Review Article

Dioscorides' Investigations on Pharmacological Properties of *Pistacia lentiscus* L. and *Marrubium Vulgare* L.: Two Plants with Timeless Medicinal Use

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Abstract

Pistacia lentiscus L. and Marrubium vulgare L. are two plants described by Pedanius Dioscorides that have been examined for their use in medicine. This review aimed to determine whether the pharmacological properties of these two plants identified by Dioscorides are consistent with modern pharmacological data. There will also be a record of the chemicals identified by these plants from different studies and their contributions to disease control. A hundred literature references were studied in this review work but only 51 references were included. Many of the substances isolated from *P.lentiscus* and *M.vulgare* have pharmacological properties described by Dioscorides. The pharmacological properties of these two plants have been certified by modern techniques described in several of the articles mentioned in this mini review. Many studies have shown that mastic oil (originated from *P.lentiscus*) has a chemotype dominated by monoterpene hydrocarbons, alcohols, aldehydes, ethers, oxides, furans, sesquiterpene hydrocarbons and monoterpene hydrocarbons with specific biological effects. The chemical composition of the aerial parts of *Marrubium vulgare* consist of y-eudesmol, β - citronellol, citronellyl formate, germacrene D, flavonoids and polyphenolic compounds. It can be concluded that the results are highly consistent with the observations of Dioscorides. Further studies can reveal if the rest of the plants listed in the book De Materia Medica are related to the pharmacological properties recently reported. There are many substances with pharmacological use in plants described by Dioscorides that have remained largely unnoticed to date. Many texts written so far contain a wealth of knowledge. This information combined with state-of-the-art techniques could lead to faster and more targeted results in the field of herbal medicine.

Keywords: De Materia Medica, Marrubium vulgare, Dioscorides, Medicinal use, Pistacia lentiscus, Pharmacology

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Introduction

Pedanius Dioscorides of Anazarbus was a Greekspeaking physician, pharmacist and pharmacologist who lived in the 1st century AD (ca AD 40-80). He was born in Anazarbus, an ancient city at Cilicia, under the Roman empire (1). Dioscorides studied botany and pharmacology under Areius of Tarsus and traveled to Crete, Egypt, Petra and Greek mainland collecting information about the medical uses of herbs, minerals and animal products (2). He gathered in his travels information on more than 700 plants and 1000 medicines included in a five-volume book entitled Peri hules iatrikes (De Materia Medica) (3). His method was to associate the drug with its clinical results, free from any supernatural mood that was as an innovative process changing the world of pharmacology (4). In this mini review, an attempt was made to relate the pharmacological properties of two plants, i.e. Pistacia lentiscus and Marrubium vulgare, that were described by Dioscorides, with their pharmacological actions at present. Pistacia lentiscus is an evergreen shrub which is found in the eastern Mediterranean area and belongs to the Anacardiaceae family. The variety chia is cultivated exclusively on the south side of the island of Chios for the special resin it produces and is known as mastic. Dioscorides made very extensive reports for mastic and its therapeutic properties and found it effective in cleaning the teeth and healing stomach aches as well as chronic cough. Moreover, he reported that it could contribute to blood coagulation and is effective on intestinal disorders (5).

Marrubium vulgare (white horehound or common horehound) which is the most representative plant among the Marrubium species is a member of the Lamiaceae family. This perennial aromatic herb is native to Europe and Asia (India and Iran). In the third volume of *De Materia Medica*, Dioscorides gives a full description of *Marrubium vulgare*. Dioscorides considered it a stimulant, expectorant, deobstruent, carminative and local anodyne. Moreover, he maintained that the leaves together with honey could be given to those who suffer from tuberculosis, asthma and cough. It is also able to drain the phlegm form the breast. Furthermore, it induces induce menstruation and expel the placenta in women. After mixing the leaves with honey, cataplasms are formed that clean dirty abscesses. Moreover it reduces jaundice (14, 19).

Materials and Methods

The articles published on P. lentiscus and M. vulgare were searched and downloaded using the popular academic search engine Google Scholar and the academic databases of SCOPUS and PubMed. The criteria for the inclusion of the studies in the present work were the existence of approved methods for the determination of chemicals in these plants and the existence of strong literature reports on their pharmacological action. On the contrary, studies with an unclear method were excluded, which simply assumed that the substances contained in these plants could have some uses. The last criterion was the date of the article. An attempt was made to include the most updated bibliography. Other literature sources were also used including books. In a time period from March to September 2020, about 100 literature articles were studied and 51 literature references were included in this mini review. The keywords used in this search were Dioscorides, Marrubium vulgare, Pistacia lentiscus, De Materia Medica, medicine properties, antibacterial, and antifungal. A specific strategy was followed for this work. The initial selection of the plants was made after an extensive search in the works of Dioscorides. Sunsequently, the pharmacological uses of these plants were recorded as mentioned by Dioscorides. This was followed by an extensive search in contemporary articles related to the work of the ancient Greek doctor. The articles selected are those which (using modern techniques) certify the pharmacological properties of the substances derived from these plants. Finally, we tried to quantify the results by showing the number of articles that certify each pharmacological property that Dioscorides has described for each of these plants.

Results and Discussion

Many studies have shown that mastic oil has a chemotype dominated by monoterpene hydrocarbons, mainly α -pinene (75.6 %) and β -myrcene (16.6 %) that together constitute over 90 % of the oil. Moreover,

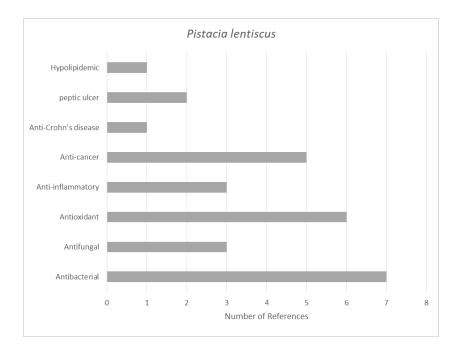
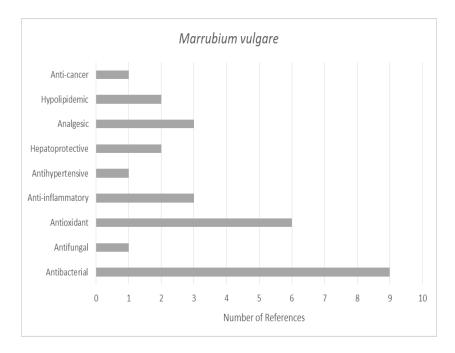
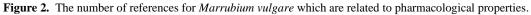


Figure 1. The number of references for Pistacia lentiscus which are related to pharmacological properties. Marrubium vulgare L.





mastic oil contains trace amounts of alcohols (linalool, cis-3-pinen2-ol, trans-pinocarveol), aldehydes (α campholenal), ethers (o-methyloanisole, anethole), oxides (α -pinene oxides), furans (perillene), sesquiterpene hydrocarbons (β -caryophyllene) and monoterpene hydrocarbons other than the major ones such as β -pinene, limonene and camphene (6-7).

These substances seem to have a variety of biological effects (Table 1).

Gas chromatography has revealed the chemical composition of the aerial parts of *Marrubium vulgare*, consisting of y-eudesmol, β - citronellol, citronellyl formate, germacrene D, flavonoids and polyphenolic compounds. The biological effects of these compounds

Biological Activity	Reference No
Antibacterial	[6], [8], [12], [13], [38], [41], [44]
Antifungal	[6], [38], [42]
Antioxidant	[8], [12], [39], [41], [42], [47]
Anti-inflammatory	[7], [43], [46]
Anti-cancer	[7], [10], [11], [40], [48]
Anti-Crohn's disease	[8]
peptic ulcer	[12], [45]
Hypolipidemic	[9]

 Table 1: Biological Activities of Mastic.

Table 2: Biological Activities of Marrubium vulgare L.

Biological Activity	Reference No
Antibacterial	[20], [25], [26], [27], [28], [29], [30], [32], [36]
Antifungal	[25]
Antioxidant	[28], [31], [33], [35], [36], [37]
Anti-inflammatory	[19], [22], [50]
Antihypertensive	[23]
Hepatoprotective	[24], [51]
Analgesic	[21], [27], [34]
Hypolipidemic	[18], [49]
Anti-cancer	[29]

have been investigated (Table 2) (14-19).

To summarize the results, it can be concluded that they highly consistent with the observations of Dioscorides. The strong antibacterial, antioxidant and anti-inflammatory activities of *Pistacia lentiscus* L. and *Marrubium vulgare* L. may explain the medicinal effects of these plants as described in the book *De Materia Medica*. Further studies can reveal if the rest of the plants listed at the book *De Materia Medica* are related to pharmacological properties recently reported. Further investigations on substances with pharmacological use in plants described by Dioscorides that have been ignored to date are required to be conducted.

Conclusion

The present study revealed that there are significant data in the modern literature that support the pharmacological properties of *Pistacia lentiscus* L. and *Marrubium vulgare* L. Modern techniques have identified the existence of chemicals and their associations with the treatment of specific diseases. In

the present work, a stapling of all this knowledge that was scattered in the bibliography was made. It was also found that the pharmacological properties of these plants as described in the texts of Dioscorides are in agreement with the results of modern studies. This is a good indication of the scientificity of this ancient text of pharmacology. Moreover, further explorations are necessary to establish the validity of other observations of Dioscorides on the pharmacological properties of other plants as described in his texts. Finally, in a reverse process we could look for new pharmacological properties in plants based on the observations of Dioscorides that have not been investigated so far.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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