



From natural product chemistry to natural ingredient discovery and exploitation

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# Outline

- Presentation of the research group
- Natural products and cosmetics
- The Agrocos project a success story
- Industry-Academia the future

<sup>1</sup>st EDP focus group on cosmetics and food supplements based on natural resources, Cluj, North-West Region of Romania, May 26th 2016

# Our group

- The University of Athens was founded in 1847, being the oldest in the Balkan region and the Western Mediterranean
- The research group of Prof. Leandros
   Skaltsounis is natural product
   chemistry oriented with focus on
   cosmetic-nutraceutical applications
   and drug discovery
- One of the most active research groups, with more than 30 members (post-docs, PhD candidates, research associates, technicians)



# Infrastructure and resources

Our group has a range of state-of-the-art infrastructure for:

### • Extraction – isolation – purification

Microwave/Ultrasound extraction, Supercritical Fluids Extraction,
 Countercurrent Partition Extraction/Chromatography, several
 MPLC/prep HPLC

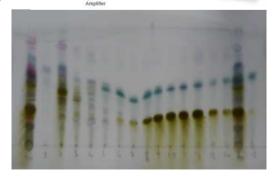


### Analysis and structure elucidation

 Bruker NMR 200, 400, 600 MHz, Orbitrap UHPLC-HRMS platform (ESI, APPI, APCI), SFC-MS, SPME-GC-MS, GC-FID, UHPLC-DAD/FLD, HPLC-DAD/ELSD/RI, HPTLC densiometric platform

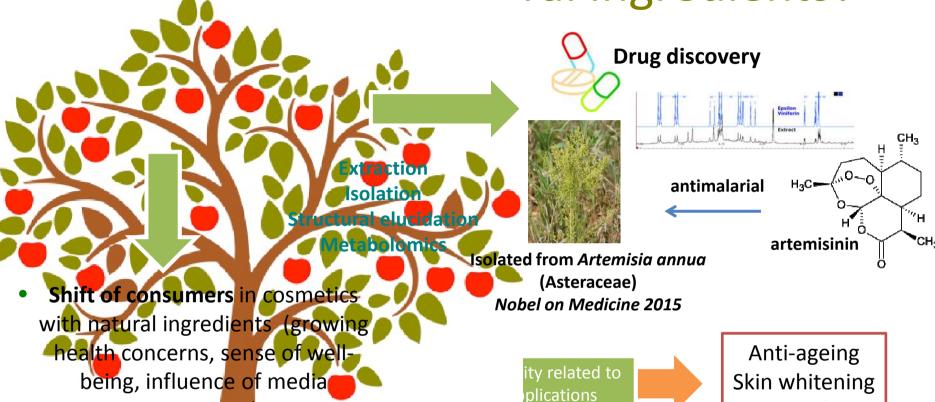
### Access to natural resources:

- Global, Mediterranean and Greek biodiversity (plants, fungi, terrestrial organisms)
- Library of more than 3000 extracts/1500 compounds (natural products/organic synthesis



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Natural products Natural ingredients?



• Natural active ingredients comprise 3% of total cosmetic sales in Europe (projected to be over 10% in the coming years)

attention.

Extraction
Enrichment

Determination of active components

Antioxidant



# AGROCOS: From Biodiversity to Chemodiversity: Novel Plant Produced Compounds with Agrochemical and Cosmetic interest

- > Granted under the 7<sup>th</sup> framework programme
- ➤ Call: Food, Agriculture and Fisheries, and Biotechnology

  Topic Prospecting for novel plant-produced compounds (FP7-KBBE-2009-3)
- > Duration: 4 years
- ➤ Budget: ~ 4.000.000 €





### Consortium

National and Kapodistrian University of Athens, Greece (NKUA, 1. Coordinator)





2. University of Basel, **Switzerland** (UNIBAS)



3. Centre National de la Recherche Scientifique, France (CNRS)





- **ECOFOG (French Guyane)** a.
- ICSN (New Caledonia, Madagascar) b.
- Universidad de Panamá, Panama (CIFLORPAN) 4.













7. KORRES SA, **Greece** (KORRES)



8. Bruker BioSpin GmbH, Germany (BRUKER)



National Center for Scientific Research "Demokritos", Greece (NCSR) 9.





National and Kapodistrian University of Athens







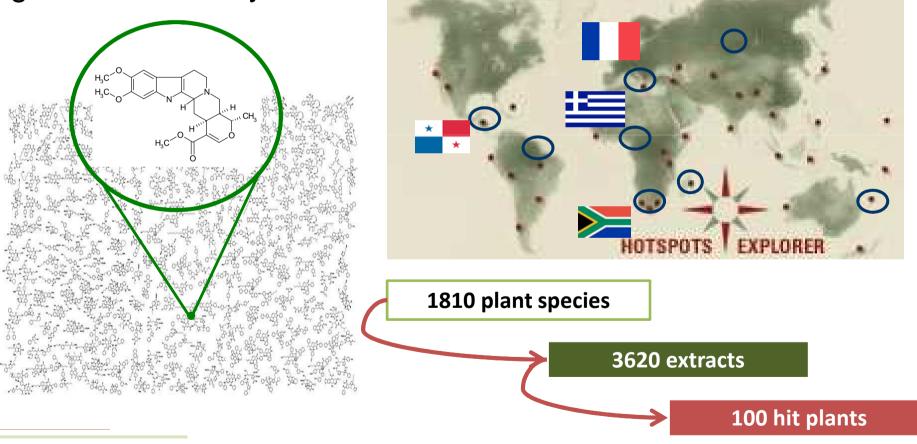




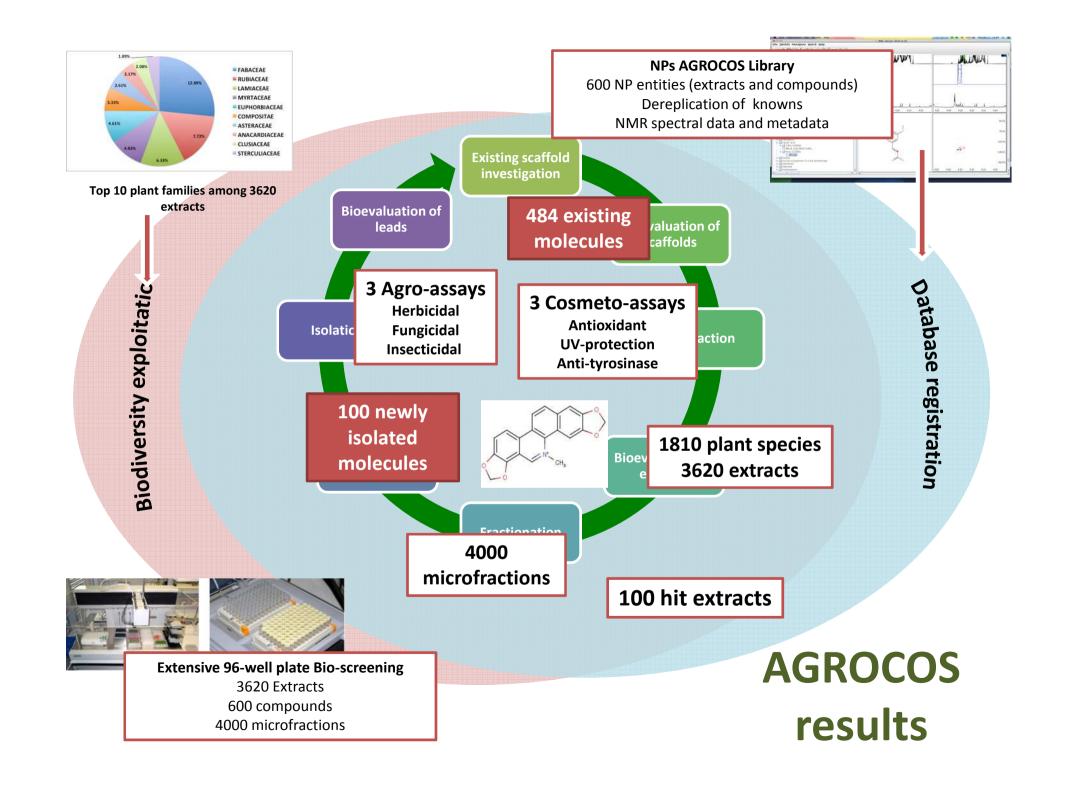
# Core target achieved

Discovery of plant derived small molecules with development potential as new cosmetic/agrochemical agents, from the

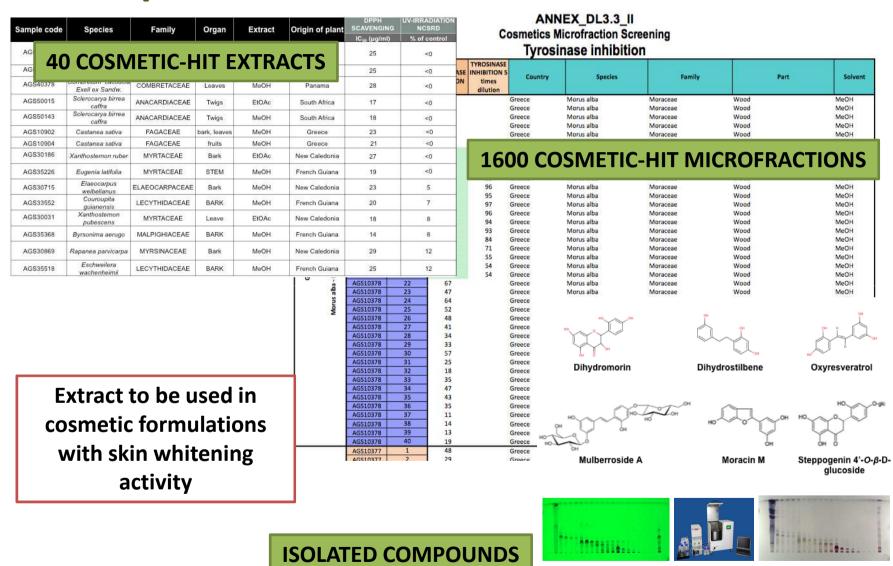
global biodiversity.



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# **Development Cosmetics**







### **RESULT:**

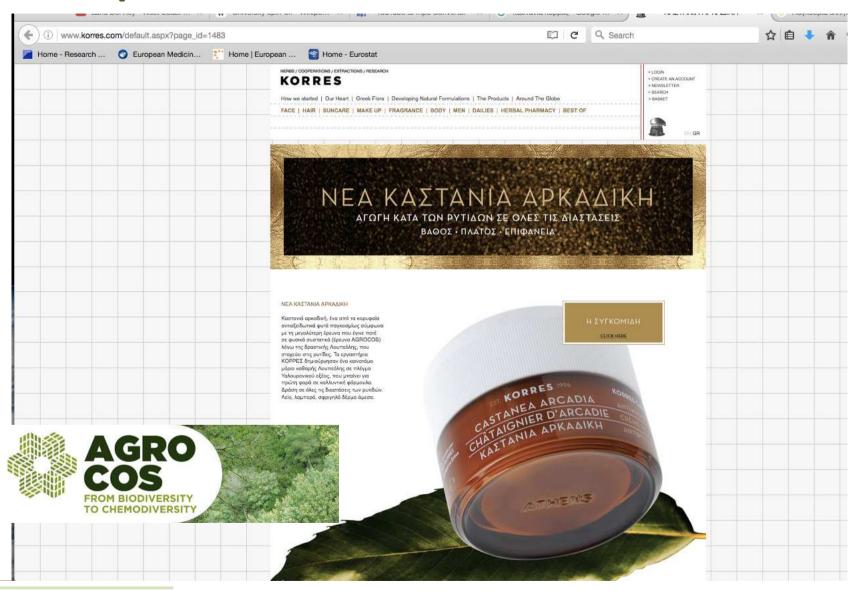
Launch of a full skincare antiaging line based on Agrocos findings / antiaging properties of Fagacea

Stay tuned, in pharmacies & department stores around the world in 2016!





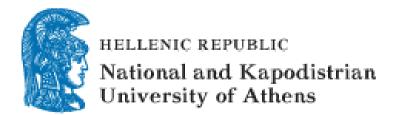
# **Development Cosmetics**





# PharmaGnose is a spin-off company of the University of Athens





### **Academic staff members from**

- University of Athens
- Agricultural University of Athens
- NCSR Demokritos

### **Experienced researchers**

## The team

### Main staff involved

- 7 Academic staff
- 5 Experienced researchers

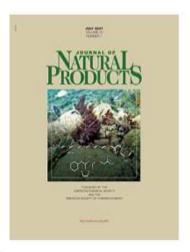
### **Available human resources**

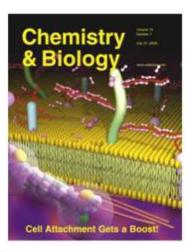
- Highly qualified experts in research and development (chemists, pharmacists, physicists)
- Highly trained technical staff
- Financial manager



## **Publications**

- 230 Publications in international journals
   (Nature Med., Oncogene, Chem.Biol, Org. Lett. J.Med.Chem, J. Agric. Food Chem., J.Nat.Prod., Phytochemistry, Tetrehedron Lett., etc)
- 12 Monographs & Review articles
- 270 Seminars/Posters in international conferences
- Supervision of >20 PhD thesis









# **Infrastructure 1/3**

# **Laboratories With State of the Art equipment**

### **Extraction** (Classical & Innovative technologies)

- Maceration unit
- Accelerated Solvent Extraction unit
- Supercritical Fluid Extraction unit
- Microwave Assisted Extraction unit

### **Isolation**

- High Speed Counter Current Chromatography
- High Performance Liquid Chromatography
- Medium Pressure Liquid Chromatography

### **Synthesis & in silico studies**

- Buchi Syncore apparatus (combinatorial synthesis)
- Silicon Graphics workstations
- Linux cluster & Software





# **Infrastructure 2/3**

### **Analysis**

- Analytical HPLC with Diode Array, Evaporative Light Scattering & Refractive Index detectors
- LC-MS with ESI & APCI ionization sources
- UPLC with DAD detector
- High-Resolution MS + ESI, APCI & APPI ionization sources
- SFC-MS
- GC-MS systems + EI and CI ionization sources, GC-FID apparatus
- Head-space analysis
- HPTLC Camag platform

### **Structural elucidation**

- NMR spectrometers
- Mass Spectrometers
- FT-IR
- UV/Vis
- Polarimeter, melting point apparatus





# **Infrastructure 3/3**

### **Formulation**

- Spray
- Two lyophilization units
- 2D barcoding system for encoding & storage

### **Fermentation/Bioevaluation**

- Incubators
- Bioreactor
- Autoclave
- Plate reader





- 1000 L Distillation/extraction unit
- 200 L Distillation unit
- 100 L essential oil distillator
- 500 L & 600 L extraction vessels
- Adsorption resin columns
- 100 L Vacuum dessicator
- 20 L Rotary evaporators
- Lyophilization unit
- 63 L reactor for medicinal chemistry preparations

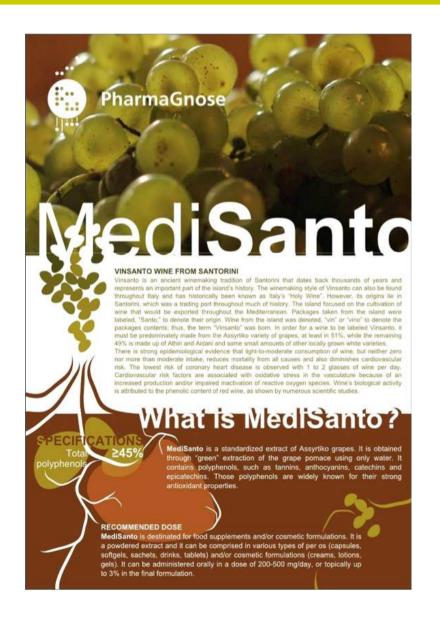


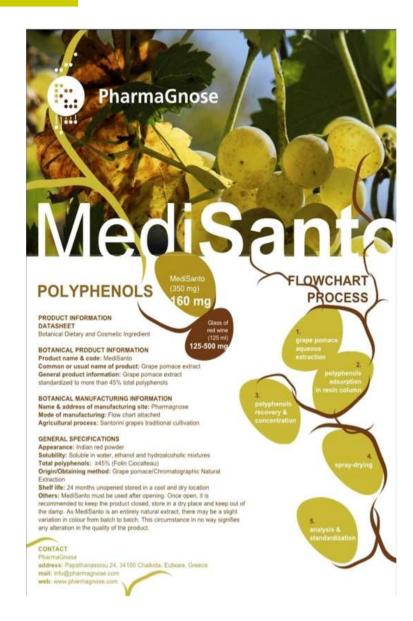
### The services

Analytical Services

Method development for

- extraction, separation, isolation
- structural identification
- analysis of natural products
- analogues development
- and pilot scale production
- R&D Contract research for early stage discovery process







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### What is FleurdeSafran?

Pleur de Sefren is a standardized extract of Crooce sethnic petale. It is obtained through "green" extraction of the petals using hydrosicoholic michanes. It is enriched in phenois, such se flavonoide and anthocyanins. These compounds are widely known for their strong anticidant properties.

#### Composition

\*\*Second glycodrides (haempfand 7-O-glucopyranosy-3-O-apphanosida, kaampfand 3-O-apphanosida, kaampfan

min. 15% <100 µg/ml



#### Information datasheet

**Hotorical cosmetic Ingredient** 

#### Botanical product information

Product name: Floor<sub>de</sub>/befren

Common or usual name of product: Crocus sudvue policie

General product information: Crocus entires posts entract standardized to more than 15% lotal polyphorate.

#### Botanical manufacturing information

Manufacturing alts: PromaGrose SA, Greece Blode of secretaring: Fire their classed Agricultural process: Groups eather trafficest cultivation

#### General specifications

Appearance: Violat blue powder Setubilitie: Boluble in water, ethanet and hydroalcuhotic michanse

Total polypherote: #15% (Folis Cloculines)
Origin/Oblaining anothesis Crocus assistas polybridizonalographic Natural Entreeting

Whelf life: 24 months unspensed alonet in a cool and dry location server the 24 months unspense assure in a cost and or source.

Otheres: Resuggitation mast be used after operating. Once opers, it is recommended to keep the product cheed, elsee in a dry place and large cut of the dump. As Placegatiation is an entirely resture surbed, there may be a slight western in colour from batch to batch. This chountains in no way eight sentian in the quality of the product.

hermesku 34, 34100 Chafdde, Eubone, Green

### lowchart

orocus petals hydrosicoholic

polyphenola adsorption In reein column

apmy-drying



considered as a synthet of beauty and love. The impress of the common captured and preserved in the face of common which by an archeol embad.

Bed can be broad back to bilitard three in the biblish East, and later to the ballon miscoribrari. A Pensian advantat, the sicharski Autonom, is that one he beauth best he billions from in the billions facilities in the billions advantable of A Persinn advantable he district the sub-from a considerable in the south part of the process of sub-freeling some sends from core positive in the south print the most and announcement of, extends of the positive heart of the positive from the south core considerable properties by various effects groups. The positive process will defice receive a finite properties by the positive from the positive

1 Sealer 19 Collection of the Collection of the

#### What is Rosanle? Resente is a standardized

extract of Rose demascens petals. It is "nearg" riguordt banlatdo extraction of the petals using only water. It is enriched in flavonoids, such as knompforol, guercetin and rutin. Those flavonote are widely known for their strong anticoddent

proportion.

#### Composition

Recenile contains mainly three flavonois (issempfarol, quercetin and autin), pharylethenol and their glysosides phenylethanol p glucopyranceide ∢ quercotin-3-0 p glucopyranceide ∢ quarcetin-3-0-p-guicopyramostic-4 quarcetin-3-0-p-guicopyramostic-4 keempferoi-3-0-p-guicopyramostic-4 keempferoi-3-0-p-arabinofuramoramostic-4

keemple of 3-0-5-glucopyranoutie 4 keemple of 3-0-(6'-0-p-courseveyt)-5-glucopyranoutie 4

**Total Phenolic Content** min. 20%

Antioxidant activity (DPPH IC,s) <50 µg/ml



#### Information datasheet Botanical cosmeto ingredient

#### Botanical product information

Product name: Rosenie Common or usual name of product: Rise damescene petab

General product information: Passe demanance public extract standardized to more than 20% total polyphanols

#### **Botanical manufacturing information**

Menufesturing site: PhermeCnose SA, Creece Mode of manufacturing: Flow chart attached Applicational process: Ross demescene treational outlivesion

#### General specifications

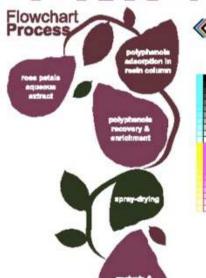
Appearance: Indian red powder fieldfillg: Soluble in water, etheno and hydroelocholic mictures. Total polyphenois: 200% (Folin Clossiters.) Origin/Obtaining method: Ross demasours petrial Chrometographic Natural Extraction

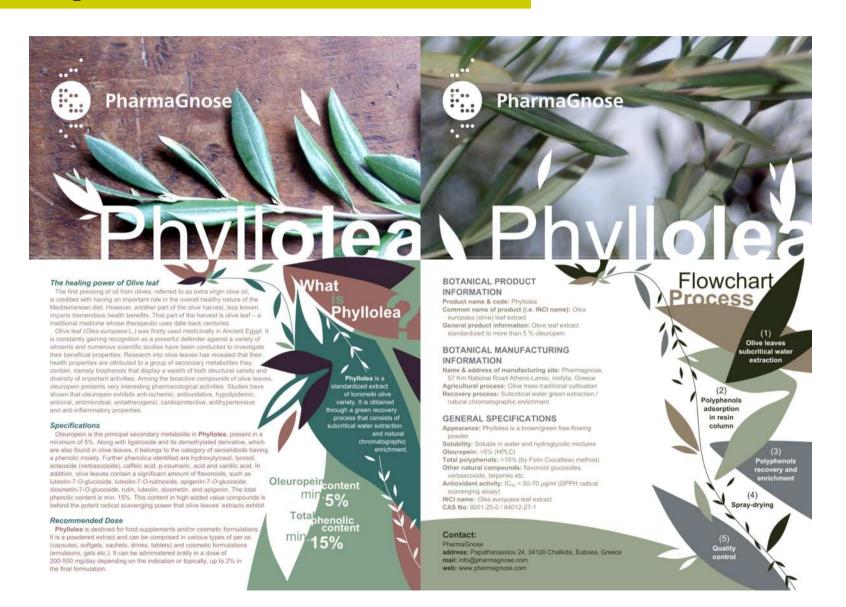
Shelf Me: 24 months unopened stored in a cool and dry location Others: Rosen's must be used after opening. Once open, it is recommended to keep the product closed, store in a dry place and keep out of the demp. As Russen's is an entirely natural extract, there may be a alight verteton in colour from batch to batch. This

droumstance in no very signifies any absention in the quality of the

#### Pharma Coose

achtrees: Papelhamassiou 24, 34100 Challchie, Eubose, Green mait info@pharmegnose.com







tage of Grocce, Italy, Spain and Morocco according to Linesco, has as been evidenced to promote commany health and promote longevity<sup>5</sup>. It is ong low in saturated fat and high in monouncaturated fat and dietary fiber. One of the ght to be the health effects of olives and olive oil, which characterize the Meditemanean rs with strong anticoldant, anti-inflammatory and cardioprotective properties are contained in uch as hydroxytyrosol, tyrosol, verbascoside, cleocanthal and cleacin. The EFSA Panel on Dietelic cots. Nutrition and Allergies (NDA Fishel) has approved the relationship between the daily intake of 5 mg of olive oil polyphenois (standardized by the content of hydroxytyrosol and its derivatives) and the protection of LDL particles from coddative stress?,



Oleamed is a standardized, "green" olive extract from the fruit of a specific greek variety, Amfissis (Oles europsea var. rotunda). It is obtained through environmentally friendly extraction processes. It exhibits a characteristic composition, rich in hydroxytyrosol (which is approved by EFSA for heart and coronary health claims) and tyrosol among other phenolics which have been shown to possess antioxident properties by protecting body cells and LDL from oxidative damages, according to EFSA. It also promotes skin health and retards skin aging through the scavenging of free radicals.

### Specifications

Oleamed is standardized in hydroxytyrosol and guarantees high total phenolic content demonstrating high antioxidant activity during DPPH radical scavenging activity tests.

- Mydroxytyrosol content : ≥7%
- Total polyphenois : ≥17%
- DPPH radical scavenging activity: IC<sub>so</sub> <100 µg/ml.</p>

### Recommended dose

Oleamed is destinated for food supplements and/or cosmetic formulations, it is a powdered olive fruit extract with maitodextrine and it can be comprised in various types of per os (capsules, softgels, sachets, drinks, tablets) and/or cosmetic formulations (creams, lotions, gets). It can be administered orally in a dose of 50-100 mg/day, or topically up to 2% in the final formulation.



#### **Botanical product information**

Product name: Oleamed

Common or usual name of product: Olive fruit extract General product information: Olive fruit extract standardized to more than 7% hydroxytyrosol.

#### Botanical manufacturing information

Manufacturing site: PharmaGnose, Greece Mode of manufacturing: Flow chart attached Agricultural process: Greek alives traditional cultivation

#### General specifications

Appearance: beige powder

Solubility: Soluble in water, ethanol and hydroalocholic martures

Hydroxytyresel: 28% (HPLC)

Total polyphenols: ≥17% (Folin Ciocaltesu)

Lipids: 8-10% Proteins: 2-4%

Energy: 300 koal/100 g

Antioxidant activity: ICso <100 µg/ml (DPPH radical acavenging

Origin/Obtaining method: Olive Fruit/Chromatographic Natural Extraction

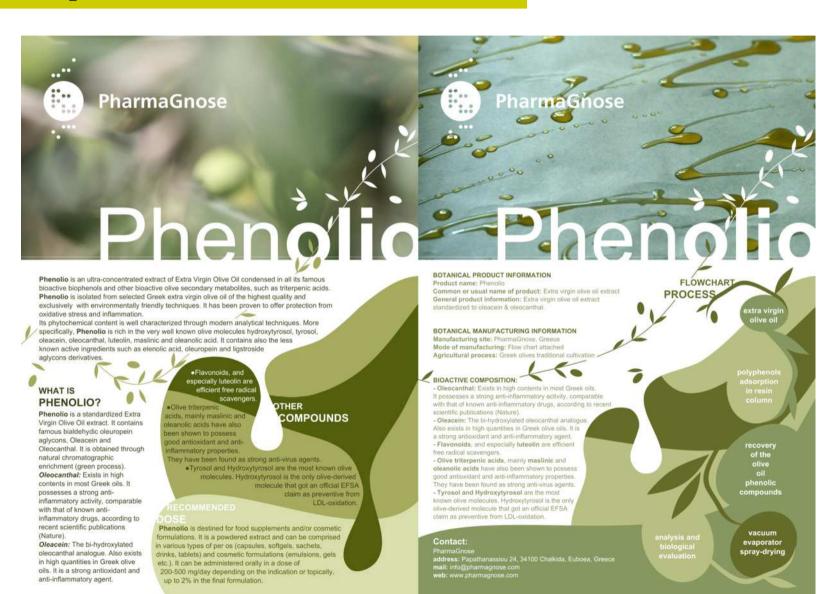
Shelf life: 24 months unopened stored in a cool and dry location Others: Oleamed must be used after spening. Once open, it is recommended to keep the product closed, store in a dry place and keep out of the damp. As Cleamed is an entirely natural extract. there may be a slight variation in colour from batch to hatch. This circumstance in no way signifies any alteration in the quality of the product.

#### Contact:

address: Papathanessiou 24, 34100 Chalkida, Eubosa, Greece mall: info@pharmagnose.com

web: www.pharmagnose.com





# Thank you very much for your attention!



