

1 **Nutritional composition, antioxidant activity and isolation of**
2 **scopoletin from *Senecio nutans*: Support of new and ancestral uses**

3 Claudio Parra,^{a,*} Emilio Soto,^a Gloria León,^b Cristian O. Salas,^c Michael Heinrich,^d

4 Carlos Echiburú-Chau,^{a,e}

5 ^a*Laboratorio de Química Médica y Productos Naturales, Centro de Investigaciones del*
6 *Hombre en el Desierto (CIHDE), Arica, Chile;* ^b*Departamento de Química, Facultad de*
7 *Ciencias, Universidad de Tarapacá, Arica, Chile;* ^c*Departamento de Química*
8 *Orgánica, Facultad de Química, Pontificia Universidad Católica de Chile, Santiago,*
9 *Chile;* ^d*Research Cluster 'Biodiversity and Medicines' / Centre for Pharmacognosy and*
10 *Phytotherapy', UCL School of Pharmacy, London, UK;* ^e*Facultad de Ciencias de la*
11 *Salud, Universidad de Tarapacá, Arica, Chile*

12
13 *Corresponding Author; e-mail: cparra@cihde.cl

14

15 **Nutritional composition, antioxidant activity and isolation of scopoletin**
16 **from *Senecio nutans*: Support new and ancestral uses**

17 Continuing with our study about the characterization of *Senecio nutans* Sch. Bip.,
18 we have isolated and identified a simple coumarin, scopoletin, that could be
19 relevant for the biological properties of the species related with the ancestral
20 medical uses. This is the first report of scopoletin from *S. nutans*. In addition, was
21 analyzed for its antioxidant activity using the ABTS and FRAP method as well
22 providing the first nutritional analyses of this plant from northern Chile
23 highlands.

24 Keywords: *Senecio nutans*, scopoletin, nutritional composition, antioxidant
25 activity, ethnopharmacology.

26 **1. Introduction**

27 New plant-based health foods, nutraceuticals and botanicals have been developed from
28 a wide range of species (Bernal et al. 2011, Heinrich and Prieto 2008), but the potential
29 of Chilean plants remains underexplored. In the highlands of northern Chile, inhabitants
30 have a variety of vegetal species with ancestral uses due its beneficial characteristics
31 (Castro and Villagrán, 2004). One of these species is *Senecio nutans* Sch. Bip. (syn.: *S.*
32 *graveolens* Wedd), locally known as *chachacoma*, *chachacoma del campo*,
33 *chachacoma del cerro*, *tola*, *tola hembra*, which grows 3000 meters above sea level
34 (m.a.s.l.) and is widely used by the local Andean communities for mountain sickness
35 characterized by symptoms such as headache, dizziness, vomiting and fatigue (Castro
36 and Villagrán 2004, Martínez *et al.* 2006). In continuation with our phytochemical
37 investigation of *Senecio nutans*, here we report, the nutritional composition, antioxidant
38 activity and the isolation of a compound corresponding to a coumarin derivative found
39 in other *Senecio* specie (Dupre *et al.* 1990), but never in *S. nutans*.

40 **2. Results and discussion**

41 The powdered plant was analyzed for proximate composition by AOAC methods
42 (AOAC 2005). The parameters determined were moisture (8.70%), total ash (7.19%),
43 total lipids (14.31%), crude protein (8.18%), and crude fiber (13.23%). These values are
44 slight compared with other medicinal plants studied, such variation might have resulted
45 from extreme environment growing conditions of *S. nutans* (Alonso-Amelot 2008).
46 Lipid concentration in *S. nutans* is significantly higher in comparison to other medicinal
47 plants, presenting contents between 1% and 4%. Despite the high fat content in this
48 plant, which is a potential nutritional risk, the antimicrobial activity of the essential oil
49 showed effect against *Micrococcus luteus*, and *Staphylococcus aureus*, also antifungal
50 effect on *Candida albicans* (Pérez *et al.* 1999). The total carbohydrate (57.09%) was
51 calculated by difference with the other parameters. Carbohydrates represent the major
52 component measured in *chachacoma*, giving a significant nutritional value to this herb.
53 Accumulated carbohydrate reserves function as a source of monosaccharides that are
54 used during growth and development of the plant, especially for primary and secondary
55 metabolism of high levels of non-structural carbohydrates (free sugars, starch and
56 fructan) that may be associated with bioactive secondary metabolites, such as
57 flavonoids and phenols (Ibrahim *et al.* 2010).

58 The content of macro and micronutrients showed that the main elements are: potassium
59 (2130 ± 0.01 mg/100g), calcium (1390 ± 0.02 mg/100g), magnesium (290 ± 0.02
60 mg/100g), phosphorus (230 ± 0.11 mg/100g), sodium (190 ± 0.01 mg/100g), iron
61 (10.41 ± 0.29 mg/100g), manganese (8.48 ± 0.24 mg/100g), copper (1.18 ± 0.03
62 mg/100g), and zinc (0.67 ± 0.03 mg/100g). In addition, the iron content found in
63 *chachacoma* was higher in comparison with other *Senecio* species investigated (Ajiboye
64 *et al.* 2013). This is an important nutritional fact since studies indicated that iron is
65 involved in pivotal processes such as erythropoiesis and intracellular oxygen transport

66 reactions. In fact, its deficiency leads to behavioral changes and biochemical changes in
67 the brain (de Oliveira *et al.* 2001). In this study, we assessed the polyphenolic profile of
68 aerial parts of *S. nutans* evaluating its antioxidant capacity and the total phenolic and
69 flavonoid content. The aerial parts were extracted with ethanol. Antioxidant capacity
70 was measured and correlated with the total phenolic and flavonoid contents. The total
71 phenolic and flavonoid contents, the extraction yield and antioxidant capacity measured
72 by FRAP and ABTS are given in Table S1. The flavonoid content of *chachacoma*
73 extract forms about 72% of its total phenolic content (Table S1). This plant had higher
74 total polyphenols content (20.58 ± 0.59 mg GAE/g DW) compared to other Andean
75 plants (Chirinos *et al.* 2013). Recent studies indicate that phenolic compounds in
76 medicinal plants possess significant antioxidant efficacy and powerful scavenging
77 activity against free radicals (Jaberian *et al.* 2013). In this case the total antioxidant
78 activity was performed using electron transfer methods, such as ABTS and FRAP
79 assays. The *chachacoma* extract showed a FRAP value (27.65 ± 0.06 $\mu\text{mol TE/g DW}$),
80 slightly less when compared to those reported for other medicinal plants (Simirgiotis,
81 Quispe, Bórquez, *et al.* 2016, Simirgiotis, Quispe, Mocan, *et al.* 2016), while *S. nutans*
82 ABTS values for aerial parts extract (13.01 ± 0.08 $\mu\text{mol TE/g DW}$) were higher than
83 medicinal plants like *Amaranthus caudatus* (Kiwicha), *Chenopodium quinoa* (Quínu),
84 among others (Chirinos, Pedreschi, Rogez, Larondelle and Campos 2013). Finally, from
85 the ethanolic extract, using column chromatography, we isolated and identified 7-
86 hydroxy-6-methoxy-2*H*-chromen-2-one, also known as scopoletin, according to the
87 method described by Islam *et al.* (Islam *et al.* 2013). This compound is also known as a
88 constituent of many different medicinal plants (Elgamal *et al.* 1993) and has been
89 intensely investigated as a reversible and selective MAO inhibitor (Basu *et al.* 2016)
90 and an inhibitor of acetylcholinesterase (AChE), butyrylcholinesterase (BChE), and β -

91 site amyloid precursor protein cleaving enzyme 1 (BACE1), relevant for anti-Alzheimer
92 effects (Ali *et al.* 2016). The NMR assignments are in agreement with the ones reported
93 in the literature (San Martín *et al.* 1980). It is interesting the existence of this coumarin
94 in *S. nutans* because it supports and presents a rational explanation for the use of this
95 ancestral plant and its traditional use for the cure of the mountain sickness for its
96 vasodilator effect. (Elgamal, Shalaby, Duddeck and Hiegemann 1993, Ruphin *et al.*
97 2016).

98 In conclusion, this work presents the first report of the isolation of scopoletin from
99 *Senecio nutans* related with ancestral medicinal uses in northern Chile, and the
100 antioxidant activity of the extract can be consider for new uses of this native plant.

101 **Supplementary material**

102 Experimental details and table relating to this study are available online.

103 **Acknowledgements**

104 We are thankful to Gloria Rojas for identification and registration of *S. nutans*
105 specimens in the Chilean National History Natural Museum (MNHN). This study was
106 supported by REDES 140002 (CONICYT).

107 **Reference**

108 Ajiboye B, Ibukun E, Edobor G, Ojo A, Onikanni S. 2013. Chemical composition of
109 *Senecio biafrae* leaf. Scientific journal of biological sciences.2:152-159.

110 Ali MY, Jannat S, Jung HA, Choi RJ, Roy A, Choi JS. 2016. Anti-Alzheimer's disease
111 potential of coumarins from *Angelica decursiva* and *Artemisia capillaris* and structure-
112 activity analysis. Asian Pac J Trop Med. Feb;9:103-111.

113 Alonso-Amelot M. 2008. High altitude plants, chemistry of acclimation and adaptation.
114 Stud Nat Prod Chem.34:883-982.

115 AOAC. 2005. Official methods of analysis ,18th ed. Gaithersburg, MD: AOAC
116 International.

- 117 Basu M, Mayana K, Xavier S, Balachandran S, Mishra N. 2016. Effect of scopoletin on
118 monoamine oxidases and brain amines. *Neurochemistry international*.93:113-117.
- 119 Bernal J, Mendiola J, Ibáñez E, Cifuentes A. 2011. Advanced analysis of nutraceuticals.
120 *Journal of pharmaceutical and biomedical analysis*.55:758-774.
- 121 Castro V, Villagrán C. 2004. *Ciencia Indígena de los Andes del Norte de Chile*. *Ciencia*
122 *Indígena de los Andes del Norte de Chile*.
- 123 Chirinos R, Pedreschi R, Rogez H, Larondelle Y, Campos D. 2013. Phenolic compound
124 contents and antioxidant activity in plants with nutritional and/or medicinal properties
125 from the Peruvian Andean region. *Industrial Crops and Products*.47:145-152.
- 126 de Oliveira ACC, Perez AC, Merino G, Prieto JG, Alvarez AI. 2001. Protective effects
127 of *Panax ginseng* on muscle injury and inflammation after eccentric exercise.
128 *Comparative Biochemistry and Physiology Part C: Toxicology &*
129 *Pharmacology*.130:369-377.
- 130 Dupre S, Bohlmann F, Knox E. 1990. Prenylated p-hydroxyacetophenone derivatives
131 from the giant *Senecio johnstonii*. *Biochemical systematics and ecology*.18:149-150.
- 132 Elgamal MHA, Shalaby NM, Duddeck H, Hiegemann M. 1993. Coumarins and
133 coumarin glucosides from the fruits of *Ammi majus*. *Phytochemistry*.34:819-823.
- 134 Heinrich M, Prieto JM. 2008. Diet and healthy ageing 2100: will we globalise local
135 knowledge systems? *Ageing research reviews*.7:249-274.
- 136 Ibrahim MH, Jaafar HZ, Rahmat A, Rahman ZA. 2010. The relationship between
137 phenolics and flavonoids production with total non structural carbohydrate and
138 photosynthetic rate in *Labisia pumila* Benth. under high CO₂ and nitrogen fertilization.
139 *Molecules*.16:162-174.
- 140 Islam MN, Jung HA, Sohn HS, Kim HM, Choi JS. 2013. Potent α -glucosidase and
141 protein tyrosine phosphatase 1B inhibitors from *Artemisia capillaris*. *Archives of*
142 *pharmaceutical research*.36:542-552.

- 143 Jaberian H, Piri K, Nazari J. 2013. Phytochemical composition and in vitro
144 antimicrobial and antioxidant activities of some medicinal plants. Food
145 chemistry.136:237-244.
- 146 Martínez JL, Calvo CA, Laurido C. 2006. Medicinal plants used in Chile for the
147 treatment of hypertension and mountain sickness. African Journal of Traditional,
148 Complementary and Alternative Medicines.3.
- 149 Pérez C, Agnese AM, Cabrera JL. 1999. The essential oil of *Senecio graveolens*
150 (Compositae): chemical composition and antimicrobial activity tests. Journal of
151 ethnopharmacology.66:91-96.
- 152 Ruphin FP, Barthelemy F, Guy R, Oscar RA, Adolphe R, Zhao M, Marchioni E, Baholy
153 R, Marcelin S. 2016. Vasodilator effects of *Cymbopogon pruinosis* (Poaceae) from
154 Madagascar on isolated rat thoracic aorta and structural elucidation of its two bioactive
155 compounds. Journal of Pharmacognosy and Phytochemistry.5:46.
- 156 San Martín A, Rovirosa J, Becker R, Castillo M. 1980. Diterpenoids from *Baccharis*
157 *tola*. Phytochemistry.19:1985-1987.
- 158 Simirgiotis MJ, Quispe C, Bórquez J, Mocan A, Sepúlveda B. 2016. High resolution
159 metabolite fingerprinting of the resin of *Baccharis tola* Phil. from the Atacama Desert
160 and its antioxidant capacities. Industrial Crops and Products.94:368-375.
- 161 Simirgiotis MJ, Quispe C, Mocan A, Villatoro JM, Areche C, Bórquez J, Sepúlveda B,
162 Echiburu-Chau C. 2016. UHPLC high resolution orbitrap metabolomic fingerprinting of
163 the unique species *Ophryosporus triangularis* Meyen from the Atacama Desert,
164 Northern Chile. Revista Brasileira de Farmacognosia.

165

166