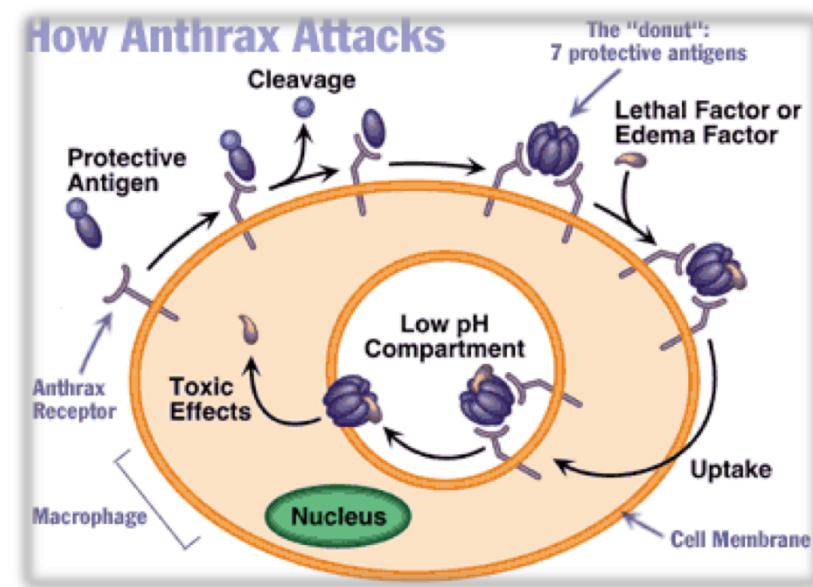
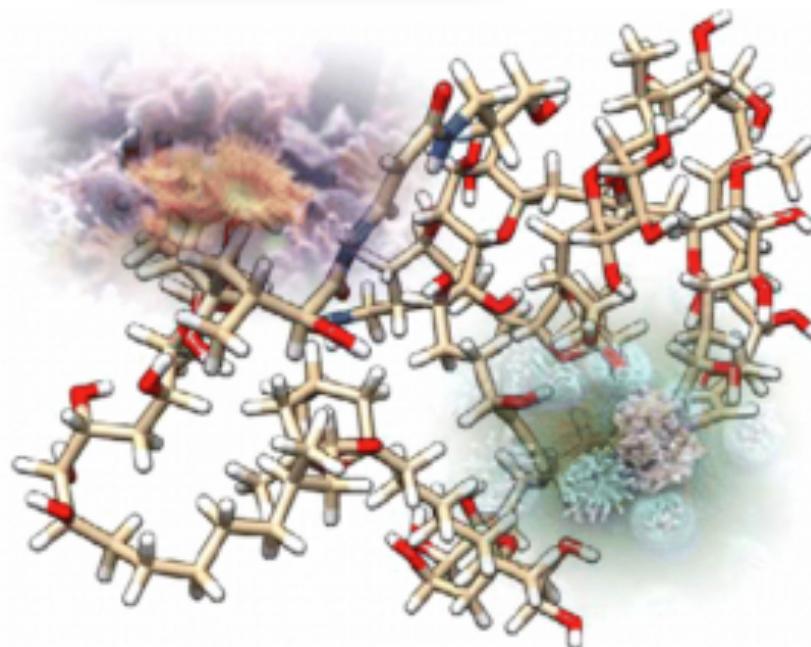
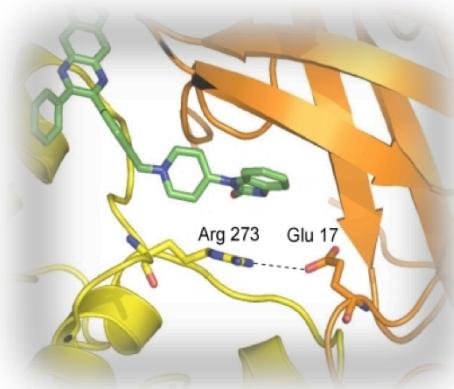


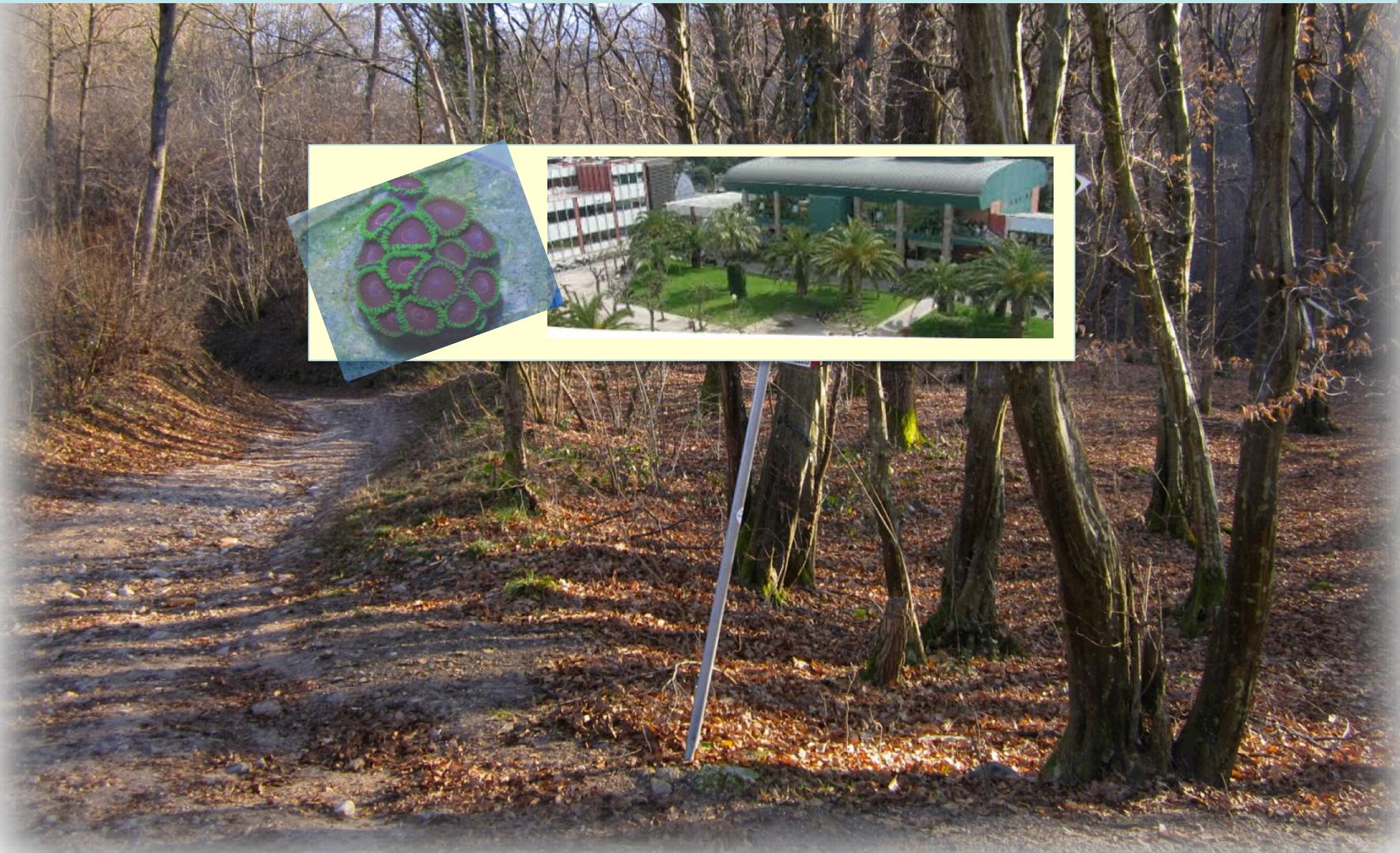


Alla ricerca dell'elisir di lunga vita dell'uomo e ... del vino!

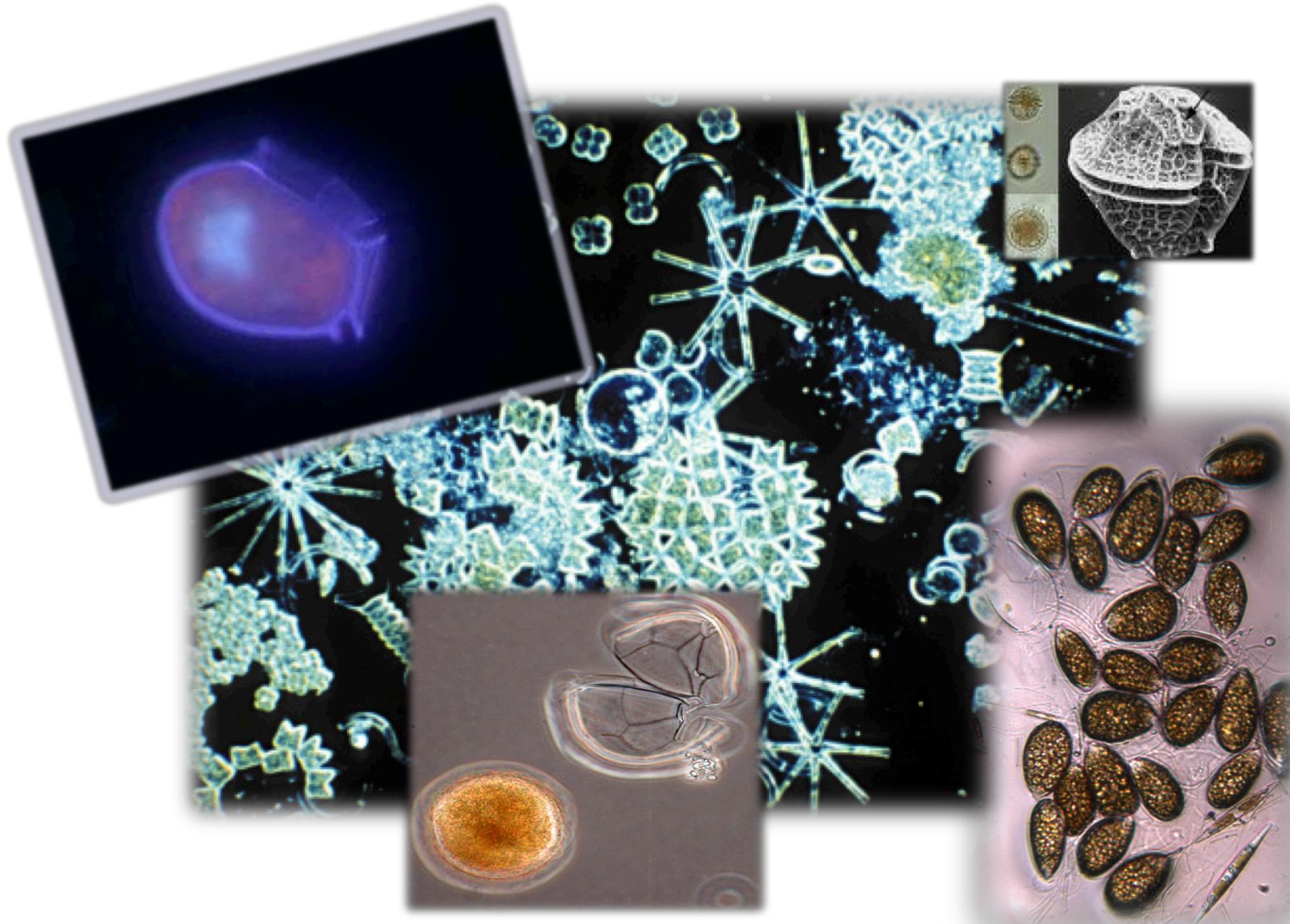




Laurea in CTF e Dottorato di Ricerca in chimica delle sostanze naturali: le biotossine marine



Il mare pullula di microalghe...

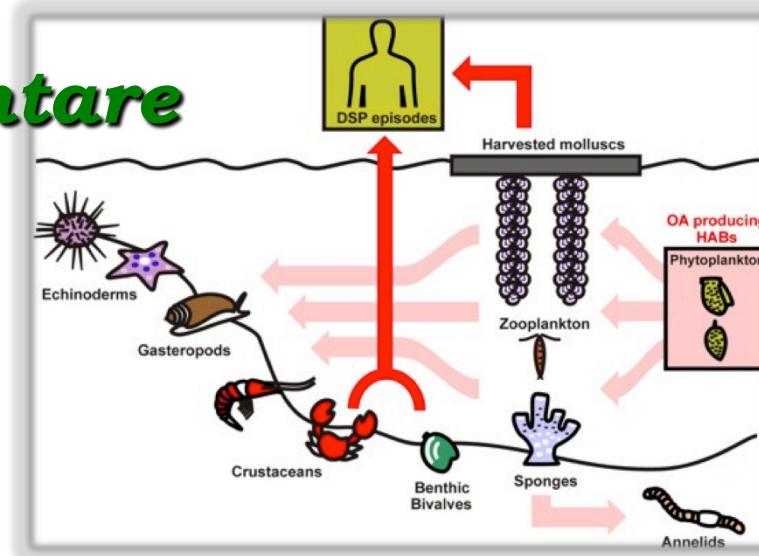


In che modo le biotossine arrivano all'uomo

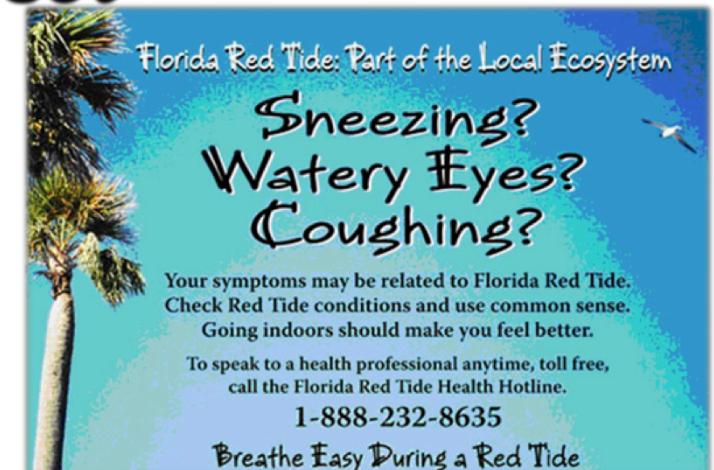


1) Catena alimentare

2) Contatto diretto

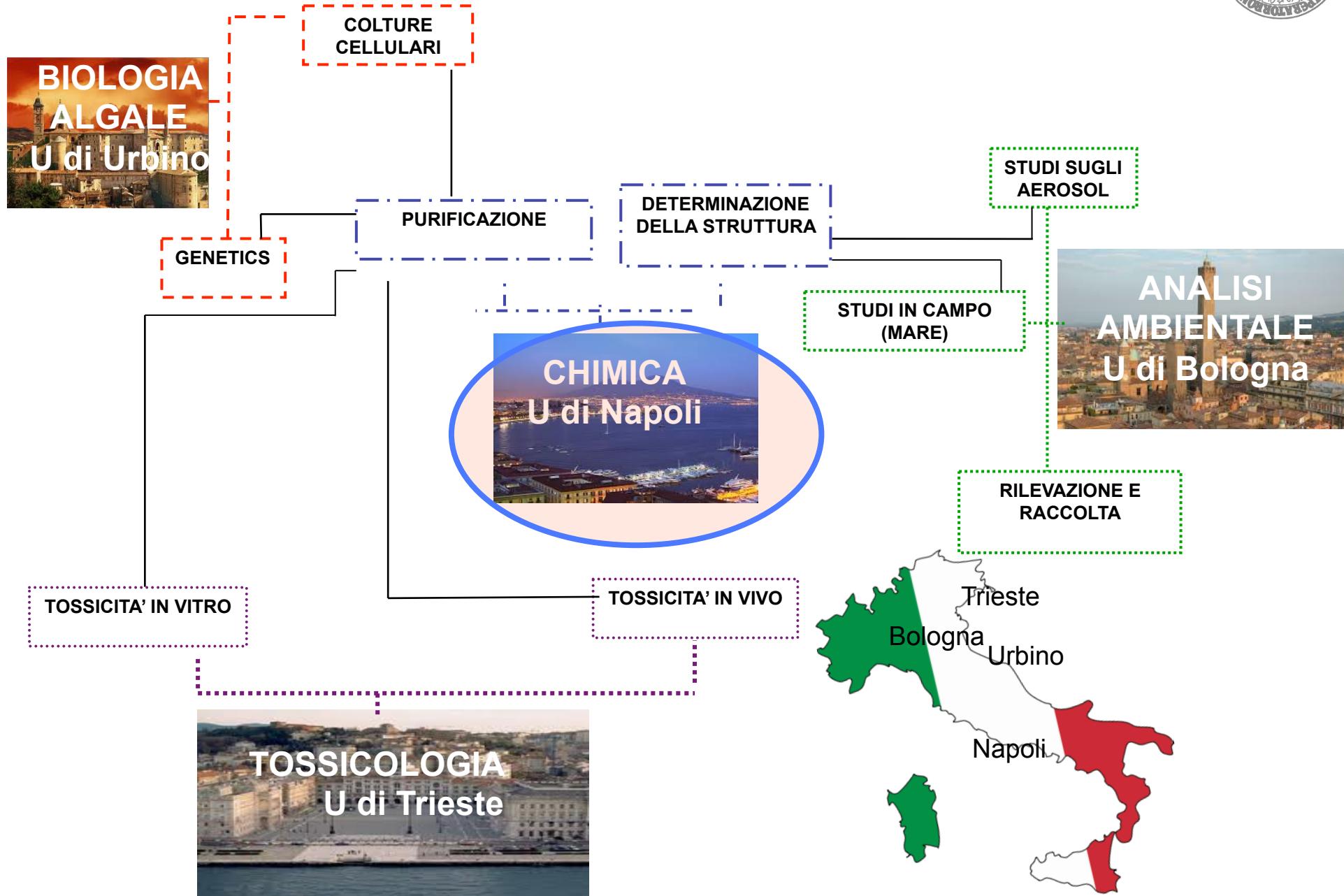


3) Aerosol





Il network italiano per le biotossine



Il Network internazionale sulle biotossine

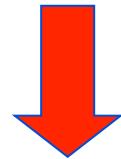




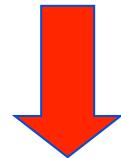
ISOLAMENTO DELLE TOSSINE



200-300 KG
Di molluschi contaminati
o Milioni di cellule di microalghe



Centinaia di grammi di estratti

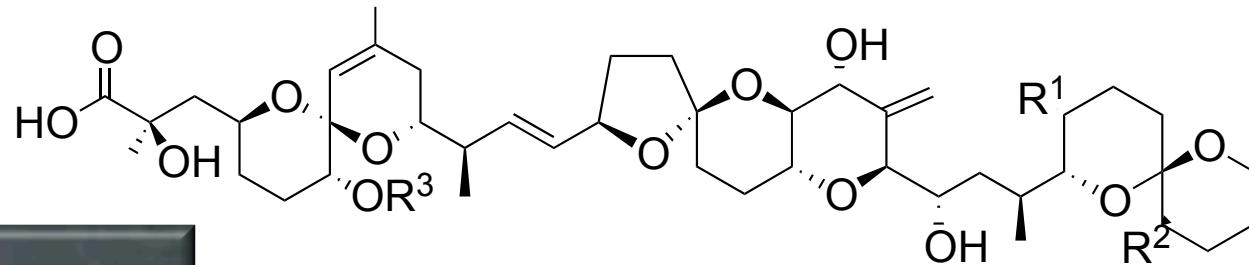
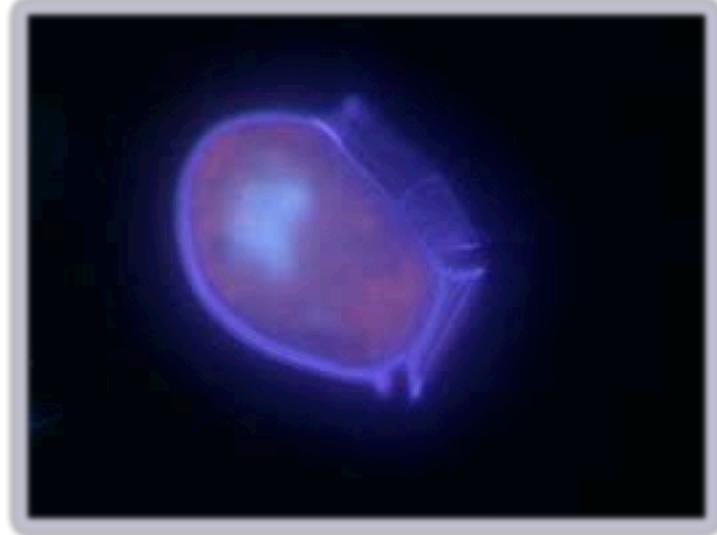


grammi di contaminanti e solo
Poche centinaia di µg di tossine
allo stato puro

Determinazione stereostretturale
Mediante NMR



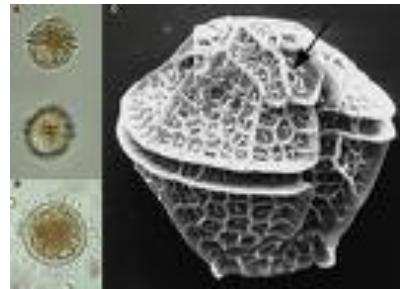
1989 Nel mar Adriatico settentrionale...



Acido Okadaico
da *Dinophysis fortii*

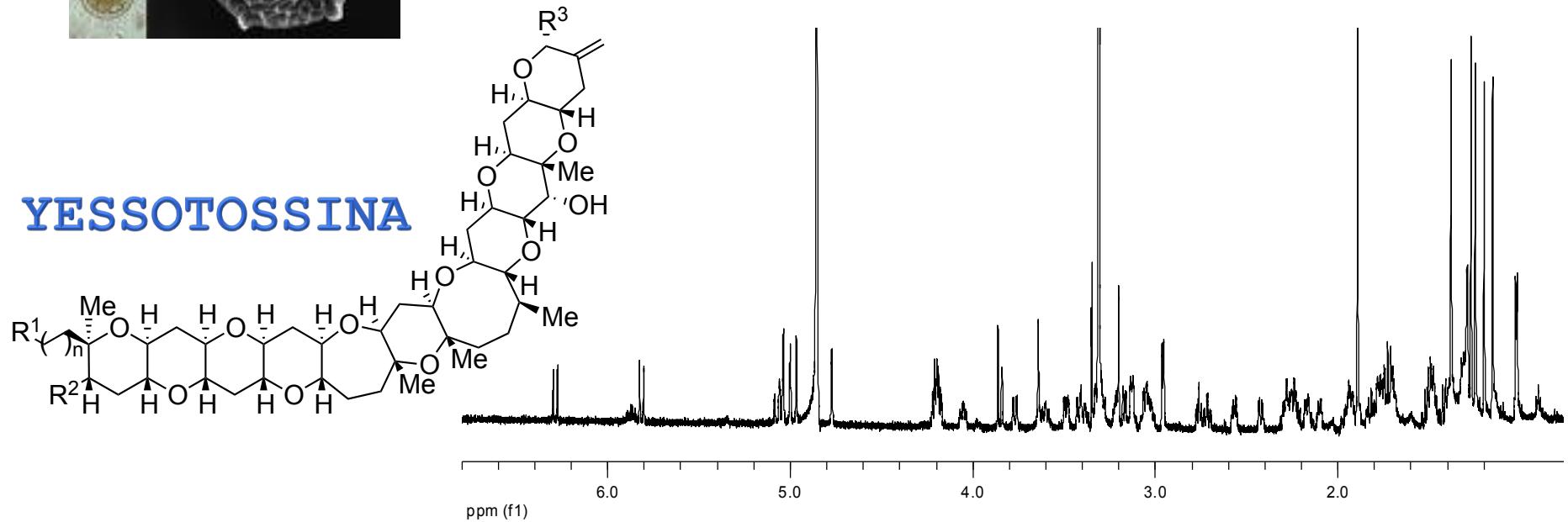


DAL 1995 Nel mar Adriatico settentrionale...



Protoceratium reticulatum

YESSOTOSSINA



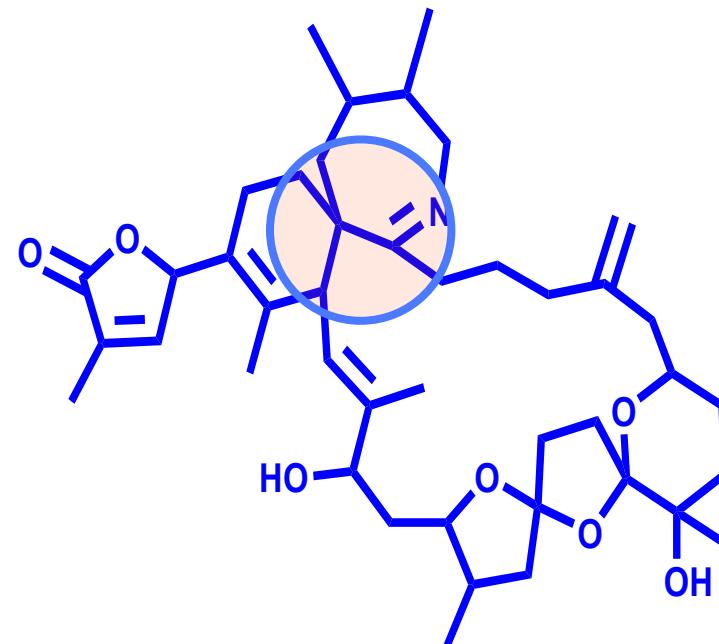
P.Ciminiello, E.Fattorusso, M.Forino, S.Magno, R.Poletti, M.Satake, and T.Yasumoto
Toxicon, 1997, 35, 177-183



DAL 2000



Alexandrium ostenfeldii



Spirolides...

ESTATE 2005...GENOVA



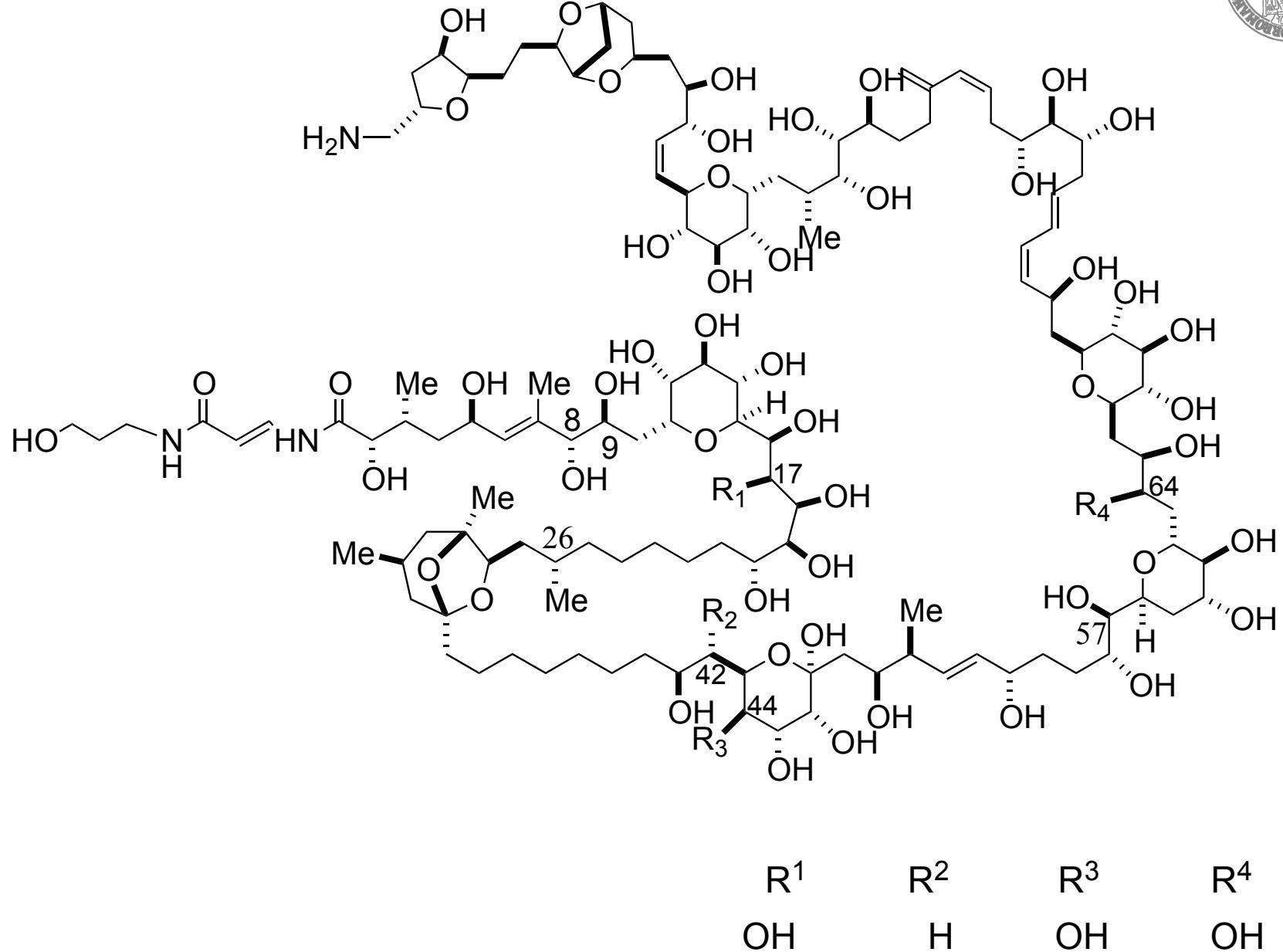
- *febbre*
- *broncococostrizione*
- *tosse*
- *rinite*
- *congiuntivite*



**Alte concentrazioni di
Ostreopsis ovata nel mar Ligure**



Palitossina:





Messa a punto di un metodo LC/MS Per la palitossina

LC parameters:

Column: 3mm C-18 Gemini (150 × 2.00 mm)

Mobile phase: A = water, B = 95% acetonitrile in water, both the phases added of 30 mM of acetic acid

Flow: 0.2 mL/min

Gradient: t= 0 min, 20% B;
t = 20 min, 100% B; t = 14 min, 100% B



MS parameters:

Declustering potential 1V

Focusing potential 390 V

Entrance potential 11 V

Temperature 0 °C

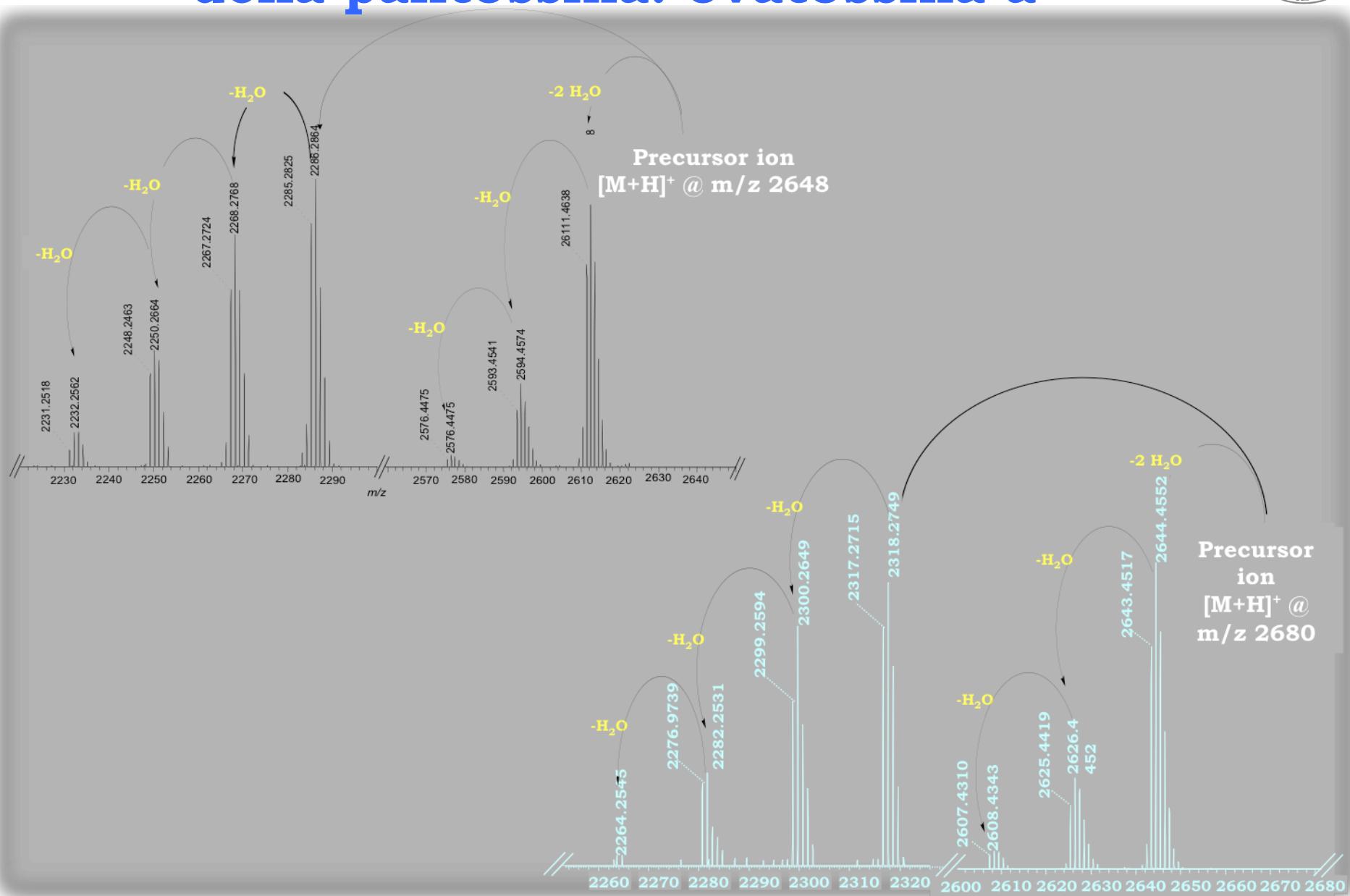
Collision Energy 50 eV

Cell exit potential 10 V

Collision Gas 7



identificazione di un nuovo analogo della palitossina: ovatossina-a





European Food Safety Authority

EFSA Journal 2009; 7(12):1393

“... Hazard identification and characterisation

Further information is needed on toxicity of palytoxin-group toxins, particularly of ovatoxin-a, to better characterise their oral toxicity and relative potencies...”





Isolamento

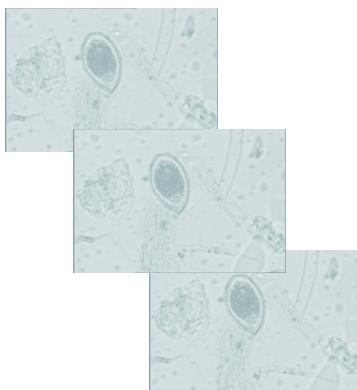
circa **80** litri
Di colture di O.
ovata
(**100,000,000** cellule)



MeOH: H₂O
1 : 1



Ripartizione
contro
CH₂Cl₂



Combiflash
360g C-18
eluita con un
gradiente di
acqua:
propanolo



Centrifugazione
5500 rpm
(30 min)

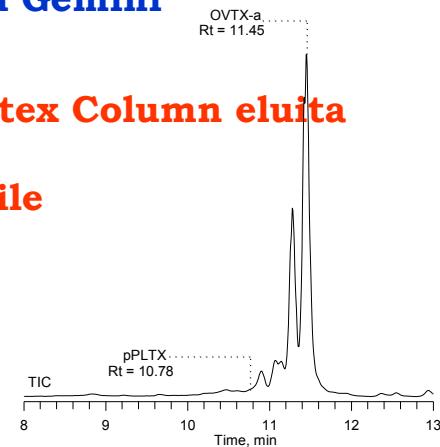


HPLC

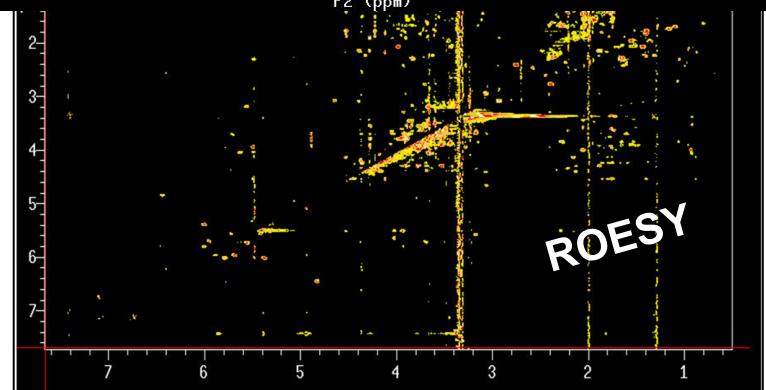
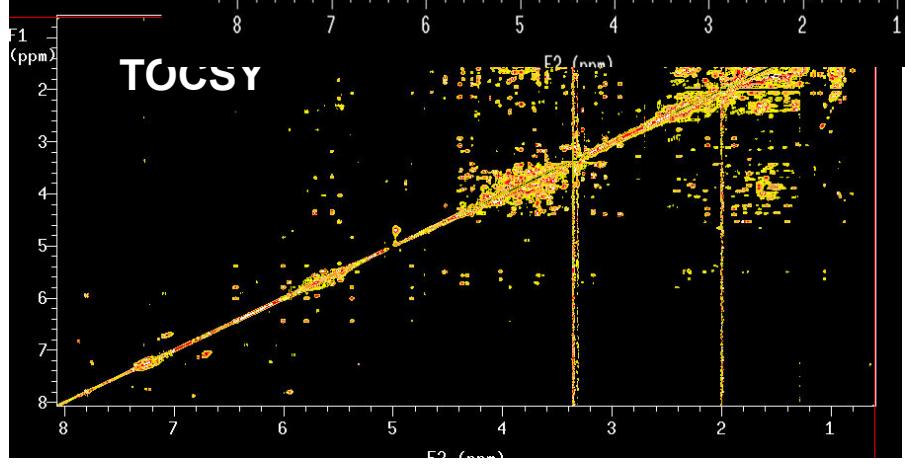
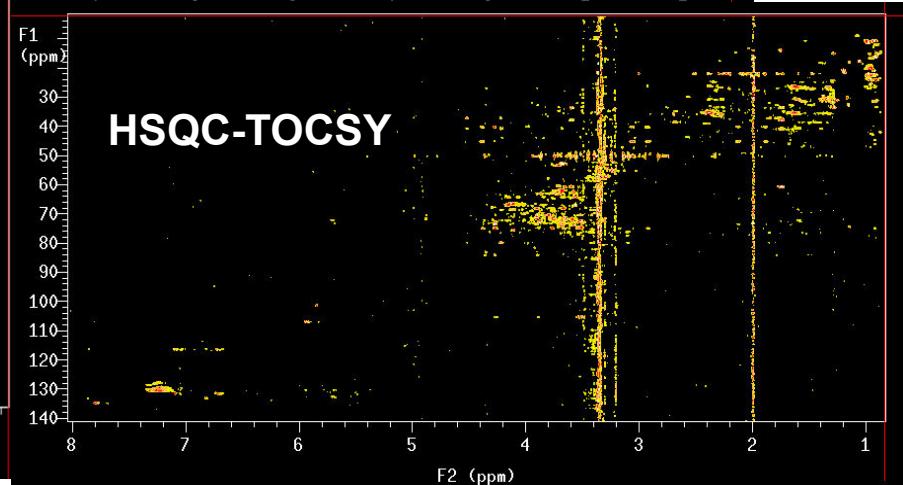
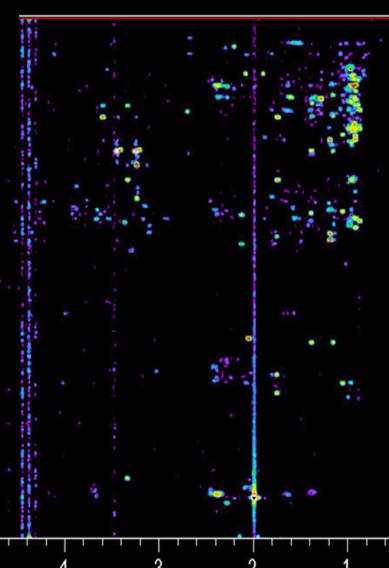
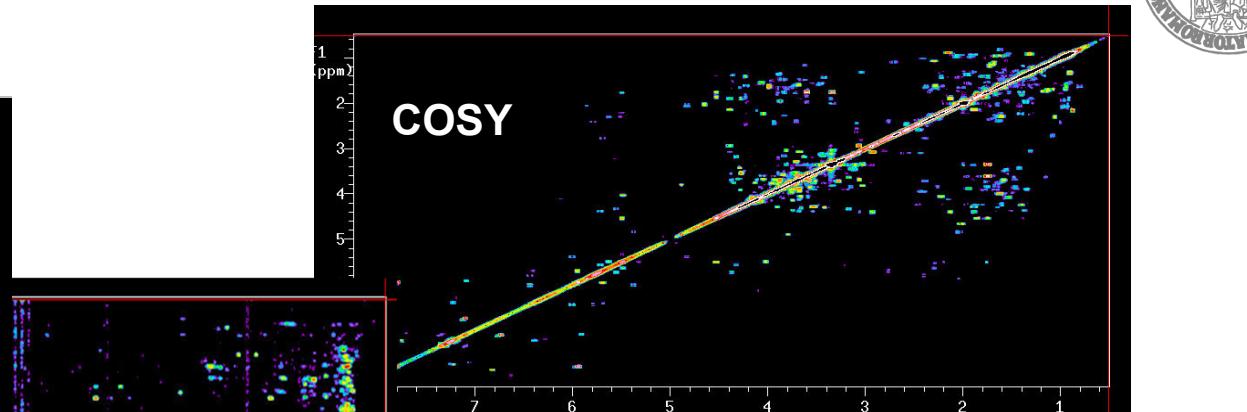
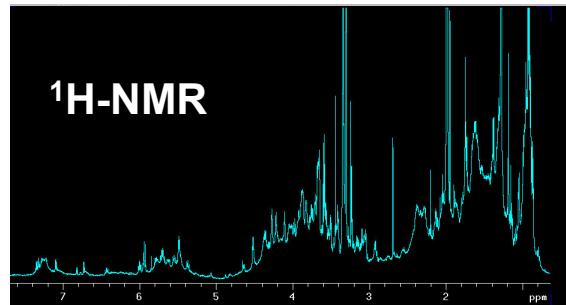


1) HPLC 10u Gemini

2) HPLC 2.6 u Kinetex Column eluita
con un gradiente
Di acqua/acetonitrile

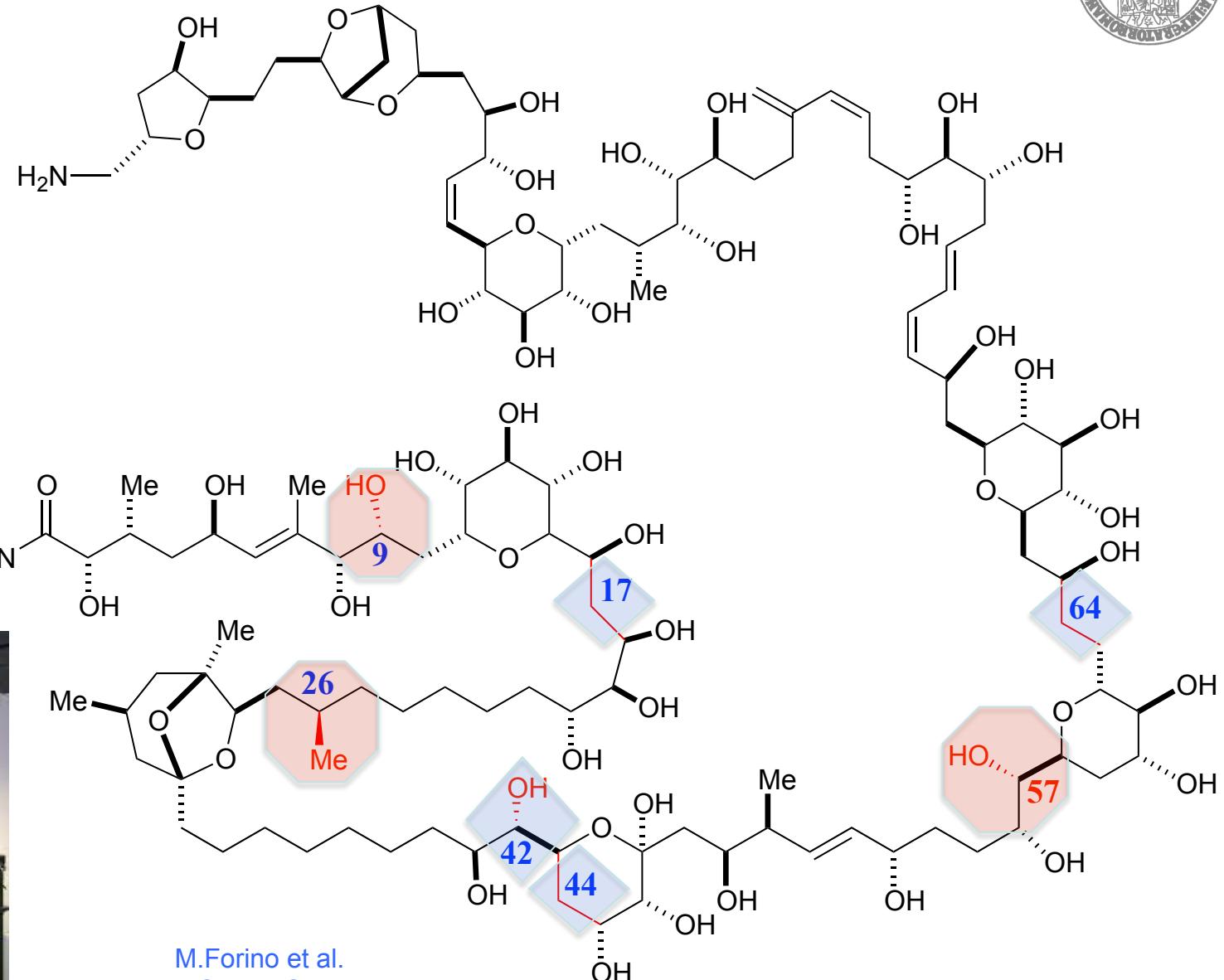


NMR studies on ovatoxin-a





Stereostruutura dell'ovatossina-a



M.Forino et al.
J. Am. Chem. Soc. 2011,
Chemistry-A Europ. J. 2012
Journal of organic chemistry 2014

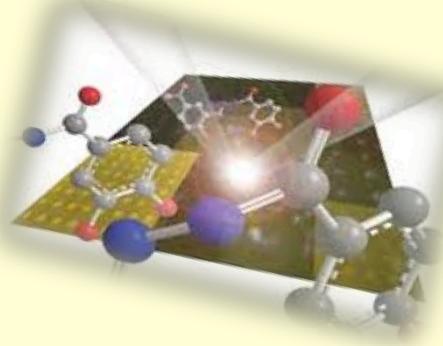




Laurea in CTF e Dottorato di Ricerca in chimica delle sostanze naturali: le biotossine marine

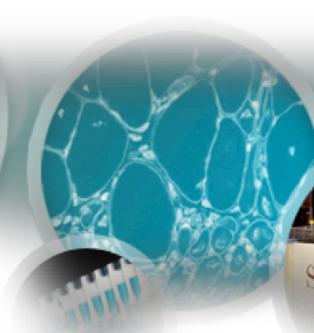
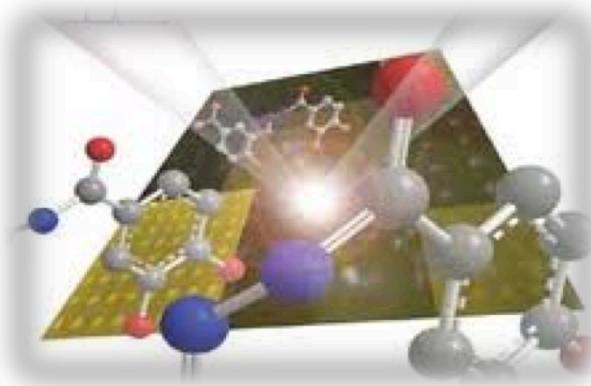


Drug discovery:
Sanford-Burnham Institute
di San Diego-California:
malattie infettive e neurodegenerative





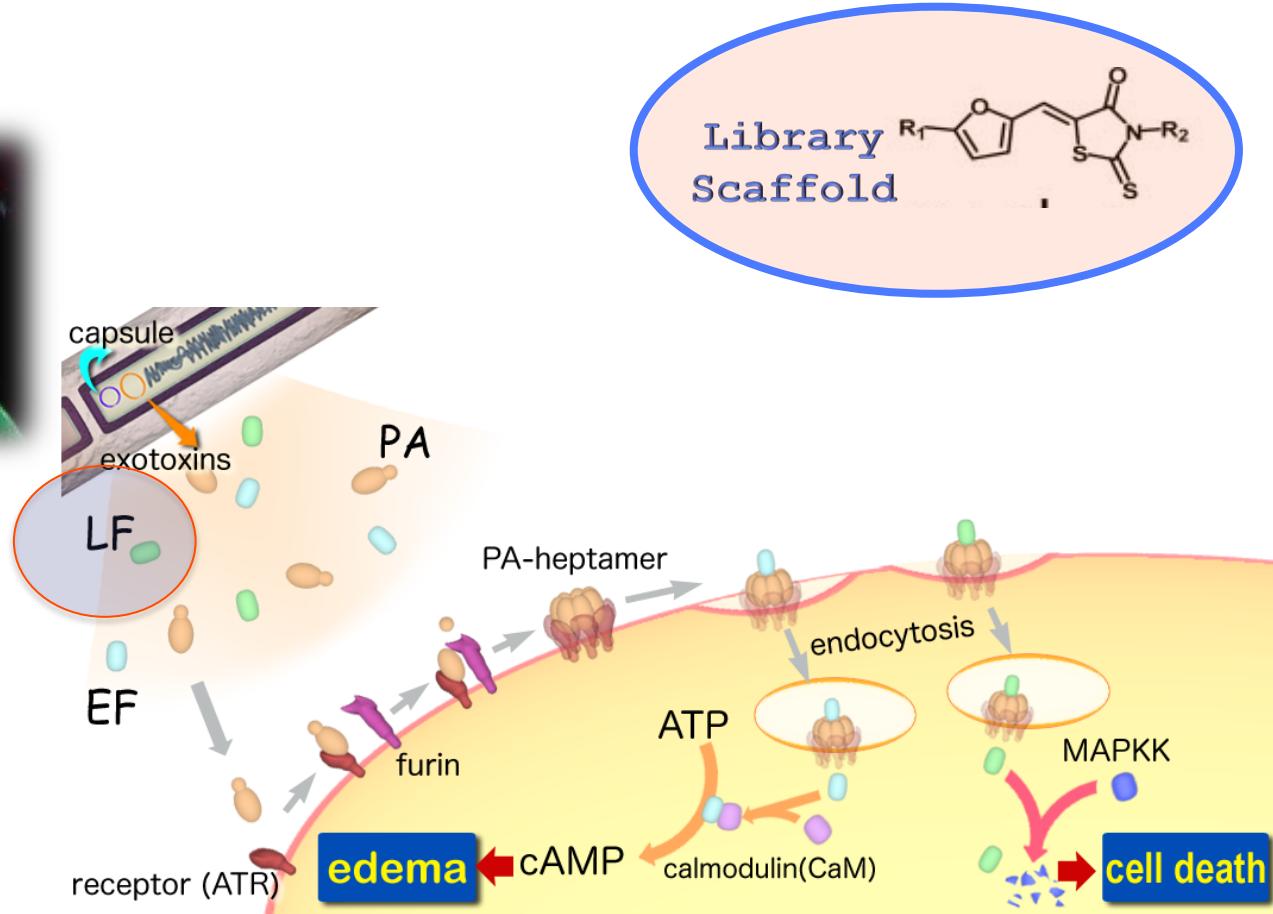
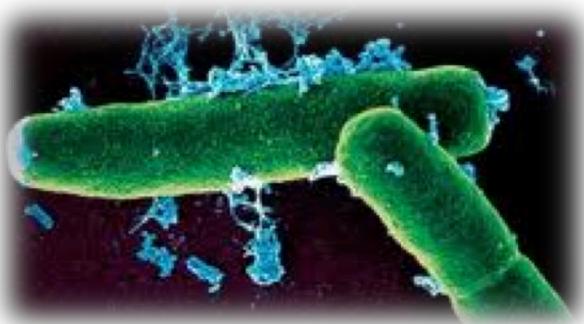
Drug Discovery



**1) Approfondimento di tecniche NMR
(^{19}F e spettri proteine-ligandi)**

**2) Messa a punto di saggi enzimatici
basati sulla fluorescenza**

Scoperta di inhibitori Dell'anthrax lethal factor

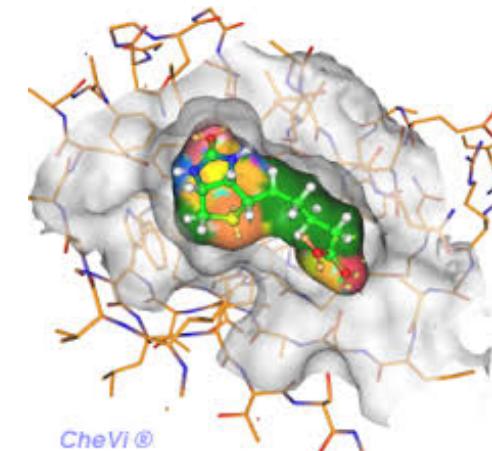


M. Forino et al.

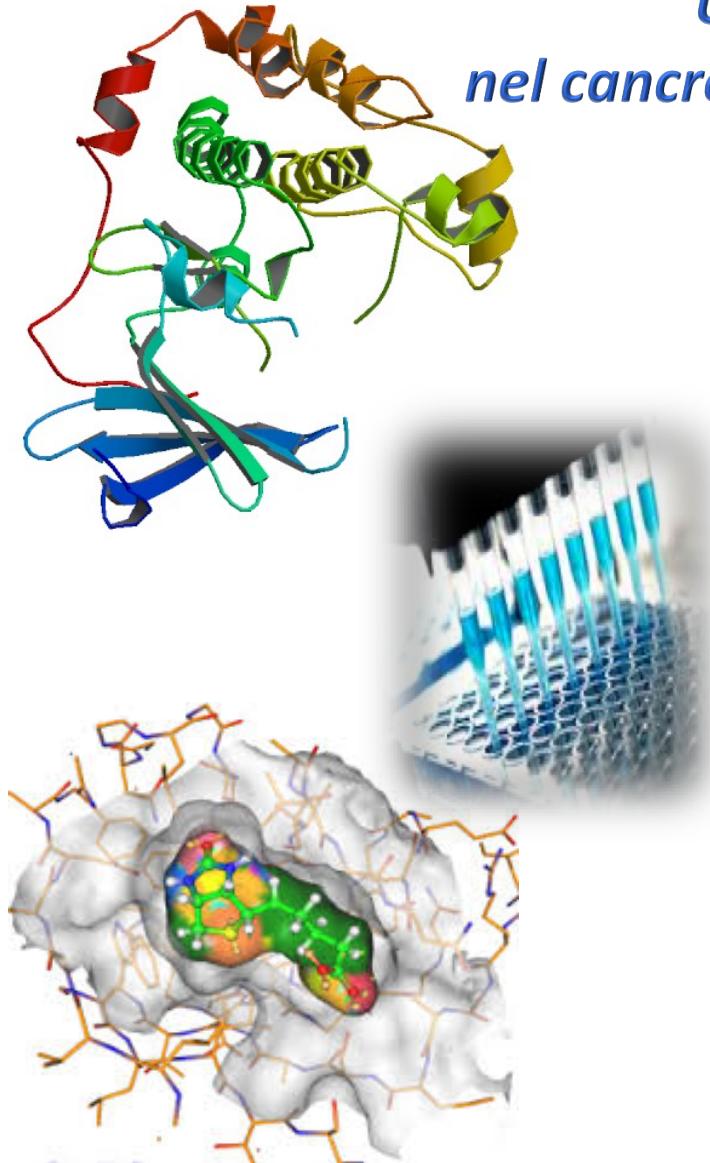
- NMR-based techniques in the hit identification, *Expert Opinion*, 2004
- Efficient synthetic inhibitors of anthrax lethal factor, *PNAS*, 2005
- Anthrax lethal factor protease inhibitors, *J. Med. Chem.*, 2006

Sintesi organica guidata da molecular docking

#	R ₁	R ₂	IC ₅₀ (μ M)	#	R ₁	R ₂	IC ₅₀ (μ M)
BI-9B9b	H	-CH ₂ COOH	140	12	Cl-C ₆ H ₄ -	H	7.4
1			300	13	Br-C ₆ H ₄ -Cl	H	7.0
2	Cl-C ₆ H ₄ -	-H ₂ C-	150	14	HO ₂ C-C ₆ H ₄ -	-H ₂ C-C ₆ H ₄ -	6.0
3	F-C ₆ H ₄ -	-CH ₂ CH=CH ₂	50	15	I-C ₆ H ₄ -	-CH ₂ COOH	5.5
4	O ₂ N-C ₆ H ₄ -	-C ₆ H ₄ -OH	37.7	16	HO ₂ C-C ₆ H ₄ -	-C ₆ H ₄ -NO ₂	4.8
5		-H ₂ C-	36.3	17		-CH ₂ COOH	3.1
6		-H ₂ CH ₂ C-	31.9	18	HO ₂ C-C ₆ H ₄ -	-C ₆ H ₄ -CF ₃	2.9
7		-(CH ₂) ₃ COOH	20	19	O ₂ N-C ₆ H ₄ -	-CH ₂ CH ₂ COOH	2.7
8		-CH ₂ CH ₂ COOH	12.8	20	HO ₂ C-C ₆ H ₄ -Cl	-CH ₂ CH=CH ₂	2.7
9	O ₂ N-C ₆ H ₄ -	-H ₂ C-	12.6	21	Br-C ₆ H ₄ -	-(CH ₂) ₃ COOH	2.3
10	HO ₂ C-C ₆ H ₄ -	-H ₂ C-	9.9	BI-MFM3	Cl-C ₆ H ₄ -	-CH ₂ CH ₂ COOH	0.8 (K _i)
11		-CH ₂ COOH	9.1				



Scoperta di inibitori dell' Akt1



*Una proteina coinvolta soprattutto
nel cancro al seno e allo stomaco, nonché in malattie
neurodegenerative*

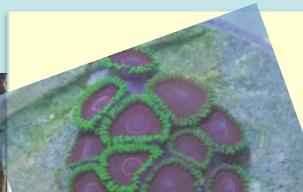
Molecule	ID	Structure	IC ₅₀ (μM)	Ki (μM)
1	6025233		2.6	1.1
2	5809365		4.5	3.9
3	5378650		25.1	20.8

M.Forino et al.

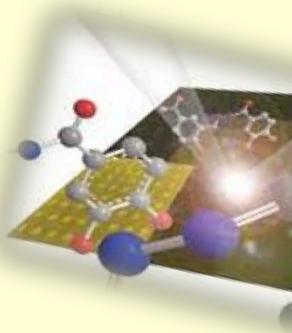
- Discovery of a novel class of Caspase Inhibitors, *J. Med. Chem.*, 2005
- Virtual docking approach to protein kinase B inhibition, *J. Med. Chem.*, 2005



**Laurea in CTF e
Dottorato di Ricerca in chimica delle sostanze naturali:
le biotossine marine**



**Drug discovery:
Samford-Burnham Institute
di San Diego-California:
malattie infettive e neurodegenerative**



**La ricerca scientifica a servizio
della medicina tradizionale**

Bacche di Goji

Forino et al. Food Chem 2016, 194, 1254-1259
Phytochemistry 2017, 144, 52-57



Le sorbe

Forino et al. Food Chem 2015, 178, 306-310

Foglie di noce

Forino et al. J. Functional Food 2016, 26, 731-738



Foglie di vite

Forino et al. Fitoterapia 2018, 125, 13-17

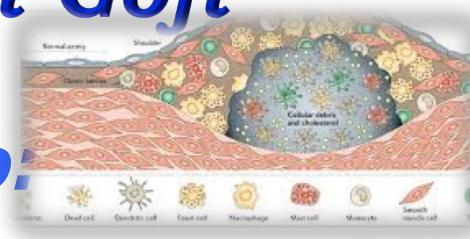


Il Luppolo

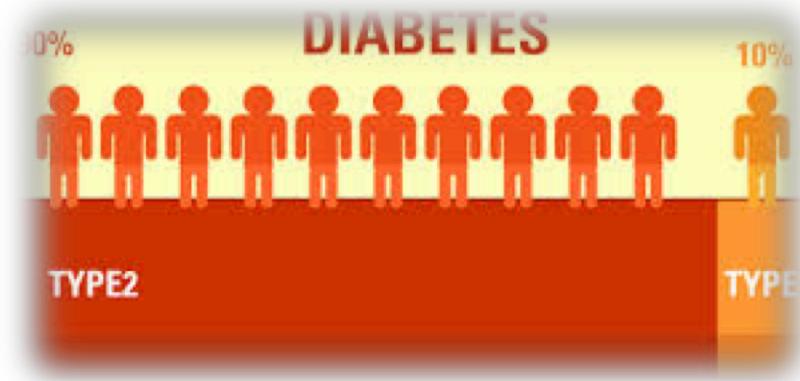
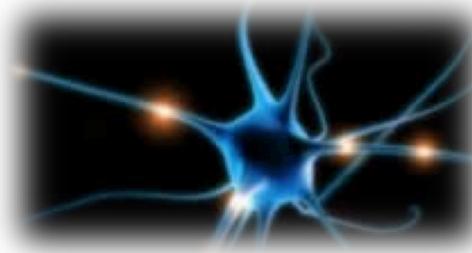
Forino et al. J. Nat. Prod. 2016, 79, 590-597

Proprietà biologiche delle bacche di Goji

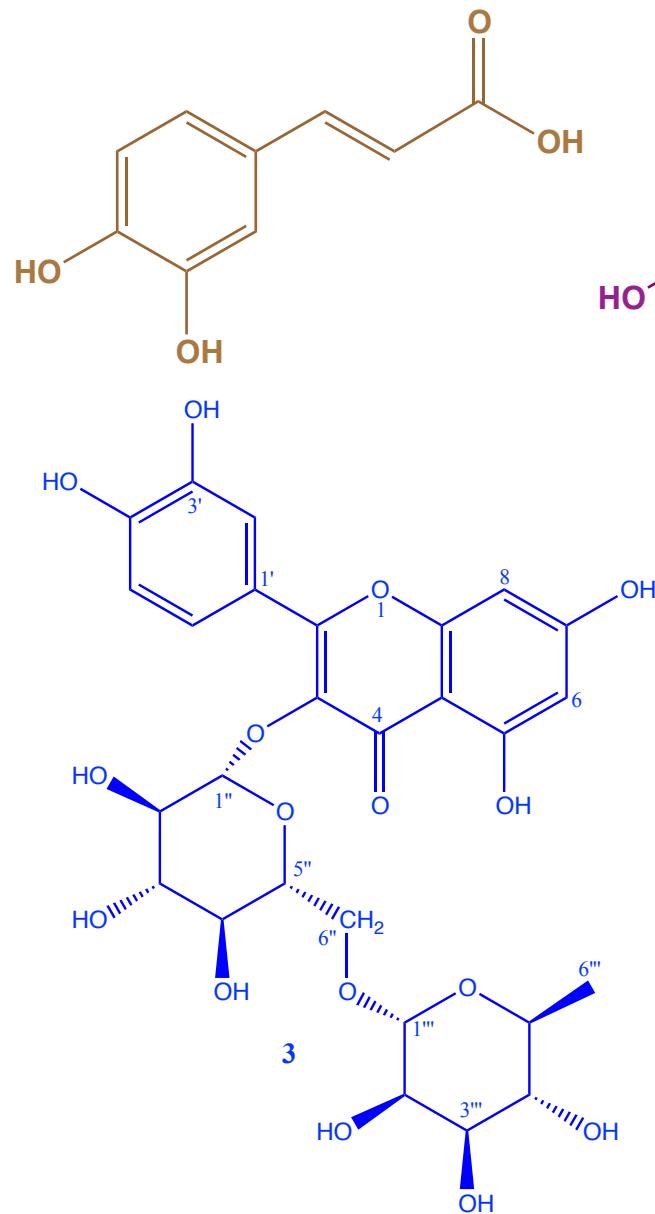
Malattie dell'invecchiamento:



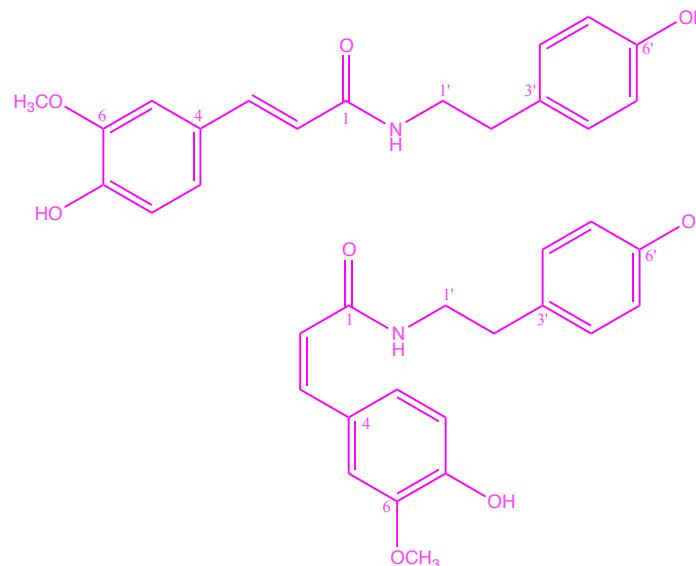
- *Malattie cardiovascolari*
- *neurodegenerazione*
- *diabete*



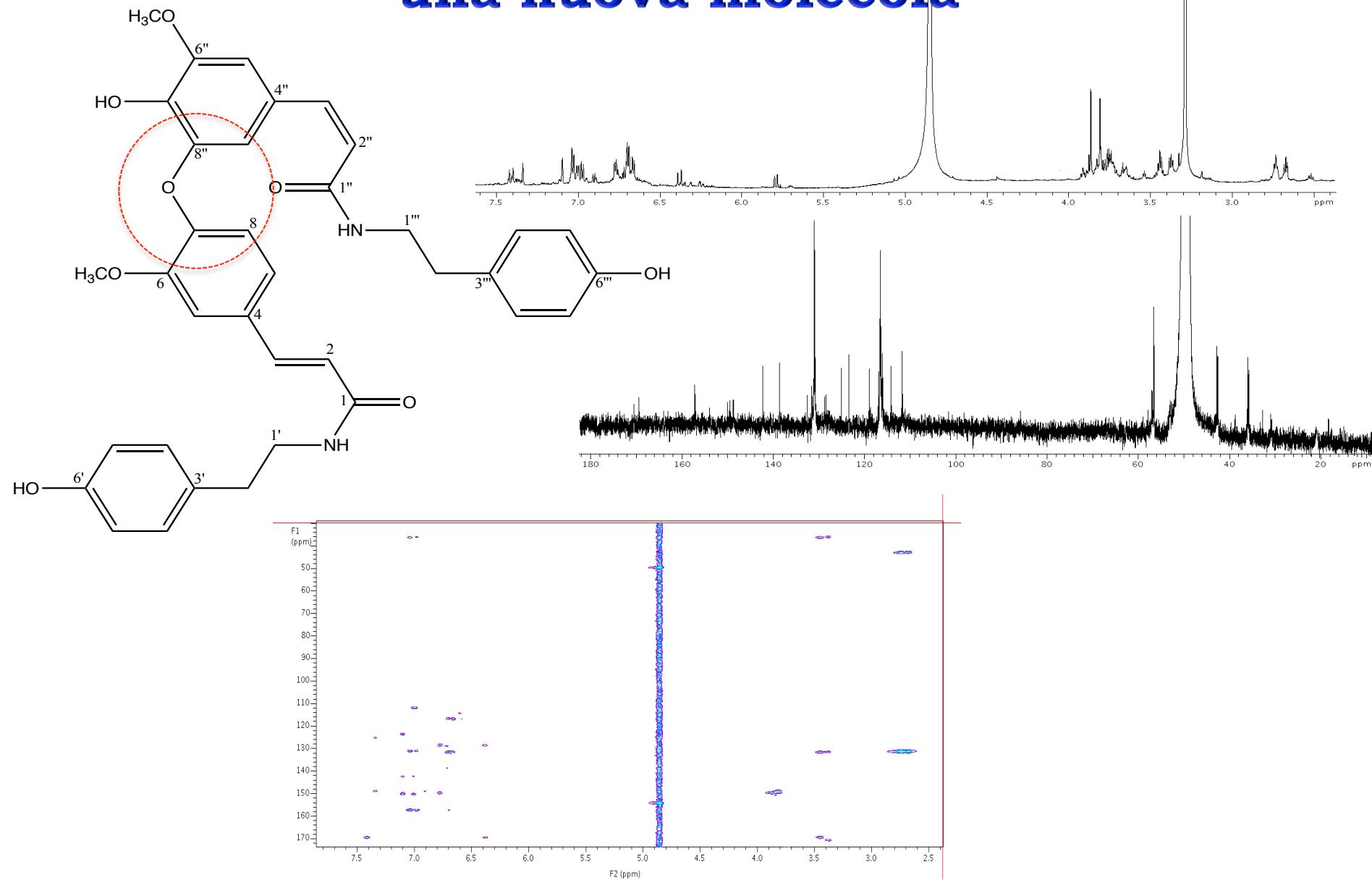
Molecole bioattive già note



Compound	mg
Caffeic acid	1,7
p-Coumaric acid	2,5
Rutin	4,1
Scopoletin	2,8
<i>N</i> - <i>trans</i> -feruloyl tyramine	1,3
<i>N</i> - <i>cis</i> -feruloyl tyramine	0,8

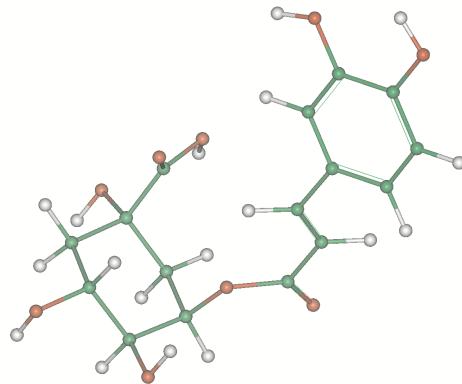
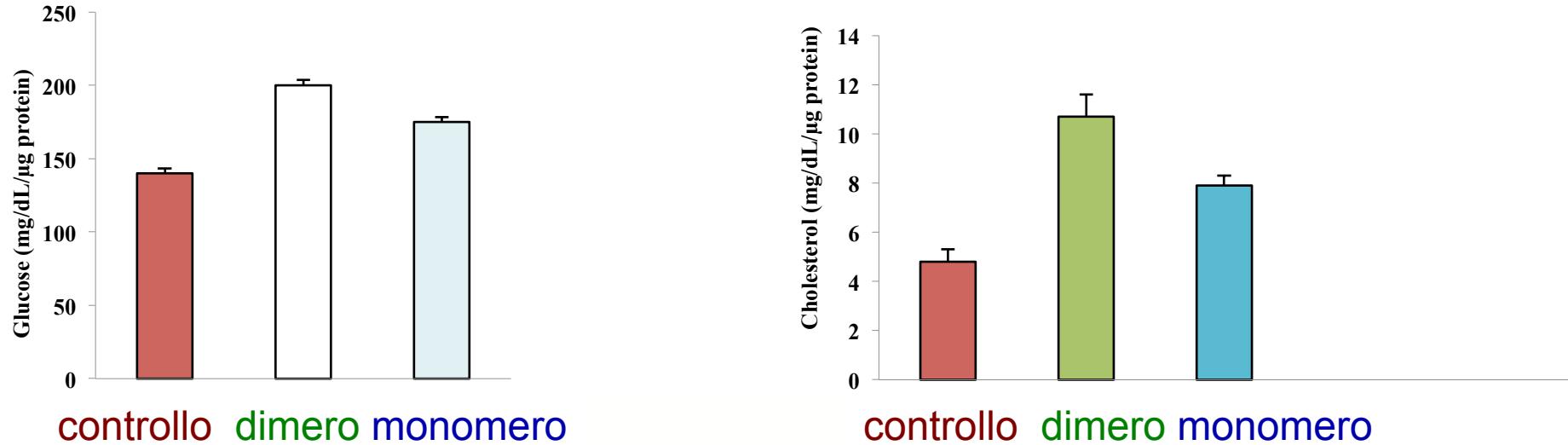


Il più abbondante composto antiossidante è una nuova molecola



Valutazione dell'attività biologica Su cellule HepG2

(human hepatocellular carcinoma)





LUPPOLO



L'interesse per il luppolo...

- *Produzione della birra*

- *Sedativo*

- *Antimicrobico*

- *Antitumorale*

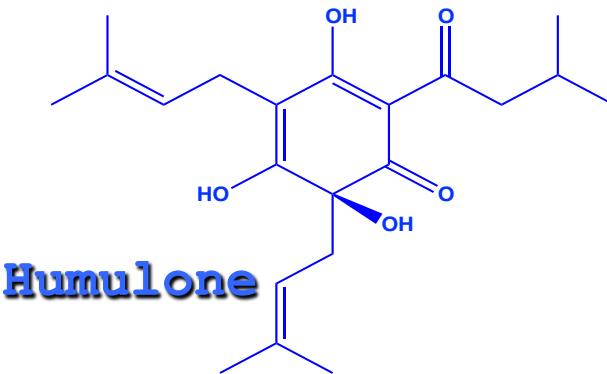


A photograph showing several green hop cones and some leafy branches. The cones are large, rounded, and textured. A single hop leaf with serrated edges is visible on the right side.

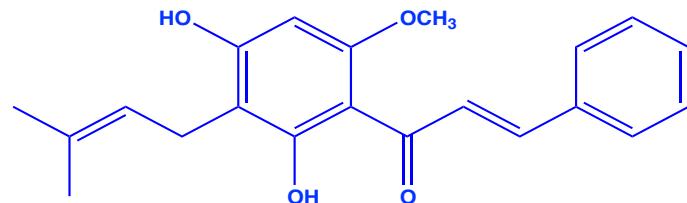
Conservante

*Conferire il tipico
Sapore amaro*

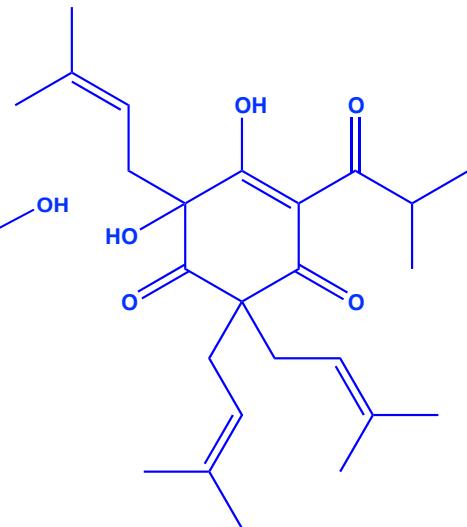
Principali metaboliti secondari del loppolo già noti



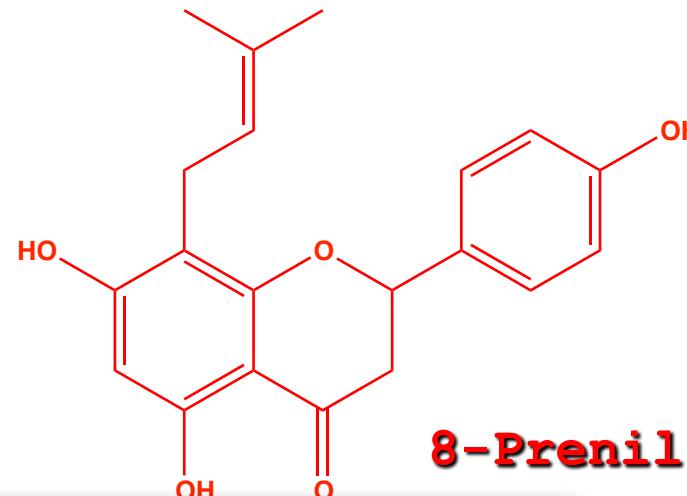
Humulone



Xanthumolo



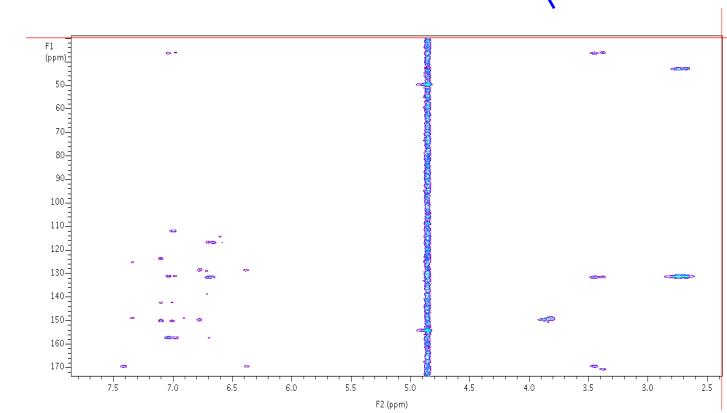
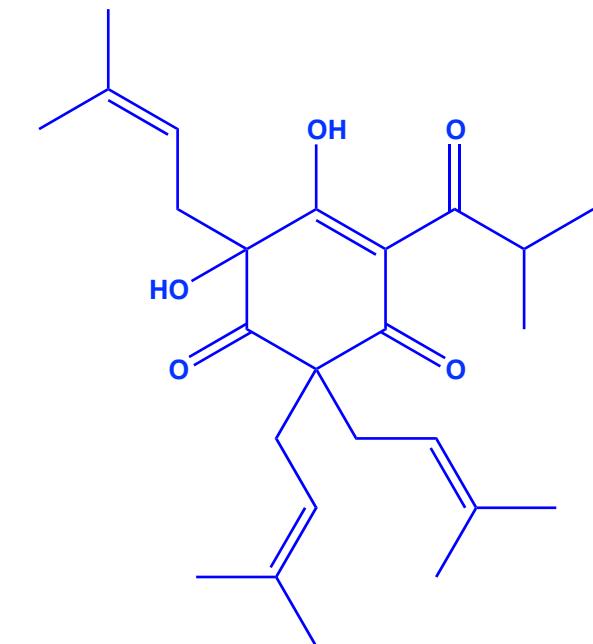
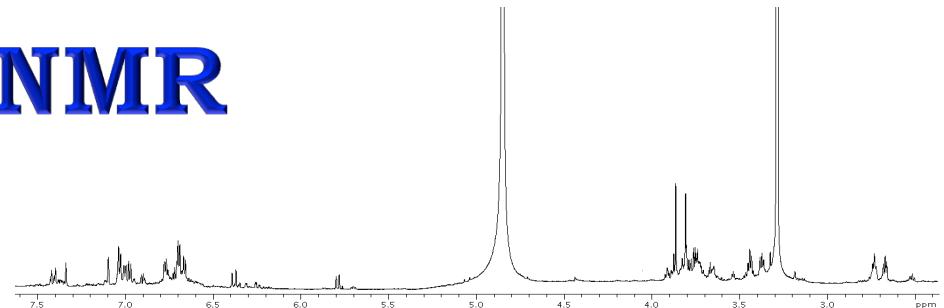
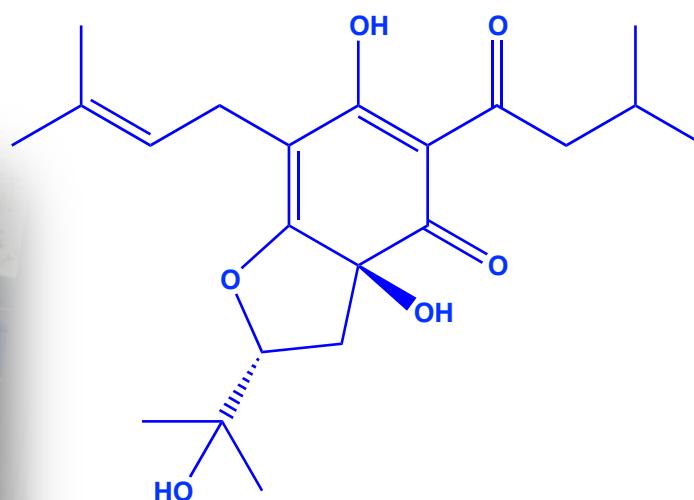
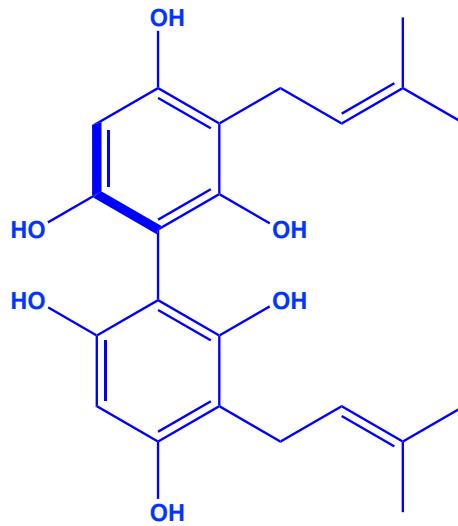
Lupulone



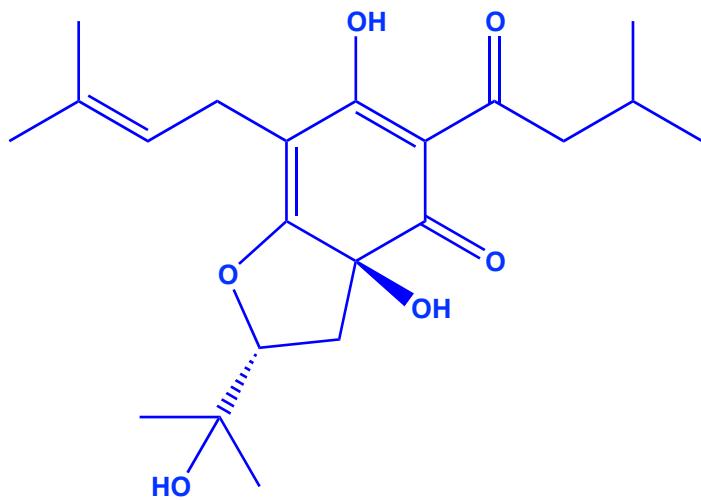
8-Prenil-naringenina

FITOESTROGENO

Studi NMR

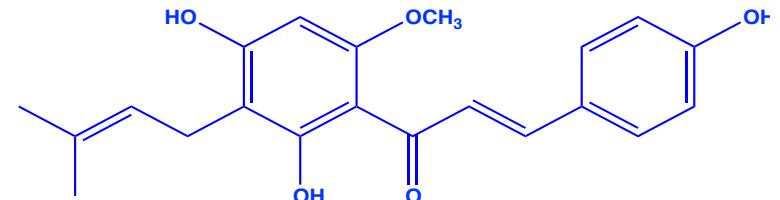
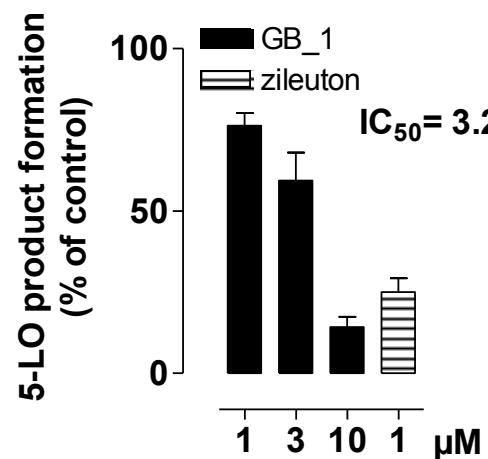


Valutazione dell'attività antiinfiammatoria



4-idrossicolupulone

IC₅₀ 5.9 mM



Xanthumolo

IC₅₀ 2.1 mM

Effect of the compound on isolated 5-LO stimulated with AA (20 μM)

Settembre 2017: Dipartimento di Agraria



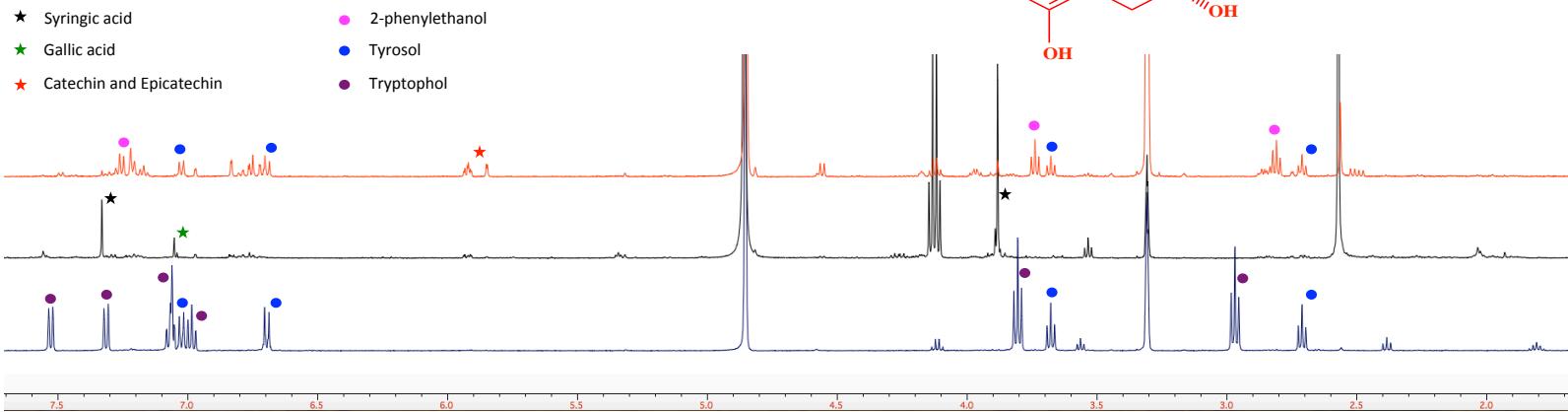
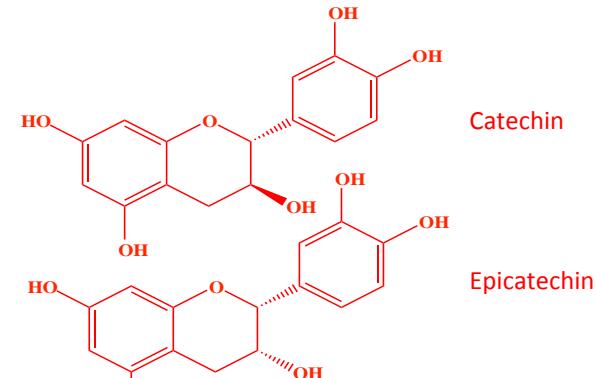
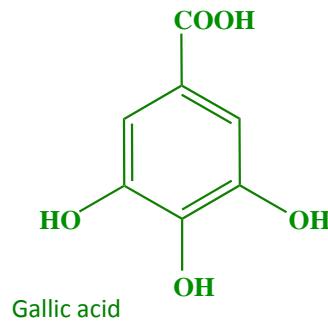
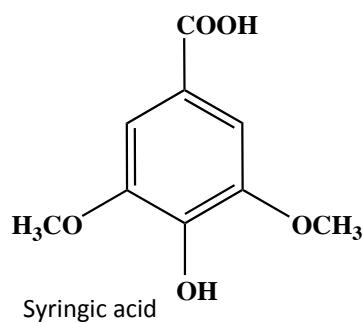
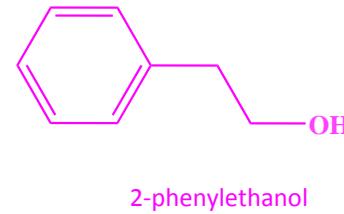
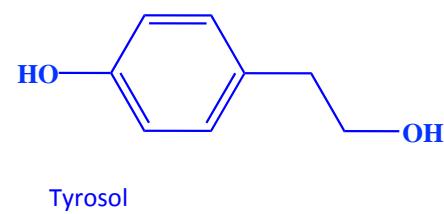
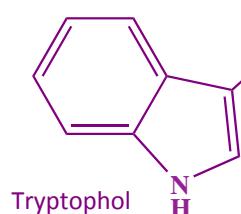
● **Conoscenza della chimica del vino**



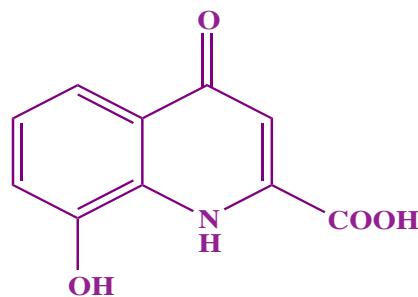
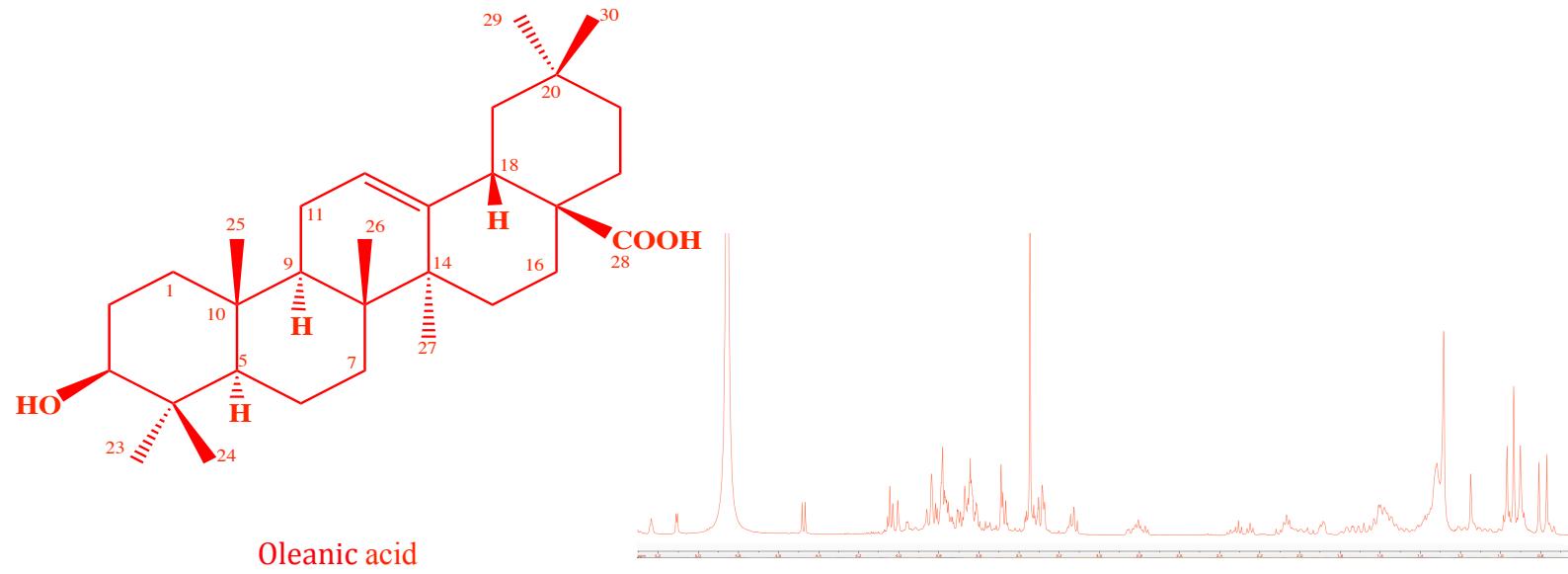


Analisi dei metaboliti Bioattivi delle uve e nel vino

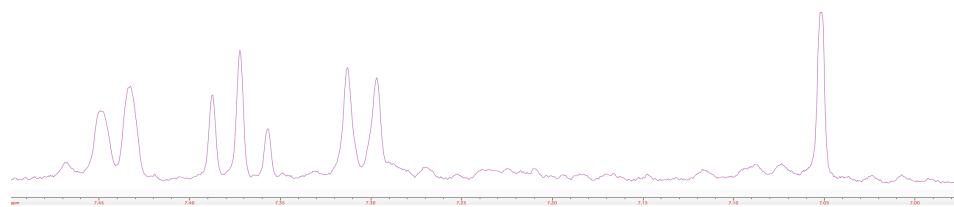
Principali metaboliti secondari Presenti nel vino



Nuovi metaboliti bioattivi Presenti nel vino

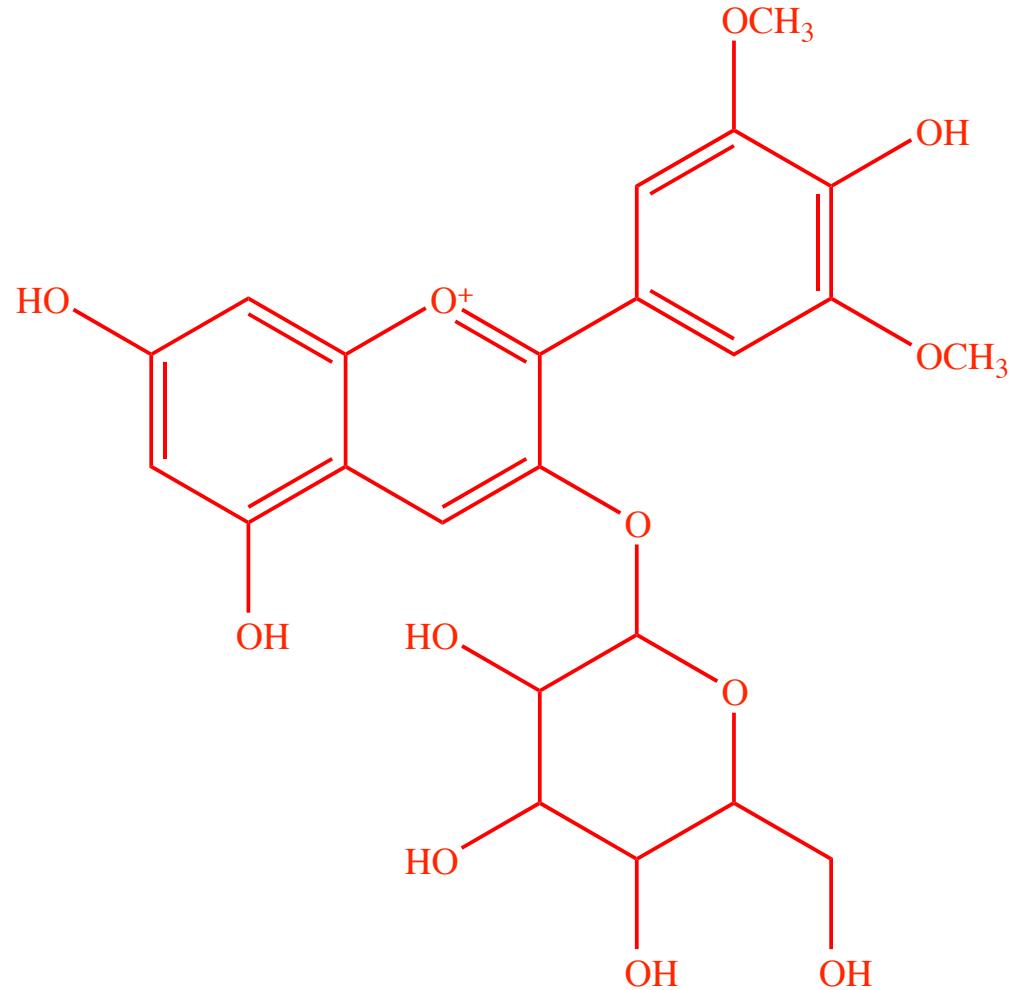


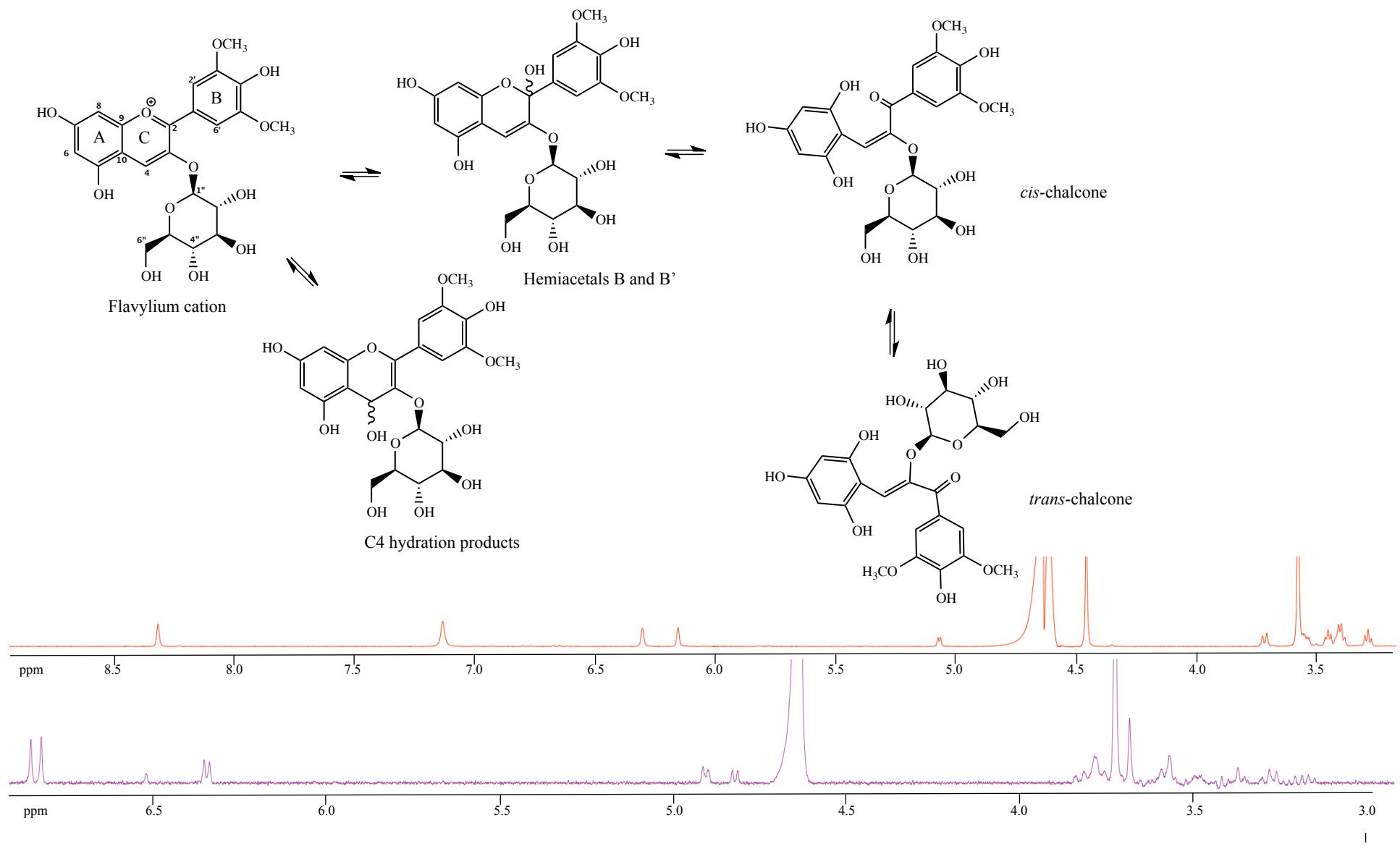
Xanthurenic acid



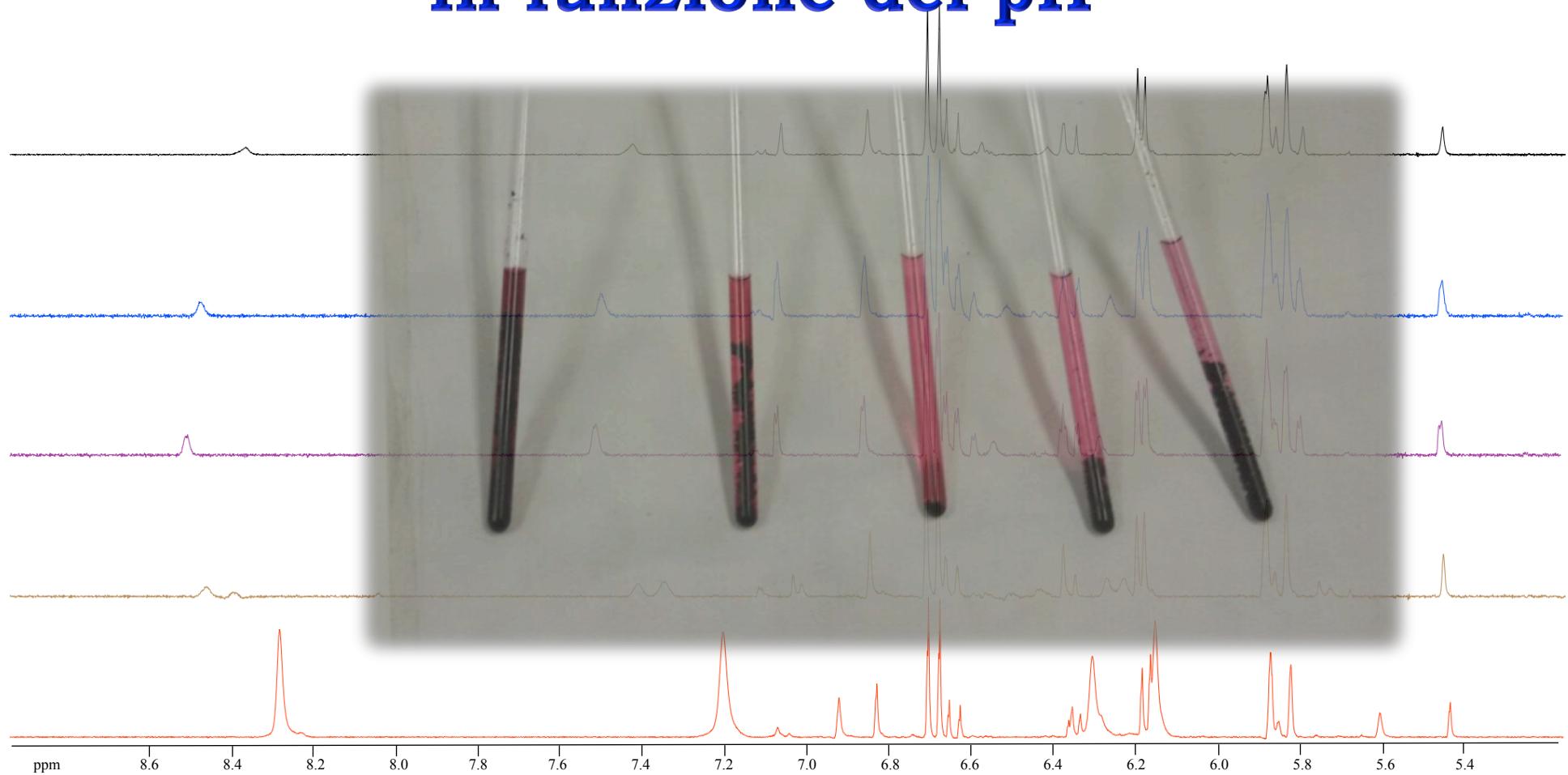
Forino et al. Food Chem. 2019, 278, 495-501

La malvidina: buona per la salute Buona per il vino





La solubilità della malvidina in funzione del pH



Forino et al. J.Agric. Food Chem. 2019;
doi: 10.1021/acs.jafc.8b05895



Alla ricerca dell'elisir di lunga vita
dell'uomo e ... del vino!

