Abstract: Background: Native Americans have had a rich ethnobotanical heritage for treating diseases, ailments, and injuries. Cherokee traditional medicine has provided numerous aromatic and medicinal plants that not only were used by the Cherokee people, but were also adopted for use by European settlers in North America. Methods: The aim of this review was to examine the Cherokee ethnobotanical literature and the published phytochemical investigations on Cherokee medicinal plants and to correlate phytochemical constituents with traditional uses and biological activities. Results: Several Cherokee medicinal plants are still in use today as herbal medicines, including, for example, yarrow (Achillea millefolium), black cohosh (Cimicifuga racemosa), American ginseng (Panax quinquefolius), and blue skullcap (Scutellaria lateriflora). This review presents a summary of the traditional uses, phytochemical constituents, and biological activities of Cherokee aromatic and medicinal plants. Conclusions: The list is not complete, however, as there is still much work needed in phytochemical investigation and pharmacological evaluation of many traditional herbal medicines.

Keywords: Cherokee; Native American; traditional herbal medicine; chemical constituents; pharmacology

1. Introduction

Natural products have been an important source of medicinal agents throughout history and modern medicine continues to rely on traditional knowledge for treatment of human maladies [1]. Traditional medicines such as Traditional Chinese Medicine [2], Ayurvedic [3], and medicinal plants from Latin America [4] have proven to be rich resources of biologically active compounds and potential new drugs. Several plant-derived drugs are in use today, including, for example, vinblastine (from Catharanthus roseus (L.) G. Don, used to treat childhood leukemia); paclitaxel (from Taxus brevifolia Nutt., used to treat ovarian cancer); morphine (from Papaver somniferum L., used to treat pain); and quinine (from Cinchona spp., used to treat malaria) [5]. Not only are phytochemicals useful medicines in their own right, but compounds derived from them or inspired by them have become useful medicines [6,7]. For example, Artemisia annua L., a plant originally used in Traditional Chinese Medicine to treat fever, is the source of artemisinin, a clinically-useful antimalarial sesquiterpenoid [8]; the antihypertensive drug reserpine, isolated from the roots of Rauvolfia serpentina (L.) Benth. ex Kurz., has been used in Ayurveda to treat insanity, epilepsy, insomnia, hysteria, eclampsia, as well as hypertension [9]; Dysphania ambrosioides (L.) Mosyakin and Clemants (syn. Chenopodium ambrosioides L.) is used in several Latin American cultures as an internal anthelmintic and external antiparasitic [4] and has shown promise for treatment of cutaneous leishmaniasis [10]. The biological activity of D. ambrosioides has been attributed to the monoterpenoid endoperoxide ascaridole.

Unfortunately, much of the traditional medicine knowledge of Native North American peoples has been lost due to population decimation and displacement from their native lands by European conquerors (see, for example: [11–14]). Nevertheless, there are still some remaining sources of...
information about Native American ethnobotany [15,16]. In addition, there are several sources of Cherokee ethnobotany [17–22].

The Cherokee Native Americans are a tribe of Iroquoian-language people who lived in the southern part of the Appalachian Mountain region in present-day northern Georgia, eastern Tennessee, and western North Carolina and South Carolina at the time of European contact [13] (Figure 1A). During and after the American Revolution, Cherokee wars with European settlers resulted in the surrender of vast amounts of territory. Gold was discovered on Cherokee land in north Georgia and the Treaty of New Echota (1835) ceded all Cherokee land east of the Mississippi River to the United States. Congress passed the Indian Removal Act in 1830, and the forced eviction of as many as 16,000 Cherokee took place during the fall and winter of 1838–1839 to a new territory in north-eastern Oklahoma (Figure 1B). During this “Trail of Tears”, an estimated one-fourth of the Cherokee died. However, at the time of the removal, a few hundred Cherokee successfully escaped to the mountains of western North Carolina, forming what is now the Eastern Band of Cherokee Indians.

In this review, I have consulted the ethnobotanical sources for plants used in Cherokee traditional medicine [15–24] and I have carried out a literature search using Google Scholar, PubMed, ResearchGate, and Science Direct for phytochemical analyses on the plant species. Note that in many instances, the phytochemistry was determined by plants not collected in the south-eastern United States; many of the species have been introduced to other parts of the world and some species are native to other continents besides North America. The phytochemistry, therefore, may be affected by the different geographical and climatic conditions [25]. Sources reporting the phytochemical constituents, regardless of geographical origin, have been included.
Figure 1. Cherokee territorial lands [26]. (A) "Map of the former territorial limits of the Cherokee 'Nation of' Indians", i.e., prior to displacement of Euro-Americans. (B) "Map showing the territory originally assigned Cherokee 'Nation of' Indians", i.e., after the forcible relocation known as the "Trail of Tears".

2. Cherokee Aromatic Medicinal Plants and Their Phytochemical Constituents

The plants used by the Cherokee people for traditional medicines for which the phytochemistry has been investigated are summarized in Table 1.
Table 1. List of Cherokee aromatic medicinal plants, their traditional uses, and phytochemical constituents and biological activities.

| Scientific Name | Family        | Common Name | Cherokee Use                | Part Used | Chemical Constituents and Activities                                                                 | Ref.   |
|-----------------|---------------|-------------|-----------------------------|-----------|-------------------------------------------------------------------------------------------------------|--------|
| *Acer rubrum* L. | Sapindaceae   | Red maple   | analgesic (cramps), eye soreness | bark      | Leaves: 1-O-galloyl-α-L-rhamnose, 1-O-galloyl-β-D-glucose, gallic acid, methyl gallate, ethyl gallate, m-digallate, ethyl digallate | [15]   |
|                 |               |             |                             |           | Leaves: gallic acid, methyl gallate, ethyl gallate, m-digallate, ethyl m-digallate, 1-O-galloyl-β-D-glucose, 1-O-galloyl-α-L-rhamnose, kaempferol 3-O-β-D-glucoside, kaempferol 3-O-β-D-galactoside, quercetin 3-O-β-D-glucoside, quercetin 3-O-β-L-rhamnoside and quercetin | [27]   |
|                 |               |             |                             |           | Leaves: major gallotannins: maplexin B, ginnalin B, ginnalin C, ginnalin A, maplexin F and a pair of isomers, 6-O digalloyl-2-O-galloyl-1,5-anhydro-D-glucitol and 2-O digalloyl-6-O-galloyl-1,5-anhydro-D-glucitol; ginnalin A was the predominant gallotannin | [28]   |
|                 |               |             |                             |           | Bark: catechin, epicatechin gallate, procyanidin A₄, procyanidin A₂, quercetin-3-O-α-L-rhamnopyranoside, quercetin-3-O(3′-O-galloyl)-α-L-rhamnopyranoside, quercetin-3-O(2′-O-galloyl)-α-L-rhamnopyranoside, rotrachelogenin-6′-O-β-D-glucopyranoside, 7,8-dihydroxy-6-ethoxy coumarin, phloridzin, methyl vanillate, 3,5-dihydroxy-4-methoxybenzoic acid, and 3-methoxy-4-hydroxyphenol-1-O-β-D-(6′-O-galloyl)-glucopyranoside | [29]   |
|                 |               |             |                             |           | Bark: gallotannins, named maplexins A-E; showed α-glucosidase inhibitory activity | [30]   |
|                 |               |             |                             |           | Bark: gallotannins, maplexins F-I; phenolic glycosides, rubrumosides A-B. The maplexins showed α-glucosidase inhibitory activity | [31]   |
|                 |               |             |                             |           | Bark: Maplexins C and D showed cytotoxic activity on HCT-116 and MCF-7 cells | [32]   |
|                 |               |             |                             |           | Leaves and flowers: 2-methoxy-1-O-galloyl-myo-inositol, 1-O-(3′-methoxy-galloyl)-β-D-glucose | [33]   |
| *Acer saccharinum* L. | Sapindaceae   | Silver maple | analgesic (cramps), eye soreness | bark      | Leaves: methyl gallate; cytotoxic to B16 melanoma in mice | [15]   |
|                 |               |             |                             |           | Leaves: glucitol-core containing gallotannins (GCCs), ginnalins A-C, maplexins B, D, and F; phenolics, methyl syringate, methyl gallate, and 3-methoxy-4-hydroxyphenol-1-β-D-(6-galloyl)-glucopyranoside; sesquiterpenoid pubinird A | [34]   |
| Scientific Name         | Family       | Common Name | Cherokee Use           | Part Used | Chemical Constituents and Activities                                                                 | Ref.  |
|------------------------|--------------|-------------|------------------------|-----------|------------------------------------------------------------------------------------------------------|-------|
| *Achillea millefolium* L. | Asteraceae   | Yarrow      | hemorrhages (leaves), fever (infusion) | leaves    | Herb: 5-hydroxy-3,6,7,4′-tetramethoxyflavone, artemetin, casticin | [15]  |
|                        |              |             |                        |           | Herb: chlorogenic acid, vicemin-2, luteolin-7-O-glucoside, rutin, apigenin-7-O-glucoside, luteolin, and apigenin | [35]  |
|                        |              |             |                        |           | Herb: apigenin, luteolin, centauredin, β-sitosterol, 3β-hydroxy-11α,13-dihydro-costunolide, desacylmatricarin, leucodin, achill, 8α-angeloy-lexocodin and 8α-angeloy-achillin | [38]  |
|                        |              |             |                        |           | Herb: chlorogenic acid, rutin, luteolin 7-O-glucoside, 1,3-dicaffeoylquinic acid, 1,4-dicaffeoylquinic acid, 3,4-dicaffeoylquinic acid, apigenin 4′-O-glucoside, apigenin 7-O-glucoside, luteolin 4′-O-glucoside, 3,5-dicaffeoylquinic acid; luteolin and apigenin 7-O-glucoside showed notable antiplasmodial activity | [39]  |
|                        |              |             |                        |           | Herb: 5-O-caffeoylquinic acid, quercetin O-hexoside, 3,4-O-dicaffeoylquinic acid, quercetin O-acetylhexoside, cis-3,5-O-dicaffeoylquinic acid, trans-3,5-O-dicaffeoylquinic acid, 4,5-O-dicaffeoylquinic acid, apigenin 7-O-glucoside, luteolin O-acetylhexoside, apigenin O-acetylhexoside | [40]  |
|                        |              |             |                        |           | Herb: chlorogenic acid, 3,5-dicaffeoyl quinic acid, 4,5-dicaffeoyl quinic acid, apigenin 7-O-glucoside, luteolin | [41]  |
|                        |              |             |                        |           | Flowers: methyl achimillate A, methyl achimillate B, methyl achimillate C, all three compounds active against P-388 leukemia in vivo (mouse) | [42]  |
|                        |              |             |                        |           | Herb: dihydrodehydrodiconiferyl alcohol 9-O-β-D-glucopyranoside, apigenin, apigenin-7-O-β-D-glucopyranoside, luteolin, luteolin-7-O-β-D-glucopyranoside, rutin, 3,5-dicaffeoylquinic acid, and chlorogenic acid; apigenin and luteolin showed in vitro estrogenic activity | [43]  |
|                        |              |             |                        |           | Herb: hydroalcoholic extract showed antinociceptive activity | [44]  |
|                        |              |             |                        |           | Herb: rutin, schaftoside, isoschaftoside, luteolin-7-O-glucoside (major), apigenin-7-O-glucoside (major), luteolin-7-malonylglicoside, apigenin-7-malonylglicoside, luteolin, apigenin | [45]  |
|                        |              |             |                        |           | Herb: five flavonoids (apigenin, luteolin, centauredin, casticin and artemetin) and five sesquiterpenoids (paulitin, isopaulitin, paulostachyin C, desacylmatricarin and sintrin); centaureadin, casticin, and paulitin showed good in vitro cytotoxic activity on HeLa, MCF-7, and A-431 cells | [46]  |
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|--------------------------------------|------|
| Aesculus pavia L. | Sapindaceae | Red buckeye | tumors, infections (poultice of nuts) | nuts | Fruits: polyhydroxyoleane triterpenoid saponins (aesculiosides Ia–Ie, IIa–IId, and IVa–IVc) | [54] |
| Fruits: 13 polyhydroxyoleane pentacyclic triterpenoid saponins, aesculiosides Ia–IIa, and Ila–IIIa, together with 18 known compounds: aesculiosides Ia–Ie, IIa–IId, and IVa–IVc, 3-O-[β-D-galactopyranosyl(1→2)-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-β,15a,16a,21β,22α,28-hexahydroxyolean-12-ene, 3-O-[β-D-glucopyranosyl(1→2)-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-β,16a,21β,22α,24β,28-hexahydroxyolean-12-ene, 3-O-[β-D-galactopyranosyl(1→2)-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-β,16a,21β,22α,24β,28-pentahydroxyolean-12-ene, R1-barrigenol, scopolin, and 5-methoxyscopolin. Aesculioside Ic, 3-O-[β-D-galactopyranosyl(1→2)-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-β,15a,16a,21β,22α,28-hexahydroxyolean-12-ene, 3-O-[β-D-glucopyranosyl(1→2)-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-β,16a,21β,22α,24β,28-hexahydroxyolean-12-ene, 3-O-[β-D-galactopyranosyl(1→2)-α-L-arabinofuranosyl(1→3)-β-D-glucuronopyranosyl-21,22-O-diangeloyl-β,16a,21β,22α,24β,28-pentahydroxyolean-12-ene, showed broad cytotoxic activity | [55] |
| Herb EO: 1,8-cineole (24.6%), camphor (16.7%), α-pinene (10.2%), weak antimicrobial activity on *Streptococcus pneumoniae*, *Clostridium perfringens*, and *Candida albicans* | [48] |
| Herb EO: germacrene D (6.1%), chamazulene (48.3%); shows antitypanosomal activity (*Trypanosoma cruzi*) | [49] |
| Herb EO: α-pinene (0.6–10.0%), camphene (0.4–15.4%), β-pinene (1.9–38.7%), limonene (1.4–3.8%), γ-terpinene (3.5–13.1%), β-caryophyllene (4.4–13.8%), germacrene D (1.7–10.7%), cadinene (0.7–32.2%) | [50] |
| Herb supercritical CO\(_2\) extract: myrcene (4.9%), p-cymene (5.4%), 1,8-cineole (16.2%), γ-terpinene (9.4%), camphor (38.4%), bornyl acetate (4.3%) | [51] |
| Herb EO: β-pinene (4.3%), 1,8-cineole (15.2%), β-cubebene (4.0%), germacrene D (14.1%), τ-cadinol (4.4%) | [52] |
| Herb EO: sabinene (5.4%), 1,8-cineole (24.5%), trans-sabinene hydrate (10.2%), cis-sabinene hydrate (4.6%), camphor (4.9%), terpinen-4-ol (5.6%), bornyl acetate (4.0%), germacrene D (7.2%) | [53] |
Table 1. Cont.

| Scientific Name | Family        | Common Name      | Cherokee Use                  | Part Used     | Chemical Constituents and Activities                                                                 | Ref.   |
|-----------------|---------------|------------------|-------------------------------|---------------|-----------------------------------------------------------------------------------------------------|--------|
| *Aesculus pavia* L. | Sapindaceae   | Red buckeye      | tumors, infections (poultice of nuts) | nuts          | Fruits: oleane saponins (vaccaroside A, vaccaroside B), showed in vitro cytotoxic activity on FL normal human amniotic cells and A-549 human lung carcinoma cells [56] |
| *Ageratina altissima* (L.) R.M. King and H. Rob. (syn. *Eupatorium rugosum* Houtt.) | Asteraceae     | White snakeroot | fever, tonic, urinary diseases | root         | Leaves: oleane saponins (escins Ia, Ib, Ila, Ilb, Illa) [57]                          |
| *Allium canadense* L. | Amaryllidaceae | Meadow garlic    | cathartic, diuretic           | entire plant  | Herb: cysteine sulfoxides: methin, allin, propin [63]                                           |
| *Allium cernuum* Roth | Amaryllidaceae | Nodding onion   | fever                         | entire plant  | Herb: diosgenin [64]                                                                              |

**Fruits:** oleane saponins (vaccaroside A, vaccaroside B), showed in vitro cytotoxic activity on FL normal human amniotic cells and A-549 human lung carcinoma cells [56]

**Leaves:** prenylated coumarin pavietin; flavonol glycosides quercetin 3-O-α-rhamnosi (quercitrin), quercetin 3-O-α-arabinosi, and isorhamnetin 3-O-α-arabinosi (distichin). Pavietin showed antifungal activity on *Guignardia aesculi* [57]

**Aerial parts:** tremetone, 6-hydroxytremetone, dehydrotremetone; tremetone cytotoxic on murine melanoma (B16F1) cells [60]

**Aerial parts:** tremetone, dehydrotremetone [61]

**Aerial parts:** tremetone, 6-hydroxytremetone, dehydrotremetone, dehydrotremetone, 2-senecioyl-4-acetylphenol, 2-senecioyl-4-(1-methoxyethyl)phenol, 6-acetyl-2,2-dimethylchroman-4-one, 6-acetyl-7-methoxy-2,2-dimethylchromene, 6-acetyl-8-methoxy-2,2-dimethylchromene, 6,7-dimethoxy-2,2-dimethylchromene, and 6-(1-hydroxyethyl)-7-methoxy-2,2-dimethylchromene. Tremetone, hydroxygremetone, dehydrotremetone toxic in goldfish assay [62]

**Herb:** cysteine sulfoxides: methin, allin, propin [63]

**Herb:** diosgenin [64]
| Scientific Name | Family           | Common Name     | Cherokee Use               | Part Used  | Chemical Constituents and Activities                                                                 | Ref. |
|-----------------|------------------|-----------------|-----------------------------|------------|-----------------------------------------------------------------------------------------------------|------|
| *Allium tricoccum* | Amaryllidaceae   | Wild leek       | tonic (entire plant)         | entire plant | Herb: methanesulfiniothioic acid S-methyl ester, methanesulfiniothioic acid S-2-propenyl ester, 2-propene-1-sulfiniothioic acid S-methyl ester, methanesulfiniothioic acid S-(E)-1-propenyl ester, methanesulfiniothioic acid S-(Z)-1-propenyl ester, (E)-1-propenesulfiniothioic acid S-2-propenyl ester (allicin), 1-propenesulfiniothioic acid S-2-propenyl ester, 2-propene-1-sulfiniothioic acid S-(E)-1-propenyl ester, 2-propene-1-sulfiniothioic acid S-(Z)-1-propenyl ester, (E)-1-propenesulfiniothioic acid S-2-propenyl ester, 1-propenesulfiniothioic acid S-(E)-1-propenyl ester, (E)-1-propenesulfiniothioic acid S-2-propenyl ester, methyl 1-(methylsulfinyl)propyl disulfide, methyl (E)-1-(1-propenylsulfinyl)propyl disulfide, 1-(methylsulfinyl)propyl disulfide, (E)-1-propenyl 1-(2-propenylsulfinyl)propyl disulfide, 2-propenyl 1-(2-propenylsulfinyl)propyl disulfide, (E)-1-propenyl 1-(1-propenylsulfinyl)propyl disulfide, diosgenin saponin: diosgenin 3-O-[α-rhamnosyl(1→2)]-β-glucoside, 3-O-[α-rhamnosyl(1→2)]-β-glucoside, 3-O-[α-rhamnosyl(1→2)]-β-glucoside, several of these saponins showed molluscicidal activity | [65] |
| *Allium vineale* | Amaryllidaceae   | Wild garlic     | carminative, cathartic,   | entire plant | Herb: molluscicidal saponins (nuatigenin 3-O-[α-rhamnosyl(1→2)]-β-glucoside, 3-O-[α-rhamnosyl(1→2)]-β-glucoside | [66] |

[Table 1. Cont.]
Table 1. Cont.

| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|-------------------------------------|------|
| **Medicinal Herbs**<sup>1</sup> | | | | | | |
| *Aralia nudicaulis* L. | Araliaceae | Wild sarsaparilla | root infusion taken as a blood tonic | root | Herb: flavones: chrysoeriol-7-([2''-O-4'']-feruloyl)]-β-D-glucoside, chrysoeriol, isorhamnetin-3-β-D-glucoside, and quercetin | [68] |
| | | | | | Herb EO: methyl (E)-1-propenyl disulfide (2.6-12.5%), benzaldehyde (up to 16.4%), dimethyl trisulfide (3.8-17.4%), allyl (E)-1-propenyl disulfide (7.9-12.5%), allyl methyl trisulfide (7.9-13.2%), diallyl trisulfide (2.8-10.5%), p-vinylguaiacol (52-6.5%), 5-methyl-1,2,3,4-tetrahydiane (up to 6.1%) | [69] |
| *Aralia spinosa* L. | Araliaceae | Devil’s walking stick | root (poisonous) used for emetic, venereal diseases | root | Leaf EO: (2E)-hexenal (13.8-29.8%), myrcene (13.9-15.1%), β-caryophyllene (8.2-15.7%), α-humulene (1.9-4.9%), germacrene D (28.0-37.3%), (E)-nerolidol (1.2-10.4%) | [70] |
| *Arnica cordifolia* Hook. | Asteraceae | Arnica | pain reliever, anti-inflammatory | flowers | Aerial parts: flavonoids: hispidulin, genkwanin, quercetin 3-methyl ether, quercetin 3-gentiobioside, quercetin 3-diglucoside, 6-methoxykaempferol 3-glicoside, isouercitrin, astragalin, neptirin, and glucofuselolin | [71] |
| *Aruncus dioicus* (Walter) Fernald | Rosaceae | Goatsbeard | beaten root applied to bee stings | root | Phytchemistry of Eurasian varieties studied, but not North American varieties | [72] |
| *Aruncus dioicus* var. *kamtschaticus* (Maxim.) H. Hara<sup>a</sup> | Rosaceae | Goatsbeard | beaten root applied to bee stings | root | Aerial parts: aruncin A, aruncin B, aruncide A, aruncide B, aruncide C; aruncin B showed cytotoxic activity on Jurkat T cells | [73] |

<sup>1</sup> Certain scientific names were not converted into natural language due to their uniqueness or complexity. The provided information is based on the content of the table and the context of the listed scientific names, families, common names, Cherokee uses, and chemical constituents.
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|----------------|--------|-------------|--------------|-----------|-------------------------------------|------|
| *A. dioicus* var. *kamtschaticus* | *A* | Aerial parts: aruncin B, cytotoxic to Jurkat T cells (apoptosis, microtubule damage) | [77] |
| *A. dioicus* var. *kamtschaticus* a | *A* | Aerial parts: palmitic acid, 10-monocosanol, pentacosan-1-ol, phytol, β-sitosterol, β-sitosterol-3-β-D-glucopyranoside, 2,4-dihydroxycinnamic acid, hyperoside, uridine, and adenosine; β-sitosterol-3-β-D-glucopyranoside cytotoxic to HL-60 cells; 2,4-dihydroxycinnamic acid and hyperoside showed antioxidant (DPPH radical-scavenging) activity | [78] |
| *A. dioicus* var. *kamtschaticus* a | *A* | Aerial parts: sambunigrin, prunasin, aruncide A, aruncide C, 1-O-caffeoyl-β-D-glucopyranose, and caffeic acid; aruncide C cytotoxic to HeLa cells; aruncide A cytotoxic to HL-60 cells; 1-O-caffeoyl-β-D-glucopyranoside cytotoxic to MCF-7 cells | [79] |
| *A. dioicus* (Italy) | *A* | Young shoots: 4-O-cafeoylglucose, chlorogenic acid, dicaffeoylglucose isomer I, dicaffeoylglucose isomer II, 3,5-dicafeoylquinic acid, prunasin | [80] |

*Asarum canadense* L. Aristolochi-aceae Wild ginger vermicide (root), wounds (poultice of leaves) root, leaves | Leaves: chalcone glycosides (chalconaringenin 2′,4′-di-O-glucoside and chalconaringenin 2′-O-glucoside-4′-O-gentiobioside) and flavonol glycosides (quercetin 3-O-glucoside, quercetin 3-O-rhamnoside, quercetin 3-O-rhamnopyranoside, kaempferol 3-O-galactoside, kaempferol 3-O-glucoside, kaempferol 3-O-galactoside-7-O-rhamnoside and iso-rhamnetin 3-O-rhamnopyranoside) | [81] |
| Rhizome EO: 4-methyleugenol (44.5%), linalyl acetate (41.1%), geraniol (7.4%), linalool (5.3%) | [82] |
| Rhizome EO: 4-methyleugenol (53.6%), linalool (19.4%), 4-terpineol (6.9%) | [83] |
| Rhizome EO: 4-methyleugenol (53.6%), linalool (12.5%), 4-terpineol (6.9%) | [84] |

*Asclepias tuberosa* L. Apocyn-aceae Butterfly weed cough root | Roots: steroids (ascandroside, Δ5-calotropin, Δ5-calotropin 3′-O-β-D-glucoside, Δ5-calotropin (3′S)-3′-thiazolidinone, Δ5-calotropin (3′R)-3′-thiazolidinone-5-oxide) | [86] |
| Roots: Pregnane steroid (ikemagenin, lineolon, pleurogenin) glycosides | [87] |
| Aerial parts: Pregnane steroid glycosides (tuberosides A1–L2) | [88] |
| Aerial parts: Pregnane steroid glycosides (tuberosides B1 and B2) | [89] |
| Scientific Name          | Family           | Common Name      | Cherokee Use           | Part Used | Chemical Constituents and Activities                                                                 | Ref. |
|-------------------------|------------------|------------------|------------------------|-----------|------------------------------------------------------------------------------------------------------|------|
| *Asclepias tuberosa* L. | Apocynaceae      | Butterfly weed   | cough                  | root      | Roots: Pregnane steroid glycosides (tuberosides A₀, B₀, B₁, C₁, D₁, D₂, E₂, F₂, G₁, H₁, I₂, I₃, K₁, K₂, M₁, N₁, O₁, P₁, and Q₁) | [22] |
| *Baptisia australis* (L.) R. Br. | Fabaceae        | Wild indigo      | cold infusion          | plant     | Flavonoids: afrormosin 7-0-β-D-glucoside, apigenin 7-0-β-D-glucoside, luteolin 7-0-β-D-glucoside, formononetin 7-0-β-D-glucoside, formononetin, and afrormosin; coumarin triflorizin | [91] |
|                         |                  |                  |                        |           | Isoflavonoid: texasin 7-0-β-D-glucoside                                                                 | [92] |
| *Berberis canadensis* Mill. | Berberidaceae    | American barberry | bark infusion for diarrhea | bark      | Alkaloids: (+)-sparteine and (-)-N-methylcytisine                                                     | [93] |
|                         |                  |                  |                        |           | Callus culture: isouquinoline alkaloid jatrorrhizine                                                 | [94] |
| *Betula nigra* L.       | Betulaceae       | River birch      | dysentery, colds       | leaves    | Bud EO: benzyl alcohol (2.4-5.0%), nonanal (0.7-6.6%), eugenol (28.7-55.3%), tricosane (1.6-8.0%), heptacosane (6.2-39.1%) | [95] |
|                         |                  |                  |                        |           | Leaf EO: linalool (9.8-19.2%), eugenol (6.7-13.5%)                                                   | [95] |
|                         |                  |                  |                        |           | Bark EO: hexanal (0.8-5.8%), (Z)-hexenol (0-7.8%), o-methylarilose (0.3-5.3%), octanoic acid (0.2-7.4%), eugenol (trace-8.8%), decanoic acid (0.6-24.4%), dodecanoic acid (0.7-29.2%), palmitic acid (8.8-43.7%), heptacosane (2.5-24.3%) | [95] |
|                         |                  |                  |                        |           | Bark: betulonaldehyde, lupeol, betulin, betulinic acid, betulin caffeate                             | [96] |
|                         |                  |                  |                        |           | Buds: combretol, 5-hydroxy-3,4′,7-trimethoxyflavone                                                | [97] |
|                         |                  |                  |                        |           | Buds: 3,5-dihydroxy-4′,7-dimethoxyflavone                                                            | [98] |
| *Callicarpa americana* L. | Lamiaceae        | American beautyberry | Alabama tribe of Native Americans (not Cherokee) used a decoction of roots/branches sweat bath for rheumatism, fever | roots, branches | | [15] |
### Table 1. Cont.

| Scientific Name       | Family      | Common Name          | Cherokee Use                              | Part Used                                                                 | Chemical Constituents and Activities                                                                 |
|-----------------------|-------------|----------------------|-------------------------------------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| **Callicarpa americana** |             |                      |                                           | Leaf EO: 1-octen-3-ol (8.5%), β-pinene (8.8%), α-humulene (10.1%), humulene epoxide II (13.9%), intermediol (9.5%), callicarpenal (4.3%); the EO was selectively toxic toward the cyanobacterium Oscillatoria perornata | [99]                                                                                                   |
|                       |             |                      |                                           | Leaf EO: α-humulene, humulene epoxide II, intermediol, callicarpenal; intermediol and callicarpenal showed mosquito repellent activity (*Aedes aegypti*, *Anopheles stephensi*) | [100]                                                                                                  |
|                       |             |                      |                                           | Leaves: callicarpenal and intermediol; both showed tick repellent activity | [101]                                                                                                  |
|                       |             |                      |                                           | Fruiting branches: clerodane diterpenoids:                              | [102]                                                                                                  |
|                       |             |                      |                                           | 12(S),16ξ-hydroxy-16ξ-methoxycleroda-3,13-dien-15,16-olide,              |                                                                                                       |
|                       |             |                      |                                           | 12(S)-hydroxy-16ξ-methoxycleroda-3,13-dien-15,16-olide,                 |                                                                                                       |
|                       |             |                      |                                           | 12(S)-hydroxycleroda-3,13-dien-15,16-olide,                             |                                                                                                       |
|                       |             |                      |                                           | 16ξ-hydroxycleroda-3,11(E),13-trien-15,16-olide,                         |                                                                                                       |
|                       |             |                      |                                           | 3β,12(S)-dihydroxycleroda-4(18),13-dien-15,16-olide, and                |                                                                                                       |
|                       |             |                      |                                           | 12(S)-hydroxycleroda-3,13-dien-15,16-olide,                             |                                                                                                       |
|                       |             |                      |                                           | 16ξ-hydroxycleroda-3,11(E),13-trien-15,16-olide,                         |                                                                                                       |
|                       |             |                      |                                           | 12(S),16ξ-dihydroxycleroda-3,13-dien-15,16-olide,                       |                                                                                                       |
|                       |             |                      |                                           | 16ξ-hydroxycleroda-3,13-dien-15,16-olide,                               |                                                                                                       |
|                       |             |                      |                                           | 2-formyl-16ξ-hydroxy-3-A-norcleroda-2,13-dien-15,16-olide,              |                                                                                                       |
|                       |             |                      |                                           | 12(S),16ξ-dihydroxycleroda-3,13-dien-15,16-olide,                       |                                                                                                       |
|                       |             |                      |                                           | 16ξ-hydroxycleroda-3,11(E),13-trien-15,16-olide,                         |                                                                                                       |
|                       |             |                      |                                           | 12(S)-hydroxycleroda-3,13-dien-15,16-olide,                             |                                                                                                       |
|                       |             |                      |                                           | 16ξ-hydroxycleroda-3,11(E),13-trien-15,16-olide,                         |                                                                                                       |
|                       |             |                      |                                           | 12(S)-hydroxycleroda-3,13-dien-15,16-olide,                             |                                                                                                       |
|                       |             |                      |                                           | 16ξ-hydroxycleroda-3,13-dien-15,16-olide,                               |                                                                                                       |
|                       |             |                      |                                           | 2-formyl-16ξ-hydroxy-3-A-norcleroda-2,13-dien-15,16-olide,              |                                                                                                       |
|                       |             |                      |                                           | showed broad-spectrum cytotoxic activity                                 |                                                                                                       |
| **Calycanthus floridus** | Calycanth-aceae | Eastern sweetshrub | bark sap used on sores; bark infusion used on hives. Root strong emetic. |                                                            | Flowers: anthocyanin pigments: cyanidin-3-glucoside, cyanidin-3-rutinoside                            | [15]                                                                                                  |
|                       |             |                      |                                           | Herb EO: α-pinene, 1,8-cineole (major), borneol, bornyl acetate           | [103]                                                                                                  |
|                       |             |                      |                                           | Herb EO: (E)-β-ocimene (13.8%)                                          | [104]                                                                                                  |
| **C. floridus var. oblongifolius** |             |                      |                                           | FloraEO: α-pinene (10.2%), β-pinene (8.6%), 1,8-cineole (33.1%), bornyl acetate (14.1%), α-terpinyl acetate (5.8%), elemol (8.2%) | [105]                                                                                                  |
| Boudford and Spongberg (Iran)       |             |                      |                                           | Herb EO: (E)-β-ocimene (13.8%)                                          | [106]                                                                                                  |
| **C. floridus var. oblongifolius** (Iran) |             |                      |                                           | Stem EO: α-pinene (10.0%), β-pinene (7.2%), 1,8-cineole (31.7%), bornyl acetate (12.6%), α-terpinyl acetate (6.8%), elemol (9.0%) | [107]                                                                                                  |
| Scientific Name                      | Family            | Common Name | Cherokee Use                                                                 | Part Used  | Chemical Constituents and Activities                                                                                                    | Ref.  |
|-------------------------------------|-------------------|-------------|--------------------------------------------------------------------------------|------------|------------------------------------------------------------------------------------------------------------------------------------------|-------|
| *Caulophyllum thalictroides* (L.)  | Berberidaceae     | Blue cohosh | root decoction given as sedative and anticonvulsive; root taken internally to treat rheumatism | root       | Roots: alkaloids: N-methylcytisine, baptifoline, anagyrine, magnoflorine (major)                                                        | [108] |
|                                     |                   |             |                                                                                 |            | Roots: quinolizidine alkaloids: N-methylcytisine, baptifoline (major), anagyrine                                                        | [109] |
|                                     |                   |             |                                                                                 |            | Roots: alkaloids: thalictroidine, taspine, magnoflorine, anagyrine, baptifoline, 5,6-dehydro-α-isolupanine, α-isolupanine, lupanine, N-methylcytisine, and sparteine; N-methylcytisine showed teratogenic activity | [110] |
|                                     |                   |             |                                                                                 |            | Roots: piperidine alkaloids (caulophyllumine A, caulophyllumine B), quinolizidine alkaloids (anagyrine, lupanine, O-acetylbaptifolin, N-methylcytisine), oleanane saponins (caulosides A, B, C, D, G, H, leonticin D, ciwujianoside A, saponin PE) | [111] |
|                                     |                   |             |                                                                                 |            | Roots: alkaloids, O-acetylbaptifolin, anagyrine, caulophyllumine B, lupanine showed cytochrome-P450 inhibitory activity                    | [112] |
|                                     |                   |             |                                                                                 |            | Roots: oleanane saponins: caulosides A, B, C, D, G, leonticin D, and 3-O-β-D-glucopyranosyl(1→2)-α-L-arabinopyranosyl-ehinosyctic acid 28-O-α-L-rhamnopyranose(1→4)-β-D-glucopyranoside | [113] |
|                                     |                   |             |                                                                                 |            | Roots: 22 oleanane saponins; several showed cytotoxicity on HL-60 cells                                                              | [114] |
|                                     |                   |             |                                                                                 |            | Roots: oleanane saponins caulosides A-D exert anti-inflammatory effects by inhibiting expression of iNOS and proinflammatory cytokines | [115] |
| *Ceanothus americanus* L.          | Rhamnaceae        | New Jersey tea | root infusion taken for "bowel complaints"                                     | root       | Root bark: peptide alkaloids (ceanothine A, B, Ceanotheamine A, B)                                                                  | [116] |
|                                     |                   |             |                                                                                 |            | Root bark: peptide alkaloid amercine                                                                                                | [117] |
|                                     |                   |             |                                                                                 |            | Root bark: peptide alkaloids (ceanothine D, E, frangularine, adouetine-X, adouetine-Y)                                               | [118] |
| *Cercis canadensis* L.             | Fabaceae          | Redbud      | bark infusion used for severe coughs                                             | inner bark | Bark EO: 1-hexanol (23.3%), hexanoic acid (18.2%), (2E)-hexenoic acid (3.4%)                                                        | [119] |
| *Chelone glabra* L.                | Plantaginaceae    | Balmony     | herb used to treat skin problems; herb infusion taken as a digestive tonic      | herb       | Leaves: iridoid glycoside catalpol                                                                                                    | [120] |
| Scientific Name       | Family       | Common Name | Cherokee Use          | Part Used | Chemical Constituents and Activities                                                                                                                                                                                                 | Ref. |
|----------------------|--------------|-------------|-----------------------|-----------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|
| **Cichorium intybus** | **Asteraceae**| Chickory    | infusion of root as tonic | root      | Sesquiterpene lactones (8-deoxylactucin, lactucin, lactupicrin)                                                                                                                                                                    | 15   |
|                      |              |             |                       |           | Leaves and roots: sesquiterpene lactones (lactucin, 11β,13-dihydrolactucin, jacquinelin, 8-deoxylactucin, lactucopicrin, crepidiaside B, loliolide), p-hydroxyphenylacetic acid methyl and ethyl esters, cichoniside B, sonchuside A, ixerisoside D, magnolialide | 121  |
|                      |              |             |                       |           | Root: sesquiterpene lactones (lactucin, lactupicrin)                                                                                                                                                                                 | 122  |
|                      |              |             |                       |           | Leaves and roots: sesquiterpene lactones (guaianolides, lactucin, lactucopicrin, 11β,13-dihydrolactucin)                                                                                                                                 | 123  |
|                      |              |             |                       |           | Flowers: anthocyanin pigments: delphinidin 3,5-di-O-(6-O-malonyl-β-D-glucoside) and delphinidin 3-O-(6-O-malonyl-β-D-glucoside)-5-O-β-D-glucoside; delphinidin 3-O-β-D-glucoside-5-(6-O-malonyl-β-D-glucoside) and delphinidin 3,5-di-O-β-D-glucoside | 124  |
| **Cimicifuga racemosa** | **Ranunculaceae** | Black cohosh | root used to stimulate menstruation; root infusion used for rheumatism, coughs, colds | root      | Rhizome: triterpene glycosides (actein, 27-deoxyactein, cimicifugoside M, and cimicifugoside)                                                                                                                                       | 15   |
| (L.) Nutt. (syn. *Actaea racemosa* L.) |              |             |                       |           | Rhizome: triterpene glycosides (cimiaceroside A, 25-O-methylcemigenol-3-O-β-D-xylopyranoside, 27-deoxyactein, 23-O-acetylsengmanol-3-O-β-D-xylopyranoside, 16β,23,22β,25-diepoxy-12β-acetoxy-3β,23,24β-trihydroxy-9,19, cyclolanost-7-ene-3-O-β-D-xylopyranoside) | 126  |
|                      |              |             |                       |           | Rhizome: triterpene glycosides (12β-acetoxycimigenol-3-O-β-D-xylopyranoside, 25-acetoxycimigenol xyloside, cimigenol-3-O-β-D-xylopyranoside, acetylshengmanol 3-O-β-D-xylopyranoside, foetidinol-3-O-β-xyloside, cimicifugoside H-2, 25-O-methylcemigenol xyloside, 21-hydroxycimigenol-3-O-β-D-xylopyranoside, 24-en-7,8-didehydrocimigenol-3-xyloside, cimidahurinine, cimidahurine, and cimufugin) | 127  |
|                      |              |             |                       |           | Rhizome: triterpene glycosides (cimiracemosides A–H, 27-deoxyactein, 26-deoxycimicifugoside, actein, acetyl shengmanol xyloside, cimicifugoside (cimiragensol-3-O-β-D-xylopyranoside), cimiaceroside A, 12β-hydroxycimigenol-3-O-β-D-xylopyranoside, and 12β-hydroxycimigenol-3-O-α-L-arabinopyranoside) | 128  |
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|-------------------------------------|------|
| Rhizome: triterpene glycosides (cimigenol) 3-O-α-L-arabinopyranoside, 25-O-methoxycimigenol 3-O-α-L-arabinopyranoside, 12β-hydroxycimigenol 3-O-α-L-arabinopyranoside, 27-deoxyactein, actein, cimiracemoside F, cimiracemoside G, cimiracemoside H, 25-O-acetyl-12β-hydroxycimigenol 3-O-α-L-arabinopyranoside, 23-O-acetylcimigenol 3-O-α-L-arabinopyranoside, (2R,23R,24S)-12β-acetyloxy-16β,22,25-diepoxy-23,24-dihydroxy-9,19-cyclolanostan-3β-yl α-L-arabinopyranoside) | | | | | | [130] |
| Rhizome: triterpene glycosides (cimiracemoside H, 26-deoxyactein, 23-O-acetylcimigenol 3-O-β-D-xylopyranoside, actaeaepoxide 3-O-β-D-xylopyranoside, 25-O-acetylcimigenol 3-O-α-L-arabinopyranoside, 25-O-acetylcimigenol 3-O-β-D-xylopyranoside) | | | | | | [131] |
| Rhizome: triterpene glycosides (actein, 23-epi-26-deoxyactein, 23-O-acetylcimigenol 3-O-β-D-xylopyranoside, cimiracemoside D, 25-O-acetylcimigenol 3-O-β-D-xylopyranoside, and cimigenol) | | | | | | [132] |
| Rhizome: triterpene xylosides (cimipodocarpaside) | | | | | | [133] |
| Rhizome: triterpene xylides (cimigenol xyloside, 26-deoxyactein, cimicifugoside H-1, and 24-acetylhydroshengmanol xyloside) | | | | | | [134] |
| Rhizome: triterpene xylides (isocimipodocarpaside, 23-epi-26-deoxycimicifugoside, 23-epi-26-deoxyactein, 25-anhydrocimigenol xyloside, 25-O-acetylcimigenol xyloside, 3′-O-acetylcimicifugoside H-1) | | | | | | [135] |
| Rhizome: Cimicidol 3-O-β-D-xyloside (slightly hepatotoxic) | | | | | | [136] |
| Rhizome: fukiic and piscidic acid esters: (2E-caffeoylfukiic acid (fukinolic acid), 2E-feruloylfukiic acid (cimicifugic acid A), 2E-isofuruloylfukiic acid (cimicifugic acid B), 2E-feruloylpiscidic acid (cimicifugic acid E) and 2E-isofuruloylpiscidic acid (cimicifugic acid F), free caffeic, ferulic and isoferulic acids) | | | | | | [137] |
| Rhizome: phenylpropanoid esters (cimiracemates A–D) | | | | | | [138] |

Table 1. Cont.
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| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|-------------------------------------|------|
| **Collinsonia canadensis** L. | Lamiaceae | Heal-all | decoction taken as emetic | leaves | Rhizome: polyphenolics (actaealactone, cimicifugic acid G, protocatechuc acid, protocatechualdehyde, p-coumaric acid, caffeic acid, methyl caffeate, ferulic acid, ferulate-1-methyl ester, isoferulic acid, 1-isoferuloyl-â-D-glucopyranoside, fukinolic acid, and cimicifugic acids A, B, and D–F) | [141] |
| **Collinsonia canadensis** L. | Lamiaceae | Heal-all | decoction taken as emetic | leaves | Rhizome: alkaloids (cyclocimipronidine, cimipronidine methyl ester, cimipronidine, dopargine, salsolinol, 3-hydroxytyrosol 3-O-glucoside) | [142] |
| **Conyza canadensis** (L.) Cronquist (syn. *Erigeron canadensis* L.) | Asteraceae | Horseweed | leaves used for toothache | leaves | Leaf EO: germacrene D (46.0%), β-caryophyllene (5.3%), elemicin (3.6%), β-elemene (3.3%) | [143] |
| **Conyza canadensis** (L.) Cronquist (syn. *Erigeron canadensis* L.) | Asteraceae | Horseweed | decoction of herb used to treat diarrhea | herb | Roots: triterpene glycosides, hederagenin-3-O-α-L-arabinopyranoside (leontoside A), 3-O-α-L-arabinopyranosylcollinsogenin (collinsonin), 3-O-β-D-glucopyranosyl(1′′→3′)α-L-arabinopyranosylhederagenin (collinsonidin) | [144] |
| **Conyza canadensis** (L.) Cronquist (syn. *Erigeron canadensis* L.) | Asteraceae | Horseweed | leaves used for toothache | leaves | Leaf and stem exudates: flavonoids, 2,5-dihydroxy-6,7-dimethoxyflavanone, baicalein-6,7-dimethyl ether, norwogenin-7,8-dimethyl ether, and tectochrysin (5-hydroxy-7-methoxyflavone) | [145] |
| **Mikasuki and Seminole** | | | Native Americans used the plant to treat sore throats and respiratory complaints | | | [146] |
| **Conyza canadensis** (L.) Cronquist (syn. *Erigeron canadensis* L.) | Asteraceae | Horseweed | leaves used for toothache | leaves | Whole plant: β-sitosterol, stigmasterol, β-sitosterol 3-O-β-D-glucoside, harmine, and sphingolipid | [147] |
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|--------------------------------------|------|
| Whole plant: sphingolipids, 1,3,5-trihydroxy-2-hexadecanoylamino-(6E,9E)-heptacosdiene, 1,3,5-trihydroxy-2-hexadecanoylamino-(6E,9E)-heptacosdiene-1-O-glucopyranoside, 1,3-dihydroxy-2-hexanoylamino-(4E)-heptadecene; p-hydroxybenzoic acid, 3,5-dihydroxybenzoic acid, 3,5-dimethoxybenzoic acid, 3β-hydroxyolean-12-en-28-oic acid, and 3β-erythrodiol | | | | | [148] |
| Aerial parts: triterpenoid erigeronol (showed potent anti-melanoma cytotoxicity) | | | | | [149] |
| Whole plant: conyzolide, conyzoflavone (both showed antimicrobial activities) | | | | | [150] |
| Whole plant: 8R,9R-dihydroxymatricarinate methyl ester, matricarine methyl ester, matricarine lactone, 3β,16β,20β-trihydroxytaraxast-3-0-palmitoyl ester, friedelin, friedelinol, β-sitosterol, α-spinasterol, 3-isopropenyl-6-oxoheptanoic acid, 9-hydroxy-10Z,12E-octadecenoic acid, (+)-hydroxydihydrodieneocarvenol, 3′,4′,5,7-tetrahydroxydihydroflavone, 9,12,13-trihydroxy-10(Z)-octadecenoic acid | | | | | [151] |
| Whole plants: phenylprobanoyl esters (rel-(1S,2R,3R,5S,7R)-methyl 7-caffeoyloxymethyl-2-hydroxy-3-feruloyloxy-6,8-dioxabicyclo[3.2.1]octane-5-carboxylate, rel-(1S,2R,3R,5S,7R)-methyl 7-feruloyloxymethyl-2-hydroxy-3-feruloyloxy-6,8-dioxabicyclo[3.2.1]octane-5-carboxylate, and rel-(1R,2R,3R,5S,7R)-methyl 7-feruloyloxymethyl-2-feruloyloxy-3-hydroxy-6,8-dioxabicyclo[3.2.1]octane-5-carboxylate) | | | | | [152] |
| Aerial parts: enyne derivatives, (2Z,8Z)-matricaria acid methyl ester, (4Z,8Z)-matricaria lactone, and (4Z)-lachnophyllum lactone | | | | | [153] |
| Aerial parts: (4Z)-lachnophyllum lactone, (4Z,8Z)-matricaria lactone, (2Z,8Z)-matricaria acid methyl ester; (4Z)-lachnophyllum lactone and (4Z,8Z)-matricaria lactone showed antifungal activity against Aspergillus niger, Cladosporium sp., and Penicillium digitatum | | | | | [154] |
| Flowering parts: polyphenolic-polysaccharide (anticoagulant, antiplatelet activity) | | | | | [155] |
| Roots: dihydroxypyranones conyzapyranone A and B; 4E,8Z-matricaria-lactone, 4E,8Z-matricaria-γ-lactone, 9,12,13-trihydroxy-10(Z)-octadecenoic acid, epifriedelanol, friedelin, taraxerol, simiarenol, spinasterol, stigmasterol, β-sitosterol, and apigenin; conyzapyranone B, 4E,8Z-matricaria-γ-lactone, and spinasterol showed cytotoxic activity | | | | | [156,157] |
| Roots: triterpenoid 3β-erythrodiol (inhibits MKN-45 gastric cell proliferation) | | | | | [158] |
| Roots: salicylic acid, methyl gallate | | | | | [159] |
| Roots: lanostane triterpenoids conyzagenin-A, conyzagenin-B | | | | | [160] |
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|-------------------------------------|------|
| Coreopsis tinctoria Nutt. | Asteraceae | Tickseed | root tea for diarrhea | Aerial parts EO: limonene (76.0%), α-santalene (5.8%), δ-3-carene (3.9%), myrcene (3.6%) | [161] |
| | | | root | Aerial parts EO: limonene (57.9–81.1%), (E)-β-ocimene (0.7–9.1%), trans-α-bergamoten (5.6–8.9%), (Z)-β-farnesene (tr-11.1%). | [162] |
| | | | | Aerial parts EO: limonene (50.0–70.3%) and (E)-β-ocimene (4.0–7.5%) | [163] |
| | | | | Aerial parts EO: limonene (70.0%), trans-α-bergamotene (7.0%) | [164] |
| | | | | Aerial parts EO: limonene (77.7–89.4%), trans-α-bergamotene (1.5–3.8%), β-pinene (0.8–6.6%), carvone (0.5–1.8%) | [165] |
| | | | | Aerial parts EO: (E)-β-Farnesene (14.6%), spathulenol (14.1%) and limonene (12.3%) | [166] |
| | | | | Aerial parts EO: limonene (31.2%), camphene (14.2%) and germacrene D (11.3%) | [167] |
| | | | | Aerial parts EO: limonene (68.3%), δ-3-carene (15.9%) | [168] |
| | | | | Root EO: (2Z,8Z)-matricaria ester (88.2–93.9%) | [169] |

Plant: polyacetylenes, (2S)-(3Z,11E)-decadiene-5,7,9-triyne-1,2-diol and (2E)-(3E,11Z)-decadiene-5,7,9-triyne-1,2-diol | [170] |

Plant: seven compounds made up the major contributions of antioxidant activity in C. tinctoria, including okanin, isoakanin, marein, flavanomarein, 5,7,8,3′-tetrahydroxyflavanone-7-O-glucoside, 3,5-dicaffeoylquinic acid, and chlorogenic acid | [171] |

Flowers: C14 polyacetylene glycosides coreosides A–D | [172] |

Buds: C14 polyacetylene glycosides coreosides E and F | [173] |

Flowers: C14 polyacetylene glycosides coreosides A, B, D, and E | [174] |

Flowers: chalcone marein, flavanone flavanomarein | [175] |

Flowers: chalcone okanin-4′-O-β-D-glucopyranoside; flavonoids flavanomarein okanin-4′-O-β-D-glucopyranoside, quercetatin 7-O-β-D-glucopyranoside, (2R,3R)-dihydroquercetin 7-O-β-D-glucopyranoside, okanin, quercetin, butein, 2S-3′,4′,7′-triarylhydroxyflavanone, (2R,3R)-3,4′,5,6,7-penta-arylhydroxyflavanone, (2R,3R)-3,4′,5,6,7-penta-arylhydroxyflavanone, and 2S-3′,5,5′,7-tetraarylhydroxyflavanone | [176] |

Flowers: flavonoids (flavanomarein, flavanokanin, quercetatin-7-O-glucoside, marein) | [177] |

Flowers: flavonoids (+)-catechin, kaempferol-3-O-glycoside, quercetin-3-O-glycoside, quercetin-3-O-rutinoside | [178] |
Table 1. Cont.

| Scientific Name          | Family     | Common Name   | Cherokee Use                                      | Part Used                                      | Chemical Constituents and Activities                                      | Ref. |
|--------------------------|------------|---------------|---------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------------------|------|
| *Cornus florida* L.      | Cornaceae  | Dogwood       | bark chewed for headache                          | bark                                          | Flowers: flavonoids (taxifolin, taxifolin-7-O-β-D-glucopyranoside, isookanin, flavanomarein, quercetagetin-7-O-β-D-glucopyranoside, 5,7,3′,5′-tetrahydroxyflavanone-7-O-β-D-glucopyranoside), chalcones (okanin, marenin), and phenolic acids (chlorogenic acid, 3,5-di-O-cafeoylquinic acid, 4,5-di-O-cafeoylquinic acid) | [179]|
|                          |            |               | bark decoction used for fevers, body aches; bark poultice used on sores/ulcers | bark                                          |                                                                           |      |
| *Datura stramonium* L.   | Solanaceae | Jimson weed    | leaf poultice applied to boils, leaves smoked for asthma | leaves                                        | Flowers: quercetagetin-7-O-glucoside, marenin (major), 1,3-dicaffeoylquinic acid, okanin, acetylmarein | [180]|
|                          |            |               |                                                   |                                               |                                                                           |      |
|                          |            |               |                                                   |                                               | Flowers: taxifolin-7-O-glucoside, flavanomarein, quercetagetin-7-O-glucoside, okanin 4′-O-glucoside, okanin, chlorogenic acid | [181]|
|                          |            |               |                                                   |                                               |                                                                           |      |
|                          |            |               |                                                   |                                               | Flowers: chlorogenic acid, (R/S)-flavanomarein, butin-7-O-β-D-glucopyranoside, isookanin, taxifolin, 5,7,3′,5′-tetrahydroxyflavanone-7-O-β-D-glucopyranoside, marenin, and okanin | [182]|
|                          |            |               |                                                   |                                               |                                                                           |      |
|                          |            |               |                                                   |                                               | Fruits: flavonoids (marenin, flavanomarein, quercetagetin-7-O-glucoside, okanin aurone, leptosidin, luteolin, apigenin) and phenolic acids (chlorogenic acid, caffeic acid) | [183]|
|                          |            |               |                                                   |                                               |                                                                           |      |
|                          |            |               |                                                   |                                               | Cornus florida. Bark: saponins (sarsapogenin-O-β-D-xylopyranosyl-(1→2)-β-D-galactopyranoside and sarsapogenin-O-β-D-glucopyranosyl-(1→2)-β-D-galactopyranoside) | [185]|
| *Diospyros virginiana* L. | Ebenaceae  | Persimmon     | bark infusion for venereal diseases, sore throat and mouth; syrup for oral thrush, bloody discharge from bowels | bark                                          |                                                                           | [17] |
|                          |            |               |                                                   |                                               |                                                                           |      |
|                          |            |               |                                                   |                                               |                                                                           | [186]|
|                          |            |               |                                                   |                                               |                                                                           | [187]|
|                          |            |               |                                                   |                                               |                                                                           | [188]|
|                          |            |               |                                                   |                                               |                                                                           | [189]|
|                          |            |               |                                                   |                                               |                                                                           | [190]|

**Ref.** - References for the chemical constituents and activities.
### Table 1. Cont.

| Scientific Name | Family       | Common Name     | Cherokee Use                  | Part Used          | Chemical Constituents and Activities                                                                 | Ref. |
|-----------------|--------------|-----------------|-------------------------------|--------------------|------------------------------------------------------------------------------------------------------|------|
| *Epilobium angustifolium* L. | Onagraceae   | Fireweed        | eye conditions due to asthma, allergies | herb               | Herb: quercetin 3-O-(6′′-galloyl)-galactoside, kaempferol 3-O(6′′-p-coumaryl)-glucoside, quercetin 3-O-glucuronide, oenothein B; oenothein B inhibited the endopeptidases neutral endopeptidase (NEP) and angiotensin converting enzyme (ACE) | [190]|
|                 |              |                 |                               |                    | Herb: oenothein B (a dimeric macrocyclic ellagitannin) inhibits proliferation of SK-N-SK and PC-3 cells | [190]|
|                 |              |                 |                               |                    | Herb: oenothein B enhances IFNy production by lymphocytes                                           | [190]|
|                 |              |                 |                               |                    | Herb: ellagitannins (oenothein B, oenothein A, tetramer, pentamer, hexamer, heptamer)             | [190]|
|                 |              |                 |                               |                    | Flowers and leaves: ellagitannins (oenothein B, oenothein A, tetramer, pentamer, hexamer, heptamer) | [190]|
| *Equisetum hyemale* L. | Equiset-aceae | Horsetail        | infusion taken for kidneys    | plant              | Stems: (E)-feruloyl-4-β-glucoside, (Z)-feruloyl-4-β-glucoside, (E)-caffeoyl-3-β-glucoside, kaempferol 3-sophoroside-7-β-glucoside, herbacetin-3-sophoroside-8-β-glucoside | [190]|
| *Eryngium puccinellum* Michx. | Apiaceae     | Baneberry, Rattlesnake master | remedy for snakebites | root               | Aerial parts: 2-(sophorosyl)-1-(4-hydroxyphenyl)etheneone                                           | [190]|
|                 |              |                 | remedy for snakebites         |                    | Plant extracts showed inhibition of *Crotalus* proteases                                           | [190, 17]|
|                 |              |                 | urinary-tract inflammation modulator | root               | Aerial parts EO: polyacetylenes (falkarinone, falkarinol, yuccifolol, 1,8-heptadecadiene-4,6-diyn-3,9-diol) | [200]|
|                 |              |                 |                               |                    | Leaf EO: α-pinene (7.6%), terpinolene (17.8%), β-carophyllene (6.2%), germacrene D (18.3%), bicyclogermacrene (8.8%), falkarinol (9.6%) | [200]|
|                 |              |                 |                               |                    | Root EO: α-pinene (4.7%), terpinolene (25.8%), 2,3,6-trimethylbenzaldehyde (13.9%), trans-β-bergamotene (18.6%) | [200]|
|                 |              |                 |                               |                    | Whole plant: triterpenoid saponins (eryngiosides A-L, saniculasaponin III), flavonoid (kaempferol) glycosides, polyphenolics (caffeates) | [200]|

Fruits: polyphenolics (methyl gallate, gallic acid, luteolin, quercetin, myricetin, quercitin 3-O-α-rhamnoside, myricetin 3-O-β-glucoside, myricetin 3-O-β-glucuronide)

Roots: 4-hydroxy-5,6-dimethoxy-2-naphthalene-2-carbaldehyde, 12,13-didehydro-20,29-dihydrobetulin, 7-methyljuglone, diospyrin, isodiospyrin, shinarolone, lupeol, betulin, betulinic acid, betulinaldehyde, and ursolic acid
Table 1. Cont.

| Scientific Name          | Family    | Common Name      | Cherokee Use                          | Part Used | Chemical Constituents and Activities                                           | Ref.     |
|--------------------------|-----------|------------------|---------------------------------------|-----------|-------------------------------------------------------------------------------|----------|
| Erythronium americanum  | Liliaceae | Trout Lily       | leaves crushed and juice poured over wounds | leaves    | The phytochemistry of E. yuccifolium has been reviewed                       | [205]    |
|                          |           |                  |                                       |           |                                                                                |          |
| Eupatorium maculatum L.  | Asteraceae| Joe-Pye weed     | root infusion for kidney, dropsy      | root      |                                                                                | [15]     |
|                          |           |                  |                                       |           | α-Methylenebutyrolactone                                                      | [206]    |
| Eupatorium perfoliatum L.| Asteraceae| Boneset          | infusion of the plant taken as a tonic, for colds, sore throat, and influenza | plant    |                                                                                | [15]     |
|                          |           |                  |                                       |           | Aerial parts: guianolide and germacranolide sesquiterpene lactones, flavonoids (eupafolin, hispidulin, patuletin, and kaempferol) | [209]    |
|                          |           |                  |                                       |           | Aerial parts: guianolide and germacranolide sesquiterpene lactones            | [15]     |
|                          |           |                  |                                       |           | Leaves: polyphenolics (protocatechuic acid, hyperoside, quercetin, rutin)      | [210]    |
|                          |           |                  |                                       |           | Aerial parts: extracts show anti-inflammatory activity, but not immunostimulatory activity | [213]    |
|                          |           |                  |                                       |           | Aerial parts: caffeic acid derivatives (5-cafeoylquinic acid (chlorogenic acid), 3-cafeoylquinic acid (neochlorogenic acid) and 3,5-dicafeoylquinic acid, 2,5-dicafeoylglycic acid, 3,4-dicafeoylglycic acid, and 2,4- or 3,5-dicafeoylglycic acid) | [214]    |
|                          |           |                  |                                       |           | Aerial parts: glycosides of kaempferol and quercetin; quianolides              | [216]    |
|                          |           |                  |                                       |           | Aerial parts EO: (E)-Anethole (16.5%), carvone (7.6%), selin-11-en-4a-ol (5.5%) | [217]    |
| Fagus grandifolia        | Fagaceae  | American Beech   | nuts chewed for worms                  | nuts      | Bark: monolignols [(Z)-coniferyl alcohol, (Z)-sinapyl alcohol, (Z)-coniferin, (Z)-isoconiferin, (Z)-syringin] | [155]    |
| Frasera caroliniensis    | Gentianaceae| American Columbo | root used to treat dysentery           | root      | Root: xanthones (1-hydroxy-2,3,4,7-tetramethoxyxanthone, 1-hydroxy-2,3,4,5-tetramethoxyxanthone, 1-hydroxy-2,3,7-trimethoxyxanthone, 1-hydroxy-2,3,5-trimethoxyxanthone, 1-hydroxy-2,3,5-trimethoxyxanthone, swerchirin, 1,3-dihydroxy-4,5-dimethoxyxanthone) | [218]    |
Table 1. Cont.

| Scientific Name                  | Family          | Common Name       | Cherokee Use                          | Part Used     | Chemical Constituents and Activities                                                                 | Ref. |
|---------------------------------|-----------------|-------------------|--------------------------------------|---------------|------------------------------------------------------------------------------------------------------|------|
| *Fraxinus americana* L.          | Oleaceae        | American ash      | tonic of inner bark taken for liver and stomach problems | bark          | Plant: iridoid (loganic acid), secoiridoid (gentiopicroside), and xanthones [1,3-diOH-4,5-diMeO-xanthone, 1-OH-2,3,5-triMeO-xanthone, 1-OH-2,3,4,5-tetraMeO-xanthone, 1-OH-2,3,4,7-tetraMeO-xanthone, 1,8-diOH-3,5-diMeO-xanthone (swerchirin)] | [218]|
|                                 |                 |                   |                                      |               | Bark: oleoside, syringin, hydroxypinoresinol glycoside, verbascoside, ligustroside                      | [15] |
|                                 |                 |                   |                                      |               | Leaves: secoiridoid glucosides (demethylligstroside, (2”R)-2”-hydroxyoleuropein, (2”S)-2”-hydroxyoleuropein, fraxamoside, framerosi, oleoside dimethyl ester, oleuropein, ligstroside, nuezhenide, (2”R)-2”-methoxyoleuropein, (2”S)-2”-methoxyoleuropein) | [219]|
|                                 |                 |                   |                                      |               | Seeds: catechins (epicatechin, catechin-3-O-gallate, epigallocatechin, epigallocatechin-3-O-gallate, epigallocatechin-(4β-8)-epicatechin, epicatechin-3-O-gallate-(4β-8)-epigallocatechin-3-O-gallate), procyanidins (procyanidin B-1, procyanidin B-3) | [220]|
| *Geranium maculatum* L.          | Geraniaceae     | Wild geranium     | cuts, sores, oral thrush             | plant         | Plant EO: citronellol (38%), geraniol (16%), citronellyl formate (10.4%), and linalool (6.45%)        | [221]|
| *Hamamelis virginiana* L.        | Hamamelidaceae  | Witch hazel       | bark infusion used on sores          | bark          | Bark: hamamelitannin cytotoxic to HT-29 colon tumor cells                                            | [222]|
|                                 |                 |                   |                                      |               | Leaves: gallotannins (hydrolyzable tannins: monogalloyl, heptagalloyl, octagalloyl, and nonagalloyl hexoses), caffeoylquinic acids (3-, and 5-), kaempferol glycoside                               | [223]|
|                                 |                 |                   |                                      |               | Bark: polymeric proanthocyanidins (condensed tannins).                                               | [224]|
|                                 |                 |                   |                                      |               | Bark: tannins, antioxidant, cytotoxic to SK-Mel-28 melanoma cells                                      | [225]|
|                                 |                 |                   |                                      |               | Bark: condensed (proanthocyanidins) and hydrolyzable (galloylhamameloses) tannins                       | [226]|
| *Helenium autumnale* L.          | Asteraceae      | Sneezeweed        | root infusion used to prevent menstruation after childbirth, dried leaves used to induce sneezing | roots, leaves | Apparently the root extract has not been examined                                                    | [15] |
|                                 |                 |                   |                                      |               | Aerial parts: dihydromexicanin E                                                                      | [227]|
|                                 |                 |                   |                                      |               | Aerial parts: flexuosin A                                                                           | [228]|
|                                 |                 |                   |                                      |               | Aerial parts: helenalin                                                                              | [229]|
|                                 |                 |                   |                                      |               | Aerial parts: tenuulin                                                                               | [230]|
|                                 |                 |                   |                                      |               |                                                                                                     |      |
| Scientific Name          | Family           | Common Name       | Cherokee Use                  | Part Used     | Chemical Constituents and Activities                                                                 | Ref. |
|-------------------------|------------------|-------------------|-------------------------------|---------------|------------------------------------------------------------------------------------------------------|------|
| *Helenalin*              |                  |                   |                               |               | Helenalin is cytotoxic (human epithelial type 2, HEp-2, cells)                                        | [232]|
| Whole plant: *carolenin* | and *carolenalin*|                   |                               |               | Whole plant: *carolenin* and *carolenalin*                                                            | [233]|
| Flowers: *helenalin*    | *autumnolide*    |                   |                               |               | Flowers: *helenalin*, *autumnolide*, mesicanin I, *helenalin* is cytotoxic                             | [234]|
| Plant: *dihydroflorilenalin*|                |                   |                               |               | Plant: *dihydroflorilenalin*                                                                        | [235]|
| Plant: 4-O-tigloyl-11,13-dihydroautumnolide|          |                   |                               |               | Plant: 4-O-tigloyl-11,13-dihydroautumnolide                                                          | [236]|
| *Helenalin*              |                  |                   |                               |               | Rhizomes: alkaloids (berberine, 8-oxotetrahydrothalifendine, canadine, and β-hydrastine); berberine shows antitubercular activity| [237]|
| Aerial parts: *berberine*|                 |                   |                               |               | Rhizomes: *berberine* alkaloids (berberine, β-hydrastine, canadine and canadaline); berberine is antibacterial. | [238]|
| Rhizomes: *alkaloids*   | *berberine*,     |                   |                               |               | Rhizomes: *alkaloids* (berberine, canadine, β-hydrastine, and isocorypalmine)                        | [239]|
| Rhizomes: *alkaloids*   | *hydastinine*,   |                   |                               |               | Rhizomes: *alkaloids* (hydastinine, hydrastine, canadine, berberine, canadine)                      | [240]|
| Aerial parts: *leaves*  | *hydrastinine*,  |                   |                               |               | Leaves: 3′,4′-dimethoxy-2-(methoxycarbonyl)benzoic acid, 3,3′,5,5′-tetrahydroxy-7,4′-dimethoxy-6,8-C-dimethyl-flavone, (±)-chilenine, (2R)-5,4′-dihydroxy-6-C-methyl-7-methoxy-flavanone, 5,4′-dihydroxy-6,8-di-C-methyl-7-methoxy-flavanone, noroxyhydrastinine, oxyhydrastinine, 4′,5′-dimethoxy-4-methyl-3′-oxo-(1,2,5,6-tetrahydro-4H-1,3-dioxole)-4′,5′-benzo[1-ε]1,2-oxazocin)-2-spiro-10-phtalan| [241]|
| *Hypericum gentianoides*| *Hyperikeae*     | *St. John’s wort* | root poultice used for stakebite| root          | Leaves: flavonoids (sideroxylin, 8-desmethyl-sideroxylin, and 6-desmethyl-sideroxylin); inhibit N or A multidrug resistance pump; synergistic antibacterial activity with berberine | [242]|
| Aerial parts: *acyl-phloroglucinols* | *saroaspidin A, uliginosin A*| Hyperaspidinol (Hyperaspidinol) | St. John's wort | root | Aerial parts: acyl-phloroglucinols (saroaspidin A, uliginosin A, hyperaspidinol) | [243]|
| Aerial parts: *acyl-phloroglucinols* | *saroaspidin A, uliginosin A*| Hyperaspidinol (Hyperaspidinol) | St. John's wort | root | Aerial parts: acyl-phloroglucinols (5′-prenyl-phlorisobutyrophenone, saroaspidin A, uliginosin A, hyperaspidinol) | [244]|
| Aerial parts: *chlorogenic acid, hyperoside, isoquercitrin, quercitrin, quercetin, at least 9 acyl-phloroglucinols (not identified). The acyl-phloroglucinols fraction reduced prostaglandin E2 synthesis in mammalian macrophages* | | | | | Aerial parts: chlorogenic acid, hyperoside, isoquercitrin, quercitrin, quercetin, at least 9 acyl-phloroglucinols (not identified). The acyl-phloroglucinols fraction reduced prostaglandin E2 synthesis in mammalian macrophages | [245]|

Table 1. Cont.
| Scientific Name          | Family             | Common Name | Cherokee Use          | Part Used | Chemical Constituents and Activities                                                                 | Ref.  |
|-------------------------|--------------------|-------------|-----------------------|-----------|------------------------------------------------------------------------------------------------------|-------|
| *Hypericum hypericoides* (L.) Crantz | Hypericaceae       | St. John’s wort | root poultice used for stakebite | root      | Roots: prenylated benzophenones (clusianone, 7-epi-clusianone, 18-hydroxy-7-epi-clusianone, 18-hydroxyclusianone, and 18-hydroxyhyperibone K) | [246] |
| *Iris versicolor* L.    | Iridaceae          | Blue flag, Snake lily | eyewash               | root      | powerful cathartic rhizome                                                                                       | [18]  |
|                         |                    |             |                       |           | root poultice used to treat sores                                                                                 | [24]  |
|                         |                    |             |                       |           | Rhizomes: iridals (17,26-dihydroxyiridial, 16-hydroxyiridial, 17-hydroxyiridial, 26-hydroxyiridial, 10-deoxy-17-hydroxyiridial, iriversical) | [247] |
| *Juglans nigra* L.      | Jugland-aceae      | Black walnut | bark infusion used on sores | bark      | Bark: juglone, α-hydroxyjuglone-4-glucoside, myricetin, myricitrin, sakuranetin, sakuranin, and neosakuranin | [15]  |
|                         |                    |             |                       |           | Unripe fruit: naphthoquinones (dihydroplumbagin, 3-methylplumbagin, isoplumbagin)                               | [248] |
|                         |                    |             |                       |           | Husk: naphthoquinones (juglone, plumbagin, regiolone), sterols (stigmasterol, β-sitosterol), flavonoids (taxifolin, kaempferol, quercetin, myricetin) | [249] |
|                         |                    |             |                       |           | Leaf EO: α-Pinene (6.3–11.4%), β-caryophyllene (17.3–20.4%), germacrene D (7.1–22.5%), juglone (1.0–8.8%) | [250] |
| *Juncus effusus* L.     | Juncaceae          | Common rush  | plant decoction used as emetic | plant     | Medullae: p-Coumaroylglycerides (juncysyl esters A and B)                                                    | [15]  |
|                         |                    |             |                       |           | Plant: cinnamoylglycerols (1-O-coumaroylglycerol, 1-O-feruloylglycerol, 1-O-coumaroylglycerol, juncysyl ester A, 1-O-(4-methoxycinnamoylglycerol), 1-O-(4-methoxycinnamoylglycerol), 1-O-(4-methoxycinnamoylglycerol), 2-O-(4-methoxycinnamoylglycerol), 1,2-di-O-feruloylglycerol, 1,3-di-O-coumaroylglycerol) | [252] |
|                         |                    |             |                       |           | Plant: 8-dihydroxy-1,7-dimethyl-8-vinyl-10,11-dihydro-dibenz[b,f] oxepin (showed brine shrimp lethality)      | [253] |
|                         |                    |             |                       |           | Stems: cycloartane glucosides (juncosides II-V)                                                              | [254] |
|                         |                    |             |                       |           | Plant: cycloartane triterpenoids (lagerenol, cycloartane-3β,24S,25-triol, cycloart-22Z-ene-3β,25-diol, sterculin A, cycloart-25-ene-3β,24-diol, 3-hydroxycycloart-25-ene-24-one, 24S,25-epoxycycloartan-3β-ol) | [255] |
|                         |                    |             |                       |           | Plant: cycloartane glucoside juncoside I                                                                     | [256] |
|                         |                    |             |                       |           | Medullae: phenanthrenes (juncunins E–G, dehydrojuncuenins D–E), juncuin E cytotoxic to MCF-7 and HeLa cells | [257] |
Table 1. Cont.

| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|--------------------------------------|------|
| Underground parts: phenanthrenes (dehydroeffusol, juncusol), compounds showed UVA light-enhanced antimicrobial activities due to DNA binding | | | | | | [259] |
| Plant: phenanthrenes (4-ethenyl-9,10-dihydro-1,8-dimethyl-2,7-phenanthrenediol, 4-ethenyl-9,10-dihydro-7-methoxy-1,8-dimethyl-2-phenanthrenol, 4-ethenyl-9,10-dihydro-3,8-dimethyl-1,7-phenanthrenediol, 4-ethenyl-9,10-dihydro-7-methoxy-3,8-dimethyl-1-phenanthrenol, 4-ethenyl-9,10-dihydro-7-hydroxy-8-methyl-2-phenanthrenecarboxylic acid) | | | | | | [260] |
| Plant: phenanthrenes (juncuenin F 2-methyl ether, 4-formyl-9,10-dihydro-3,7-dihydroxy-2,8-dimethylphenanthrene, 5-ethenyl-9,10-dihydro-1,7-dimethyl-2,3-phenanthrenediol, 9,10-dihydro-1,7-dihydroxy-4-(1-hydroxyethyl)-2,8-dimethylphenanthrene, 9,10-dihydro-6,6-dihydroxy-5-(1-hydroxyethyl)-1,7-dimethylphenanthrene, 9,10-dihydro-2,6-dihydroxy-5-(1-methoxyethyl)-1,7-dimethylphenanthrene, 4-ethenyl-9,10-dihydro-7-hydroxy-8-methyl-1-phenanthrenecarboxylic acid) | | | | | | [261] |
| Plant: phenanthrenes (2-hydroxy-7-(hydroxymethyl)-1-methyl-5-vinyl-9,10-dihydrophenanthrene, 2-hydroxy-6-(hydroxymethyl)-1-methyl-5-vinyl-9,10-dihydrophenanthrene, 2-hydroxy-5-(hydroxymethyl)-1,7-dimethyl-9,10-dihydrophenanthrene, 2,7-dihydroxy-5-(hydroxymethyl)-1,8-dimethyl-9,10-dihydrophenanthrene, 2-hydroxy-5-(hydroxymethyl)-7-methoxy-1,8-dimethyl-9,10-dihydrophenanthrene, 5-(1-ethoxy)-2,7-dihydroxy-1,8-dimethyl-9,10-dihydrophenanthrene, 2-hydroxy-1,7-dimethyl-9,10-dihydrophenanthrene-[5,6-b]-4',5'-dihydro-4',5'-dihydrofuran) | | | | | | [262] |
| Plant: phenanthrene glucosides (Effusides I–V) | | | | | | [263] |
| Aerial parts: phenanthrenes (7-carboxy-2-hydroxy-1-methyl-5-vinyl-phenanthrene, 2,7-dihydroxy-1-methyl-5-aldehyde-9,10-dihydrophenanthrene, dehydroeffusol, dehydrojuncusol, 7-carboxy-2-hydroxy-1-methyl-5-vinyl-9,10-dihydrophenanthrene, 8-carboxy-2-hydroxy-1-methyl-5-vinyl-9,10-dihydrophenanthrene, effusol, and juncusol; effusol and juncusol showed anxiolytic and sedative activities) | | | | | | [264] |
| Medullae: diterpenoid effusenone A, phenanthrene (5-hydroxymethyl)-1-methylphenanthrene-2,7-diol, pyrenes 1-methylpyrene-2,7-diol and 7-methoxy-8-methylpyren-2-ol | | | | | | [265] |
| Medullae: phenanthrenes (effusol, dehydroeffusol, dehydroeffusol) | | | | | | [266] |
| Medullae: phenanthrenes (effusol, dehydroeffusol, juncusol, dehydrojuncusol, juncuenin B, dehydrojuncuenin B, juncuenin D, and effususol A), flavonoids (luteolin and luteolin 5-methyl ether), and 4-hydroxy-2,3-dimethyl-2-non-en-4-olide) | | | | | | [267] |
Table 1. Cont.

| Scientific Name | Family     | Common Name | Cherokee Use                                      | Part Used          | Chemical Constituents and Activities                                                                 | Ref. |
|-----------------|------------|-------------|--------------------------------------------------|--------------------|------------------------------------------------------------------------------------------------------|------|
| Juniperus virginiana L. | Cupress-aceae | Eastern red cedar | decoction of berries given for worms; infusion of some part taken for colds; ointment used on skin diseases | various            | Plant: tetrahydropyrene glucosides (4,5,9,10-tetrahydro-2,7-dihydroxy-1,6-dimethylpyrene monoglucoside and diglucoside) [268] |
|                 |            |             |                                                  |                    | Medullae: phenanthrene dimers (effususins A–D); effususins A and B showed cytotoxic activity against several tumor cell lines; effususin B showed inflammatory activity (inhibition of NO production in LPS-stimulated RAW 264.7 cells) [269] |
|                 |            |             |                                                  |                    | Phenanthrenes from medullae of Juncus effusus show cytotoxic activity against several tumor cell lines; some also show inhibition of NO production indicating anti-inflammatory potential [270] |
|                 |            |             |                                                  |                    | The phenanthrene dehydroeffusol shows anxiolytic and sedative effects (mouse model) [271] |
|                 |            |             |                                                  |                    | The phenanthrenes effusol and dehydroeffusol activate GABA<sub>A</sub> receptors, explaining the traditional Chinese use of the plant as a sedative and anxiolytic agent [272] |
| Lactuca canadensis L. | Asteraceae | Canada lettuce | infusion taken for pain and calming nerves | plant              | Roots: sesquiterpene lactones (3-epizaluzanin C glucoside, 9-hydroxydehydroeleucodin glucoside, zaluzanin C, 11β,13-dihydrozaluzanin C, 3-epizaluzanin C, 11β,13-dihydro 3-epizaluzanin C, vernoflexuoside, 11β,13-dihydro vernoflexuoside, macroclinside A, ixerin F, picriside B, santamarin, 11β,13-dihydro santamarin, arnemefolin, 1-epidehydrosoerivanin, armefolin, 1-episoerivanin, 3α-hydroxyreynosin and 1-epierivanin) [277] |
| Scientific Name          | Family            | Common Name | Cherokee Use                        | Part Used | Chemical Constituents and Activities | Ref. |
|-------------------------|-------------------|-------------|-------------------------------------|-----------|--------------------------------------|------|
| *Liatris spicata* (L.)  | Asteraceae        | Blazing star| tonic, tincture used on pains       | root      | Flavonoid glycosides: quercitin 3-glucoside, quercitin 3-rutinoside, and quercitin 3-glucoside-7-rhamnoside | [15] |
|                         |                   |             |                                     |           | Leaf: major volatiles: α-pinene, mesityl oxide, β-pinene, myrcene, 2,4-heptadienal, β-caryophyllene, germacrene D, caryophyllene oxide | [278] |
|                         |                   |             |                                     |           | Aerial parts: guaianolide sesquiterpenoid spicatin | [280] |
|                         |                   |             |                                     |           | Corms (underground stems): sterols (stigmasterol and its 3-O-glucoside), triterpene (obtusifoliyl acetate), benzofurans: (euparin and 6-hydroxy-3-methoxysteretone), phenolic acids (protocatechuic, vanillic and ferulic acid) and a sesquiterpene lactone igalan. Iglan showed cytotoxic activity on Hep-G2 cells | [281] |
| *Lindera benzoin* (L.)  | Lauraceae         | Spicebush   | infusion for measles, cough         | bark      | Leaf EO: 6-methyl-5-hepten-2-one (42.9%), β-caryophyllene (7.7%), bicyclogermacrene (5.1%), b-cadinene (4.9%), and (E)-nerolidol (4.8%) | [15] |
|                         |                   |             |                                     |           | Twigs EO: α-pinene (5.9%), sabine (6.8%), α-phellandrene (4.2%), 1,8-cineole (45.4%), α-terpineol (6.8%) | [282] |
|                         |                   |             |                                     |           | Fruit EO: myrcene (4.7%), α- phellandrene (64.6%), β- phellandrene (11.2%) | [283] |
|                         |                   |             |                                     |           | Fruit: (6Z,9Z)-pentadecadien-2-one, (6Z,9Z,12Z)-pentadecatrien-2-one, (E)-nerolidol, isolinderanolide, isolinderenolide, isoobtusilactone A, obtusilactone A, isoobtusilactone B, obtusilactone C, and linderanolide | [284] |
| *Liquidambar styraciflua* | Altingiaceae     | Sweet gum   | inner bark for diarrhea, externally for wounds, sores, ulcers | bark      | Bark: shikimic acid | [15] |
|                         |                   |             |                                     |           | Bark: pentacyclic triterpenoids (25-acetoxy-3α-hydroxysterol-12-en-28-oic acid, 3α,25-dihydroxyol-12-en-28-oic acid, 6β-hydroxy-3-oxo-29(29)-en-28-oic acid, and 3,11-dioxolane-12-en-28-oic acid); 25-acetoxy-3α-hydroxyol-12-en-28-oic acid showed broad cytotoxic activity against a panel of human tumor cell lines | [285] |
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|-------------------------------------|------|
| *Liriodendron tulipifera* L. | Magnoliaceae | Tulip tree | bark infusion taken for pinworms, cholera, coughs, rheumatism | bark | Bark: lignans (liriosol, syringic acid methyl ester, pinoresinol, syringaresinol), aporphine alkaloids (O-methyl-N-noraporphine, N-(2-hydroxy-2-phenylethyl)-benzamidine) | [292] |
| | | | | | Bark: aporphine alkaloids (asimilobine, norushinsunine, norglaucine, liriodenine, anonaine, oxoglucine); the aporphine alkaloids showed antimalarial activity | [293] |
| | | | | | Leaves: germacranolide sesquiterpenoids (peroxyferolide, lipiferolide); showed antiproliferative and cytotoxic activities | [293] |
| | | | | | Leaves: aporphine alkaloids (anonaine, norstephalagine, liridinine, normuciferine, caaverine, lirindine, lyciscamine), a coumarin (scopoletin), a germacranolide (epitulipinolide diepoxide), polyphenolics (β-oryzanol, formylsyringaldehyde, syringaldehyde, syringic acid, vanillic acid), sterols (β-sitosterol, stigmasteryl); anonaine, liridinine, lyciscamine, and epitulipinolide diepoxide significantly inhibited proliferation of A375 melanoma cells | [294] |
| | | | | | Leaves: germacranolide (dihydrocrypysaroside, 11,13-dehydrolanuginolide, laurenbiolide) and guaianolide (β-cyclofiferolide) sesquiterpenoids | [295] |
| | | | | | Aerial parts: lignans (sesamin, syringaresinol, dihydrodehydrodiconiferyl alcohol, salvinal, guaiacylglycerol-5-O-4′-dihydroconiferyl ether, guaiacylglycerol-8-O-4′-sinapyl alcohol ether, tanegol, 5,5′-dimethoxy-7-o xoariciresinol), phenolics (3-hydroxy-4-methoxyacetophenone, 4-acetoxyethylphenol), germacranolide (paramicholide), and blumenol A | [296] |
| Scientific Name | Family          | Common Name       | Cherokee Use                                                                 | Part Used         | Chemical Constituents and Activities                                                                 | Ref. |
|-----------------|-----------------|-------------------|------------------------------------------------------------------------------|-------------------|------------------------------------------------------------------------------------------------------|------|
| Lobelia cardinalis L. | Campanu-laceae | Cardinal flower   | root infusion for worms, rheumatism; leaf infusion for colds, fever; root poultice for sores | root, leaves      | Roots: germacranolides (tulipinolide, epitulipinolide)                                               | [297]|
|                  |                 |                   |                                                                              |                   | Leaf EO: (Z)-β-Ocimene (6.1–59.4%), (E)-β-ocimene (4.4–24.0%), β-elemene (8.2–23.5%), germacrene D (4.8–43.5%), bicyclogermacrene (3.0–21.5%); β-ocimenes cytotoxic to MDA-MB-231 and HEK293 cells | [298]|
|                  |                 |                   |                                                                              |                   | Bark EO: α-Pinene (6.7–11.3%), camphene (1.1–5.0%), β-pinene (6.0–19.1%), myrcene (2.4–11.7%), limonene (4.5–12.0%), β-phellandrene (up to 13.7%), (Z)-β-ocimene (30.6–53.9%), bornyl acetate (2.6–13.3%) | [299]|
| Lobelia inflata L. | Campanu-laceae | Indian tobacco    | root poultice used on pains; root/leaf poultice used on ringworm, insect bites | root, leaves      | Aerial parts: alkaloid lobinaline                                                                    | [15] |
|                  |                 |                   |                                                                              |                   | Hairy root culture: diacetylene triol lobetyol + glucosides lobetyolin and lobetyolinin              | [300]|
|                  |                 |                   |                                                                              |                   | Leaves: anthocyanin cyanidin-3-O-(6-O-[4-(3-p-coumaroyl-O-α-rhamnopyranosyl)-β-glucopyranosyl]-5-O-β-glucopyranoside | [301]|
| Lobelia siphilitica L. | Campanu-laceae | Great blue lobelia | root infusion for worms; leaf infusion for colds, fever                      | root, leaves      | Aerial parts: piperidine alkaloids (lobeline, lobelianine, norlobeline, norlobelanine, lobelanidine, norlallosemidamine, 8-ethyl-10-phenyllobelolidol, 8-ethyl-10-phenyllobelolidol) | [15] |
|                  |                 |                   |                                                                              |                   | Aerial parts: piperidine alkaloids (8,10-diphenyllobelidiol, 8,10-diphenyllobelidiol, 8-ethyl-10-phenyl-lobelolidol, 8-ethyl-10-phenyl-lobelolidol, 8-ethyl-10-phenyl-dehydrolobelolidol, 8-ethyl-10-phenyl-dehydrolobelolidol, lobeline, lobelidine, lobelanine) | [302]|
| Lycopus virginicus L. | Lamiaceae      | Virginia bugleweed | tea, root applied to snakebite                                               | plant, root       | Aerial parts: piperidine alkaloids (lobeline, cis-8,10-diphenyllobelidol, (S)-2-[25,6R]-1-methyl-6-(2-oxo-2-phenylethyl)piperidin-2-yl]1-phenylthethyl acetate, 6-[([E]-2-3-methoxyphenylethenyl)]-2,3,4,5-tetrahydrpyridine) and the diacetylene lobelolin | [15] |
| Scientific Name | Family         | Common Name | Cherokee Use            | Part Used  | Chemical Constituents and Activities                                                                                                                                                                                                 | Ref.   |
|-----------------|----------------|-------------|-------------------------|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| *Magnolia acuminata* (L.) | Magnoli-aceae | Cucumber magnolia | bark infusion for toothache | bark       | Aerial parts: flavone glucuronides (7-O-β-D-glucuronides of apigenin, acacetin, and luteolin as well as the methyl ester of apigenin 7-O-β-D-glucuronide)                                                                                       | [307]  |
|                  |                |             |                         |            | Root bark: lignans (calopiptin, galgravin, veraguensin, and acuminatin)                                                                                                                                                                  | [308]  |
|                  |                |             |                         |            | Root bark: alkaloids (anolobine, N-methylidcarpine methiodide, N,N′-dimethyl-2,11,11-dihydro-1,10-dimethoxyaporphine iodide), lignans (calopiptin, galgravin, veraguensin, acuminatin), sesquiterpene lactone (costunolide), sterol (β-sitosterol) | [309]  |
|                  |                |             |                         |            | Leaves: alkaloids (asimilobine, lirioderine, norarmepavine, roemerine, armepavine, magnocurarine, magnoflorine)                                                                                                                        | [310]  |
| *Menispernum canadense* L. | Menisperm-aceae | Common moonseed | root used for skin diseases | root       | Roots: alkaloid dauricine                                                                                                                                                                                                               | [311]  |
|                  |                |             |                         |            | Roots: alkaloids (acutumine, acutumidine, dauricine, daurinoline, N′-desmethyldauricine, magnoflorine, N,N-dimethyldauricine, dehydrocheilanthifoline)                                                                                    | [312]  |
| *Monarda didyma* L. | Lamiaceae | Scarlet beebalm | infusion abortifacient; poultice for colds, headache | leaves     | Several essential oil chemotypes are known                                                                                                                                                                                            | [15]   |
|                  |                |             |                         |            | Floral EO: sabine (5.0%), γ-terpinene (5.3%), p-cymene (11.0%), linalool (64.5%)                                                                                                                                                       | [313]  |
|                  |                |             |                         |            | Leaf EO: linalool (74.2%), bornyl acetate (5.7%), germacrene D (5.3%)                                                                                                                                                                    | [313]  |
|                  |                |             |                         |            | Commercial EO (Pam'innov, Le Chaffaut-Saint-Julson, Provence, France): geraniol (89.5%)                                                                                                                                                 | [314]  |
|                  |                |             |                         |            | Leaf EO: δ-3-carene (4.5%), p-cymene (10.5%), γ-terpinene (9.3%), thymol (57.3%), EO showed antifungal and DPPH radical inhibitory activities                                                                                               | [315]  |
|                  |                |             |                         |            | Leaf EO: γ-terpinene (7.0%), α-terpinene (7.0%), p-cymene (20.1%), borneol (11.7%), 1-octen-3-ol (21.7%), thymol (12.3%), thymoquinone (10.1%)                                                                                         | [316]  |
|                  |                |             |                         |            | Leaf EO: γ-terpinene (6.6%), p-cymene (33.9%), thymol (38.0%), thymoquinone (12.8%)                                                                                                                                                       | [316]  |
|                  |                |             |                         |            | Leaf EO: p-cymene (17.0%), carvacrol (69.7%)                                                                                                                                                                                            | [316]  |
|                  |                |             |                         |            | Leaf EO: p-cymene (17.0%), linalool (29.3%), 1-octen-3-ol (9.8%), thymol (5.5%), thymoquinone (22.3%)                                                                                                                                     | [316]  |
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|----------------|--------|-------------|--------------|-----------|--------------------------------------|------|
| *Monarda fistulosa* L. | Lamiaceae | Wild bergamot | fevers, colds | plant | Several subspecies are known | [15] |
| *Oenothera biennis* L. | Onagraceae | Evening primrose | eye conditions due to asthma, allergies; poultice on boils | root | | [15] |

Leaf EO: α-terpineol (35.9%, 99% L-enantiomer), thymol methyl ether (14.0%), linalool (5.0%, 100% L-enantiomer) | WNS" 

Leaves and flowers: flavonoids (rutin, hyperoside, quercitrin, luteolin, quercetin) | [320] |

Leaf EO: p-cymene (9.2%), thymol (72.9%), carvacrol (6.8%), thymoquinone (5.8%) | [316] |

Aerial parts EO: myrcene (8.1%), α-phellandrene (13.7%), β-phellandrene (17.0%), p-cymene (13.5%), thymol (26.5%) | [322] |

Aerial parts EO: myrcene (35.4%), 1-octen-3-ol (10.3%), carvacrol (39.1%); the EO and carvacrol showed good mosquito (*Aedes aegypti*) repellent activity | [323] |

Aerial parts EO: myrcene (8.6–8.7%), α-phellandrene (13.7–14.0%), p-cymene (13.2–13.3%), thymol (28.4–33.4%); EO showed anticandidal and antibacterial activity | [318] |

Leaf EO: α-terpineol (35.9%, 99% L-enantiomer), thymol methyl ether (14.0%), linalool (5.0%, 100% L-enantiomer) | WNS" 

Leaf EO: p-cymene (21.2%), 1-octen-3-ol (7.1%), carvacrol (46.8%), thymoquinone (21.3%) | [316] |

Aerial parts EO (M. didyma var 80-1A): p-cymene (8.2%), linalool (55.4%), geraniol (20.7%); EO inhibited mycelial growth spore germination of *Botrytis cinerea* | [317] |

Aerial parts EO: p-cymene (12.6%), γ-terpinene (15.9%), thymol (41.2%), carvacrol (15.2%); EO inhibited mycelial growth spore germination of *Botrytis cinerea* | [317] |

Aerial parts EO: δ-3-carene (4.1–4.5%), p-cymene (10.2–10.3%), γ-terpinolene (9.2%), thymol (59.4–64.3%); EO showed anticandidal and antibacterial activity. | [318] |

Aerial parts EO: p-cymene (10.3%), terpinolene (9.2%), thymol (59.3%); EO showed anti-germination activity against several "weed" seeds | [319] |
| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|----------------|--------|-------------|--------------|-----------|-------------------------------------|------|
| *Panax quinquefolius* L. | Araliaceae | American ginseng | root used as tonic | root | | |
| Root (wild): ginsenosides [Rb₁ (2.81%), Rb₂ (0.09%), Rb₃ (0.42%), Rd (0.29%), Re (1.42%), and Rg₁ (0.94%)] | | | | | [333] |
| Root: ginsenosides [Rb₁, Rb₂, Re, Rd, Re, and Rg₁] | | | | | [334] |
| Root (cultivated): ginsenosides [Rb₁ (3.70%), Rb₂ (0.05%), Re (0.41%), Rd (0.42%), Re (0.50%), and Rg₁ (0.13%)] | | | | | [335] |
| Root (cultivated): ginsenosides [Rb₁ (1.85%), Rb₂ (0.04%), Rb₃ (0.04%), Re (0.29%), Rd (0.29%), Re (2.05%), Rg₁ (0.25%), and F₁ (0.20%)] | | | | | [336] |
| Root (cultivated): polyacetylenes (falcarinol, panaxydol) | | | | | [337] |
| Root (cultivated): ginsenosides [Rb₁ (4.94%), Rb₂ (0.04%), Re (0.39%), Rd (0.60%), Re (1.75%), and Rg₁ (0.13%)] | | | | | [338] |
| Leaves (wild): ginsenosides [Rb₁ (0.17%), Rb₂ (1.04%), Re (0.18%), Rd (1.08%), Re (0.93%), and Rg₁ (0.14%)] | | | | | [333] |
| Leaves (cultivated): ginsenosides [Rb₁ (0.28%), Rb₂ (1.82%), Rb₃ (4.64%), Re (0.56%), Rd (2.82%), Re (3.42%), Rg₁ (0.96%), and F₁ (1.94%)] | | | | | [336] |
| Review of chemical analysis of *P. quinquefolius* | | | | | [339] |
| Review of pharmacology and toxicology of *P. quinquefolius* | | | | | [340] |
| Review of ginsenosides in *P. quinquefolius* | | | | | [341] |
| Review of pharmacology of *P. quinquefolius* | | | | | [342] |
| Scientific Name                        | Family        | Common Name | Cherokee Use           | Part Used | Chemical Constituents and Activities                                                                 | Ref. |
|---------------------------------------|---------------|-------------|------------------------|-----------|-----------------------------------------------------------------------------------------------------|------|
| Panax trifolius L.                    | Araliaceae    | Dwarf ginseng | root used as tonic    | root      | Leaves: flavonoids (kaempferol-3,7-dirhamnoside and kaempferol-3-gluco-7-rhamnoside), ginsenosides (ginsenoside-Rd, -Rc, -Rb3 and notoginsenoside-Fe) | [343]|
|                                       |               |             |                        |           | Leaves: ginsenosides (Ro, Rb1, Rb2, Rc)                                                             | [344]|
| Parthenocissus quinquefolia (L.)      | Vitaceae      | Virginia creeper | infusion taken for jaundice |           | Stem: resveratrol oligomers, parthenocissins A and B, were isolated in addition to three known stilbenes (resveratrol, piceatannol, resveratrol 3-glucoside) | [345]|
| Parthenocissus quinquefolia (L.)      | Vitaceae      | Virginia creeper | infusion taken for jaundice |           | Stem: oligostilbenes, parthenocissins M and N, together with two known compounds, miyabenol C and ε-viniferin | [346]|
| Parthenocissus quinquefolia (L.)      | Vitaceae      | Virginia creeper | infusion taken for jaundice |           | Leaves: β-amyryl palmitate; shows thrombin inhibitory activity                                   | [347]|
| Passiflora incarnata L.               | Passifloraceae | Passion flower | root infusion used for boils, earache, to wean babies; poultice for wounds | root      | Plant: C-Glycosidic flavonoids (schaftoside, isoschaftoside, isovetexin-2′-O-glucopyranoside and isoorientin-2′-O-glucopyranoside) | [348]|
| Passiflora incarnata L.               | Passifloraceae | Passion flower | root infusion used for boils, earache, to wean babies; poultice for wounds | root      | Plant: flavonoid glycosides (vicenin-2′, schaftoside, isoschaftoside isoorientin-2′-O-glucoside, orientin, novirhin-2′-O-glucoside, swertisin, orientin isovitexin, vitexin) | [349]|
| Passiflora incarnata L.               | Passifloraceae | Passion flower | root infusion used for boils, earache, to wean babies; poultice for wounds | root      | Plant: flavonoid glycoside (isoscoparin-2′-O-glucoside)                                              | [350]|
| Passiflora incarnata L.               | Passifloraceae | Passion flower | root infusion used for boils, earache, to wean babies; poultice for wounds | root      | Plant: C-glycosidic flavonoid (6-β-D-glucopyranosyl-8-β-D-ribopyranosyl apigenin)                     | [351]|
| Phytolacca americana L.               | Phytolaccaceae | Pokeweed     | poultice used for ulcers; root infusion used for eczema | root      | The phytochemistry of P. incarnata has been reviewed                                                  | [352]|
| Phytolacca americana L.               | Phytolaccaceae | Pokeweed     | poultice used for ulcers; root infusion used for eczema | root      | Roots: triterpenoid saponins (phytolaccasides A, D, E)                                               | [353]|
| Phytolacca americana L.               | Phytolaccaceae | Pokeweed     | poultice used for ulcers; root infusion used for eczema | root      | Roots: triterpenoid saponin (phytolaccoside B)                                                      | [354]|
| Phytolacca americana L.               | Phytolaccaceae | Pokeweed     | poultice used for ulcers; root infusion used for eczema | root      | Roots: triterpenoid saponins (phytolaccasaponins B, E, G)                                           | [355]|
| Phytolacca americana L.               | Phytolaccaceae | Pokeweed     | poultice used for ulcers; root infusion used for eczema | root      | Roots: triterpenoid saponins (phytolaccasaponins N1–N5, esculetoside H, esculetoside A = phytolaccoside E, esculetoside M, esculetoside B = phytolaccoside B, esculetoside S, esculetoside R-28-O-glucoside, esculetoside L) | [356]|
| Phytolacca americana L.               | Phytolaccaceae | Pokeweed     | poultice used for ulcers; root infusion used for eczema | root      | Roots: phytosterol α-spinasterol                                                                | [357]|
| Scientific Name         | Family      | Common Name | Cherokee Use                                                                 | Part Used | Chemical Constituents and Activities                                                                 | Ref.         |
|-------------------------|-------------|-------------|------------------------------------------------------------------------------|-----------|----------------------------------------------------------------------------------------------------------------|-------------|
| *Pinus virginiana* Mill. | Pinaceae    | Pine        | wash for skin ulcers/sores; sap used on stubborn sores; syrup from inner bark for coughs/congestion; inner bark used for intestinal worms and parasites. | bark      | Bark EO: α-pinene (43.1%), β-pinene (24.8%), β-phellandrene (13.9%)                                           | [18]        |
|                         |             |             |                                                                              |           | Leaf EO: α-pinene (22.8%), β-pinene (25.1%), β-phellandrene (14.3%), α-terpineol (8.7%)                             | [273]       |
| *Plantago lanceolata* L. | Plantaginaceae | Narrowleaf plantain | infusion or poultice used for bites and stings | plant | Herb: purpureaside A, lavandulifolioside B, acteoside, luteolin-3',7-diglucuronide, isoacteoside, luteolin-7-glucuronide, and luteolin | [358]       |
|                         |             |             |                                                                              |           | Herb: phenolic acids: p-hydroxybenzoic acid, vanillic acid, gallic acid, cinnamic acid, chlorogenic acid (major); flavonoids: apigenin, luteolin, luteolin-7-O-glucoside. Extract shows antioxidant, COX-1-inhibitory, 12-LOX-inhibitory, and weak cytotoxic activity | [359]       |
|                         |             |             |                                                                              |           | Herb: iridoid glycosides: aucubin and catalpol                                                                   | [360]       |
| *Plantago major* L.     | Plantaginaceae | Common plantain | infusion or poultice used for bites and stings | plant | Review, Herb: aucubin, melittoside, asperuloside, melampyroside, plantarenaloside, zeoroside, majoroside, 10-hydroxyjasmonoside, 10-acetoxysinfloside, acteoside, plantamajoside | [364]       |
|                         |             |             |                                                                              |           | Review, Herb: caffeic acid derivatives (caffeic acid, chlorogenic acid, plantamajoside, acteoside), flavonoids (apigenin 7'-glucoside, baicalein, hispidulin, hispidulin 7'-glucuronide, homoplantaginin, luteolin 7-glucoside, luteolin 7-diglucoside, luteolin 6-hydroxy-4'-methoxy-7'-galactoside, nepetin 7'-glucoside, plantaginin, scutellaran), iridoid glycosides (asperuloside, aucubin, catalpol, gardoside, geniposidic acid, majoroside, 10-acetoxysinfloroside, 10-hydroxysinfloroside, melittoside), triterpenoids (oleanolic acid, ursolic acid, 18β-glycyrrhetinic acid). Bioactivities of extracts includes wound healing activity, anti-inflammatory, analgesic, antioxidant, weak antibiotic, immune modulating and antiulcerogenic activity | [365]       |
|                         |             |             |                                                                              |           | *P. major* compounds showed antiviral activity: caffeic acid on herpesvirus (HSV-1) and adenovirus (ADV-3); chlorogenic acid on ADV-11 | [366]       |
| Scientific Name | Family | Common Name            | Cherokee Use                    | Part Used | Chemical Constituents and Activities                                                                 | Ref.         |
|-----------------|--------|------------------------|---------------------------------|-----------|------------------------------------------------------------------------------------------------------|-------------|
| *Platanus occidentalis* L. | Platanaceae | American sycamore | infusion of inner bark for cough, measles, urinary infection | bark       | Herb: anti-MRSA flavonoids (kaempferol 3-O-α-L-(2′,3′-di-E-p-coumaroyl)rhamnoside, kaempferol 3-O-α-L-(2′-E-p-coumaroyl-3″-Z-p-coumaroyl)rhamnoside, and kaempferol 3-O-α-L-(2′,3′-di-Z-p-coumaroyl)rhamnoside) | [15]         |
| *Podophyllum peltatum* L. | Berberidaceae | Mayapple | anthelmintic, sores | root       | Roots: aryltetralin lignans (podophyllotoxin, picropodophyllotoxin, α-peltatin, β-peltatin, desoxypodophyllotoxin) | [15]         |
|                  |         |                        |                                 |            | Roots: aryltetralin lignans (podophyllotoxin, 4′-demethylpodophyllotoxin, α-peltatin, β-peltatin, desoxypodophyllotoxin, podophyllotoxone, isopicropodophylline, 4′-demethylisopicropodophyllotoxin, and 4′-demethylisopicropodophylline) | [373]        |
|      |         |                        |                                 |            | Plants: aryltetralin lignans (podophyllotoxin 4-O-β-D-glucopyranoside, epipodophyllotoxin 4-O-β-D-glucopyranoside, 4′-demethylpodophyllotoxin, α-peltatin, epipodophyllotoxin, podophyllotoxin, β-peltatin, 1,2,3,4-dehydrodesoxypodophyllotoxin) | [375]        |
| *Polygala senega* L. | Polygalaceae | Seneca snakeroot | snakebite | root       | Root: triterpenoid saponin senegen-II                                                           | [376]        |
|                  |         |                        |                                 |            | Root: triterpenoid saponins (senegen III, senegen IV)                                           | [377]        |
|                  |         |                        |                                 |            | Root: oligosaccharide esters (senegose A, senegose B, senegose C, senegose D, senegose E)         | [378]        |
|      |         |                        |                                 |            | Root: oligosaccharide esters (senegose F, senegose G, senegose H, senegose I)                    | [379]        |
|      |         |                        |                                 |            | Root: oligosaccharide esters (senegose J, senegose K, senegose L, senegoseM, senegose N, senegose O) | [380]        |
Table 1. Cont.

| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|--------------------------------------|------|
| *Polygonum aviculare* L. | Polygon-aceae | Prostrate knotweed | fish poison | plant | Root: triterpenoid saponins (senegen II, senogen III, *E*-senegasaponin A, *E*-senegasaponin B, *Z*-senegasaponin A, *Z*-senegasaponin B, *Z*-senegen II, *Z*-senegen III) | [381] |
| | | | | | Root: essential oil [hexanoic acid (33.6%), methyl salicylate (26.5%), n-hexanal (5.3%) and o-cresol (3.5%)] | [382] |
| | | | | | Root: triterpenoid saponins (senegen II, senogen III, senegen IV, senegasaponin A, senegasaponin B) | [383] |
| *Polygonum hydropiper* L. | Polygon-aceae | Marshpepper knotweed | fish poison | plant | Plant: lignan aviculin; flavonoids (juglanin, avicularin, astragalin, and betmidin) | [384] |
| | | | | | Plant: naphthoquinone 6-methoxyplumbagin, also β-sitosterol, oleanolic acid, and 5,6,7,4′-tetramethoxyflavone | [385] |
| | | | | | Aerial parts: flavonoids (avicularin, liquiritin, cinaroside) | [386] |
| | | | | | Plant: flavonol glucuronides [myricetin 3-O-β-D-glucuronide, mearsetin 3-O-β-D-glucuronide, quercetin 3-O-β-D-glucuronide, isorhamnetin 3-O-β-D-glucuronide, kaempferol 3-O-β-D-glucuronide, kaempferol 3-O-[2′-O-acetyl-β-D-glucuronide], isorhamnetin 3-O-[2′-O-acetyl-β-D-glucuronide], quercetin 3-O-[2′-O-acetyl-β-D-glucuronide], quercetin 3-O-[3′-O-acetyl-β-D-glucuronide], and kaempferol 3-O-[3′-O-acetyl-β-D-glucuronide]] | [387] |
| | | | | | Leaves: flavonoids (myricetin, quercetin, kaempferol, myricitrin, desmanthin-1, isoquercitrin, avicularin, juglanin) and gallic acid | [388] |
| | | | | | Aerial parts: flavonoids (avicularin, juglanin, myricitrin, isoastragalin, isoquercitrin, kaempferol-5,7-di-O-β-D-glucopyranoside, and kaempferol 5-O-α-L-rhamnopyranosyl(1→2)-O-β-D-glucopyranoside), lignan aviculin, and loliolide and 1,6-digalloylglucose | [389] |
| *Polygonum hydropiper* L. | Polygon-aceae | Marshpepper knotweed | fish poison | plant | Plant: polygodial | [390] |
| | | | | | Plant: drimane sesquiterpenoids (warburanal, polygodial, isopolygodial, polygonal, isodrimeninol, drimenol, confertifolin) | [391] |
| | | | | | Plant: flavonoids [rutin (0.58-0.93%), hyperin (0.37-0.63%), isoquercitrin (0.08-0.38%), quercitrin (0.55-0.95%), catechin (0.06-0.09%), epicatechin (0.05-0.08%), quercitin (0.28-0.65%), kaempferol (0.28-0.53%), isorhamnetin (0.03-0.04%)] | [392] |
Table 1. Cont.

| Scientific Name          | Family            | Common Name          | Cherokee Use                                      | Part Used                                                                 | Chemical Constituents and Activities                                                                                   | Ref.       |
|--------------------------|-------------------|----------------------|--------------------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|------------|
| *Polymnia canadensis* L. | Asteraceae        | Whiteflower leafcup  | Houma Native American use (not Cherokee) applied | leaves                                                                   | Leaves: drimane sesquiterpenoids (polygenic acid, 11-ethoxycinnamolide, polygodial acetal, valdivioside, and fuegin), drimane norsesquiterpenoids (isopolygalic and polygone) | [393]      |
|                          |                   |                      | a leaf poultice to swellings                     |                                                                           |                                                                                                                        |            |
| *Polymnia uvedalia* (L.) | Asteraceae        | Leafcup, Bear’s foot | bruised root used on cuts, burns                 | root                                                                     | Germacranolide sesquiterpenoids (uvedalin, isouvedalin, 2′,3′-dehydromelnerin A, 9-hydroxy-2′,3′-dehydromelnerin A), ent-kaurane diterpenoids (ent-12-hydroxy-16-kauren-19-oic acid, ent-18-hydroxy-16-kauren-19-oic acid derivatives, ent-16-kauren-3,19-diol derivatives, ent-12,18-di-hydroxy-16-kauren-19-oic acid derivatives) | [247]      |
| (syn. Smallanthus uvedalia (L.) Mack.) |                   |                      |                                                  |                                                                           |                                                                                                                        |            |
| Scientific Name            | Family         | Common Name | Cherokee Use     | Part Used | Chemical Constituents and Activities                                                                 | Ref.       |
|---------------------------|----------------|-------------|------------------|-----------|--------------------------------------------------------------------------------------------------------|-----------|
| Prunella vulgaris L.       | Lamiaceae      | Heal-all    | sore throat, cuts, burns | plant     | Leaf EO: selin-1 1-en-4a-ol (14.9%), cis-eudesma-6,11-diene (9.4%), 1,10-di-epi-cubenol (8.0%), spathulenol (5.8%) and germacrene D (5.1%) | [402]     |
|                           |                |             |                  |           | Leaf EO: aromadendrene (55.4%), cucumber alcohol (8.5%) and phytol (5.1%)                              | [403]     |
|                           |                |             |                  |           | Aerial parts: rosmarinic acid, ursolic acid, oleanolic acid                                           | [404]     |
|                           |                |             |                  |           | Aerial parts: rosmarinic acid, ursolic acid, oleanolic acid                                           | [405]     |
|                           |                |             |                  |           | Aerial parts: four triterpenes, i.e., betulinic acid, ursolic acid, 2a,3a-dihydroxyurs-12-en-28-oic acid, and 2a-hydroxyursolic acid | [406]     |
|                           |                |             |                  |           | Aerial parts: polyacetylenic acids (octadeca-9,11,13-triyne acid and trans-octadec-13-ene-9,11-diyne acid) | [407]     |
|                           |                |             |                  |           | oleanane-skeleton triterpenoid saponins, 3(β,4β,16α)-16a-carboxy-16,24-dihydroxy-28-norolean-12-en-3-yl-1β-D-glucopyranosidouronic acid, (3β,4β,16α)-17-carboxy-16,24-dihydroxy-28-norolean-12-en-3-yl-1β-D-glucopyranosidouronic acid methyl ester, and (3β,4β)-24-hydroxy-16-oxo-28-norolean-12-en-3-yl-4-O β-xylopyranosyl-β-D-glucopyranosidouronic acid | [408]     |
|                           |                |             |                  |           | Aerial parts: 15 triterpene acids (olenic acid, ursolic acid, 2a,3a,19a-trihydroxyurs-12-en-28-oic acid, 2a,3a-dihydroxyurs-12-en-28-oic acid, maslinic acid, 2a,3a,19a,23-tetrahydroxyurs-12-en-28-oic acid, 2a,3a,23-trihydroxyurs-12-en-28-oic acid, 2a,3β-dihydroxyurs-12-en-28-oic acid, 2a,3β,24-trihydroxyolea-12-en-28-oic acid, (12R,13S)-2a,3a,24-trihydroxy-12,13-cycloartane-14-en-28-oic acid, 2a,3a,24-trihydroxyurs-12,20(30)-dien-28-oic acid, 2a,3a,24-trihydroxyolea-12-en-28-oic acid, 2a,3β,19a,24-tetrahydroxyurs-12-en-28-oic acid 28-O-β-glucopyranoside, 2a,3a,19a,24-tetrahydroxyurs-12-en-28-oic acid 28-O-β-glucopyranoside, prunuloside A); four flavonoids (quercetin 3-β-D-glucopyranoside, kaempferol 3-0-a-L-rhamnopyranosyl(1→6)-β-D-glucopyranoside, kaempferol 3-β-D-glucopyranoside, quercetin 3-0-a-L-rhamnopyranosyl(1→6)-β-D-glucopyranoside), four phenolics (caffeic acid, p-hydroxybenzoic acid, rosarinic acid, and 2-hydroxy-3-(3′,4′-dihydroxyphenyl)propanoic acid); and a diterpene (trans-phytol) | [409]     |
Table 1. Cont.

| Scientific Name          | Family   | Common Name     | Cherokee Use             | Part Used   | Chemical Constituents and Activities                                                                 | Ref. |
|--------------------------|----------|-----------------|--------------------------|-------------|------------------------------------------------------------------------------------------------------|------|
| *Prunus serotina* Ehrh. | Prunaceae | Black cherry    | bark infusion for colds  | bark        | Aerial parts: polyphenolics (butyl rosmarinate, ethyl rosmarinate, methyl rosmarinate, rosmarinic acid, 3,4,α,3-trihydroxy-methyl phenylpropionate, and p-coumaric acid) [410]  |
|                          |          |                 |                          |             | Aerial parts: phenolics (quercetin, rutin, rosmarinic acid, caffeic acid, chlorogenic acid ferulic acid, protocatechuic acid) [411]  |
|                          |          |                 |                          |             | Aerial parts: polygalacerebroside, ursolic acid, β-amyrin, quercetin, quercetin-3-O-β-D-galactoside, α-spinasterol, stigmasterol, β-sitosterol, daucosterol [412]  |
| *Pseudognaphalium*       | Asteraceae| Rabbit tobacco  | infusion of herb for coughs, colds, flu | herb        | Leaves: flavonoids (avicularin, nourtin, hyperoside, narcissin, rutin, quercetin 3-O-neohesperidoside, 3-O-(2′-O-α-L-rhamnopyranosyl)-β-D-galactopyranoside) [413]  |
| *obtusifolium* (L.)     |          |                 |                          |             | Leaves: chlorogenic acid (1.08-2.30%), rutin (0.10-0.35%), hyperoside (1.20-2.23%), reynoutrin (0.06-0.44%), guajiverin (0.07-0.22%), avicularin (0.98-1.82%), juglanin (0.04-0.20%) [414]  |
| Hilliard and B.L. Burtt  |          |                 |                          |             | Leaves: triterpenoids (corosolic acid (0.137%), oleanolic acid (0.129%), ursolic acid (0.884%)) [415]  |
| (syn. *Gnaphalium*       |          |                 |                          |             | Leaves: hyperoside, prunin, ursolic acid [416]  |
| *obtusifolium* L.)      |          |                 |                          |             | Leaves: chlorogenic acid, hyperoside, benzaldehyde [417]  |
|                         |          |                 |                          |             | Leaf EO: benzyl alcohol (20.3%), benzaldehyde (12.1%), cinnamyl alcohol (4.7%), cinnamaldehyde (4.1%) [416]  |
|                         |          |                 |                          |             | Flowers: chlorogenic acid (0.65-1.96%), rutin (0.17-0.31%), hyperoside (0.08-1.59%), reynoutrin (0.08-0.21%), guajiverin (0.10-0.28%), avicularin (0.20-0.95%), juglanin (0.08-0.16%) [414]  |
|                         |          |                 |                          |             | Bark: triterpenoids (ursolic acid, ursolic aldehyde, 2α,3α-dihydroxysper-12-en-28-oic acid) [418]  |
|                         |          |                 |                          |             | Bark: flavonoids (4′-methoxynaringenin, naringenin, dihydrokaempferol, eriodictyol) [419]  |
| *Pseudognaphalium*       | Asteraceae| Rabbit tobacco  | infusion of herb for coughs, colds, flu | herb        | Plant: flavonoid obtusifolin [420]  |
| *obtusifolium* (L.)     |          |                 |                          |             | Plant: flavonoids (gnaphalin A, methylgnaphalin) [421]  |
| Hilliard and B.L. Burtt  |          |                 |                          |             | Plant: flavonoid 3,5,7-trihydroxy-6,8-dimethoxyflavone [422]  |
| Scientific Name         | Family         | Common Name     | Cherokee Use                          | Part Used | Chemical Constituents and Activities                                                                 | Ref.       |
|-------------------------|----------------|-----------------|---------------------------------------|-----------|------------------------------------------------------------------------------------------------------|------------|
| *Pycnanthemum flexuosum* (Walter) Britton, Sterns and Poggenb. | Lamiaceae      | Mountain mint   | leaf infusion for headache, colds, fevers | leaves    | Whole plant: vanillic acid 1-O-[β-D-apiofuranosyl]-β-D-glucopyranoside, (4S,5R)-4-hydroxy-5-phenyl-tetrahydrofuran-2-one, luteoline 7-O-[β-D-glucopyranosyl]-1→2)-β-D-glucopyranoside, 4′-O-methyllypolaetin 7-O-[β-D-glucopyranosyl]-(1→2)-β-D-glucopyranoside, apigenin 7-O-[6-O-acetyl-β-D-glucopyranosyl]-(1→2)-β-D-glucopyranoside, isoquercitrin 4-O-methyl ether 7-O-[6-O-acetyl-β-D-glucopyranosyl]-(1→2)-β-D-glucopyranoside, apigenin 7-O-[6-O-(E-coumaroyl)β-D-glucopyranoside], 3′-hydroxy-4-O-methylisoquercitrin 7-O-[6-O-acetyl-β-D-glucopyranosyl]-(1→2)-6,8-0-acetyl-β-D-glucopyranoside, acteoside, leucosceptoside A, martynoside, artselaeroside A, stachyoside B, and chlorogenic acid | [423]      |
| *Quercus alba* L.         | Fagaceae       | White oak       | bark infusion for dysentery, antiseptic, fever | bark      | Bark: tannins                                                                                       | [424]      |
| *Ranunculus acris* L. *a* | Ranunculaceae  | Tall buttercup   | leaf poultice for abscesses; leaf infusion for sore throat | leaves    | Aerial parts: ranunculin                                                                            | [425]      |
| *Rhamnus caroliniana* Walter | Rhamnaceae     | Buckthorn       | itching skin, sores                     | berries, bark | Bark: chrysophanol, phywicin, ararobin, orachrysone, 1-docosanol                                    | [426]      |
| *Rhus glabra* L.          | Anacardiaceae  | Smooth sumac    | bark decoction to wash blisters         | bark      | Bark EO: chrysarobin (24.2%), piperine (15.4%), and pacharin (7.5%)                                  | [426]      |
|                          |                |                 |                                       |           | Branches: methyl gallate, 3,5-dihydroxy-4-methoxybenzoic acid, gallic acid, methyl gallate and 3,5-dihydroxy-4-methoxybenzoic acid showed antibacterial activity | [427]      |
|                          |                |                 |                                       |           | Leaves: myo-inositol, 1-docosanol, β-sitosterol, β-sitosterol glucoside, mixture of homologous alkanes (C₁₄-C₃₅, major heptacosane) | [428]      |
| Scientific Name       | Family              | Common Name | Cherokee Use                          | Part Used | Chemical Constituents and Activities                                                                 | Ref.   |
|-----------------------|---------------------|-------------|---------------------------------------|-----------|------------------------------------------------------------------------------------------------------|--------|
| *Rhus hirta* Harv. ex Engl. | Anacardi-aceae       | Staghorn sumac | bark decoction to wash blisters    | bark      | Fruits: major components: sumadin B-3-O-(2”-gallloyl)-galactoside-3’’’-O-glucoside, 7-O-methyl-cyanidin-3-O-(2”-gallloyl)-galactoside; shows anti-oxidant activity | [429]  |
| **Rhus spp. (as above)** | Anacardi-aceae       | Infusion of berries for urinary tract infections, thrush | berries   | Fruits: major components: sumadin B-3-O-(2”-gallloyl)-galactoside-3’’’-O-glucoside, 7-O-methyl-cyanidin-3-O-(2”-gallloyl)-galactoside; shows anti-inflammatory activity | [430]  |
| *Robinia pseudacacia* L. | Fabaceae            | Black locust | bark chewed as emetic                | bark      | Bark: lectins (RPbAI and RPrAI)                                                                        | [15]   |
| **Rubus allegheniensis** Porter | Rosaceae            | Allegheny blackberry | leaf infusion for diarrhea | leaves   | Root: lectins (RPbAI and RPrAI)                                                                       | [435]  |
| **Rubus idaeus** L. *a*    | Rosaceae            | Red raspberry | leaf infusion for pain; root infusion cathartic | roots, leaves | Leaf extract: triterpenoids (tormentic acid, euscaphic acid, myrianthic acid, ziyu glycoside II, sericic acid, and 19-hydroxy-2,3-secours-12-ene-2,3,28-trioic acid 3-methyl ester) | [436]  |
| **Rubus idaeus** L. *a*    | Rosaceae            | Red raspberry | leaf infusion for pain; root infusion cathartic | roots, leaves | Leaf extract: triterpenoid glycosides (3β-(O-β-D-glucopyranosyl)-olean-12-ene-1α,2α,3β-triol, 28-(O-β-D-glucopyranosyl)-urs-12-ene-2α,3β,19α-trihydroxy-28-oic acid, and 3β-(O-β-D-glucopyranosyl)-olean-12-ene-1α,2α,3β-trihydroxy-28-oic acid) | [437]  |
Table 1. Cont.

| Scientific Name         | Family          | Common Name        | Cherokee Use                        | Part Used | Chemical Constituents and Activities                                                                 | Ref. |
|-------------------------|-----------------|--------------------|-------------------------------------|-----------|------------------------------------------------------------------------------------------------------|------|
| **Leaf extracts:**      |                 |                    |                                     |           | tannins (ellagic acids, ellagitannins, sanguin H-6 and H-10, and the trimers lambertianin D and lambertianin C, as well as methyl gallate), phenolic acids (chlorogenic acid, p-coumaric, ferulic, protocatechuic, gentisic, caffeoylhartc, feruloylhartc, and p-coumaroyl-glucoside acids, as well as p-hydroxybenzoic and vanillic acids), terpenoids (terpinolene, 3-oxo-α-ionol, α- and β-amyrin, squalene and cycloartenol) |      |
| **Rudbeckia fulgida**   | Asteraceae      | Orange coneflower  | root used for ear medicine          | root      | Leaf EO: β-caryophyllene (10.0%), γ-muurolene (8.9%), germacrene D (30.1%), δ-cadinene (17.8%)         | [439]|
| **Rudbeckia hirta**     | Asteraceae      | Black-eyed Susan   | root infusion taked for sexually transmitted diseases (STDs) | root      | Leaf EO: (2E)-hexenal (20.2%), (E)-β-ocimene (15.2%), γ-muurolene (8.1%), germacrene D (23.6%), δ-cadinene (16.2%) | [440]|
| **Rudbeckia laciniata** | Asteraceae      | Souchan, Green-headed coneflower | tonic, skin wash | leaves | Aerial parts: lignans ((+)4,4’-O-diangeloylpinoresinol, (+)4,4’-O-diangeloylmethioresinol, (+)4,4’-O-diangeloylsyringaresinol, and (+)-syringaresinol) | [441]|
|                         |                 |                    |                                     |           | Aerial parts: flavonoid glycosides (quercetin 3-O-α-L-arabinofuranosyl(1”→6”)-β-D-galactopyranoside, quercetin 3-O-α-L-arabinopyranosyl(1”→6”)-β-D-galactopyranoside, quercetin 3-O-β-D-xylopyranosyl(1”→2”)-β-D-glucopyranoside, and quercetin 3-O-β-D-glucopyranoside, isorhamnetin 3-O-β-D-glucopyranoside), quinic acid derivatives (3,5-O-trans-dicaffeoylquinic acid methyl ester, 3,5-O-trans-dicaffeoylquinic acid methyl ester, 3,4-O-trans-cafeoylquinic acid methyl ester, 3,4-O-trans-cafeoylquinic acid methyl ester, 3,4-O-trans-cafeoylquinic acid methyl ester, 3,4-O-trans-cafeoylquinic acid methyl ester, 3,4-O-trans-cafeoylquinic acid, 3,5-O-trans-dicaffeoylquinic acid) | [442]|
|                         |                 |                    |                                     |           | Roots: sesquiterpene rudbeckianone                                                                   | [443]|
|                         |                 |                    |                                     |           | Roots: sesquiterpene lactone rudbeckiolide                                                          | [444]|
| **Sambucus canadensis** | Adoxaceae       | American elder     | berry infusion for rheumatism; infusion of flowers taken for fever; leaves used to wash sores | plant     | Root extract: sesquiterpenoids (sesquiterpene, igalan, lacinan-8-ol)                                | [445]|

References:
[439] [440] [441] [442] [443] [444] [445]

(Rudbeckia fulgida Aiton Asteraceae Orange coneflower root used for ear medicine root [15]
(Rudbeckia hirta L. Asteraceae Black-eyed Susan root infusion taken for sexually transmitted diseases (STDs) root [15]
(Rudbeckia laciniata L. Asteraceae Souchan, Green-headed coneflower tonic, skin wash leaves [15]
(Sambucus canadensis L. Adoxaceae American elder berry infusion for rheumatism; infusion of flowers taken for fever; leaves used to wash sores plant [15]
### Table 1. Cont.

| Scientific Name | Family | Common Name | Cherokee Use | Part Used | Chemical Constituents and Activities | Ref. |
|-----------------|--------|-------------|--------------|-----------|--------------------------------------|------|
| **Flowers:** | | | | | | |
| rutin | | | | | | [446] |
| **Fruits:** | | | | | | |
| anthocyanins (cyanidin 3-sambubioside-5-glucoside, cyanidin 3,5-diglucoside, cyanidin 3-sambubioside, cyanidin 3-glucoside, cyanidin 3-O-(6-O-Z-p-coumaroyl-2-O-β-D-xylopyranosyl)-β-D-glucopyranoside-5-O-β-D-glucopyranoside, cyanidin 3-O-(6-O-E-p-coumaroyl-2-O-β-D-xylopyranosyl)-β-D-glucopyranoside-5-O-β-D-glucopyranoside (major), cyanidin 3-O-(6-O-E-p-coumaroyl-2-O-β-D-xylopyranosyl)-β-D-glucopyranoside) | | | | [447] |
| **Rhizome:** | | | | | | |
| alkaloids (sanguinarine, chelerythrine, protopine) | | | | | | [450] |
| alkaloids [protopine (0.32–0.74%), allocryptopine (0.34–0.77%), sanguinarine (1.38–4.45%), chelerythrine (0.99–2.57%), chelurubine (0.37–0.87%), chelilutine (0.78–1.83%), sanguilutine (0.49–1.03%)] | | | | | | [451] |
| alkaloids (sanguinarine and chelerythrine-antimycobacterial) | | | | | | [452] |
| alkaloids (sanguinarine, chelerythrine, protopine-anti-Helicobacter pylori) | | | | | | [453] |
| alkaloids (sanguinarine (2.81–3.96%), chelerythrine (1.38–2.88%)) | | | | | | [454] |
| alkaloids (sanguinarine, chelerythrine, sanguilutine, chelurubine, chelirubine, protopine, and allocryptopine) | | | | | | [455] |
Table 1. Cont.

| Scientific Name | Family       | Common Name      | Cherokee Use                                                                 | Part Used | Chemical Constituents and Activities                                                                 | Ref. |
|-----------------|--------------|------------------|------------------------------------------------------------------------------|-----------|-----------------------------------------------------------------------------------------------------|------|
| *Sassafras albidum* (Nutt.) Nees | Lauraceae    | Sassafras        | bark decoction for skin diseases, sexually-transmitted diseases; poultice for wounds and sores | bark      | Leaf EO: (3Z)-hexenol (2.5–9.9%), α-pinene (3.2–12.2%), camphene (0.3–5.4%), limonene (5.7–16.6%), linalool (3.5–6.7%), neral (9.9–18.1%), geranial (10.7–26.5%), β-caryophyllene (5.1–12.5%), caryophyllene oxide (0.4–19.0%) | [456]|
|                 |              |                  |                                |           | Root EO: safrole (85%), camphor (3.25%), and methyleugenol (1.10%)                                      | [457]|
|                 |              |                  |                                |           | Bark EO: α-pinene (37.9–61.5%), camphene (2.9–5.1%), β-pinene (10.0–13.0%), 1,8-cineole (7.3–10.0%), and α-terpineol (4.2–11.6%) | [458]|
|                 |              |                  |                                |           | Bark: sesamin, spinescin, β-sitosterol, hexatriacontanol, and 1-triacontanol; sesamin and spinescin showed antileishmanial activity | [459]|
| *Saururus cernuus* L. | Saururaceae  | Lizard’s tail     | mashed roots poultice for wounds                                             | root      | Aerial parts: lignans (austrobailignan-5, veraguensin, guaiacin, saucercoxin)                           | [460]|
|                 |              |                  |                                |           | Plant: lignans (manassantin A, manassantin B, saucercoxin)                                             | [461]|
|                 |              |                  |                                |           | Aerial parts: indole alkaloids (sauristolactam, cepharanone B)                                        | [462]|
|                 |              |                  |                                |           | Aerial parts: lignans (saururin, saururenin, saururinone, austrobailignan 6, calopiptin, galbacin, zuonin A) | [463]|
|                 |              |                  |                                |           | Aerial parts: lignans (sauriol A, sauriol B)                                                          | [464]|
|                 |              |                  |                                |           | Aerial parts: lignans (licrin A, sauercoxin, dihydroguaiaretic acid, sauriol A, sauritol B, saucercoxin, and saucercoxin methyl ether) | [465]|
|                 |              |                  |                                |           | Aerial parts: diterpenoid 12,13-dehydrogeranylgeraniin                                                | [466]|
|                 |              |                  |                                |           | Aerial parts: lignans (manassantin B, 4-O-demethylmanassantin B)                                      | [467]|
|                 |              |                  |                                |           | Stems and leaves: lignans (manassantin A, manassantin B, manassantin B4, 4-O-methylsaucercoxin, vorrucosin, austrobailignan-5) | [468]|
| *Scutellaria lateriflora* L. | Lamiaceae    | Blue skullcap     | root infusion for monthly period, diarrhea; root decoction to expel afterbirth, for breast pains, and for nerves | root      | Review                                                                                               | [469]|

**Review**
### Table 1. Cont.

| Scientific Name   | Family       | Common Name       | Cherokee Use               | Part Used                        | Chemical Constituents and Activities                                                                 | Ref. |
|-------------------|--------------|-------------------|-----------------------------|----------------------------------|------------------------------------------------------------------------------------------------------|------|
| *Senecio aureus* L. | Asteraceae    | Golden ragwort    | infusion of plant taken to prevent pregnancy/induce abortions | plant                            | Eremophilane sesquiterpenoids (trans-9-oxofuranoelemiphilane, 8a-ethoxy-10aH-ermophileneolide, 3a-angeloyloxy-9-oxo-10aH-furanoelemiphilane) | [479]|

Aerial parts ED: δ-cadinene (27%), calamenene (15.2%), β-selinene (9.2%), α-cubenene (4.2%), α-humulene (4.2%), and α-bergamotene (2.8%) 
[470]

Aerial parts: neo-clerodane diterpenoids (scutelaterin A, scutelaterin B, scutelaterin C, ajugapitin, and scutecyprol A) 
[471]

Herb: flavonoids baicalin and baicalein (aglycone) 
[472]

Aerial parts: indole alkaloids (melatonin, serotonin); flavonoids (baicalin, baicalein, wogonin, scutellarin) 
[473]

Herb: flavonoids (viscidulin III, chrysos, baicalin, oroxylin A, wogonin); phenolics (trans-verbascoside, trans-martynoside) 
[474]

Aerial parts: coumarins (scuteflorin A, scuteflorin B, decursin) 
[475]

Stem: flavonoids [scutellarin (0.08%); phenolic [acteoside (0.05%)]] 
[476]

Root: flavonoids [baicalin (0.05%), baicalein (0.06%), wogonin (0.20%), oroxylin A (0.02%)] 
[476]

Leaf: flavonoids [scutellarin (0.92%), baicalin (0.05%)] 
[476]

Aerial parts: flavonoids (apigenin, luteolin, baicalein, wogonin, 6-methoxy-luteolin 4'-methyl ether, isoscutellarin 8-O-β-D-glucuronide, apigenin 7-O-β-D-glucuronide, luteolin 7-O-β-D-glucuronide, baicalin, wogonin 7-O-β-D-glucuronide, wogonin 7-O-β-D-glucuronide methyl ester, eriodictyol, naringenin, naringenin 7-O-β-D-glucuronide), phenolics (acteoside, nonoside D, leucosceptoside A, martynoside, isosceposide); lignan (syringaresinol 4'-O-β-D-glucopyranoside) 
[477]

Aerial parts: flavonoids (norwogonin-7-O-glucuronide, baicalin, dihydrobaicalin, galangin-7-O-glucuronide, dihydrooroxylin A,7-O-glucuronide, oroxylin A,7-O-glucuronide, wogonin-7-O-glucuronide, 5,7-dihydroxy-6,8-dimethoxyflavone-7-O-glucuronide, dihydrowogonin-7-O-glucuronide, baicalin, wogonin, oroxylin A, chrysin); phenolic (5-(β-D-glucopyranosyl)-3-hydroxy-trans-stilbene-2-carboxylic acid) 
[478]
| Scientific Name      | Family               | Common Name     | Cherokee Use         | Part Used | Chemical Constituents and Activities                                                                 | Ref. |
|----------------------|----------------------|-----------------|----------------------|-----------|-------------------------------------------------------------------------------------------------------|------|
| *Silphium compositum* | Asteraceae           | Rosin weed      | tonic                | plant     | Leaves: flavonoid glycosides (isorhamnetin 3-O-α-L-rhamnosyl (1″″′→6″)-O-β-D-galactopyranoside 7-O-β-L-apiofuranoside, quercetin 3-O-α-L-rhamnosyl (1″″′→6″)-O-β-D-galactopyranoside 7-O-β-L-apiofuranoside, quercetin 3-O-α-L-rhamnosyl (1″″′→6″)-O-β-D-galactopyranoside, and quercetin 3-O-β-D-galactopyranoside) | [15] |
| *Solanum carolinense* L. | Solanaceae           | Carolina horsenettle | leaf infusion for worms | leaves    | Leaves: steroidal glycoside (carolinoside) is shown to be O-(α-pentulopyranosyl)-(1→4)-O-(α-L-arabinopyranosyl)-(1→1)-D-glucopyranose | [15] |
| *S. odora* Aiton     | Asteraceae           | Goldenrod       | bee stings, sore throat  | flowers   | Roots: ethyl N,N-bis(4-dimethylaminobutyl) carbamate (solaurethine). Other compounds reported for the first time in this species include solamine (principal base), cuscohygrine and anabasine | [481] |
| *S. odora* f. odora  | Asteraceae           | Goldenrod       | bee stings, sore throat  | flowers   | Flowering parts EO: methyl chavicol (70.8%), myrcene (12.5%), methyl eugenol (5.8%), limonene (4.5%) | [15] |
| *Stillingia sylvatica* L. | Euphorbiaceae       | Queen’s delight | root tincture for STDs | root      | Roots: stillingia factors S1–S6 (2-hydroxydaphnetoxin diterpenoids) | [484] |
| *Symphyotrichum novae-angliae* (L.) G.L. Nesom (syn. *Aster novae-angliae* L.) | Asteraceae       | New England aster | root poultice for pain | root      | Leaf EO: (2E)-hexenal (31.0%), α-pinene (16.4%), germacrene D (25.5%), β-cadinene (14.3%) | [440] |
| *Thalictrum dioicum* L. | Ranunculaceae       | Early meadowrue | root infusion for diarrhea | root     | Bis-benzylisoquinoline alkaloids (thalctropine, thalidoxine, pennsylvanine, thalmetaline, thalictrogamine) | [485] |
| *Tilia americana* L.  | Tiliaceae            | American basswood | inner bark decoction for diarrhea, coughs, boils | bark      | Pallidine and corydine alkaloids | [487] |
| *T. americana* var. mexicana (Schldl.) Hardin | Tiliaceae            | American basswood | inner bark decoction for diarrhea, coughs, boils | bark      | Flowers: quercetin and kaempferol derivatives; showed sedative and anxiolytic activity | [488] |
Table 1. Cont.

| Scientific Name                  | Family         | Common Name     | Cherokee Use                                | Part Used          | Chemical Constituents and Activities                                                                 | Ref. |
|----------------------------------|----------------|-----------------|---------------------------------------------|--------------------|--------------------------------------------------------------------------------------------------------|------|
| *T. americana* var. *mexicana*   |                |                 | Flowers: tiliroside, quercetin, quercitrin, kaempferol; showed anxiolytic activity |                    | [489]                                                                                                   |      |
| *T. americana* var. *mexicana*   |                |                 | Flowers: quercetin; showed analgesic activity |                    | [490]                                                                                                   |      |
| *T. americana* var. *mexicana*   |                |                 | Flowers: quercetin, kaempferol; showed anxiolytic activity |                    | [491]                                                                                                   |      |
| *T. americana* var. *mexicana*   |                |                 | Flowers and leaves: flavonoids quercetin, rutin, isoquercetin; extract showed anticonvulsant activity |                    | [492]                                                                                                   |      |
| *Tsuga canadensis* (L.) Carrière | Pinaceae       | Eastern hemlock | bark poultice for itching skin; stem tips for kidneys | bark, leaves       | Foliar EO: α-pinene (17.6%), camphene (11.5%), isobornyl acetate (43.4%) | [15] |
|                                  |                |                 |                                             |                    | Foliar EO: α-pinene (13.2%), camphene (7.8%), isobornyl acetate (42.9%)                               | [493]|
|                                  |                |                 |                                             |                    | Foliar EO: tricyclene (1.6–5.1%), α-pinene (4.1–15.1%), camphene (3.0–11.1%), myrcene (0.5–21.1%), isobornyl acetate (22.0–55.8%), α-humulene (3.6–9.8%), germacrene D (1.4–21.3%) | [494]|
|                                  |                |                 |                                             |                    | Foliar EO: tricyclene (3.1–7.8%), α-pinene (11.6–22.7%), camphene (7.8–15.9%), isobornyl acetate (32.8–50.7%), α-humulene (up to 9.2%), germacrene D (up to 6.4%) | [495]|
|                                  |                |                 |                                             |                    | Foliar EO: α-pinene (13.9, 5.4%), camphene (13.3, 3.4%), limonene (6.0, 7.0%), piperitone (4.3, 7.7%), isobornyl acetate (38.6, 37.0%) | [496]|
| *Viburnum prunifolium* L.        | Adoxaceae      | Black haw shrub | bark infusion as tonic for female bleeding   | bark               | Bark: biflavonoid amentoflavone | [497]|
|                                  |                |                 |                                             |                    | Bark: indoid glycosides (2-O-acetyldihydrostemsid, 2-O-trans-p-coumaroyldihydrostemsid, 2-O-acetylpatrinosid, and patrinoside) | [498]|
| *Vicia caroliniana* Walter       | Fabaceae       | Vetch           | pains, rheumatism                            | plant              | Bark: 1-methyl-2,3-dibutyl hemimellitrate | [499]|
|                                  |                |                 |                                             |                    | Aerial parts EO: phytone (2.2–21.5%), methyl roughanate (1.9–29.5%), palmitic acid (9.9–28.1%), (E)-phytol (15.8–36.1%) | [500]|
| *Xanthorrhiza simplicissima* Marshall | Ranunculaceae | Yellow root     | root infusion for cramps, as tonic           | root               |                                                                                                         | [501]|
| Scientific Name          | Family    | Common Name          | Cherokee Use                                      | Part Used | Chemical Constituents and Activities                                                                 | Ref. |
|-------------------------|-----------|----------------------|---------------------------------------------------|-----------|------------------------------------------------------------------------------------------------------|------|
| Zanthoxylum americanum  | Rutaceae  | Common prickly ash   | bark infusion for swollen joints                  | bark      | Root: alkaloids (berberine, jatrorrhizine, magnoflorine) [502]                                       |      |
|                         |           |                      |                                                   |           | Whole plant: alkaloids berberine and puntarenine [503]                                              |      |
|                         |           |                      |                                                   |           | Roots: bisbenzylisoquinoline alkaloids (obamegine and oxyacanthine) [504]                            |      |
| Zanthoxylum clava-herculis | Rutaceae  | Hercules’s club       | Houma tribe of Native Americans (not Cherokee) used the bark for toothache | bark      | Bark: pyranocoumarins (dipetaline, alloxanthoxyletin, xanthoxyletin, xanthyletin) and lignans (sesamin, asarinin) [505] |      |
|                         |           |                      |                                                   |           | Leaf EO: α-thujene (0.2–5.6%), limonene (43.6–73.0%), 1,8-cineole (12.9–43.3%), linalool (up to 11.3%) [506] |      |
|                         |           |                      |                                                   |           | Bark EO: sabinene (47.0%), limonene (18.7%), terpinen-4-ol (12.9%) [507]                            |      |
|                         |           |                      |                                                   |           | Bark: asarinin, sesamin, neoherculin, xanthoxylol-γ,γ-dimethylallyl ether, pipertol-γ,γ-dimethylallyl ether, pluviatol-γ,γ-dimethylallyl ether [508] |      |
|                         |           |                      |                                                   |           | Bark: chelerythrine [509]                                                                             |      |

* Non-native.  † Commercial (dōTERRA) essential oil.  ‡ W. N. Setzer (unpublished).
3. Cherokee Aromatic Medicinal Plants Currently in Use as Herbal Medicines

3.1. Achillea millefolium L.

*Achillea millefolium* (yarrow) is native to temperate regions of the Northern Hemisphere but has been introduced worldwide [510]. The traditional medical uses of *A. millefolium* have been reviewed and the plant has been used since ancient times as a wound-healing agent and to treat gastrointestinal complaints [510–512]. Consistent with this, the Cherokee have also used *A. millefolium* as an antihemorrhagic; for healing wounds, treating bloody hemorrhoids and bloody urine, and for bowel complaints [15,17,510]. In addition, infusions of *A. millefolium* have been used as a treatment for fever [15,17,510]. Yarrow extract has shown spasmogenic effects on murine and human gastric antrum, consistent with its traditional use to treat dyspepsia [513]. In a double-blind clinical trial, *A. millefolium* ointment was shown to reduce pain, inflammation, and ecchymosis in episiotomy wound healing [514].

The essential oils of *A. millefolium* have shown wide variation depending on geographical location and growing season. Volatile oil samples from Turkey [48] and Macedonia [51] were dominated by 1,8-cineole and camphor, whereas the essential oil from Lavras, Brazil, was rich in chamazulene [49]. The essential oil from Lithuania showed wide variation in composition depending on morphological type (flower color) as well as plant phenology [50]; γ-terpinene and cadinene (isomer not identified) were the major components during the flowering phase, but β-pinene was abundant during the vegetative phase. Conversely, *A. millefolium* leaf essential oil from Portugal was rich in 1,8-cineole during the flowering phase, but germacrene D dominated the oil during the vegetative phase [53].

The non-volatile chemical components of *A. millefolium* are generally dominated by phenolics (e.g., chlorogenic acid and other quinic acid derivatives) and flavonoids and flavonoid glycosides (e.g., luteolin, apigenin, and quercetin, and their glycosides) [38–42,44,46,47]. Chlorogenic acid has shown in vivo wound-healing properties in rat models [515,516]. Likewise, the flavonoid apigenin [517,518] as well as an apigenin glycoside [519] have shown in vivo wound-healing effects in rodent models. Similarly, luteolin [520–522], luteolin-7-O-glucoside [523], quercetin [524–526] and several quercetin glycosides [527–531] have shown wound-healing effects.

3.2. Caulophyllum thalictroides (L.) Michx.

A decoction of the roots of *C. thalictroides* (blue cohosh) has been used by the Cherokee as an anticonvulsive (to treat “fits and hysterics”) and antirheumatic [15]. The plant is also used as a gynecological aid, to promote childbirth and to treat womb inflammation [15]. These traditional uses are in apparent contrast to the observed toxic effects (convulsions, respiratory paralysis) of the plant observed in range animals such as sheep [108]. The rhizome of *C. thalictroides* contains several quinolizidine alkaloids, including N-methylcytisine (also known as caulophylline), baptifoline, anagyrine, and lupanine [108,110,112]. *N*-Methylcytisine is known to stimulate the central nervous system, and in high doses causes convulsions followed by paralysis [532]. Acute lupanine toxicity is characterized by neurotoxic effects including decreased cardiac contractility, blocking of ganglionic transmission and contraction of uterine smooth muscle [533]. This latter effect explains the traditional Cherokee use to promote childbirth. Apparently, lupanine, in lower doses, does not exhibit sub-chronic, chronic, reproductive, or mutagenic toxic effects [533]. Both *N*-methylcytisine [110] and anagyrine [534] have been shown to be teratogenic, however. The aporphine alkaloid magnoflorine, on the other hand, has shown sedative and anxiolytic effects [535] and may be responsible for the anti-convulsive and sedative uses of *C. thalictroides* in Cherokee traditional medicine.

Lee and co-workers [115] have shown that the oleanolic acid glycosides caulosides A–D exert anti-inflammatory effects by way of inhibiting expression of inducible nitric oxide synthase (iNOS) and the pro-inflammatory cytokines tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6). The anti-inflammatory effects of *C. thalictroides* triterpene saponins are consistent with the Cherokee traditional uses to treat rheumatism and inflammation.
3.3. Cimicifuga racemosa (L.) Nutt. (syn. Actaea racemosa L.)

Black cohosh (C. racemosa) has been a popular herbal supplement for many years [536]. The plant is reputed to possess anti-inflammatory, diuretic, sedative, and antitussive activities [511], and the root has been reported to have estrogic activity [537–539]. Fukinolic acid [137] and formononetin [511] have been reported to be estrogic constituents of C. racemosa rhizome. The traditional Cherokee use of C. racemosa rhizome to stimulate menstruation [15] is consistent with the reported estrogic activity. There have been conflicting reports regarding the estrogic activity of C. racemosa rhizome, however [540–542], and a survey of 13 populations of C. racemosa in the eastern United States failed to detect the presence of formononetin [543]. Molecular docking studies have suggested that C. racemosa triterpenoids are unlikely estrogen receptor binding agents, but any estrogic activity of C. racemosa extract is probably due to phenolic components such as cimicifugic acid A, cimicifugic acid B, cimicifugic acid G, cimiciphenol, cimiciphenone, cimiracemate A, cimiracemate B, cimiracemate C, cimiracemate D, and fukinolic acid [544]. Although recent evidence suggests the estrogen receptor not to be a target of C. racemosa phytochemical constituents, other biomolecular targets may be involved. Rhizome extracts of C. racemosa have been shown to interact with the serotonin receptor [545], the µ-opioid receptor [546,547] as well as the γ-aminobutyric acid type A (GABA_A) receptors [548]. Modulation of these receptors may contribute to some of the biological effects of C. racemosa extracts.

Reviews of several randomized clinical trials have failed to demonstrate efficacy of C. racemosa on menopausal symptoms [549,550]. However, one randomized, placebo-controlled double-blind clinical trial with menopausal women, concluded that C. racemosa extract showed superiority over a placebo in ameliorating menopausal disorders [551]. Clinical studies have generally suggested C. cimicifuga use to be safe, but there have been some case reports indicating safety concerns [552].

The Cherokee have also used infusions of C. racemosa rhizome to treat rheumatism, coughs, and colds [15]. Aqueous extracts of C. racemosa have demonstrated reduction of the release of pro-inflammatory cytokines interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), and interferon-gamma (IFN-γ) in whole blood, and the prominent active component responsible was isoferulic acid [553]. The ethyl acetate fraction of the aqueous extract of C. racemosa was also shown to suppress the release of TNF-α, due to cimiracemate A [554]. Aqueous extracts reduced inducible nitric oxide synthase (iNOS) protein expression as well as iNOS mRNA levels, but did not inhibit iNOS enzymatic activity; the triterpenoid glycoside 23-epi-26-deoxyactein was found to be the active principle in the extract [555]. These effects likely explain the anti-inflammatory activities of C. racemosa and their traditional uses to treat rheumatism and other inflammatory diseases.

3.4. Hamamelis virginiana L.

Hamamelis virginiana, American witch hazel, is a shrub or small tree, native to eastern North America. Several Native American tribes have used the plant for numerous medicinal purposes. Decotions of the bark or the stems of witch hazel have been used as a topical lotion for cuts, bruises, insect bites, external inflammations, and other skin problems [15]. In addition, the Cherokee people took infusions of witch hazel for periodic pains, to treat colds, sore throats, and fevers. Modern uses of witch hazel include treatment of hemorrhoids, inflammation of the mouth and pharynx (leaf only), inflammation of the skin, varicose veins, wounds and burns [537]. Hamamelis virginiana leaves contain up to 10% tannins, including gallic acid, polygallocatein, hamamelitin and analogs, flavonoids, and proanthocyanidins [511], which are responsible for the observed astrigent, anti-inflammatory, and hemostatic effects [537]. The bark also contains hamamelitin and analogs, and proanthocyanidins [511].

The aqueous ethanol extract of H. virginiana showed anti-inflammatory activity in the croton oil mouse ear edema test [556] as well as the induced rat paw edema assay, confirming its use as an anti-inflammatory agent [557]. The extract also showed notable antiviral activity against Herpes simplex virus type 1 (HSV-1) [556]. Hamamelitin and galloylated proanthocyanidins from H. virginiana were found to be potent inhibitors of 5-lipoxygenase (5-LOX) [558]. Hamamelis
proanthocyanidins were found to stimulate cell growth of keratinocytes, enhancing cell growth, and are likely responsible for the dermatological use of tannin-containing witch hazel preparations [559]. *Hamamelis* tannins have also shown cytotoxic activity against HT-29 human colorectal adenocarcinoma cells [223] and antiviral activity against influenza A virus and human papillomavirus [560].

The anti-inflammatory activity of witch hazel was demonstrated in a clinical study using a lotion prepared from *H. virginiana* distillate, which showed suppression of erythema after ultraviolet (UVB) light exposure [561]. Similarly, in a clinical trial with patients suffering from atopic eczema, a cream containing *H. virginiana* distillate significantly reduced skin desquamation, itching and redness [562]. Of course, *H. virginiana* distillate will not contain tannins.

3.5. *Hydrastis canadensis* L.

Goldenseal (*Hydrastis canadensis*), a perennial herb in the Ranunculaceae, is native to eastern North America from Ontario, Canada, south to Alabama and Georgia [563]. The Cherokee used the root decoction of goldenseal as a tonic and wash for local inflammations; took the root decoction orally to treat cancer, dyspepsia, and general debility [15]. Goldenseal is still used in herbal medicine to control muscle spasms, treat cancer, increase blood pressure, treat gastrointestinal disorders, manage painful and heavy menstruation, treat infections topically, and reduce swelling [537,564].

The major components in goldenseal root are isoquinoline alkaloids hydrastine, berberine, and canadine, and berberine likely accounts for the biological activities of goldenseal. Berberine has shown in vitro cytotoxic activity to HeLa human epitheliod cervix carcinoma, SK-OV-3 human ovarian carcinoma, HEp2 human laryngeal carcinoma, HT-29 human colorectal adenocarcinoma, MKN-45 human gastric cancer, HepG2 human hepatocellular carcinoma, MCF-7 and MDA-MB-231 human breast adenocarcinoma cell lines [565–568]. The cytotoxicity of berberine can be attributed to DNA intercalation [569–571] and modulation of the human epidermal growth factor receptor 2 (HER2)/phosphatidylinositol-3-kinase (PI3K)/protein kinase B (Akt) signaling pathway [572,573]. Berberine has also shown antibacterial activity against *Staphylococcus aureus* [238,574], and *Helicobacter pylori* [453]; antiparasitic activity against *Entamoeba histolytica*, *Giardia lamblia*, *Trichomonas vaginalis*, *Trypanosoma brucei*, *Trypanosoma congolense*, *Leishmania braziliensis panamensis*, *Leishmania major*, and *Plasmodium falciparum* [575–578]; and anti-inflammatory activity in a serotonin-induced mouse paw edema assay [579]. In a randomized, double-blind, placebo-controlled clinical trial with patients suffering from acute watery diarrhea due to cholera, berberine showed a significant reduction in stool volume compared to the placebo [580]. Several clinical studies have demonstrated antihyperlipidemic effects of berberine in humans [581].

3.6. *Juncus effusus* L.

*Juncus effusus* (common rush) is native to North and South America, Europe, Asia, and Africa [563]. There are numerous varieties and subspecies of *J. effusus* with at least two in eastern North America [582]. The Cherokee took a decoction of the plant as an emetic, while an infusion was used to wash babies to strengthen them and prevent lameness [15]. In Chinese Traditional Medicine (TCM), *J. effusus* is used as a sedative, anxiolytic, antipyretic, and to reduce swelling. Extracts of *J. effusus* have revealed several cinnamoylglycerides [252,253], cycloartane triterpenoids [255–257], phenanthrenes [258–264,266,267,269–272,583,584], and pyrenes [265,268]. Dehydroeffusol, effusol, and juncusol, phenanthrenes isolated from *J. effusus*, have shown anxiolytic and sedative effects in a mouse model [264,271], likely due to modulation of the gamma-amino butyric acid type A (GABA<sub>A</sub>) receptor [272]. The GABA<sub>A</sub> modulatory activity may account for the TCM use of *J. effusus* as a sedative and anxiolytic agent. Several *J. effusus* phenanthrenes have shown inhibition of NO production in lipopolysaccharide (LPS)-activated murine macrophage RAW 264.7 cells, indicating anti-inflammatory activity [270].
3.7. Panax quinquefolius L.

American ginseng (Panax quinquefolius) is a member of the Araliaceae and is native to eastern North America [585]. Ginseng root from P. ginseng or P. notoginseng, has been used for thousands of years in the Asian traditional medicine. Panax quinquefolius is currently cultivated in the United States, Canada, and China, and is used as a medical tonic worldwide. Native Americans have used P. quinquefolius for numerous medical problems as well as a general tonic [15], and European settlers had also utilized this plant for similar purposes [586]. The Cherokee used the root as an expectorant, to treat colic, oral thrush, and as a general tonic [15].

The phytochemistry and pharmacology of P. quinquefolius has been reviewed several times [333,339,341,342]. The major components in P. quinquefolius roots are triterpenoid glycosides, the ginsenosides, as well as several polyacetylenes. The ginsenosides have shown anti-inflammatory, antiproliferative, hepatoprotective, cardioprotective, neuroprotective, cholesterol-lowering, and cognitive improvement [340].

Several clinical trials have been carried out using P. quinquefolius extracts. In terms of cognitive function, a randomized, double-blind, placebo-controlled crossover trial, P. quinquefolius extract showed significant improvement in working memory, choice reaction time and “calmness” [587]. A clinical trial to study the effects of P. quinquefolius extract on cancer-related fatigue showed a promising significant trend in relieving fatigue [588]. Panax quinquefolius extracts were found to be clinically effective in preventing upper respiratory infections in healthy adult senior citizens [589,590].

3.8. Sanguinaria canadensis L.

Bloodroot (Sanguinaria canadensis, Papaveraceae) is native to eastern North America [591]. The plant has been used by Native Americans as a traditional medicine for a variety of ailments [455]. The Cherokee used a decoction of the root, in small doses, for coughs, lung inflammations, and croup, and a root infusion was used as a wash for ulcers and sores [15]. The roots are rich in isoquinoline alkaloids, including sanguinarine, chelerythrine, sanguilutine, chelilutine, sanguirubine, chelirubine, protopine, and allocryptopine [455]. The traditional Cherokee uses of bloodroot as a cough medicine/respiratory aid as well as for treating ulcers and sores can be attributed to the antimicrobial activities of the isoquinoline alkaloids [592]. Thus, for example, sanguinarine has shown antimicrobial activity against methicillin-resistant Staphylococcus aureus (MRSA) [593], biofilm-forming Candida spp. [594], Mycobacterium spp. [452], and Helicobacter pylori [453].

3.9. Scutellaria lateriflora L.

Infusions of the roots of blue skullcap (Scutellaria lateriflora, Lamiaceae) were used by the Cherokee for monthly periods and to treat diarrhea; root decoctions were used as an emetic to expel afterbirth and to remedy breast pains [15]. Interestingly, the aerial parts, rather than the roots, are currently used as an herbal medicine as an anxiolytic, sedative and antispasmodic [511,537,595,596].

The phytochemistry and pharmacology of S. lateriflora have been reviewed [469]. The secondary metabolites from the aerial parts of S. lateriflora are dominated by flavonoid glycosides (baicain, dihydrobaicain, lateriflorin, ikonnikoside I, scullarin (scutellarein-7-O-glucuronide), and oroxylin A-7-O-glucuronide, and 2-methoxy-chrysin-7-O-glucuronide), flavonoid aglycones (baicalein, oroxylin A, wogonin, and lateriflorein), phenylpropanoids (caffeic acid, cinnamic acid, p-coumaric acid, and ferulic acid), and clerodane diterpenoids (scutelaterin A, scutelaterin B, scutelaterin C, ajugapitin, and scutecyprol A) [469]. The essential oil from the aerial parts of S. lateriflora (collected in northern Iran) was composed largely of sesquiterpene hydrocarbons, δ-cadinene (27%), calamenene (15.2%), β-elemene (9.2%), α-cubenene (4.2%), α-humulene (4.2%), and α-bergamotene (2.8%) [470].

The flavonoids scullarin and baicain and the phenylpropanoid ferulic acid have shown in vitro estrogenic effects [597,598], and may be responsible for the traditional Cherokee uses of S. lateriflora.
Consistent with the current herbal medicinal use of *S. lateriflora*, the plant has shown anti-convulsant activity in rodent models of acute seizures, attributable to the flavonoid constituents [474]. Baicalin has shown anti-convulsant activity in pilocarpine-induced epileptic model in rats [599], while wogonin has shown anti-convulsant effects on chemically-induced and electroshock-induced seizures in rodents [600]. In addition, scutellarin has shown relaxant activity using rodent aorta models [601,602], while wogonin showed smooth muscle relaxant activity in rat aorta [603] and rat uterine smooth muscle [604]. On the other hand, both baicalin and baicalein inhibited NO-mediated relaxation of rat aortic rings [605]. Baicalein and baicalin have shown anxiolytic activity [606]. Apparently, baicalin and wogonin exert their anxiolytic effects through allosteric modulation of the GABA<sub>A</sub> receptor by way of interaction at the benzodiazepine site [607,608]. Conversely, baicalein promotes anxiolytic effects via interaction with non-benzodiazepine sites of the GABA<sub>A</sub> receptor [609]. There have apparently been no clinical trials on the root extracts of *S. lateriflora*.

However, in randomized, double-blind, placebo-controlled crossover clinical trials, the anxiolytic effects of *S. lateriflora* herbal treatments significantly enhanced overall mood without reducing cognition or energy [610,611].

### 4. Conclusions

This is not a complete list of the phytochemistry of Cherokee aromatic medicinal plants. Numerous plants described in the Cherokee ethnobotanical literature [15–24] have not been investigated for phytochemical constituents or pharmacological activity. In addition, in many instances the phytochemistry is not sufficiently characterized, particularly in terms of the plant tissues used in Cherokee traditional medicine. In this review, there are numerous instances where the phytochemical constituents and the biological activities associated with them correlate with the traditional Cherokee uses of the plant, but there are several instances where there is no apparent correlation. Therefore, much work is needed to add to our knowledge of the pharmacological properties of the chemical components, not to mention potential synergistic or antagonistic interactions.

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