## Le spezie

Salute, alimentazione e ricerca



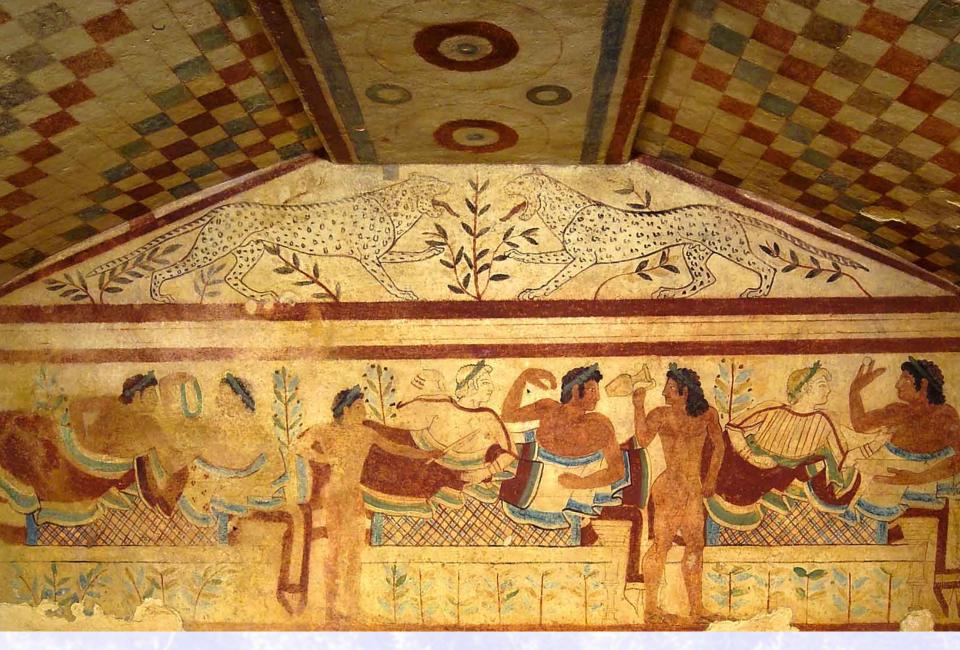
Rosmarino: aromatico rimedio per la terapia del dolore

Lorenzo Di Cesare Mannelli

Università di Firenze, Neurofarba







Necropoli etrusca di Tarquinia



Manuscript of the *Pseudo-Apuleius XI century,* St. Augustine's Abbey, Canterbury

"There's rosemary, that's for remembrance, pray you love, remember."

Shakespeare, Hamlet



*Tractatus de herbis,* Italian herbal, XIII century, British Library



Jacques-Louis David (1748-1825), The Coronation of Empress Josephine by Napoleon

Chardin, "Perfumer of Their Imperial and Royal Majesties," recorded Napoleon's use of 162 bottles of rosemary water in the first three months of 1806.

## Rosmarinus officinalis

The hydroalcoholic extracts from *R*. officinalis have been recognized as safe by EFSA (2008) and their use is authorized as natural antioxidant and preservatives of foods.



#### Leaf extracts show:

- inhibition of acetylcholinesterase activity, improving memory impairment in the rat (Ozarowski et al., 2013)
- anti-inflammatory effects (Emami et al., 2013)
- redox unbalance regulatory properties



## Rosmarinus officinalis & Pain





## **Nociceptive vs Neuropathic Pain**

## Nociceptive Pain

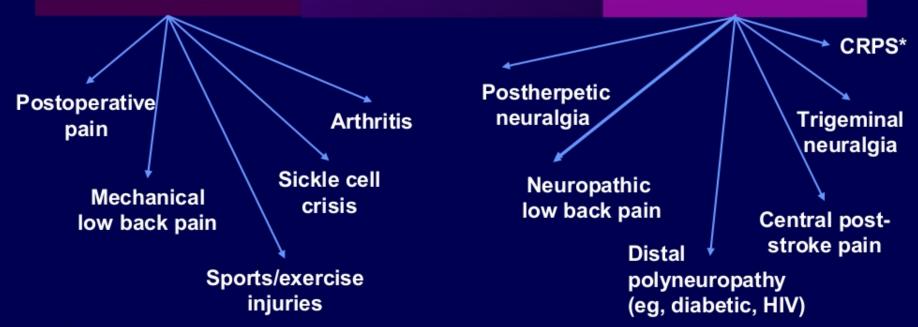
Caused by activity in neural pathways in response to potentially tissue-damaging stimuli

#### **Mixed Type**

Caused by a combination of both primary injury and secondary effects

#### Neuropathic Pain

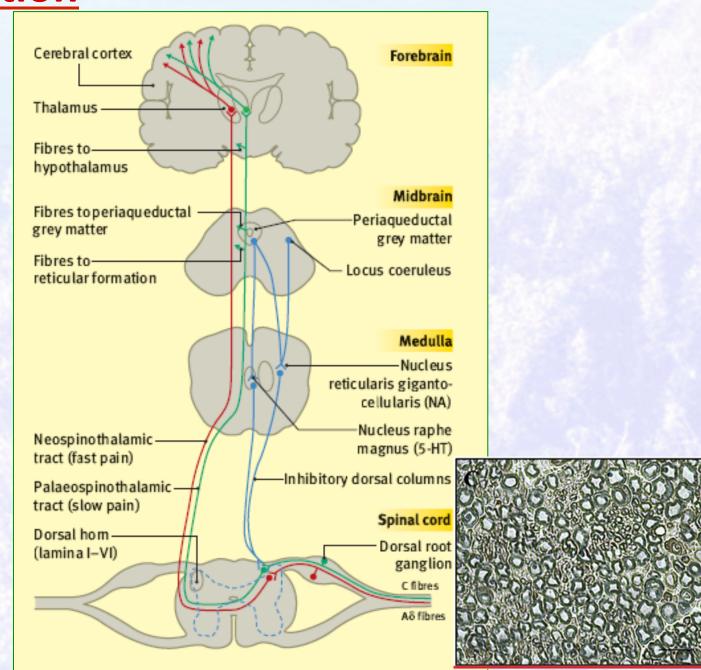
Initiated or caused by primary lesion or dysfunction in the nervous system



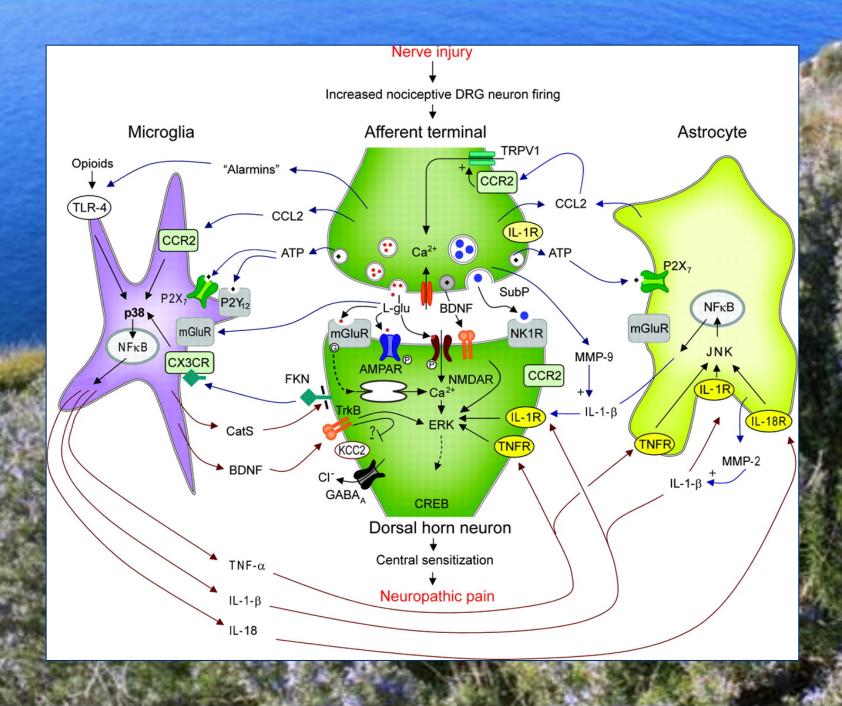
\*Complex regional pain syndrome

#### **Pain modulation**

The pathological aspects of NP involve a maladaptive response of the nervous system characterized by peripheral and central sensitization as well as by spinal disinhibition



Von Hehn et al., Neuron, 2012



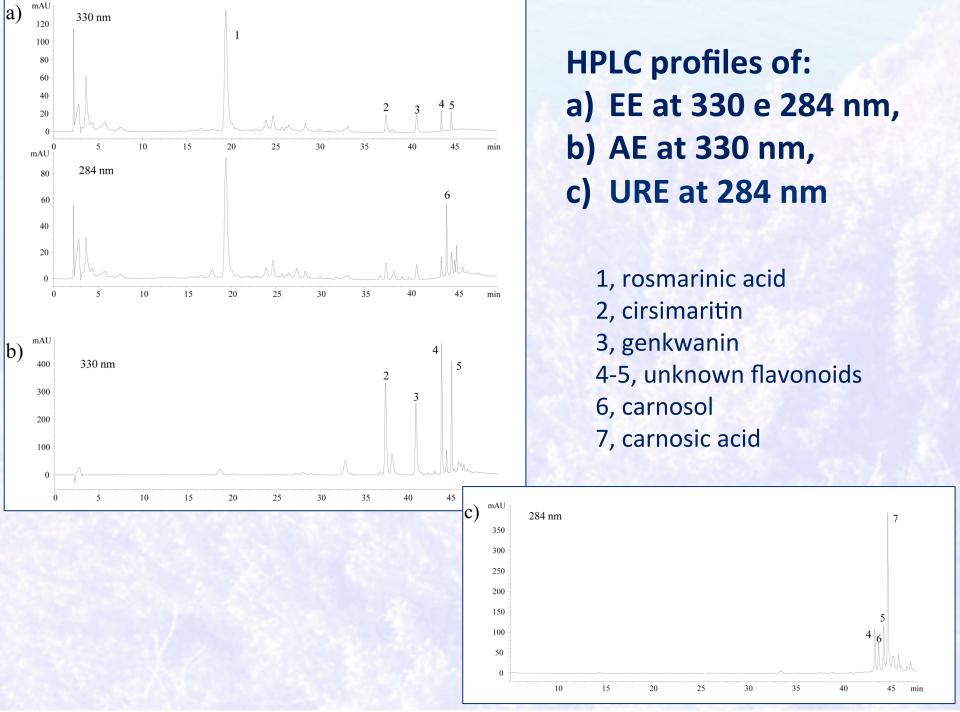




Evaluation of rosemary extract fractions in a preclinical model of neuropathic pain induced by damage of the sciatic nerve (Bennett and Xie, 1988)

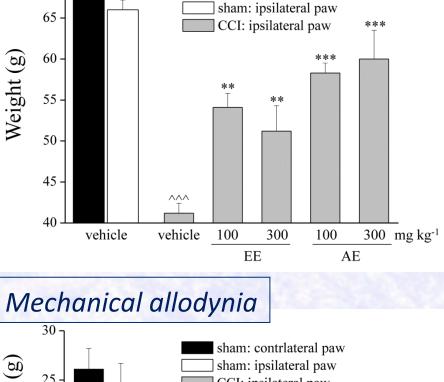
- Ethanolic extract (EE)
- Acetone extract (AE)
- *n*-hexane-ultrasound assisted-extraction (URE*prel* and URE)





#### Mechanical hyperalgesia

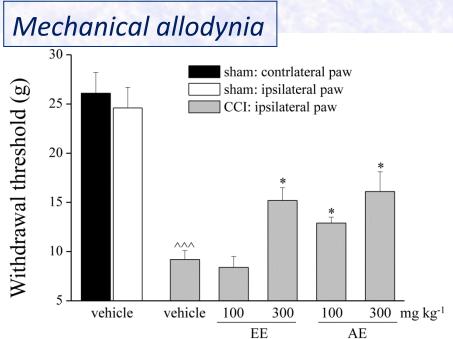
70 -

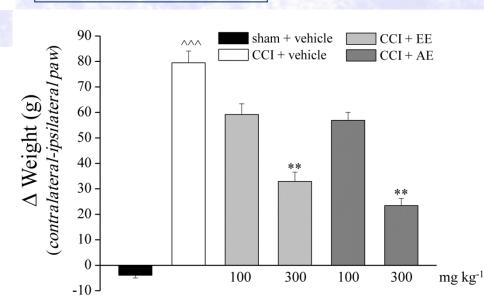


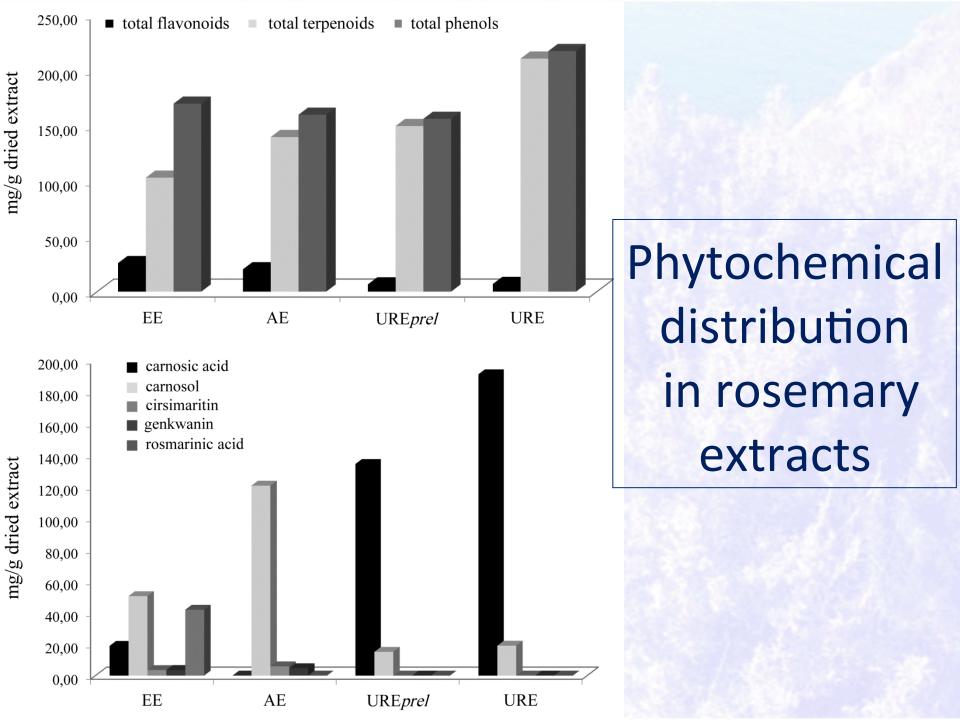
sham: contrlateral paw

## Pain measurements

#### Spontaneous pain

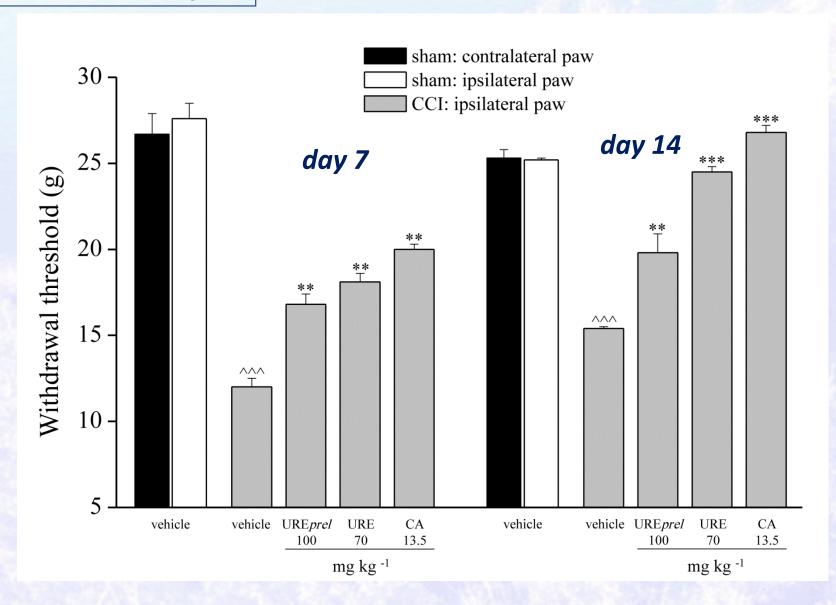






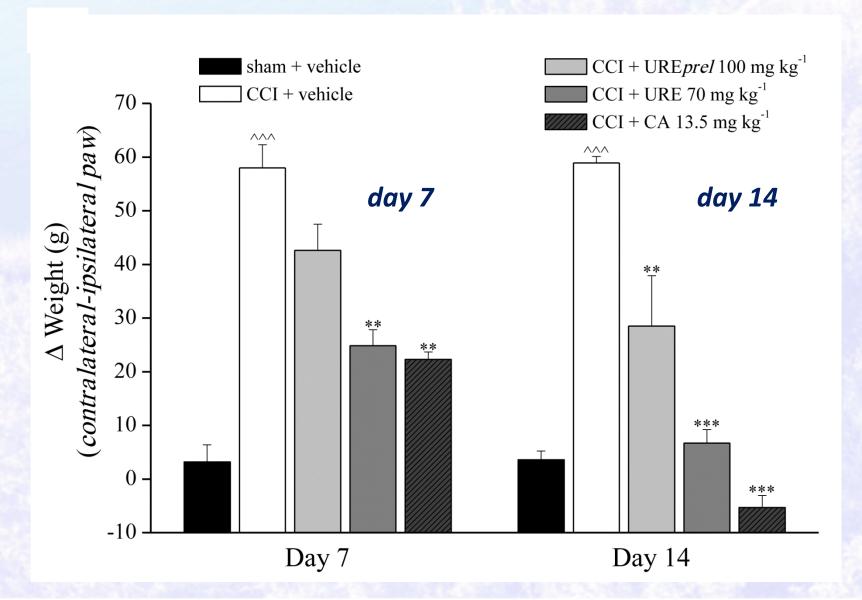
#### Pain measurements

#### Mechanical allodynia

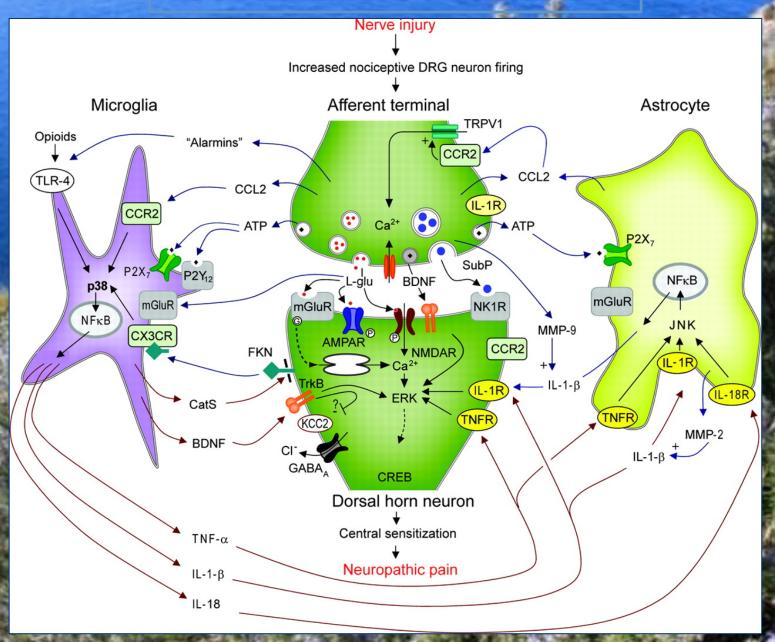


#### Pain measurements

#### Spontaneous pain

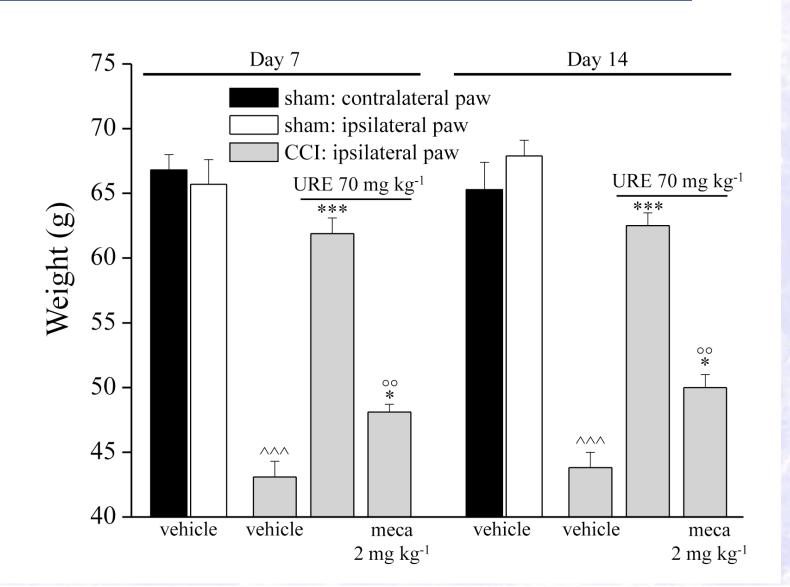


## Possible mechanism?

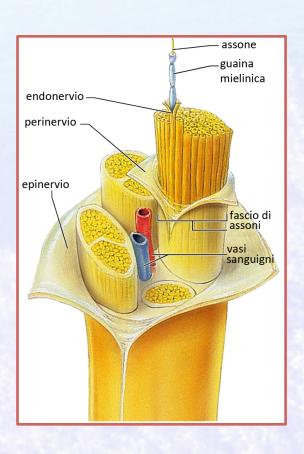


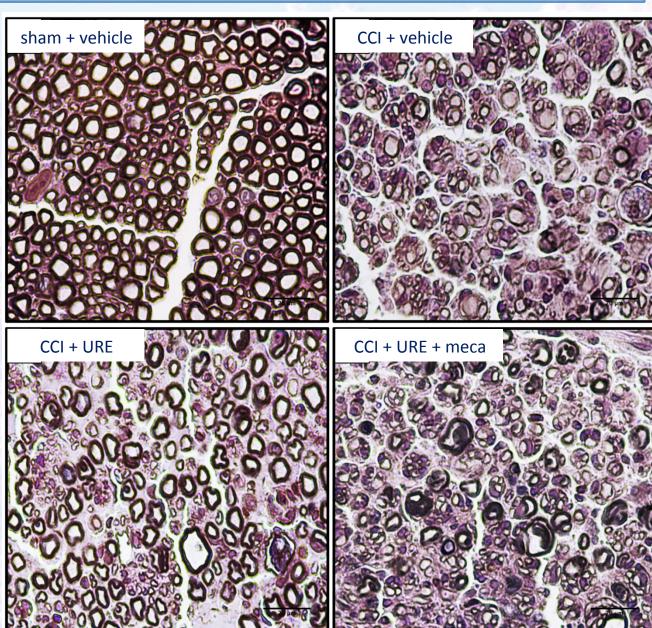
## Pain & nAChR

#### The nicotinic antagonist mecamilamine prevents URE efficacy



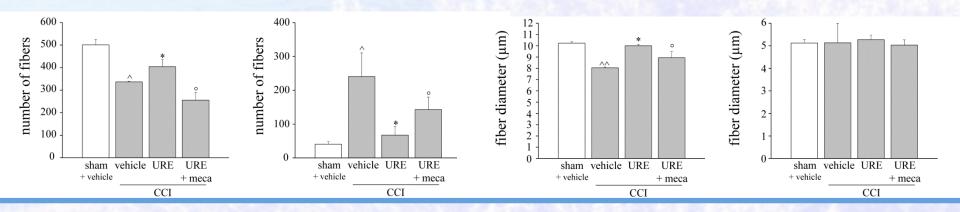
### Neuroprotective effect of URE: sciatic nerve

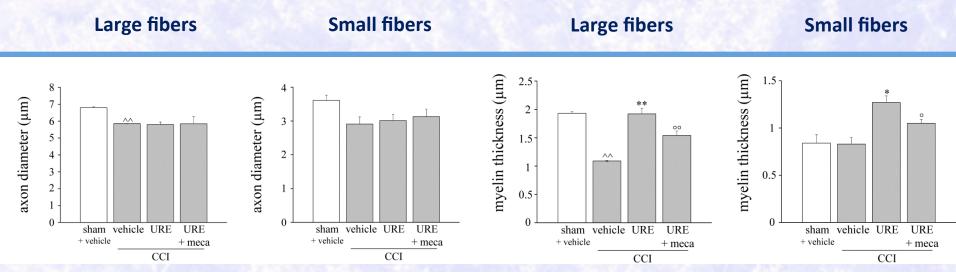




900 μm proximally to the injury

# Neuroprotective effect of URE: sciatic nerve





#### **Conclusions**

- The hexane-ultrasound extract from Rosmarinus officinalis L. (URE) reduces neuropathic hypersensitivity
- URE improves neurorestoration
- URE efficacy is mainly related to the terpenoid fraction
- Nicotinic receptors are involved in the pharmacodynamic mechanism of URE

University of Florence,
Dept Neurofarba
Section of Pharmacology and Toxicology

Prof. Carla Ghelardini

Dr Elena Lucarini Dr. Laura Micheli Dr. Mario Maresca Dr. Barbara Tenci Dr. Elena Trallori



...We are thankful to Prof. Nadia Mulinacci
University of Florence,
Neurofarba, Pharmaceutical and Nutraceutical division

