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Review

Review on *Cardamine diphylla* (Michx.) A. wood (*Brassicaceae*): Ethnobotany and glucosinolate chemistry

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ABSTRACT

Ethnopharmacological relevance: *Cardamine diphylla* (Michx.) A. Wood, commonly called toothwort, is a spring perennial herb belonging to the *Brassicaceae* family. This endemic plant of Eastern North America has been widely used by multiple American First Nations (i.e. indigenous people of North America) for food and medicine for centuries.

Approach and methods: The aim of the review is to describe the botany, ethnopharmacology, phytochemistry, and bioactivity of *Cardamine diphylla*. The review covers literature on *Cardamine diphylla*, and the alternative name *Dentaria diphylla*, from English and French language sources.

Results: Multiple traditional uses of *Cardamine diphylla* by American First Nations are well documented. Initial health studies showed that the tested concentrations of the extract were not toxic against brine shrimp larvae and the same extract had a weak free-radical scavenging activity. However, bioactive compounds in the form of aliphatic and indole glucosinolates and some indole alkaloids have been isolated from this plant. Ecological research regarding *Cardamine diphylla*-insect interactions (such as feeding and oviposition) is also available in the literature.

Conclusions: The wide range of traditional uses by multiple American First Nations suggests that the antibacterial, antiviral, immunostimulant, analgesic, antipyretic, and anti-inflammatory activities of this plant should be explored in in vitro and in vivo tests. Traditional modes of preparation of the plant suggest that some of the medicinal properties could certainly be attributed to glucosinolate degradation products (i.e. isothiocyanates), but a clear assignment of active molecules and mechanisms of action remain to be elucidated. The presence of glucosinolates indicates that the plant could be probed for cancer chemopreventive properties. Overall, the review shows that more investigation is necessary to determine the possible benefits of *Cardamine diphylla* extracts to pharmaceutical companies as a nutraceutic specialty phytotherapeutic agent against respiratory (cold and sore throat) or gastrointestinal problems.

Contents

Abbreviations: $ABTS^{+\bullet}$, 2,2′-Azino-bis(3-ethylbenzthiazoline-6-sulfonic acid); CYP, Cytochrome P450; $DPPH^{\bullet}$, Diphenylpicrylhydrazyl radical; GC, Gas chromatography; GL, Glucosinolate; GLs, Glucosinolates; HPLC, High performance liquid chromatography; ITC, Isothiocyanate; ITCs, Isothiocyanates; LC–MS, Liquid chromatography–mass spectrometry; SC_{50}, Half maximal scavenging activity

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1. Introduction

Cardamine diphylla (Michx.) A. Wood is a spring perennial herb belonging to the *Brassicaceae* family and an endemic plant to Eastern North America. *Cardamine diphylla* was assigned to the *Cardamine* genus in 1877 by Wood (1877). *Dentaria diphylla* Michx. is a commonly used synonym that was previously assigned by Michaux (1820) in 1820. The word *Cardamine* is derived from the Greek word *kardamon*, a name used by Dioscorides for "cress" (Gray, 1908). *Dentaria* is from Latin, *dens*, meaning "tooth". This refers to the form of the rhizome in certain species (Lamoureux, 1975) and to the bidentate nectary of the corolla (Provancher, 1892). *Diphylla* means "with two leaves" in Latin. The plant was well-known to American First Nations and early European settlers. The common names used for *Cardamine diphylla* in a number of different languages are given in Table 1.

As part of our continued interest in the chemistry and biology of the plants from the *Brassicaceae* family and in particular of *Cardamine diphylla*, we reviewed the literature regarding the occurrence, botanical description, ethnopharmacology, phytochemistry, and biological activity of the plant. The review covers the literature up to 2012. Future research activities and pharmaceutical applications of this under-researched plant emerge from this review.

2. Occurrence, botanical description and ethnopharmacology

2.1. Occurrence

Cardamine diphylla is an uncommon plant which can be found growing near streams or swampy areas within forested regions (McKay and Catling, 1979). This plant usually grows together in colonies and in shady regions (McKay and Catling, 1979). In Canada, *Cardamine diphylla* is found in the provinces of New Brunswick, Nova Scotia, Quebec and Ontario, while in the United States, it is found from Michigan to Kentucky, South Carolina to Wisconsin, in Tennessee, and Pennsylvania (Erichsen-Brown, 1979; Horsley et al., 2008; Stehn et al., 2011; Weatherbee and Crow, 1992).

The plant is considered to be a good indicator species of sugar maple (*Acer saccharum* Marsh.) health in New Hampshire and Vermont (Horsley et al., 2008).

The compensation point -the amount of sunlight needed for the photosynthetic rate to equal the rate of respiration—is 0.4%. This is notable as being rather low (Greller, 1988). However, this is not surprising due to the forested habitat that the plant prefers. The light saturation point is 3.8% for *Cardamine diphylla* and is unusually low due to its shady habitat. The maximum photosynthetic rate is 36.6 μmol CO_2 g^{-1} s^{-1} (Greller, 1988).

2.2. Botanical description

2.2.1. The rhizome

Cardamine diphylla emerges from underground stems which grow horizontally (Fig. 1), and are referred to as rhizomes (Chambers et al., 1996). The rhizomes are elongated and "toothed" (Torrey and Gray, 1969). They usually grow close to the surface and have a pungent, peppery odour which is a characteristic of the mustard family (McKay and Catling, 1979). The rhizomes are long and continuous, thickened at the nodes, and green or white (Radford et al., 1968). This species tends to spread rapidly from the crisp and edible rootstocks (Smith, 1966). The rhizomes are constricted at intervals representing a single year′s growth, the segments being easily separable (Scoggan, 1978).

2.2.2. The stem

The stem (Fig. 1) is a continuous rootstock and is notched on the way up (Homer, 1918). It grows from 20 to 40 cm in height (Radford et al., 1968). The plant can be easily multiplied by rootstock division when the plant is dormant.

2.2.3. The leaf

The leaves (Fig. 1) appear approximately half way up the stem (Torrey and Gray, 1969). The leaves are described as crenate (meaning having a margin with low, rounded or scalloped projections) or serrated; with the teeth mucronate (meaning ending abruptly in a sharp point). They are rarely lobed, can be ciliate or are otherwise glabrous. The basal leaves are ovate to elliptic and are often evergreen; they measure 10 cm long by up to 6 cm wide (Radford et al., 1968). The leaf has a linear to lanceolate shape. The petioles are 10–15 cm long and the stem has two leaves (Radford et al., 1968). The petioles are sub-opposite, 1–2 cm long (Radford et al., 1968), short-petiolulate and rhombic-ovate or oblong-ovate (Gray, 1908). The lifespan of the leaf is usually greater than ten weeks

Table 1
Vernacular names of *Cardamine diphylla*.

Tribe/language	Name	References
Abnaki	kondouhi′jak meaning "little veins" referring to the winding roots through soil	Lamoureux (1975), Rousseau (1947)
Cherokee	anahlskwalʌ·ski translated to "crowsfoot" or "crowfoot"	Perry (1974)
Delaware	"little burr"	Tantaquidgeon (1942, 1972)
English	Crinkled, crinkleroot, pepper-root, toothache-root, toothwort, twin-leafed toothwort, white flowered toothwort, trickle, trickle-root, two toothed pepper-root	Hamel and Chiltoskey (1975), Yanovsky (1936), Newcomb (1977), Erichsen-Brown (1979), Coffey (1993)
French	Carcajou, corson, dentaire à deux feuilles, snicroût meaning "snake-root" due to its inter-twined roots	Lamoureux (1975), Black (1980)
Iroquois	a-tsa, ɪkde′hɛks (Onondaga), o$^{/ɛ}$djia^{ɛ}	Rousseau (1945), Waugh (1916), Herrick (1977)
Malecite	ka/djiwuk "something growing in a hiding place"	Mechling (1959)