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Medicinal plants used for musculoskeletal disorders in Navarra and their pharmacological validation

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ABSTRACT

Ethnopharmacological relevance: This paper provides important ethnopharmacological information on plants used in musculoskeletal disorders in Navarra.

Material and methods: Information was collected using semi-structured ethnobotanical interviews. In order to confirm the pharmacological validation of the uses, monographs from Official International Agencies (ESCO, Commission E, WHO and EMA) were reviewed. A literature review was conducted focusing on the plants that were widely used but had no published monograph.

Results: A total of 199 pharmaceutical uses were reported, for 38 plants and 24 families, mainly represented by *Asteraceae* and *Lamiaceae* (11%, each), *Rosaceae* (8%) and *Boraginaceae*, *Cucurbitaceae*, *Equisetaceae*, *Malvaceae*, *Oleaceae* and *Urticaceae* (5%, each). The most frequently used parts were the aerial parts, roots, followed by inflorescences and leaves. Nine out of 38 plants (24%) and 123 uses (62%), had already been pharmacologically validated.

Conclusions: The authors propose to validate four species for their use in musculoskeletal disorders: *Verbena officinalis*, *Symphytum tuberosum*, *Hypericum perforatum* and *Equisetum* ssp.

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1. Introduction

Traditional medicine is used globally and has a rapidly growing economic importance. In developing countries, traditional medicine is often the only accessible and affordable treatment available. Moreover, this medicine is becoming more and more popular in many developed countries (Bussmann, 2013). Among the positive aspects of traditional medicine, researchers have pointed to its diversity, flexibility, ease of access, continued acceptance in developing countries and increasing popularity in developed countries, relative low cost, low levels of technological inputs, relatively low side effects and increasing economic importance (Payyappallimana, 2010).

The musculoskeletal system is an organ system that gives humans the ability to move using their muscular and skeletal systems. The term musculoskeletal disorder is used to describe a variety of conditions that affect the muscles, cartilage, tendons, ligaments, joints, and other connective tissue, which are usually progressive and associated with pain. Musculoskeletal conditions are the most common cause of severe long term pain and disability in the EU and lead to significant healthcare and social support costs (The European Musculoskeletal Conditions

Surveillance and Information Network, 2012). As a major cause of work absence and incapacity they also have a significant economic cost through lost productivity. They can seriously affect the quality of life of those. Typically around 50% of the EU population report musculoskeletal pain at one or more sites for at least one week in the last month (www.ec.europa.eu). Different types of manual therapies and medications such as non-steroidal anti-inflammatories or opioids may be used to treat inflammation or pain. The medicinal plants can also be considered for the treatment of these diseases (Cameron and Chrubasik, 2013).

Previous studies carried out by our research group in Navarra showed that the ailments commonly treated by traditional medicine are digestive (Calvo et al., 2013), dermatological (Cavero et al., 2013), cardiovascular (Calvo and Cavero, 2014) and respiratory (Cavero and Calvo, 2014) diseases. Following on from this, the aims of the present paper are: (i) to collect information using monographs from Official International Agencies to confirm the pharmacological validation of the uses and (ii) to propose highly plants reported for these diseases for pharmacological validation.

2. Methodology

Information has been collected for 12 years, since 2003 to the present, using semi-structured ethnobotanical interviews with 667 informants in 265 locations (Navarra, Spain) following the

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methodology described in previous papers (Calvo et al., 2011; Cavero et al., 2011a, 2011b).

In order to confirm the pharmacological validation of the uses claimed by the informants, monographs from Official International Agencies: ESCOP (2003–2009), Commission E (Blumenthal et al., 2000), WHO (1999–2009) and EMA (www.ema.europa.eu/ema/index) were reviewed. A literature review was carried out for the plants that were reported to be in widespread use, for which no monograph exists.

3. Results and discussion

A total of 199 pharmaceutical uses were reported, belonging to 38 plants (82% native and 18% introduced species from other continents, or other European regions). The complete catalog of the ethnoflora of the surveyed territory is given in Akerreta (2009).

The 38 medicinal plants belong to 24 families (Tables 1 and 2), mainly represented by Asteraceae and Lamiaceae (11%, each), Rosaceae (8%) and Boraginaceae, Cucurbitaceae, Equisetaceae, Malvaceae, Oleaceae and Urticaceae (5%, each).

The most frequently used parts of the plants were its aerial parts (58%), roots (9%), flowered aerial parts and leaves (8% each), bulbs (5%), fruits and inflorescences (3% each) and stem (2%).

Plants were used fresh (84%), dry (3%), or either (12%) and lost knowledge (1%) for administration in different forms. The percentage of external uses was three times higher than that for internal uses (72% and 27%, respectively, lost knowledge 1%), and the most important forms of preparation was direct application of the plant, or the macerated in oil, vinegar, or alcohol (47%), poultice (36%), to rub with wine or water decoction or infusion (10%) and ointment (6%). The most important excipients of poultices preparation was eggwhite, olive oil and infusion. For internal uses, infusion (47%), decoction (20%), food (18%), maceration in alcohol or in anisette (12%) and juice (2%) were used.

Nine out of 38 plants (24%) and 123 of 199 popular uses (62%) had already been pharmacologically validated for musculoskeletal diseases by ESCOP, Commission E, WHO and EMA Monographs (Table 1). It is important to highlight that two of nine plants already had monographs in the four agencies taken into consideration.

Two out of nine plants (22%) shown in Table 1 had no monograph in the European Pharmacopoeia and/or Real Farmacopea Española.

The remaining plants (76%, 76 uses, Table 2) were reported for musculoskeletal troubles and need to be screened through standard scientific procedures for their actions. We found that the most widely treated affections fell into seven pathological categories: back pains (3%), bruises (25%), muscular pains (17%), rheuma (26%), sprains and strains (16%), strengthen bones and bone fractures (11%), and tendinitis (3%).

The external administration of the macerated in oil and ointment with wax and olive oil of *Agrimonia eupatoria* was cited (2 uses of 76 total uses, 3%) for the back pains.

In this study, the results showed that *Verbena officinalis* was employed for bruises (16 uses of 76 total uses, 21%), muscular pains (4 uses, 5%) and rheuma (4 uses, 5%). A poultice of aerial parts using eggwhite as excipient is well known as the famous “verbena omelette” for these affections. In the same way, olive oil or alcohol maceration of flowered aerial parts from *Hypericum perforatum* was used for bruises (2 uses, 3%) and muscular pains (4 uses, 5%).

The two reported applications of roots from *Symphytum tuberosum* was for sprains and twists (9 uses, 12%) and for rheuma (1 use, 1%). It is important to highlight that in the first case, the external use was crushed and placed between cloths.

The sterile aerial part of two species of horsetail, *Equisetum arvense* and *Equisetum telmateia*, were cited to bone problems and to strengthen and for broken bones (5 uses, 7%). With the same therapeutic indication, *Portulaca oleracea* was also cited (2 uses, 3%); it is also remarkable that for tendinitis, this plant was the only cited (2 uses, 3%).

In summary, it is important to highlight that the most widely cited plant for musculoskeletal affections were *V. officinalis*, *H. perforatum*, *S. tuberosum* and *Equisetum* ssp.

V. officinalis, commonly known as vervain and verbena, has been used as folk medicine for thousands of years for the treatment of abdominal mass, amenorrhea, dysmenorrhea, malaria, pharyngitis, carbuncles, edema, etc. Previous studies carried out have shown the importance from the ethnopharmacological point of view for dermatological (Cavero et al., 2013), digestive (Calvo et al., 2013) and respiratory (Cavero and Calvo, 2014) problems.

Regarding musculoskeletal problems, a review of literature from ethnopharmacological studies has showed that *V. officinalis* is used in different regions of Spain: Aragon, Basque Country, Catalonia, Navarra and Valencian Community; additionally, four ethnopharmacological references were found in other areas: Italian Republic, Portuguese Republic and Republic of Bulgaria (Akerreta, 2009, and references cited therein; Cavero et al., 2011a; Menendez-Baceta et al., 2014).

Pharmacological studies employing *in vitro* and animal models have found that verbena has anti-inflammatory (Speroni et al., 2007), topical analgesic (Sarris, 2007; Calvo, 2006) and antioxidant (Rehecho et al., 2011) activity. From the phytochemical point of view, the main constituents include iridoids, flavonoids and terpenoids (Rehecho et al., 2011; Zhang et al., 2011). These compounds, along with pharmacological spectrum mentioned above could support the use of verbena for the treatment of bruises, muscle pains and rheuma.

S. tuberosum is a perennial plant commonly known as comfrey. Two species of comfrey were used in Navarra without distinction for the symptomatic treatment of sprains and twists, *S. officinale* and *S. tuberosum*. The use of *S. officinale* for this therapeutic indication is scientifically supported by Official International Agencies (Table 2). *S. officinale* roots have been used in the traditional medicine externally (as ointment, compresses, or alcoholic maceration) for treatment of disorders of the locomotor system and inflammatory disorders of joints, bone fractures and distortions (Stickel and Seitz, 2000). In recent years, several references to support the use of this species have been published for the treatment of osteoarthritis of the knee (Chrubasik and Grunwald, 2007; Smith and Jacobson, 2011) and subacute low back pain (Jurcău and Jurcău, 2013). However, *S. tuberosum* is more used in Spain: Aragon, Catalonia and Navarra (Akerreta et al., 2009 and references cited therein; Cavero et al., 2011a). The botanical similarity of both species can justify the same therapeutic use (Tarle and Kosi-Culibrk, 1994).

St. John's wort (*H. perforatum*) has been intensively investigated for its antidepressant activity, but dermatological and musculoskeletal applications also have a long tradition. Traditional use of these preparations was characterized by external applications, such as oils or tinctures are used for the treatment of minor wounds, sunburns, bruises, contusions, myalgia, sciatica, rheumatism, lumbago, cramps, muscular pains, and many others (Wölfle et al., 2014). Clinical research works in this field have been scarce compared to the numerous trials about depression and other psychiatric indications. Consequently, the European Medicines Agency regards none of these applications as scientifically well established but accepts the use of topical preparations for “symptomatic treatment of minor inflammations of the skin and as an aid in the healing of minor wounds” in the context of traditional

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