Solidago chilensis Meyen (Asteraceae), a medicinal plant from South America. A comprehensive review: ethnomedicinal uses, phytochemistry and bioactivity

Bruno Gastaldi, César AN Catalán, Fresia M Silva-Sofrás & Silvia B González

1 Chemistry Department, Natural and Health Sciences Faculty, National University of Patagonia San Juan Bosco, Esquel, Argentina
2 National Council of Scientific and Technical Research of Argentina (CONICET), Esquel, Argentina
3 Chemistry Institute of Northwestern Argentina (INQUINOA-CONICET), Organic Chemistry Institute, Faculty of Chemistry, Biochemistry and Pharmacy, National University of Tucumán, Tucumán, Argentina

Abstract: Solidago chilensis Meyen (Asteraceae) is a medicinal and aromatic herb widely distributed in South America. From 2000 to the present numerous articles on this species have been published, mainly in the last decade where the pharmacological studies and articles on its secondary metabolites have risen sharply. S. chilensis has potential beneficial effects on human health, particularly as an anti-inflammatory because of its high flavonoid content. This work describes the research carried out on this species with emphasis on biological and phytochemical studies.

Keywords: Solidago chilensis, Solidago microglosa, antioxidant activity, anti-inflammatory activity, solidagenone, quercetin, quercetrin.

Resumen: Solidago chilensis Meyen (Asteraceae) es una hierba aromática y medicinal, ampliamente difundida en Sudamérica. A partir del año 2000 se publicaron numerosos estudios sobre esta planta, particularmente en la última década donde se incrementó sensiblemente el estudio de sus propiedades farmacológicas y de la química de sus metabolitos secundarios. Es una planta con propiedades potencialmente beneficiosas para la salud humana, destacándose particularmente por su actividad antiinflamatoria que puede ser atribuida al elevado contenido en flavonoides. En este trabajo revisamos exhaustivamente los antecedentes de esta planta desde un enfoque cronológico, con énfasis en los estudios biológicos y fitoquímicos.

Palabras clave: Solidago chilensis, Solidago microglosa, actividad antioxidante, actividad antiinflamatoria, solidagenona, quercetina, quercetrina..
INTRODUCTION

Initials considerations

An exhaustive chronological review on *Solidago chilensis* Meyen (Asteraceae) with emphasis on the biological studies and its secondary metabolites chemistry is presented.

Interest on this species is booming. Figure 1 shows the cumulative number of publications for *S. chilensis* in the period 1970-2017. The number of publications has skyrocketed in the last decade (2007-2017).

Figure 1


*S. chilensis* is a very promising species. Due to its wide range of distribution covering different ecosystems of South America, comparative phytochemical and biological studies on plants collected at different sites are needed to detect intraspecific variations (chemotypes). Studies are also needed to know seasonal variations and changes associated with the growth phase of the plant.

Valverde *et al.* (2012) emphasize the importance of this medicinal plant in Brazil where it is being widely used by people and companies (private and public). In 2010 the Brazilian Ministry of Health considered *S. chilensis* as a plant with potential to generate products of pharmaceutical interest for the Brazilian Unified Health System. Currently this species is under cultivation in the Agroecological Platform of Phytomedicines (PAF) at Campus Fiocruz Atlantic Forest (CFMA)-Río de Janeiro.

General description and distribution

*Solidago chilensis* Meyen (Asteraceae) is a native species to South America that grows between 0 and 2500 meters above sea level. It is an herbaceous plant with abundant rhizomes that can reach up to 1.4 meters in height. It has an erect and leafy stem, the flowers arrangement is a typical dense pyramidal inflorescence. Figure 2 shows a representative picture of this plant. The first report and description of this plant was made by F. Meyen (1834) and in Argentina by Spegazzini (1897) under the synonymy *S. linearifolia* var. *brachypoda*.

A recent anatomical study was done by Hernandez *et al.* (2013) who noted epidermal characteristics of a xerophile species; also identified essential oils reservoirs in different organs of the plant. The chromosome composition for *S. chilensis* is 2n = 2x = 18 (Dematteis *et al.*, 2007; Laphitz & Semple, 2015; Semple, 2016).
According to Catalog of vascular plants of South Cone (http://www.darwin.edu.ar) and Correa (1971), in Argentina this plant occurs in Buenos Aires, Catamarca, Chaco, Chubut, Cordoba, Corrientes, Entre Ríos, Formosa, Jujuy, La Pampa, La Rioja and Mendoza provinces. In Brazil it is mainly found in the states of Rio Grande Do Sul and Santa Catarina. In Chile it grows in Region I, Region III, Region IV, Region V, Region VI, Region VII, Region VIII, Region IX, Region X, Region XI, Juan Fernández archipelago and Metropolitan Santiago Region. In Paraguay it is found in Alto Paraguay and Cordillera. In Uruguay its presence has been reported in Montevideo, Paysandú and Soriano.

Laphitz & Semple (2015) made up a map of the current distribution of S. chilensis, although we consider the actual distribution is wider, since the species is found also in Brazil (Valverde et al., 2012). In Figure 3 we propose an updated map of S. chilensis distribution in South America. In addition Silva et al. (2008) recorded S. chilensis in the Madeira Islands of Portugal, where it could have arrived by sea.

![Figure 2](image_url)

**Figure 2**

*S. chilensis* photography

**Synonyms and common names**

**Synonyms**

According to Catalog of vascular plants of South Cone (http://www.darwin.edu.ar) and The Plan List (http://www.theplantlist.org), the main accepted synonyms are: *Solidago linearifolia* DC., *Solidago microglossa* DC. Other synonyms registered in...

It should be noted that Laphiz (2009) and Laphiz & Semple (2015) consider that *S. chilensis* and *S. microglossa* are different species with different anatomical characteristics (stem hair length). However, in South America both species have the same popular use and a similar phytochemical profile. The morphological differences of *S. microglossa* could be attributed to a morphotype adapted to the environmental conditions of the northern populations. It would be very useful to perform chemotaxonomic and molecular analysis to confirm whether we are dealing with a single species or not, as well as if there exist variations in the phytochemical profile among populations of different habitats.

At this point it should be noted that *S. microglossa* is the only synonym that remains in use in current literature. So, and according to Mercandeli *et al.* (2012), in pharmacognosy and related areas it could be considered as a species with two accepted names: *S. chilensis* and *S. microglossa*.

**Figure 3**

**Distribution for S. chilensis in South America**

Common names

“Golden rod” is the most used common name of this plant and for members of genus *Solidago* in general. Other common names in Argentina and Chile are "vara amarilla" (yellow stick), "lanceta" (lancet), "punta de lanza" (spearhead), "romerillo amarillo" (yellow romerillo), (Alonso & Desmachelier, 2005). Mapuche names in Argentina and Chile: pfelel, felel (González & Molares, 2004). Brazilian common names: arnica, arnica-brasileira, arnicahorta, arnica-de-terreiro, arnica-brasil, arnica-silvestre, erva-federal, erva-lanceta,
ethnomedicinal uses

*S. chilensis* has variety of uses in the countries where it is present. According to Ferrari et al. (2014) and Mercandeli et al. (2012), the plant is used for numerous purposes and conditions. Ethnopharmacological uses are mostly related to inflammatory conditions and can be explained by the high contents of flavonoids in the plant.

**Argentina**

Argentinean literature cites it has been used as vulnerary, anti-gonorrhea and because of its revulsive properties. The root has been used as a sedative and for headaches, in addition to being used as baths for children with nervous problems. (Toursarkissian, 1980; Marzocca, 1997; Nuñez & Cantero, 2000).

Alonso & Desmachelier (2005) state *S. chilensis* has similar uses to *S. virgaurea*, a species widely known in Europe and Japan. The most common use is as infusion or decoction of aerial parts or roots. These authors report its use as sedative, diuretic, anti-inflammatory and for wound healing. Forcone (2004) also mentions it is used as a therapeutic agent for renal and urinary inflammations.

**Brazil**

In Brazilian popular medicine, it is recommended as a diuretic, analgesic and anti-inflammatory to treat burns and rheumatic disease, among others (Gouland et al., 2007; Liz et al., 2008). It is observed that most common use in folk medicine is related to inflammatory conditions, being used in the reduction of pain and edema, characteristic symptoms of inflammation (Valverde et al., 2012). Mercandeli et al. (2012) indicated that this plant have antiseptic, analgesic, and healing properties. Other uses include treating rheumatic and lumbar pain, contusions, wounds, and inflammations caused by insect bites. Also it is used as a gastrointestinal stimulant, healing and antiseptic.

**Chile**

The plant is used to treat symptomatology related to inflammation (Schmeda-Hirschmann et al., 2002).

**Paraguay**

Degen et al. (2005) indicate the plant has been used for kidney diseases.

**Uruguay**

The infusion of *S. chilensis* has been reported as antilithic, since it is used preventively and as a therapeutic agent for renal and urinary inflammations (Güntner et al., 1999). The study of the RI index (Relative Importance) made by Ferrari et al. (2014) in an ethnobotanic survey, reported a RI = 100% for *S. chilensis*, which means that the plant is used for numerous purposes and conditions.

**Phytochemistry**

The most relevant compounds isolated from *S. chilensis* are shown in Figure 4.

**Phenolic compounds and antioxidant activity**

In 1981 appeared in Buenos Aires-Argentina the first report on phenolic compounds from aerial parts of *S. chilensis* where several flavonoids were isolated and identified: isorhamnetin, quercetin 3-O-rhamnoside, quercetin 3-O-galactoside, and rutin. (Gutierrez et al., 1981). Günter et al. (1999) from plants collected at Montevideo-Uruguay, reported that the inflorescences are a source of free and glycosidic flavonoids derived from kaempferol, quercetin and others. In the same work, the antioxidant properties of different flower extracts and fractions containing flavonoids were studied. The total antioxidant capacity of the extracts was monitored spectrophotometrically measuring the color loss of solutions of ß-carotene in presence of 0.1% hydrogen peroxide. The most effective fraction was composed of 50% quercetin which has more effective antioxidant activity than butylated hydroxytoluene (BHT), a food industry synthetic antioxidant. Russo and Garbarino (2008) indicated that *S. chilensis* showed antioxidant activity similar to other *Solidago* species.

Tamura et al. (2009) investigated the main components of a hydroalcoholic extract (93% ethanol) from aerial parts of plants collected in São Paulo-Brazil. The extract was analyzed using high pressure liquid chromatography coupled to a diode detector and a mass spectrometer (HPLC–DAD–MS). The major components of the extract were

Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas/21
rutin and two caffeoylquinic acid derivatives.

From an ethanol extract Sabir et al. (2012) in Santa María-Brazil reported the following values in terms of milligrams of compound per gram of freeze-dried extract (mg/g): total phenolics (226 mg/g), total flavonoids (115.2 mg/g), quercetin (quercetin-3-O-α-L-rhamnoside) (51.9 mg/g), gallic acid (24.1 mg/g), rutin (3.82 mg/g), quercetin (2.57 mg/g). The extract showed high antioxidant activity. In a similar approach, from an aqueous extract of leaves, Löbler et al. (2013) also in Santa María-Brazil, identified and quantified: quercetin (441.4 mg/g), chlorogenic acid (95.7 mg/g) and rutin (46.9 mg/g).

Roman et al. (2015) from Chapecó-Brazil, using HPLC with the internal standard method, identified quercetin as the main flavonoid in hydroalcoholic extracts. The amount of quercetin was 0.2916 g of quercetin/g of total extract, so they concluded that aerial parts of S. chilensis contain 6.5% of quercetin. In similar works, Schneider et al. (2015) and Vechia et al. (2016) found, respectively, 2.4% and 5.29% of quercetin in the aerial parts, and the amount of quercetin is proposed as a quality control marker of the plant drug. Barros et al. (2016) also reported quercetin for a Santa Catarina-Brazil collection, where the flavonoid azeliny was also identified.

Gastaldi et al. (2016a) in Esquel-Argentina with a dietary approach found the following values for one infusion cup (250 ml) prepared from 5.0 g of air dried aerial parts (flowers, leaves and stems): ascorbic acid (Vitamin C); a total phenol content equivalent to 93 mg of gallic acid and a total flavonoid content equivalent to 69 mg of quercetin.

**Terpenes**

The first report on terpenoids was in 1980 that showed dihydroxycarotenoids as the main carotenoids of S. chilensis (Caffini et al., 1980).

From the roots of populations from Buenos Aires-Argentina, two well-known furan diterpenes were isolated by Gutierrez et al. (1981): junceic acid and solidagenone. Solidagenone, a highly bioactive molecule, was also isolated from plants collected in Asunción-Paraguay (Schmeda-Hirschmann, 1988) and tested in mice.

Composition of the essential oil from aerial parts has been analyzed by gas chromatography-flame ionization detector-mass spectrometry (GC-FID-MS) in two Argentina populations: one from Santa Fe province (Vila et al., 2002) and the other from Chubut province (Gonzalez et al., 2013; Gastaldi et al., 2016b). In the essential oil from the Santa Fe collection, pumiloxide, an unusual labdane diterpene, was found to be one of the major components, up to 15.3%; other important components were limonene 15.4%, caryophyllene oxide 3.5%, β-elemene 3.4%, γ-cadinene 8.2%, and germacrene D 3.1%. The composition of the essential oil of the population from Chubut was analyzed during four years; the main identified components being myrcene 8.2%, α-phellandrene 13.1%, limonene 46.6% and germacrene D 43%. A high content of limonene and germacrene D was found in both populations from Argentina.

**Other compounds**

Gutierrez et al. (1981) reported the presence of hydrocarbons in flowers and leaves. The flowers have hydrocarbons of 22 to 35 carbons, mostly C29 10.46%, C31 52.19%, C32 5.50%, C33 18.74% and C35 4.17%. The leaves have hydrocarbons of 17 to 37 carbons, mostly C31 69.04%, C32 3.88% and C34 7.31%.

Using histochemical methods Hernandez et al. (2013) identified inulin, lipophilic substances and starch.

The seasonal variation of saponins in plants collected in Beriso, Buenos Aires, Argentina was studied by Arrambarri & Hernandez (2014). The saponins content was determined by the height of the foam formed. Saponins were always present in underground organs (roots and rhizomes), but leaves collected at the end of summer and early autumn (March-April) also gave a highly positive reaction. Accordingly, March and April are the most suitable months to extract saponins from S. chilensis under natural conditions.

**BIOACTIVITY**

**Cell assays**

Razmilic & Schmeda (2000) studied the cytotoxicity of diterpene solidagenone and four semi-synthetic derivatives in L 1210, BHK and COS 7 cell lines that exhibited inhibitory concentrations 50 (IC50) between 10-100 μg/mL. They also studied possible mechanisms of anti-inflammatory activity on glucocorticoid-mediated signal transduction and found activities between 1-25 μg/mL.

Bagatini et al. (2009) using the Allium cepa test showed that infusions of this plant have
cytotoxic but not mutagenic effect. They showed the existence of antiproliferative and cytotoxic activities suggesting a possible therapeutic potential to inhibit the cell cycle in eukaryotic organisms. Accordingly, Gastaldi et al. (2016a) investigated the antiproliferative effect of the infusion on colon cancer cell line T84, finding an effective concentration 50 (EC50) of 0.16 mg/ml; this is a promising result suggesting that this plant has potential to inhibit the proliferation of colon cancer cells.

Freitas et al. (2008) analyzed the effect of aqueous extracts on the osmotic stability of human erythrocytes. In this assay the extract displayed simultaneously hemolytic and anti-hemolytic effects. The hemolytic activity may be related to the presence of saponins that form complexes with sterols, proteins and phospholipids, thereby modifying membrane permeability. The antagonistic anti-haemolytic activity may be related to flavonoids that can be incorporated into erythrocyte membranes. The presence of these antagonistic effects reflects the heterogeneous nature of the extract and indicates a need to fractionate it to characterize the components responsible for each effect.

Gastaldo et al. (2012) reported that a water-ethanol extract increases the release of cytokines in human cultured cells. It should be noted that this reference presents highly summarized information without in-depth analysis.

Figure 4
Some relevant compounds isolated from *S. chilensis*. Flavonoids: a) quercetrin (= quercetin-3-O-α-L-rhamnoside); b) quercetin; c) rutin. Terpenoids: d) pumiloxide; e) solidagenone; f) limonene; g) germacrene D; h) γ-cadinene.
Antimicrobial and antifungal activity

Vila et al. (2002) showed that the essential oil from leaves of S. chilensis is an efficient antifungal against the dermatophyte fungi Microsporum gypseum and Trichophyton mentagrophytes. The oil was more efficient than Amphotericin B and Nystatin whilst resulted inactive against other filamentous fungi such as Aspergillus fumigatus, Fusarium oxysporum and Penicillium purpurogenum. Cryptococcus neoformans was slightly sensitive only at the highest dose assayed (10 ul).

Duarte et al. (2005) reported that the essential oil displayed anti Candida albicans activity, whereas the ethanolic extract had no effect on this opportunistic fungus. The concentrations assayed were between 0.03 and 2 mg/ml.

Avancini et al. (2008) reported that a 10% decoction of aerial parts of S. chilensis was active against Staphylococcus aureus (Gram-positive) while it had no effect against Salmonella choleraesuis (Gram negative). A potential veterinary application is suggested due to the positive result against S. aureus, the main bacterium responsible for bovine mastitis.

Morel et al. (2006) tested the essential oil from leaves and a methanolic extract from roots against Staphylococcus aureus ATCC 6538p, Staphylococcus epidermidis (ATCC 12228), Klebsiella pneumoniae (ATCC 10031), Escherichia coli (ATCC 25792), Salmonella setubal (ATCC 19796), Bacillus subtilis (ATCC 6633), Pseudomonas aeruginosa ATCC 27853, Saccharomyces cerevisiae (ATCC 2601) and Candida albicans (ATCC 10231). The methanol extract showed weak activity against the tested microorganisms with a minimal inhibitory concentration (MIC) >1 mg/ml while the essential oil effectively inhibited the growth of all tested microorganisms.

Rafael et al. (2009) determined the antimicrobial activity of aqueous extracts of rhizomes against Staphylococcus aureus (ATCC 25922), Escherichia coli (ATCC 25923) and Pseudomonas aeruginosa (ATCC 27853). The extracts showed the following MIC values: P. aeruginosa 3.1 mg/ml, E. coli 6.2 mg/ml, S. aureus 6.2 mg/ml. The positive control using gentamicin as reference drug presented the following MIC values: P. aeruginosa 0.62 ug/ml, E. coli 1.25 ug/ml, S. aureus 0.62 ug/ml.

The potential use in dentistry has been tested by Freires et al. (2010) using the microdilution method. The tooth decay producing bacterium Streptococcus mutans (ATCC 25175) and Lactobacillus casei (ATCC 7469) were exposed to different concentrations of a commercial tincture of the plant. The MICs were 7.81 and 1.95 mg/ml respectively. These results show the potential of the tincture in dental clinic as an alternative and low cost method in the prevention of dental caries.

Animal studies

Anticuercerogenic and gastroprotective activities

Schmeda-Hirschmann et al. (2002) studied the anticylcerogenic effect of diterpene solidagenone and some semi-synthetic derivatives in mice. They found that a dose of 100 mg/Kg exerted a significant effect, equivalent to the control drug lansoprazole (20 mg/Kg).

In other work, Bucciarelli et al. (2010) analyzed the gastroprotective activity and acute toxicity of an aqueous extract in ulcerogenic models induced in female of albino mice. They studied the activity of aqueous extracts of inflorescences and compared it with the anticylcer reference drug omeprazole. The following doses of extract were tested: 125, 250, 400, 800, 1200 and 2000 mg/Kg. The extract gave promising results regarding anticylcerogenic activity which can be attributed to the flavonoid content. No toxic effects were observed. For this reason, the authors consider it as a promising plant for the development of new anticylcerogenic agents.

Barros et al. (2016) also studied the gastroprotective activity of a methanolic extract in doses 100-300 mg/Kg. The gastroprotective effect was investigated in acute gastric ulcer models and the anticypertory activity was assessed in vivo and in vitro. They concluded that S. chilensis extract promotes gastroprotection and gastric healing by diversified and complementary modes of action. Flavonoids, especially quercitrin and afzelin, are related to its antioxidant and anticypertory properties in parallel to its beneficial effect on the mucus production. In agreement with Bucciarelli et al. (2010), this plant is considered a possible natural resource in the search for anticylcer compounds, mainly flavonoids.

Hepatotoxicity, hepatoprotection

Neto et al. (2004) exposed a group of rats to 16.1 mg/Kg of aqueous extract in form of daily intraperitoneal injections for 14 days. They report
the lack of significant changes in the serum levels of alanine aminotransferase and aspartate, indicating that extract was not hepatotoxic at the dose assayed. However, the lethal dose 50 (LD₅₀) and lethal dose 100 (LD₁₀₀) in rats were 54.7 and 86.2 mg/Kg respectively, only 3.4 and 5.4 times higher than therapeutic dose (16.1 mg/Kg), which means that the extract does not have enough safety margin to be used to prevent intoxication.

In a recent work, Sabir et al. (2012) reported a significant hepatoprotective effect of an ethanol extract against paracetamol induced liver injury (250 mg/Kg). The animals received oral doses of 100 or 200 mg/Kg, per day for 7 days. However, the authors suggest the need for more detailed in vivo studies to establish the safety and bioavailability of plant extract.

**Hypoglycemic and hypolipidemic activities**

Roman et al. (2015) carried out a test in order to analyze the hypolipidemic and antioxidant effects of S. chilensis hydroalcoholic extract (HAE) on cholesterol-fed rats. Rats treated with extract (150, 300, and 600 mg/Kg) and quercetin decreased serum levels of total cholesterol and triglycerides similar to control drug simvastatin. Moreover, treatment with HAE and quercetin decreased 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase activity (35.1% on average) and increased the amount of fecal cholesterol (38.2% on average). This study suggested that hypolipidemic effects of HAE are associated with it modulating the activity of HMG-CoA reductase and its interference in the reabsorption and/or excretion of intestinal lipids. S. chilensis and quercetin, may thus be effective as cholesterol-lowering agents and in preventing atherosclerosis.

Schneider et al. (2015) evaluated the hypoglycemic and hypolipidemic effects of HAE from S. chilensis aerial parts in rats. The study showed that a glucose dose of 4 g/Kg can considerably increase serum glucose level which was mitigated by a single oral dose of HAE at 500 mg/kg for 180 min following glucose administration. Rats treated with HAE (125, 250 or 500 mg/Kg) showed decreased serum total cholesterol, more than glibenclamide drug at 10 mg/Kg. They conclude that HAE of S. chilensis may be effective in maintaining glucose homeostasis by reducing serum glucose levels and total cholesterol.

**Anti-inflammatory activity**

Goulart et al. (2007) made the first work of preclinical relevance to study the anti-inflammatory activity. The aim was to investigate the anti-inflammatory effect and mechanism of action of aqueous extracts obtained from rhizomes, leaves and inflorescences of S. chilensis in a mouse model of pleurisy induced by carrageenan. The results indicated that infusions at 25-50 mg/Kg inhibited leukocytes, neutrophils and exudation. The extracts also inhibited myeloperoxidase, adenosine-deaminase, and tumours necrosis factor alpha (TNF-α), and induced a decrease in the nitric oxide and interleukin-1 beta levels. An important anti-inflammatory effect is demonstrated, inhibiting cell infiltration and also decreasing pro-inflammatory mediators released into the site of the inflammatory process. Similar results have been obtained by Liz et al. (2008) and Gastaldo et al. (2012) using the mouse “air pouch” inflammation model.

Using Wistar rats as an experimental model, Tamura et al. (2009) showed the anti-inflammatory effects of alcoholic and hydroalcoholic extracts of aerial parts of S. chilensis on oedema and leucocyte trafficking. Their results indicated that topical (12.5 - 50 mg/kg) or intraperitoneal (25 or 50 mg/Kg) administration of the extract reduced ear oedema formation (> 25% reduction). Intraperitoneal applications of 25 mg/Kg of extract inhibited the migration of polymorphonuclear cells into the inflamed cavity (about 50%). Besides, the rolling behaviour and adherence of circulating leukocytes to postcapillary venules of the mesentery network was diminished (50%), but the mast cell degranulation in the perivascular area was not affected. In conclusion, local and systemic anti-inflammatory effects of the extract are demonstrated, and implicate the inhibition of leukocyte-endothelial interactions as an important mechanism of action.

Assini et al. (2013) reported the anti-inflammatory assay of formalin, based on the direct injection of formalin in the paws of mice. The aqueous extract (25, 50 and 250 mg/Kg) was administered by the oral route 30 minutes prior to behavioural test. In this test the extract produced significant analgesic and anti-inflammatory effects.

**Activity on the central nervous system**

In order to determine possible antidepressant and locomotor-type activities, Assini et al. (2013)
performed "open field test" and "forced swimming test" on Swiss mice. Experiments were performed with doses of 25, 50 and 250 mg/Kg. Results indicate that aqueous extract from *S. chilensis* did not show antidepressant-type activity. A reduction in the locomotor activity was noted at the highest administered level (250 mg/Kg), suggesting an effect on the central nervous system, although this could also be due to a peripheral muscular relaxing effect of the extract.

**Burn healing**
Catarino *et al.* (2015) carried out a study to evaluate possible synergic effect of laser therapy and hydroalcoholic extract of *S. chilensis* as phytotherapeutic agent to heal experimental second-degree burns in Wistar rats. The application of an extract combined with 670 nm laser promoted favourable responses in tissue repair in this experimental model.

**Others**
Rafael *et al.* (2009) studied the in vitro antiplatelet effect using a turbidimetric method. In this assay, the platelet aggregation is induced by adenosine diphosphate (ADP). The aqueous extract (400 μg/mL) of *S. chilensis* was effective in inhibiting the platelet aggregation stimulated by ADP with a 45% of inhibition. The observed effect may have important benefits over atherothrombotic diseases, although in vivo studies should be done to corroborate this activity.

Guarda *et al.* 2016 investigated the insecticide potential of *S. chilensis* and other Brazilian plants on the mosquito *Aedes aegypti*, vector of many tropical diseases. They worked with aqueous extract at concentrations of 125, 250, 500, 750 and 1000 μg/ml. The percentage efficiency was 0% for *S. chilensis*, so this extract does not have any lethal activity on *A. aegypti* larvae.

**CLINICAL TRIALS**
The first clinical trial of *S. chilensis* was carried out by Silva *et al.* (2010). The authors evaluated a gel preparation based on ethanol extract in treating lumbago (low back pain). The effectiveness of *S. chilensis* used externally was examined in placebo-controlled double-blind clinical pharmacological studies. Two daily skin applications of a gel containing a 5% extract in glycerol were administered for 15 days to ten volunteers in a placebo group and to an equal number in a test group. Statistical analyses of the results demonstrated a significant reduction in the perception of pain and a significant increase in flexibility of patients in the test group as compared with those receiving only the placebo.

Latter, the same group demonstrated the effectiveness of *S. chilensis* fluid extract used externally for treating tendinitis of flexor and extensor tendons of wrist and hand. Results showed a significant reduction in the perception of pain in the arms in the test group, when it was compared to those receiving only the placebo (Silva *et al.*, 2015).

**DISCUSSION AND CONCLUSIONS**
*S. chilensis* is an herb widely distributed in South America that in the last years has aroused attention by its varied properties and apparent low or nil toxicity. According to the publications analyzed in this review, this herb has potential as a source of antilulcerogenic, hypoglycemic and hypolipidemic compounds and to be used in the formulation of anti-inflammatory preparations for external use. Preclinical evidence (Mercandeli *et al.*, 2012) and two clinical trials with preparations for external use (Silva *et al.*, 2010; Silva *et al.*, 2015) showed no adverse reactions or toxicity of the extracts tested.

Due to the plethora of active metabolites produced by this plant (phenolic compounds, flavonoids, saponins, diterpenes, essential oil, etc.), long-term studies on pure bioactive components or purified and standardized fractions are required to establish relationships with the observed properties as well as possible synergistic effects.

Interestingly, quercetin-3-O-α-L-rhamnoside (quercetrin) -one of the main components in the aerial parts- is widely cited in collections from northern Brazil but not reported in southern populations, probably due to existence of different chemical races. On the other hand, solidagenone, an antilulcerogenic diterpene, is a major metabolite in the rhizomes and could be used for quality control of underground parts of the plant. Studies on populations from Paraguay, Uruguay, Chile and Bolivia are scarce or nonexistent and further comparative investigations to detect possible chemotypes in terms of phenolic profile, flavonoids, diterpenes, saponins and essential oil are needed. In addition, research on variation in the type and content of active metabolites according to the stage of development of the plant will provide
extremely useful information. Recently an experimental crop of this species was started in Rio de Janeiro, Brazil to homogenize quality and promote a sustainable harvesting for productive purposes without affecting natural populations. Initiatives of this type should be promoted and encouraged in order to protect wild genotypes of this species.

ACKNOWLEDGMENTS.
This work has been partially supported by a grant from Consejo de Investigaciones de la Universidad Nacional de Tucumán (CIUNT). B.G. thanks Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET)-Argentina, and Facultad de Ciencias Naturales y Ciencias de la Salud (UNPSJB)-Argentina for a fellowship.

REFERENCES
Freires IA, Alves LA, Jovito VC, Almeida LFD, Castro RD, Padilha WWN. 2010. In vitro antibacterial and antiadherent activities of tinctures from Schinus terebinthifolius
(Aroeira) and Solidago microglossa (Arnica) on dental biofilm forming bacteria. Odon Clin Cient 9: 139 - 143.


Nuñez C, Cantero JJ. 2000. Las plantas medicinales del sur de la provincia de Córdoba. Editorial de la Fundación Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas/28
Unidad Nacional de Río Cuarto, Río Cuarto, Argentina.