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Resins and gums in historical *iatrosophia* texts from Cyprus – a botanical and medico-pharmacological approach

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This study explores historical *iatrosophia* texts from Cyprus from a botanical and medico-pharmacological point of view focusing on remedies containing resins and gums. The *iatrosophia* are a genre of Greek medical literature of Byzantine origin and can be described as medicine handbooks which serve as therapeutic repositories containing recipes or advice. To extract and analyze information on plant usage in such sources – which are largely unedited texts and so far have not been translated – we investigate (i) the relationship of the *iatrosophia* to Dioscorides' *De Materia Medica* as well as historic pharmaceutical books or standard texts on modern phytotherapy and (ii) the validity of the remedies by comparing them to modern scientific data on reported biological activities. In the six texts investigated 27 substances incorporating plant exudates are mentioned. They are obtained from over 43 taxa of higher plants and in particular are used to treat dermatological, gastrointestinal, and respiratory tract conditions. The comparison to historic pharmaceutical books and phytotherapy texts reflects the gradual decline of the use of plant exudates in Western medicine. While remarkable parallels to Dioscorides' text exist, the non-Dioscoridean influence suggests a complex pattern of knowledge exchange. Overall, this resulted in an integration of knowledge from so far poorly understood sources. The comparison with bioscientific data reveals a fragmentary picture and highlights the potential of these unexplored substances and their uses. Where relevant bioscientific data are available, we generally found a confirmation. This points to a largely rational use of the associated remedies. Taken together, the *iatrosophia* are a valuable resource for ethnopharmacological and natural product research. Most importantly they contribute to the understanding of the development of herbal medicines in the (Eastern) Mediterranean and Europe.

Keywords: historical texts, *iatrosophia*, Cyprus, Eastern Mediterranean, resins, gums

INTRODUCTION

The present study is part of a larger project which explores the herbal materia medica and its use in historical *iatrosophia* texts from Cyprus as well as modern herbal knowledge in the island's monasteries where some of these texts were written. The term *iatrosophia* (ιατροσόφια), meaning medical wisdom, can be applied to both orally transmitted medicinal recipes and corresponding medical texts in Greek. This study focuses on the textual sources which constitute themselves a special genre of medical literature of Byzantine origin.

Among the many drugs described in these texts, resins, and gums are endowed with a special relevance. Humans have employed resins for very diverse purposes including esthetic, ceremonial, or therapeutic uses but also in arts and industry. As they often belonged to the most sought after materials, they have been traded between the different cultures around the world from the earliest times. Around the middle of the second millennia before the Common Era (CE) trade routes were established which brought resins to the Mediterranean region. Amber from the Baltic region was traded to the Mycenaeans and the Phoenicians brought the material by ship from northern Europe. Frankincense or myrrh was supplied to Egypt from of a place called Punt, which is believed to have lied in the region of Sudan, Ethiopia, or Somalia (Serpico, 2000, p. 438; Langenheim, 2003, pp. 257–267). In the following centuries the incense road leading from the south-coast of the Arabian Peninsula northwards to the Mediterranean coast was established and by 500 BCE a substantial trade existed with the ancient Greek world (Langenheim, 2003, pp. 283–287). Resins were not only brought to the Mediterranean but the region itself is notable for a number of resin producing trees, shrubs, or herbs (Howes, 1950). Pedanius Dioscorides (first century CE), in his περὶ ὕλης ἰατρικῆς (*peri ylēs iatrikēs*), better known by its Latin title *De Materia Medica*, mentioned that styrax, mastic, scammony, various coniferous resins, as well as ladanum and resin of the terebinth could be obtained from places in the Eastern Mediterranean. For the latter two he particularly noted Cyprus as provenance (Berendes, 1902; Chrysanthis, 1942). Archeological excavations at Pyrgos–Mavrorachi, a metallurgic Bronze age site near the south-coast of the island dated to the nineteenth century BCE brought several relicts of plant exudates to light, some of them were identified as pine or terebinth resins (Lentini, 2004, cited in Hadjikyriakou, 2007, pp. 50, 154–55). A Mycenaean tablet of the same era mentioned a substance called *ki-ta-no*, now interpreted as terebinth resin which appears to have been imported to Crete from Cyprus or Syria (Karageorghis, 1996, p. 66).

We previously investigated the species contained in a *iatrosophia* text from Cyprus (Lardos, 2006). The fact that quite a number of plant exudates were mentioned in this text together with the absence of published studies which discuss this specific class of natural products in the context of historical medical texts has prompted us to undertake the present study. Here we apply a special procedure for unlocking information on species and their uses in up to now non-translated and largely unedited *iatrosophia* texts. Based on the classification of medicinal uses into greater categories we highlight similarities and differences between the *iatrosophia* and (i) Dioscorides' *De Materia Medica*, (ii) historic pharmaceutical books from the era when plant drugs were still included in mainstream medicine, and (iii) authoritative texts of modern phytotherapy which serve as scientific standards of herbal medicinal products in Europe. By implementing specific points of the protocol for analyzing historical texts by Buenz et al. (2004) we attempt to examine the validity of the medicinal uses mentioned in the texts by comparing them with reported bioactivity data and at the same time identify previously unexplored cases.

IATROSOPHIA TEXTS

Many earlier historians showed little enthusiasm for the *iatrosophia,* considering them as "diluted and clouded extraction of ancient knowledge with all sorts of superstitious ingredients and invocations" (e.g., Bloch, 1902, p. 512). As commonly understood today, these texts developed in the context of Byzantine hospitals where they served as handbooks for the daily medical practice containing recipes and therapeutic advice (Varella, 1999, p. 579; Touwaide, 2007, pp. 160–161). They can best be described as therapeutic compendia, which contain extracts from classical or Byzantine sources and which often were reproduced on previous compilations (Touwaide, 2007, p. 149). Earliest examples might reach back to the tenth century CE but they certainly became abundant from the fifteenth century onwards (Touwaide, 2007, p. 149; Zisper, 2009, p. 9). After the end of the Byzantine Empire (1453) hospitals of the Byzantine tradition were restricted to Greek orthodox monasteries spread over many parts of the previous empire or to monastic foundations in great cities now part of Greece or Turkey. The tradition of the *iatrosophia* continued in these monasteries but also in the secular environment among the Greek-speaking population of the Ottoman Empire. The examples produced in this era had a marked influence on the medicine of this group of population (Varella, 1999, pp. 579–583). As illustrated by the text of a traditional healer from Crete or the one from a monastery in Cyprus this tradition was continued until the first decades of the twentieth century (Clark, 2002, p. 339; Lardos, 2006).

The existing literary sources available for the compilation of the first *iatrosophia* texts included the healing lore of Greek and Roman antiquity and the earlier Byzantine time. Such a list would probably include the Hippocratic texts, Dioscorides, and Galen. Perhaps of greater importance were the Byzantine authors like Oribasius, Aetios of Amida, Alexander of Tralles and Paulus Aegineta. They wrote between the fourth and seventh century CE (Scarborough, 1984, pp. 213, 221–229). By consulting the works of contemporary scholars the writers of the *iatrosophia* might also have included elements of Arabic/Islamic medicine. Islamic medicine, which had hitherto borrowed from Byzantium exerted a marked influence on Byzantine therapeutic practice from the tenth century CE onwards and especially between the thirteenth and fourteenth century CE (Varella, 1995; Bennett, 2000; Touwaide, 2007, pp. 163–164). The writers of the hospital and medical craft texts (virtually the *iatrosophia*) distilled what they found useful from the available sources and supplemented it with new information. Brevity as well as easy access to reliable recipes and recorded practical experience from the bedside was what counted most for them (Bennett, 2000, pp. 280–281; Touwaide, 2007, pp. 150–154, 160–161). As Clark (2002, p. 358) could demonstrate by investigating a *iatrosophion* from Crete – written in 1930 – a commitment to preserve the past combined with the capacity to adapt to changed conditions and incorporate new learning are inherent qualities of this tradition.

Today, several *iatrosophia* texts have survived in monasteries or private collections in Greece or Cyprus (Varella, 1999, p. 580; Lardos, unpublished results). Individual manuscripts are also stored in public libraries for example in London, Oxford, Paris, and Vienna (Touwaide, 2007, p. 156; Zisper, 2009, pp. 14–27). In a survey including roughly 700 Greek medical manuscripts produced during the Ottoman era it was found that 45% of them belong to this category (Varella, 1999, p. 578). The lack of existing inventories and difficulties in identifying corresponding texts in the bulk of medical manuscripts are major points which hampered the study of the *iatrosophia* in the past. To counteract this drawback Touwaide (1992, p. 75) has launched a research program to establish a computerized inventory of all Greek medical manuscripts currently known in library collections (Touwaide, 2007, pp. 156–157).

HISTORICAL TEXTS FROM THE MEDITERRANEAN AS AN ETHNOPHARMACOLOGICAL RESEARCH TOOL

With the ongoing socio-structural changes in the societies of the Mediterranean region local, mainly orally transmitted knowledge about the uses of plants as medicine and food appears to be declining. It has been demonstrated that in this area information on the local use of plants is increasingly restricted to people of middle age or beyond (Nebel et al., 2006; Gonzalez-Tejero et al., 2008). The consequence of the generational shift with the associated loss of knowledge has forced researchers to emphasize the importance to gather endangered knowledge but also to define creative ways how to reintroduce this knowledge to younger generations of the local societies (Nebel et al., 2006; Hadjichambis et al., 2008). While the loss of pre-existing knowledge seems to be unavoidable to some extent, other perspectives to access information on plant use have opened up. Historical texts from the various medical traditions in and around the Mediterranean basin have become established as a rewarding tool for ethnobotanical or ethnopharmacological research. A number of studies have been published recently which analyzed and contextualized the content of written sources from this area (Lardos, 2006; López-Muñoz et al., 2006; Pardo-de-Santayana et al., 2006; Touwaide, 2007, pp. 168–173; Lev and Amar, 2008; Pollio et al., 2008; Leonti et al., 2009; De-Vos, 2010; Leonti et al., 2010). Historical texts can also provide a unique gateway to discover new medicinal agents. One prominent example to illustrate the role such texts could play in this respect is Gerard's "Herball" (see, e.g., Buenz et al., 2004; Cordell and Colvard, 2005). Since its publication in Britain at the end of the sixteenth century, eighteen different pharmaceuticals were developed from plants that are described in

this source and 16 of those became approved drugs (Cox, 1998). It has been argued that a careful and systematic re-examination of medicinal plants mentioned historical texts provides an invaluable source for the development of new drugs (Holland, 1994; Riddle, 1996, 2002; Buenz et al., 2004; Fiore et al., 2005). Recent studies were able to corroborate many of the plant uses in historical texts with reported biological activities or identify promising candidates for the development of new drugs (Buenz et al., 2005; Adams et al., 2009, 2011). The previously unexplored atun tree (*Atuna racemosa* Raf., Chrysobalanaceae) from Samoa which had been identified as candidate in the text analysis of Rumphius's *Ambonese Herbal* in fact exhibited a pharmacological activity that corresponded to the historical use (Buenz et al., 2006).

CLASSIFICATION AND PROPERTIES OF RESINS AND GUMS

To define resins and to group them various concepts representing different scientific approaches and disciplines have been suggested. Based on the fact that resins usually are intermixed with other exudates three groups are commonly recognized: resins, balsams, and gum resins (Wolff-Berlin, 1928, p. 50). Resins dissolved in volatile oils are generally called balsams. However, for some researchers balsams are a type of oleo resins restricted to phenolic resins mainly composed of benzoic or cinnamic acids and their esters. Resins mixed with polysaccharides are called gum resins or oleo gum resins if they additionally contain volatile oils (Howes, 1950; Berger, 1964, pp. 1–3; Bruneton, 1995, p. 224). All these resinous exudates can also be classed by the main chemical components of the fraction that is soluble in organic solvents. In doing so, two main groups can be distinguished, terpenoid and phenolic resins. Terpenoid resins predominantly contain mono- or sesquiterpenes in their volatile and di- and triterpenes in their non-volatile fraction while in phenolic resin phenylpropanoids or lipophilic flavonoids are the major groups of compounds. Additionally several mixed resins are known or such which do not fit in these categories (Langenheim, 2003, pp 23–44, 306, 341, 412).

As a consequence of this phytochemical diversity, gums, and resins have often been confused and both terms are used rather loosely (Hepper, 1987; Langenheim, 2003, pp. 23–24, 45). Exudate gums are amorphous solids which basically consist of mixtures of polysaccharides (Boer and Ella, 2000, p. 15). They are readily distinguished from resins and products of a rubbery nature by the fact that they are miscible with water but insoluble in organic solvents (Howes, 1949, p. 5). Depending on their solubility properties in water true gums can be divided in soluble, insoluble and half soluble or semi-insoluble gums (Howes, 1949, p. 5; Mantell, 1949).

Most resins are obtained by tapping or applying incisions to the bark of trees or shrubs. The exudate is collected either when still fluid or in a solid state after the more volatile compounds have evaporated. Such harvesting methods are dramatic interventions for the plant organism and can lead to its debilitation. Moreover, the industrial exploitation of wild populations of resin or gum producing species raises concerns in terms of biodiversity. For example, *Pistacia atlantica* trees from which fruits are collected to extract terebinth oil should not be tapped since this would have a negative impact on the fruit production (Panaretos, 1979). Because of the recent overexploitation of agar wood several *Aquilaria* species are threatened with extinction, as a consequence all Thymelaeaceae known as a source for the material have now been classified into the CITES Appendix II (Ito and Honda, 2005). As illustrated by Langenheim (2003, p. 466) at the example of resin use in tropical ecosystems, the challenge, here too, is to develop "a balance of economic success and sustainable management."

MATERIALS AND METHODS

SEARCH FOR *IATROSOPHIA* TEXTS

This study involves six *iatrosophia* texts (**Table 1**) to which we have gained access through a hand-search in various libraries in Cyprus and the United Kingdom as well as in the 21 monasteries taking part in the ethnobotanical field study in Cyprus as part of the overall project. Most of the texts seem to have been in circulation on the island during the Ottoman (1571–1878) and British era (1878–1960) (Kargotis, 1951; Chrysanthis, 1966). They were written by monks (IM, GP – see **Table 1** for the full names of the texts) and traditional healers (KYP) or stood in connection to some priests (IPM, IPP). While two of the six (IM, KYP) were demonstrably produced in Cyprus, the status of further three (IPM, IPP, KI) is ambiguous in this respect. The *Geoponikon* (GP) from Agapios Landos originates from Crete but printed copies of the manuscript were produced in Venice as early as 1643 (Kostoula, 1991) and distributed in Cyprus in the following centuries (Spanopoulos, 1935, p. 53; Georgiadis, 1995, p. 134). In all but one case (KYP) the texts could be accessed using print editions of the original manuscript.

Table 1 | The six investigated *iatrosophia* texts.

Text-code	Original manuscript Title Author (year), Place of origin	Working copy[a] Text type Editor (year), Place	Rec.[b]
GP	*Geoponikon*	Print edition	143
	Agapios Landos (1585–1656)	D. D. Kostoula (1991),	+64*
	Crete GR, edit. Venice, 1643	Volos GR	
IM	*Iatrosophikon Antidotarion*	Print edition	493
	Mitrophanous (1790–1867)	Filaretos (1924),	
	Mon. of Makhairas CY, 1849	Makhairas CY	
IPM	*Iatrosophi tou Papa Michaïli*	Print edition	39
	? Michaïlis	G. Petridis (2000),	
	? Vasa (Koilani) CY, undated	Limassol CY	
IPP	*Iatrosophikon Papa tis Petras*	Print edition	13
	Anonymous	G. I. Spanopoulos (1935),	
	? Petra CY, ca. eighteenth century	Nicosia CY	
KI	*Ena Kypriako Iatrosophi*	Print edition	67
	Anonymous	K. Chrysanthis (1951),	
	? CY, undated	Nicosia CY	
KYP	*Kyprianarion*	Manuscript (copy)	24
	Velephantou (1913),	Anonymous (1978),	
	Lefkosia (Nicosia) CY	Athens GR	
Total number of recipes containing plants as ingredients			779

[a] *See reference list for full citations.*
[b] *Counted number of recipes which contain plants as ingredients and which are destined for use in humans.*
**In addition to the 143 recipes, 64 chapters dealing with plants and their virtues were counted.*

PROTOCOL FOR THE ANALYSIS OF *IATROSOPHIA* TEXTS

For analyzing the texts a multi-step protocol was developed (**Figure 1**). In steps 1 and 2 information about the use of plants was extracted and itemized according to recipe or chapter, substance name, part used, mode of preparation, way of application, and use. Every mentioning of a substance in one of the texts was entered in the database as a separate record (the term "substance" is used as a substitution for both plant and plant part or product in the consecutive text). The resulting inventory provided the base for the second part of the protocol (steps 3–6) which involved the selection of a specific substance class, the identification of the species and the categorization of the uses. The third part of the protocol involved the investigation from a medicinal and pharmacological point of view (steps 7–10).

Extraction and translation (steps 1 and 2)

The information was extracted by reading through the entire text. All the texts were written in the vernacular Greek of the respective time, some of them with a Cypriot-Greek coloring. The language is relatively well comprehensible to a reader with knowledge of Modern Greek. When required, specific dictionaries, etymological lexica (Hadjiioannou, 2000; Papangellou, 2001), or glossaries (Myrianthopoulos, 1925; Kostoula, 1991) were consulted. The disorders or symptoms that were mentioned in a recipe were first translated using popular medicinal and medicinal literature or glossaries dealing with the topic of the local nomenclature of diseases (Myrianthopoulos, 1925; Kyriazis, 1926; Chrysanthis, 1944, 1988; Kyprianou, 1987). Ancient names of conditions were cross-checked with their correspondents in the "Deutsches Krankheitsnamen-Buch" (Höfler, 1899). Complementary information

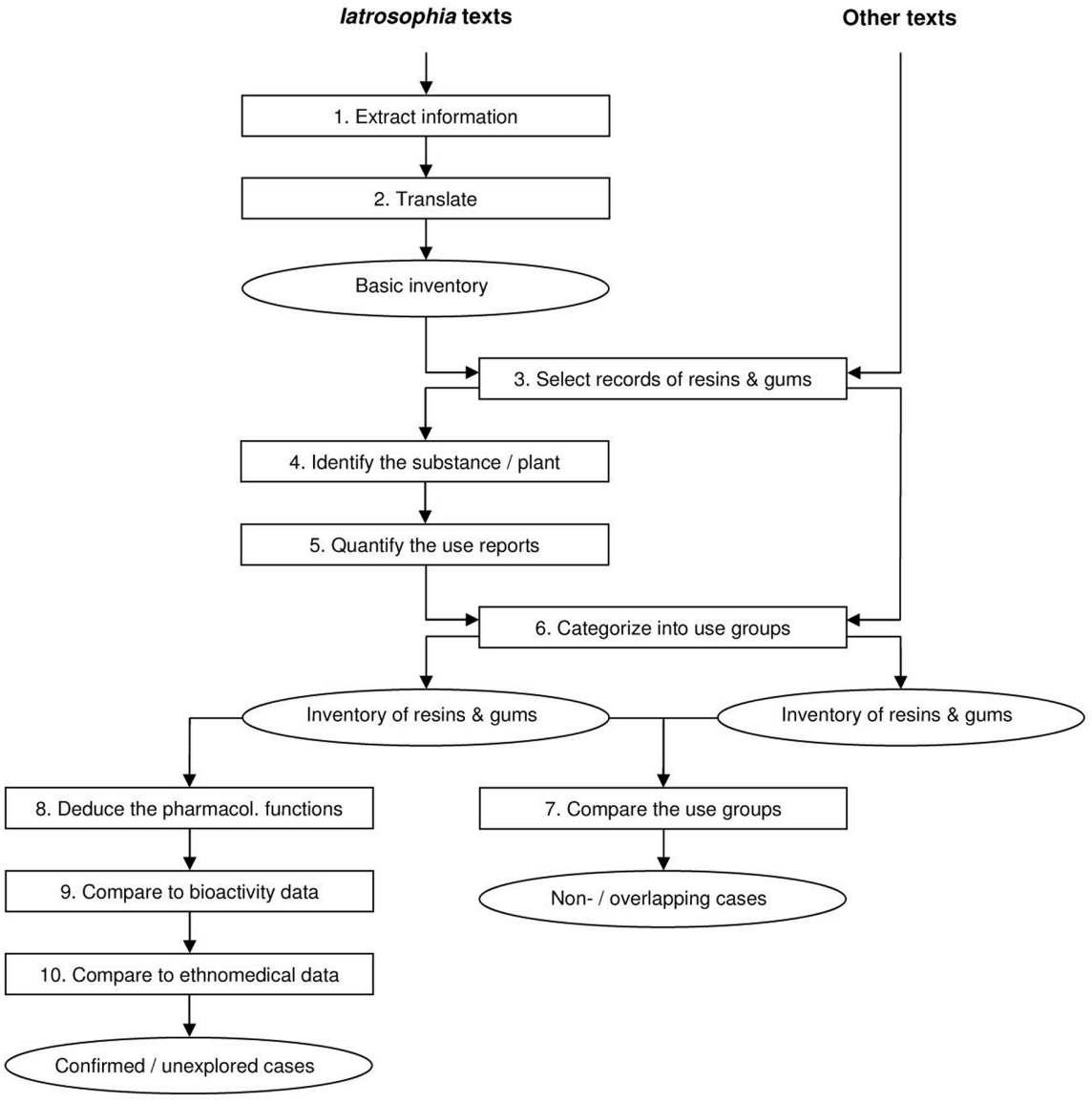

FIGURE 1 | Flowchart of the 10 steps in the analysis of the *iatrosophia* texts. Steps 3 and 6 were also applied on other texts (i.e., Dioscorides' *De Materia Medica*, historic pharmaceutical books and standard texts of modern phytotherapy) and served to establish a separate inventory of resins and gums of their owns.

including the general medical situation and the diseases prevalent on the island at that time was drawn from books on the local history of medicine (Koureas, 2006; Marangou and Georgiadis, 2006; Stavridis, 2006). Particular care was taken to retain the original wording of a use mentioned in a text. The translated use was then cross-checked with a German edition of "Harrison's principles of internal medicine" (Dietel et al., 2003) or "Health Topics" of the Medline Plus database[1] and if required transcribed into the appropriate clinical term. To accomplish this, a clear understanding of the mentioned condition was essential. However, many of the medicinal uses were ambiguous and sometimes difficult to link to a particular clinical term. For example, the condition "wound on the leg that opens again and again out of its own" can be interpreted as a chronic wound perhaps associated with infection and inflammation or more specifically a venous ulcer.

Selection of records and identification of the substances (steps 3 and 4)

From the established basic inventory records referring to resin and gum exudates were selected. These also included related products such as volatile oil separated through distillation of the resin or wood tar which usually was obtained through a dry distillation by burning resinous wood in an oven (Blaschek et al., 2007).

By applying linguistic and pharmacognostic criteria a substance was first identified on the basis of the substance name and then assigned to the appropriate botanical source. To establish the identity of a substance the *iatrosophia* name was cross-referenced with plant or substance names listed in:

(i) Historical texts including *De Materia Medica* of Dioscorides (Berendes, 1902; Wellmann, 1906/1907/1914) and the "Medical Compendium in Seven Books" of Paulus Aegineta (Adams, 1844/1846/1847; Heiberg, 1921/1924). They were available in Ancient Greek as digitized texts from TLG® (Thesaurus Linguae Graecae), University of California, Irvine and in English or German translations as scanned books including also commentaries about the identity of drugs and their sources. Berendes' (1902) German translation of Dioscorides was accessed via the online catalog of Heilpflanzen-Welt (multi MED vision GbR) and Adams' (1844/1846/1847) English translation of Paulus Aegineta downloaded as PDF file from Bibliothèque Interuniversitaire de Medicine et d'Odontologie, Paris. In addition appropriate publications on the materia medica of historical texts of ancient Greek, Byzantine, medieval Arabic/Islamic, and Ottoman origin which listed original names were consulted (Langkavel, 1866; Tschirch and Lippmann, 1933; Riddle, 1987; Varella, 1995; Aliotta et al., 2003; Lev and Amar, 2008; Ölker and Direkçi, 2009).

(ii) Lexica, glossaries, etymological keys, and botanical literature containing beside Greek also Cypriot-Greek or Turkish names (Gennadios, 1914; Myrianthopoulos, 1925; Panaretos, 1967; Kostoula, 1991; Viney, 1994; Hadjiioannou, 2000; Papangellou, 2001; Hadjikyriakou, 2007).

(iii) Miscellaneous references including popular medicinal, pharmaco-historical, and ethnobotanical literature as well as dictionaries of the Greek or Turkish language (for all references see **Table 2**).

After the identity had been established the substance was assigned to the appropriate botanical source based on the information in up-to-date or if necessary also earlier pharmacognostic reference books (Richter, 1827; Tschirch and Stock, 1935/1936; Howes, 1949; Berger, 1964; List et al., 1972; Langenheim, 2003; Blaschek et al., 2007; Nussinovitch, 2010) and other scientific literature. In cases where the respective species can be found in Cyprus this was done using the "Flora of Cyprus" (Meikle, 1977/1985) or other botanical literature on the local flora (Della, 1999; Tsintides et al., 2002; Hadjikyriakou, 2007). All references were cross-checked. Scientific plant names were checked with the Tropicos, Missouri Botanical Garden[2], or International Plant Name Index[3].

Quantification and categorization of the use reports into use groups (steps 5 and 6)

Following the approach of Kufer et al. (2005) every use of a substance mentioned in one of the texts was counted as one use report (UR). Records referring to identical uses of a substance *within the same text* were considered duplicates and removed from the list. Finally, every medicinal use was categorized into 1 of the 12 pre-established medicinal use groups (UGs) largely based on body systems: CA – Cardiovascular and blood, EE – Ears and eyes, DE – Dermatological, FV – Fevers (including malaria), GI – Gastrointesinal and hepatic, GY – Gynecological, HA – Headache and migraine, MS – Musculosceletal, OC – Oral cavity, RE – Respiratory tract, UG – Urogenital, VA – Various conditions.

Comparison to uses mentioned in other texts (step 7)

To reveal similarities of the use pattern of a substance, a comparison was conducted between the UGs treated by the uses mentioned in *iatrosophia* and those mentioned in: (i) Berendes' (1902) German translation of *De Materia Medica* of Dioscorides; (ii) Western pharmaceutical books from the era before plant drugs were largely abandoned from mainstream medicine including British Pharmaceutical Codex, 2nd Edition (Council of the Pharmaceutical Society of Great Britain, 1911) and United States Dispensatory (Remington and Woods, 1918). They both were accessed via the online catalog of Henriette's Herbal Homepage; (iii) Authoritative standard texts of phytotherapy in Europe including German Commission E Monographs (BGA, 1978–1994), British Herbal Compendium, Volume 1 (Bradley, 1992), Potter's Herbal Cyclopedia (Williamson, 2003), Hagers Enzyklopädie der Arzneistoffe und Drogen (Blaschek et al., 2007) and ESCOP monographs (ESCOP, 2009). For this purpose, every medicinal use of a substance mentioned in these references was categorized into one of the 12 UGs [see Quantification and Categorization of the use Reports into Use Groups (Steps 5 and 6)]. For each substance the established UGs were then juxtaposed to those in *iatrosophia* and evaluated based on the number of UGs of the substances the compared texts had in common.

Comparison to reported bioactivity data (step 8 and 9)

To enable a one-to-one association between the substance and the mentioned use the detailed comparison to reported bioactivity data was conducted involving only simple remedies. These are remedies that include only one active substance, as opposed to compound

[1]http://www.nlm.nih.gov/medlineplus/

[2]http://www.tropicos.org/

[3]www.ipni.org

Table 2 | Identification of the substance names mentioned in the *iatrosophia*.

Name in *iatrosophia*[a]	Correspondent name[b]	Cent.[c]	Reference[d]	Substance[e]
bouchoúr yiági	*buhur yağı*	16	Ölker and Direkçi (2009)	Storax, liquid (exotic grade)
	bouchoúri yag	19	Hanbury (1857)	
	bukhur yaghy	19	Hanbury (1857)	
	bohur	20	Viney (1994, p. 250)	
katráni, katrán	*qatrân*	10	Tschirch and Lippmann (1933, p. 1361)	(1) Cedar tar
	qitrân	11–13	Lev and Amar (2008, p. 497)	
	katran	≤19	Lev (2002)	
	katran	21	Lev and Amar (2002)	
	qitrân	11–13	Lev and Amar (2008, p. 497)	(2) Pine tar
	kara katran	21	Sezik et al. (2001)	
	katrámi, katrás	≤20	Gennadios (1914, p.782)	(3) Wood tar (of conifers)
	katránin, katrás	≤21	Papangellou (2001)	
kechripárin, chechripárin	*kechrimpári*	≤20	Gennadios (1914, p. 411)	Amber (fossilized resin)
	kechripárin	≤20	Myrianthopoulos (1925)	
	kechrimpári	21	Webster's Online Dictionary[d]	
kechriparóladon	*kechrimpári // ládi, -ládo*	21	Webster's Online Dictionary[d]	Amber oil
kómmi arapikón, kómmi aravikón	*komidē arapikōn*	03–13	Langkavel (1866, p. 1.2)	Gum arabic
	kómmi aravikón	≤20	Gennadios (1914, p. 28)	
	aravikó kómmi	21	Webster's Online Dictionary[d]	
kommídi	*kommi […] amygdalēs, -kerasōn, -tes kokkomyleas*	01	Berendes (1902, 1.157, 174, 176), Wellmann (1906/1907/1914, 1.113, 121, 123)	Gum of various *Prunus* species such as almond, cherry, plum
	kerasia […] kommi, kokkymēleas […] kommi	07	Adams (1844/1846/1847, 7.3, 167, 180), Heiberg (1921/1924, 7.3.21)	
	kommídi	≤20	Gennadios (1914, p. 534)	
	komídin	≤20	Myrianthopoulos (1925)	
	kómmi	20	Panaretos (1979)	
kommídi tis kerasiás, komídi (=píssa) tis kkerashiás	*kommi tōn kerasōn*	01	Berendes (1902, 1.157), Wellmann (1906/1907/1914, 1.113)	Cherry gum
	kerasia […] kommi	07	Adams (1844/1846/1847, 7.3, 167), Heiberg (1921/1924, 7.3.10)	
	kérasos […] kommi	≤20	Gennadios (1914, p. 492)	
	komídin […] tis keraséas, píssa tis keraséas	≤20	Myrianthopoulos (1925)	
komídi (kolitsána) tou moúsklou kai tou damaskínou	*kommi tēs kokkomyleas*	01	Berendes (1902, 1.157, 174, 176), Wellmann (1906/1907/1914, 1.113, 121, 123)	Plum gum
	kokkymēleas […] kommi	07	Adams (1844/1846/1847, 7.3, 180), Heiberg (1921/1924, 7.3.21)	
	moúskla (kokomílo)	≤20	Kostoula (1991)	
	damáskino	21	Webster's Online Dictionary[d]	
ládanon	*lēdanon, ladanon*	≤02 BCE	Arnold-Apostolides (1985, p. 396); Riddle (1987, p. 59)	Ladanum
	ladanon	01	Berendes (1902, 1.128), Wellmann (1906/1907/1914, 1.97)	
	ladanon	07	Aliotta et al., (2003, p. 7.3, 208), Heiberg (1921/1924, 7.3.11)	
	ládanon	≤20	Gennadios (1914, p. 512)	

(Continued)

Table 2 | Continued

Name in *iatrosophia*[a]	Correspondent name[b]	Cent.[c]	Reference[d]	Substance[e]
ládin tou kapnismátou	*kápnisma*	≤20	Gennadios (1914, p. 972)	Storax, liquid (local grade)
	kápnisma	20	Panaretos (1979)	
	kápnisma (tou Ayíou Neophútou)	21	Hadjikyriakou, (2007, p. 102)	
lívanos (*arsenikós*), *lívanos áspros*	*libanos, libanōtos (arsēn)*	≤02 BCE	Aliotta et al.,(2003, p. 395), Riddle (1987, p. 59)	Frankincense (*olibanum*)
	libanos	01	Berendes (1902, 1.81), Wellmann (1906/1907/1914, 1.68)	
	libanōtos	07	Adams (1844/1846/1847, 7.3, 217), Heiberg (1921/1924, 7.3.11)	
	lívanos	≤20	Gennadios (1914, p. 202)	
machmoudiá	*machmoutá*	03–13	Langkavel (1866, p. 146.1)	Scammony
	mahmûda	11–13	Lev and Amar (2008, p. 280)	
	mahmûde, mahmudiye otu	16	Ölker and Direkçi (2009)	
	mamoutiá	≤20	Gennadios (1914, p. 764)	
	machmoudiá	≤20	Myrianthopoulos (1925)	
mastíchin	*mastichē*	01	Berendes (1902, 1.90), Wellmann (1906/1907/1914, 1.70)	Mastic
	mastichē	07	Adams (1844/1846/1847, 7.3, 243), Heiberg (1921/1924, 7.3.12)	
	mastichē	≤20	Gennadios (1914, p. 640)	
	mastíchin	≤20	Papangellou (2001)	
mávron kápnisman (=*chalváni*)	*chalbanē*	≤02 BCE	Aliotta et al., (2003, p. 400)	Galbanum
	chalbanē	01	Berendes (1902, 3.87(97)), Wellmann (1906/1907/1914, 3.83)	
	chalbanē	07	Adams (1844/1846/1847, 7.3, 398), Heiberg (1921/1924, 7.3.22)	
	galvánon, chalváni	≤20	Gennadios (1914, p. 218)	
	chalváni	≤20	Myrianthopoulos (1925)	
mýrra, mýrra dialektí	*mýrra, smýrna*	≤20	Gennadios (1914, p. 170)	Myrrh
	mýrra	≤20	Myrianthopoulos (1925)	
	mýrra	21	Webster's Online Dictionary[d]	
mýrra xylalá	*xylaloē*	11	Tschirch and Lippmann (1933, p. 1348), Varella (1995)	(1) Agar wood, gaharu wood, aloe wood (*lignum aloes*)
	xylalás	≤20	Gennadios (1914, pp. 2–3)	
	xylalás	≤20	Hadjiioannou (2000)	
	xylalás	≤20	Papangellou (2001)	
	mýrra	≤20	Gennadios (1914, p. 170)	(2) Myrrh
	mýrra	≤20	Myrianthopoulos (1925)	
neft yiági	*néfti*	≤20	Gennadios (1914, p. 825)	Pine turpentine oil
	neft yiagí	≤20	Myrianthopoulos (1925)	
	neft yağı	21	Webster's Online Dictionary[d]	
píssa áspri tou péfkou, píssa péfkou áspri (=retsína), píssa, píssa tou péfkou, retsína, retsíni tou péfkou	*rētinē[…] peukinē*	01	Berendes (1902, 1.92), Wellmann (1906/1907/1914, 1.71)	Pine resin (*resina alba communis*), crude turpentine (*terebinthina*), rosin (*colophonium*)

(Continued)

Table 2 | Continued

Name in *iatrosophia*[a]	Correspondent name[b]	Cent.[c]	Reference[d]	Substance[e]
	rētinai […] peukinē	07	Adams (1844/1846/1847, 7.3, 317), Heiberg (1921/1924, 7.3.17)	
	retsína […] ton péfkon	≤20	Gennadios (1914, p. 824–825)	
	píssa […] tis péfkis	≤20	Myrianthopoulos (1925)	
	píssa, retsínan apó ta péfka	20	Panaretos (1979)	
píssa mávri	*píssa […] mávri*	≤20	Myrianthopoulos (1925)	Pine resin, cooked *(resina nigra)*
	píssa	20	Panaretos (1979)	
	mávri píssa	≤20	Papangellou (2001)	
píssa pikrís amygdaliás, píssa tis athashiás tis pikrís	*amygdalēs […] kommi*	01	Berendes (1902, 1.176), Wellmann (1906/1907/1914, 1.123)	Bitter almond gum
	athashiá […] píssa	≤20	Myrianthopoulos (1925)	
	athashiá […] píssa	≤20	Papangellou (2001)	
	píssa […] amygdaliés	20	Panaretos (1979)	
píssa tis elaías	*dakryon […] elaia*	01	Berendes (1902, 1.141), Wellmann (1906/1907/1914, 1.105)	Olive resin
	dakryon […] agrian elaian	07	Adams (1844/1846/1847, 7.3, 100), Heiberg (1921/1924, 7.3.5)	
	elaiodákryon	≤20	Gennadios (1914, p. 265)	
píssa tou xylalá	*xylaloē*	11	Tschirch and Lippmann (1933, p. 1348), Varella (1995)	(1) Agar wood, gaharu wood, aloe wood (*lignum aloes*)
	xylalás	≤20	Gennadios (1914, p. 2–3)	
	xylalás	≤20	Hadjiioannou (2000)	
	xylalás	≤20	Papangellou (2001)	
	píssa tou xylalá	≤20	Gennadios (1914, p. 783, 923)	(2) Benzoin
	píssa tou xylalá	≤20	Myrianthopoulos (1925)	
	píssa tou xylalá	20	Arnold-Apostolides (1985)	(3) Storax, solid (*styrax*)
	píssa tou xylalá	20	Panaretos (1967)	
sarí katrán	*qitrân*	11–13	Lev and Amar (2008, p. 497)	Cypress tar
	sarí katrán	20	Chrysanthis (1940)	
	servi	20	Viney (1994, p. 4)	
	servi	21	Hadjikyriakou, (2007, p. 55)	
smýrna	*smyrna*	≤02 BCE	Riddle (1987, p. 59)	Myrrh
	smyrnē	01	Chrysanthis(1940, p. 1.77), Wellmann (1906/1907/1914, 1.64)	
	smyrnē	07	Adams (1844/1846/1847, 7.3, 348), Heiberg (1921/1924, 7.3.18)	
	mýrra, smýrna	≤20	Gennadios (1914, p. 170)	
trimintína, trementína	*rētinē terebinthinē*	01	Wellmann (1906/1907/1914, 1.66), Berendes (1902, 1.91)	(1) Terebinth resin
	rētinē terebinthinē, terebinthinē	07	Adams (1844/1846/1847, 1.45, 58, 3.22., 414), Heiberg (1921/1924, 1.45.1, 3.22.13)	
	tremantinē	03–13	Langkavel (1866, p. 11.4)	
	trimintína	18–19	Hadjikyriakou (2007, p. 153)	
	trimintína	20	Chrysanthis (1942)	
	trementína	20	Panaretos (1979)	

(Continued)

Table 2 | Continued

Name in *iatrosophia*[a]	Correspondent name[b]	Cent.[c]	Reference[d]	Substance[e]
	trementína	≤20	Gennadios (1914, p. 825)	(2) Crude turpentine of the pine (*terebinthina*)
	trimintína píssa	≤20	Myrianthopoulos (1925)	
tzam sákkizi	*tzam […] sakiz*	≤20	Gennadios (1914, p. 768, 824–25)	Pine resin
	çam sakızı	20	Honda et al. (1996)	
	çam sakızı	21	Webster's Online Dictionary[d]	
trimintína venétini	*trementína // Venetía*	21	Webster's Online Dictionary[d]	Venice turpentine
válsamon tis Mékkas	*válsamon tis Mékkas*	≤20	Gennadios (1914, p. 170)	Balsam of Mecca
	válsamon tis Mékkas	≤20	Myrianthopoulos (1925)	

[a]*Names are listed as mentioned in the texts. The transliteration of the substance names in Latin letters basically follows the ISO code 843 1997 TR for Modern Greek with a few adjustments to improve the approximation of the code to the correct phonetic reproduction (e.g., Greek γι- as yi- at the beginning of a word; Cypriot-Greek -σια as -sha).*

[b]*Names mentioned in the cited reference, which were considered a match with the corresponding iatrosophia name. For the conversion of Ancient or Medieval Greek names (references until 1453 CE) the transliteration scheme of the American Library Association ALA-LC 1997 for Greek of The Library of Congress was used [http://www.loc.gov/catdir/cpso/roman.html (accessed December 03, 2010)].*

[c]*Century, -ies (CE) from which the correspondent name is documented based on the cited references. Cases referring to BCE are specified.*

[d]*http://websters-online-dictionary.org/*

[e]*Identity of the iatrosophia name based on the information contained in the cited references. In cases where the name can refer to more than one substance, all possible interpretations are separately listed and indicated with individual numbers (e.g., 1, 2, 3).*

remedies which contain two or more of them. The method was adopted from the protocol for analyzing historical texts introduced by Buenz et al. (2004, 2005) and included two basic steps, the extrapolation of the pharmacological functions of a substance and the cross-referencing to reported bioactivity data. In a first step the pharmacological therapy required for the treatment of the respective condition was looked up in "Goodman and Gilman's pharmacological basis of therapeutics" (Brunton et al., 2006) or "Health Topics" of the Medline Plus database[4]. The pharmacological properties of the suggested therapy were deduced or, if specified, directly adopted and assigned to the respective substance as presumable pharmacological functions. In doing so, we relatively strictly adhered to the information stated in these references and at the same time disregarded less common causes of a respective disease. The procedure is illustrated by the following example: According to recipe GP PMH 05 crude gum Arabic should be eaten to stop the "flux of the belly," which according to Höfler (1899, p. 29, "Bauchfluss") is diarrhea. Most cases of diarrhea are caused by a disturbed intestinal water and electrolyte balance or altered intestinal motility, a medical intervention would include liquid- and electrolyte replacement, bulk-forming agents, motility, or secretory inhibitors. Diarrhea can also be associated with inflammatory bowel disease or microbial infection (Brunton et al., 2006). Assuming that gum Arabic would in fact be able to influence diarrhea bulk-forming, antimotility, antisecretory, anti-inflammatory, or antibiotic effects are likely to be involved in its action. Next, the Web of Knowledge (ISI Web of Knowledge Service for UK Education, Thomson Reuters) and EMBASE (Elsevier Science Publishers) were surveyed for bioactivity data of the respective substance using flexible combinations of substance or species name together with the deduced pharmacological functions as search words. The reported activities were then compared with the associated pharmacological functions and cross-referenced.

[4]http://www.nlm.nih.gov/medlineplus/

Comparison to ethnomedical information (step 10)

The simple remedies in *iatrosophia* were compared to *De Materia Medica* of Dioscorides (Berendes, 1902) and "Medical Compendium in Seven Books" of Paulus Aegineta (Adams, 1844/1846/1847). Dioscorides had a distinct influence on the development of the medicinal knowledge in areas from northern Europe to the Indian Ocean (Riddle, 1985, p. xvii). Paulus Aegineta's early Byzantine work is a "distillation of classical drug theory which captured the essence" (Scarborough, 1984, p. 229). As he wrote before the emergence of Arabic/Islamic medicine an influence on his work from this side could be excluded.

RESULTS AND DISCUSSION

IDENTITY OF THE SUBSTANCES AND THEIR BOTANICAL SOURCES

The identification of plant exudates mentioned in historical texts is notoriously difficult. Before determining the botanical source the substance itself has to be identified by referencing to names cited in the literature. For this purpose we also consulted annotated historical texts. However, several problems remain in terms of the identification of plants mentioned in ancient texts (Piomelli and Pollio, 1994). As highlighted by Riddle (1985, p. xxv), the various authorities who sought to identify the plants mentioned in Dioscorides' *De Materia Medica* do not always agree and there are real possibilities for error. Dawkins (1936) was of the opinion that ancient plant names can only be interpreted with certain vagueness and Raven et al. (2000) additionally highlighted the unreliability of some identifications in authoritative dictionaries of ancient Greek plant names.

We were in the comfortable situation that the majority of the over 40 substance names of resins, gums, and related products encountered in the *iatrosophia* (**Table 2**) were common names which are still known today. In only two cases either no entirely matching (*mýrra xylalá* – myrrh or agar wood) or only one correspondent name (*sarí katrán* – cypress tar) could be found in the literature and this leaves the established identity particularly

uncertain. However, in the majority of the other cases at least three correspondents in Greek, Turkish, and sometimes Arabic were found enabling a straightforward attribution to a defined substance. They included Cypriot-Greek vernacular names (e.g., *píssa tis athashiás tis pikrís* – bitter almond gum) and trade names (e.g., *válsamon tis Mékkas* – balsam of Mecca) or such that can be traced far back in history, sometimes for two millennia or more (e.g., *lívanos* – frankincense, *ládanon* – ladanum, *mastíchin* – mastic). Assuming that over the centuries the name has not been applied to different herbal drugs, this demonstrates a remarkable continuity of the popular plant nomenclature of the respective cases. Sibthorp was surprised when locals he met on his botanical excursions to Greece in 1787 used the nomenclature of Dioscorides and Theophrastus to name the plants (Bruce, 1970). Although Fraas (1845, p. ix), who contributed to the exploration of the local flora in the nineteenth century CE, was clearly more skeptical and argued that many plant names of the Greek antiquity had recently been reintroduced into the Greek language to purport a cultural continuity, he admitted that particularly among the names of cultivated plants such with true ancient roots could be found. Hanlidou et al. (2004) showed that a great number of the herbs sold on the market of Thessaloniki today have names which are related to those in Dioscorides.

More difficulties posed those substance names with several possible interpretations. They could be attributed to different material obtained from sometimes taxonomically unrelated species (e.g., *trimintína* – terebinth resin or crude pine resin, *píssa tou xylalá* – agar wood, benzoin, or solid storax). Perhaps typical for plant exudates, in many cases the botanical source is not restricted to one single species because the material simply can be collected from several more or less closely related taxa. This appears to be connected with traditional concepts of species demarcations which do not necessarily overlap with those of the Linnean binomial nomenclature. Cases like these can best be comprehended by considering them as plant complexes as suggested by Linares and Bye (1987). A group of different species consisting of one "label" plant and several substitutes share the same name and have common qualities and uses.

Finally, the identification procedure yielded a list of at least 27 different substances (**Table 3**). With the help of standard texts and additional appropriate references they could be attributed to their respective botanical source. However, in the case of cedar tar and cypress tar the attribution is ambiguous because of the lack of corresponding information in the available references. The 27 substances were obtained from over 43 taxa out of 13 families and included various kinds of resins, gums, tars, and volatile oils. Seven of the resins could be categorized as terpenoid resins obtained from species which are members of the Anacardiaceae, Burseraceae, and Pinaceae. Phenolic resins were only found in the Styracaceae. Various of them were of miscellaneous nature containing substantial portions of both terpenoid and phenolic compounds, belonging to the Altingiaceae, Apicaceae, Cistaceae, and Convolvulaceae. Five of the substances were pure gums belonging to the Rosaceae and Fabaceae. Twelve of the substances were obtained from exotic species originating from Southeast Asia, Middle East, Europe and the neighboring region. The botanical sources of the remaining 15 substances were trees and shrubs which can be found in the Cypriot flora either spontaneously growing or cultivated.

INVENTORY OF RESINS AND GUMS

The 27 substances were used as ingredients in 118 recipes which corresponded to 224 URs (9.4% of the total URs in our database; **Table 3**). Since a recipe may contain more than one plant ingredient and can be indicated for manifold uses the number of URs exceeds the number of recipes. The great majority of the URs concerned medicinal uses, only nine were non-medicinal ones such as the use as paint for church icons or incense. The by far most important use was for dermatological conditions accounting for 35.8% of all medicinal URs followed by gastrointestinal and hepatic conditions (18.6%) and respiratory tract diseases (12.1%; **Figure 2**). Of the 26 substances used medicinally 14 were applied both orally and topically, some of them even in a scent remedy, and others either only orally (seven) or topically (five). Altogether nine of them were listed in more than five medicinal recipes.

Of those, mastic is the substance most frequently mentioned, the resin was used as an ingredient in 42 recipes. Conditions distributed over 10 of the 12 UG were identified, in particular dermatological (17 URs), respiratory (16 URs), gastrointestinal and hepatic (14 URs), and ears and eyes (10 URs). Although *Pistacia lentiscus* is a widespread shrub in the Mediterranean, the main source of supply for commercial mastic has apparently always been the Eastern Aegean island of Chios. Here, the resin is harvested by making incisions to the bark of the small trees of *P. lentiscus* var. *chia* (Desf.) Poir. (Flückiger and Hanbury, 1874, pp.142–145; Howes, 1950; Serpico, 2000, p. 434).

Products of pines such as resins, turpentine oil, and wood tar were mentioned in overall 30 recipes. Recipes, which included crude or cooked pine resins were distributed over 7 UGs, above all dermatological complaints (17 URs). Until the early twentieth century the collection of pine resin and the production of tar in particular from *Pinus brutia* or *P. nigra* subsp. *pallasiana* was of some commercial importance in Cyprus (Zeilinger, 1997, p. 140; Tsintides et al., 2002, pp. 77–79; Hadjikyriakou, 2007, pp. 47–49).

Frankincense also called olibanum was mentioned in 28 recipes. The conditions they treated were distributed over 8 UGs and mainly concerned dermatological (20 URs) but also gastrointestinal and hepatic or urogenital uses (each with 6 URs). Southern Arabia and African regions south of Egypt were the main provenances of the oleo gum resin (Serpico, 2000, p. 439). Several *Boswellia* species of this area produce frankincense, of certain importance are *B. sacra* from southern Oman and Yemen, *B. carteri*, *B. frereana*, *B. bhau-dajiana* from Somalia and *B. papyrifera* from Sudan, Ethiopia, and other places in East Africa (Howes, 1950; Serpico, 2000, pp. 438–439; Langenheim, 2003, p. 363; Blaschek et al., 2007).

Terebinth resin was mentioned in 20 recipes distributed over four medicinal UGs. The majority of the uses concerned dermatological (16 URs) followed by gastrointestinal and hepatic (4 URs) conditions. Blaschek et al. (2007) as earlier Tschirch and Stock (1935/1936, 2.2.1, p. 383) indicate *Pistacia terebinthus* as the source. In contrary, botanical references on resin producing terebinths from Cyprus mention *P. atlantica* and not to *P. terebinthus* (Chrysanthis, 1942; Panaretos, 1967; Tsintides et al., 2002, p. 258; Hadjikyriakou, 2007, pp. 152–155). This inconsistency was highlighted by Meikle (1977/1985, p. 368) and it has been suggested that the confusion owed to variations in past botanical nomenclature considering *P. atlantica* as a variety of *P. terebinthus* (Mills and White, 1989). In the past, Cyprian turpentine or Cyprus balsam, in fact, had some importance as an item of

Table 3 | Botanical sources of the substances and their uses in the *iatrosophia*.

Substance[a]	Botanical source[b]	Family[c]	Classification[d]	Stat.[e]	Rec.[f]	Uses[g]	Appl.[h]	Reference
Agar wood, gaharu wood, aloe wood (*lignum aloes*)	*Aquilaria malaccensis* Lam. (syn. *A. agallochum* Roxb. ex Finl.), *A. beccariana* Tiegh., *A. hirta* Ridl., *A. sinensis* (Lour.) Spreng., *Gonystylus* spp., *Gyrinops* spp.	Thymelaeaceae	Resinous wood/MR	ex	9* + 1*	DE (5), EE (1), MS (2), OC (1) + RE (2), VA (1)	o, t	Blaschek et al. (2007), Ito and Honda (2005), Langenheim (2003, pp. 448–450)
Amber	Fossil resins from conifers and angiosperms	n.d.	Fossilized resin	ex	1	EE (3), HA (1), RE (3), VA (1)	o, t	Langenheim (2003, pp. 143–195), Serpico (2000, pp. 451–454)
Amber oil	Fossil resins from conifers and angiosperms		Volatile oil	ex	1	RE (1)	o	Langenheim (2003, pp. 143–195), Serpico (2000, pp. 451–454)
Almond gum	*Prunus dulcis* (Mill.) D.A. Webb/var. *amara* (DC.) Buchheim[1]	Rosaceae	Gum	sp	2*	Paint for icons (2)	–	Howes (1949, p. 78), Mantell (1949), Nussinovitch (2010, pp. 229–230)
Bitter almond gum	*Prunus dulcis* (Mill.) D.A.Webb/var. *amara* (DC.) Buchheim[1]	Rosaceae	Gum	sp	2	DE (2)	t	Howes (1949, p. 78), Mantell (1949), Nussinovitch (2010, pp. 229–230)
Balsam of Mecca	*Commiphora opobalsamum* Engl.	Burseraceae	Oleo resin/T	ex	1	DE (1)	t	Blaschek et al. (2007)
Cedar tar	*Cedrus libani* A.Rich. subsp. *brevifolia* (Hook.f.) Meikle	Pinaceae	Wood tar	sp	3*	DE (1), GI (1), MS (1)	o, t	Arnold-Apostolides (1985)
Cherry gum	*Prunus avium* (L.) L.	Rosaceae	Gum	sp	4 + 2*	EE (1), GI (1), RE (2), UG (1), VA (1) + paint for icons (2)	o	Arnold-Apostolides (1985), List et al. (1972), Nussinovitch (2010, pp.128–140)
Cypress tar	*Cupressus sempervirens* L.[2]	Cupressaceae	Wood tar	sp	1	DE (1)	t	Mills and White (1994, pp. 102–103)
Frankincense (*olibanum*)	*Boswellia sacra* Flueck., *B. bhau-dajiana* Birdw., *B. carteri* Birdw., *B. frereana* Birdw., *B. papyrifera* Hochst.	Burseraceae	Oleo gum resin/T	ex	28	DE (20), FV (1), GI (6), MS (1), OC (3), RE (4), UG (6), VA (1), incense (1)	o, t	Blaschek et al. (2007), Deutsche Apothekerschaft (1935), Howes (1950), Langenheim (2003, p. 363), Pharmacopoea Helvetica (1933), Serpico (2000, p. 438)
Galbanum	*Ferula gummosa* Boiss. (syn. *F. galbaniflua* Boiss. and Buhse, syn. *Peucedanum galbanifluum* Boiss. and Buhse), *F. kokanika* Regel and Schmalh., *F. schair* Borszcz., *F. rubricaulis* Boiss.	Apiaceae	Gum resin/MR	ex	1	GY (1)	o	Blaschek et al. (2007), List et al. (1972), Serpico (2000, pp. 442–443)
Gum arabic	*Acacia senegal* (L.) Willd., *A. seyal* Delile, *A. nilotica* (L.) Willd. ex Delile	Fabaceae	Gum	ex	3	GI (1), paint for icons (2)	o	Berger (1964, pp. 142–143), Blaschek et al. (2007), Langenheim (2003, p. 46), Nussinovitch (2010, pp. 39–42)
Ladanum	*Cistus incanus* subsp. *creticus* (L.) Heyw. (syn. *Cistus creticus* L. and *Cistus villosus* var. *creticus* (L.) Boiss.), *Cistus creticus* L. subsp. *creticus*[3]	Cistaceae	Resin/MR	sp	7	DE (3), GI (3), VA (1)	o, s, t	Blaschek et al. (2007), Hadjikyriakou (2007, p. 172), Meikle (1977/1985, p. 182), Tsintides et al. (2002, p. 289)

(Continued)

Table 3 | Continued

Substance[a]	Botanical source[b]	Family[c]	Classification[d]	Stat.[e]	Rec.[f]	Uses[g]	Appl.[h]	Reference
Mastic	*Pistacia lentiscus* L.	Anacardiaceae	Resin/T	sp	42	DE (17), EE (10), FV (2), GI (14), GY (1), HA (5), OC (4), RE (16), UG (1), VA (5), incense (1)	o, t	Blaschek et al. (2007)
Myrrh	*Commiphora molmol* Engl. ex Tschirch (syn. *C. myrrha* var. *molmol* Engl.), *C. abyssinica* Engl, *C. schimperi* Engl.	Burseraceae	Gum resin/T	ex	8 + 1*	DE (1), EE (3), FV (1), GI (5), GY (1), HA (1), RE (4), VA (1), incense (1) + RE (2), VA (1)	o, s, t	Blaschek et al. (2007)
Olive resin	*Olea europea* L.	Oleaceae	Gum resin	sp	5	DE (4), OC (1)	t	Arnold-Apostolides (1985), Tschirch and Stock (1935/1936, p. 2.2.2, 1756)
Pine resin (*resina alba/communis*), crude turpentine (*terebinthina*), rosin (*colophonium*), black rosin (*resina nigra*)	*Pinus brutia* Ten., *P. halepensis* Mill, *P. nigra* Arnold subsp. *pallasiana* (Lamb.) Holmboe	Pinaceae	Gum	sp	23	DE (17), EE (1), GI (1), GY (1), MS (1), OC (1), RE (1)	o, t	Arnold-Apostolides (1985), Hadjikyriakou (2007, pp. 47–50), List et al. (1972), Meikle (1977/1985, pp. 24–25), Richter (1827, p. 125), Sezik et al. (2001), Tsintides et al. (2002, pp. 77–80)
Pine tar (*pix nigra*)	*Pinus brutia* Ten., *P. halepensis* Mill, *P. nigra* Arnold subsp. *pallasiana* (Lamb.) Holmboe	Pinaceae	Oleo resin/T	sp	3*	DE (1), GI (1), MS (1)	o, t	Arnold-Apostolides (1985), Hadjikyriakou (2007, pp. 47–50), List et al. (1972), Meikle (1977/1985, pp. 24–25), Richter (1827, p. 125), Sezik et al. (2001), Tsintides et al. (2002, pp. 77–80)
Pine turpentine oil	*Pinus brutia* Ten., *P. halepensis* Mill, *P. nigra* Arnold subsp. *pallasiana* (Lamb.) Holmboe	Pinaceae	Wood tar	sp	4	DE (1), MS (1), RE (1), UG (1)	o, t	Arnold-Apostolides (1985), Hadjikyriakou (2007, pp. 47–50), List et al. (1972), Meikle (1977/1985, pp. 24–25), Richter (1827, p. 125), Sezik et al. (2001), Tsintides et al. (2002, pp. 77–80)
Plum gum	*Prunus domestica* L.	Rosaceae	Volatile oil	sp	1 + 2*	UG (1) + paint for icons (2)	o	Arnold-Apostolides (1985), Howes (1949, p. 78); Nussinovitch (2010, p. 141)
Scammony	*Convolvulus scammonia* L.[4]	Convolvulaceae	Gum resin/MR	ex	2	FV (2), GI (4), RE (2), VA (1)	o	Blaschek et al. (2007), Langenheim (2003, p. 420)
Storax, liquid (exotic)	*Liquidambar orientalis* Mill.	Altingiaceae	Oleo resin/P	ex	3	DE (5), EE (1), MS (2), OC (1)	o, t	Hanbury (1857), Meikle (1977/1985, p. 655)
Storax, liquid (local)	*Liquidambar styraciflua* L., = *L. orientalis* Mill.?[5]	Altingiaceae	Oleo resin/P	cu	1	DE (1)	t	Hadjikyriakou (2007, pp. 102–105), Meikle (1977/1985, p. 655)
Storax, solid (*st*)	*Styrax officinalis* L.	Styracaceae	n.c.	sp	9*	DE (5), EE (1), MS (2), OC (1)	o, t	Hanbury (1857), Howes (1950), List et al. (1972), Marzell and Paul (1979, p. 523), Meikle (1977/1985, p. 1088)

Sumatra or Siam benzoin	*Styrax benzoin* Dryand., *S. parallelonerum* Perk. or *S. tonkinensis* Craib ex Hartwich	Styracaceae	Balsam/P	ex	9*	DE (5), EE (1), MS (2), OC (1)	o, t	Blaschek et al. (2007), Hovaneissian et al. (2006)
Terebinth resin (*terebinthina chiotica/cypria*)	*Pistacia atlantica* Desf., (*P terebinthus* L.)	Anacardiaceae	Oleo resin/T	sp	20	DE (16), GI (4), RE (1), UG (2), bed bug repellent (1)	o, t	Blaschek et al. (2007), Hadjikyriakou (2007, pp.152–55), Meikle (1977/1985, pp. 367–368), Mills and White (1994, p. 108), Panaretos (1967), Tsintides et al. (2002, pp. 257–258)
Venice turpentine	*Larix decidua* Mill	Pinaceae	Oleo resin/T	ex	1	UG (1)	o	Blaschek et al. (2007), Mills and White (1994, pp. 100–102)

[a]*Where appropriate, the substance name was supplemented by the pharmaceutical name in italic.*
[b]*The nomenclature was verified with Tropicos, Missouri Botanical Garden or the International Plant Name Index (IPNI).*
[c]*Classification and nomenclature of angiosperm families follows the Angiosperm Phylogeny Website (Stevens, 2001 onwards).*
[d]*The classification of the substances primarily follows Blaschek et al. (2007). The discrimination of resins in terpenoid or phenolic resins follow Langenheim (2003): T-predominantly terpenoid compounds, P-predominantly phenolic compounds, MR-miscellaneous resins. Olive resin was only mentioned in Tschirch and Stock (1935/1936). Solid storax was not categorized (n.c.) in any of the used references.*
[e]*The status of a taxon in Cyprus follows Della (1999): cu-cultivated, sp-spontaneous (native, naturalized or endemic). Plants not mentioned in this reference were classified as exotics (ex).*
[f]*Number of iatrosophia recipes mentioning the substance. In a number of cases more than one interpretation was possible for the associated substance name (cf.* ***Table 2****). The number of recipes linked with such cases are marked (*) and separately listed.*
[g]*Medicinal uses were classified into 12 use groups (UGs) (key to the abbreviations see Quantification and Categorization of the Use Reports into Use Groups (Steps 5 and 6)]. Uses linked to substance names with more than one interpretation possible interpretation, are separately listed (+).*
[h]*Way of application of a remedy according to the recipe: o-oral, s-scent, t-topical.*
[i]*The species instead of the infraspecific taxon was mentioned in the used references; [2]Resin instead of tar of this species was mentioned in the used reference; [3]According to Hadjikyriakou (2007, pp. 172–174) this infraspecific taxon is the primary source of ladanum in Cyprus; [4]Several other European and Middle Eastern Apocynaceae or Convolvulaceae provided certain local qualities of scammony (Blaschek et al., 2007); [5]Local Liquidambar trees were conditionally classed as L. styraciflua in the "Flora of Cyprus" (Meikle, 1977/1985, p. 655). Recently this identification has been put in question in favor of L. orientalis (Hadjikyriakou, 2007, pp. 102–105).*

FIGURE 2 | Distribution of the use reports (URs) of records referring to resins and gums over the 12 medicinal use groups [key to the abbreviations see Quantification and Categorization of the Use Reports into Use Groups (Steps 5 and 6)].

commerce for the island (Thiselton-Dyer, 1885; Tschrich and Stock, 1935/1936, p. 2.2.1, 384). Today, specifically in the Pafos area, the resin is still collected to produce a traditional chewing gum called *pafitikí píssa* (Mills and White, 1989; Hadjikyriakou, 2007, p. 153).

Overall 10 recipes can be associated with agar wood, they treated conditions distributed over 6 UGs. Agar wood is the fragrant resinous wood of trunk and roots from several tropical Thymelaeaceae in particular *Aquilaria* species of Southeast Asia (Langenheim, 2003, p. 448). As suggested by an account from the fourteenth century, "aloe wood" was actually available in medieval Cyprus (Heyd, 1879, p. 9, 559). Interestingly, agar wood or aloe wood was not referred to by Dioscorides' name *agallochōn* (Berendes, 1902, 1.21) but by (*píssa tou*) *xylalá*, the Cypriot-Greek reproduction of *xylaloē* (Gennadios, 1914, pp. 2–3) and provides a clue about the origin of this knowledge. Simeon Seth, a Jewish Byzantine doctor of the eleventh century, who played an important role in the transmission of Eastern, in particular Islamic medicine, to the Byzantine Empire, seems to be the first of the Greek writing authors who described the drug in detail by using the name *xylaloē* (Langkavel, 1866, p. xi 17t; Tschrich and Lippmann, 1933, p. 1348; Varella, 1995).

Nine of the above recipes can also be associated with benzoin or solid storax both obtained from members of the Styracaceae. Two different kinds of benzoin are recognized; Sumatra benzoin from *Styrax benzoin* and *S. parallelonerum*, both found in Indonesia and Malaysia, and Siam benzoin from *S. tonkinensis* found in Laos, Thailand, Vietnam, and Malaysia or other related species (Blaschek et al., 2007). The first report which unequivocally refers to this resin comes from the fourteenth century Arab traveler Ibn Batuta. It was suggested that the Arabic name *luban djawi* (frankincense of Java) was later changed to *banjawi* to finally give benjoin or benzoin (Flückiger and Hanbury, 1874, p. 362; Tschirch and Lippmann, 1933, p. 1383). The only representative

of the Styracaceae in the Mediterranean and native to Cyprus is *Styrax officinalis* (Meikle, 1977/1985), the source of solid storax. It should be noted that the substance commonly known by the name storax or styrax today is the exudate from *Liquidambar* species (see, e.g., Hovaneissian et al., 2006). However, according to Hanbury (1857) the original and classical storax was the "solid storax" produced by *S. officinalis* which in modern times disappeared from commerce and was replaced by the "liquid storax" obtained from *Liquidambar orientalis*. This view is adhered to in up-to-date standard texts (see, e.g., Blaschek et al., 2007). There is a still ongoing dispute whether *S. officinalis* does produce a resin at all. In morphological studies of stem samples from trees growing near Izmir (western Turkey) no resin production was observed and, therefore, Zeybek (1971) concluded that plants from this part of Anatolia do not produce it. However, based on reports of resin producing trees in southeastern Turkey, the author underscored the potential importance of geographical varieties. Interestingly, both Dioscorides (Berendes, 1902, 1.79) and Pliny (Bostock and Riley, 1855, p. 12.55) in writing about *styrax*, mentioned that the product comes from places now in southeastern Turkey, western Syria, or Lebanon but also from Cyprus and Crete. In fact, Hadjikyriakou (2007, p. 229) provided photographic evidence of fresh running resin on a previously injured stem of a living *S. officinalis* tree from a place at the entrance of the Karpas peninsula in northeastern Cyprus.

Myrrh was mentioned in nine recipes including uses distributed over 8 UGs. The majority of them concerned respiratory (6 URs) and gastrointestinal and hepatic conditions (5 URs). The gum resin is collected from several species of the large genus *Commiphora*, a commonly accepted source is *C. molmol* (*C. myrrha* var. *molmol*; Serpico, 2000, pp. 439–442; Blaschek et al., 2007).

Ladanum was mentioned in seven recipes the uses of which concerned 3 UGs. Both Dioscorides (Berendes, 1902, 1.128) and Pliny (Bostock and Riley, 1855, p. 12.37) stressed that the preferred quality of ladanum comes from Cyprus while the other main provenance was Arabia including the district bordering Syria. Ladanum had been collected and even exported from the island at least until the end of the nineteenth century (Thiselton-Dyer, 1885; Gennadios, 1914; Warren, 2002). Of the four indigenous *Cistus* species only *Cistus incanus* subsp. *creticus* (syn. *Cistus creticus* and *Cistus villosus* var. *creticus*) plays a role as a source of ladanum here, as well as on Crete (Warren, 2002). Hadjikyriakou (2007, pp. 172–174) mentions *Cistus creticus* L. subsp. *creticus* as the source of ladanum which in contrary to subsp. *eriocephalus* (Viv.) Greuter et Burdet, the other local infraspecific taxon, is glandular, strongly resinous and aromatic. In Meikle (1977/1985) the names *Cistus creticus* L. var. *creticus* and var. tauricus (Presl) Dunal, respectively, are used.

RELATIONSHIP TO DIOSCORIDES AND WESTERN STANDARD TEXTS

Conceptually, this comparative analysis joins similar approaches based on retrospective explorations of diachronic data as illustrated by Heinrich et al. (2006). Of specific relevance for the present case are findings suggesting a substantial influence of Dioscorides' *De Materia Medica* on the development of both the materia medica in European historical texts (De-Vos, 2010) and the orally transmitted popular medicine in regions of the Mediterranean such as Sardinia, Sicily, and Campania (Italy; Leonti et al., 2009, 2010). The *iatrosophia* too show remarkable parallels with Dioscorides' text. Roughly two-thirds (18 of 26) of the plant exudates used medicinally here were already listed in this ancient treatise, 16 of them showed some degree of consistency in the UGs and 8 out of these were used to treat conditions of exactly the same UGs. Of all 74 UGs included in the *iatrosophia* and associated with these 18 substances, 46 UGs (62.2%) are also found in *De Materia Medica* (**Table 4**). On the other hand changes in terms of numbers and kinds of UGs of substances common to both systems were observed. In particular the only moderate consistency in the UGs of substances which were well known to Dioscorides, some of them originating from the Eastern Mediterranean, such as frankincense, mastic, pine resins, and agar wood or solid storax is notable. While in *iatrosophia* agar wood, amber, frankincense, and mastic were used in a more diverse way, for almond gum, galbanum, ladanum, and olive resin this was the case in *De Materia Medica*. In fact, the mean number of UGs treated per substances was even higher in the latter (4.6) than the former (3.6) indicating that in general a substance was used in more diverse ways in *De Materia Medica*. Analogous results were reported by Leonti (2011) based on a comparison between recent field-based studies from Campania with Matthioli's edition of Dioscorides (Leonti et al. 2010). Those substances not mentioned in Berendes' (1902) translation of Dioscorides concerned tars and volatile oils or resins of local and exotic species (benzoin, balsam of Mecca, liquid storax). They appear to have been introduced in later centuries, some of them perhaps via Islamic medicine as illustrated by the case of benzoin (see Inventory of Resins and Gums). The differences to Dioscorides altogether may be linked to changes in the prevalence of diseases or the influence of other sources.

The comparison to historic pharmaceutical books and modern standard texts of phytotherapy reflects the gradual decline of the use of plant exudates in Western medicine and simultaneously demonstrates the presence of substances in the *iatrosophia* which have never become established here. While 16 of the 26 substances were mentioned in historic pharmaceutical books only 11 of them remained in the modern standard texts of phytotherapy. Similarly, 14 cases showed some degree of consistency in the UGs between *iatrosophia* and historic pharmaceutical books, only nine cases did so between *iatrosophia* and the phytotherapy texts. Of all 65 UGs included in the *iatrosophia* and associated with the 16 substances used in the historic pharmaceutical books, 41.5% (27 UGs) are also found in the latter. The analogous percentage of the phytotherapy texts is 34.8% (16 UGs; based on 46 UGs included in the *iatrosophia* and associated with 11 substances; **Table 4**). The mean number of UGs treated per substance was slightly lower than in *iatrosophia* (3.6), namely 3.0 in the historic pharmaceutical books and 2.5 in the phytotherapy texts. While the highest number of same UGs was found with the uses of myrrh mentioned in the historic pharmaceutical books (five of six UGs), substances with a wide range of indication in *iatrosophia* such as mastic or frankincense had an overall low degree of consistency (10–30%). The general reduction in the use of plant exudates is partly due to the fact that for several reasons in modern phytotherapy old uses were abandoned. A substance may have become obsolete, at least for certain indications or applications, because

Table 4 | Comparison of the substances and UGs included in the *iatrosophia* to those of other texts.

	Iatros.	Dioscorides' *De Materia Medica*				Historic pharmaceutical books				Modern phytotherapy texts			
Substances[a]	**#UGs[b]**	**Incl.[c]**	**#UGs[b]**	**#Same UGs[d]**	**%Same UGs[e]**	**Incl.[c]**	**#UGs[b]**	**#Same UGs[d]**	**%Same UGs[e]**	**Incl.[c]**	**#UGs[b]**	**#Same UGs[d]**	**%Same UGs[e]**
Agar wood	6	Yes	3	2	33.3	No	0	0	–	No	0	0	–
Amber	4	Yes	1	0	0.0	No	0	0	–	No	0	0	–
Amber oil	1	No	0	0	–	Yes	1	1	100.0	No	0	0	–
Balsam of Mecca	1	No	0	0	–	No	0	0	–	No	0	0	–
Bitter almond gum	1	Yes	4	1	100.0	No	0	0	–	No	0	0	–
Cedar tar	3	No	0	0	–	No	0	0	–	No	0	0	–
Cherry gum	5	Yes	5	5	100.0	No	0	0	–	No	0	0	–
Cypress tar	1	No	0	0	–	No	0	0	–	No	0	0	–
Frankincense	8	Yes	4	3	37.5	Yes	3	2	25.0	Yes	2	2	25.0
Galbanum	1	Yes	7	1	100.0	Yes	4	1	100.0	Yes	3	0	0.0
Gum arabic	1	Yes	2	1	100.0	Yes	1	0	0.0	Yes	2	1	100.0
Ladanum	3	Yes	7	3	100.0	Yes	3	2	66.7	No	0	0	–
Mastic	10	Yes	6	6	60.0	Yes	3	3	30.0	Yes	1	1	10.0
Myrrh	8	Yes	9	7	87.5	Yes	6	5	62.5	Yes	4	3	37.5
Olive resin	2	Yes	5	2	100.0	No	0	0	–	No	0	0	–
Pine resins	7	Yes	5	4	57.1	Yes	4	3	42.9	No	0	0	–
Pine tar	4	Yes	6	3	75.0	Yes	2	2	50.0	Yes	2	2	50.0
Pine turpentine oil	4	No	0	0	–	Yes	7	3	75.0	Yes	2	2	50.0
Plum gum	1	Yes	2	1	100.0	No	0	0	–	No	0	0	–
Scammony	4	Yes	6	2	50.0	Yes	3	1	25.0	No	0	0	–
Storax, liquid (exotic)	4	No	0	0	–	Yes	2	1	25.0	Yes	3	2	50.0
Storax, liquid (local)	1	No	0	0	–	Yes	2	1	100.0	Yes	3	1	100.0
Storax, solid	4	Yes	4	1	25.0	No	0	0	–	No	0	0	–
Sumatra/siam benzoin	4	No	0	0	–	Yes	4	1	25.0	Yes	3	2	50.0
Terebinth resin	4	Yes	5	4	100.0	Yes	1	1	25.0	No	0	0	–
Venice turpentine	1	Yes	1	0	0.0	Yes	1	0	0.0	Yes	3	0	0.0
	93		82	46			47	27			28	16	

[a] *Substances used medicinally in the iatrosophia.*
[b] *Total number of use groups (UGs) treated by the medicinal uses of the respective text(s).*
[c] *Indicates if a substances is included for medicinal purposes in the respective text(s).*
[d] *Number of UGs included in the iatrosophia which are also found in the respective text(s).*
[e] *Percentage of UGs included in the iatrosophia which are also found in the respective text(s).*

of toxicological concerns (e.g., oil of turpentine, scammony) or potential allergic reactions (e.g., crude turpentine, colophony; Williamson, 2003; Blaschek et al., 2007). On the other hand new indications of ancient drugs with a long tradition have found their way into modern phytotherapy as illustrated by the gastrointestinal and musculo-sceletal uses of Indian frankincense or the gastrointestinal uses of gum Arabic (Williamson, 2003; Blaschek et al., 2007; ESCOP, 2009).

COMPARISON OF THE SIMPLE REMEDIES TO ETHNOMEDICAL AND BIOACTIVITY DATA

The great majority of the medicinal URs concerned plant uses listed in compound remedies. Overall 17 simple remedies (14.4%) were counted, they involved 23 medicinal URs (10.7%) with 12 different substances. In **Table 5** the simple remedies are presented together with their deduced pharmacological functions. The results of the cross-referencing to reported biological activities are shown

Table 5 | Simple remedies in the *iatrosophia*: interpretation of the mentioned use and deduced pharmacological functions.

Recipe[a]	Substance[b]	Mentioned use[c]	Form of Administr.[d]	Interpretation[e]	Deduced pharmacological functions[f]
IM 14.3	Agar wood, benzoin, or, solid storax	Fracture of the head	Filling for the fracture	Open cranial fracture	Anti-inflammatory Antimicrobial Wound healing promotion
IM 63.03	Agar wood, benzoin, or solid storax	Podalgia	Beverage	Gout and rheumatic conditions (incl. arthritis, athrosis)	Analgesic Anti-inflammatory Immunomodulatory
GP PME 01	Cherry gum	It relieves the cough but also the liver, it helps the eyesight and makes your face look bright.	Beverage	Productive or dry cough	Antitussive Bronchodilatating Expectorant
				Liver health	Beneficial effect on liver diseases
				Vision improvement	Vision improving effects
				Healthy and bright complexion	Beneficial effect on liver or kidney diseases
GP PME 02	Cherry gum	Beneficial in stones	Beverage	Gall, kidney or bladder stones	Stone-dissolving/-expelling
GP ΡΞΙΓ 02	Frankincense	Every kind of rheumatism	Ointment	Rheumatic conditions	Analgesic Anti-inflammatory Immunomodulatory
IM 134.05	Galbanum	If the child dies in her [the mother's] belly	Beverage	Abortion of a dead fetus	Abortive Antispasmodic
GP PMH.05	Gum arabic	Concerning the flux of the belly	Snack or beverage	Diarrhea	Antibiotic Anti-inflammatory Antimotility Antisecretory Bulk-forming effect
IM 48.02	Ladanum	Hemorrhoids and spots inside and outside of the anus	Poultice	Hemorrhoids accompanied by anal excema	Analgesic Anti-inflammatory Antimicrobial
IM 128.03	Ladanum	To stop hair loss	Fumigation	Alopecia	Antifungal Beneficial effects on hair cycle 5-Alpha-reductase inhibition
IM 64.02	Pine resin	Rheumatic diseases and podalgia	Poultice	Rheumatic conditions and gout	Analgesic Anti-inflammatory Immunomodulatory
GP PKΘ 06	Plum gum	It dissolves the stones of dysuria	Beverage	Gall, kidney or bladder stones, dysuria	Antibiotic Stone-dissolving/-expelling
IM 41.05	Scammony	It purges "depositions and poisons," keeps off fevers, shivers, quartan fevers.	Beverage	Cathartic, prophylactic against fevers including malaria	Antibacterial Antimalarial Antiviral Cathartic
IM 89.03	Terebinth resin	Old ulcers	Poultice	Infected ulcerative wounds	Anti-inflammatory Antimicrobial
IM 137.05	Terebinth resin	Diarrhea in small children	Fumigation	Diarrhea in infants	Antibiotic Anti-inflammatory Antimotility Antisecretory

(Continued)

Table 5 | Continued

Recipe[a]	Substance[b]	Mentioned use[c]	Form of Administr.[d]	Interpretation[e]	Deduced pharmacological functions[f]
IM 149.03	Terebinth resin	For those who cannot urinate	Snack	Impaired urination possibly related to bladder stones, urinary tract infections, BPH or prostate cancer	Alpha-receptor antagonistic effect 5-Alpha-reductase inhibition Antibiotic Anticancer Stone-dissolving/-expelling
KI 9.01	Terebinth resin	Deep wounds that need a filling	Ointment	Incisions caused by sharp or cutting implements	Analgesic Antimicrobial Wound healing promotion
KI 10.01	Terebinth resin	Pestilent ulcers and foul ulcers	Ointment	Infected ulcerative or malignant wounds	Anticancer Anti-inflammatory Antimicrobial

[a]*Signature of the recipe, the first two capitals indicate the respective text (see* ***Table 1****).*
[b]*Corresponding to the homonymous column in* ***Table 3****.*
[c]*Uses were translated by retaining the original wording as far as possible.*
[d]*Oral applications: beverage, snack; Topical applications: filling, fumigation, ointment, poultice.*
[e]*The mentioned uses were interpreted as described in 2.2.1.*
[f]*The deduction of the pharmacological functions was conducted as described in 2.2.6.*

in **Table 6**. In the following sections for each substance the simple remedies are first compared to relevant ethnomedical data and then the reported biological activities as listed in **Table 6** are reviewed. Here, we primarily considered studies that were conducted with the respective substance (including full extracts or fractions). Studies that solely investigated isolated compounds or another plant part of the same or a closely related species were included mainly if no other data were available but then only if they stood in relationship to the respective substance. In Section "Evaluation of the Reported Bioactivity Data" the results of the comparison to the bioactivity data are evaluated.

(i) Agar wood – Aquilaria spp. and other Thymelaeaceae, (ii) benzoin – S. benzoin, S. paralleloneurum, S. tonkinensis, or (iii) solid storax – S. officinalis

In the third recipe on page 14 of the *Iatrosophikon* of Mitrophanous (recipe IM 14.03) pounded "*píssa tou xylalá*" is applied on an open fracture of the cranial bone obviously to protect the injury and promote healing. In IM 63.03 the pounded substance is dissolved in rum and then extracted in the sun for 8 days, the resulting "tincture" is drunk as a remedy against podalgia. The name "*píssa tou xylalá*" can be attributed to all of the above three substances (i, ii, iii).

(i) Both Dioscorides (Berendes, 1902, 1.21) and Paulus Aegineta (Adams, 1844/1846/1847, 7.3, 18) discussed agar wood by the name of *agallochon* without, however, mentioning any uses related to the above recipes. In a series of *in vitro* tests a 70% ethanolic extract from powdered agar wood of *Aquilaria sinensis* showed anti-inflammatory properties (Yam, 2007, pp. 81–88). The extract had no inhibitory effect on cyclooxygenase activity but specifically reduced 5-lipoxygenase activity with an IC_{50} value around 30 μg/ml.

(ii) As in the case of Dioscorides, none of the drugs discussed by Paulus Aegineta seems to refer to benzoin. Today, Sumatra benzoin is known as an ingredient in Friar's Balsam which is used as a vulnerary agent to protect and disinfect the skin (Williamson, 2003). Depending on quality and origin, 70–80% of Sumatra benzoin consist of free benzoic and cinnamic acids and their corresponding esters. Free benzoic acid (up to 20%), its esters (70–95%) and the triterpene α-siaresinolic acid (6%) are the main constituents of Siam benzoin (Blaschek et al., 2007). Benzoic acid is conventionally used as a preservative by the food industry due to its antimicrobial activity. Mycopol®, a preparation containing benzoic acid beside other active compounds has a long history of use in the treatment of fungal skin infections and is beneficial in a large number of patients (Steppert, 1966). Preparations of the balsams from *S. benzoin* and *S. tonkinensis* were studied for their phagocytotic activity in mice inoculated with *E. coli*. The 95% ethanolic extract of the latter species and the insaponifiable fractions of both species showed to protect at least four of five animals (50 mg/kg, intraperitoneally; Delaveau et al., 1980).

(iii) Although Dioscorides listed various indications for solid storax (Berendes, 1902, 1.79, *styrax*) and Paulus Aegineta employed it in many remedies (Adams, 1844/1846/1847), no relationship between these ancient uses and those described in the two *iatrosophia* recipes presented above could be found. Phytochemical or pharmacological properties of solid storax have not been explored so far.

Cherry gum – Prunus avium

According to recipe PME 01 in the *Geoponikon* (GP PME 01) drinking every morning cherry gum dissolved in water should relieve cough, improve liver health and vision as well as "make the face look bright." While in GP PME 02 the gum dissolved in wine is recommended in stones. Looking at Dioscorides' account on the gum (Berendes, 1902, 1.157) reveals that the *iatrosophia* appear to have borrowed from this reference. Paulus Aegineta, too, mentioned the above recipe for stone affections and the gum's ability to ease "asperities of the trachea" (Adams, 1844/1846/1847, 7.3, 167).

Table 6 | Cross-referencing of deduced pharmacological functions to reported biological activities.

Substance[a]	Deduced pharmacological functions[b]	Matching biological activities reported in the studies[c]	Study type[d]	Stud.[e]
Agar wood	Analgesic Anti-inflammatory Antimicrobial Immunomodulatory Wound healing promotion	Anti-inflammatory, 1×	*In vitro*	1
Cherry gum	Antitussive	[Indirect hepatoprotective, 1×]	*in vivo*[1]	2
	Beneficial effect on liver or kidney diseases	[Improved metabolic profile in chronic renal failure, 1×]	*In vivo*[1]	
	Bronchodilatating Expectorant Stone-dissolving/-expelling Vision improving effects			
Frankincense	Analgesic	Anti-inflammatory, 3×	*In vitro*, *in vivo*	3
	Anti-inflammatory	Decrease of cytokine levels (immunomodulatory), 1×	*In vivo*	
	Immunomodulatory			
Galbanum	Abortifacient	Spasmolytic	*In vitro*	1
	Effects on uterine contractility			
Gum arabic	Antibiotic	Improved recovery rates from diarrhea, 1×	*In vivo*	4
	Anti-inflammatory	Proabsorptive (antisecretory), 2×	*In vivo*	
	Antimotility	No significant antidiarrheal effects, 1×	Clinical[2]	
	Antisecretory Bulk-forming effect			
Ladanum	Analgesic	Antibacterial, 2×	*In vitro*	4
	Antifungal	Antioxidant (anti-inflammatory), 1×	*In vitro*[3]	
	Anti-inflammatory	No significant anti-inflammatory effect, 2×	*In vitro*[3], *in vivo*[4]	
	Antimicrobial Effects with a beneficial action on the hair cycle 5-Alpha-reductase inhibition			
Pine resin	Analgesic	Analgesic, 1×	*In vivo*	3
	Anti-inflammatory	Anti-inflammatory, 2×	*In vivo*[4], *in vivo*[3]	
	Immunomodulatory			
Plum gum	Antibiotic	No data available	–	0
	Stone-dissolving/-expelling			
Scammony	Antibiotic	Antibacterial (antibiotic), 1×	*In vitro*[4]	1
	Antimalarial Antiviral Cathartic			
Solid storax	Analgesic	No data available	–	0
	Anti-inflammatory Antimicrobial Immunomodulatory Wound healing promotion			
Sumatra or Siam benzoin	Analgesic	Antifungal, 1×	Case reports[2,4]	2

(Continued)

Table 6 | Continued

Substance[a]	Deduced pharmacological functions[b]	Matching biological activities reported in the studies[c]	Study type[d]	Stud.[e]
	Anti-inflammatory	Phagocytotic (antibacterial), 1×	*In vivo*	
	Antimicrobial			
	Immunomodulatory			
	Wound healing promotion			
Terebinth resin	Alpha-receptor antagonistic effect	Antibacterial, 1×	*In vitro*[4]	7
	Analgesic	Antimicrobial (antibiotic), 1×	*In vitro*	
	Antibiotic	Anti-hypernociceptive (analgesic), 1×	*In vivo*[4]	
	Anticancer	Anti-inflammatory, 3×	*In vivo*[4], *in vivo*[3]	
	Anti-inflammatory	Inhibition of LDL oxidation (anti-inflammatory), 1×	*In vitro*	
	Antimicrobial	Leucotriene inhibition (anti-inflammatory), 1×	*In vitro*[4]	
	Antimotility			
	Antisecretory			
	Wound healing promotion			
	5-Alpha-reductase inhibition			

[a]*Corresponding to the homonymous column in* ***Table 5****.*
[b]*Corresponding to the homonymous column in* ***Table 5****. All pharmacological functions referring to the same substance were consolidated.*
[c]*Where appropriate the deduced pharmacological function to which the reported activity was cross-references is added in parenthesis. Activities in squared brackets refer to studies conducted with an analogous substance from a taxonomically unrelated species (see footnote 4). The figure indicates the number of studies reporting the corresponding activity.*
[c]*Type of the study reporting the corresponding activity.*
[d]*Number of studies included in the comparison.*
The study was conducted with: [1]gum arabic, [2]a compound preparation that included additional further active constituents, [3]a different plant part, [4]isolated compounds only..

The symptoms listed in GP PME 01 could be related to a defined disease of some specific organ or, in their entirety, a complex systemic disease or even intoxication. While cherry gum can hardly boast of bioactivity data, another natural gum typically composed of sugar polymers is comparatively well explored. Namely, for gum Arabic a number of the actions have been suggested which are related to some of the pharmacological functions deduced from the above recipes. In Sudan, the gum is prescribed in chronic renal failure (CRF) due to its ability to decrease uremia levels or reduce the frequency of dialysis. In a preliminary study involving 36 CRF patients, a significant improvement of the metabolic profile could be observed in the groups receiving 50 g gum Arabic daily in comparison to baseline and control (Ali et al., 2008). Although gum Arabic seems to lack a direct hepatoprotective action, 100 mg administered intraperitoneally suppressed macrophage activation and attenuated the extent of liver injury in a rat model of induced hepatic necrosis (Mochida et al., 1996).

Frankincense – Boswellia sacra, B. bhau-dajiana, B. carteri, B. frereana, B. papyrifera

In recipe GP ΡΞΓ 02 an ointment containing frankincense, pig fat, and egg white was prepared for the topical treatment of "every kind of rheumatism." The Roman encyclopedist Celsus (ca. 25 BCE – 50 CE), wrote that frankincense was beneficial in the treatment of gout (Martinez et al., 1989) and Paulus Aegineta applied it in a powder-mix for the same condition (Adams, 1844/1846/1847, 7.13, 539).

The majority of studies conducted with *Boswellia* resins refer to Indian frankincense from *B. serrata*, which according to the ESCOP monographis indicated for "relief of painful osteoarthritis" or "treatment of inflammatory bowel disease." Numerous studies have been conducted both with the resin and its constituents, they suggest among others anti-inflammatory and immunomodulatory activities (ESCOP, 2009). Some of these data are based on boswellic acids. These pentacyclic triterpenic acids are characteristic for *Boswellia* resins including those from African or Arabian species and, therefore, relevant in the context of the above *iatrosophia* remedy. In fact, studies reviewed by Moussaieff and Mechoulam (2009) showed the potential of these compounds in animal models of arthritic conditions.

However, studies actually conducted with the resin of African or Arabian *Boswellia* species are limited. One of these studies investigated the anti-inflammatory activity of extract fractions and triterpene acids isolated from the resin of *B. carteri* in TPA-induced ear edema in mice. Topically applied hexane- and EtOAc-soluble fractions (1.0 mg/ear) exhibited potent inhibitory activities (91–94% inhibition, $p < 0.01$ significant from control). Isolated di- and triterpenes, with the exception of incensole acetate, exhibited marked anti-inflammatory activities (ID_{50} values of 0.05–0.49 mg/ear). Some of the compounds were equally or more active than the positive controls hydrocortisone (ID_{50} 0.03 mg/ear) or indomethacine (ID_{50} 0.3 mg/ear) respectively (Banno et al., 2006). The resin of *B. carteri* (*B. carterii*) was also investigated for its potential to influence adjuvant-induced arthritis in rats. The tested acetone extract administered intragastrally at a dose of 0.9 g/kg (average body weight: 224.63 g) significantly suppressed arthritic scores, attenuated paw edema and decreased cytokine levels (TNF-α, IL-1 β), compared to control (Fan et al., 2005).

In an *in vitro* model of osteoarthritis, 100 μg/ml of an absolute ethanol extract from the resin of *B. frereana* (the dose was selected as a result of a dose response study on isolated articular chondrocytes) showed a protective effect against cartilage loss by inhibiting breakdown of the collagenous matrix mainly through inhibition of pro-inflammatory mediators (Blain et al., 2010).

Galbanum – Ferula gummosa, F. kokanika, F. schair, F. rubricaulis

According to recipe IM 134.05 drinking pounded galbanum in water will expel a dead embryo/fetus. The same use was mentioned by the authors of "On the Diseases of Women," one of the Hippocratic treatises (Riddle, 1992), by Dioscorides (Berendes, 1902: 3.87(97)) as well as by Paulus Aegineta (Adams, 1844/1846/1847, 3.61, 611).

The use of uterine stimulating herbs during pregnancy is regarded as a potential risk factor for a spontaneous abortion (Johns and Sibeko, 2003). Although the ancient use might suggest to place galbanum among these herbs, no studies reporting contractile effects on the uterus are available. Based on its traditional use in the treatment of diarrhea, Sadraei et al. (2001) instead investigated the spasmolytic effects of essential oil and extracts of the gum resin from *Ferula gummosa* on the contraction of isolated rat ileum. Ether, petrol and methanol extracts inhibited the contractions induced by 80 mM KCl most potently (IC_{50} values: 0.55, 1.4, and 7.5 μg/ml, respectively). Etheric or petrolic extracts attenuated the maximum attainable response of ACh with IC_{50} values of 10 or 5.1 μg/ml, respectively. The authors argued that at least part of the inhibitory effect was due to α- and β-pinene, two common constituents of the essential oil, ether, and petrol extracts. As shown in a study with the essential oil of *Bupleurum fruticosum* L., another Apiaceae, fractions containing substantial amounts of these two monoterpenes are able to exert antispasmodic effects on the uterus of the rat (Lorente et al., 1989). While this points to some possibly relevant effects, no direct evidence for the induction of labor or abortion exists for galbanum. Perhaps the *iatrosophia* use of galbanum should not be linked to a later stage of pregnancy as purported by the wording of the above recipe but rather to earlier stages or fertility control in general. Rosemary (*Rosmarinus officinalis* L., Lamiaceae), for example, has known antispasmodic *in vivo* effects on the uterus and is used in tea mixtures for fertility control in Central America (Lemonica et al. (1996).

Gum arabic – Acacia senegal, A. seyal, A. nilotica

The gum ingested with old wine and some food is said to be a remedy in diarrhea (GP PMH 05). Dioscorides in discussing *akakia*, used the juice of the pods to "bind a loose belly" and was also acquainted with the astringent properties of the gum (Berendes, 1902, 1.133). Paulus Aegineta was mixing *akakia* with other herbs for the treatment of dysentery (Adams, 1844/1846/1847, 7.12, 530–531, 534–535). Finally, the gum has been reported as a dysentery remedy from Senegal (Watt and Breyer-Brandwijk, 1962, cited in Maiga et al., 2005).

Published studies on biological effects of the gum have been reviewed in detail by Ali et al. (2009). In particular the effects on the gastrointestinal tract were rated positively; Gum Arabic improved small intestinal absorption of sodium and water in two rat models of induced diarrhea (Wapnir et al., 1997; Codipilly et al., 2006). Other rats recovering from diarrhea induced by cathartic agents gained more weight and had lower fecal output when additionally supplemented with the gum (Teichberg et al., 1999). In general, the *in vivo* data suggest a potential benefit of gum Arabic in the context of diarrhea and malabsorption caused by infection or intestinal dysfunction.

In a multicenter randomized placebo controlled study 144 boys aged 1–36 months suffering from diarrhea received an oral rehydration solution with or without a mixture containing 9% gum Arabic in addition to other non-digestible carbohydrates. However, since no significant group differences in stool volume, duration of diarrhea, duration of hospital stay and need of intravenous rehydration could be observed, the mixture was considered ineffective (Hoekstra et al., 2004).

Ladanum – Cistus incanus subsp. creticus

To heal hemorrhoids accompanied by an anal eczema, 10 dr (*drámi*) ladanum were heated in 4 dr olive oil, spread on a piece of cloth and applied as a poultice on the affected area. This treatment should be continued for 8 days (IM 48.02). According to recipe IM 128.03 exposing the scalp to smoke of ladanum would stop hair loss. In fact, Ladanum was used to treat hair loss by Dioscorides (Berendes, 1902, 1.128) as well as by Paulus Aegineta (Adams, 1844/1846/1847, 3.1.5/8, 339 and 7.3.11, 208). While both of them knew of its applications in liniments or plasters (Adams, 1844/1846/1847, 7.18.8, 578; Berendes, 1902, 1.128), in particular the latter author made specific reference to abscesses, furuncles, or ulcers (Adams, 1844/1846/1847, 4.34.2, 94–95 and 4.39.1, 103). (for synonyms see Inventory of Resins and Gums and **Table 3**)

While no data are available regarding alopecia, a number of studies investigated potential actions of the *Cistus* resinor its compounds that could be of relevance in the treatment of hemorrhoids or eczema. Ladanum from *C. creticus* subsp. *creticus* exerted only a weak antibacterial activity against *Staphylococcus aureus, S. epidermidis,* and *S. hominis* (MIC 2 mg/ml; Demetzos et al., 1999), although its chloroform–methanolic extract showed some inhibitory activity against several bacteria (*Acinetobacter anitratus, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, S. aureus*; Kalpoutzakis et al., 1998). Isolated sclareol and another labdane type diterpene inhibited the growth of the three tested *Staphylococcus* germs with a MIC of 0.1 mg/ml which is 100-fold lower than streptomycin (Demetzos et al., 1999).

Because ladanum is exuded from the glandular hairs of stem and leaf (Hadjikyriakou, 2007, p. 174), bioactivity data on lipophilic compounds of the leaves or corresponding lipophilic extracts should not be disregarded; Pure ethanolic extracts of *C. incanus* subsp. *tauricus* and *C.* aff. *creticus* at a dose of 10 μg/ml showed an antioxidant effects with TEAC values of 3.6 and 2.5, respectively (Trolox: $IC_{50} = 0.63 \pm 0.02$ μg/ml). However, no significant inhibition of the tested inflammatory parameters (IL-6, IL-1β, TNF-α, PGE_2, NF-κB) could be shown (Taila et al., 2008). Similarly, in an anti-inflammatory model, no significant effect on the skin barrier repair could be observed with two labdane diterpenes from the leaves of *C. creticus* subsp. *eriocephalus* (Viv.) Greuter and Burdet which were applied on the back of hairless mice (5% solution, 25 μl/cm^3) previously exposed to UV-B irradiation (Demetzos et al., 2001).

Pine resin – Pinus brutia, P. halepensis, P. nigra subsp. pallasiana

For the therapy of rheumatic conditions and podalgia a poultice is prepared using *píssa mávri* (IM 64.2). This name denotes cooked resin known as *resina nigra* (**Table 2**), the dark-colored quality of rosin (Richter, 1827). The pounded substance is dissolved in hot barley gruel, the mass is then spread on a piece of cloth of the size of the affected area be it the knee, ankle, or hand. Dioscorides mentioned that one of the properties common to all resins was their warming effect (1.91), in particular "burnt" resin was used in plasters or ointments (1.93; Berendes, 1902). Paulus Aegineta mentioned poultices containing "turpentine" for the treatment of rheumatic diseases and gout (Adams, 1844/1846/1847, 3.78, 663, 665). Arnold-Apostolides (1985) recorded several medicinal uses of topical applications of resin and tar from *P. brutia*, *P. nigra* ssp. *pallasiana,* and *P. halepensis* from various places in Cyprus. Similar uses and applications were also reported in another ethnobotanical study conducted in western Anatolia (Turkey) for the resin from *P. nigra* ssp. *pallasiana* and *P. brutia* (Honda et al., 1996).

These poultices act as a rubefacients, irritants, and counter-irritants. They certainly will achieve an increase of blood flow in the area of application, which may favor the absorption of anti-inflammatory secondary metabolites. In this context, an ethyl alcohol extract of turpentine (crude pine resin) from *Pinus nigra* ssp. *pallasiana* showed an *in vivo* anti-nociceptive effect when administered internally thus supporting the existence of such active principles. The extract revealed a dose-dependent analgesic effect in a writhing response in mice induced by acetic acid at a dose of 25 mg/kg. Metamizol at 200 mg/kg and the resin extract at 50 mg/kg showed a comparable effect (Gülçin et al., 2003). However, the pharmacological effects of topically applied preparations can only be of any relevance in arthritic inflammations if the active principle is able to penetrate the skin. In fact, certain of the possibly involved compounds show a topical bioavailability and suggest direct anti-inflammatory effects. The diterpene abietic acid, for example, is one of the major compounds in the non-volatile fraction of the resin of *P. brutia* (Gören et al., 2010). In a TPA-induced mouse ear edema model topically applied abietic acid inhibited the development of swelling in a significant and dose-dependent manner. The highest dose (1 mg/ear) showed an inhibitory effect of 74.8% being in the similar range as the effect of indomethacin (0.5 mg/ear, inhibitory effect approx. 90%; Fernández et al., 2001).

Another study investigated the *in vivo* anti-inflammatory activity of an ethyl-acetate extract from the bark of *P. brutia* in comparison to Pycnogenol®, a standardized bark extract of French maritime pine *Pinus maritima* Lam. In the carrageenan induced rat paw edema model the intraperitoneal administration of each of the preparations inhibited paw-swelling dose-dependently exhibiting significant anti-inflammatory activities at doses of 75 and 100 mg/kg. At these doses *P. brutia* extract also showed a significantly stronger activity than 10 mg/kg of indomethacin (Ince et al., 2009).

Plum gum – Prunus domestica

According to GP PKΘ 06 drinking plum gum dissolved in red wine also dissolves the "stones of dysuria." This recipe, obviously related to the doctrine of signatures and an alternative of GP PME 02 (cf. 3.4.2), was already mentioned by Dioscorides (Berendes, 1902, 1.175) and again by Paulus Aegineta (Adams, 1844/1846/1847, 7.3, 180). From the villages of Cyprus plum gum was reported as a tonic, laxative, and vermifuge in substitution of more expensive gums (Arnold-Apostolides, 1985). No bioactivity data were available for this exudate.

Scammony – Convolvulus scammonia

In IM 41.05 a drink is prepared by mixing 1/3 dr scammony and 1 dr of sugar in some water. This remedy would purge easily expelling all "depositions and poisons." Repeating the therapy after 1 month would keep off "fevers, shivers, and quartan fevers" (malaria caused by *Plasmodium malariae*) for the rest of the year. Although Dioscorides was well acquainted with the purgative effects of scammony [Berendes, 1902, 1.168(171)] and Paulus Aegineta applied the drug in numerous simple and compound remedies for this purpose (Adams, 1844/1846/1847, 7.3, 341 and 7.4, 481), neither of them mentioned fever or malaria. Unlike these two, the physician Alexander of Tralles from Lydia in Asia Minor, who wrote in the sixth century, highlighted the usefulness of scammony in "quartan" and other fevers linking their cause to excessive "bile and phlegm" (Puschmann, 1878/1879, p. 1.384).

Beside *Convolvulus scammonia*, several other species of the Apocynaceae and Convolvulaceae provide some sort of scammony, the resinous exudates obtained from the root. Mexican scammony, for example, is obtained from *Ipomoea orizabensis* (G. Pelletin) Ledeb. ex Steud., Convolvulaceae. This and the former species are recognized to act as laxatives or drastic purgatives due to the resin glycosides present in the exudate (Williamson, 2003; Blaschek et al., 2007). A number of these resin glycosides including scammonins isolated from *Ipomoea tricolor* and *I. orizabensis* were tested against different *S. aureus* strains. Synergistic effects between these compounds were observed, revealing direct bactericidal (MIC values 4–32 μg/ml compared to 0.25 and 64 μg/ml for tetracyclin), resistance disabling or antibiotic potentiating effects (Pereda-Miranda et al., 2006). However, studies investigating the potential of scammony or its compounds against malaria causing pathogens (*Plasmodium* spp.) are lacking.

Terebinth resin – Pistacia atlantica (P. terebinthus)

In recipes KI 9.01/10.01 and IM 89.03 terebinth resin was pounded, mixed with egg yolk and used as a ointment or applied in a poultice for the treatment of infected, ulcerative, or malignant wounds and deep cuts. To ease urination problems the pounded resin was spread on a piece of bread and eaten (IM 149.03). The latter use could be related to bladder stones, some infection, prostate hyperplasia or cancer. Dioscorides in referring to all resins highlighted their diuretic properties, their use in leprosy or in plasters, poultices, and ointments (Berendes, 1902, 1.91). Paulus of Aegina was making copious use of (*rētinē*) *terebinthinē* in topical applications such as plasters or ointments for abscesses, swellings, foul, and spreading ulcers or phagedena (Adams, 1844/1846/1847, 4.41, 4.44, 7.17–7.20). Several references from the Roman Antiquity and the European Renaissance to early modern periods mention the use of the terebinth resin to treat various cancers, tumors, carcinomas and indurations (Hartwell, 1967). Recent accounts on the use of resin from *P. atlantica* are equally limited as such for *P. terebinthus*.

One report from Iraq documents that resin from *Pistacia* trees (*P. atlantica* Desf. and *P. khinjuk* Stocks in Hook.) was applied as an antiseptic to wounds by local inhabitants (Guest and Al-Rawi, 1966, p. 107). Another recipe (IM 137.05) recommends exposing an infant to the smoke of terebinth resin to stop diarrhea. Medicinal smokes are popular in many cultures; the treatment of diarrhea by smoke inhalation has also been reported from Guyana and North America for leaves and stems of two members of the Lauraceae but the understanding of the pharmacodynamics of medicinal smokes is limited (Ben Amar, 2006).

Bioactivity studies investigating the resin of *P. atlantica* are lacking and quantitative analytical data are restricted to the volatile fraction. The crude oleo resin is rich in essential oil, 32.6% were measured in samples from Morocco with α-pinene accounting for 42.9% (Barrero et al., 2005). Corresponding figures for the variety *P. atlantica* var. *mutica* were 22.0 and 70.0%, respectively (Delazar et al., 2004). Different qualities of essential oil of the resin from *P. atlantica* were tested for their antimicrobial potential against seven bacteria (*E. coli, E. cloacae, K. pneumoniae, Xanthomonas maltophilia, P. aeruginosa, Enterococcus faecalis, S. aureus*) and three different strains of *C. albicans*. The MIC for the Gram-positive and Gram-negative bacteria were ≤10 and 10^2 μg/ml, respectively, and for *C. albicans* between 10^3 and 1 mg/ml (Benabderrahmane et al., 2009).

Alpha-pinene isolated from the turpentine oil of *Pinus pinaster* Aiton exhibited a distinctive bioactivity against various isolates of *Actinomadura madurae* with MICs ranging between 3.3 and 5.0 μl/ml (positive control streptomycin: 29.8–50.0 μl/ml) and a minimum microbicidal concentration (MMC) of 10.0 μl/ml (streptomycin: 50.0–75.0 μl/ml). This pathogen is the main cause of actinomycetoma, an infectious skin disease which is able to eventually form a tumor and cause problematic secondary infections (Stojkovic et al., 2008). The same monoterpene compound isolated from the essential oil of *Ugni myricoides* (Kunth) O. Berg, Myrtaceae, was investigated for its anti-hypernociceptive potential in a model of neuropathic pain of the sciatic nerve in mice. Alpha-pinene orally applied at doses of 25 and 50 mg/kg was capable of abolishing the hypernociceptive response with inhibitions of 64 and 89%, respectively. This effect was comparable to gabapentin, a drug clinically used to treat neuropathic pain (70 mg/kg, orally applied: inhibition of 88%; Quintão et al., 2010).

The potential of resin extracts from *P. terebinthus* L. var. *chia* to protect LDL from oxidation was dependent on the polarity of the solvent and ranged between 27.0 and 49.5%. A corresponding extract from Chios mastic gum (*P. lentiscus* L. var. *chia*) showed a distinctly higher protection rate sometimes more than doubling the one achieved with the terebinth resin (Andrikopoulos et al., 2003).

Anti-inflammatory and anti-phospholipase A_2 activities of a methanolic extract from *P. terebinthus* L. galls were investigated in a number of animal models. In TPA- or EEP-induced mouse ear edema models topically applied extract (1 mg/ear) revealed a 58 or 44%, respectively, inhibition of chronic inflammatory swelling. Orally applied extract (200 mg/kg) inhibited paw edema induced by PLA_2 from two different types of venoms by 48–67% (Giner-Larza et al., 2000). In partially identical mouse models the same group tested four different triterpenes from *P. terebinthus* L. galls administered in concentrations between 0.3 and 1 mg/kg topically and 30 mg/kg intraperitoneally (Giner-Larza et al., 2001 and 2002). Two isoforms, masticadienonic acid and masticadienolic acid, were also found in turpentine resin (Blaschek et al., 2007). They both showed significant inhibitory activities in ear and paw edemas. The latter additionally inhibited leukotriene B_4 production in rat polymorphonuclear leukocytes with an IC_{50} of 16.6 μM (apigenin IC_{50} of 13 μM; Giner-Larza et al., 2002).

Evaluation of the reported bioactivity data

Altogether 28 studies were included in this comparison (**Table 6**). Although several further studies were found in the literature search, the unusual high concentrations of the test samples applied in the respective assays eventually questioned the significance of the suggested biological activities and made us abstain from including them. Similar observations were made by Adams et al. (2009) when discussing the results of bioscientific studies in relationship to the uses described in the European Renaissance herbals. This problem was addressed by Gertsch (2009) in a commentary regarding the interpretation of molecular pharmacological data in ethnopharmacological publications. The author argued that much of the problem is related to a misemployment of the concentration-effect paradigm and the overinterpretation of *in vitro* data.

The comparison of the deduced pharmacological functions with matching biological activities reported in the literature revealed an overall fragmentary picture in terms of the available data (**Table 6**). While for cherry gum (*Prunus avium*) no matching data were found, plum gum (*Prunus domestica*), solid storax (*S. officinalis*) and, apart from its essential oil, terebinth resin from *P. atlantica* do not appear to have been explored at all. For the remaining 9 of the 12 substances, which to a certain extent have been the subject of medicinal or pharmacological research, one or more studies were available that reported some sort of matching effects. Frankincese, gum Arabic and pine resin had corresponding bioactivity data for at least half of the deduced pharmacological functions. The majority of the associated data were linked to studies including mainly *in vitro* (11) and animal models (14) only two studies included data from patients. In several of these models, however, isolated compounds, extracts from other plant parts or compound preparations and not the substance mixture were tested. Some of the studies referring to gum Arabic, ladanum, and turpentine resin also reported inactivity, weak, or non-significant effects. Nevertheless, in the great majority of the cases the available studies reported positive results. At least four cases have appropriate data available which allows to draw direct conclusions on the putative pharmacological effectiveness of the respective substance, because the associated *in vivo* studies were actually conducted with the plant exudate or its full extract and showed meaningful results; For the *iatrosophia* use of pine resin in rheumatic conditions and podalgia corresponding evidence is available demonstrating the analgesic potential of a crude resin extract from *P. nigra* subsp. *pallasiana*. Moreover, both from other historical texts as well as ethnobotanical studies various topical applications of pine resins were reported. Overlapping uses with ethnobotanical data "can lend strength and credibility to a lead which originated from a historical text" (Hunt, 1996, p. 92). Ethnomedical uses supporting the findings of animal studies were reported too for applications of gum Arabic as a diarrhea remedy, frankincense from *Boswellia carteri* in the treatment of rheumatic diseases and Sumatra or Siam benzoin as an antiseptic agent.

CONCLUSIONS

Firstly, this study provides a systematic ethnopharmacological approach to analyze largely unedited historical texts and highlights some conceptual issues and specific challenges inherent to such a work. The integration of a diachronic aspect in the identification procedure of the substance names allowed us to show a remarkable continuity of the nomenclature in several cases. Such an approach can also provide important clues about the point of time a drug or its use had been introduced, its origin or the trade routes involved.

The comparison based on the number of UGs in common demonstrates parallels with Dioscorides' *De Materia Medica* in roughly two-thirds of the investigated substances and within those in again roughly two-thirds of the concerned UGs. On the other hand it points to the presence of a relevant share of knowledge not connected with this ancient treatise. This is particularly notable when considering the importance plant exudates already played in antiquity, the comprehensiveness of *De Materia Medica* and the pronounced relationship of this text to the Eastern Mediterranean. When speaking about plant habitats Dioscorides most frequently made references to places in Asia Minor (Turkey), on the Greek mainland, in Egypt and Syria (Riddle, 1985, p. 3). Moreover, Dioscorides' text must have been readily available to Byzantine medical writers, without the need of translations. The reliance on the plant lore of earlier written sources is one of the main characteristics of the Byzantine materia medica (Stannard, 1984, p. 205). Taken together, one would expect an even greater influence of Dioscorides on the *iatrosophia* than the one observed in this study. In this context, the non-Dioscoridean influence suggests a complex pattern of knowledge exchange. Overall, this resulted in an integration of knowledge from so far poorly understood sources.

The application of ethnopharmacological concepts in the analysis of the simple remedies provides rational criteria to estimate the potential therapeutic effectiveness of the plant uses. In the majority of the cases where relevant bioactivity data were available we found a confirmation pointing to the putative validity of many of the other not yet investigated plant uses in the *iatrosophia*. Numerous remedies are labeled as "tried and tested successfully" by their authors and underscore the practical nature of this knowledge. One can assume that many of these remedies have repeatedly undergone selection based on their perceived safety, tolerability and effectiveness. Perhaps they are best described as the distillate of what was found best and most useful from preceding sources, like, for example, remedies of Byzantine medicine in general (Bennett, 2000). Therefore, the *iatrosophia* are a rewarding tool to inspire the development of herbal drugs based on multicomponent extracts but also phytochemical or pharmacological research. If integrated in models for studying the development of herbal medicines in the (Eastern) Mediterranean or Europe these texts offer unique scientific insight.

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