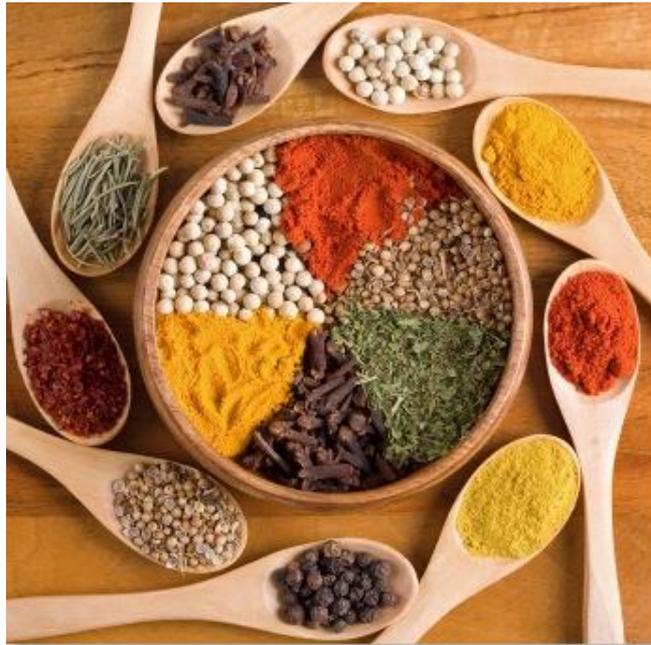


# NUTRACEUTICA E INFIAMMAZIONE GASTROINTESTINALE

**Mario Dell'Agli**

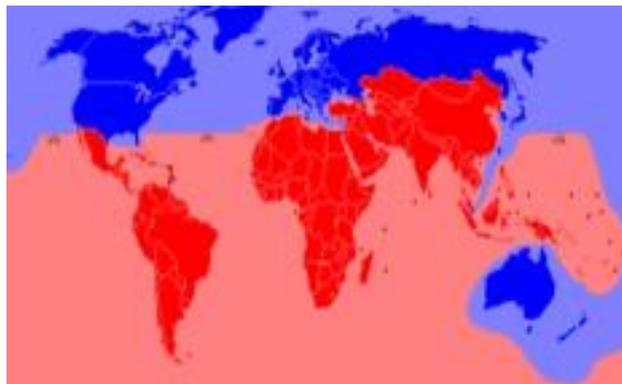
**Laboratorio di Farmacognosia, Dipartimento di Scienze Farmacologiche  
e Biomolecolari, Università degli Studi di Milano**



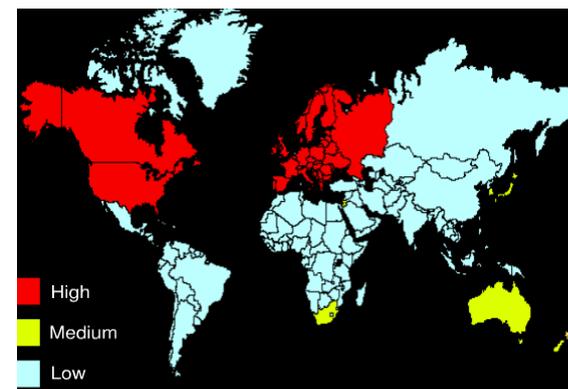
# LE PATOLOGIE GASTROINTESTINALI

## EPIDEMIOLOGIA

- 10 milioni di persone soffrono di patologie del tratto gastrointestinale in Italia;
- si stima che il 50% della popolazione mondiale sia infettata da *Helicobacter pylori*. L'infezione è più comune tra asiatici, ispanici ed afroamericani;
- la sindrome del colon irritabile è il disturbo intestinale più frequente e, in Italia, interessa il 25% circa della popolazione;



Incidenza di *H. pylori* (in rosso)

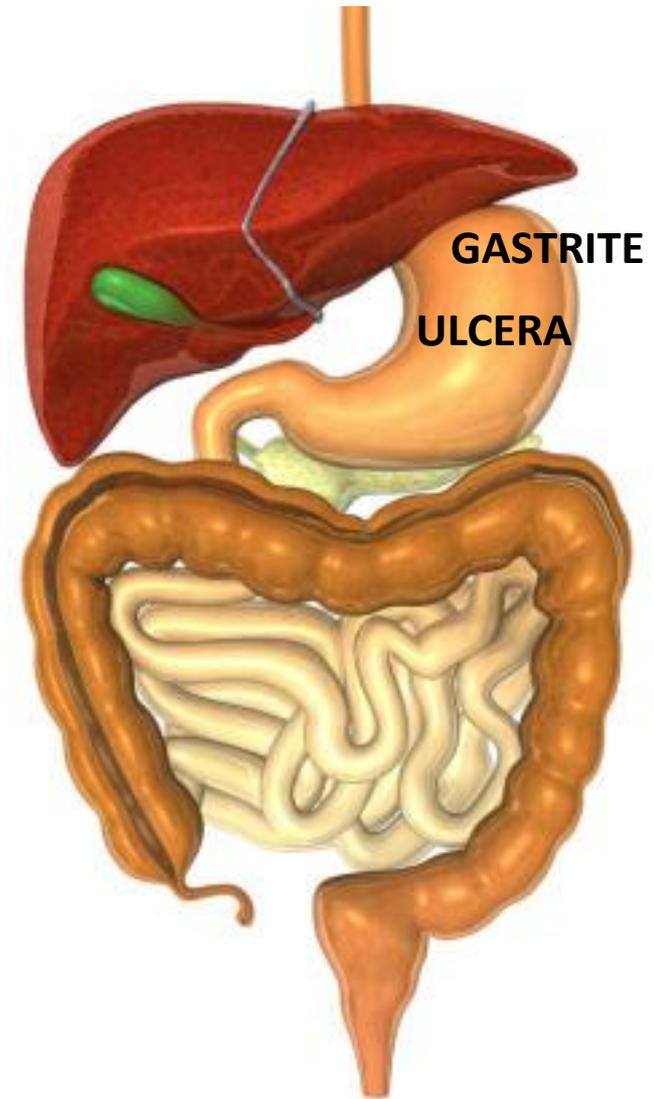
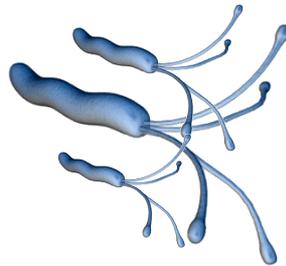


Incidenza di IBD

# LE INFIAMMAZIONI GASTRICHE

**GASTRITE:** infiammazione della mucosa gastrica causata da disordini del sistema immunitario, abuso di farmaci o alcool, presenza di *Helicobacter pylori*

**ULCERA:** erosione della mucosa fino alla completa perforazione della parete

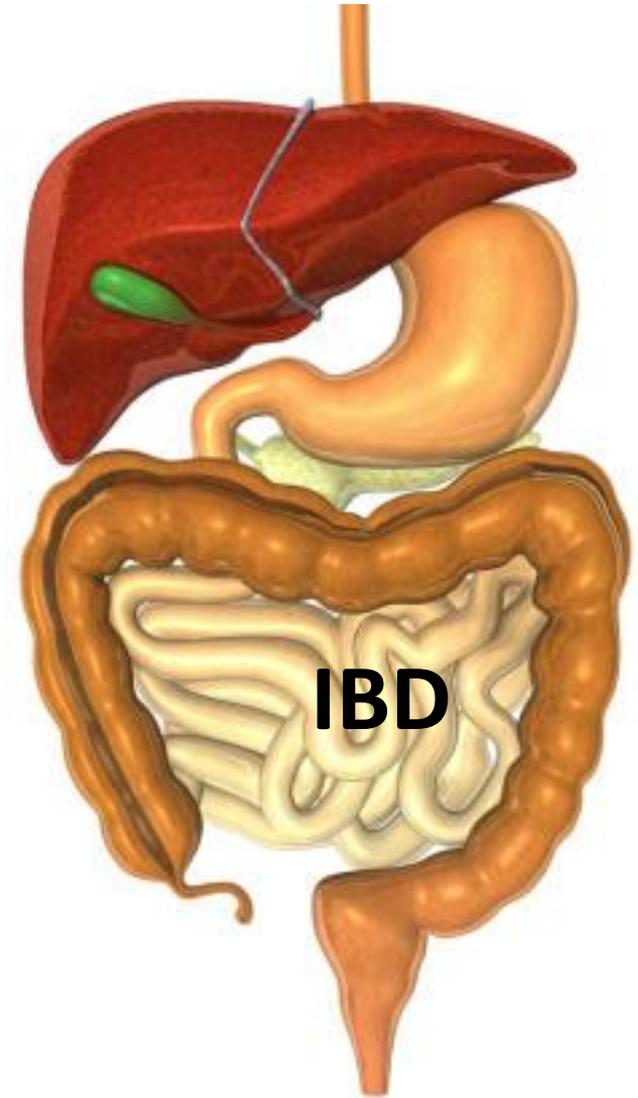


# LE INFIAMMAZIONI INTESTINALI

**COLITE ULCEROSA:** infiammazione cronica intestinale che coinvolge la mucosa del colon/retto

**MORBO DI CROHN:** infiammazione cronica intestinale a base autoimmune che può coinvolgere tutto il tratto intestinale

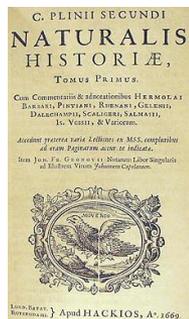
**SINTOMI:** diarrea, perdita di peso, anemia, sanguinamento rettale, dolori addominali, febbre



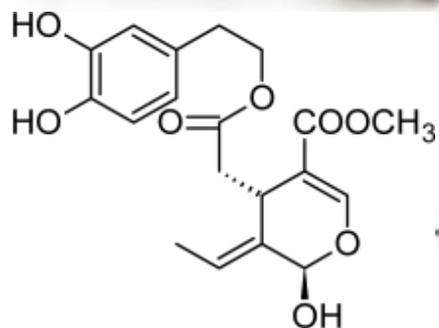
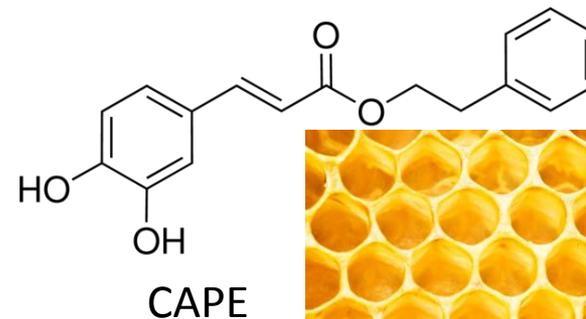
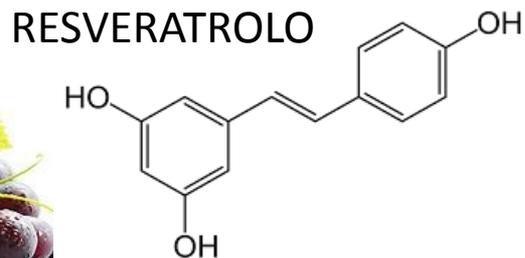
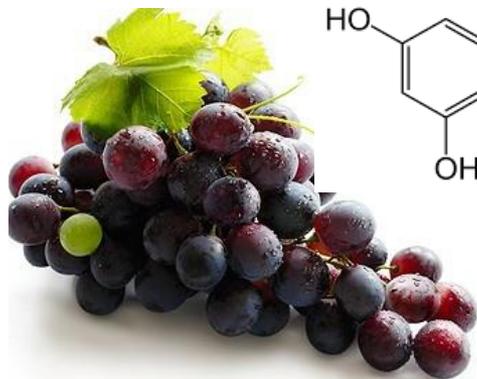
# LE PIANTE UTILI NEL TRATTO GASTROINTESTINALE

## L'USO TRADIZIONALE

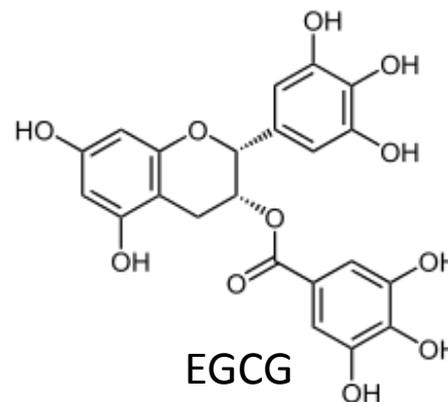
- **TAMARINDO:** utilizzato da tempi immemorabili in Egitto ed India e, successivamente, dagli Arabi, che ne scoprirono le sue proprietà lassative
- **CANNELLA:** Portoghesi e Olandesi la esportavano dall'isola di Ceylon fin dal XVI secolo per utilizzarla come spezie e per contrastare alcune forme infiammatorie di origine batterica a carico del tratto gastrointestinale
- **ZENZERO:** utilizzato da millenni in India e Cina e citato da Plinio per le sue proprietà eupeptiche, carminative e digestive (*Naturalis Historia*, XII-28)



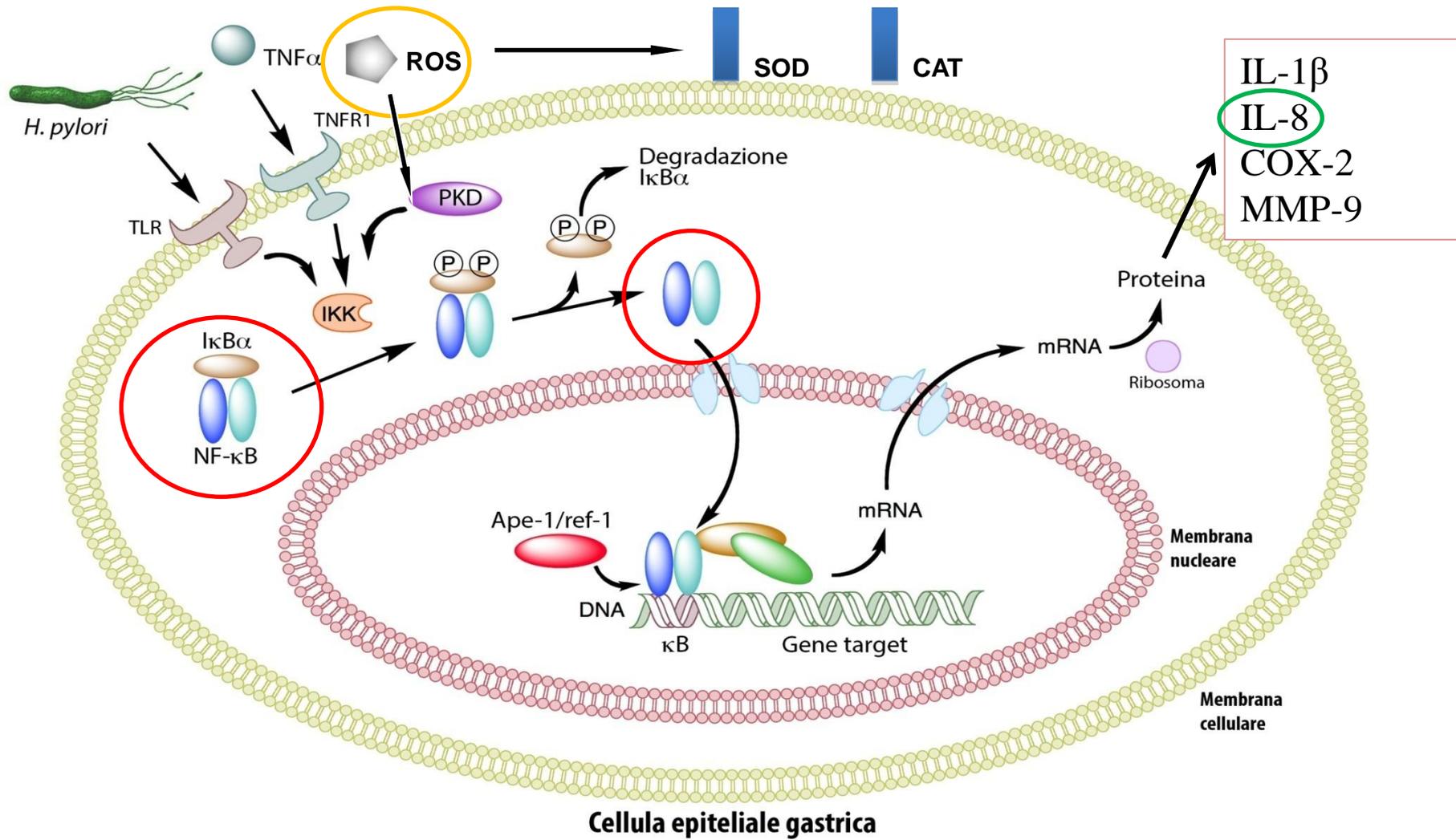
# NUTRACEUTICI E INFIAMMAZIONE



OLEUROPEINA  
AGLICONE



# ATTIVAZIONE DI NF- $\kappa$ B

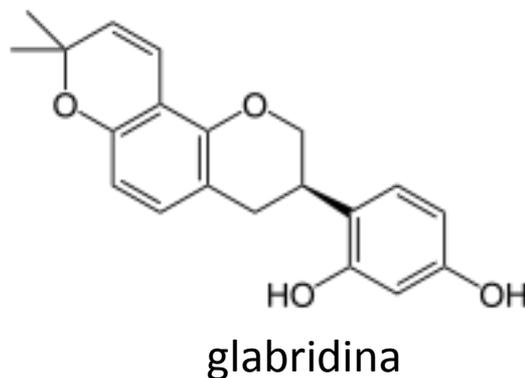




# LIQUIRIZIA E GASTRITE

Treatment	Dose	Study design	Effects	References
GutGard <sup>a</sup> (n = 55) Placebo (n = 52), quadruple therapy: amoxicillin, omeprazole, metronidazole in both groups	150 mg, 60 days	Double-blind placebo-controlled trial	Treatment with GutGard was more effective in reducing <i>Helicobacter pylori</i> and gastric load	Puram <i>et al.</i> , 2013
Bismuth (n = 20) Licorice (n = 20)	500 mg/3 times/30 days 500 mg/3 times/30 days	Double-blind study	Administration of licorice instead of bismuth subnitrate could effectively heal peptic ulcer and eradicate <i>H. pylori</i> pathologically	Rahnama <i>et al.</i> , 2013

Groups	Days	n	HpSA	
			Hp <sup>+</sup>	Hp <sup>-</sup> (%)
GutGard	0	50	50	0 (0)
Placebo		50	50	0 (0)
GutGard	30	50	50	0 (0)
Placebo		50	50	0 (0)
GutGard	60	50	22	28* (56)
Placebo		50	48	2 (4)



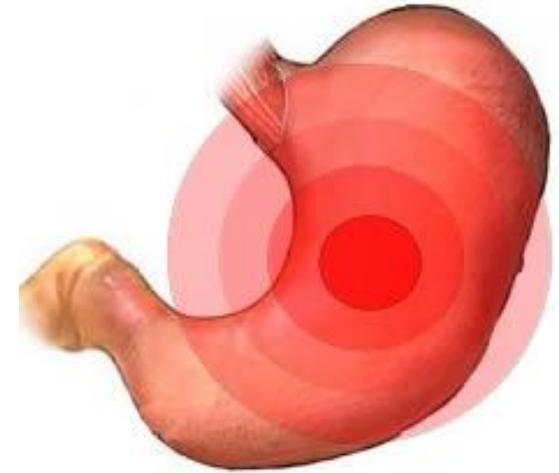
*Glycyrrhiza glabra* L. riduce la proliferazione di *H. pylori* gastrico

Tratto da Hosseinzadeh H. et al. Phytoter. res. 2015

# PIANTE PER LA GASTRITE: LIQUIRIZIA

## STUDI CLINICI

- 15 pazienti con ulcera peptica sono stati trattati con 9g/die di radice per 1-3 mesi;
- Miglioramento significativo già dopo 2 mesi dall'inizio del trattamento:
- Diminuzione del bruciore epigastrico (76% dei pazienti);
- Completa guarigione in oltre il 50% dei casi (Chaturvedi GN, 1979)

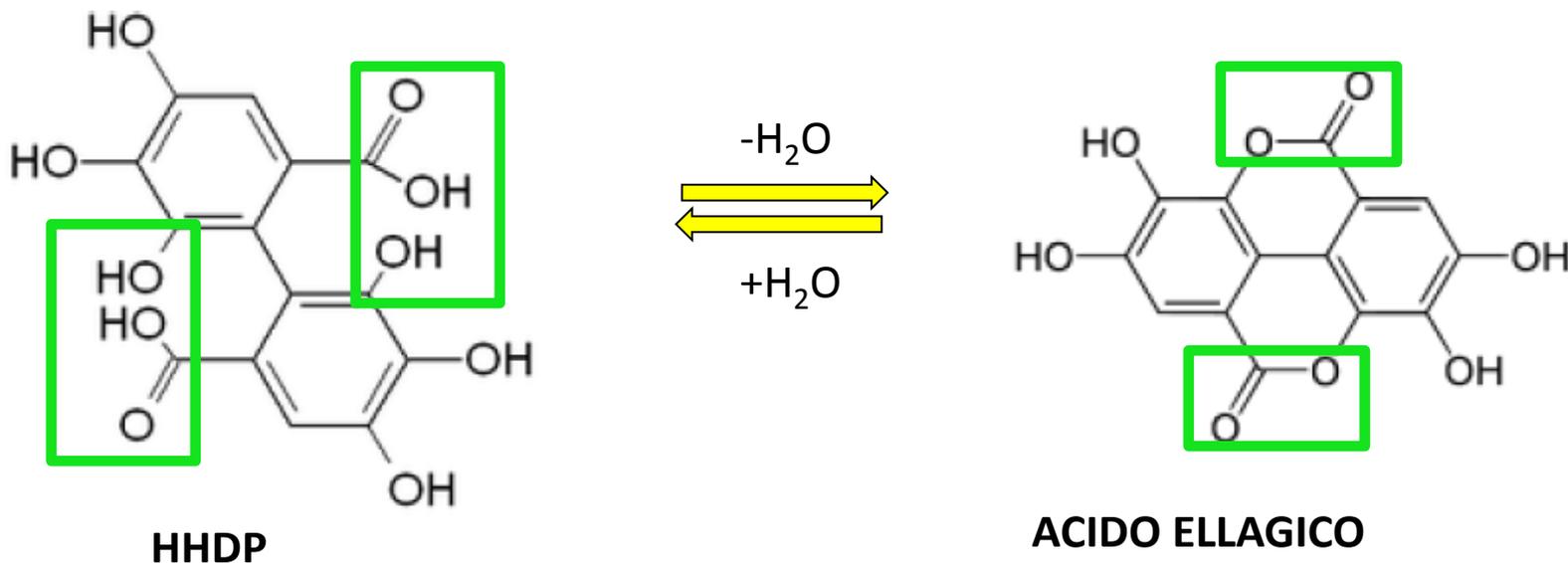


# GLI ELLAGITANNINI

## DEFINIZIONE

*ESAIDROSSIDIFENOIL ESTERI DI ZUCCHERI*

*Molecole costituite da uno zucchero il cui gruppo ossidrilico è esterificato con l'acido esaidrossidifenico (HHDP)*



# LE FONTI DI ELLAGITANNINI



*Ribes nigrum* L.



*Rubus idaeus* L.



*Punica granatum* L.

**ELLAGITANNINI**



*Juglans regia* L.

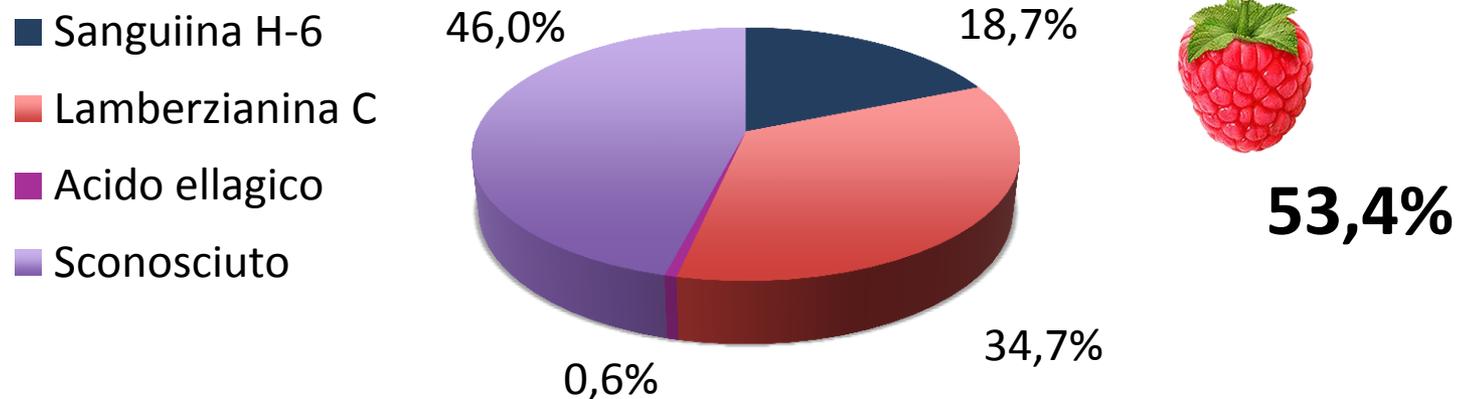
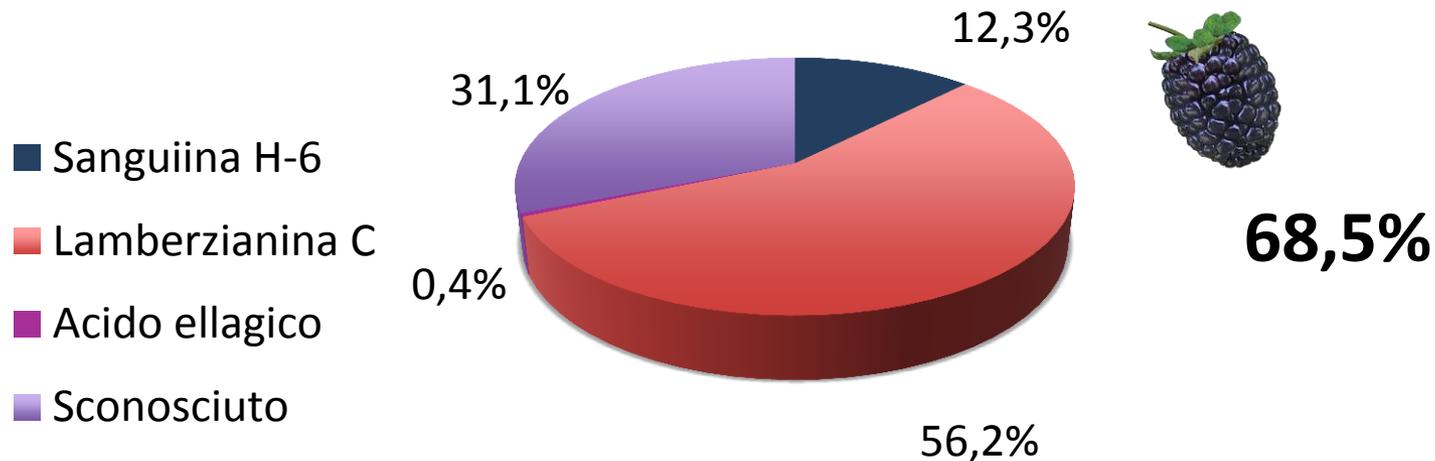


*Castanea sativa* Miller



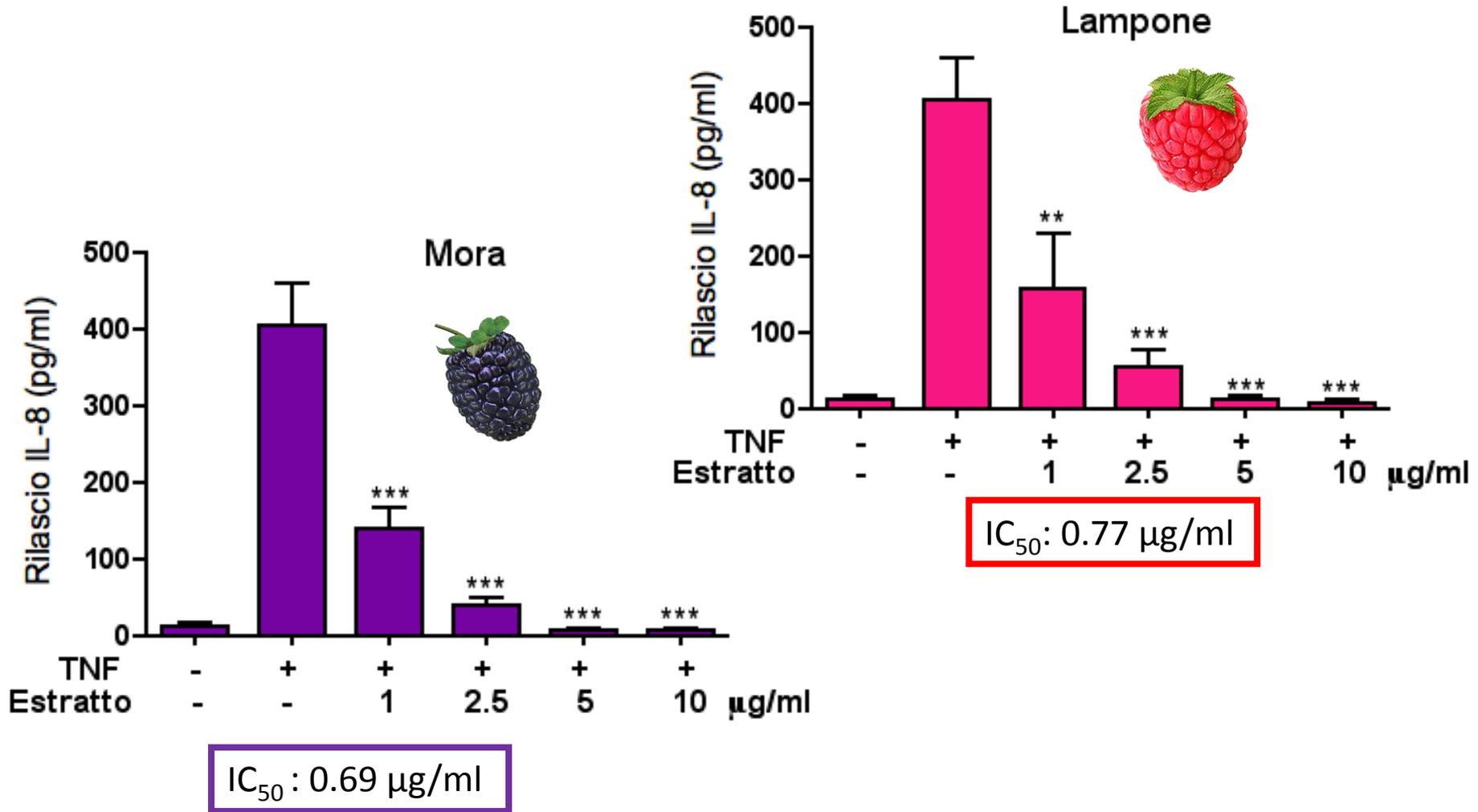
*Rubus fruticosus* L.

# COMPOSIZIONE DEGLI ESTRATTI



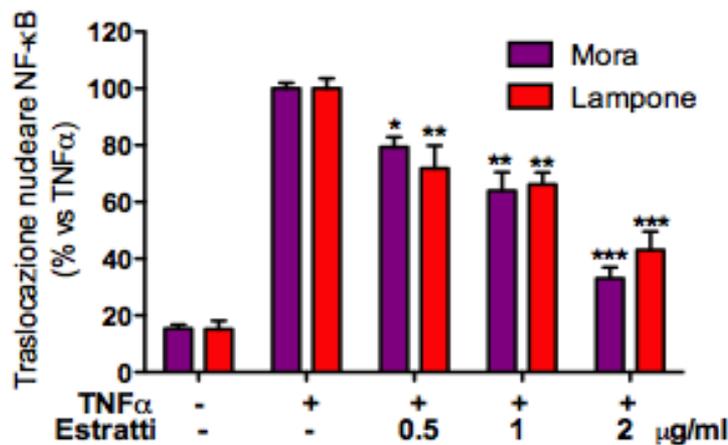
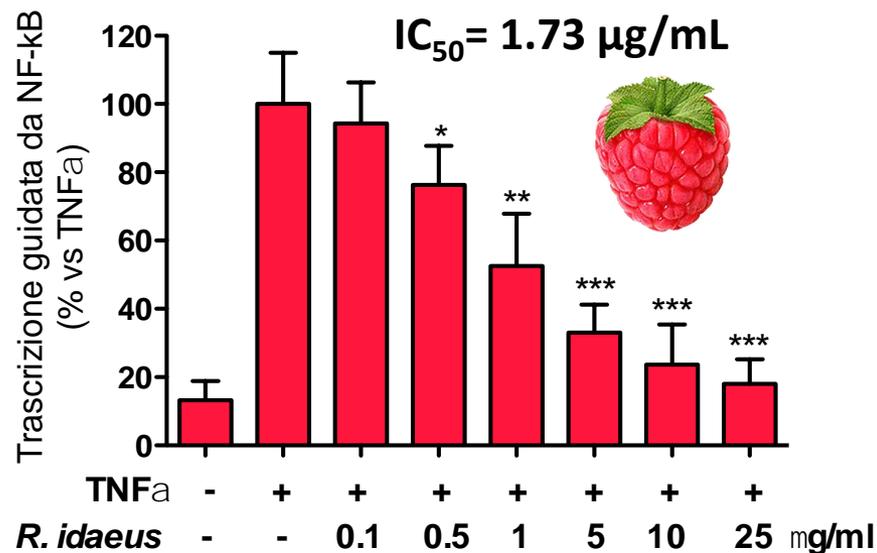
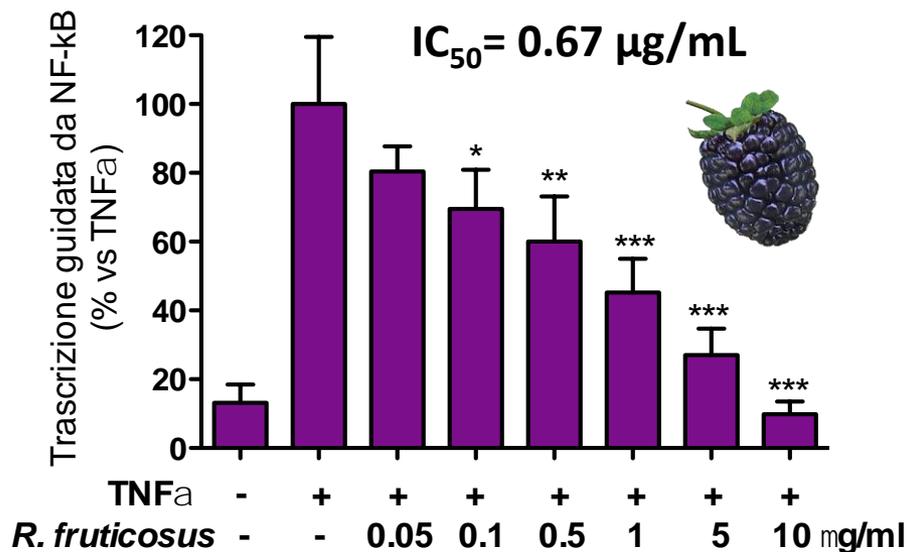
# EFFETTO SULLA SECREZIONE DI IL-8

## Cellule epiteliali gastriche umane



Sangiovanni E. et al., PLoS One 2013

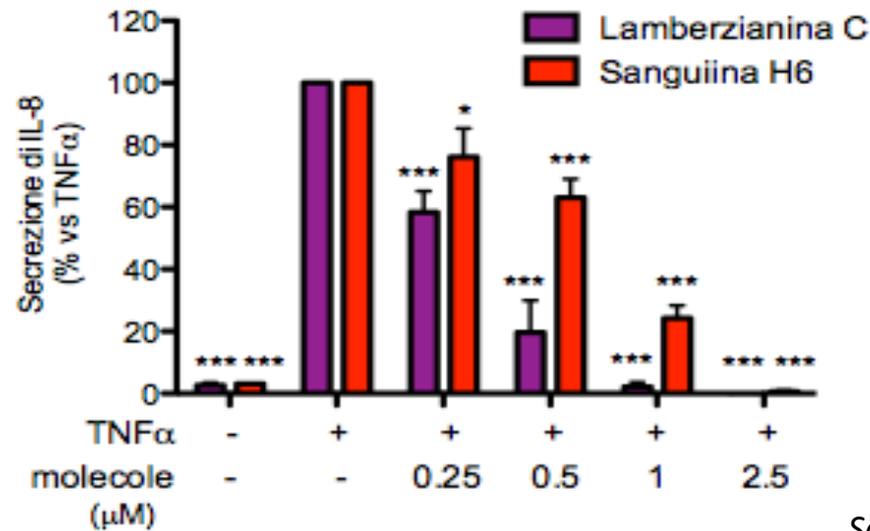
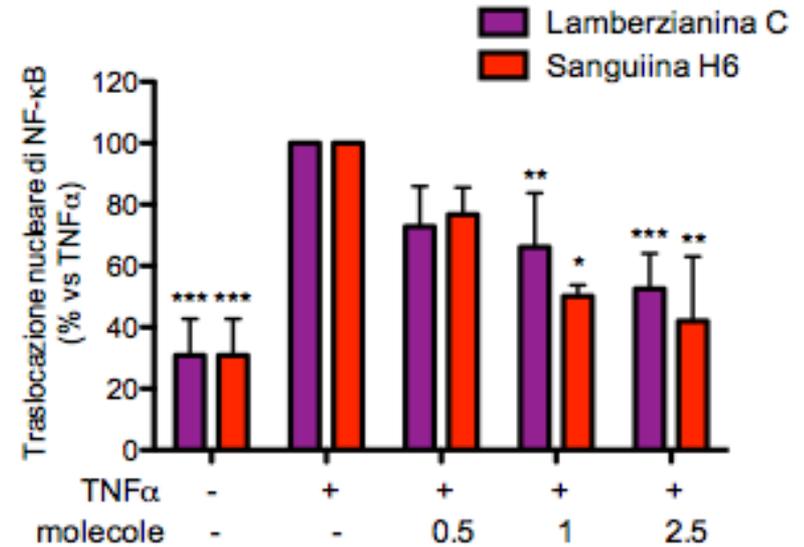
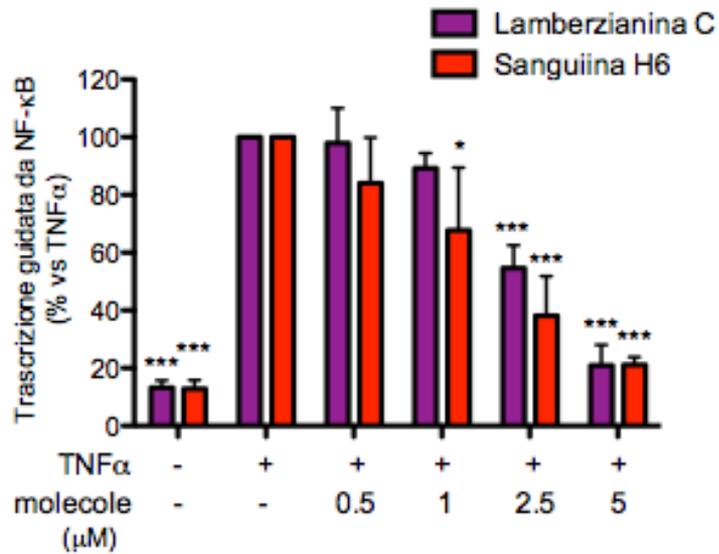
# EFFETTO DEGLI ESTRATTI SU NF-κB



\*p < 0.05; \*\*p < 0.01; \*\*\*p < 0.001

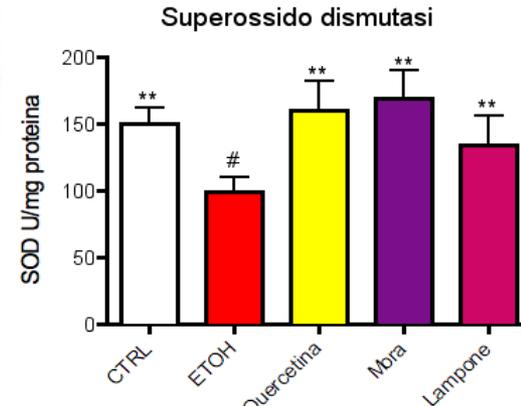
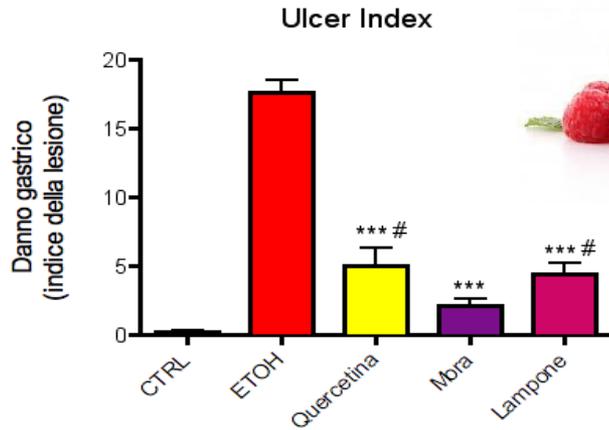
Sangiovanni E. et al., PLoS One 2013

# GLI ELLAGITANNINI: NF- $\kappa$ B E IL-8



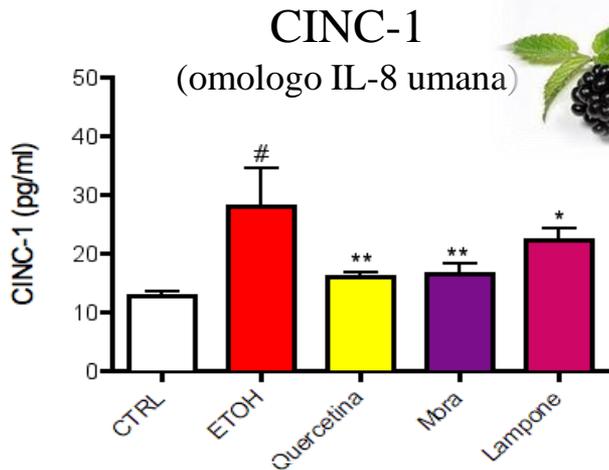
Sangiovanni E. et al., PLoS One 2013

# GLI ELLAGITANNINI PREVENGONO IL DANNO GASTRICO Modello in vivo

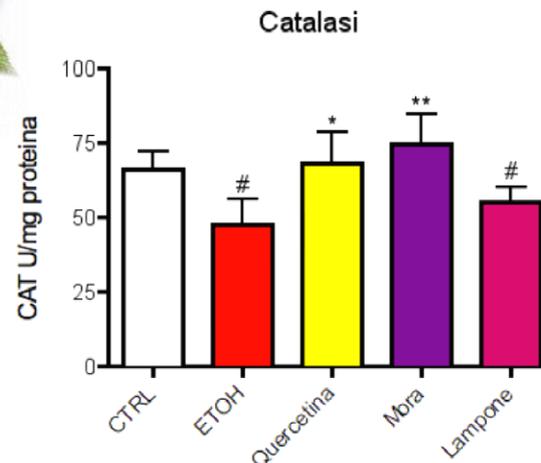


\*\*\* P<0.001 vs EtOH # P<0.05 vs mora

\*\* P<0.01 vs EtOH # P<0.05 vs controllo



\*\* P<0.01 vs EtOH \* P<0.05 vs EtOH  
# P<0.05 vs controllo

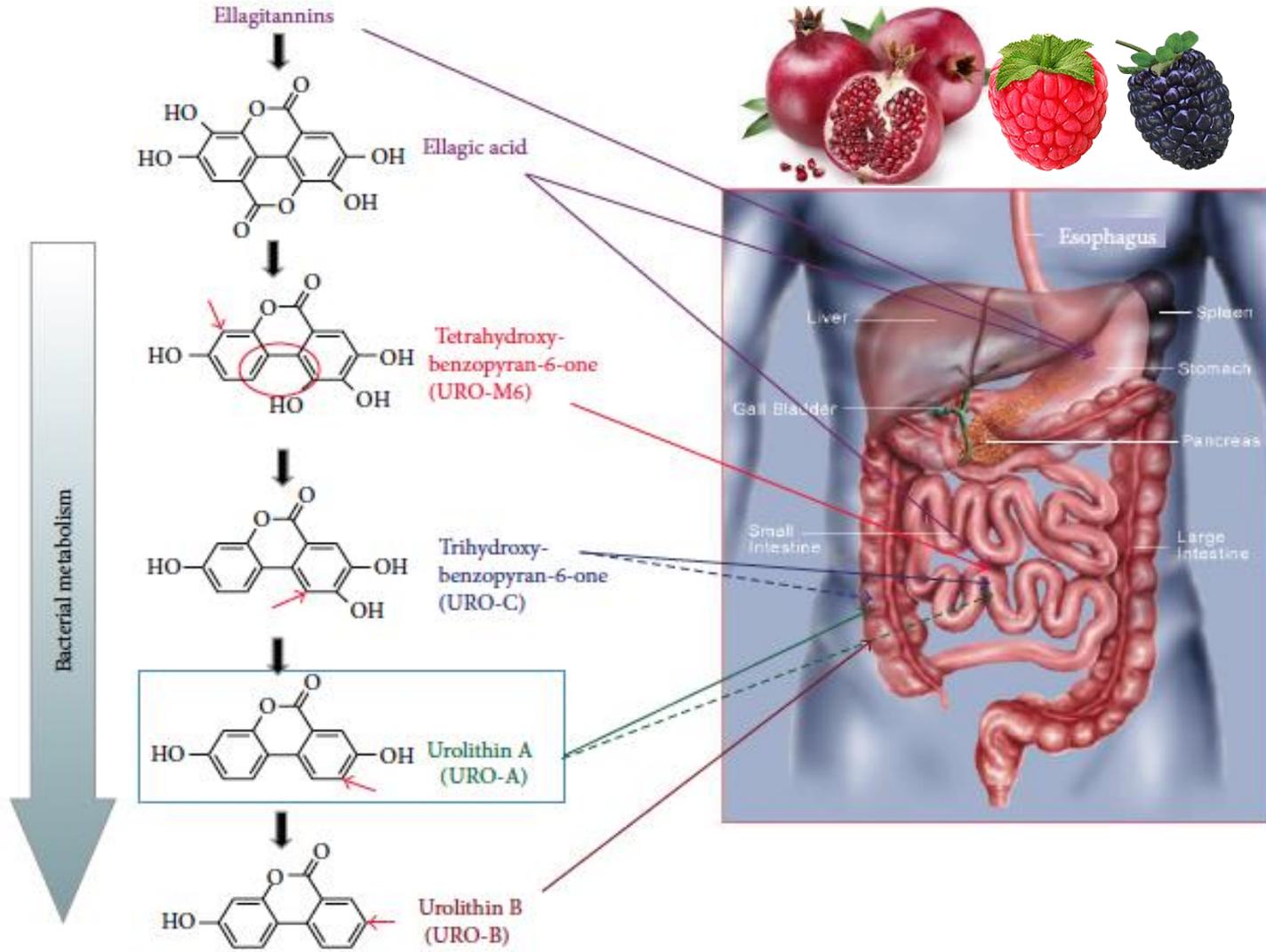


\*\* P<0.01 vs EtOH \*P<0.05 vs EtOH  
#P<0.05 vs ctrl

Estratti: 20 mg/kg, quercetina: 100 mg/kg

*Sangiovanni E. et al., PLoS One 2013*

# METABOLISMO DEGLI ELLAGITANNINI



Tratta da Espin J.C. et al., EBCAM, 2013

# GLI EFFETTI BENEFICI DELLE PIANTE

## INFIAMMAZIONE INTESTINALE



*Aloe vera* L.



*Artemisia absinthium* L.



*Andrographis paniculata* Wall.



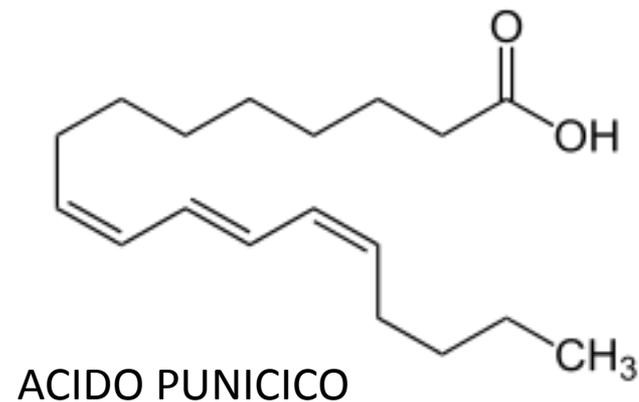
*Boswellia serrata* Roxb.

# I PRODOTTI VEGETALI E LE IBD

Herbal preparation	Study design	Number of patients	IBD type	Dose	Comparator	Frequency	Endpoint
<i>Aloe vera</i>	Randomized, double-blind controlled study	44	UC	100 mL twice/day	Placebo	4 weeks	<i>Aloe vera</i> produced a significantly better clinical response than in those receiving placebo. The Simple Clinical Colitis Activity Index and histological scores decreased significantly during treatment with <i>Aloe vera</i> but not with placebo
<i>Andrographis paniculata</i> (HMPL-004)	Randomized, double-blind multicentre study	120	UC	1.2 g/day	Mesalazine (4.5 mg/day)	8 weeks	There were no significant differences between the two treated groups when considering the clinical efficacy rates or the safety profile
	Randomized, double-blind placebo-controlled study	224	UC	1.2 g/day and 1.8 g/day	Placebo	8 weeks	Patients treated with the extract, mainly at the highest doses, were more likely to achieve clinical response than those receiving placebo, whereas the incidence of adverse events was similar among groups, although the occurrence of rash was higher in the HMPL-004 extract groups
<i>Artemisia absinthium</i>	Randomized, double-blind multicentre study	40	CD	3 × 500 mg/day	Placebo	10 weeks	After 8 weeks of treatment with wormwood, there was almost complete remission of symptoms in 65% of the patients, whereas no beneficial effect was observed in those receiving the placebo
	Randomized, double-blind multicentre study	20	CD	3 × 750 mg/day (in addition to standard therapy)	Standard therapy + placebo	6 weeks	Wormwood administration promoted the clinical improvement of the symptoms in all the patients. The beneficial effect was associated with a significant decrease in TNF $\alpha$ serum levels in comparison with those obtained in the placebo group, where no amelioration in the disease was observed
<i>Boswellia serrata</i> (Gum resin)	—	?	UC	750 mg (3 × 250 mg)	Sulfasalazine 3 g (3 × 1 g)	6 weeks	All parameters tested improved after treatment with <i>Boswellia serrata</i> gum resin, with the results being similar compared to controls: 82% out of treated patients went into remission; in case of sulfasalazine remission rate was 75%
(Gum resin)	—	30	UC?	900 mg (3 × 300 mg)	Sulfasalazine 3 g (3 × 1 g)	6 weeks	Patients showed an improvement in several parameters: stool properties, histopathology, and scanning electron microscopy, besides haemoglobin, serum iron, calcium, phosphorus, proteins, total leukocytes, and eosinophils. The remission was higher in patients treated with <i>Boswellia serrata</i>
(Boswelan)	Randomized, double-blind, multicentre placebo-controlled study	82	CD	2.4 g/day	Placebo	12 months (52 weeks)	Boswelan showed a safety profile during the long-term therapy but the results obtained did not show a higher efficacy when compared with placebo

# OLIO DI SEMI DI MELOGRANO

- Acido grasso polinsaturo presente in elevate concentrazioni (64-83%) nell'olio di semi di melograno
- **Acido punico** è un potente agonista di PPARgamma
- Diminuisce lo stato di ulcerazione, il danno tissutale in modelli di colite indotta da DSS e TNBS
- Non sono presenti studi clinici



# CONCLUSIONI

- Diversi prodotti di origine vegetali sono utilizzati per gli **effetti benefici sul tratto gastrointestinale**;
- Molti di questi prodotti sono validati da un **utilizzo millenario**, sebbene gli **studi clinici** siano, in alcuni casi, **scarsi** o addirittura assenti;
- Il **destino metabolico** dei principi attivi presenti nel fitocomplesso deve essere seriamente considerato;
- La liquirizia e gli ellagitannini sembrano essere particolarmente promettenti nelle infiammazioni del tratto gastrico, mentre l'olio di semi di melograno e Boswellia nelle IBD



# RINGRAZIAMENTI

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- Dr. Enrico Sangiovanni



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