



ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ

Εθνικόν και Καποδιστριακόν
Πανεπιστήμιον Αθηνών

— ΙΔΡΥΘΕΝ ΤΟ 1837 —

ΤΜΗΜΑ ΦΑΡΜΑΚΕΥΤΙΚΗΣ

ΤΟΜΕΑΣ ΦΑΡΜΑΚΟΓΝΩΣΙΑΣ & ΧΗΜΕΙΑΣ

ΦΥΣΙΚΩΝ ΠΡΟΪΟΝΤΩΝ

Ο ρόλος των εθνοφαρμακολογικών μελετών στη σύγχρονη θεραπευτική

Δρ. Νεκτάριος Αληγιάννης
Αναπληρωτής Καθηγητής

Traditional Medicine & Globalization



Traditional medicine is the sum total of the knowledge, skill, and practices based on the **theories, beliefs, and experiences** indigenous to different cultures, **whether explicable or not**, used in the **maintenance of health** as well as in the **prevention, diagnosis, improvement or treatment** of physical and mental illness

- In **developed countries**, adaptations of traditional medicine are termed **complementary and alternative medicine**



- In **developing countries** herbal medicines are mostly the only **available and affordable treatment option**



Traditional Medicine (TM) in Modern Times

In some **Asian** and **African** countries, up to **80%** of the population relies on **TM** for their **primary health care** needs

- ✓ Traditional Chinese medicine
- ✓ Ayurveda
- ✓ Siddha medicine
- ✓ Unani
- ✓ Traditional African medicine
- ✓ Muti, Ifá etc



- **Inappropriate use** of traditional medicines or practices can have **negative** or **dangerous** effects
- **Further research** is needed to ascertain the **efficacy** and **safety** of such practices and medicinal plants used by traditional medicine systems

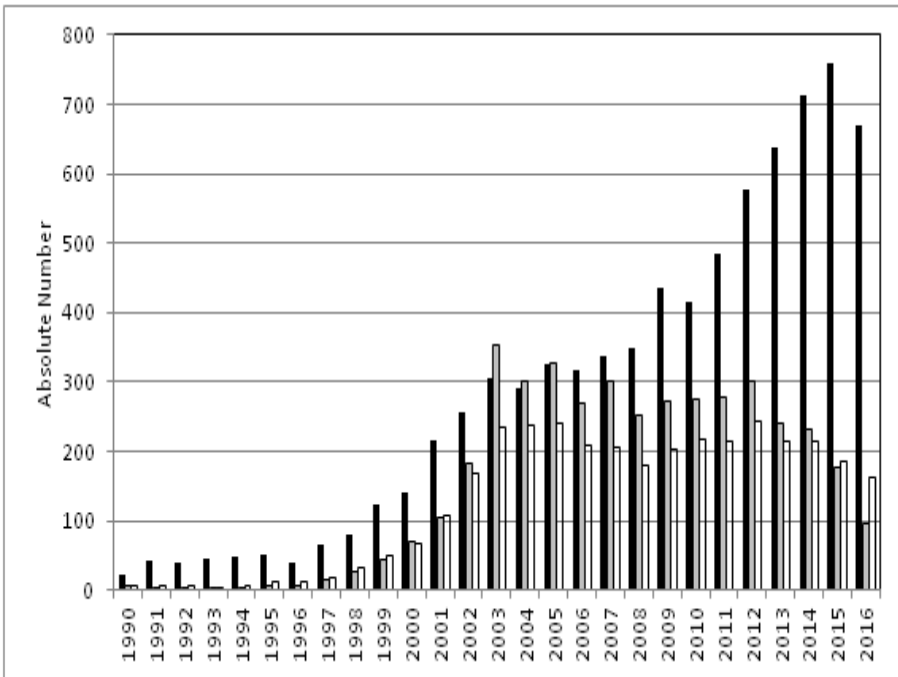
Herbal Medicine (HM) - Definition



Herbal medicines (HM) are remedies containing crude “**herbs, herbal materials, herbal preparations and finished herbal products that contain as active ingredients parts of plants, or other plant materials, or combinations**”

- **Authorized herbal medicinal products** according to the European Union framework for medicines regulation [EC 2001/83 – 2004/24]
- **Botanical or dietary herbal supplements** used for medicinal purposes like in the United States and almost all other countries, and
- Single, individual preparations that are prepared and/or **used by the consumers themselves or prescribed by a herbal practitioner or a physician**

Trends in Herbal Medicine Use: Increasing Use and Popularity



Running total of the number of research papers listed on PubMed from **1990-2016** containing the terms:

- “**herbal medicine – phytotherapy**”
(**white bar** reduced 1/10)
- “herbal medicine-phytotherapy and **clinical trials**” (gray bar)
- “herbal medicine-phytotherapy and **safety aspects**” (adverse reactions or events, black bar)

In the 21st century, with the increased efficacy in pharmacological effects of medicinal plants, herbal medicine has been considered as a promising future medicine for the management of health care

Trends in Herbal Medicine Use: Return to Nature

❖ **4 billion people (80% of the world's population) use herbal medicines for one or other aspect of primary health care**

- growing recognition that the natural products have **less side effects than synthetic pharmaceuticals**
- easy availability of natural products at affordable prices
- improved access to health information
- changing values and lower tolerance against paternalism

❖ **In the developing countries the rate of population which use herbs could be as high as 95%**

- Botanical/herbal products and preparations are usually **the only accessible and affordable treatment options**
- Encouragement to use traditional plant medicine **to accomplish needs unmet by modern systems**

Trends in Herbal Medicine Use: Return to Nature

- ❖ **In industrialized countries, 10-50 % of the population regularly uses herbal products**
 - It is estimated that in Europe, North America, and other developed countries, more than **50% of the population have used herbal medicinal approaches** at least once in life
 - About **70%-90% of the population in Canada and Germany** have used herbal medicines at least once in their life
 - In the United States, it is believed that **158 million of the adult population use herbal medicines** and its use is continually being increased
 - It has been estimated that **70% of all medical doctors in France and Germany** are regularly prescribing herbal medicine

However, there are also increasing concerns about the **safety, standardization, efficacy, quality, availability, and commercialization** of herbal products

Hellenic (Greek) Traditional Medicine in modern times

After 1960 a significant reduction in the use of medicinal plants was observed

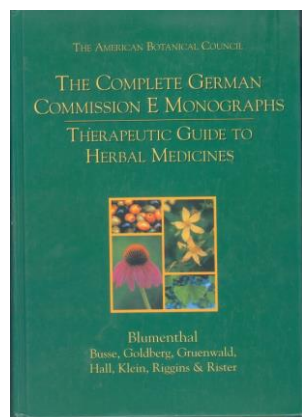
- Only the elderly people still keep the tradition, while younger people do not seem interested to the herbal remedies
- People without scientific knowledge about the healing properties of herbs engage with their commercial exploitation
- The efficacy and safety of herbs was questioned
- The uses of Greek traditional medicinal plants has not been recorded nor documented until now in a systematic way
- Traditional medicine is based on knowledge transmitted orally

✓ **the risk of extinction of Greek folk medicine is evident**

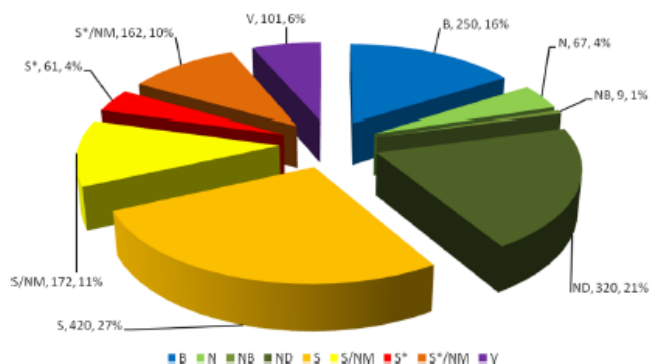
Herbal Medicine use: The role of Herbal Monographs

The appropriate medicinal use is described in **well recognized herbal monographs** provided by the:

- **Committee on Herbal Medicinal Products (HMPC) of the European Medicines Agency (EMA; available via www.ema.europa.eu)**
- **European Scientific Cooperative on Phytotherapy (ESCOP; available via www.escop.com)**
- **World Health Organization (WHO; available via apps.who.int).**



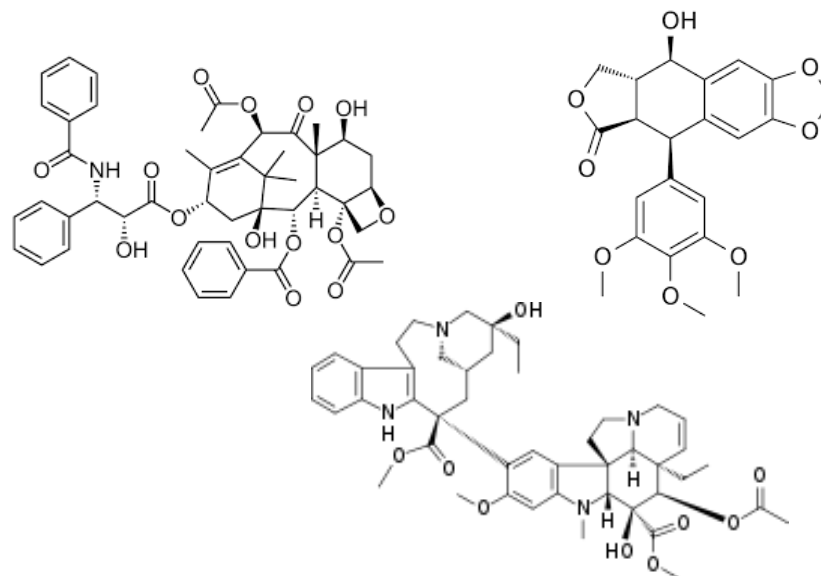
From Herbal Medicine to Drug discovery



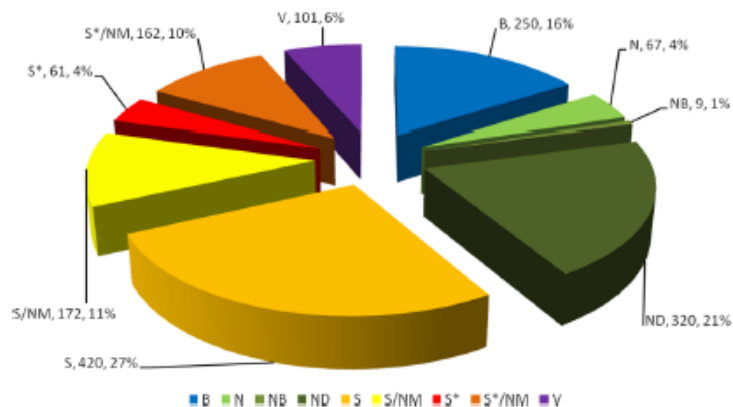
All new approved drugs 1981–2014

- “B”: Biological, large peptides or Proteins
- “N”: Natural product
- “NB”: Natural product “botanical drug”
- “ND”: Derived from a natural product
- “S”: Totally synthetic drug
- “S*”: Made by total synthesis - pharmacophore from a natural product
- “V”: Vaccine

Medicinal plants are considered as rich sources of phytochemical ingredients which play a vital role for the development of new drugs

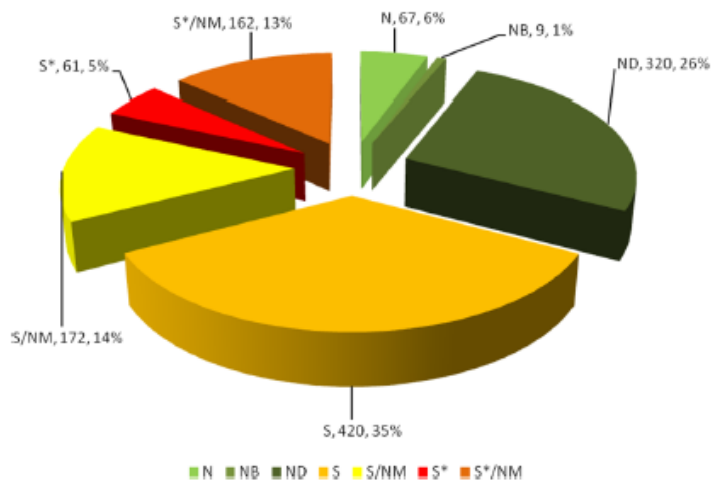


Φυσικά προϊόντα ως πηγές νέων φαρμάκων

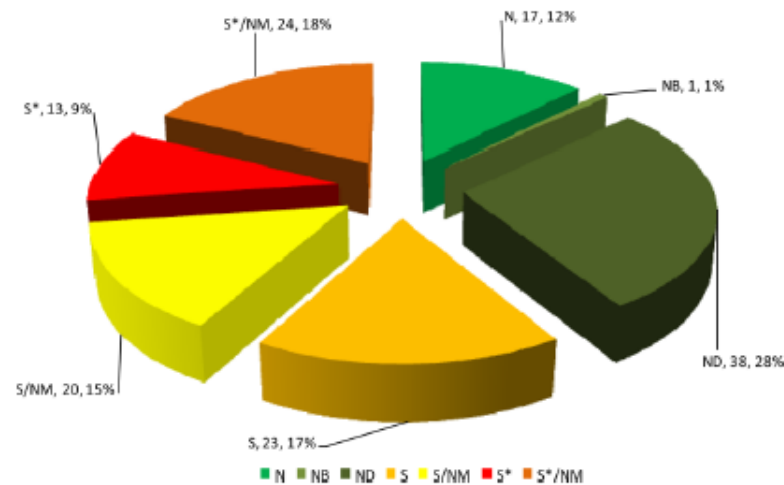


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All small-molecule approved drugs 1981–2014



Small-molecule anticancer drugs 1940s–2014

Εθνοφαρμακολογία

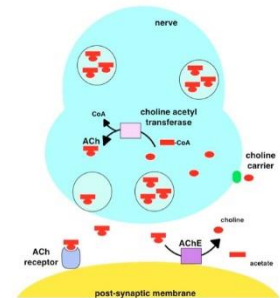
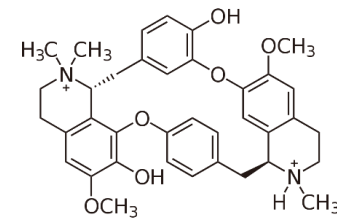
Αντικείμενο αποτελεί η διεξοδική διερεύνηση των βιολογικά ενεργών ουσιών που παρατηρήθηκαν ή χρησιμοποιήθηκαν στα πλαίσια της παραδοσιακής κουλτούρας των λαών (Bruhn & Holmstedt, 1981)



Chondrodendron tomentosum



Strychnos toxifera



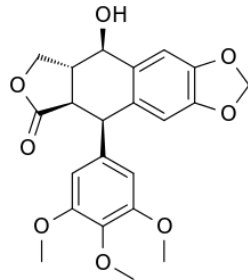
Claude Bernard
(1813-1878)

Εθνοφαρμακολογία

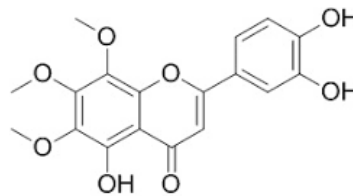
Η Εθνοφαρμακολογία δεν εστιάζει μόνο στην παραδοσιακή χρήση των φυτών αλλά δίνει έμφαση και στην επιστημονική διερεύνηση και τεκμηρίωση



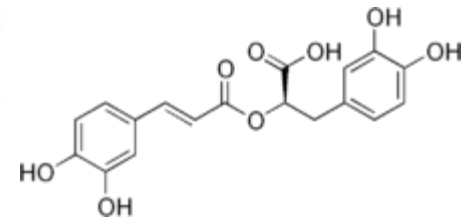
Hyptis verticillata Jacq.
(Lamiaceae)



Podophyllotoxin

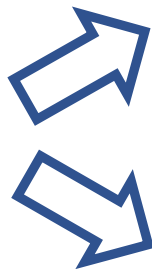


Sideroflavone



Rosmarinic acid

Traditional medicine
(*Lowland Mixe of
Oaxaca, Mexico*)



Plant is ground up with a little alcohol or the mashed leaves



Skin infections

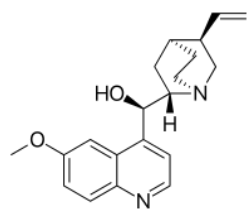
A tea is prepared of fresh leaves



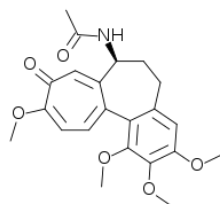
Inflammation,
gastrointestinal pain

Ethnopharmacology in drug discovery

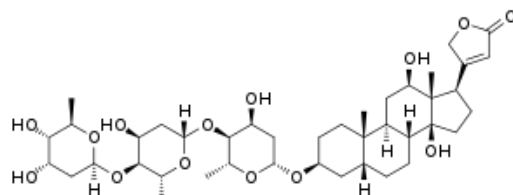
Herbal sources	Active ingredients
<i>Cinchona succirubra</i> Pav [syn. <i>C. pubescens</i> Vahl] (Rubiaceae)	Quinine
<i>Colchicum autumnale</i> L. (Colchicaceae)	Colchicine
<i>Digitalis</i> spp. (Scrophulariaceae)	Digitalis glycosides
<i>Papaver somniferum</i> L. (Solanaceae)	Morphine, codeine, papaverine
<i>Physostigma venenosum</i> Balfour (Fabaceae s.str.)	Physostigmine
<i>Pilocarpus jaborandi</i> Holmes (Rutaceae)	Pilocarpine



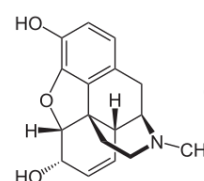
Quinine



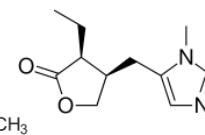
Colchicine



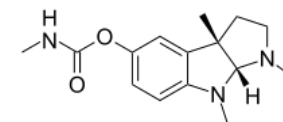
Digoxin



Morphine



Pilocarpine



Physostigmine

25% of the modern medicines have been derived from plants being used in traditional medicine

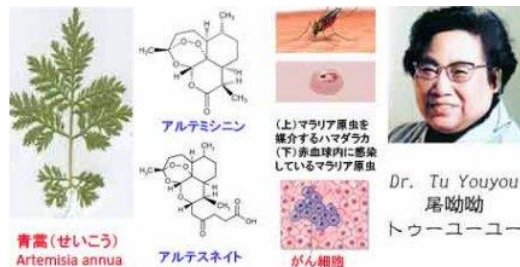
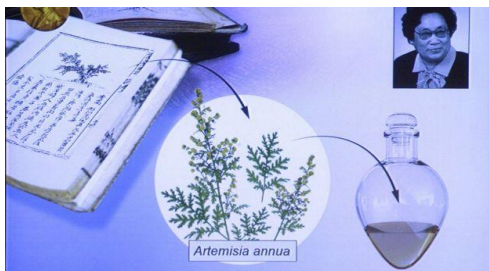
Traditional Chinese Medicine (TCM)



Dr. TU Youyou has been honored for her discovery of the antimalarial compound artemisinin

Artemisinin... is a true gift from old Chinese medicine. But this is not the only instance in which the wisdom of Chinese medicine has borne fruit

- 240,000 compounds had already been tested for use as potential antimalarial drugs
- Tu Youyou turned to Chinese **medical texts** from the Zhou, Qing and Han Dynasties
- It was reported that the sweet wormwood *Artemisia annua* (Asteraceae) was used in China around 400 AD. to cure "intermittent fevers"
- Artemisinin proved a spectacularly effective drug against malaria by rapidly killing *Plasmodium* parasites at an early stage in their development
- Artemisinin, is part of current combination therapy for malaria saving hundreds of thousands of lives per year



Chinese medicine will help us conquer life-threatening diseases worldwide, and that people across the globe will enjoy its benefits for health promotion

Ο σύγχρονος ρόλος της Εθνοφαρμακολογίας

- Η νυχτερίδα τρέφεται όχι με το κρέας των θυμάτων τους αλλά με το αίμα τους
- Ένα ανεπαίσθητο δάγκωμα προκαλούσε το θάνατο λόγω αιμορραγίας
- Η νυχτερίδα ήταν γνωστή ως νυχτερίδα - βρυκόλακας



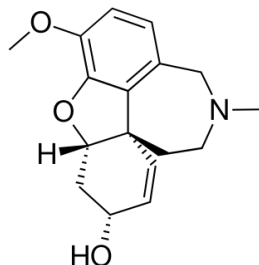
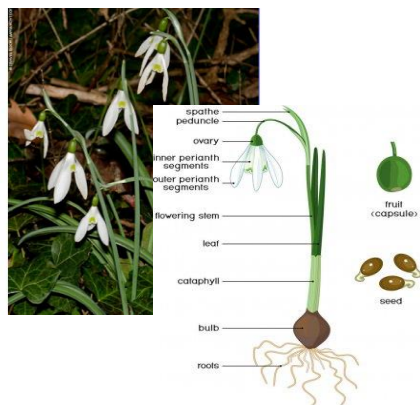
Desmodus rotundus

Το σάλιο της νυχτερίδας περιέχει την δεσμοτεπλάση, μιας πεπτιδικής φύσεως ουσία η οποία διαθέτει θρομβολυτικές ιδιότητες

Είναι σε κλινική φάση III για Θρομβόλυση σε οξεία ισχαιμία των κάτω άκρων

Ethnopharmacology in Drug Discovery

The most correct view is to look for the identity of the plant in an anticholinergic antidote



- In 1950 the Bulgarian Ethnopharmacologist Paskov recorded the habit of the population of some villages in use of the drug
- The villagers rubbed the sexes of the plant on affected areas
- The further pharmacognostic study led to his isolation alkaloid galantamine
- Pharmacological research has shown that galantamine inhibits acetylcholinesterase, the an enzyme that causes it to break down neurotransmitter acetylcholine
- Acetylcholine plays important role in both muscle contraction and maintaining muscle tone
- Thus, galantamine has been used successfully in the treatment of neuritis and neuralgia
- In 1980 it was found that the drug is able to penetrate him blood-brain barrier
- in 2001 the galantamine was approved by FDA for Alzheimer's disease (Reminyl®)
- Narcissus bulb (*Narcissus pseudonarcissus*) was found so rich in galantamine used in crops in Belgium



Αντικείμενα

- Συστηματική αναζήτηση, καταγραφή και διάσωση δεδομένων από έργα των Αρχαίων Ελλήνων Ιατρών, χειρόγραφα βυζαντινής και μεταβυζαντινής περιόδου και πληροφορίες παραδοσιακής θεραπευτικής που μεταφέρονται με τον προφορικό λόγο (Διατήρηση πολιτισμικής κληρονομιάς)
- Αναζήτηση δεδομένων παραδοσιακής θεραπευτικής για την ασφαλή και αποτελεσματική χρήση δρογών φυσικής προέλευσης (Κατάρτιση μονογραφιών)
- Συμβολή στην ανακάλυψη βιοδραστικών φυσικών προϊόντων για την ανάπτυξη φαρμάκων, καλλυντικών προϊόντων και συμπληρωμάτων διατροφής

Εθνοβοτανικές μελέτες

Είναι κρίσιμη η επιλογή της περιοχής στην οποία λαμβάνει χώρα η μελέτη (Νήσος Κρήτη)

✓ Η χλωρίδα της Κρήτης περιλαμβάνει περίπου 1.800 φυτικά είδη, εκ των οποίων το 10% είναι ενδημικά

✓ Πολλά από τα φυτά της Κρήτης χρησιμοποιήθηκαν για αιώνες από τους Κρήτες για την αντιμετώπιση διαφόρων παθήσεων

✓ Πρακτικές παραδοσιακής θεραπευτικής εφαρμόζονται ακόμη σε αρκετές ορεινές περιοχές της Κρήτης

✓ Εθνοβοτανικές μελέτες έδειξαν ότι η παραδοσιακή θεραπευτική αντικαθίσταται ολοένα και περισσότερο από τη Δυτική Ιατρική

Εθνοβοτανικές μελέτες

❖ Αρχικά χρησιμοποιούνται ερωτηματολόγια, με σκοπό να εντοπισθούν οι άνθρωποι που έχουν γνώσεις σχετικά με τις θεραπευτικές ιδιότητες των βοτάνων



Περιοχή μελέτης στη Σητεία



Περιοχή μελέτης στον Αποκόρωνα

✓ 500 Ερωτηματολόγια μοιράστηκαν σε κατοίκους περιοχών της Σητείας (η κυριότερη πόλη της ανατολικής Κρήτης) και του Αποκόρωνα (η Βορειοανατολικότερη γωνιά του νομού Χανίων)

✓ Οι άνθρωποι κλειδιά (109) εντοπίστηκαν μετά από επεξεργασία των δεδομένων που υπήρχαν στα συμπληρωμένα ερωτηματολόγια αλλά και τις υποδείξεις του τοπικού πληθυσμού των περιοχών μελέτης

Εθνοβοτανικές μελέτες

- ❖ Σε δεύτερη φάση λαμβάνει χώρα η συστηματική συλλογή πληροφοριών παραδοσιακής θεραπευτικής με τη χρήση ημι-δομημένων συνεντεύξεων



Οι συνεντεύξεις συνήθως γίνονται με ανθρώπους που έχουν γεννηθεί και έχουν περάσει το μεγαλύτερο μέρος της ζωής τους στην περιοχή μελέτης

- ✓ Σε ένα σύνολο 109 πληροφοριοδοτών έγιναν συνεντεύξεις σε σχεδόν 20 χωριά από την καθεμιά περιοχή μελέτης
- ✓ Για κάθε βότανο έχουν καταγραφεί τα ακόλουθα στοιχεία: **τοπικό όνομα, περιγραφή φυτού, περιοχή συλλογής, μέθοδοι ξήρανσης και διατήρησης, μέρη του φυτού που χρησιμοποιούνται, μέθοδος παρασκευής, δοσολογία & τρόπος χορήγησης**

Ethnobotanical Study of Medicinal Plants Used in Central Macedonia, Greece

Ethymia Eleni Tsioutsiou¹, Paolo Giordani², Effie Hanlidou³, Marco Biagi⁴, Vincenzo De Feo⁵, Laura Cornara⁶

¹ Department of Pharmacognosy and Natural Products Chemistry, Faculty of Pharmacy, National and Kapodistrian University of Athens, Athens, Greece

² Department of Pharmacy, University of Genoa, Viale Cembrano, 4, 16148 Genoa, Italy.

³ Laboratory of Systematics, Botany and Phytochemistry, School of Biology, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece;

⁴ Department of Physical Sciences, Earth and Environment, University of Siena, Via Laterina, 8, 53100 Siena, Italy;

⁵ Department of Pharmacy, University of Salerno, Via Giovanni Paolo II, 132, 84084 Fisciano (Salerno), Italy;

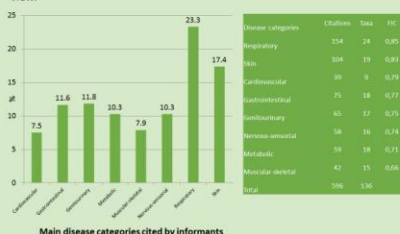
⁶ Department of Earth, Environment and Life Sciences, University of Genoa, Corso Europa 26, 16132 Genoa, Italy.

INTRODUCTION

- Medicinal plants have represented for thousands of years the only remedy for various diseases. **Phytotherapy still maintains an important role in the treatment of many diseases in Greece.** Despite this fact, only few studies explored the use of plants in folk Greek medicine (1, 2, 3, 4).
- The present study is aimed to collect, analyze and evaluate **ethnobotanical and pharmacological information on the use of medicinal plants in Central Macedonia, N. Greece.**
- The study was conducted in the area of two small cities, Edessa and Naoussa, and their nearby villages. The selection of the areas was based on the **rich flora**, and on the **cultural differences** among the population.
- The population consists mainly of **four groups**:
 - Dopioi**, i.e., the local people that remained after the migrations of the first quarter of the 20th century. Many of them speak a local Slavic-based dialect while others are Greek-speaking;
 - Pontians**, which come from the Greek population lived in the shores of the Black Sea since antiquity;
 - Mikrasiates** or **prosyfges** (meaning refugees), descendants of the Greeks of Asia Minor;
 - Vlachs** or **Aromanians**, people mostly living in montane regions and occupied in animal husbandry, who speak a Latin-based language.

RESULTS AND CONCLUSIONS

The final database included **87 taxa** belonging to 48 plant families, **Lamiaceae (21%)** and **Asteraceae (13%)** being the most represented, followed by **Rosaceae (6%)**. Cultivated plants are less frequently used, whereas the information collected is mainly referring to wild taxa, which were used to treat **8 ailment categories**. The greatest number of plants was used to treat **respiratory (FIC 0,85)**, **skin (0,83)**, **cardiovascular (0,78)**, **gastro-intestinal (0,77)** and **genito-urinary (0,76)** diseases. The most used parts of the plant were flowers and inflorescences (40%), followed by aerial parts (22%), leaves (16%), fruits and seeds (15%), and underground parts (8%). Principal methods of herbal preparations included infusion or decoction (76%), maceration in alcohol or oil (12%), used raw (7%), poultice (3%), and other (2%). The most cited species were *Hypericum perforatum*, *Matricaria chamomilla*, *Sideritis scardica* (endemic species), *Tilia platyphyllos*, and *Sambucus nigra*. The results demonstrated that the traditional knowledge of medicinal plants in Edessa and Naoussa is well preserved but a large part of Macedonia remains poorly explored from the ethnobotanical point of view.



Disease Categories	Number	Sex	FIC
Respiratory	124	24	0,80
Skin	104	19	0,81
Cardiovascular	39	9	0,79
Gastrointestinal	75	18	0,77
Genito-urinary	65	17	0,75
Genito-urinary	54	16	0,74
Metabolic	19	18	0,71
Musculo-skeletal	47	11	0,66
TOTAL	596	136	

MATERIALS AND METHODS

Ethnobotanical investigations were conducted from May 2016 to June 2017. The data were gathered through questionnaires, extensive dialogues, informal and semi-structured interviews with **96 native informants** (59 women, 37 men), who had personal experience in self-medication using herbs. The informants were requested to indicate vernacular names, parts of the plant used, **folk uses** and **preparation procedures**. In many cases specific recipes, preparations and their sources were cited. The interviews included visits in the field together with the informants in order to collect specimens and identify the medicinal plants. The information collected is referred to wild and cultivated species. The taxa were identified using Standard Floras and monographs and voucher specimens are deposited at the Herbarium of the Aristotle University of Thessaloniki (TAU).



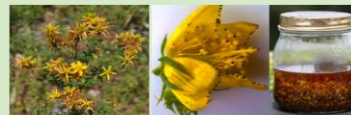
Popular remedies: *Origanum majorana* aerial part and *Arum italicum* flower

The FIC (Informant Consensus Factor)

was calculated as follows:

$$FIC = \frac{(nur-nt)}{(nur-1)}$$

where **nur** is the number of use citations in each category and **nt** is the number of used taxa (5).



Preparation of oleoile from *Hypericum perforatum* flowers.



Plants with Unusual Medicinal Uses

Among the taxa used for treating prostatitis (Genito-urinary category), the use of *Paliurus spino-christi* dried fruits and *Equisetum arvense* aerial part has been frequently reported by the informants.

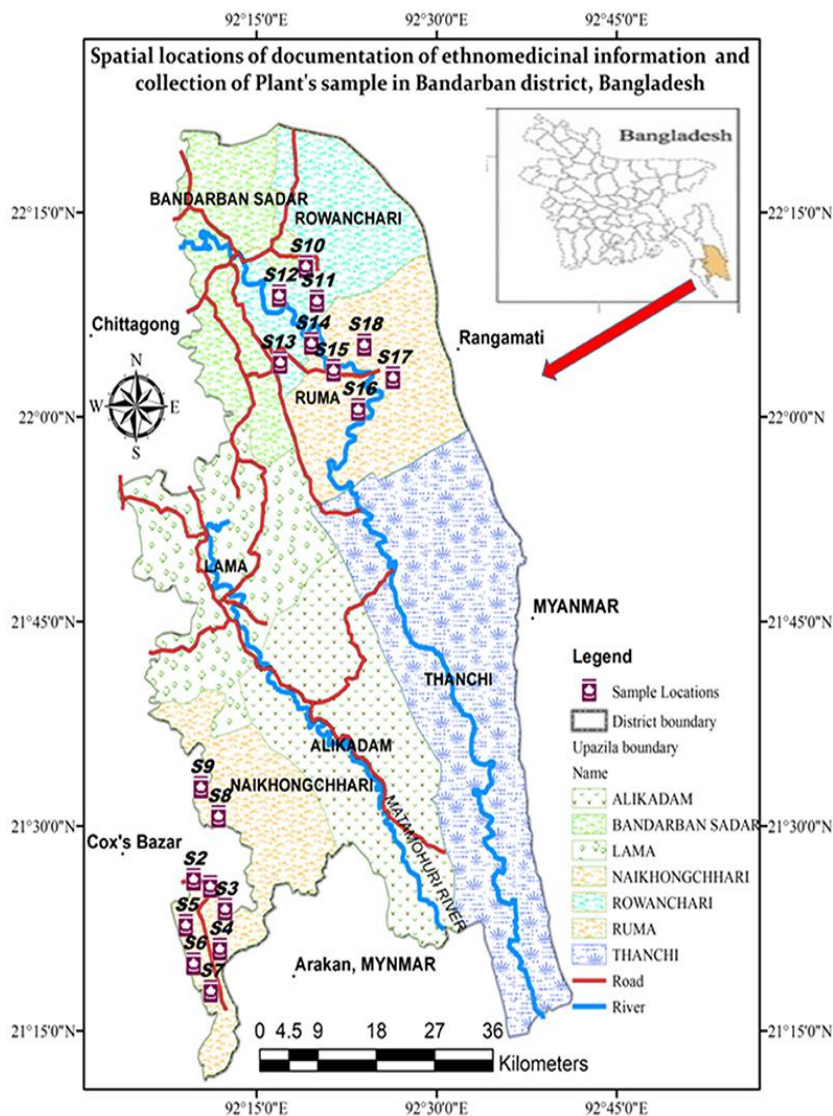
Some examples of unusual medicinal uses reported in the present study are:

- Cuscuta campestris* stems are applied topically against bee stings.
- Cynoglossum creticum* fruits have been reported to be eaten to treat a skin disease called "myrmecia" (Greek "myrmigkia" = ant), a word used all over Greece for the common skin warts caused by HPV (Human Papilloma Virus).
- Helianthus tuberosus* fragmented tuber is indicated as decoction against constipation.
- Hyssopus officinalis* aerial parts are used as analgesic to treat headache.

REFERENCES

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Quantitative Ethnobotany of Medicinal Plants Used by Indigenous Communities in the Bandarban District of Bangladesh



- A total of 12 indigenous communities live within the studied area of which three i.e., Chak, Marma, and Tanchayanga were selected for the present study
- To maximize documentation, initial contacts were established with indigenous students and local people (notably the Karbari, or headmen) to identify the traditional healers of the selected communities
- The main objective of the current study was to comprehensively document the ethnomedicinal information from the traditional healers of these three communities

Demography of Informants

Factor	Categories	Chak community	Marma community	Tanchayanga community	Total no. of persons	Percentage (%)
Sex	Male	25	74	30	129	74
	Female	9	25	11	45	26
Profession	Government employee	0	5	3	8	4.60
	Teacher	1	3	1	5	2.87
	Farmer	14	33	19	66	37.93
	House wife	6	10	5	21	12.07
	Unemployed	9	24	6	39	22.41
	Professional herbalist	5	21	9	35	20.12
Age	<30	0	11	4	15	8.62
	30–40	6	19	5	30	17.24
	40–50	10	25	18	53	30.46
	50–60	11	22	13	46	26.44
	>60	7	16	7	30	17.24

A total of 174 informants were interviewed. Out of these, 129 (74%) were male and 45 (26%) were female. As the Marma were the largest community in the study area, a larger number of informants (99) were interviewed from that community, compared to those from the Chak and Tanchayanga communities

❖ *Informant Consensus Factor (ICF)*

$$FIC = (Nur - Nt) / (Nur - 1)$$

“Nur” refers to the total number of use reports for each disease cluster

“Nt” refers the total number of species used for that cluster

The ICF values ranged from 0.65 to 0.77. The highest ICF value of 0.77 was for digestive system disorders followed by parasitic infections (0.76) and treatment of snake and insect bites (0.75), while the lowest ICF value was 0.50 for neurological and psychological disorders

❖ *Use Value (UV)*

$$UV = \sum / N$$

“U” refers to the number of uses mentioned by the informants
for a given species

“N” refers to the total number of informants interviewed

If a plant has a high UV score that indicates there are many use reports for that plant

❖ *Frequency of Citation (FC)*

$$FC = (\text{Number of times a particular species was mentioned}) / (\text{total number of times that all species were mentioned}) \times 100$$

❖ *Relative Frequency of Citation (RFC)*

The RFC index was evaluated by dividing the number of informants who mentioned the use of the species (FC) by the total number of informants participating in the survey (N).

The ethnomedicinal plants species having high RFC values indicated their abundant use and widespread knowledge among the local communities

Overview of ethnobotanical knowledge *Albania, Cyprus, Greece and Turkey*

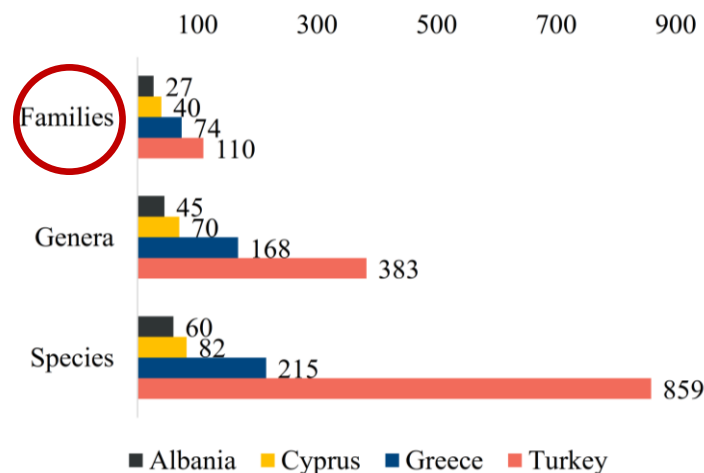
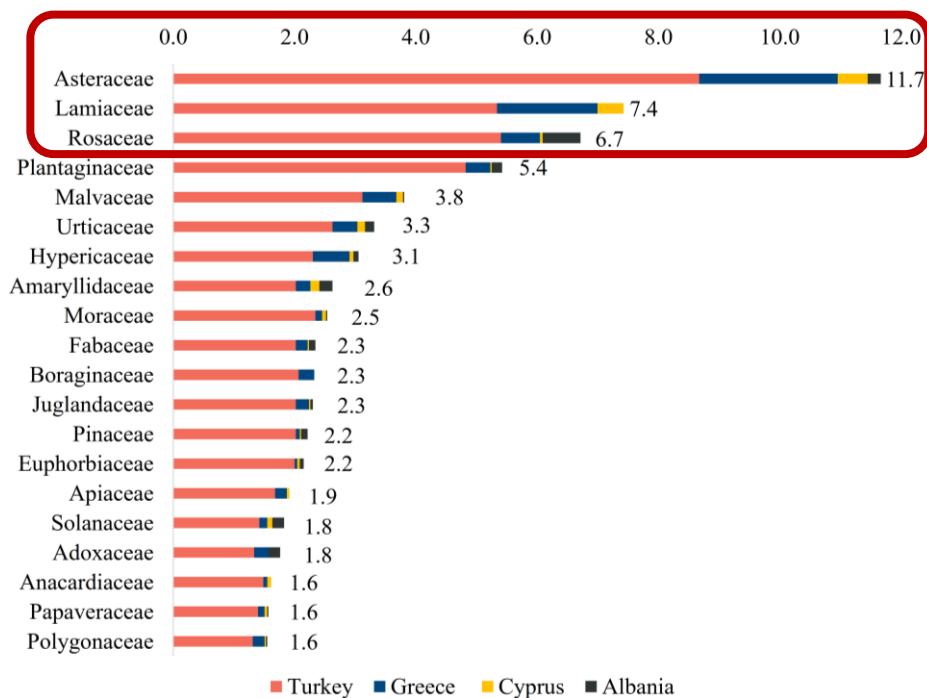


- **Distinct flora** due to the geographical and ecological characteristics of the **Balkan Peninsula and Mediterranean Sea**
- Use of **common** medicinal plants against various **skin ailments** because of **historical connection** among those countries

Results

Albania, Cyprus, Greece and Turkey

Most cited families in relation to skin ailment reports



Families: 111

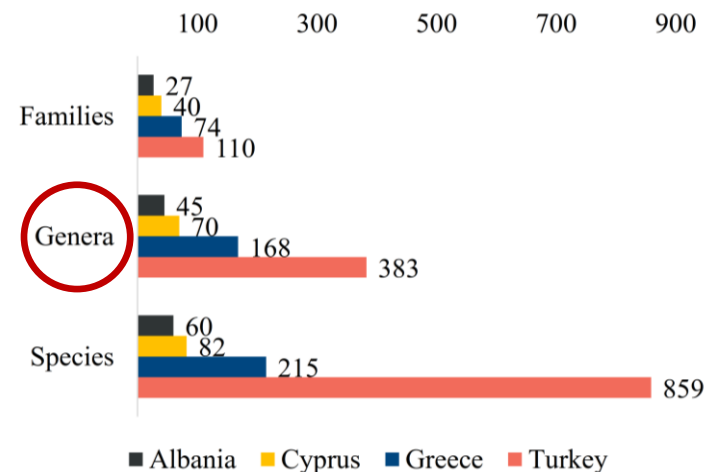
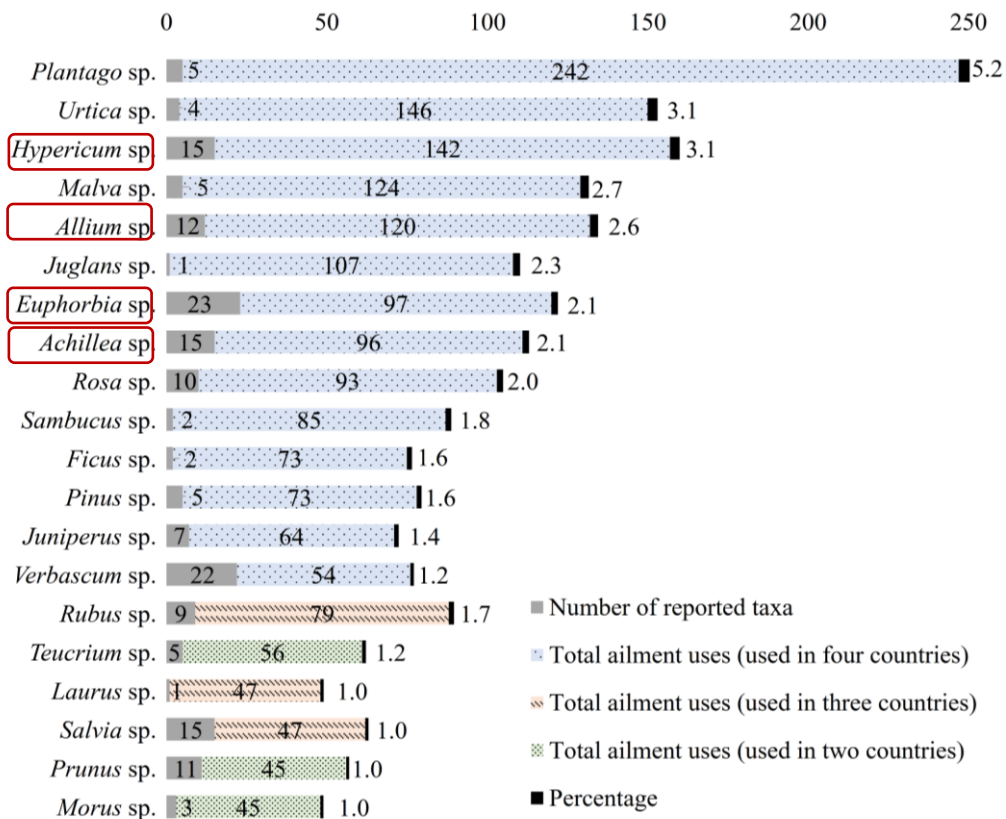
Genera: 418

Taxa (species & subspecies): 967

Results

Albania, Cyprus, Greece and Turkey

Most cited plant genera in relation to skin ailment reports



Families: 111

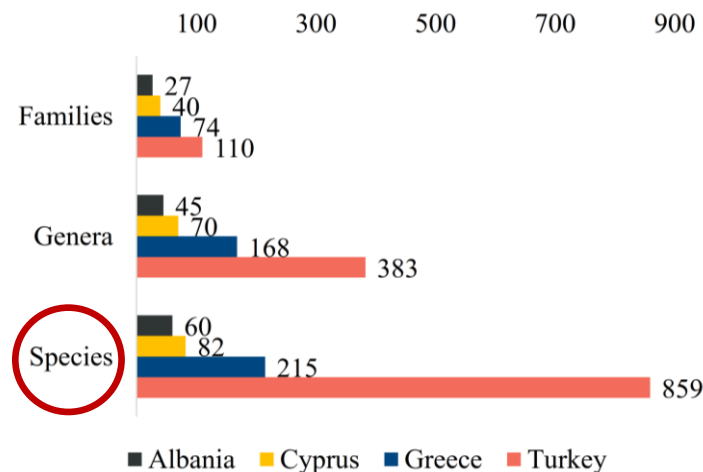
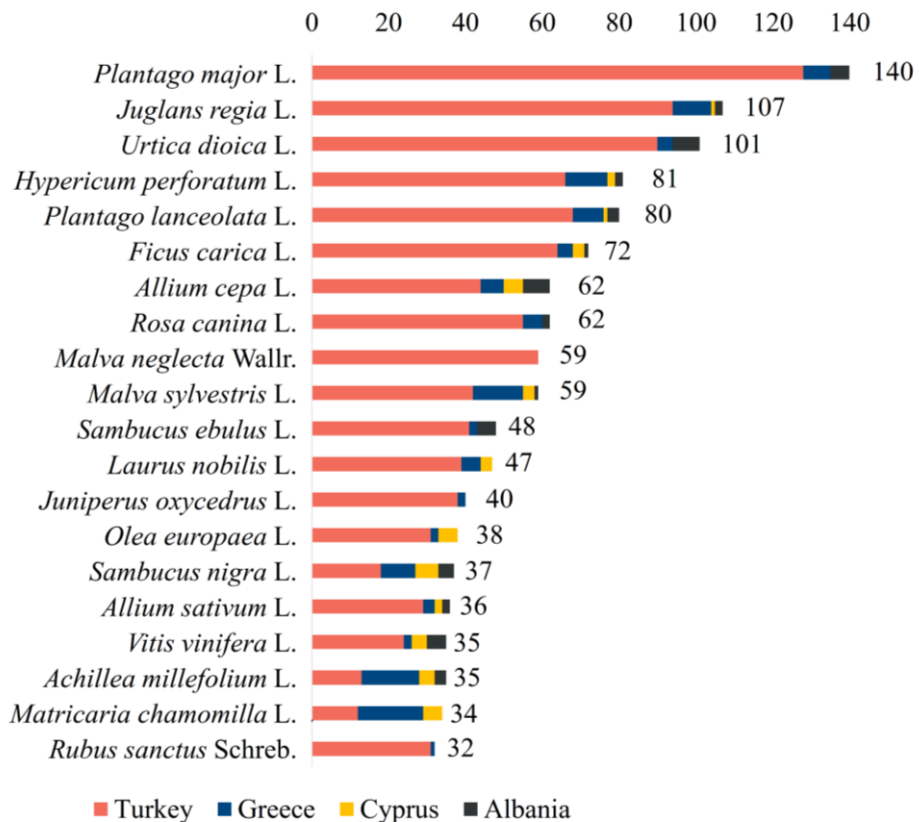
Genera: 418

Taxa (species & subspecies): 967

Results

Albania, Cyprus, Greece and Turkey

Most cited plant species in relation to skin ailment reports

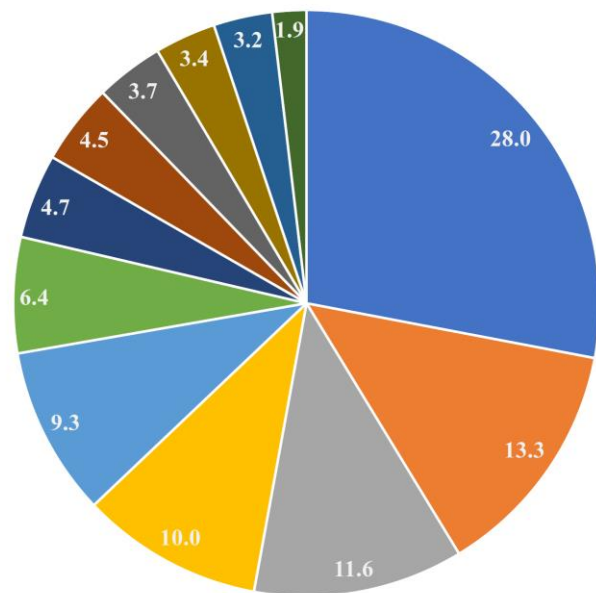


Families: 111

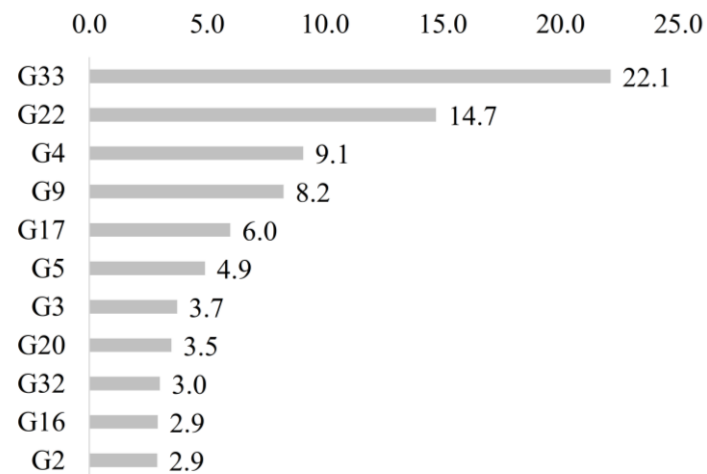
Genera: 418

Taxa (species & subspecies): 967

Most cited plant parts & skin ailments categories



- Leaves (28.0%)
- Fruits (11.6%)
- Roots/Rhizome/Radix (9.3%)
- Seeds (4.7%)
- Stems (3.7%)
- Bark (3.2%)
- Aerial parts (13.3%)
- Flowers/Inflorescence (10.0%)
- Whole plant/Herb (6.4%)
- Other (Bulbs, Essential oil etc.) (4.5%)
- Latex (3.4%)
- Resin (1.9%)



G33: Wounds, Sores, Trauma

G22: Hemorrhoids, Piles

G4: Fungal and bacterial infections, Mycodermatitis, etc.

G9: Boils, Abscess, Inflamed wounds

G17: Eczema

G5: Inflammation

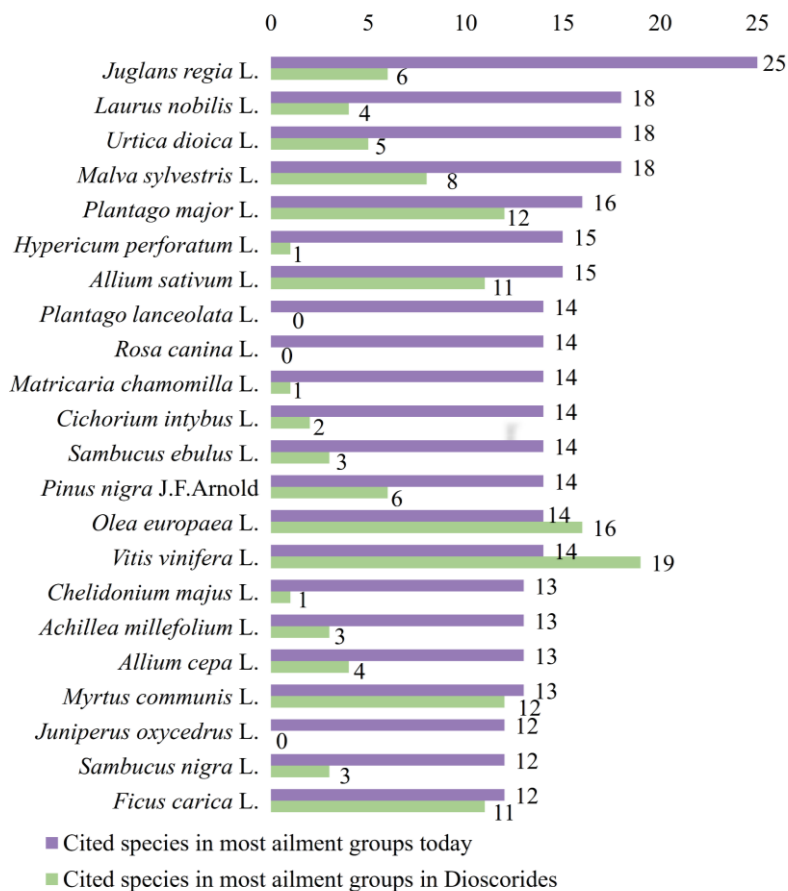
G3: Bleeding, Hemorrhage

G20: Excrescences (warts, raised moles), Skin Tumors

G32: Skin ailments (undefined)

G16: Animal bites, Insect stings

Plant species used in most ailment groups



Plant species	Common skin ailments groups
<i>Juglans regia</i> L.	G2, G4, G5, G9, G16, G33
<i>Laurus nobilis</i> L.	G5, G16
<i>Urtica dioica</i> L.	G4, G9, G16, G33
<i>Malva sylvestris</i> L.	G4, G5, G6, G16, G33, G34
<i>Plantago major</i> L.	G3, G4, G5, G9, G16, G20, G23, G33
<i>Hypericum perforatum</i> L.	G33
<i>Matricaria chamomilla</i> L.	G6
<i>Olea europaea</i> L.	G4, G5, G6, G9, G20, G33, G36
<i>Pinus nigra</i> J.F.Arnold	G2, G4, G9, G16, G33
<i>Rosa canina</i> L.	No skin related uses reported in 'Dioscorides: Materia Medica'
<i>Sambucus ebulus</i> L.	G5, G16, G33
<i>Vitis vinifera</i> L.	G4, G5, G6, G9, G10, G14, G16, G25, G29, G33
<i>Achillea millefolium</i> L.	G3, G9, G33
<i>Allium cepa</i> L.	G2, G9, G16
<i>Allium sativum</i> L.	G2, G10, G16, G29, G33
<i>Chelidonium majus</i> L.	G23
<i>Myrtus communis</i> L.	G1, G2, G9, G28, G33
<i>Plantago lanceolata</i> L.	Not mentioned in 'Dioscorides: Materia Medica'
<i>Ficus carica</i> L.	G4, G9, G16, G20, G33
<i>Juniperus oxycedrus</i> L.	Not mentioned in Dioscorides 'Dioscorides: Materia Medica'
<i>Sambucus nigra</i> L.	G5, G33

- ✓ Despite the high number of ethnobotanical studies conducted in **Turkey (103 studies with 859 different taxa)** in comparison to those conducted in Greece (**14 studies with 215 different taxa**), the percentage of common taxa reported is high (**63.3%** of all species recorded in surveys conducted in Greece)
- ✓ Inhabitants of both European part and Mediterranean coastline of Turkey have been in constant contact with Greek and other Balkan people
- ✓ Out of **215** different taxa reported in Greek ethnobotanical studies, **105 taxa (48.8%) were mentioned in 'Dioscorides: De Materia Medica'**

The limited number of surveys should raise concern because many populations, especially in remote areas, still possess vital knowledge

□ Data of published ethnobotanical studies



Country	Number of ethnobotanical surveys
Bosnia-Herzegovina	4
Bulgaria	2
Croatia	6
Italy	41
Kosovo	4
Montenegro	1
North Macedonia	3
Romania	5
Slovenia	1
Serbia	5
Turkey	101
Cyprus	5
Albania	6
Greece	14

- ✓ 198 ethnobotanical studies conducted in the Balkans have been recorded
- ✓ Data on the treatment of skin diseases have been extracted and recorded
- ✓ Their evaluation contributed to the selection of plant species to be studied

Data of published ethnobotanical studies

Code	Botanical name	Family	SD1	SD2	SD3	SD4	SD5	SD6	SD7	SD8	SD9	SD10	SD11	SD12	SD13	SD14	SD15	SD16	SD17	SD18	SD19	SD20	SD21	SD22	SD23	SD24	Total scoring
ETHTR557	<i>Plantago major L.</i>	Plantaginaceae	36	2	3			43	4		1		4		2	4	1		10	3						5	118
ETHIT243	<i>Malva sylvestris L.</i>	Malvaceae	17	7	5		4	19	2	2					2	1		1	5	2					6	13	86
ETHTR395	<i>Juglans regia L.</i>	Juglandaceae	7	13	3	5	3	3	4		1		2	1	1	11	1	1	16	1	1		2	5	2	1	84
ETHTR794	<i>Urtica dioica L.</i>	Urticaceae	6	3	1	15		3	4	1				2	1	13			24			1		1	2	5	82
ETHTR379	<i>Hypericum perforatum L.</i>	Hypericaceae	36	8			2	3							1			1	6	2		1				2	62
ETHTR319	<i>Ficus carica L.</i>	Moraceae	2	1				4	1		1		25		8	6			12							1	61
ETHTR555	<i>Plantago lanceolata L.</i>	Plantaginaceae	24		1			18							3	1			5	1						3	56
ETHIT376	<i>Sambucus nigra L.</i>	Adoxaceae	12	5			1	3		4		1	1		2		2		4	2	1				2	5	45
ETHTR446	<i>Malva neglecta Wallr.</i>	Malvaceae	14	1				13		2									11					1	1	8	51
ETHIT269	<i>Olea europea L.</i>	Oleaceae	18	2	2	3				1	1							1	1	5	1	1			1	5	42
ETHIT302	<i>Plantago major L.</i>	Plantaginaceae	20	4	3		1	10		2					9											2	51
ETHTR626	<i>Rosa canina L.</i>	Rosaceae	3	3					4	1			1			6			28	2				1		3	52
ETHIT025	<i>Allium sativum L.</i>	Amaryllidaceae	6	7	2	2	1		1		4		2		13				1		1				1	4	45
ETHIT449	<i>Urtica dioica L.</i>	Urticaceae	1	3	2	14	1	1	1	2				8	1				4	2					3		43
ETHIT178	<i>Ficus carica L.</i>	Moraceae	3		1		2	2			8	1	19		3				1							2	42
ETHIT209	<i>Hypericum perforatum L.</i>	Hypericaceae	26					1		2	2				1			1							2	1	36
ETHTR673	<i>Sambucus ebulus L.</i>	Adoxaceae	9	2				4	2	3			1		4	3			9							1	38
ETHTR051	<i>Allium cepa L.</i>	Amaryllidaceae	10	1		1		14		5					1				2			1				2	37
ETHIT403	<i>Solanum tuberosum L.</i>	Solanaceae	19	4						2		1			4			1	1							2	34

✓ 1289 different taxa were recorded

- Botanical name
- Family
- Plant part used
- Preparation
- Total number of references (Total scoring)
- Number of references per group of skin disorders

✓ The most cited skin disorders

Code	Scin Disorders	Number of Citations
SD1	Sores, Trauma, Wounds	2019
SD17	Haemorrhoids, Piles	905
SD2	Fungal & bacterial infections	730
SD6	Boils, Abscess, Furuncles	567
SD24	Skin Inflammation	486
SD23	Skin ailments, Skin diseases	453
SD14	Eczema	331
SD11	Warts, Moles, Skin Tumors	321

□ Data of published ethnobotanical studies

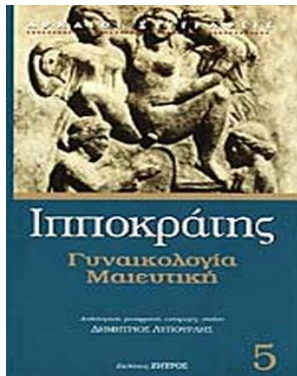
✓ Determination of selection criteria

- Proportional representation of promising plant species for each category of skin diseases
- Potential activity on more than one biological or pharmacological targets
- Preference in herbs which belong to Greek flora

✓ Consideration into account of specific factors

- **Relative Frequency of Citations (RFC):** the fraction of published studies referring to the therapeutic use of a plant species against skin diseases
- **Use Value (UV):** the total number of medicinal use citations in all publications against all skin disorders divided by the total number of published studies (198)
- **Fidelity Level (FL):** the fraction of published studies in which is referred the therapeutic use of a plant species against a specific group of skin diseases

Ιπποκράτης ο Κώος 'Γυναικολογία - Μαιευτική'



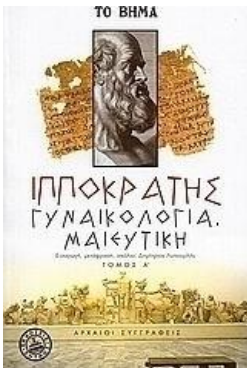
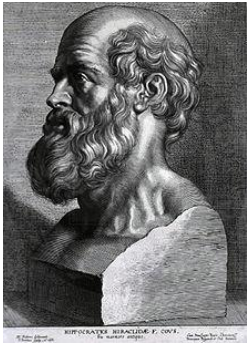
Πεδάνιος Διοσκουρίδης 'De Materia Medica'



Πληροφορίες παραδοσιακής
θεραπευτικής

**Φυσικά προϊόντα με
οστεοπροστατευτικές ιδιότητες**

❑ Ιπποκράτης (460 π.Χ. – 377 ή 356 π.Χ.)



- ✓ Απομάκρυνε τη θεραπευτική από τη μαγεία και τη δεισιδαιμονία
- ✓ Εισήγαγε τον επιστημονικό τρόπο σκέψης και την συστηματική ιατρική παρατήρηση
- ✓ Ιπποκρατικό αξίωμα: “Ο ιατρός πρέπει να ωφελεί τον άρρωστο ή τουλάχιστον να μην τον βλάπτει (Ασκέειν, περί τα νοσήματα δύο, ωφελέειν ή μη βλάπτειν)”
- ✓ Η θεραπευτική του μέθοδος, εκτός από τη χρήση βοτάνων (336 δρόγες), περιελάμβανε ειδική διαίτα και αλλαγές στον τρόπο ζωής
 - «Αν οι άνθρωποι ζούσαν και τρέφονταν σωστά δεν θα υπήρχαν αρρώστιες»
 - «Φάρμακό σας ας γίνει η τροφή σας και η τροφή σας ας γίνει φάρμακό σας»
- ✓ Ο Ιπποκράτης θεωρούσε ότι αυτά τα φυτά είναι γνωστά στους θεραπευτές και ανέφερε μόνο τα ονόματα, χωρίς βοτανική περιγραφή
- ✓ Μαιευτική-Γυναικολογία: *Περί παρθενίων, Περί γυναικείας φύσιος, Περί γυναικείων α' και β', Περί αφόρων, Περί επικυήσεως, Περί επταμήνου, Περί οκταμήνου, Περί εγκατατομής εμβρύου*

☐ Πεδάνιος Διοσκουρίδης (1^{ος} μ.Χ. αιώνας)



✓ Ως στρατιωτικός ιατρός, είχε την ευκαιρία να ταξιδεύει συνεχώς και να συλλέγει για θεραπευτικά συστατικά από όλο τον Ρωμαϊκό και Ελληνικό κόσμο

✓ Το έργο του 'Περί ύλης ιατρικής' ήταν το αποτέλεσμα προσωπικής παρατήρησης, απαλλαγμένο από προκαταλήψεις και δεισιδαιμονίες

✓ Τα πιο σημαντικά ελληνικά χειρόγραφα διατηρούνται σε μονές του Αγίου Όρους

✓ Θεωρείται ο διασημότερος φαρμακογνώστης και φαρμακολόγος της αρχαιότητας

✓ Σώζονται αρκετοί χειρόγραφοι κώδικες, οι οποίοι περιγράφουν διαφορετικό αριθμό φυτικών φαρμάκων (Συνολικά περίπου 600)



Byzantine *De Materia Medica*
(15th century)



➤ Αντικείμενο της μελέτης:

- ✓ Αξιοποίηση των γνώσεων των αρχαίων Ελλήνων Ιατρών και πληροφοριών παραδοσιακής θεραπευτικής
- ✓ Αναγνώριση ειδών με πιθανή επίδραση στις διαταραχές του εμμηνορροϊκού κύκλου και την υγεία των οστών
- ✓ Αξιολόγηση χημικού φορτίου και βιολογικών ιδιοτήτων
- ✓ Αξιολόγηση των οστεοπροστατευτικών ιδιοτήτων των φυτικών παρασκευασμάτων και των συστατικών τους
- ✓ Ανάδειξη του πλούτου της ελληνικής χλωρίδας



Η συστηματική μελέτη των φυτικών δρογών που αναφέρονται στα έργα 'De Materia Medica' (Διοσκουρίδης) και 'Γυναικολογία-Μαιευτική' (Ιπποκράτης) για την ανακάλυψη βιοδραστικών φυσικών προϊόντων με πιθανές ευεργετικές επιδράσεις έναντι της οστεοπόρωσης

Φαρμακολογικός στόχος

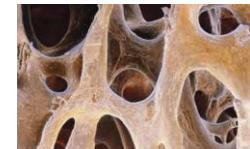
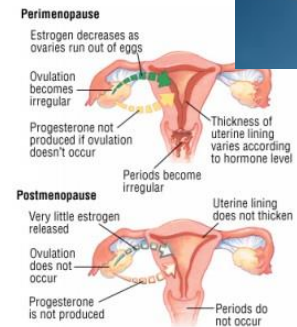
Οστεοπροστατευτικοί παράγοντες

- ✓ Εμμηνόπαυση, φυσιολογική περίοδος στη ζωή μιας γυναίκας κατά την οποία σταματά η εμμηνορρυσία
- ✓ Εμφανίζεται κατά μ.ό. σε γυναίκες ηλικίας περίπου 50 ετών
- ✓ Σταδιακή έκπτωση της λειτουργίας των ωθηκών και συνεπάγεται την ελάττωση ζωτικών ορμονών (π.χ. οιστρογόνα)
- ✓ Osteoporosis I

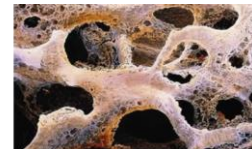


- **Αύξηση του αριθμού των οστεοκλαστών**
- **Ασαφής οστεοβλαστική δραστηριότητα**
- **Μείωση της οστικής πυκνότητας**

Οι εμμηνοπαυσιακές γυναίκες εμφανίζουν αυξημένη νοσηρότητα και θνησιμότητα από οστεοπόρωση και στεφανιαία νόσο



Φυσιολογικό οστό



Οστεοπορωτικό οστό

➤ Πληροφορίες για αντιμετώπιση γυναικολογικών δυσλειτουργιών

γλήχων· οί δὲ βλῆχρον, οί δὲ ἀρσενάκανθον, Ῥωμαῖοι πουλεγίουμ, ἝΑφροὶ ἀπουλεγουμ, Γάλλοι ἄλβολον, οί δὲ γαλίοψις.
Πόα γνώριμος, θερμαντική, λεπτυντική, πεπτική.
ποθεῖσα δὲ ἔμμηνα καὶ δεύτερα καὶ ἔμβρυα ἄγει·

Dioscorides Pedanius 'De material medica':

- *Volume III (Book III), section 31, lines 1-3*
- *Volume III (Book III), chapter 31, section 31, lines 1-2*



Mentha pulengium
(Lamiaceae)



- ✓ Ρύθμιση του εμμηνορροϊκού κύκλου
- ✓ Θεραπεία αμηνόρροιας και δυσμηνόρροιας
- ✓ Ρύθμιση της γαλακτόρροιας
- ✓ Πρόκληση έκτρωσης
- ✓ Αντιμετώπιση εξάψεων και εφιδρώσεων



➤ Πληροφορίες ευεργετικών επιδράσεων στην υγεία των οστών

ἴρις· Ἰλλυρικὴ φύλλα φέρει ὅμοια ξιφίω, μείζονα δὲ καὶ πλατύτερα καὶ λιπαρώτερα, ἄνθη ἐπὶ καυλῶν παράλληλα, ἐπικαμπῆ, **ποικίλα**· ἢ γὰρ **λευκὰ** [ἢ ὠχρὰ] ἢ **μήλινα** ἢ **πορφυρᾶ** ἢ **κυανίζοντα** ὁρᾶται, ὅθεν διὰ τὴν ποικιλίαν ἀπεικάσθη Ἰριδι τῆ οὐρανία.

*Dioscorides Pedanius 'De material medica':
Volume I (Book I), chapter 1, section 1, lines 1-4*

- ✓ Το γένος *Iris* περιλαμβάνει 260–300 είδη και υποείδη
- ✓ Το όνομά της προήλθε από την ελληνική λέξη 'ίριδα' (το όνομα της ελληνικής θεότητας 'Ίριδα')
- ✓ Πιστεύεται ότι το όνομα προέκυψε από την ευρεία ποικιλία χρωμάτων των ανθέων διαφόρων ειδών



Iris illyrica - I. florenina
(Iridaceae)



➤ Πληροφορίες ευεργετικών επιδράσεων στην υγεία των οστών



Το ρίζωμα της ίριδας:

- ✓ σχηματίζει γόνατα και είναι ευώδες
- ✓ κόβεται και ξηραίνεται υπό σκιά
- ✓ επάγει την έμμηνο ρύση
- ✓ Έχει επουλωτικές ιδιότητες και ευεργετική επίδραση στα οστά

*Dioscorides Pedanius
'De material medica'*

ρίζαι δὲ ὕπεισι γονατώδεις, στερεαί,
εὐώδεις,

ἄς δεῖ μετὰ τὴν τομὴν ξηράναντας ἐν σκιά
καὶ διείραντας λίνῳ ἀποτίθασθαι.

Volume I (Book I), chapter 1, section 1, lines 5-7

σὺν οἴνῳ δὲ ποθεῖσαι ἄγουσιν ἔμμηνα.

Volume I, chapter 1, section 2, lines 8-11

ξηραὶ δὲ πληροῦσιν ἔλκη καὶ
ἀνακαθαίρουσι μετὰ μέλιτος καὶ τὰ
ἐψιλωμένα τῶν ὀστέων σαρκοῦσιν.

Volume I, chapter 1, section 3, lines 4-5

Δεδομένα παραδοσιακής θεραπευτικής

Οστεοπροστατευτικοί παράγοντες

Ρίζες *Salvia miltiorrhiza* ('Danshen')



Κινέζικη παραδοσιακή θεραπευτική

Αντιμετώπιση του εμμηνοπαυσιακού συνδρόμου

In vivo οστεοπροστατευτική δράση

Διτερπένια (*tanshinone-type*)

Αναστολή δραστηριότητας οστεοκλαστών

Kim et al. *Immunopharmacol. & Immunotoxicol.*, 2008, 30 (2), 347-364

Ρίζες *Berberis aristata* ('Daruharidra')



Αγιουβερδική παραδοσιακή θεραπευτική

Εμμηνοπαυσιακές δυσλειτουργίες & οστεοπόρωση

In vivo οστεοπροστατευτική δράση

Yogesh et al. *J. Ethnopharmacology*, 2011, 134, 334-338

Σύγχρονα επιστημονικά δεδομένα

Οστεοπροστατευτικοί παράγοντες

Φυτικών εκχυλισμάτων (Mountain tea)



Υδατικά εκχυλίσματα *Sideritis euboica* & *S. clandestina* subsp. *clandestina*

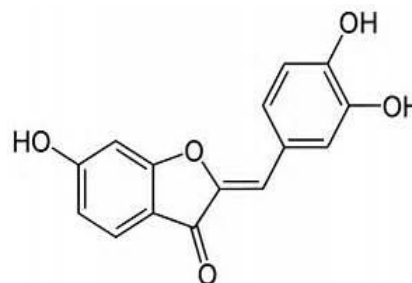
Επαγωγή διαφοροποίησης οστεοβλαστών

In vivo οστεοπροστατευτική δράση του υδατικού εκχυλίσματος *S. euboica*

Kassi et al. *J. Agric. Food Chem.*, 2004, 52 (23), 6956-6961.

Dontas et al. *Menopause*, 2011, 18 (8), 915-922.

Απομονωμένων ενώσεων (Sulfuretin)



Η σουλφουρετίνη επάγει τη δραστηριότητα των οστεοβλαστών και πιθανότατα διαθέτει οστεοπροστατευτική δράση

Αποτελεί σημαντικό μεταβολίτη του ξύλου του είδους *Rhus verniciflua* (οικ. Anacardiaceae)

Το χρυσόξυλο (*Cotinus coggygria*) ανήκει στο γένος *Rhus* (syn. *Rhus cotinus*)

Song et al. *Mol. Cell. Biochem.*, 2015, 410, 55-63.

Διάγραμμα ροής

Οστεοπροστατευτικοί παράγοντες



Χαρακτηριστικά ελληνικής χλωρίδας

- Αξιοσημείωτη ποικιλότητα ειδών, λόγω της γεωγραφικής θέσης και των έντονων γεωλογικών και κλιματολογικών αντιθέσεων
- Το 15,6% της χλωρίδας αποτελείται από ενδημικά είδη
- Το 40% των φυτικών ειδών της Ευρώπης το συναντάμε στην Ελλάδα
- Συλλέχθηκαν 82 (67.7%) από τις επιλεγμένες φυτικές δρόγες



Παρ' ότι λοιπόν η Ελλάδα αποτελεί ένα από τα μεγαλύτερα κέντρα πλούσιας χλωριδικής ποικιλότητας ('biodiversity hotspots'), ελάχιστες βιβλιογραφικές αναφορές τη συσχετίζουν με την ανεύρεση οστεοπροστατευτικών παραγόντων

Έλεγχος φυτικών εκχυλισμάτων Οστεοπροστατευτικοί παράγοντες



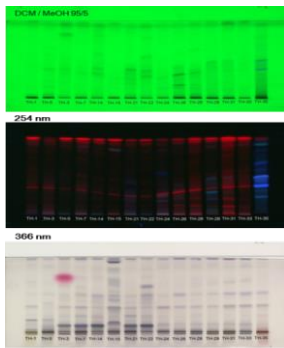
EtOAc
MeOH



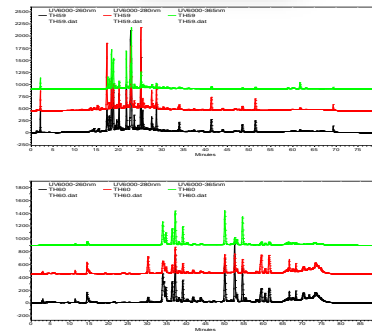
82 φυτικές δρόγες

169 φυτικά παρασκευάσματα

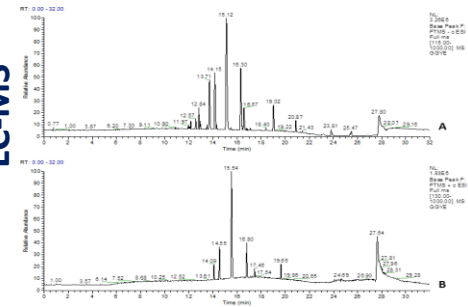
HPTLC



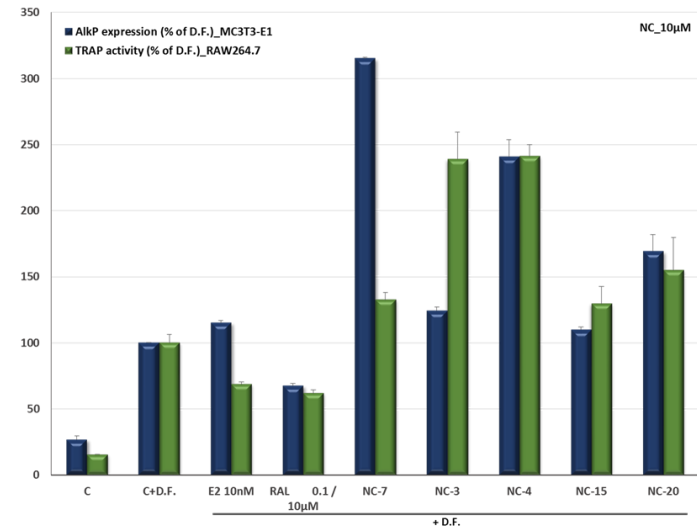
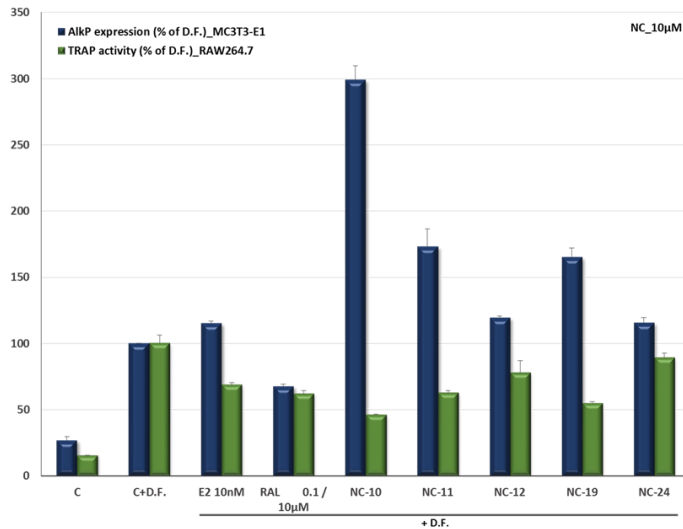
HPLC



LC-MS

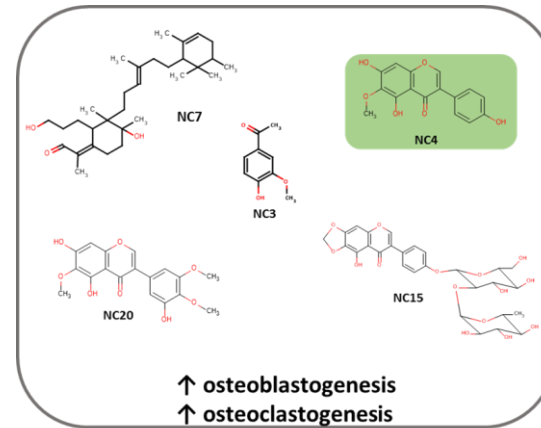
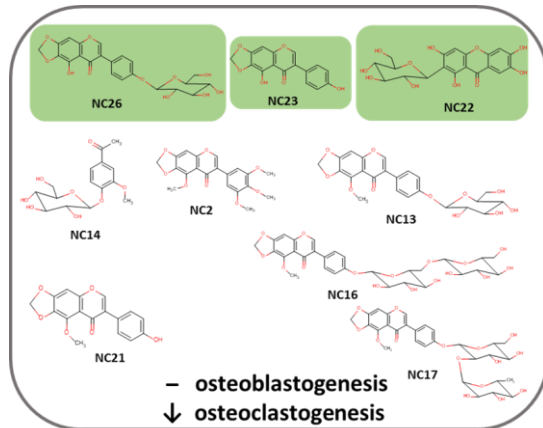
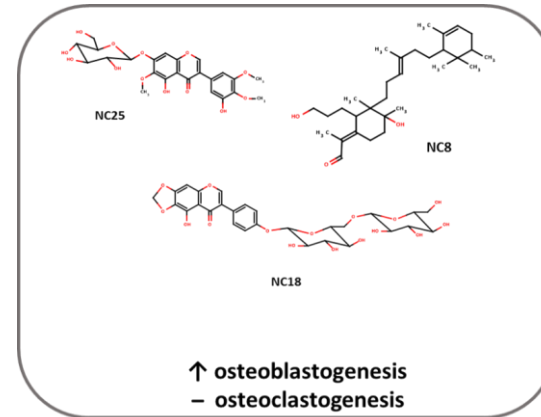
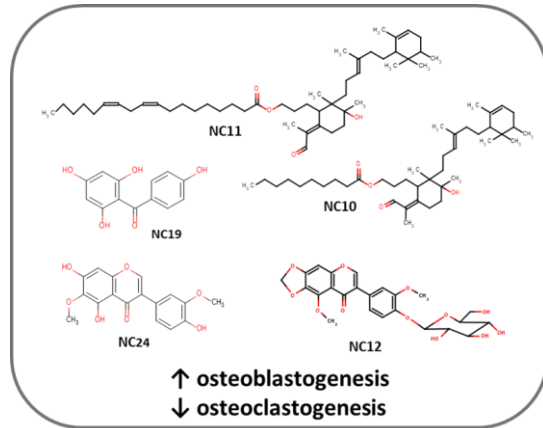


Extract	Plant part – Extraction solvent	MC3T3-E1 induction of AlkP activity (% of Differentiation factors_DF)			ISHIKAWA Induction of AlkP activity (% of E ₂ at 1nM)	MCF-7 Induction of AlkP activity (% της E ₂ 0,1nM)
		10 µg/ml	1 µg/ml	0.1 µg/ml	1 µg/ml	1 µg/ml
1	<i>Acanthus spinosus</i> (aerial)-EtOAc	120.3±6.6	90.0±0.8	89.4±0.9	M	ND
158	<i>Schinus molle</i> (leaves)-MeOH	127.8±1.1	107.1±4.3	104.6±2.3	M	ND
24	<i>Cupressus sempervirens</i> (forma horizontalis) (fruit)-MeOH	152.3±4.8	112.1±1.3	90.9±7.9	M	ND
28	<i>Juniperus communis</i> subsp. <i>communis</i> (branches, leaves, fruit)-MeOH	151.6±0.4	104.4±3.5	100.6±1.9	M	ND
29	<i>Iris attica</i> (all)-EtOAc	205.5±33.6	107.7±4.1	94.7±0.3	W 30.8±0.7	ND
30	<i>Iris attica</i> (all)-MeOH	167.8±11.5	95.7±2.2	93.7±2.3	W 12.1±0.2	ND
31	<i>Iris germanica</i> (roots)-EtOAc	260.1±20.8	211.0±16.1	116.5±7.9	M	ND
32	<i>Iris germanica</i> (roots)-MeOH	225.5±24.3	152.5±7.9	103.5±3.2	M	ND
33	<i>Iris unguicularis</i> subsp. <i>cretensis</i> (roots)-EtOAc	90.9±13.4	109.7±4.9	107.9±9.3	F (83.6±12.5)	F (66.7±4.0)
34	<i>Iris unguicularis</i> subsp. <i>cretensis</i> (roots)-MeOH	121.5±5.4	109.0±1.8	101.6±3.8	P (33.7±0.9)	M
138	<i>Mentha aquatica</i> (aerial)-MeOH	121.4±2.4	93.4±1.4	88.2±1.4	F (76.7±26.2)	F (84.9±7.7)
141	<i>Mentha pulegium</i> (aerial)-EtOAc	92.3±13.2	117.2±4.1	99.3±4.1	M	ND
121	<i>Morus alba</i> (wood)-EtOAc	138.9±1.2	108.9±1.6	112.5±1.8	P (34.9±1.4)	M
122	<i>Morus alba</i> (wood)-MeOH	119.2±1.0	99.9±0.7	106.9±0.5	W 27.7±1.1	ND
74	<i>Morina persica</i> (aerial)-MeOH	119.7±2.1	106.5±1.9	104.2±1.1	M	ND
75	<i>Pinus heldreichii</i> (leaves, branches d <1,5cm)-EtOAc	130.5±12.4	104.7±2.3	92.3±4.3	M	ND
76	<i>Pinus heldreichii</i> (leaves, branches d <1,5cm)-MeOH	165.4±3.4	99.1±2.2	97.3±3.3	F (82.6±1.4)	F (142.4±15.9)
77	<i>Abies cephalonica</i> (cortex and branches)-EtOAc	141.9±14.6	102.9±2.3	107.4±8.3	M	ND
78	<i>Abies cephalonica</i> (cortex and branches)-MeOH	125.6±0.6	96.1±2.0	95.1±1.9	P (55.9±3.9)	F (80.6±6.2)



Αξιολόγηση απομονωμένων ουσιών (10 μM) ως προς τη διαφοροποίηση οστεοβλαστικών MC3T3-E1 (AlkP δραστικότητα) και οστεοκλαστικών RAW264.7 (TRAP activity) κυττάρων

Ελιδοφόροι οστεοπροστατευτικοί παραγοντες από το *Iris germanica*



“...but then when people were born and died, they forgot a lot of the herbs, for what kind of remedy each one was determined by God and now they are looking for them. For this reason everyone who recognizes a herb it is a sin not to share it with the others”

Andrea Pieroni & Cassandra L. Quave. Ethnobotany and Biocultural Diversities in the Balkans