Available online at www.sciencedirect.com
ScienceDirect
Journal of Ethnopharmacology 116 (2008) 469–482
Journal of ETHNO-PHARMACOLOGY
www.elsevier.com/locate/jethpharm

Continuity and change in the Mediterranean medical tradition: *Ruta* spp. (rutaceae) in Hippocratic medicine and present practices

A. Pollio[a], A. De Natale[b], E. Appetiti[c], G. Aliotta[d], A. Touwaide[c,*]

[a] *Dipartimento delle Scienze Biologiche, Sezione di Biologia Vegetale, University "Federico II" of Naples, Via Foria 223, 80139 Naples, Italy*
[b] *Dipartimento Ar.Bo.Pa.Ve, University "Federico II" of Naples, Via Università 100, 80055 Portici (NA), Italy*
[c] *Department of Botany, National Museum of Natural History, Smithsonian Institution, PO Box 37012, Washington, DC 20013-7012, USA*
[d] *Dipartimento di Scienze della Vita, Seconda Università di Napoli, Via Vivaldi, Caserta, Italy*

Received 3 October 2007; received in revised form 20 December 2007; accepted 20 December 2007
Available online 3 January 2008

Abstract

Ethnopharmacological relevance: *Ruta* is a genus of Rutaceae family. It features mainly shrubby plants, native to the Mediterranean region and present in traditional medicine of this region since Antiquity. The three most diffused species *Ruta chalepensis* L., *Ruta graveolens* L., and *Ruta montana* (L.) L., are morphologically poorly differentiated and were probably interchangeably used during Antiquity.
Aim of the study: Hippocratic and contemporary medical applications of the *Ruta* genus in the Mediterranean were compared to check if they result from a continuity of use from the ancient times to nowadays.
Results: *Ruta* spp. was mainly employed in medical preparations by Hippocratic physicians as an abortifacient and emmenagogue. In addition to gynaecological conditions, in several treatises of the *Corpus Hippocraticum* *Ruta* spp. were also recommended as a specific remedy against pulmonary diseases. *Ruta* spp. leaves and also roots and seeds, were administered for internal use by Hippocratic physicians after having been soaked in wine or mixed with honey or its derivatives. Contemporary traditional uses of *Ruta* spp. have been assessed in detail in the whole Mediterranean area.
Conclusion: Nowadays, *Ruta* spp. is used to treat different conditions but, as a general rule, the external uses are preferred as the toxicity of the plant is widely acknowledged.

Keywords: *Corpus Hippocraticum*; Ethnobotany; Traditional plant use; Medicinal plants

1. Introduction

In his recent synthesis on traditional uses of plants in Italy, the ethnobotanist Paolo Maria Guarrera lists 100+ uses for the following species of *Ruta*: *Ruta angustifolia* Pers., *Ruta chalepensis* L., *Ruta corsica* DC., and *Ruta graveolens* L. (Guarrera, 2006). All these species are shrubs, whose bluish-green leaves emit a powerful odour and have a bitter taste. *Ruta* spp. is among the most-used genera in contemporary Italian traditional medicine, economic botany, and folk life. Such possible intensive use is not specific to Italy, but is also documented for other geographical areas of the Mediterranean (Boulos, 1983; Aliotta et al., 1995; San Miguel, 2003) and other continents (Penso, 1983). Significantly, the *Ruta* genus (family Rutaceae) was already abundantly used in the most ancient systematic record of medical practice of the Mediterranean world, the so-called *Corpus Hippocraticum*, that is, the collection of 62 treatises written between the 5th century BCE and the 2nd century CE that were attributed at a certain point of time to Hippocrates (b. 465 – d. between 375 and 350 BCE). In this paper, we compare the Hippocratic and contemporary medical applications of the *Ruta* genus in the Mediterranean basin in order to verify possible similarities and, should they be numerous and significant enough, to check if they result from a continuity of use from the ancient times to nowadays.

* Corresponding author. Tel.: +1 202 633 0967; fax: +1 202 633 0967.
E-mail address: touwaida@si.edu (A. Touwaide).

0378-8741/$ – see front matter © 2008 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.jep.2007.12.013

2. Materials and methods

Outlines of Ruta spp. in ancient literature

The first therapeutic indications of *Ruta* spp. (called *pêganon*; see below for the discussion of the identification) in ancient Greek medical literature can be found in nine Hippocratic treatises, none of which is by Hippocrates himself. The treatises are listed below (English and most commonly used Latin titles) in their plausible chronological order with some information on their origin and contents (Jouanna, 1992) and with references to their original text (Greek) and translation (English or French):

- *Diseases III* (*De morbis III*) (Hippocrates vol. VI, translator Potter, 1988): this work contains the description of a certain number of diseases ordered from head to toe (*a capite ad calcem*). Data are from the so-called School of Cnidus and are usually dated to the middle or end of the 5th century BCE.
- *Diseases II* (*De morbis II*) (Hippocrates vol. V, translator Potter, 1988): the medical information in this treatise, similar to that in *Diseases III* and arranged in the same way, probably dates back to mid-5th century BCE, even though the work itself might have been written later. It is generally believed that the material at the origin of the work comes from the so-called School of Cnidus.
- *Nature of women* (*De natura muliebri*) (Hippocrates vol. VII, translator Littré, 1851): as for the previous treatise, the information contained in this work is of the mid-5th century BCE, although the work itself was written sometime later. The title does not correspond to the contents, but to a first section that was added later. The main part of the work is made of descriptions of diseases, mainly of the womb, as in the previous two.
- *Diseases of women I-II* (*De morbis mulierum I-II*) (Hippocrates vol. VIII, translator Littré, 1853): this is a collection of mid-5th century BCE data.
- *Sterile women* (*De sterilitate mulierum*) (Hippocrates vol. VIII, translator Littré, 1853): the data in this treatise are of the same period and origin as those of the previous, that is, mid-5th century and the supposed School of Cnidus. However, such data have been reorganized and rewritten (possibly several times), perhaps in the 4th century. Both deal with the diseases of women from menarche to pregnancy, childbirth to sterility. They also include lists of remedies.
- *Internal affections* (*De affectionibus interioribus*) (Hippocrates vol. VI, translator Potter, 1988): this work probably comes from the so-called School of Cnidus and might be attributed to the years 400-390 BCE. It is a series of reports on clinical cases ordered without strict head to toe regularity.
- *Ulcers* (*De vulneribus*) (Hippocrates vol. VIII, translator Potter, 1995): a 5th/4th century BCE work, this treatise deals with certain wounds, including ulcers. In the second part, it lists medicines for their treatment.
- *Regimen* (*Regimen*) Hippocrates. et al. (1931)(Hippocrates vol. IV, translator Jones, 1931): though similar in contents to the Hippocratic treatises from the supposed School of Kos, this is a rather independent work, traditionally dated to the 5th or the 4th century BCE.
- *Affections* (*De affectionibus*) (Hippocrates vol. V, translator Potter, 1988): this work, which can probably be dated to the 380s BCE, somewhat resembles other Hippocratic treatises from the Cnidian School, although it also differs substantially from Cnidus teaching.

Data collected from these works were complemented by means of additional medical and scientific literature, listed here in chronological order:

- the *Problems* (*Problêmata*) (Aristotle, books 1–21, translator Hett, 1978): once attributed to Aristotle himself (384–322 BCE), they are now more correctly attributed to his school, being notebooks in which the teachers and students of the school wrote down both the scientific questions they were interested in and the solutions each of them could bring over time. This explains why some questions have been repeatedly treated, sometimes in contradictory ways.
- *De materia medica* (in Greek *peri ulês iatrikês*, Greek text by Wellmann, 1906–1914 and English translation by Beck, 2005) by Dioscorides (1st century CE). Often considered as herbal, the work is in fact an encyclopaedia of the natural products from the three reigns (vegetal, mineral, and animal) used at Dioscorides' time, and known to him, for therapeutic purposes.
- the *Natural History* (*Naturalis Historia*) of the encyclopaedist Pliny (23/24-79 CE). In this all-encompassing work made of 38 books (each devoted to a specific topic), Pliny analysed the medicinal uses of plants in books 20–27 (Jones, 1951, 1956).

Finally, medical and therapeutic elements need to be complemented with botanical information. The main source on this point is the work traditionally known as *Historia plantarum*, but more correctly cited as *Enquiry into plants* (1916–1926), by the so-called Father of Botany, Theophrastus (387–278 BCE), as well as another work by the same author, *De causis plantarum* (1976–1990).

As for data on contemporary uses of *Ruta* spp., they have been collected from modern ethnobotanical literature mentioned in the bibliographical list at the end of the article and summarized in Table 2.

Data on the uses of medicinal plants in the *Corpus Hippocraticum* have been compiled on the basis of the original Greek text by Alain Touwaide and databased by Emanuela Appetiti (ACCESS database). This material has already permitted a first analysis of the uses of plants in the *Corpus Hippocraticum* (Aliotta et al., 2003). Additional work is underway by Alain Touwaide. Traditional medical indications of *Ruta* spp. currently used for therapeutic purposes in Mediterranean area have been collected from the literature listed below and databased by Antonino De Natale (Table 2).

3. Results and discussion

3.1. Identification of pêganon as Ruta spp. in ancient texts

An abundant literature has been devoted to the identification of the plants mentioned in ancient literature according to Linnean binomial nomenclature (Touwaide, 1997, 1998; for the *Corpus Hippocraticum* more specifically, also see Moisan, 1990). The historian of medieval botany and herbalism Jerry Stannard (1961) renewed the question by suggesting to combine philological and phytogeographical data, and to complete these data with the morphological information to be found in *Enquiry into plants* by Theophrastus, which was written approximately a century after the most ancient treatises of the *Corpus Hippocraticum*. More recently, an interdisciplinary research conducted by a team associating philology, botany, and pharmacology (Aliotta et al., 2003) concluded that many authors who have worked on the topic since the early 19th century generally agree on the identification of a large majority of the plants mentioned in the *Corpus Hippocraticum*. Such a conclusion has been confirmed by Buenz et al. (2004), for whom the identification of the plant-based prescriptions in the *Corpus Hippocraticum* – supposedly totalling 257 items – is uncertain for only 11 plants.

Post-Linnean authors are almost unanimous in considering that the Greek phytonym *pêganon* corresponds to the evergreen shrub *Ruta graveolens* L. (André, 1985). The plant is not described in any of the treatises of the *Corpus Hippocraticum*, maybe because it was well known, as its high number of therapeutic uses suggest. The earliest botanical descriptions of it are found in Theophrastus' *Enquiry into plants* (*HP*) and *De causis plantarum* (*CP*). *Ruta* spp. is described sometimes as a typical evergreen undershrub (*HP* 1.3.1 and 1.9.4) and sometimes as a vegetable (*CP* 2.5.3, 6.14.7, 6.14.12, 6.20.1). As an undershrub it can assume a tree habit (*HP* 1.3.4), with dry wood (*HP* 6.7.3) and fleshy leaves (*HP* 1.10.4), which can degenerate (*HP* 1.9.4). Theophrastus also affirms that *Ruta* spp. was a cultivated pot-herb (*HP* 7.4.1), although he is ambiguous about the existence of a wild and a cultivated species: while early in *HP* he affirms that only one species of the plant was known (*HP* 7.4.1), later on in the same treatise he affirms that the cultivated plant differs somewhat from the wild one, this latter having "leaves and stalks smaller and rougher", and being "more pungent and stronger in taste" (*HP* 7.6.1). Similarly in *CP*, when he analyses the difference in fragrance in cultivated and wild species of *Ruta* spp., he affirms that fragrance can become too pungent in wild varieties (*CP* 6.20.1; the text is significant, defining the wild variety as resembling the cultivated one, without clearly distinguishing the characteristics of the wild species). He may have grouped a variety of plants under the name *pêganon* as is shown by his comment that "various plants are called *Ruta* spp." (*HP* 1.10.4). Whatever the case, according to Theophrastus, *Ruta* spp. is propagated through a cutting from a branch (*HP* 2.1.3 and 7.2.1) or from a detached sucker, as well as from other parts (*CP* 1.4.2). Seed propagation is also possible, although, according to Theophrastus, some deny it because it is slow (*HP* 7.2.1). The plant dislikes dung (*HP* 7.5.1) and benefits from saline water as is shown by the fact that it improves when watered with it (*CP* 2.5.3). To paraphrase the Greek text, ashes are applied to its roots to protect them from worms and decomposition (*CP* 3.17.1), and the plant gets hard and dry, but, when it has grown up again after being cut down, it is larger, finer, and juicier (*CP* 3.19.2). When growing "in a fig tree", it is of the best quality as fig juice feeds *Ruta* spp. and provides a remedy to *Ruta* spp. if necessary as it is hot (*CP* 5.6.10). The fragrance of the plant is analysed in some detail in *CP*. It is defined as dry, pungent, and astringent, and considered to occur not in the fruit, but in the other parts of the plant (*CP* 6.14.7). Such fragrance becomes worse when dryness goes too far, and is too pungent and harsh (*CP* 6.14.12). In such case, it is as pungent and untempered as to become disagreeable (*CP* 6.16.7).

In the *Problems* from Aristotle's school, *Ruta* spp. is mainly mentioned as a cultivated and edible plant, often associated with figs and eaten at the beginning of meals, since it was thought valuable against evil-eye (Aristotle, books 1-21, translator Hett, 1978).

Dioscorides in *De Materia Medica* (3.45) does not add any new element to Theophrastus' description. However, he more clearly affirms the existence of a wild species which he considers harsher than the cultivated species and unfit to eat, just like the species growing in mountains. Also he explicitly mentions that the cultivated species growing close to fig trees is more edible.

Pliny gives some information in *Naturalis Historia*, particularly on the cultivation of *Ruta* spp. For him, indeed, it is sown in spring and after the autumn equinox (19.156), grows both from seeds and cuttings (19.121), and blossoms in a bunch (19.100).

In spite of this good general correspondence between the characteristics of *Ruta* spp. in Theophrastus and those of *Ruta graveolens* L., it cannot be excluded that other members of the genus *Ruta* could have been collected and used by Hippocratic physicians time for the same medicinal purposes as *Ruta graveolens* L. The centre of diversity for *Ruta* spp. covers indeed the entire Mediterranean area, with some species endemic only to Corsica and the Canary Islands, and others with a larger distribution not necessarily limited to the Mediterranean area but extending to Africa, Asia, and the American continent. The species with the widest diffusion are *Ruta chalepensis* L. (including *Ruta angustifolia* Pers.) and *Ruta graveolens* L., the latter also being frequently cultivated. *Ruta montana* (L.) L. is also widespread in the Mediterranean area, mainly in dry and rocky habitats (Tutin et al., 1968). The taxonomy of *Ruta* spp. is based on the floral morphology, and species limits are not currently well known, but are the object of a continuing study of species boundaries and biogeographic patterns (Salvo and Conti, in press). *Ruta graveolens* L., *Ruta chalepensis* L. (included the variety *angustifolia*) and *Ruta montana* (L.) L. might have been confused (or associated) by the physicians of the *Corpus Hippocraticum*, particularly because the flower of the three species is neither described nor mentioned as a descriptor in ancient medical texts, and all three species have partially overlapping geographical distribution patterns.

Table 1
Rue (*pêganon*) in Hippocratic treatises

Medicinal uses	Preparation	Other plants in the same medicine	Identification of the plants	Hippocratic treatise
Abortive (potion)	(a) Rue, *mintha*, and *koriannon* with powdered *kedros*or *kuparittos* wood, drunken in wine. (b) Hydromel mixture of roots of rue and *lapathon*, with ashes and shrimps macerated in wine	(a1) *Mintha*; (a2) *koriannon*; (a3) *kedros*; (a4) *kuparittos*. (b) *Lapathon*	(a1) *Mentha* sp., *Mentha spicata* L.; (a2) *Coriandrum sativum* L.; (a3) *Juniperus oxycedrus* L. s.l.; (a4) *Cupressus sempervirens* L. (b) *Rumex conglomeratus* Murray, *Ruta patientia* L.	*Morb. mul.*, I, 78 *Morb. mul.*, I, 91
Angina (throat)	Leaves of rue, *mintha*, *origanon*, *selinon* and *thumbra*, macerated with *nitron* (soda) in *melikraton* (honey and water) and diluted with water and vinegar (external use: gargles)	(1) *Mintha*; (2) *origanon*; (3) *selinon*; (4) *thumbra*	(1) *Mentha* sp., *Mentha spicata* L.; (2) *Origanum* sp., *Origanum vulgare* L. s.l., *Origanum vulgare* L. subsp. *viridulum* (Martin-Donos) Nyman; (3) *Apium graveolens* L., *Petroselinum crispum* (Mill.) A.W. Hill; (4) *Satureja thymbra* L., *Thymbra spicata* L.	*Morb.*, II, 26
Conception (to help to conceive)	After an emetic potion, leaves of rue are kept in the nose and in the ears while the woman sleeps			*Morb. mul.*, I, 75
Delivery of placenta	Potion of rue in black sweet wine, or rue mixed with honey			*Morb. mul.*, I, 45
Delivery of placenta	To eat cooked *krambê* with rue and *linozôstis*	(1) *Krambê*; (2) *linozôstis*	(1) *Brassica cretica* Lam., *Brassica oleracea* L.; (2) *Mercurialis annua* L.	*Morb. mul.*, I, 45
Diet (to dry the body)	Rue is included among the foods that "dry the body"			*Aff.*, 43
Emmenagogue (potion)	Potion of *krithê* straw macerated in water, with oil, powdered rue and *krambê* leaves	(1) *Krithê*; (2) *krambê*	(1) *Hordeum distichon* L., *Hordeum vulgare* L.; (2) *Brassica cretica* Lam., *Brassica oleracea* L.	*Nat. mul.*, 59
Gynecologic affection	Fumigation with compresses made of powdered asphalt from Zakynthos island, hare's hair, rue, dry *koriannon*	*Koriannon*	*Coriandrum sativum* L.	*Morb. mul.*, II, 206
Gynecologic affection	Pessary made of *krambê* and rue	*Krambê*	*Brassica cretica* Lam., *Brassica oleracea* L.	*Morb. mul.*, I, 74 *Nat. mul.*, 109
Hysteria (gynecological affection)	Mixture of sulfur, *kardamômon*, rue and *kuminon aithiopikon* in wine	(1) *Kardamômon*; (2) *kuminon aithiopikon*	(1) *Elettaria cardamomum* (L.) Maton; (2) *Cuminum cyminum* L.	*Nat. mul.*, 68
Inflammation around wounds (poultice, external use)	*Malachê* leaves pounded in wine, with leaves of rue and *origanon chlôrê* mixed with linseeds roasted and powdered	(1) *Malachê;* (2) *origanon chlôrê;* (3) *linon*	(1) *Malva pusilla* Sm. and/or *Malva sylvestris* L.; (2) *Origanum vulgare* L. subsp. *viridulum* (Martin-Donos) Nyman; (3) *Linum usitatissimum* L.	*Vuln.*, 11
Menstrual flows (metrorrhagia)	Seeds of *selinon*, *knidê*, *mêkôn* with barley flour, *elaia* gall, nut gall, *erusimon*, *glêchôn*, mixed legumes, *origanon*, and rue in water	(1) *Selinon*; (2) *knidê*; (3) *mêkôn*; (4) *elaia*; (5) *erusimon*; (6) *glêchôn*; (7) *origanon*	(1) *Apium graveolens* L., *Petroselinum crispum* (Mill.) A.W. Hill; (2) *Urtica dioica* L., *Urtica urens* L., *Urtica pilulifera* L.; (3) *Papaver somniferum* L. or not identified; (4) *Olea europaea* L.; (5) *Sisymbrium officinale* (L.) Scop.; *Sisymbrium polyceratium* L.; (6) *Mentha pulegium* L.; (7) *Origanum* sp., *Origanum vulgare* L. s.l., *Origanum vulgare* L. subsp. *viridulum* (Martin-Donos) Nyman	*Morb. mul.*, II, 113
Peripneumonia (potion)	*Akalêphê*, *aron mega, daukos, napu,* rue, and *silfion juice,* mixed in honey and vinegar and dissolved in water	(1) *Akalêphê*; (2) *aron mega;* (3) *daukos*; (4) *napu*; (5) *silfion*	(1) *Urtica dioica* L., *Urtica urens* L.; (2) *Arum italicum* Mill. s.l., *Arum maculatum* L.; (3) *Athamanta cretensis* L., *Malabaila aurea* (Sibth. et Sm.) Boiss.; (4) *Brassica nigra* (L.) W.D.J. Koch, *Sinapis alba* L. s.l.; (5) unknown (*Ferula tingitana* L.?)	*Morb.* III, 15
Phthisis (7, 196, 17)	Rue, *mintha*, *koriannon*, fresh *mêkôn*, *ôkimon*, *fakos*, juice of *roê glukeiê* and *roê oinôdês* macerated in a mixture of black sweet wine and water and mixed with *orobos* flour, poultice of *krithê* and grated goat's cheese	(1) *Selinon*; (2) *anêthon*; (3) *mintha*; (4) *koriannon*; (5) *mêkôn*; (6) *ôkimon*; (7) *fakos*; (8) *roê glukeiê* and r*oê oinôdês*; (9) *orobos*; (10) *krithê*	(1) *Apium graveolens* L., *Petroselinum crispum* (Mill.) A.W. Hill; (2) *Anethum graveolens* L.; (3) *Mentha* sp., *Mentha spicata* L.; (4) *Coriandrum sativum* L.;(5) *Papaver somniferum* L. or not identified; (6) *Ocimum basilicum* L.; (7) *Lens culinaris* Medik.; (8) *Punica granatum* L.; (9) *Vicia ervilia* (L.) Willd.; (10) *Hordeum distichon* L., *Hordeum vulgare* L.	*Aff. int.*, 12
Phthisis (larynx)	Rue is among the few pot-herbs included in this alimentary regimen			*Morb.*, II, 50
Pleurisy (peripneumonie)	Rue, *thumbra*, *elelisfakon*, *origanon* in wine	(1) *Elelisfakon*; (2) *origanon*; (3) *thumbra*	(1) *Salvia* sp. pl.; (2) *Origanum* sp., *Origanum vulgare* L. s.l., *Origanum vulgare* L. subsp. *viridulum* (Martin-Donos) Nyman; (3) *Satureja thymbra* L., *Thymbra spicata* L.	*Morb.*, II, 47
Post partum affection	Potion of powdered seeds of *krêthmon*, *seseli*and rue, in wine	(1) *Krêthmon*; (2) *seseli*	(1) *Crithmum maritimum* L.; (2) *Molopospermum peleponnesiacum* (L.) Koch, *Tordylium officinale* L.	*Morb. mul.*, I, 78
Post partum affection	Rue in wine is quoted among other remedies for this affection			*Ster.*, 234
Post-partum fever	Soup of rue flour			*Morb. mul.*, I, 35
Pregnancy (problems)	Sulfur, rue, *kardamômon*, and *kuminon aithiopikon* powdered and dissolved in wine	(1) *Kardamômon*; (2) *kuminon aithiopikon*	(1) *Elettaria cardamomum* (L.) Maton; (2) *Cuminum cyminum* L.	*Morb. mul.*, I, 34
Pulmonary apoplexy	*Elelisfakon*, *thumbra*, *origanon*, *uperikon*and rue mixed with barley flour in sweet wine	(1) *Elelisfakon*; (2) *origanon*; (3) *thumbra*; (4) *uperikon*	(1) *Salvia* sp. pl.; (2) *Origanum* sp., *Origanum vulgare* L. s.l., *Origanum vulgare* L. subsp. *viridulum* (Martin-Donos) Nyman; (3) *Satureja thymbra* L., *Thymbra spicata* L.; (4) *Hypericum coris* L., *Hypericum empetrifolium* Willd., *Hypericum triquetrifolium* Turra	*Morb.*, II, 64
Spleen affections	Diet			*Aff. int.*, 30

Table 1 (*Continued*)

Medicinal uses	Preparation	Other plants in the same medicine	Identification of the plants	Hippocratic treatise
Uterin *erusipelas* (inflammation)	Leaves of *aktê* boiled with rue (or *origanon* or *thumbra*)	(1) *Aktê* (2. *origanon* or 3. *thumbra*)	(1) *Sambucus ebulus* L., *Sambucus nigra* L.; (2. *Origanum* sp., *Origanum vulgare* L. s.l., *Origanum vulgare* L. subsp. *viridulum* (Martin-Donos) Nyman; 3. *Satureja thymbra* L., *Thymbra spicata* L.)	*Morb. mul.*, II, 174 bis
Uterine affections	Rue leaves and seeds are included in potions useful against uterine affections			*Nat. mul.*, 32
Uterine suffocation	*Agnos* and *glukusidê* seeds, or *abrotonon* or *panakes*, *ammôniakon*, rue, juice of *mêkônion upnôtikon*, all in wine water of rue (maceration) is quoted among other remedies for this affection	(1) *Agnos*; (2) *glukusidê*; (3) *abrotonon*; (4) *panakes*; (5) *ammôniakon*; (6) *mêkôn*	(1) *Vitex agnus-castus* L.; (2) *Paeonia officinalis* L.; (3) *Artemisia arborescens* L.; (4) *Opopanax chironium* (L.) Koch, *Echinophora tenuifolia* L., *Ferulago campestris* (Besser) Grec.; (5) *Ferula orientalis* L.; *Dorema ammoniacum* D. Don; (6) *Papaver somniferum* L. or not identified	*Morb. mul.*, II, 201
Uterus hardening	Cataplasmata made with a decoction of barley or wheat flour with rue			*Morb. mul.*, II, 161
Uterus shifting	Fumigation of *kupeiros*, *kalamos*; *schoinos murepsikê*; *kardamômon*; *kuminon aithiopikon*; *anêson*; *uperikon*; *marathon* and dried rue in white, very odorous and astringent wine	(1) *Kupeiros*; (2) *kalamos*; (3) *schoinos murepsikê*; (4) *kardamômon*; (5) *kuminon aithiopikon*; (6) *anêson*; (7) *uperikon*; (8) *marathon*	(1) *Cyperus longus* L., *Cyperus rotundus* L.; (2) (uncertain) *Acorus calamus* L.; (3) *Andropogon schoenanthus* L., *Cymbopogon nardus* (L.) Rendle; (4) *Elettaria cardamomum* (L.) Maton; (5) *Cuminum cyminum* L.; (6) *Pimpinella anisum* L.; (7) *Hypericum coris* L., *Hypericum empetrifolium* Willd., *Hypericum triquetrifolium* Turra; (8) *Foeniculum vulgare* Mill.	*Morb. mul.*, II, 133

3.2. Therapeutic uses of Ruta spp. in the Corpus Hippocraticum

3.2.1. Therapeutic indications

The several therapeutic uses of *pêganon* in the Hippocratic treatises listed above are presented in Table 1 and can be summarized as follows. *Ruta* spp. was prescribed to treat pulmonary diseases (*Morb. III*, 15 and *Morb. II* 47 and 64), included *phthisis* (*Aff. Int.*,12; *Morb. II*, 50), which might correspond at least in part to modern tuberculosis (Stannard, 1961). *Ruta* spp. draughts were also used as a gargle against throat angina (*Morb II*, 26), and to reduce a swelling of the spleen, which might be one of the symptoms of malaria (*Aff. Int.*, 30). *Ruta* spp. is also included among the herbs employed externally to cure wounds (*Vuln.*, 11).

The major number of therapeutic uses of *Ruta* spp. is in the field of gynaecology. *Ruta* spp. was mainly used for the treatment of various ailments of the womb, which are not necessarily well identified. *Usteria*, for example, which does not correspond by any means to the process described by this term in modern neuropsychiatry, was considered to be a move of the uterus within the female body. In so doing, it could disturb respiration, provoking the so-called *uterine suffocation*, as well as other vital functions. It seems reasonable to consider that the term was a generic one to designate any kind of uterine condition (Potter, 1990). *Ruta* spp. was also prescribed for menses disturbance, be it their regulation, amenorrhea or excess. It was administered both as an abortive and to help conception. It was prescribed to treat all the possible disturbances during pregnancy, during the delivery, to expel the placenta, and against puerperal fever.

The use of *Ruta* spp. for different, and sometimes opposite, gynaecological conditions might result from the fact that the *Corpus Hippocraticum* is a collection of treatises from different times, locations, and also methodological approaches to pharmacological treatment of disease. There were mainly two ways to treat disease: by administering medicines counteracting disease mechanisms according to the principle *contraria contrariis* (principle of contrary) or by imitating disease mechanisms according to *similia similibus* (principle of similarity). In both cases, medicines were credited with the role of restoring the right balance of the physiological components of the body, which, in the specific case of the Hippocratic system(s) were the four humours: blood, phlegm, yellow bile and black bile. As *Ruta* spp. was credited with hot and dry properties, it could be used either to treat inflammations (heat against heat; principle of similarity) or to reduce any excess of fluids in the body (heat against moisture and cold; principle of contrary).

It might be worth mentioning that the name *pêganon* has been interpreted by philologists as deriving from a Greek root of which the verb *pêgnumi* is another derivative (André, 1985). Yet the root and, hence, the verb derived from it, mean *to flow* or *to make flow*, something that might refer to the use of *Ruta* spp. as an abortifacient. If so, the very name of the plant might have been produced on the basis of its use according to the principle of contrary (*contraria contrariis*). The heat with which *Ruta* spp. was credited was applied to provoke an elimination

Table 2
Modern phytotherapeutic uses of *Ruta* spp. in the Mediterranean area (countries are in alphabetical order)

Country	Medicinal uses	Preparation	Species	Part(s) used	Literature
Algeria	Anti-helmintic; circulatory system affection; digestive; mental disorders; poisoning	Not indicated	*R. c.*	Whole plant	MEDUSA
	Abortive; genital system disorders (*emmenagogue*)	Not indicated	*R. g.*		Trotter, 1915
	Anti-helmintic, digestive, general malaise, mental disorders, pain killer (*antispasmodic, headaches, rubefiant*)	Not indicated	*R. m.*	Leaves, young leaves, flower tips, flower buds	MEDUSA
Bulgaria	Abortive; anti-inflammatory; anti-helmintic; sedative	Maceration	*R. g.*	Aerial parts	Leporatti and Ivancheva (2003)
Cyprus	Anti-helmintic (*helminthiasis*); diarrhoea; dropsy; eye affection (*swollen and inflamed eye*); insect bite; headache; mental disorders; pain killer (*intestine ache, teeth*); poisoning (*antidote*); respiratory system affections (*coughs and cold*); skin affection (*paronychia, ringworm, scabies*); snake bite. *Rare uses*: plague; profilactic in cholera; tonic	External; internal	*R. c.*	Leaves, root, seed, tip of shoot	Lardos (2006)
	Injuries and wounds, mental disorders	Not indicated	*R. c.*	Leafy stems, stems	MEDUSA
Greece	(1) Abortive; (2) antiseptic; (3) pain killer (*headache*); (4) pregnancy/birth; skin affection (5. *eczema*, 6. *disorders*)	(1) Plant juice; (2) and (3) powdered leaves and flowers in strong vinegar on the head to cure headache; (4) and (5) infusion mixed with red wine; (6) powdered leaves and flowers in raki and alcohol to rub the body cures flu	*R. c.*	leaves, flower tips	MEDUSA
	Abortive; genito-urinary system disorders (*prostate*); mental disorders (*anti-convulsive*); poisoning, sedative. *Rare uses*: obesity	Infusion	*R. g.*	Aerial parts	Hanlidou et al. (2004)
Israel	Sedative (*pacifying children*)	Not indicated	*R.*	Branches	Lev and Amar (2000)
	Genito-urinary system disorders; mental disorders (*nervous pain*); pain killer (*disorders muscular-skeletal system*); respiratory system affections. *Rare uses*: system disorders; sensory disorders	Not indicated	*R. c.*	Leaves	MEDUSA
	(1) Ear affection; (2) eye affection; (3) mental disorders (*nervous system*); (4) pain killer (*arthritic pains*, *back ache*); (5) poisoning, (6) skin affection	(1), (2), (4) and (6) leaves and stems are put in glass bottle. Bottle is then filled with olive oil, put in sunny location for 15 days and then applied externally to affected areas; (3) and (5) an infusion is prepared from 100 g in 1 l of water and taken internally, 15–20 cc, 1–2 times/day	*R. c.*	Leaves, stems	Said et al. (2002)
Italy	Pain-killer	Poultice prepared with *Allium sativum* L., *Ruta* sp., *Mentha* spp., *Artemisia* spp. on the wrist	*R.*	Whole plant	Cirelli (1853), Jamalio (1918)
	Rare uses: tertian and quartan ferver	*Ruta* sp., *Mentha* spp., *Artemisia* spp. juice drunken (potion)			
	Injuries and wounds; skin affections (*burns, sores*)	Honeycomb wax, olive oil, *Ruta* sp., vergin animal fat	*R.*		De Martino (1959)
	Anti-helmintic	*Ruta* sp. and incense cooked in oil and topically applied	*R.*	Whole plant	Nardi (1978), Jamalio (1918)
	(1) Abortive; (2) injuries and wounds (*heal cuts*); (3) to relieve sciatic pains	(1) Infusion; (2) and (3) cataplasmata	*R. c.*	Leaves	Galt and Galt (1978)
	(1) Anti-helmintic, (2) injuries and wounds (*lenitive and resolvent for tumefactions, haematomas and bruises*), (3) pain killer (*rheumatic pains*). *Rare uses*: renal lithiasis and stinking urine	(1a) Squeeze fresh material and take juice orally; (1b). smell fresh plant; (2) fresh or dry, prepare decoction and use liquid for compresses; (3) fresh, mash and apply to anus fresh, prepare decoction and take orally	*R. c.*	Aerial parts	Amico and Sorce (1997)
	Digestive; pain killer (*anti-rheumatic*)	(1) Poultice, external use; (2) infusion	*R. c.*	Roots, branches	Ballero et al. (1994)
Italy	(1) Anti-helmintic; (2) digestive	(1a) Decoction used to prepare clysteres; (1b) crushed plant for cataplasmata (external use); (1c) external application of *Ruta chalepensis* L. leaves and *Allium sativum* L. bulbils; (2) leaves chewed	*R. c.*	Leaves	Chiovenda-Bensi (1960)
	Anti-helmintic	Decoction with milk	*R. c.*	Leaves	Catanzaro (1970)
	Anti-helmintic. *Rare uses*: insect bites	Decoction (sometimes with *Allium sativum* L.) external application	*R. c.*	Aerial parts leaves	Guarrera et al. (2005b)
	Repellent and insecticide (*remove mosquitos and other insects*)	Infusion of leaves picked in spring was rubbed vigorously on to the skin	*R. c.*	Leaves	Guarrera (1999)
	Anti-inflammatory; antiseptic	The healer chews on fresh leaves, then breathes on the eyes of patient affected by conjunctivitis or other eye infections	*R. c.*	Leaves	Palmese et al. (2001)
	Digestive; aperient	Infusion, aromatised grappa	*R. c.*	Aerial parts	Pieroni (2000)
	(1) Anti-helmintic (*helminthiasis*); (2) pain killer (*toothache*, *pain reliever*)	(1) Leaves decoction; (2) direct application	*R. g.*	1. Leaves, 2. branches	Ballero et al. (2001)
	(1) Anti-helmintic (*for children*); pain killer (2. *intestine ache*, 3. *stomach ache*)	(1a) Juice of Ruta *graveolens* L. and *Mentha* spp.; (1b) leaves in salads or soup; (2) cataplasmata (external use); (3) decoction	*R. g.*	Leaves	Bandini (1961)
	(1) Anti-helmintic; (2) pain killer (*anti-rheumatic*)	(1a) Cataplasmata (external use) on the abdomen; (1b) decoction; (2a) tincture 1: dried leaves of *Ruta graveolens* L., and orange, seeds of mustard macerated in alcohol; (2b) tincture 2: *Ruta graveolens* L. leaves, mustard seeds, *Juglans regia* L. nuts and dried leaves of *Calamintha nepeta* (L.) Savi s.l. macerated in alcohol	*R. g.*	Whole plant, leaves	Barbagallo et al. (1979)

	Pain killer (1. *analgesic*, 2. *anti-rheumatic*, 3. *head-ache*); 4. respiratory system affections, 5. skin affection (*scabies*)	(1) Decoction or fresh juice; (2) fumigation of decoction, cooked with *Ruta graveolens* L. and *Sambucus ebulus* L.; (2) and (4) oleolite to rub the painful parts; (3) rubbed on the head; (5) fried in pork fat and sulfur	*R. g.*	Leaves, tips	Barone (1963)
	Rare uses: bladder affections	Decoction in black wine, with *Ruta graveolens* L., *Mentha* sp., *Rubus* sp.			
	Anti-inflammatory	Plant crushed and used to prepare cataplasmata (external use)	*R. g.*	Flowers	Cavara (1954)
	Anti-helmintic	Cataplasmata made with *Ruta graveolens* L., *Mentha* spp., *Artemisia* spp. cooked in vinegar. poultice prepared with *Allium sativum* L., *Ruta graveolens* L., *Mentha* spp., *Artemisia* spp. (external use)	*R. g.*	flower tips, leaves	Cirelli (1853)
	Digestive; circulatory system affection (*hypotensive*)	Medicated wine and the tincture	*R. g.*	Whole fresh plant	De Feo et al. (1992b)
	Anti-helmintic (*escharotic*, *vermifuge*); antiseptic (*antiputrefactive*); digestive; genital system disorders (*emmenotropic*); injuries and wounds; pain killer (*caries*, *decongestant and antispasmodic for injured parts or for arthritic pains*, *toothaches*)	Decoction of aerial parts (internal use), emmenotropic, digestive, antiputrefactive. Infusion of leaves with tops of *Origanum vulgare* L. and *Mentha suaveolens* Ehrh. (external use), vermifuge. Decoction of leaves (external use), decongestant and antispasmodic for injured parts or for arthritic pains. Juice of fresh plant (external use), escharotic. Crushed leaves with bulbs of *Allium sativum* L. and aerial parts of *Petroselinum crispum* (Mill.) A.W. Hill (external use), vulnerary. Crushed leaves with coarse salt (external use), toothaches, caries. Eating fresh fruit, as anti-rheumatic	*R. g.*	Aerial parts, leaves	De Feo et al. (1992a)
	(1) Abortive; (2) anti-helmintic; (3) aperient; (4) circulatory system affection (*peripheric vasodilatator*); pain killer (5. *anti-rheumatic*, 6. *headache accompanied by vertigo*) *externally* (7. *anti-rheumatic*); poisoning (8. *antiparasitic*, 9. *antidote for poisoning*); skin affection *externally:* (10. *to halt subcutaneous bleeding*, 11. *decongestant*). *Rare uses*: (12) mild laxative; (13) tonic	(1), (2), (4), (7), (9), (10), (11) decoction of aerial part; (3), (5), (6), (12), (13) infusion of aerial part; (8) powdered dried leaves	*R. g.*	Aerial parts, leaves	De Feo and Senatore (1993)
	Pain killer (*anti-rheumatic*)	Oleolite (the plant fried in olive oil and topically applied)	*R. g.*	Entire plant	De Natale and Pollio (2007)
	Anti-helmintic	Eaten in salad; chewed in small quantities with sugar and honey	*R. g.*	Leaves	Guarrera et al. (2005a)
	(1) Anti-helmintic (*children*); (2) repellent and insecticide	(1a) Decoction of leaves, often with olive oil and *Allium sativum* L.; (1b) the juice of the crushed plant in water or leaflets on bread; (1c) crushed plant was hung around a child's neck or a maceration of the plant in aniseed liquid inhaled; (1d) crushed plant rubbed on the stomach, temples and palms of the hands; (1e) pancakes of flour, water and *Ruta graveolens* L.; (1f) made to sniff the leaves; (2) fresh plant; decoction of aerial part rubbed on scalps afflicted with lice	*R. g.*	Leaves, aerial parts	Guarrera (1999)
	(1) Anti-helmintic, (2) pain killer	(1) Decoction; (2) macerated in olive oil, filtered and rubbed on	*R. g.*	Leaves	Leporatti and Corradi (2001)
	(1) Anti-helmintic; (2) against intestinal pains; (3) to heal the "*mal d'arco*"	(1) Cold infusion (crushed with or without *Allium sativum* L. bulbs, after having removed the internal part of the bulb); (2) crushed in a cold infusion; (3) ritual object	*R. g.*	aerial parts	Pieroni et al. (2002)
	(1) Skin affection (*anti-acne*); (2) to heal muscular pains, and as anti-diaphoretic	(1) Poultice made by crushing the leaves in a mortar; (2) macerated in alcohol, in external applications	*R. g.*	Leaves	Pieroni et al. (2004a)
	Pain killer (*muscular pains*)	Oleolite (plant is fried in olive oil) in topical application; enolite	*R. g.*	Aerial parts	Pieroni et al. (2004b)
	Anti-helmintic	Used very sparely in salad or chewed in small quantities with sugar and honey	*R. g.*	Small leaves	Pieroni et al. (2005)
	Digestive; anti-helmintic; pain killer (*muscular pains*)	Not indicated	*R. g.*	Aerial parts	Pieroni and Quave (2005)
	Anti-inflammatory; resolutive; pain killer (*external analgesic)*	Plant warmed up or fried in olive oil or beef marrow. Oil then massaged against muscular pain, in case of rheumatism or sciatica. Fresh leaves mashed and macerated 40 h in alcohol or boiled and used as a poultice against pains	*R. g.*	LEAVES	Scherrer et al., 2004
	(1) Anti-helmintic; (2) anti-inflammatory; (3) injuries and wounds; (4) pain killer (*anti-rheumatic*)	(1) and (2) decoction; (3) poultice on wounds; (4a) massages; (4b) applied to the abdomen	*R. g.*	Flower tips, leaves	Uncini Manganelli and Tomei (1999)
Jordan	Digestive (*indigestion*); mental disorders (*nervosity*); pain killer (*arthritis*). *Rare uses*: general weakness	Not indicated	*R. c.*	Shoots	Abu-Irmaileh and Afifi (2003)
	Internal desease (*antidiabetic*); pain killer (*antispasmodic*); scorpion bite; sudorific	Not indicated	*R. c.*	Leaves	Aburjai et al. (2007)
Libya	Sedative (*local pacifying children*)	Not indicated	*R.*	Branches	Lev and Amar (2002)
	Tonic (*for new-born babies*)	Potion	*R.*	Aerial parts	Trotter (1915)
	Pain killer (*anti-rheumatic*)	Oleolite	*R. c.*		Chiovenda (1937)
	Injuries and wounds (*haematomas*); pain killer (*rheumatic pains*)	Oleolite	*R.c.*	Leaves, seeds	Trotter (1915)

Table 2 (*Continued*)

Country	Medicinal uses	Preparation	Species	Part(s) used	Literature
Morocco	Ear affection (*pain*)	Topical use (washing)	*R.c.*	Leaves	El-Hilaly et al. (2003)
	(1) Ear infection (*pain*); (2) diuretic; anti-helmintic; pain killer (*rheumatic pains*); (3) headache	(1) Mixed with olive oil (topic use); (2) infusion; (3) lives applied externally	*R. m.*	Aerial parts	Merzouki et al. (2000)
	Genito-urinary system disorders; poisonings; mental disorders; respiratory system disorders. *Rare uses*: religious uses antifertility agents abortifacients ritual	Oil, fumigations, infusions, drinkable decoctions, injections, sometimes in association with *Cannabis sativa* L.	*R. m.*	Whole plant	MEDUSA
Near East	Circulatory system affection (*haemorrhoids*); eye affections; genito-urinary system disorders (*sexual diseases*); injuries and wounds (*wounds*); mental disorders (*psychiatric, epilepsy*); pain killer (*stomach*, *intestine*, *teeth*); poisoning (*animals bites and poisons*); skin affections (*burns*, *diseases*, *inflammations*) *Rare uses*: heat, internal diseases	Not indicated	*R.*		Lev (2002)
Palestine	Pain killer (*rheumatism*, *arthritis*)	Not indicated	*R. c.*		Ali-Shtayeh et al. (2000)
Portugal	Internal desease (*antihypercholesterolaemic*); diarrhoea; against intestinal pains	Infusion	*R. c.*	Aerial parts	Novais et al. (2004)
	Rare uses: antifungal in plants	Direct use, Topical	*R. c.*	Stems	Agelet and Vallès (2003)
	Anti-helmintic. *Rare uses*: against bloating	Fresh plant	*R. c.*	Aerial parts	Blanco (1996)
	Sedative	Infusion	*R. c.*, *R. g.*	Aerial parts	Bonet et al. (1999)
	(1) Antiseptic (*antigangrenous*); (2) antiseptic (*post-labour*); (3) antiseptic (*eye infection*), injuries and wounds (*haematomas*)	(1) Embrocation; (2) enema; (3) tisane	*R. c.*	Aerial parts	Bonet and Valles (2007)
	(1) Abortive; (2) ear affections; (3) eye affections; (4) injuries and wounds (*wounds*); pain killer (5., 6. *intestine ache, menstrual ache,* 7. *stomach ache*). *Rare uses*: to strengthen the hairs	(1) Decoction; (2) fumigation; (3),(4), (7) infusion; (6) oleolite rubbed on the skin; (5) cataplasmata locally applied	*R. g.*	(1), (2), (4), (5), (6) aerial parts; (7) dried leaves; (3) flowers	Fresquet Febrer et al. (2001)
Spain	(1) Antiseptic; (2) gastro-intestinal affection (*stomach ache, diarrhoea, digestive*); (3) haemorrhoids; (4) pain killer; (5) respiratory system affection (*sore throat*); (6) sedative. *Rare uses*: (7) head swimming	(1) liniment; (2), (6), (7) decoction; (3) pomade; (4) poultice, lotion; (5) poultice	*R. c.*	Aerial parts	Rigat et al. (2007)
	(1) Abortive; anti-helmintic (2. *intestinal worms in children*, 3. *vermifuge*); (4) aperient; circulatory system affection (5. a*gainst rhagades*; 6. *varicose veins, haemorrhoids*); (7) digestive; (8) ear affections; (9) eye affections; (10) genito-urinary system disorders (*inflammation of male and female genitalia*); injuries and wounds (11. *ulcers*; 12. *wounds, swellings*); pain killer (13. *headache*, 14. and 15. *rheumatisms and pains*, 7. *stomach ache*, 16. *toothache*); (17) respiratory system affection; skin affection (18. *acne*, 19. burnings; 20. *pimples*, *nail infections*; 21. *skin parasites*, *lices*; 22. *warts, eczema*); sedative (23. *sedative*, 24. *weaning of babies*)	(1) concentrated infusion; (2) infusion alone or with *Mentha x piperita* L., *Thymus mastichina* L. and *Thymus zygis* L.; (3) rubbed on the stomach, fresh or with oil, bread dough; (4) infusion, alcoholic beverages; (4), (5), and (24) local application on the breast; (6) infusion; (7) macerated in alcoholic beverages. Oleolite rubbed on the skin; (8) oil from the fried plant locally applied; (9), (10) decoction; (11) infusion or decoction also with other plants; (12) and (19) external application of fresh plant or decoctions, or oleolites; (13) poultice with *Aloysia citriodora* Palau, or a twin held in the hairs, sniffing the vapours of the boiled plant; (14) alcoholic tincture, or the plant fried in lard, bath in *Ruta* sp. decoction, application of a poultice; (15) oil extract rubbed on the skin; (16) part of the plant chewed, mouth washes with the juice of the plant, or with infusion or decoction in water or wine, oil from the fried plant rubbed on the teeth with a cotton plug, *Ruta* sp., together with *Crocus longiflorus* Raf. and *Allium sativum* L. held in a bag around the neck;	*R. c.* *R. m.*	From (1) to (14) and from (17) to (31) aerial parts; (15) leaves, floral buds; (16) shoots, roots	San Miguel (2003)
	Rare uses: (25) against diarrhea; (26) blood tonic; (27) delivery aid; (28) delivery of placenta; (29) fevers; (30) fevers of children; (31) to strengthen the hairs; (32) tonic, reconstituent	(17) local application or eaten with honey, wine or milk; (18) with *Thymus vulgaris* L. and *Rosmarinus officinalis* L. mixed in alcohol and locally applied; (20) fresh or boiled locally applied; (21) locally applied; (22) rubbing of the plant, applied with oil; (23) infusion at low concentration (25), (26), and (28) infusion; (27) infusion in small doses or oleolite rubbed on the womb; (29) infusion or decoction; (30) poultice with *Medicago sativa* L., sardines, *Nicotiana tabacum* L., snails, yeast and vinegar applied to feet; (31) locally applied; (32) infusion, with boiled water or with hot chocolate, rubbed on arms and legs with oil, *Allium sativum* L. or lard	*R. g.*		
	Abortive, circulatory system affection (vasoregulator)	Decoction	*R. c.*	Leaves, fruits	Vázquez et al. (1997)

Tunisia	Abortive, antiseptic (*infections/infestations*), ear affections (*otitis*), genito-urinary system disorders, pain killer (*muscular disorders – skeletal system, rheumatism*), skin affection	Not indicated	*R. c.*	Leaves	MEDUSA
Turkey	Pain killer (*pain in stomach*)	Mashed, mixed with a bit of virgin oil and coconut; eat the fresh aerial parts	*R. g.*	aerial parts	Uzun et al. (2004)
	(1) Skin affection (*psoriasis*). *Rare uses*: (2) malaria	(1), (2) maceration in olive oil	*R. g.*	(1) Leaves, (2) flowers	Kultur (2007)
	(1) Anti-helmintic (*for babies*); (2) aperient; (3) digestive (*flatulence of babies*); (4) genital system disorders (*emmenagogue*); pain killer (5. *pain killer*, 6. *stomach ache*); (7) sedative (*to relax babies*); (8) respiratory system affections (*coughs*); (9) stomach ache (*severe pains*); skin affection (10. *against heat rashes of babies*, 1. and 11. *carminative*, 3. *boils*)	(1) and (14) leaves boiled in olive oil exposed to sun for 2–3 days and external use; (2), (4) and (15) internal use: tea, oil or tablet; external use: relaxant, to cure rheumatic pains and stomach aches; (3) oil in external use; (5) mush (dried foodstuff made chiefly of curds and flour), mixed and cooked with dry or fresh leaves of *Ruta* sp., some vinegar and salt; (6) smashed *Ruta* sp. leaves eaten in small quantities; (7) poultice: leaves of *Ruta* sp. roasted in olive oil with some flour; (8) and (13) ointment made with *Allium sativum* L., black cumin (*Nigella* sp.) seeds pounded mixed with fresh leaves of *Ruta* sp. and roasted in olive oil; (9) infusion; (10) *Ruta* sp. leaves pounded with *Nigella* seeds, nutmeg (*Myristica fragrans* Houtten.) and sugar; (11) see (10)	*R. c.* and *R. g.*	Leaves, seeds	Akalin and Ertuğ (2002–2003)
	Rare uses: (12) palpitation of the heart; (13) croup; (14) on armpits; (15) sudorific	(12) Seeds eaten			

Species: (R.) *Ruta* spp., (R. c.) *Ruta chalepensis* L., (R. g.) *Ruta graveolens* L., (R. m.) *Ruta montana* (L.) L.

of supplementary humidity in the female body resulting from child-bearing.

The uses of *Ruta* spp. in the *Corpus Hippocraticum* changed significantly over time. If we do not take into consideration the gynaecological indications, *Ruta* spp. seems indeed to have mainly been used as a medicine against pulmonary and throat irritations in the most ancient treatises. Later, there is still an indication for a pulmonary disease (*phthisis*), but there are also new ones: wounds and a swelling of the spleen. Also, the dietary properties of *Ruta* spp. are formulated in an abstract and theoretical way (hot and dry). All this suggests not only a possible expansion of the use of the plant, something that might suggest therapeutic experiments, but also an attempt to express the several uses of the plant by means of a theoretical property (i.e. hot or dry) that might account for the several individual applications.

3.2.2. Preparations

Ruta spp. was used entirely (the fresh plant) or in parts, especially the leaves, but also its seeds, and, less frequently, its roots (Table 1). For internal use, *Ruta* spp. was administered after having been soaked in wine or mixed with honey or its derivatives (Table 1).

As for the excipients for internal administration, wine was among the most used in Hippocratic pharmaco-therapy. Several varieties are mentioned, ranging from *rêtinês* (a resin-flavoured wine) to black or white ones. It could be young or old, sweet or dry, perfumed, mixed with water or pure. Wine use was not limited to an excipient, as it was also credited with therapeutic properties and was frequently prescribed in the cure of different diseases and recommended as an *anodynê* – i.e. an analgesic – of very valuable efficacy.

Honey was another excipient. It was used pure or in such derivatives as *melikraton*, a mixture of honey and water, and *oxugluku*, a mixture of vinegar and honey. Just like wine, it was an excipient and a therapeutic substance of its own, particularly used for the treatment of respiratory and gynaecological troubles, as well as for conditions of the skin and eyes (Byl, 1996).

Sometimes Hippocratic medicines were made of several active substances. *Ruta* spp. was mixed with other herbs, the most frequent of which were *koriannon* (*Coriandrum sativum* L.), *kardamōmon* (*Elettaria cardamomum* White et Maton) and *kuminon aithiopikon* (*Cuminum cyminum* L.). All these species are not native to the Greek mainland and arrived probably from Near East. Laskaris (1996) has suggested that these plants are related to ancient healing cults diffused in Crete. Other plants mixed with *Ruta* spp. in Hippocratic prescriptions are *mintha* (*Mentha* sp., *Mentha spicata* L.), *ôkimon* (*Ocimum basilicum* L.), and *origanon* (*Origanum* sp., *Origanum vulgare* L. s.l., *Origanum vulgare* L. subsp. *viridulum* (Martin-Donos) Nyman). All share with *Ruta* spp. the fact of having been credited with hot and dry properties according to the system of the four qualities, four elements of the world, and four humours. The combination of these plants with *Ruta* spp. was probably justified by their common therapeutic action, and their mixture was perhaps aimed at reinforcing such action.

Table 3
Comparison between hippocratic and modern therapeutic uses of rue

		Corpus Hippocraticum	Algeria	Bulgaria	Cyprus	Greece	Israel	Italy	Jordan	Libya	Morocco	Near East	Palestine	Spain	Tunisia	Turkey
conception and pregnancy	abortive	●	●	●		●		●		●				●	●	
	conception (help to conceive)	●														
	delivery of placenta	●														
	post partum affection	●														
	pregnancy/birth					●										
	pregnancy problems	●														
dermatological affections	antiseptic	●							●							
	inflammation around wounds				●			●		●		●		●		
	injuries and wounds					●	●	●				●		●	●	●
	skin affection															
gastrointestinal affections	anti-helmintic		●	●				●	●					●		●
	aperient							●						●		●
	digestive		●					●	●					●		●
	tonic									●						
gynaecological affections	emmenagogue	●	●							●						●
	hysteria	●														
	metrorrhagia	●														
	uterine affections	●														
	uterine erysipelas	●														
	uterine suffocation	●														
	uterus hardening	●														
	uterus shifting	●														
nervous system / sense affections	sedative			●		●	●		●					●		
	mental disorders		●		●	●	●		●		●	●				
	ear affection						●							●	●	
	eye affection						●					●		●		
respiratory system affections	angina (throat)	●														
	peripneumonia	●						●			●			●		
	phthisis	●														
	phthisis (larynx)	●														
	pleurisy	●														
	pulmonary apoplexy	●														
	pulmonary affection						●	●			●			●		●
skeleto-muscular affections	anti-inflammatory							●	●							
	pain killer		●			●	●	●	●	●		●	●	●	●	●
other	circulatory system affection		●					●				●		●		
	diet (to dry the body)	●														
	general malaise		●													
	genito-urinary system disorders		●			●	●	●		●	●	●		●	●	●
	repellent and insecticide							●								
	poisoning		●			●	●	●				●				
	spleen affections	●														

3.3. Contemporary traditional uses of Ruta spp.

Available documentation on contemporary traditional uses of *Ruta* spp. in the Mediterranean basin varies from region to region. For Spain and Italy, and, to a lesser extent, Turkey, a conspicuous corpus of ethnopharmacological data is documented, whereas information is scanty and often vague for the rest of contemporary Mediterranean world. However, some common features in the therapeutic uses of *Ruta* spp. can be evidenced.

Leaves are the most frequently used part of the plant, but it is also common to administer the entire aerial parts. Flowers and roots only are used in few unrelated locations, while they are used in association with the leaves for the same conditions elsewhere. Use of seeds has been reported prevalently in Turkey (Akalin and Ertuğ, 2002–2003).

Therapeutic indications cover a wide range of medical conditions affecting almost all parts of human body, even though in many cases they are general and do not refer to any specific part of the body. This is particularly evident for the countries with no recent detailed ethnopharmacological study such as Algeria, Morocco, and Tunisia. In addition, the indications for Eastern Europe (Bulgaria, Cyprus, and Greece) are far from being precise in the current state of research. Focusing on Spain, Italy, and Turkey, it is possible to have a clearer idea of the actual medicinal uses of the plant, although the resulting picture is not homogeneous. In Spain, *Ruta* spp. is mainly prescribed to cure menstrual disorders and as abortifacients, and also against digestive disorders (San Miguel, 2003). Anthielminthic and vermifuge are by far the most common properties throughout Italy, including Sicily and Sardinia. Anti-inflammatory and analgesic properties are second to the previous. A survey carried out among herbalists in 40 provinces of Turkey has revealed that the plant is mainly prescribed as a laxative (Akalin and Ertuğ, 2002–2003), whereas field investigation evidenced that therapeutic indications vary from region to region, and include a wide array of diseases (Table 2).

The most frequent type of preparation for internal use is infusions and/or decoctions of *Ruta* spp. leaves, whereas for external use direct application of fresh leaves or juice is the standard type of administration. Oleolites made by frying *Ruta* spp. leaves in olive oil are frequent in Spain and Italy. They are recommended against rheumatisms. A similar preparation is used in Turkey to prepare a cataplasm against severe cough and croup (Akalin and Ertuğ, 2002–2003).

Ruta spp. is frequently used with other herbs. Complex recipes are rarely described. In Italy and Spain *Ruta* spp. is most frequently associated with members of *Origanum*, *Mentha*, *Nepeta* or *Thymus* genera, and also garlic (*Allium* sp. pl.). Of the two cases of plants being mixed with *Ruta* spp. in Turkey, one includes *Nigella* seeds (Akalin and Ertuğ, 2002–2003). *Nigella*, particularly *Nigella sativa* L., is frequently used in folk recipes in the Near East against numerous conditions, mainly involving the vascular and respiratory systems (Aliotta et al., 2003).

The comparison between the *Corpus Hippocraticum* and modern Mediterranean ethnopharmacology (Table 3) evidences differences not only in the uses, something that led the early-20th century German pharmacognosist Rudolf Schmid (1919) to omit *Ruta* spp. from among the plants of antiquity still used at that time, but also, and perhaps more significantly, in the ways of preparing medicines made of *Ruta* spp.

In the *Corpus Hippocraticum, Ruta* spp. was macerated in, and administered with wine, or mixed with hydromel. In other cases, *Ruta* spp. was pounded, mixed into wine, and immediately drunk (Table 1). Although hot water extracts (both as decoctions and infusions) were used by Hippocratic practitioners, there is no mention of these preparations for *Ruta* spp. By contrast, both infusions and decoctions represent the most diffused way of preparing higher medicinal plants, including *Ruta* spp., in modern Mediterranean ethnopharmacognosy. It is well known that the choice of a solvent influences the chemical composition of the extract, both quantitatively and qualitatively. Although none of the extractants is ideal, wine, considered as a diluted ethanolic solvent, should ensure high rates of extraction of non-polar and polar substances, also at ambient temperature. On the other hand, water extracts, which are carried out at high temperature (>90 °C), could damage thermo-labile compounds (Eloff, 1998). Administering *Ruta* spp. leaves after maceration in wine might ensure the preservation of the major chemical constituents of the plant.

4. Conclusions

Ruta spp. has been constantly present in the Western therapeutic from Hippocratic medicine on. Not only did Dioscorides and Galen (*On the mixtures and properties of simple medicines*) mention it in their major works on materia medica, but also late antique manuals of therapeutics such as the *Medicines from Vegetables and Fruits* by Gargilius Martialis (d. 260 CE) and the Pseudo Apuleius, which was written sometimes in the 4th century CE and circulated widely in the pre-1100 Western world, devoted each a paragraph to the plant. The more typically Western recipe book known as the *Lorscher Book of Medicines*, used sometimes around 800 BC in the Abbey of Lorsch in Carolingian Germany, included it in several prescriptions. In the Arabic world, *Ruta* spp. is present in the major syntheses on materia medica by al Biruni (973–1048 CE), al Ghafiqi (d. ca. 1160 CE) and ibn al Baytar (ca. 1204–1248), as well as in other therapeutic works as those of ibn Butlan (d. 1063 CE [?]) and his contemporary ibn Ridwan (ca 980–1060 CE). After the translation of Arabic medicine into Latin from the late-11th to the 13th century, Arabic pharmacological knowledge was available in the West. *Ruta* spp. appeared in the many versions of the *Tacuinum Sanitatis*, an adaptation of ibn Butlan's work, as well as in the so-called *Circa Instans* and *Book on Simple Medicines* from the Salerno school, which were among the most diffused and influential works on medicinal plants in the Late Middle Ages. With the rediscovery of Greek scientific texts in the Renaissance, the information to be found in Dioscorides' *De materia medica* was again available and abundantly commented on, particularly by Pietro Andrea Mattioli (1501–1577), whose repeated new editions of his commented translation of Dioscorides' treatise contributed to popularize the traditional Greek uses of plants, including *Ruta* spp. New 16th-century herbals such as the *History of Plants* (1542) by Leonhart Fuchs (1501–1566), rooted

in ancient science, expanded on it, and integrated local uses of plants into traditional knowledge, among others *Ruta* spp. At the turn of the 19th–20th centuries, Georg Dragendorf included it in his manual entitled *Die Heilpflanzen der verschiedenen Völker und Zeiten. Ihre Anwendung, wesentlich Bestandtheile und Geschichte. Ein Handbuch für Ärzte, Apotheker, Botaniker und Droguisten* (Stuttgart, 1898), which was a sort of summary of traditional uses.

The medicinal uses of *Ruta* species in the *Corpus Hippocraticum* were preserved at least in part over time. Nevertheless, during the centuries, *Ruta* spp. was prevalently administered against eye affections and different kinds of aches, and as an antidote against poisons and venomous bites by various animals. Also, the plant got an increasingly growing symbolic value. Thanks to its numerous little leaves, it was used to sprinkle the Holy Water and to bless people in the Roman rites of the Catholic Church. Known for this reason as *Herb of grace* (Cleene and Lejeune, 2003), *Ruta* spp. was among the first plants introduced by Europeans in the New World. Heinrich et al. (2006) have suggested that this religious role contributed to promote the therapeutic uses of *Ruta* spp. in Latin America.

The ethnopharmacology of *Ruta* spp. in the Mediterranean area does not seem to have been influenced by the symbology and ritual uses of the plant. *Ruta* spp. was considered by Hippocratic physicians as a remedy mainly suitable for women diseases and, secondarily, as an effective *pharmakon* in the cure of pulmonary affections. Although these indications have remained alive in circum-Mediterranean countries through the centuries, there is now a greater awareness of the potential toxicity of the plant. Current recommended therapeutic indications of *Ruta* spp. are no longer related to the gynaecological sphere, with the exception of the use as an abortifacient. *Ruta* spp. is still used internally in the treatment of pulmonary diseases, and externally as an antihelmintic and antirheumatic (something that constitutes the most frequent uses of the plant). Often it is treated at high temperature before being administered. These current indications seem to suggest that a shift towards a safer application occurred at a certain point in time. If so, this evolution might have been among the factors that contributed to eliminate many of the Hippocratic uses.

References

Abu-Irmaileh, E.B., Afifi, U.F., 2003. Herbal medicine in Jordan with special emphasis on commonly used herbs. Journal of Ethnopharmacology 89, 193–197.

Aburjai, T., Hudaib, M., Tayyem, R., Yousef, M., Qishawi, M., 2007. Ethnopharmacological survey of medicinal herbs in Jordan, the Ajloun Heights region. Journal of Ethnopharmacology 110, 294–304.

Agelet, A., Vallès, J., 2003. Studies on pharmaceutical ethnobotany in the region of Pallars (Pyrenees, Catalonia, Iberian Peninsula). Part II. New or very rare use of previously known medicinal plants. Journal of Ethnopharmacology 84, 211–227.

Akalin, E., Ertuğ, F., 2002-2003. An anatomical and ethnobotanical study on *Ruta* species in Turkey. Journal of Faculty of Pharmacology, Istanbul 35–36, 121–132.

Aliotta, G., Cafiero, G., Oliva, A., Pinto, E., 1995. Ethnobotany of (*Ruta* graveolens L.): an overview. Delpinoa, nuova serie 37–38, 63–72.

Aliotta, G., Piomelli, D., Pollio, A., Touwaide, A., 2003. Le piante medicinali del «Corpus Hippocraticum». Guerini e Associati, Milano, p. 483.

Ali-Shtayeh, M.S., Yaniv, Z., Mahajna, J., 2000. Ethnobotanical survey in the Palestinian area: a classification of the healing. Journal of Ethnopharmacology 73, 221–232.

Amico, E.A., Sorce, E.G., 1997. Medicinal plants and phytotherapy in Mussomeli area (Caltanissetta, Sicily, Italy). Fitoterapia 68, 143–159.

André, J., 1985. Les noms de plantes dans la Rome antique. Belles Lettres, Paris, p. 333.

Aristotle. Problems. Books 1-21, Greek text and English translation by W.S. Hett, 1978. The Loeb Classical Library, Harvard University Press, Cambridge (Mass) and London, p. 480.

Ballero, M., Bruni, A., Sacchetti, G., Mossa, L., Poli, F., 1994. Indagine etnofarmacobotanica del territorio di Arzana (Sardegna orientale). Annali di Botanica, Studi sul Territorio (Roma) 52, pp. 489–500.

Ballero, M., Poli, F., Sacchetti, G., Loi, M.C., 2001. Ethnobotanical research in the territory of Fluminimaggiore (south-western Sardinia). Fitoterapia 72, 788–801.

Bandini, A., 1961. Le piante della medicina tradizionale nell'alta valle di Vara (Liguria orientale). Webbia 16, 143–163.

Barbagallo, C., Grillo, M., Meli, R., 1979. Note sulle piante officinali spontanee e coltivate del territorio di Cesarò (Messina). Fitoterapia 2, 57–66.

Barone, R., 1963. Le piante della medicina popolare nel territorio di Falconara e San Lucido (Calabria). Webbia 17, 329–357.

Beck, L.Y., 2005. Pedanius Dioscorides of Anazarbus, De materia medica. Translated. Olms-Weidmann, Hildesheim, Zürich, and New York (Altertumswissenschaftliche Texte und Studien 38), p. 540.

Blanco, E., 1996. El Caurel, las plantas y sus habitantes. Estudio etnobotánico de la Sierra del Caurel (Lugo): la importancia de las plantas para nuestros antepasados. Fundación Caixa Galicia, A Corunha, p. 203.

Bonet, À.M., Parada, M., Selga, A., Vallès, J., 1999. Studies on pharmaceutical ethnobotany in the regions of L'Alt Empordà and Les Guilleries (Catalonia, Iberian Peninsula). Journal of Ethnopharmacology 68, 145–168.

Bonet, M.A., Valles, J., 2007. Ethnobotany of Montseny biosphere reserve (Catalonia, Iberian Peninsula): Plants used in veterinary medicine. Journal of Ethnopharmacology 110, 130–147.

Boulos, L., 1983. Medicinal plants of North Africa. Reference Pubns, U.S.A., p. 286.

Buenz, E.J., Schnepple, D.J., Bauer, B.A., Elkin, P.L., Riddle, J.M., Motley, T.J., 2004. Techniques: Bioprospecting historical herbal texts by hunting for new leads in old tomes. TRENDS in Pharmacological Sciences 25, 494–498.

Byl, S., 1996. La thérapeutique par le miel dans le corpus hippocraticum. In: Garofalo, I., Lami, A., Manetti, D., Roselli, A. (Eds.), Aspetti della terapia nel Corpus Hippocraticum. Atti del IXe Colloque international hippocratique (Pisa, 25–29 settembre 1996). Firenze: Olschki, 1999. (Accademia Toscana di scienze e lettere "La Colombaria". Studi 183), pp. 119–124.

Catanzaro, F., 1970. Le piante officinali del territorio di Bivona (Agrigento) nella tradizione popolare. Fitoterapia 41, 66–84.

Cavara, C., 1954. Coltivazione delle Piante officinali – con cenni sul loro uso in terapia o nella medicina popolare. Delpinoa (appendice al tomo XXIV), 171.

Chiovenda, E., 1937. L'utilizzazione della flora spontanea nelle nostre Colonie. Società Italiana per il Progresso delle Scienze, Roma, p. 31.

Chiovenda-Bensi, C., 1960. Florula medicinale delle Cinque Terre. Webbia 15, 631–641.

Cirelli, F., 1853. Il Regno delle due Sicilie descritto ed illustrato. VII–VII. Stabilimento Poligrafico di Tiberio Pansini, Napoli, p. 96.

Cleene, M.D., Lejeune, M.C., 2003. Compendium of Symbolic and Ritual plants in Europe, vol. 2. Man & Culture Publishers, Ghent.

De Feo, V., Ambrosio, C., Senatore, F., 1992a. Traditional phytotherapy in Caserta Province. Campania, southern Italy, Fitoterapia 63, pp.337–349.

De Feo, V., Aquino, R., Menghini, A., Ramundo, E., Senatore, F., 1992b. Traditional phytotherapy in the Peninsula Sorrentina, Campania, Southern Italy. Journal of Ethnopharmacology 36, 113–125.

De Feo, V., Senatore, F., 1993. Medicinal plants and phytotherapy in the Amalfitan Coast, Salerno Province, Campania, Southern Italy. Journal of Ethnopharmacology 39, 39–51.

De Martino, E., 1959. Sud e Magia. Feltrinelli Editore, Milano.
De Natale, A., Pollio, A., 2007. Plants species in the folk medicine of Montecorvino Rovella (inland Campania, Italy). Journal of Ethnopharmacology 109, 295–303.
El-Hilaly, J., Hmammouchi, M., Lyoussi, B., 2003. Ethnobotanical studies and economic evaluation of medicinal plants in Taounate province (Northern Morocco). Journal of Ethnopharmacology 86, 149–158.
Eloff, J.N., 1998. Which extractant should be used for the screening and isolation of antimicrobial components from plants? Journal of Ethnopharmacology 60, 1–8.
Fresquet Febrer, J.L., Blanquer Roselló, G., Galindo Dobón, G., Gallego Estrada, F., García de la Cuadra Arizo, R., López Bueno, J.A., Sanjosé Pí A., 2001. Inventario de las plantas medicinales de uso popular en la ciudad de Valencia. http://www.uv.es/medciensoc/sumario13.html, Last update 24-11-2003. Medicina y Ciencias Sociales 13.
Galt, A.H., Galt, J.W., 1978. Peasant use of some wild plants on the island of Pantelleria Economic Botany. Sicily 32, 20–26.
Guarrera, P.M., 1999. Traditional antihelmintic, antiparasitic and repellent uses of plants in Central Italy. Journal of Ethnopharmacology 68, 183–192.
Guarrera, P.M., 2006. Usi e tradizioni della flora italiana. Aracne, Roma, p432.
Guarrera, P.M., Forti, G., Marignoli, S., 2005a. Ethnobotanical and ethnomedicinal uses of plants in the district of Acquapendente (Latium, Central Italy). Journal of Ethnopharmacology 96, 429–444.
Guarrera, P.M., Salerno, G., Caneva, G., 2005b. Folk phytotherapeutical plants from Maratea area (Basilicata). Journal of Ethnopharmacology 99, 367–378.
Hanlidou, E., Karousou, R., Kleftoyanni, V., Kokkini, S., 2004. The herbal market of Tessaloniki (N Greece) and its relation to the ethnobotanical tradition. Journal of Ethnopharmacology 91, 281–299.
Heinrich, M., Kufer, J., Leonti, M., Pardo-de-Santayana, M., 2006. Ethnobotany and ethnopharmacology – Interdisciplinary links with the historical sciences. Journal of Ethnopharmacology 107, 157–160.
Hippocrates, vol. IV. Regimen, Greek text and English translation by W.H.S. Jones, 1931. The Loeb Classical Library, Harvard University Press, Cambridge (Mass.) and London, pp. 223–419.
Hippocrates. vol. V. Affections. Diseases I. Diseases II. Greek text and English translation by P. Potter, 1988. The Loeb Classical Library, Harvard University Press, Cambridge (Mass.) and London, p. 352.
Hippocrates. vol. VI. Diseases III. Internal Affections. Regimen in Acute Diseases. Greek text and English translation by P. Potter, 1988. The Loeb Classical Library, Harvard University Press, Cambridge (Mass.) and London, pp. 1–64, 65–256.
Hippocrates. vol. VII. De natura muliebri. In: Oeuvres complètes de Hippocrate: Traduction nouvelle avec le texte grec en regard. Translation by E. Littré, 1851. J.B. Bailliere, Paris, pp. 310–431.
Hippocrates. vol. VIII. De morbis mulierum. In: Oeuvres complètes de Hippocrate: Traduction nouvelle avec le texte grec en regard. Translation by E. Littré, 1853. J.B. Bailliere, Paris, pp. 1–407.
Hippocrates. vol. VIII. De sterilitate mulierum. In: Oeuvres complètes de Hippocrate: Traduction nouvelle avec le texte grec en regard. Translation by E. Littré, 1853. J.B. Bailliere, Paris, pp. 408–463.
Hippocrates. vol. VIII. Glands. Fleshes. Prorrhetic I-II. Physician. Use of Liquids. Ulcers. Haemorrhoids and Fistulas, Greek text and English translation by P. Potter The Loeb Classical Library, Harvard University Press, Cambridge (Mass.) and London, 1995, pp. 339–376.
Jamalio, A., 1918. La Regina del Sannio. Federico & Ardia Editori, Napoli, p. 198.
Jones W.H.S., 1951. Pliny, Natural History, books 20-23, with an English translation. Harvard University Press, Cambridge (Mass.) and London (Loeb Classical Library no. 392), Harvard University Press, Cambridge (Mass.) and London, p. 532.
Jones, W.H.S., 1956. Pliny, Natural History, books 24-27, with an English translation. Harvard University Press, Cambridge (Mass.) and London (Loeb Classical Library no. 393), Harvard University Press, Cambridge (Mass.) and London, p. 562.
Jouanna, J., 1992. Hippocrate. Fayard, Paris, p. 648.
Kultur, S., 2007. Medicinal plants used in Kirklareli Province (Turkey). Journal of Ethnopharmacology 111, 341–364.
Lardos, A., 2006. The botanical materia medica of the Iatrosophikon-A collection of prescriptions from a monastery in Cyprus. Journal of Ethnopharmacology 104, 387–406.
Laskaris, J., 1996. Archaic healing cults as a source for Hippocratic pharmacology. In: I. Garofalo, A. Lami, D. Manetti and A. Roselli (Eds.), Aspetti della terapia nel Corpus Hippocraticum. Atti del IXe Colloque international hippocratique (Pisa, 25-29 settembre 1996). Firenze: Olschki, 1999. (Accademia Toscana di scienze e lettere “La Colombaria”. Studi 183), pp. 1–12.
Leporatti, M.L., Corradi, L., 2001. Ethnopharmacobotanical remarks on the Province of Chieti town (Abruzzo, Central Italy). Journal of Ethnopharmacology 74, 17–40.
Leporatti, M.L., Ivancheva, S., 2003. Preliminary comparative analysis of medicinal plants used in the traditional medicine of Bulgaria and Italy. Journal of Ethnopharmacology 87, 123–142.
Lev, E., 2002. Reconstructed materia medica of the Medieval and Ottoman al-Sham. Journal of Ethnopharmacology 80, 167–179.
Lev, E., Amar, Z., 2000. Ethnopharmacological survey of traditional drugs sold in Israel at the end of the 20th century. Journal of Ethnopharmacology 72, 191–205.
Lev, E., Amar, Z., 2002. Ethnopharmacological survey of traditional drugs sold in the Kingdom of Jordan. Journal of Ethnopharmacology 82, 131–145.
Merzouki, A., Ed-derfoufi, F., Molero Mesa, J., 2000. Contribution to the knowledge of Rifian traditional medicine II: Folk medicine in Ksar Lakbir district (NW Morocco). Fitoterapia 71, 278–307.
Moisan, M., 1990. Lexique du vocabulaire botanique d’Hippocrate. Université Laval, Laboratoire de recherches hippocratiques, Document 7, Québec, Canada, p. 90.
Nardi, C., 1978. Storia di un feudo del Fortore, la Baronia di Montefalcone. Tipografica Sannio, Circello (BN), p. 251.
Novais, M.H., Santos, I., Mendes, S., Pinto-Gomes, C., 2004. Studies on pharmaceutical ethnobotany in Arrabida Natural Park (Portugal). Journal of Ethnopharmacology 93, 183–195.
Palmese, M.T., Uncini Manganelli, R.E., Tomei, P.E., 2001. An ethnopharmacobotanical survey in the Sarrabus district (south-east Sardinia). Fitoterapia 72, 619–643.
Penso, G., 1983. Index plantarum medicinalium totius mundi eorumque synonimorum. OEMF. Milano, p1026.
Pieroni, A., 2000. Medicinal plants and food medicines in the folk traditions of the upper Lucca Province, Italy. Journal of Ethnopharmacology 70, 235–273.
Pieroni, A., Dibra, D., Grishaj, G., Grishaj, I., Maçai, S.G., 2005. Traditional phytotherapy of the Albanians of Lepushe. Northern Albanian Alps, Fitoterapia 76, pp. 379–399.
Pieroni, A., Nebel, S., Quave, C.L., Heinrich, M., 2002. Ethnopharmacy of the ethnic Albanians (Arbëreshë) of northern Basilicata Italy. Fitoterapia 73, 217–241.
Pieroni, A., Quave, C.L., 2005. Traditional pharmacopoeias and medicines among Albanians and Italians in southern Italy: A comparison. Journal of Ethnopharmacology 101, 258–270.
Pieroni, A., Quave, C.L., Lorena, V., Mangino, P., Sabbatini, G., Santini, L., Boccetti, T., Profili, M., Ciccioli, T., Rampa, L.G., Antonini, G., Girolamini, C., Cecchi, M., Tomasi, M., 2004a. Ethnopharmacognostic survey on the natural ingredients used in folk cosmetics, cosmeceuticals and remedies for healing skin diseases in the inland Marches, Central-Eastern Italy. Journal of Ethnopharmacology 91, 331–344.
Pieroni, A., Quave, C.L., Santoro, R.F., 2004b. Folk pharmaceutical knowledge in the territory of the Dolomiti Lucane, inland southern Italy. Journal of Ethnopharmacology 95, 373–384.
Potter, P., 1990. Methods and Issues/Problématiques et methodes. Ancient Texts and the Historian, Canadian Bulletin of Medical History – Bulletin Canadien the Histoire de la Medicine 1, 169–176.
Rigat, M., Bonet, M.A., Garcia, S., Garnatje, T., Valles, J., 2007. Studies on pharmaceutical ethnobotany in the high river Ter valley (Pyrenees, Catalonia, Iberian Peninsula). Journal of Ethnopharmacology 113, 267–277.
Said, O., Khalil, K., Fulder, S., Azaizeh, H., 2002. Ethnopharmacological survey of medicinal herbs in Israel, the Golan Heights and the West Bank region. Journal of Ethnopharmacology 83, 251–265.

Salvo, G., Conti, E. Investigating the monophyly and biogeographic history of *Ruta* (Rutaceae) with chloroplast DNA sequence data. Annual Meeting of Botanical Society of America, California State University Chico – Sistematics section, abstract no. 181, in press.

San Miguel, E., 2003. *Ruta* spp. (*Ruta* L., Rutaceae) in traditional Spain: frequency and distribution of its medicinal and symbolic applications. Economic Botany 57, 231–244.

Scherrer, A.M., Motti, R., Weekerle, C.S., 2004. Traditional plant use in the areas of Monte Vesole and Ascea, Cilento National Park (Campania, Southern Italy). Journal of Ethnopharmacology 97, 129–143.

Schmid, R., 1919. Die noch gebräuchlichen Arzneimittel des Dioskurides. Inaugural-dissertation zur erlangung der doktorwürde der hohen medizin fakultät der Universität Tübingen, Druck H. Laupp Jr, Tübingen, p. 44.

Stannard, J., 1961. Hippocratic Pharmacology. Bulletin of History of Medicine 35, 497–518.

Theophrastus, vol. I–III. De causis plantarum. Translation by B. Einarson and G.K.K. Link, 1976–1990. The Loeb Classical Library, Harvard University Press, Cambridge (Mass.) and London, p. 440.

Theophrastus, vol. I–II. Enquiry into Plants. Translation by Hort A.F., 1916-1926. The Loeb Classical Library, Harvard University Press, Cambridge (Mass.) and London, p. 520.

Touwaide, A., 1997. Bibliographie historique de la botanique: les identifications de plantes médicinales citées dans les traités anciens après l'adoption du système de la classification botanique de Linné (1707–1778). Lettre d'informations 30, 2–22.

Touwaide, A., 1998. Bibliographie historique de la botanique: les identifications de plantes médicinales citées dans les traités anciens après l'adoption du système de la classification botanique de Linné (1707–1778). Lettre d'informations 31, 2–82.

Trotter, A., 1915. Flora economica della Libia. Tipografia dell'Unione Editrice, Roma, p. 145.

Tutin, T.G., Heywood, V.H., Burges, N.A., Valentine, D.H., Walters, S.M., Webb, D.A. (Eds.), 1968. Flora Europaea 2. Cambridge University Press, Cambridge, p. 455.

Uncini Manganelli, R.E., Tomei, P.E., 1999. Ethnopharmacobotanical studies of the Tuscan Archipelago. Journal of Ethnopharmacology 65, 181–202.

Uzun, E., Sariyar, G., Adsersen, A., Karakoc, B., Ötük, G., Oktayoglu, E., Pirildar, S., 2004. Traditional medicine in Sakarya province (Turkey) and antimicrobial activities of selected species. Journal of Ethnopharmacology 95, 287–296.

Vázquez, F.M., Suarez, M.A., Pérez, A., 1997. Medicinal plants used in the Barros Area, Badajoz Province (Spain). Journal of Ethnopharmacology 55, 81–85.

Wellmann, M., 1906–1914. Pedanii Dioscuridis Anazarbei de materia medica libri quinque. 3 vols. Weidmann, Berlin.