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Traditional Mediterranean and European herbal medicines

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ABSTRACT

Ethnopharmacological relevance: Written history allows tracing back Mediterranean and European medical traditions to Greek antiquity. The epidemiological shift triggered by the rise of modern medicine and industrialization is reflected in contemporary reliance and preferences for certain herbal medicines.
Materials and methods: We sketch the development and transmission of written herbal medicine through Mediterranean and European history and point out the opportunity to connect with modern traditions.
Results: An ethnopharmacological database linking past and modern medical traditions could serve as a tool for crosschecking contemporary ethnopharmacological field-data as well as a repository for data mining. Considering that the diachronic picture emerging from such a database has an epidemiological base this could lead to new hypotheses related to evolutionary medicine.
Conclusion: The advent of systems pharmacology and network pharmacology opens new perspectives for studying past and current herbal medicine. Since a large part of modern drugs has its roots in ancient traditions one may expect new leads for drug development from novel systemic studies, as well as evidence for the activity of certain herbal preparations.

1. Introduction

Throughout written history, medicine, horticulture and agriculture have guided the study of plants, animals, organic and inorganic products. Valuable insights into the history of medicine can be gained through cross-cultural studies of medical texts, archaeological remains, contemporary folk medicines and ethnomedical practices (Tschirch, 1910; Arber, 1953). This commentary is an integration to the supplementary series recently published by Science magazine dedicated to the Arts and Science of Traditional Medicine highlighting modern scientific approaches and perspectives to global traditional medicine with a special focus on TCM (The Art and Science of Traditional Medicine Part 1–3, 2014–2015).

Hygiene and preventive medicines, such as vaccines and the introduction of antibiotics brought about an epidemiological shift away from the burden of infectious diseases in the western world (Mann, 1984). Propelled by industrialization and warfare between the late 18th and mid 20th century, this development led to a steady decline in the reliance on herbal products for primary care and endowed us with a rising life expectancy. In parallel, changes in working habits led to a decline in everyday physical activity, while dietary patterns shifted towards the overconsumption of meat, dairy and refined products, and a lower intake of fruits, vegetables, fibres and phytochemicals in general. As a consequence multifactorial age related and life style diseases such as cancers, type II diabetes, cardiovascular diseases and neurodegenerative disorders, as well as chronic inflammatory autoimmune diseases are now at the forefront among health problems in affluent societies (Bray, 1996).

Today consumers perceive herbal medicine and plant based food products as an adjuvant or more gentle and holistic way of coping with chronic health problems and self-limiting infectious diseases. This perception is paralleled by the progress in omics approaches and network pharmacology, which have allowed the synergistic properties of herbal products to shed the “quackery” label, as they acquire a firm evidence base.

In Europe and the Mediterranean medicinal plants are being collected for use as home remedies from wild habitats and private yards, or bought in shops and markets. The renewed interest in alternative, traditional and herbal medicines in the economically more developed societies needs to be considered against the backdrop of the historical process and epidemiological changes outlined above (c.f. Etkin, 2006).

2. The written tradition

Though traditional medicine and the use of medicinal plants can be

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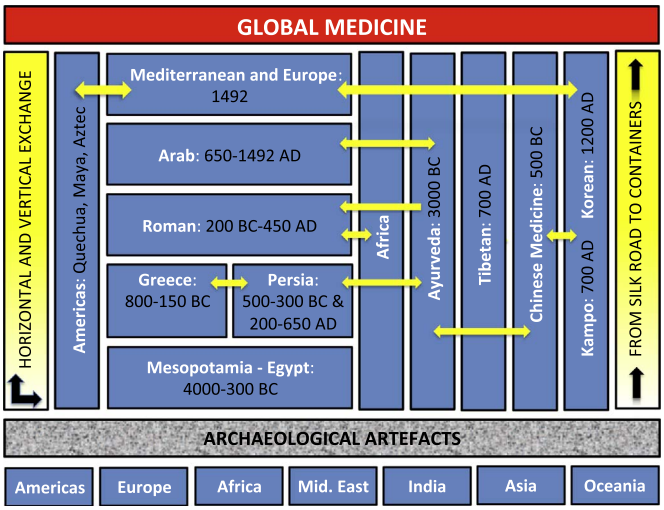

Fig. 1. Mutual influence and development of major traditional medicinal systems with focus on the Mediterranean and Europe. A range of other, more local but still important traditional medicinal systems exist in parallel. The width of the arrows does not exactly correspond with scale of imports from the specific regions.

traced back to mesopotamia and Egypt (Fig. 1), the basis of Mediterranean and European medicine was laid down during Greek antiquity and the period of the Roman Empire by physicians and philosophers, who started building a written consensus about what was considered efficacious medical knowledge (Fig. 2). The 9th book of Theophrastus of Eresos' (ca. 370–287 BCE) *Enquiry into Plants*, about the juices and the medicinal properties of plants, has preserved the earliest known fraction of a Greek herbal (Hort, 1977). The most eminent and influential classic authors were Hippocrates of Kos (ca. 460–370 BCE), Galen (129– ca. 199/200 or 216/217 CE) and Pedanios Dioscorides (1st century AD), who with great success combined both botanical and medical skills. Dioscorides' *De Materia Medica* together with Galen's first alphabetical collection of simple drugs (*De simplicium medicamentorum facultatibus libri XI*), are regarded as the most influential herbals ever written. Through the repeated copying and dissemination of their content, both texts shaped Mediterranean and European medicinal plant use until the 18th century (Singer, 1927; Urdang, 1951; Arber, 1953). Dioscorides described the medicinal use of some 600 medicinal plant species and around 900 herbal, 35 animal and 90 mineral drugs (Riddle, 1985). Around a century later Galen reported about 850 simple drugs largely overlapping with those mentioned in Dioscorides but indicating considerably fewer medicinal uses (c.f. Galenus, 1561; Leonti et al., 2015). Often, each specific plant taxon was referred to by a "code" comprising the list of its known vernacular names in different languages, the strict cross-referencing of names and uses serving as a protocol for academic rigour to ensure correct plant identification between regions, and hence the applicability of herbal texts in a wider geographical and cultural context, allowing scientific knowledge to grow and become consolidated.

The development, mutual influence and phylogeny of Greek herbals are relatively well documented, including the detection of lost copies through missing links (Tschirch, 1910; Singer, 1927). Dioscorides for instance, quotes and makes reference to a range of different authors and texts that have been preserved (e.g. works ascribed to Theophrastus and Hippocrates) and others, that are now lost or survive only in fragments (e.g. works by Sextius Niger (late 1st century BC to first half of 1st century AD) and Krateuas (ca. 100 BCE)). An important intermediate step, which facilitated the transmission of Greek and Byzantine medical knowledge into Arabic and to the medieval Islamic world were translations into Syriac (Russell, 2010). The Arab culture not only preserved classic medical knowledge, but also developed it further and enabled the transmission back to the Occident through the School of Salerno (ca. 1000–1300 CE) as well as al-Andalus (711–1492; Urdang, 1951). New and valuable insights regarding the transmission of Greco-Roman medical knowledge to the Arabic world are expected from the study of the so-called "Syriac Galen Palimpsest". This manuscript is currently the oldest known copy of Galen's work on herbal preparations and is crucial because it provides variant readings that differ from the younger Greek copies and therefore can be used to identify interpolations as well as different textual interpretations (Bhayro et al., 2013).

The classic Mediterranean *materia medica* also influenced the structure, the literary form and the content of the middle and northern European herbals. During the Middle-ages Benedictine monks were directed by monastic rule to duplicate herbals and to tend medicinal herb gardens such as those of the Abbeys of Montecassino (Italy) and St. Gall (Switzerland) (Tschirch, 1910). During the Renaissance, the classic Greco-Roman herbals and medical texts were critically analysed, commented upon and translated into modern languages receiving important print runs. However, Renaissance herbals also contained the consensus on central and northern European medical folk knowledge and were accompanied by woodcut illustrations imposing the plant identifications of the commentators. The *Gart der Gesundheit* written by Johann Wonnecke von Kaub (ca. 1430–1504), physician to the city of Frankfurt a. M. and illustrated by Erhard Reuwich (1450–1505), a Dutch graphic artist, is regarded as the first comprehensive German herbal (Müller, 2011). The *Gart der Gesundheit* contains 435 monographs and draws on Mediterranean sources, such as Pliny's Natural history (1st century AD), the *Canon medicinae* by Avicenna (Ibn Sina, ca. 980–1037), the *Pseudo-Serapion* (*Aggregator*) by Ibn Wafid (11th century, Toledo) and the *Circea Instans* by Matthaeus Platearius (12th century, School of Salerno), as well as on texts written in German and containing Middle-European knowledge such as the *Buch der Natur* (Book of Nature) by Konrad von Megenberg (1309–1374) and the *Physica* by Hildegard of Bingen (1098–1179; Mayer, 2011). The invention of the printing press triggered a boom in producing European herbals and a race among authors, who were not always exempt of nationalist sentiments. Ancient Greco-Roman knowledge was translated, commented and integrated with the documentation of traditional folk knowledge on central and northern European *materia medica* by Peter Schöffer (ca. 1425–1503), Jan Stanko (1430–1493), Jean Ruelle (1474–1537), Otto Brunfels (1488–1534), Adam Lonitzer (1528–1586), Leonhard Fuchs (1501–1566), Hieronymus Bock (1498–1554), William Turner (1508–1568), Marcin of Urzędów (1500–1573), Andrea Matthioli (1501–1578), Rembert Dodoens (ca. 1516–1585), Tabernaemontanus (1525–1590), Péter Melius Juhász (1532–1572), Simon Syrenius (1540–1611), Caspar Bauhin (1560–1624), John Gerard (1545–1612), Fabio Colonna (1567–1640) and other authors (Fig. 2). A systematic analysis regarding the questions as to what plant taxa and uses were described for the first time in which herbal, and how much information was directly adopted from the classic literature, is still lacking, however.

Also the first official pharmacopoeias drew heavily on the Greco-Roman and Arabic medical treatises. Besides Hippocrates, Pliny, Dioscorides and Galen, of particular importance were Matthaeus Platearius (12th century), Rhazes (865–925) and Avicenna (ca. 980–1037; Urdang, 1951). Due to the format and presentation adopted, the *Compositiones medicamentorum*, a formulary by the Roman Scribonius Largus (1st century AD) and three texts written after 1000 CE at the School of Salerno, i.e. the *Antidotarium Nicolai* (ca. 1100), the *Antidotarium Nicolai Myrepsi* (13th century) and the *Antidotarium* or *Grabadin of Pseudo-Mesue* (ca. 13th century), are regarded as precursors of the official city-pharmacopoeias (Urdang, 1951). Another important part of the body of work crafted at the School of Salerno stems from Constantinus Africanus (11th century), a Carthaginian herbal merchant who gathered Arabic medical texts in North Africa and translated them into Latin (Müller, 2011).

Evidence of early imports of herbal drugs and spices from the orient exist for the Roman period and is well documented for the New World and