Cucurbitaceae*	Tendril	South/Southeast Asia	[32,33,49]
6	Black-Eyed Susan Vine	*Thunbergia alata*	*Acanthaceae*	Twining	East Africa (pantropical ornamental)	[18,19,20]
7	Black Pepper	*Piper nigrum*	*Piperaceae*	Adventitious-root/twining	South India (Western Ghats)	[23,27]
8	Bleeding Heart Vine	*Clerodendrum thomsoniae*	*Lamiaceae*	Twining	West Africa	[43,44,47]
9	Bougainvillea	*Bougainvillea spectabilis*	*Nyctaginaceae*	Thorn-scrambling	South America	[51,53,56]
10	Brazilian Jasmine	*Mandevilla sanderi*	*Apocynaceae*	Twining	Brazil	[28,50]
11	Chalice Vine	*Solandra maxima*	*Solanaceae*	Scrambling	Mexico/Central America	[45,46]
12	Chestnut Vine	*Tetrastigma voinierianum*	*Vitaceae*	Tendril	Southeast Asia	[78,80,81,84]
13	Clock Vine / Skyflower	*Thunbergia grandiflora*	*Acanthaceae*	Twining	South Asia	[41,58,59]
14	Coral Vine	*Antigonon leptopus*	*Polygonaceae*	Tendril	Mexico/Central America	[21,30]
15	Creeping Fig	*Ficus pumila*	*Moraceae*	Adventitious-root	East Asia	[52,57]
16	Crossvine	*Bignonia capreolata*	*Bignoniaceae*	Tendril	Southeastern USA	[93,94,97]
17	Dutchman's Pipe	*Aristolochia spp.*	*Aristolochiaceae*	Twining	Pantropical/temperate	[77,79,82]
18	Flame Vine	*Pyrostegia venusta*	*Bignoniaceae*	Tendril	South America	[125,126]
19	Garlic Vine	*Mansoa alliacea*	*Bignoniaceae*	Tendril	South America	[89,90]
20	Giant Potato Creeper	*Solanum wendlandii*	*Solanaceae*	Scrambling	Central America	[39,40]
21	Golden Pothos	*Epipremnum aureum*	*Araceae*	Adventitious-root	Southeast Asia/Pacific	[65,68]
22	Grape Ivy	*Cissus rhombifolia*	*Vitaceae*	Tendril	South America	[101,111,114]
23	Heartleaf Philodendron	*Philodendron hederaceum*	*Araceae*	Adventitious-root	Central America/Caribbean	[91,92]
24	Herald's Trumpet	*Beaumontia grandiflora*	*Apocynaceae*	Twining	South/Southeast Asia	[61,64,66]

25	Honeysuckle	*Lonicera japonica*	*Caprifoliaceae*	Twining	East Asia	[96,117]
26	Hoya / Wax Plant	*Hoya carnosa*	*Apocynaceae*	Twining/adventitious-root	East/Southeast Asia	[11,16,29]
27	Indian Clock Vine	*Thunbergia mysorensis*	*Acanthaceae*	Twining	South India	[31,36]
28	Ivy Gourd	*Coccinia grandis*	*Cucurbitaceae*	Tendril	South/Southeast Asia, East Africa	[35,37,38]
29	Jewel of Opar	*Talinum paniculatum*	*Talinaceae*	Weak scrambling	Central/South America	[42,48]
30	Kangaroo Vine	*Cissus antarctica*	*Vitaceae*	Tendril	Australia	[54,62]
31	Madagascar Jasmine	*Stephanotis floribunda*	*Apocynaceae*	Twining	Madagascar	[55,60]
32	Malaysian Orchid	*Medinilla myriantha*	*Melastomataceae*	Scrambling	Philippines	[63,67]
33	Morning Glory	*Ipomoea purpurea*	*Convolvulaceae*	Twining	Tropical America	[69,70,71]
34	New Guinea Trumpet Vine	*Tecomanthe dendrophila*	*Bignoniaceae*	Twining	New Guinea	[72,73]
35	Passionflower	*Passiflora edulis*	*Passifloraceae*	Tendril	South America	[74,76]
36	Pink Trumpet Vine	*Podranea ricasoliana*	*Bignoniaceae*	Scrambling	Southern Africa	[75,83,86]
37	Rangoon Creeper	*Combretum indicum*	*Combretaceae*	Hook-scrambling	Southeast Asia	[85,87]
38	Rosary Vine	*Ceropegia woodii*	*Apocynaceae*	Twining	Southern Africa	[88,91,92]
39	Shatavari	*Asparagus racemosus*	*Asparagaceae*	Scrambling/hook (cladode-thorn)	South/Southeast Asia	[95,96,99]
40	Snail Vine	*Vigna caracalla*	*Fabaceae*	Tendril/twining	South America	[98,100,102]
41	Spanish Jasmine	*Jasminum grandiflorum*	*Oleaceae*	Scrambling	Himalayan foothills	[103,123,128,130]
42	Star Jasmine	*Trachelospermum jasminoides*	*Apocynaceae*	Twining/adventitious-root	East Asia	[112,131]
43	Sweet Potato	*Ipomoea batatas*	*Convolvulaceae*	Trailing/twining	Tropical America	[104,109,110]
44	Swiss Cheese Plant	*Monstera deliciosa*	*Araceae*	Adventitious-root	Central America	[105,106,107,108]
45	Guduchi / Tinospora	*Tinospora cordifolia*	*Menispermaceae*	Twining	South/Southeast Asia	[113,116,117]
46	Trumpet Creeper	*Campsis radicans*	*Bignoniaceae*	Adventitious-root	North America	[118,119]
47	Vanilla	*Vanilla planifolia*	*Orchidaceae*	Adventitious-root	Mexico/Central America	[120,132]
48	Wild Yam	*Dioscorea spp.*	*Dioscoreaceae*	Twining	Pantropical	[121,122]
49	Wisteria	*Wisteria sinensis*	*Fabaceae*	Twining	East Asia (subtropical cultivation)	[124]
50	Hadjod	*Cissus quadrangularis*	*Vitaceae*	Tendril	South Asia/Africa	[127,129]

4. Phytochemical Diversity of Tropical Vining Plants

Six large chemical classes of phytochemicals are discussed in general as a common chemical signature to the tropical vining habit, for six of the fifteen species profiled in Table 2: alkaloids, flavonoids and anthocyanins, terpenoid and steroidal saponins, terpenoids, phenolic acids, and polysaccharides.

The plant's classical classification as Amrita ("nectar of immortality") in Ayurvedic pharmacopoeia 32-34 is mainly due to the presence of isoquinoline alkaloids berberine, palmatine, diterpenoid furanolactones tinosporide and tinosporine, and a phenolic glycoside cordifolioside A. Piper nigrum, whose principal bioactive component is Piper nigrum, represents a class of chemistry more closely related to the alkamides, which include structures related to Piper longum that have been found to be possess anti-inflammatory and antineoplastic activity 15,17,35.

They are especially abundant in their flower and leaf tissues and have flavonoids and anthocyanins. The extracts of C. ternatea flowers provide a family of pH-responsive polyacylated delphinidin based anthocyanins known as ternatins that are known to contain antioxidant and possibly nootropic properties and can be employed in the nutrition industry as natural food colourant and pH indicator, as well as in the pharmaceutical industry for therapeutic use 36-39. Other anthocyanosides found in purple flesh varieties of Ipomoea batatas have also been reported to have antiproliferative activity against breast, gastric and colorectal cancer cell lines with both extrinsic and intrinsic pathways of apoptosis induction as part of the mechanism 5,40. In addition to anxiolytic mechanism 41-43, which implies a GABAergic action, passiflora species contain a unique fingerprint of C-glycosylflavones (vitexin, isovitexin and orientin), which have been mechanistically linked to non-GABAergic actions of plant compounds, including opioid receptor action and monoaminergic systems 41-43.

Phytochemistry of Asparagus racemosus and Dioscorea spp. is represented by saponins, which are steroids and triterpenoids. Dioscorea spp. is a family of plants and herbs that have been used traditionally for female reproduction tonic and as a rasayana (rejuvenative) herb; another class of steroids, the steroidal saponins 12,13,44 A of which derives from Shatavari root, diosgenin, may be found in a directly relevant and historically significant way between a tropical vine phytoconstituent and a twentieth century pharmaceuticals industry.

Momordica charantia is composed of two kinds of molecules, namely, cucurbitane-type triterpenoids and glycopeptides, which include charantin (two steroidal saponins) along with momordicosides Q/S/T, karaviloside XI and the insulin-mimetic polypeptide-p, that have been well documented for their hypoglycemic activity. Also terpenoid rich are Coccinia grandis (taraxerol) and Cissus quadrangularis (β-sitosterol and related phytosterols) which are peculiar for their pharmacology on bone-healing and anti-osteoporotic action, based on the synergy between the steroidal component and flavonoids 50-52, 52-54.

Vanilla planifolia pods when cured yield Vanillin as the major flavoursome and bioactive constituent along with Vanillic acid, p-hydroxybenzaldehyde and a number of flavonoids (rutin, quercetin, myricetin and kaempferol) which together exhibit interesting antioxidant, antimutagenic and emerging antidiabetic and anticancer activity 53,54,55,56. Finally, recently, a first class (and more recently macromolecules) of immunomodulatory polysaccharide fractions has been identified, most understood of which is the cytokine-modulating activity of Tinospora cordifolia macropharmacology. The number of representative constituents has been summarized in Table 2 and these six classes of phytochemicals colocated in a common multi-target pharmacological context in Figure 2.

Table 2. Principal phytochemical classes and representative bioactive constituents in fifteen pharmacologically well-characterised tropical vining species.

Species	Family	Major phytochemical classes	Representative bioactive constituents	Plant part(s) studied	Representative References
Tinospora cordifolia	*Menisperm aceae*	Alkaloids, glycosides, diterpenoid lactones,	Berberine, palmatine, tinosporine,	Stem, leaves, roots	[12,23]

		steroids, sesquiterpenoids	tinosporide, cordifolioside A		
Momordica charantia	*Cucurbitaceae*	Cucurbitane triterpenoids, steroidal saponins, peptides, phenolics	Charantin, momordicoside Q/S/T, karaviloside XI, polypeptide-p	Fruit, seeds, leaves, vines	[45,46,47]
Clitoria ternatea	*Fabaceae*	Anthocyanins (ternatins), flavonol glycosides, triterpenoids	Delphinidin/cyanidin-based ternatins, apigenin, clitorin	Flowers, roots, leaves	[17,18,19]
Piper nigrum	*Piperaceae*	Alkamides, essential oils, lignans	Piperine, piperlongumine-related alkamides, β-caryophyllene	Fruit (peppercorn)	[11,20]
Passiflora edulis	*Passifloraceae*	Flavonoids, saponins, cyanogenic glycosides	Vitexin, isovitexin, orientin, saponins	Leaves, fruit peel/rind	[51,52,60]
Asparagus racemosus	*Asparagaceae*	Steroidal saponins, polyphenols, alkaloids	Shatavarin I-IV, sarsasapogenin, racemosol, diosgenin	Roots	[21,25]
Bougainvillea spectabilis	*Nyctaginaceae*	Flavonoids, betalains, terpenoids, D-pinitol	Quercetin, kaempferol, D-pinitol, bougainvinones	Leaves, bracts, stem bark	[22,27,28]
Coccinia grandis	*Cucurbitaceae*	Alkaloids, flavonoids, coumarins, terpenoids	Cephalandrol, taraxerol, lupeol	Leaves, fruit, roots	[13,29,30,32]
Jasminum sambac	*Oleaceae*	Iridoid glycosides, flavonoids, essential oils	Jasminin, jasmonic acid derivatives, benzyl acetate	Flowers, leaves	[94,97]
Vanilla planifolia	*Orchidaceae*	Phenolic aldehydes, flavonoids	Vanillin, vanillic acid, p-hydroxybenzaldehyde, rutin	Cured pods (beans)	[55,61,62]
Ipomoea batatas	*Convolvulaceae*	Anthocyanins, phenolics, carotenoids	Peonidin- and cyanidin-based anthocyanins, chlorogenic acid	Tuberous root, leaves	[116,117]
Combretum indicum	*Combretaceae*	Alkaloids, flavonoids, tannins, saponins	Quisqualic acid, quercetin, rutin	Flowers, seeds, roots	[86,129]
Dioscorea spp.	*Dioscoreaceae*	Steroidal saponins	Diosgenin, dioscin, gracillin, deltonin	Tuber (rhizome)	[123,124,125]
Cissus quadrangularis	*Vitaceae*	Steroids, flavonoids, carotenoids, ascorbic acid	β-sitosterol, quercetin, kaempferol	Stem	[65,66,67]
Aristolochia spp.	*Aristolochiaceae*	Nitrophenanthrene carboxylic acids (aristolochic acids)	Aristolochic acid I and II	Roots, stem (medicinal use now restricted)	[101,102]

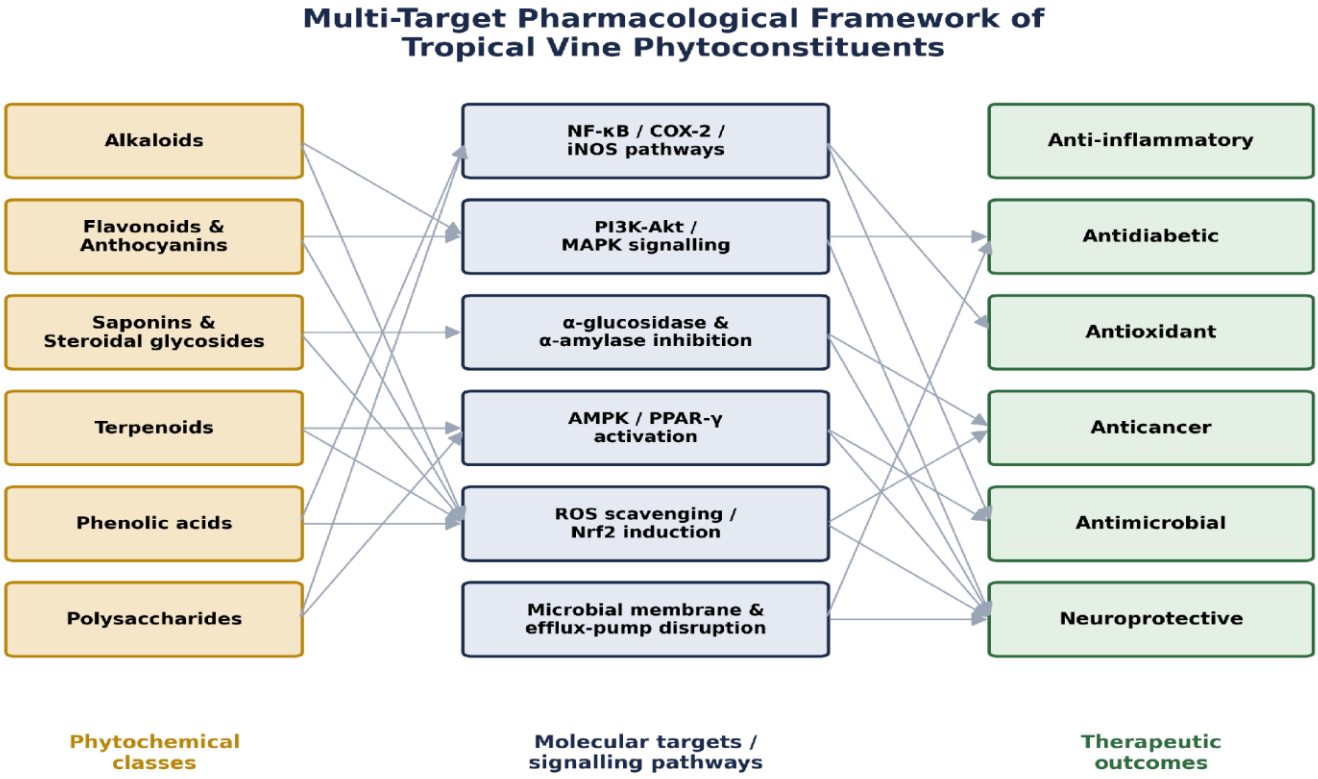


Figure 2. Multi-target pharmacological framework linking major phytochemical classes of tropical vines to molecular targets and therapeutic outcomes.

5. Multi-Target Pharmacological Properties

As concluded from the pharmacologic literature analyzed here, vining plants from the tropics show very few cases of a single and isolated bioactivity: the typical pattern is one of overlapping activities, with various mechanisms, and comprising anti-inflammatory, antioxidant, antidiabetic, antimicrobial, anticancer and neuropharmacological activity, summarized in the activity matrix of Table 3. Each class of activities is discussed in turn, focusing on the common and distinct molecular mechanisms displayed in Table 4.

Anti-inflammatory activity. Translocation of NF-κB into the nucleus and the subsequent expression of COX-2 and iNOS are the most consistently reported mechanism for anti-inflammatory activity in the species reviewed. Mechanistically, piperine is shown to block NF-kB-dependent transcription of pro-inflammatory cytokines in models of nervous, cardiovascular and gastrointestinal diseases supporting the traditional use of Piper nigrum in inflammatory and febrile diseases 35,60,61. As opposed to the more widely studied fruit, the Momordica charantia triterpenoids isolated from the charcoalated vine and leaves, have similar NF-κB and cytokine-suppressive activity 21. The anxiolytic effect of Passiflora edulis leaves is in fine parallel to the other classical indications, such as the inhibiting effects on the secretion of inflammatory mediators induced by the separation into its flavonoids and saponins fractions.

Antidiabetic activity. Tropical vines have several convergent mechanisms in their pharmacology against Diabetes. The actions of Momordica charantia are known to be via activation of AMPK pathways, inhibiting α-glucosidase and α-amylase, through increased insulin secretion from the pancreas and through enhanced glucose uptake periferally 19,20,21. The extracts from the leaves of Coccinia grandis have similar α-glucosidase inhibitory activity and insulin sensitising effects on in vivo and in vitro models 24. The antioxidant anti-diabetic effect of Bougainvillea spectabilis is accomplished in significant part by the presence of D-pinitol, which is a cyclitol that has insulin-mimetic signalling properties and is known to protect pancreatic β-cell tissue from oxidative stress 53,63. Measuring insulin-resistance amelioration effects of Tinospora cordifolia in related diseases like polycystic ovary syndrome

provides evidence of its endocrine-modulatory activity as well as insulin-resistance.

Antioxidant activity. Free-radical scavenging (DPPH, ABTS, FRAP assays) and induction of endogenous antioxidant defence (Nrf2/antioxidant response-element pathway) are found in almost all the 15 targeted species, showing the ubiquity of phenolics, flavonoids and anthocyanins intrinsic to their radical quenching capacity. Ternatin anthocyanins extracted from Clitoria ternatea and peonidinrich anthocyanins from Ipomoea batatas show specially high in vitro radicalscavenging activity with mechanistic investigations suggesting catalase and superoxide dismutase upregulation are mechanisms involved in the protective action of such anthocyanins in metabolic tissues 36–40,64.

Antimicrobial activity. The mechanisms of action of the different species reviewed above include action on bacterial membrane disruption, efflux-pump inhibition, and biofilm disruption and/or quorum-sensing disruption, which are relevant pathways in contemporary medical practice, due to the rapidly growing global challenge of antimicrobial resistance 60,65-67. Extracts of Bougainvillea glabra and B. spectabilis exhibit anti-bacterial (Gram-positive and Gram-negative) activity, with more potent activity of anthocyanin-rich fractions compared with crude extracts in some comparative tests against Gram-positive (Bacillus) and Gram-negative (Escherichia coli) strains 68. It is now suggested that this polyvalent, multi-target nature of these phytochemical antimicrobial mechanisms is beneficial when compared to single-target synthetic antibiotics insofar as simultaneous disruption of multiple pathways of bacterial survival may be less selective for the emergence of resistance 69,70.

Anticancer activity. The majority of anticancer effects reported are related to cell-cycle arrest, mostly at the G2/M and G0/G1 phases of cell cycle, or to induction of apoptosis through both death-receptor and mitochondrial (intrinsic) pathways. Vanillin not only blocks proliferation of CRC cells in G2/M phase but also in the G0/G1 phase and possesses antimutagenic effect in independent genotoxicity models 29,53 indicating that vanillin can act as a chemopreventive agent as well as directly being a cytotoxic agent. In the case of gastric carcinoma, both the mechanism of action of piperine as an anticancer agent and the list of targets has been resolved at the multi-omics level to converge on ACOT1 modulation, clearly demonstrating the value of systems-level target deconvolution for botanically derived polypharmacological agents 18. Anthocyanin extracts from I. batatas inhibit cancer cell proliferation of three cell lines, including the human breast adenocarcinoma MCF-7, gastric adenocarcinoma SNU-1 and colon adenocarcinoma WiDr, by inducing apoptosis and blocking adenoma formation in APCMIN mice fed anthocyanin-enriched diets 5,40.

Neuropharmacological activity. Passiflora species (both P. edulis and its close relative P. incarnata) have the most advanced range of clinical evidence from neuropharmacological studies reviewed (randomised controlled trials), showing anxiolytic and sleep-promoting effects, primarily through modulation of GABA-A and GABA-B receptors, but with emerging evidence suggesting other contributions, notably from opioidergic, monoaminergic and glutamatergic mechanisms 41,43,71,72. Asparagus racemosus contains sarsasapogenin which is a multi-target-directed ligand of Alzheimer's disease pathological-related amyloid-β aggregates, and increasing of anti-ageing gene expression in Parkinsonian models by shatavarin IV. Clitoria ternatea continues to have its traditional Ayurvedic classification as medhya rasayana (cognitive tonic) and there is no scientific evidence to support the nootropic and neuroprotective properties of Clitoria ternatea based on its anthocyanin and triterpenoid contents.

Other notable activities. In addition to the six main categories above, there are some species with specialised bioactivities of independent translational interest: for instance, in the case of Tinospora cordifolia 58,75, its immunomodulatory and hepatoprotective properties; Piper nigrum 15,16, its role as a bioavailability enhancer (bioenhancer) for co-administered therapeutic agents via modulation of CYP450 and P-glycoprotein; Cissus quadrangularis with its sole activity known via bone fracture healing and anti-osteoporotic pharmacology that is mechanistically linked to the compound quisqualic acid along with its flavonoids (14) and, last but not least, Irvingia gabonensis's exceptional capability to combat obesity in human subjects, as evidenced by a randomized Placebo Controlled double blind clinical trial (50).

Table 3. Multi-target pharmacological activity matrix of fifteen focal tropical vining species (✓ = activity substantiated by preclinical/clinical evidence).

Species	Anti-inflammatory	Anti-oxidant	Anti-diabetic	Antimicrobial	Anticancer	Neuro-pharmacological	Other notable activity	Representative References
Tinospora cordifolia	✓	✓	✓	✓	✓	–	Immunomodulatory, hepatoprotective	[14,17]
Momordica charantia	✓	✓	✓	✓	✓	–	Cardioprotective, hepato-renal protective	[22,23,25]
Clitoria ternatea	✓	✓	✓	✓	✓	✓	Nootropic/memory-enhancing	[27,29]
Piper nigrum (piperine)	✓	✓	–	✓	✓	✓	Bioavailability enhancer (bioenhancer)	[30,32,33,34]
Passiflora edulis / incarnata	✓	✓	✓	–	–	✓	Anxiolytic, sedative (clinical trials)	[56,62,63]
Asparagus racemosus	✓	✓	–	✓	✓ (in vitro)	✓	Galactagogue, antiulcerogenic	[45,47,48]
Bougainvillea spectabilis	✓	✓	✓	✓	–	–	Antihyperlipidaemic, hepatoprotective	[66,67,68]
Coccinia grandis	✓	✓	✓	✓	✓ (in vitro)	–	Anti-Alzheimer's (emerging), wound healing	[71]
Jasminum sambac	✓	✓	– (emerging)	✓	–	–	Antipyretic, sedative	[75,76,77]
Vanilla planifolia (vanillin)	–	✓	✓ (emerging)	–	✓ (in vitro)	–	Antimutagenic/genoprotective	[80,82,89]
Ipomoea batatas	✓	✓	✓	–	✓ (in vitro)	–	Antihyperlipidaemic	[90,111]
Combretum indicum	✓	✓	✓	✓	–	–	Anthelmintic (classical use)	[121,132]
Dioscorea spp.	✓	✓	✓ (variable)	–	✓ (diosgenin-mediated)	–	Steroid-precursor (diosgenin)	[102,118,119]
Cissus quadrangularis	✓	✓	✓	–	–	✓ (anxiolytic/antiepileptic)	Bone-fracture healing, anti-osteoporotic, anti-obesity	[100,103]
Aristolochia spp.	✓ (historical)	–	–	✓ (historical)	–	–	Nephrotoxic/carcinogenic – clinical use discontinued	[125,126,129]

Table 4. Representative molecular targets and signalling pathways underlying the principal pharmacological activity classes of tropical vine phytoconstituents.

Activity class	Principal molecular targets / pathways	Representative phytoconstituents	Representative References
Anti-inflammatory	NF-κB, COX-2, iNOS, TNF-α, IL-6 suppression	Piperine, quercetin, kaempferol, vitexin, berberine	[72,89]
Antidiabetic	AMPK activation, PPAR-γ agonism, α-glucosidase/α-amylase inhibition, GLUT4 translocation, β-cell protection	Charantin, D-pinitol, shatavarins, cucurbitane triterpenoids	[12,13,14]
Antioxidant	Nrf2/ARE pathway induction, DPPH/ABTS radical scavenging, SOD and catalase upregulation	Anthocyanins (ternatins, peonidins), vanillin, phenolic acids	[20,23,24,25]
Antimicrobial	Bacterial membrane disruption, efflux-pump inhibition, biofilm/quorum-sensing interference	Piperine, tannins, saponins, alkaloids	[92,98]
Anticancer	Cell-cycle arrest (G2/M, G0/G1), apoptosis induction (intrinsic/extrinsic pathways), ACOT1 and PI3K-Akt modulation	Vanillin, piperine, triterpenoids, anthocyanins	[29,30,31]
Neuropharmacological	GABA-A/GABA-B receptor modulation, acetylcholinesterase inhibition, monoaminergic and opioidergic modulation	Passiflora flavonoids, sarsasapogenin, ternatin anthocyanins	[59,60,61,62]
Immunomodulatory	Macrophage activation, cytokine network modulation, NK-cell stimulation	Tinospora polysaccharides, cordifolioside A, shatavarin IV	[78,80,81]

6. From Ethnomedicine to Modern Drug Discovery: Network Pharmacology and Multi-Target Approaches

The movement from ethnomedical observation towards the "-omics" approach in rational design of drug discovery is increasingly being facilitated by a systems-level analytical framework called network pharmacology, which rethinks botanical extracts as multi-component and multi-target therapeutic systems instead of impure, single-target medicines 22,23,25. The general steps of two promising methods are usually network pharmacology approaches: compound identification (by LC-MS/MS or other similar analysis platforms), target prediction (by reverse docking or database mining based on resources like TCMSP, DrugBank, STRING, etc) and constructing compound-target-pathway interaction networks, followed by the molecular docking and the in vitro / in vivo bioassay 25,77. This approach has been praised for helping elucidate many modern natural products that it has added to the understanding of the mechanistic action of herbal medicines, which historically were considered as “one herb, many effects”, and transformed to “one compound, multiple targets, multiple diseases” 77-79.

Network pharmacology methodology has the particular advantages when applied to the species of this review: first, it visualizes multi-species interactions, second, it reveals the direct interaction between species, and third, it extends the investigation to include species outside the species being studied. First, it offers a philosophical framework to guide the selection of the most promising and most relevant of the countless phytoconstituents that might be found in a crude extract for isolation and mechanistic study, based on the target-connectivity and disease-relevance scores of the compounds, rather than merely on the traditional-use inferences. Secondly, it provides a rational way to investigate synergic or antagonistic interactions among co-occurring phytoconstituents, a phenomenon commonly seen in polyherbal Ayurvedic and Traditional Chinese Medicine (TCM) formulations but hard to research in a way that fits the mould of the pharmacology of singly administered compounds (55,80,81). Third, it enables drug-repurposing analysis in which known "phytoconstituents" (piperine, diosgenin and other compounds) are computationally tested against emergent databases of drugs designed against specific disease targets, thereby generating novel therapeutic applications 27,82.

History has demonstrated that the wealth of knowledge regarding the phytochemistry of tropical vines has been translated into modern

medicine with great success. The Dioscores, in particular Diosgenin, isolated from species of Dioscorea spp., has been used for decades as the main industrial precursor for the semi-synthetic production of corticosteroids and oral-contraceptive steroids - one of the most important pharmaceutical contributions of any tropical vining species examined 45. Natural products and their semisynthetic counterparts, more globally, have seen a substantial representation - historically, in excess of one-third - of all newly approved small molecule therapeutics (SMTs) across therapeutic areas and even higher percentages in the oncology class of therapeutics 83-85. Table 5 presents a summary of the current standing of eight representative phytoconstituents from the tropical vinelands discussed in this review, from the fully industrialized use of diosgenin to the preliminary (preclinical) characterization of sarsasapogenin as a multi-target-directed neuroprotective ligand.

The overall translational journey from ethnobotanical documentation to bioassay-guided fractionation, target identification by network pharmacology, preclinical pharmacological and toxicological evaluation and the ultimate clinical translation is illustrated in figure 3. Accordingly, the current approach to drug discovery is increasingly adopting multi-omics (transcriptomics, proteomics, metabolomics), network pharmacology, as well as computational led by artificial intelligence (AI)-based prediction of compounds and their targets, which should bring speed to this pipeline and which is particularly adapted to the multi-component chemistry of vining plants from tropical regions 54,86.

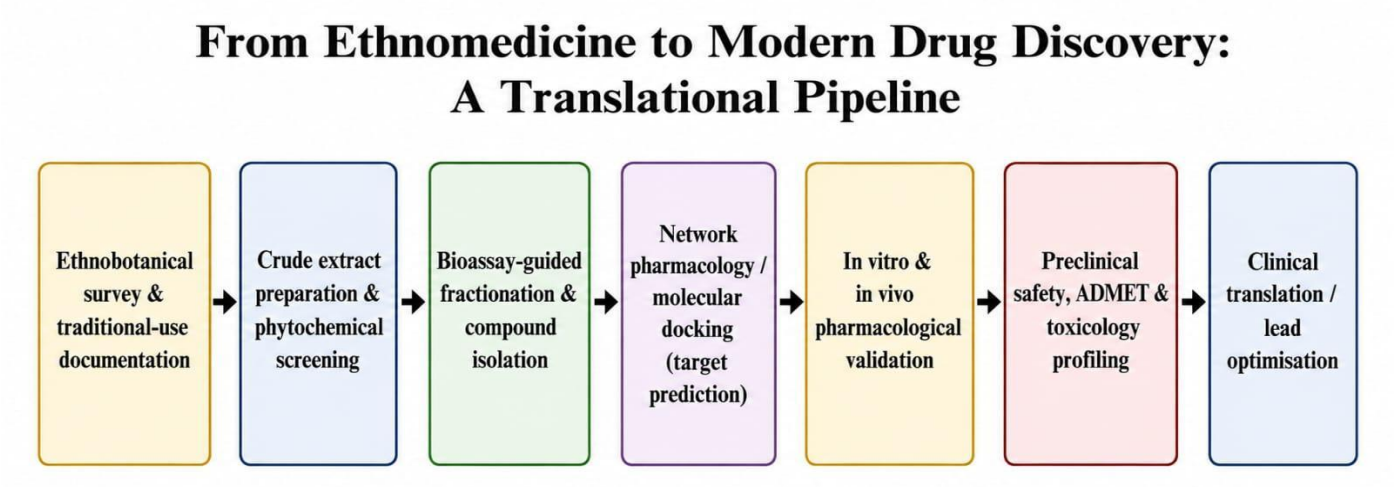


Figure 3. Translational pipeline connecting ethnobotanical documentation to modern, network pharmacology-guided drug discovery.

Table 5. Selected tropical vine-derived phytoconstituents at varying stages of the translational drug-discovery pipeline.

Phytoconstituent	Source species	Reported mechanism/target	Stage of development	Representative References
Piperine	*Piper nigrum*	NF-κB/COX-2 inhibition; CYP450 and P-glycoprotein modulation (bioenhancer)	Marketed nutraceutical bioenhancer; nanoparticle formulations in preclinical testing	[14,16,17,18]
Diosgenin	*Dioscorea spp.*	Steroidogenic precursor; PPAR-γligand	Industrial steroid-synthesis feedstock; anticancer leads in preclinical study	[33,38,39,40]

Charantin / cucurbitane triterpenoids	*Momordica charantia*	AMPK activation; insulin-secretagogue activity	Standardised extracts in clinical nutraceutical use; mechanism elucidation ongoing	[41,42]
Ternatin anthocyanins	*Clitoria ternatea*	Nrf2 induction; antioxidant/nootropic signalling	Functional-food colourant; cognitive-health formulations in early clinical study	[63,64,65]
Sarsasapogenin	*Asparagus racemosus*	Multi-target-directed ligand in amyloid aggregation (Alzheimer's disease)	Preclinical multi-target neuroprotective lead	[36,47,69]
Vanillin	*Vanilla planifolia*	Antimutagenic/genoprotective activity; G2/M cell-cycle arrest	Widely used flavour compound; anticancer nanoparticle delivery in preclinical study	[12,13,20]
D-Pinitol	*Bougainvillea spectabilis*	Insulin-mimetic signalling; pancreatic antioxidant protection	Nutraceutical antidiabetic supplement	[85,89]
Aristolochic acid	*Aristolochia spp.*	DNA adduct formation (dA-AL I, dG-AL I)	Withdrawn/restricted – regulatory case study in botanical safety	[99,112,113,114]

7. Safety, Toxicity, and Regulatory Considerations

Caution should be expressed when considering vining tropical plants in any program of rational bioprospecting, whether to guarantee their safety, standardize the acquired material, or to consider regulatory precedents, as illustrated by the genus aristolochia. Some species of this genus are traditionally employed in the ethnomedical treatment of ailments such as antipyretic, antimicrobial, and anti-inflammatory properties, and have been found to contain aristolochic acids I and II, which are now well established as strong nephrotoxins, genotoxins, and human carcinogens 51,87. Aristolochic acid metabolites form very characteristic DNA adducts (dA-AL I and dG-AL I) linked to a unique mutational signature which has been linked to the occurrence of urothelial carcinoma of the upper urinary tract, and chronic dietary exposure of the sun is now known to be linked to the development of Balkan endemic nephropathy.

There are three broad lessons that can be drawn from the aristolochic acid precedent that are relevant to this present review. In the first place, it is not possible to extrapolate generic level safety to a specific level because of the necessity for phytochemical and toxicological screening at the species level but not the genus level when constituents of various genera are pharmacologically similar. Second, extensive past or traditional use per se does not make something long-term safe, especially if used at low doses over extended periods that will not develop toxicity during the period of observation in empirical traditional use. Third, botanical adulteration and misidentification – there are documented cases of contamination of remedies completely unrelated to the disease in question, but in the case of weight loss/ slimming product status, often found in herbal slimming/ weight loss remedies – is a responsibility gap in the herbal medicine supply chain which remains both persistent and largely unaddressed.

In addition to Aristolochia, the general tropical vine pharmacopoeia is ridden with standardisation problems. The conditions under which production grows, the season for harvesting, the plant part extracted, extraction solvent and post-harvest processing all have significant effects on the phytochemical content, which further makes it difficult to find reproducibility of the pharmacological findings and uniformity of the commercial herbal products 68,73. For instance, the content of asparagus racemosus saponin is variable by several folds based on cultivation site and source (cultivated or wild) of the root 43. The same applies to antimicrobial susceptibility testing of polyphenolic compounds isolated from plants, for which no standardisation of methodology is available among various laboratories confining comparability from study to study. All these results collectively reinforce the importance of the analytical standardisation, in the form of marker-

compound quantifications by a validated HPLC or LC-MS/MS method, as a prerequisite for any tropical vine phytoconstituent that is moving forward to clinical development.

8. Conservation and Sustainability of Tropical Vining Medicinal Plants

While the pharmacologic potential cited in this review is proven, it exists in a "tension" with the increasing awareness of population loss within the wild vining medicinal plants in tropics and subtropics.The pharmacologic promise outlined throughout this review coexists with increasing awareness of population loss of wild vining medicinal plants in tropics and subtropics. The combined effects of habitat destruction, illegal and unregulated long-distance harvesting for the herbal-medicine market and the progress of climate-driven range-shifts pose a significant risk to a significant proportion of species recorded as wild resources: current scoping analysis shows that a large majority of medicinally important plant sources are still wild-harvested (89%) and that a large proportion are classed as critically endangered, endangered and vulnerable. Asparagus racemosus is a typical example of this; its ethnopharmacological review specifically stated that root harvest pressure has led to documented population decline and conservation concerns are considered as taking root harvest pressure on board so that continued pharmaceutical use of this species is areas of evident conservation concern.

These species also have traditional ecological and medicinal knowledge that is in danger. Poor ethnobotanical documentation and failure of the transfer of traditional knowledge from one generation to the next has been reported as two serious threats to plant species and the traditional knowledge associated with their use 90. This knowledge erosion is scientifically relevant: current phytochemical and pharmacological studies reviewed in this article are based on ethnobotanical claims that are often derived from traditional knowledge that is not systematically documented in peer-reviewed literature and therefore could risk irreversible loss as it is passed down to younger generations or as knowledge of its custodians fades 91,92,132.

Systematic ex situ conservation of genetic diversity (including seed banking and living collections in botanical gardens) 26,93,94, cultivation-based supply chains, tissue-culture and micropropagation methods; and community-based, sustainable wild-harvesting agreements which provide incentives for conservation in addition to traditional and commercial utilization are some of the sustainable bioprospecting strategies applicable to the tropical vines reviewed here. The preservation of undocumented and under-characterised tropical vining species may not only be an ecological necessity but also a limitation on future possibilities in natural product drug discovery 120,122,131.

9. Future Perspectives and Conclusion

Focusing on fifty representative tropical vining plants, this review has, for a subset of fifteen plants, detailedly evaluated the evidence regarding the phytochemical and pharmacological properties, and combined evidence at a summary level to analyse the plants. Three main ones are found particularly clearly. First, irrespective of the climbing mechanism used, the climbing growth habit is invariably accompanied by a phytochemically rich secondary metabolite profile dominated by alkaloids, flavonoids and anthocyanins, triterpenoid and steroidal saponins, terpenoids and phenolic acids possibly documenting resource allocation tradeoffs between chemical and structural defence. Secondly, the pharmacological activity of these phytoconstituents is in general a multi-target type and tends to converge on four large common targets, NF-κB/COX-2 inflammatory signalling, AMPK/PPAR-γ-dependent glucose homeostasis, Nrf2-dependent antioxidant defence, and apoptosis-regulating pathways, which is naturally consistent with the system-level analytical approach that network pharmacology provides. Third, although this pharmacological potential is found in all of the species studied, it is not automatically guaranteed for any species and, as the example of Aristolochia aristolochic acid stresses, toxicological characterisation of a species is still a critical need, in addition to proving efficacy, for species.

Moving forward, there are some key research questions to be highlighted. Network pharmacology and multi-omics characterisation should be expanded for the phytochemically promising species of adventitious-root and hook-scrambling vines outlined in Table 1, which have been under-investigated, with many species not yet characterised beyond a traditional use record or simple phytochemical analyses. In order to bring the pharmacology described above that is substantiated in the lab into a reproducible, controlled supply chain for clinical candidates, marker compounds need to be analytically standardised and culture-based supply chains need to be developed. Finally, the conservation of wild populations of tropical vines and their traditional ecological knowledge should not just be an environmental issue, but also a scientific priority because the future of the natural-product drug discovery “Promised Land” is ensured by the continued existence of the vines and their knowledge and expertise.

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