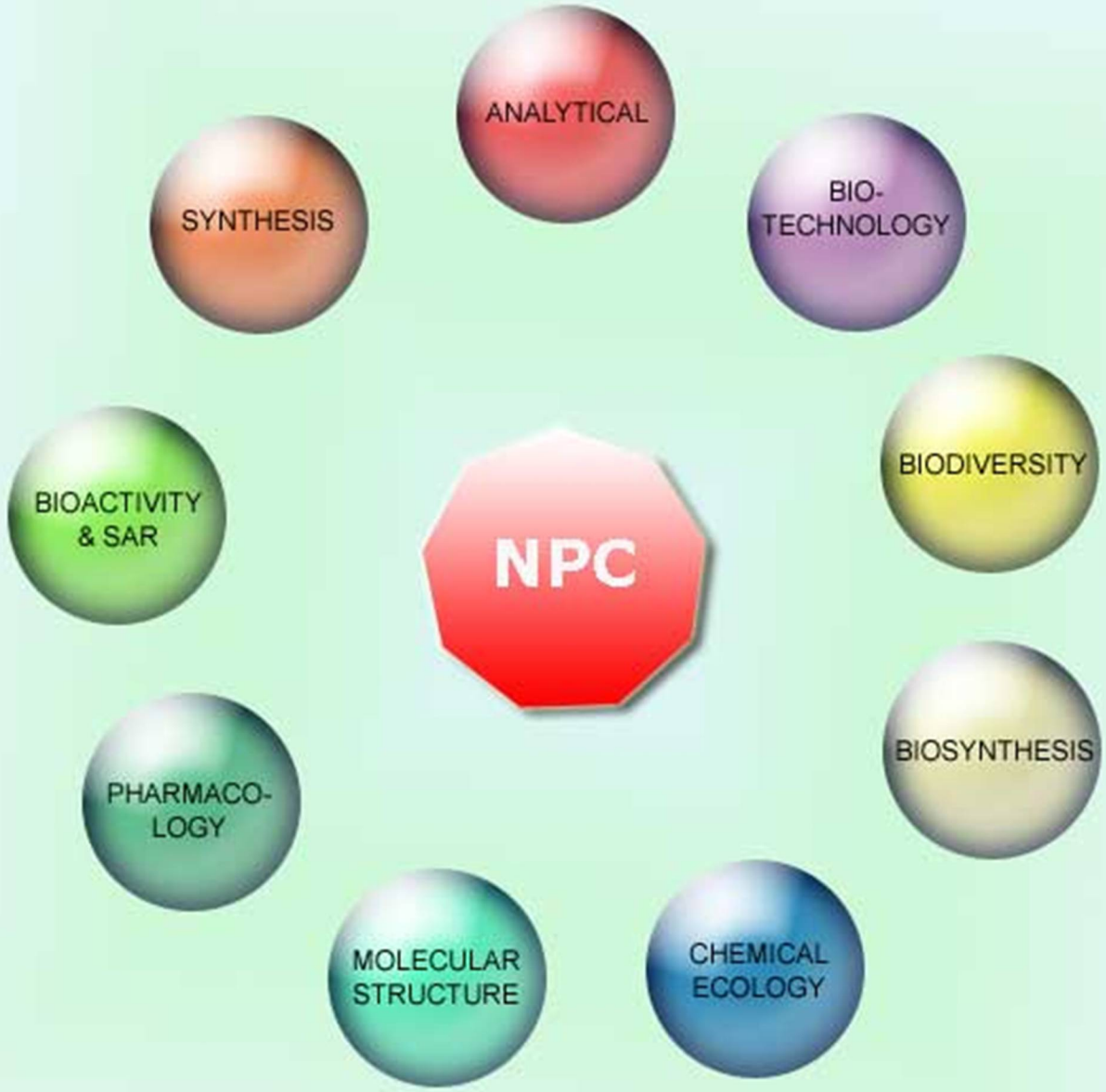
NATURAL PRODUCT COMMUNICATIONS

An International Journal for Communications and Reviews Covering all Aspects of Natural Products Research



Volume 7. Issue 12. Pages 1557-1690. 2012
ISSN 1934-578X (printed); ISSN 1555-9475 (online)
www.naturalproduct.us

NPC Natural Product Communications

INFORMATION FOR AUTHORS

Full details of how to submit a manuscript for publication in Natural Product Communications are given in Information for Authors on our Web site http://www.naturalproduct.us.

To Subscribe: Natural Product Communications is a journal published monthly. 2012 subscription price: US$1,995 (Print, ISSN# 1934-578X); US$1,995 (Web edition, ISSN# 1555-9475); US$2,495 (Print + single site online); US$595 (Personal online). Orders should be addressed to Subscription Department, Natural Product Communications, Natural Product Inc., 7963 Anderson Park Lane, Westerville, Ohio 43081, USA. Subscriptions are renewed on an annual basis. Claims for nonreceipt of issues will be honored if made within three months of publication of the issue. All issues are dispatched by airmail throughout the world, excluding the USA and Canada.

NPC Natural Product Communications

2012
Vol. 7
No. 12
1663 - 1666

Chemical Composition, Antimicrobial and Antioxidant Properties of the Volatile Oil and Methanol Extract of *Xenophyllum poposum*

Ana M. González[a], María I. Tracanna[a], Sara M. Amani[a], Carola Schuff[b], Miguel J. Poch[a], Horacio Bach[c] and César A. N. Catalán[b,*]

[a]*Cátedra de Farmacognosia*, *Facultad de Bioquímica*, *Química y Farmacia*, *Universidad Nacional de Tucumán*, *Ayacucho 491*, *4000, S. M. de Tucumán*, *Argentina*

[b]*INQUINOA-CONICET*, *Instituto de Química Orgánica*, *Facultad de Bioquímica Química y Farmacia*, *Universidad Nacional de Tucumán*, *Ayacucho 491*, *(T4000INI) S. M. de Tucumán*, *Argentina*

[c]*Department of Medicine*, *Division of Infectious Diseases*, *University of British Columbia*, *410-2660 Oak Street*, *Vancouver*, *Canada*

ccatalan@fbqf.unt.edu.ar

Received: September 7th, 2012; Accepted: October 14th, 2012

The essential oil and methanol extract of northwestern Argentina medicinal plant *Xenophyllum poposum*, collected in Catamarca province, were investigated. GC and GC-MS analyses of the essential oil identified 56 compounds accounting for 92.9%. The main components of the oil were δ-cadinene (16.5%), 6-hydroxytremetone (14.7%), *epi*-α-cadinol (12.0%), α-cadinol (8.8%), γ-cadinene (7.5%), 1-*epi*-cubenol (4.2%) and α-muurolene (3.0%). The essential oil exhibited antibacterial activities against five pathogenic strains as well as antifungal activities against two pathogenic fungi. The methanol extract showed antibacterial activity against two strains of *Staphylococcus aureus* and two pathogenic fungal strains. The main components isolated from the methanol extract were the antifungal 4-hydroxy-3-(isopenten-2-yl)-acetophenone, 6-hydroxytremetone, and tremetone. 6-Hydroxytremetone showed activity against all the fungal strains and one of the *S. aureus* strains assayed. Antioxidant and radical-scavenging properties of the methanol extract and essential oil were determined using the 2,2'-diphenyl-1-picrylhydrazyl assay and β-carotene bleaching (BCB) test. The methanol extract and the essential oil showed, respectively, moderate and weak antioxidant activity when compared to butylated hydroxytoluene.

Keywords: *Xenophyllum poposum*, *Werneria poposa*, Asteraceae, Essential oil, New chemotype, Methanol extract, Prenylated *p*-hydroxyacetophenone, 6-Hydroxytremetone, Antimicrobial activity.

Xenophyllum poposum (Philippi) V.A. Funk (syn. *Werneria poposa* Philippi) is a perennial rhizomatous plant belonging to the Asteraceae family and one of 21 species of the Andean genus *Xenophyllum* that has recently been extracted from the genus *Werneria s.l.* [1]. *X. poposum* is a fetid sub-shrub known under the common names "poposa", "pupusa" or "fosfosa" that grows in the high mountains of Northern Argentina, Northern Chile, Bolivia and Southern Peru at 4600-5300 m above sea level [2]. Infusions of its aerial parts are used in folk medicine for the treatment of hypertension, altitude sickness and digestive disorders, such as indigestion, intestinal inflammation, intestinal colics, and diarrhoea [3]. Also, it is used for abdominal pain, rheumatism, and as a food condiment for pneumonia convalescents [3,4]. This herb together with the "chachacoma" (*Senecio nutans* Sch. Bip.) and the "copa-copa" (*Artemisia copa* Phil.) are the most common Asteraceae in the Northwestern Argentina folk pharmacopeia [4]. *Xenophyllum poposum* is frequently confused with *X. incisum* and, in folk medicine, the uses for both species are essentially the same [5].

Previous investigations on *X. poposum* (under the old *Werneria poposa* label) reported the presence of (-)kaur-16-en-19-al from petrol extract, 4-hydroxy-3-(isopenten-2-yl)-acetophenone (**1**) and 4-hydroxy-3-(3′-hydroxyisopentyl)-acetophenone from the methylene chloride extract [6a], and the coumarins aesculetin, fraxetin, isoscopoletin, and dihydroisoscopoletin along with the flavonoid isorhamnetein from the methanol extract (ME) [6b]. Recently, the phytotoxic activities of the benzofuran (2*R*)-6-hydroxytremetone (**2**) isolated from this plant have been reported [7].

Following our investigations on herbs used in Andean traditional medicine [8], we report here the chemical composition, antimicrobial and antioxidant activities of both the essential oil and the methanol extract of *Xenophyllum poposum.*

GC and GC/MS analyses of the essential oil led to the identification of 56 compounds accounting for 92.9% of the oil. Table 1 shows the identified constituents, their percentages, retention indices and method of identification. The essential oil was dominated by sesquiterpenoids (72.2%) with almost equal amounts of sesquiterpene hydrocarbons (36.0%) and oxygenated sesquiterpenes (36.2%). The amount of monoterpenoids was very low representing barely 3.6% of the oil. Interestingly, the essential oil contains significant amounts of 6-hydroxytremetone (**2**) (14.7%) and tremetone (1.7%). Other major components of the volatile oil were: δ-cadinene (16.5%), **2** (14.7%), *epi*-α-cadinol (T-cadinol) (12.0%), α-cadinol (8.8%), γ-cadinene (7.5%), 1-*epi*-cubenol (4.2%) and α-muurolene (3.0%) and an unidentified sesquiterpene alcohol $C_{15}H_{26}O$ (5.8%) (Table 1).

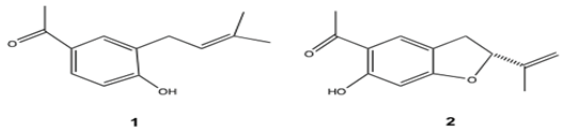
A previous investigation on *X. poposum* collected at an undisclosed location of the Argentine Puna [9] yielded a qualitative very different volatile oil, dominated by monoterpenes (76.4%), with β-pinene (21.8%), α-pinene (5.5%), terpinen-4-ol (5.3%) and α-terpinene (5.2%), as major components. The total amount of sesquiterpenoids was low (6.2%) and neither tremetone analogs nor other benzofuran derivatives were detected [9]. The dissimilar chemical composition exhibited by the essential oil of our collection strongly suggests that we are dealing with a different chemotype, a

Table 1: Chemical composition of *Xenophyllum poposum* essential oil.

Compound	%	RI_{Exp}	RI_{Lit} [13]	Identification
α-Pinene	< 0.1	933	932	a,b,c
β-Pinene	< 0.1	976	974	a,b,c
α-Phellandrene	< 0.1	1004	1002	a,b
α-Terpinene	< 0.1	1016	1014	a,b,c
p-Cymene	< 0.1	1023	1020	a,b,c
Limonene	< 0.1	1027	1024	a,b,c
β-Phellandrene	< 0.1	1028	1025	a,b
γ-Terpinene	< 0.1	1056	1054	a,b
Undecane	< 0.1	1100	1100	a,b,c
endo-Fenchol	0.2	1114	1114	a,b
cis-para-Menth-2-en-1-ol	0.1	1120	1118	a,b
1-Terpineol	0.1	1131	1130	a,b,c
Camphene hydrate	0.1	1145	1145	a,b
Isoborneol	0.1	1157	1155	a,b,c
Borneol	0.6	1167	1165	a,b,c
Terpinen-4-ol	0.5	1174	1174	a,b,c
p-Cymen-8-ol	0.1	1180	1179	a,b
α-Terpineol	1.2	1188	1186	a,b,c
Piperitone	0.2	1252	1249	a,b,c
α-Cubebene	0.1	1349	1345	a,b
α-Copaene	1.1	1377	1374	a,b
β-Caryophyllene	0.1	1420	1417	a,b,c
β-Copaene	0.1	1428	1430	a,b
Aromadendrene	0.1	1441	1439	a,b
α-Humulene	0.3	1454	1452	a,b,c
allo-Aromadendrene	1.0	1459	1458	a,b,c
cis-Muurola-4(14),5-diene	0.1	1467	1465	a,b
γ-Muurolene	0.9	1477	1478	a,b
α-Amorphene	1.1	1482	1483	a,b
trans-Muurola-4(14),5-diene	0.1	1493	1493	a,b
cis-Cadina-1,4-diene	0.5	1496	1495	a,b
α-Muurolene	3.0	1499	1500	a,b
γ-Cadinene	7.5	1511	1513	a,b,c,d
δ-Cadinene	16.5	1523	1522	a,b,c,d
trans-Cadina-1,4-diene	0.8	1533	1533	a,b
α-Cadinene	1.2	1536	1537	a,b,c
α-Calacorene	1.1	1545	1544	a,b
Spathulenol	0.4	1578	1577	a,b,c
Viridiflorol	0.1	1591	1592	a,b
β-Oplopenone	0.4	1606	1607	a,b
1,10-*di-epi*-Cubenol,	1.1	1616	1618	a,b
Dehydrotremetone	0.1	1622	-	b,c
1-*epi*-Cubenol	4.2	1626	1627	a,b
Sesquiterpene alcohol $C_{15}H_{26}O$*	5.8	1634	-	a,b
epi-α-Cadinol (T-cadinol)	12.0	1638	1638	a,b,c,d
epi-α-Muurolol	1.7	1641	1640	a,b,c
α-Muurolol	1.7	1645	1644	a,b,c
α-Cadinol	8.8	1652	1652	a,b,c,d
Cadalene	0.4	1672	1675	a,b
Tremetone	1.7	1727	-	b,c,d
6-Hydroxytremetone	14.7	1854	-	b,c,d
Nonadecane	0.2	1900	1900	a,b
Eicosane	0.1	2000	2000	a,b
Heneicosane	0.2	2100	2100	a,b
Docosane	< 0.1	2200	2200	a,b
Tricosane	0.1	2300	2300	a,b
Monoterpene hydrocarbons	0.4			
Oxygenated monoterpenes	3.2			
Sesquiterpene hydrocarbons	36.0			
Oxygenated sesquiterpene	36.2			
p-hydroxyacetophenone derivatives	16.5			
Others	0.6			
TOTAL IDENTIFIED	**92.9**			

[a] Retention index (RI) on an HP-5 capillary column; [b] Mass spectrum; [c] Co-injection with an authentic sample; [d] ^{1}H NMR; * EIMS *m/z* (rel. abund. %): 222 [M^+] (3); 207 (7); 204 (23); 189 (24); 161 (55); 147 (8); 133 (20); 121 (28); 109 (100); 93 (44); 81 (28); 69 (23); 55 (26); 43 (32); 41 (40).

trait frequently found in aromatic plants. It is worth to note that later collections of *X. poposum* performed by us in December 2005, March 2009 and March 2011 at the same location (Cerro Pabellón, Catamarca province) yielded volatile oils with chemical compositions essentially identical to the March 2003 collection. The stability of the chemical profile during several years of plants gathered at the same place strongly supports that our collection reperesents a true chemotype. The essential oil composition of the samples collected in 2005, 2009 and 2011 is available on request to the corresponding author.



1 **2**

Besides, GC-MS analysis of another sample of *X. poposum* purchased at an herbal store in Tucumán city (see *Plant Material*) showed that it belonged to the same chemotype of our Cerro Pabellón collection as its essential oil was dominated by sesquiterpenoids (72.8%), with δ-cadinene (18.8%), *epi*-α-cadinol (10.0%), γ-cadinene (9.1%), α-cadinol (5.7%), α-muurolene (3.3%) and 1-*epi*-cubenol (1.8%) as main components, which were accompanied by a significant amount of **2** (11.8%).

Most of the relevant components of the essential oil from *X. poposum* are bioactive compounds. Thus, **2** (14.7% in the essential oil) displays potent anticancer activity against HL-60 human leukaemia and HeLa cell lines [10a], plant growth inhibitory [10b], anti HIV-1 [10c] and allergenic [10d] activities. In turn, *epi*-α-cadinol (T-cadinol) (12.0%) induces dendritic cells from human monocytes and drive Th1 polarization [11a]. It has also been shown that T-cadinol inhibits induced intestinal hypersecretion in mice and electrically induced contractions of the isolated guinea pig ileum [11b], and possesses calcium antagonist properties [12a]. T-cadinol (12%) and α-cadinol (8.8%) were also reported to suppress the nitric oxide production induced by lipopolisaccharides and possess significant anti-inflammatory activity [12b]. α-Cadinol also exhibits strong antimite activity against *Dermatophagoides pteronyssinus* and *D. farinae* [12c].

The methanol extract (ME) of *X. poposum* exhibited a moderated scavenging effect in comparison to butylated hydroxytoluene (BHT) (IC_{50} = 160 ppm for ME; 17 ppm for BHT), while the esential oil and compounds **1** and **2** were inactive (Figure 1). With the β-carotene bleaching method, both the ME and the essential oil showed a moderate antioxidant activity (35,9% and 27,1% resp.) in comparison to BHT (Figure 2).

The antibacterial screening of essential oil (Table 2) showed antibacterial activities against *P. aeruginosa* and both *E. coli* and *S. aureus* strains assayed. In addition, it showed antibacterial activity against the clinical strains *B. cepacia* and *H. alvei*, but at concentrations of 1.1 mg/mL. Furthermore, a strong antifungal activity against filamentous fungi was observed with minimal inhibitory concentrations (MICs) varying between 0.025-0.05 mg/mL. The ME was only active against both *S. aureus* strains assayed, but also showed similar antifungal activities as the essential oil against filamentous fungi. Interestingly, **2** exhibited weak antibacterial and antifungal activities, but a significant antifungal activity against *A. fumigatus*.

In conclusion, *X. poposum* contains significant amounts of several powerful bioactive compounds. The known inhibitory effects of T-cadinol on intestinal hypersecretion and ileum contractions [11b] as well as its calcium antagonist properties [12a] are consistent with the use of *X. poposum* in folk medicine to treat digestive disorders such as indigestion, intestinal inflammation, intestinal colics, abdominal pain and hypertension [3,4]. In addition, because of the co-occurrence of so many bioactive compounds, it should be expected that the consumption of this herb has powerful effects that deserve to be investigated in depth. To the best of our knowledge, this is the first study reporting the antioxidant and antimicrobial activities of *X. poposum* and the existence of a well-defined essential oil chemotype.

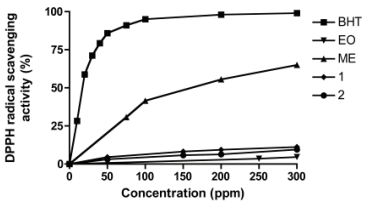


Figure 1: Scavenging effect of essential oil (EO) and methanol extract (ME) of *X. poposum*, compounds **1** and **2** and BHT. Free radical scavenging activity was determined by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical assay. BHT was used as a control. Shown is the mean ± SD of three independent experiments.

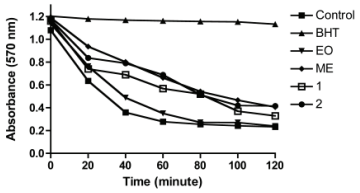


Figure 2: Antioxidant activity of essential oil (EO) and methanol extract (ME) of *X. poposum*, compounds **1** and **2**, and BHT at 1000 ppm in β-carotene-linoleate model system. Shown is the mean ± SD of three independent experiments.

Table 2: Minimal Inhibitory Concentrations (mg/mL) of essential oil and ME from *X. poposum*.

Organism	Essential Oil	ME	**2**
Bacteria			
Acinetobacter baumannii	1.0	R	1.0
*Burkholderia cepacia**	1.17	NA	NA
*Enterobacter gergoviae**	R	NA	NA
Escherichia coli ATCC 35218	0.74	NA	NA
Escherichia coli ATCC 25922	0.95	R	1.0
*Hafnia alvei**	1.11	NA	NA
Pseudomonas aeruginosa	0.71	NA	NA
Salmonella typhimurium	R	R	1.0
Staphylococcus aureus	0.5	0.25	R
Staphylococcus aureus MRSA	0.25	0.25	0.75
Fungi			
Aspergillus fumigatus	0.025	0.25	0.025
Candida albicans	R	R	0.75
Cryptococcus neoformans	R	R	1.0
Trichophyton rubrum	0.05	0.05	0.75

R= resistant. *Clinical isolate. NA= Not assayed.

Experimental

Plant Material: Aerial parts of wild growing *X. poposum* (Philippi) V.A. Funk were collected at Cerro Pabellón at 4600 m above sea level, Andalgalá Department, province of Catamarca, Argentina, in March 2003 during the flowering period. A voucher specimen has been deposited in the herbarium of Miguel Lillo Institute (LIL 29301), Tucumán, Argentina. Later collections carried out in December 2005, March 2009 and March 2011 at the same place yielded essential oils (GC-MS analysis) practically identical to the 2003 collection. Also, a commercial sample of aerial parts of *X. poposum* purchased in February 2006 at a herbal store in Tucumán city and supposedly gathered in the Calchaquí mountains, Tafí del Valle Department, Tucumán province, belonging to the same phytogeographical region of our collections in Catamarca province, was hydrodistilled to yield an essential oil with a chemical composition (see below) resembling the collection at Cerro Pabellón (Table 1).

Methanol extract preparation and essential oil preparation: Air-dried aerial parts of *X. poposum* (100 g) were macerated with MeOH for 4 days. After filtering, the solvent was evaporated at reduced pressure to yield 13.2 g of ME, which was used for the antioxidant and antimicrobial assays. The essential oil was obtained by hydrodistillation of aerial parts (200 g) for 3 h in a Clevenger-type apparatus. A yield of 1.3 mL 0.65% (v/w) was obtained. Qualitative and quantitative analyses of the essential oil were carried out using a Hewlett-Packard 5890 series II GC with flame ionization detector (FID), equipped with a capillary HP-5 column (5% phenyl methyl silicone, 30 m x 0.32 mm; 0.25 μm film thickness) with nitrogen as carrier gas (1.1 mL/min). The oven was programmed for 75ºC (4 min), 75º-180º (2ºC/min) and 220º-280º (10ºC/min). Injection volume was 0.1 μL, split mode. Injector and detector temperatures were maintained at 250ºC and 270ºC, respectively. The relative amounts of individual components are based on the peak areas obtained with an integrator HP 3395 without FID response factor correction. Retention indices (RI) were obtained by co-injection of a series of standard *n*-hydrocarbons C_8-C_{18} and the oil sample using the oven temperature program suggested by Adams [13] (60ºC to 246ºC at 3 ºC/min). The GC-MS analysis was carried out with a 5973 Hewlett Packard selective mass detector (quadrupole), source 70 eV, coupled to a HP 6890 GC fitted with a HP-5MS column (5% phenylmethyl siloxane, 30 m x 0.25 mm; film thickness 0.25 μm) with helium as carrier gas (1.0 mL/min; constant flow). Injection port was maintained at 250ºC, GC-MS interphase at 275ºC, ion source 230ºC, and MS Quad at 150ºC. The oven was programmed as above. The injection volume was 0.1 μL (split 1:80). The identification of the individual components was based on: (a) Computer matching with commercial mass spectra libraries (NBS75K, NIST, WILEY) and comparison with mass spectra available in our files, (b) Comparison of GC retention indexes (RIs) on an HP-5 column [13]. RIs were obtained by co-injection of a series of *n*-hydrocarbons C_8-C_{18} with the oil sample. For RI measurements, an oven temperature program of 60°C to 246°C at 3°C/min was used [13]; (c) Co-injection with authentic samples (whenever available), (d) Tremetone and **2** were also isolated from the ME by column chromatography on Sigel 230-400 Mesh using hexane-EtOAc mixtures of increasing polarity as eluting solvent and characterized by NMR spectroscopy.

Isolation of 4-hydroxy-3-(isopenten-2-yl)-acetophenone (1), tremetone and 6-hydroxytremetone (2): A portion of ME (2.1 g) was subjected to column chromatography over Si gel (105 g; Merck 70-230 mesh) using *n*-hexane with increasing amounts of EtOAc (0-40%) to yield 67 fractions, which were monitored and reunited on the basis of their TLC profiles and analyzed by GC-MS. Frs. 17-21 were reunited (96 mg) and re-chromatographed over Si gel (Merck 230-400 mesh) using *n*-hexane-EtOAc mixtures of increasing polarity to give 77 mg of **2**. Frs. 28-30 (14 mg) after preparative TLC (hexane-EtOAc 4:1; two developments) gave 8 mg of tremetone. Frs. 39-52 (915 mg) gave a solid residue, which on re-crystallization from *n*-heptane-ethyl acetate afforded 672 mg of crystalline 4-hydroxy-3-(isopenten-2-yl)-acetophenone (**1**), mp 96ºC. The structure of compounds **1** and **2** was confirmed by NMR spectroscopy. Compound **1** possesses significant antifungal properties [14] and was by far the main component in the ME of *X. poposum*.

Antioxidant activity: The antioxidant activities of the essential oil and ME of *X. poposum* as well as compounds **1** and **2**, were measured in terms of hydrogen donating or radical scavenging capability using the stable radical DPPH as reagent. The method described by Wei and T. Shibamoto [15] with slight modifications was used. The assay was carried out in triplicate. DPPH inhibition (I%) by the samples was calculated according to the formula: I%= (A_{blank}-A_{sample}/A_{blank}) x 100, where A_{blank} is the absorbance of the control reaction (containing all reagents except the test compound), and A_{sample} is the absorbance of the blank plus test compound. Extract concentration providing 50% inhibition (IC_{50}) was calculated from the graph by plotting inhibition percentage against extract concentration. The antioxidant activity was determined

according to the β-carotene bleaching method [16]. Absorbance was measured at 20 min intervals until the color of β-carotene disappeared in the control reaction (t=120 min). Relative antioxidant activities (RAA%) of the extract and oil were calculated from the equation: RAA% = (A_{Sample}/A_{BHT}) x 100, where A_{BHT} is the absorbance of the positive control BHT, and A_{Sample} is the absorbance of the extract and oil. Experiments were performed in triplicate. Antioxidant capacities of the samples were compared with those of BHT and the control.

Antimicrobial activity: Antibacterial assays were performed using the agar diffusion method against *Acinetobacter baumannii* (ATCC BAA-747), *Escherichia coli* (ATCC 35218 and 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Salmonella typhimurium* (ATCC 13311), *Staphylococcus aureus* (ATCC 25923) and Methicillin-Resistant *Staphylococcus aureus* (MRSA) (ATCC 700698). Multi-resistant clinical isolates of *Burkholderia cepacia, Enterobacter gergoviae,* and *Hafnia alvei* provided by Dr. Cristina Estrella, Hospital Centro de Salud, San Miguel de Tucumán, Argentina, were also assayed. Antifungal activities were performed using the yeast-like *Candida albicans* (provided by Vancouver General Hospital, BC, Canada) and *Cryptococcus neoformans* var. *grubii* (kindly provided by Dr. Karen Bartlet, University of British Columbia, BC, Canada), while *Aspergillus fumigatus* (ATCC 1022) and *Trichophyton rubrum* (ATCC 18758) represented filamentous fungi. Bacteria were grown in Brain Heart Infusion broth fungi. (Laboratories Britania, Argentina) at 37ºC for 18 h, and resuspended in sterile physiological saline with reference to the value 0.5 of the McFarland scale (1.5 x 10^8 colony forming unit /mL). Briefly, plates were prepared with a base layer of Müeller–Hinton agar (10 mL) and wells (6 mm of diameter) were made on the surface of the media. Different concentrations (50 µL) of essential oil and ME were placed in the wells. 25 µL of gentamicin and amphotericin B (0.05 mg/mL) were used as positive control for bacteria and fungi, respectively. Fungal strains were grown in Sabouraud broth (B&D), and the antifungal activity against filamentous fungi was assessed from spores obtained as reported Spores were harvested by rubbing the top of sporulated colonies in 2 mL Sabouraud broth containing 10% glycerol. Spores were aliquoted and kept at -20ºC. For yeast-like fungi, the same protocol used for bacterial strains was used, but using Sabouraud broth. The microorganisms were incubated at 37°C aerobically and after 24 h of incubation, the zones of inhibition were measured. Bacterial growth inhibition was determined as the diameter of the inhibition zones around the well. The growth inhibition diameter was an average of four measurements, taken in 90 degrees apart. MIC values were determined by conventional agar plate dilution method [17]. All tests were performed in triplicate.

Statistic Analysis: A *t*-student test was used for statistical analysis. A P value <0.05 was considered significant.

Acknowledgements - This work was financially supported by Consejo de Investigaciones de la Universidad Nacional de Tucumán (CIUNT) and Consejo Nacional de Investigaciones Científicas y Técnicas de la República Argentina (CONICET). The authors warmly thank Dr. Viviana Vildoza for providing the standard strains of microorganisms.

References

[1] Funk VA. (**1997**) *Xenophyllum*, a new Andean genus extracted from *Werneria* s.l. (Compositae: Senecioneae). *Novon*, *7*, 235-241.
[2] Zuloaga FO, Morrone O. (**1999**) Catálogo de las plantas vasculares de la República Argentina. Missouri Botanical Garden Press, Missouri, USA.
[3] Alonso J, Desmarchelier C. (**2006**) Plantas Medicinales Autóctonas de la Argentina. Ediciones Fitociencia, Buenos Aires, Argentina.
[4] Giberti GC. (**1983**) Herbal folk medicine in northwestern Argentina: Compositae. *Journal of Ethnopharmacology*, *7*, 321-341.
[5] de Marchese MJA, de Heluani CS, Catalán CAN, Griffin CA, Vaughn Jr. JB, Herz W. (**2007**) Incisol, an alcohol with a novel sesquiterpene skeleton from *Xenophyllum incisum*. *Biochemical Systematics and Ecology*, ***35***, 169-175.
[6] (a) Ponce MA, Gros GE. (**1991**) Prenylated aromatic ketones from *Werneria poposa*. *The Journal of the Argentine Chemical Society*, ***79***, 197-200; (b) Ponce MA, Gros GE. (**1995**) A flavonoid and coumarins from *Werneria poposa. Ibid.* ***83***, 93-95.
[7] Romano E, Raschi AB, Gonzalez AM, Jaime G, Fortuna MA, Hernandez LR, Bach H, Benavente AM. (**2011**) Phytotoxic activities of (2*R*)-6-hydroxytremetone. *Plant Physiology and Biochemistry*, ***49***, 671-675.
[8] Lizarraga E, Castro F, Fernández F, de Lampasona MP, Catalán CAN. (**2012**) Antioxidant, hemolytic and cytotoxic activities of *Senecio* species used in traditional medicine of northwestern Argentina. *Natural Product Communications*, ***7***, 607-608.
[9] Abella L, Cortella AR, Velasco-Negueruela A, Perez-Alonso MJ. (**2000**) Ethnobotany, volatile oils and secretion tissues of *Werneria poposa* from Argentina. *Pharmaceutical Biology*, ***38***, 197-203.
[10] (a) Liu Q, Shen L, Wang T, Chen J, Qi W, Gao K. (**2010**) Novel modified furanoeremophilane-type sesquiterpenes and benzofuran derivatives from *Ligularia veitchiana*. *Food Chemistry*, ***122***, 55-59; (b) Cespedes CL, Uchoa A, Salazar JR, Perich F, Pardo F. (**2002**) Plant growth inhibitory activity of *p*-hydroxyacetophenones and tremetones from Chilean endemic *Baccharis* species and some analogous: A comparative study. *Journal of Agricultural and Food Chemistry,* ***50***, 2283–2292; (c) Piacente S, Aquino R, de Tommasi N, Pizza C, de Ugaz OL, Orellana HC, Mahamood N. (**1994**) Constituents of *Werneria ciliolata* and their in *vitro* anti-HIV activity. *Phytochemistry*, ***36***, 991–996; (d) Hausen BM, Helmke B. (**1995**) Butenylbithiophene, α-terthienyl and hydroxytremetone as contact allergens in cultivars of marigold (Tagetes sp.). *Contact Dermatitis*, ***33***, 33–37.
[11] (a) Takei M, Umeyama A, Arihara S. (**2006**) T-cadinol and calamenene induce dendritic cells from human monocytes and drive Th1 polarization. *European Journal of Pharmacology*, ***537***, 190-199; (b) Claeson P, Andersson R, Samuelsson G. (**1991**) T-cadinol: a pharmacologically active constituent of scented myrrh: introductory pharmacological characterization and high field ^{1}H- and ^{13}C-NMR data. *Planta Medica*, ***57***, 352-356.
[12] (a) Claeson P, Zygmunt P, Hogestatt ED. (**1991**) Calcium antagonistic properties of the sesquiterpene T-cadinol: a comparison with nimodipine in the isolated rat aorta. *Pharmacology and Toxicology*, ***69***, 173-177; (b) Tung YT, Huang CC, Ho ST, Kuo YH, Lin CC, Lin CT, Wu JH. (**2011**) Bioactive phytochemicals of leaf essential oils of *Cinnamomum osmophloeum* prevent lipopolysaccharide/D-galactosamine (LPS/D-GalN)-induced acute hepatitis in mice. *Journal of Agriculture and Food Chemistry*, ***59***, 8117-8123; (c) Chang ST, Chen PF, Wang SY, Wu HH. (**2001**) Antimite activity of essential oils and their constituents from *Taiwania cryptomerioides*. *Journal of Medical Entomology*, ***38***, 455-457.
[13] Adams R. (**2007**) Identification of essential oil components by Gas Chromatography/ Quadrupole Mass Spectroscopy, 4th Edition. Allured Publishing Corporation, Carol Stream, Illinois, USA.
[14] Tomás-Barberán F, Iniesta-Sanmartin E, Tomás-Lorente F, Rumbero A. (**1990**) Antimicrobial phenolic compounds from three Spanish *Helichrysum* species. *Phytochemistry*, ***29***, 1093-1095.
[15] Wei A, Shibamoto T. (**2007**) Antioxidant activities and volatile constituents of various essential oils. *Journal of Agriculture and Food Chemistry*, ***55***, 1737-1742.
[16] Jayaprakasha GK, Singh RP, Sakariah KK. (**2001**) Antioxidant activity of grape seed (*Vitis vinifera*) extracts on peroxidation models *in vitro*. *Food Chemistry*, ***73***, 285-290.
[17] Basualdo J, Coto C, De Torres R. (**1996**) Microbiología Biomédica. Buenos Aires, Argentina: Atlante.

Review/Account

Natural Product Communications
2012
Volume 7, Number 12

Contents

Continued inside backcover