

Review: Northern Ontario medicinal plants

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Hassan, H. M., Jiang, Z.-H., Syed, T. A. and Qin, W. 2012. **Review: Northern Ontario medicinal plants.** Can. J. Plant Sci. **92**: 815–828. The majority of scholarly investigations conducted in the 20th century have provided the incentive for establishing plants as sources of diverse phytochemicals. With infectious and cancerous diseases causing millions of mortalities worldwide, and the advent of resistant strains, the discovery of new antimicrobial and anticancer agents is crucial. Hence, included in this review is a novel list of 48 northern Ontario medicinal plants that may be sources of antifungal, antibacterial and/or anticancer phytochemicals. A total of two ferns and allied plants, two sedges and grasses, six trees, four shrubs, one vine and 33 herbs were identified. These plants were accumulated through interviews with native Elders and a survey of ethnobotanical literature on northern Canadian species of medicinal plants. We also present a critical review of their potential constituents, medicinal properties, and analysis of four promising plants (skullcaps, devil's club, St. John's wort and evergreens). Skullcaps and St. John's wort are model plants with documented anticancer, antibacterial and antifungal bioactivities. However, a considerable gap in ethnopharmacological data was found for species of skullcaps (*Scutellaria galericulata*, *S. parvula* and *S. lateriflora*) and St. John's wort (*Hypericum mutilum*, *H. majus*, *H. canadense*) growing in northern Ontario. These findings provide promising incentives in the ethnopharmacological community for medicinal research in this region.

Key words: Traditional medicine, northern Ontario, medicinal plants, anti-microbial, anti-cancer, drug discovery

Hassan, H. M., Jiang, Z.-H., Syed, T. A. et Qin, W. 2012. **Revue: Les plantes médicinales du nord de l'Ontario.** Can. J. Plant Sci. **92**: 815–828. On doit à la majorité des études érudites effectuées au XX^e siècle la propension de chercher dans les plantes une source de nombreux composés phytochimiques. Avec les millions de décès dans le monde qu'engendrent les maladies infectieuses et cancéreuses et avec l'avènement de souches antibiorésistantes, il est capital de trouver de nouveaux agents antibactériens et anticancéreux. C'est pourquoi les auteurs proposent une liste inédite de 48 plantes médicinales poussant dans le nord de l'Ontario et susceptibles de renfermer des substances antifongiques, antibactériennes ou anticancéreuses. Deux fougères et plantes similaires, deux carex et graminées, six arbres, quatre arbustes, une vigne et 33 herbes ont ainsi été identifiées. Ces plantes ont été sélectionnées à la suite d'entretiens avec des sages autochtones et du dépouillement de la documentation ethnobotanique sur les espèces médicinales du Nord canadien. Les auteurs procèdent aussi à une revue critique de leurs composants et propriétés médicinales éventuels, et analyse quatre végétaux prometteurs (la véronique en écusson, le bois piquant, le millepertuis et les conifères). La véronique et le millepertuis sont des plantes modèles dont les propriétés anticancéreuses, antibactériennes et antifongiques ont été bien étayées. Néanmoins, il existe de sérieuses lacunes dans les données ethnopharmacologiques sur les diverses espèces de véronique (*Scutellaria galericulata*, *S. parvula* and *S. lateriflora*) et de millepertuis (*Hypericum mutilum*, *H. majus*, *H. canadense*) poussant dans le nord de l'Ontario. Ces constatations promettent d'inciter les spécialistes en ethnopharmacologie à parcourir la région à la recherche de plantes médicinales.

Mots clés: Médecine ancestrale, nord de l'Ontario, plantes médicinales, antibactérien, anticancéreux, découverte de médicaments

Global cancer statistics estimated a global count of 12.7 million new cancer cases and 7.6 million cancer related mortalities to have occurred in 2008; approximately 56% of the cases and 64% of the deaths occurred in economically developing countries (Jemal et al. 2011). According to an estimate by Ames et al. (1995), one in four deaths in America is due to cancer. Moreover, infectious diseases are also a major problem, particularly in developing countries. Worldwide, one in three deaths is the result of an infectious or communicable

disease (Lopez 2006). This problem can be traced to the evolution of multiple drug-resistant strains of pathogenic bacteria due to a concentrated use of existing antimicrobial drugs (Ahmad et al. 1998). These issues have created immense clinical problems in the treatment of cancer and infectious diseases.

The agricultural industry also suffers from the advent of microbial infestations on crops (Hadacek and Greger 2000). Recent studies estimate that the world will need

Abbreviations: AML, acute myeloid lymphoma; DPPH, 2,2-diphenyl-1-picrylhydrazyl; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; MIC, minimum inhibitory concentration

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70 to 100% more food by 2050, and the population is expected to increase to 9 billion people (Gomiero et al. 2011). We face the challenge of increasing demand for food, and limited land for agricultural growth. With plant pathogens causing a 20% worldwide reduction in crop yield (Oerke et al. 1994), the use of fungicides and bactericides remain an integral part of agriculture and food protection.

NATURAL PRODUCTS AS PROMISING ASPECTS

The medicinal properties of various plant extracts have been documented since the 5th century BC. It is estimated that more than two-thirds of current drugs are derived from plant sources (Coe and Anderson 1996). In the areas of cancer and infectious diseases, 60 and 70% of all drugs, respectively, originated from plant sources between 1981 and 2002 (Newman and Cragg 2007). Furthermore, scrutiny of medical indications by source of compounds has demonstrated that natural products and related drugs are used to treat 87% of all categorized human diseases, including antibacterial, anticancer, anticoagulant, antiparasitic, and immunosuppressant agents, among others (Newman et al. 2003). Between 2001 and 2005, 23 new drugs of plant origin were introduced to treat diseases such as cancer, fungal infections, bacterial infections, diabetes, atopic dermatitis, Alzheimer's syndrome, and genetic diseases such as tyrosinaemia and Gaucher's disease (Lam 2007). Despite the tremendous success of drug discovery from natural sources, the pharmaceutical industry has retracted its investigation of plants as sources of novel chemicals (Farnsworth and Morris 1976; Coe and Anderson 1996; Lam 2007).

There are major economic incentives for the discovery of natural products. Herbal therapy is a way of life for almost 80% of the people in rural areas, especially those in Asia, Latin America and Africa (Shale et al. 1999). According to a World Health Organization survey, about 70–80% of the total world population depends on herbal remedies as a source of their primary health care (Chan 2003). It is estimated that in the United States of America, approximately 30% of the population uses \$13 billion worth of alternative or herbal remedies per year (Keen et al. 1994). A relatively recent telephone survey by National Population Health Survey reported that 15% of 11 424 Canadian adults surveyed had used natural products within the previous 2 d (Singh and Levine 2007). Another survey of Canadian breast cancer patients found that 25% reported usage of herbal medicines as a supplementary treatment for breast cancer (Smith and Boon 1999). The great demand for herbal products, and the diminishing forestry in northern Ontario, should force the industry and research community to investigate plants in this region for sources of phytochemicals for the treatment of cancer and infectious diseases.

NORTHERN ONTARIO MEDICINAL PLANTS WITH POTENTIAL BIOACTIVE SUBSTANCES

There has been considerable research in Canada on medicinal plants collected by Aboriginal First Nations individuals (Westfall and Glickman 2004). Jones et al. (2000) tested 18 medicinal plants used by First Nations in eastern Canada for their anti-fungal properties against opportunistic human pathogens. They discovered 13 plants contained anti-fungal properties, and that medical knowledge held by First Nations significantly correlated with laboratory findings. Fraser et al. (2007) assessed 36 medicinal plants from two Cree communities (Whapmagoostui and Mistissini) for antioxidant activity via 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay and their ability to protect human low-density lipoprotein from oxidation. Upon comparison of antioxidant activity of these 36 medicinal plants with 16 extracts not utilized for medicinal purposes, a positive correlation was found between the established traditional knowledge of Cree Elders and the radical scavenging activity of these plants. Essentially, plants used by the Native Indians towards the cure of a certain illnesses have more therapeutic potential than a randomly chosen sample (Arnason et al. 1981).

The list of northern Ontario medicinal plants was compiled through interviews with native Elders and a survey of ethnobotanical literature (Arnason et al. 1981; Mowrey 1990; Willard et al. 1992; Bryan et al. 1993; Chevallier 1996; Hälvä and Craker 1996; Heatherly 1998; Argus et al. 1999; Small and Catling 1999; Li 2000; Etkin 2008; MacKinnon 2009). The criteria for plant selection was based on North American First Nations' ethnobotanical medicinal plant trends (Jones et al. 2000), which states that plants used in the treatment of burns, cuts, infections, diarrhea, and mouth conditions are likely to contain antimicrobial substances. Plants used in the alleviation of cancers were also included in the list. A total of two fern and allied plants, two sedges and grasses, six trees, four shrubs, one vine and 33 herbs were accumulated with reference to their conventional medicinal names (Table 1). Overall, 105 different species of plants are listed due to the existence of various species within the conventional nomenclature. The potential secondary metabolite(s) of plants were identified via a rigorous literature analysis of their medicinal properties. No prior herbal research has been documented for northern Ontario; as such, this is the first report of medicinal plants in this region.

RESEARCH ON MEDICINAL PLANTS OF NORTHERN ONTARIO

Northern Ontario constitutes 87% of the land mass of the province of Ontario, but contains only 6% of the provincial population. Unlike urban centers, it is renowned for investment in forestry and many industries resort to forestry resources for economic stability and diversification (Duinker et al. 1991). This region has a large diversity of plant species used in traditional

Table 1. List of 48 Northern Ontario medicinal plants

Conventional name	Plant family	Botanical name	Medicinal properties	Potential constituent(s)
<i>Filicinophyta</i>				
Clubmosses	Lycopodiaceae: "Clubmoss"	<i>Lycopodium annotinum</i> , <i>L. clavatum</i> , <i>L. complanatum</i> , <i>L. dendroideum</i> , <i>L.</i> <i>inundatum</i> , <i>L. lucidulum</i> , <i>L.</i> <i>sabiniifolium</i> , <i>L. selago</i> , <i>L. sitchense</i> , <i>L. tristachyum</i> , <i>L. × zelleri</i>	Antifungal, antibacterial, antiviral (Orhan et al. 2007); relieve spasms, increase urine flow, estrogenic; reduce pain, fever, inflammation; insecticidal (Ibrahim et al. 2001; Ainge et al. 2002)	Lycodine type alkaloids (Nagai et al. 2005), lycopodine alkaloids (Orhan et al. 2007), tetracyclic alkaloids (Yin et al. 2006), clavine alkaloid (Wink and Schneider 1990), huperizine A (Orhan et al. 2007)
Common horsetail	Equisetaceae: "Horse tail"	<i>Equisetum arvense</i> L., <i>E. fluviatile</i> L., <i>E. palustre</i> L., <i>E. pratense</i> Ehrh., <i>E. sylvaticum</i> L., <i>E. variegatum</i>	Teas used to treat gout, gonorrhoea, stomach problems, bronchitis, tuberculosis and infection (Feresin et al. 2003), antioxidant (Amarowicz et al. 2004)	Antioxidant phenolics and proteins (Nagai et al. 2005), saponins, alkaloids (Abascal and Yarnell 2008)
<i>Planti</i>				
Balsam poplar	Salicaceae: willow	<i>Populus balsamifera</i> L., <i>P. tremuloides</i> , <i>P.</i> <i>grandidentata</i>	Used to treat diarrhea, fevers, skin problems, worms, inflammation; antimicrobial, antifungal (Mathes 1963; Isaeva et al. 2010)	Monoterpenes (Bryant et al. 1992), sesquiterpenoids (Mattes et al. 1987), phenolic glycosides (Mattes et al. 1987), flavonoids (Isaeva et al. 2010), tannins (Schimel et al. 1996)
Horse chestnut	Hippocastanaceae: buckeye	<i>Aesculus hippocastanum</i>	Used to treat blood circulatory problems and varicose veins; has anti-edema, anti-inflammatory, and free radical scavenging properties (Lou et al. 2004); antimicrobial (Fant et al. 1999)	Flavonoids (Kapusta et al. 2007), saponins (Benthin et al. 1999), triterpenoid glycoside (Loew and Kaszkin 2002), polyphenols (Lou et al. 2004), antimicrobial proteins (Fant et al. 1999)
Juniper	Cupressaceae: juniper	<i>Juniperus communis</i> L., <i>J. horizontalis</i>	Treatment of pneumonia, fever, colds, coughs, rheumatic joints, inflammation, diarrhea; antimicrobial (Matovic et al. 1996)	Tannins (Matovic et al. 1996), alkaloids, terpenoids, flavonoids, sterols (Wink 1987; Kumar et al. 2010)
Mossy cup oak	Fagaceae: beech	<i>Quercus macrocarpa</i>	Used to treat diarrhea, toothaches, skin infections, cuts, sore throats, burns; has antiviral and antibacterial properties (Güllüce et al. 2004)	Tannins (De La Rosa et al. 2001), phenolic acids (Cantos et al. 2003), polyphenols (Scalbert and Haslam 1987)
White elm	Ulmaceae: elm	<i>Ulmus americana</i> L.	Used to treat inflammation, diarrhea, burns, heartburn, antibacterial (Lee et al. 1992), antifungal (Burden and Kemp 1984)	Cerato ulmin (Richards and Takai 1988), phenolics (Witzell and Martin 2008), sesquiterpenes (Burden and Kemp 1984)
White spruce	Pinaceae: pine	<i>Picea glauca</i> , <i>P.</i> <i>mariana</i>	Used to treat infection (Johnk et al. 2005), insect bites, cuts (Johnk et al. 2005), scrapes	Camphor (Roy and Bergeron 1990), polyphenolics (Ralph et al. 2006), β -sitosterol (Dreikorn 2000), monoterpenes, 4-allyl-lansinol (Ibrahim et al. 2001)
<i>Magnoliophyta</i>				
Quack grass	Poaceae: grass	<i>Elymus repens</i> L. ^z	Antiseptic, laxative: used to treat fever, syphilis, jaundice, swollen and rheumatic limbs, chest pain, poor eyesight; affects crop development and reduce crop yields (An et al. 2005)	2,4-dihydroxy-1,4-benzoxazin-3-one, vanillin, β -hydroxybutyric-, 4-hydroxycinnamic-, ferulic-, vanillic-, syringic- and protocatechuic acids (An et al. 2005); allelopathic aglycans (Hagen 1989)
Sweet grass		<i>Hierochloa odorata</i>	Treat coughs, fever, venereal infections (Mohagheghzadeh et al. 2006)	Coumarin (Small and Catling 1999), antioxidant (Kumar et al. 2010), 8-dihydroxycoumarin (Krishnaiah et al. 2007)
<i>Coniopherophyta</i>				
Devil's club	Poaceae: dog bane	<i>Oplopanax horridus</i> ^z	Hypoglycemic (Large et al. 1938), antibacterial (Kobaisy et al. 1997), antiviral (Tai et al. 2006), antioxidant (McCutcheon et al. 1995); used to treat diabetes, colds, bronchitis, pneumonia; anticancer (Sun et al. 2010)	Polyynes (Kobaisy et al. 1997); sesquiterpenoids (Small and Catling 1999); hydrophobic anticancer metabolites (Sun et al. 2010); diynes (Copp 2003); phenolic glycosides (Huang et al. 2011)

Table 1 (Continued)

Conventional name	Plant family	Botanical name	Medicinal properties	Potential constituent(s)
Dogwood or bunchberry	Cornaceae: dogwood	<i>Cornus canadensis</i> L. ² , <i>C. alternifolia</i> , <i>C. rugosa</i> Lam., <i>C. stolonifera</i>	Anti-inflammatory, fever-reducing, pain killer; used to treat diarrhea, dysentery and burns, infections (Post and Urban 1995)	Antioxidant phenolics (Mulabagal and Tsay 2004; Tanaka et al. 2003)
Common bearberry	Ericaceae: heath	<i>Arctostaphylos uva-ursi</i>	Used to treat urinary tract infections, diarrhea, bladder problems, bronchitis, bleeding, cystitis (Abascal and Yarnell 2008); has antiseptic effects, anti-bacterial (Puupponen-Pimiä et al. 2001; Betoni et al. 2006), antioxidant properties (Amarowicz et al. 2004)	Phenolic glycoside arbutin, tannins (Small and Catling 1999), antibacterial polyphenol (Betoni et al. 2006), arbutin (Abascal and Yarnell 2008)
Prince's pine	Pyrolaceae: wintergreen	<i>Chimaphila umbellata</i> ²	Antimicrobial; used to treat infections, fevers, colds, sore throats, coughs, backaches, stomachaches, bladder problems, cystitis (Abascal and Yarnell 2008)	Antifungal compound (Galván et al. 2008), arbutin (Abascal and Yarnell 2008)
<i>Anthophyta</i> Common hops	Cannabaceae: hemp	<i>Humulus lupulus</i> ²	Antibacterial; used to relieve tumors, pneumonia, wounds, toothaches, fevers, painful swellings, boils; anti-HIV (Yazaki et al. 2009)	α acids, β acids, prenylated chalcones (De Keuleire et al. 2003); prenylated flavonoids, humulone and lupulone, phloroglucinol derivatives (Yazaki et al. 2009)
<i>Magnoliophyta</i> Bittercress and cuckooflower	Brassicaceae: mustard	<i>Cardamine parviflora</i> L., <i>C. pennsylvanica</i> , <i>C. pratensis</i> L.	Used to treat fevers, colds, sore throats, headaches, heart palpitations, chest pains, gas, stomach upset, lack of appetite; may contain anti-cancer substances (Daniel 2006)	Glucosinolates (Gurevitch et al. 2002), tropane alkaloids (Broek et al. 2006)
Black-eyed Susan and wild goldenglow	Asteraceae: sunflower	<i>Rudbeckia hirta</i> L., <i>R. laciniata</i> L.	Used to treat inflammation, indigestion, sores, snakebites, swellings, earaches; antimicrobial (Luczkiewicz and Cisowski 2001)	Polyacetylenes (Arnason et al. 1981); flavonoids, phenolic acids, anthocyanins (Luczkiewicz and Cisowski 2001); sesquiterpene lactones, pulchelin E (Luczkiewicz et al. 2002)
Bloodroot	Papaveraceae: poppy	<i>Sanguinaria canadensis</i> L. ²	Used to treat vomiting, diarrhea, gas, stomachaches, ulcers, tuberculosis; antibacterial, antifungal, anti-inflammatory, antioxidant, antitumor (Arnason et al. 1981)	Sanguinarine alkaloids (Arnason et al. 1981), Benzophenanthridine alkaloids (Arnason et al. 1981)
Blue cohosh	Berberidaceae: barberry	<i>Caulophyllum thalictroides</i>	Used to treat pelvic inflammatory disease, colic, sore throat, inflammation, fevers, infections (Gottshall and Lucas 1949)	Quinolizidine alkaloids (Roy and Bergeron 1990)
Canadian goldenrod	Asteraceae: sunflower	<i>Solidago canadensis</i> , <i>S. multiradiata</i>	Used to treat rheumatism, neuralgia, headaches, sore throat, kidney stones, ulcers; contains antioxidant and antiseptic substances (Abascal and Yarnell 2008)	Flavonoids, glycosides, saponins (Abascal and Yarnell 2008); phenolic acids (Buchsbaum et al. 1984)
Chamomiles		<i>Matricaria maritima</i> L., <i>M. matricarioides</i>	Antibacterial (Pastirova et al. 2004), anti-ulcer, antiviral, anti-inflammatory (Pastirova et al. 2004)	Sesquiterpenes, polyacetylenes, flavonoids, coumarins (Pastirova et al. 2004)
Cocklebur		<i>Xanthium strumarium</i> L.	Antibacterial, antifungal, antimalarial (Cerdeiras et al. 2007)	Carboxyatractyloside (Cutler 1985); 8- <i>epi</i> -tomentosin, xanthanolides (Park et al. 2001)
Common geranium	Geraniaceae: geranium	<i>Geranium bicknellii</i>	Antiseptic (Dorman and Deans 2000), anti-diuretic; used to treat toothaches	Terpenoids, phenylpropanoid eugenol (Dorman and Deans 2000); tannins and polyphenols (Scalbert and Haslam 1987)

Table 1 (Continued)

Conventional name	Plant family	Botanical name	Medicinal properties	Potential constituent(s)
Common yarrow	Asteraceae: sunflower	<i>Achillea millefolium</i> L.	Antiseptic, antibacterial (Vasinauskienė et al. 2006), anti-inflammatory, anti-spasmodic; used to treat diarrhea, urinary tract infections (Woods-Panزارu et al. 2009)	Isovaleric acid, camphor, azulenes, dehydromatracharia ester (Armason et al. 1981); lactones, sterols, flavonoids (Armason et al. 1981)
Common and rough dandelion	Asteraceae: sunflower	<i>Taraxacum ceratophorum</i> , <i>T. officinale</i>	Antimicrobial, lower sugar and cholesterol level, anti-inflammatory, immune stimulant; treat liver, urinary tract issues (Woods-Panزارu et al. 2009)	Sesquiterpene lactones (Michalska and Kistel 2003), phenolics (Hudec et al. 2007); Taraxacin, taraxerin, taraxerol, taraxasterol, inulin, gluten, gum, potash, choline, levulin, putin (Small and Catling 1999)
Fireweeds	Onagraceae: evening primrose	<i>Epilobium angustifolium</i> L., <i>E. ciliatum</i> , <i>E. leptophyllum</i> , <i>E. palustre</i> L.	Used to treat inflammation, burns, boils, sores, rashes, mouth ulcers, yeast infections (Iwashina and Kitajima 2000)	Flavonoids, myricetin, sitosterol (Small and Catling 1999); tannins (Armason et al. 1981), other phenolics (Romani et al. 2002), 3-O-D-glucuronide (Romani et al. 2002)
Flax	Linaceae: flax	<i>Linum perenne</i> L., <i>L. usitatissimum</i> L.	Used to prevent breast, prostate and colon cancer (Hemmati et al. 2007)	Justicidin B, glycosides of 7-hydroxyjusticidin B (Hemmati et al. 2007); lignans, arylidihydro-naphthalene (Hemmati et al. 2007); podophyllotoxin (Hemmati et al. 2007)
Gentians	Gentianaceae: gentian	<i>Gentiana linearis</i> , <i>G. amarella</i> ; <i>Gentianopsis crinita</i> , <i>G. detonsa</i>	Used to treat fever, indigestion, jaundice, skin diseases, heartburn; antimicrobial properties (Dorman and Deans 2000)	Secoiridoid glucosides –gentiopicroside (Mulabagal and Tsay 2004)
Gumweed	Asteraceae: sunflower	<i>Grindelia squarrosa</i>	Used to treat bladder inflammation caused by fungi or food (Hoffmann et al. 1993)	Alkaloids (Hazlett and Sawyer 1998), diterpenes, polyphenolics (Hoffmann et al. 1993)
Heal-all	Lamiaceae: mint	<i>Prunella vulgaris</i>	Antibacterial, antiviral, anti-inflammatory (Jirovský et al. 2007)	Rosmarinic acid, phenolic acids (Jirovský et al. 2007); ursolic acid, oleanolic acid (Wink 1987)
Knotweeds and smartweed	Polygonaceae: buckwheat	<i>Polygonum arifolium</i> , <i>amphibium</i> L., <i>P. hydrophiper</i> L., <i>P. lapathifolium</i> L., <i>P. pensylvanicum</i> L., <i>P. punctatum</i> , <i>P. scabrum</i> , <i>P. viviparum</i> L.	Known for treating various types of cancer (Yildirim et al. 2003); used to treat diarrhea, fever, chills, stomach pain, kidney problems, heart trouble, bleeding problems, antiseptic (Sato et al. 2000), antibacterial (Datta et al. 2000)	Phenolcarboxylic acids, flavonoids, anthraquinones, stilbenes (Nonaka et al. 1982); sesquiterpene acid (Datta et al. 2000)
Leaf mustard and wild turnip	Brassicaceae: mustard	<i>Brassica juncea</i> , <i>B. rapa</i> L.	May have anti-cancer substances (Daniel 2006); tonic for fevers, croup, asthma, headaches; antibacterial (Armason et al. 1981)	Tropane alkaloids (Jing-Yan and Zhao-Pu 2010), glucosinolates (De La Rosa et al. 2001)
Marsh yellow cress		<i>Rorippa palustris</i>	Used to treat inflammation, infection, anemia, bronchitis (Bussmann et al. 2008)	Isothiocyanates (Ishimoto et al. 2000), tropane alkaloids (Brock et al. 2006), glucosinolates (Gurevitch et al. 2002)
Northern St. John's wort	Guttiferiferae: St. John's wort	<i>Hypericum multum</i> , <i>H. perforatum</i> , <i>H. majus</i> , <i>H. ellipticum</i> , <i>H. canadense</i>	Anti-inflammatory, antibacterial (Dall'Agno et al. 2003); used to treat diarrhea, worms, coughs, depression, tuberculosis, tumors, cuts, ulcers, neurological disorders (Murch et al. 2003), cancer (Murch et al. 2003)	Hypericin, pseudohypericin, hyperforin (Murch et al. 2003); phenolics, chlorogenic acid, quercitrin, quercetin, rutin, apigenin-7-O-glucoside (Çirak et al. 2007)
Pearly everlasting	Asteraceae: sunflower	<i>Anaphalis margaritacea</i>	Used to treat swollen mucus membranes, paralysis; have anti-inflammatory, astringent effects; antimicrobial (Borchardt et al. 2008)	Polyacetylenes, pentaynes (Borchardt et al. 2008)
Pitcher plant	Sarraceniaceae: pitcher plant	<i>Sarracenia purpurea</i> L.	May have anticancer, antiviral, antimicrobial properties (Etkin 2008)	Comaine alkaloids (Carlson et al. 1948); triterpenes, phytosterols, sesquiterpenes (Etkin 2008)

Table 1 (Continued)

Conventional name	Plant family	Botanical name	Medicinal properties	Potential constituent(s)
Plantains	Plantaginaceae: plantain	<i>Plantago major</i> L., <i>P. media</i> L.	Used to treat inflammation, diarrhea, toothaches, headaches, bronchitis, sore throats, laryngitis, coughs, tuberculosis, infections (Jelager et al. 1998)	Iridoid glycosides aucubin and catalpol (Fajer et al. 1992)
Shepherd's purse	Brassicaceae: mustard	<i>Capsella bursa-pastoris</i>	May have anti-cancer substances (Daniel 2006)	Flavonoids, glucosinolates, saponins, volatile oils and sulfur containing compounds (Daniel 2006); tropane alkaloids (Brock et al. 2006)
Skullcaps	Lamiaceae: mint	<i>Scutellaria galericulata</i> L., <i>S. lateriflora</i> L., <i>S. parvula</i> ,	Used to treat cancer (Scheck et al. 2006); anti-inflammatory (Smith and Culvenor 1981); antioxidant, anticonvulsant, antibacterial, anti-viral (Shang et al. 2010)	Flavonoids (Abascal and Yarnell 2008); baicalin, baicalein, wogonin (Murch et al. 2003), diterpenes (Shang et al. 2010), phenophorbide (Fajer et al. 1992), apigenin (Sato et al. 2000)
Sorrels	Oxalidaceae: wood sorrel	<i>Oxalis acetosella</i> L., <i>O. stricta</i> L.	Used to treat inflammation, diarrhea, urinary tract infections, sprains, boils and pimples, traumatic injuries, infections (Feresin et al. 2003)	Benzoquinones, phenols (Feresin et al. 2003); oxalic acid (Wink 1987)
Skunk cabbage	Arum	<i>Symplocarpus foetidus</i> ²	Treatment of epileptic seizures, applied to wounds, rheumatism; potentially antifungal (Edilimesi 2002)	Antifungal nitro compounds (Edilimesi 2002)
Spreading dog bane	Papocynaceae: dog bane	<i>Apocynum androsaemifolium</i> L., <i>A. cannabinum</i> L.	Used to treat headaches, insomnia, constipation, indigestion, rheumatism, liver disease, syphilis; Antitumor properties (Murthy et al. 2011)	Indole alkaloids (Murthy et al. 2011), monoterpene indole alkaloids (Mishra et al. 2006), latex (Jing-Yan and Zhao-Pu 2010)
Sundews	Droseraceae: sundew	<i>Drosera anglica</i> , <i>D. intermedia</i> , <i>D. linearis</i> , <i>D. rotundifolia</i>	Antibacterial, antiviral, antifungal, anticancer, used to treat coughs, arynitis, pertussis, tracheitis, catarrh, tuberculosis, asthma, chronic bronchitis, ulcers, insecticidal (Bekesiova et al. 1999; Pareek et al. 2005)	Polyphenolics (Bekesiova et al. 1999); naphthoquinones, plumbagin, flavanoids (Pareek et al. 2005)
Swamp and common milkweed	Asclepiadaceae: milkweed	<i>Asclepias incarnate</i> L., <i>A. syriaca</i> L.	Used for treating blindness; stomachaches, asthma, bowel problems, rheumatism, intestinal worms; Milky sap applied to cuts and burns to infections and irritations (Wittstock and Gershenzon 2002)	Latex containing surface cardenolides (Wittstock and Gershenzon 2002)
Sweet flag	Alismataceae: water plantain	<i>Acorus calamus</i> L. ²	CNS-depressant, anti-inflammatory, antioxidant, antispasmodic, memory enhancing, antidiarrheal, anti-helminthic; insecticidal (Varma and Dubey 1999)	Phenylpropanes, monoterpenes, sesquiterpenoids, β -asarone (Small and Catling 1999); phenolics (Gurevitch et al. 2002)
Sweet coltsfoot	Asteraceae: sunflower	<i>Petasites frigidus</i>	Inhibits bacterial growth; used to treat inflammation, swelling, burns, sores and skin diseases; anti-carcinogenic	Pyrrrolizidine alkaloids (Smith and Culvenor 1981)
Wild onions and wild chives	Liliaceae: lily	<i>Allium schoenoprasum</i> L., <i>A. stellatum</i>	Used for treatment of cuts burns, insect bites, stings; Antibacterial, antiviral, antifungal (Kumari et al. 2009)	Saponins (Benkeblia 2004), phenolics (Barile et al. 2007)
Wild ginger	Aristolochiaceae: birthwort	<i>Asarum canadense</i> L.	Used to treat coughs, stomach problems, fever, gas, stomach upset and rashes; Antibacterial, antifungal properties (Yarnell and Abascal 2008)	Anti-adhesion compounds (Yarnell and Abascal 2008), chalcone and flavanol glycosides (Iwashina and Kitajima 2000); aristolochic acid alkaloids, borneol, α -pinene terpineol, ellagic acid (Armason et al. 1981)

²Rare plant species.

aboriginal communities for various medicinal incentives. Described here are a few exemplary medicinal plants of northern Ontario that have attracted considerable interest in the ethnobotanical community.

Skullcaps (*Scutellaria* Species)

Several *Scutellaria* species are known as skullcaps (Table 1). The genus *Scutellaria* (Lamaicaea) comprises approximately 350 species (Shang et al. 2010). It is widely distributed in temperate regions and tropical mountains, including Europe, North America and South Asia. The species range from 5 cm to 1 m in height and have been used for thousands of years to alleviate heat-evil and expel superficial evils in traditional Chinese medicine (Shang et al. 2010). Skullcaps are noted for anti-proliferative, anti-cancer, antibacterial and antiviral activities. *Scutellaria baicalensis* (*Huang Qin*, as it is known in Chinese) is one of the 50 fundamental herbs in Chinese medicine (Yin et al. 2004) and a significant quantity of literature iterates its anti-cancer activity (Ye et al. 2002; Scheck et al. 2006; Kumagai et al. 2007; Parajuli et al. 2009; Shang et al. 2010). Ye et al. (2002) demonstrated that *S. baicalensis* was cytotoxic with an IC₅₀ value of 1.1, 0.9, 0.52, 0.82 and 1.1 mg mL⁻¹ to squamous cell carcinoma, breast cancer, hepatocellular carcinoma, prostate carcinoma, and colon cancer, respectively. There was a strong dose-dependent inhibition of proliferation in all cell lines tested. Scheck et al. (2006) correlated its bioactivity to the presence of phenolic compounds baicalein (1a) and baicalin (1c, Fig. 1) and concluded a possible synergistic viability when used in concert with other chemotherapeutic agents. Kumagai et al. (2007) associated the anti-proliferative effect of *S. baicalensis* with mitochondrial damage, modulation of the anti-apoptotic family of genes (Bcl), an increased level of cyclin dependent kinase inhibitor p27^{KIP1} and a

decreased level of proliferation stimulatory c-myc gene. Among other species in the genus, *S. barbata* has also been shown to exhibit strong in vitro anti-cancer activity (Cha et al. 2004; Yin et al. 2004; Shoemaker et al. 2005; Kumagai et al. 2007; Yu et al. 2007; Shang et al. 2010). Despite the documented success of this herb in treating cancer, research on northern Ontario species of *Scutellaria* (*S. galericulata*, *S. parvula* and *S. lateriflora*) is lacking. This situation presents a promising opportunity for researchers towards discovery of potential anticancer agents.

Scutellaria species also exhibit antimicrobial properties. Sato et al. (2000) isolated flavonoids from *S. barbata* that displayed selective toxicity towards methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin sensitive *S. aureus* strains (MSSA). The most potent component was found to be apigenin (1b, Fig. 1) with a minimum inhibitory concentration (MIC) of 3.9–15.6 µg mL⁻¹ against MRSA and MSSA strains. Baicalin (1c, Fig. 1), an anticancer, anti-HIV and anti-inflammatory flavanoid representing 5% of the dry weight of *S. baicalensis*, also displayed antibacterial activity with MIC₅₀ and MIC₉₀ of 1.04 and 1.30 mg mL⁻¹, respectively, against 10 different strains of *Helicobacter pylori* (Wu et al. 2008). The myriad signature bioactivities recorded for this herb promotes *Scutellaria* species as interesting subject of ethnopharmacological research.

St. John's Wort (*Hypericum* Species)

St. John's wort is a well-studied perennial herb that grows widely in Europe, Western Asia, North Africa and America (Gupta and Möller 2003). It is also known as amber, Klamath weed, millepertuis, rosin rose, or Tipton's weed (Rowe and Baker 2009). St. John's wort was utilized in ancient native traditions for over 2000 yr as a spiritual plant to alleviate sickness, misfortune,

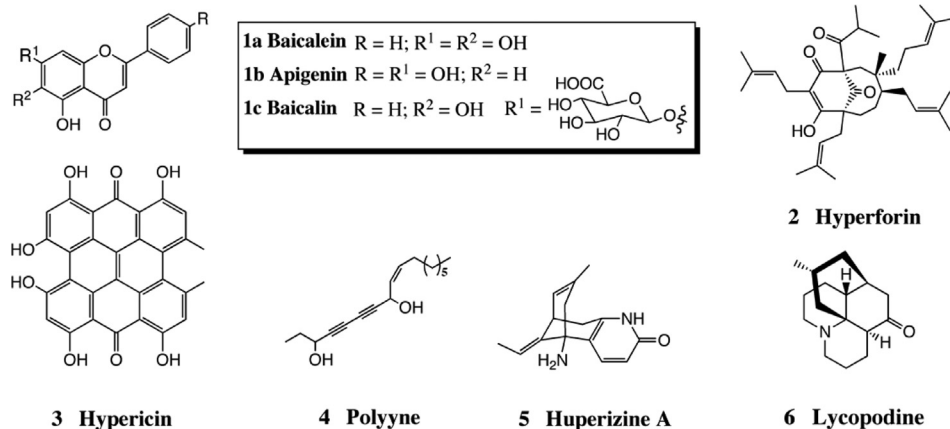


Fig. 1. Chemical structures of bioactive compounds isolated from medicinal plants: Baicalein (1a), apigenin (1b) and baicalin (1c) isolated from the roots of *Scutellaria baicalensis*; Hyperforin (2) isolated from the aerial parts of *Hypericum perforatum*; Hypericin (3) isolated from the entire *Hypericum perforatum* plant; Polyynes (4) isolated from the root bark of *Oplopanax horridus*; Huperzine A (5) and lycopodine (6) isolated from the aerial parts of *Lycopodium clavatum*.

anxiety, and depression, and served as a topical treatment for superficial wounds and burns (Gupta and Möller 2003; Rowe and Baker 2009). Five species of *Hypericum* genus are known as St. John's wort (Table 1). Active ingredients from *H. perforatum* have noted antibacterial, antidepressant, antiviral and anticancer properties. The anti-depressant activity of this herb is well debated, and has been attributed to the inhibition of norepinephrine, serotonin and dopamine synaptosomal uptake in many double blind studies (Müller et al. 1997; Gupta and Möller 2003; Carpenter 2011). However, Rapaport et al. (2011) refutes this result due to a high response measurement of placebo dose, relative to St. John's wort extract. Attention has focused on hyperforin (2) and hypericin (3) (Fig. 1) as the active ingredients behind this property (Barnes et al. 2001).

Hyperforin (2), a natural phloroglucinol isolate, is also reported to show anticancer activity. Merhi et al. (2011) discovered that hyperforin (2) inhibited the growth of acute myeloid lymphoma (AML) cell lines (U937, OCI-AML3, NB4, HL-60) by inducing apoptosis in a time- and concentration-dependent manner. Normal blood cells were not affected by the treatments. This activity has been attributed to suppression of cytochrome C oxidase-1 and 5-lipoxygenase activity, key enzymes in the formation of pro-inflammatory eicosanoids (Albert et al. 2002). Further, hyperforin (2) has been shown to act synergistically with hypericin (3) in its inhibitory effect on leukemic cell growth (Hostanska et al. 2003). The antibacterial property of hyperforin (2) has also been observed only at high concentrations, and its low potency makes it unlikely to be used for this purpose.

Preparations of *H. perforatum* are available at pharmacies, herbal medicine and health-food stores. It is considered one of the best selling herbal products. Due to the success of this herb, it is surprising that many species in this genus have not been well researched (e.g., *H. multilum*, *H. majus*, *H. canadense*). *Hypericum multilum* and *H. canadense* are species of St. John's wort found in northern Ontario. Though antibacterial activity has been reported for *H. multilum* extract (Carlson et al. 1948), the literature is significantly outdated. This presents a promising opportunity for contemporary research.

Devil's Club (*Oplopanax horridus*)

Devil's club (*Oplopanax horridus*), native to Thunder Bay, is considered one of the most important spiritual and medicinal plants by indigenous communities. It is a large shrub located in cool moist forests of western North America and is known for its large palmate leaves and erect woody stems covered in brittle spines. The hypoglycemic, antibacterial, and antioxidant properties of devil's club are well-researched. Kobaisy et al. (1997) studied the anti-microbial properties of polyne (4) isolated from the root bark of devil's club. The isolate

exhibited significant anti-*Candida*, antibacterial and antimicrobial activity, with an MIC of $10 \mu\text{g mL}^{-1}$ against *Mycobacterium tuberculosis* and isoniazid-resistant *M. avium* in a disc diffusion assay. These results are in correlation with findings that the inner bark of devil's club has been used by indigenous people to cure tuberculosis (Thommasen et al. 1990). Devil's club is also noted for its anti-proliferative, antioxidant and anti-viral activities. McCutcheon et al. (1995) studied the anti-viral activity of the inner bark methanolic extract of devil's club and found it partially inhibited the herpes virus type 1. Tai et al. (2006) documented anti-proliferative activity of inner bark extract against K562, HL60, MCF7 and MDA-MB-468 cancer cell lines. The ethanolic extracts exhibited synergistic effects when combined at non-inhibitory concentrations with non-cytotoxic concentrations of camptothecin or paclitaxel. The antiproliferative activity of devil's club extracts may be correlated with its strong antioxidant profile.

Devil's club has been widely noted in the Native community to relieve diabetic symptoms. Large et al. (1938) demonstrated that at extract concentrations of 0.1, 0.2, and 0.25 cc per lb. of body weight, a rapid reduction in blood sugar, from 35 to 70 mg 100 cc^{-1} was observed. In contrast, Thommasen et al. (1990), in a closely monitored study, reported the absence of hypoglycemic activity when administered to an insulin-dependent diabetic patient, a newly diagnosed non-insulin-dependent diabetic, and two healthy individuals. With these apparently contradictory data, further investigation is necessary to evaluate the hypoglycemic property of this plant.

Also, considering its range of bioactivities, it is surprising that few publications report the isolation and characterization of bioactive compounds from devil's club. More research needs to be geared towards this.

Evergreens

Evergreen plants have a long leaf lifespan, and are active in all seasons (Moore 1980). They encompass a wide array of trees and shrubs, including conifers, gymnosperms and angiosperms. Evergreen trees, perennials and herbs have been used in native communities to treat infection and cancer and to alleviate toothache. Prior to winter, a sappy substance called "pine gum" is harvested from juniper, jack pine, balsam fir, spruce, tamarack and other conifers, which is rubbed as a paste on wounds to prevent infection. This paste is also rubbed on teeth to mitigate toothaches. The roots of evergreen trees are harvested in the winter, according to native elders, to alleviate infections. Plantain (*Plantago major*) was reported by a Native Elder to have maintained the suppression of cancer in one chronic patient through an entire winter. Hence, this herbaceous species may contain anticancer substances.

Clubmoss (*Lycopodiaceae* family) is a low growing, non-flowering, spore-producing vascular plant that

covers approximately 80% of the soil surface in many grassland communities of the northern mixed prairie of North America (Romo 2010). In Chinese medicine, clubmoss species are prepared as a tea or poultice to treatment amnesia, contusion, swelling, schizophrenia and hematuria (Bai 1993). *Lycopodium varium* from New Zealand exhibited insecticidal activity (Ainge et al. 2002). Orhan et al. (2007) tested the antibacterial activity of *L. clavatum* and found it inhibited all the bacteria tested with an MIC range of 4–64 $\mu\text{g mL}^{-1}$. Their study also revealed antifungal and antiviral properties of this species. Further, many alkaloids have been isolated from clubmosses displaying a wide array of bioactivities. Huperzine A (5, Fig. 1), lycopodine (6, Fig. 1), serratezomines, carinatamins, and complamandine are among the alkaloids isolated that exhibit insecticidal, antibacterial, and anti-acetylcholinesterase activity, and the induction of neurotrophic factor secretion, respectively (Morita et al. 2005; Choo et al. 2007; Orhan et al. 2007; Kubota et al. 2009). Huperzine A (5) also exhibits anticholinesterase activity and is presently in phase II clinical studies for the treatment of Alzheimer's disease in elderly patients (Rafii et al. 2011). It has been used to treat myasthenia gravis, dementia and to improve senile memory (Yu et al. 1986). However, lycopodine (6) is the major alkaloid found in clubmosses (Orhan et al. 2007).

PERSPECTIVES

There has been considerable research on the isolation of bioactive substances from medicinal plants, their efficacy against diseases, potential targets, architectural characterization, and therapeutic properties. Several plant-derived drugs have been introduced onto the market, and there is significant evidence to support continued research on their extraction and isolation. For example, the famous anticancer drug Paclitaxol was isolated from pacific yew (*Taxus brevifolia*) and is now administered in the treatment of breast, lung and ovarian cancer (Jemal et al. 2011). Past experiences have taught us that plant phytochemicals possess a broad range of bioactivities against bacteria, fungi, cancer and other diseases. New procedures and advanced separation techniques may lead to the discovery of novel chemical entities previously neglected. Overall, many plant compounds remain untapped resources in medicine; as such, it is essential to investigate their therapeutic properties and chemical structures. In accordance, we propose this paper to stimulate herbal research in the uncharted forestry of the northern Ontario. Based on the abundant medicinal plant resource and the great knowledge in utilizing these plants by the First Nations in northern Ontario, there is great potential for drug discovery in this region.

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