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Medicinal plants used for dermatological affections in Navarra and their pharmacological validation ☆

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ABSTRACT

Aim of the study: This paper provides significant ethnopharmacological information on plant used in dermatological affections in Navarra.
Material 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. In order to confirm the pharmacological validation of the uses reports, the European Scientific Cooperative on Phytotherapy (ESCOP), German Commission E, World Health Organization (WHO), European Medicines Agency (EMA), European Pharmacopoeia (Ph. Eur.) and Real Farmacopea Española (RFE) monographs have been revised. A literature review has been carried out with the plants without monograph and high frequency citations, using a new tool of the University of Navarra, UNIKA.
Results: A total of 982 pharmaceutical uses are reported from the informants, belonging to 91 plants and 42 families, mainly represented by *Asteraceae*, *Lamiaceae*, *Euphorbiaceae* and *Crassulaceae*. The most frequently used parts of the plants are aerial parts followed by leaves and inflorescences. Seventeen out of 91 plants (19%) and 148 of 982 popular uses (15%), have already been pharmacologically validated.
Conclusions: The authors propose seven species for their validation (Allium cepa, Sambucus nigra, Hylotelephium maximum, *Chelidonium majus,* Ficus carica, Allium sativum and Anagallis arvensis).

1. Introduction

The modern pharmaceutical industry is paying more attention to medicinal plants as scientists rediscover that plant life is an almost infinite resource for medicine development. On the other hand, in many developed countries, traditional medicine (TM) is becoming more and more popular. The percentage of the population which has used TM at least once is 48% in Australia, 70% in Canada, 42% in USA, 38% in Belgium and 75% in France. For this reason, WHO define its role in TM by developing a strategy to address issues of policy, safety, efficacy, quality, access and rational use of TM (WHO, 2002).

Plants have been utilized as medicine throughout human history and probably even before humans evolved, given the long-standing practice of botanical medicine (Bonet and Vallès, 2007). Among the many applications of herbs in medicine include the use of these agents to treat dermatological troubles.

The skin is the largest organ of the human body and covers approximately 2 m^2. Its function is to act as a protective barrier to isolate the organism from the external environment. Physical, chemical, microbial and/or immunological factors can modify this barrier associated with loss function, resulting various dermatological problems such as wounds, callus, burns, grazes, warts, and skin problems, in general.

Previous studies carried out by our research group in Navarra have shown that one of the main ailments and/or purposes treated are dermatological problems (Akerreta et al., 2010; Calvo et al., 2011; Cavero et al., 2011a, 2011b). Similar results have been found in other ethnobotanical studies (Aburjai et al., 2007). The aims of the present paper are: (i) to do a scientific validation of the medicinal plants used for dermatological affections, and (ii) to propose plants reported in different regions of the Mediterranean basin for scientific validation.

2. Methodology

2.1. Study area

Navarra is a territory of 10,421 km^2 placed to the North of the Iberian Peninsula, where three zones can be differed: the Mountain

☆This manuscript is a etnopharmacological paper and no chemical compound appears.

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on the North, the Riverside on the South, and both separated by a zone of transition, the Middle Navarra. There are two macrobioclimates, Temperate and Mediterranean. The oceanic temperate bioclimate appears in the northern part, and is characterized by mild temperatures and high precipitation throughout the year. More to the south, as precipitation decrease the oceanic temperate bioclimate changes to the sub-Mediterranean variant and finally to the seasonal-rainfall Mediterranean bioclimate, characterized by seasonal drought. These factors provide a great diversity of plant communities and a rich flora (2650 vascular plants) (Akerreta et al., 2007a).

2.2. Field studies

Information was collected using semi-structured ethnobotanical interviews to 667 informants (55.47% women and 44.53% men, mean age are 72 years) of 265 locations. In the field work we noted for each species the local name, place and collection method, drying and preservation system, parts or organs used and method of preparation, dosage and administration (Akerreta et al., 2010; Calvo et al., 2011; Cavero et al., 2011a, 2011b). Plant vouchers were collected, mostly in collaboration with the informants, and authenticated according to Flora Iberica (Castroviejo, 1986–2011) and Flora of the Basque Country (Aizpuru et al., 2003). 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).

2.3. Plants with pharmacological validation

In order to confirm the pharmacological validation of the uses claimed by the informants, the European Scientific Cooperative on Phytotherapy (ESCOP), German Commission E, World Health Organization (WHO), European Medicines Agency (EMA), European Pharmacopoeia (Ph. Eur.) and Real Farmacopea Española (RFE) monographs have been reviewed. These monographs are responsible for evaluating the quality, security and efficacy of herbs.

The Monographs, primarily published by the German Commission E, 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 are used by herbalists, pharmacies, and medical doctors alike. Three different types of Monographs were published which determined how the 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 safety concern; 'Unapproved' monographs prohibit the normal sale of the herb because the risk of using the herb is deemed high (Blumenthal et al., 2000).

New monographs are now in the hands of 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 from the majority of countries within the European Union and from 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 summaries of pharmacological, clinical and toxicological data. These monographs provide the evidence base for the clinical use of herbal medicinal products (ESCOP, 2003–2009).

World Health Organization (WHO (1999–2009)) published a series of four volumes, the "*WHO monographs on selected medicinal plants*", includes data on quality, safety and efficacy of herbs.

The European Medicines Agency (EMA) publishes a full scientific assessment report called a *European public assessment report* for every medicine granted a central marketing authorisation by the European Commission. This search allows finding *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 Monograph and may also be found in Community list entry (www.ema.europa.eu/ema/index).

The European Pharmacopoeia 7th edition (2010) (Ph. Eur.) of the Council of Europe is a book, listing a wide range of active substances and excipients used to prepare pharmaceutical products in Europe. It includes more than 2000 specific and general monographs, including herbal drugs, among them. The monographs give quality standards for all the main medicines used in Europe. All medicines sold in the 36 Member States of the European Pharmacopoeia must comply with these quality standards so that consumers have a guarantee for products obtained from pharmacies and other legal suppliers (European Pharmacopoeia 7th edition, 2010).

The Real Farmacopea Española 3rd edition (2005) (RFE) is an authorized and revised translation of the European Pharmacopoeia, and also includes Spanish peculiar monographs (Real Farmacopea Española 3rd edition, 2005).

2.4. Plant without pharmacological validation

A literature review has been carried out with the plants without monograph and very employed, using a new tool of the University of Navarra, UNIKA, which allows to search at the same time in the main sources of information (www.unav.es/biblioteca/unika/informacion.html): Institutional catalogue, DADUN (digital repository of the University of Navarra), and SABIO (access system and search for information online).

UNIKA presents the following advantages in comparison with a traditional search: (i) searches are carried out against an index of several hundreds of millions of records; (ii) the contents of this resource correspond exclusively to academic and scientific quality documents; (iii) the process of search is simple and intuitive; (iv) the system presents the possibilities of access to full-text electronic or printed.

References to published work were researched using as keywords the Latin name of the species, for example "*Anagallis arvensis*".

3. Results and discussion

A total of 982 pharmaceutical uses are reported from the informants, belonging to 91 plants (73% native and 27% introduced species from other continents, or other European regions). The complete catalogue of the ethnoflora of the surveyed territory is given in (Akerreta, 2009).

The 91 medicinal plants belong to 42 families, mainly represented by *Asteraceae* (18%), *Lamiaceae* (10%), *Euphorbiaceae* (7%), *Crassulaceae* (4%), *Boraginaceae*, *Clusiaceae*, *Liliaceae*, *Malvaceae*, *Rosaceae* and *Scrophulariaceae* (3%, each one) are the most represented family.

The most frequently used parts of the plants are aerial parts (23%), leaves (22%), inflorescences (13%), flowered aerial parts (8%), bulbs (7%), latex (5%), and internal barks and sterile aerial parts (4%, each one).

Plants are used fresh (90%) for administration in different forms. The percentage of external uses is 98% and the most important forms of preparation are direct application (41%), poultice (29%), ointment

(15%), clean with infusion or decoction (9%) and olive oil or alcohol maceration (3%). The most important excipients of poultices preparation are honey, olive oil and white of eggs.

Seventeen out of 91 plants (19%) and 148 of 982 popular uses (15%), reported in the present survey, have already been pharmacologically validated for dermatological affections by ESCOP, Commission E, WHO and EMA Monographs (Table 1). It is important to highlight that only one of seventeen plants, *Calendula officinalis*, present monographs in the four agencies taken into consideration in this study.

Two out of them have previously been reported in other studies but not yet pharmacologically validated: *Arctium minus* and *Verbena officinalis* (indicated as 2[b] in Table 1). Activity in the indications listed has not been adequately demonstrated. Since the claimed efficacies have not been documented, a therapeutic application cannot be recommended.

Table 1
Plants with pharmacological validation.

Plant (Family, voucher specimen)	Part used	Ph	Preparation	Popular use	Monograph
Achillea millefolium L. ssp. *millefolium* (*Asteraceae*, 21175)	Inflorescence	A	Boiled in poultice; clean with infusion	Wounds	3,4
			Ointment with wax and olive oil	Disinfection of whitlows	3,4
Agrimonia eupatoria L. ssp. *eupatoria* (*Rosaceae*, 21932)	Aerial part	A, B	Boiled and placed between cloths; ointment with wax and olive oil	Wounds	1
Althaea officinalis L. (*Malvaceae*, 18805)	Root	A	Boiled in poultice	Wounds	3
Arctium minus Bernh. (*Asteraceae*, 21193)	Root		Clean with decoction	Herpes	2[b]
			Clean with infusion	Clean skin	2[b]
			Maceration in alcohol	Dandruff	2[b]
	Leaf		Clean with decoction	Eczema; ringworm; scabies	2[a,b]
			Direct application	Boils; heal wounds; wounds	2[a,b]
			Roasted in poultice	Pimples	2[a,b]
Calendula officinalis L. (*Asteraceae*, 18787)	Inflorescence	A, B	Maceration in oil	Wounds	1,2,3,4
			Ointment with wax and olive oil	Burns; heal wounds; pimples; skin problems; skin spots; wounds	1,2,3,4
			Ointment with wax, honey and olive oil	Skin infections	1,2,3,4
Chamaemelum nobile (L.) All. (*Asteraceae*, 21222)	Inflorescence	A, B	Ointment with wax and olive oil	Use for everything (burns; furuncles; pimples; wounds,…)	2
Equisetum arvense L. (*Equisetaceae*, 18670)	Aerial part	A, B	Clean with infusion	Children stinging, clean wounds	2
			Ointment with wax and olive oil; roasted and placed between cloths	Burns; crap out of wounds; grazes	2
Hypericum perforatum L. ssp. *perforatum* (*Clusiaceae*, 21559)	Flowed aerial part	A, B	Maceration in oil over 30–40 days	Burns, skin problems, wounds	2
			Ointment with wax and olive oil	Burns; wounds	2
	Flower	A, B	Clean with infusion	Eczema	2[a]
			Maceration in oil over 30–40 days	Burns; moisturize dry skin; wound healing	2[a]
Hypericum perforatum L. ssp. *angustifolium* (DC.) A. Fröhl. (*Clusiaceae*, 21558)	Flowed aerial part	A, B	Maceration in oil over 30–40 days	Burns; wounds	2
Juglans regia L. (*Juglandaceae*, 18681)	Leaf		Boiled in poultice	Herpes	2
			Clean with decoction	Chilblain; wounds	2
			Compresses with the decoction	Herpes; pain caused by herpes	2
Linum usitatissimum L. (*Linaceae*, 21246)	Seed	A	Boiled with milk and apply between cloths	Infections	1,2
Plantago lanceolata L. (*Plantaginaceae*, 21887)	Leaf	A, B	Boiled in poultice; clean with infusion; roasted in poultice	Wounds	2
			Direct application	Cure ills; foot problems; mosquito bites; wounds	2
Plantago lanceolata L. (*Plantaginaceae*, 21887)	Aerial part	A, B	Direct application	Burns	2
Rosmarinus officinalis L. (*Lamiaceae*, 21658)	Aerial part	B	Boiled and placed between cloths	Boils; furuncles; wounds	1
			Clean with decoction; crush with a little white wine; ointment with wax, olive oil and a small glass of red wine	Wounds	1
	Flowed aerial part	B	Ointment with wax and olive oil	Pimples	1
Salvia officinalis L. (*Lamiaceae*, 21676)	Aerial part	A, B	Clean with infusion	Wounds	4
Thymus vulgaris L. (*Lamiaceae*, 21713)	Aerial part	A, B	Clean with decoction; ointment with wax, honey and olive oil	Wounds	3
	Flowed aerial part		Clean with infusion	Wounds	3
Verbena officinalis L. (*Verbenaceae*, 21770)	Leaf	A, B	Poultice	Wounds	2[b]
	Flowed aerial part	A, B	Boiled and roasted with oil and egg whites, in poultice	Skin infection	2[b]
			Ointment with wax and olive oil	Crap out of wounds; skin problems	2[b]
			Poultice with egg white	Eczema; pimples; warts; wounds; wounds disinfection	2[b]
			Roasted in poultice	Boils; crap out of wounds	2[b]

Ph: Pharmacopeia; A: European Pharmacopoeia; B: Real Farmacopea Española; I: Internal; E: External; 1: ESCOP monograph; 2: German Commission E monograph; 3. WHO monograph; 4: EMA monograph.

[a] Different part used.
[b] Neutral German Commission E monograph.

Table 2
Plant without pharmacological validation (mentioned by three or more independent informants).

Affection	Plant (Family, voucher specimen)	Part used	Preparation (number of use reports)	FU	TFC
BALDNESS	*Urtica dioica* L. (*Urticaceae*, 21747)	Aerial part	Clean with decoction (4)	4	4
BURNS	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	Poultice with boiled or roasted bulb (39)	39	66
	Hylotelephium maximum (L.) Holub (*Crassulaceae*, 19685)	Leaf	Direct application (3)	3	
	Sambucus nigra L. ssp. *nigra* (*Adoxaceae*, 21815)	Internal bark, inflorescence	Ointment with wax and olive oil (24)	24	
CALLUS (callosity). HARD SKINS	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	Poultice with boiled or roasted bulb (20)	20	41
	Sambucus nigra L. ssp. *nigra* (*Adoxaceae*, 21815)	Internal bark, inflorescence	Ointment with wax and olive oil (21)	21	
GRAZES	*Sambucus nigra* L. ssp. *nigra* (*Adoxaceae*, 21815)	Internal bark, inflorescence	Ointment with wax and olive oil (8). Clean with infusion (2)	10	10
PIMPLES					
Acne	*Urtica dioica* L. (*Urticaceae*, 21747)	Aerial part	Decoction (3). Clean with decoction (1)	4	165
Boils, *furuncles*, *grains*	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	Poultice with boiled or roasted bulb (66). Direct application (7)	73	
	Allium sativum L. (*Liliaceae*, 21718)	Bulb	Warned with olive oil and direct application (6)	6	
	Equisetum telmateia Ehrh. (*Equisetaceae*, 21394)	Sterile aerial part	Boiled with wine in poultice (2). Clean with infusion (2)	4	
	Hylotelephium maximum (L.) Holub (*Crassulaceae*, 19685)	Leaf	Direct application (6)	6	
	Malva sylvestris L. (*Malvaceae*, 21825)	Aerial part, flower	Boiled in poultice (6)	6	
	Sambucus nigra L. ssp. *nigra* (*Adoxaceae*, 21815)	Internal bark, leaf, inflorescence	Ointment with wax and olive oil (9). Sahumerio (2). Clean with infusion (1)	12	
Whitlows (*felons*)	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	Poultice with boiled or roasted bulb (49). Boiled in poultice (5)	54	
SKIN PROBLEMS	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	Poultice with boiled or roasted bulb (3)	3	3
WART (*antiviral*)	*Allium sativum* L. (*Liliaceae*, 21718)	Bulb	Direct application (4)	4	80
	Chelidonium majus L. (*Papaveraceae*, 18712)	Latex	Direct application (29)	29	
	Euphorbia characias L. ssp. *characias* (*Euphorbiaceae*, 21505)	Latex	Direct application (5)	5	
	Euphorbia helioscopia L. ssp. *helioscopia* (*Euphorbiaceae*, 21509)	Latex	Direct application (3)	3	
	Euphorbia peplus L. (*Euphorbiaceae*, 21512)	Latex	Direct application (3)	3	
	Ficus carica L. (*Moraceae*, 21839)	Infrutescence latex	Direct application (36)	36	
WOUNDS (*anti-haemorrhagic*, *antiseptic healing*)	*Allium cepa* L. (*Liliaceae*, 19324)	Bulb	Poultice with boiled or roasted bulb (72). Direct application (9)	81	
	Allium sativum L. (*Liliaceae*, 21718)	Bulb	Warned with olive oil and direct application (7). Direct application (3)	10	
	Anagallis arvensis L. (*Primulaceae*, 21912)	Whole plant, aerial part, flowered aerial part	Boiled in poultice (9). Clean with decoction (4). Ointment with wax and olive oil (4). Clean with infusion (1)	18	313
	Carduus pynocephalus L. ssp *pynocephalus* (*Asteraceae*, 21214)	Stem	Direct application (7)	7	
	Chelidonium majus L. (*Papaveraceae*, 18712)	Latex	Direct application (12)	12	
	Cirsium arvense (L.) Scop. (*Asteraceae*, 21241)	Aerial part	Direct application (4)	4	
	Euphorbia characias L. ssp. *characias* (*Euphorbiaceae*, 21505)	Latex	Direct application (4)	4	
	Hylotelephium maximum (L.) Holub (*Crassulaceae*, 19685)	Aerial part, leaf	Direct application (75)	75	
	Malva sylvestris L. (*Malvaceae*, 21825)	Leaf, aerial part, flowered aerial part	Boiled in poultice (6). Clean with decoction (1)	7	
	Plantago major L. ssp. *major* (*Plantaginaceae*, 18716)	Leaf	Direct application (3)	3	
	Sambucus nigra L. ssp. *nigra* (*Adoxaceae*, 21815)	Internal bark, inflorescence	Ointment with wax and olive oil (78). Warned with oil in poultice (3). Clean with infusion (2)	83	
	Tussilago farfara L. (*Asteraceae*, 18656)	Leaf	Direct application (4)	4	
	Umbilicus rupestris (Salisb.) Dandy (*Crassulaceae*, 21347)	Leaf	Direct application (5)	5	

FC: frequency of uses; TFC: total frequency of uses.

It is important to highlight that Commission E establishes a risk of use to *Hypericum perforatum* because of a photosensitization is possible, especially in fair-skinned individuals.

On the other hand, it must be taken into account that plants listed in Table 1 have monograph in the European Pharmacopoeia and/or Real Farmacopea Española, with the exception of *Juglans regia*.

In addition, all these plants are marketed in Spain for these dermatological indications in different pharmaceutical forms (Vanaclocha and Cañigueral, 2003); information is available online (www.fitoterapia.net) for health professionals.

The remaining 74 plants (of total 91; 81%) are being reported for dermatological troubles and need to be screened through standard scientific procedures for their activities. Taking into consideration only the uses mentioned by three or more independent informants (682 uses, Table 2), the most treated affections are grouped in eight pathological affections: baldness (0.6%), burns (10%), callus or hard skins (6%), pimples (24%), grazes (1.5%), skin problems (0.4%), wart (12%) and wounds (46%).

The poultice with boiled or roasted bulb of *Allium cepa* is employed for the treatment of burns (59% of total uses for this affection), callus or hard skins (49%), furuncles and pimples (44%), boils, whitlows (33%), and wounds (26%).

An ointment with wax and olive oil prepared with the internal bark or inflorescence of *Sambucus nigra* used for grazes (80%), callus or hard skins (51%), burns (36%), wounds (25%), and boils, furuncles, pimples (5%).

The leaves or aerial parts of *Hylotelephium maximum* by direct application are applied for wounds (24%), and boils, furuncles, pimples (4%).

It is important to highlight the importance of the latex plants by direct application to the treatment of warts: *Ficus carica* (45%), *Chelidonium majus* (36%), *Euphorbia characias* (6%), *Euphorbia helioscopia* and *Euphorbia peplus* (4%, each one). *Chelidonium majus* (4%) and *Euphorbia characias* (1%) are employed also for the treatment of wounds.

In addition to the plants mentioned above, many species have been found for the treatment of wounds: *Anagallis arvensis* and *Malva sylvestris* (6% and 2%, respectively) in different forms of applications (boiled, ointment or clean with tisane); *Allium sativum* (3%), *Carduus pynocephalus* and *Umbilicus rupestris* (2%, each one), *Cirsium arvense*, *Tusilago farfara* and *Plantago major* (1%, each one) by direct application.

Allium sativum and *Malva sylvestris* (4%, each one), and *Equisetum telmateia* (2%), are used for boils, furuncles and pimples.

One aspect to highlight is that *Urtica dioica* has been cited only for the treatment of baldness and acne, *Allium cepa* for whitlows and skin problems, *Sambucus nigra* for grazes, *Ficus carica* for warts, and *Anagallis arvensis* for wounds.

Fig. 1 shows that the most used species and their frequency of citation in the different dermatological troubles are: *Allium cepa* (270 uses of 682 total uses, 40%), *Sambucus nigra* (150 uses, 22%), *Hylotelephium maximum* (84 uses, 12%), *Chelidonium majus* (41 uses, 6%), *Ficus carica* (36 uses, 5%), *Allium sativum* (20 uses, 3%), and *Anagallis arvensis* (18 uses, 3%).

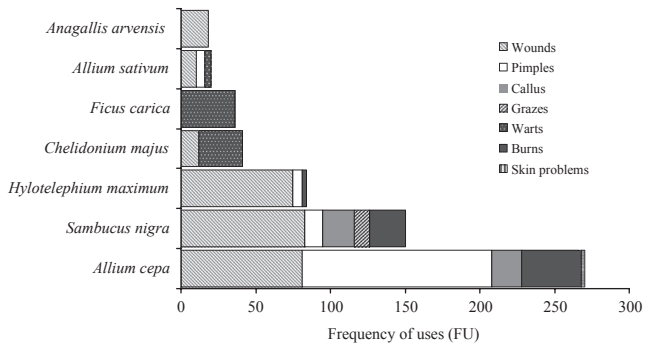

Fig. 1. The most used species and their frequency of use in the different dermatological affections.

Numerous ethnopharmacological studies carried out in other areas of the Mediterranean region have shown the same therapeutic applications for these plants: Federal Democratic Republic of Ethiopia, Hashemite Kingdom of Jordan, Hellenic Republic, Islamic Republic of Iran, Islamic Republic of Pakistan, Italian Republic, Kingdom of Morocco, Kosovo, Montenegro, Palestine, Portuguese Republic, Republic of Bulgaria, Republic of India, Republic of Serbia, Republic of Turkey, Russia/Ukraine, Spain and Syrian Arab Republic (Table 3).

The fleshy bulbs of *Allium cepa* are used medicinally as well as for food. In this study, the results have showed that onion is employed for the treatment of wounds (81 of 270 uses, 30%), pimples (127 uses, 47%), callus (20 uses, 7%), burns (39 uses, 15%) and skin problems in general (3 uses, 1%) (Fig. 1). Many scientific articles have confirmed these pharmacological activities and their correlation with the phytochemical composition (Bora and Sharma, 2009; Nath et al., 2010). Volatile oils of onion have been shown antimicrobial (Kim et al., 2011; Santas et al., 2010; Skerget et al., 2009), antiviral (Romeilah et al., 2010) and proved to be very effective against gram positive bacteria (Omoloso and Vagi, 2001; Ramos et al., 2006; Saxena et al., 2010), antifungal (Cornago et al., 2011; Lanzotti et al., 2012b) activity. On the other hand, flavonoids (Pérez-Gregorio et al., 2010; Rodríguez Galdón et al., 2008), pigments such as anthocyanins (Can et al., 2012; Steimer and Sjoberg, 2011) and organosulfur compounds (Borjihan et al., 2010) possess antioxidant (Lu et al., 2011; Roldán-Marín et al., 2009; Santas et al., 2010; Skerget et al., 2009), and anti-inflammatory (Rogerio et al., 2010; Takahashi and Shibamoto, 2008) activity. Flavonoids have been reported as one of the most important components of wound healing. The enhanced wound healing may be due to free radical scavenging action and the antibacterial property of the phytoconstituents present in it which either due to their individual or additive effect fastens the process of wound healing. This could be the reason for prohealing activity of onion (Shenoy et al., 2009).

In a various phytochemical study performed of *Sambucus nigra* were found to contain flavonoids (Wach et al., 2007), anthocyanins and tannins (Denev et al., 2010; Veberic et al., 2009a, 2009b), triterpenoids and volatile compounds (Jäger et al., 2009). These compounds are secondary metabolites widely distributed in the higher plant kingdom and are known to show diverse biological and pharmacological actions and its have been evaluated for their in vitro antioxidant (Barros et al., 2011; Kolodziej and Drozdzal, 2011; Srabovic et al., 2011), antiviral (Uncini Manganelli et al., 2005), anti-inflammatory (Barak et al., 2002), antibacterial (Hearst et al., 2010) and antifungal (Farcasanu et al., 2006; Soares et al., 2000) activity.

Hylotelephium maximum is a medicinal plant used to cure many types of inflammatory skin diseases. The leaves (without the external cuticle), are used to promote healing and reduce skin inflammation and pain, and contain various components (Bonina et al., 1996). The major components are flavonoids (Mulinacci et al., 1995a, 1995b; Sturm et al., 1999), polysaccharides (Sendl et al., 1993) and lactones (Fung et al., 1990). Flavonoids possess a strong protective effect against UV-induced skin erythema in vivo and possess strong antioxidant/free radical scavenging properties (Bonina et al., 1996). On the other hand, the anti-inflammatory and immunologically activity of polysaccharides have been also demonstrated (Sendl et al., 1993).

Latex is widely distributed in plants and contains various secondary metabolites, like terpenoids, phenolics, alkaloids, and proteins, namely, proteases (Oliveira et al., 2010). Two of seven

Table 3
Top seven plants without pharmacological validation.

Plant	Ethnobotanical studies
Allium cepa L.	SPAIN: *Andalusia* (Fernández-Ocaña, 2000; González-Tejero, 1989; Martínez-Lirola et al., 1997), *Aragon* (Ferrández and Sanz, 1993; Villar et al., 1987), *Basque Country* (Peillen, 1994), *Canary Islands* (Pérez and Hernández, 1999), *Cantabria* (Pardo de Santayana, 2004), *Castile-La Mancha* (Verde, 2002), *Catalonia* (Agelet, 1999; Bonet et al., 1999; Muntané, 2005; Parada et al., 2002), *Navarra* (Fernández, 1990; Ormazábal, 1973), *Principality of Asturias* (San Miguel, 2004), *Region of Murcia* (Obón and Rivera, 1991), *Valencian Community* (Mulet, 1991) HELLENIC REPUBLIC (Malamas and Marselos, 1992) ISLAMIC REPUBLIC OF IRAN (Ghorbani, 2005) ITALIAN REPUBLIC (Ballero et al., 2001; De Feo et al., 1992; De Feo and Senatore, 1993; Guarrera, 1999, 2005; Guarrera et al., 2005a; Motti et al., 2009; Pieroni et al., 2004) KINGDOM OF MOROCCO (Merzouki et al., 2000) PALESTINE (Ali-Shtayeh et al., 2000) PORTUGUESE REPUBLIC (Camejo-Rodrigues, 2001; Camejo-Rodrigues et al., 2003; Novais et al., 2004) REPUBLIC OF TURKEY (Sezik et al., 2004)
Sambucus nigra L. ssp. *nigra*	SPAIN: *Andalusia* (Benítez, 2007; González-Tejero, 1989), *Aragon* (Ferrández and Sanz, 1993; Villar et al., 1987), *Basque Country* (Letona, 1979; Aguirre, 2005), *Cantabria* (Pardo de Santayana, 2004), *Castile-La Mancha* (Verde, 2002), *Catalonia* (Agelet, 1999; Agelet et al., 2002; Bonet and Vallès, 2006; Muntané, 2002, 2005; Parada, 2007; Parada et al., 2002; Rigat, 2005; Rigat et al., 2007; Vallès et al., 2004), *Galicia* (Blanco et al., 1999), *Navarra* (Cavero et al., 2011a, 2011b; Fernández, 1981, 1990; Irigaray, 1977a, 1977b; Lapuente, 1972), *Principality of Asturias* (San Miguel, 2004), *Region of Murcia* (Obón and Rivera, 1991), *Valencian Community* (Mulet, 1991) ITALIAN REPUBLIC (Bullitta et al., 2007; Cornara et al., 2009; De Feo and Senatore, 1993; Guarrera, 2005; Guarrera et al., 2005a, 2005b; Passalacqua et al., 2007; Pieroni, 2000; Pieroni and Quave, 2005; Pieroni et al., 2004; Leporatti and Corradi, 2001) KOSOVO (Mustafa et al., 2012) PORTUGUESE REPUBLIC (Camejo-Rodrigues, 2001; Pinto, 2005) REPUBLIC OF TURKEY (Kültür, 2007) SYRIAN ARAB REPUBLIC (Carmona et al., 2005)
Hylotelephium maximum (L.) Holub	SPAIN: *Andalusia* (Casado, 2003; Espinosa et al., 2001a; Fernández-Ocaña, 2000; Ortuño, 2003), *Aragon* (Ferrández and Sanz, 1993; Villar et al., 1987), *Catalonia* (Agelet, 1999; Bonet and Vallès, 2006; Carrió et al., 2012; Vallès et al., 2002), *Navarra* (Akerreta et al., 2007b; Fernández, 1981) MONTENEGRO (Menkovic et al., 2011)
Chelidonium majus L.	SPAIN: *Andalusia* (González-Tejero, 1989; González-Tejero et al., 1990), *Aragon* (Ferrández and Sanz, 1993; Villar et al., 1984, 1987), *Basque Country* (Aguirre, 2005; Letona, 1979; Peillen, 1994), *Canary Islands* (Pérez and Hernández, 1999), *Cantabria* (Pardo de Santayana, 2004), *Castile-La Mancha* (Verde, 2002), *Catalonia* (Agelet, 1999; Agelet et al., 2000; Bonet and Vallès, 2006; Muntané, 2002, 2005; Parada, 2007; Parada et al., 2002; Rigat, 2005), *Galicia* (Blanco et al., 1999), *Navarra* (Fernández, 1981, 1990; Irigaray, 1977a, 1977b, 1979; Ormazábal, 1973), *Principality of Asturias* (San Miguel, 2004), *Valencian Community* (Mulet, 1991) ITALIAN REPUBLIC (De Feo et al., 1992; De Feo and Senatore, 1993; Guarrera, 2005; Guarrera et al., 2005a; Leporatti and Corradi, 2001; Leporatti and Ivancheva, 2003; Pieroni, 2000) MONTENEGRO (Menkovic et al., 2011) PORTUGUESE REPUBLIC (Camejo-Rodrigues, 2001; Novais et al., 2004; Pinto, 2005) REPUBLIC OF BULGARIA (Leporatti and Ivancheva, 2003) REPUBLIC OF SERBIA (Jarić et al., 2007) REPUBLIC OF TURKEY (Kültür, 2007) RUSSIA/UKRAINE (Moskalenko, 1987)
Ficus carica L.	SPAIN: *Andalusia* (Benítez, 2007; Casado, 2003; Casana, 1993; Espinosa et al., 2001a; Fernández-Ocaña, 2000; González-Tejero, 1989; Guirao-Moral, 1992; Martínez-Lirola et al., 1997; Ortuño, 2003), *Aragon* (Ferrández and Sanz, 1993; Villar et al., 1987), *Basque Country* (Aguirre, 2005; Etniker-Euskalerria, 2004; Letona, 1979), *Canary Islands* (Pérez and Hernández, 1999), *Cantabria* (Pardo de Santayana, 2004), *Castile-La Mancha* (Verde, 2002), *Catalonia* (Agelet, 1999; Agelet et al., 2000; Bonet and Vallès, 2002. 2006; Carrió and Vallès, 2012; Muntané, 2002, 2005; Parada, 2007; Parada et al., 2002), *Navarra* (Cavero et al., 2011b; Etniker-Euskalerria, 2004; Fernández, 1990), *Principality of Asturias* (San Miguel, 2004), *Region of Murcia* (Obón and Rivera, 1991), *Valencian Community* (Mulet, 1991) HELLENIC REPUBLIC (Hanlidou et al., 2004; Malamas and Marselos, 1992) ISLAMIC REPUBLIC OF IRAN (Ghorbani, 2005) ISLAMIC REPUBLIC OF PAKISTAN (Matin et al., 2001) ITALIAN REPUBLIC (Ballero et al., 2001; De Feo et al., 1992; Guarrera, 2005; Guarrera et al., 2005a, 2005b; Leporatti and Corradi, 2001; Motti et al., 2009; Pieroni, 2000; Pieroni and Quave, 2005; Scherrer et al., 2005) KINGDOM OF MOROCCO (Merzouki et al., 2000) PORTUGUESE REPUBLIC (Pinto, 2005) REPUBLIC OF INDIA (Jain et al., 2005)
Allium sativum L.	SPAIN: *Andalusia* (Benítez, 2007; Casado, 2003; Fernández-Ocaña, 2000; González-Tejero, 1989), *Aragon* (Ferrández and Sanz, 1993; Villar et al., 1984, 1987), *Basque Country* (Peillen, 1994), *Canary Islands* (Pérez and Hernández, 1999), *Cantabria* (Pardo de Santayana, 2004), *Castile-La Mancha* (Verde, 2002), *Castile-León* (González et al., 2011), *Catalonia* (Agelet, 1999; Bonet and Vallès, 2006; Carrió and Vallès, 2012; Carrió et al., 2012; Muntané, 2002, 2005; Parada, 2007; Parada et al., 2002; Rigat, 2005), *Extremadura* (Vallejo Villalobos et al., 2008), *Navarra* (Akerreta et al., 2007b; Cavero et al., 2011b; Fernández, 1981, 1990; Nieto, 1992), *Principality of Asturias* (San Miguel, 2004), *Region of Murcia* (Obón and Rivera, 1991), *Valencian Community* (Mulet, 1991) FEDERAL DEMOCRATIC REPUBLIC OF ETHIOPIA (Yinegar et al., 2007) HASHEMITE KINGDOM OF JORDAN (Aburjai et al., 2007; Al-Quran, 2011) ISLAMIC REPUBLIC OF PAKISTAN (Ishtiaq et al., 2007) ITALIAN REPUBLIC (Ballero et al., 2001; De Feo and Senatore, 1993; Guarrera, 1999; Guarrera et al., 2005a; Pieroni and Quave, 2005; Pieroni et al., 2002, 2004; Scherrer et al., 2005) KINGDOM OF MOROCCO (Merzouki et al., 2000) PALESTINE (Ali-Shtayeh et al., 2000) PORTUGUESE REPUBLIC (Camejo-Rodrigues, 2001; Pinto, 2005) REPUBLIC OF BULGARIA (Petkov, 1986) REPUBLIC OF INDIA (Rajan et al., 2002; Saskia et al., 2006) REPUBLIC OF TURKEY (Goncagul and Ayaz, 2010)
Anagallis arvensis L.	SPAIN: *Andalusia* (González-Tejero, 1989), *Aragon* (Villar et al., 1987), *Basque Country* (Etniker-Euskalerria, 2004), *Navarra* (Akerreta et al., 2007a; 2007b; Cavero et al., 2011a; Fernández, 1981, 1990; Ormazábal, 1973) ITALIAN REPUBLIC (Leporatti and Ivancheva, 2003)

plants analysed in Fig. 1 (*Chelidonium majus* and *Ficus carica*) possess this type of substance to remove warts on the body.

Pharmacological studies from *Chelidonium majus* L. has demonstrated the cytotoxic (Hu and Wang, 2009; Spiridonov et al., 2005), antimicrobial (Kokoska et al., 2002; Saglam and Arar, 2003), antibacterial (Zuo et al., 2008) and antifungal (Meng et al., 2009) activities, which support some of the traditional uses (Yang et al., 2011). *Chelidonium majus* displays a variety of biological properties due to the alkaloids (Gu et al., 2010; Suchomelová et al., 2007), acids and hydroxycinnamic acid derivates (Hahn and Nahrstedt, 1991, 1993), flavonoids (Kurkin and Artamonova, 2007; Stancic-Rotaru et al., 2002) components.

Many scientific articles of *Ficus carica* have confirmed the pharmacological activities like as antioxidant (Oliveira et al., 2010), antibacterial (Lazreg-Aref et al., 2012), antiviral and cytotoxic (Aref et al., 2011a, 2011b); and their correlation with the phytochemical composition: phenolic compounds (Caliskan and Polat, 2011; Vallejo et al., 2012), phenolic acid (Teixeira et al., 2009), flavonoids (Ali et al., 2011; Teixeira et al., 2009), anthocyanins (Duenas et al., 2008), coumarins (Ali et al., 2011; Chung et al., 2011; Lazreg-Aref et al., 2012;), essential oils (Gozlekci et al., 2011; Silva et al., 2010), and proteolytic enzymes like diastase, esterase, lipase, catalase, and peroxidase (Chang et al., 2011; Yan et al., 2011).

Allium sativum is frequently used as a spice on food and as medicinal plant due to its various reported activities such as anti-atherogenic, antihypertensive, lipid-lowering, antiatherosclerotic, antiprotozoal, anthelmintic, antibacterial, antifungal, antiviral, and recently as anticancerous and antithrombotic (Bhandari, 2012). Garlic contains allinase, alliin and allicin. Externally, it has been used to treat infections and wounds, mainly. In this sense, numerous pharmacological studies have demonstrated the antibacterial (Ayazi et al., 2011; Daka, 2011), antimicrobial (Goncagul and Ayaz, 2010a, 2010b), antifungal (Lalitha et al., 2011; Lanzotti et al., 2012a) and antitumor (Iciek et al., 2009) activity and their correlations with these phytochemical composition. On the other hand, some organosulfur compounds and flavonoids (Kim et al., 2000) have been found a high radical scavenging activity (Othman et al., 2011), and recently the anti-inflammatory activity of *Allium sativum* has been described (Jayanthi and Dhar, 2011).

Anagallis arvensis ("scarlet pimpernel") have been reported to contain saponins and flavonoids (Aliotta et al., 1992; Kawashty et al., 1998; Shoji et al., 1994a, 1994b); few works on biological effects have also been published: antifungal (López et al., 2008; Qasem, 2011), antiviral against herpes simplex virus (Amoros et al., 1987, 1988), molluscicidal (Abdel-Gawad et al., 2000), antimicrobial and anti-inflammatory (López et al., 2011), antioxidant (López et al., 2008) and cytotoxic effect in neuronal and cancer cell lines (López et al., 2013) properties. According to constituents, flavonoids are well-known for antioxidant and anti-inflammatory activities (Pietta, 2000) whereas many saponins have been described as anti-inflammatory and antifungal agents (Bruneton, 2001). All the properties demonstrated by these in vitro assays may explain the uses of the plants as wound healing remedies.

Numerous ethnobotanic, phytochemical and pharmacological studies with *Allium cepa*, *Sambucus nigra*, *Hylotelephium maximum*, *Chelidonium majus*, *Ficus carica*, *Allium sativum* and *Anagallis arvensis* suggest that medicinal plants have proved to be effective for prevention and cure of dermatological troubles and can be used after its validation to improve upon, leading to relatively inexpensive, effective, and safe therapies.

4. Concluding remarks

A large proportion of the population of developing countries uses traditional medicine alone, or in combination with Western drugs to treat a wide variety of ailments. The medicinal plants have been described for treating dermatological troubles. Many of them have been used since the ancient times and their knowledge passed from generation to generation. For this reason, its therapeutic efficacy and safety can be backed.

Nineteen percent of the medicinal plants used in Navarra for dermatological problems have been pharmacologically validated by official international organizations. Of the remaining 81%, the authors highlight seven species for their validation (*Allium cepa*, *Sambucus nigra*, *Hylotelephium maximum*, *Chelidonium majus*, *Ficus carica*, *Allium sativum* and *Anagallis arvensis*). These species are commonly used in traditional medicine of Navarra and in other regions of the Mediterranean basin. To this end, in vitro and in vivo pharmacological studies and phytochemical analyses of some of the reported plants from the survey area are underway for their pharmacological validation.

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