

## ORIGINAL ARTICLE

### The Plant Material of Medicine

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#### ABSTRACT

The oldest illustrated and most valuable document in the history of pharmaceutical and herbal writing is *De materia medica*, i.e. materials of medicine, a precursor to the modern pharmacopoeia and one of the most influential herbal books in history of sciences; this work was written by Dioscorides in his native Greek, during the first century AD. Although the original text of Dioscorides herbal has never been found, numerous manuscripts of his work (mostly illustrated) reproduced between 2nd and 15th century AD; however, unlike the original, they contain alphabetically listed plants that have been used for therapy. The first Greek version was published in 1499 and the first Latin version in 1516. It is likely that the first translated manuscript in Arabic appeared during the 9th century. In these texts the presented plant classification is pre-Linnaean. Unlike many classical authors, Dioscorides' work was not rediscovered in the Renaissance, because the five volume text on materials of medicine never left circulation. Nowadays, increasing interest for natural products reminds us of Dioscorides' aspects and it introduces studies in biodiversity, plant distribution, plant environmental physiology, ethnopharmacology, biosynthesis and biomimetic synthesis of substances, natural history, medieval culture and methodology. In the mean time, the medical tradition with the immortelle, herbal treasure has been influenced by new discoveries; while scientists are practicing the ancient herbal lore, new components are distinguished. As a matter of fact, the story of the herbal can be told almost continuously from the 5th century BC.

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#### Key words:

#### Introduction

Dioscorides was a Greek physician who lived in the first century of the Christian era (c. 40 – c. 90 AC). He was born in Anazarba, a town in south-eastern Asia Minor and probably studied at nearby Tarsus, which was renowned as a centre for the study of medicine and pharmacology. He became a military surgeon under Roman Emperors and he was a contemporary of Pliny the Elder. Dioscorides, after much direct observation of herbs in their native habitats and careful practical experience on the medicinal uses of hundreds of plants (some minerals and few animals), he started to write in Greek their medical properties in 65 AD; this was the basis for pharmacology, medicine and herbal writing until the 16th century. The original text does not exist, but this work was, for about 1,500 years, the supreme authority due to the practical nature of its contents.

The oldest known manuscript of Dioscorides' text, is a magnificent manuscript dated about 512 AD, known as the Juliana Anicia codex of Dioscorides, (better known as the codex *Vindobonensis*, or the codex *Constantinopolitanus*, or the Vienna codex). Also, it is considered to be a splendid monument of botanical art (Premestein, 1903; Collins, 2000; Lack, 2001). Hence, the most famous copy of Dioscorides' work is an illuminated Byzantine manuscript produced for Anicia Juliana, the daughter of the emperor Flavius Anicius Olybrius of the western empire, in 472 AD. The codex comprises 491 folios and it contains almost 400 full-page paintings of plants,

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each facing a full page of a description of the plant and its properties. It is likely that the plant drawings contained therein have been derived much earlier, at least as far back as the 2nd century AD, while they were not surpassed in quality for about 1,000 years. It has been repeatedly published in literature that they resemble the actual designs of Crateuas the rhizotomos (i.e. the root-cutter) and early plant illustrator. Crateuas was a rhizotomist and herb gatherer, whose own illustrated herbal (Rhizotomicon) has been lost (2nd century BC). Dioscorides speaks respectfully of him in his preface. According to Singer (1927), eleven illustrations in the codex *Vindobonensis*, which are especially well drawn and include quotations from Crateuas, may have been copied from an earlier work. Riddle (1985) argues that both Crateuas and Dioscorides originally were written on papyrus scrolls. Their drawings would have been in ink wash; otherwise, the paint would have cracked and flaked off as the scroll was rolled and unrolled. The paintings on parchment in the Vienna Dioscorides seem to be too finely detailed to have been copied from such crude originals. Also, it has been argued that original text of the *De materia medica* was not originally illustrated. This might be assumed from the text, which very often does not describe the plant but only its medicinal uses; an accompanying illustration often would have been required if the text was to make sense.

It has to be mentioned that the earliest known illustration of a plant is a drawing of symphytum or comfrey (*Symphytum officinale* L.), from a fragment known as the Johnson Papyrus, made c. 400 AD. The action of plant illustration and drawing was a tool of scientific value, related with plant identification, until the beginning of the 20th century (Lack and Ibáñez, 1997; Janick and Paris, 2006; Rhizopoulou, 2007b). It is of greatest interest and importance to search through the methodology, the nomenclature and the etymology of scientific names of plants, for the interpretation of plant names used by Dioscorides and his precursors.

It has been argued that the codex was written either in Constantinople or in Alexandria. As it passed through the hands of various owners, the codex of Anicia was amended with the names of plants in Greek, Arabic, Turkish and Hebrew and annotations in French. Ogier Ghislain de Busbecq (1522-1592), ambassador of the Emperor Ferdinand I to the Ottoman court of Süleyman, attempted to purchase the Anicia codex in 1562. In 1569 Emperor Maximilian II did acquire the Anicia codex for the imperial library in Vienna, now the Austrian National Library (Österreichische Nationalbibliothek), where it is designated *Codex Vindobonensis Med. Graecum 1* (from the word *Vindobona*, i.e. the old Latin name for Vienna) or, more simply, the Vienna Dioscorides.

Many other illustrated Greek manuscripts of Dioscorides have survived, one of the most important of which is the 7th century codex *Neapolitanus*, housed in the Bibliotheca National, Naples, Italy and another one in the library of a monastery on the Holly Mountain Athos, in Greece.

In his preface, Dioscorides indicates that, instead of presenting the materials of medicine (i.e. *materia medica*) in alphabetical order, which he complains, "splits off genera and properties from what most resembles them", he is using a different arrangement and he describes the classes according to the properties of the individual substances. His scheme was to organize them by category or class and then by the physiological effect of a substance on the body. Nevertheless, copyists of *De materia medica* alphabetized his material, completely rearranging its original schema (Riddle, 1985; Beck, 2005). Thus, in the Anicia codex, the chapters of *De materia medica* have been rearranged, the plants alphabetized and their descriptions augmented with observations from Galen and Crateuas.

The *materia medica* was copied repeatedly, throughout Europe and Middle East with some variations, over the next 15 centuries. The first English translation was made from one of the Greek manuscripts of Dioscorides, between 1652 and 1655 by the botanist John Goodyer and it was entitled "The Greek herbal of Dioscorides, illustrated by a Byzantine AD512, Englished by John Goodyer AD1655", but it was not published until 1934 (edited by Robert T. Gunther in Oxford). Some years ago, a brief epitome of the new herbal or history of plants –translated by Henry Lyte and William Ram– was published by Rembert Dodoens (London 1606). Dioscorides' Greek text was published in a definitive edition by Max Wellmann (Pedanii Dioscuridis Anazarbei De Materia Medica), from various extant versions, from 1906 to 1914. Then, Riddle (1985) published his work entitled "Dioscorides on Pharmacy and Medicine" (Reeds, 1987). Another work entitled "Dioscorides de materia medica, being an herbal with many other materials written in the first century of the Common Era. An extended version in modern English" was written by T.A. Osbaldeston and R.P.A. Wood (Johannesburg, 2000). Recently, Beck (2005) has rendered Wellmann's Greek edition into English; these are the only English texts of Dioscorides' remarkable book since the seventeenth century.

An attempt was made to present some applications based on ancient knowledge of plant material, in order to identify properties of extracts from tissues mentioned in codices that have been observed by using modern infrastructure. Also, our attention was to look for the earliest surviving manuscripts of Dioscorides' work.

## Materials and Methods

Since we are competent in Greek and professionals in plant biology (S.R.) and medicine (A.K.), our research focuses on plant species presented in codices, ancient manuscripts and fragments. As a matter of fact, we are studying original, classical texts, trying to understand the usage and application of materials of medicine, as well as the origin of plant names.

## Results and Discussion

The unique aspect of Dioscorides' method of presentation was that he listed plants not alphabetically by name, as did many herbals, but in groups with similar pharmacological actions in the human body; thus listing together types of plants such as those with sedative or anti-inflammatory properties. The alphabetical herbal recession was made perhaps in the third or the fourth century AD (Singer, 1927; Collins, 2000). Under the umbrage of a bewildering variety of medical and magical theories, generations of people took herbs as medicines when they were sick or injured; when they were fearful of bad spirits and germs; when they wanted to preserve good health; or when they wanted to control the reproductive process. Sometimes the medicine was prescribed by a doctor, but more often it was self-prescribed or recommended by friends or relatives; people acted largely on oral information, as they did when learning manners, cooking, sewing and art (Heilmeyer, 2007). Most could not read or write, at least not to the extent of comprehending a complex pharmaceutical-medical manuscript (even if one had existed). In addition, the concepts and technical vocabulary of early times did not permit rapid development of plants' identification. For example, St. John's wort (*Hypericum perforatum*) is considered an alternative treatment for rheumatism, arthritis and aching muscles. Juniper (*Juniperus oxycedrus*) berries figured as a material with anti-fungal properties. Myrtle (*Myrtus communis*) berries were widely used in medicine and cosmetics; myrtle juice squeezed from fresh berries was considered beneficial for the stomach. Immense power has been ascribed to sage (*Salvia officinalis*, with the strong, pleasant fragrance) that has been cultivated in medieval gardens (Brubaker, 2002). The olive tree (*Olea europaea*) is among the oldest cultivated plants on earth (Rhizopoulou 2007a) and the physicians described its curative properties. More examples from a medical herbal are given in Table 1.

Dioscorides exhibited a sophisticated appreciation of the effects of plants beyond the Hippocratic philosophy (5th century BC), that all diseases and treatments were based on the rhythm of the four humours of the body, i.e. yellow bile (summer), black bile (autumn), phlegm (winter) and blood (summer); this was also included in philosophical aspects of Aristotle and Theophrastus (4th century BC). This unique contribution of Dioscorides has been described in detail (Reeds, 1976; Riddle, 1985).

Dioscorides made personal observations of the specific properties of drugs and presented them through illustrations for the first time, during the 1st century A.D.; almost all the physician authors from Galen to Azam Khan have quoted Dioscorides. It seems likely that during periods when the knowledge of Greek was more restricted, Dioscorides' work was translated into Latin, Arabic, Armenian, German, Italian, French and English (El-Gammal, 1997; Walther and Wolf, 2001).

**Table 1:** Some examples from an herbal that is a medical document (through centuries of human civilization).

Common name	Ancient name	Scientific name	Uses, causes	Components
Acotine (blue racket)	Aconiton	<i>Aconitum napellus</i>	febrifuge, gastric anesthetic, cough	aconitine (heart treatment)
Birthwort, snake root	Aristolochia	<i>Aristolochia rotunda</i>	wounds of the head, childbirth	aristolochic acid
Bryony	Ampelos thermatikon	<i>Bryonia alba</i> <i>Bryonia cretica</i>	purgative	bryonin, bryonidin, resin, oil, bryomarin glycoside
Cretan dittany	Dicatmnon, elelifaskos	<i>Dictamnus albus</i> , <i>Origamun dictamnus</i>	antispasmodic tonic, diuretic, antihelmintic	dictamnolide (4-methoxyfuro [2, 3-b] quinoline), volatile inflammable oil
Cyclamen	Cyclaminos	<i>Cyclamen persicum</i>	antibacterial, emetic, purgative	cyclamin (3-acetyloleandromycin)
Dyers madder (rose madder)	Ereuthedamon	<i>Rubia tinctorium</i>	pains in the loins,	ruberythric acid, rubiadin
Hellebore	Eleboros	<i>Helleborus orientalis</i>	ulcers, emetic, poisonous	sapogenin, cevadine, veratrine, cardiac glycoside
Hemlock	coneion	<i>Conium maculatum</i>	poisonous, weakness, sleepiness, paralysis, vomiting hydrochloride	coniine, citurine, 2-propylpiperidine, conicine hydrobromide and
Jimson weed	Strychnos manikos	<i>Datura stramonium</i>	madness, asthma	atropine, hyoscyamine, hyoscyamine, scopolamine
Mandrake	Mandragoras	<i>Mandragoras officinalis</i>	madness, lethargy, antispasmodic anaesthetic (up to 1846)	hyoscyamine, podophyllotoxin, picropodophyllin, peltanins
Mistletoe	Exos, Ixos	<i>Viscum album</i>	neoplasia, cancer, cytotoxic, immuno-stimulatory	viscotoxine, lectins; fermented extracts from <i>V. album</i> in Iscador (Urech <i>et al.</i> , 2005)
Oleander	Onotheras	<i>Nerium oleander</i>	toxic, cardiac insufficiency	cardiac glycoside oleandrin (folinerin)
Rosemary	Libanotis, karpinos	<i>Rosmarinus officinalis</i>	perfumes, soaps, shampoos	essential oil (1,8-cineole 2-ethyl- 4,5-dimethylphenol and camphor)
Treacle	Chamaidrys	<i>Teucrium scorodonia</i>	ulcers, wounds, fractures	tannin, scordein, oil, sudofiric acid

Since, the plants were there (millions years ago), it would be expected that Dioscorides had predecessors who observed and wrote on properties of herbals, i.e. Hippocrates, Diocles, Theophrastus (Rhizopoulou, 2004), Sextus Niger, Crateuas and others (Rhizopoulou, 2005). According to Beck (2005 and references therein) *De materia medica* may reflect the long-term influence of concepts derived from Theophrastus' *De causis plantarum*. The generations who came after him used his work for the data base of their pharmacy and medicine.

With the development of printing and the so-called Renaissance (1450-1600), Dioscorides was not rediscovered by the humanists, the way other classical authors supposedly were, because his work had never left circulation (Givens *et al.*, 2006; Rhizopoulou *et al.*, 2008). The Greek text of Dioscorides was published once in the 15th century and five times in the 16th century. During this period seven Latin and three Arabic translations appeared. One verified edition of a Latin translation was published in the fifteenth century and forty-nine editions in the sixteenth. There were thirty-six different Latin commentaries involving ninety-six separate printings from 1478 to 1600. Forty-three separate printings were produced in modern vernacular translations into Italian, French, German, Czech, Spanish, Dutch, English and Arabic. They are as impressive in size as they are expressive in medical content. The above mentioned references concern only the editions and commentaries. If we were to include his imitators-those whose contributions were based, at least in part, on Dioscorides' foundation-the numbers increase so substantially as to be unmanageable.

The commentators who directly expounded on Dioscorides' text were generally a) medical practitioners and b) university professors who lectured on his work (Reeds, 1976; Stearn, 1976; Scarborough, 1978; Pavord, 2005). The intensity of interest and refinement of his part of the educational curriculum in sixteenth-century Universities in Europe led to a splintering of the study of the materials of medicine into the specialties of botany, pharmacology and medicine (Mabberley, 1998). As important as the scale of his work was, the quality of his information and his organization by drug affinities were potentially of greater significance. It seems relatively clear how he could accomplish to obtain most of his information through direct observation. The ability to synthesize so much empirical data almost certainly would have been based on experience. Dioscorides must have made his observations in clinical situations, because it is highly unlikely that he could have acquired the knowledge in any other way. He must have been a practicing doctor, trained in the Hippocratic way of Hellenistic physicians. His mentor, Areios, stressed drug therapy in his practice in Tarsus, a pharmacology centre, at that period. Although, it is not clear that, as a physician military or not, Dioscorides travelled in the eastern Mediterranean provinces, it is presumed that he talked with local people about their remedies, he observed the effects of drugs on patients' bodies and he identified drug affinities. Above all, he had the ability to observe nature in the Levant, to collect specimens from native plants and then to base his working postulates on empirical data.

## Conclusion

Dioscorides' understanding of properties of plant material may be close to the order that we perceive in the behaviour of natural products. Thus, an understanding and the appreciation of his work tells us far more about early science. Successors to Dioscorides took simples and mixed them to control multiple results. For a long time after Dioscorides, the tendency was to develop medicines containing many natural substances. This direction was not reversed, until the sixteenth century; the reversal came about partly with the observation that a simple, that is, a single natural-product drug, was itself a mixture of compounds. Unobtrusively, Dioscorides offered science a direction, but it took more than fifteen hundred years to catch up with him.

Dioscorides was one of the first people to point out that anyone wanting experience in these matters must encounter the plants as shoots newly emerged from the earth, plants in their prime and plants in their decline; actually, these are aspects of current research in plant biology.

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Where did this revival of plants as medicine come from? How do you forge your own path through all the noise? Herbalist Sade Musa shares how history and healing intersect. Our ancestors went to great lengths to retain their knowledge of medicinal and edible plants so that we may continue to use them. Enslaved Africans risked their very safety to smuggle plants of cultural, spiritual, and medical importance during the Middle Passage. The Irish labored to protect their own ancient herbal legacies against the destruction of repeated invasions. It's a testament to the resilience of people that they preserved their healing traditions, despite being faced with incredible hardship such as forced migration from their motherlands. One of the disadvantages of using plants as a raw material for medicine is maintaining a supply: the plant may be difficult to grow and, since the compounds are often found in very low concentrations, extraction may be costly. The first patient to be treated with penicillin (which is derived from fungi) died not because the medicine was harmful but because the supply ran out. To study the compounds in depth, and perhaps even test as a new medicine, large quantities are required. Many scientists work on natural product synthesis: producing compounds found in nature in the laboratory. Peter Bernstein, Digest Editor for Bioorganic and Medicinal Chemistry comments: In this article the use of natural products combined with phenotypic screening has been highlighted as a source of new drugs. In these texts the presented plant classification is pre-Linnaean. Unlike many classical authors, Dioscorides' work was not rediscovered in the Renaissance, because the five volume text on materials of medicine never left circulation. Nowadays, increasing interest for natural products reminds us of Dioscorides' aspects and it introduces studies in biodiversity, plant distribution, plant environmental physiology, ethnopharmacology, biosynthesis and biomimetic synthesis of substances, natural history, medieval culture and methodology.