Published in final edited form as:
J Herb Med. 2013 June 1; 3(2): 47–51. doi:10.1016/j.hermed.2013.01.001.

Ethanolic Extracts of California Mugwort (*Artemisia douglasiana* Besser) Are Cytotoxic against Normal and Cancerous Human Cells

Himali Somaweera[a], **Gary C. Lai**[a,b], **Rachel Blackeye**[a,b,c], **Beverly Littlejohn**[b,d], **Justine Kirksey**[b,c], **Richard M. Aguirre**[b,c], **Vince LaPena**[e,f], **Anna Pasqua**[b,g], and **Mary McCarthy Hintz**[a,b,*]

[a]Department of Chemistry, California State University, Sacramento, California, USA

[b]Science Educational Equity Program, California State University, Sacramento, California , USA

[c]Duckwater Shoshone Tribe, Nevada, USA

[d]Department of Biological Sciences, California State University, Sacramento, California, USA

[e]Nor Rel Muk Wintu Tribe, California, USA

[f]Interpretative Specialist and Naturalist, Effie Yeaw Nature Center, Sacramento County Parks Department, Sacramento, California, USA

[g]Susanville Indian Rancheria, California, USA

Abstract

California mugwort (*Artemisia douglasiana* Besser) is used by many tribes throughout California to treat a variety of conditions, including colds, allergies, and pain. California mugwort is also utilized as women's medicine. Its use is on the rise outside of Native communities, often without the guidance of a traditional healer or experienced herbalist. Because it has been shown to have antiproliferative activity against plant and animal cells, we investigated whether California mugwort extracts have an effect on normal human cells as well as estrogen receptor positive (ER^+) and estrogen receptor negative (ER^-) human breast cancer cells. Ethanolic and aqueous extracts of *A. douglasiana* leaves were tested for cytotoxicity against unstimulated normal human peripheral blood mononuclear cells (hPBMC), as well as against an ER^+ human breast cancer cell line (BT-474) and an ER^- human breast cancer cell line (MDA-MB-231). An ethanolic leaf extract killed hPBMC, BT-474, and MDA-MB-231 cells with IC_{50} values of 23.6 ± 0.3, 27 ± 5, and 37 ± 4 μg/ml, respectively. An aqueous extract killed hPBMC with an IC_{50} value of 60 ± 10 μg/ml, but had no effect on the two cancer cell lines at concentrations up to 100 μg/ml. The results of this study indicate that the cytotoxicity of California mugwort extends to normal human cells, as well as cancerous cells. Therefore, until further is known about the safety of this medicine, caution should be taken when consuming extracts of California mugwort, whether as a tincture or as a tea.

*Corresponding author Postal address: Department of Chemistry, California State University, Sacramento, 6000 J Street, Sacramento, CA 95819-6057 Telephone: + 1.916.278.6519 Fax: + 1.916.278.4640 mccarthy@csus.edu.

Keywords

Artemisia douglasiana; California mugwort; cytotoxicity; Native American Traditional Medicine

1. Introduction

California mugwort (*Artemisia douglasiana* Besser; Figure 1), which grows throughout the western regions of the Americas, is sacred to many tribes in California. Traditional medicinal uses of this plant by California tribes are many: as a diuretic, a stimulant, and a tonic (Garcia and Adams, 2005); to treat asthma, flus, colds, bronchitis, and fevers (Chestnut, 1902; Bocek, 1982); for relieving pain associated with headaches, broken bones, arthritis, and rheumatism (Baker, 1981; Chestnut, 1902; Barrett and Gifford, 1933; Bocek, 1982); and more. As women's medicine, mugwort tea is drunk to treat premenstrual syndrome, dysmenorrhea, and amenorrhea; to ease hot flashes and other menopausal symptoms; and to terminate difficult pregnancies (Chestnut, 1902; Zigmond, 1981; Baker, 1981; Strike, 1994; Adams and Garcia, 2006). In most instances, a tea is made from the leaves, but the leaves are sometimes heated or burned and the fumes or smoke inhaled, or they are used as a poultice, depending on the malady (Chestnut, 1902; Barrett and Gifford, 1933; Zigmond, 1981; Bocek, 1982; Garcia and Adams, 2005). California mugwort is also used medicinally in other areas of the western hemisphere. In Argentina, the chewed leaves are used to treat peptic ulcers and external sores (Giordano et al., 1990; Ariza Espinar and Bonzan, 1992). Besides mugwort's medicinal uses, it is also used to keep mold, insects, and other pests at bay in food stores and residences (Vince LaPena, unpublished; Baker, 1981; Bocek, 1982; Duncan, 1991).

This wide range of uses led to a number of investigations into the pharmacological properties of California mugwort: *In vitro* studies demonstrated that California mugwort possesses antifungal activity due to the active principal vulgarone B (Meepagala et al., 2003); antibacterial (Oh et al., 1968; Vega et al., 2009) and antioxidant (Maria et al., 2000) activities due to the active principle dehydroleucodine (DhL); and antiviral activity (Garcia et al., 2003). Vulgarone B also has *in vivo* antimolluscidal activity (Meepagala et al., 2004; Joshi et al., 2005). Oral administration of an infusion of California mugwort or DhL is cytoprotective against ethanol-induced gastric injury in rats and mice (Giordano et al., 1990; Piezzi et al., 1992; Piezzi et al., 1995), attributable to a reduction in reactive oxygen species in the stomach (Repetto et al., 2003) and an increase in gastric mucus synthesis (Guardia et al., 1994; Penissi and Piezzi, 1999). Further investigations have demonstrated that DhL possesses anti-inflammatory activity when administered orally, subcutaneously, or intraperitoneally into rats (Guardia et al., 2003), *in vitro* anti-trypanosomatid activity (Brengio et al., 2000; Barrera et al., 2008), antiproliferative activity against plant cells (Lopez et al., 2002) and animal cells (Cruzado et al., 2005; Preistap et al., 2012) *in vitro*, and cytotoxicity against vascular smooth muscle cells *in vitro* (Polo et al, 2007). DhL also is lethal to amphibian embryos (Moreno et al., 2012), inhibits maturation of amphibian oocytes (Sanchez Toranzo et al., 2007), and inhibits aromatase *in vitro* (Blanco et al., 1997).

California mugwort leaves contain the neurotoxin α-thujone, which constitutes 10% to 68% of the essential oil (Garcia et al., 2003; Setzer et al., 2004). Although α-thujone is not readily extracted by water, it is extracted by ethanol (Tegtmeier and Harnischfeger, 2006). It is, therefore, not surprising that tinctures of *A. douglasiana* are not consumed in Native communities, and that non-Native herbalists are urged to use caution when prescribing tinctures (Christopher Hobbs, personal communication).

Based on its widespread use, its ability to arrest the cell cycle (Lopez et al., 2002; Cruzado et al., 2005; Sanchez Toranzo et al., 2007; Preistap et al., 2012), its differential effects on different types of mammalian cells (Polo et al., 2007; Preistap et al., 2012), and its contraindication during pregnancy (Adams and Garcia, 2006), we believe it is imperative to assess the safety of this medicine toward other normal human cells. Additionally, because of its use as women's medicine, we investigate the possibility that there is a differential effect on cells that express the estrogen receptor. Here, we compare the effects of a tea and a tincture on unstimulated normal human peripheral blood cells (hPBMC) to their effects on an estrogen-receptor negative (ER^-) and an estrogen-receptor positive (ER^+) human breast cancer cell line.

2. Materials and Methods

2.1 Plants

A. douglasiana leaves were collected from a single stand on the eastern bank of the American River, north of the Guy West Bridge in Sacramento, California (latitude: 38 33 49.3236, longitude: −121 25 13.5156), in the spring of 2009. The plant was identified by naturalist and Nor Rel Muck Wintu Tribal Member Vince LaPena and by California State University, Sacramento, (CSUS) botany professor *emeritus* and herbarium curator Michael Baad. A voucher specimen is stored in the CSUS herbarium.

2.2 Extract Preparations

Leaves were air dried for 3-4 days, then finely chopped. An ethanol extract (tincture) was prepared by stirring 200 g of leaves in 5.0 L of 95 % ethanol (HPLC grade, Fisher Scientific) for 2 days at room temperature. An aqueous extract was prepared by stirring 10.0 g of leaves in 250 ml of deionized water for 2 days at room temperature. Extracts were vacuum-filtered through 3 mm filter paper (Whatman), then through a 0.45 μm filter (FisherBrand). The filtrate was evaporated to dryness by rotary evaporation (ethanol extract) or lyophilization (aqueous extract). The residue was dissolved in 95% ethanol or deionized water to a concentration of 10.0 mg/mL. Extract stocks were sterilized by filtration through a 0.20 μm filter (FisherBrand) and stored at −20°C.

2.3 Cell Culture

2.3.1 Normal Human Peripheral Blood Mononuclear Cells—Blood was obtained from an anonymous donor at the CSUS Health Center or at the University of California, Davis, Center for Regenerative Medicine, according to a protocol approved by the CSUS Human Subjects Institutional Review Board. Peripheral blood mononuclear cells (hPBMC) were isolated using Fico/liteH (Atlanta Biologicals), following manufacturer's instructions. Cells were resuspended in growth media, which consisted of Improved Minimal Essential Media (Zinc Option, Richter's Modification, with 2 mg/L L-glutamine, 2 mg/L L-proline, 50.0 μg/ml L-gentamicin sulfate; Invitrogen Corporation) containing 10% heat-inactivated fetal bovine serum (Qualified Australian sourced; Invitrogen Corporation), 50 IU/ml penicillin, 50 μg/ml streptomycin, and 10 mM 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid.

2.3.2 Human Breast Cancer Cells—Human breast cancer cell lines MDA-MB-231 and BT-474 were purchased from American Type Culture Corporation and maintained in growth medium in T-25 tissue culture flasks (Corning CoStar) in a humidified incubator at 37°C and 5% CO_2 atmosphere. Cells were maintained and harvested in their logarithmic growth phase.

2.3.3 Cytotoxicity Assays—Extract dilutions were prepared by adding sterile deionized water or 95% ethanol to each extract or to the positive control (doxorubicin). Test media was prepared by adding 1% (v/v) of the various dilutions to growth media. This concentration of solvent in the culture media affected the growth of the cells (data not shown), so test results were compared to negative controls containing 1% (v/v) sterile water or 1% (v/v) 95% ethanol in culture media, as appropriate.

For the adherent cell lines MDA-MB-231 and BT-474, 100 μL of cell suspension (5.0×10^5 cells/ml) were seeded into each well of a 96-well microtiter plate, plates were incubated for 48 hours, then the growth medium was aspirated and replaced with 100 μL of control or test medium. For the non-adherent hPBMC, 50 μl of cell suspension (5.0×10^6 cells/ml) were seeded into each well, plates were incubated for 48 hours, then 50 μL of control or test medium was added to the growth medium in each well. Plates were incubated for an additional 48 hours, then the relative number of viable cells was assessed using an MTS ([-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt) Assay (CellTiter 96Aqueous One Solution, Promega Corp.). The absorbance of the formazan product was measured at 490 nm with a microtiter plate reader (BioRad).

2.3.4. Determination of IC_{50} values—The average absorbance (ten replicates per concentration) was plotted *vs.* the log of the concentration, and the IC_{50} (the concentration that produced half the maximal response) was calculated using ED50Plus V1.0 software (Vargas, 2011).

3. Results

3.1 Cytotoxicity of A. douglasiana Extracts on Normal and Cancer Cells

To compare the effect of California mugwort extracts on normal and cancer cells, the IC_{50} values were determined for ethanolic and aqueous mugwort extracts against hPBMC, BT-474, and MDA-MB-231. Test media containing 1% (v/v) ethanolic extract completely killed all cells at extract concentrations less than 100 μg/ml, compared to control media (containing 1% (v/v) ethanol). Comparing the IC_{50} values (Table 1), ethanolic extracts were just as active against hPBMC as against the ER^+ cell line BT-474 and more effective against hPBMC than against the ER^- cell line MDA-MB-231.

Although test media containing 1% (v/v) aqueous extract were not as cytotoxic as those containing ethanolic extracts, they were still active against hPBMC, killing 50% of the cells at extract concentrations of 60 ± 10 μg/ml and killing all cells at 100 μg/ml, compared to cells treated with control media (containing 1% (v/v) water). Aqueous extracts did not have a significant effect on the two breast cancer cell lines at the concentrations tested.

4. Discussion

Healers within and outside of Native communities hold that mugwort tea is safe to drink, but that tinctures should be consumed for only a short time, if at all. Safety concerns about tinctures center on their effects on women's reproductive cycles (Adams and Garcia, 2006) and/or the possibility of neurotoxicity due to thujones (Adams and Garcia, 2006; Christopher Hobbs, personal communication). Besides the concern about neurotoxicity, this study brings up another safety concern about *A. douglasiana* tinctures - cytotoxicity against normal human cells. We have shown that an ethanolic extract is significantly more cytotoxic than an aqueous extract against both normal and cancerous human cells *in vitro* (Table 1). This is in agreement with the results of Polo et al. (2007), who showed that DhL is cytotoxic to normal rat vascular smooth muscle cells. Interestingly, Preistap et al. (2012) showed that neither Dhl nor the related compound dehydroparishin (DhP) killed normal human

melanocytes or rat melanoma cells, at least at the concentrations used in that study. It is noteworthy that the PBMC used in the present study were not stimulated to proliferate, whereas the cells in the other two studies were proliferating. This is the first time that *A. douglasiana* or its active principals have been tested on normal, non-proliferating mammalian cells.

The cytotoxic agent(s) in our extract have yet to be isolated, but DhL and DhP are likely candidates. The fact that, in this study, the aqueous *A. douglasiana* extract possesses some cytotoxicicity implies that DhP or another polar compound is responsible for the cytotoxicity of the aqueous extract, since DhL is not readily soluble in water (Brengio et al., 2000). Interestingly, the aqueous extract is cytotoxic against normal hPBMC but not against cancerous human cells (Table 1).

The use of California mugwort as women's medicine led us to also compare the effects of *A. douglasiana* extracts on ER^+ and ER^- cells. There was a slight but statistically significant difference in the effect of the ethanolic extract on these two types of cells, with the ER^+ cell line being slightly more sensitive than the ER^- cell line. However, this difference is so small that it is unlikely to contribute to the medicinal properties. It is more likely that the importance of California mugwort in women's medicine is due to the inhibitory action of DhL on estrogen biosynthesis (Blanco et al., 1997).

Besides its cytotoxicity against mammalian cells, *A. douglasiana* extracts possess a wide range of other pharmacological activities. Some of these activities (bactericidal, molluscidal, fungicidal, and embryocidal) may be due to the same mechanism of action as that responsible for its cytotoxicity toward mammalian cells. However, the gastric cytoprotective activity that is the basis of its use in treating peptic ulcers (Giordiano et al., 1990) is clearly not due to the same mode of action as the cytotoxicity. *In vivo* studies have shown that DhL induces an increase in the rate of synthesis of gastric mucus (Guardia et al., 1994; Penissi and Piezzi, 1999). DhL also reduces the levels of reactive oxygen species, both *in vitro* (Maria et al., 2000) and *in vivo* (Repetto et al., 2003).

A. douglasiana is used for different medicinal purposes in South and North America - to treat peptic ulcers in Argentinean folk medicine, and as women's medicine and pain relief in California. This difference in medicinal uses may be a result of different secondary metabolites in the two populations (Bohlmann et al., 1982; Jakupovic et al., 1986; Rodriguez et al., 1990).

5. Conclusion

California tribes continue to use *A. douglasiana* as a women's medicine and to treat pain, colds and allergies. Medicinal use within Native communities is guided by oral tradition and is usually supervised by a traditional healer. California mugwort is also used outside of Native communities, where it is much less regulated. Our results show that California mugwort may possess general cytotoxicity. Until this is fully investigated, these results should serve as a caution to those using this medicine to do so under the supervision of a traditional healer or an experienced herbalist.

Acknowledgments

HS was supported by the Jo-Ann Bulf Memorial Grant through CSUS. GL was supported by a Graduate Diversity Grant from CSUS. JK and RB were supported by a Bridges to the Baccalaureate Grant (No. R25-GM056645) from the National Institute of General Medical Sciences. RA was supported by a Louis Stokes Alliance for Minority Participation Grant (No. HRD-0802628) from the National Science Foundation.

6. References

Adams JD Jr. Garcia C. Women's health among the Chumash. Evidence-based complementary and alternative medicine. Evid-Based Compl Alt. 2006; 3:125–31.

Ariza Espinar L, Bonzan N. El mático de la región de Cuyo (Argentina). Acta Farmaceutica Bonaerense. 1992; 11:139–145.

Baker, MA. Thesis. Humboldt State University; Arcata, California: 1981. The Ethnobotany of the Yurok, Tolowa, and Karok Indians of Northwest California.

Barrera PA, Jimenez-Ortiz V, Tonn C, Giordano O, Galanti N, Sosa MA. Natural sesquiterpene lactones are active against *Leishmania mexicana*. J Parasitol. 2008; 94(5):1143–9. [PubMed: 18576826]

Barrett SA, Gifford EW. Miwok Material Culture. Bulletin of the Public Museum of the City of Milwaukee. 1933; 2(4):117–376.

Blanco JG, Gill RR, Alvarez CI, Patrito LC, Genti-Raimondi S, Flury A. A novel activity for a group of sesquiterpene lactones : inhibition of aromatase. FEBS Lett. 1997; 409:396–400. [PubMed: 9224697]

Bocek B. Ethnobotany of the Costanoan Indians. Economic Botany. 1982; 38(2):240–55.

Brengio SD, Belmonte SA, Guerreiro E, Giordano OS, Pietrobon EO, Sosa MA. The sesquiterpene lactone dehydroleucodine (DhL) affects the growth of cultured epimastigotes of *Trypanosoma cruzi*. J Parasitology. 2000; 86(2):407–12.

Chestnut VK. Plants Used by the Indians of Mendocino County, California. U.S. National Herbarium Contributions. 1902; 7:295–408.

Cruzado M, Castro C, Fernandez D, Gomez L, Roque M, Giordano OE, Lopez LA. Dehydroleucodine inhibits vascular smooth muscle cell proliferation in G2 phase. Cell Mol Bio (Noisy.-le-grand). 2005; 51:525–30. [PubMed: 16309576]

Duncan, JW. Thesis. San Fransisco State College; San Francisco, California: 1961. Maidu Ethnobotany.

Garcia, C.; Adams, J. Healing with Medicinal Plants of the West – Cultural and Scientific Basis for Their Use. Abedus Press; La Crescenta, California: 2005.

Garcia CC, Talarico L, Almeida N, Colombres S, Duschatzky C, Damonte EB. Virucidal activity of essential oils from aromatic plants of San Luis, Argentina. Phytother Res. 2003; 17:1073–5. [PubMed: 14595590]

Giordano OS, Guerreiro E, Pestchanker MJ, Guzman J, Pastor D, Guardia T. The gastric cytoprotective effect of several sesquiterpene lactones. J Nat Prod. 1990; 53:803–9. [PubMed: 2095374]

Guardia T, Guzmán JA, Pestchanker MJ, Guerreiro E, Pelzer L. Mucus synthesis and sulfhydryl groups in cytoprotection mediated by dehydroleucodine, a sesquiterpene lactone. J Nat Prod. 1994; 57:507–9. [PubMed: 8021651]

Guardia T, Juarez AO, Guerreiro E, Guzmán JA, Pelzer L. Anti-inflammatory activity and effect on gastric acid secretion of dehydroleucodine isolated from *Artemisia douglasiana*. J Ethnopharmacol. 2003; 88:195–8. [PubMed: 12963142]

Joshi RC, Meepagala KM, Sturtz G, Cagauan AG, Mendoza CO, Dayan FE, Duke SO. Molluscicidal activity of vulgarone B from *Artemisia douglasiana* (Besser) against the invasive, alien, mollusc pest, *Pomacea canaliculata* (Lamarck). Int J Pest Manage. 2005; 51:175–80.

Lopez ME, Giordano OS, Lopez LA. Sesquiterpene lactone dehydroleucodine selectively induces transient arrest in G2 in *Allium cepa* root meristematic cells. Protoplasma. 2002; 219:82–8. [PubMed: 11926070]

Maria AOM, Repetto M, Llesuy S, Giordano O, Guzman J, Guerreiro E. Antioxidant activity of *Artemisia douglasiana* Besser extract and dehydroleucodine. Phytotherapy Research. 2000; 14:558–60. [PubMed: 11054852]

Meepagala KM, Kuhajek JM, Sturtz GD, Wedge DE. Vulgarone B, the antifungal constituent in the steam-distilled fraction of *Artemisia douglasiana*. J Chem Ecol. 2003; 29:1771–80. [PubMed: 12956506]

Meepagala KM, Sturtz G, Mischke CC, Wise D, Duke SO. Molluscicidal activity of vulgarone B against ram's horn snail (*Planorbella trivolvis*). Pest Manag Sci. 2004; 60:479–82. [PubMed: 15154515]

Moreno L, Juárez AO, Pelzer LE. Lethal effect of dehydroleucodine (DhL) on amphibian *Bufo arenarum* embryos. Food Chem Toxicol. 2012; 50:672–74. [PubMed: 22240414]

Oh HK, Jones MB, Longhurst WM. Comparison of rumen microbial inhibition resulting from various essential oils isolated from relatively unpalatable plant species. Appl Microbiol. 1968; 16:39–44. [PubMed: 5636470]

Penissi AB, Piezzi RS. Effect of dehydroleucodine on mucus production: a quantitative study. Digest Dis Sci. 1999; 44(4):708–12. [PubMed: 10219826]

Piezzi RS, Guzmán JA, Guardia T, Pestchanker MJ, Guerreiro E, Giordano OS. Dehydroleucodine prevents ethanol-induced necrosis in the rat gastric mucosa. A histological study. Microsc Electron Bio. 1992; 16(1):45–55.

Piezzi R, Guzmán J, Guardia T, Pestchanker M, Guerreiro E, Giordano O. Dehydroleucodine prevents ethanol induced necrosis in the mice duodenal mucosa. A histological study. Biocell. 1995; 19:27–33.

Polo LM, Castro CM, Cruzado MC, Collino CJG, Cuello-Carrión FD, Ciocca DR, Giordano OS, Ferrari M, López LA. 11,13-dihydro-dehydroleucodine, a derivative of dehydroleucodine with an inactivated alkylating function conserves the anti-proliferative activity in G2 but does not cause cytotoxicity. Eur J Pharmacol. 2007; 556:19–26. [PubMed: 17134695]

Preistap HA, Galvis A, Rivero N, Costantino V, Lopez LA, Barbieri MA. Dehydroleucodine and dehydroparishin-B inhibit proliferation and motility of B16 melanoma cells. Phytochem Lett. 2012; 5:581–85.

Repetto M, Maria A, Guzman J, Giordano O, Llesuy S. Protective effect of *Artemisia douglasiana* Besser extracts in gastric mucosal injury. J Pharm Pharmacol. 2003; 55(4):551–557. [PubMed: 12803778]

Sanchez Toranzo G, Giordano OS, Lopez LA, Buehler MI. Effect of dehydroleucodine on meiosis reinitiation in *Bufo arenarum* denuded oocytes. Zygote. 2007; 15(2):183–7. [PubMed: 17462111]

Setzer WN, Vogler B, Schmidt JM, Leahy JG, Rives R. Antimicrobial activity of *Artemisia douglasiana* leaf essential oil. Fitoterapia. 2004; 75:192–200. [PubMed: 15030924]

Strike, SS. Ethnobotany of the California Indians. Vol. Vol 2. Aboriginal Uses of California's Indigenous Plants. Koeltz Scientific Books; Champaign, Illinois: 1994.

Tegtmeier M, Harnischfeger G. Methods for the reduction of thujone content in pharmaceutical preparations of *Artemisia*, *Salvia* and *Thuja*. Eur J Pharm Biopharm. 1994; 40:337–40.

Vargas, MH. [accessed August 21, 2012] www.sciencegateway.org/protocols/cellbio/drug/data/ed50v10.xls

Vega AE, Wendel GH, Maria AOM, Pelzer L. Antimicrobial activity of *Artemisia douglasiana* and dehydroleucodine against *Helicobacter pylori*. J Ethnopharmacol. 2009; 124:653–5. [PubMed: 19422904]

Zigmond, ML. Kawaiisu Ethnobotany. University of Utah Press; Salt Lake City, Utah: 1981.

Figure 1.
Artemisia douglasiana Besser (California mugwort)

Table 1

IC_{50} values (μg/mL) of aqueous and ethanolic extracts of California mugwort

Test Sample	**Cell Line**		
	hPBMC	MDA-MB-231	BT-474
***A. douglasiana* (aqueous)**	60 ± 10	>100	> 100
***A. douglasiana* (ethanolic)**	23.6 ± 0.3	37 ± 4	27 ± 5
Doxorubicin	1.0 ± 0.1	1.2 ± 0.2	1.6 ± 0.1