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Murcia, 21st November 2016

Dear Editor of the Journal of Ethnopharmacology

We are pleased to submit the revised manuscript of our paper (5th revision)

Is there nothing new under the sun? The influence of herbals and pharmacopoeias on ethnobotanical traditions in Albacete (Spain)

By

Diego Rivera ^{a*}, Alonso Verde ^b, Concepción Obón ^c, Francisco Alcaraz ^a, Candelaria Moreno ^d, Teresa Egea ^{c,g}, José Fajardo ^b, José Antonio Palazón ^f, Arturo Valdés ^b, Maria Adele Signorini ^e, Piero Bruschi ^g

We expect it will suit as a satisfactory revision for publication in JEP.

A handwritten signature in blue ink, appearing to read 'Diego Rivera'.

Sincerely yours.

Diego Rivera on behalf of the authors.

Journal of Ethnopharmacology AUTHOR CHECKLIST

Dear Author,

It frequently happens that on receipt of an article for publication, we find that certain elements of the manuscript, or related information, is missing. This is regrettable of course since it means there must be a delay in processing the article while we obtain the missing details.

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Dear Miguel,

We are extremely grateful for the exhaustive language editing.

I accepted as a rule, but one by one, all changes introduced.

We also modified these still obscure sentences; following the suggestion of the reviewer.

We, for sake of consistence deleted all texts like (Fig. 1 approx. here) since the reviewer marked some for deletion and others not.

We expanded GMT as suggested.

Due to compatibility issues, some problems were detected in the file for legends, captions and supplementary material. Therefore, we accepted all suggested changes and proceeded to copy these to the original documents also in the figures in order to keep the structure of figures and tables unaltered.

Best regards

Diego Rivera

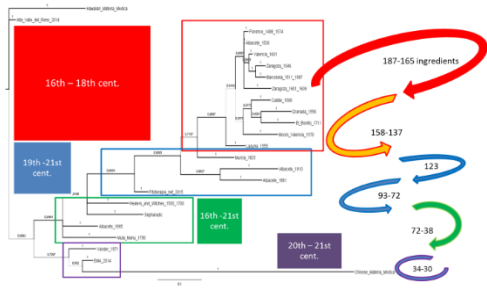
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*Graphical Abstract



- The c. 200 ingredients, local and exotic, represent the late medieval consensus
- These ingredients progressively disappear from pharmacy
- Ethnobotany, Sephardic and Healers mainly share local ingredients
- Modern phytotherapy retains only c. 15 % of the ingredients

Arancel of medicines Albacete (Spain) 1526



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Ethnopharmacological relevance: This paper has two overarching aims: (1) presenting the results of studying the Albacete tariff of medicines of 1526 and (2) broadly analyzing the origin and influences of medicinal traditional knowledge in the region of Albacete, Spain. We use historical and modern literature that may have influenced this knowledge. Our primary goal was to determine the ingredients used in the pharmacy in the 16th century CE in Albacete through the analysis of the tariff, and our secondary goal was to investigate until when ingredients and uses present in pharmacy and herbals persisted in later periods.

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Methods: The identity of medicines and ingredients was determined by analyzing contemporary pharmacopoeias and classical pharmaceutical references. We analyzed further 21 sources (manuscripts, herbals, and books of medicines, pharmacopoeias, pharmacy inventories, and modern ethnobotanical records) for the presence/absence of ingredients and complex formulations of the tariff. Using factorial and cluster analysis and Bayesian inference applied to evolution models (reversible-jump Markov chain Monte Carlo), we compared textual sources. Finally, we analyzed the medicinal uses of the top 10 species in terms of frequency of citation to assess the dependence of modern ethnobotanical records on Renaissance pharmacy and herbals, and, ultimately, on Dioscorides.

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Results: In Albacete 1526, we determined 101 medicines (29 simple drugs and 72 compound medicines) comprising 187 ingredients (85% botanical, 7.5% mineral, and 7.5% zoological substances). All composed medicines appear standardized in the pharmacopoeias, notably in the pharmacopoeia of Florence from 1498. However, most were no longer in use by 1750 in the pharmacy, and were completely absent in popular herbal medicine in Albacete 1995 as well as in Alta Valle del Reno (Italy) in 2014. Among the ingredients present in different formulation are the flowers of *Rosa gallica*, honey (*Apis mellifera*), the roots of *Nardostachys jatamansi*, and *Convolvulus scammonia*, pistils of *Crocus sativus*, grapes and raisins (*Vitis vinifera*), rhizomes of *Zingiber officinale*, bark of *Cinnamomum verum*, leaves and fruits of *Olea europaea*, mastic generally of *Pistacia lentiscus*, and wood of *Santalum album*. The statistical analysis of sources produces four well-separated clusters (Renaissance Herbals and Pharmacopoeias, Ethnobotany and Folk Medicine, Old phytotherapy, and Modern phytotherapy including Naturopathy) confirming our a priori classification. The clade of Renaissance Herbals and Pharmacopoeias appears separated from the rest in 97% of bootstrapped trees. Bayesian inference produces a tree determined by an initial set of

1 two well-distinct core groups of ingredients: 64, locally used in Mediterranean Europe
2 during centuries; and 45, imported, used in pharmacy during centuries. Complexity
3 reached its maximum in Albacete 1526 and contemporary pharmacopoeias, gradually
4 decreasing over time. The analysis of medicinal uses of the top 10 ingredients showed
5 low coincidence between Dioscorides and different Renaissance herbals or medical
6 treatises and of all of them with ethnobotany in Albacete.
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10 **Conclusions:** Regarding our question: is there something new under the sun? In
11 some aspects, the answer is “No”. The contrast between expensive drugs, highly valued
12 medicines, and unappreciated local wild medicinal plants persists since the Salerno’s
13 school of medicine. Old medicine in Mediterranean Europe, as reflected by Albacete
14 1526 tariff of medicines, involved strict formulations and preferences for certain
15 ingredients despite other ingredients locally available but underappreciated. This
16 confirms the fact that any system of medicine does not get to use all available
17 resources. Ethnobiological records of materia medica, in rural areas of Albacete,
18 describe systems with a high degree of stability and resilience, where the use of local
19 resources, largely wild but also cultivated, is predominant in contrast with the weight
20 of imported exotic products in pharmacy.
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Is there nothing new under the sun? The influence of herbals and pharmacopoeias on ethnobotanical traditions in Albacete (Spain)

Diego Rivera ^{a*}, Alonso Verde ^b, Concepción Obón ^c, Francisco Alcaraz ^a, Candelaria Moreno ^d, Teresa Egea ^{c,g}, José Fajardo ^b, José Antonio Palazón ^f, Arturo Valdés ^b, Maria Adele Signorini ^e, Piero Bruschi ^g

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ABSTRACT:

Ethnopharmacological relevance: This paper has two overarching aims: (1) presenting the results of studying the Albacete tariff of medicines of 1526 and (2) broadly analyzing the origin and influences of medicinal traditional knowledge in the region of Albacete, Spain. We use historical and modern literature that may have influenced this knowledge. Our primary goal was to determine the ingredients used in the pharmacy in the 16th century CE in Albacete through the analysis of the tariff, and our secondary goal was to investigate until when ingredients and uses present in pharmacy and herbals persisted in later periods.

Methods: The identity of medicines and ingredients was determined by analyzing contemporary pharmacopoeias and classical pharmaceutical references. We analyzed further 21 sources (manuscripts, herbals, and books of medicines, pharmacopoeias, pharmacy inventories, and modern ethnobotanical records) for the presence/absence of ingredients and complex formulations of the tariff. Using factorial and cluster analysis and Bayesian inference applied to evolution models (reversible-jump Markov chain Monte Carlo), we compared textual sources. Finally, we analyzed the medicinal uses of the top 10 species in terms of frequency of citation to assess the dependence of modern ethnobotanical records on Renaissance pharmacy and herbals, and, ultimately, on Dioscorides.

Results: In Albacete 1526, we determined 101 medicines (29 simple drugs and 72 compound medicines) comprising 187 ingredients (85% botanical, 7.5% mineral, and 7.5% zoological substances). All composed medicines appear standardized in the pharmacopoeias, notably in the pharmacopoeia of Florence from 1498. However, most were no longer in use by 1750 in the pharmacy, and were completely absent in popular herbal medicine in Albacete 1995 as well as in Alta Valle del Reno (Italy) in 2014. Among the ingredients present in different formulation are the flowers of *Rosa gallica*, honey (*Apis mellifera*), the roots of *Nardostachys jatamansi*, and *Convolvulus scammonia*, pistils of *Crocus sativus*, grapes and raisins (*Vitis vinifera*), rhizomes of *Zingiber officinale*, bark of *Cinnamomum verum*, leaves and fruits of *Olea europaea*, mastic generally of *Pistacia lentiscus*, and wood of *Santalum album*. The statistical analysis of sources produces four well-separated clusters (Renaissance Herbals and Pharmacopoeias, Ethnobotany and Folk Medicine, Old phytotherapy, and Modern phytotherapy including Naturopathy) confirming our a priori classification. The clade

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Conclusions: Regarding our question: is there something new under the sun? In some aspects, the answer is “No”. The contrast between expensive drugs, highly valued medicines, and unappreciated local wild medicinal plants persists since the Salerno’s school of medicine. Old medicine in Mediterranean Europe, as reflected by Albacete 1526 tariff of medicines, involved strict formulations and preferences for certain ingredients despite other ingredients locally available but underappreciated. This confirms the fact that any system of medicine does not get to use all available resources. Ethnobiological records of materia medica, in rural areas of Albacete, describe systems with a high degree of stability and resilience, where the use of local resources, largely wild but also cultivated, is predominant in contrast with the weight of imported exotic products in pharmacy.

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Keywords:

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Ethnobotany; herbals; medicinal plants; multivariate and Bayesian analysis; pharmacopoeias; traditional medicine

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Abbreviations

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A1526 – tariff of medicines of the city of Albacete of 1526; AHPAB – Provincial Archive of Albacete (Spain); CE – Christian era; DEP – Dependent; EMA – European Medicines Agency; ETHN – Medical Ethnobotany; GTR – General time reversible nucleotide substitution model; HMPC – European Medicines Agency's Committee on Herbal Medicinal Products; ICD-10 – International Statistical Classification of diseases and Related Health Problems 10th Revision; MAAC – Marginal groups and alternative or complementary systems of medicine; PCoA – Principal coordinates analysis; PHCL – Pharmaceutical classical; PHMO – Pharmaceutical modern; rjMCMC– Reversible-jump Markov chain Monte Carlo; SOU – Source; TPL – The Plant List.

1 Introduction

All ethnopharmacological research refers to one, several, or numerous plant or animal species, fungi, algae, microorganisms, minerals, or rocks that unambiguously are subject of ethnopharmacological uses. Recently, Leonti et al. (2010) questioned that to what extent studies on contemporary medicinal plant use in Europe over the last two to three decades contain autochthonous traditional knowledge. They estimate that for Campania (Italy), Matthioli's effect is not negligible and lies between 14 and 25% with a high probability.

Leonti (2011) denounced, "apart from empirically learned medicinal and pharmacological properties, the selection of medicinal plants is dependent on cognitive features, ecological factors and cultural history".

At the beginning of the 16th century CE, the repertory of single and compound medicines officially used by physicians in Western Europe was still strongly influenced by the medical school of Salerno (south of Naples, Italy) and medieval works of Mesue, Nicolao Salernitano, and al-Razi (Anonymous 1513, 1519, De Laredo 1534, Razi 1529, Sylvio 1550). Extremely complex herbal formulations involving dozens of expensive substances were usual. Their complexity and frequent adulteration made necessary the definition of standards for crude drugs, processing, and formulations. The pharmacopoeias codified these standards.

The first official pharmacopoeia, issued in Florence (Tuscany in Italy) in 1498 under the name of "*Nuovo Ricettario*", intended to secure uniformity in the kind, quality, composition, and strength of remedies approved to prevent fraudulent or inappropriate substitutions and manipulations (Fittipaldi 2011, I-Dodici-Reformatori 1567, 1574; Urdang, 1951). The kingdoms of Aragon and Valencia in Spain soon adopted these standards.

In this context, it prevailed among physicians a preference for expensive complex medicines prepared with exotic products and an underestimation of cheaper local wild medicinal plants. One of the aphorisms of the school of Salerno outlines this: *Res dare pro rebus, pro verbis verba solemus. Pro vanis verbis, montanis utimur herbis. Pro caris rebus, pigmentis et speciebus* that could be translated as "things pay for things, words pay for words in kind. For vain words give the cheapest herbs you find (the herbs in the mountains). For high fees give such precious drugs, as are pigments and spices" (Meaux-Saint-Marc, 1861; Odronaux, 1870).

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However, since early 16th century CE, the works of Ruel (Ruellio) (1516) and Fuchs (1542) critically revised the European *materia medica* followed by the numerous editions of Matthioli (1544, 1549, 1563, 1573) in Italian or in Latin (id. 1565), and the Spanish versions of Jarava (1557) and Laguna (1555, 1566, 1570) (Fig. 1). Overall, these works revalorized numerous local wild plants, always referring to the authority of the encyclopedic work of Dioscorides, compiled in the first century CE. In addition, these works gave a new approach to the use of medicinal plants, focusing on European species, questioning complex mixtures that included many Asian species (due to the frequency of fraudulent substitutions), and opening the door to the introduction of American species.

Leonti et al. (2009) mention that Dioscorides' *De Materia Medica* had few or no competition for most of the time, and therefore, this book was able to homogenize knowledge about medicinal plants all over Europe and the Mediterranean.

Recently, one of the present authors (Candelaria Moreno) recovered from the Provincial Archives of Albacete (Spain) several manuscripts dated from the 16th century CE onward pertaining to the area of pharmacy. These manuscripts were a promising source of information, geographically localized, for comparison with the contemporary pharmacopoeias to determine the degree of uniformity in medicines in use in Europe, and with medicinal ingredients and uses recorded in ethnobotanical studies between 1995 and 2002 in the same area.

Furthermore, these included the "Arancel" of medicines A1526 (Fig. 2). "Arancel" in Spanish means a kind of tax, also an official price, which determines the amounts to be paid for various services or goods, or established to remunerate certain professionals (Real Academia Española, 2016). The A1526 is a list of official prices for medicines sold in Albacete and therefore offers a much more precise information than the list of taxes imposed to all imported goods in Granada in 1501, which only included some drugs (Trillo, 1996).

Ethnobotany and ethnopharmacology of Albacete have been a subject of different studies, articles, and books (Fajardo *et al.*, 2000; Rivera *et al.*, 2006; Verde 2002; Verde *et al.*, 1998, 2008). These studies and historic manuscripts offer an opportunity, difficult to equal, for the comparison of relationships between the pharmacy at the time immediately previous and later to that of Laguna and Matthioli, the subsequent stages of *materia medica* and present ethnobotany. However, to obtain a

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better representation of this evolution, it is necessary to broaden the range of samples in terms of geography, chronology, and systems of medicine.

This paper has two overarching aims: (1) presenting the results of studying the tariff and (2) broadly analyzing the origin and influences of medicinal traditional knowledge focusing on Albacete. Our first target was to determine the ingredients used in the pharmacy in the 16th century CE in Albacete and, second, how long ancient formulations, ingredients, and uses from the pharmacy and herbals persisted in later periods, and to determine their influence in the present pharmaceutical ethnobotany.

2 Material and Methods

2.1 General procedure

We summarize in Fig. 3 and explain in detail in the next section the sequential process of analysis that we follow to address the above objectives.

Starting from the document A1526, to determine the differential presence of ingredients, formulations, and uses in well-characterized sources at different periods, we “a priori” selected to test the following:

Renaissance herbals and pharmacopoeias. Pharmacopoeias, herbals, and inventories of local pharmacies, showing strong medieval influence, and of late-Renaissance renewal of herbalism and medicine (16th to early 18th century CE).

Old phytotherapy. Pharmaceutical sources from mid-18th to early 20th centuries CE, where plants were still substantial part of the materia medica.

Modern phytotherapy. Here, we included modern evidence-based phytotherapy (21st century CE) and other alternative approaches such as naturopathy, which employ medicinal plants.

Ethnobotany and folk medicine. Here, we included present medical ethnobotany in Albacete and Alta Valle del Reno (border between Tuscany and Emilia Romagna, Italy). In addition, we analyzed different marginal groups, which along the history of Spain, practiced alternative or complementary systems of medicine (local healers, “Moriscos” and Sephardic).

As we intend to compare a large number of sources based on the presence/absence or on frequencies of 187 ingredients, it is necessary to use statistical techniques. To confirm that the detected relationships are not simply an artifact of the calculation procedure, we used four different methods that complement each other and provide consistency if their results are matched.

2.2 Data collection

2.2.1 Manuscripts analyzed

The number of basic manuscript documents that are analyzed is five. First, the Tariff of Medicines approved in Albacete in 1526 (A1526) (Fig. 2) (known as *Arancel*, AHPAB, MUN.C.125) [cited as Albacete 1526 in Figs.] (Supplementary Table 1).

Second, the inventory made by the pharmacist Custodio José Carvajal of the tools, books, vases, and medicinal materials of a pharmacy in El Bonillo (Albacete) in 1711 (Hernández, 2007; AHPAB C 3525) [cited as El Bonillo 1711 in Figs.].

Third and fourth, the inspection acts in 1881 and 1910 for the pharmacies of Andrés Picazo [cited as Albacete 1881 in Figs.] and Jesús Leal [cited as Albacete 1910 in Figs.] in Albacete (AHPAB, MUN.C.125), respectively.

Fifth, the collection of recipes attributed to physician Miguel Tendero at Mula (Murcia) c. 1790 (González, 1996) [cited as Mula Manu 1790 in Figs.]. The last four manuscripts represent different Old phytotherapy approaches.

2.2.2 Bibliographical sources

Further, we analyze inventories, dated 16th and 17th centuries CE, of medicinal products from three pharmacies in Granada (De-la-Obra et al., 2009; Luque et al., 2006) [cited as Granada 1556 in Figs.], Zaragoza (Andrés, 1991) [cited as Zaragoza 1601-1609 in Figs.], and Castile (Madrid) (Davis and López, 2010) [cited as Castile 1599 in Figs.].

We included from Murcia the materia medica of 1823 (Authenac, 1823) [cited as Murcia 1823 in Figs.]. We analyzed the *Ricettario Fiorentino* (first European pharmacopoeia) using the editions of 1498 (College of Physicians, 1498; Fittipaldi, 2011), 1567 and 1574 (I-Dodici-Reformatori, 1567; 1574) (Fig. 4) [cited as Florence 1498-1574 in Figs.].

We confirmed ingredients in A1526 by analyzing the pharmacopoeias of Barcelona (Domenech and Pau, 1587; Duch, 2000) [cited as Barcelona 1511-1587 in Figs.], Valencia (Valentian College of Pharmacists 1601) [cited as Valencia 1601 in Figs.], and Zaragoza (Moliné, 1998, Sagaun and Aznarez, 1546) [cited as Zaragoza 1546 in Figs.]. However, from these sources, we only obtained lists of ingredients with Latin or Spanish pharmaceutical names.

We retrieved and downloaded from seven online repositories: Archive (2015), *Biblioteca Digital Hispánica* (BNE, 2015), *Bibliothèque numérique Medica* (Medica, 2015), Biodiversity Heritage Library (BHL, 2015), *Digitale Bibliothek* (GNM, 2015),

Gallica (2015), and Google Books (Google, 2015), classical texts, cited above, and those used to determine pathologies.

2.2.3 Data from other historical sources

Another challenge was to document the medicinal species used outside the main pharmaceutical circuits, in the 16th century CE and later. The *Relaciones mandadas hacer por Felipe II* (Carrilero et al., 2014), which is a systematic census of resources of the kingdom of Castile, contains information explicitly “not included in the pharmacists’ manuals”, of medical relevance, but scarce. Three marginal groups exist in the Castilian society: Moors, healers, and witches; and Sephardic communities had reputation of heterodox medical knowledge.

1- Sephardic. We analyzed the “*Sefer Refuot*” tradition of folk medicine among Sephardic communities in the Mediterranean (assuming these can reflect pharmaceutical knowledge of Jews before their expulsion from Spain in 1492). Sephardic communities compile traditional remedies in Judeo-Spanish. Such compilations appeared in Salonica (Greece) in 1855, Istanbul and Smyrna (Turkey) in 1870 and 1878 (Albarral, 2014; Levy and Levy, 1991; Romeu, 2010; Shaul, 1986; 1992) [cited as Sephardic in Figs.].

2- Moors. Several manuscripts of the 16th century CE contain exhaustive lists of medicines used by the Moors (*Moriscos*) of Valencia (Labarta, 1981; Labarta and Barceló, 1988) and Castile (Vázquez, 1994; Vazquez and Bustos, 1998) [cited as Moors Valencia 1570 in Figs.]. Numerous Moors were conventional physicians in the Christian kingdoms of Spain for centuries. However, during the 16th century CE, their activities became suspicious and marginal, before their prosecution and expulsion from Spain (Moriscos, 2016; Pérez, 2014).

3- Healers. The “*Inquisición*” tribunals were active from late 15th until the beginning of the 19th century CE. In their records, the medicines used by healers and witches in their activities are directly documented (Blázquez, 1991; Cirac, 1942; Laza, 1958) [cited as Healers and Witches 1500–1700 in Figs.]. The archives of the *Consejo de Inquisición* (Alonso, 2016) consist of 1345 books and 3621 files that are now at the *Archivo Histórico Nacional*, plus those of the numerous territorial tribunals (Toledo, Sevilla, Llerena, Granada, Zaragoza, etc.). Some, like those of Zaragoza (Iranzo, 2011), are available online. The information from the tribunal of Toledo (Cirac, 1942) is particularly useful in terms of medicinal ingredients.

2.2.4 *Present ethnobiological data*

1 The document A1526 clearly belongs to the Italian tradition (medical school of
2 Salerno). It follows the standards codified in Florence and later adopted in Spain. Thus,
3 we analyzed the ethnobotanical studies of Albacete and a similar ethnobotanical
4 context in Toscana-Emilia Romagna geographically close to Florence. However, to
5 generalize our hypotheses, more ethnopharmacological studies should be used.
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10 The ethnobiological catalog of 358 medicinal plants (including other drugs from
11 zoological and mineral origin) for Albacete is based on records collected in open semi-
12 structured interviews, which were conducted in Albacete province (Spain) (38°15'–
13 39°15' N, 0°54'–2°54' W, average elevation 700 m) from 1995 to 2002. This
14 information is compiled, and voucher specimens cited by Verde (2002) are deposited in
15 herbarium ALBA (University of Castilla La Mancha, Spain) (numbers in
16 Supplementary Table 2) [cited as Albacete 1995 in Figs.].
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20 Similarly, the catalog of 116 medicinal substances is analyzed and recorded as
21 used in rural areas of Alta Valle del Reno (Italy) (44°05'–44°11' N, 10°54'–11°06' E,
22 average elevation 700 m) (which also includes local drugs from zoological origin). This
23 information is compiled, and voucher specimens cited by Egea (2016) are deposited in
24 herbarium FIAF (numbers in Supplementary Table 2) (University of Firenze, Italy)
25 [cited as Alta Valle del Reno 2014 in Figs.]. We expect that the pharmaceutical culture
26 reflected in the successive Florence pharmacopoeias could have influenced Alta Valle
27 del Reno even more closely than Albacete.
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30 2.2.5 *Data from Modern phytotherapy approaches*

31 We analyzed three different modern phytotherapy approaches. First, the catalog
32 of herbal substances designated for assessment by the European Medicines Agency's
33 committee on Herbal Medicinal Products (HMPC) and the European Union herbal
34 monographs, which offer a list of substances of present medical interest at an European
35 level (EMA, 2014) [cited as EMA 2014 in Figs.]. According to EMA (2014), because
36 herbal substances are obtained from plants, algae, fungi, and lichens, they implicitly
37 exclude substances of zoological and mineral origin.
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41 Second, we analyzed the catalog of herbal products available in the Spanish
42 market (Fitoterapia.net, 2015) [cited as Fitoterapia.net 2015 in Figs.]. This eclectic and
43 comprehensive list includes almost every one herbal product and ingredient available in
44 pharmacies and herbal shops of Spain. Here, the concept of herbal is wider, comprising
45 substances like propolis, royal jelly, or medicinal clay.
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1 Third, we analyzed Vander (1971) who was highly influential in Spain's folk
2 medicine in the 1970s and later on (Rivera and Obón, 1996) [cited as Vander 1971 in
3 Figs.].
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5 2.2.6 *Data on Medicinal uses* 6

7 The list A1526 does not contain references to a determined use of the 101
8 medicines. However, we assume that medicinal uses of the medicines in A1526 were
9 those described in contemporary sources. Therefore, we analyzed the sources such as
10 Alonso de Chirino, died in 1431; whose book "*Menor Daño de Medicina*" appeared in
11 numerous editions during the 15th and 16th centuries (Herrera, 1973) [cited as Chirino
12 c. 1490 CE in Figs.].
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18 Andrea Matthioli (1549) and Andrés Laguna (1555) present similar medicinal
19 uses attributed to Dioscorides in each monograph of single ingredients (simples) [cited
20 as Dioscorides 1st cent CE in Figs.]. In addition, Matthioli and Laguna record different
21 contemporary medicinal uses [cited as Matthioli 1549 CE or Laguna 1555 CE in Figs.].
22 Laguna (1555) closely follows Matthioli (1549) presenting, first, in regular characters
23 the Spanish translation of each Dioscorides' monograph, presumably from a Latin
24 version of the Greek original, and second, in *italics*, the comments and uses by Laguna
25 and their contemporaries. These were sometimes similar and, often, different.
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32 We ensured that separate indications are attributed to Dioscorides (which are
33 almost identical in both analyzed versions of Laguna (1555) and Matthioli (1549)) from
34 those annotated by Laguna or Matthioli from their personal experiences. To verify
35 ingredient names, images, and uses by Matthioli and Laguna, we similarly revised other
36 editions cited in the introduction of this paper and listed in the references.
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42 2.3 *Geographical coverage and Maps* 43

44 Overall, consulted sources concentrate in Spain and Italy (Fig. 5). We draw
45 maps using The Generic Mapping Tools (2014). The EMA (2015) has published
46 HMPC monographs in Brussels and London. It has established each particular
47 monograph on data collected from all over Europe and therefore does not represent
48 knowledge specifically developed in Brussels or London. However, it is here
49 georeferenced linked to Brussels (the capital city of the European Union) (Fig. 5).
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54 2.4 *Standardization of data* 55

56 2.4.1 *Identification of formulations, ingredients and species* 57

58 At the beginning of the 16th century CE, pharmaceutical formulations in
59 European countries were subject to standards established, first, in the pharmacopoeia of
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Florence (Italy) in 1498. This and other pharmacopoeias specify for each formulation the list of ingredients, their quantities, preparation procedures, and often, indications. Further, the pharmacopoeias include for each ingredient a monograph defining criteria of quality and purity (Rodríguez et al., 2012). Therefore, to analyze this “*Arancel*” further, and to identify species and ingredients, we assessed contemporary (15–17th centuries CE) Spanish and Italian pharmacopoeias.

There is always a doubt: how reliable is the species-level identification of a pre-Linnaean description, for example, of a rose or a grass? Yet, due to their relevance as drugs, it is possible to follow in detail the history of each one of these 187 ingredients. The works of Clusius (1601), Bauhin (1671), and Tournefort (1700) “*Institutiones rei herbariae*”, in chronological sequence, are particularly relevant for this purpose.

Linné analyzed these works and gave the modern equivalence of names in his *Materia Medica* (Linnaeus, 1749; Schreber, 1782) and “*Species Plantarum*” (Linnaeus, 1753). Scientific names of vascular plants were subsequently actualized using the *Farmacopea Española* (Real Academia de Medicina, 1865) and others (Davis and López, 2010; Haller, 1771; Kew, 2016; López, 2015; Rivera et al., 2012; WHO, 2015).

However, for 10% of ingredients, depending on the resources consulted (including standard pharmacognosy literature), we reach quite different identifications (different species but also different genera) (Suppl. Table 2). This uncertainty mainly affects exotic imported ingredients whose origins were unknown to the pharmacists.

Healers and witches between 1500 and 1700 and Sephardic, and Mula Manu in 1790 used Spanish vernacular names. We analyzed particularly their coincidence with those in Albacete 1526 or the Spanish names recorded for the ingredients in the pharmacopoeias and those by Laguna (1555) or Verde (2002).

We assessed taxonomic and nomenclatural veracity by comparing with existing standard regional floras, and with the botanical literature available at BHL (2015), and databases (Anthos, 2015; Euromed, 2011; GRIN, 2015; IPNI, 2005; NCBI, 2013; Tropicos, 2012) and, most importantly, standardized according to The Plant List (2015) and to the procedures suggested by Rivera et al. (2014). It was not necessary to develop a strategy for resolving conflicts between The Plant List and other taxonomic reference works because we did not detect any such conflicts for the species treated.

However, concerning *Corylus* nuts, we adopted the distinction in four categories made by Miller (1752) between hazelnuts (*Corylus avellana* L.), cobnuts (hybrids *C. avellana* x *C. maxima*), filberts (*C. maxima* Mill.), and large Spanish nut (*C. hispanica*

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Mill. ex D.Rivera et al.). This last (*Corylus hispanica*) supplied the “avellana” nuts used in the pharmaceutical formulations of the 16th and later centuries CE in Spain (Rivera et al. 1997).

Groups of plants and other ingredients with similar qualities and uses (i.e. ethnotaxonomic species complexes or pharmaceutical names of drugs), which in historical texts, are often described in one chapter. We identified these collectively using an inclusive scientific taxon name. Thus, the identification was not restricted to “the label species”. For example, “Dragacanthi” was identified in the sense of *Astracantha gummifera* (Labill.) Podlech/*Astragalus clusii* Boiss, “Gálbano” as *Ferula gummosa* Boiss. (incl. *Ferulago galbanifera* (Mill.) W.D.J.Koch) or “Sticados” as *Lavandula stoechas* L./*Thymus moroderi* Pau ex Martínez. For modern ethnobotanical sources, we computed the presence when the use of at least one of the species of the complex was documented. This had minimal influence on the analysis because these complexes have very low representation in ethnobotanical sources analyzed.

Drugs from zoological and mineral origin appear, with different relevance, in all sources analyzed except EMA (2015). We updated mineral ingredients nomenclature according to the New International Mineralogical Association List of Minerals (IMA, 2016) and Duffin et al (2013), and ingredients of zoological origin using the Global Biodiversity Information Facility (GBIF, 2015).

2.4.2 Standardized Medicinal uses

Pathologies were determined according to the different studies of paleopathology and history of medicine cited by Martínez-Francés et al. (2015). In respect to standardization of indications and pathologies, we adopt in the present review the standards of the ICD-10 (International Statistical Classification of Diseases and Related Health Problems 10th Revision) (WHO, 2014).

2.5 Data Analysis

2.5.1 Presence of ingredients of the A1526 tariff in other sources

Once the list of 187 ingredients of Albacete tariff 1526 [Albacete 1526] was determined, we proceeded to determine their presence/absence in a set of other 21 sources (Figs. 6–8). In the analysis, we did not use the complete lists of ingredients of all sources. The sources represent, a priori, the following main four categories:

Renaissance herbals and Pharmacopoeias. Pharmaceutical sources with strong medieval influence or associated to the late Renaissance renewal of medicine: Four pharmacopoeias [Barcelona 1511–1587, Florence 1498–1574, Valencia 1601, and

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Zaragoza 1546]. Four inventories of pharmacies [Castile 1599, El Bonillo 1711 (which is transitional to next category), Granada 1556, Zaragoza 1601–1609]. Herbals [Laguna 1555] (identical in terms of ingredients with Andrea Matthioli (1549)).

Old phytotherapy. Later pharmaceutical sources where plants were still a substantial part of the materia medica: two inventories of local pharmacies [Albacete 1881, Albacete 1910] and one eclectic list of *Materia Medica* [Murcia 1823].

Modern phytotherapy (EMA and Naturopathy). This includes modern evidence-based phytotherapy (21st century CE) in the form of the official list of monographs by the European Medicines Agency [EMA, 2014]. We also analyzed the catalog of herbal products available in Spain [Fitoterapia.net 2015] and a 20th-century CE naturopathy book of medicinal plants [Vander 1971].

Ethnobotany and Folk Medicine. Ethnobotany is represented by Albacete province (Spain) 1995–2015 [Albacete 1995], and Alta Valle del Reno (Italy) 2012–2015 [Alta Valle del Reno 2014]. Folk medicine here includes, a priori, four sources attributable to alternative or complementary systems of medicine: First, local healers (remedies recorded by the Spanish Inquisition in Castile) [Healers and witches 1500–1700]. Second, physician-Moors in Valencia 1573–1593 [Moors Valencia 1570]. Third, the Sephardic Tradition [Sephardic]. Fourth, the recipes in a manuscript dated c. 1790, which is an apocryphal attributed to the authority of Dr. Fr. Miguel Tendero, who served as a physician in Mula (Murcia) c. 1760 [Mula Manu 1790] (Gonzalez, 1996).

As described later, the “a priori” ascription of some of the above sources to the four main categories will require further examination because of the results of our analyses.

The 187 variables are the different ingredients determined (Supplementary Table 2). For each one of the 22 units (the 22 sources), the presence/absence of each ingredient of the Albacete tariff of 1526 is determined. Therefore, it represents the possibility of reproducing similar drug compounds in terms of the availability of crude drugs. The result is a crude matrix of presence/absence of ingredients (Supplementary Table 3).

2.5.2 Geographical origin of ingredients in A1526

Each ingredient of the Albacete tariff 1526 was identified and classified in terms of local (widely available in Western Europe through cultivation or collection in wild populations) or imported (exotic product only available in Europe through long-distance commerce) (Fig. 6). We linked these to their main biogeographical profiles

1 and zones of origin (Fig. 7) as Widespread, Eastern Asiatic, Euro-Siberian, Indian,
2 Irano-Turanian, Malaysian, Mediterranean, Paleotropical, Saharo-Arabian, Sudano-
3 Zambezi, according to Rivera et al. (2012) and GBIF (2015).
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5 The 22 sources analyzed were georeferenced using Google Earth®. The tool
6 Ruler–Line allowed to measure the distance between Albacete and the rest of localities
7 on the ground (Fig. 8).
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9 *2.5.3 Weighting of the different ingredients in the A1526 tariff*

10 In addition to the presence/absence of ingredients, we have identified the
11 number of formulations in which each ingredient appears. Several ingredients appeared
12 in more than one single formulation in the 101 single and compound medicines of the
13 tariff A1526. This allows producing a list of ingredients in the order of decreasing
14 frequencies. We then calculated the weight of the ingredients for each of the remaining
15 sources by following the same criteria (Supplementary Table 4).
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18 We also produced a list for the ensemble of ethnobotanical medicinal plants and
19 other resources of Albacete and their frequencies on the base of available evidence.
20 These frequencies, however, are not equivalent. The frequencies in the tariff only give
21 us an idea of multivalency of each ingredient within the set of the listed medicines.
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23 We calculated the ethnobotanical data frequencies in terms of the sum of the
24 number of remedies in which each informant uses this ingredient, along the entire set of
25 informants. Therefore, we only use them to establish a ranked list of the 25 most
26 important ingredients in each context (Table 1). In addition, we determined the core
27 ingredients within the set of sources in terms of the number of sources that reported
28 each, which ranges between 2 and 21 (Table 1).
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30 *2.5.4 Ordination and classification of sources based on the lists of ingredients*

31 To determine how different these 22 sources are, considering as a reference the
32 187 ingredients of the Albacete 1526, we calculated the pairwise differences between
33 samples in form of a dissimilarity matrix.
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35 The crude matrix of presence/absence of ingredients was used to compute a
36 dissimilarity matrix using Darwin 6 V.6.0.9 (2015-04-15) (Perrier, Flori & Bonnot,
37 2003; Perrier & Jacquemoud-Collet, 2006).
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39 The Sokal-Sneath dissimilarity index was calculated ($d_{ij} = \frac{2(b+c)}{a+2(b+c)}$), where d_{ij} is the dissimilarity between samples i and j , a : number of
40 variables where $x_i =$ presence and $x_j =$ presence, b : number of variables where $x_i =$
41 presence and $x_j =$ absence and c : number of variables where $x_i =$ absence and $x_j =$
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absence. The dissimilarity is =0 for two samples sharing the 187 ingredients and =1 for two samples that present 0 ingredients shared.

For this index, “presence” modality is only informative, while “absence” modality mainly expresses an absence of information. This index considers that a common absence for two units is uninformative to measure their dissimilarity (Perrier & Jacquemoud-Collet, 2006). Therefore, similarity here reflects the number of coinciding ingredients, and dissimilarity is inversely proportional to this.

These pairwise dissimilarities can be represented in a multidimensional space, but to obtain meaningful graphic representation of these relationships in a two-dimensional plane, we used factorial and cluster analysis.

We used an ordination method, principal coordinates analysis (from now abbreviated in the text as PCoA), to obtain an overall representation of diversity within samples with the lowest possible dimensional space. PCoA can be viewed as a more general form of principal components analysis (abbreviated as PCA) that provides a direct ordination of the samples and is useful in situations where there are more variables than samples (Kovach, 2007). In general, the first axes (3 or 4) summarize a large part of the complete space information. Planes of axis 1-2, 1-3, 2-3... are sufficient to exhibit the main structure of the data. The part of information retained by each axis is given by the percent inertia (the eigenvalue of this axis on the sum of all eigenvalues) (Perrier & Jacquemoud-Collet, 2006) (Fig. 9).

Factorial analysis family, including PCoA, offers a consistent ordination of samples. However, the definition of groups that we represent with circles in the figures is still a heuristic process and requires the use of more precise techniques to obtain a classification.

Cluster analysis is a term used to name a set of numerical techniques in which the main purpose is to divide the objects of study into discrete groups according to the characteristics of the objects (Kovach, 2007).

We used the agglomerative hierarchical method that arranges the clusters into a hierarchy so that the relationships between different groups are apparent. Minimum variance clustering (Ward’s method) focuses on determining how much variation is present within each cluster. Thus, the clusters will tend to be as distinct as possible because the criterion for clustering is to have the least amount of variation (Kovach, 2007) (Fig. 10). Ward’s method produces a single tree.

1 To further reduce the uncertainty in the structure of the tree, we used a
2 bootstrapped matrix (20,000 bootstraps) and a tree construction method that uses the
3 trees inferred from these bootstrapped dissimilarities to assess the uncertainty of the
4 tree structure.
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7 The Neighbor-Joining method proposed by Saitou and Nei (1987) uses the
8 criterion of relative neighborhood, weighted average for dissimilarity updating, and
9 adjustment to an additive tree distance. A bootstrap value is given to each edge that
10 indicates the occurrence frequency of this edge in the bootstrapped trees. Bootstrap
11 values range between 0 and 100 (Fig. 11). High bootstrap values supporting an edge
12 (near 100) represent high consistence of the cluster to the right of this edge; on the
13 contrary, low scores (particularly below 40) imply that data do not support this
14 particular cluster.
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21 *2.5.5 Assessing the influence of classical sources and Modern phytotherapy in* 22 *ethnobotanical records* 23 24

25 We further used another method of the factorial analysis family to contrast the
26 hypotheses for the influence of classical sources and Modern phytotherapy in
27 ethnobotanical records. To simplify, we labeled samples according to three main
28 categories by cultural context: Pharmaceutical classical (PHCL) that includes
29 **Renaissance Herbals and Pharmacopoeias** and **Old phytotherapy**. Ethnobotanical
30 (ETHN) that includes **Ethnobotany and Folk Medicine**. Pharmaceutical modern
31 (PHMO) that includes **Modern phytotherapy (EMA and Naturopathy)**. According
32 to the origin of information, the uses were labeled as hypothetically dependent (DEP)
33 or as a, presumably, source (SOU).
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42 Among the above, we classify as either influential sources of information
43 (herbals, pharmacopoeias, and popular books) (SOU) or as dependent (marginal
44 systems, ethnobotanical data and, evidently, catalogs and tariffs of medicines which
45 obviously were subject to pharmacopoeial standards) (DEP). Therefore, dependent
46 sources would hypothetically cluster closer to their direct sources. We also aim at
47 determining relative distances between sources classified as either PHCL, ETHN, or
48 PHMO (Fig. 12).
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54 With this purpose, we used a second crude matrix based on the weighting of
55 each ingredient to compute correspondence analysis using FactoMineR: an R package
56 for multivariate analysis (Husson et al., 2009; Lê, et al., 2008). Correspondence
57 analysis is conceptually similar to principal component analysis (PCoA), but applies to
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categorical rather than continuous data and distance is “Chi-squared” measure. The chi square dissimilarity index was calculated. This measure expresses a value x_{ik} as its contribution to the sum x_i on all variables and is a comparison of unit profiles.

$$d_{ij} = \sqrt{\sum_1^k \frac{x_{..}}{x_{.k}} \left(\frac{x_{jk}}{x_{.i}} - \frac{x_{jk}}{x_{.j}} \right)^2}$$

where d_{ij} : dissimilarity between units i and j ; x_{ik} , x_{jk} : values of variable k for units i and j ; $x_{.i}$, $x_{.j}$, $x_{.k}$: mean for units i and j or variable k ; $x_{..}$: overall mean. K : number of variables.

In many comparative studies, correspondence analysis provides an optimal summary of the structure of the original data (Kovach, 2007). Similar to that in PCoA, we graphically represented relationships against the main axes (Fig. 12).

2.5.6 Bayesian analysis of ingredients

The study of the evolutionary history and relationships among different versions of the materia medica in general and of the evolution of the A1526 list of ingredients can be improved, in particular, using the phylogenetic inference methods, which are routinely used in the study of relationships among individuals or groups of organisms (e.g. species, or populations). Thus, we, further, recurred to Bayesian methods, which offer the possibility of working in terms of likelihood, credibility, and conditional probabilities.

Despite being controversial, Bayesian analysis has been applied to the detection of over and underused taxonomic groups in ethnobotany and ethnopharmacology (Leonti et al., 2012; Moerman, 2012; Weckerle et al., 2011; 2012).

Here, we wanted to compare different lists of ingredients with reference to the A1526 to generate a phylogenetic classification that reflects the relationships and dependencies between those lists in terms of deletions of the 187 basic ingredients, from an evolutionary perspective.

We could translate here the Darwinian idea of “survival of the fittest” as “Survival of the ingredient that will leave the most copies of itself in successive generations”. Therefore, “which will be used most often, in most formulations and by most people”. Nevertheless, we must not exclude non-Darwinian models, considering that part of the materia medica evolution is likely random, in parallel with neutral mutation and genetic drift (King and Jukes, 1969) in genes and organisms.

1 For this analysis, we utilized the current version of MrBayes 3.2.6, released
2 November 25, 2015. MrBayes is a program for Bayesian inference and model choice
3 across a wide range of phylogenetic and evolutionary models.
4

5 MrBayes uses Markov chain Monte Carlo (MCMC) methods to estimate the
6 posterior distribution of model parameters (Huelsenbeck et al., 2015; Ronquist et al.,
7 2011). A Markov chain is a mathematical model for stochastic systems whose discrete
8 or continuous states are governed by a transition probability. The current state in a
9 Markov chain only depends on the most recent previous state. Monte Carlo is the art of
10 approximating an expectation by the sample mean of a function of simulated random
11 variables (Anderson, 1999).
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18 In phylogenetics, an outgroup is a group of organisms that serve as a reference
19 group when determining the evolutionary relationship among three or more
20 monophyletic groups of organisms. We use outgroup as a point of comparison for the
21 ingroup—the set of organisms under study—that specifically allows the phylogeny to
22 be rooted. Because the polarity (direction) of character change can only be determined
23 on a rooted phylogeny, the choice of outgroup is essential for understanding the
24 evolution of traits along a phylogeny. Therefore, an appropriate outgroup must be
25 unambiguously outside the clade of interest in the phylogenetic study, but they must be
26 related to the ingroup, close enough for meaningful comparisons to the ingroup
27 (Wikipedia, 2016). In our case, we added a pair of extra samples based on the Hawaiian
28 traditional pharmacopoeia (Bishop Museum, 2015; Hilgenkamp and Pescaia, 2003),
29 and the Chinese Materia Medica (Hempfen and Fischer, 2007; Hsu et al., 1986), which
30 are supposed to be relatively unrelated with the different sources analyzed (Fig. 13).
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42 For taking full advantage of the possibilities of analysis available in Mr. Bayes,
43 we adopted the DNA 4×4 nucleotide model assuming that phylogenetic models are
44 appropriate to describe historical and cultural transitions in materia medica preferences
45 (Supplementary Tables 5a and 5b). Therefore, we assume the conversion of the
46 weighted ingredient list into an ACGT nucleotide chain with substitution rates, but
47 excluding insertions, and deletions.
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53 Thus, we, first, diagonalized the matrix ordering samples in columns by
54 decreasing number of ingredients (left to right) and ingredients in rows by decreasing
55 number of samples in which the ingredient was present (from top to bottom). Second,
56 we converted values of variables (frequencies of each ingredient in each source = $f(i)_s$)
57 in four categories as follows: $f(i)_s = 0$, coded as A; $1 \leq f(i)_s \leq 3$, coded as C; $4 \leq f(i)_s \leq 6$,
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1 coded as G; $7 \leq f(i)_s \leq 14$, coded as T (Supplementary Tables 4 and 5). With transition
2 rates set as follows, first A-C= 2, A-G= 5, A-T= 8, C-G= 3, C-T= 7, G-T= 4, and
3 second A-C= 8, A-G= 5, A-T= 2, C-G= 7, C-T= 3, G-T= 6. With the above, we
4 adopted a heuristic approach to facilitate the use of models in which we assume that
5 transition rates are either directly or inversely proportional to the frequencies. Note that
6 converting absence = $f(i)_s = 0 = A$ is not a neutral decision. This way we transform the
7 coincidence in missing ingredients for each pair of samples in informative, it is
8 computed and may influence the general structure of the tree. We could alternatively
9 have treated absence as a gap or as missing information. Hence, it is relevant to
10 compare previous results of presence/absence matrix with those of our Bayesian model.
11

12 We addressed the model uncertainty by model averaging using reversible-jump
13 MCMC (rjMCMC), where the chain integrates over the joint prior probability density
14 of a given model in the usual manner, but also jumps between all 203 possible
15 candidate substitution models, visiting each model in proportion to its marginal
16 probability (Huelsenbeck et al., 2004).
17

18 The pool of candidate models is calculated by the Bell number, which for n
19 elements is the sum of the Stirling numbers of the second kind (Bell, 1934a, b). The
20 Markov chain sampling over the space of all possible reversible substitution models,
21 including the GTR model, and all models derived from it, by grouping the six rates in
22 various combinations, waives the restrictions imposed when choosing a single
23 substitution model. We did not observe the differences in the structure of the resulting
24 tree with transition rates either inversely or directly proportional to the frequency of
25 ingredients.
26

27 2.5.7 Medicinal use comparison

28 To determine dissimilarities and coincidences in the medicinal uses, because of
29 the effort required, we could not review the use of the 187 ingredients; hence, we
30 analyzed a subset of 10 ingredients. This subset presents the characteristic of being the
31 most relevant (frequent) in the two contrasting sources: Arancel of 1526 and modern
32 ethnobotany of Albacete.
33

34 Of the 187 ingredients, we selected the top 10 which in decreasing order of
35 frequency appeared both in the two key lists (A1526 and modern ethnobiological
36 records of Albacete) (Table 1). Therefore, we generated five different lists of uses for
37 each one of the 10 ingredients (Dioscorides, Chirino, Laguna, and Matthioli) and the
38 Albacete's ethnobotanical one.
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1 We calculated for each ingredient and source the number of different diseases
2 treated belonging to each one main category of diseases and related health problems of
3 ICD-10 (WHO, 2014) (Fig. 14).
4

5 We systematized information in a crude matrix with 46 units, which are
6 different versions of 10 ingredients (I) from five different sources (S) and 20 variables
7 (K) which are categories of diseases and related health problems (Supplementary Table
8 6). Variables received values ranging between 0 and 100 representing the percentage of
9 the total medicinal uses recorded for each unit. Therefore, 100 means that in this unit,
10 100% of uses concentrate in one single ICD-10 main category.
11

12 We must emphasize that each ingredient is treated in five separate versions
13 (codified in Fig. 15A with the abbreviations of the five sources analyzed) to check
14 whether their uses coincide in this analysis. There are only 46 versions for the 10
15 ingredients instead of 50 because Chirino does not mention uses for *Rosmarinus* and
16 *Olea*, and Matthioli did not mention contemporary uses of honey and saffron. We do
17 not conclude that no such ingredients appear in Matthioli's works, but for these
18 simples, their uses are attributed in full to Dioscorides.
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20 We analyzed this matrix using the same methods described above for frequency
21 data. We drew a hierarchical tree with the Ward's minimum variance criterion (Fig.
22 15A).
23

24 Further, we summarized this matrix in one with five units (Supplementary Table
25 7), which are the 5 different sources and 20 variables simply by adding the values for
26 all ingredients in each variable of the previous matrix. Therefore, we calculated the
27 value of each cell (V) as follows:
28

$$29 V_{s,k} = \sum_{j=1}^n f(I_{j,k}),$$

30 where n is the number of ingredients reported useful for a category of diseases k within
31 a source s and f is the percentage of use for each ingredient. We analyzed this matrix
32 using the same methods described above for frequency data. We drew a hierarchical
33 tree with Ward's minimum variance criterion (Fig. 15B).
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35 **3 Results and discussion**

36 *3.1 The tariff of medicines of Albacete (Spain) in 1526*

37 The tariff (A1526) (Fig. 2) is mainly written in Spanish, with minor use of
38 Latin, following a Spanish writing style known as "*Procesal encadenada*", which was
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1 widely used in the 16th century in Spain in the notarial ambit and by the Audience
2 scribes.

3
4 It comprises a total of 101 different medicines with Spanish or Latin names that
5 appear classified into 11 main categories: (1) single or simple, (2) gums (and resins),
6 (3) syrups, (4) ointments, (5) preserves, (6) electuaries, (7) laxative (*Mediçinas*
7 *solutivas conpuestas*), (8) pills, (9) distilled waters, (10) oils, and (11) confections.
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11 Of these, 29 medicines are single ingredient, and 72 are more or less complex
12 mixtures of active ingredients. Simples receive in A1526 names similar to those used in
13 Laguna (1555, 1566, and 1570) (Supplementary Tables 1 and 2). Complex drug
14 combinations in A1526 receive the standard names of the epoch (Supplementary Table
15 1), influenced by Razi, Mesue and Nicolao (Anonymous, 1513 and 1519; De-Laredo,
16 1534; Razi, 1529; Sylvio, 1550), and their standardized composition is detailed in
17 contemporary pharmacopoeias.
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21 Each one formulation includes from 2 to 35 ingredients (on average 7.43,
22 standard deviation 7.44) (Supplementary Table 1) according to the standards of the
23 pharmacopoeias of Florence 1498, Barcelona 1511, Zaragoza 1546, and Valencia 1601
24 (Supplementary Table 2).
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28 It is remarkable the high degree of overlap in terms of medicines with the
29 pharmacopoeia of Florence. Of the 101 medicines listed (simple and compound), 97
30 appear in the pharmacopoeia of Florence 1498 (Fittipaldi, 2011; I-Dodici-Reformatori,
31 1567 and 1574). Lesser overlaps, 85, 84, and 60 respectively, are found with the
32 pharmacopoeias of Zaragoza 1546 (Moliné, 1998; Sagaun and Aznarez, 1546),
33 Valencia 1549–1601 (Valentian College of Pharmacists, 1601), and Barcelona
34 (Domenech and Pau, 1587; Duch, 2000).
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38 One hundred and eighty-seven different ingredients were involved in such
39 formulations (Supplementary Table 1). Ingredients are, in an 85% of plant origin, and,
40 in a 7.5% each, mineral or zoological substances. Over 90% of the organisms
41 investigated in ethnobotanical studies are vascular plants. The remaining 10% includes
42 animals, fungi, algae, microorganisms, minerals, and rocks (Rivera et al., 2014); thus,
43 proportions are similar to those in the list analyzed.
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47 Plant organs and substances most often involved in the formulations are as
48 follows: fruits and seeds 25.13%, aerial parts 14.44%, and gums and resins 11.76%,
49 and they differ from modern ethnobiological records in their percentages (Table 2).
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1 The ingredients of A1526 belong to 83 families of organisms (69 botanical and
2 14 zoological), whereas modern ethnobiological records in Albacete account to 102
3 families (99 botanical and 3 zoological).
4

5 Most frequent plant families in A1526 are Leguminosae (20.86% of drug
6 combinations), Apiaceae (20.32%), and Asteraceae (17.11%). It differs from modern
7 ethnobotanical records mostly in the high proportion of Leguminosae in A1526 and in
8 the absence of Cistaceae (Table 3).
9
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11 To note that zoological resources no longer recorded belong to the families
12 Bombycidae, Buthidae, Castoridae, Cervidae, Coralliidae, Elephantidae, Kerriidae,
13 Phasianidae, Physeteridae, Pteriidae, and Ursidae and the botanical ones to Acoraceae,
14 Adoxaceae, Altingiaceae, Amaranthaceae, Cannabinaceae, Capparaceae, Colchicaceae,
15 Combretaceae, Convolvulaceae, Dryopteridaceae, Fomitopsidaceae, Myristicaceae,
16 Nitrariaceae, Nymphaeaceae, Phyllanthaceae, Santalaceae, Styracaceae, and
17 Zingiberaceae.
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19 Imported ingredients from outside Europe are approximately 50%, and the rest
20 are locally produced (cultivated) or gathered in Albacete (Fig. 6), which notably differs
21 from modern ethnobotanical records. In Albacete 1995, above 90% of ingredients were
22 local and most were wild.
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25 The biogeographical profile shows the relevance of tropical regions of Asia and
26 Africa (Fig. 7) as sources of crude drugs, which in modern local ethnobotanical records
27 are irrelevant.
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32 We must emphasize that the profile of the knowledge of the Spanish population
33 in the rural areas is suffering in the 21st century a profound change in the sense of a
34 deep loss of knowledge associated with trivialization. This has led to the Spanish
35 authorities to start the Spanish inventory of traditional knowledge related to
36 biodiversity (Pardo et al., 2012).
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40 However, data collected in the villages of Albacete in the last decade of the 20th
41 century still reflect a rich and diversified local culture and is little influenced by
42 globalization (Verde, 2002). This explains the high proportion of local species.
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45 3.2 *Abandonment and persistence over time of ingredients and drug combinations*

46 Simples and, mostly, drug formulations recorded in A1526 gradually
47 disappeared with time, as these were no longer present in later catalogs. Figure 8 shows
48 how shared ingredients were rather more dependent on chronological than on
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1 geographical grounds, and decreased over time (process of deletion in evolutionary
2 terms).

3 Most complex mixtures essentially disappeared between 1600 and 1750 CE
4 (Table 4), although some persisted until 1910.

5 This does not mean that the whole set of ingredients of these mixtures
6 disappeared in parallel, because most persisted. However, numerous botanical and
7 zoological ingredients, and almost all mineral and fossil substances, to 33, were no
8 longer present in the analyzed repertories since 1750 and another 40 from 1910 onward
9 (Table 5). Most ingredients that were no longer in use were imported (41), but some
10 (23) are wild and a few ones (9) are locally cultivated.

11 Ingredients, largely of plant origin, to 114, are still in use (in the analyzed
12 sources) in Modern phytotherapy and/or local medical-pharmaceutical ethnobotany.
13 Thus, at present, nearly 61% of the A1526 ingredients remain as usual materia medica
14 (Tables 5 and 6).

15 Sixty-nine ingredients (from the 187 in A1526) (Table 6) are still in use in
16 medical ethnobotany sources. Most are locally cultivated (42); some (23) are wild
17 species, and a few ones (4) are imported from outside Europe. It is worth mentioning
18 that of these 69 ingredients, only 15 are exclusively found in ethnobotanical sources,
19 and the remaining 54 are also used in Modern phytotherapy.

20 Forty-five species and substances that are not persisted in local ethnobotanical
21 records are consulted but are still present in the naturopathic medicine and Modern
22 phytotherapy (Table 6) from another singular group. Most are imported (22), some (15)
23 are widely cultivated, and a few ones (8) are wild species. It is evident that especially
24 those wild or locally cultivated species from this last list are used in ethnobotanical
25 sources of Western Europe, although they were not recorded in our two samples
26 (Albacete and Alta Valle del Reno).

27 *3.3 Relationships of the 1526 tariff for medicines of Albacete (Spain) with other* 28 *catalogs, herbals, pharmacopoeias and ethnobotanical information based on* 29 *the ingredients*

30 Based on the presence/absence of ingredients, the principal coordinates analysis
31 (PCoA) of sources produced a graphical display where four groups are apparent (Fig.
32 9) with relatively low uncertainty. However, the adscription of Murcia 1823 and
33 Fitoterapia.net 2015 is doubtful.

1 Overall, the classification generated through hierarchical cluster using the
2 Ward's minimum variance criterion (Fig. 10) confirmed these four groups, but the
3 doubts about Murcia 1823 and Fitoterapia.net 2015 remain unsolved. Finally, the
4 weighted neighbor tree (Fig. 11) furnishes on the base of 20,000 bootstrapped trees the
5 level of support for the different groups and subgroups, and again adscription of Murcia
6 1823 and Fitoterapia.net 2015 remains doubtful. It is worthy of notice the high support
7 (97%) for the clade of **Renaissance Herbals and Pharmacopoeias** opposed to another
8 clade (with 99% support) that comprises the rest of sources.

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14 The correspondence analysis (Fig. 12 A), based on weighted presence of
15 ingredients, graphically represents the intermediate position of Murcia 1823 between
16 the **Renaissance Herbals and Pharmacopoeias** and **Old phytotherapy**, as a link
17 between both groups. Here we detect a similar intermediate position of Fitoterapia.net
18 2015 between **Ethnobotany and Folk Medicine** and the sources ascribed to Old
19 phytotherapy.

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25 Within the group of **Renaissance Herbals and Pharmacopoeias**, A1526 links
26 first with the pharmacopoeia of Florence 1498–1574, and other pharmacopoeias
27 (Concordia Barcinonese 1511–1587, Valencia 1601, and Zaragoza 1553), with a 95%
28 of support (Fig. 11).

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34 Other more or less contemporary and geographically close sources (Castile
35 Zamudio de Alfaro 1592–1599, El Bonillo 1711, Granada 1556, Zaragoza Hospital
36 1601–1609) slide down sequentially together with the Spanish Renaissance version of
37 Dioscorides' herbal (Laguna, 1555) and the recipes and lists of medicines written by
38 the seemingly marginal group of Moors from Valencia 1573–1593. Both conforming a
39 major group that receives a support of 97% (Fig. 11).

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44 We, a priori, included the Moors from Valencia 1573–1593 within
45 **Ethnobotany and Folk Medicine** category assuming their supposed marginal status.
46 However, both ordination (Fig. 9) and classification (Figs. 10 and 11) clearly show it as
47 part of the **Renaissance Herbals and Pharmacopoeias** group.

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53 Although marginal in social sources of Spain, the Moors practiced medicine and
54 used the simple and compound medicines according to their eastern Islamic traditions
55 and culture. Therefore, the Moors use the same medicinal ingredients as official
56 pharmacy of their epoch, deeply influenced by Islamic medicine, and, thus, show little
57 relationships with modern ethnobotanical records.

1 This cluster reflects a common cultural substrate of medicine and materia
2 medica in the 16th century CE, not only in Spain but also across Europe. The Salerno
3 school of medicine and oriental medical traditions, which evolved in Islamic countries,
4 strongly influenced it. This materia medica is rich in exotic materials imported from
5 India, Southeast Asia, and tropical regions of Africa (Fig. 7) and zoological and
6 mineral substances play a relevant role (Table 2), especially in complex drug
7 formulations, some including over 30 different ingredients.
8

9 We did not find any of the 72 complex drug combinations of A1526 in use
10 among informants interviewed since 1995 in either Albacete or Alta Valle del Reno. In
11 fact, there are very few combinations of more than two or three ingredients.
12

13 Although complex drug compounds with c. 40 different ingredients were
14 recorded in Madeira (Portugal) (Rivera and Obón 1995a and b) and in Syria, Lebanon,
15 Turkey and, used by the immigrants from these countries, in Great Britain, France, and
16 Germany (Carmona et al., 2005; Obón et al., 2014), this is in fact extremely infrequent
17 in modern ethnobotanical records in Europe.
18

19 Noticeably, 16th century CE herbals including those by Matthioli and Laguna
20 seriously questioned the reliability, quality, and purity of exotic materia medica widely
21 used by their contemporary pharmacists, and together with the introduction of
22 American medicinal substances, contributed to the decrease in the use of oriental
23 products.
24

25 As noted above, over time, the presence in the catalogs of exotic oriental
26 substances decreased. This is observed, particularly, in ethnobotanical modern records
27 of Albacete (rural areas) where the materia medica is substantially local (Fig. 6) and
28 mainly presents a Mediterranean and Euro-Siberian biogeographical profile (Fig. 7).
29 Coincidences with A1526 gradually decrease (Fig. 8) in **Modern phytotherapy** and
30 present ethnobotany.
31

32 Here, it is worth to mention Murcia 1823, locally published and in use in the
33 pharmacies of the city of Murcia in the beginning of the 19th century, which is a
34 Spanish translation of a French materia medica. Its eclectic and conservative nature
35 places it as a transitional source between **Renaissance Herbals and Pharmacopoeias**
36 and **Old phytotherapy** (Figs. 9, 10 and 12). This led to its classification as an outlier
37 with low support in Fig. 11.
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39 The **Old phytotherapy** cluster (Fig. 9) links close the inventories of two
40 pharmacies in Albacete (19th and early 20th centuries CE). The online Vade Mecum of
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herbal products in Spain (Fitoterapia.net 2015) appears next to this group and seemingly associated to it in ordination analyses (Figs. 9 and 12). The presence in this cluster of the Vade Mecum along with **Old phytotherapy** is explained because the Spanish herbal market superpose different tendencies including old-fashioned traditional local products, modern evidence-based rational phytotherapy products, and recently introduced oriental medicines. Given the eclectic and comprehensive nature of fitoterapia.net, it somewhat overlaps with the ethnobotanical cluster. Thus, classification analysis shows its relationships with **Ethnobotany and Folk Medicine** (Fig. 10 and 11).

Curiously, a third cluster **Modern phytotherapy** (EMA and Naturopathy) closely links a naturopathy popular book (Vander, 1971), published in Spain but with strong central European influence, and the official catalog of herbal monographs by the HMPC of the European Medicines Agency (EMA 2015). Ordination analysis (Fig. 9 and 12) clearly show this relationship, which is confirmed in the classification (Fig. 10), and receives 99% support in the bootstrapped weighted neighbor joining tree (Fig. 11).

Among the key objectives of HMPC are:

First, maintain EU herbal monographs and list entries as an up-to-date and consistent base for national procedures according to available scientific data and state of the art.

Second, to identify and collect criteria for assessment needs, according to market relevance, using available data from National Competent Authorities and Interested parties (HMPC, 2015a).

Both available evidence and market priorities determined a strong Central European bias in the herbal substances proposed to HMPC for assessment (HMPC, 2015b). Noticeably, the catalog of herbal products available in Spain (Fitoterapia.net 2015) does not integrate into this cluster, being instead closer to **Old phytotherapy** and **Ethnobotany and Folk Medicine** groups.

Moreover, the ethnobotanical records from Albacete (Spain) and Alta Valle del Reno (Italy) form a cluster in the classification generated following the minimum variance Ward's criterion (Fig. 10) within the **Ethnobotany and Folk Medicine** group. Both also appear to be associated in the ordination generated in the PCoA (Fig. 9). However, the classification generated with weighted neighbor joining method, clusters

1 within a cascade ethnobotanical and folk medicine sources, ending just with the
2 Modern phytotherapy (EMA and Naturopathy) group, with 94% support.

3
4 The Sephardic traditional medicines, and the Inquisition records (Healers and
5 witches 1500–1700) containing repertoires of medicines and recipes of local healers
6 and witches that were processed by the Inquisition tribunals, appear in the ordination
7 analysis close to Albacete 1995 (Figs. 9 and 12). Classification supports this
8 association (Figs. 10 and 12). These present in common with Albacete 1995 and Alta
9 Valle del Reno 2014 the use of simple drugs or low complexity combinations and the
10 use of easily accessible local resources, which are often foods and food ingredients.

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12 The Mula 1760 manuscript of folk medicine is clearly associated to the
13 **Ethnobotany and Folk Medicine** group both by ordination (Fig. 9) and classification
14 analysis (Figs. 10 and 11).

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16 Ingredients that are locally available in Mediterranean areas of Europe, wild or,
17 most often grown in relatively small home-gardens are the most frequent items in these
18 five ethnobotanical sources. Therefore, we did not find neither any complex formula of
19 those used in A1526 nor rare exotic ingredients.

20
21 Concerning ingredient frequencies, differences are noticeable in terms of
22 presence/absence of exotic imported products (Table 1). Forty percent of the most
23 frequent ingredients in A1526 are imported substances, which in the ethnobotanical
24 records are irrelevant. In parallel, 18 of the 25 most frequent medicinal plants in the
25 Albacete 1995 ethnobotanical records (Table 1) were not involved in the standard
26 formulations of A1526.

27 28 29 30 31 32 33 34 35 36 37 38 39 40 *3.4 Dependence of ethnobotanical records from external sources and ingredients*

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42 We assessed the hypothesis for a dependence of ethnobotanical records with
43 respect to classical or modern pharmaceutical sources through a correspondence
44 analysis (Fig. 12 B) with negative results. The ethnobotanical samples appear together
45 without close links to “external” sources (SOU).

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47 We assumed “a priori” that medicinal ingredients from the Moors of Valentia
48 1570 CE were part of a local tradition, on the basis of the classification as healers of the
49 medical practitioners of this ethnic group. Nevertheless, the analysis shows clearly that
50 this source directly links those in **Renaissance Herbals and Pharmacopoeias**. It is
51 unrelated to other contemporary sources like healers and witches 1500–1700 (Fig.
52 12B). It appears next to **Old phytotherapy**. As we expected, we found a higher
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differentiation for modern ethnobotanical sources in Spain (Albacete) and in Italy (Alta Valle del Reno) (Fig. 12).

The Bayesian inference and model choice across a wide range of phylogenetic and evolutionary models (Huelsenbeck et al., 2004) applied to the weighted matrix of ingredients and sources (Supplementary Table 4) transformed into a four-states matrix (Supplementary Table 5 A and B) furnish a model, which, largely, coincides with those resulting of the previous classifications. This evolutionary model reflects relationships in an almost sequential form (Fig. 13).

The tree (Fig. 13) presents an inverted chronological sequence, where modern sources appear near the base and A1526 and associated sources at the tip. The tree depicts from the top to the base a pattern of decreasing complexity and exoticness, determined by a set of three well distinct core groups of species. First, 15, mostly local species used in Mediterranean Europe during centuries and here recorded exclusively in ethnobotanical sources. Second, 45, mostly imported, used in pharmacy during centuries. Third, 69, mostly cultivated, used in both.

The 69 species (Table 6) vertebrate the tree from A1526 to Albacete 1995 and EMA, and vice versa. The continuous use of these 69 ingredients is documented for, at least, the last 500 years. The complexity reached a maximum represented by A1526 and contemporary pharmacopoeias (between 164 and 187 ingredients shared), which gradually decreased over time through a process, lead in its beginnings by Matthioli and Laguna (150 ingredients), of revalorization of European materia medica and incorporation of new drugs. Therefore, from an evolutionary perspective, the A1526 clade is a “dead end”.

The outgroup Hawaiian Materia Medica (Fig. 13) (only four coinciding ingredients) roots the tree and clearly influenced the exclusion from the main tree of Alta Valle del Reno 2014 (36 ingredients shared with A1526), which questions its place in previous analysis. Alternatively, we defined as outgroup Chinese Materia Medica (47 coinciding ingredients), but the structure of the tree obtained was similar (not shown). Therefore, it is pertinent to note what is discriminant is not only the total but also the specific set of ingredients shared.

At the base of the tree, with a low support, but noteworthy, is the clade represented by **Modern phytotherapy** (the HMPC of EMA and naturopathy), which show an incipient tendency to form an independent clade with affinity toward the Chinese Materia Medica (Fig. 13), which merits further investigations. With such a low

1 number of ingredients, between 30 and 40 in each source, random coincidences with
2 large lists of hundreds of ingredients, like those of the Traditional Chinese Medicine,
3 are possible. These may have influenced this rare association. Nevertheless, the fact is
4 that several ingredients retained in EMA and naturopathy are part of the Chinese
5 Materia Medica.
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9 The cluster of A1526, classical pharmacopoeias, and herbals appears to be
10 supported with a probability of 0.97 (Bayesian probabilities are expressed with values
11 between 0 and 1) at the end of a clade. Just in parallel with Murcia 1823 and forming,
12 in turn, a clade with probability 0.99 with two lists of pharmacies from Albacete, dating
13 1881 and 1910 (Fig. 13). The whole appears basally connected with the list of
14 Fitoterapia.net with probability 0.98. Therefore, the **Old phytotherapy** cluster takes
15 the place of a bridge between **Renaissance Herbals and Pharmacopoeias** and the
16 cluster of **Ethnobotany and Folk Medicine** that gradually unfolds toward the basal
17 positions of the tree.
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20 3.5 *Did alternative and complementary medicines exist during the sixteenth* 21 *century CE in Europe?* 22 23

24
25 The aforementioned analyses suggest the existence of a sort of common medical
26 practice based on the use of local inexpensive resources and extremely simple
27 formulations in parts of Mediterranean Europe. A medicine for the poor, partially
28 known and underrated by the medical establishment since, at least the times of the
29 medical school of Salerno.
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33 Although the official system of medicine was well established across Europe,
34 this was not the unique healthcare system available. As mentioned above, the evidence
35 of medical practices existing in parallel with the official system of medicine was
36 frequent in Europe and not only in rural areas.
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40 Laguna (1555), for instance, mentions that he personally experienced the care of
41 a half-witch (in his words) in 1543 in the city of Metz (Lorraine), who cured him of an
42 irreducible insomnia by stuffing henbane leaves (*cf. Hyoscyamus aureus* L.) within his
43 pillow.
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47 Healers were numerous and, often, considered suspicious of heterodox
48 practices. They were repeatedly denounced to the religious tribunals of the *Inquisición*,
49 not only in Spain (Walker, 2005), as it is attested in the archives (Blazquez, 1991;
50 Cirac, 1942).
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In parallel, there existed a wealth of medical knowledge transmitted within families from grandmothers to daughters and granddaughters, specific for minor and chronic diseases, which has been documented in the Sephardic tradition and present patterns and use ingredients similar to those of our ethnobotanical records from Albacete 1995 and, to some extent, to those of Alta Valle del Reno 2014. Note that Sephardic Jews were expelled from Spain in 1492 and maintained their Spanish traditions and language to present times in their places of exile (Levy and Levy, 1991; Romeu, 2010; Shaul, 1986).

The Systematic inventory of resources raised by the officials of Felipe II in the Kingdom of Castile (Carrilero et al., 2014) furnished further evidence. For instance, at Chinchilla (Albacete) on February 8, 1576: “This city is abundant of sage and thyme, infinite licorice grows by this city and much lavender, so much that can be loaded several carriages of such. It grows also in this mountain, great abundance of a purgative herb that is **not written in the codices of herbalists**, here they call *burfalaga* or *sanamonda*. In the kingdom of Murcia they call *yerba de Ricote*. It is herb, which very easily, purge the humors: phlegm, choleric and melancholy, taken with an egg or with a little honey. Puts admiration for those who do not know by how easy it is to purge by vomiting and stool”.

Actually, this herb is *Thymelaea tartonraira* (L.) All., which still grows in Chinchilla and whose aerial parts in decoction are reported in ethnobotanical interviews as a laxative to treat constipation in Alcazozo, Peñarrubia (Balazote), Peñas de San Pedro and Puente Torres (Valdeganga), all four localities of the province of Albacete (Verde, 2002).

The same source (Carrilero et al., 2014) furnishes evidence for the commercial flux of medicinal substances from some of these mountains to the large cities, and the high proportion of local medicinal substances in rural pharmacies.

For instance, at Yeste (Albacete) on December 7, 1576: “There are herbs and such and so many; that come to look for them from the Kingdom of Valencia and elsewhere. And of these, the pharmacies are supplied, in this land if not of some drugs brought from outside”. This suggests a difference, which merits exploration between the pharmacies of small towns in rural areas and those of the large cities at least during the 16th century. In this case, seems that poor medicines in the sense of Salerno predominate in the former.

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Therefore, evidence exists for a parallel array of alternative medical practices and practitioners, which interacted with the official medical staff and often complemented their services during centuries in Spain.

Our analyses show the close relationships, in terms of ingredients used, of this alternative medicine with the medical information recorded through the ethnobotanical fieldwork.

Furthermore, the absence in A1526 of ingredients such as *Thymelaea* and different Cistaceae (*Cistus* and *Helianthemum* spp.), despite their presence and uses in the area, reflects the principle that any system of medicine does not get to use all available resources and therefore, the repertoire of ingredients is determined not only by their local availability. This involves a series of preferences derived from the system of medicine and his explicative model, and, in general, of worldview and culture.

3.6 Medicinal uses of relevant ingredients

We analyzed 212 different ethnobotanical medicinal uses in the province of Albacete for the top 10 medicinal plants and substances (in bold in Table 1). As A1526 did not include explicit mention to the purposes of each medicinal formula and ingredient, we analyzed the medicinal uses of these substances in three main references of the epoch Alonso de Chirino (Herrera 1973), the Dioscorides herbal edited by Andrés Laguna (1555) and Matthioli (1549).

We recorded in Chirino 100 medicinal uses. In Laguna (1555), we found 202 uses attributed to Dioscorides and 63 personally added by Andrés Laguna himself. Matthioli (1549) added 41 uses, and allowed to confirm those 202 uses attributed to Dioscorides by Laguna.

This gives a different profile of uses for each source with relatively higher coincidence among Chirino and Dioscorides, a close coincidence of Laguna and Matthioli and a relatively independent profile for the ethnobotanical records from Albacete (Fig. 14) with a high proportion of diseases of the circulatory system, the respiratory system and those related with pregnancy, childbirth, and the puerperium.

The hierarchical cluster based on frequencies of main ICD-10 diseases categories for the top 10 ingredients using the Ward's minimum variance criterion (Fig. 15A) shows that, on the basis of the uses attributed by Dioscorides, at least 6 medicinal plants out of 10 present a high degree of coincidence and thus are relatively interchangeable.

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There is no coincidence between the different sources in the specific medicinal uses for a determined plant or substance. Furthermore, we found coincidences for completely different substances (Fig. 15A).

It is exceptional to find coincidences such as those for *Crocus sativus* between Dioscorides original prescriptions and those recommended by Andrés Laguna in the next paragraph of the same book (Laguna 1555).

Coincidences of ethnobotanical records with the analyzed herbals are equal to zero, at least in terms of the profile of medicinal uses for each one of the 10 main ingredients.

The medicinal use analysis of the top 10 ingredients shows that the single coincidence in all 10 substances are medicinal and useful. Nevertheless, each author organizes these for different purposes within their repertoires of medicinal resources (Fig. 15). Therefore, overall, the profile of medicinal uses depended primarily on the cultural preferences of medical practitioners and schools and epidemiological constraints (main causes of morbidity and mortality) rather than on the specific pharmacological properties of each plant and substance.

4 Conclusions

The aforementioned analysis yields a range of immediate and far-reaching conclusions relevant to ethnobotanists and ethnopharmacologists:

Old medicine in Mediterranean Europe and concretely in Albacete (Spain) as reflected by A1526 relied in certain ingredients in despite of others locally available but which were underappreciated, confirming that any system of medicine does not get to use all available resources and therefore, the repertoire of ingredients is determined not only by their local availability. However, a relatively substantial part of this materia medica consisted of local ingredients, which persist in the ethnobotanical records but others are also lost.

One hundred and nine ingredients, largely of plant origin, are still in use (within the analyzed sources) in Modern phytotherapy (45) or pharmaceutical ethnobotany (64). Thus, at present, nearly a 58% of the A1526 ingredients remain as usual materia medica.

Different analysis confirmed the four distinct styles of materia medica: Renaissance Herbals and Pharmacopoeias, Old phytotherapy, Ethnobotany and Folk Medicine and finally Modern phytotherapy, characterized by the set of ingredients

1 retained from the initial list of 187 from the A1526 in terms of number and specific
2 ingredients.

3 A substantial difference amongst ethnobotanical (Albacete and Alta Valle del
4 Reno), and pharmaceutical materia medica, consists in the almost exclusive use of local
5 resources in ethnobotanical sources. This contrasts with the weight of imported exotic
6 products in pharmacy (even in 16th-century CE herbals, pharmacopoeias, and
7 pharmacies).

8 Another difference is the generalized use of simples or drug formulations much
9 less complex than the mixtures with numerous ingredients in Renaissance and Old (and
10 in some respects Modern) pharmaceutical phytotherapy sources.

11 Medicinal uses for specific substances show notable differences between the
12 analyzed herbals. Coincidences of ethnobotanical records from Albacete with the
13 analyzed herbals in terms of the profile of medicinal uses are equal to zero.

14 An exhaustive revision of original documents of healers and witches as these
15 appear recorded in several Inquisition archives, most unpublished but others now
16 available online, from an ethnopharmacological perspective would offer novel and
17 significant evidence. A systematic recording and analysis of medical Sephardic
18 traditions is necessary and urgent especially concerning the materia medica.

19 Regarding our question: is there something new under the sun? The analyzed
20 evidence suggests, first, that the contrast between highly valued expensive drugs and
21 unappreciated local wild medicinal plants, in the field of conventional medicine as
22 evidenced by the Salerno school of medicine, persists. Second, ethnobotany, in rural
23 areas of Albacete, describes systems with a high degree of stability and resilience. In
24 these systems, the use of local resources, largely wild but also cultivated, was and still
25 is predominant.

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Is there nothing new under the sun? The influence of herbals and pharmacopoeias on ethnobotanical traditions in Albacete (Spain)

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ABSTRACT:

Ethnopharmacological relevance: This paper has two overarching aims: (1) presenting the results of studying the Albacete tariff of medicines of 1526 and (2) ~~broadly analyzing~~ ~~a wider analysis of~~ the origin and influences of medicinal traditional knowledge in the region of Albacete, ~~(Spain)~~. We use historical and modern ~~literature written sources~~ that may have influenced this knowledge. Our ~~primary~~ ~~first~~ goal was to determine the ingredients used in the pharmacy in the 16th century CE in Albacete through the analysis of the tariff, and ~~our secondary goal was~~ ~~second~~, to investigate until when ingredients and uses present in pharmacy and herbals persisted in later periods.

Methods: The identity of medicines and ingredients was determined ~~by~~ analyzing contemporary pharmacopoeias and classical pharmaceutical references. We analyzed, further 21 sources (manuscripts, herbals, and books of medicines, pharmacopoeias, pharmacy inventories, and modern ethnobotanical records) for the presence/absence of ingredients and complex formulations of the tariff. Using factorial and cluster analysis, and Bayesian inference applied to evolution models (reversible-jump Markov chain Monte Carlo), we compared textual sources. Finally, we analyzed the medicinal uses of the top ~~10~~ ~~ten~~ species in terms of frequency of citation, ~~in order~~ to assess the dependence of modern ethnobotanical records on Renaissance pharmacy and herbals, and, ultimately, on Dioscorides.

Results: ~~In~~ ~~We determined, in~~ Albacete 1526, ~~we determined~~ 101 medicines (29 simple drugs and 72 ~~compound composed~~ medicines) comprising 187 ingredients (85% botanical, 7.5% mineral, ~~and~~ 7.5% zoological substances). All composed medicines appear standardized in the pharmacopoeias, notably in the ~~pharmacopoeia~~ ~~Pharmacopoeia of the city~~ of Florence from 1498. However, most were no longer in use by 1750 in the pharmacy, and ~~were~~ completely absent in popular herbal medicine in Albacete 1995 as well as in Alta Valle del Reno (Italy) in 2014. Among the ingredients present in different formulation are the flowers of *Rosa gallica*, honey (*Apis mellifera*), the roots of *Nardostachys jatamansi*, and *Convolvulus scammonia*, pistils of *Crocus sativus*, grapes and raisins (*Vitis vinifera*), rhizomes of *Zingiber officinale*, bark of *Cinnamomum verum*, leaves and fruits of *Olea europaea*, mastic generally of *Pistacia lentiscus*, and wood of *Santalum album*. The statistical analysis of sources produces four well-separated clusters (Renaissance Herbals and

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1 Pharmacopoeias, Ethnobotany and Folk Medicine, Old phytotherapy, and Modern
2 phytotherapy including Naturopathy) confirming our a priori classification. The clade
3 of Renaissance Herbals and Pharmacopoeias appears separated from the rest in 97% of
4 bootstrapped trees. Bayesian inference produces a tree determined by an initial set of
5 two well-~~distinct~~ core groups of ingredients: 64, ~~locally~~~~local~~ used in Mediterranean
6 Europe during centuries; and 45, imported, used in pharmacy during centuries.
7 Complexity reached ~~its~~ maximum ~~in~~ Albacete 1526 and contemporary
8 pharmacopoeias, gradually decreasing over time. The analysis of medicinal uses of the
9 top ~~10~~~~ten~~ ingredients showed low coincidence between Dioscorides and different
10 Renaissance herbals or medical treatises and of all of them with ethnobotany in
11 Albacete.

12 **Conclusions:** Regarding our question: is there something new under the sun? In
13 some aspects, ~~the answer there~~ is “No”.~~not~~ The contrast between expensive drugs,
14 highly valued medicines, and unappreciated local wild medicinal plants, persists since
15 the Salerno’s school of medicine. Old medicine in Mediterranean Europe, as reflected
16 by Albacete 1526 tariff of medicines, involved strict formulations and preferences for
17 certain ingredients ~~in~~ despite ~~other ingredients of others~~ locally available but
18 underappreciated. This confirms the fact that any system of medicine does not get to
19 use all available resources. Ethnobiological records of materia medica, in rural areas of
20 Albacete, describe systems with a high degree of stability and resilience, where the use
21 ~~of~~~~predominate~~ local resources, largely wild but also cultivated, is predominant in
22 contrast with the weight of imported exotic products in pharmacy.

23 **Keywords:**

24 Ethnobotany; herbals; medicinal plants; multivariate and Bayesian analysis;
25 pharmacopoeias; traditional medicine

26 **Abbreviations**

27 A1526 – tariff of medicines of the city of Albacete of 1526; AHPAB –
28 Provincial Archive of Albacete (Spain); CE – Christian era; DEP – Dependent; EMA –
29 European Medicines Agency; ETHN – Medical Ethnobotany; GTR – General time
30 reversible nucleotide substitution model; HMPC – European Medicines Agency's
31 Committee on Herbal Medicinal Products; ICD-10 – International Statistical
32 Classification of diseases and Related Health Problems 10th Revision; MAAC –
33 Marginal groups and alternative or complementary systems of medicine; PCoA –
34 Principal coordinates analysis; PHCL – Pharmaceutical classical; PHMO –

Pharmaceutical modern; rjMCMC– Reversible-jump Markov chain Monte Carlo; SOU
– Source; TPL – The Plant List.

1 Introduction

All ethnopharmacological research refers to one, several, or numerous plant or animal species, fungi, algae, microorganisms, minerals, or rocks that unambiguously are subject of ethnopharmacological uses. Recently, Leonti et al. (2010) questioned that to what extent studies on contemporary medicinal plant use in Europe over the last two to three decades contain autochthonous traditional knowledge. They estimate that for Campania (Italy), Matthioli's effect is not negligible and lies between 14 and 25% with a high probability.

Leonti (2011) denounced, “apart from empirically learned medicinal and pharmacological properties, the selection of medicinal plants is dependent on cognitive features, ecological factors and cultural history”.

At the beginning of the 16th century CE, the repertory of single and compound medicines officially used by physicians in Western Europe was still strongly influenced by the medical school of Salerno (south of Naples, Italy) and medieval works of Mesue, Nicolao Salernitano, and al-Razi (Anonymous 1513, 1519, De Laredo 1534, Razi 1529, Sylvio 1550). Extremely complex herbal formulations involving dozens of expensive substances were usual. Their complexity and frequent adulteration made necessary the definition of standards for crude drugs, processing, and formulations. The pharmacopoeias codified these standards.

The first official pharmacopoeia, issued in Florence (Tuscany in Italy) in 1498 under the name of “*Nuovo Ricettario*”, intended to secure uniformity in the kind, quality, composition, and strength of remedies approved to prevent fraudulent or inappropriate substitutions and manipulations (Fittipaldi 2011, I-Dodici-Reformatori 1567, 1574; Urdang, 1951). The kingdoms of Aragon and Valencia in Spain soon adopted these standards.

In this context, it prevailed among physicians a preference for expensive complex medicines prepared with exotic products and an underestimation of cheaper local wild medicinal plants. One of the aphorisms of the school of Salerno outlines this: *Res dare pro rebus, pro verbis verba solemus. Pro vanis verbis, montanis utimur herbis. Pro caris rebus, pigmentis et speciebus* that could be translated as “things pay

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1 for things, words pay for words in kind. For vain words give the cheapest herbs you
2 find (the herbs in the mountains). For high fees give such precious drugs, as are
3 pigments and spices” (Meaux-Saint-Marc, 1861; Odrónaux, 1870).

4 ~~Fig. 1 approx. here.~~

5 However, since early 16th century CE, the works of Ruel (Ruellio) (1516) and
6 Fuchs (1542) critically revised the European *materia medica* ~~followed~~-~~Followed~~ by the
7 numerous editions of Matthioli (1544, 1549, 1563, 1573) in Italian or in Latin (id.
8 1565), and the Spanish versions of Jarava (1557) and Laguna (1555, 1566, 1570) (Fig.
9 1). Overall, these works revalorized numerous local wild plants, always referring to the
10 authority of the encyclopedic work of Dioscorides, compiled in the first century CE. In
11 addition, these works~~These~~ gave a new approach to the use of medicinal plants,
12 focusing on European species, questioning complex mixtures that included many Asian
13 species (due to the frequency of fraudulent substitutions), and ~~opening~~~~opened~~ the door
14 to the introduction of American species.

15 Leonti et al. (2009) mention that Dioscorides’ *De Materia Medica* had few or
16 no competition for most of the time, and therefore, this book was able to homogenize
17 knowledge about medicinal plants all over Europe and the Mediterranean.

18 Recently, one of ~~the present authors~~ (Candelaria Moreno) recovered from the
19 Provincial Archives of Albacete (Spain) several manuscripts dated from the 16th
20 century CE ~~onward~~~~onwards~~ pertaining to the area of ~~pharmacy~~~~Pharmacy~~. These
21 ~~manuscripts~~ were a promising source of information, geographically localized, for
22 comparison with the contemporary pharmacopoeias ~~in order~~ to determine the degree of
23 uniformity in medicines in use in Europe, and with medicinal ingredients and uses
24 recorded in ethnobotanical studies between 1995 and 2002 in the same area.

25 Furthermore, these included the “Arancel” of medicines A1526 (Fig. 2).
26 “Arancel” in Spanish means a kind of tax, ~~but~~ also an official price, which determines
27 the amounts ~~that are~~ to be paid for various services or goods, or established to
28 remunerate certain professionals (Real Academia Española, 2016). The A1526 is a list
29 of official prices for medicines sold in Albacete and therefore offers a much more
30 precise information than the list of taxes imposed to all imported goods in Granada in
31 1501, which only included some drugs (Trillo, 1996).

32 Ethnobotany and ethnopharmacology of Albacete ~~have~~~~has~~ been a subject of
33 different studies, articles, and books (Fajardo *et al.*, 2000; Rivera *et al.*, 2006; Verde
34 2002; Verde *et al.*, 1998, 2008). These studies and historic manuscripts offer an

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1 opportunity, difficult to equal, for the comparison of ~~relationships~~relations between the
2 pharmacy at the time immediately previous and later to that of Laguna and Matthioli,
3 the subsequent stages of materia medica and present ethnobotany. However, ~~in order to~~
4 ~~obtain~~get a better representation of this evolution, ~~it~~ is necessary to broaden the range
5 of samples in terms of geography, chronology, and systems of medicine.
6
7

8 ~~Fig. 2 approx. here.~~

9 This paper has two overarching aims: ~~(1)~~; presenting the results of studying the
10 tariff and ~~(2) broadly analyzing a wider analysis of~~ the origin and influences of
11 medicinal traditional knowledge focusing on Albacete. Our first target was to
12 determine the ingredients used in the pharmacy in the 16th century CE in Albacete and,
13 second, how long ancient ~~formulations~~formulas, ingredients, and uses from the
14 pharmacy and herbals persisted in later periods, and to determine their influence in the
15 present pharmaceutical ethnobotany.
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18 2 Material and Methods

19 2.1 General procedure

20 We summarize in Fig. 3 and explain in ~~detail in the various paragraphs of~~ the
21 next section the sequential process of analysis that we follow to address the above
22 objectives.
23

24 ~~Fig. 3 approx. here.~~

25 Starting from the document A1526, ~~being our objective~~ to determine the
26 differential presence of ingredients, formulations, and uses in well-characterized
27 sources at different periods, we “a priori” selected to test the following:
28

29 **Renaissance herbals and ~~pharmacopoeias~~Pharmacopoeias.** Pharmacopoeias,
30 herbals, and inventories of local pharmacies, showing strong medieval influence, and of
31 late-Renaissance renewal of herbalism and medicine (16th to early 18th century CE).
32

33 **Old phytotherapy.** Pharmaceutical sources from mid-18th to early 20th
34 centuries CE, where plants were still substantial part of the materia medica.
35

36 **Modern phytotherapy.** Here, we ~~included~~include modern evidence-based
37 phytotherapy (21st century CE) and other alternative approaches such as naturopathy,
38 which employ medicinal plants.
39

40 **Ethnobotany and ~~folk medicine~~Folk Medicine.** Here, we ~~included~~include
41 present medical ethnobotany in Albacete and ~~in~~ Alta Valle del Reno (border between
42 Tuscany and Emilia Romagna, Italy). In addition, we analyzed different marginal
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1 groups, which along the history of Spain, practiced alternative or complementary
2 systems of medicine (local healers, “Moriscos” and Sephardic).

3
4
5 As we intend to compare a large number of sources based on ~~the presence/~~
6 absence or on frequencies of 187 ingredients, it is necessary to use statistical
7 techniques. To confirm that the detected relationships are not simply an artifact of the
8 calculation procedure, we ~~used~~~~have worked with~~ four different methods that
9 complement each other and, ~~if they match their results,~~ provide consistency if their
10 results are matched.

11 2.2 Data collection

12 2.2.1 Manuscripts analyzed

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17 The number of basic manuscript documents that are analyzed ~~is~~~~are~~ five. First,
18 the Tariff of Medicines approved in Albacete in 1526 (A1526) (Fig. 2) (known as
19 *Arancel*, AHPAB, MUN.C.125) [cited as Albacete 1526 in Figs.] (Supplementary
20 Table 1).

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Second, the inventory made by the pharmacist Custodio José Carvajal of the
tools, books, vases, and medicinal materials of a pharmacy in El Bonillo (Albacete) in
1711 (Hernández, 2007; AHPAB C 3525) [cited as El Bonillo 1711 in Figs.].

Third and fourth, the inspection acts in 1881 and 1910 for the pharmacies of;
~~respectively;~~ Andrés Picazo [cited as Albacete 1881 in Figs.] and Jesús Leal [cited as
Albacete 1910 in Figs.] in Albacete (AHPAB, MUN.C.125), ~~respectively.~~

Fifth, the collection of recipes attributed to physician Miguel Tendero ~~physician~~
at Mula (Murcia) c. 1790 (González, 1996) [cited as Mula Manu 1790 in Figs.]. The
~~four~~ last four manuscripts represent different Old phytotherapy approaches.

2.2.2 Bibliographical sources

Further, we analyze inventories, dated 16th and 17th centuries CE, of medicinal
products from three pharmacies in Granada (De-la-Obra et al., 2009; Luque et al.,
2006) [cited as Granada 1556 in Figs.], Zaragoza (Andrés, 1991) [cited as Zaragoza
1601-1609 in Figs.], and Castile (Madrid) (Davis and López, 2010) [cited as Castile
1599 in Figs.].

We ~~included~~~~include~~ from Murcia the materia medica of 1823 (Authenac, 1823)
[cited as Murcia 1823 in Figs.]. We analyzed the *Ricettario Fiorentino* (first European
pharmacopoeia) using the editions of 1498 (College of Physicians, 1498; Fittipaldi,
2011), 1567 and 1574 (I-Dodici-Reformatori, 1567; 1574) (Fig. 4) [cited as Florence
1498-1574 in Figs.].

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1 We confirmed ingredients in A1526 by analyzing the pharmacopoeias of
2 Barcelona (Domenech and Pau, 1587; Duch, 2000) [cited as Barcelona 1511-1587 in
3 Figs.], Valencia (Valentian College of Pharmacists 1601) [cited as Valencia 1601 in
4 Figs.], and Zaragoza (Moliné, 1998, Sagaun and Aznarez, 1546) [cited as Zaragoza
5 1546 in Figs.]. However, from these sources, we only ~~obtained~~ lists of ingredients
6 with Latin or Spanish pharmaceutical names.
7

8 ~~Fig. 4 approx. here.~~

9 We retrieved and downloaded from seven ~~online~~ repositories: Archive
10 (2015), *Biblioteca Digital Hispánica* (BNE, 2015), *Bibliothèque numérique Medica*
11 (Medica, 2015), Biodiversity Heritage Library (BHL, 2015), *Digitale Bibliothek*
12 (GNM, 2015), *Gallica* (2015), and Google Books (Google, 2015), classical texts, cited
13 above, and those used to determine pathologies.
14

15 2.2.3 Data from other historical sources

16 Another challenge was to document the medicinal species used outside the main
17 pharmaceutical circuits, in the 16th century CE and later. The *Relaciones mandadas*
18 *hacer por Felipe II* (Carrilero et al., 2014), which is a systematic census of resources of
19 the kingdom of Castile, contains information explicitly “not included in the
20 pharmacists’ manuals”, of medical relevance, but scarce. Three marginal groups ~~exist~~
21 in the Castilian society: Moors, healers, and witches; and Sephardic communities had
22 reputation of heterodox medical knowledge.
23

24 **1- Sephardic.** We analyzed the “*Sefer Refuot*” tradition of folk medicine among
25 Sephardic communities in the Mediterranean (assuming these can reflect
26 pharmaceutical knowledge of Jews before their expulsion from Spain in 1492).
27 Sephardic communities compile traditional remedies in Judeo-Spanish. Such
28 compilations appeared in Salonica (Greece) in 1855, Istanbul and Smyrna (Turkey) in
29 1870 and 1878 (Albarral, 2014; Levy and Levy, 1991; Romeu, 2010; Shaul, 1986;
30 1992) [cited as Sephardic in Figs.].
31

32 **2- Moors.** Several manuscripts of the 16th century CE contain exhaustive lists
33 of medicines used by the Moors (*Moriscos*) of Valencia (Labarta, 1981; Labarta and
34 Barceló, 1988) and Castile (Vázquez, 1994; Vazquez and Bustos, 1998) [cited as
35 Moors Valencia 1570 in Figs.]. Numerous Moors were conventional physicians in the
36 Christian kingdoms of Spain ~~for~~ during centuries. However, during the 16th century CE,
37 their activities became suspicious and marginal, ~~before prior to~~ their prosecution and
38 expulsion from Spain (Moriscos, 2016; Pérez, 2014).
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3- Healers. The “*Inquisición*” tribunals were active from late 15th until the ~~beginning~~~~beginnings~~ of the 19th century CE. In their records, ~~are directly documented~~ the medicines used by healers and witches in their activities ~~are directly documented~~ (Blázquez, 1991; Cirac, 1942; Laza, 1958) [cited as Healers and Witches 1500–1700 in Figs.]. The archives of the *Consejo de Inquisición* (Alonso, 2016) consist ~~of~~ 1345 books and 3621 files that are now at the *Archivo Histórico Nacional*, plus those of the numerous territorial tribunals (Toledo, Sevilla, Llerena, Granada, Zaragoza, etc.). Some, like those of Zaragoza (Iranzo, 2011) ~~are~~ available online. The information from the tribunal of Toledo (Cirac, 1942) is particularly useful in terms of medicinal ingredients.

2.2.4 Present ethnobiological data

The document A1526 clearly belongs to the Italian tradition (medical school of Salerno). It follows the standards codified in Florence and later adopted in Spain. Thus, we analyzed the ethnobotanical studies of Albacete and a similar ethnobotanical context in Toscana-Emilia Romagna geographically close to Florence. However, to generalize our hypotheses, more ethnopharmacological studies should be used.

The ethnobiological ~~cataloge~~~~atalogue~~ of 358 medicinal plants (~~includingbut also~~ other drugs from zoological and mineral origin) for Albacete is based on records collected in open semi-structured interviews, which ~~were conducted~~~~took place~~ in Albacete province (Spain) (38°15'—39°15' N, 0°54'—2°54' W, average elevation 700 m) from 1995 to 2002. This information is compiled, and voucher specimens cited by Verde (2002) are deposited in herbarium ALBA (University of Castilla La Mancha, Spain) (numbers in Supplementary ~~Table~~~~Tab.~~ 2) [cited as Albacete 1995 in Figs.].

Similarly, ~~is analyzed~~ the ~~cataloge~~~~atalogue~~ of 116 medicinal substances ~~is analyzed and~~ recorded as used in rural areas of Alta Valle del Reno (Italy) (44°05'—44°11' N, 10°54'—11°06' E, average elevation 700 m) (which also includes local drugs from zoological origin). This information is compiled, and voucher specimens cited by Egea (2016) are deposited in herbarium FIAF (numbers in Supplementary ~~Table~~~~Tab.~~ 2) (University of Firenze, Italy) [cited as Alta Valle del Reno 2014 in Figs.]. We expect that the pharmaceutical culture reflected in the successive Florence pharmacopoeias could have influenced Alta Valle del Reno even more closely than Albacete.

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2.2.5 Data from Modern phytotherapy approaches

We analyzed three different ~~modern~~Modern phytotherapy approaches. First, the ~~catalogue~~catalogue of herbal substances ~~that are~~ designated for assessment by the European Medicines Agency's committee on Herbal Medicinal Products (HMPC) and the European Union herbal monographs, which offer a list of substances of present medical interest at an European level (EMA, 2014) [cited as EMA 2014 in Figs.]. ~~According~~Herbal substances ~~come according~~ to EMA (2014), ~~because herbal substances are obtained~~ from plants, algae, fungi, and lichens, ~~they~~therefore implicitly ~~exclude~~excluding substances of zoological and mineral origin.

Second, we analyzed the ~~catalog~~Catalogue of herbal products available in the Spanish market (Fitoterapia.net, 2015) [cited as Fitoterapia.net 2015 in Figs.]. This eclectic and comprehensive list includes almost every one herbal product and ingredient available in pharmacies and herbal shops of Spain. Here, the concept of herbal is wider, comprising substances like propolis, royal jelly, or medicinal clay.

Third, we analyzed Vander (1971) ~~whowhich~~ was highly influential in Spain's folk medicine in the 1970s and later on (Rivera and Obón, 1996) [cited as Vander 1971 in Figs.].

2.2.6 Data on Medicinal uses

The list A1526 does not ~~containe~~contains references to a determined use of the 101 medicines. However, we assume that medicinal uses of the medicines in A1526 were those described in contemporary sources. Therefore, we analyzed ~~the~~ sources such as Alonso de Chirino, died in 1431; whose book "*Menor Daño de Medicina*" appeared in numerous editions during the 15th and 16th centuries (Herrera, 1973) [cited as Chirino c. 1490 CE in Figs.].

Andrea Matthioli (1549) and Andrés Laguna (1555) present similar medicinal uses attributed to Dioscorides in each monograph of single ingredients (simples) [cited as Dioscorides 1st cent CE in Figs.]. ~~In addition~~Additionally, Matthioli and Laguna record different contemporary medicinal uses [cited as Matthioli 1549 CE or Laguna 1555 CE in Figs.]. Laguna (1555) closely follows Matthioli (1549) presenting, first, in regular characters the Spanish translation of each Dioscorides' monograph, presumably from a Latin version of the Greek original, and second, in *italics*, the comments and uses by Laguna and their contemporaries. These were sometimes similar and, often, different.

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We ~~ensured that~~~~took care to~~ separate indications are attributed to Dioscorides (which are almost identical in both analyzed versions of Laguna (1555) and Matthioli (1549)) from those annotated by Laguna or Matthioli ~~from~~ their personal experiences. ~~To~~~~In order to~~ verify ingredient names, images, and uses ~~by~~ Matthioli and Laguna, we similarly revised other editions cited in the introduction of this paper and listed in the references.

2.3 Geographical coverage and Maps

Overall, consulted sources concentrate in Spain and Italy (Fig. 5). We draw maps using The Generic Mapping Tools GMT (2014). The EMA (2015) ~~has published~~ HMPC monographs in Brussels and London. ~~It has established~~ EMA ~~establish~~ each particular monograph on data collected from all over Europe and ~~therefore~~ does not represent knowledge specifically developed in Brussels or London. However, it is here georeferenced linked to Brussels (the capital city of the European Union) (Fig. 5).

~~Fig. 5 approx. here.~~

2.4 Standardization of data

2.4.1 Identification of formulations, ingredients and species

At the ~~beginning~~ beginnings of the 16th century CE, pharmaceutical formulations in European countries were subject to standards established, first, in the pharmacopoeia of Florence (Italy) in 1498. This, and other pharmacopoeias, specify for each formulation the list of ingredients, their quantities, preparation procedures, and, often, indications. Further, the pharmacopoeias include for each ingredient a monograph defining criteria of quality and purity (Rodríguez et al., 2012). Therefore, ~~in order~~ to analyze this “*Arancel*” further, and to identify species and ingredients, we assessed contemporary (~~15-15th~~ to 17th centuries CE) Spanish and Italian pharmacopoeias.

There is always ~~at~~ the doubt; how reliable is the species-level identification of a pre-Linnaean description, ~~for example,~~ e.g. of a rose or a grass? Yet, due to their relevance as drugs, it is possible to follow in detail the history of each one of these 187 ingredients. The works of Clusius (1601), Bauhin (1671), and Tournefort (1700) “*Institutiones rei herbariae*”, in chronological sequence, are particularly relevant for this purpose.

Linné analyzed these works and gave the modern equivalence of names in his *Materia Medica* (Linnaeus, 1749; Schreber, 1782) and “*Species Plantarum*” (Linnaeus,

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1 1753). Scientific names of vascular plants were subsequently actualized using the
2 *Farmacopea Española* (Real Academia de Medicina, 1865) and others (Davis and
3 López, 2010; Haller, 1771; Kew, 2016; López, 2015; Rivera et al., 2012; WHO, 2015).

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6 However, for ~~a~~ 10% of ingredients, depending on the resources consulted
7 (including standard pharmacognosy literature ~~)~~ we reach quite different identifications
8 (different species but also different genera) (Suppl. Table 2). This uncertainty mainly
9 affects exotic imported ingredients whose origins were unknown to the pharmacists.

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12 Healers and witches ~~between~~ 1500 ~~and~~ -1700 ~~and~~; Sephardic, and Mula Manu
13 ~~in~~ 1790 used Spanish vernacular names. We analyzed particularly their coincidence
14 with those in Albacete 1526 or the Spanish names recorded for the ingredients in the
15 pharmacopoeias and those by Laguna (1555) or Verde (2002).

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18 We assessed taxonomic and nomenclatural veracity by comparing with existing
19 standard regional floras, and with the botanical literature available at BHL (2015), and
20 databases (Anthos, 2015; Euromed, 2011; GRIN, 2015; IPNI, 2005; NCBI, 2013;
21 Tropicos, 2012) and, most importantly, standardized according to The Plant List (2015)
22 and to the procedures suggested by Rivera et al. (2014). It was not necessary to develop
23 a strategy for resolving conflicts between The Plant List and other taxonomic reference
24 works, because we did not detect any ~~such conflicts~~ for the species treated.

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26
27 However, concerning *Corylus* nuts, we adopted the distinction in four categories
28 made by Miller (1752) between hazelnuts (*Corylus avellana* L.), cobnuts (hybrids *C.*
29 *avellana* x *C. maxima*), filberts (*C. maxima* Mill. ~~)~~ and large Spanish nut (*C.*
30 *hispanica* Mill. ex D.Rivera et al.). ~~This~~ ~~These~~ last (*Corylus hispanica*) ~~supplied~~
31 the “*avellana*” nuts used in the pharmaceutical formulations of the 16th and later
32 centuries CE in Spain (Rivera et al. 1997).

33
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35 ~~Groups~~ ~~Concerning groups~~ of plants and other ingredients with similar qualities
36 and uses (i.e. ethnotaxonomic species complexes or pharmaceutical names of drugs),
37 which in historical texts, are often described in one chapter. We identified these
38 collectively using an inclusive scientific taxon name. Thus, the identification was not
39 restricted to “the label species”. For example, “*Dragacanthi*” was identified in the
40 sense of *Astracantha gummifera* (Labill.) Podlech ~~+~~ *Astragalus clusii* Boiss, “*Gálbano*”
41 as *Ferula gummosa* Boiss. (incl. *Ferulago galbanifera* (Mill.) W.D.J.Koch) or
42 “*Sticados*” as *Lavandula stoechas* L. ~~+~~ *Thymus moroderi* Pau ex Martínez. ~~For~~ ~~We,~~ ~~for~~
43 modern ethnobotanical sources, ~~we~~ computed the presence ~~whenif it was documented~~
44 the use of at least one of the species of the complex ~~was documented~~. This had minimal
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1 influence on the analysis because these complexes have very low representation in
2 ethnobotanical sources analyzed.

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5 | Drugs from zoological and mineral origin appear, with different relevance, in all
6 sources analyzed except EMA (2015). We updated mineral ingredients nomenclature
7 according to the New International Mineralogical Association List of Minerals (IMA,
8 2016) and Duffin et al (2013), and ingredients of zoological origin using the Global
9 Biodiversity Information Facility (GBIF, 2015).

12 2.4.2 *Standardized Medicinal uses*

13 | Pathologies were determined according to the different studies of
14 paleopathology and history of medicine cited by Martínez-Francés et al. (2015). In
15 respect to standardization of indications and pathologies, we adopt in the present
16 review the standards of the ICD-10 (International Statistical Classification of Diseases
17 and Related Health Problems 10th Revision) (WHO, 2014).

22 2.5 *Data Analysis*

23 2.5.1 *Presence of ingredients of the A1526 tariff in other sources*

24 | Once ~~determined~~ the list of 187 ingredients; of Albacete tariff 1526 [Albacete
25 1526] was determined, we proceeded to determine their presence/absence in a set of
26 other 21 sources (~~Figs~~Fig. 6 ~~to~~ 8). ~~In~~We did not used in the analysis, we did not use
27 the complete lists of ingredients of all sources. The sources represent, a priori, the
28 following main four categories:
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33 | **Renaissance herbals and Pharmacopoeias.** Pharmaceutical sources with
34 strong medieval influence or associated to the late Renaissance renewal of medicine:
35 Four pharmacopoeias [Barcelona 1511–1587, Florence 1498–1574, Valencia 1601,
36 and Zaragoza 1546]. Four inventories of pharmacies [Castile 1599, El Bonillo 1711
37 (which is transitional to next category), Granada 1556, Zaragoza 1601–1609]. Herbals
38 [Laguna 1555] (identical in terms of ingredients with Andrea Matthioli (1549)).

39 | **Old phytotherapy.** Later pharmaceutical sources where plants were still a
40 substantial part of the materia medica: two inventories of local pharmacies [Albacete
41 1881, Albacete 1910] and one eclectic list of *Materia Medica* [Murcia 1823].

42 | **Modern phytotherapy (EMA and Naturopathy).** This includes modern
43 evidence-based phytotherapy (21st century CE) in the form of the official list of
44 monographs by the European Medicines Agency [EMA, 2014]. We also
45 ~~analyzed~~analyze the ~~cataloge~~catalogue of herbal products available in Spain
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[Fitoterapia.net 2015] and a 20th-century CE naturopathy book of medicinal plants [Vander 1971].

Ethnobotany and Folk Medicine. Ethnobotany is represented by Albacete province (Spain) 1995–2015 [Albacete 1995], and Alta Valle del Reno (Italy) 2012–2015 [Alta Valle del Reno 2014]. Folk medicine here includes, a priori, four sources attributable to alternative or complementary systems of medicine: First, local healers (remedies recorded by the Spanish Inquisition in Castile) [Healers and witches 1500–1700]. Second, physician-Moors in Valencia 1573–1593 [Moors Valencia 1570]. Third, the Sephardic Tradition [Sephardic]. Fourth, the recipes in a manuscript dated c. 1790, which is an apocryphal attributed to the authority of Dr. Fr. Miguel Tintero, ~~whowhich~~ served as a physician in Mula (Murcia) c. 1760 [Mula Manu 1790] (Gonzalez, 1996).

As ~~described we will~~ later ~~see~~, the “a priori” ascription of some of the above sources to the four main categories will require further examination because of the results of our analyses.

The 187 variables are the different ingredients determined (Supplementary ~~TableTab.~~ 2). For each one of the 22 units (the 22 sources), ~~is determined~~ the presence/absence of each ingredient of the Albacete tariff of 1526 ~~is determined.~~ Therefore, ~~it represents~~ ~~represent~~ the possibility of reproducing similar drug compounds in ~~termsfunction~~ of the availability of crude drugs. The result is a crude matrix of presence/absence of ingredients (Supplementary ~~TableTab.~~ 3).

2.5.2 Geographical origin of ingredients in A1526

Each ingredient of the Albacete tariff 1526 was identified and classified in terms of local (widely available in Western Europe through cultivation or collection in wild populations) or imported (exotic product only available in Europe through long-distance commerce) (Fig. 6). We linked these to their main biogeographical profiles and zones of origin (Fig. 7) as Widespread, Eastern Asiatic, Euro-Siberian, Indian, Irano-Turanian, Malaysian, Mediterranean, Paleotropical, Saharo-Arabian, Sudano-Zambezian, according to Rivera et al. (2012) and GBIF (2015).

The 22 sources analyzed were georeferenced using Google ~~Earthearth~~®. The tool Ruler—Line allowed to measure the distance between Albacete and the rest of localities on the ground (Fig. 8).

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2.5.3 *Weighting of the different ingredients in the A1526 tariff*

In addition to the presence-/absence of ingredients, we have identified the number of formulations in which each ingredient appears. Several ingredients appeared in more than one single formulation in the 101 single and compound medicines of the tariff A1526. This allows producing a list of ingredients in the order of decreasing frequencies. We then ~~calculated~~calculate the weight of the ingredients for each of the remaining sources by following the same criteria (Supplementary ~~TableTab.~~ 4).

We also produced a list for the ensemble of ethnobotanical medicinal plants and other resources of Albacete and their frequencies on the base of available evidence. These frequencies, however, are not equivalent. The frequencies in the tariff only give us an idea of multivalency of each ingredient within the set of the listed medicines.

We calculated the ethnobotanical data frequencies in terms of the sum of the number of remedies in which each informant uses this ingredient, along the entire set of informants. Therefore, ~~we only we~~ use them to establish a ranked list of the 25 most important ingredients in each context (~~TableTab.~~ 1). In addition, we determined the core ingredients within the set of sources in terms of the number of sources that reported each, which ranges between 2 and 21 (~~TableTab.~~ 1).

2.5.4 *Ordination and classification of sources based on the lists of ingredients*

~~To~~In order to determine how different these 22 sources are, considering as a reference the 187 ingredients of the Albacete 1526, we calculated the pairwise differences between samples in form of a dissimilarity matrix.

The crude matrix of presence/absence of ingredients was used to compute a dissimilarity matrix using Darwin 6 V.6.0.9 (2015-04-15) (Perrier, Flori & Bonnot, 2003; Perrier & Jacquemoud-Collet, 2006).

The Sokal-Sneath dissimilarity index was calculated ~~(un2)~~ ($d_{ij} = 2(b+c) / a+2(b+c)$), where d_{ij} is the dissimilarity between samples i and j , a : number of variables where $x_i =$ presence and $x_j =$ presence, b : number of variables where $x_i =$ presence and $x_j =$ absence and c : number of variables where $x_i =$ absence and $x_j =$ absence. The dissimilarity is $=0$ for two samples sharing the 187 ingredients and $=1$ for two samples ~~that~~which present 0 ingredients shared.

For this index, ~~“presence” only “presence”~~ modality is only informative, while ~~“absence”~~ modality ~~“absence” expressing~~ expresses an absence of information. This index considers that a common absence for two units is uninformative to measure their dissimilarity (Perrier & Jacquemoud-Collet, 2006). Therefore, similarity here

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1 reflects the number of coinciding ingredients, and dissimilarity is inversely proportional
2 to this.

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5 These pairwise dissimilarities can be represented in a multidimensional space,
6 but, ~~in order~~ to obtain meaningful graphic representation of these relationships in a
7 two-dimensional plane, we used factorial and cluster analysis.

8
9 We used an ordination method, principal coordinates analysis (~~from now~~
10 ~~abbreviated in the text as~~ PCoA), to ~~obtaining~~ an overall representation of diversity
11 within samples with the lowest possible dimensional space. ~~PCoA~~ can be viewed as a
12 more general form of principal components analysis (~~abbreviated as~~ PCA) that
13 ~~provides~~ gives a direct ordination of the samples and is useful in situations where there
14 are more variables than samples (Kovach, 2007). In general, the first axes (3 or 4)
15 summarize a large part of the complete space information. Planes of axis 1-2, 1-3, 2-
16 3... are sufficient to exhibit the main structure of the data. The part of information
17 retained by each axis is given by the percent inertia (the eigenvalue of this axis on the
18 sum of all eigenvalues) (Perrier & Jacquemoud-Collet, 2006) (Fig. 9).

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Factorial analysis family, including PCoA, offers a consistent ordination of
samples. However, the definition of groups that we represent with circles in the figures
is still a heuristic process and requires the use of more precise techniques ~~in order~~ to
obtain a classification.

Cluster analysis is a term used to name a set of numerical techniques in which
the main purpose is to divide the objects of study into discrete groups ~~according~~
~~to based on~~ the characteristics of the objects (Kovach, 2007).

We used the agglomerative hierarchical method that arranges the clusters into a
hierarchy so that the relationships between different groups are apparent. Minimum
variance clustering (Ward's method) focuses on determining how much variation is
~~present~~ within each cluster. ~~Thus in this way~~, the clusters will tend to be as distinct as
possible ~~because, since~~ the criterion for clustering is to have the least amount of
variation (Kovach, 2007) (Fig. 10). Ward's method produces a single tree.

~~To in order to~~ further ~~reducing~~ the uncertainty in the structure of the tree,
we used a bootstrapped matrix (20,000 bootstraps) and a tree construction method that
uses the trees inferred from these bootstrapped dissimilarities to assess the uncertainty
of the tree structure.

The Neighbor-Joining method proposed by Saitou and Nei (1987) uses the
criterion of relative neighborhood, weighted average for dissimilarity updating, and

1 adjustment to an additive tree distance. A bootstrap value is given to each edge that
2 indicates the occurrence frequency of this edge in the bootstrapped trees. Bootstrap
3 values range between 0 and 100 (Fig. 11). High bootstrap values supporting an edge
4 (near 100) represent high consistence of the cluster to the right of this edge; on the
5 contrary, low scores (particularly below 40) ~~imply that mean~~ data do not support this
6 particular cluster.
7

11 2.5.5 *Assessing the influence of classical sources and Modern phytotherapy in* 12 *ethnobotanical records*

13 We further used another method of the factorial analysis family to contrast the
14 hypotheses for the influence of classical sources and Modern phytotherapy in
15 ethnobotanical records. ~~To~~~~in order to~~ simplify, we ~~labeled~~~~labelled~~ samples according to
16 three main categories by cultural context: Pharmaceutical classical (PHCL) that
17 includes **Renaissance Herbals and Pharmacopoeias** and **Old phytotherapy**.
18 Ethnobotanical (ETHN) that includes **Ethnobotany and Folk Medicine**.
19 Pharmaceutical modern (PHMO) that includes **Modern phytotherapy (EMA and**
20 **Naturopathy)**. According to the origin of information, ~~the~~~~and~~ uses were
21 ~~labeled~~~~labelled~~ as hypothetically dependent (DEP) or as a, presumably, source (SOU).
22

23 ~~Among~~~~Amongst~~ the above, we classify as either influential sources of
24 information (herbals, pharmacopoeias, and popular books) (SOU) or as dependent
25 (marginal systems, ethnobotanical data and, evidently, ~~catalog~~~~catalogues~~ and tariffs of
26 medicines which obviously were subject to pharmacopoeial standards) (DEP).
27 Therefore, dependent sources would hypothetically cluster closer to their direct
28 sources. We also aim at determining relative distances between sources classified as
29 either PHCL, ETHN, or PHMO (Fig. 12).
30

31 With this purpose, we used a second crude matrix based on the weighting of
32 each ingredient to compute ~~correspondence~~~~Correspondence~~ analysis using
33 FactoMineR: an R package for multivariate analysis (Husson et al., 2009; Lê, et al.,
34 2008). Correspondence analysis is conceptually similar to principal component analysis
35 (PCoA), but applies to categorical rather than continuous data and distance is “Chi-
36 squared” measure. The chi square dissimilarity index was calculated. This measure
37 expresses a value x_{ik} as its contribution to the sum x_i on all variables and is a
38 comparison of unit profiles.
39

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$$d_{ij} = \sqrt{\sum_{k=1}^K \frac{x_{.k}}{x_{i,k}} \left(\frac{x_{jk}}{x_{i,k}} - \frac{x_{jk}}{x_{j,k}} \right)^2}$$

~~where~~ ~~Where~~ d_{ij} : dissimilarity between units i and j ; x_{ik} , x_{jk} : values of variable k for units i and j ; x_i , x_j , $x_{.k}$: mean for units i and j or variable k ; $x_{.}$: overall mean. K : number of variables.

In many comparative studies, correspondence analysis ~~provides~~ ~~gives~~ an optimal summary of the structure of the original data (Kovach, 2007). ~~Similar to that~~ ~~As~~ in PCoA, we graphically represented relationships against the main axes (Fig. 12).

2.5.6 Bayesian analysis of ingredients

The study of the evolutionary history and relationships among different versions of the materia medica in general and ~~in particular~~ of the evolution of the A1526 list of ingredients can be improved, ~~in particular~~, using the phylogenetic inference methods, which are routinely used in the study of relationships among individuals or groups of organisms (e.g. species, or populations). Thus, we, further, recurred to Bayesian methods, which offer the possibility of working in terms of likelihood, credibility, and conditional probabilities.

~~Despite being controversial~~, Bayesian analysis has been applied ~~to, not without controversy, for~~ the detection of over and underused taxonomic groups in ethnobotany and ethnopharmacology (Leonti et al., 2012; Moerman, 2012; Weckerle et al., 2011; 2012).

Here, we wanted to compare different lists of ingredients with reference to the A1526, ~~in order~~ to generate a phylogenetic classification that reflects the relationships and dependencies between those lists in terms of deletions of the 187 basic ingredients, from an evolutionary perspective.

We could translate here the Darwinian idea of “survival of the fittest” as ~~“~~Survival of the ingredient that will leave the most copies of itself in successive generations”. Therefore, “which will be used most often, in most formulations and by most people”. Nevertheless, we must not exclude non-Darwinian models, considering that part of the materia medica evolution is likely random, in parallel with neutral mutation and genetic drift (King and Jukes, 1969) in genes and organisms.

For this analysis, we utilized the current version of MrBayes 3.2.6, released November 25, 2015. MrBayes is a program for Bayesian inference and model choice across a wide range of phylogenetic and evolutionary models.

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1 MrBayes uses Markov chain Monte Carlo (MCMC) methods to estimate the
2 posterior distribution of model parameters (Huelsenbeck et al., 2015; Ronquist et al.,
3 2011). A Markov chain is a mathematical model for stochastic systems whose ~~states;~~
4 discrete or continuous ~~states;~~ are governed by a transition probability. The current state
5 in a Markov chain only depends on the most recent previous state. Monte Carlo is the
6 art of approximating an expectation by the sample mean of a function of simulated
7 random variables (Anderson, 1999).

8 In phylogenetics, an outgroup is a group of organisms that serve as a reference
9 group when determining the evolutionary relationship among three or more
10 monophyletic groups of organisms. We use outgroup as a point of comparison for the
11 ingroup—the set of organisms under study—that specifically allows the phylogeny to
12 be rooted. Because the polarity (direction) of character change can only be determined
13 on a rooted phylogeny, the choice of outgroup is essential for understanding the
14 evolution of traits along a phylogeny. ~~Therefore, an~~ appropriate outgroup must be
15 unambiguously outside the clade of interest in the phylogenetic study, but ~~they~~ must
16 be related to the ingroup, close enough for meaningful comparisons to the ingroup
17 (Wikipedia, 2016). In our case, ~~of~~ we added a pair of extra samples based ~~on~~ the
18 Hawaiian traditional pharmacopoeia (Bishop Museum, 2015; Hilgenkamp and Pescaia,
19 2003), and the Chinese Materia Medica (Hempfen and Fischer, 2007; Hsu et al., 1986),
20 which are supposed to be relatively unrelated with the different sources analyzed
21 (~~Fig~~ 13).

22 For taking full ~~advantage~~ of the possibilities of analysis available in Mr.
23 Bayes, we adopted the DNA ~~4x4x4~~ nucleotide model assuming that phylogenetic
24 models are appropriate to describe historical and cultural transitions in materia medica
25 preferences (Supplementary ~~Tables~~ 5a and 5b). Therefore, we assume the
26 conversion of the weighted ingredient list into an ACGT nucleotide chain with
27 substitution rates, ~~but excluding~~ insertions, and deletions.

28 Thus, we, first, diagonalized the matrix ~~ordering samples in columns by~~
29 ~~decreasing~~ number of ingredients ~~(left to right)~~ ~~per sample~~ and
30 ~~ingredients in rows by decreasing~~ the number of samples ~~in which the~~ ingredient ~~was~~
31 ~~present (from top to bottom)~~. Second, we ~~converted~~ values of variables
32 (frequencies of each ingredient ~~in each source = $f(i)_s$ in four categories~~) as follows: ~~$f(i)_s$~~
33 ~~= 0, coded as =A;~~ ~~$1 \leq f(i)_s \leq 3$, coded as =C;~~ ~~$4 \leq f(i)_s \leq 6$, coded as =G;~~ ~~$7 \leq f(i)_s \leq$~~
34 ~~14, coded as =T~~ (Supplementary ~~Tables~~ 4 and 5). With transition rates ~~set~~ as

1 follows, first A-C= 2, A-G= 5, A-T= 8, C-G= 3, C-T= 7, G-T= 4, and second A-C= 8,
2 A-G= 5, A-T= 2, C-G= 7, C-T= 3, G-T= 6. With the above, we adopted a heuristic
3 approach to facilitate the use of models in which we assume that transition rates are
4 either directly or inversely proportional to the frequencies. Note that
5 converting ~~Converting~~ absence = $f(i)$, =frequency 0 = A is not a neutral decision. This;
6 because this way we transform the coincidence in missing ingredients for each pair of
7 samples in informative, it is computed and may influence the general structure of the
8 tree. We could alternatively have treated absence as a gap or as missing information.
9 Hence, it is relevant to compare ~~Hence, the relevance of comparing~~ previous results of
10 presence/absence matrix with those of our Bayesian model ~~models~~.

11 We addressed the model uncertainty by ~~means of~~ model averaging using
12 reversible-jump MCMC (rjMCMC), where the chain integrates over the joint prior
13 probability density of a given model in the usual manner, but also jumps between all
14 203 possible candidate substitution models, visiting each model in proportion to its
15 marginal probability (Huelsenbeck et al., 2004).

16 The pool of candidate models is calculated by the Bell number, which for n
17 elements is the sum of the Stirling numbers of the second kind (Bell, 1934a, b). The
18 Markov chain sampling over the space of all possible reversible substitution models,
19 including the GTR model, and all models derived from it, by grouping the six rates in
20 various combinations, waives the restrictions imposed when choosing a single
21 substitution model. We did not observe the ~~observed~~ differences in the structure of the
22 resulting tree with transition rates either inversely or directly proportional to the
23 frequency of ingredients.

24 2.5.7 Medicinal use ~~uses~~ comparison

25 To ~~In order to~~ determine dissimilarities and coincidences in the medicinal uses,
26 because of the effort required, we could not review the use of the 187 ingredients;
27 hence, ~~so~~ we analyzed ~~had to resort to analyze~~ a subset of 10 ingredients ~~ten~~. This
28 subset presents the characteristic of being the most relevant (frequent) in the two
29 contrasting sources: Arancel of 1526 and modern ethnobotany of Albacete.

30 Of ~~Out of~~ the 187 ingredients, we selected the top 10 ~~ten~~ which in decreasing
31 order of frequency appeared both in the two key lists (A1526 and modern
32 ethnobiological records of Albacete) (Table 1). Therefore, we generated ~~raised~~ five
33 different lists of uses for each one of the 10 ~~ten~~ ingredients (Dioscorides, Chirino,
34 Laguna, and Matthioli) and the Albacete's ethnobotanical one.

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~~Table 1 approx. here.~~

We calculated for each ingredient and source the number of different diseases treated belonging to each one main category of diseases and related health problems of ICD-10 (WHO, 2014) (Fig. 14).

We systematized information in a crude matrix with 46 units, which are different versions of 10 ingredients (I) from five different sources (S) and 20 variables (K) which are categories of diseases and related health problems (Supplementary ~~Table~~~~Tab.~~ 6). Variables received values ranging between 0 and 100 representing the percentage of the total medicinal uses recorded for each unit. Therefore, 100 means that in this unit, ~~a 100% percent~~ of uses concentrate in one single ICD-10 main category.

We must emphasize that each ingredient is treated in five separate versions (codified in Fig. 15A with the abbreviations of the five sources analyzed) to check whether their uses coincide ~~or not~~ in this analysis. There are only 46 versions for the 10 ingredients instead of 50 because Chirino does not mention uses for *Rosmarinus* and *Olea*, and Matthioli ~~did not mention contemporary uses of mentioned~~ honey and saffron. ~~We~~~~In the case of Matthioli we~~ do not ~~concludesay~~ that no such ingredients appear ~~in Matthioli's works, but for these simples,~~ but their uses are attributed in full to Dioscorides, ~~and Matthioli describes nothing, in his commentary on contemporary uses, which itself does in the rest of the ingredients.~~

We analyzed this matrix using the same methods described above for frequency data. We ~~drew~~~~draw~~ a hierarchical tree with the Ward's minimum variance criterion (Fig. 15A).

Further, we summarized this matrix in one with five units (Supplementary ~~Table~~~~Tab.~~ 7), which are the 5 different sources and 20 variables simply by adding the values for all ingredients in each variable of the previous matrix. Therefore, we calculated the value of each cell (V) as follows:

$$V_{s,k} = \sum_{j=1}^n f(I_{j,k}),$$

~~-~~where n is the number of ingredients reported useful for a category of diseases k within a source s and f is the ~~percentage~~~~percentage~~ of use for each ingredient. We analyzed this matrix using the same methods described above for frequency data. We ~~drew~~~~draw~~ a hierarchical tree with ~~the~~ Ward's minimum variance criterion (Fig. 15B).

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3 Results and discussion

3.1 The tariff of medicines of Albacete (Spain) in 1526

The tariff (A1526) (Fig. 2) is mainly written in Spanish, with minor use of Latin, following a Spanish writing style known as “*Procesal encadenada*” which was widely used in the 16th century in Spain in the notarial ambit and by the Audience scribes.

It comprises a total of 101 different medicines with Spanish or Latin names that appear classified into 11 main categories: (1) single, (2) gums (and resins), (3) syrops, (4) ointments, (5) preserves, (6) electuaries, (7) laxative (*Medicinas solutivas conpuestas*), (8) pills, (9) distilled waters, (10) oils, and (11) confections.

Of these, 29 medicines are single ingredient, and 72 are more or less complex mixtures of active ingredients.

Simples receive in A1526 names similar to those used in Laguna (1555, 1566, and 1570) (Supplementary Tables 1 and 2). Complex drug combinations in A1526 receive the standard names of the epoch (Supplementary Table 1), influenced by Razi, Mesue and Nicolao (Anonymous, 1513 and 1519; De-Laredo, 1534; Razi, 1529; Sylvio, 1550) and their standardized composition is detailed in contemporary pharmacopoeias.

Each one formulation includes from 2 to 35 ingredients (on average 7.43, standard deviation 7.44) (Supplementary Table 1) according to the standards of the pharmacopoeias of Florence 1498, Barcelona 1511, Zaragoza 1546, and Valencia 1601 (Supplementary Table 2).

It is remarkable the high degree of overlap in terms of medicines with the pharmacopoeia of Florence. Of the 101 medicines listed (simple and compound) 97 appear in the pharmacopoeia of Florence 1498 (Fittipaldi, 2011; I-Dodici-Reformatori, 1567 and 1574). Lesser overlaps, 85, 84, and 60 respectively, are found with the pharmacopoeias of Zaragoza 1546 (Moliné, 1998; Sagaun and Aznarez, 1546), Valencia 1549–1601 (Valentian College of Pharmacists, 1601), and Barcelona (Domenech and Pau, 1587; Duch, 2000).

One hundred and eighty-seven different ingredients were involved in such formulations (Supplementary Table 1). Ingredients are, in an 85% of plant origin,

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1 and, in a 7.5% each, mineral or zoological substances. Over 90% of the organisms
2 investigated in ethnobotanical studies are vascular plants. The remaining 10% includes
3 animals, fungi, algae, microorganisms, minerals, and rocks (Rivera et al., 2014); thus,
4 proportions are similar to those in the list analyzed.
5
6

7
8 Plant organs and substances most often involved in the formulations are as
9 follows: fruits and seeds 25.13%, aerial parts 14.44% and gums and resins 11.76%,
10 and they differ from modern ethnobiological records in their percentages (Table 2).
11
12

13 ~~Table 2 approx. here.~~

14 ~~Table 3 approx. here.~~

15
16 The ingredients of A1526 belong to 83 families of organisms (69 botanical and
17 14 zoological), whereas ~~while~~ modern ethnobiological records in Albacete account to
18 102 families (99 botanical and 3 zoological).
19

20
21 Most frequent plant families in A1526 are Leguminosae (20.86% of drug
22 combinations), Apiaceae (20.32%) and Asteraceae (17.11%). It differs from
23 modern ethnobotanical records mostly in the high proportion of Leguminosae in A1526
24 and in the absence of Cistaceae (Table 3).
25

26
27 To note that zoological resources no longer recorded belong to the families
28 Bombycidae, Buthidae, Castoridae, Cervidae, Coralliidae, Elephantidae, Kerriidae,
29 Phasianidae, Physeteridae, Pteriidae, and Ursidae and the botanical ones to Acoraceae,
30 Adoxaceae, Altingiaceae, Amaranthaceae, Cannabinaceae, Capparaceae, Colchicaceae,
31 Combretaceae, Convolvulaceae, Dryopteridaceae, Fomitopsidaceae, Myristicaceae,
32 Nitrariaceae, Nymphaeaceae, Phyllanthaceae, Santalaceae, Styracaceae, and
33 Zingiberaceae.
34
35

36
37 Imported ingredients from outside Europe are approximately ~~a~~ 50% and the
38 rest are locally produced (cultivated) or gathered in Albacete (Fig. 6) ~~in~~ which notably
39 differs from modern ethnobotanical records. In Albacete 1995, above 90% of
40 ingredients were local and most were wild.
41
42

43
44 ~~Fig. 6 approx. here.~~

45
46 The biogeographical profile shows the relevance of tropical regions of Asia and
47 Africa (Fig. 7) as sources of crude drugs, which in modern local ethnobotanical records
48 are irrelevant.
49
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52 ~~Fig. 7 approx. here.~~
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1 We must emphasize that the profile of the knowledge of the Spanish population
2 in the rural areas is suffering in the 21st century a profound change in the sense of a
3 deep loss of knowledge associated with ~~a~~-trivialization. This has led to the Spanish
4 authorities to start the Spanish inventory of traditional knowledge related to
5 biodiversity (Pardo et al., 2012).
6
7

8 However, data collected in the villages of Albacete in the last decade of the 20th
9 century still reflect a rich and diversified local culture and is, little influenced by
10 globalization (Verde, 2002). This explains the high proportion of local species.
11
12

13 3.2 *Abandonment and persistence over time of ingredients and drug combinations*

14 Simples and, mostly, drug formulations recorded in A1526 gradually
15 disappeared with time, as these were no longer present in later catalogs.
16 ~~Figure catalogues~~. ~~Fig.~~ 8 shows how shared ingredients were rather more dependent on
17 chronological than on geographical grounds, and decreased over time (process of
18 deletion in evolutionary terms).
19

20 Most complex mixtures essentially disappeared between 1600 and 1750 CE
21 (Table 4), although some persisted until 1910.
22

23 ~~Fig. 8 approx. here.~~

24 ~~Table 4 approx. here.~~

25 This does not mean~~means~~ that the whole set of ingredients of these mixtures
26 disappeared in parallel, because~~since~~ most persisted. However, numerous botanical and
27 zoological ingredients, and almost all mineral and fossil substances, to 33, were no
28 longer present in the analyzed repertories since 1750 –and another 40 from 1910
29 onward~~onwards~~ (Table 5). Most ~~the~~-ingredients that were no longer in use were
30 imported (41), but some (23) are wild and a few ones (9) are locally cultivated~~farmed~~.
31
32

33 ~~Table 5 approx. here.~~

34 Ingredients, largely of plant origin, to 114, are still in use (in the analyzed
35 sources) in Modern phytotherapy and/or local medical-pharmaceutical ethnobotany.
36 Thus, at present, nearly ~~a~~-61% of the A1526 ingredients remain as~~a~~ usual materia
37 medica (Tables 5 and 6).
38

39 ~~Sixty-nine~~~~To 69~~ ingredients (from the 187 in A1526); (Table 6) are still in use
40 in medical ethnobotany sources. Most are locally cultivated (42); ~~but~~ some (23) are
41 wild species, and a few ones (4) are imported from outside Europe. It is worth
42 mentioning~~to mention~~ that ~~out~~ of these 69 ingredients, only 15 are exclusively found in
43 ethnobotanical sources, and the remaining 54 are also used in Modern phytotherapy.
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Forty-five species and substances that are not persisted in local ethnobotanical records are consulted but are still present in the naturopathic medicine and Modern phytotherapy (Table 6) ~~from form~~ another singular group. Most are imported (22), ~~but~~ some (15) are widely cultivated, and a few ones (8) are wild species. It is evident that especially those wild or locally cultivated species from this last list are used in ethnobotanical sources of Western Europe, although they were not recorded in our two samples (Albacete and Alta Valle del Reno).

~~Table 6 approx. here.~~

3.3 *Relationships of the 1526 tariff for medicines of Albacete (Spain) with other ~~catalogse~~ catalogues, herbals, pharmacopoeias and ethnobotanical information based on the ingredients*

Based on the presence/~~the~~ absence of ingredients, the principal coordinates analysis (PCoA) of sources ~~produced~~ produces a graphical display where four groups are apparent (Fig. 9) with relatively low uncertainty. However, ~~there~~ the adscription of Murcia 1823 and Fitoterapia.net 2015 is doubtful.

~~Fig. 9 approx. here.~~

Overall, the classification generated through hierarchical cluster using the Ward's minimum variance criterion (Fig. 10) confirmed these four groups, but the doubts about Murcia 1823 and Fitoterapia.net 2015 remain unsolved. Finally, the weighted neighbor tree (Fig. 11) ~~furnishes~~ furnish on the base of 20,000 bootstrapped trees the level of support for the different groups and subgroups, and again adscription of Murcia 1823 and Fitoterapia.net 2015 remains doubtful. It is worthy ~~worth~~ of notice the high support (97%) for the clade of **Renaissance Herbals and Pharmacopoeias** opposed to another clade (with 99% support) that comprises the rest of sources.

The correspondence analysis (Fig. 12 A), based on weighted presence of ingredients, graphically represents the intermediate position of Murcia 1823 between the **Renaissance Herbals and Pharmacopoeias** and **Old phytotherapy**, as a link between both groups. Here we ~~We~~ detect ~~here~~ a similar intermediate position of Fitoterapia.net 2015 between **Ethnobotany and Folk Medicine** and the sources ascribed to Old phytotherapy.

Within the group of **Renaissance Herbals and Pharmacopoeias**, A1526 links first with the pharmacopoeia of Florence 1498–1574, and other pharmacopoeias (Concordia Barcinonense 1511–1587, Valencia 1601, and Zaragoza 1553), with a 95% of support (Fig. 11).

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Other more or less contemporary and geographically close sources (Castile Zamudio de Alfaro 1592–1599, El Bonillo 1711, Granada 1556, Zaragoza Hospital 1601–1609) slide down sequentially together with the Spanish Renaissance version of Dioscorides' herbal (Laguna, 1555) and the recipes and lists of medicines written by the seemingly marginal group of Moors from Valencia 1573–1593. Both conforming a major group that receives a support of 97% (Fig. 11).

We, a priori, included the Moors from Valencia 1573–1593 within **Ethnobotany and Folk Medicine** category assuming their supposed marginal status. However, both ordination (Fig. 9) and classification (Figs. 10 and 11) clearly show it as part of the **Renaissance Herbals and Pharmacopoeias** group.

Although marginal in social sources of Spain, the Moors practiced ~~a~~ medicine and used the simple and compound medicines according to their eastern Islamic traditions and culture. Therefore, ~~the Moorsthey~~ use the same medicinal ingredients as official pharmacy of their epoch, deeply influenced by Islamic medicine, and, thus, show little relationships with modern ethnobotanical records.

This cluster reflects a common cultural substrate of medicine and materia medica in the 16th century CE, not only in Spain but also across Europe. The Salerno school of medicine and oriental medical traditions, which evolved in Islamic countries, strongly influenced it. This materia medica is rich in exotic materials imported from India, Southeast Asia, and tropical regions of Africa (Fig. 7) and zoological and mineral substances play a relevant role (Table 2), especially in complex drug formulations, some including over 30 different ingredients.

We ~~didhave~~ not ~~findfound~~ any of the 72 complex drug combinations of A1526 in use among informants interviewed since 1995 in either Albacete or Alta Valle del Reno. In fact, there are very few combinations of more than two or three ingredients.

Although complex drug compounds with c. 40 different ingredients were recorded in Madeira (Portugal) (Rivera and Obón 1995a and b) and in Syria, Lebanon, Turkey and, used by the immigrants from these countries, in Great Britain, France, and Germany (Carmona et al., 2005; Obón et al., 2014), ~~;) this is in fact extremely infrequent in modern ethnobotanical records in Europe.~~

Noticeably, 16th century CE herbals including those by Matthioli and Laguna seriously questioned the reliability, quality, and purity of exotic materia medica widely used by their contemporary pharmacists, and together with the introduction of

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1 American medicinal substances, contributed to the decrease in the use of oriental
2 products.

3
4 As noted above, over time, the presence in the ~~catalogseatalogues~~ of exotic
5 oriental substances decreased. This is observed, particularly, in ethnobotanical modern
6 records of Albacete (rural areas) where the materia medica is substantially local (Fig. 6)
7 and mainly presents a Mediterranean and Euro-Siberian biogeographical profile (Fig.
8 7). Coincidences with A1526 gradually decrease (Fig. 8) in **Modern phytotherapy** and
9 present ethnobotany.

10
11 Here, it is worth to mention Murcia 1823, locally published and in use in the
12 pharmacies of the city of Murcia in the ~~beginningbeginnings~~ of the 19th century, which
13 is a Spanish translation of a French materia medica. Its eclectic and conservative nature
14 places it as a transitional source between **Renaissance Herbals and Pharmacopoeias**
15 and **Old phytotherapy** (~~FigsFig.~~ 9, 10 and 12). This led to its classification as an
16 outlier with low support in Fig. 11.

17
18 The **Old phytotherapy** cluster (Fig. 9) links close the inventories of two
19 pharmacies in Albacete (19th and early 20th centuries CE). The online Vade Mecum of
20 herbal products in Spain (Fitoterapia.net 2015) appears next to this group and
21 seemingly associated to it in ordination analyses (~~FigsFig.~~ 9 and 12). The presence in
22 this cluster of the Vade Mecum along with **Old phytotherapy** is explained because the
23 Spanish herbal market superpose different tendencies including old-fashioned
24 traditional local products, modern evidence-based rational phytotherapy products, and
25 recently introduced oriental medicines. Given the eclectic and comprehensive nature of
26 fitoterapia.net, it somewhat overlaps with the ethnobotanical cluster. Thus,
27 classification analysis shows its relationships with **Ethnobotany and Folk Medicine**
28 (Fig. 10 and 11).
29

30
31 ~~Fig. 10 approx. here.~~

32
33 ~~Fig. 11 approx. here.~~

34
35 Curiously, a third cluster **Modern phytotherapy** (EMA and Naturopathy)
36 closely links a naturopathy popular book (Vander, 1971), published in Spain but with
37 strong central European influence, and the official ~~catalogeatalogue~~ of herbal
38 monographs by the HMPC of the European Medicines Agency (EMA 2015).
39 Ordination analysis (Fig. 9 and 12) clearly show this relationship, which is confirmed
40 in the classification (Fig. 10) and receives a 99% support in the bootstrapped weighted
41 neighbor joining tree (Fig. 11).

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1 Among the key objectives of HMPC are:
2

3 First, maintain EU herbal monographs and ~~list~~List entries as an up-to-date and
4 consistent base for national procedures according to available scientific data and state
5 of the art.
6

7 Second, to identify and collect criteria for assessment needs, according to
8 market relevance, using available data from National Competent Authorities and
9 Interested parties (HMPC, 2015a).
10

11 Both available evidence and market priorities determined a strong Central
12 European bias in the herbal substances proposed to HMPC for assessment (HMPC,
13 2015b). Noticeably, the ~~catalogue~~catalogue of herbal products available in Spain
14 (Fitoterapia.net 2015) does not ~~integrate~~integrates into this cluster, being instead closer
15 to **Old phytotherapy** and **Ethnobotany and Folk Medicine** groups.
16

17 Moreover, the ethnobotanical records from Albacete (Spain) and Alta Valle del
18 Reno (Italy) form a cluster in the classification generated following the minimum
19 variance Ward's criterion (Fig. 10) within the **Ethnobotany and Folk Medicine** group.
20 Both ~~also~~ appear ~~to be~~ associated in the ordination generated in the PCoA (Fig. 9).
21 However, the classification generated with weighted neighbor joining method, clusters
22 within a cascade ethnobotanical and folk medicine sources, ending just with the
23 Modern phytotherapy (EMA and Naturopathy) group, with ~~a~~94% support.
24

25 The Sephardic traditional medicines, and the Inquisition records (Healers and
26 witches 1500 ~~to~~ 1700) containing repertoires of medicines and recipes of local healers
27 and witches that were processed by the Inquisition tribunals, appear in the ordination
28 analysis close to Albacete 1995 (Figs. 9 and 12). Classification supports this
29 association (Figs. 10 and 12). These present in common with Albacete 1995 and Alta
30 Valle del Reno 2014 the use of simple drugs or low complexity combinations and the
31 use of easily accessible local resources, which are often foods and food ingredients.
32

33 The Mula 1760 manuscript of folk medicine is clearly associated to the
34 **Ethnobotany and Folk Medicine** group both by ordination (Fig. 9) and classification
35 analysis (~~Figs~~Fig. 10 and 11).
36

37 Ingredients that are locally available in Mediterranean areas of Europe, wild or,
38 most often grown in relatively small home-gardens are the most frequent items in these
39 five ethnobotanical sources. Therefore, we did not ~~find~~found neither any complex
40 formula of those used in A1526, nor rare exotic ingredients.
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1 Concerning ingredient frequencies, (~~Table 1~~) differences are noticeable in terms
2 of presence/absence of exotic imported products (~~Table 1~~). ~~Forty percent~~. ~~A 40%~~ of the
3 most frequent ingredients in A1526 are imported substances, which in the
4 ethnobotanical records are irrelevant. In parallel, ~~18 out~~ of the 25 most frequent
5 medicinal plants in the Albacete 1995 ethnobotanical records (Table 1) were not
6 involved in the standard formulations of A1526.

11 3.4 *Dependence of ethnobotanical records from external sources and ingredients*

12 We assessed the hypothesis for a dependence of ethnobotanical records with
13 respect to classical or modern pharmaceutical sources through a
14 ~~correspondence~~ ~~Correspondence~~ analysis (Fig. 12 B) with negative results. The
15 ethnobotanical samples appear together without close links to “external” sources
16 (SOU).
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20 We assumed “a priori” that ~~lists of~~ medicinal ingredients from the Moors of
21 Valentia 1570 CE were part of a local tradition, on the ~~basis~~ ~~base~~ of the classification as
22 healers of the medical practitioners of this ethnic group. Nevertheless, the analysis
23 shows clearly that this source directly links those in **Renaissance Herbals and**
24 **Pharmacopoeias**. It is unrelated to other contemporary sources like ~~healers~~ ~~Healers~~ and
25 witches 1500–1700 (Fig. 12B). It appears next to **Old phytotherapy**. As we expected,
26 we found a higher differentiation for modern ethnobotanical sources in Spain
27 (Albacete) and in Italy (Alta Valle del Reno) (Fig. 12).
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33 ~~Fig. 12 approx. here.~~

34 The Bayesian inference and model choice across a wide range of phylogenetic
35 and evolutionary models (Huelsenbeck et al., 2004) applied to the weighted matrix of
36 ingredients and sources (Supplementary ~~TableTab~~. 4) transformed into a four–states
37 matrix (Supplementary ~~TableTab~~. 5 A and B) furnish a model, which, largely,
38 coincides with those resulting of the previous classifications. This evolutionary model
39 reflects relationships in an almost sequential form (Fig. 13).
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44 ~~Fig. 13 approx. here.~~

45 The tree (Fig. 13) presents an inverted chronological sequence, where modern
46 sources appear near the base and A1526 and associated sources at the tip. The tree
47 depicts from the top to the base a pattern of decreasing complexity and exoticness,
48 determined by a set of three well distinct core groups of species. First, 15, mostly local
49 species used in Mediterranean Europe during centuries and here recorded exclusively in
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1 ethnobotanical sources. Second, 45, mostly imported, used in pharmacy during
2 centuries. Third, 69, mostly cultivated, used in both.

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5 The 69 species (Table 6) vertebrate the tree from A1526 to Albacete 1995 and
6 EMA, and vice versa. The continuous use of these 69 ingredients is documented for, at
7 least, the last 500 years. The complexity reached a maximum represented by A1526
8 and contemporary pharmacopoeias (between 164 and 187 ingredients shared), which
9 gradually decreased over time through a process, ~~lead~~ in its beginnings by
10 Matthioli and Laguna (150 ingredients), of revalorization of European materia medica
11 and incorporation of new drugs. Therefore, from an evolutionary perspective, the
12 A1526 clade is a “dead end”.

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17 The outgroup Hawaiian Materia Medica (Fig. 13) (only ~~four~~ coinciding
18 ingredients) roots the tree and clearly influenced the exclusion from the main tree of
19 Alta Valle del Reno 2014 (36 ingredients shared with A1526), which questions its
20 place in previous analysis. Alternatively, we defined as outgroup Chinese Materia
21 Medica (47 coinciding ingredients) but the structure of the tree obtained was similar
22 (not shown). Therefore, it is pertinent to note what is discriminant is not only the total
23 but ~~also~~ the specific set of ingredients shared.

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30 At the base of the tree, with a low support, but noteworthy, is the clade
31 represented by **Modern phytotherapy** (the HMPC of EMA and naturopathy) which
32 show an incipient tendency to form an independent clade with affinity ~~toward~~
33 the Chinese Materia Medica (Fig. 13) which merits further investigations. With such a
34 low ~~number~~ of ingredients, between 30 and 40 in each source, random
35 coincidences with large lists of hundreds of ingredients, like those of the Traditional
36 Chinese Medicine, are possible. These may have influenced this rare association.
37 Nevertheless, the fact is that several ingredients retained in EMA and naturopathy are
38 part of the Chinese Materia Medica.

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43 The cluster of A1526, classical pharmacopoeias, and herbals appears ~~to be~~
44 supported with a probability of 0.97 (Bayesian probabilities are expressed with values
45 between 0 and 1) at the end of a clade. ~~Just~~ in parallel with Murcia 1823 and
46 forming, in turn, a clade with probability 0.99 with two lists of pharmacies from
47 Albacete, dating 1881 and 1910 (Fig. 13). The whole appears basally connected with
48 the list of Fitoterapia.net with probability 0.98. Therefore, the **Old phytotherapy**
49 cluster takes the place of a bridge between **Renaissance Herbals and**

1 **Pharmacopoeias** and the cluster of **Ethnobotany and Folk Medicine** that gradually
2 unfolds ~~toward~~towards the basal positions of the tree.

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5 3.5 *Did alternative and complementary medicines exist during the sixteenth*
6 *century CE in Europe?*

7
8 The ~~aforementioned~~above analyses suggest the existence of a sort of common
9 medical practice based on the use of local inexpensive resources and extremely simple
10 formulations in parts of Mediterranean Europe. A medicine for the poor, partially
11 known and underrated by the medical establishment since, at least the times of the
12 medical school of Salerno.

13
14 Although the official system of medicine was well established across Europe,
15 this was not the unique ~~healthcare~~health-care system available. As mentioned above,
16 the evidence of medical practices existing in parallel with the official system of
17 medicine was frequent in Europe and not only in rural areas.

18
19 Laguna (1555), for instance, mentions that he personally experienced the care of
20 a half-witch (in his words) in 1543 in the city of Metz (Lorraine), who cured him of an
21 irreducible insomnia by stuffing henbane leaves (*cf. Hyoscyamus aureus* L.) within his
22 pillow.

23
24 Healers were numerous and, often, considered suspicious of heterodox
25 practices. They were repeatedly denounced to the religious tribunals of the *Inquisición*,
26 not only in Spain (Walker, 2005), as it is attested in the archives (Blazquez, 1991;
27 Cirac, 1942).

28
29 In parallel, ~~there~~ existed a wealth of medical knowledge transmitted within
30 families from grandmothers to daughters and granddaughters, specific for minor and
31 chronic diseases, which has been documented in the Sephardic tradition and present
32 patterns and use ingredients similar to those of our ethnobotanical records from
33 Albacete 1995 and, to some extent, to those of Alta Valle del Reno 2014. Note that
34 Sephardic Jews were expelled from Spain in 1492 and maintained their Spanish
35 traditions and language to present times in their places of exile (Levy and Levy, 1991;
36 Romeu, 2010; Shaul, 1986).

37
38 The Systematic inventory of resources raised by the officials of Felipe II in the
39 Kingdom of Castile (Carrilero et al., 2014) furnished further evidence. For instance,
40 at Chinchilla (Albacete) ~~on the 8~~ February ~~8~~, 1576: “This city is abundant of sage and
41 thyme, infinite licorice grows by this city and much lavender, so much that can be
42 loaded several carriages of such. It grows also in this mountain, great abundance of a
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2 purgative herb that is **not written in the codices of herbalists**, here they call *burfalaga*
3 or *sanamonda*. In the kingdom of Murcia they call *yerba de Ricote*. It is herb, which
4 very easily, purge the humors: phlegm, choleric and melancholy, taken with an egg or
5 with a little honey. Puts admiration for those who do not know by how easy it is to
6 purge by vomiting and stool”.

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Actually, this herb is *Thymelaea tartonraira* (L.) All., which still grows in Chinchilla and whose aerial parts in decoction are reported in ethnobotanical interviews as a laxative to treat constipation in Alcadozo, Peñarrubia (Balazote), Peñas de San Pedro and Puente Torres (Valdeganga), all four localities of the province of Albacete (Verde, 2002).

The same source (Carrilero et al., 2014) furnishes evidence for the commercial flux of medicinal substances from some of these mountains to the large cities, and the high proportion of local medicinal substances in rural pharmacies.

For instance, at Yeste (Albacete) ~~on the~~ 7 December 7, 1576: “There are herbs and such and so many; that come to look for them from the Kingdom of Valencia and elsewhere. And of these, the pharmacies are supplied, in this land if not of some drugs brought from outside”. This suggests a difference, which merits exploration between the pharmacies of small towns in rural areas and those of the large cities at least during the 16th century. In this case, seems that poor medicines in the sense of Salerno predominate in the former.

Therefore, evidence exists for a parallel array of alternative medical practices and practitioners, which interacted with the official medical staff and often complemented their services during centuries in Spain.

Our analyses show the close relationships, in terms of ingredients used, of this alternative medicine with the medical information recorded through the ethnobotanical fieldwork.

Furthermore, the absence in A1526 of ingredients such as *Thymelaea* and different Cistaceae (*Cistus* and *Helianthemum* spp.), despite their presence and uses in the area, reflects the principle that any system of medicine does not get to use all available resources and therefore, the repertoire of ingredients is determined not only by their local availability. This involves a series of preferences derived from the system of medicine and his explicative model, and, in general, of worldview and culture.

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3.6 Medicinal uses of relevant ingredients

We analyzed 212 different ethnobotanical medicinal uses in the province of Albacete for the top ~~10~~^{ten} medicinal plants and substances (in bold in Table 1). ~~As~~
~~Since~~ A1526 did not ~~include~~^{included} explicit mention to the purposes of each medicinal formula and ingredient, we analyzed the medicinal uses of these substances in three main references of the epoch Alonso de Chirino (Herrera 1973), the Dioscorides herbal edited by Andrés Laguna (1555) and Matthioli (1549).

We recorded in Chirino 100 medicinal uses. In Laguna (1555), we found 202 uses attributed to Dioscorides and 63 personally added by Andrés Laguna himself. Matthioli (1549) added 41 uses, and allowed to confirm those 202 uses attributed to Dioscorides by Laguna.

This gives a different profile of uses for each source with relatively higher coincidence among Chirino and Dioscorides, a close coincidence of Laguna and Matthioli and a relatively independent profile for the ethnobotanical records from Albacete (Fig. 14) with a high proportion of diseases of the circulatory system, the respiratory system and those related with pregnancy, childbirth, and the puerperium.

~~Fig. 14 approx. here.~~

The hierarchical cluster based on frequencies of main ICD-10 diseases categories for the top ~~10~~^{ten} ingredients using the Ward's minimum variance criterion (Fig. 15A) shows that, on the ~~basis~~^{base} of the uses attributed by Dioscorides, at least ~~6~~^{six} medicinal plants out of ~~10~~^{ten}, present a high degree of coincidence and thus are relatively interchangeable.

There is no coincidence between the different sources in the specific medicinal uses for a determined plant or substance. Furthermore, we found coincidences for completely different substances (Fig. 15A).

It is exceptional to find coincidences such as those for *Crocus sativus* between Dioscorides original prescriptions and those recommended by Andrés Laguna in the next paragraph of the same book (Laguna 1555).

~~Fig. 15 approx. here.~~

Coincidences of ethnobotanical records with the analyzed herbals are equal to zero, at least in terms of the profile of medicinal uses for each one of the ~~10~~^{ten} main ingredients.

The medicinal ~~use~~^{uses} analysis of the top ~~10~~^{ten} ingredients shows that the single ~~one~~ coincidence ~~in~~^{is} all ~~10~~^{ten} substances are medicinal and useful. Nevertheless,

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1 each author organizes these for different purposes within their repertoires of medicinal
2 resources (Fig. 15). Therefore, overall, the profile of medicinal uses depended primarily
3 on the cultural preferences of medical practitioners and schools and epidemiological
4 constraints (main causes of morbidity and mortality) rather than on the specific
5 pharmacological properties of each plant and substance.
6
7

8 **4 Conclusions**

9
10 The ~~aforementioned~~ analysis ~~yields~~ ~~gives rise to~~ a range of immediate and
11 far-reaching conclusions relevant to ethnobotanists and ethnopharmacologists:
12

13 Old medicine in Mediterranean Europe and concretely in Albacete (Spain) as
14 reflected by A1526 relied in certain ingredients in despite of others locally available but
15 which were underappreciated, confirming that any system of medicine does not get to
16 use all available resources and therefore, the repertoire of ingredients is determined not
17 only by their local availability. However, a relatively substantial part of this materia
18 medica consisted of local ingredients, which persist in the ethnobotanical records but
19 others are also lost.
20

21 One hundred ~~and~~ nine ingredients, largely of plant origin, are still in use (within
22 the analyzed sources) in Modern phytotherapy (45) or pharmaceutical ethnobotany
23 (64). Thus, at present, nearly a 58% of the A1526 ingredients remain ~~asa~~ usual materia
24 medica.
25

26 Different analysis confirmed the four distinct styles of materia medica:
27 Renaissance Herbals and Pharmacopoeias, Old phytotherapy, Ethnobotany and Folk
28 Medicine and finally Modern phytotherapy, characterized by the set of ingredients
29 retained from the initial list of 187 from the A1526 in terms of number and specific
30 ingredients.
31

32 A substantial difference amongst ethnobotanical (Albacete and Alta Valle del
33 Reno), and pharmaceutical materia medica, consists in the almost exclusive use of local
34 resources in ethnobotanical sources. This contrasts with the weight of imported exotic
35 products in pharmacy (even in 16th-century CE herbals, pharmacopoeias, and
36 pharmacies).
37

38 Another difference is the generalized use of simples or drug formulations much
39 less complex than the mixtures with numerous ingredients in Renaissance and Old (and
40 in some respects Modern) pharmaceutical phytotherapy sources.
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1 Medicinal uses for specific substances show notable differences between the
2 analyzed herbals. Coincidences of ethnobotanical records from Albacete with the
3 analyzed herbals in terms of the profile of medicinal uses are equal to zero.
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5
6 An exhaustive revision of original documents of healers and witches as these
7 appear recorded in several Inquisition archives, most unpublished but others now
8 available online, from an ethnopharmacological perspective would offer novel and
9 significant evidence. A systematic recording and analysis of medical Sephardic
10 traditions is necessary and urgent especially concerning the materia medica.
11

12
13 Regarding our question: is there something new under the sun? The analyzed
14 evidence suggests, first, that the contrast between highly valued expensive drugs and
15 unappreciated local wild medicinal plants, in the field of conventional medicine as
16 evidenced by the Salerno school of medicine, ~~still~~ persists. Second, ethnobotany, in
17 rural areas of Albacete, describes systems with a high degree of stability and resilience.
18 In these systems, ~~was and yet is predominant~~ the use of local resources, largely wild but
19 also cultivated, was and still is predominant.
20
21

22 **5 Acknowledgments**

23 **~~5 Acknowledgements~~**

24 We would like to thank Dr. Bernat Vanaclocha for granting full access to the
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26 comments of reviewers who have helped to improve this work.
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Is there nothing new under the sun? The influence of herbals and pharmacopoeias on ethnobotanical traditions in Spain. Tables

Tab. 1. The 25 most frequent species and ingredients.

In: **A.** Albacete tariff 1526 (25 from 187 ingredients), **B.** Albacete 1995 (ethnobotany) (25 from 358 simples, including medicinal flora and fauna) and **C.** In the entire set of sources analyzed (25 from 187 ingredients). **Color codes: Blue:** most frequent species present in at least two lists. **Green:** imported from outside Europe. In **bold** are marked the selected species for analysis of medicinal uses. **Note:** (1) water is also a common ingredient in Albacete 1995, even if not mentioned by the informants, since remedies are often prepared as decoctions, infusions or similar.

Albacete 1526	Medicines	Albacete 1995	Counts	The set of sources	Sources
Rosa gallica L. "Officinalis" (and related cultivars) (flowers)	14	<i>Chiliadenus glutinosus</i> (L.) Fourr.	71	Olea europaea L. (leaves and fruits)	21
Apis mellifera L. (honey)	12	Rosmarinus officinalis L. (aerial parts)	39	<i>Pimpinella anisum</i> L.	21
<i>Nardostachys jatamansi</i> (D.Don) DC.	11	Olea europaea L. (leaves and fruits)	38	Rosmarinus officinalis L. (aerial parts)	21
<i>Convolvulus scammonia</i> L.	9	<i>Malva sylvestris</i> L.	36	Apis mellifera L. (honey)	20
Crocus sativus L. (pistils)	9	<i>Thymus mastichina</i> L.	33	<i>Artemisia absinthium</i> L.	20
H ₂ O Water (1)	9	Ficus carica L. (leaves, latex and figs)	29	Foeniculum vulgare Mill. (leaves and fruits)	20
Vitis vinifera L. (grapes and raisins)	9	<i>Euphorbia serrata</i> L.	27	Rosa gallica L. "Officinalis" (flowers)	20
<i>Zingiber officinale</i> Roscoe	9	<i>Juniperus oxycedrus</i> L.	27	<i>Apis mellifera</i> L. (wax)	19
<i>Cinnamomum verum</i> J.Presl.	8	<i>Lithodora fruticosa</i> (L.) Griseb.	27	<i>Apium graveolens</i> L.	19
Olea europaea L. (leaves and fruits)	8	Mentha pulegium L. (aerial parts)	26	<i>Cichorium intybus</i> L.	19
<i>Pistacia lentiscus</i> L. and rarely <i>P. terebinthus</i> L.	8	Ruta angustifolia Pers. and R. graveolens L. (aerial parts)	25	<i>Fumaria officinalis</i> L.	19
<i>Santalum album</i> L.	8	<i>Sideritis hirsuta</i> L.	25	<i>Mentha x piperita</i> L.	19
<i>Apis mellifera</i> L. (wax)	7	<i>Thymus orospedanus</i> H. del Villar	25	<i>Prunus dulcis</i> (Mill.) D.A.Webb	19
Foeniculum vulgare Mill. (leaves and fruits)	7	<i>Lavandula latifolia</i> Medik.	24	<i>Saccharum officinarum</i> L.	19
<i>Piper longum</i> L.	7	<i>Sideritis tragoriganum</i> Lag.	24	Vitis vinifera L. (grapes and raisins)	19
<i>Piper nigrum</i> L.	7	<i>Daphne gnidium</i> L.	23	<i>Althaea officinalis</i> L.	18
<i>Syzygium aromaticum</i> (L.) Merr. & L.M.Perry	7	<i>Marrubium vulgare</i> L.	23	<i>Cinnamomum verum</i> J.Presl.	18
<i>Viola odorata</i> L.	7	<i>Matricaria chamomilla</i> L.	23	Crocus sativus L. (pistils)	18

<i>Aloe vera</i> (L.) Burm.f.	6	<i>Paronychia suffruticosa</i> (L.) DC.	23	<i>Cuminum cyminum</i> L.	18
<i>Apium graveolens</i> L.	6	<i>Sedum spectabile</i> Boreau	21	<i>Glycyrrhiza glabra</i> L.	18
<i>Artemisia absinthium</i> L.	6	<i>Sideritis leucantha</i> Cav. subsp. <i>bourgeana</i> (Boiss & Reuter) Alcaraz et al.	21	<i>Papaver somniferum</i> L.	18
<i>Astracantha gummifera</i> (Labill.) Podlech/ <i>Astragalus clusii</i> Boiss.	6	<i>Juglans regia</i> L. var. <i>regia</i>	20	<i>Pinus sylvestris</i> L. (resin)	18
<i>Glycyrrhiza glabra</i> L.	6	<i>Acinos arvensis</i> (Lam.) Dandy	19	<i>Ruta angustifolia</i> Pers. and <i>R. graveolens</i> L. (aerial parts)	18
<i>Pimpinella anisum</i> L.	6	<i>Foeniculum vulgare</i> Mill. (leaves and fruits)	19	<i>Syzygium aromaticum</i> (L.) Merr. & L.M.Perry	18
<i>Saccharum officinarum</i> L.	6	<i>Malva nicaeensis</i> All.	19	<i>Viola odorata</i> L.	18

Tab. 2. Comparison of drug types (parts and substances).

A. Albacete tariff 1526 (16 types). **B.** Albacete tariff 1526, coinciding ingredients (11 types) with Albacete Ethnobotany 1995. **C.** Albacete Ethnobotany 1995–2015, complete medicinal flora and fauna (13 types).

A. Albacete 1526	%	B. Albacete 1526 U Albacete 1995	%	C. Albacete 1995	%
Fruits and seeds	25.13	Aerial parts	29.31	Aerial parts	47.32
Aerial parts	14.44	Fruits and seeds	29.31	Fruits and seeds	13.78
Exudates (Gum and resin)	11.76	Roots	12.07	Leaves	12.87
Roots	8.02	Flowers	10.35	Flowers	9.09
Mineral substances	7.49	Exudates (Gum and resin)	6.90	Roots	2.78
Flowers	7.49	Whole plant	3.45	Exudates (Gum and resin)	1.78
Animal substances	7.49	Honey	1.72	Wood	0.79
Rhizomes	5.88	Bulbs	1.72	Bark	0.79
Leaves	3.21	Mineral substances	1.72	Rhizomes	0.58
Whole plant	2.67	Rhizomes	1.72	Bulbs	0.58
Wood	2.14	Animal substances	1.72	Wax	0.54
Bark	1.07	Leaves	0	Animal substances	0.25
Bulbs	1.07	Bark	0	Honey	0.21
Honey	0.53	Wood	0	Mineral substances	<0.1
Wax	0.53	Wax	0	Whole plant	<0.1
Buds	0.53	Buds	0	Buds	<0.1

Tab. 3. A comparison of the top twenty families of plants and animals.

A. Albacete tariff 1526 (from 83 families). **B.** Albacete tariff 1526, matching ingredients (from 34 families) with Albacete Ethnobotany 1995. **C.** Albacete Ethnobotany 1995, entire set of medicinal flora and fauna. **Color codes: Green:** represented in the list by exotic species imported in Europe.

A. Albacete 1526	%	B. Albacete 1526 – Albacete 1995 (only identical ingredients)	%	C. Albacete 1995 (medicinal repertory)	%
Leguminosae	20.86	Lamiaceae	15.52	Lamiaceae	21.71
Apiaceae	20.32	Apiaceae	12.07	Asteraceae	9.92
Asteraceae	17.11	Asteraceae	6.90	Rosaceae	5.15
Lamiaceae	15.51	Leguminosae	5.17	Cistaceae	3.15
Rosaceae	12.83	Iridaceae	3.45	Apiaceae	3.03
Lauraceae	11.23	Rosaceae	3.45	Caryophyllaceae	2.91
Zingiberaceae	10.16	Papaveraceae	3.45	Malvaceae	2.74
Poaceae	9.63	Solanaceae	3.45	Poaceae	2.62
Crassulaceae	6.42	Pinaceae	3.45	Leguminosae	2.20
Papaveraceae	6.42	Adiantaceae	1.72	Cupressaceae	2.16
Burseraceae	5.88	Malvaceae	1.72	Liliaceae	2.16
Portulacaceae	5.88	Boraginaceae	1.72	Rutaceae	1.99
Ranunculaceae	5.88	Apidae	1.72	Euphorbiaceae	1.91
Rutaceae	5.35	Aristolochiaceae	1.72	Thymelaeaceae	1.91
Adoxaceae	4.81	Gentianaceae	1.72	Oleaceae	1.78
Caryophyllaceae	4.81	Aspleniaceae	1.72	Solanaceae	1.78
Castoridae	4.81	Betulaceae	1.72	Crassulaceae	1.66
Myrtaceae	4.81	Convolvulaceae	1.72	Boraginaceae	1.45
Polygonaceae	4.81	Asparagaceae	1.72	Polygonaceae	1.45
Punicaceae	4.28	Moraceae	1.72	Scrophulariaceae	1.41

Tab. 4. Disappearance over time of formulations in the sources analyzed.

Complex mixtures		
Type	Disappeared between 1600 and 1750 CE	Persisting until 1910
Electuaries	<i>filonio mayor, micleta,</i>	
Tinctures	<i>lauda</i>	
Syrups	<i>açetosa simple, bisançies, loch de pino</i>	<i>oximel compuesto, sticados</i>
Ointments	<i>populeo, palma, dialtea, desopilativo, dolor de costado, confortativo, basilia mayor, Aragón, maçiatòn</i>	<i>Resis, Agripa</i>
Tonics	<i>abatis, letuariis de gemis, aromático rosado, de pliris arçéticon, diaçimino</i>	<i>diagarganti frio</i>
Resolutive	<i>díacatalineo, letuario de çumo de rosas, diasen, letuario yndio, diafinico, letuario Elescofi</i>	<i>diaprunis de simple, diaprunis laxativo</i>
Pills	<i>sinequibus, cocheas, aureas, aureas de yera, fétidas mayors</i>	
Antidotes	<i>emagogo, tría fera magna, requies magna</i>	<i>triacca Mitridato</i>

Tab. 5. Ingredients disappeared between 1600 and 1910 CE in the sources analyzed.

Botanical Ingredients (Represented by the species name)	
	1600–1750
	<i>Alpinia zerumbet</i> (Pers.) B.L.Burt & R.M.Sm., <i>Aquilaria malaccensis</i> Lam., <i>Blackstonia perfoliata</i> (L.) Huds., <i>Cheilocostus speciosus</i> (J.Koenig) C.D.Specht., <i>Cichorium endivia</i> L., <i>Cuscuta epithimum</i> (L.) L., <i>Cymbopogon martini</i> (Roxb.) W.Watson, <i>Cyperus esculentus</i> L., <i>Limonium supinum</i> (Girard) Pignatti, <i>Mandragora officinarum</i> L., <i>Nardostachys jatamansi</i> (D.Don) DC., <i>Nuphar lutea</i> L., <i>Ranunculus aconitifolius</i> L., <i>Rosa bicolor</i> Jacq., <i>Silene vulgaris</i> (Moench) Garecke, <i>Solanum nigrum</i> L., <i>Terminalia bellirica</i> (Gaertn.) Roxb., <i>Terminalia chebula</i> Retz., <i>Terminalia citrina</i> Roxb. ex Fleming, <i>Tetraclinis articulata</i> (Vahl) Mast., <i>Valeriana celtica</i> L., <i>Vicia ervilia</i> (L.) Willd.
	1750–1910
	<i>Amomum subulatum</i> Roxb., <i>Asarum europaeum</i> L., <i>Atriplex hortensis</i> L., <i>Capparis sicula</i> Duhamel, <i>Citrullus colocynthis</i> (L.) Schrad., <i>Colchicum</i> sp., <i>Commiphora africana</i> (A.Rich.) Endl., <i>Commiphora gileadensis</i> (L.) C.Chr., <i>Convolvulus scammonia</i> L., <i>Curcuma zedoaria</i> (Christm.) Roscoe, <i>Cymbopogon schoenanthus</i> (L.) Spreng., <i>Dorema ammoniacum</i> D.Don, <i>Ecballium elaterium</i> (L.) A.Rich., <i>Euphorbia resinifera</i> O.Berg, <i>Ferula assa-foetida</i> L., <i>Ferula gummosa</i> Boiss. (incl. <i>Ferulago galbanifera</i> (Mill.) W.D.J.Koch), <i>Ferula persica</i> Willd., <i>Helleborus orientalis</i> Lam. (not <i>H. niger</i> L.), <i>Laricifomes officinalis</i> (Vill.) Kotl. & Pouzar, 1957 (= <i>Polyporus officinalis</i> Fries), <i>Liquidambar orientalis</i> Mill., <i>Mimusops elengi</i> L., <i>Operculina turpethum</i> (L.) Silva Manso, <i>Opopanax chironium</i> (L.) W.D.J.Koch, <i>Peucedanum ostruthium</i> (L.) W.D.J.Koch, <i>Phoenix dactylifera</i> L., <i>Phyllanthus emblica</i> L., <i>Portulaca oleracea</i> L., <i>Styrax officinalis</i> L., <i>Ziziphus jujuba</i> Mill.,
Zoological Ingredients (represented by the species name)	
	1600–1750
	<i>Bombyx mori</i> (= <i>Phalaena mori</i> L., 1758) Silk, <i>Elephas maximus indicus</i> (Cuvier), 1798, <i>Pinctada radiata</i> (Leach, 1814) Pearl, <i>Ursus arctos</i> L., 1758
	1750–1910
	<i>Buthus occitanus</i> Amoreux, 1789, <i>Castor fiber</i> L., 1758, <i>Cervus elaphus</i> L., 1758, <i>Gallus gallus</i> L., 1758, <i>Kerria lacca</i> Targ.–Tozz., 1884 (= <i>Coccus lacca</i> Kerr, 1782), <i>Moschus chrysogaster</i> Hodgson, 1839, <i>Physeter macrocephalus</i> L., 1758
Mineral and fossil substances	
	1600–1750
	Al ₂ O ₃ sapphires, Amber, Au gold, Be ₃ Al ₂ (SiO ₃) ₆ emerald, Fe ₃ Al ₂ Si ₃ O ₁₂ garnet almandine, lapis lazuli (mainly lazurite), SiO ₂ sard similar to carnelin
	1750–1910
	KAl(SO ₄) ₂ ·12H ₂ O Hydrated potassium aluminum sulfate, PbO (Litharge), (PbCO ₃) ₂ ·Pb(OH) ₂ White lead, ZrSiO ₄ Jacinth Zircon

Tab. 6. Persisting ingredients in the sources analyzed.

INGREDIENTS PERSISTING IN USE IN NATUROPATHIC MEDICINE AND OFFICIAL PHYTOTHERAPY AND THE MEDITERRANEAN ETHNOBOTANICAL AND ETHNOPHARMACOLOGICAL RECORDS ANALYZED

Botanical ingredients

Adiantum capillus-veneris L., *Aloe vera* (L.) Burm.f., *Althaea officinalis* L., *Anchusa azurea* Mill., *Apium graveolens* L., *Artemisia absinthium* L., *Borago officinalis* L., *Centaureum erythraea* Rafn., *Cichorium intybus* L., *Cinnamomum verum* J.Presl., *Corylus hispanica* Mill. ex D.Rivera & al., *Crocus sativus* L., *Cuminum cyminum* L., *Daucus carota* subsp. *drepanensis* (Arcang.) Heywood, *Ficus carica* L., *Foeniculum vulgare* Mill., *Fumaria officinalis* L., *Glycyrrhiza glabra* L., *Hedera helix* L., *Iris × germanica* L., *Laurus nobilis* L., *Lavandula stoechas* L. / *Thymus moroderi* Pau ex Martínez, *Matricaria chamomilla* L., *Mentha pulegium* L., *Mentha spicata* L. juice, powdered and essential oil, *Mentha × piperita* L., *Ocimum basilicum* L., *Olea europaea* L., *Paeonia officinalis* L., *Papaver somniferum* L., *Petroselinum crispum* (Mill.) Fuss, *Pimpinella anisum* L., *Pinus pinaster* Aiton, *Piper nigrum* L., *Polypodium vulgare* L., *Prunus domestica* L., *Prunus dulcis* (Mill.) D.A.Webb, *Punica granatum* L., *Rosa gallica* L. "Officinalis", *Rosmarinus officinalis* L., *Ruta graveolens* L., *Saccharum officinarum* L., *Salvia officinalis* subsp. *lavandulifolia* (Vahl) Gams, *Sambucus nigra* L., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Trifolium pratense* L., *Triticum aestivum* L. Starch, *Viola odorata* L.

Zoological Ingredients

Apis mellifera L., 1758, honey and wax

Mineral and fossil substances

H₂O,

INGREDIENTS EXCLUSIVELY PERSISTING IN USE IN THE MEDITERRANEAN ETHNOBOTANICAL AND ETHNOPHARMACOLOGICAL RECORDS ANALYZED

Botanical ingredients

Aristolochia fontanesii Boiss. & Reut., *Ceterach officinarum* Willd., *Cydonia oblonga* Mill., *Drimys maritima* (L.) Stearn., *Hyoscyamus albus* L., *Hyoscyamus niger* L., *Juniperus thurifera* L., *Lactuca sativa* L., *Lupinus albus* L., *Peganum harmala* L., *Pinus pinea* L., *Sempervivum tectorum* L., *Umbilicus horizontalis* (Guss.) DC., *Vitis vinifera* L., raisins or wine

Zoological Ingredients

Sus scrofa domestica Erxleben, 1777, fat

INGREDIENTS EXCLUSIVELY PERSISTING IN THE NATUROPATHIC MEDICINE AND OFFICIAL PHYTOTHERAPY

Botanical ingredients

Acorus calamus L., *Alpinia galanga* (L.) Willd., *Ammi visnaga* (L.) Lam., *Astracantha gummifera* (Labill.) Podlech/*Astragalus clusii* Boiss., *Boswellia sacra* Flueck., *Bryonia cretica* L., *Cassia fistula* L., *Chelidonium majus* L., *Cinnamomum camphora* (L.) J.Presl, *Cinnamomum cassia* (L.) J.Presl, *Citrus aurantium* L., *Citrus medica* L., *Commiphora myrrha* (Nees) Engl., *Cymbopogon nardus* (L.) Rendle, *Dryopteris filix-mas* (L.) Schott, *Elettaria cardamomum* (L.) Maton, *Euphrasia officinalis* L., *Geum urbanum* L., *Humulus lupulus* L., *Hyssopus officinalis* L., *Myristica fragrans* Houtt. (macis and nut), *Myrtus communis* L., *Nigella sativa* L., *Origanum majorana* L., *Pinus sylvestris* L., *Piper longum* L., *Pistacia lentiscus* L. / *Pistacia terebinthus* L., *Plantago afra* L., *Populus nigra* L., *Pterocarpus santalinus* L.f., *Rheum officinale* Baill., *Sambucus ebulus* L., *Santalum album* L., *Senna alexandrina*

Mill., *Tamarindus indica* L., *Tanacetum balsamita* L., *Tanacetum parthenium* (L.) Sch.Bip., *Trigonella foenumgraecum* L., *Zingiber officinale* Roscoe.

Zoological Ingredients

Bos taurus L., 1758 butter, *Corallium rubrum* L., 1758,

Mineral and fossil substances

Ag Silver, ClNa Salt, $KC_4H_5O_6$ potassium bitartrate,

Arancel 1526

Albacete

Fig. 1. Dioscorides' *Materia Medica* edited and commented by Laguna, published in Anvers 1555 CE (National Library of Spain).



Fig. 2. “Arancel” (Tariff for medicines) Albacete (Spain) 1526 CE (Provincial Archive of Albacete).

Item Description	Price (Dramas)
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Fig. 3. Sequence of the study. 1–3. Determining the identity and weight of ingredients. 4–6. Determining the presence and weight of these ingredients in sources of different nature. 7. Ordination, classification, and main groups of the different sources based on the presence/absence and weights of ingredients. 8. Evolution of relationships among the different sources based on ingredients (Bayesian). 9. Comparison based on medicinal uses (Cluster analysis).

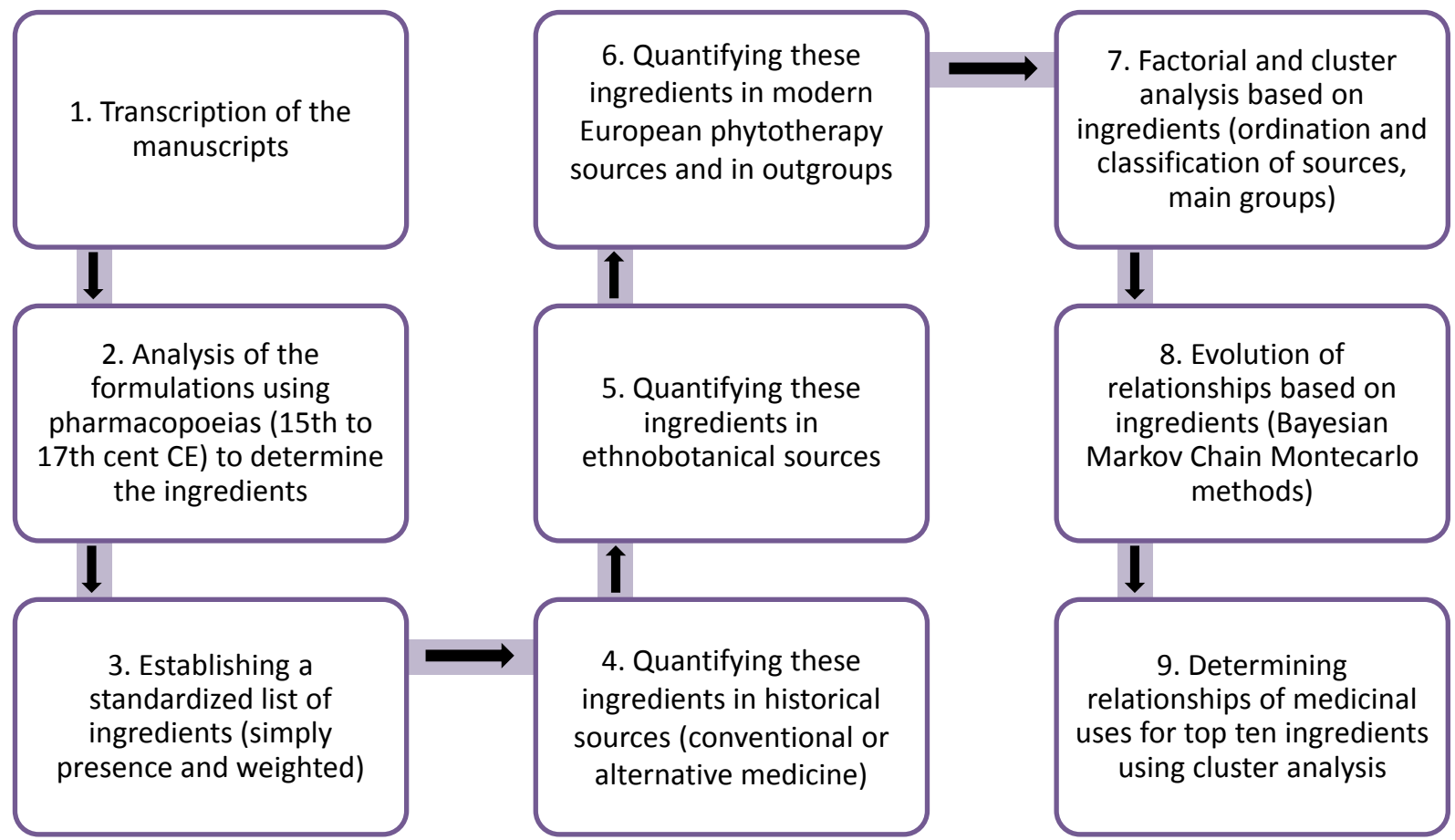


Fig. 4. Pharmacopoeias consulted to determine formulations and ingredients. **1.** Florence (Italy) 1498 CE. **2.** Barcelona (Spain) 1511 CE. **3.** Zaragoza (Spain) 1546 CE. **4.** Florence (Italy) 1567 CE. **5.** Florence (Italy) 1574 CE. **6.** Barcelona (Spain) 1587 CE. **7.** Valencia (Spain) 1601 CE. **8.** Spain 1865 CE.



Fig. 5. Geographical localization of analyzed documental sources. 1. Albacete 1526, 2. Albacete 1910, 3. Albacete 1881, 4. Castile 1599, 5. Barcelona 1511–1587, 6. El Bonillo 1711, 7. Albacete 1995, 8. Alta Valle del Reno 2014, 9. EMA 2014, 10. Fitoterapia.net 2015, 11. Florence 1498–1574, 12. Granada 1556, 13. Healers and Witches 1500–1700, 14. Laguna 1555, 15. Moors Valencia 1570, 16. Murcia 1823, 17. Sephardic (in Smyrna but also data from Salonica), 18. Mula Manu 1790, 19. Valencia 1601, 20. Vander 1971, 21. Zaragoza 1546, 22. Zaragoza 1601–1609.

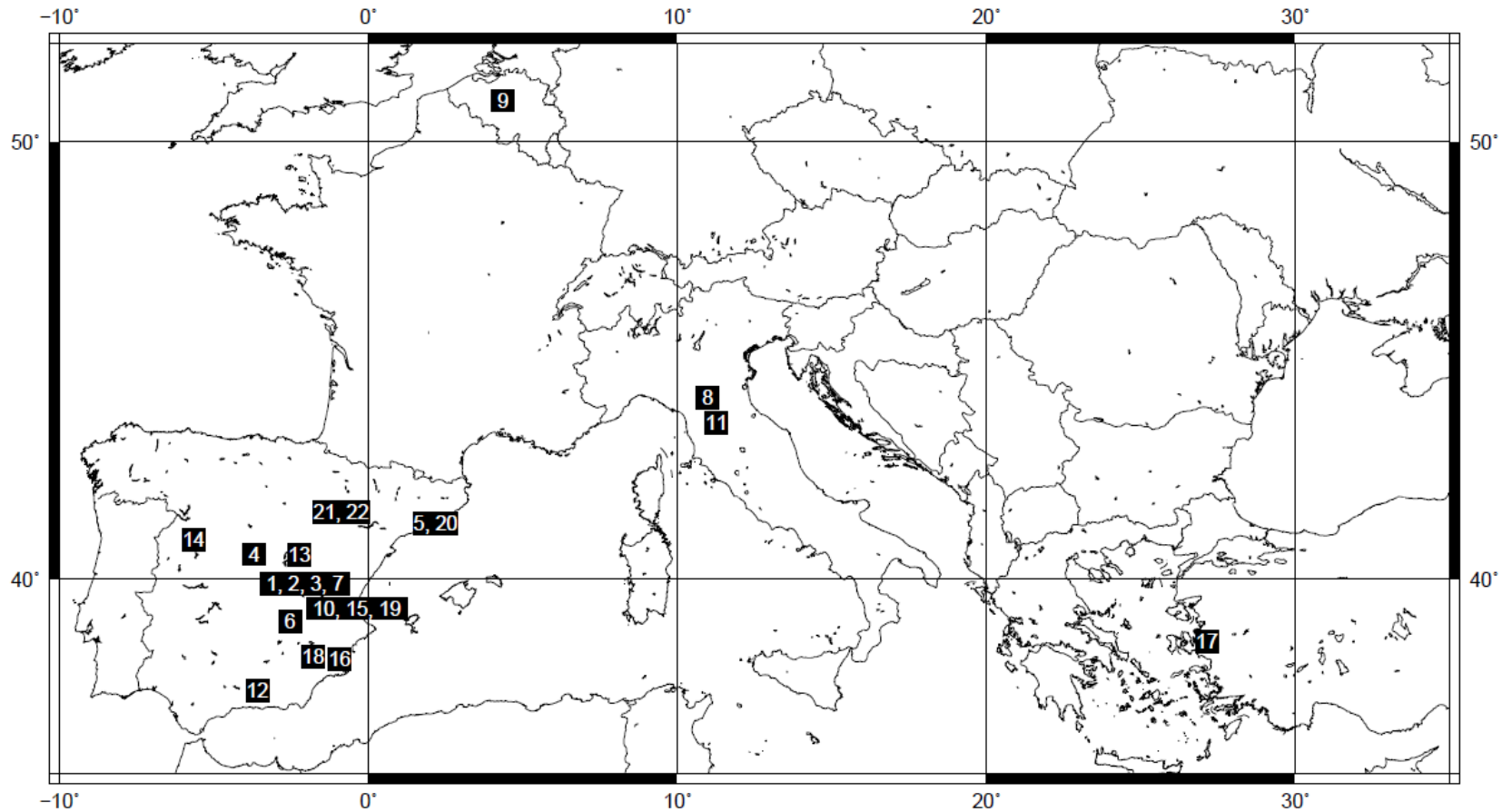


Fig. 6. Relative importance of imported and local species and medicinal substances in percentage of the total number of ingredients shared with Albacete 1526. **Color code: Red and yellow.** Renaissance Herbals and Pharmacopoeias. **Green.** Ethnobotany and Folk Medicine. **Blue.** Old Phytotherapy. **Purple.** Modern Phytotherapy.

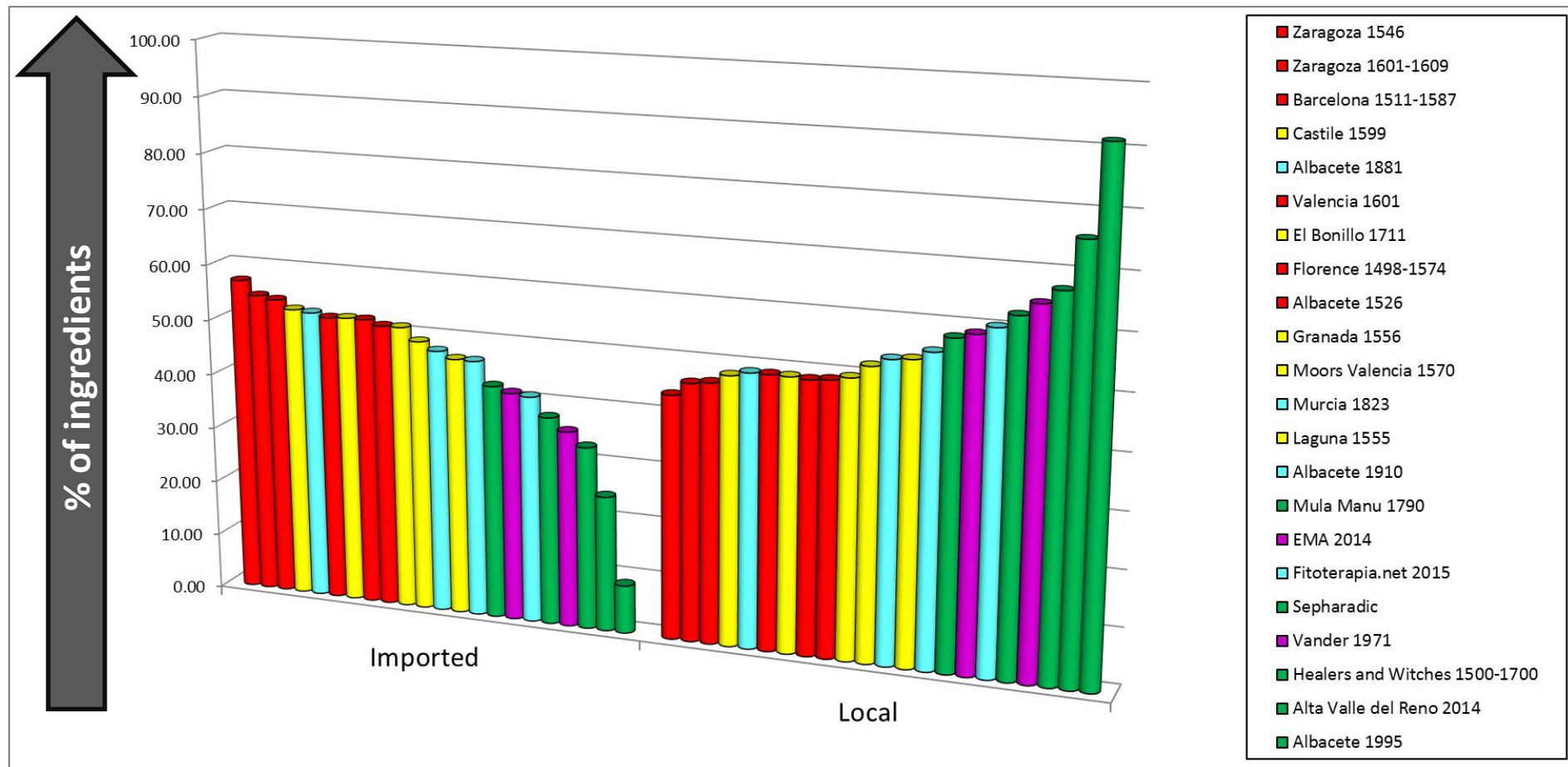
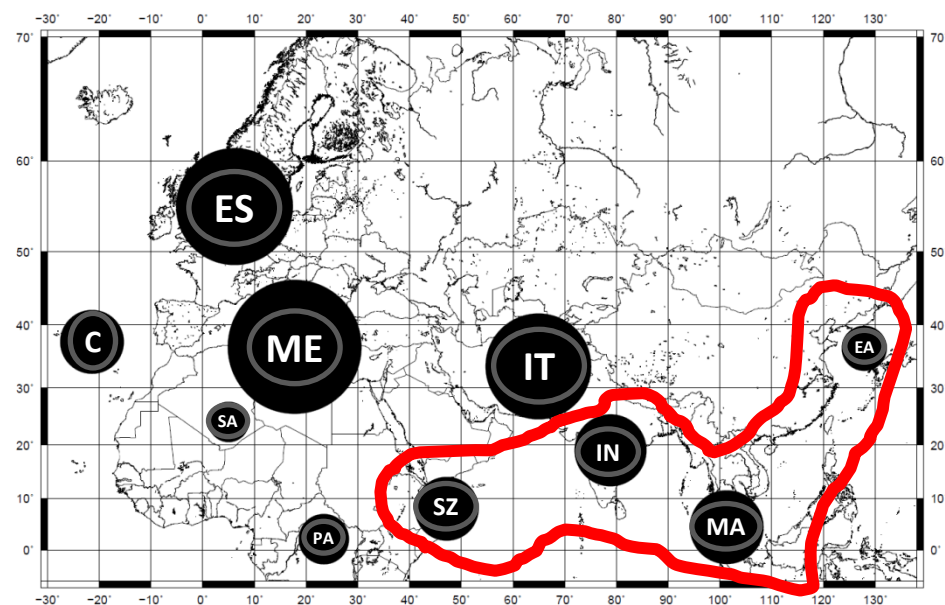
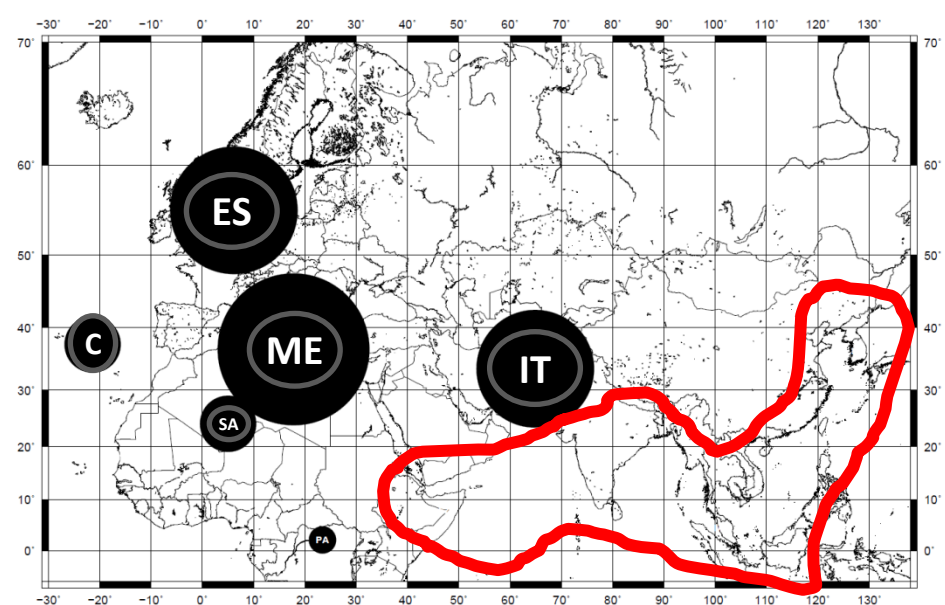


Fig. 7. Biogeographical provenance of medicinal species and substances. **A.** Albacete 1526 CE. **B.** Albacete 1995.
Abbreviations: C Widespread, EA Eastern Asiatic, ES Euro-Siberian, IN Indian, IT Irano-Turanian, MA Malaysian, ME Mediterranean, PA Paletropical, SA Saharo-Arabian, SZ Sudano-Zambezan.



A



B

Fig. 8. Analysis of patterns of deletion of ingredients in function of time, distance and system of medicine (Degree of coincidence in the repertoires of ingredients using georeferenced data). **Axes:** x = distance, straight line, in km, y = time elapsed since 1526, in calendar years, z = Surfaces of the circles are directly proportional to the number of coincidences with the ingredients of the 1526 Albacete's Tariff for medicines. Smaller circles, thus, represent samples with high deletion rate. **Color codes for main systems and periods:** Red, orange and yellow. Renaissance Herbals and Pharmacopoeias. Green. Ethnobotany and Folk Medicine. Blue. Old Phytotherapy. Purple. Naturopathy and Modern Phytotherapy.

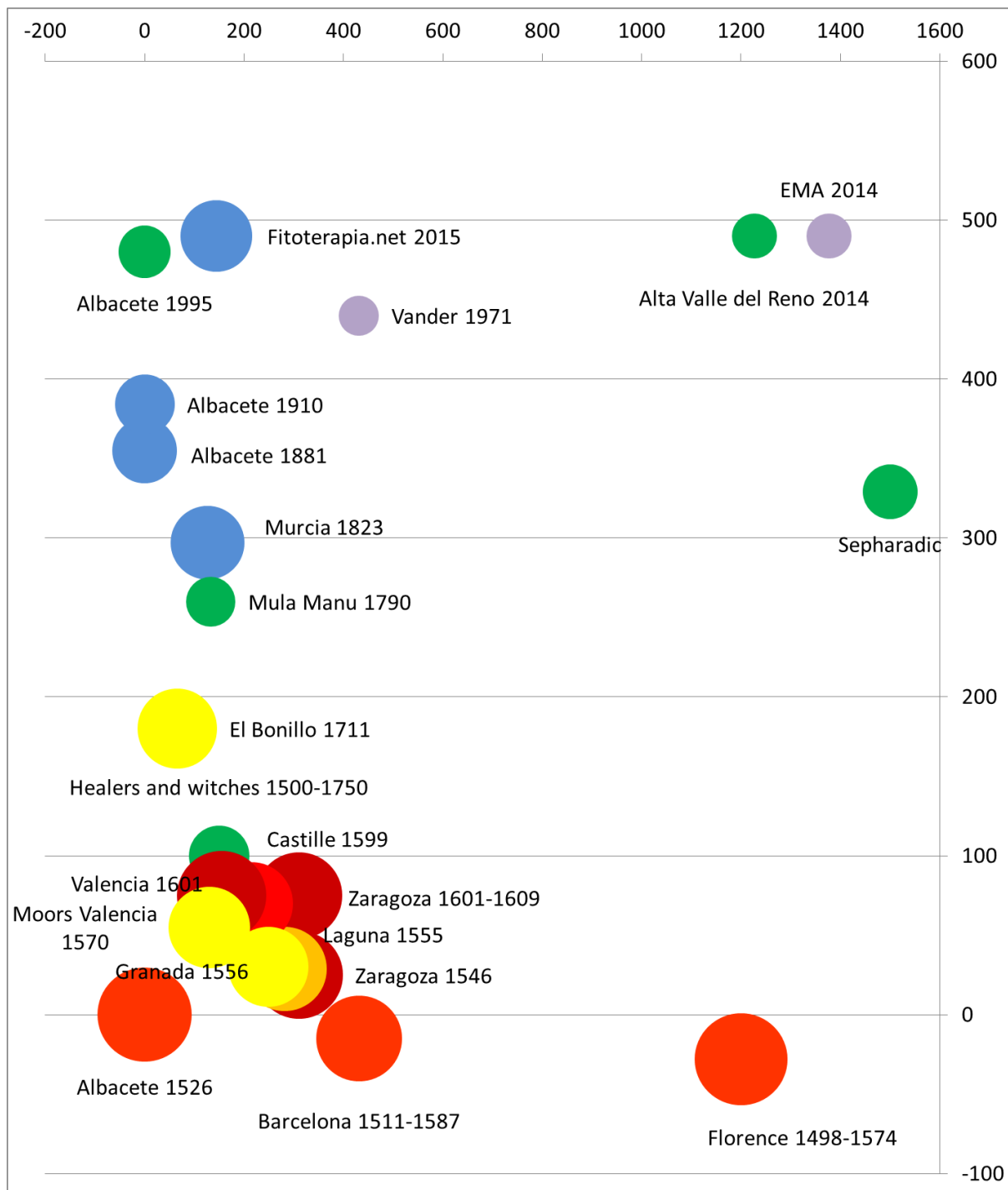


Fig. 9. Factorial analysis based on the presence/absence of the Albacete's 1526 set of 187 ingredients (PCoA). Percentage of inertia axis $x = 23.09$, $y = 20.8$. **Color code: Red.** Classical pharmacy (Renaissance Herbals and Pharmacopoeias). **Green.** Ethnobotany and Folk Medicine. **Blue.** Old Phytotherapy. **Purple.** Naturopathy and Modern Phytotherapy.

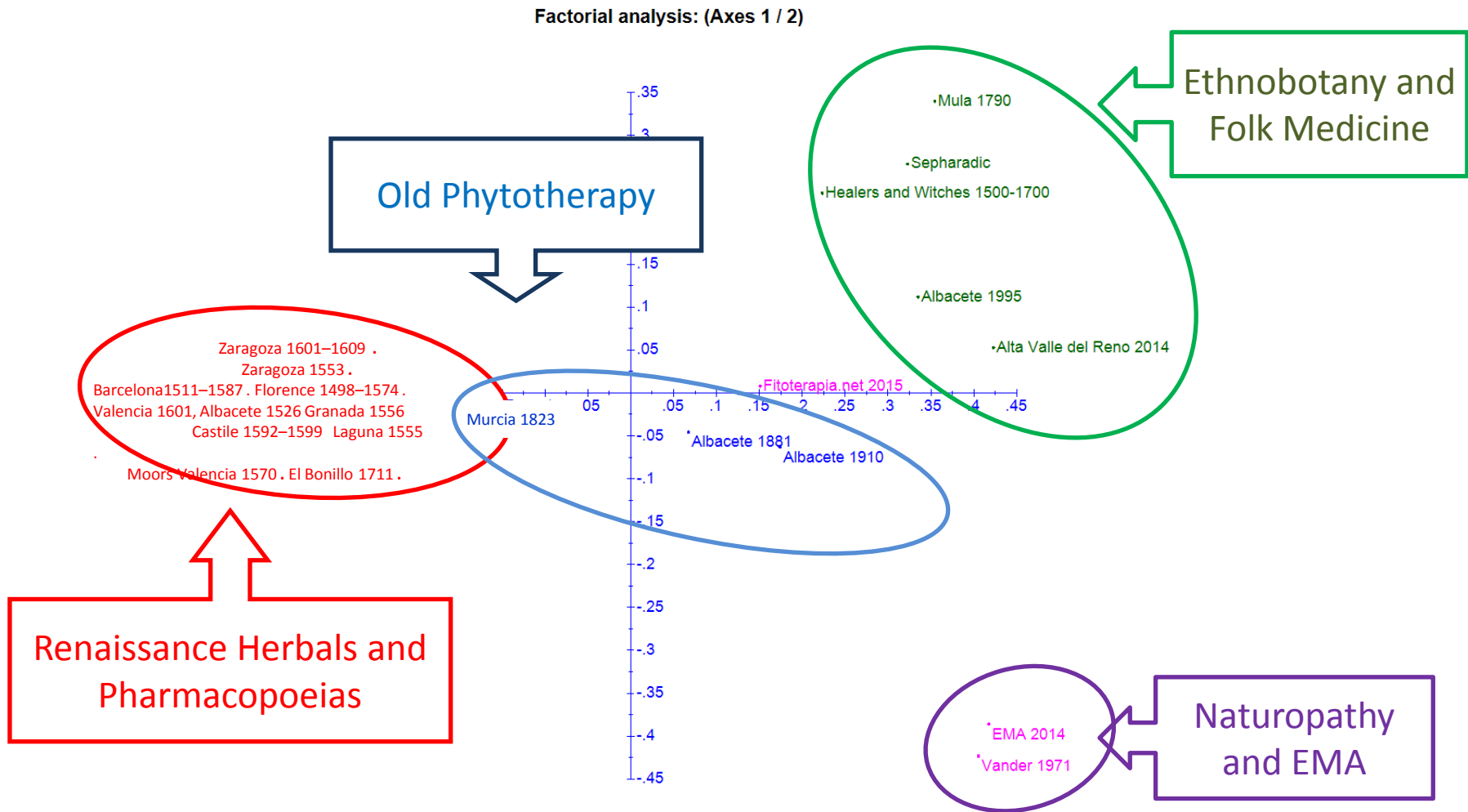


Fig. 10. Hierarchical cluster based on the presence/absence of the Albacete 1526 set of 187 ingredients using the Ward's minimum variance criterion. **Color code: Red.** Classical pharmacy (Renaissance Herbals and Pharmacopoeias). **Green.** Ethnobotany and Folk Medicine. **Blue.** Old Phytotherapy. **Purple.** Naturopathy and Modern Phytotherapy.

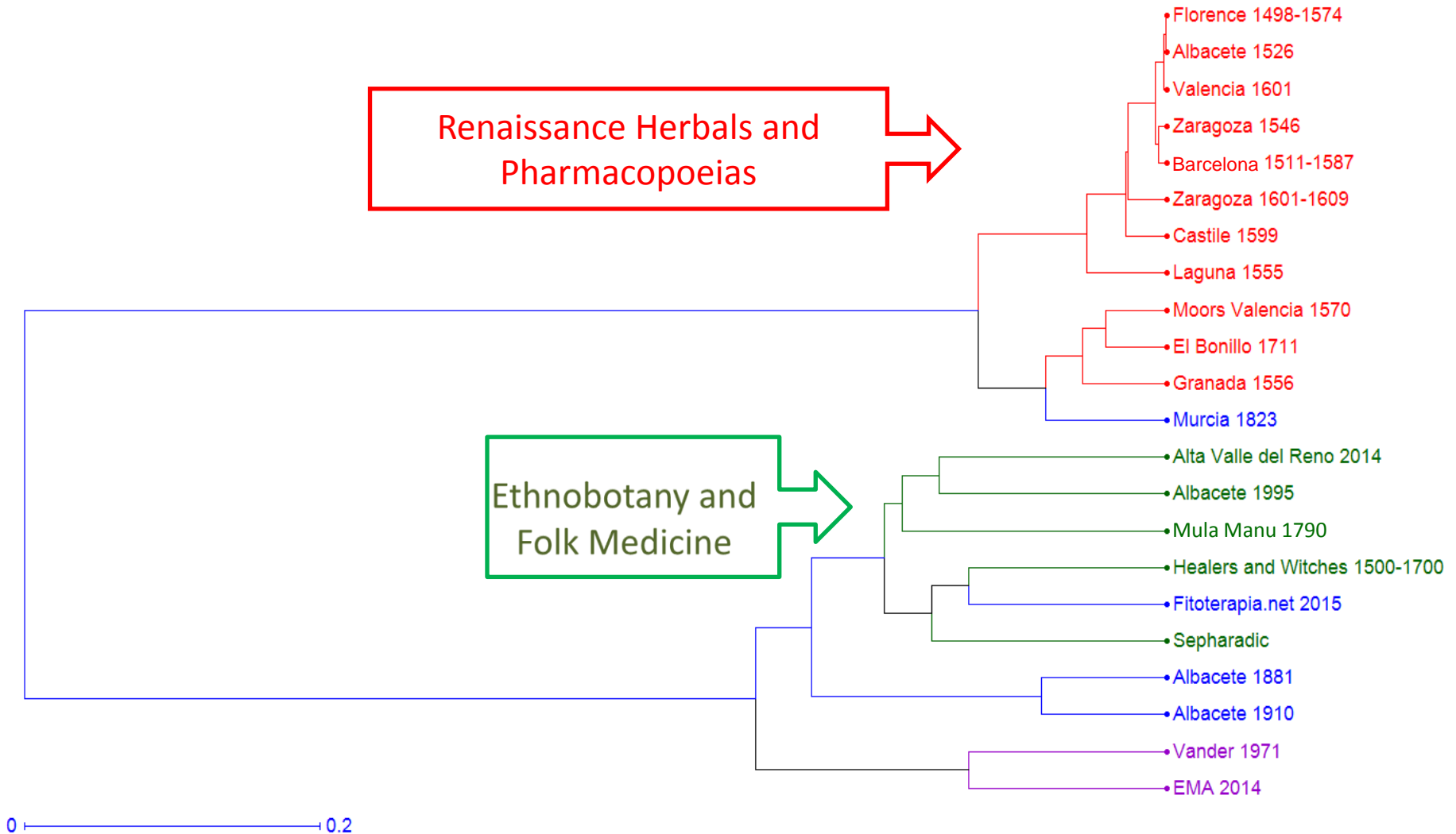


Fig. 11. Hierarchical cluster based on the presence/absence of ingredients using the Weighted Neighbor Joining criterion. Values at edges represent percentage of coincidence in 20,000 bootstrapped trees. **Color code: Red.** Classical pharmacy (Renaissance Herbals and Pharmacopoeias). **Green.** Ethnobotany and Folk Medicine. **Blue.** Old Phytotherapy. **Purple.** Naturopathy and Modern Phytotherapy.

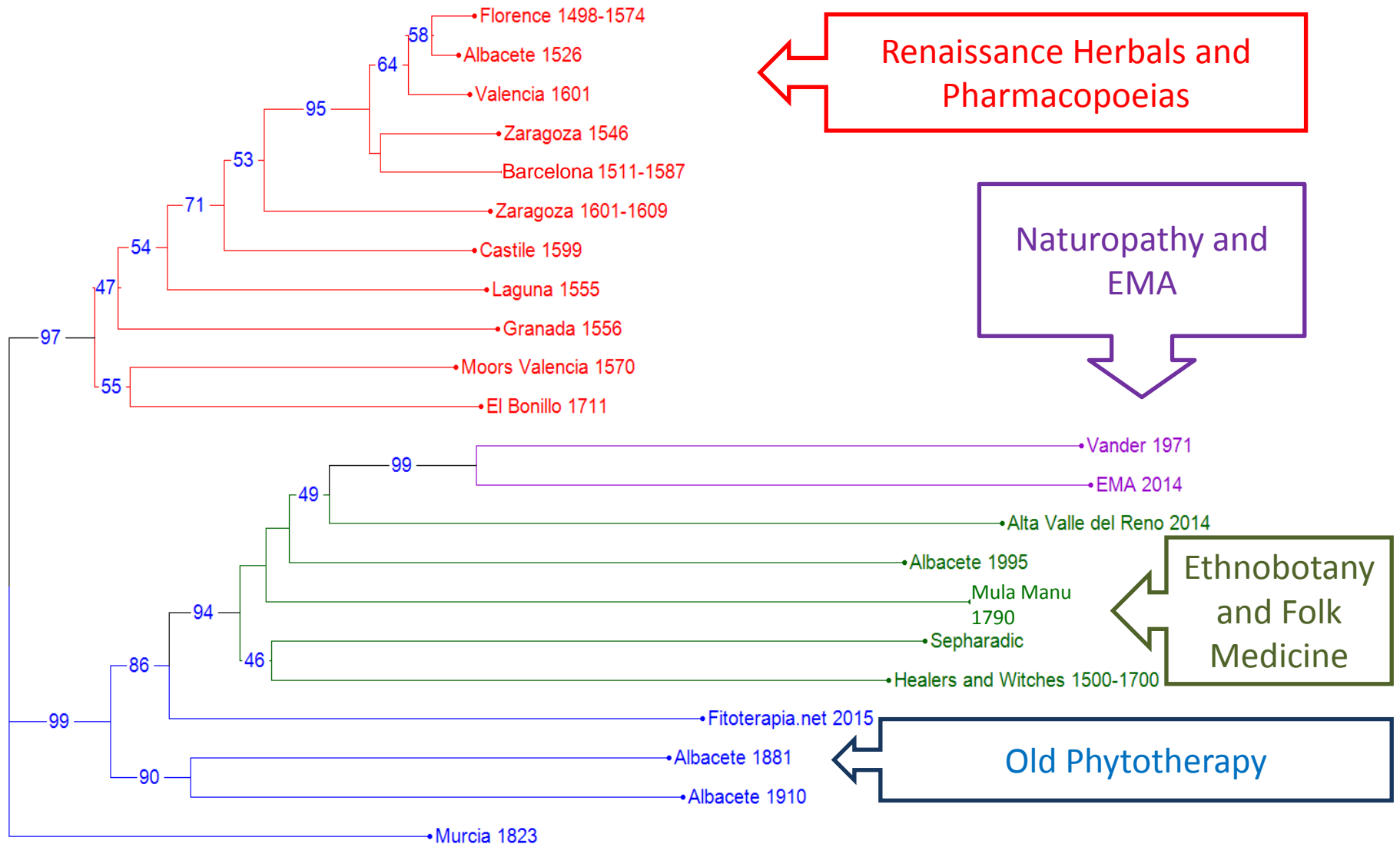


Fig. 12. A. Correspondence Analysis (CA) based on weighting of the A1526 set of 187 ingredients. **B.** Analysis of the hypotheses for dependence of ethnobotanical medicinal uses. **Abbreviations, color codes and “a priori” classification:** **ETHN**, Ethnobotany and Folk Medicine (**Green**); **PHCL**, Classical pharmacy (Renaissance Herbals and Pharmacopoeias) (**Red**) and Old Phytotherapy (**Blue**); **PHMO**, Naturopathy and Modern Phytotherapy (**Purple**), **DEP**, dependent, **SOU**, Source. **Ab16**, Albacete 1526 (PHCL, DEP); **Ab20**, Albacete 1910 (PHCL, DEP); **Ab19**, Albacete 1881 (PHCL, DEP); **Za16**, Castile 1599 (PHCL, SOU); **CB16**, Barcelona 1511–1587 (PHCL, SOU); **Bo18**, El Bonillo 1711 (PHCL, DEP); **EB19**, Albacete 1995 (ETHN, DEP); **EAVR**, Alta Valle del Reno 2014 (ETHN, DEP); **EMag**, EMA 2014 (PHMO, SOU); **FT20**, Fitoterapia.net 2015 (PHMO, DEP); **Fl15**, Florence 1498–1574 (PHCL, SOU); **GR16**, Granada 1556 (PHCL, SOU), **HW16**, Healers and witches 1500–1700 (ETHN, DEP); **La16**, Laguna 1555 (PHCL, SOU); **MV16**, Moors Valencia 1570 (ETHN, DEP); **Mu19**, Murcia 1823 (PHCL, DEP); **SeTr**, Sephardic (ETHN, DEP); **Va17**, Valencia 1601 (PHCL, SOU); **Van**, Vander 1971 (PHCL, SOU); **Za16**, Zaragoza 1546 (PHCL, SOU); **Za17**, Zaragoza 1601–1609 (PHCL, DEP).

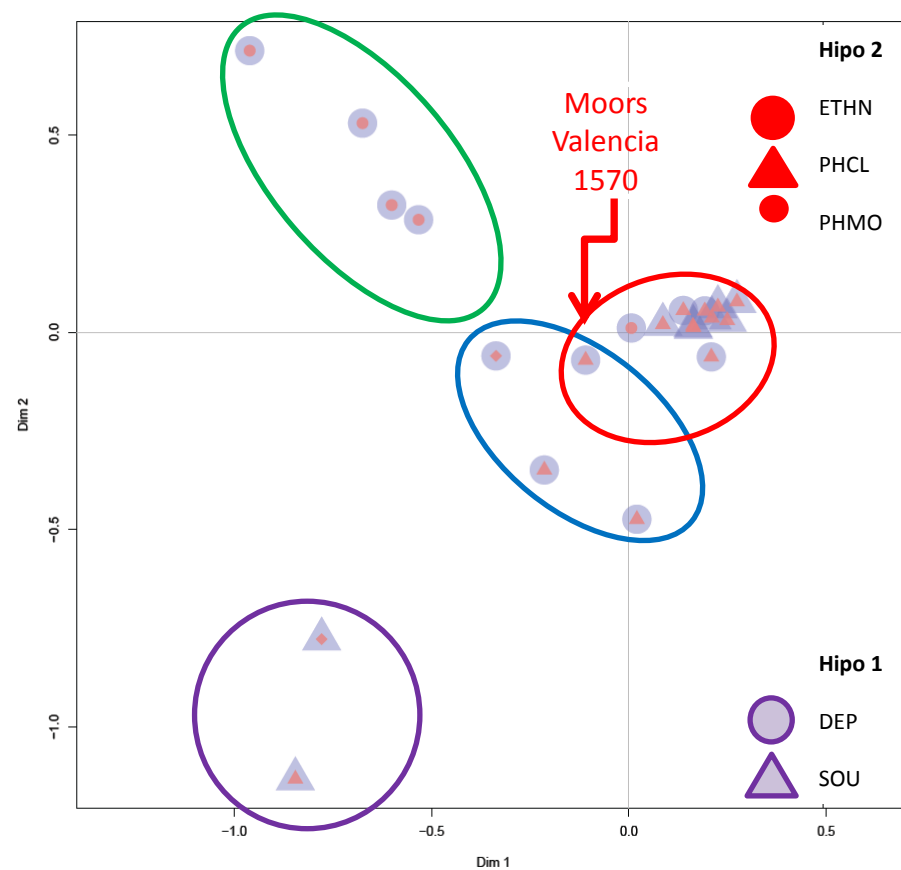
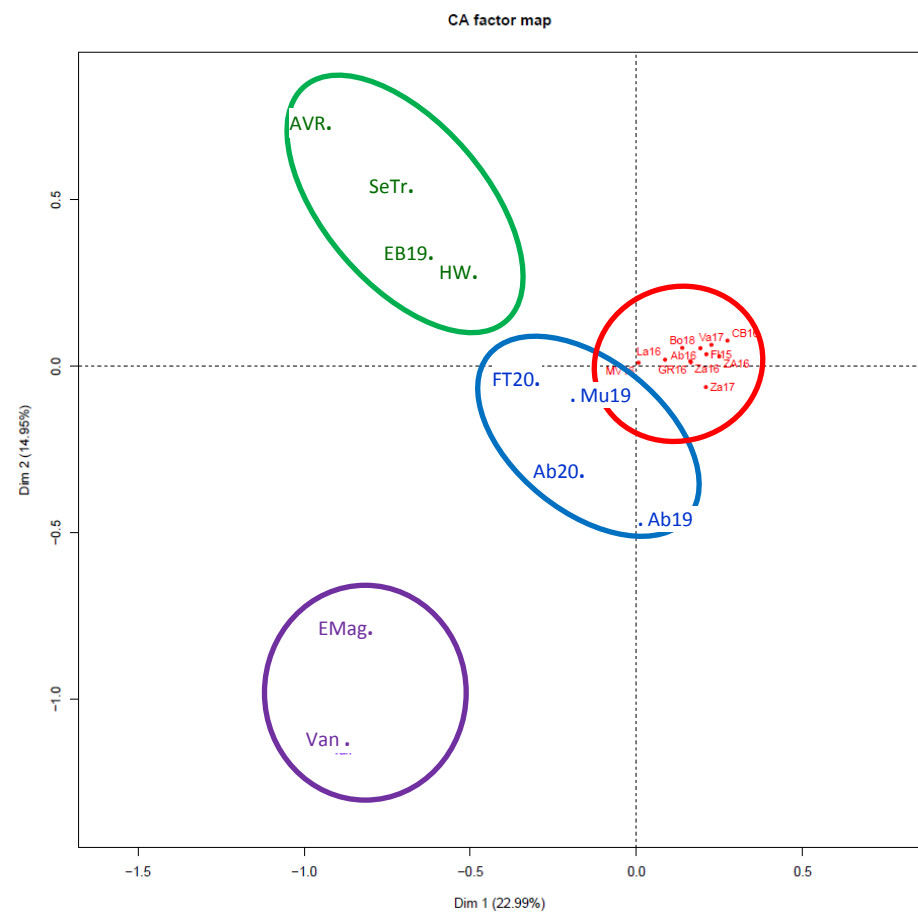


Fig. 13. Summary tree from the Bayesian rjMCMC analysis, with posterior probabilities (0–1) labeled at the edges. Left decreasing ingredients pattern. **Color code: Red.** Classical pharmacy (Renaissance Herbals and Pharmacopoeias). **Green.** Ethnobotany and Folk Medicine. **Blue.** Old Phytotherapy. **Purple.** Naturopathy and Modern Phytotherapy.

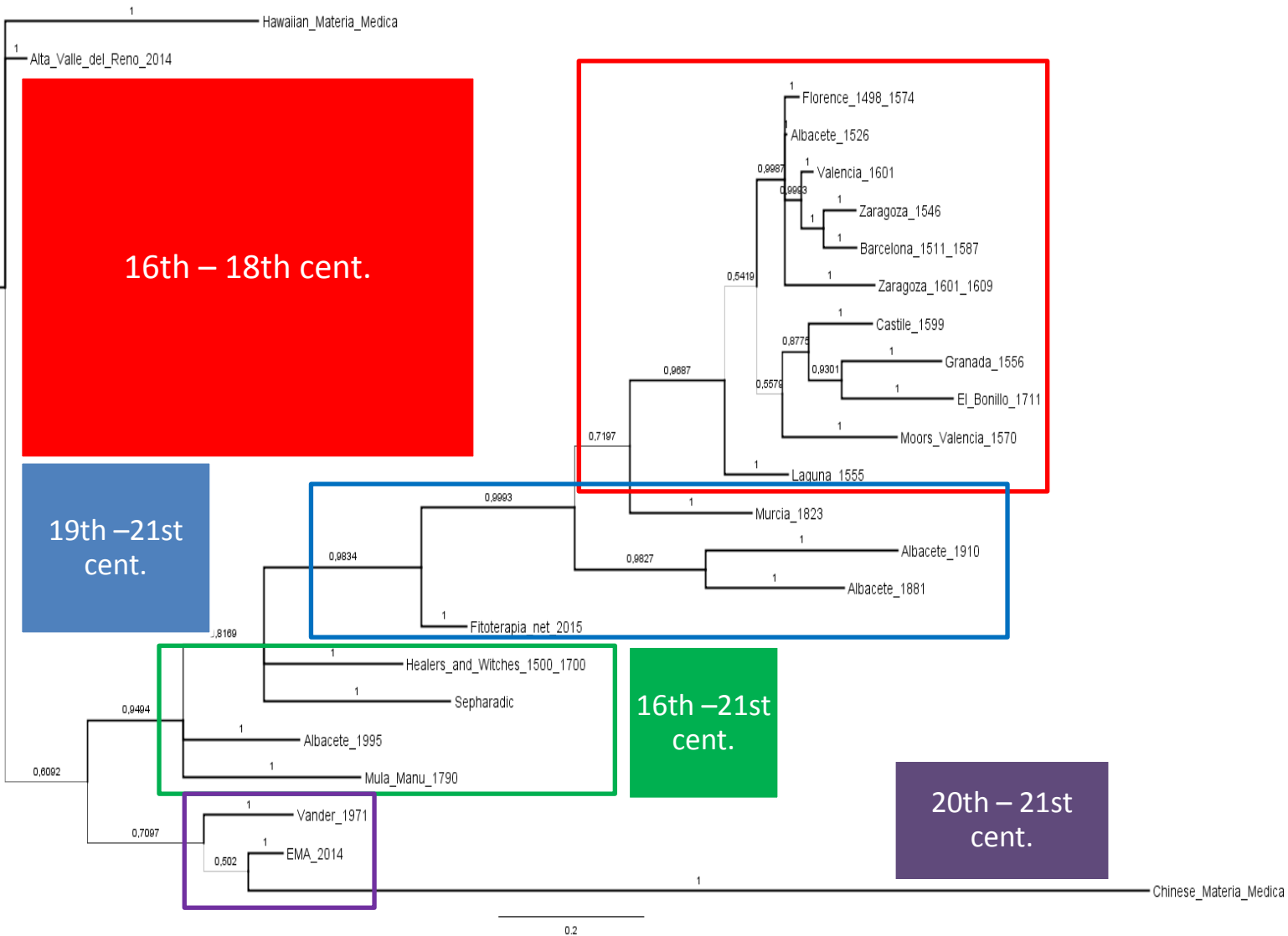


Fig. 14. Profiles based on frequencies of the 22 main categories of diseases and related health problems ICD-10 (WHO 2014) for the medicinal uses of **top 10 shared species**. **A.** Albacete 1995 (Ethnobotany Albacete). **B.** Dioscorides 1st cent CE (in Laguna, 1555; Matthioli 1549). **C.** Andrés Laguna c. 1550 CE (Laguna, 1555). **D.** Alonso de Chirino c. 1490 CE (Herrera, 1973). **Codes:** **I** Certain infectious and parasitic diseases; **II** Neoplasms; **III** Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; **IV** Endocrine, nutritional, and metabolic diseases; **V** Mental and behavioral disorders; **VI** Diseases of the nervous system; **VII** Diseases of the eye and adnexa; **VIII** Diseases of the ear and mastoid process; **IX** Diseases of the circulatory system; **X** Diseases of the respiratory system; **XI** Diseases of the digestive system; **XII** Diseases of the skin and subcutaneous tissue; **XIII** Diseases of the musculoskeletal system and connective tissue; **XIV** Diseases of the genitourinary system; **XV** Pregnancy, childbirth, and the puerperium; **XVIII** Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified; **XIX** Injury, poisoning, and certain other consequences of external causes; **XX** External causes of morbidity and mortality; **XXI** Factors influencing health status and contact with health services.

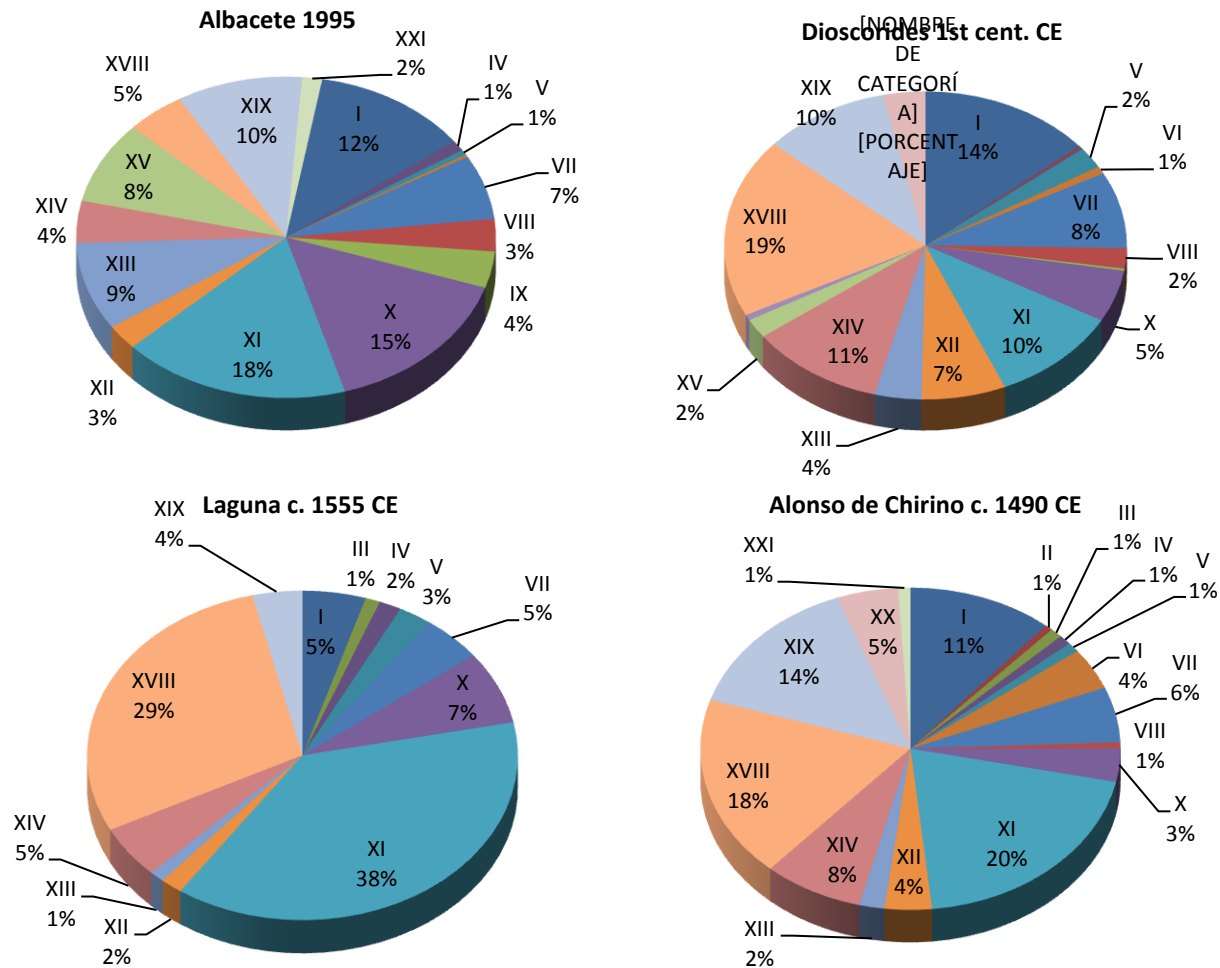
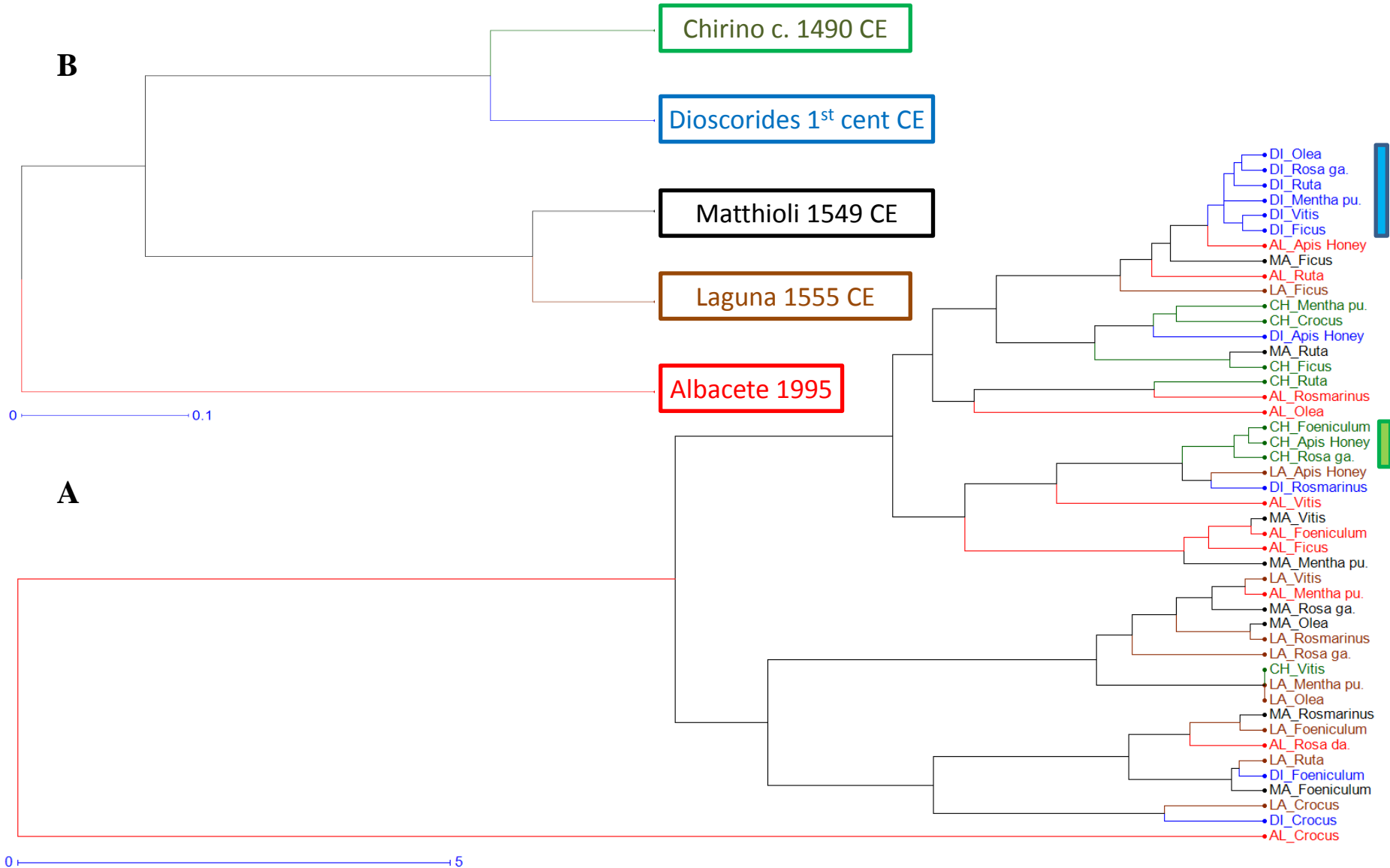


Fig. 15. Hierarchical clusters based on the 22 main categories of diseases and related health problems ICD-10 for **A** the 46 versions of the top 10 shared ingredients in the five analyzed sources in term of percentages and **B** summarized for the five sources using in both the Ward's minimum variance criterion. **Color code and abbreviations: Red (AL)**, Albacete 1995 (Verde, 2002). **Green (CH)**, Chirino c. 1490 CE (Herrera 1973). **Blue (DI)**, Dioscorides 1st cent CE (Laguna 1555, Matthioli 1549). **Brown (LA)**, Andrés Laguna 1555 CE (Laguna 1555), **Black (MA)** Matthioli 1549 CE (Matthioli 1549). **Right Side Vertical Bars:** Blue and Green mark coincidence of uses between different specie.



Supplementary material 1.

Albacete 1526 Tariffs for medicines Species and formulations

Supplementary Table 1. Catalogue of medicines in Albacete 1526 Tariff with their ingredients

Single

01. **Ruybarvo** (*Rheum officinale* Baill.)
02. **Tamarindos** (*Tamarindus indica* L.)
03. **Canna fistola** (*Cassia fistula* L.)
04. **Turbit** (*Ipomoea turpethum* L.)
05. **Sen** (*Senna alexandrina* Mill.)
06. **Polipodio calçino** (*Polypodium vulgare* L.)
07. **Agárico** (*Laricifomes officinalis* (Vill.) Kotl. & Pouzar, 1957 (= *Polyporus officinalis* Fries))

Gumresins

08. **Mirra** (*Commiphora myrrha* (Nees) Engl.)
09. **Almáçiga** (*Pistacia terebinthus* L.)
10. **Bedelio** (*Commiphora africana* (A.Rich.) Endl.)
11. **Serapino** (*Ferula persica* Willd.)
12. **Apopanaco** (*Opopanax chironium* (L.) W.D.J.Koch)
13. **Aremonya-que** (*Dorema ammoniacum* D.Don)
14. **Estoraque** (*Liquidambar orientalis* Mill.)
15. **Calamita** (*Styrax officinalis* L.)
16. **Ençienso** (*Boswellia sacra* Flueck.)
17. **Gálbano** (*Ferula gummosa* Boiss. (incl. *Ferulago galbanifera* (Mill.) W.D.J.Koch))
18. **Lauda** (*Crocus sativus* L., *Papaver somniferum* L., *Vitis vinifera* L.)
19. **Gum yedre** (*Hedera helix* L.)

Syrups

20. **Xarabe de violado** (*Viola odorata* L.)
21. **Xarabe açetosa simple** (*Saccharum officinarum* L., *Vitis vinifera* L.)
22. **Xarabe de jujubas** (*Ziziphus jujuba* Mill.)
23. **Xarabe de liquiriçia** (*Glycyrrhiza glabra* L.)
24. **Xarabe de Ysopo** (*Hyssopus officinalis* L.)
25. **Xarabe de asensios** (*Artemisia absinthium* L., *Cydonia oblonga* Mill.)
26. **Xarabe oximel conpuesto** (*Apis mellifera* L. Honey, *Apium graveolens* L., CINa Salt, *Foeniculum vulgare* Mill., *Pimpinella anisum* L., *Vitis vinifera* L.)
27. **Xarabe de fumisterre** (*Fumaria officinalis* L.)
28. **Xarabe de menta** (*Mentha x piperita* L.)
29. **Xarabe de (e)pitimo** (*Cuscuta epithymum* (L.) L.)
30. **Xarabe de sticados** (*Cinnamomum verum* J.Presl., *Crocus sativus* L., *Cymbopogon martini* (Roxb.) W.Watson, *Lavandula stoechas* L. / *Thymus moroderi* Pau ex Martínez, *Nardostachys jatamansi* (D.Don) DC., *Origanum majorana* L., *Pimpinella anisum* L., *Piper longum* L., *Piper longum* L., *Piper nigrum* L., *Tanacetum parthenium* (L.) Sch.Bip., *Vitis vinifera* L., *Zingiber officinale* Roscoe)
31. **Açivarra conpuesta** (*Aloe vera* (L.) Burm.f.)
32. **Xarabe de Bisañçies** (*Apium graveolens* L., *Borago officinalis* L., *Cichorium intybus* L., *Cydonia oblonga* Mill., *Humulus lupulus* L., *Punica granatum* L.)
33. **(Xarabe) de loch de pino** (*Adiantum capillus-veneris* L., *Astracantha gummifera* (Labill.) Podlech/ *Astragalus clusii* Boiss., *Bos taurus* L., 1758, *Corylus hispanica* Mill. ex D.Rivera & al , *Glycyrrhiza glabra* L., *Iris x germanica* L., *Phoenix dactylifera* L., *Pinus pinea* L. Pine nuts, *Prunus dulcis* (Mill.) D.A.Webb, *Prunus dulcis* (Mill.) D.A.Webb, *Saccharum officinarum* L., *Triticum aestivum* L. Starch, *Vitis vinifera* L.)

Ointments

34. **Ungüento sandalino** (*Santalum album* L., *Sus scrofa domestica* Erxleben, 1777)
35. **Ungüento populeo** (*Hyoscyamus niger* L., *Populus nigra* L., *Sempervivum tectorum* L., *Solanum nigrum* L., *Sus scrofa domestica* Erxleben, 1777, *Umbilicus horizontalis* (Guss.) DC., *Viola odorata* L.)
36. **Ungüento palma** (PbO Litharge, *Sus scrofa domestica* Erxleben, 1777)

37. **Dialtea** (*Althaea officinalis* L., *Apis mellifera* L. Wax, *Drimia maritima* (L.) Stearn., *Ferula gummosa* Boiss. (incl. *Ferulago galbanifera* (Mill.) W.D.J.Koch), *Hedera helix* L., *Olea europaea* L., *Pinus pinaster* Aiton, *Pistacia terebinthus* L., *Trigonella foenumgraecum* L.)
38. **Ungüento desopilativo** (*Artemisia absinthium* L., *Cichorium intybus* L., *Foeniculum vulgare* Mill., *Olea europaea* L., *Petroselinum crispum* (Mill.) Fuss, *Prunus dulcis* (Mill.) D.A.Webb, *Vitis vinifera* L.)
39. **Ungüento ent dolor de costado** (*Apis mellifera* L. Wax, *Apium graveolens* L., *Capparis sicula* Duhamel, *Olea europaea* L.)
40. **Ungüento confortativo** (*Apis mellifera* L. Wax, *Artemisia absinthium* L., *Cinnamomum verum* J.Presl., *Corallium rubrum* L., 1758, *Cuscuta epithymum* (L.) L., *Cymbopogon schoenanthus* (L.) Spreng., *Cyperus esculentus* L., *Matricaria chamomilla* L., *Mentha spicata* L. Juice, *Mentha spicata* L. Oil, *Mentha spicata* L. Powder, *Nardostachys jatamansi* (D.Don) DC., *Rosa gallica* L. "Officinalis", *Sambucus nigra* L.)
41. **Ungüento de resis** ($(\text{PbCO}_3)_2 \cdot \text{Pb}(\text{OH})_2$, *Apis mellifera* L. Wax, *Cinnamomum camphora* (L.) J.Presl, *Olea europaea* L., *Rosa gallica* L. "Officinalis")
42. **Ungüento Agripa** (*Apis mellifera* L. Wax, *Bryonia cretica* L., *Drimia maritima* (L.) Stearn., *Dryopteris filix-mas* (L.) Schott, *Ecballium elaterium* (L.) A.Rich., *Iris × germanica* L., *Olea europaea* L., *Sambucus ebulus* L., *Trifolium pratense* L.)
43. **Ungüento Basilia mayor** (*Apis mellifera* L. Wax, *Olea europaea* L., *Pinus pinaster* Aiton, *Pinus sylvestris* L.)
44. **Ungüento Aragón** (*Cuminum cyminum* L., *Euphorbia resinifera* O.Berg, *Laurus nobilis* L., *Olea europaea* L., *Origanum majorana* L., *Pistacia terebinthus* L., *Ruta graveolens* L., *Salvia officinalis* subsp. *lavandulifolia* (Vahl) Gams)
45. **Ungüento maçiatòn** (*Apis mellifera* L. Wax, *Boswellia sacra* Flueck., *Gallus gallus* L., 1758, *Laurus nobilis* L., *Nardostachys jatamansi* (D.Don) DC., *Olea europaea* L., *Rosmarinus officinalis* L., *Ruta graveolens* L., *Ursus arctos* L., 1758)

Preserves

46. **Conserva violada** (*Viola odorata* L.)
47. **Conserva rosada** (*Rosa gallica* L. "Officinalis")
48. **Conserva de buglosa** (*Anchusa azurea* Mill.)
49. **Conserva de flor de borrajas** (*Borago officinalis* L.)
50. **Conserva de cantaliso** (*Lavandula stoechas* L. / *Thymus moroderi* Pau ex Martínez)
51. **Conserva de capilveneris** (*Adiantum capillus-veneris* L.)
52. **Conserva de nenúfar** (*Nuphar lutea* L.)

Electuaries

Herbal electuaries are blends of honey or sugar and herbs, which with addition of alcohol can be transformed into cordial beverages.

53. **De diarodón** (*Rosa gallica* L. "Officinalis")
54. **De abatis** (*Aquilaria malaccensis* Lam., *Asarum europaeum* L., *Cervus elaphus* L., 1758, *Glycyrrhiza glabra* L., *Moschus chrysogaster* Hodgson, 1839, *Nardostachys jatamansi* (D.Don) DC., *Rosa gallica* L. "Officinalis", *Saccharum officinarum* L., *Santalum album* L.)
55. **De letuariis de gemis** (Ag Silver, Al_2O_3 Sapphires, *Alpinia galanga* (L.) Willd., *Alpinia zerumbet* (Pers.) B.L.Burtt & R.M.Sm., Amber, *Apis mellifera* L. Honey, *Aquilaria malaccensis* Lam., Au Gold, $\text{Be}_3\text{Al}_2(\text{SiO}_3)_6$ Emerald, *Cinnamomum cassia* (L.) J.Presl, *Cinnamomum verum* J.Presl., *Citrus medica* L., *Corallium rubrum* L., 1758, *Crocus sativus* L., *Curcuma zedoaria* (Christm.) Roscoe, *Elephas maximus indicus* (Cuvier), 1798, $\text{Fe}_3\text{Al}_2\text{Si}_3\text{O}_{12}$ Garnet Almandin, *Limonium supinum* (Girard) Pignatti, *Mimusops elengi* L., *Moschus chrysogaster* Hodgson, 1839, *Myristica fragrans* Houtt. (Macis), *Nardostachys jatamansi* (D.Don) DC., *Phyllanthus emblica* L., *Physeter macrocephalus* L., 1758, *Pinctada radiata* (Leach, 1814) Pearl, *Piper longum* L., *Ranunculus aconitifolius* L., *Rosa gallica* L. "Officinalis", *Silene vulgaris* (Moench) Garcke, SiO_2 Sard similar to Carnalin, *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Zingiber officinale* Roscoe, ZrSiO_4 Jacinth Zircon,
56. **De aromático rosado** (*Citrus medica* L., *Pterocarpus santalinus* L.f., *Rosa gallica* L. "Officinalis", *Santalum album* L.)
57. **De pliris arcéticon** (*Alpinia galanga* (L.) Willd., *Aquilaria malaccensis* Lam., *Bombyx mori* (= *Phalaena mori* L., 1758) Silk, *Cinnamomum camphora* (L.) J.Presl, *Cinnamomum cassia* (L.) J.Presl, *Cinnamomum verum* J.Presl., *Citrus medica* L., *Cymbopogon schoenanthus* (L.) Spreng., *Cyperus esculentus* L., *Elephas maximus indicus* (Cuvier), 1798, *Elettaria cardamomum* (L.) Maton, *Glycyrrhiza glabra* L., *Limonium supinum* (Girard) Pignatti, *Liquidambar orientalis* Mill., *Moschus chrysogaster* Hodgson, 1839, *Myristica fragrans* Houtt. (Nutmeg), *Myrtus communis* L., *Nardostachys jatamansi* (D.Don) DC., *Ocimum basilicum* L., *Origanum majorana* L., *Piper longum* L., *Piper nigrum* L., *Pistacia terebinthus* L., *Rosa gallica* L. "Officinalis", *Rosa gallica* L. "Officinalis", *Silene vulgaris* (Moench) Garcke, *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Tanacetum balsamita* L., *Viola odorata* L., *Zingiber officinale* Roscoe)
58. **Dia sándalos** (*Pterocarpus santalinus* L.f., *Santalum album* L.)
59. **Diaçimino** (*Apis mellifera* L. Honey, *Cuminum cyminum* L., *Elettaria cardamomum* (L.) Maton, *Piper nigrum* L., *Piper nigrum* L., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Zingiber officinale* Roscoe)
60. **Diagarganti frio** (*Astracantha gummifera* (Labill.) Podlech/ *Astragalus clusii* Boiss.)

Laxative (Medicinas solutivas compuestas)

61. **El díacatalineo** (*Polypodium vulgare* L., *Rheum officinale* Baill., *Senna alexandrina* Mill., *Tamarindus indica* L., *Viola odorata* L.)
62. **Diaprunis de simple** (*Glycyrrhiza glabra* L., *Prunus domestica* L., *Pterocarpus santalinus* L.f., *Rheum officinale* Baill., *Santalum album* L., *Senna alexandrina* Mill., *Tamarindus indica* L., *Viola odorata* L.)
63. **Letuario de cumo de rosas** (*Convolvulus scammonia* L., *Convolvulus scammonia* L., *Elephas maximus indicus* (Cuvier), 1798, *Pterocarpus santalinus* L.f., *Rosa gallica* L. "Officinalis", *Santalum album* L.)
64. **Diaprunis laxativo** (*Prunus domestica* L., *Vitis vinifera* L.)
65. **Diasen** (*Alpinia galanga* (L.) Willd., *Bombyx mori* (= *Phalaena mori* L., 1758) Silk, *Cinnamomum verum* J.Presl., *Corallium rubrum* L., 1758, *Corylus hispanica* Mill. ex D.Rivera & al , *Crocus sativus* L., *Curcuma zedoaria* (Christm.) Roscoe, *Elettaria cardamomum* (L.) Maton, Lapis lazuli (mainly Lazurite), *Nardostachys jatamansi* (D.Don) DC., *Ocimum basilicum* L., *Pinctada radiata* (Leach, 1814) Pearl, *Piper longum* L., *Piper nigrum* L., *Rosmarinus officinalis* L., *Senna alexandrina* Mill., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Zingiber officinale* Roscoe)
66. **Letuario yndio** (*Apis mellifera* L. Honey, *Convolvulus scammonia* L., *Ipomoea turpethum* L., *Saccharum officinarum* L.)
67. **Diafinico** (*Alpinia galanga* (L.) Willd., *Apis mellifera* L. Honey, *Aquilaria malaccensis* Lam., *Cinnamomum verum* J.Presl., *Convolvulus scammonia* L., *Daucus carota* subsp. *drepanensis* (Arcang.) Heywood, *Foeniculum vulgare* Mill., *Ipomoea turpethum* L., *Myristica fragrans* Houtt. (macis), *Phoenix dactylifera* L., *Pimpinella anisum* L., *Piper longum* L., *Prunus dulcis* (Mill.) D.A.Webb, *Ruta graveolens* L., *Vitis vinifera* L., *Zingiber officinale* Roscoe)
68. **Confeçion de fici** (*Ficus carica* L.)
69. **Letuario Elescofi** (*Apis mellifera* L. Honey, *Convolvulus scammonia* L., *Ipomoea turpethum* L., $KC_4H_5O_6$ Potassium bitartrate, *Myristica fragrans* Houtt. (Nut), *Phyllanthus emblica* L., *Polypodium vulgare* L., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Zingiber officinale* Roscoe)

Pills

70. **Píldoras de ruybarvo** (*Rheum officinale* Baill.)
71. **Píldoras (aureas Cocheas) sinequibus** (*Aloe vera* (L.) Burm.f., *Convolvulus scammonia* L., *Foeniculum vulgare* Mill.,
72. **Píldoras (aureas) Cocheas** (*Aloe vera* (L.) Burm.f., *Apis mellifera* L. Honey, *Artemisia absinthium* L., *Citrullus colocynthis* (L.) Schrad., *Convolvulus scammonia* L.,
73. **Píldoras aureas** (*Aloe vera* (L.) Burm.f., *Apium graveolens* L., *Astracantha gummifera* (Labill.) Podlech/*Astragalus clusii* Boiss., *Citrullus colocynthis* (L.) Schrad., *Convolvulus scammonia* L., *Crocus sativus* L., *Ferula assa-foetida* L., *Pimpinella anisum* L., *Pistacia terebinthus* L., *Rosa bicolor* Jacq., *Trigonella foenumgraecum* L.)
74. **Píldoras aureas de vera** (*Aloe vera* (L.) Burm.f., *Asarum europaeum* L., *Astracantha gummifera* (Labill.) Podlech/*Astragalus clusii* Boiss., *Cinnamomum cassia* (L.) J.Presl, *Commiphora africana* (A.Rich.) Endl., *Commiphora gileadensis* (L.) C.Chr., *Crocus sativus* L., *Nardostachys jatamansi* (D.Don) DC., *Pistacia terebinthus* L.)
75. **Píldoras de fumistera** (*Fumaria officinalis* L.)
76. **Píldoras de ermodátiles** (*Colchicum* sp.)
77. **Píldoras Fétidas mayores** (*Aloe vera* (L.) Burm.f., *Castor fiber* L., 1758, *Cinnamomum verum* J.Presl., *Citrullus colocynthis* (L.) Schrad., *Commiphora africana* (A.Rich.) Endl., *Convolvulus scammonia* L., *Crocus sativus* L., *Cuscuta epithymum* (L.) L., *Dorema ammoniacum* D.Don, *Euphorbia resinifera* O.Berg, *Ferula persica* Willd., *Ipomoea turpethum* L., *Iris × germanica* L., *Nardostachys jatamansi* (D.Don) DC. , *Opopanax chironium* (L.) W.D.J.Koch, *Peganum harmala* L., *Zingiber officinale* Roscoe)

Distilled waters

78. **Agua de asensios** (*Artemisia absinthium* L., H₂O Water)
79. **Agua de menta** (*Mentha x piperita* L., H₂O Water)
80. **Agua rosada** (*Rosa gallica* L. "Officinalis", H₂O Water)
81. **Agua de azahar** (*Citrus aurantium* L., H₂O Water)
82. **Agua de hinojo** (*Foeniculum vulgare* Mill., H₂O Water)
83. **Agua de ufrasia** (*Euphrasia officinalis* L., H₂O Water)
84. **Agua de çiridonia** (*Chelidonium majus* L., H₂O Water)
85. **Agua de ruda** (*Ruta graveolens* L., H₂O Water)
86. **Agua de escolopendia** (*Ceterach officinarum* Willd. (not *Asplenium scolopendrium* L.), H₂O Water)

Oils

87. **Olio nardino** (*Nardostachys jatamansi* (D.Don) DC.)
88. **Olio mastiçino** (*Pistacia terebinthus* L.)
89. **Olio de almendras dulces** (*Prunus dulcis* (Mill.) D.A.Webb)
90. **Olio de escorpiones** (*Buthus occitanus* Amoreux, 1789)
91. **Olio de baçis laurí** (*Laurus nobilis* L.)
92. **Olio de castoreo** (*Castor fiber* L., 1758)
93. **Olio de uforbio** (*Euphorbia resinifera* O.Berg)

Confections

94. **Triaca mitridato** (*Apis mellifera* L. Honey, *Astracantha gummifera* (Labill.) Podlech/ *Astragalus clusii* Boiss., *Capparis sicula* Duhamel, *Castor fiber* L., 1758, *Ferula gummosa* Boiss. (incl. *Ferulago galbanifera* (Mill.) W.D.J.Koch), *Hedera helix* L., *Laricifomes officinalis* (Vill.) Kotl. & Pouzar, 1957 (= *Polyporus officinalis* Fries), *Pistacia terebinthus* L., *Tetraclinis articulata* (Vahl) Mast. , *Vitis vinifera* L.,
95. **Azeyte Dia lacca** (*Kerria lacca* Targ.-Tozz., 1884 (= *Coccus lacca* Kerr, 1782)
96. **Diacopurma** (*Diacurcuma*) (*Crocus sativus* L.)
97. **Antídoto emagogo** (*Acorus calamus* L., *Amomum subulatum* Roxb., *Apis mellifera* L. Honey, *Apium graveolens* L., *Aristolochia fontanesii* Boiss. & Reut., *Artemisia absinthium* L., *Asarum europaeum* L., *Atriplex hortensis* L., *Blackstonia perfoliata* (L.) Huds., *Capparis sicula* Duhamel, *Cassia fistula* L., *Centaurium erythraea* Rafn., *Commiphora gileadensis* (L.) C.Chr. (Twigs), *Commiphora myrrha* (Nees) Engl., *Cuminum cyminum* L., *Cymbopogon schoenanthus* (L.) Spreng., *Cyperus esculentus* L., *Daucus carota* subsp. *drepanensis* (Arcang.) Heywood, *Foeniculum vulgare* Mill., *Glycyrrhiza glabra* L., *Helleborus orientalis* Lam. (not *H. niger* L.), *Juniperus thurifera* L., $\text{KAl(SO}_4)_2 \cdot 12\text{H}_2\text{O}$ hydrated potassium aluminium sulfate, *Laurus nobilis* L., *Lupinus albus* L., *Mentha pulegium* L., *Nardostachys jatamansi* (D.Don) DC., *Nigella sativa* L., *Paeonia officinalis* L., *Pimpinella anisum* L., *Piper nigrum* L., *Ruta graveolens* L., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Tanacetum parthenium* (L.) Sch.Bip., *Vicia ervilia* (L.) Willd.)
98. **Tría fera magna** (*Acorus calamus* L., *Alpinia galanga* (L.) Willd., *Ammi visnaga* (L.) Lam., *Apis mellifera* L. Honey, *Apium graveolens* L., *Cheilocostus speciosus* (J.Koenig) C.D.Specht., *Cinnamomum cassia* (L.) J.Presl, *Curcuma zedoaria* (Christm.) Roscoe, *Cymbopogon martini* (Roxb.) W.Watson, *Cymbopogon nardus* (L.) Rendle, *Cyperus esculentus* L., *Foeniculum vulgare* Mill., *Geum urbanum* L., *Hyoscyamus albus* L., *Iris × germanica* L., *Liquidambar orientalis* Mill., *Mandragora officinarum* L., *Ocimum basilicum* L., *Petroselinum crispum* (Mill.) Fuss, *Peucedanum ostruthium* (L.) W.D.J.Koch, *Pimpinella anisum* L., *Piper longum* L., *Rosa gallica* L. "Officinalis", *Saccharum officinarum* L., *Syzygium aromaticum* (L.) Merr. & L.M.Perry, *Valeriana celtica* L.)
99. **Requies magna** (*Apis mellifera* L. Honey, *Astracantha gummifera* (Labill.) Podlech / *Astragalus clusii* Boiss., *Cichorium endivia* L., *Cinnamomum verum* J.Presl., *Elephas maximus indicus* (Cuvier), 1798, *Hyoscyamus albus* L., *Lactuca sativa* L., *Mandragora officinarum* L., *Myristica fragrans* Houutt. (Nutmeg), *Papaver somniferum* L., *Plantago afra* L., *Portulaca oleracea* L., *Pterocarpus santalinus* L.f., *Rosa gallica* L. "Officinalis", *Saccharum officinarum* L., *Santalum album* L., *Viola odorata* L.)
100. **Filonio mayor** (*Apis mellifera* L. Honey, *Crocus sativus* L., *Hyoscyamus niger* L., *Papaver somniferum* L., *Piper nigrum* L., *Tanacetum parthenium* (L.) Sch.Bip.
101. **Micleta** (*Phyllanthus emblica* L., *Terminalia bellirica* (Gaertn.) Roxb., *Terminalia chebula* Retz., *Terminalia citrina* Roxb. ex Fleming)

Supplementary Table 2. Catalogue of ingredients with their families (those of biological origin) or classes (minerals and rocks)

The vernacular and pharmaceutical names are those in the *Arancel* (in *Italics*) and the rest of analyzed sources. Ethnobotanical voucher specimens deposited and revised by A. Verde (ALBA, MUB) and Teresa Egea (FIAF). Codes for references: 1. Real Academia de Medicina de Madrid, 1865; 2. The Plant List, 2015; 3. Haller, 1771; 4. Linnaeus, 1753; 5. Kew, 2016; 6. Laguna, 1555; Duffin et al., 2013.

<i>Species</i>	Family	Part / type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
Animals and plants						
<i>Acorus calamus</i> L.	Acoraceae	Rhizome	Acori, Ácoro	-	-	3, 4, 6
<i>Adiantum capillus-veneris</i> L.	Pteridaceae	Whole plant	<i>Capilvéneris</i> , Culantrillo de pozo	6135	-	3, 4, 6
<i>Aloe vera</i> (L.) Burm.f.	Xanthorrhoeaceae	Bitter gum from leaves	<i>Açivarra</i> , Acíbar, Aloe hiera picra, Aloe, Aloes	-	-	2, 3, 4
<i>Alpinia galanga</i> (L.) Willd. / <i>Kaempferia galanga</i> L.	Zingiberaceae	Rhizome	Galanga, Trociscorum galange, Galange	-	-	2, 3, 4
<i>Alpinia zerumbet</i> (Pers.) B.L.Burt & R.M.Sm. / <i>Zingiber zerumbet</i> (L.) Roscoe ex Sm.	Zingiberaceae	Rhizome	Trociscorum zerumbet	-	-	2, 5
<i>Althaea officinalis</i> L.	Malvaceae	Roots	<i>Dialtea</i>	6215	-	3, 4, 6
<i>Ammi visnaga</i> (L.) Lam. / <i>Trachyspermum ammi</i> (L.) Sprague	Apiaceae	Fruits	Ameos	-	-	1, 2, 5, 6
<i>Amomum subulatum</i> Roxb. / <i>Amomum verum</i> Blackw.	Zingiberaceae	Fruits	Amomi	-	-	2, 5
<i>Anchusa azurea</i> Mill. / <i>Anchusa officinalis</i> L.	Boraginaceae	Flowers	<i>Buglosa</i>	4191	-	1, 2, 5, 6
<i>Apis mellifera</i> L. Honey	Apidae	Honey	Miel, Miel espumada, Melle, Mellis, Mellis espumatis	-	-	1
<i>Apis mellifera</i> L. Wax	Apidae	Wax	Cera, Cera blanca, Cerae albae	-	-	1
<i>Apium graveolens</i> L.	Apiaceae	Roots	Apio, Apii	-	-	1, 2, 5, 6
<i>Aquilaria malaccensis</i> Lam.	Thymelaeaceae	Wood	Linaloe, Linaloes, Ligni aloes	-	-	1, 2, 3, 4, 5, 6
<i>Aristolochia fontanesii</i> Boiss. & Reut. (= <i>Aristolochia longa</i> L.)	Aristolochiaceae	Roots	<i>Aristolochia longa</i>	-	-	1, 2, 3, 4, 5, 6
<i>Artemisia absinthium</i> L.	Asteraceae	Aerial parts	<i>Asensios</i> , Axenjos, Ajenjo, Absintio, Artemisia	6170	-	1, 2, 4, 5, 6
<i>Asarum europaeum</i> L.	Aristolochiaceae	Leaves	Ásaro, Asari, Assaro	-	-	1, 2, 3, 4, 5, 6
<i>Astracantha gummifera</i> (Labill.) Podlech / <i>Astragalus clusii</i> Boiss. / <i>Astragalus tragacantha</i> L.	Leguminosae	Gum	<i>Diagarganti</i> , Dragacanthi, Tragacanto, Alquitira, Tragacanthi	-	-	1, 2, 3, 4, 5
<i>Atriplex hortensis</i> L.	Amaranthaceae	Fruits	Atriplicis, Armuelles	-	-	1, 2, 3, 4, 5, 6
<i>Blackstonia perfoliata</i> (L.) Huds. / <i>Centaurea centaurium</i> L.	Gentianaceae / Asteraceae	Aerial parts	<i>Centaurea maioris</i>	-	-	1, 2, 3, 4, 5, 6
<i>Bombyx mori</i> (= <i>Phalaena mori</i> L., 1758) Silk	Bombycidae	Animal substance	Serici combusti, Seda quemada	-	-	3, 6

<i>Species</i>	Family	Part/ type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
<i>Borago officinalis</i> L.	Boraginaceae	Flowers	<i>Borrajas</i>	-	-	1, 2, 4, 5, 6
<i>Bos taurus</i> L., 1758	Bovidae	Animal substance	Butyri recentis	-	-	3, 6
<i>Boswellia sacra</i> Flueck.	Burseraceae	Gum	<i>Ençiense</i> , Incienso, Insinsi, Olíbano	-	-	1, 2, 5, 6
<i>Bryonia cretica</i> L., rarely <i>B. alba</i> L.	Cucurbitaceae	Roots	Brionia, Nueza blanca	6086	-	1, 2, 3, 4, 5, 6
<i>Buthus occitanus</i> Amoreux, 1789	Buthidae	Animal substance	<i>Buthus</i> , Escorpiones, Alacrán, Alagransi	-	-	6
<i>Capparis sicula</i> Duhamel / <i>C. spinosa</i> L. / <i>C. orientalis</i> Veill.	Capparaceae	Roots	Alcaparras, Caperibus, Capparis	-	-	1, 2, 3, 4, 5, 6
<i>Cassia fistula</i> L.	Leguminosae	Fruits	<i>Canna fistola</i> , Cassia fistula, Quasi fistulah	-	-	1, 2, 3, 4, 5, 6
<i>Castor fiber</i> L., 1758	Castoridae	Animal substance	<i>Castóreo</i> , Castorio, Quastur, Castorei	-	-	1, 2, 3, 5, 6
<i>Centaureum erythraea</i> Rafn.	Gentianaceae	Aerial parts	Centaurea minoris, Centaura	6168	-	1, 2, 3, 4, 5, 6
<i>Cervus elaphus</i> L., 1758	Cervidae	Animal substance		-	-	1, 2, 3, 5, 6
<i>Ceterach officinarum</i> Willd. (not <i>Asplenium scolopendrium</i> L.)	Aspleniaceae	Aerial parts	<i>Escolopendia</i> , Doradilla, Escolopendia	6087	-	1, 2, 3, 4, 5, 6
<i>Cheilocostus speciosus</i> (J.Koenig) C.D.Specht. / <i>Costus afer</i> Ker Gawl.	Costaceae	Rhizome	Costo	-	-	2, 5, 6
<i>Chelidonium majus</i> L.	Papaveraceae	Aerial parts	<i>Çiridonia</i> , Celidonia	1402	38924, 38979	1, 2, 3, 4, 5, 6
<i>Cichorium endivia</i> L.	Asteraceae	Leaves	Escarola, Scariolae	-	-	1, 2, 3, 4, 5
<i>Cichorium intybus</i> L.	Asteraceae	Roots	<i>Bisançies</i> , Bizancis, Achicorias, Endivia	2323	39027, 38934, 38957, 39066	1, 2, 3, 4, 5, 6
<i>Cinnamomum camphora</i> (L.) J.Presl	Lauraceae	Exudate	Camphorae, Alcanfor, Canfore	-	-	1, 2, 3, 4, 5, 6
<i>Cinnamomum cassia</i> (L.) J.Presl	Lauraceae	Bark	Cassia lignea, Cinamomo	-	-	1, 2, 3, 4, 5, 6
<i>Cinnamomum verum</i> J.Presl.	Lauraceae	Wood	Canela, Cinnamomum	-	-	1, 2, 3, 4, 5, 6
<i>Citrullus colocynthis</i> (L.) Schrad.	Cucurbitaceae	Fruits	Coloquintida, Coloquintide	-	-	1, 2, 3, 4, 5, 6
<i>Citrus aurantium</i> L.	Rutaceae	Flowers	<i>Azahar</i> , Aqua napha	-	-	1, 2, 5, 6
<i>Citrus medica</i> L.	Rutaceae	Fruits	Corticum citri, Zidra corceças, Actirón, Cidra	-	-	1, 2, 3, 4, 5, 6
<i>Colchicum</i> sp.	Colchicaceae	Bulb	<i>Ermodátiles</i> , Irmidatilis, Armudatíl, Colchico	-	-	1, 2, 3, 4, 5, 6
<i>Commiphora mukul</i> (Hook. ex Stocks) Engl. / <i>Commiphora africana</i> (A.Rich.) Endl.	Burseraceae	Exudate	<i>Bedelio</i> , Bdelium, Bdelio	-	-	1, 2, 3, 5, 6
<i>Commiphora gileadensis</i> (L.) C.Chr.	Burseraceae	Exudate	Xilobalsamo, Silubalsami, Xylobalsami	-	-	1, 2, 3, 4, 5, 6
<i>Commiphora myrrha</i> (Nees) Engl.	Burseraceae	Exudate	<i>Mirra</i> , Commiphora myrrha, Myrrhae	-	-	1, 2, 3, 4, 5, 6
<i>Convolvulus scammonia</i> L.	Convolvulaceae	Roots	Escamonea, Diagridio, Escamonea de Alepo, Scamonii, Diagridi	-	-	1, 2, 3, 4, 5, 6

<i>Species</i>	Family	Part/ type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
<i>Corallium rubrum</i> L., 1758	Coralliidae	Animal substance	Coral rubio, Coralli rossi, Coralu rubri	-	-	1, 2, 3, 5, 6
<i>Corylus hispanica</i> Mill. ex D.Rivera & al	Betulaceae	Fruits	Avellanas, Nociuole, Avellanarum	6136	-	1, 2, 3, 4, 5, 6
<i>Crocus sativus</i> L.	Iridaceae	Flowers	Azafrán, Crocus, Ze' afrán, Safra	5994	-	1, 2, 3, 4, 5, 6
<i>Cuminum cyminum</i> L.	Apiaceae	Fruits	Çimino, Diaçimino, Cominos, Cymini	-	-	1, 2, 3, 4, 5, 6
<i>Curcuma zedoaria</i> (Christm.) Roscoe	Zingiberaceae	Rhizome	Cedoaria, Zeodariae	-	-	1, 2, 3, 4, 5, 6
<i>Cuscuta epithymum</i> (L.) L. / <i>C. europaea</i> L.	Convolvulaceae	Whole plant	<i>Epitimo</i> , Abitimu, Cuscuta, Epithimi	-	-	1, 2, 3, 4, 5, 6
<i>Cydonia oblonga</i> Mill.	Rosaceae	Fruits	Codoño, Cotognie	4914	-	1, 2, 3, 4, 5, 6
<i>Cymbopogon martini</i> (Roxb.) W.Watson (not <i>Acorus calamus</i>)	Poaceae	Leaves	Cálamo aromatico, Calami aromatici	-	-	2, 3, 4, 5, 6
<i>Cymbopogon nardus</i> (L.) Rendle	Poaceae	Leaves	Espinacardo, Spica nardi	-	-	1, 2, 3, 4, 5, 6
<i>Cymbopogon schoenanthus</i> (L.) Spreng.	Poaceae	Leaves	Esquinante, Schinanthi, Schoenanthi	-	-	1, 2, 3, 4, 5, 6
<i>Cyperus esculentus</i> L. / <i>C. longus</i> L. / <i>C. rotundus</i> L.	Cyperaceae	Rhizome	Cipero, Cyperi	-	-	1, 2, 3, 4, 5, 6
<i>Daucus carota</i> subsp. <i>drepanensis</i> (Arcang.) Heywood	Apiaceae	Fruits	Pastinaca salvatica cioè dauci, Dauci	-	-	1, 2, 3, 4, 5
<i>Dorema ammoniacum</i> D.Don	Apiaceae	Exudate	<i>Aremonya-que</i> , Armónico, Resina amoniaco	-	-	1, 2, 3, 5
<i>Doronicum pardalianches</i> L.	Asteraceae	Roots	Framentorum Deronigi	-	-	2, 3, 4, 5, 6
<i>Drimia maritima</i> (L.) Stearn.	Asparagaceae	Bulb	Squille, Scilla, Cipolla squilla	6005	-	1, 2, 3, 4, 5, 6
<i>Dryopteris filix-mas</i> (L.) Schott	Dryopteridaceae	Whole plant	Helecho, Helecho macho	-	39064	1, 2, 3, 4, 5, 6
<i>Ecballium elaterium</i> (L.) A.Rich.	Cucurbitaceae	Fruits	Ecballium, Elaterium	0090	-	1, 2, 3, 4, 5, 6
<i>Elephas maximus indicus</i> (Cuvier), 1798	Elephantidae	Animal substance, Ivory	Spodii, Espodio, Limaturae heboris	-	-	1, 2, 3, 4, 5, 6
<i>Elettaria cardamomum</i> (L.) Maton	Zingiberaceae	Fruits	Cardamomi, Cardamomo	-	-	1, 2, 3, 4, 5, 6
<i>Euphorbia resinifera</i> O.Berg / <i>E. antiquorum</i> L. / <i>E. canariensis</i> L.	Euphorbiaceae	Exudate	<i>Uforbio</i> , Euforbio, Euphorbi	-	-	1, 2, 3, 4, 5, 6
<i>Euphrasia officinalis</i> L.	Orobanchaceae	Aerial parts	<i>Ufrasia</i> , Eufragia, Eufrasia	-	-	1, 2, 3, 4, 5, 6
<i>Ferula assa-foetida</i> L.	Apiaceae	Exudate	Assafoetida, Asafétida	-	-	1, 2, 3, 4, 5, 6
<i>Ferula gummosa</i> Boiss. (incl. <i>Ferulago galbanifera</i> (Mill.) W.D.J.Koch)	Apiaceae	Exudate	<i>Gálbano</i> , Galbani	-	-	1, 2, 3, 4, 5, 6
<i>Ferula persica</i> Willd.	Apiaceae	Exudate	<i>Serapino</i> , Serapinum, Sagapeno, Sagapenum	-	-	1, 2, 3, 4, 5, 6
<i>Ficus carica</i> L.	Moraceae	Fruits	<i>Fici</i> , Fiqus, Higos	1361	-	1, 2, 3, 4, 5, 6
<i>Foeniculum vulgare</i> Mill.	Apiaceae	Fruits	<i>Finico</i> , <i>Diafinico</i> , <i>Hinojo</i> ,	MUB43848	39098	1, 2, 3, 4, 5, 6

<i>Species</i>	Family	Part/ type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
<i>Fumaria officinalis</i> L.	Papaveraceae	Aerial parts	Foeniculum, Finojo <i>Fumisterre</i> , <i>Fumistera</i> , Fumaria, Lisader	2937	-	1, 2, 3, 4, 5, 6
<i>Gallus gallus</i> L., 1758)	Phasianidae	Animal substance	Enjundia de Gallina, Grasso di pollo	-	-	1, 2, 4, 5, 6
<i>Geum urbanum</i> L.	Rosaceae	Roots	Cariofilada, Ghariofilata, Hierba de San Benito	-	-	1, 2, 3, 4, 5, 6
<i>Glycyrrhiza glabra</i> L.	Leguminosae	Roots	<i>Liquiriçia</i> , Requilitia, Regalíz, Glycyrrhiza, Liquiricie	MUB46485	-	1, 2, 3, 4, 5, 6
<i>Hedera helix</i> L.	Araliaceae	Exudate	<i>Gum yedre</i> , <i>Yedra</i> , Hiedra, Hedera	2981	-	1, 2, 3, 4, 5, 6
<i>Helleborus orientalis</i> Lam. (not <i>H. niger</i> L.)	Ranunculaceae	Aerial parts	Hellebori negri, Heléboro negro	-	-	1, 2, 3, 4, 5, 6
<i>Humulus lupulus</i> L.	Cannabaceae	Flowers	Lúpulo, Lupppli, Lupuli	-	-	1, 2, 3, 4, 5, 6
<i>Hyoscyamus albus</i> L.	Solanaceae	Fruits	Iusquiamo, Sucquiame, Beleño blanco, Beleño	MUB48039	-	1, 2, 3, 4, 5, 6
<i>Hyoscyamus niger</i> L.	Solanaceae	Fruits	Beleño, Veleño	4623	-	1, 2, 3, 4, 5, 6
<i>Hyssopus officinalis</i> L.	Lamiaceae	Aerial parts	<i>Ysopo</i> , Hisopo	6028	-	1, 2, 3, 4, 5, 6
<i>Iris × germanica</i> L.	Iridaceae	Rhizome	Gigli celesti, Ghiaggiuolo, Lirio, Lirio cárdeno	MUB27276	-	1, 2, 3, 4, 5, 6
<i>Juniperus thurifera</i> L. / rarely <i>J. phoenicea</i> L.	Cupressaceae	Exudate	Sabinae, Savina	5181	-	1, 2, 3, 4, 5, 6
<i>Kerria lacca</i> Targ.- Tozz., 1884 (= <i>Coccus</i> <i>lacca</i> Kerr, 1782)	Kerriidae	Animal substance	<i>Laca</i> , Goma laca, Laccha	-	-	1, 3, 6
<i>Lactuca sativa</i> L.	Asteraceae	Fruits	Lactugha, Lechuga, Lactuca	-	-	1, 2, 3, 4, 5, 6
<i>Laricifomes officinalis</i> (Vill.) Kotl. & Pouzar, 1957 (= <i>Polyporus</i> <i>officinalis</i> Fries)	Fomitopsidaceae	Aerial parts	<i>Agárico</i> , Agarici	-	-	1, 3, 4, 6
<i>Laurus nobilis</i> L.	Lauraceae	Fruits	<i>Lauri</i> , Laurel	MUB47700	-	1, 2, 3, 4, 5, 6
<i>Lavandula stoechas</i> L. / <i>Thymus moroderi</i> Pau ex Martínez	Lamiaceae	Flowers	<i>Stichados</i> , Cantalso, Stichados, Cantueso, Cantueso	6104, 6178, 6177	-	1, 2, 3, 4, 5, 6
<i>Limonium supinum</i> (Girard) Pignatti	Plumbaginaceae	Rhizome	Ben roho, Behen rubi	-	-	1, 2, 3, 4, 5, 6
<i>Liquidambar orientalis</i> Mill.	Altingiaceae	Exudate	<i>Estoraque</i> , Estoraque liquido, Storace	-	-	1, 2, 5, 6
<i>Lupinus albus</i> L.	Leguminosae	Fruits	Lupini, Altramuces	1207	-	1, 2, 3, 4, 5, 6
<i>Mandragora</i> <i>officinarum</i> L.	Solanaceae	Roots	Mandragora	-	-	1, 2, 3, 4, 5, 6
<i>Matricaria chamomilla</i> L.	Asteraceae	Flowers	Manzanilla, Mañanilla, Matricaria	6110	38892	1, 2, 3, 4, 5, 6
<i>Mentha pulegium</i> L.	Lamiaceae	Aerial parts	Puleggií, Puleggio, Poleo	6022	-	1, 2, 3, 4, 5, 6
<i>Mentha spicata</i> L. Juice	Lamiaceae	Aerial parts	Yerbabuena, Hierbabuena, Menta sativa	6076	-	1, 2, 3, 4, 5, 6
<i>Mentha spicata</i> L. Oil	Lamiaceae	Aerial parts	Yerbabuena,	6076	38895	1, 2, 3, 4, 5,

<i>Species</i>	Family	Part / type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
			Hierbabuena, Menta sativa			6
<i>Mentha spicata</i> L. Powder	Lamiaceae	Aerial parts	Yerbabuena, Hierbabuena, Menta sativa	6076	38895	1, 2, 3, 4, 5, 6
<i>Mentha x piperita</i> L.	Lamiaceae	Aerial parts	<i>Menta</i> , Menta sarraceni	6143, 6131	-	1, 2, 3, 4, 5, 6
<i>Mimusops elengi</i> L.	Sapotaceae	Fruits	Alphelengemic	-	-	1, 2, 5
<i>Moschus chrysogaster</i> Hodgson, 1839	Moschidae	Animal substance	Almizcle, Muscho, Musci	-	-	1, 3
<i>Myristica fragrans</i> Houtt. (Macis)	Myristicaceae	Fruits	Macis	-	-	1, 2, 3, 4, 5, 6
<i>Myristica fragrans</i> Houtt. (Nut)	Myristicaceae	Fruits	Noce moschade, Nucis muscate, Nuez moscada	-	-	1, 2, 3, 4, 5, 6
<i>Myrtus communis</i> L.	Myrtaceae	Fruits	Murtones, Arrayán, Mirtilorum	6126	-	1, 2, 3, 4, 5, 6
<i>Nardostachys jatamansi</i> (D.Don) DC.	Caprifoliaceae	Rhizome	<i>Nardino</i> , Nardo, Spigha aromatica, Spice	-	-	1, 2, 5, 6
<i>Nigella sativa</i> L.	Ranunculaceae	Fruits	Nigella, Neguilla, Melanthii	-	-	1, 2, 3, 4, 5, 6
<i>Nuphar lutea</i> (L.) Sm. / <i>Nymphaea alba</i> L.	Nymphaeaceae	Fruits	<i>Nenífar</i> , Nenufarro	-	-	1, 2, 3, 4, 5, 6
<i>Ocimum basilicum</i> L.	Lamiaceae	Aerial parts	Basaliconis, Alhavaka, Ocimum, Albahaca	6058	-	1, 2, 3, 4, 5, 6
<i>Olea europaea</i> L.	Oleaceae	Fruits	Oley, Olea, Ulive, Oliva, Olivo	3442	-	1, 2, 3, 4, 5, 6
<i>Operculina turpethum</i> (L.) Silva Manso	Convolvulaceae	Roots	<i>Turbit</i> , Turbith	-	-	1, 2, 3, 4, 5, 6
<i>Opopanax chironium</i> (L.) W.D.J.Koch	Apiaceae	Exudate	<i>Apopanaco</i> , Opopanaco, Opopanax	-	-	1, 2, 3, 4, 5, 6
<i>Origanum majorana</i> L. and related species	Lamiaceae	Aerial parts	Mayorana, Maiorana, Majorana, Mejorana	-	-	1, 2, 3, 4, 5, 6
<i>Paeonia officinalis</i> L.	Paeoniaceae	Roots	Paeoniae, Peonia	6235	-	1, 2, 3, 4, 5, 6
<i>Papaver somniferum</i> L.	Papaveraceae	Exudate	Papaveri Bianchi, Adormideras	6060	-	1, 2, 3, 4, 5, 6
<i>Peganum harmala</i> L.	Nitrariaceae	Aerial parts	Harmel, Alharmel	5238	-	2, 3, 4, 5, 6
<i>Petroselinum crispum</i> (Mill.) Fuss	Apiaceae	Aerial parts	Prezzemolo, Perejil	-	-	1, 2, 3, 4, 5, 6
<i>Peucedanum ostruthium</i> (L.) W.D.J.Koch	Apiaceae	Roots	Peucedano, Struthium	-	-	1, 2, 3, 4, 5, 6
<i>Phoenix dactylifera</i> L.	Arecaceae	Fruits	Dátiles, Datteri, Palma, Dátiles, Diyafaniqun, Dactylorum	-	-	1, 2, 3, 4, 5, 6
<i>Phyllanthus emblica</i> L.	Phyllanthaceae	Fruits	Micleta, Miqlit, Mirabolano	-	-	1, 2, 3, 4, 5, 6
<i>Physeter macrocephalus</i> L., 1758	Physeteridae	Animal substance	Ambar gris, Ambar negro	-	-	1
<i>Pimpinella anisum</i> L.	Apiaceae	Fruits	Anís, Anís verde, Anisum	-	-	1, 2, 3, 4, 5, 6
<i>Pinctada radiata</i> (Leach, 1814) Pearl	Pteriidae	Animal substance	Albarum margaritarii, Perle forate, perle non forate	-	-	1, 3
<i>Pinus pinaster</i> Aiton	Pinaceae	Exudate	Rezine, Resina de	5172	-	1, 2, 5

<i>Species</i>	Family	Part / type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
<i>Pinus pinea</i> L. Pine nuts	Pinaceae	Fruits	pino <i>Pino (piñones), Granorum pini, Pinnocchi, Piñones</i>	6140	-	1, 2, 3, 4, 5, 6
<i>Pinus sylvestris</i> L.	Pinaceae	Exudate	Pez, Pez negra, Pez de Borgoña	-	-	1, 2, 3, 4, 5, 6
<i>Piper longum</i> L.	Piperaceae	Fruits	Piperis longi, Peppe lungho, Pimienta larga	-	-	1, 2, 3, 4, 5, 6
<i>Piper nigrum</i> L.	Piperaceae	Fruits	Bibri. Pebre, Piperis nigri, Pimienta blanca	-	-	1, 2, 3, 4, 5, 6
<i>Pistacia lentiscus</i> L. and rarely <i>P. terebinthus</i> L.	Anacardiaceae	Exudate	<i>Almáciga, Mastiçino, Mastice, Mastic, Almáciga</i>	43817, 3182	-	1, 2, 3, 4, 5, 6
<i>Plantago afra</i> L. / <i>P. indica</i> L. / <i>P. ovata</i> L.	Plantaginaceae	Fruits	Psillii, Psilio, Zaragatona	-	-	1, 2, 3, 4, 5, 6
<i>Polypodium vulgare</i> L.	Polypodiaceae	Whole plant	<i>Polipodio calçino, Polipodio</i>	-	38923	1, 2, 3, 4, 5, 6
<i>Populus nigra</i> L.	Salicaceae	Buds	<i>Populeo, Álamo negro yemas frescas, Occhi di popolo</i>	-	39115	1, 2, 3, 4, 5, 6
<i>Portulaca oleracea</i> L.	Portulacaceae	Aerial parts	Porcellana, Portulacae, Verdolaga	-	-	1, 2, 3, 4, 5, 6
<i>Prunus domestica</i> L.	Rosaceae	Fruits	<i>Diaprunis, Prunis, Susine, Prunas, Prunus</i>	-	-	1, 2, 3, 4, 5, 6
<i>Prunus dulcis</i> (Mill.) D.A.Webb	Rosaceae	Fruits	<i>Almendras dulces, Amygdalarum dulcium excorticarum, Mandorle</i>	1549	-	1, 2, 3, 4, 5, 6
<i>Pterocarpus santalinus</i> L.f.	Leguminosae	Wood	<i>Sándalos, Sándalo rojo, Sandali rossi, Santali rubri</i>	-	-	1, 2, 5, 6
<i>Punica granatum</i> L.	Lythraceae	Fruits	Granada, Granado, Melagrane	6259	-	1, 2, 3, 4, 5, 6
<i>Rheum officinale</i> Baill. / <i>R. palmatum</i> L.	Polygonaceae	Leaves	<i>Ruybarbo, Reubarbero, Rheum, Ruibarbo, Rubarbiru</i>	-	-	1, 2, 3, 4, 5, 6
<i>Rosa bicolor</i> Jacq.	Rosaceae	Flowers	Rosas rojas	-	-	1, 2, 5, 6
<i>Rosa gallica</i> L. "Officinalis"	Rosaceae	Flowers	<i>Rosada, Diarodón, Rosas, Rose</i>	-	38897	1, 2, 5, 6
<i>Rosmarinus officinalis</i> L.	Lamiaceae	Aerial parts	Romero, Ramerino, Rosmarinus	6093	-	1, 2, 3, 4, 5, 6
<i>Ruta graveolens</i> L.	Rutaceae	Aerial parts	<i>Ruda, Ruta</i>	-	-	1, 2, 3, 4, 5, 6
<i>Saccharum officinarum</i> L.	Poaceae	Aerial parts	Açucar, Azacar, Azúcar, Zucchero, Sacchari	-	-	1, 2, 3, 4, 5, 6
<i>Salvia officinalis</i> subsp. <i>lavandulifolia</i> (Vahl) Gams and other subsp.	Lamiaceae	Aerial parts	Salvia	6195	-	1, 2, 3, 4, 5, 6
<i>Sambucus ebulus</i> L.	Adoxaceae	Fruits	Yezgo, Yezgos	3370	38902, 39091	1, 2, 3, 4, 5, 6
<i>Sambucus nigra</i> L.	Adoxaceae	Flowers	Sauco, Sambucho, Sambucus	6252	38900, 38908	1, 2, 3, 4, 5, 6
<i>Santalum album</i> L.	Santalaceae	Wood	<i>Sandalino, Sándalos, Sándalo, Sándalo blanco, Santali albi, Santali</i>	-	-	1, 2, 3, 4, 5, 6

<i>Species</i>	Family	Part / type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
<i>Sempervivum tectorum</i> L.	Crassulaceae	Aerial parts	citrini Sopravvivo, Siempreviva mayor	-	-	1, 2, 3, 4, 5, 6
<i>Senna alexandrina</i> Mill.	Leguminosae	Fruits	<i>Sen, Diasen</i> , Sena, Casia, Sen de España	-	-	1, 2, 3, 4, 5, 6
<i>Silene vulgaris</i> (Moench) Garcke	Caryophyllaceae	Rhizome	Been bianco, Behen blanco, Ben blanco	-	39075, 38925, 38913	1, 2, 3, 4, 5, 6
<i>Solanum nigrum</i> L.	Solanaceae	Fruits	Solano negro, Solano hortense	MUB48114	-	1, 2, 3, 4, 5, 6
<i>Styrax officinalis</i> L.	Styracaceae	Exudate	<i>Calamita</i> , Lapis chalamita, Styrax calamita, Estoraque	-	-	1, 2, 3, 4, 5, 6
<i>Sus scrofa domestica</i> Erxleben, 1777	Suidae	Animal substance	Cerdo, Puerco, Porcini	-	-	1
<i>Syzygium aromaticum</i> (L.) Merr. & L.M.Perry	Myrtaceae	Flowers	Cariofilorum, Clavos, Gherofani	-	-	1, 2, 3, 4, 5, 6
<i>Tamarindus indica</i> L.	Leguminosae	Fruits	<i>Tamarindos</i> , Thamerindi, Tamar indi	-	-	1, 2, 3, 4, 5, 6
<i>Tanacetum balsamita</i> L.	Asteraceae	Flowers	Balsamite, Balsamita	MUB43841	39015	1, 2, 3, 4, 5, 6
<i>Tanacetum parthenium</i> (L.) Sch.Bip.	Asteraceae	Flowers	Pelite, Pyrethrum, Tanacetum	-	-	1, 2, 3, 4, 5, 6
<i>Terminalia bellirica</i> (Gaertn.) Roxb.	Combretaceae	Fruits	Mirabolani bellirici	-	-	2, 3, 4, 5, 6
<i>Terminalia chebula</i> Retz.	Combretaceae	Fruits	Micleta, Mirabolos quebulos	-	-	2, 3, 4, 5, 6
<i>Terminalia citrina</i> Roxb. ex Fleming	Combretaceae	Fruits	Mirabolani citrini, Micleta, Miroblanos cetrinos	-	-	2, 3, 4, 5, 6
<i>Tetraclinis articulata</i> (Vahl) Mast.	Cupressaceae	Exudate	Sandaraca, Sandaracha, Sandareca	-	-	2, 3, 5, 6
<i>Trifolium pratense</i> L.	Leguminosae	Aerial parts	Trébol	6204	38911	2, 5, 6
<i>Trigonella foenumgraecum</i> L.	Leguminosae	Fruits	Alholva, Alolvas, Fenugreci, Trigonella	-	-	1, 2, 3, 4, 5, 6
<i>Triticum aestivum</i> L. Starch	Poaceae	Fruits	Amyli id est amydi, Almidón, Amil	MUB48267	-	1, 2, 3, 4, 5, 6
<i>Umbilicus horizontalis</i> (Guss.) DC.	Crassulaceae	Aerial parts	Omblijo de Venus	-	-	1, 2, 3, 4, 5, 6
<i>Ursus arctos</i> L., 1758	Ursidae	Animal substance	Grasso d'orso, Enjundia de oso	-	-	3
<i>Valeriana celtica</i> L.	Caprifoliaceae	Roots	Spigha celticha, Espica céltica	-	-	1, 2, 3, 4, 5, 6
<i>Vicia ervilia</i> (L.) Willd.	Leguminosae	Fruits	Arveja, Aruejas, Oroví	-	-	2, 3, 4, 5, 6
<i>Viola odorata</i> L.	Violaceae	Flowers	<i>Violado</i> , Viole mammole, Violetas, Violas secas, Violarum	1791	-	1, 2, 3, 4, 5, 6
<i>Vitis vinifera</i> L. fruits and derivatives through fermentations	Vitaceae	Fruits	Uvas pasa, Uve passe, Aceto, Vinagre, Vino	6231	-	1, 2, 3, 4, 5, 6
<i>Zingiber officinale</i> Roscoe	Zingiberaceae	Rhizome	Gengibre, Zingiberis, Agengibre	-	-	1, 2, 3, 4, 5, 6
<i>Ziziphus jujuba</i> Mill.	Rhamnaceae	Fruits	<i>Jujubas</i> , Xinjoles, Azofeyfas	-	-	1, 2, 3, 5, 6
Minerals and rocks						
(PbCO ₃) ₂ ·Pb(OH) ₂	Carbonates	Mineral,	Albayalde, Cerusa	-	-	1, 7

<i>Species</i>	Family	Part / type	Vernacular and pharmaceutical names	Vouchers ALBA	Vouchers FIAF	Selected References
White lead		powder				
Amber	Fossilized tree resins	Powder	Frumentum charabe	-	-	1, 7
ZrSiO ₄ Jacinth Zircon	Gemstones	Mineral, powder	Jacintos, Iacinti, Hyacinthi	-	-	3, 7
Be ₃ Al ₂ (SiO ₃) ₆ Emerald	Gemstones	Powder	Fragmentorum egmaradi, smaragdi	-	-	3, 7
Au Gold	Metals	Gold leaf	Foliorum auri	-	-	3, 7
Ag Silver	Metals	Powder	Folium argenti	-	-	3, 7
SiO ₂ Sard similar to Carnalin	Mineral, semi-precious gemstones	Powder	Sardini	-	-	3, 7
PbO (Litharge)	Oxides	Mineral, Crystals, scales or powder	<i>Palma</i> , Litargirio d'argento, Litargirio, Ungüento palma	-	-	1, 3
ClNa Common Salt	Salts	Mineral, Halite or Sea salt crystals	Sal	-	-	1, 3
Lapis lazuli (mainly Lazurite)	Semi-precious gemstones	Powder	Lapislazzuli, Lapislázuli	-	-	3, 7
KC ₄ H ₅ O ₆ Potassium bitartrate	Tartrates	Mineral, White crystalline powder	Tartarii solubilis, Cremor tártaro	-	-	7
Al ₂ O ₃ Sapphires	Gemstones	Powder	Frumentorum zaphiri, Saphiri	-	-	3, 7
Fe ₃ Al ₂ Si ₃ O ₁₂ Garnet Almandine	Semi-precious gemstones	Mineral, Powder	Granatorum, Granati	-	-	3, 7
KAl(SO ₄) ₂ ·12H ₂ O Hydrated potassium aluminium sulfate	Sulfates	Mineral, Crystals	Allume bianco, Pierre d'alun, Stypteriae, Alum	-	-	1, 3

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Albacete 1881	1	0	0	0	0	1	0	0	1	0	0	0	1	1	1	1	0	1
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	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Granada 1556	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1
	1	1	1	0	0	1	0	1	1	0	1	1	1	1	1	1	1	0	1
	1	0	0	1	1	1	1	1	1	0	1	1	1	0	1	1	0	1	1
	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	0	0	1
	1	1	1	0	1	0	1	1	1	1	1	1	0	1	1	1	1	1	0
	0	1	0	0	1	1	1	0	0	1	0	1	1	0	1	1	1	0	0
	1	1	1	1	1	0	0	1	1	1	0	1	1	1	1	1	1	1	1
	1	1	1	1	0	1	1	1	1	1	0	1	1	0	1	1	0	0	1
	0	1	1	1	1	0	1	1	1	1	1	1	1	0	1	0	1	1	0
	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	0	1	0
Healers and Witches 1500-1700	1	0	1	0	0	0	0	0	0	0	1	1	0	0	0	1	1	1	0
	0	1	0	0	0	0	0	0	0	0	1	1	0	1	0	0	0	0	1
	0	0	1	1	0	1	0	1	0	1	0	0	0	0	0	1	0	0	0
	0	1	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	0	0	0	0	0	0	0	1	0	0	0	1	0	0	1	1	1	0	0
	0	1	0	0	1	0	0	1	0	0	0	1	0	1	1	1	1	1	0
	0	1	0	0	1	0	1	0	0	1	0	1	0	1	0	0	1	0	0
	0	1	1	1	1	1	0	0	1	0	0	1	0	0	0	1	1	1	0
	0	0	0	0	0	0	1	0	1	0	1	0	1	1	1	1	1	0	0
Laguna 1555	1	1	1	1	0	0	1	0	0	1	1	1	1	1	1	1	1	1	1
	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	0
	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
	0	0	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	0
	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0
	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	0
	1	0	0	0	1	1	1	1	1	0	1	1	1	1	1	1	0	1	0
Moors Valencia 1570	1	0	1	0	1	0	1	1	0	1	0	0	0	1	1	1	1	1	0
	1	1	1	1	0	0	0	1	1	1	1	0	1	1	1	1	1	1	0
	0	0	0	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	0	0
	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1	0
	1	0	1	0	1	1	1	1	0	0	0	0	1	1	1	1	1	1	0
	1	1	1	1	1	0	1	1	1	1	1	0	1	1	1	0	0	1	1
	0	1	1	1	0	1	1	1	1	0	1	1	0	1	1	1	1	0	1

	1	1	1	1	1	1	0	0	1	1	1	0	0	1	1	1	1	1	0
	1	1	1	1	1	0	1	1	1	1	0	0	1	1	1	1	0		
Murcia 1823	0	0	0	1	0	0	1	1	0	1	0	1	1	1	1	1	1	0	1
	1	1	1	1	0	0	0	0	1	1	1	1	0	1	1	1	1	0	1
	0	0	0	1	1	0	1	1	1	0	0	1	0	0	0	1	1	1	1
	1	1	1	0	1	1	0	1	0	0	1	1	1	1	0	1	1	1	0
	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	0	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1
	1	1	0	1	1	1	1	1	1	0	1	0	0	1	1	0	0	0	1
	0	1	1	1	1	0	1	1	0	0	1	0	0	0	1	0	1	1	0
	1	0	0	0	0	0	1	1	0	0	0	0	1	1	1	1	1	1	0
Sephardic	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	0	0	0
	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	0
	0	0	0	1	0	1	0	0	1	1	0	0	0	0	0	0	0	1	1
	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	1	1	1	1	0	0	1	0	0	0	1	1	0	0	0	0	1
	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	1	0	0
	1	1	1	0	0	0	1	1	0	1	0	0	0	1	1	0	1	0	0
	1	0	0	0	1	0	1	1	0	0	0	1	0	1	0	1	0	0	0
	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
Mula Manu 1790	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0
	0	1	0	0	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0
	0	0	0	1	0	1	0	0	0	1	1	0	0	0	0	0	0	1	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	0	0
	0	0	0	0	0	0	0	0	1	0	0	0	1	0	1	0	0	0	0
	0	1	0	0	0	1	0	1	0	0	0	0	0	0	1	0	0	0	0
	0	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	1	0	0
	0	0	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	0
Valencia 1601	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Vander 1971	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	0	0	0	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0
	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	1
	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1
	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0

	0	0	0	0	1	1	0	1	1	0	0	0	1	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
	0	1	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	1
	0	1	1	1	0	1	0	1	0	0	1	0	0	0	0	0	0	1	0
	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0
Zaragoza 1546	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	0
	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1
	1	0	1	0	1	1	1	1	1	1	1	1	0	1	0	0	0	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1
Zaragoza 1601–1609	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1
	1	1	1	0	1	1	0	0	1	0	1	1	1	1	0	1	0	1	1
	1	1	0	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1
	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1
	0	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0
	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1	1

Supplementary Table 4. Matrix (22 x 187) weighted of each one ingredient in the 22 sources, exclusively in function of the forms it is present and its role in the complex formulations of the Albacete tariff

Localities (PbCO ₃) ₂ -Pb(OH) ₂	Acorus calamus L.	Adiantum capillus-veneris L.	Ag Silver	Al ₂ O ₃ Sapphires	Aloe vera (L.) Burm.f.	Alpinia galanga (L.) Willd.	Alpinia zerumbet (Pers.)
B.L.Burt & R.M.Sm.	Althaea officinalis L. Amber	Ammi visnaga (L.) Lam.	Amomum subulatum Roxb.	Anchusa azurea Mill.	Apis mellifera L. Honey	Apis mellifera L. Wax	Apium
graveolens L.	Aquilaria malaccensis Lam.	Aristolochia fontanesii Boiss. & Reut.	Artemisia absinthium L.	Asarum europaeum L.	Artemisia absinthium L.	Astracantha gummifera (Labill.) Podlech/	
Astragalus clusii Boiss.	Atriplex hortensis L.	Au Gold	Be ₃ Al ₂ (SiO ₃) ₆ Emerald	Blackstonia perfoliata (L.) Huds.	Bombyx mori (= Phalaena mori L. 1758) Silk	Borago officinalis L. Bos	
taurus L. 1758	Boswellia sacra Flueck.	Bryonia cretica L.	Buthus occitanus Amoreux 1789	Capparis sicula Duhamel	Cassia fistula L.	Castor fiber L. 1758	Centaurium erythraea Rafn.
	Cervus elaphus L. 1758	Ceterach officinarum Willd. (not Asplenium scolopendrium L.)	Cheilocostus speciosus (J.Koenig) C.D.Specht.	Chelidonium majus L.	Cichorium endivia		
L.	Cichorium intybus L. Cinnamomum camphora (L.) J.Presl	Cinnamomum cassia (L.) J.Presl	Cinnamomum verum J.Presl.	Citrullus colocynthis (L.) Schrad.	Citrus aurantium L. Citrus		
medica L.	CINa Salt	Colchicum sp.	Commiphora africana (A.Rich.) Endl.	Commiphora gileadensis (L.) C.Chr.	Commiphora gileadensis (L.) C.Chr. (Twigs)	Commiphora myrrha (Nees)	
Engl.	Convolvulus scammonia L.	Corallium rubrum L. 1758	Corylus hispanica Mill. ex D.Rivera & al	Crocus sativus L.	Cuminum cyminum L.	Curcuma zedoaria (Christm.) Roscoe	
	Cuscuta epithimum (L.) L.	Cydonia oblonga Mill.	Cymbopogon martini (Roxb.) W.Watson	Cymbopogon nardus (L.) Rendle	Cymbopogon schoenanthus (L.) Spreng.	Cyperus esculentus	
L.	Daucus carota subsp. drepanensis (Arcang.) Heywood	Dorema ammoniacum D.Don	Drimia maritima (L.) Stearn.	Dryopteris filix-mas (L.) Schott	Ecballium elaterium (L.) A.Rich.	Elephas maximus	
indicus (Cuvier) 1798	Elettaria cardamomum (L.) Maton	Euphorbia resinifera O.Berg	Euphrasia officinalis L.	Fe ₃ Al ₂ Si ₃ O ₁₂ Garnet	Almandin	Ferula assa-foetida L. Ferula gummosa	
Boiss. (incl. Ferulago galbanifera (Mill.) W.D.J.Koch)	Ferula persica Willd.	Ficus carica L.	Foeniculum vulgare Mill.	Fumaria officinalis L.	Gallus gallus L. 1758)	Geum urbanum L.	
	Glycyrrhiza glabra L. H ₂ O Water	Hedera helix L.	Helleborus orientalis Lam. (not H. niger L.)	Humulus lupulus L.	Hyoscyamus albus L. Hyoscyamus niger L.	Hyssopus officinalis L.	

	Ipomoea turpethum L.	Iris × germanica L.	Juniperus thurifera L.	KAl(SO ₄) ₂ ·12H ₂ O hydrated potassium aluminium sulfate	KC ₄ H ₅ O ₆ Potassium bitartrate	Kerria lacca Targ.-Tozz. 1884													
	(= Coccus lacca Kerr 1782)	Lactuca sativa L.	Lapis lazuli (mainly Lazurite)	Laricifomes officinalis (Vill.) Kotl. & Pouzar 1957 (= Polyporus officinalis Fries)	Laurus nobilis L.	Lavandula stoechas													
	L. / Thymus moroderi Pau ex Martínez	Limonium supinum (Girard) Pignatti	Liquidambar orientalis Mill.	Lupinus albus L.	Mandragora officinarum L.	Matricaria chamomilla L.													
	pulegium L.	Mentha spicata L. Juice	Mentha spicata L. Oil	Mentha spicata L. Powder	Mentha x piperita L.	Mimusops elengi L.	Moschus chrysogaster Hodgson 1839												
	Houtt. (Macis)	Myristica fragrans Houtt. (Nut)	Myrtus communis L.	Nardostachys jatamansi (D.Don) DC.	Nigella sativa L.	Nuphar lutea L.	Ocimum basilicum L.	Olea europaea L.											
		Opopanax chironium (L.) W.D.J.Koch	Origanum majorana L.	Paeonia officinalis L.	Papaver somniferum L.	PbO (Litharge)	Peganum harmala L.	Petroselinum crispum (Mill.)											
Fuss		Peucedanum ostruthium (L.) W.D.J.Koch	Phoenix dactylifera L.	Phyllanthus emblica L.	Physeter macrocephalus L. 1758		Pimpinella anisum L.	Pinctada radiata (Leach 1814)											
Pearl		Pinus pinaster Aiton	Pinus pinea L. Pine nuts	Pinus sylvestris L.	Piper longum L.	Piper nigrum L.	Pistacia terebinthus L.	Plantago afra L.	Polypodium vulgare L.										
		Populus nigra L.	Portulaca oleracea L.	Prunus domestica L.	Prunus dulcis (Mill.) D.A.Webb	Pterocarpus santalinus L.f.	Punica granatum L.	Ranunculus aconitifolius L.	Rheum officinale										
Baill.		Rosa bicolor Jacq.	Rosa gallica L. "Officinalis"	Rosmarinus officinalis L.	Ruta graveolens L.	Saccharum officinarum L.	Salvia officinalis subsp. lavandulifolia (Vahl) Gams												
		Sambucus ebulus L.	Sambucus nigra L.	Santalum album L.	Sempervivum tectorum L.	Senna alexandrina Mill.	Silene vulgaris (Moench) Garcke	SiO ₂ Sard similar to Carnalin											
		Solanum nigrum L.	Styrax officinalis L.	Sus scrofa domestica Erxleben 1777	Syzygium aromaticum (L.) Merr. & L.M.Perry	Tamarindus indica L.	Tanacetum balsamita L.												
		Tanacetum parthenium (L.) Sch.Bip.	Terminalia bellirica (Gaertn.) Roxb.	Terminalia chebula Retz.	Terminalia citrina Roxb. ex Fleming	Tetraclinis articulata (Vahl) Mast.													
		Trifolium pratense L.	Trigonella foenumgraecum L.	Triticum aestivum L. Starch	Umbilicus horizontalis (Guss.) DC.	Ursus arctos L. 1758	Valeriana celtica L.	Vicia ervilia (L.) Willd.											
		Viola odorata L.	Vitis vinifera L.	Zingiber officinale Roscoe	Ziziphus jujuba Mill.	ZrSiO ₄ Jacinth Zircon													
Albacete 1526	1	2	2	1	1	6	5	1	1	1	1	1	1	1	12	7	6	4	1
	6	3	6	1	1	1	1	2	2	1	2	1	1	3	2	3	1	1	1
	1	1	1	2	2	4	8	3	1	3	1	1	3	1	1	2	9	3	2
	9	3	3	3	2	2	1	3	4	2	2	2	1	1	4	3	3	1	1
	1	3	2	1	7	2	1	1	6	9	3	1	1	2	2	1	5	4	1
	1	1	1	1	1	2	4	2	2	3	1	2	1	1	1	1	1	2	1
	3	2	3	1	11	1	1	3	8	2	3	1	3	1	1	2	1	2	3
	1	6	2	2	1	1	7	7	8	1	3	1	1	2	5	5	1	1	4
	1	14	2	5	6	1	1	1	8	1	4	2	1	1	1	2	7	3	1
	3	1	1	1	1	2	1	1	1	1	1	1	7	9	9	1	1		
Florence 1498–1574	1	2	2	1	1	6	5	1	1	1	1	1	1	1	12	7	6	4	1
	6	3	6	1	1	1	1	2	2	1	2	1	1	3	2	3	1	1	1
	1	1	1	2	2	4	8	3	1	3	1	1	3	1	1	2	9	3	2
	9	3	3	3	2	2	1	3	4	2	2	2	1	1	4	3	3	1	1
	1	3	2	1	7	2	1	1	6	2	3	1	1	2	2	1	5	4	1
	1	1	1	1	1	2	4	2	2	3	1	2	1	1	0	0	0	2	1
	3	2	3	1	11	1	1	3	8	2	3	1	3	1	1	2	1	2	3
	1	6	2	2	1	1	7	7	8	1	3	1	1	2	5	5	1	1	4
	1	14	2	5	6	1	1	1	8	1	4	2	1	1	1	2	7	3	1
	3	1	1	1	1	1	2	1	1	1	1	1	7	9	9	0	1		
Ethnobotany Alta Valle del Reno		0	0	0	0	0	0	0	6	0	0	0	0	0	0	0	12	7	0
	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	1
	0	1	0	0	0	2	0	0	8	0	0	0	0	0	0	0	0	0	0
	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	1	7	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	1	0	0	4	0	0	0	1	0	1	0	1	1	1
	2	0	0	0	0	0	0	0	0	3	8	0	0	0	0	0	0	2	0
	0	0	0	0	0	0	1	0	0	7	0	0	3	0	0	2	0	0	0
	0	0	0	0	2	0	6	1	0	1	0	1	0	0	0	0	0	0	7
	0	0	0	0	0	0	0	1	0	1	0	0	0	0	7	9	0	0	0

Vander	0	0	2	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	6
	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	1	0	1	0
	0	0	2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2	0
	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0
	0	0	0	7	2	0	1	6	0	0	0	1	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0
	0	0	1	0	0	0	3	0	0	0	0	0	0	0	2	0	0	0	0
	6	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	4	0
	14	2	5	0	1	0	1	0	0	4	0	0	0	0	0	0	3	0	0
	0	0	0	0	0	2	0	0	0	0	0	7	0	0	0	0	0	0	0
European Medicines Agency	0	0	0	0	0	0	0	6	0	0	1	0	0	0	0	0	0	0	0
	0	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
	0	0	0	0	2	0	0	8	0	0	0	0	0	0	0	0	2	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	0	0	7	2	0	0	6	0	3	0	1	0	0	0	0	0
	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2
	0	0	0	0	0	0	0	0	0	8	0	0	1	0	0	0	0	0	0
	0	0	6	0	0	0	0	0	0	8	1	1	0	0	0	0	0	0	0
	4	0	14	2	0	0	1	0	1	0	0	4	0	0	0	0	0	7	0
	0	3	0	0	0	0	0	2	0	0	0	0	0	0	0	9	0	0	0
Sepharadic Tradition	0	0	0	0	0	0	0	0	0	0	0	0	0	0	12	7	6	0	0
	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0	1	0
	0	0	0	0	2	0	8	0	0	3	1	0	0	0	0	0	0	0	2
	9	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	0	0	1	7	2	1	0	0	9	0	0	0	2	2	0	0	0	0
	1	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	2	0
	0	2	3	1	0	0	0	3	8	0	3	0	0	0	1	2	0	2	0
	0	3	0	0	0	1	0	7	8	0	0	0	1	0	5	0	1	0	0
	0	14	2	0	6	0	0	0	0	0	0	0	0	0	0	0	7	3	0
	0	0	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0	0	0
Zaragoza Hospital 1601–1609	1	2	2	1	1	6	5	1	1	1	1	0	1	1	6	6	6	6	3
	1	6	3	6	0	1	1	0	0	2	0	2	1	1	3	0	3	0	1
	1	1	1	0	2	1	1	8	3	1	3	1	1	1	0	0	2	9	3
	1	9	3	2	3	2	1	0	3	4	1	2	2	1	1	4	3	3	1
	1	1	3	2	0	7	2	1	0	6	7	3	1	1	2	2	1	5	4
	1	0	1	1	0	1	2	4	2	1	2	1	2	1	0	1	1	1	2
	1	2	2	1	1	11	0	1	2	7	2	2	1	3	1	1	2	1	2
	3	1	6	2	2	0	1	7	3	8	1	3	1	1	1	3	5	1	1
	4	1	14	2	3	2	1	1	1	8	1	4	1	1	1	0	2	7	3
	0	3	1	1	1	1	1	2	0	1	1	1	0	7	5	9	1	1	0
Albacete Picazo 1881	1	0	0	0	0	1	0	0	1	0	0	0	1	1	2	1	0	1	0
	6	0	6	0	0	0	0	0	2	0	2	1	1	0	2	3	1	1	0
	0	0	0	2	2	0	0	3	1	3	1	3	0	0	2	9	3	0	0
	9	3	0	0	0	0	0	0	0	0	2	2	1	1	0	3	3	0	0
	1	3	2	0	7	2	0	0	6	4	0	1	1	2	2	1	5	4	0
	0	1	1	1	0	2	1	0	0	3	0	0	1	0	0	0	0	1	0

	3	0	3	1	0	0	0	0	2	2	0	1	3	1	0	0	0	0	0
	1	1	0	2	0	1	0	0	8	1	0	0	0	0	2	5	0	0	4
	0	14	2	0	6	0	1	1	8	0	4	0	0	0	0	7	3	0	
	3	0	0	0	0	1	0	0	0	0	0	0	7	2	9	0	0	0	
Healers and witches 1500–1750	1	0	2	0	0	0	0	0	0	0	1	1	0	0	0	12	7	6	0
	0	6	0	0	0	0	0	0	0	0	1	2	0	1	0	0	0	0	1
	0	0	1	1	0	1	0	8	0	1	3	1	0	0	0	0	2	0	0
	0	9	3	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	0	0	0	0	0	0	0	1	0	0	0	3	0	0	2	2	1	0	0
	0	1	0	0	1	0	0	4	0	0	0	1	0	1	1	1	1	1	0
	0	3	0	0	1	0	1	0	0	8	0	3	0	3	0	0	2	0	0
	0	1	6	0	2	1	1	0	7	8	0	3	1	0	0	5	0	0	0
	0	1	14	2	5	6	0	0	1	0	0	4	0	0	0	1	2	7	0
	0	0	0	0	0	0	1	0	1	0	1	0	1	7	8	9	1	0	0
Concordia Barcinonese 1511–1587				1	2	1	1	1	5	5	1	1	1	1	1	0	11	5	5
	4	1	3	3	6	1	1	1	1	2	1	1	1	1	1	2	1	3	1
	1	0	1	0	1	1	2	4	7	3	0	3	1	1	2	1	1	1	8
	2	2	8	3	3	2	2	2	1	2	3	2	1	2	1	1	4	3	3
	0	1	1	2	1	0	5	2	1	1	6	0	2	1	1	2	2	1	3
	4	1	1	0	1	1	1	1	4	1	2	2	1	2	0	1	0	0	0
	1	1	3	2	2	1	9	1	0	3	6	1	3	1	2	1	1	1	1
	2	2	1	6	2	2	1	1	7	7	7	1	1	1	1	2	4	4	1
	1	4	1	11	2	4	6	1	1	0	7	1	3	2	1	1	0	2	6
	2	1	3	1	1	1	1	1	2	1	1	1	1	1	6	7	8	1	1
Zaragoza 1553				1	2	1	1	6	5	1	1	1	1	1	10	5	5	4	1
	4	3	5	1	1	1	1	2	2	1	2	1	0	2	1	3	1	1	0
	1	1	0	1	2	4	6	3	0	3	1	1	3	1	1	2	8	2	2
	8	3	3	2	2	2	1	2	3	2	1	2	1	1	3	3	3	1	1
	1	3	2	0	6	2	1	1	6	7	2	1	1	1	2	0	5	4	1
	1	0	1	0	1	2	4	1	2	3	1	1	0	1	0	0	0	2	1
	3	2	1	1	10	1	1	3	6	2	3	1	1	1	1	1	1	2	2
	1	6	2	2	1	1	7	7	8	0	2	1	0	2	4	4	1	1	4
	1	12	2	5	5	1	1	1	6	1	4	2	1	1	1	2	6	2	1
	3	1	1	1	1	1	2	1	1	1	1	1	7	7	8	0	1		
Laguna 1555				1	2	2	0	0	6	0	1	1	1	1	12	7	6	4	1
	6	3	0	1	0	0	0	2	2	1	2	1	1	3	2	3	0	0	1
	1	1	0	2	2	4	8	3	1	3	1	1	3	1	1	2	9	3	2
	9	3	3	3	2	2	1	0	0	2	2	2	1	1	4	3	3	1	0
	0	3	2	1	7	2	1	1	6	9	3	1	1	2	2	1	5	4	0
	0	0	1	1	0	2	4	2	2	3	1	2	0	1	1	1	1	2	0
	0	0	0	1	10	1	1	3	8	2	3	1	3	1	1	0	1	2	0
	0	6	0	1	1	1	7	7	8	1	3	1	1	2	5	5	1	0	4
	1	14	2	5	6	1	1	1	8	1	4	2	0	1	1	2	0	3	0
	3	0	0	0	1	1	2	1	1	0	1	1	7	9	9	1	0		
Castilla Zamudio de Alfaro 1592–1599				1	2	1	0	0	5	3	0	1	0	1	1	1	10	6	6
	2	1	5	3	5	1	0	0	1	1	2	0	2	1	1	3	2	3	1

	1	0	1	1	1	2	1	2	5	3	0	1	1	1	2	1	1	2	8
	1	1	8	3	2	2	2	2	1	1	2	2	2	1	1	2	2	2	3
	1	0	1	3	2	0	7	1	1	1	4	6	3	1	1	2	2	1	4
	3	1	1	0	1	1	1	2	4	2	0	2	1	2	0	1	0	0	0
	1	0	1	1	1	0	8	1	1	2	8	2	2	1	3	1	1	2	1
	1	1	0	6	1	2	0	1	5	6	7	1	2	1	1	2	3	5	1
	0	4	1	8	2	5	5	1	1	0	8	1	4	0	0	1	0	2	4
	3	0	3	1	1	1	1	1	2	0	1	1	1	1	6	8	6	1	0
Valencia 1601	1	2	2	1	1	1	5	5	1	0	1	1	1	1	11	5	5	4	1
	5	3	6	1	1	1	1	2	2	1	1	1	1	2	2	3	1	1	0
	1	0	1	2	2	4	8	3	1	3	1	1	3	1	1	2	8	3	2
	8	3	3	3	2	2	1	3	4	2	2	1	1	1	4	3	3	0	1
	1	2	2	1	7	2	1	1	6	4	2	1	1	2	2	1	4	4	1
	1	0	1	1	1	1	4	2	2	2	1	2	1	1	1	1	1	2	1
	3	2	2	1	11	1	1	3	6	2	3	1	2	1	1	2	1	2	2
	1	6	2	1	1	1	7	7	7	1	2	1	1	1	5	4	1	1	4
	1	13	2	4	6	1	1	1	6	1	4	2	1	1	2	2	6	2	1
	3	1	1	1	1	1	1	1	1	1	1	1	7	7	8	1	1		
Moriscos Valencia 1573-1593	1		0	2	0	0	0	5	5	0	1	0	0	0	1	11	7	6	2
	0	6	1	2	1	0	0	0	1	2	1	2	0	1	3	2	3	1	1
	0	0	0	0	1	2	0	7	3	0	3	1	1	1	1	1	2	8	3
	1	9	3	1	3	2	1	0	3	0	1	1	2	1	1	2	3	3	0
	0	1	2	1	1	7	2	1	0	6	9	2	0	1	1	2	1	5	4
	0	1	0	1	0	1	2	4	2	0	0	0	0	1	1	1	1	1	2
	0	3	1	2	1	9	0	1	3	8	1	2	0	3	1	1	0	0	2
	1	0	6	2	2	0	1	4	7	8	0	1	1	0	2	2	4	1	0
	4	1	13	2	5	5	1	0	0	6	1	3	0	0	1	1	2	7	3
	0	3	1	1	1	1	0	2	1	1	1	0	0	6	7	9	1	0	
Granada 1556	1	2	2	0	1	0	5	0	1	0	1	1	1	1	11	7	5	4	1
	6	3	5	0	0	1	0	2	2	0	2	1	1	3	2	3	1	0	1
	1	0	0	1	1	1	6	3	0	3	1	1	0	1	1	0	5	3	1
	8	3	2	3	1	1	1	3	4	2	0	2	1	1	3	3	0	0	1
	1	1	2	0	6	0	1	1	6	9	3	1	0	1	2	1	5	4	0
	0	1	0	0	1	1	4	0	0	3	0	1	1	0	1	1	1	0	0
	3	1	1	1	9	0	0	3	8	2	0	1	3	1	1	2	1	2	3
	1	4	1	2	0	1	3	4	8	0	3	1	0	2	5	4	0	0	4
	0	13	2	5	5	0	1	1	6	1	4	2	0	1	0	2	4	3	0
	2	1	1	1	0	1	1	0	1	1	1	1	5	3	4	1	0		
El Bonillo 1711	1	1	1	2	0	0	3	1	0	1	0	0	1	1	11	7	6	4	1
	6	3	5	1	0	1	1	2	2	1	2	0	1	3	2	3	1	1	0
	0	0	0	2	2	0	6	3	1	3	1	1	3	0	1	2	9	3	0
	3	3	2	3	1	2	0	1	4	2	2	1	0	0	3	2	3	0	1
	1	3	2	0	7	2	1	0	6	9	3	1	0	0	1	1	2	4	1
	1	1	1	0	0	1	4	1	0	0	1	0	1	1	1	1	1	1	0
	3	2	2	1	9	1	0	0	8	2	3	1	3	1	1	2	0	2	3
	1	4	0	2	0	1	6	6	8	0	0	1	0	2	5	4	0	0	4

	0	12	1	5	5	0	0	1	6	1	0	0	0	1	0	2	6	0	0
	3	1	1	1	0	0	2	0	1	1	1	1	6	7	4	1	1	0	1
Murcia 1823	0	0	0	2	0	0	6	3	0	1	0	1	1	1	10	6	5	0	1
	6	3	5	1	0	0	0	0	2	1	2	1	0	3	2	3	1	0	1
	0	0	0	2	1	0	5	3	1	0	0	1	0	0	2	8	3	1	
	8	3	2	0	1	2	0	3	0	0	2	2	1	1	0	2	3	1	0
	1	3	2	1	5	2	0	1	6	9	3	1	1	1	2	1	4	4	1
	1	1	0	0	0	1	0	2	0	3	0	0	1	1	1	1	1	2	0
	3	1	2	1	1	0	1	2	7	2	3	1	3	1	0	2	1	2	3
	1	4	0	1	1	1	2	6	1	0	3	0	0	2	4	0	0	0	4
	0	12	1	4	5	0	1	1	0	0	3	0	0	0	1	0	6	3	0
	3	0	0	0	0	0	2	1	0	0	0	0	6	9	7	1	1	0	0
Albacete 1910	1	0	2	0	0	0	6	0	0	1	0	0	0	1	10	6	5	0	0
	6	0	5	0	0	0	0	0	2	0	0	0	0	0	1	3	1	0	0
	0	0	0	2	1	4	0	3	1	3	1	0	0	0	2	8	3	0	0
	7	0	0	0	1	0	0	0	0	0	2	1	1	0	0	0	0	0	0
	1	1	0	0	1	2	0	0	6	5	0	0	0	1	2	1	0	4	0
	0	1	0	0	0	2	0	0	0	3	0	0	0	0	0	0	0	1	0
	3	0	0	1	0	0	0	0	8	0	0	0	3	1	0	0	0	0	0
	0	4	0	1	0	1	0	0	0	0	0	1	0	2	4	0	0	0	4
	0	13	1	4	5	1	0	1	6	1	3	0	0	0	1	2	0	3	0
	2	0	0	0	0	0	1	0	0	0	0	0	6	2	0	1	0	0	0
Fitoterapia.net 2015	0	2	2	1	0	6	5	0	1	0	1	0	0	0	12	7	6	0	0
	6	0	6	0	0	0	0	2	1	2	1	0	0	2	0	1	0	0	0
	0	1	0	2	2	4	8	0	1	3	1	0	0	0	2	0	3	2	2
	9	3	0	0	0	1	0	0	2	0	0	0	0	0	3	0	1	0	0
	0	0	0	1	7	2	0	0	6	9	3	0	1	0	0	1	0	4	0
	0	1	0	0	0	0	4	2	0	0	0	0	1	1	1	1	2	0	0
	0	2	3	1	0	1	0	3	8	0	3	0	3	0	0	2	0	0	0
	0	6	0	1	0	1	7	7	0	1	3	1	0	2	5	5	1	0	4
	0	14	2	5	6	1	1	1	8	0	4	0	0	0	0	0	7	3	1
	3	0	0	0	0	1	1	1	0	0	0	0	7	0	9	0	0	0	0
Ethnobotany Albacete 1990–2015	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0	1	12	0	6
	0	1	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	0	1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
	0	2	9	3	0	3	2	0	0	0	0	2	0	2	0	0	0	0	0
	0	0	0	0	0	1	7	2	0	0	6	9	3	0	0	2	2	0	0
	4	1	0	0	0	0	0	0	4	2	0	0	1	0	1	1	1	1	1
	2	0	0	0	0	0	0	0	0	3	8	0	0	1	3	0	1	2	1
	0	0	0	6	0	2	1	0	0	0	0	0	0	0	0	0	5	0	1
	0	0	0	0	2	5	0	1	0	1	0	0	0	0	0	0	0	2	0
	0	1	0	0	0	0	0	1	0	1	1	0	0	0	9	0	0	0	0

Supplementary Table 5. Transformed matrix (22 x 187) from weighted to four classes (ACGT) of each one ingredient in the 22 sources, exclusively in function of the forms it is present and its role in the complex formulations of the Albacete tariff. A. Crude matrix. B. Nexus format matrix

A. Crude matrix

Localities	Alpinia zerumbet (Pers.) B.L.Burt & R.M.Sm.	Au Gold	Mimusops elengi L.	Ranunculus aconitifolius L.	SiO2 Sard similar to Carnalin	Al2O3 Sapphires	Limonium supinum (Girard)												
Pignatti	Ag Silver	Tanacetum balsamita L.	Opopanax chironius (L.) W.D.J.Koch	Umbilicus horizontalis (Guss.) DC.	Capparis sicula Duhamel	Cuscuta epithimum (L.) L.													
	Cymbopogon schoenanthus (L.) Spreng.	Elephas maximus indicus (Cuvier) 1798	Fe3Al2Si3O12 Garnet Almandin	Blackstonia perfoliata (L.) Huds.	ZrSiO4 Jacinth Zircon														
	Be3Al2(SiO3)6 Emerald	Tetraclinis articulata (Vahl) Mast.	Cheilocostus speciosus (J.Koenig) C.D.Specht.	Commiphora gileadensis (L.) C.Chr.	Cymbopogon nardus (L.)														
Rendle	Cyperus esculentus L.	Silene vulgaris (Moench) Garcke	Ammi visnaga (L.) Lam.	Lapis lazuli (mainly Lazurite)	Mandragora officinarum L.	Nuphar lutea L.	Pinctada												
radiata (Leach 1814) Pearl	Atriplex hortensis L.	Commiphora gileadensis (L.) C.Chr. (Twigs)	Terminalia bellirica (Gaertn.) Roxb.	Terminalia chebula Retz.	Terminalia citrina Roxb. ex														
Fleming	Valeriana celtica L.	Acorus calamus L.	Amomum subulatum Roxb.	Aquilaria malaccensis Lam.	Bombyx mori (= Phalaena mori L. 1758) Silk	Solanum nigrum L.	Ursus arctos L.												
1758	Nardostachys jatamansi (D.Don) DC.	Alpinia galanga (L.) Willd.	Asarum europaeum L.	Peucedanum ostruthium (L.) W.D.J.Koch	Phyllanthus emblica L.	Juniperus thurifera													
L.	Curcuma zedoaria (Christm.) Roscoe	Cymbopogon martini (Roxb.) W.Watson	Sempervivum tectorum L.	Cydonia oblonga Mill.	PbO (Litharge)	Ferula gummosa Boiss. (incl.													
Ferulago galbanifera (Mill.) W.D.J.Koch	Laricifomes officinalis (Vill.) Kotl. & Pouzar 1957 (= Polyporus officinalis Fries)	Citrullus colocynthis (L.) Schrad.	Convolvulus scammonia L.																
	Colchicum sp.	Ecballium elaterium (L.) A.Rich.	Ferula assa-foetida L.	Ferula persica Willd.	Ipomoea turpethum L.	Buthus occitanus Amoreux 1789	Euphorbia resinifera O.Berg												
	Helleborus orientalis Lam. (not H. niger L.)	Liquidambar orientalis Mill.	Kerria lacca Targ.-Tozz. 1884 (= Coccus lacca Kerr 1782)	Aristolochia fontanesii Boiss. & Reut.	Castor fiber L.														
1758	(PbCO3)2·Pb(OH)2	Commiphora africana (A.Rich.) Endl.	Santalum album L.	Paeonia officinalis L.	Corallium rubrum L. 1758	Elettaria cardamomum (L.) Maton	Humulus lupulus												
L.	Ceterach officinarum Willd. (not Asplenium scolopendrium L.)	Geum urbanum L.	Piper longum L.	Pterocarpus santalinus L.f.	Tamarindus indica L.	Tanacetum parthenium (L.) Sch.Bip.													
	Zingiber officinale Roscoe	Anchusa azurea Mill.	Aloe vera (L.) Burm.f.	Cassia fistula L.	Astracantha gummifera (Labill.) Podlech/ Astragalus clusii Boiss.	Rheum officinale Bail.													
	Euphrasia officinalis L.	KC4H5O6 Potassium bitartrate	Cinnamomum cassia (L.) J.Presl	Plantago afra L.	Prunus domestica L.	Salvia officinalis subsp. lavandulifolia (Vahl) Gams													
	Trigonella foenumgraecum L.	Lavandula stoechas L. / Thymus moroderi Pau ex Martinez	Glycyrrhiza glabra L.	Cichorium intybus L.	Borago officinalis L.	Centaurium erythraea Rafn.													
	Moschus chrysogaster Hodgson 1839	Amber	Chelidonium majus L.	Cichorium endivia L.	Styrax officinalis L.	Vicia ervilia (L.) Willd.	Nigella sativa L.	Pinus pinea L.	Pine										
nuts	Rosa bicolor Jacq.	Sus scrofa domestica Erxleben 1777	Physeter macrocephalus L. 1758	Citrus aurantium L.	Polypodium vulgare L.	Ziziphus jujuba Mill.	Populus nigra L.												
	Laurus nobilis L.	Commiphora myrrha (Nees) Engl.	Hyssopus officinalis L.	Adiantum capillus-veneris L.	Pinus pinaster Aiton	Sambucus nigra L.	Senna alexandrina Mill.												
	Althaea officinalis L.	Viola odorata L.	Portulaca oleracea L.	Lactuca sativa L.	KAl(SO4)2·12H2O hydrated potassium aluminium sulfate	Bos taurus L. 1758	Cervus elaphus L. 1758												
	Punica granatum L.	Gallus gallus L. 1758)	Lupinus albus L.	Myristica fragrans Houtt. (Macis)	Phoenix dactylifera L.	Boswellia sacra Flueck.	Citrus medica L.												
	Myristica fragrans Houtt. (Nut)	Origanum majorana L.	Hyoscyamus albus L.	Ocimum basilicum L.	Petroselinum crispum (Mill.) Fuss	Pistacia terebinthus L.	Mentha x piperita												
L.	Matricaria chamomilla L.	Cinnamomum camphora (L.) J.Presl	Corylus hispanica Mill. ex D.Rivera & al	Hyoscyamus niger L.	Myrtus communis L.	Foeniculum vulgare Mill.	Crocus												
sativus L.	Rosmarinus officinalis L.	Ficus carica L.	Bryonia cretica L.	Sambucus ebulus L.	Daucus carota subsp. drepanensis (Arcang.) Heywood	Dorema ammoniacum D.Don	Mentha pulegium												
L.	Mentha spicata L. Juice	Mentha spicata L. Oil	Mentha spicata L. Powder	Peganum harmala L.	Triticum aestivum L. Starch	Trifolium pratense L.	Drimia maritima (L.) Stearn.												
	Dryopteris filix-mas (L.) Schott	CiNa Salt	H2O Water	Hedera helix L.	Iris x germanica L.	Piper nigrum L.	Cinnamomum verum J.Presl.	Cuminum cyminum L.	Papaver										
somniferum L.	Pinus sylvestris L.	Ruta graveolens L.	Syzygium aromaticum (L.) Merr. & L.M.Perry	Apis mellifera L. Wax	Apis mellifera L. Wax	Apium graveolens L.	Fumaria officinalis L.	Prunus dulcis											
(Mill.) D.A.Webb	Saccharum officinarum L.	Vitis vinifera L.	Apis mellifera L. Honey	Artemisia absinthium L.	Rosa gallica L. "Officinalis"	Olea europaea L.	Pimpinella anisum												
L.																			
Albacete_1526	C	C	C	C	C	C	C	C	C	C	C	C	C	C	G	C	C	C	C
	C	C	C	C	C	G	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	G	C	C	C	T	G	C	C	C	C	C	C	C	C	C	C	C	C
	T	C	C	C	C	G	C	C	C	C	C	C	C	C	T	C	C	C	C
	C	C	C	T	G	C	C	T	C	G	C	G	G	C	C	G	C	C	C
	C	C	G	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	C	G	C	C	C	C	C	G	C	T	C	C	C	C	C	C	C	C
	C	C	C	C	C	C	C	C	T	C	C	C	C	C	C	C	T	T	C

	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	C	G	T
	T	C	C	C	G	T	T	G	C	G	G	T	T	G	T	G	C	C
Florence_1498_1574	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	G	C	C	C	T	G	C	C	C	C	C	C	C	C	C	C	C
	T	C	C	C	C	G	C	C	C	C	C	C	C	C	T	C	C	C
	C	C	C	T	G	C	C	C	C	C	G	C	G	C	C	C	C	C
	C	C	G	C	C	C	C	C	C	C	T	C	C	C	C	C	C	C
	A	C	C	C	C	C	C	C	G	C	C	C	C	C	C	C	C	C
	C	C	C	C	C	C	C	C	C	A	C	C	C	C	C	T	T	C
	C	C	C	C	C	A	A	A	A	C	C	C	C	C	C	C	G	T
Valencia_1601	T	C	C	C	G	T	T	G	C	C	G	T	T	G	T	G	C	C
	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	G	C	C	C	T	G	C	C	C	C	C	C	C	C	C	C	C
	T	C	C	C	C	G	C	C	C	C	C	C	C	C	G	C	C	C
	C	A	C	T	G	C	C	C	C	C	C	C	C	A	A	C	C	C
	C	C	G	C	C	C	C	C	C	A	C	C	C	C	C	C	C	C
	C	C	C	C	C	C	C	C	C	A	T	C	C	C	C	C	T	C
	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T
Zaragoza_1546	T	C	C	C	G	G	G	C	C	C	G	T	T	G	T	G	C	C
	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	G	C	C	C	T	G	C	C	C	C	C	C	C	C	C	C	C
	T	C	C	C	C	G	A	C	C	C	C	C	C	C	C	C	C	C
	C	A	C	T	G	C	C	C	C	C	C	C	C	A	G	A	C	C
	C	C	G	C	C	C	C	C	C	G	T	C	A	A	C	C	A	C
	A	C	C	C	A	C	C	C	C	A	T	A	A	C	C	C	C	C
	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	T	C
	A	C	C	C	C	A	A	A	A	A	C	G	T	G	T	G	C	C
Barcelona_1511_1587	G	C	C	C	G	G	G	C	C	C	G	T	T	G	T	G	G	C
	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	C	G	C	C	C	T	G	C	C	C	C	C	C	C	C	C	C
	C	T	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	C	A	C	T	G	C	C	T	A	G	C	A	G	A	A	C	C
	C	C	C	G	C	C	C	C	C	A	C	C	A	C	C	C	C	C
	C	C	C	C	C	C	C	C	C	A	C	C	A	C	C	C	C	C
	C	C	C	C	C	C	C	C	C	A	C	C	A	C	C	C	C	C
	C	A	C	C	C	C	C	A	A	A	A	C	C	C	C	A	C	G
Zaragoza_1601_1609	T	T	C	C	C	G	G	G	G	C	G	G	T	T	T	G	G	A
	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
	C	C	A	C	C	T	G	C	C	C	C	C	C	C	C	C	C	C
	T	C	C	C	C	G	C	C	C	C	C	C	C	C	T	C	C	C

El_Bonillo_1711	A	A	A	A	A	A	A	A	A	C	C	C	C	C	C	C	C	C
C	A	A	A	A	G	A	A	A	A	A	A	C	C	C	C	C	C	C
C	G	C	C	C	T	C	C	C	A	C	C	C	C	C	C	C	C	C
T	C	A	C	C	C	C	C	C	C	C	C	C	C	C	G	C	C	C
A	A	A	G	G	A	C	G	C	C	C	G	C	A	C	A	C	C	A
C	C	G	C	C	C	C	A	A	A	A	A	A	A	A	C	C	C	A
C	C	G	C	C	C	C	C	C	A	C	G	C	A	C	A	C	C	A
C	C	C	C	C	C	C	A	A	C	T	C	A	C	C	C	C	C	A
A	A	A	C	C	C	C	C	C	C	C	A	C	A	C	C	T	C	G
A	C	C	C	G	G	T	G	C	G	G	G	T	T	G	T	T	G	A
Murcia_1823	A	A	A	A	A	A	A	A	A	C	C	C	C	A	C	A	A	A
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	C
A	A	A	A	A	A	C	C	C	C	C	C	C	C	A	A	A	A	A
C	A	A	A	A	C	A	C	C	C	C	A	C	C	A	A	A	C	A
T	C	C	C	C	G	A	C	C	C	C	C	C	C	A	A	A	C	C
C	C	C	C	A	C	C	C	T	C	G	C	G	G	C	C	A	C	C
C	C	G	C	C	C	C	C	A	A	A	A	A	A	C	A	A	C	A
C	A	A	C	C	C	C	C	C	A	C	A	A	A	C	A	A	C	A
C	C	C	A	C	C	C	C	C	C	C	C	C	C	C	A	T	C	A
C	C	C	A	C	C	C	C	C	C	A	C	A	C	C	A	T	G	G
G	C	C	C	G	G	G	G	C	G	G	T	T	G	T	T	G	A	A
Fitoterapia_net_2015	A	A	A	A	A	A	A	A	A	C	A	A	A	A	A	A	A	A
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
A	A	A	A	A	A	A	G	A	A	A	A	A	A	A	A	A	A	A
C	A	A	T	G	A	C	A	A	A	A	A	A	A	A	T	A	C	C
C	A	A	C	C	C	C	A	T	A	G	C	G	G	C	G	A	C	C
A	C	G	C	C	C	C	C	C	C	C	A	A	A	A	A	A	C	C
C	A	C	C	C	C	C	A	C	C	C	A	C	C	C	A	C	A	A
C	C	C	C	A	C	C	C	C	C	C	A	C	A	C	A	C	T	A
T	C	C	C	G	T	T	G	C	A	G	C	A	T	A	T	T	G	G
Albacete_1881	A	A	A	A	A	A	A	A	A	A	C	A	A	A	A	A	A	A
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
T	C	C	C	C	G	C	C	C	C	C	C	C	C	C	C	C	C	C
C	A	A	A	G	C	C	C	C	T	C	C	G	C	A	C	A	C	A
A	A	G	C	C	C	C	C	C	A	A	A	A	A	A	A	A	C	A
A	A	C	C	C	A	C	C	C	A	G	C	T	A	C	A	C	A	A
A	A	C	C	C	A	C	A	A	A	A	T	C	C	C	A	C	A	A
A	C	C	C	A	T	C	C	C	A	C	G	C	C	C	C	G	T	A
Albacete_1910	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
T	A	A	A	C	A	A	A	A	A	A	C	A	A	C	A	C	G	A
A	A	A	A	A	C	C	A	A	C	G	C	G	A	C	G	A	C	C
A	A	G	C	C	C	C	A	A	A	A	A	A	A	A	C	A	C	A

	C	C	A	C	C	C	C	C	C	C	G	A	A	A	A	A	A	A	A
	A	A	A	C	A	A	C	A	A	A	C	A	C	C	C	C	C	C	C
	A	A	A	A	C	A	A	A	A	A	C	A	C	C	C	C	C	C	C
Healers_and_Witches_1500_1700	A	A	C	C	G	A	G	G	C	G	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	C	C	C	C	G	C	C	C	C	C	G	C	C	C	C	C	C	C	C
	C	C	A	A	C	C	A	C	C	C	C	T	A	C	C	C	C	C	C
	T	C	A	A	A	A	A	C	C	C	C	A	C	C	A	C	C	C	A
Albacete_1995	A	T	T	C	C	C	G	T	T	G	A	G	G	T	T	G	T	T	G
	A	A	A	A	A	A	A	A	A	A	A	C	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	C	A	A	A	A	A	A	C	A	A	A	A	A	A	A	A	A	C
	A	C	G	C	A	C	A	A	A	A	A	A	A	A	C	A	C	A	A
	A	A	G	A	A	C	C	C	C	A	C	A	A	A	C	A	A	C	C
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	T	T
	C	A	A	C	A	C	C	C	C	C	C	C	C	C	A	A	T	C	G
Chinese_Materia_Medica	A	C	C	A	G	A	A	G	C	G	A	T	T	G	A	T	T	G	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	T	A	A	G	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	G	A	G	T	G	T	G	C	T	A	A	A	G	A	A	A	A	A	A
	G	A	A	A	G	A	A	A	T	A	A	G	A	A	A	A	A	A	C
	G	A	A	A	G	A	A	A	A	G	A	A	A	A	A	A	A	A	A
	A	G	A	A	A	A	A	A	T	A	A	A	A	A	A	A	A	T	T
	A	G	A	A	G	A	G	A	A	G	A	A	A	A	T	A	T	A	G
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Sepharadic	C	T	A	A	A	A	T	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	C	C	C	C	C	C	C	C	C	T	C	C	C	C	C	C	C	C	C
	C	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	T
Mula_1790	T	C	A	C	A	T	T	G	C	G	G	T	T	A	T	T	C	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A


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Barcelona_1511_1587      CCCCCACACCCCCACCCGCCCCACCGCCCCCCCCCCCCCCCCCTCACCCCGTCACCCCCAAACCCCCACGTTCCCGGGGGCGTTCTGG
Zaragoza_1601_1609     CCACCCAAAAACCCCCCGCCCGCTCAAACCCCCCCCCCCCCCTCCCCCCCTCACCCACCCACCCCTCGCTCCCTGGCCCGGGTTG
Castile_1599           CCCCACCACCACCCCGCCCCAGCGCCACCCCCCCCCCCCTCACCCATTACCCCCAAACACCCCGCCGGCCGGCGTTGTTG
Laguna_1555            CCAACCACCCCCACCCCGCCCGCTCCACACCCACCCATCACCCCTTCCCCCCCCCCCCCTCGTTCCCGATGCGGTTGTTG
Granada_1556           CCCCCAAAAACAAACCACCCGACCCGCGAAAAAACACCCCCACCCCTACCCCGTCACCCAACCCACCCCTCGGGCCCGGTGAGGCTGTTG
Moors_Valencia_1570    CCCCCAAACAAACCAACCCGCCCCACCGAACCCACCCCCCCCACTCCACCTCCAACCCCCCCAACACTCGGGCCCGGTGCGGTTGTTG
El_Bonillo_1711       CCCCCAAACCAACCCACCGCCCCACGAACCCACCCCCCCCACTCCACCTCCAACCCCCCCAACACTCGGGCCCGGTGCGGTTGTTG
Murcia_1823           CCCCCAAACAACACCCCAACCCCGAACCAAAACCCACCCCCCCCGTCCCCACCCCAACCATCGGGCCCGGGGGCGTTGTTG
Albacete_1910         CCCCCAAACAAAAACACCACCCCGAAAAAACAACAAACACACCCCTAAAAACAAAAACCCCGAGAAACCGAGGCGGCTGTTG
Albacete_1881         CCCCCAAAAAACCACAAACCCACCGCTACAACAAAAACCCACAATCCACCTTACCACAAAAACCCCGAGAACCCATCCCGCCGCTCC
Vander_1971           CCCCCAAAAAACCACAAACACGCTAAAAAACCACAAACACTACAAAAAACAACAAAAAAGAAACAAAAAGTAG
EMA_2014              CACAAAAAACAACAAACAAACGCAAAAAAATCCAAAAATACAAAAAACAATAAAATAACAAAAAGTTG
Fitoterapia_net_2015  CCAACAAACAAACACACCCACGCCCCCGCTAAACACAACACCCACCCCACTTCCCCACCCCACTCGTTCCCGTTGCGGATGTTG
Albacete_1995         CACAAAAAACACAAAAAGAACCACAAAAACAAAAACCCACCACCTTCCAACACCCCCCCCAATCGAACAGAGCGATTGATG
Alta_Valle_del_Reno_2014  CCCAAAAAACAAAAACAAGAAAAAATACAAAAACAAAAAACCCACCACAATACAAAAACCCACAAAAATTAATAAAGTTAATA
Healers_and_Witches_1500_1700  AAACCCCCCCCCCCCCCGCCCCGCTACCCACCAACCCACCACTACCACCATCAAAAACCCACCACCACATTCCCGTTGAGGTTGTTG
Sepharmac             AAAAAAAAAAAAAAAAAAAAAAAAAACCCCCCCCCCCCTTCCAAAAAACAACAACTAATTCACATTGCGGTTATTC
Mula_Manu_1790        AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAACCCCCCCCCCCCTCGTTCCCGTTGCGGTTGTTG
Hawaiian_Materia_Medica  AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGAAAAAA
Chinese_Materia_Medica  AAATTTAAAAAATAGAAGAAAAACAAGAGTTTGAGAGAGAAGAAATATAGAAAAAATAAAATAAAAAAAAAA

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END;

Supplementary Table 6. Matrix in percentage of medicinal uses for each one of the 46 versions of the top 10 ingredients in 5 different sources of the Albacete tariff considering the ICD-10 main categories of diseases.

Codes: I Certain infectious and parasitic diseases, II Neoplasms, III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism, IV Endocrine nutritional and metabolic diseases, V Mental and behavioural disorders, VI Diseases of the nervous system, VII Diseases of the eye and adnexa, VIII Diseases of the ear and mastoid process, IX Diseases of the circulatory system, X Diseases of the respiratory system, XI Diseases of the digestive system, XII Diseases of the skin and subcutaneous tissue, XIII Diseases of the musculoskeletal system and connective tissue, XIV Diseases of the genitourinary system, XV Pregnancy childbirth and the puerperium, XVI Certain conditions originating in the perinatal period, XVIII Symptoms signs and abnormal clinical and laboratory findings not elsewhere classified, XIX Injury poisoning and certain other consequences of external causes, XX External causes of morbidity and mortality, XXI Factors influencing health status and contact with health services.

Latin name	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	XVI	XVIII	XIX	XX	XXI
AL_Rosa da.	0	0	0	0	0	0	60	0	0	0	0	0	0	0	0	0	40	0	0	0
AL_Apis Honey	0	0	0	0	0	0	0	0	0	20	40	20	0	0	0	0	0	20	0	0
AL_Rosmarinus	3	0	0	0	0	3	5	0	3	26	8	0	21	5	0	0	5	10	0	13
AL_Olea	11	0	0	3	0	0	0	0	26	0	5	5	0	5	0	0	0	42	0	3
AL_Crocus	0	0	0	0	0	0	0	17	0	0	0	0	0	0	83	0	0	0	0	0
AL_Ficus	21	0	0	0	0	0	0	0	0	59	3	0	17	0	0	0	0	0	0	0
AL_Mentha pu.	15	0	0	4	0	0	0	0	4	7	52	0	0	15	0	0	0	4	0	0
AL_Vitis	67	0	0	0	0	0	0	0	0	0	0	0	33	0	0	0	0	0	0	0

AL_Ruta	0	0	0	4	0	0	0	16	4	0	36	0	12	12	0	0	0	16	0	0
AL_Foeniculum	5	0	0	0	5	0	0	0	0	42	32	0	5	5	0	0	0	5	0	0
DI_Rosa ga.	8	0	0	0	0	0	8	8	0	8	23	8	0	8	0	0	15	15	0	0
DI_Apis Honey	12	0	0	0	0	0	6	6	0	12	0	0	0	6	0	6	12	24	18	0
DI_Rosmarinus	50	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	50	0	0	0
DI_Olea	10	3	0	0	0	0	8	0	0	0	21	13	5	10	0	0	13	18	0	0
DI_Crocus	0	0	0	0	22	0	33	0	0	0	11	0	0	11	0	0	11	11	0	0
DI_Ficus	17	0	0	2	0	2	2	2	2	13	7	17	2	11	0	0	7	11	4	0
DI_Mentha pu.	0	0	0	0	0	0	0	0	0	6	17	17	11	17	11	0	17	6	0	0
DI_Vitis	32	0	0	0	0	0	0	0	0	14	9	9	9	14	0	0	14	0	0	0
DI_Ruta	9	0	0	0	0	6	6	6	0	3	3	6	11	17	0	0	20	11	3	0
DI_Foeniculum	0	0	0	0	0	0	18	0	0	0	9	0	0	18	9	0	27	9	9	0
LA_Rosa ga.	0	0	11	0	0	0	0	0	0	0	56	0	11	0	0	0	22	0	0	0
LA_Apis Honey	25	0	0	0	0	0	0	0	0	25	0	0	0	0	0	0	25	25	0	0
LA_Rosmarinus	10	0	0	0	0	0	0	0	0	10	20	0	0	0	0	0	60	0	0	0
LA_Olea	0	0	0	0	0	0	0	0	0	0	100	0	0	0	0	0	0	0	0	0
LA_Crocus	0	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0	75	0	0	0
LA_Ficus	0	0	0	17	0	0	0	0	0	17	17	17	0	17	0	0	17	0	0	0
LA_Mentha pu.	0	0	0	0	0	0	0	0	0	0	100	0	0	0	0	0	0	0	0	0
LA_Vitis	0	0	0	0	0	0	0	0	0	20	60	0	0	10	0	0	10	0	0	0
LA_Ruta	13	0	0	0	0	0	13	0	0	0	13	0	0	25	0	0	25	13	0	0
LA_Foeniculum	0	0	0	0	0	0	33	0	0	0	33	0	0	0	0	0	33	0	0	0
CH_Rosa ga.	27	0	0	0	0	7	7	0	0	13	13	0	0	7	0	0	27	0	0	0
CH_Apis Honey	23	5	0	0	0	9	5	5	0	14	14	9	0	0	0	0	18	0	0	0
CH_Crocus	20	0	0	0	0	0	0	0	0	0	0	20	0	0	0	0	20	20	20	0
CH_Ficus	0	0	0	0	0	0	0	0	0	0	0	0	0	25	0	0	25	50	0	0
CH_Mentha pu.	20	0	0	0	0	10	0	0	0	0	0	0	0	30	0	0	0	30	10	0
CH_Vitis	0	0	0	0	0	0	0	0	0	0	100	0	0	0	0	0	0	0	0	0
CH_Ruta	0	0	8	8	8	8	0	0	0	0	0	0	15	0	0	0	23	15	8	8
CH_Foeniculum	22	4	0	0	0	4	9	4	0	4	22	0	0	9	0	0	22	0	0	0
MA_Rosa ga.	30	0	0	0	0	0	0	0	10	0	40	0	0	0	0	0	20	0	0	0
MA_Rosmarinus	0	0	0	0	0	0	33	0	0	0	67	0	0	0	0	0	0	0	0	0
MA_Olea	0	0	0	0	0	0	0	0	0	0	50	0	0	0	0	0	50	0	0	0
MA_Ficus	0	0	0	0	0	0	0	0	0	0	33	33	0	33	0	0	0	0	0	0
MA_Mentha pu.	0	0	0	0	0	0	0	0	0	40	0	0	0	40	0	0	20	0	0	0
MA_Vitis	0	0	0	0	0	0	0	0	0	40	40	0	0	0	0	0	20	0	0	0
MA_Ruta	0	0	0	0	0	0	0	0	0	0	17	0	0	0	0	0	50	33	0	0
MA_Foeniculum	0	0	0	0	0	0	29	0	0	0	14	0	0	29	14	0	14	0	0	0

Supplementary Table 7. Matrix (5 x 20) with the sum of percentage of uses for each one of the 46 versions of medicinal uses of the top 10 ingredients in 5 different sources of the Albacete tariff considering the ICD-10 main categories of diseases

Codes: I Certain infectious and parasitic diseases, II Neoplasms, III Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism, IV Endocrine nutritional and metabolic diseases, V Mental and behavioural disorders, VI Diseases of the nervous system, VII Diseases of the eye and adnexa, VIII Diseases of the ear and mastoid process, IX Diseases of the circulatory system, X Diseases of the respiratory system, XI Diseases of the digestive system, XII Diseases of the skin and subcutaneous tissue, XIII Diseases of the musculoskeletal system and connective tissue, XIV Diseases of the genitourinary system, XV Pregnancy childbirth and the puerperium, XVI Certain conditions originating in the perinatal period, XVIII Symptoms signs and abnormal clinical and laboratory findings not elsewhere classified, XIX Injury poisoning and certain other consequences of external causes, XX External causes of morbidity and mortality, XXI Factors influencing health status and contact with health services.

Categories	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV	XV	XVI	XVIII	XIX	XX	XXI
Ethnobotany	121	0	0	10	5	3	65	33	37	154	176	25	88	42	83	0	45	97	0	15
Dioscorides 1st cent. AD	139	2	0	2	22	8	81	21	2	55	105	68	38	109	20	6	189	102	34	0
Laguna 16th cent. AD	48	0	11	17	25	0	46	0	0	72	378	17	11	52	0	0	287	38	0	0
Chirino 15th cent. AD	89	5	8	8	8	33	45	5	0	27	160	29	15	62	0	0	146	115	38	8
Matthioli 16th cent. AD	30	0	0	0	0	0	62	0	10	80	261	33	0	102	14	0	174	33	0	0