PROFESSIONAL ARTICLE

EvoS Journal:
Evolutionary Studies and Higher Education

Exploring the Interface between Plant Diversity and Culture: The Phylogeny as a Pharmacological and Pedagogical Tool cultivating Plant Appreciation in an Undergraduate Classroom

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ABSTRACT

Traditional medicine systems value herbal medicine with many cultures in developing countries still reliant on these practices to maintain health. Medicinal plants can be studied and compared using phylogenetic analysis to determine if related plants are used similarly by different cultures. These patterns of cultural convergence could highlight plant families of specific pharmacological importance. The phylogeny of medicinal plants has been previously shown to depict cultural convergence among immigrant groups in New York City (NYC). As part of a class project, undergraduate students of medicinal botany at Pace University-NYC reconstructed the phylogeny of traditionally used medicinal plants compiled from the class textbook (Heinrich et al., 2023, chp. 16), with their medicinal applications mapped on the phylogeny. Students were also asked to interview their elders to include a prominent medicinal plant from their cultural background. Ten families: Zingiberaceae, Ranunculaceae, Apiaceae, Solanaceae, Apocynaceae, Myrtaceae, Anacardiaceae, Malvaceae, Euphorbiaceae, and Rhamnaceae depicted patterns of cultural convergence and collectively were primarily used for gastrointestinal, musculoskeletal, and antibiotic/anti-parasitic applications. These patterns of cultural convergence suggest intrinsic phytochemistry shared by members of these families, resulting in their common medicinal uses that may be further investigated pharmacologically. Based on student feedback, the phylogeny was an effective pedagogical tool that allowed us to bridge multidisciplinary fields–traditional medicine, plant diversity, and evolutionary pharmacology, providing an interface that not only enriched student learning, but moreover, offered a novel approach that could facilitate drug discovery from plant natural products.

KEYWORDS

Drug Discovery, Ethnomedicine, Evolutionary Pharmacology, Herbal Medicine, Medicinal Plants, Natural Products, Phytochemistry

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INTRODUCTION

Herbal medicine is the use of plants or plant products for healing or therapeutic purposes. Humans have used plants and other natural products as medicine to heal wounds and treat ailments since prehistoric times (Yuan et al., 2016). Many indigenous cultures around the world have knowledge of different medicinal plants that have been passed down for centuries (Ahmad et al., 2013). Traditional medicines are extremely significant to this day, as they can be the only form of healthcare available in certain parts of the world. Herbal medicines have been used to maintain general health and well-being, as well as to relieve symptoms of numerous chronic conditions such as cancer, asthma, or rheumatoid arthritis (Heinrich et al., 2023).

Several traditional herbal medicines have served as the basis for important pharmaceutical drug discoveries (Fabricant & Farnworth, 2001). Analgesics like morphine and aspirin, antimalarials such as artemisinin and quinine, and anticancer drugs such as irinoctan are some examples of pharmaceuticals developed from plants with traditional uses (Fabricant & Farnsworth, 2001). Willow bark (*Salix* spp.) infusions have been used for centuries for their analgesic and antipyretic effects, and this led to their clinical development into aspirin by the Bayer pharmaceutical company in 1899 (Rubira, 2011; Heinrich et al., 2023). Atropine, a derivative of plants like *Atropa belladonna* and *Mandragora officinarum* (Solanaceae), has been noted by Greek philosopher Theophrastus in the 4th c. BC as being useful for sleeplessness, while Dioscorides listed wine of mandrake as a possible anesthetic in the 1st c. AD (Holzman, 1998). Originally isolated from *A. belladonna* leaves in 1833, atropine now serves as an essential pharmaceutical for treating acute arrhythmias and for dilating pupils (Heinrich et al., 2023). Similarly, digoxin, extracted from *Digitalis lanata* leaves in 1930, was heralded by William Withering in 1785 for its efficacy in managing heart failure, known then as "dropsy" (Cartwright, 2015; Heinrich et al., 2023). Today, digoxin is still used in treating tachycardia and heart failure (Heinrich et al., 2023). These instances exemplify the invaluable contributions of traditional medicine to modern drug discovery.

An important part of the modern pharmaceutical drug discovery process is searching for new natural products to test. Most large pharmaceutical companies have the capability to screen at least 1,000 or more substances a week via high throughput in vitro assays, and so they are driven to find expeditious ways of obtaining new natural products to test (Fabricant & Farnsworth 2001). Pharmaceutical companies may execute random selection of natural products to test, in which discovered bioactivity may be serendipitous; or a chemotaxonomic approach, in which prior knowledge from closely related plants is used to inform natural products to screen; or ethnobotanical, wherein knowledge by an indigenous group for a particular plant informs the screening process. Information-driven approaches use a combination of these, linked in a database to avoid repeated discovery of known compounds (dereplication, Heinrich et al., 2023). In a recent review, Davis and Choisy (2024) called for a holistic, interdisciplinary approach combining evolutionary ecology, molecular biology/biochemistry, and ethnopharmacology to catalyze pharmacological discoveries.

The phylogeny can be utilized as a tool to interface between ethnomedicine and plant diversity. The predictive potential of phylogenies offers an opportunity for

bioprospecting from traditional medicine, as originally exemplified by Saslis-Lagoudakis et al. (2012). By assigning traits to nodes rather than individual taxa, phylogenies may offer an alternative or complementary method to the approaches traditionally employed by pharmaceutical companies, thus enhancing the prospects for pharmacological discoveries. For example, Guzman and Molina (2018) conducted a phylogenetic investigation involving 139 plant species to identify potential new sources of cardiovascular drugs. Seven of the 71 plant families were identified as pharmacologically significant, given that many members of these families shared a common cardiovascular mechanism of action (Guzman & Molina 2018). They found that Apiaceae and Brassicaceae exhibited diuretic and antihypertensive properties, while Fabaceae and Lamiaceae displayed thrombolytic/anticoagulant activity (Guzman & Molina 2018). This also implies that untested members of Apiaceae or Brassicaceae, for example, could be pharmaceutically developed into new diuretic medication. Other studies conducted by Alrashedy and Molina (2016) and Prasad et al. (2019) have demonstrated the significance of the plant phylogeny in identifying families rich in natural products possessing psychoactive and antibiotic properties, respectively. These studies underscore the potential for pharmaceutical companies to strategically focus on these botanical groups in their bioprospecting endeavors.

Interfacing between chemotaxonomy and ethnobotany, Xavier and Molina (2016) used a plant phylogeny to look for patterns of cultural convergence in traditional uses of medicinal plants among immigrant groups in New York City (NYC), one of the most ethnically diverse cities in the world. The confluence of various immigrant cultures within this city, coupled with the widespread availability of their traditional herbal remedies, makes NYC an intriguing venue for exploring the intricacies of urban ethnobotany. Xavier and Molina (2016) defined cultural convergence as multiple cultures using related medicinal plants within a group or clade similarly, possibly arising from independent discoveries of these plants' medicinal uses, and could be indicative of evolutionarily conserved bioactivity within the clade that may be further explored pharmacologically. After surveying immigrant herbal store owners for medicinal plants, they carry and subsequently reconstructing the phylogeny of these plants, 10 plant families demonstrated cultural convergence and were important in the traditional medicine practices of immigrant cultures. For example, many members of Apiaceae and Zingiberaceae were found to have been disproportionately used for gastrointestinal concerns (Xavier & Molina 2016). Additional plants from Native American and Western herbalism were added to the phylogenetic scaffold in Xavier and Molina (2016), highlighting the relative importance of small ordinal clades such as Dipsacales and Fagales for their applications in nervous and gastrointestinal uses, respectively (Molina, 2018).

In this study, we similarly used the plant phylogeny to identify patterns of cultural convergence of medicinal plant uses among different cultural groups, as tabulated in chapter 16 of Heinrich et al. (2023). This was undertaken as part of a collaborative project in an undergraduate medicinal botany class offered at Pace University-NYC in Fall 2023. The diverse cultural backgrounds of the 16 students in the class presented a pedagogical advantage, as they were tasked with interviewing their elders to identify a prominent medicinal plant species for integration into the phylogeny. Elucidating patterns of cultural convergence in this study did not only highlight pharmacologically relevant plant clades, but consequently impressed upon

the students the vital intersection between ethnomedicine and plant diversity in guiding natural product research. By integrating phylogenetic analysis, ethnobotanical knowledge, and student-driven research, our study aims to bridge traditional medicinal practices with modern pharmacological discovery while also serving as an educational tool in undergraduate botany courses.

MATERIALS AND METHODS

Bio 296D was a new undergraduate course in medicinal botany first offered at Pace University-NYC in Fall 2023 with 16 students. The textbook for the class was "Fundamentals of Pharmacognosy and Phytotherapy" by Heinrich et al. (2023). The final class project was to find patterns of cultural convergence by reconstructing the phylogeny of traditional medicinal plant species enumerated by Heinrich et al. (2023) in chapter 16, representing Western (Table 16.1.1: including European and North American medicinal traditions, incorporating Anglo-American, Germanic, and Mediterranean herbal practices), East Asian (16.2.2: traditional medicinal systems from China, Japan, and Korea), Ayurvedic (16.3.4: represents plants used in Ayurvedic, Siddha, and Unani medicine, which are practiced in India), Southeast Asian (16.3.6: traditional herbal medicine practices from Indonesia, Malaysia, and Singapore), African (16.4.1: ethnobotanical knowledge systems across the African continent), American (16.5.1: includes indigenous medicinal knowledge from North, Central, and South America), Australian (16.6.1: medicinal plants in aboriginal Australia), and Māori (16.6.2: representing the indigenous Rongoā Māori medicinal practices of New Zealand) cultures–consolidated into Table 1 here.

Table 1. Consolidated list of traditional medicinal plants from various cultures compiled by Heinrich et al. (2023) in chapter 16, and their medicinal applications. Medicinal plants provided by students are indicated by "*".

Plant Species	Family	Traditional medicinal uses	Culture
Sambucus nigra	Adoxaceae	R	Western
Carpobrotus glaucescens	Aizoaceae	S	Australian
Allium sativum	Amaryllidaceae	CV	Western
Boophone disticha	Amaryllidaceae	N, MS, S	African
Anacardium occidentale	Anacardiaceae	GI, CV, AB	Southeast Asian

Mangifera indica	Anacardiaceae	GI, R, MS	Ayurvedic
Semecarpus anacardium	Anacardiaceae	MS, S, Other	Ayurvedic
Xylopia aethiopica	Annonaceae	GI, R, MS	African
Angelica sinensis	Apiaceae	Gy, MS	East Asian
Bupleurum falcatum	Apiaceae	GI	East Asian
Centella asiatica	Apiaceae	N, S	Western, Ayurvedic
Cuminum cyminum	Apiaceae	GI, E	Ayurvedic
Trachyspermum ammi	Apiaceae	GI, CV, AB	Ayurvedic
Alstonia scholaris	Apocynaceae	GI, AB	Southeast Asian
Catharanthus roseus	Apocynaceae	CV, Other	African
Cryptolepis sanguinolenta	Apocynaceae	AB	African
Gymnema sylvestre	Apocynaceae	E	Ayurvedic
Hemidesmus indicus	Apocynaceae	GI, MS, AB, E, S	Ayurvedic
Holarrhena spp.	Apocynaceae	GI, MS, E, S	Ayurvedic, African
Hunteria umbellata	Apocynaceae	CV, MS, AB, E	African
Leptadenia reticulata	Apocynaceae	N, AB, S, Other	Ayurvedic

Marsdenia cundurango	Apocynaceae	GI, Other	American
Rauvolfia vomitoria	Apocynaceae	GI, N, MS, CV	African
Voacanga africana	Apocynaceae	Gy, Mr, AB	African
Ilex paraguayensis	Aquifoliaceae	N, Other	American
Pinellia ternata	Araceae	GI, N, MS, Other	East Asian
Hedera helix	Araliaceae	R	Western
*Panax ginseng**	Araliaceae	N, Gy, Mr, Other	Western, East Asian, China*
Serenoa repens	Arecaceae	Mr	Western, American
Asparagus spp.	Asparagaceae	GI, Gy, MS	East Asian, Ayurvedic
Ruscus aculeatus	Asparagaceae	CV	Western
Aloe ferox	Asphodelaceae	GI, MS, AB, S	African
Phormium tenax	Asphodelaceae	S	Māori
Arctium lappa	Asteraceae	R, S	East Asian
Artemisia annua	Asteraceae	MS, AB	East Asian
Atractylodes lancea	Asteraceae	GI	East Asian
Calendula officinalis	Asteraceae	S	Western

Cynara cardunculus	Asteraceae	GI	Western
Echinacea spp.	Asteraceae	R	Western, American
Matricaria chamomilla	Asteraceae	N	Western
*Neurolaena lobata**	Asteraceae	R, MS	Trinidad*
Silybum marianum	Asteraceae	GI	Western
Tanacetum parthenium	Asteraceae	MS	Western
Vernonia amygdalina	Asteraceae	GI, MS	African
Berberis spp.	Berberidaceae	GI, MS, AB, S	Ayurvedic, American
Podophyllum peltatum	Berberidaceae	GI, AB, Other	American
Handroanthus chrysotrichus	Bignoniaceae	AB, Other	American
Kigelia africana	Bignoniaceae	MS, AB, S	African
Boswellia serrata	Burseraceae	GI, R, MS	Ayurvedic
Commiphora wightii	Burseraceae	CV, E, S, Other	Ayurvedic
Lobelia inflata	Campanulaceae	N	American
*Platycodon grandiflorus**	Campanulaceae	GI, R	South Korea*
Humulus lupulus	Cannabaceae	N	Western

Crateva nurvala	Capparaceae	U	Ayurvedic
Lonicera japonica	Caprifoliaceae	GI, R, MS	East Asian
Valeriana officinalis	Caprifoliaceae	N	Western
Carica papaya	Caricaceae	Gy, Mr	African
Catha edulis	Celastraceae	R, N	African
Garcinia spp.	Clusiaceae	N, MS, AB, Other	Southeast Asian, African
Combretum micranthum	Combretaceae	CV, MS, Other	African
Ipomoea pes-caprae	Convolvulaceae	MS, AB, S	Australian
Rhodiola rosea	Crassulaceae	N	Western
Cucurbita pepo	Cucurbitaceae	Mr	Western
Momordica charantia	Cucurbitaceae	CV, E	Ayurvedic
Cyperus rotundus	Cyperaceae	GI, N, Gy, MS, E	East Asian, Ayurvedic
Dioscorea villosa	Dioscoreaceae	GI, Gy, MS, Other	American
Diospyros mespiliformis	Ebenaceae	GI, AB	African
Ephedra sinica	Ephedraceae	R	East Asian
Arctostaphylos uva-ursi	Ericaceae	U	Western

Vaccinium macrocarpon	Ericaceae	U, Other	Western, American
Erythroxylum coca	Erythroxylaceae	N	American
*Croton tiglium**	Euphorbiaceae	GI, CV, AB, S	Peru*
Euphorbia spp.	Euphorbiaceae	GI, R, AB, S	Ayurvedic, African
Ricinus communis	Euphorbiaceae	GI, Mr, AB, S	African
Abrus precatorius	Fabaceae	GI, N, Gy	Ayurvedic
Acacia spp.	Fabaceae	GI, MS, AB, E	Ayurvedic, Australian
Aspalathus linearis	Fabaceae	N, E, Other	African
Astragalus propinquus	Fabaceae	R	East Asian
*Bauhinia variegata**	Fabaceae	GI, AB	Costa Rica*
Caesalpinia bonduc	Fabaceae	GI, MS, AB, S	Ayurvedic
Cajanus cajan	Fabaceae	CV	African
Cyclopia intermedia	Fabaceae	CV, E, Other	African
Glycine max	Fabaceae	Gy	Western
Glycyrrhiza spp.	Fabaceae	GI, R, E	Western, East Asian
Senna spp.	Fabaceae	GI, AB	Western, Ayurvedic

Sophora flavescens	Fabaceae	GI, R, AB, S	East Asian
Styphnolobium japonicum	Fabaceae	CV	East Asian
Trifolium pratense	Fabaceae	Gy	Western
Trigonella foenum-graecum	Fabaceae	CV, Gy, MS, E, S	Ayurvedic
Gentiana lutea	Gentianaceae	GI	Western
Pelargonium sidoides	Geraniaceae	R	Western, African
Ginkgo biloba	Ginkgoaceae	N	Western
Hamamelis virginiana	Hamamelidaceae	MS, S, Other	Western,
Hypericum perforatum	Hypericeae	N	Western
Hypoxis hemerocallidea	Hypoxidaceae	R, Mr, MS	African
Mentha piperita	Lamiaceae	GI	Western
*Ocimum basilicum**	Lamiaceae	AB, S	Italy*
*Origanum syriacum**	Lamiaceae	GI, N, AB	Morocco*
Orthosiphon aristatus	Lamiaceae	CV, MS, AB, U	Southeast Asian
Perilla frutescens	Lamiaceae	MS, Other	East Asian
Salvia spp.	Lamiaceae	CV, Gy, R	East Asian, Western

Scutellaria baicalensis	Lamiaceae	GI	East Asian
*Sideritis syriaca**	Lamiaceae	R	Albania*
Vitex spp.	Lamiaceae	Gy, MS, S	Western, Ayurvedic
Cinnamomum spp.	Lauraceae	GI, Gy, MS, AB, E, Other	East Asian, Southeast Asian
Lawsonia inermis	Lythraceae	GI, CV, S	Ayurvedic
Punica granatum	Lythraceae	GI, CV, Gy, AB	Ayurvedic
Abelmoschus moschiatus	Malvaceae	Gy, Mr, MS	Southeast Asian
Cola spp.	Malvaceae	GI, N, MS	African
Gossypium herbaceum	Malvaceae	GI, Mr, S, Gy	Ayurvedic
*Hibiscus sabdariffa**	Malvaceae	GI, CV, E, Other	African, Mexico*
*Tilia cordata**	Malvaceae	R, N	Italy*
Trillium erectum	Melanthiaceae	S, Other	American
Azadirachta indica	Meliaceae	MS, AB	Ayurvedic
*Swietenia mahagoni**	Meliaceae	GI	Haiti*
Tinospora sinensis	Menispermaceae	GI, MS, AB, E, Other	Ayurvedic
Peumus boldus	Monimiaceae	GI, U,	American

Ficus spp.	Moraceae	GI, MS, AB, E, S	Ayurvedic, African, Australian
Moringa oleifera	Moringaceae	MS, E, Other	Ayurvedic
Eucalyptus spp.	Myrtaceae	MS	Australian
Kunzea spp.	Myrtaceae	GI, MS, O, S	Māori
Psidium guajava	Myrtaceae	CV, MS, AB, E	Southeast Asian
Syzygium spp.	Myrtaceae	GI, R, AB, O, S, E	Ayurvedic
Nelumbo nucifera	Nelumbonaceae	GI, CV, Other	Ayurvedic
Boerhaavia diffusa	Nyctaginaceae	GI, CV, R, MS, U	Ayurvedic
*Jasminum officinale**	Oleaceae	S	Pakistani*
Oenothera biennis	Onagraceae	S	American
Gastrodia elata	Orchidaceae	CV, N	East Asian
Rehmannia glutinosa	Orobanchaceae	R, MS, U, S	East Asian
Paeonia lactiflora	Paeoniaceae	CV, MS	East Asian
Fumaria indica	Papaveraceae	GI, AB, MS	Ayurvedic
Passiflora incarnata	Passifloraceae	N	Western
Turnera diffusa	Passifloraceae	Gy, Mr, Other	American

Harpagophytum procumbens	Pedaliaceae	MS	Western, African
Sesamum indicum	Pedaliaceae	GI, R, Gy	Ayurvedic
Cedrus deodara	Pinaceae	MS, S, Other	Ayurvedic
Macropiper excelsum	Piperaceae	GI, AB, O, S	Māori
Piper guineense	Piperaceae	GI, R, MS, Other	African
Bacopa monnieri	Plantaginaceae	N, MS	Ayurvedic
Picrorriza kurroa	Plantaginaceae	GI, MS	Ayurvedic
Plantago ovata	Plantaginaceae	GI	Western
Coix lacryma-jobi	Poaceae	GI, MS, U	East Asian
Cymbopogon citratus	Poaceae	MS, AB, S	Southeast Asian
Rheum palmatum	Polygonaceae	GI, S	East Asian
Aconitum carmichaelii	Ranunculaceae	GI, CV, MS	East Asian
Actaea racemosa	Ranunculaceae	Gy	Western, American
Coptis chinensis	Ranunculaceae	GI, AB, E, S	East Asian
Hydrastis canadensis	Ranunculaceae	GI, AB	American
Nigella sativa	Ranunculaceae	CV, E, S, Other	Ayurvedic

Frangula spp.	Rhamnaceae	GI	Western, American
Pomaderris kumeraho	Rhamnaceae	GI, R, AB, S	Māori
Ziziphus jujuba	Rhamnaceae	GI, CV	East Asian
Crataegus spp.	Rosaceae	CV	Western
*Prunus spp.**	Rosaceae	GI, R, Mr, MS	Western, African, American, England*
*Rosa spp.**	Rosaceae	MS, S	Western, Syria*
Rubus idaeus	Rosaceae	Gy	Western
Carapichea ipecacuanha	Rubiaceae	GI, AB	American
Cinchona spp.	Rubiaceae	MS, AB	American
Morinda citrifolia	Rubiaceae	CV, R, MS, Other	Southeast Asian
Pausinystalia johimbe	Rubiaceae	Mr, Other	African
Rubia cordifolia	Rubiaceae	GI, MS, AB, S	Ayurvedic
Agathosma betulina	Rutaceae	GI, R, Mr, U	African
Murraya koenigii	Rutaceae	GI, E, S	Ayurvedic
Salix spp.	Salicaceae	MS	Western
Aesculus hippocastanum	Sapindaceae	CV	Western

Dodonaea polyandra	Sapindaceae	O	Australian
Paullinia cupana	Sapindaceae	N, Other	American
Schisandra chinensis	Schisandraceae	R, GI, Other	East Asian
Eremophila spp.	Scrophulariaceae	MS	Australian
Brucea antidysenterica	Simaroubaceae	GI, S	African
Eurycoma longifolia	Simaroubaceae	N, Mr, Other	Southeast Asian
Picrasma excelsa	Simaroubaceae	AB	American
Quassia amara	Simaroubaceae	AB	American
Smilax spp.	Smilacaceae	MS, S, Other	American
Duboisia hopwoodii	Solanaceae	N	Australian
*Lycium barbarum**	Solanaceae	GI, R, N, Other	East Asian, China*
Solanum spp.	Solanaceae	GI, MS	Ayurvedic, Australian
Taxus baccata	Taxaceae	Other	American
Urtica dioica	Urticaceae	Mr	Western
Cissus quadrangularis	Vitaceae	GI, MS	Ayurvedic
Vitis vinifera	Vitaceae	CV	Western

Aframomum spp.	Zingiberaceae	GI, MS, AB	African
Alpinia galanga	Zingiberaceae	GI, MS, AB, Other	Southeast Asian
*Curcuma longa**	Zingiberaceae	GI, MS, Other	Western, Southeast Asia, Egypt*
Elettaria cardamomum	Zingiberaceae	GI, CV	Ayurvedic
Kaempferia galanga	Zingiberaceae	CV, R, MS	Southeast Asian
Zingiber officinale	Zingiberaceae	GI, R	Western, East Asian
Tribulus terrestris	Zygophyllaceae	GI, MS, U, Other	East Asian

To incorporate students' cultural perspectives, interviews were conducted with family members, including grandparents, parents, aunts, and uncles, to identify a prominent medicinal plant from their cultural background. These interviews were open-ended and designed to elicit qualitative insights into the plant's perceived medicinal uses. Responses were collected and categorized by medicinal application, aligned with the existing classifications from Heinrich et al. (2023). These cultural plants were marked with "*" in Table 1 including the student's cultural background/geographic origin. At the conclusion of the semester, students were also asked how incorporating a medicinal plant from their cultural background influenced their appreciation of medicinal plant diversity, cultural heritage, and natural product research.

For each plant species, only the genus was noted, such that congeneric species were only listed once, with their respective cultures and traditional medicinal uses indicated (Table 1). The traditional medicinal uses indicated by Heinrich et al. (2023) were categorized into: gastrointestinal (GI, including liver uses); cardiovascular (CV); respiratory (R, including immune support/tonic uses; nervous (N, including psychiatry), gynecological (Gy, including lactation), male reproductive (Mr); musculoskeletal (MS, including anti-inflammatory uses and use for pain, fever); antiparasite/antibiotic (AB), endocrine (E, excluding reproductive hormones); urinary (U, including kidney uses); dentistry/oral (D); skin/dermatology (S). Any use outside these categories was placed in "Other". Multiple uses may be indicated for a plant genus and are indicated in Table 1.

The phylogeny for these plant genera was reconstructed following methods in Xavier and Molina (2016). A representative rbcL sequence for each genus was obtained from Genbank using Blastn (Zhang et al., 2000, except for 6 species that

did not have corresponding sequences in Genbank). The DNA sequences were imported into Geneious Prime 2023.2.1 (Biomatters, Ltd.) aligned with MAFFT v7.490 (Katoh & Standley 2013) and phylogenetically analyzed using PhyML v. 3.3.20180621 (Guindon et al., 2010). The medicinal applications were mapped on the PhyML phylogeny (transformed into a cladogram) using ITOL (Interactive Tree of Life, www.itol.embl.de). We analyzed the phylogeny for cultural convergence, defined here as three or more plant genera within the same plant family with majority (> 50%) of these genera being used for the same medicinal category by multiple cultures.

RESULTS

The plant phylogeny shows, that out of the 188 species from 85 plant families including culturally important plants provided by students (Table 1), 10 families (Zingiberaceae, Ranunculaceae, Apiaceae, Solanaceae, Apocynaceae, Myrtaceae, Malvaceae, Anacardiaceae, Euphorbiaceae and Rhamnaceae) showed patterns of cultural convergence (Fig. 1), with at least 1% of their respective genera estimated to be medicinal when generic diversity was accounted for (= number of medicinal genera in phylogeny divided by total number of genera in the family, Christenhusz & Byng, 2016). Rubiaceae, though with 5 genera represented here, did not meet this cutoff (total number of genera is 590).

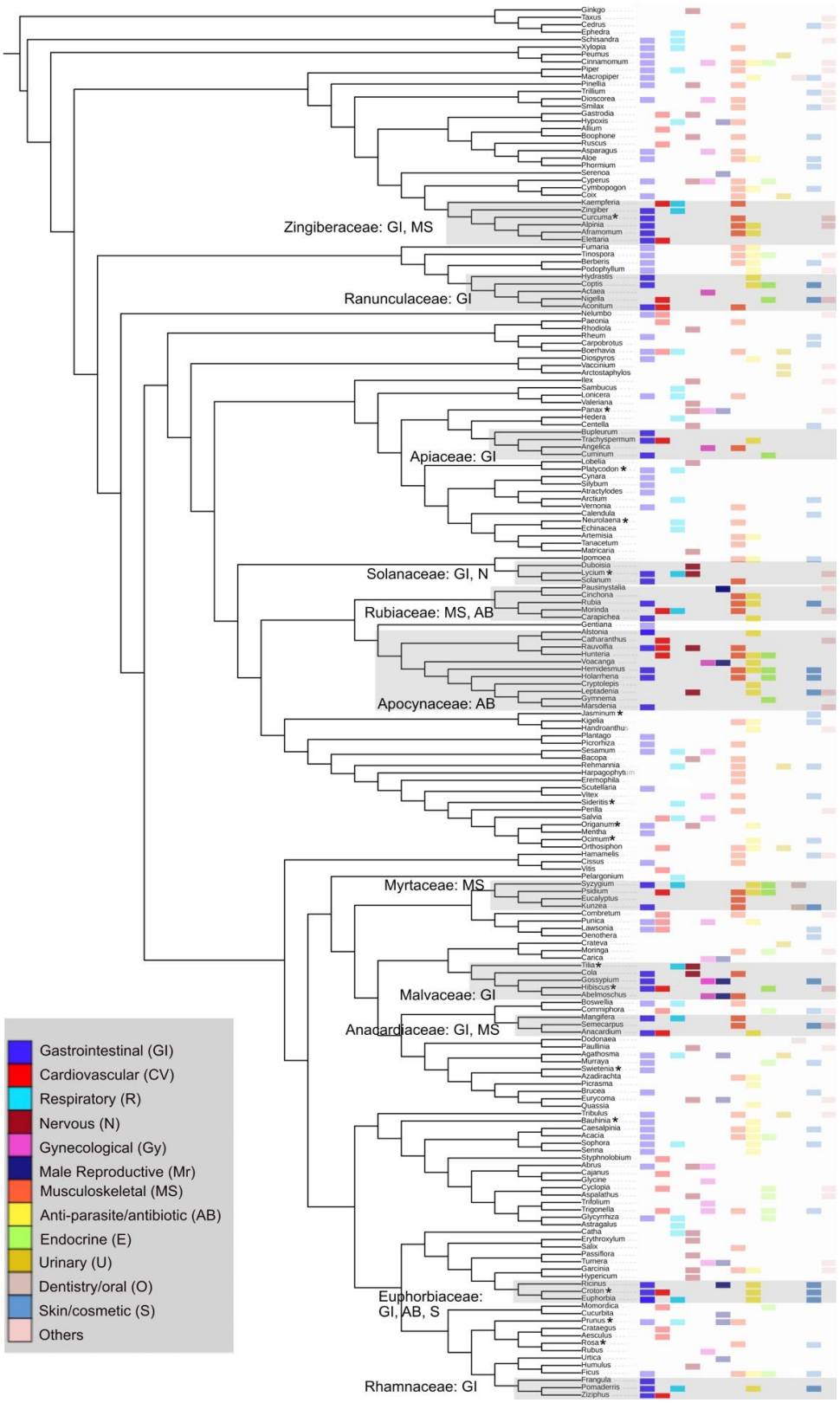
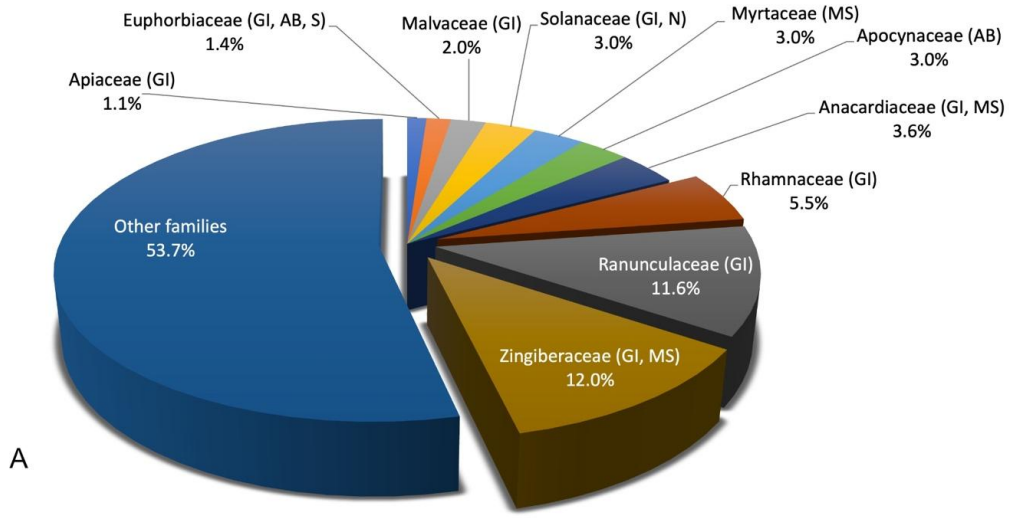

Zingiberaceae: GI, MS
Ranunculaceae: GI
Apiaceae: GI
Solanaceae: GI, N
Rubiaceae: MS, AB
Apocynaceae: AB
Myrtaceae: MS
Malvaceae: GI
Anacardiaceae: GI, MS
Euphorbiaceae: GI, AB, S
Rhamnaceae: GI
Gastrointestinal (GI)
Cardiovascular (CV)
Respiratory (R)
Nervous (N)
Gynecological (Gy)
Male Reproductive (Mr)
Musculoskeletal (MS)
Anti-parasite/antibiotic (AB)
Endocrine (E)
Urinary (U)
Dentistry/oral (O)
Skin/cosmetic (S)
Others

Figure 1. Phylogeny of traditional medicinal plants enumerated by Heinrich et al. (2023) in chapter 16, including plants medicinally important to students' cultural background (indicated with "*"). Plant families with three or more plant genera with majority (>50%) of these genera being used for the same medicinal category, as indicated by colored boxes, are highlighted/shaded.

Zingiberaceae (12%), Ranunculaceae (11.6%), and Rhamnaceae (5.5%) were the most medicinally important plant families across cultures (Fig. 2A). The "Other families" category comprises 53.7% of plant families analyzed. Gastrointestinal (GI) use (18%) was the most predominant medicinal application across cultures, followed by musculoskeletal (MS, 15%) and antibiotic (AB, 11%) uses (Fig. 2B).



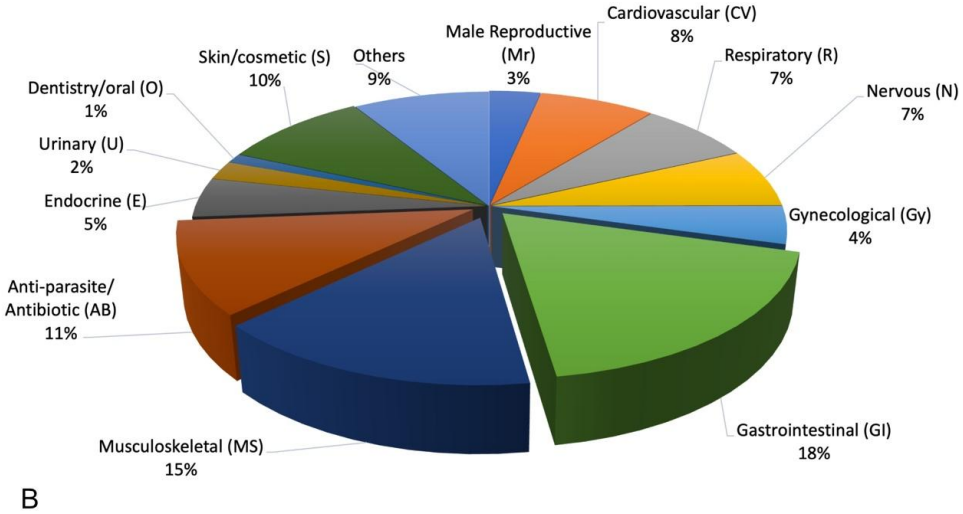


Figure 2. Relative proportions of medicinal plant families (A) and their medicinal applications (B). A. When generic diversity is accounted for among plant families depicting cultural convergence, Zingiberaceae, Ranunculaceae, and Rhamnaceae were proportionally most medicinally important across cultures. B. Gastrointestinal (GI) use (18%) was the most predominant medicinal application across cultures, followed by musculoskeletal (MS, 15%) and antibiotic (AB, 11%) uses.

DISCUSSION

In this study, we aimed to reconstruct a phylogeny of medicinal plants traditionally used in various cultures to discover patterns of cultural convergence. From the phylogeny, of the 85 plant families represented, 10 families (Zingiberaceae, Ranunculaceae, Apiaceae, Solanaceae, Apocynaceae, Myrtaceae, Malvaceae, Anacardiaceae, Euphorbiaceae, and Rhamnaceae) demonstrated patterns of cultural convergence (Fig. 1) with at least 1% of their respective genera estimated to be medicinal when generic diversity was accounted for (Fig. 2A). The “Other families” category comprises 53.7% of plant families analyzed. This suggests that while patterns of cultural convergence are identifiable in certain plant families, a significant proportion of medicinal plants did not meet the generic diversity cutoff and do not exhibit strong phylogenetic clustering. This may be due to the regional specificity of certain plant uses. Patterns of cultural convergence shown here do not appear to be an artifact of the species diversity within these plant families, as the most species-rich families such as Asteraceae, Orchidaceae, Fabaceae, and Poaceae (Christenhusz and Byng 2016) did not display such patterns in this study. Additionally, across all the cultures included in this study, the top three traditional applications for herbal medicine were related to gastrointestinal (GI), musculoskeletal (MS), and antibiotic uses (AB), at 18%, 15%, and 11%, respectively (Fig. 2B).

The patterns of cultural convergence in medicinal plant selection identified in our study may reflect deep evolutionary tendencies shaped by pathogen pressures, as proposed by Hagen et al. (2023). They suggest that early humans' reliance on plant secondary metabolites was driven by pathogen pressures, reinforcing the idea that phylogenetic clustering of medicinal plants is not merely a cultural artifact but also an evolutionary consequence. Our findings support this perspective, as plant families with known bioactive compounds were independently selected across multiple cultures for similar medicinal purposes, such as related plants with antibiotic properties.

It is important to note that because our study was based on the medicinal plant tables found in chapter 16 of Heinrich et al. (2023), our reconstructed phylogeny may not be fully representative of all the traditionally important medicinal plants used in various cultures. For example, a notable omission from our phylogeny is the set of traditional medicinal plants used in Middle Eastern/Islamic culture, as they were not included in the tables by Heinrich et al. (2023). Similar phylogenetic studies which included Middle Eastern herbal medicine were able to identify certain plant families which showed cultural convergence, such as Burseraceae for musculoskeletal pain, Apiaceae for urinary issues (Xavier & Molina 2016), Fabaceae for antibiotic uses, and Lamiaceae for both gastrointestinal and respiratory uses (Xavier & Molina, 2016;

Molina, 2018). Nonetheless, we found familial patterns of cultural convergence mostly consistent with previous studies (Xavier & Molina 2016; Molina, 2018), as well as additional families, which we discuss below.

Phytochemistry of Plants for Gastrointestinal Ailments

Based on our phylogeny, we were able to identify several plant families with patterns of cultural convergence for addressing gastrointestinal (GI) conditions. In members of Zingiberaceae, Apiaceae, and Malvaceae, the presence of volatile essential oils with high terpene and terpenoid content may explain their usage in GI treatments (Kumari et al., 2014). Additionally, Zingiberaceae is known to contain phenolic compounds which have been experimentally shown to have gastroprotective effects (Mao et al., 2019). One member of Zingiberaceae, *Kaempferia*, was not noted for GI uses, but given the predictive utility of the phylogeny, it may have GI applications. Experimentally, *Kaempferia* extracts were found to relieve inflammation caused by the ulcerogenic bacteria *Helicobacter pylori* in mammalian cells (Nemidkanam et al., 2020).

The pharmacological activity of members of Ranunculaceae is likely explained by the presence of alkaloids. Both *Hydrastis* and *Coptis* have been found to be rich in isoquinoline alkaloids (Hao et al., 2015). *Hydrastis* is used as an astringent which stimulates the muscles of the GI tract, and *Coptis* is used to treat dysentery, gastroenteritis, stomatitis, and ulcers (Hao 2019). *Aconitum,* another genus within Ranunculaceae, is also rich in alkaloids, and aqueous extracts have experimentally shown antidiarrheal effects by restoring gut microbiota (Zhang et al., 2023). *Actaea* was not marked for GI use in our phylogeny, but with other Ranunculaceae members having GI use, it is possible that *Actaea* does as well. There is experimental evidence of *Actaea racemosa* possessing serotonergic phytochemicals (Gödecke et al., 2009), and serotonin has been found to strongly regulate the gastrointestinal system (Terry & Margolis, 2017). *Nigella* also had no GI use in our phylogeny, but there is experimental evidence that thymoquinone, one of its primary active phytochemicals, is capable of reducing gastric acid secretion and inhibiting the depletion of gastric mucosa, indicating it could be used to treat gastritis or dyspepsia (Jarmakiewicz-Czaja et al., 2023).

Members of Rhamnaceae also demonstrated cultural convergence for GI use. *Frangula* bark preparations have been proven effective at treating occasional constipation, and this is thought to be due to the hydroxyanthracene derivatives contained within (European Medicines Agency, 2019). Phytochemical studies of *Pomaderris kumeraho* revealed that it contains quercetin, kaempferol, saponins, myricyl acetate, and ellagic acid, among others (Cain & Cambie, 1959). Experimentally, it was determined that kaempferol may have protective effects against ulcerative colitis in mice by regulating the gut microbiota (Qu et al., 2021).

In Malvaceae, *Cola* has been found to contain numerous active phytochemicals including alkaloids, tannins, flavonoids, saponins, and phenols, with *Cola anomala* extracts having experimentally proven anti-diarrhea effects in rats (Ekalu & Habila, 2020). In another study, *Hibiscus sabdariffa* extracts significantly protected against gastric mucosal injury in various ulcer models in rats (Alqasoumi et al., 2010). *Tilia* was not noted for GI use in our phylogeny, but there is experimental

evidence that *Tilia cordata* extracts can induce contraction of intestinal smooth muscle cells via cholinergic phytochemicals, such as flavonoid glycosides (Al-Essa et al., 2007). No experimental studies were found supporting the traditional use of *Gossypium herbaceum* for GI purposes, though it could have unexplored properties for this application.

Members of Solanaceae possess solanaceous alkaloids such as atropine, nicotine, hyoscyamine, and scopolamine that contribute to their GI and nervous/psychoactive effects (Alrashedy & Molina, 2016; Knox et al., 2024). For example, hyoscyamine is an anticholinergic used to treat GI disorders, and scopolamine is another anticholinergic alkaloid used to treat nausea and vomiting (Knox et al., 2024). *Lycium* is a solanaceous plant presented by a Chinese student who reported on its traditional use for GI and psychoactive applications consistent with previously published research.

Anacardiaceae also showed cultural convergence for GI use, with *Anacardium occidentale* extracts having experimentally proven antidiarrheal effects, which could be due to synergy between its phytochemicals (Omolaso et al., 2021). Another member of Anacardiaceae, *Mangifera indica*, is known to be rich in polyphenols such as gallic acid which have been shown to help reduce inflammation in the intestines by modulating the gut microbiome (Kim et al., 2021).

Phytochemistry of Plants for Musculoskeletal Ailments

Members of Zingiberaceae, Anacardiaceae, and Myrtaceae all showed patterns of cultural convergence for musculoskeletal (MS) applications (including anti-inflammatory uses and use for pain, fever). The anti-inflammatory effects of Zingiberaceae members may be explained by the presence of phenolic compounds such as curcumin (Lakhan et al., 2015). Phenolic compounds have been shown to inhibit pro-inflammatory compounds (Ambriz-Pérez et al., 2016). *Zingiber officinale,* while not noted for MS applications in our phylogeny, has experimental evidence supporting its use in relieving pain, supporting the phylogenetic pattern observed here. In a blind study comparing the anti-inflammatory effects of ibuprofen and ginger in postsurgical pain, it was found that no significant differences were observed between the two groups, indicating ginger is as effective as ibuprofen in treating musculoskeletal pain (Rayati et al., 2017).

The MS activity of members of Anacardiaceae is likely due to the presence of polyphenols (flavonoids) and triterpenoids. In rats, *Semecarpus anacardium* extracts were experimentally found to have anti-inflammatory activity, which were attributed to flavonoids and other synergistic compounds (Ramprasath et al., 2004). *Anacardium officinale* extracts (Baptista et al., 2020) and *Mangifera indica* extracts (Ojewole, 2005), were experimentally shown to demonstrate anti-inflammatory activities, possibly attributed to their flavonoid and triterpene content. *Rhus sylvestris,* another member of Anacardiaceae not included in our study, has experimentally been found to contain triterpene compounds which possess anti-inflammatory properties by blocking inflammatory cytokine secretion (Ding et al., 2009). These findings support the predictive utility of the phylogeny, as the pattern of cultural convergence of MS use extends beyond the genera included in the study. It is noteworthy that Anacardiaceae is closely related to Burseraceae, which has been previously

identified as phylogenetically important for alleviating inflammation and pain, possibly mediated by the triterpene (boswellic) acid content of members of the family (Xavier & Molina, 2016). In Myrtaceae, the anti-inflammatory effects can likely be attributed to the presence of essential oils (Maiolini et al., 2023). One member of Myrtaceae, *Kunzea spp.*, is used commercially as an anti-inflammatory cream (www.zea.com.au). *Syzygium* extracts, which contain numerous phytochemicals including flavonoids and terpenes, were experimentally shown to significantly inhibit inflammation and pain in mice (Rauf et al., 2022).

Phytochemistry of Plants for Antibiotic Uses

Members of both the Euphorbiaceae and Apocynaceae families exhibited patterns of cultural convergence in their application as antibiotics (AB). These families represent additional antibiotic-rich groups with pharmacological significance, which was not apparent in earlier studies (Molina, 2018; Prasad et al., 2019). *Euphorbia* extracts were experimentally tested for antimicrobial activity, and several species in the genera were found to be effective antibacterial agents, with differing effects due to different phytochemicals among species (Kirbag et al., 2013). Additionally, *Euphorbia* latex is known to contain triterpene derivatives and esters, which may contribute to the AB activity (Benjamaa et al., 2022). *Croton* essential oils were found to contain terpene derivatives, which demonstrated antibacterial activity against *Staphylococcus aureus* (Daouda et al., 2014). Interestingly, a student with Peruvian background reported on the antibacterial uses of *Croton lecheri* in the treatment of wounds and dermatitis. Extracts of the confamilial *Ricinus communis* were determined to contain terpenoids, flavonoids, and tannins, and had effective AB activity against the pathogens tested (Suurbaar et al., 2017).

The phylogeny also highlighted the antibacterial utility of Apocynaceae, which is also supported by a review paper collating antibacterial properties of various members of the family (Anand et al., 2020). Perturbation of redox status of bacterial cells was the underlying antibiotic mechanism, while reducing incidence of antibiotic resistance (Anand et al., 2020).

The Phylogeny is a Pedagogical Tool Bridging Plant and Cultural Diversity

A major goal of this study was to assess the pedagogical value of using the phylogeny to enhance ethnobotanical appreciation among undergraduate students through a class project. Incorporating medicinal plants used by students or their family members leveraged the cultural diversity of the 16 students in the class, making the learning experience more personal and engaging. The open-ended nature of interviews encouraged students to develop critical thinking skills by analyzing traditional medicinal practices. Categorizing responses using scientific classifications (Heinrich et al., 2023) required students to bridge cultural knowledge with scientific frameworks, reinforcing interdisciplinary learning. Students attested that this made the study more personal and engaging allowing them to test whether their elder's use is an "old wives' tale," as one student described it, or supported by phylogenetic evidence. The realization that, as undergraduates, they can contribute data gathered

literally from their 'doorstep,' as one student put it, and potentially shape scientific research outside the classroom was edifying to them.

Students have developed an appreciation for the pragmatic utility of the phylogeny in guiding natural product research, facilitating prediction of bioactivity for less-studied members of a clade and validation of traditional therapies through patterns of cultural convergence. They reported that this experiential learning approach, integrating personal and ancestral knowledge into phylogenetic analysis provided a tangible connection between their academic coursework and real-world applications. This project has consequently inspired multiple students from the class to pursue independent studies, as part of their biology capstone research at Pace, on the application of the plant phylogeny for unraveling patterns in evolutionary pharmacology. Future iterations of this course may incorporate additional cultural contexts, such as Middle Eastern and Islamic traditional medicine, to enhance inclusivity and broaden the scope of student engagement. The phylogeny was an effective pedagogical tool that allowed us to bridge multidisciplinary fields–traditional medicine, plant diversity, and evolutionary pharmacology, providing an interface that not only enriched student learning, but also offered a novel approach that could facilitate drug discovery from plant natural products.

Data Availability Statement

The data that support the findings of this study are available in Genbank at https://www.ncbi.nlm.nih.gov/genbank/. These data were derived from the following resources available in the public domain: https://www.ncbi.nlm.nih.gov/genbank/

Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

Ahmad, A., Husain, A., Mujeeb, M., Khan, S. A., Najmi, A. K., Siddique, N. A., Damanhouri, Z. A., & Anwar, F. (2013). A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pacific Journal Tropical Biomedicine*, *3*(5), 337-352. doi:10.1016/S2221-1691(13)60075-1

Al-Essa, M. K., Mohammed, F. I., Shafagoj, Y. A., & Afifi, F. U. (2007). Studies on the direct effects of the alcohol extract of *Tilia cordata*. on dispersed intestinal smooth muscle cells of guinea pig. *Pharmaceutical Biology*, *45*(3), 246–250. https://doi.org/10.1080/13880200701213195

Alqasoumi, S., Al-Dosari, M., Al-Sohaibani, M., Al-Howiriny, T., Al-Yahya, M., & Rafatullah, S. (2010). Gastric ulcer protective activity of *Hibiscus sabdariffa:* An experimental, biochemical and histological study. *Clinical and*

Experimental Medical Journal CEMED, *4*(1), 115-127. https://doi.org/10.1556/CEMED.4.2010.1.12

Alrashedy NA, Molina J. The ethnobotany of psychoactive plant use: A phylogenetic perspective. *PeerJ*. 4, e2546. doi:10.7717/peerj.2546

Ambriz-Perez, D. L., Leyva-Lopez, N., Gutierrez-Grijalva, E. P., & Heredia, J. B. (2016). Phenolic compounds: Natural alternative in inflammation treatment. A review. *Cogent Food & Agriculture*, *2*(1). https://doi.org/10.1080/23311932.2015.1131412

Anand, U., Nandy, S., Mundhra, A., Das, N., Pandey, D. K., & Dey, A. (2020). A review on antimicrobial botanicals, phytochemicals and natural resistance modifying agents from Apocynaceae family: Possible therapeutic approaches against multidrug resistance in pathogenic microorganisms. *Drug resistance updates: Reviews and commentaries in antimicrobial and anticancer chemotherapy*, *51*, 100695. https://doi.org/10.1016/j.drup.2020.100695

Baptista, A. B., Sarandy, M. M., Gonçalves, R. V., Novaes, R. D., Gonçalves da Costa, C., Leite, J. P. V., & Peluzio, M. D. C. G. (2020). Antioxidant and anti-inflammatory effects of *Anacardium occidentale* L. and *Anacardium microcarpum* D. extracts on the liver of IL-10 knockout mice. *Evidence-based Complementary and Alternative Medicine*, *2020*, 3054521. https://doi.org/10.1155/2020/3054521

Benjamaa, R., Moujanni, A., Kaushik, N., Choi, E. H., Essamadi, A. K., & Kaushik, N. K. (2022). Euphorbia species latex: A comprehensive review on phytochemistry and biological activities. *Frontiers in Plant Science* 13, 1008881. doi: 10.3389/fpls.2022.1008881

Cain, B. F., & Cambie, R. C. (1959). Leaf extractives of Pomaderris elliptica Labill. *New Z. J. Sci.,* 2, 240–243.

Cartwright, A. C. (2015). *The British Pharmacopoeia 1864 to 2014 Medicines International Standards and the State*. Ashgate Publishing, Limited.

Christenhusz, M. J. M., & Byng, J. W. (2016). The number of known plants species in the world and its annual increase. *Phytotaxa*, 261, 201. https://doi.org/10.11646/phytotaxa.261.3.1

Davis, C. C., & Choisy, P. (2024). Medicinal plants meet modern biodiversity science. Curr Biol. 2024 Feb 26;34(4):R158-R173. doi:10.1016/j.cub.2023.12.038.

Ding, Y., Nguyen, H. T., Kim, S. I., Kim, H. W., & Kim, Y. H. (2009). The regulation of inflammatory cytokine secretion in macrophage cell line by the chemical constituents of Rhus sylvestris. *Bioorganic & Medicinal Chemistry Letters*, *19*(13), 3607–3610. https://doi.org/10.1016/j.bmcl.2009.04.129

Daouda, T., Prevost, K., Gustave, B., Joseph, D. A., Nathalie, G., Raphaël, O., Rubens, D., Jean Claude, C., Mireille, D., & Felix, T. (2014). Terpenes, Antibacterial and Modulatory Antibiotic Activity of Essential Oils from *Croton hirtus* L' Hér. (Euphorbiaceae) from Ivory Coast. *Journal of Essential Oil Bearing Plants*, *17*:4, 607-616, doi:10.1080/0972060X.2014.958550

Ekalu, A., & Habila, J. D. (2020). Phytochemistry, pharmacology and medicinal uses of *Cola* (Malvaceae) family: A review. *Medicinal Chemistry Research*, *29*(12), 2089–2105. https://doi.org/10.1007/s00044-020-02637-x

European Medicines Agency (2019). *Frangula bark*. https://www.ema.europa.eu/en/documents/herbal-summary/frangula-bark-summary-public_en.pdf Accessed 29 December, 2023.

Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives*, 109 Suppl 1, 69-75. doi:10.1289/ehp.01109s169

Gödecke, T., Nikolic, D., Lankin, D. C., Chen, S. N., Powell, S. L., Dietz, B., Bolton, J. L., van Breemen, R. B., Farnsworth, N. R., & Pauli, G. F. (2009). Phytochemistry of cimicifugic acids and associated bases in *Cimicifuga racemosa* root extracts. *Phytochemical analysis: PCA*, *20*(2), 120–133. https://doi.org/10.1002/pca.1106

Guindon, S., & Gascuel, O. (2013). A simple fast and accurate algorithm to estimate large phylogenies by maximum likelihood. *Syst. Biol.*, *52*, 696–704.

Guzman, E., & Molina, J. (2018). The predictive utility of the plant phylogeny in identifying sources of cardiovascular drugs. *Pharmaceutical biology*, *56*(1), 154–164. https://doi.org/10.1080/13880209.2018.1444642

Hagen, E. H., Blackwell, A. D., Lightner, A. D., & Sullivan, R. J. (2023). Homo medicus: The transition to meat eating increased pathogen pressure and the use of pharmacological plants in Homo. *American Journal of Biological Anthropology*, *180*(4), 589–617. https://doi.org/10.1002/ajpa.24718

Hao, D. C., Xiao, P. G., Ma, H. Y., Peng, Y., & He, C. N. (2015). Mining chemodiversity from biodiversity: Pharmacophylogeny of medicinal plants of Ranunculaceae. *Chinese Journal of Natural Medicines*, *13*(7), 507–520. https://doi.org/10.1016/S1875-5364(15)30045-5

Hao, D. C. (2019). *Ranunculales Medicinal Plants*. Academic Press.

Heinrich, M., Barnes, J., Gibbons, S., & Williamson, E. M. (2023). Fundamentals of Pharmacognosy and Phytotherapy (4th ed.). Churchill Livingstone/Elsevier.

Holzman, R. S. (1998) The Legacy of Atropos, the Fate Who Cut the Thread of Life. *Anesthesiology*, *89*(1):241–249. https://doi.org/10.1097/00000542-199807000-00030

Jarmakiewicz-Czaja, S., Zielińska, M., Helma, K., Sokal, A., & Filip, R. (2023). Effect of *Nigella sativa* on Selected Gastrointestinal Diseases. *Current Issues in Molecular Biology*, *45*(4), 3016–3034. https://doi.org/10.3390/cimb45040198

Katoh, K., & Standley, D. (2013). MAFFT multiple sequence alignment software version 7: improvements in performance and usability. *Molecular Biology & Evolution,* 30, 772–778.

Kim, H., Castellon-Chicas, M. J., Arbizu, S., Talcott, S. T., Drury, N. L., Smith, S., & Mertens-Talcott, S. U. (2021). Mango (*Mangifera indica* L.) polyphenols: Anti-inflammatory intestinal microbial health benefits, and associated mechanisms of actions. *Molecules* *26*(9), 2732. https://doi.org/10.3390/molecules26092732

Kirbag, S., Erecevit, P., Zengin, F., & Guvenc, A. N. (2013). Antimicrobial activities of some *Euphorbia* species. *African Journal of Traditional, Complementary, and Alternative Medicines:* *10*(5), 305–309. https://doi.org/10.4314/ajtcam.v10i5.13

Knox, C., Wilson, M., Klinger, C. M., Franklin, M., Oler, E., Wilson, A., Pon, A., Cox, J., Chin, N. E. L., Strawbridge, S. A., Garcia-Patino, M., Kruger, R.,

Sivakumaran, A., Sanford, S., Doshi, R., Khetarpal, N., Fatokun, O., Doucet, D., Zubkowski, A., Rayat, D. Y., & Wishart, D. S. (2024). DrugBank 6.0: The DrugBank Knowledgebase for 2024. *Nucleic acids research*, *52*(D1), D1265–D1275. https://doi.org/10.1093/nar/gkad976

Kumari, S., Pundhir, S., Priya, P., Jeena, G., Punetha, A., Chawla, K., Jafaree, Z. F., Mondal, S., & Yadav, G. (2014). EssOilDB: a database of essential oils reflecting terpene composition and variability in the plant kingdom. *Database, 2014,* bau120. http://dx.doi.org/10.1093/database/bau120

Lakhan, S. E., Ford, C. T., & Tepper, D. (2015). Zingiberaceae extracts for pain: a systematic review and meta-analysis. *Nutrition journal*, *14*, 50. https://doi.org/10.1186/s12937-015-0038-8

Maiolini, T. C. S., Nicácio, K. J., Rosa, W., Miranda, D. O., Santos, M. F. C., Bueno, P. C. P., Lago, J. H. G., Sartorelli, P., Dias, D. F., Chagas de Paula, D. A., & Soares, M. G. (2023). Potential anti-inflammatory biomarkers from Myrtaceae essential oils revealed by untargeted metabolomics. *Natural Product Research*, 1–8. https://doi.org/10.1080/14786419.2023.2283758

Mao Q. Q., Xu X. Y., Cao S. Y., Gan R. Y., Corke H., Beta T., & Li H. B. (2019). Bioactive compounds and bioactivities of Ginger (*Zingiber officinale* Roscoe). *Foods, 8*(6):185. doi:10.3390/foods8060185.

Molina, J. (2018). Phylogenetic analysis of traditional medicinal plants: Discovering new drug sources from patterns of cultural convergence. In: McKenna, D, ed. *Ethnopharmacologic Search for Psychoactive Drugs*, *Vol. 2: 50 years of research*. Santa Fe, NM: Synergetic Press.

Nemidkanam, V., Kato, Y., Kubota, T., & Chaichanawongsaroj, N. (2020). Ethyl acetate extract of Kaempferia parviflora inhibits Helicobacter pylori-associated mammalian cell inflammation by regulating proinflammatory cytokine expression and leukocyte chemotaxis. *BMC Complementary Medicine and Therapies*, *20*(1), 124. https://doi.org/10.1186/s12906-020-02927-2

Ojewole J. A. (2005). Antiinflammatory, analgesic and hypoglycemic effects of *Mangifera indica* Linn. (Anacardiaceae) stem-bark aqueous extract. *Methods and Findings in Experimental and Clinical Pharmacology*, *27*(8), 547–554. https://doi.org/10.1358/mf.2005.27.8.928308

Omolaso, B. O., Oluwole, F. S., Odukanmi, O. A., Adesanwo, J. K., Ishola, A. A., & Adewole, K. E. (2021). Evaluation of the gastrointestinal anti-motility effect of *Anacardium occidentale* stem bark extract: A mechanistic study of antidiarrheal activity. *Journal of Pharmaceutical Analysis*, *11*(6), 776–782. https://doi.org/10.1016/j.jpha.2020.06.009

Prasad M. A., Zolnik C. P., & Molina, J. (2019). Leveraging phytochemicals: The plant phylogeny predicts sources of novel antibacterial compounds. *Future Sci OA. 5*(7), FSO407. doi:10.2144/fsoa-2018-0124.

Qu, Y., Li, X., Xu, F., Zhao, S., Wu, X., Wang, Y., & Xie, J. (2021). Kaempferol alleviates murine experimental colitis by restoring gut microbiota and inhibiting the LPS-TLR4-NF-κB axis. *Frontiers in Immunology*, *12*, 679897. https://doi.org/10.3389/fimmu.2021.679897

Ramprasath, V. R., Shanthi, P., & Sachdanandam, P. (2004). Anti-inflammatory effect of *Semecarpus anacardium* Linn. Nut extract in acute and chronic

inflammatory conditions. *Biological & Pharmaceutical Bulletin*, *27*(12), 2028–2031. https://doi.org/10.1248/bpb.27.2028

Rauf, A., Al-Awthan, Y. S., Khan, I. A., Muhammad, N., Ali Shah, S. U., Bahattab, O., Al-Duais, M. A., Sharma, R., & Rahman, M. M. (2022). In vivo anti-inflammatory, analgesic, muscle relaxant, and sedative activities of extracts from *Syzygium cumini* (L.) Skeels in mice. *Evidence-based Complementary and Alternative Medicine, 2022*, 6307529. https://doi.org/10.1155/2022/6307529

Rayati, F., Hajmanouchehri, F., & Najafi, E. (2017). Comparison of anti-inflammatory and analgesic effects of Ginger powder and Ibuprofen in postsurgical pain model: A randomized, double-blind, case-control clinical trial. *Dental Research Journal*, *14*(1), 1–7. https://doi.org/10.4103/1735-3327.201135

Rubira E. R. (2011) *The evolution of drug discovery: From traditional medicines to modern drugs*. Weinheim: Wiley-Vch.

Saslis-Lagoudakis, C. H., Savolainen, V., Williamson, E. M., Forest, F., Wagstaff, S. J., Baral, S. R., Watson, M. F., Pendry, C. A., & Hawkins, J. A. (2012). Phylogenies reveal predictive power of traditional medicine in bioprospecting. *Proceedings of the National Academy of Sciences, 109*(39), 15835–15840. https://doi.org/10.1073/pnas.1202242109

Suurbaar, J., Mosobil, R., & Donkor, A. M. (2017). Antibacterial and antifungal activities and phytochemical profile of leaf extract from different extractants of Ricinus communis against selected pathogens. *BMC Research Notes*, *10*(1), 660. https://doi.org/10.1186/s13104-017-3001-2

Terry, N., & Margolis, K. G. (2017). Serotonergic mechanisms regulating the GI tract: Experimental evidence and therapeutic relevance. *Handbook of Experimental Pharmacology*, *239*, 319–342. https://doi.org/10.1007/164_2016_103

Xavier, C., & Molina, J. (2016). Phylogeny of medicinal plants depicts cultural convergence among immigrant groups in New York City. *Journal of Herbal Medicine*, *6*(1), 1-11.

Yuan, H., Ma Q., Ye, L., & Piao, G. (2016). Traditional medicine and modern medicine from natural Products. *Molecules, 21*, 559. doi:10.3390/molecules21050559

Zhang, D., Cheng, H., Zhang, Y., Zhou, Y., Wu, J., Liu, J., Feng, W., & Peng, C. (2023). Ameliorative effect of Aconite aqueous extract on diarrhea is associated with modulation of the gut microbiota and bile acid metabolism. *Frontiers in Pharmacology, 14*, 1189971. doi:10.3389/fphar.2023.1189971

Zhang, Z., Schwartz, S., Wagner, L., & Miller, W. (2000). A greedy algorithm for aligning DNA sequences. *Journal of Computational Biology, 7*, 203–214.