

# ORIENTATESI

Cdl in Chimica e Scienze Chimiche

**Scegli i tuoi  
esperimenti con...**

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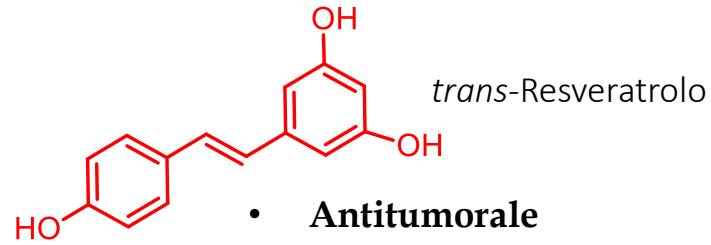
# Sintesi di prodotti naturali e **non** con «bioattività»:

**1. Anti-tumorali**  
**(dimeri del resveratrolo)**  
**(PRIN 2022 PNNR)**

**2. Anti-virali e anti-tumorali**  
**(inibitori dell'HIV proteasi,**  
**peptidomimetici)**  
**(PRIN 2022)**

# DIMERI DEL RESVERATROLO ED ATTIVITA' BIOLOGICA

## 1. Anti-tumorali (dimeri del resveratrolo)



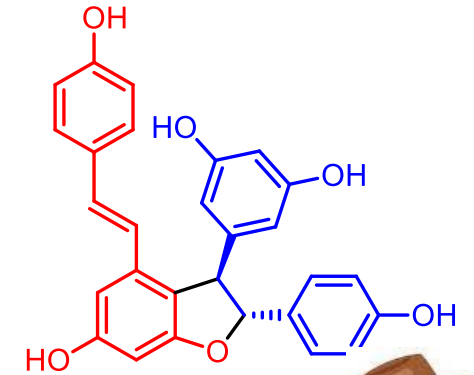
*v. Chem. Int. Ed.* **2012**, *51*, 6824–6826

- **Antitumorale**
- **Antiossidante**
- **Antiaggregante**

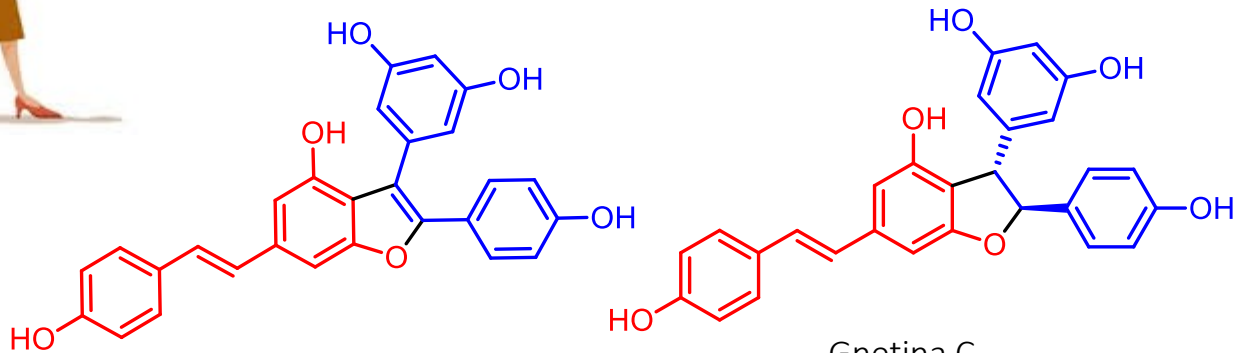
**Trova la differenza**

*trans*- $\epsilon$ -Viniferina

- **Antitumorale**
- **Antileucemico**
- **Antiossidante**



*Biochimie*, **2008**, *90*, (11–12), 1674–1684



Anigopreissina A

Gnetina C

- **Antiaggregante**
- **Antiossidante**
- **Inibitore dell'angiogenesi**

*Bioorg. Med. Chem. Lett.* **2010**, *20*, 3441

*Amurensina H*

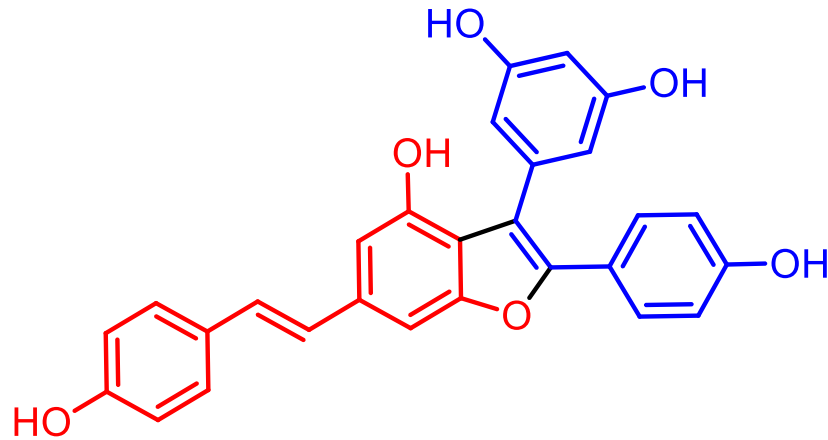
- **Antiinfiammatorio**
- **Anti asmatico**
- **Inibitore del fattore TNF - $\alpha$**

*Acta Pharmacologica Sinica* **2006**, *27*, 735

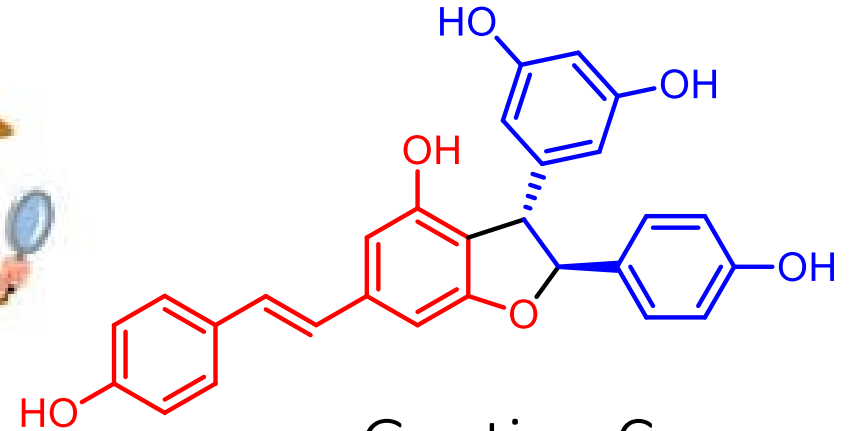


# DIMERI DEL RESVERATROLO ED ATTIVITA' BIOLOGICA

## 1. Anti-tumorali (dimeri del resveratrolo)



Anigopreissina A



Gnetina C

- **Antiaggregante**
- **Antiossidante**
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*Bioorg. Med. Chem. Lett.* 2010, 20, 3441



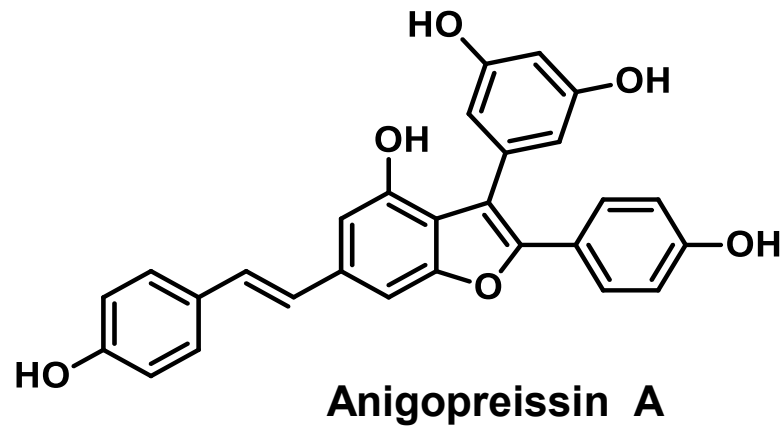
250 g di radici 2,4 mg



50 g di rizomi 100 µg



77 g di bulbi 12.2 mg



- ✿ It prevents and/or fights against the wrinkles of the skin
- ✿ It has low antimicrobial activity against *S. aureus* e *S. pyogenes*.
- ✿ It inhibits HIV-1 reverse transcriptase

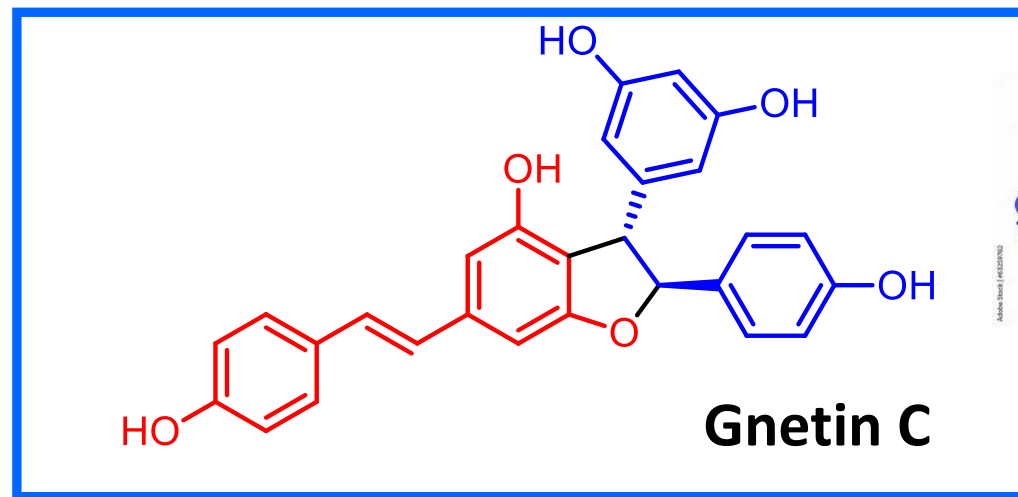
B. Schneider *et al.* *Phytochemistry* **1996**, 471.

S. Urban *et al.* *J. Nat. Prod.* **2015**, 78, 1600.

M. Eloffsson *et al.* *Advanced Synthesis & Catalysis*, **2016**, 358(24), 4085.



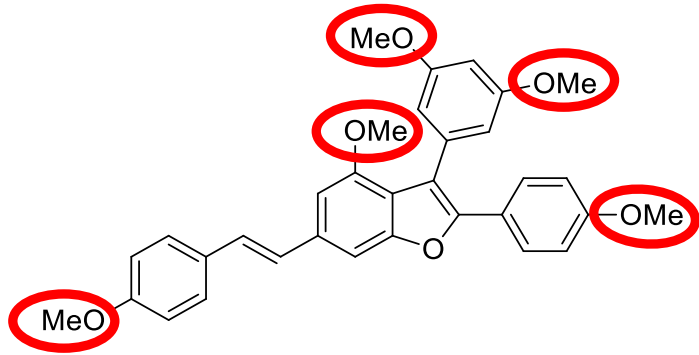
Dai semi di Melinjo  
*Gnetum gnemon* (Gnetaceae)



**No total synthesis !!**

- Inibitore della attività della tirosinasi e quindi della biosintesi della melanina; agente preventivo contro iperpigmentazione, agente
- Inibitore dell'angiogenesi (prevenzione e trattamento del cancro);
- Moderata attività antimicrobica;
- Inibitore aggregazione piastrinica
- Inibitore delle placche b-amiloidi
- Fase preclinica nel trattamento cancro prostatico

# Cosa sappiamo dell'Anigopreissina A permetilata (PAA) ?

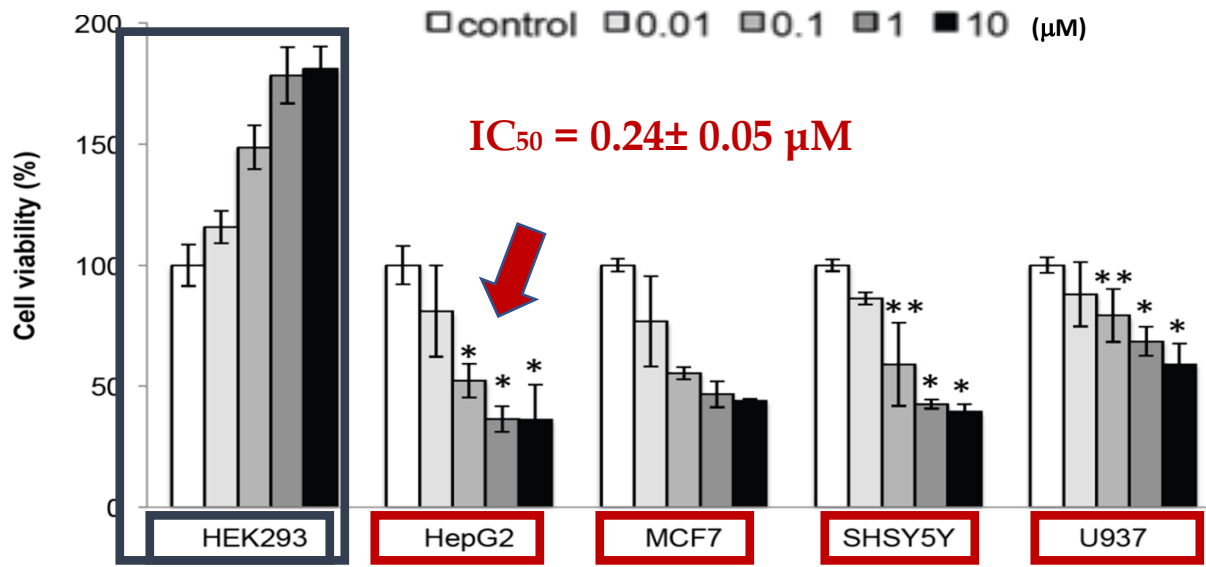


Metilazione dei gruppi ossidrilici

↑ Permeabilità membrana cellulare

↑ Biodisponibilità

↑ Stabilità metabolica

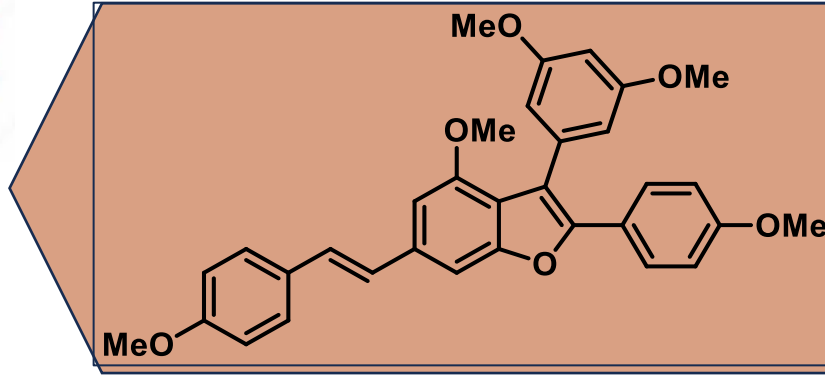


8 passaggi

Resa Totale 20%

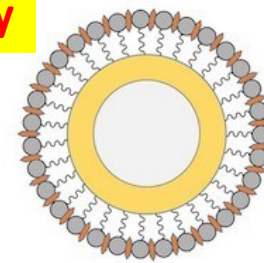
# Studio di Drug Delivery della PAA

2



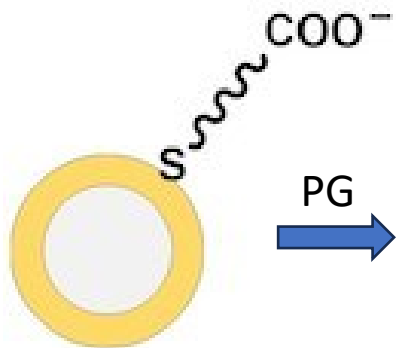
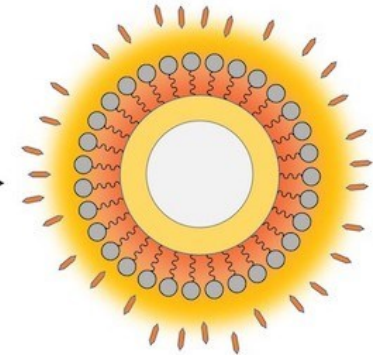
Drug Delivery

STRATEGY B



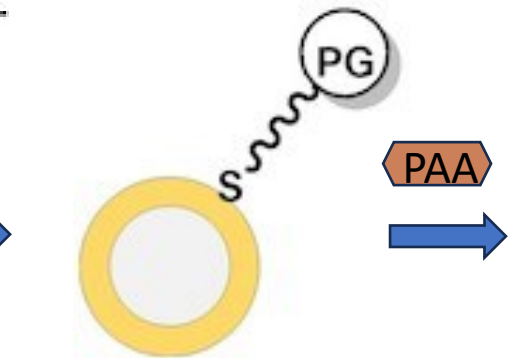
Au-Nanoshell

NIR



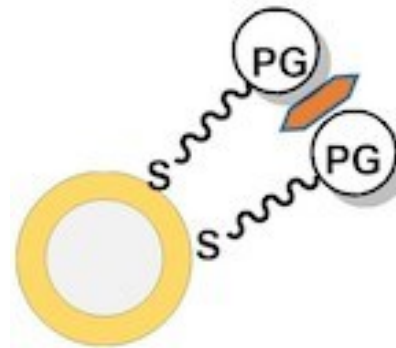
Au-Nanoshell

PG



PG= Photolabile Group

PAA



Interazioni  $\pi - \pi$

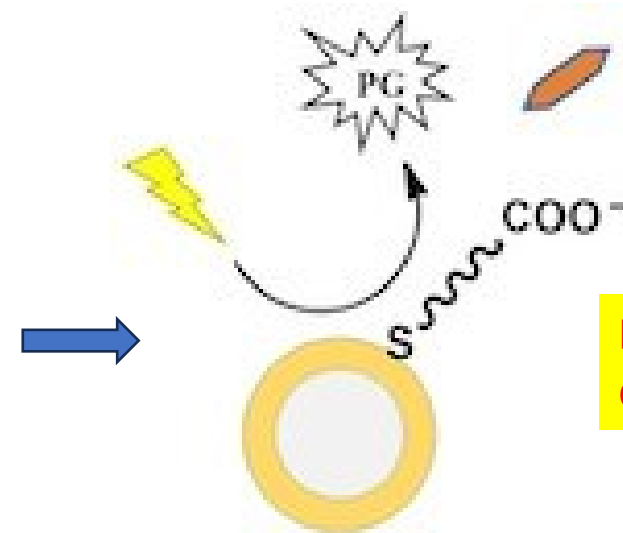


Foto-rilascio della molecola

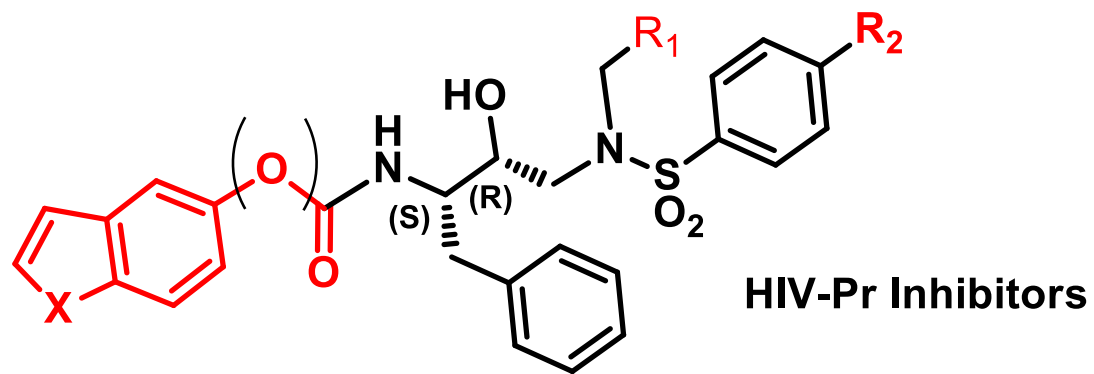
“PRIN PNRR 2022” funded by the European Union- *Next Generation EU* (Gold Nanostructures for Benzofuryl-based Anti-tumoral Photoinduced Drug Delivery Systems)



3

# Quali altri bersagli ci attendono?

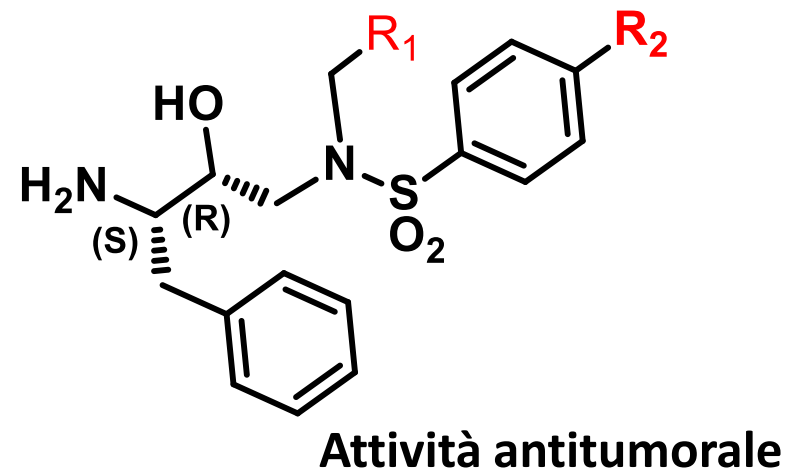
## Nuovi potenziali inibitori dell'HIV proteasi.....



X = O, NH, S

R<sub>1</sub> = iPr, Ph

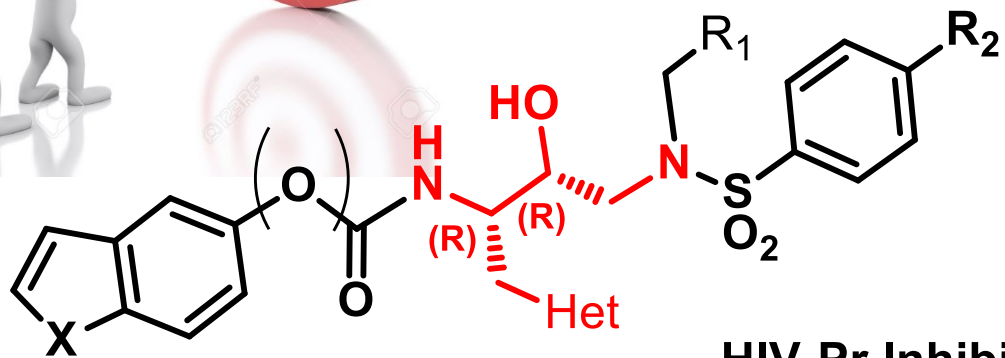
R<sub>2</sub> = 4-OMe, 4-NO<sub>2</sub>, 3,4-diMeO



IC<sub>50</sub> = ≤0.6 nM (X=O,NH, S)



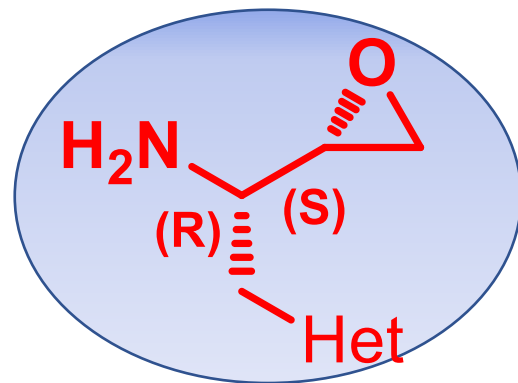
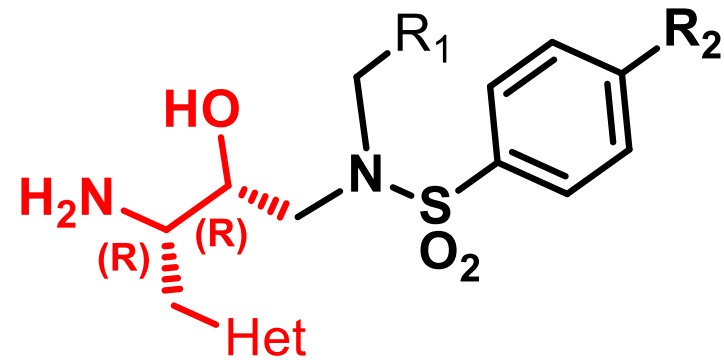
3



X = O, NH, S

R<sub>1</sub> = iPr, Ph

R<sub>2</sub> = 4-OMe, 4-NO<sub>2</sub>, 3,4-diMeO



# How are drugs discovered ?

Drug Discovery and Development and Delivery and so on...



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**Via aspettiamo numerosi!!!**