Evidence for the Safe Use of the Extract from the Brazilian Arnica, *Solidago chilensis* Meyen, in Primary Health Care

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**ABSTRACT**

In Brazil, the National Policy on Medicinal Plants has stimulated the use of plants in primary health care, validating the traditional medicine and pointing to the lack of a consistent set of evidence that supports their uses and indications by ethnobotany and ethnopharmacology. This paper aims to make a systematic review of the scientific literature to gather evidence on indications and safety of use of extracts of *Solidago chilensis*. The bibliographic research was carried out using terms derive from the title, and all the published papers were downloaded, covering at least the last five years, and it was focused on preclinical and clinical studies with extracts of *S. chilensis* in the databases of Web of Science, BIREME, SciELO, PubMed, Scirus and Highwire. Phytochemical analysis carried out on many studies showed that among the chemical constituents of *S. chilensis* are sesqui- and diterpenes, flavonoids and other substances, and the diterpene solidagenone was identified as a marker of the extract that has demonstrated gastroprotective activity in different experimental models of ulcer induced in animals without signs of toxicity at doses above 600 mg/kg. Another studies show that the anti-inflammatory effect in rats has been given by inhibiting the exudation of leukocytes, especially neutrophils, as well as through inhibition of myeloperoxidase, adenosine deaminase, and tumor necrosis factor-α (TNF-α), decreased induction of nitric oxide synthesis and levels of interleukin-1β. Studies show that solidagenone at a concentration of 100 mg/kg showed activity similar to lansoprazole (20 mg/kg), the effect occurs without changes in the gastric mucosa or on acid secretion. The aqueous and alcoholic extracts showed anti-inflammatory activity and may act in a satisfactory way in cases involving the inflammatory response, such as injuries due to trauma, repetitive stress, pain, and healing. The inhibition of anti-inflammatory response is on the base of all these described effects. In spite of the fact that *S. chilensis* has been used since ancient times in Brazilian traditional medicine, and the existence of preclinical pharmacological end toxicological evidence for its efficacy as an inhibitor of anti-inflammatory response, we could find only a single clinical trial study carried out in treating lumbago. In this lack of clinical pharmacology and toxicology evidence for its uses, its safety and therapeutic indications are guaranteed, up to this moment, by traditional knowledge.

**Keywords:** Safe Use; Primary Health Care; Traditional Knowledge; Anti-Inflammatory

1. Introduction

Despite the diversity of drugs developed by pharmaceutical industry, the traditional indigenous herbal medicine is still practiced in many Brazilian rural areas as therapeutic practices in primary health care. The World Health Organization (WHO) has emphasized the importance of indigenous traditional medicine since, in most rural areas of developing countries still using these drugs as first choice in health care and thus, building a history of traditional use of medicinal plants [1,2].

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Considering the widespread use of medicinal plants in Brazilian folk medicine, they are currently objects of many researches on the search for evidence for their therapeutic use. There is a wide use of these plants in Brazil as complementary health treatments, as a consequence of the high Brazilian biodiversity indexes that make traditional communities in close contact with natural resources [3]. Brazilian National Policy for medicinal plants and phytomedicines validated and stimulated the use of those traditionally known medicinal plants in primary health care [4]. In the context of that policy, from which the National Program of Medicinal Plants was derived, a trend in investigations was established, leading the phytomedicine practice to include the traditional knowledge as an important argument not only for the use of plants in primary health care [5], but also for the official registry of phytomedicines in Brazilian Ministry of Health [6].

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Among the plants used in Brazilian traditional Medicine, the name “arnica” became popular after the arrival of European immigrants, principally the Italians, at the end of the 19th century. These new settlers gave this name to the plants they encountered in Brazil that had aromas similar to that of * Arnica montana* L., that grew in Europe, and that will be nominated, from now on, as European arnica [7,8]. Despite of the fact of not always adequate or successful, early European immigrants sought correspondence between Brazilian native plants and the Old World species that they had been familiar with. This gave rise to the identification of various Brazilian “arnicas” that were recognized for their analgesic and anti-inflammatory properties [8].

One of the Brazilian arnicas, *Solidago chilensis* Meyen, belongs to the family Asteraceae [9]. This herb had already received another binomial name that is now taken as nomenclatural synonym for the former one, *Solidago microglossa* DC, and under that name it took part of the 1st edition of Brazilian Pharmacopeia [10] for its antiseptic, analgesic, and healing properties [11]. This plant is also referred as “arnica-do-campo” [12] and “erva-lanceta” [13]. The uses attributed it include treating rheumatic and lumbar pain, contusions, wounds, and inflammations caused by insect bites [14,15]. From now on it will be here referred in this paper as Brazilian arnica.

The investigation of phytochemical constituents from *S. chilensis* revealed the presence of flavonoids and saponins, substances known by their anti-inflammatory, antispasmodic and antiuretic effects. However, there are few evidence on those pharmacological properties for this phytomedicine, that were produced through clinical trials [16]. So, this paper aims to make a systematic review on the preclinical and clinical evidence for the use of the *S. chilensis* in inflammatory processes.

2. Traditional Clinical Indications of Uses of *Solidago chilensis*

Some indigenous communities, for example, the Mapuche, who live in arid Patagonia (Argentina) use this herb for medicinal and edible use for subsistence [17,18]. In Brasil, its use as a substitute for the specie European arnica *A. montana* seems to be due to their similar pharmacological effect, particularly for the treatment of infections and inflammation, such as chronic nephritis, cystitis, urethritis and rheumatism [19,20]. In addition, its fresh rhizomes are used as a diuretic, appetite stimulant, anthelmintic and aerial parts as anti-inflammatory [21].

This species has medicinal properties indications as antispasmodic, anti-hemorrhagic, anti-inflammatory, anti-rheumatic beckic, bitter, stomachic, toothache, vulnerary, and is also indicated for bruising, swelling, sores, weakness of joints, bruises, rheumatism, trauma and varicose veins [2]. Also assigned by the taxonomic synonym *S. microglossa* [22], this species properties as anti-inflammatory, analgesic, antirheumatic, and anti-hemorrhagic. It was placed in the second group of plants known and used by most pharmacists [23]. Its topical use is indicated in injuries, bumps, sprains, strains, bruises, falls, swelling, pain, trauma, among others [24] and is externally used as a substitute for *A. montana* to treat those illnesses [25]. The indication of the leaves of this species also can be done as a stimulant to gastro-intestinal wound healing and as anti-inflammatory agent [26].

However, this wide range of medicinal uses that arise from the traditional knowledge has not always been supported by preclinical or clinical evidence.

3. Preclinical Trail Evidence

Some pharmacological studies had demonstrated the gastroprotective effect of solidagenone in induced lesions in mouse models, in which some of its derivatives showed a statistically significant effect and reduction in lesion indices [27]. These effects seem to act through different and complementary mechanisms, many of them exhibit as a common characteristic, the stimulation of mucosal defensive factors and the modulation of the aggressive ones [28,29].

Other studies on gastroprotective activity showed that the terpenes and its derivatives from *S. chilensis* are effective in different experimental models of induced ulcer in animals without signs of toxicity at doses above 600 mg/kg. In addition, solidagenona at a concentration of 100 mg/kg showed activity similar to lansoprazole (20 mg/kg), the effect occurs without changes in the gastric mucosa or on acid secretion [30].

Several studies have shown that, due to the phytochemicals from *Solidago* species, they seem to possess anti-inflammatory properties, emerging at this point several possibilities to understand the mechanism of action of the extract of *S. chilensis*. Since its phytochemicals are bioavailable in the tissue layers beneath the skin and considering that both pain and inflammation have autacoids such as prostaglandins in their mediation, they may be involved in a common mechanism of action [27].

Anti-inflammatory effects and the mechanism of action of the glycolic extracts obtained from rhizomes, leaves and inflorescences of *S. chilensis* inhibited leukocytes, neutrophils and exudation in the mouse model of pleurisy in the inflammation induced by carrageenan. They also inhibited myeloperoxidase, adenosine-deaminase, and tumor necrosis factor alpha (TNF-α), and induced decreasing in the nitric oxide, and interleukin-1β levels, demonstrating an important anti-inflammatory effect, inhibiting cells infiltration and also decreasing pro-inflammatory mediators release into the site of the inflammatory process [31].
4. Evidence for the Use of *Solidago chilensis* in Primary Health Care

The fluid glycolic extract of *S. chilensis* was effective in treating lumbago and increasing lumbar flexibility when compared to a placebo treatment. The significant improvements observed indicated that the phytochemicals present in the extract were able to satisfactorily permeate the skin. The results obtained contribute to the evaluation of *S. chilensis* as a medicinal plant useful in the treatment of lumbago [32].

The properties reported to *S. chilensis* have been considered as consequences of its phytochemical constituents, such as flavonoids, phenolics, acetophenone, carotenoid, glycosides, essential oil, saponins, terpenes, lactones, and the dihydro-helenalin helenalin, which are the most studied anti-phlogistic lactones [33], among other active constituents [34].

Cyclooxygenase 2-dependent prostaglandin E2 (COX2/PGE2) is one of the important mediator abundantly produced in injured nerves and involved in the genesis of neuropathic pain. There are some novel proposed mechanisms underlying the role of COX2/PGE2 in injured nerves in the genesis of neuropathic pain. Long lasting COX2/PGE2 in injured nerves may induce chronic effects on nociceptors to facilitate the synthesis of pain-related molecules by stimulating injured or spared axons. COX2/PGE2 may also induce chronic effects on local inflammatory cells in injured nerves to facilitate the synthesis of inflammatory mediators via autocrine and paracrine pathways [35].

Prostaglandins are not the only inflammation mediators that have been involved in pain. The interleukin IL-1β is a pro-inflammatory cytokine has been implicated in pain, inflammation and autoimmune conditions that have been involved in various pain states, including the role of the intracellular complex, the inflammasome, which regulates IL-1β production. There are evidence of the importance of IL-1β in both in the induction and in the maintenance of pain in chronic states. Taken together, evidence of the importance of IL-1β in animal and human pain states, suggests that blockade of IL-1β be considered as a therapeutic opportunity [36].

Extracts of *S. chilensis* has a significant anti-inflammatory action on acute inflammatory responses and that its inhibitory activity may be due not only to the inhibition of pro-inflammatory mediators, but also to the inhibition of leucocyte infiltration [31,37]. These facts make clear that the use of *S. chilensis* can come to contribute to the reversal of the inflammatory process thereby reverse frames of morbidity.

These facts points to a probable mechanism for the action of the extract of *S. chilensis*. If the phyto-pharmacologically active substances from this species can be are into the tissues below the skin, and if the pain as well as the inflammation have common mediators [32,35,38], it is possible that these compounds may act by controlling the mediators synthesis or accumulation, and that the extracts have anti-inflammatory activity, as indicated by ethnobotanical studies [15].

A marker of the extract of *S. chilensis* is the solidagenone, a labdane diterpene that was isolated from ethanol: ethyl ether extract seems to be one of those responsible for anti-inflammatory activity and gastroprotective, thus presenting a yield of 6.56% from the extract obtained from a mixture of ethyl ether: ethanol (1:1), also showing the immunomodulatory effect through its property of inhibition of nitric oxide in peritoneal macrophages of BALB/C [21].

Caffeoylquinic acid derivatives, one of the major components of *S. chilensis* hydroalcoholic extract have also been found in polar extract of the roots of another species known as Brazilian “amica do cerrado”, *Lychnopora ericoides* Mart. (Asteraceae) likewise demonstrated analgesic effects (when administered orally), with the markers 3,5-di-O-[E]-caffeoylquinic, 4,5-di-O-[E]-caffeoylquinic, and 3,4,5-[E]-tri-O-caffeoylquinic. They demonstrated significant analgesic activity in skin scarification tests induced by acetic acid [39].

Since that the phytochemicals present in the extract are able to satisfactorily permeate the skin [32], it can be inferred that extracts of *Solidago* can be applied in cases of healing, and that for it to occur it is necessary the presence of various cytokines and cells that make use of inflammatory process for tissue reconstruction [40].

5. Conclusions

The phytochemical analysis of *S. chilensis* allows us to affirm the potential of this plant on the anti-inflammatory for acting in the cells and markers of inflammatory response. These factors are likely to affirm the potential gastroprotective widely cited in this manuscript as well as its effect on wound healing and analgesia.

In spite of the fact that *S. chilensis* has been used since ancient times in Brazilian traditional medicine, and the existence of preclinical pharmacological end toxicological evidence for its efficacy as an inhibitor of anti-inflammatory response, we could find only a single clinical trial study carried out in treating lumbago. In this lack of clinical pharmacology and toxicology evidence for its uses, its efficacy and safety is up to this moment guaranteed by traditional knowledge.

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REFERENCES


[31] S. Goulart, M. I. Moritz, K. L. Lang, R. Liz, E. P. Schen-


