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Original article

The pharmacological validation of medicinal plants used for digestive problems in Navarra, Spain

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Abstract

Introduction: To provide significant ethnopharmacological information on the plants used to treat digestive problems in the Navarra region of Spain.

Materials and methods: Information was collected using semi-structured, ethnobotanical interviews with 667 informants (mean age 72; 55.47% women, 44.53% men) in 265 locations. Monographs from the European Scientific Cooperative on Phytotherapy (ESCOP), the German Commission E, the World Health Organization (WHO), the European Medicines Agency (EMA), the European Pharmacopoeia (Ph. Eur.) and the Real Farmacopea Española (RFE) were used to confirm and validate the pharmacological actions for the reported uses of these plants. In cases when frequently reported plants were not covered by a monograph, a literature review was performed using a new tool from the University of Navarra: the UNIKA database.

Results: A total of 1214 pharmaceutical uses were reported by the informants of this study; these uses originated from 126 plants and 47 families and were mainly represented by *Asteraceae*, *Lamiaceae* and *Rosaceae*. The most frequently used parts of the plants were the inflorescences, followed by the flowered aerial parts and fruits. Thirty-three out of 126 plants (26%) and 322 of their identified 1214 popular uses (27%), have already been pharmacologically validated.

Conclusions: The authors propose that four species should be explored and validated (*Santolina chamaecyparissus* ssp. *squarrosa*, *Jasonia glutinosa*, *Jasonia tuberosa* and *Prunus spinosa*) because these species are frequently mentioned and show promise for therapeutic treatments.

Keywords: Digestive; Gastroenterological symptoms; Pharmacological validation; Traditional knowledge; Ethnopharmacology; Navarra

Introduction

The modern pharmaceutical industry is paying increased attention to medicinal plants as a resource for medicine development [1].

Additionally, in many developed countries, traditional medicine (TM) is becoming more and more prevalent. The percentage of the population that has used TM at least once in their lifetime is 48% in Australia, 70% in Canada, 42% in the USA, 38% in Belgium and 75% in France [2]. For this reason, the WHO has defined its role in TM by developing a strategy to address the issues of policy, safety, efficacy, quality, access and the rational use of TM [2].

Plants have been utilized as medicines throughout human history [3]. The use of herbs as medicines to treat ailments of the digestive tract is widespread. The human digestive system is a complex series of glands and hollow organs that process food. To use the food, the body must break it down into smaller molecules to build and nourish cells and to provide energy, and the body must also excrete the waste byproducts. The inner layer of these hollow organs is called the mucosa. In the mouth, stomach, and small intestine, the mucosa contains tiny glands that produce juices to help digest food. Two solid organs (the liver and pancreas) produce or store digestive chemical juices that reach the small intestine [4]. Taking into consideration that disorders of this system are usually closely interrelated, the medicinal plants

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used for treatment tend to be multipurpose and can be used for a variety of digestive symptoms and disorders [5].

Previous studies carried out by our research group in Navarra [6–9] have shown that the main ailments and/or purposes of treatment in traditional medicine are digestive problems, including carminative, tonic, aperitif, stomach ache, digestive, intestinal problems, evil tripe, diarrhea, liver problems, gallbladder problems, indigestion, toothache and a bad mood. The aim of the present paper is to identify the medicinal plants used for digestive problems in different regions of the Mediterranean basin that should be pharmacologically validated.

Methods

Study area

Navarra is a territory of 10,421 km^2 in the northern part of the Iberian Peninsula and can be differentiated into three zones: the mountains in the north, the riverside in the south, and a transitional zone, middle Navarra, that separates these two regions. In this region, there are two macro-bioclimates, the temperate and Mediterranean bioclimates. The oceanic temperate bioclimate appears in the northern part of the territory and is characterized by mild temperatures and high precipitation throughout the year. In the middle zone, the precipitation decreases, and the oceanic temperate climate with seasonal rainfall changes from the sub-Mediterranean variant with seasonal rainfall to the far south Mediterranean variant, which is characterized by a seasonal drought. These factors provide a great diversity of plant communities and a rich flora, with 2650 vascular plants [10].

Field studies

Information was collected using semi-structured ethnobotanical interviews with 667 informants (55.47% women and 44.53% men, mean age 72 years) in 265 locations. During the period of our study (2002–2012), we realized that elderly people possessed greater knowledge of the utilization of medicinal plants compared to the younger generation. In addition, the younger generations showed less interest in traditional practices, mostly due to a poor recognition of traditional medicine and the availability of modern health facilities. A similar scenario has been suggested by ethnobotanical studies in developed countries [3]. Interviews are generally carried out spontaneously with people who were born or have lived most of their lives in the region studied. The search for the informants in this study was performed by contacting participants through the following approaches: (a) town halls; (b) geriatrics and pensioners' clubs; (c) pharmacists in rural areas; (d) family, friends and contacts; and (e) spontaneous meetings [6–9].

During our field work, we noted, for each species, the local name, place and collection method, the drying and preservation system, the parts or organs used and the method of preparation, dosage and administration (Fig. 1). Plant vouchers were collected, mostly in collaboration with the informants, and authenticated according to Flora Iberica [11] and Flora of the Basque Country [12]. These specimens were authenticated by Dr. R.Y. Cavero (Department of Plant Biology–Botany). Voucher samples are kept in the PAMP Herbarium at the Faculty of Science (University of Navarra).

Plants with pharmacological validation

To confirm the pharmacological validation of the uses claimed by the informants, monographs from the European Scientific Cooperative on Phytotherapy (ESCOP), the German Commission E, the World Health Organization (WHO), the European Medicines Agency (EMA), the European Pharmacopoeia (Ph. Eur.) and the Real Farmacopea Española (RFE) were reviewed [13–18]. These monographs are responsible for evaluating the quality, security and efficacy of herbs.

The monographs, primarily published by the German European Commission, are an authoritative description of the uses and side-effects of over 300 herbs and herbal combinations (phytomedicines). The monographs are based on strict scientific investigation and are now recognized globally and used by herbalists, pharmacies, and medical doctors alike. The following three different types of monographs were published to determine how an herb would be regulated in Germany: Approved, Neutral and Unapproved. 'Approved' monographs allow for the use of the herb as a non-prescription drug; 'Neutral' monographs do not endorse a therapeutic benefit but still permit the sale of the herb without a safety concern; and 'Unapproved' monographs prohibit the normal sale of the herb because the risk of using the herb is deemed high [13].

New monographs are now produced by the European Scientific Cooperative on Phytotherapy (ESCOP) and are published under the name ESCOP Monographs. The ESCOP was founded as an umbrella organization of national associations for phytotherapy and consists of the majority of countries within the European Union as well as a number of non-EU countries. The ESCOP monographs constitute an up-to-date review of scientific information on the therapeutic uses of herbal medicines, including indications, dosage, contra-indications, interactions and undesirable effects, together with the summaries of pharmacological, clinical and toxicological data. These monographs provide the evidence base for the clinical use of herbal medicinal products [14].

The World Health Organization (WHO) published a series of 4 volumes referred to as the "*WHO monographs on selected medicinal plants*", which include data on the quality, safety and efficacy of herbs [15].

The European Medicines Agency (EMA) publishes a full scientific assessment report, called the *European public assessment report*, for every medicine granted a central marketing authorization by the European Commission. This search identifies *herbal substances* that are designated for assessment by the European Medicines Agency's Committee on Herbal Medicinal Products (HMPC). Each substance will be at a different stage of assessment, and various documents will be associated with the substance depending on where it is in the assessment process. The HMPC conclusions on the herbal substance at the end of the assessment process can be found in the final Community Herbal