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Antiviral screening of British Columbian medicinal plants

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Abstract

One hundred methanolic plant extracts were screened for antiviral activity against seven viruses. Twelve extracts were found to have antiviral activity at the non-cytotoxic concentrations tested. The extracts of *Rosa nutkana* and *Amelanchier alnifolia*, both members of the Rosaceae, were very active against an enteric coronavirus. A root extract of another member of the Rosaceae, *Potentilla arguta*, completely inhibited respiratory syncytial virus. A *Sambucus racemosa* branch tip extract was also very active against respiratory syncytial virus while the inner bark extract of *Oplopanax horridus* partially inhibited this virus. An extract of *Ipomopsis aggregata* demonstrated very good activity against parainfluenza virus type 3. A *Lomatium dissectum* root extract completely inhibited the cytopathic effects of rotavirus. In addition to these, extracts prepared from the following plants exhibited antiviral activity against herpesvirus type 1: *Cardamine angulata*, *Conocephalum conicum*, *Lysichiton americanum*, *Polypodium glycyrrhiza* and *Verbascum thapsus*.

Keywords: Antiviral activity; Ethnopharmacology (British Columbia); Traditional medicines (British Columbia); *Amelanchier alnifolia*; *Cardamine angulata*; *Conocephalum conicum*; *Ipomopsis aggregata*; *Lomatium dissectum*; *Lysichiton americanum*; *Oplopanax horridus*; *Polypodium glycyrrhiza*; *Potentilla arguta*; *Rosa nutkana*; *Sambucus racemosa*; *Verbascum thapsus*

1. Introduction

The search for selective antiviral agents, principally focused on anti-human immunodeficiency virus (HIV) agents, has been vigorous in recent years (De Clercq, 1988) but progress in the development of useful new antivirals has been painstakingly slow (Galasso, 1988). Meanwhile, frequencies of viral resistance to the relatively few anti-viral drugs currently used are increasing (De Clercq, 1993) and the problem of viral latency, the greatest obstacle to treatment of some viral infec-

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tions, remains unsolved. The increasingly urgent need to find effective therapeutics justifies not only an accelerated search for new agents but also a broader scope to such research.

Ethnopharmacological screenings provide scientists with an alternative avenue to discovery from the current mainstream approach of attempting to design narrow spectrum drugs for specific molecular targets. The ethnopharmacological approach has equal potential for identifying new antiviral compounds, yet relatively few antiviral screenings of plant ethnomedicines have been conducted to date. 'In view of the significant proportion of plant extracts that have yielded positive results in these screenings, it seems reasonable to conclude that there are probably numerous types of antiviral compounds in these materials. Further characterization of the active ingredients of some of these plants should reveal some useful compounds' (Hudson, 1990). It seems prudent, if not imperative, that researchers continue to investigate these sources before the knowledge or the plants themselves are lost.

In this report, the results of an antiviral screening of 100 methanolic plant extracts against seven viruses, as well as background ethnobotanical and pharmacological activity data for those species which exhibited antiviral activity are presented. This research was conducted as part of an ongoing project investigating the pharmacological activities of medicinal plants used by the British Columbian native peoples (McCutcheon et al., 1993; McCutcheon et al., 1994).

2. Materials and methods

2.1. Plant collection

A sampling of the British Columbian ethnobotanical literature (Turner, 1975, 1978; Turner et al., 1980, 1990) was surveyed to compile a representative list of those plants used medicinally by the native peoples of this area. The list was used in the field as a selection guide for the plant species and type of material to be collected. The collecting was carried out from May–July 1991, in five areas of the province: the Wyndel region in the Kootenay mountains, the Princeton-Penticton region in the interior, the Queen Charlotte Islands, the Fraser River canyon and the Lower Mainland. From the several hundred plant species on the ethnobotanical list, 100 specimens were collected. In order to ensure accurate botanical identifications, only plants which were in flower were collected, introducing a seasonal bias into the selection. A voucher specimen was made for each collection and these vouchers have been filed in the University of British Columbia Herbarium.

2.2. Extract preparation

The plant material was air dried and ground in a Wiley grinder with a 2 mm diameter mesh. Twenty grams of the ground material were extracted with (3 × 100 ml) methanol over 24 h. The crude methanolic extract was filtered through cheesecloth and cotton wool, and then through a Büchner funnel with a No. 4 paper filter. The filtrate was evaporated to dryness on a rotary evaporator and reconstituted with 10 ml of methanol.

2.3. Viruses and cell lines

The effect of the methanolic plant extracts on the replication of seven selected viruses representing a spectrum of viral families was assayed. The viruses selected were: bovine coronavirus (BCV, *Coronaviridae*), bovine herpesvirus type 1 (BHV1, *Herpesviridae*), bovine parainfluenza virus type 3 (BPI3, *Paramyxoviridae*), bovine rotavirus (BRV, *Reoviridae*), bovine respiratory syncytial virus (BRSV, *Paramyxoviridae*), vaccinia virus (*Poxviridae*) and vesicular stomatitis virus (VSV, *Rhabdoviridae*). Viruses were propagated in established cell lines which were maintained in vitro as monolayer cultures using Eagle's minimal essential medium (MEM) supplemented with fetal bovine serum (10% v/v) and gentamicin (10 μg/ml). The cells were incubated at 37°C in a humidified environment containing 5% CO_2. BCV, BHV1 and VSV were grown in Madin-Darby bovine kidney (MDBK) cells; BRV and vaccinia virus in African green monkey kidney (MA104) cells; BRSV in Georgia bovine kidney (GBK) cells; and BPI3 in African green monkey kidney (Vero) cells.

2.4. Antiviral assays

The abilities of dilute plant extracts to inhibit virus-specific cytopathic effects were used as a measure of antiviral activities. Near-confluent 0.3 cm^2 cell monolayers in 96-well plates (Flow Laboratories) were rinsed with serum-free MEM then each was treated with 0.2 ml of a plant extract diluted in serum-free MEM. The extracts were tested at dilutions ranging from 1×10^{-1} through 1×10^{-7}. Antiviral activities were scored using cell cultures treated with extracts diluted sufficiently (usually 1×10^{-4}) to eliminate any microscopically observable toxic effects. Two samples (Q1 and Q2) demonstrated residual toxicity at that level, hence they were scored after application at a dilution of 2.5×10^{-5}.

After 12 h of treatment at 37°C, the medium was removed and the cultures were infected with stock preparations containing approximately 100 plaque-forming units (PFU) of the respective infectious virus in 0.1 ml of MEM. Mock-infected controls received sterile cell-culture medium. After a 1 h absorption period, the inoculum was removed, the cells were washed twice with MEM then overlaid with 0.2 ml of fresh diluted plant extract. Plates were incubated at 37°C for 2–7 days, depending upon the virus-cell combination used. Cytopathic effects were scored after microscopic observation. Each treatment (+/− plant extract, +/− virus) was performed in triplicate and the entire regimen was repeated at least once for each extract tested.

3. Results

One hundred crude methanolic extracts of plants, 96 of which were used medicinally by British Columbian native peoples were screened for antiviral activity against seven viruses. The botanical names of the plants tested are listed alphabetically by genus in Table 1. Twelve plant extracts each demonstrated some antiviral activity against one virus. Scores of the degrees of inhibition of virus-induced cytopathic effects caused by treatment with these extracts are presented in Table 2. Results for vaccinia virus and VSV are not shown as none of the plant extracts were observed to inhibit the cellular cytopathology induced by these viruses at the extract dilutions used.

Table 1
Botanical names of species screened[a]

Achillea millefolium L. var. *occidentalis* DC. (Compositae) P-10 Whole plant
Alnus rubra Bong. (Betulaceae) Q-1 Bark, Q-2 Catkins
Ambrosia chamissonis (Less.) Greene var. *chamissonis* (Compositae) Q-29 Aerial parts
Amelanchier alnifolia Nutt. var. *humptulipensis* (Jones) Hitchc. (Rosaceae) P-6, P-15 Branches
Antennaria microphylla Rydb. (Compositae) P-21 Whole plant
Arctostaphylos uva-ursi (L.) Spreng. (Ericaceae) P-42a Branches, P-42b roots
Argentina egedii (Wormsk.) Rydb. (Rosaceae) Q-20 Aerial parts
Arnica cordifolia Hook. (Compositae) P-31 Aerial parts
Arnica sororia Greene (Compositae) P-7 Aerial parts
Artemisia ludoviciana Nutt. ssp. *ludoviciana* (Compositae) W-5 Aerial parts
Artemisia michauxiana Bess. (Compositae) P-29 Aerial parts
Artemisia tridentata Nutt. ssp. *tridentata* (Compositae) W-19 Branches
Aruncus dioicus (Walt.) Fern. var. *vulgaris* (maxim) Hara (Rosaceae) F-1 Branches
Asarum caudatum Lindl. (Aristolochiaceae) W-12 Whole plant
Balsamorhiza sagittata (Pursh) Nutt. (Compositae) W-18 Aerial parts, P-2 roots
Betula papyrifera Marsh (Betulaceae) P-38 Branches
Capsella bursa-pastoris Medic. (Cruciferae) W-8 Whole plant
Cardamine angulata Hook. (Cruciferae) Q-16 Roots
Ceanothus velutinus Dougl. ex Hook. (Rhamnaceae) P-39 Branches
Chaenactis douglasii (Hook.) H. et A. (Compositae) P-3 Whole plant
Chrysothamnus nauseosus (Pall.) Britt. ssp. *albicaulis* (Nutt.) H. et C. (Compositae) P-25 Branches
Clematis ligusticifolia Nutt. ex T. et G. (Ranunculaceae) P-14 Aerial parts
Conocephalum conicum (L.) Dum. (Conocephalaceae) [Hepaticae] Q-28 Thallus
Cornus canadensis L. (Cornaceae) Q-12 Aerial parts
Cornus sericea L. ssp. *sericea* (Cornaceae) W-6 Branches
Crataegus douglasii Lindl. (Rosaceae) W-14 Branches
Delphinium nuttallianum Pritz. var. *nutallianum* (Ranunculaceae) P-33 Aerial parts
Disporum trachycarpum (Wats.) Benth. et Hook. (Liliaceae) W-11 Whole plant
Empetrum nigrum L. (Empetraceae) Q-17 Branches
Epilobium minutum Lindl. (Onagraceae) P-1 Whole plant
Equisetum arvense L. (Equisetaceae) W-3 Aerial parts
Equisetum hyemale L. (Equisetaceae) P-37 Aerial parts
Erigeron filifolius (Hook.) Nutt. (Compositae) P-9 Aerial parts
Eriogonum heracleoides Nutt. (Polygonaceae) P-11 Aerial parts, P-17 roots
Fauria crista-galli (Menzies ex Hook.) Makino (Menyanthaceae) Q-19 Aerial parts
Fragaria chiloensis (L.) Mill. (Rosaceae) Q-7 Aerial parts

Table 1 (*continued*)

Botanical names of species screened[a]
Fragaria vesca L. var. *bracteata* (Heller) Staudt. (Rosaceae) W-1 Aerial parts
Gaillardia aristata Pursh (Compositae) P-8 Aerial parts
Ganoderma applanatum L. (Polyporaceae) Q-10 Whole plant
Geum macrophyllum Willd. var. *macrophyllum* (Rosaceae) Q-23 Roots
Glehnia littoralis F. Schmidt ssp. *leiocarpa* (Mathias) Hult. (Umbelliferae) Q-13 Roots
Heracleum maximum Bartr. (Umbelliferae) P-32a Aerial parts, P-32b roots
Heuchera cylindrica Dougl. ex Hook. var. *cylindrica* (Saxifraceae) W-4 Roots
Holodiscus discolor (Pursh) Maxim. (Rosaceae) F-3 Branches
Hylocomium splendens (Hedw.) B.S.G. (Hylocomiaceae) [Bryidae] Q-9 Gametophyte
Hypericum perforatum L. (Hypericaceae) P-30 Aerial parts
Ipomopsis aggregata (Pursh) Grant var. *aggregata* (Polemoniaceae) P-13a Aerial parts, P-13b roots
Juniperus communis L. (Cupressaceae) Q-25 Branches
Kalmia microphylla (Hook.) Heller ssp. *occidentalis* (Small) Taylor et MacBryde (Ericaceae) Q-5 Branches
Larix occidentalis Nutt. (Pinaceae) W-15 Branches
Ledum groenlandicum Oeder (Ericaceae) Q-4 Branches
Lobaria oregana (Tuck) Mull. (Lobariaceae) Q-11 Thallus
Lomatium dissectum (Nutt.) Math. et Const. var. *multifidum* (Nutt.) Math. et Const. (Umbelliferae) W-10 Roots
Lonicera ciliosa (Pursh) Poir. ex DC. (Caprifoliaceae) F-2 Branches
Lonicera involucrata Banks ex Spreng. (Caprifoliaceae) F-5 Branches
Lupinus sericeus Pursh ssp. *sericeus* (Leguminosae) P-12 Aerial parts
Lycopodium clavatum L. (Lycopodiaceae) Q-6 Branches
Lysichiton americanum Hulten et St. John (Araceae) Q-26 Roots
Mahonia aquifolium (Pursh) Nutt. (Berberidaceae) W-2 Roots
Maianthemum racemosum (L.) Link (Liliaceae) W-17 Rhizomes
Maianthemum stellatum (L.) Link (Liliaceae) W-13 Rhizomes
Moneses uniflora (L.) A. Gray (Ericaceae) Q-8 Aerial parts
Monotropa uniflora L. (Ericaceae) P-19 Whole plant
Nuphar lutea (L.) Sm. ssp. *polysepala* (Engelm.) E.O. Beal (Nymphaceae) Q-3b Roots, Q-3c rhizomes
Oplopanax horridus Miq. (Araliaceae) Q-14 Inner bark
Opuntia fragilis (Nutt.) Haw. (Cactaceae) F-4 Aerial parts
Osmorhiza purpurea (C. et R.) Suksdorf (Umbelliferae) Q-24 Roots
Penstemon fruticosus (Pursh) Greene (Scrophulariaceae) P-4 Branches
Philadelphus lewisii Pursh (Hydrangeaceae) P-22 Branches
Pinus contorta Dougl. ex Loud. var. *contorta* (Pinaceae) Q-18 Branches
Pinus ponderosa P. et C. Lawson (Pinaceae) W-20 Branches
Plantago major L. (Plantaginaceae) Q-22 Whole Plant
Polypodium glycyrrhiza D.C. Eaton (Polypodiaceae) Q-27 Rhizomes
Polystichum munitum (Kaulf.) Presl (Polypodiaceae) Q-15 Rhizomes
Populus tremuloides Michx. (Salicaceae) P-34 Branches
Potentilla arguta Pursh (Rosaceae) W-7 Roots
Prunus virginiana L. var. *demissa* (Nutt.) Torr. (Rosaceae) W-9 Branches
Prunus virginiana L. var. *melanocarpa* (Nels.) Sarg. (Rosaceae) P-40 Branches
Rhus glabra L. (Anacardiaceae) P-23 Branches
Ribes sanguineum Pursh (Grossulariaceae) P-18 Branches
Rosa nutkana Presl var. *nutkana* (Rosaceae) P-5 Branches
Rubus parviflorus Nutt. (Rosaceae) P-28 Branches
Salix bebbiana Sarg. (Salicaceae) P-36 Branches
Sambucus cerulea Raf. (Caprifoliaceae) P-16 Branches
Sambucus racemosa L. ssp. *pubens* (Michx.) House var. *arborescens* (T. et G.) A. Gray (Caprifoliaceae) Q-21 Branches
Sedum lanceolatum Torr. (Crassulaceae) P-20 Whole plant
Shepherdia canadensis (L.) Nutt. (Elaeagnaceae) W-16 Berries
Spiraea betulifolia Pall. (Rosaceae) P-41 Branches
Symphoricarpos albus (L.) Blake var. *laevigatus* Fern. (Caprifoliaceae) P-26 Branches
Urtica dioica L. ssp. *gracilis* (Ait.) Seland. var. *lyallii* (Wats.) Hitchc. (Urticaceae) P-27 Aerial parts
Verbascum thapsus L. (Scrophulariaceae) P-24 Leaves
Collectors for all species were A.R. McCutcheon and S.M. Ellis.

[a]Key to collection site: F, Fraser River Canyon; P, Princeton-Penticton region; Q, Queen Charlotte Islands; W, Wyndel region.

4. Discussion and conclusions

One of the inherent drawbacks of in vitro antiviral testing is the environmental sensitivity of animal cells in culture. Preparations which exert antiviral effects in vivo may not be detected in in vitro assays because of the extremely low concentrations of extract tolerated by cells in the artificial system. Even with this limitation, 12 of the 100 methanolic plant extracts screened exhibited some antiviral activity. Six of these active extracts completely inhibited virus induced cytopathic effects at the non-cytotoxic concentrations tested. As has been found in previous antiviral screenings (see

Table 2
Antiviral assay results[a]

Viruses assayed against	Corona-virus	Herpesvirus type 1	Parainfluenza virus type 3	Respiratory syncytial virus	Rotavirus
Amelanchier alnifolia (Rosaceae) P-6 Branches	++++				
Cardamine angulata (Cruciferae) Q-16 Roots		+			
Conocephalum conicum (Conocephalaceae) Q-28 Thallus		+			
Ipomopsis aggregata (Polemoniaceae) P-13			++++		
Roots					++++
Lomatium dissectum (Umbelliferae) W-10 Roots					
Lysichiton americanum (Araceae) Q-26 Roots		+			
Oplopanax horridus (Araliaceae) Q-14 Inne bark				+	
Polypodium glycyrrhiza (Polypodiaceae) Q-27 Rhizomes		+			
Potentilla arguta (Rosaceae) W-7 Branches				++++	
Sambucus racemosa (Caprifoliaceae) Q-21 Branches				++++	
Rosa nutkana (Rosaceae) P-5 Branches	++++				
Verbascum thapsus (Scrophulariaceae) P-24 Leaves		+			

[a]Classification of results: +, partial inhibition of virus-induced CPE; ++++, complete inhibition of virus-induced CPE.

Hudson, 1990 for overview), none of the extracts exhibited broad spectrum activity. Each active extract was effective against only one of the seven viruses screened.

Three of the most active extracts in this study were members of the same plant family. The branch extracts made from *Rosa nutkana* and *Amelanchier alnifolia*, both members of the Rosaceae, completely inhibited the cytopathic effects of an enteric coronavirus. A root extract of another member of the Rosaceae, *Potentilla arguta*, completely inhibited respiratory syncytial virus. Coronavirus and respiratory syncytial virus are similar in that they are both single-stranded RNA viruses which infect mucosal surfaces.

A branch tip extract of *Sambucus racemosa* (Caprifoliaceae) also completely inhibited the cytopathic effects of respiratory syncytial virus while an inner bark extract of *Oplopanax horridus* (Araliaceae) exhibited partial inhibition. A root extract of *Ipomopsis aggregata* (Polemoniaceae) completely inhibited cytopathology induced by parainfluenza virus type 3, another single-stranded RNA virus which causes respiratory disease. None of the extracts was effective against the fourth single-stranded RNA virus used in the screening, vesicular stomatitis virus.

Rotavirus is a double-stranded RNA virus that causes gastroenteritis, one of the major infectious diseases in the world today, as judged by mortality statistics (Vesikari, 1988). The only extract which exhibited activity against this serious pathogen was a *Lomatium dissectum* (Umbelliferae) root extract which completely inhibited the cytopathic effects.

Two double-stranded DNA viruses were used in this screening, herpesvirus type 1 and vaccinia virus. Herpesviruses cause respiratory, genital, conjunctival or encephalitic infections which become latent in the trigeminal ganglion. There is also a growing body of evidence that Kaposi's sarcoma is caused by a newly discovered type of herpesvirus (Chang et al., 1994; Cohen, 1995; Chang, 1995). Five of the plant extracts were found to partially inhibit the cytopathic effects of herpesvirus: *Cardamine angulata* (Cruciferae) roots, *Conocephalum conicum* (Conocephalaceae) thallus, *Lysichiton americanum* (Araceae) roots, *Polypodium glycyrrhiza* (Polypodiaceae) rhizomes and *Verbascum thapsus* (Scrophulariaceae) leaves. None of the extracts exhibited activity against vaccinia virus at the non-cytotoxic concentrations tested.

Given the pressing need for new antiviral agents and the inherent limitations of in vitro antiviral testing for such agents, the results of this screening were promising. It is possible that the elucidation of the active constituents in these plants may provide useful leads in the development of antiviral therapeutics. It is interesting to note that 10 of these 12 active plant species were traditionally used to treat what are now known as viral ailments. Eight of the active plants were used to treat the specific diseases caused by the virus that they exhibited activity against. The traditional medicinal uses, reported chemical constituents and pharmacological activities of the 12 plants which exhibited antiviral activity in this study are summarized below.

Amelanchier alnifolia Nutt. var. ***humptulipensis*** (Jones) Hitchc. (Rosaceae) (*A. florida* Lindl. var. *humptulipensis* Jones, *A. pallida* Greene, *A. parviflora* Hort. ex Loud.) Common names: Saskatoon, Serviceberry. Branch extract demonstrated strong activity against bovine coronavirus.

Decoctions of the aerial parts of *A. alnifolia* were traditionally used to treat respiratory ailments such as colds and coughs, as well as diarrhea, influenza and smallpox. Serviceberry decoctions were also used as a general tonic, reportedly good for any type of sickness (Turner, 1980; 1990).

The cyanogenic glycoside, prunasin, is a constituent of *A. alnifolia* (Majak et al., 1978). Majak et al. (1981) reported that the vegetative parts of this plant were potentially hazardous to ruminants. In spite of this toxic constituent, extracts of this plant were found to exhibit little antibacterial activity (McCutcheon et al., 1993), no antifungal activity (McCutcheon et al., 1994) and no in vitro cytotoxicity at a dilution of 1×10^{-4}. Work is in progress to isolate and identify the antiviral compound present in this plant.

Cardamine angulata Hook. (Cruciferae) Common name: Bitter Cress. Root extract showed activity against bovine herpesvirus type 1.

The Haida people used the roots of *C. angulata* mixed with 'water lily medicine' (*Nuphar lutea* ssp. *polysepala*) in a poultice for sores (Turner, personal communication). In eastern North America, the Iroquois and the Cherokee peoples were reported to have also used *Cardamine* sp. to treat colds, sore throats, fever and heart problems (Moerman, 1986).

This plant extract only exhibited very slight antibacterial and antifungal activity in previous screenings, although *N. lutea* ssp. *polysepala*, the plant that it was compounded with, had very strong antimicrobial activity (McCutcheon et al., 1993; 1994). No other reports of pharmacological activity nor reports on the chemical constituents of this plant were found in the literature.

Conocephalum conicum (L.) Dum. (Conocephalaceae) (Hepaticae) Common name: Liverwort. Thallus extract showed activity against bovine herpesvirus type 1.

The Haida people of the Queen Charlotte Islands used this plant as a cold medicine (Turner, personal communication). On Vancouver Island, the Coast Salish used it to treat cankers and sores (Turner and Bell, 1973) while the Dididaht employed it as an eye medicine (Turner in Pojar and MacKinnon, 1994). This plant extract also exhibited some antifungal activity, particularly against *Aspergillus fumigatus* (McCutcheon et al., 1994). The flavonoid, monoterpene, sesquiterpene, lipid and alkane chemistry of this species has been investigated quite extensively with over 100 chemical constituent reports in the literature.

Ipomopsis aggregata (Pursh) Grant var. ***aggregata*** (Polemoniaceae) (*Cantua aggregata* Pursh, *Gilia aggregata* (Pursh) Spreng.) Common names: Scarlet Gilia, Sky-rocket. Root extract demonstrated activity against bovine parainfluenza virus type 3.

A root infusion of *Ipomopsis aggregata* was drunk for high fever by the Okanagan-Colville people. An infusion of the aerial parts of *A. ag-*

gregata was used to 'clean out your system' and as a laxative (Turner, 1980). Moerman (1986) cited reports of the Navaho, Paiute, and Shoshone also using *I. aggregata* for colds, stomach disease, gonorrhea, syphilis, rheumatism, cathartic, emetic, physic and blood tonic.

It was previously reported that methanolic extracts of this plant showed good antibacterial and antifungal activity (McCutcheon et al., 1993; 1994). The compounds responsible for these activities have now been identified and tests are underway to determine if these compounds also have antiviral activity. Six tumor inhibiting compounds (three cucurbitacins, ipomopsin, hydroquinone and schottenol glucoside) have also been isolated from *I. aggregata* (Arisawa et al., 1985).

Lomatium dissectum (Nutt.) Math. et Const. var. ***multifidum*** (Nutt.) Math. et Const. (Umbelliferae) (*Ferula dissoluta* Wats., *F. multifida* A. Gray, *Leptoaenia multifida* Nutt., *L. purpurea* Rydb.) Common names: Chocolate Tips, Cough Root, Fern-leaved Lomatium. Root extract showed strong activity against rotavirus.

As one of the common names of this plant implies, the major medicinal use of this plant was in the treatment of pulmonary complaints such as colds and coughs, pneumonia, tuberculosis, lung hemorrhage and asthma. The root was also used in a poultice for sores, cuts, boils, bruises, sprains and broken bones. The powdered root was sprinkled on burns, boils, wounds and fresh sores to make them heal. The roots were also used in a steam-bath for rheumatism, sprains, pains of any sort and even pneumonia (Turner, 1980; 1990).

Moerman (1986) cited reports that the Blackfeet, Kawaiisu, Paiute, Shoshone and Washoe peoples also used this plant medicinally. Potential antiviral applications included: colds, coughs, sore throat, pneumonia, bronchitis, smallpox and influenza.

L. dissectum was previously reported to have antimicrobial activity (Cardellina and Vanwagenen, 1985; McCutcheon et al., 1993). The active compounds were identified as a pair of unstable, homologous 2-alkenyl-3-hydroxy-penta-2,4-dien-4-olides (Vanwegenen and Cardellina, 1986). It is not yet known whether these compounds are also responsible for the antiviral activity exhibited by this plant.

Lysichiton americanum Hulten et St. John (Aracaceae) (*Symplocarpus kamtschaticus* Bong.) Common name: Skunk Cabbage. Root extract demonstrated activity against herpesvirus type 1.

The Haida used young roots from this plant to treat fever and skin disease (Turner, personal communication). The southern Kwakiutl compounded the roots in a medicine for general weakness or undefined sickness (Turner and Bell, 1973). The Bella Coola and Gitksan peoples used the root in the treatment of stomach troubles, influenza, rheumatism, blood poisoning and boils (Smith, 1928). The Shuswap used a cold infusion of the roots for any sickness (Palmer, 1975). Gunther (1973) reported that the Klallam, Kwakiutl, Makah, Quileute, Quinault, Skokomish and Swinomish peoples in neighbouring Washington state also used *L. americanum* roots for carbuncles, body parts sore with scrofula, for general weakness or undefined sickness, as a tonic, blood purifier and physic.

Oplopanax horridus Miq. (Araliaceae) (*Echinopanax horridus* Decne et Planch., *Fatsia horrida* Benth. et Hook.) Common name: Devil's Club. Inner bark extract showed activity against respiratory syncytial virus.

O. horridus was a very important spiritual and physical medicine among the aboriginal peoples of western North America. The extensive traditional uses of Devil's Club were reviewed by Turner (1982). The inner bark was used fresh, dried or ashed in a wide variety of preparations. For external applications, it was applied directly, as a salve or as a poultice for burns, swellings, sores, boils, swollen glands and sore areas. Poultices were also applied to wounds to prevent blood poisoning and to broken bones, toothaches and abrasions to relieve the pain and swelling. Devil's Club was used in steam-baths for arthritis, rheumatism, body pain, lameness, stomach trouble and as a skin tonic (Turner, 1982).

For internal use, the inner bark was either chewed and the juice swallowed or a decoction or infusion was drunk. One of the primary medicinal uses was in the treatment of respiratory ailments such as colds, coughs, chest pains, blood spitting and tuberculosis. Devils's Club was also used internally to treat a variety of diseases including: influenza, measles, diabetes, cancer, arthritis and rheumatism. It was often taken as a tonic or blood purifier for any general sickness and especially those with fever, weight loss and general debility. In higher doses, it was used as a purgative, emetic and cathartic (Turner, 1982).

An inner bark infusion was also drunk for stomach troubles such as stomach pain, ulcers, gallstones, indigestion and constipation. It was commonly used to relieve internal pains caused by ailments as varied as broken bones to black eyes. Women drank a decoction to help expel the afterbirth, to start menstruation post partum and to treat uterine cancers (Turner, 1982). See also Smith (1928), Steedman (1929), Perry (1952), Gunther (1973), Turner and Bell (1973), Moerman (1986), Gottesfeld and Anderson (1988) and Turner and Hebda (1990).

The methanolic extract of *O. horridus* also exhibited good antibacterial and antifungal activity in previous screenings (McCutcheon et al., 1993; 1994). The essential oil of the related species *Oplopanax elatus* has also been reported to have antifungal activity (Mi et al., 1987). Chemical isolation work is in progress to identify the pharmacologically active constituents of this plant.

Polypodium glycyrrhiza D.C. Eaton (Polypodiaceae) (*P. vulgare* L., *P. falcatum* Kellogg) Common names: Licorice Fern, Licorice Root. Rhizome extract exhibited activity against bovine herpesvirus type 1.

This plant extract also exhibited antibacterial and antifungal activity (McCutcheon et al., 1993; 1994). Girre et al. (1987) reported that *P. vulgare* had antiviral activity against a herpesvirus. They found that the active principles were catechin tannins. Husson et al. (1986) also reported that the ferns *P. aureum* and *P. vulgare* had antiviral properties.

The Haida people made a poultice from the rhizomes to treat colds and coughs (Turner, personal communication). They were compounded in a decoction for stomach pain (Smith, 1928). The rhizomes were chewed and the juice swallowed for sore throats (Turner, 1973). The Thompson people also chewed the rhizomes or made an infusion from them to treat sore throats, colds and sore gums (Turner, 1990). The Oweekeno, Hanaksiala, Haisla and Kitasoo peoples also used the rhizomes for colds, coughs and sore throats (Compton, 1993). The Kwakiutl people used the rhizome juice to stop vomiting blood and a decoction of the rhizome was taken for diarrhea (Turner and Bell, 1973). The Cowlitz took an infusion of the crushed stems for measles (Gunther, 1973). Gunther (1973) also reported that the Green River, Khallam, Makah and Quinalt peoples used the rhizome as a cough medicine.

Potentilla arguta Pursh (Rosaceae) (*P. agrimonoides* Pursh, *P. artica* Hort. ex Lehm., *P. convallaria* Rydb., *P. glutinosa* Pursh) Common names: Glandular, Tall or Valley Cinquefoil. Roots extract showed activity against bovine respiratory syncytial virus. This plant extract also demonstrated good antibacterial and antifungal activity (McCutcheon et al., 1993; 1994). Polyphenols from the related species *P. erecta* were reported to exhibit antimicrobial, anti-inflammatory and capillary resistance effects (Selenina et al., 1973).

The Okanagan-Colville people steeped the roots to make an infusion drunk by women after childbirth (Turner, 1980). The Chippewa used the root to stop the bleeding after bloodletting and to treat convulsions, people who seemed to have too much blood (headache?), cuts and dysentery (Densmore, 1928). Other medicinal uses of *Potentilla* sp. were fever, sore throat, diarrhea, inflammation and as a tonic (Moerman, 1986).

Rosa nutkana Presl var. ***nutkana*** (Rosaceae) (*R. aleutensis* Crep., *R. camtschatica* Erman, *R. durandii* Crep., *R. fraxinifolia* Hook., *R. macrocarpa* Nutt. ex Raf., *R. megacarpa* Nutt. ex T. et G.) Common names: Nutkana's Rose, Wild Rose. Branch extract demonstrated strong activity against bovine coronavirus.

Among the Bella Coola people, a *R. nutkana* decoction was drunk for stomach pain (Smith, 1928). The Thompson people drank a rosehip infusion for sore or itchy throat, cough and especially coughs in babies. For diarrhea, vomiting, or women's illnesses, the branches were compounded with *Prunus virginiana* and *Cornus sericea*. The roots of *Rosa* species were boiled to make a decoction taken for syphilis and by women after childbirth (Turner, 1990). A bark decoction was used as an eyewash for cataracts or to enhance eyesight (Turner in Pojar and MacKinnon, 1994). The Skagit people used a root decoction for sore throats and as an eye wash. Decoctions were also administered to ease labor pains and used as a wash to strengthen babies. The Quileuete and Quinault peoples used the ashes in a poultice for swellings and syphilitic sores (Gunther, 1973). The Okanagan-Colville people chewed the leaves and then applied them directly to bee stings to reduce swelling and pain (Turner, 1980).

This plant extract exhibited some antibacterial activity, particularly against *Escherichia coli* but showed only slight antifungal activity (McCutcheon et al., 1993; 1994). Work is now in progress to isolate and identify the antiviral constituents.

Sambucus racemosa L. ssp. ***pubens*** (Michx.) House var. ***arborescens*** (T. et G.) A. Gray (Caprifoliaceae). (*S. arborescens* (T. et G.) Howell, *S. melanocarpa* Gray, *S. nigra* Thunb., *S. pubens* Michx. var. *aborescens* T. et G., *S. pubescens* Pers.) Common name: Red Elderberry. Branch extract exhibited activity against bovine respiratory syncytial virus.

The most common medicinal use of the root or bark of this shrub was as an emetic or purgative (Moerman, 1986; Turner, 1973, 1980; Turner and Bell, 1973). The Haida, Saanich and Cowichan Coast Salish peoples used the bark in a female medicine (Turner and Hebda, 1990; Turner, personal communication). Among the Gitksan, weakness, general illness and inability to eat were presenting symptoms indicating the use of a *S. racemosa* root bark decoction (Gottesfeld and Anderson, 1988). Gottesfeld and Anderson (1988) reported that patients were treated with this decoction during the deadly 1918 influenza epidemic. The Thompson people compounded the roots to make an infusion drunk for liver disease (Turner, 1990). Perry (1952) reported that the Thompson and Okanagan peoples used this plant for rheumatism, erysipelas and toothache.

Other traditional uses cited in Moerman (1986) included: measles, poultice to reduce swellings, footbath for aching legs and feet, lotion on open cuts or sores, wash on area infected with blood poisoning, applied to breast after childbirth to start milk flow, steam-bath to relax a woman's body after childbirth and as a physic.

This plant extract exhibited very slight antibacterial and antifungal activity in previous screenings (McCutcheon et al., 1993; 1994). Chemical isolation and identification of the antiviral constituents is in progress.

Verbascum thapsus L. (Scrophulariaceae) Common names: Common Mullein, Flannel Plant. Leaf extract demonstrated activity against bovine herpesvirus type 1. This extract showed only slight antibacterial and antifungal activity (McCutcheon et al., 1993; 1994).

Mullein was used extensively as a medicinal by aboriginal peoples throughout North America. Moerman (1986) contains sixty-nine citations for medicinal uses of *V. thapsus*, compiled from the ethnobotanical literature on eighteen different tribes. One of the most common uses cited was in the treatment of pulmonary complaints such as cold, cough, consumption and asthma. Other reported uses which imply possible antiviral activity include mumps, swollen glands, croup and fever.

Among the British Columbian peoples, the Thompson drank a leaf tea for colds and coughs. Leaf juice was rubbed on warts to remove them (Turner, 1990). The Okanagan-Colville people drank a decoction of the leaves for consumption (Turner, 1980).

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