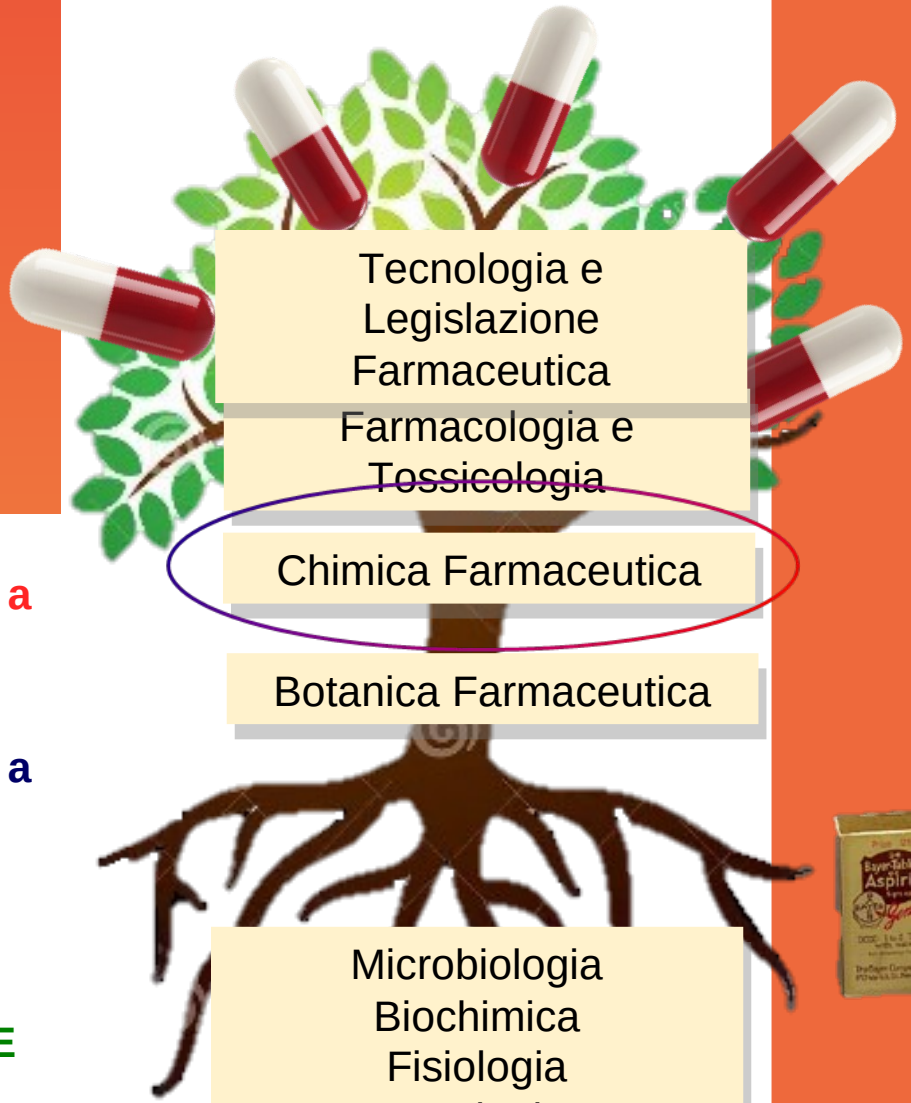
Università degli Studi
di Torino

DIPARTIMENTO DI
SCIENZA E
TECNOLOGIA DEL
FARMACO

Corso di Laurea Magistrale a ciclo unico in FARMACIA

Corso di Laurea Magistrale a ciclo unico in CHIMICA E TECNOLOGIA FARMACEUTICHE

Corso di Laurea in TECNICHE ERBORISTICHE

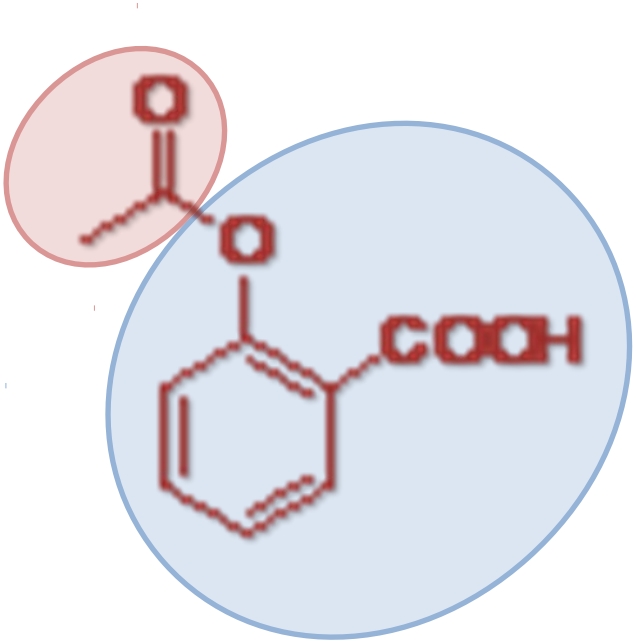






Aspirina: semplice ed efficace

Gruppo acetile



Acido salicilico

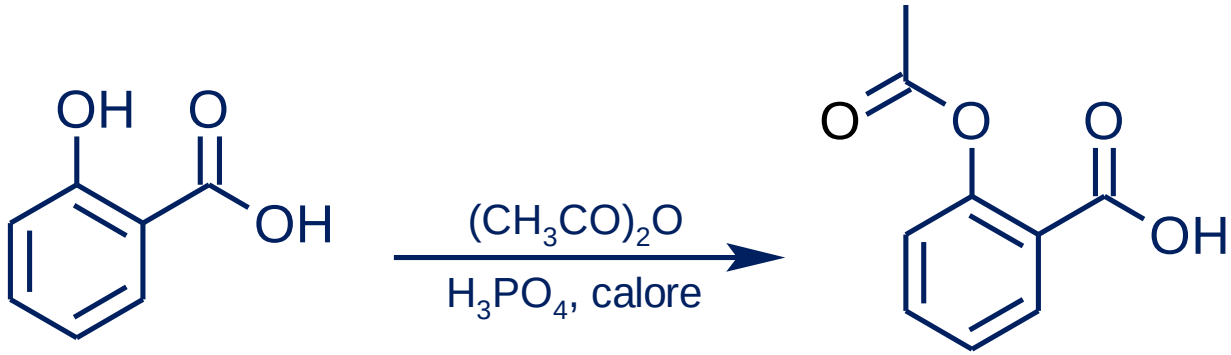
Acido acetilsalicilico

Sintesi di Kolbe dell'acido salicilico



- 1860
  - H. Kolbe e E. Lautemann producono in grandi quantità acido salicilico partendo da fenolo
- 1874
  - T. J. MacLagan utilizza la salicina, e non i decotti di corteccia, per la "cura" di un caso di reumatismo articolare acuto
  - **Il prezzo da pagare è un forte dolore di stomaco**

Sintesi dell'acido acetilsalicilico



- 1853
  - C. F. Gerhart sintetizza l'acido acetilsalicilico ma in modo non efficiente
  - **Questo composto riduce gli effetti collaterali**
- 1897
  - F. Hoffman, chimico della Bayer, mette a punto una via **semplice** ed **economica** per preparare l'acido acetilsalicilico

La storia dell'aspirina

- 1 febbraio 1899
  - La Bayer mette in commercio l'*aspirina*

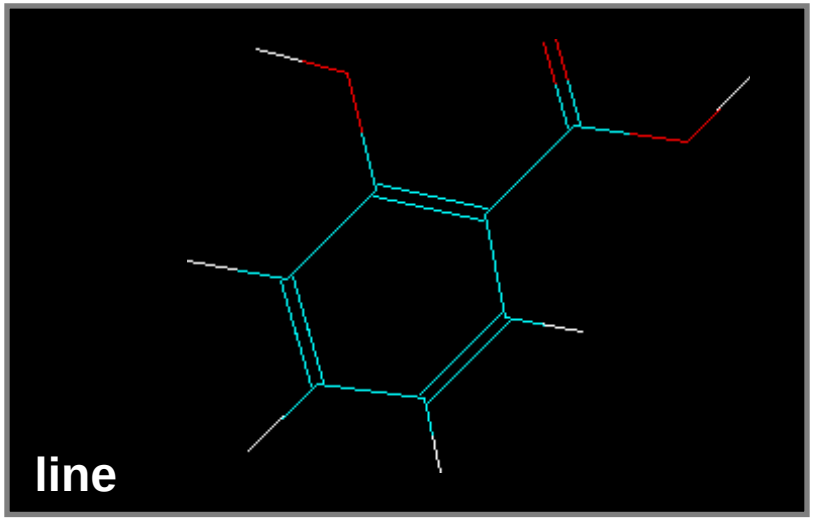


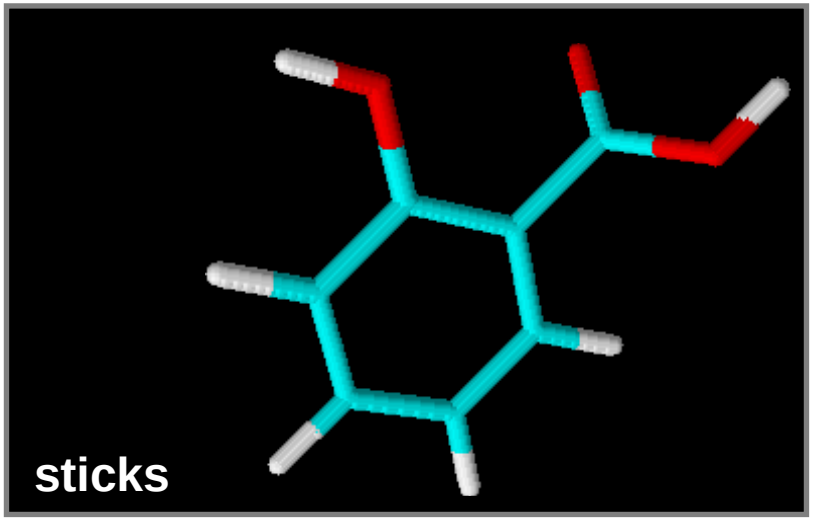
A *(cetile)*

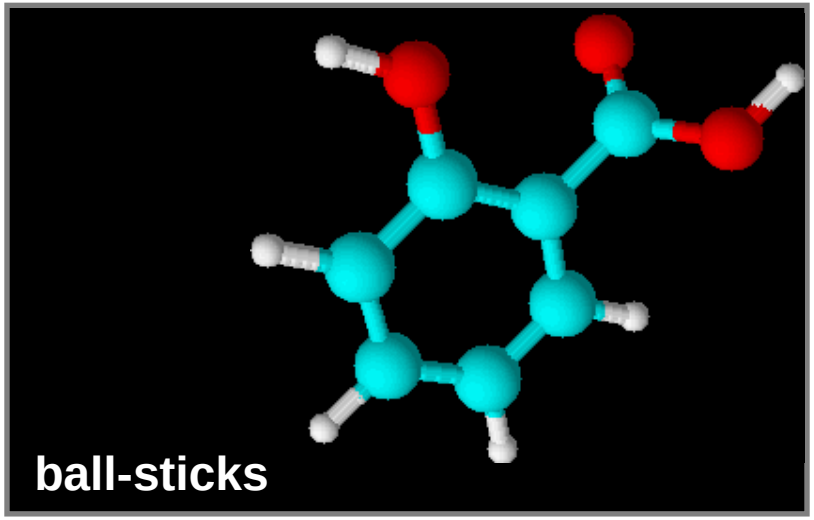
spir *(saure, da Spirea ulmaria)*

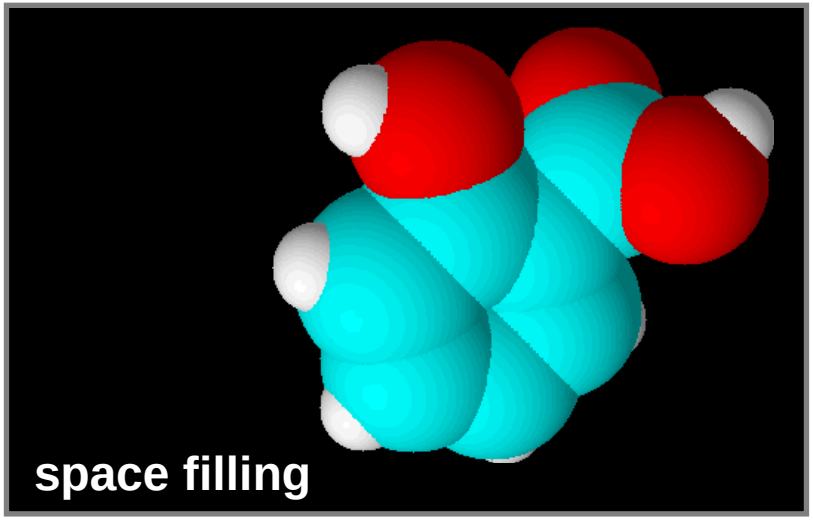
in *(suffisso per le sostanze scoperte o isolate in natura)*

La cristallografia: *i raggi X*



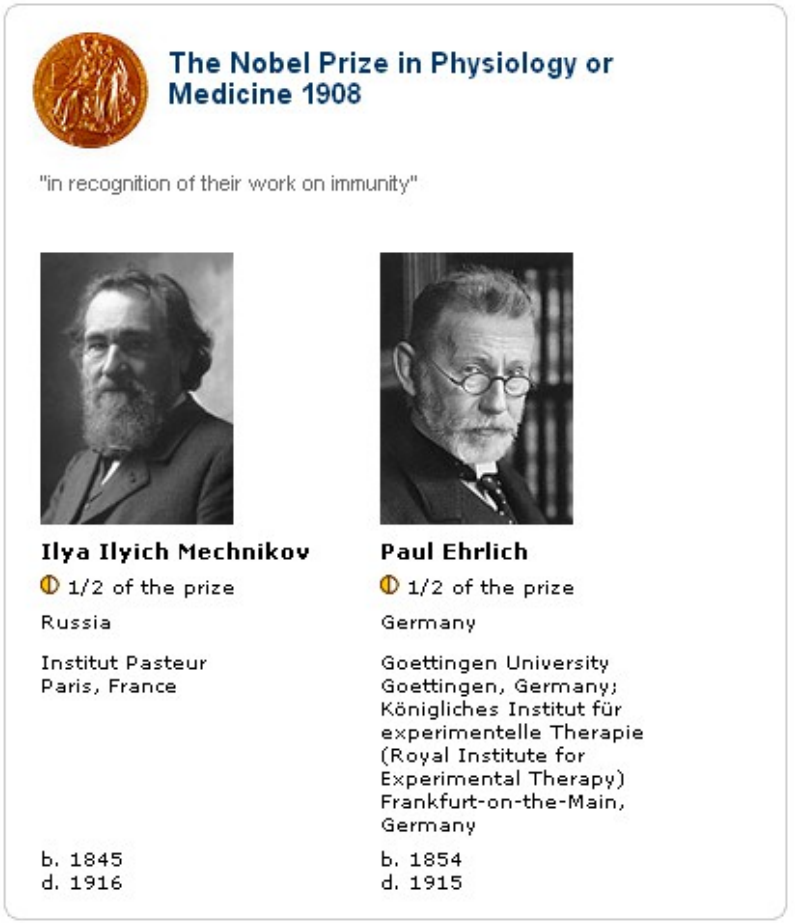






La storia dell'aspirina: *un po' oltre…*

- Le molecole non agiscono se non si legano
- "Il mio programma consiste in questo: ricavare da sostanze dotate di una certa efficacia degli omologhi e dei derivati; saggiare l'azione di ciascuno e, in base ai risultati ottenuti, cercare di arrivare a medicamenti sempre migliori"



The Nobel Prize in Physiology or Medicine 1908

"in recognition of their work on immunity"

Ilya Ilyich Mechnikov
1/2 of the prize
Russia
Institut Pasteur
Paris, France
b. 1845
d. 1916

Paul Ehrlich
1/2 of the prize
Germany
Goettingen University
Goettingen, Germany;
Königliches Institut für experimentelle Therapie (Royal Institute for Experimental Therapy)
Frankfurt-on-the-Main, Germany
b. 1854
d. 1915

http://www.nobel.se/medicine/laureates/1908/index.html

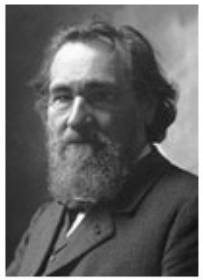
La storia dell'aspirina: *un po' oltre…*

- Per farmaco si intende ogni sostanza capace di provocare in un organismo modificazioni funzionali mediante un'azione chimica o fisica

R. Paoletti, S. Nicosia, F. Clementi, G. Fumagalli "Farmacologia generale e molecolare" UTET 1999, pag. 3

The Nobel Prize in Physiology or Medicine 1908

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The Nobel Prize in Physiology or Medicine 1982

Sune K. Bergström, Bengt I. Samuelsson, John R. Vane

- **The Nobel Prize in Physiology or Medicine 1982**
- Nobel Prize Award Ceremony
- Sune K. Bergström
- Bengt I. Samuelsson
- John R. Vane



Sune K. Bergström



Bengt I. Samuelsson



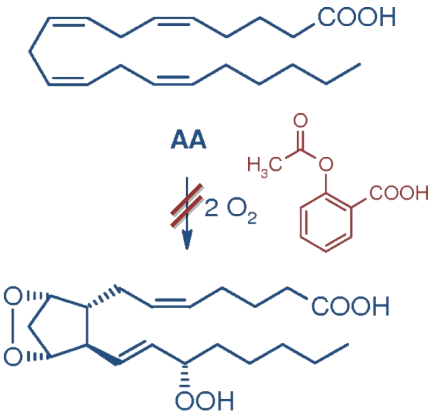
John R. Vane

The Nobel Prize in Physiology or Medicine 1982 was awarded jointly to Sune K. Bergström, Bengt I. Samuelsson and John R. Vane *"for their discoveries concerning prostaglandins and related biologically active substances"*.

Photos: Copyright © The Nobel Foundation

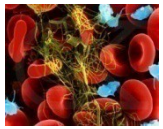


Gastroerosione come effetto collaterale principale

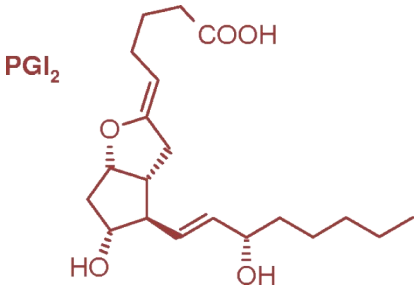


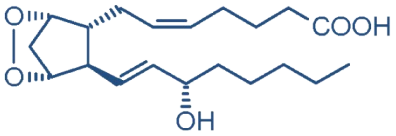
PGG_2

Aspirina:
un inibitore covalente, irreversibile dell'enzima cicloossigenasi

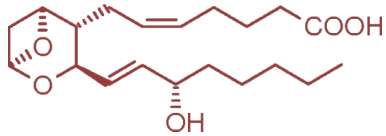


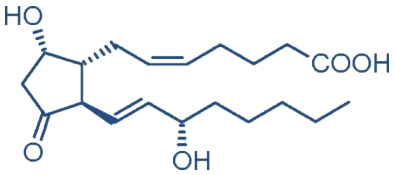
Azione antiaggregante



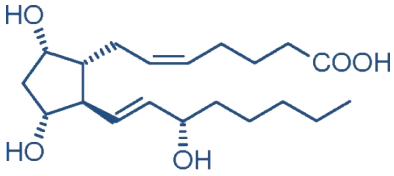


PGH_2

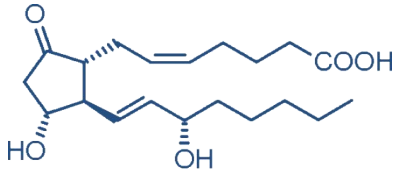




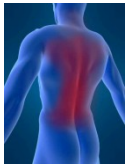
PGD_2



$PGF_{2\alpha}$



PGE_2



Analgesica



Antipiretica

Ma insomma, come funziona questa Aspirina?

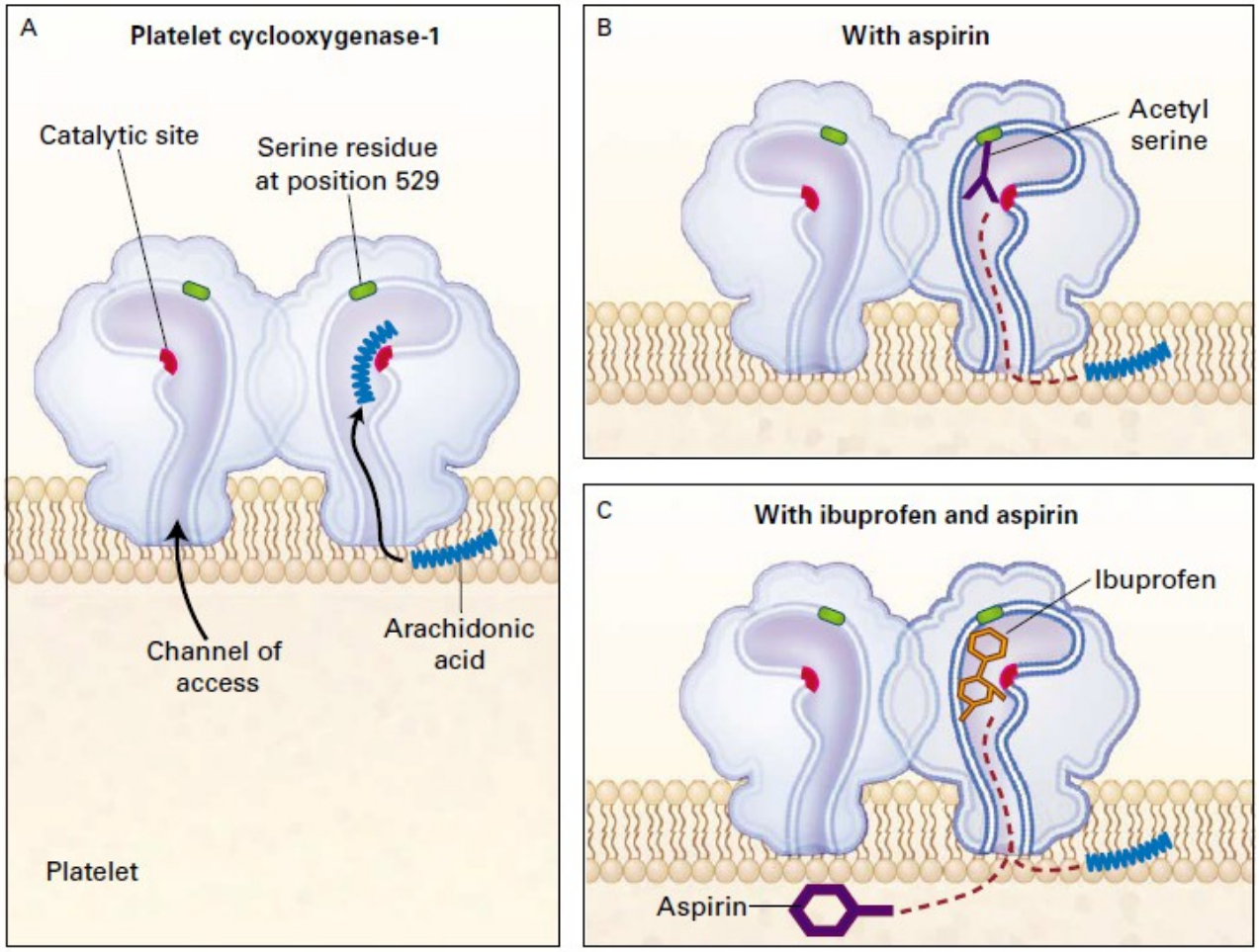
Mechanism of action of aspirin

From Wikipedia, the free encyclopedia

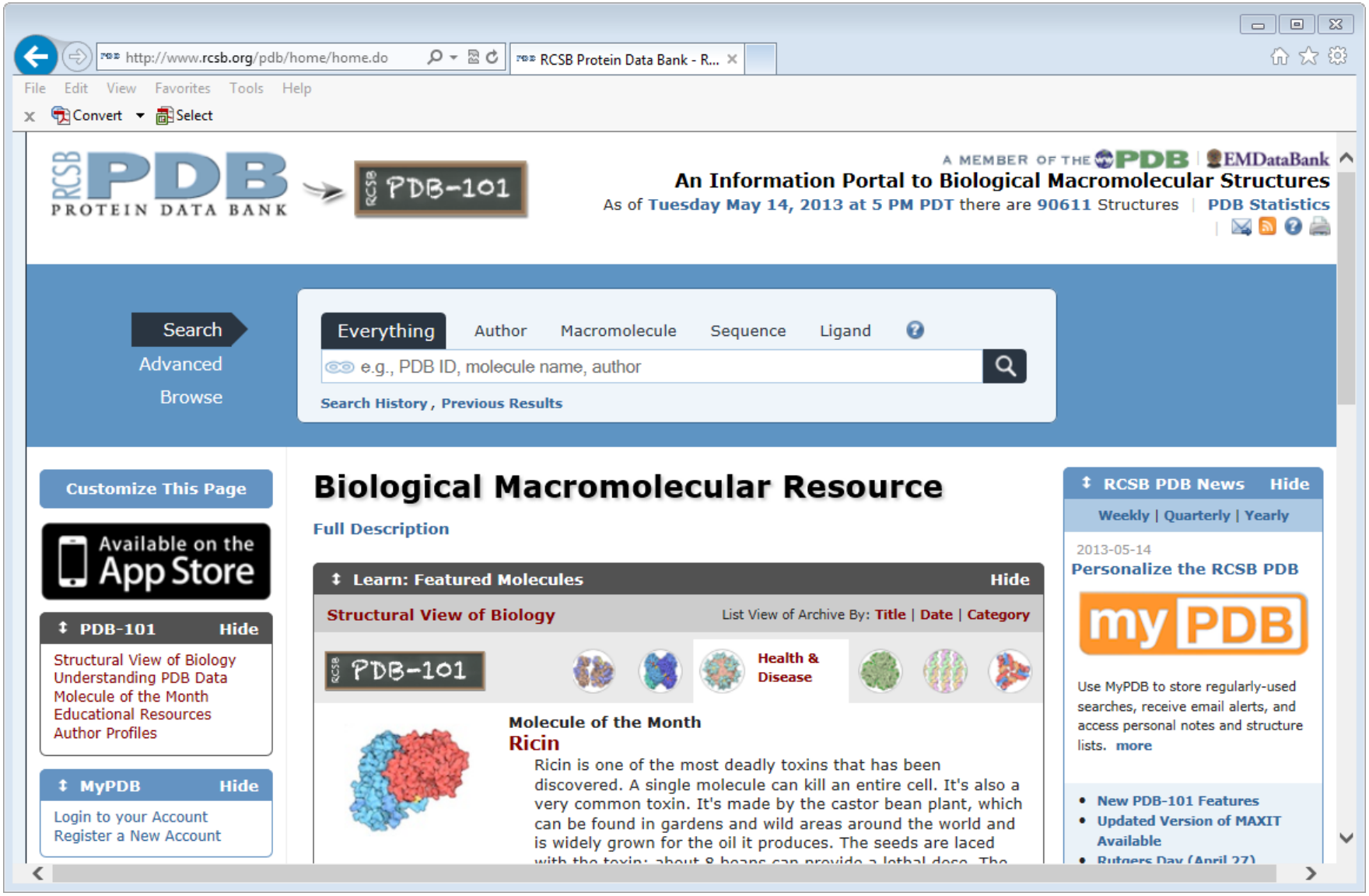
Aspirin causes several different effects in the body, mainly the reduction of inflammation, analgesia (relief of pain), the prevention of clotting, and the reduction of fever. Much of this is believed to be due to decreased production of prostaglandins and thromboxanes. Aspirin's ability to suppress the production of prostaglandins and thromboxanes is due to its irreversible inactivation of the cyclooxygenase (COX) enzyme. Cyclooxygenase is required for prostaglandin and thromboxane synthesis. Aspirin acts as an acetylating agent where an acetyl group is covalently attached to a serine residue in the active site of the COX enzyme.

C’era proprio bisogno di venire all’Università, c’è scritto pure su Wikipedia…

Effetto dell'aspirina e dell'aspirina più l'ibuprofene sulla cicloossigenasi-1 delle piastrine

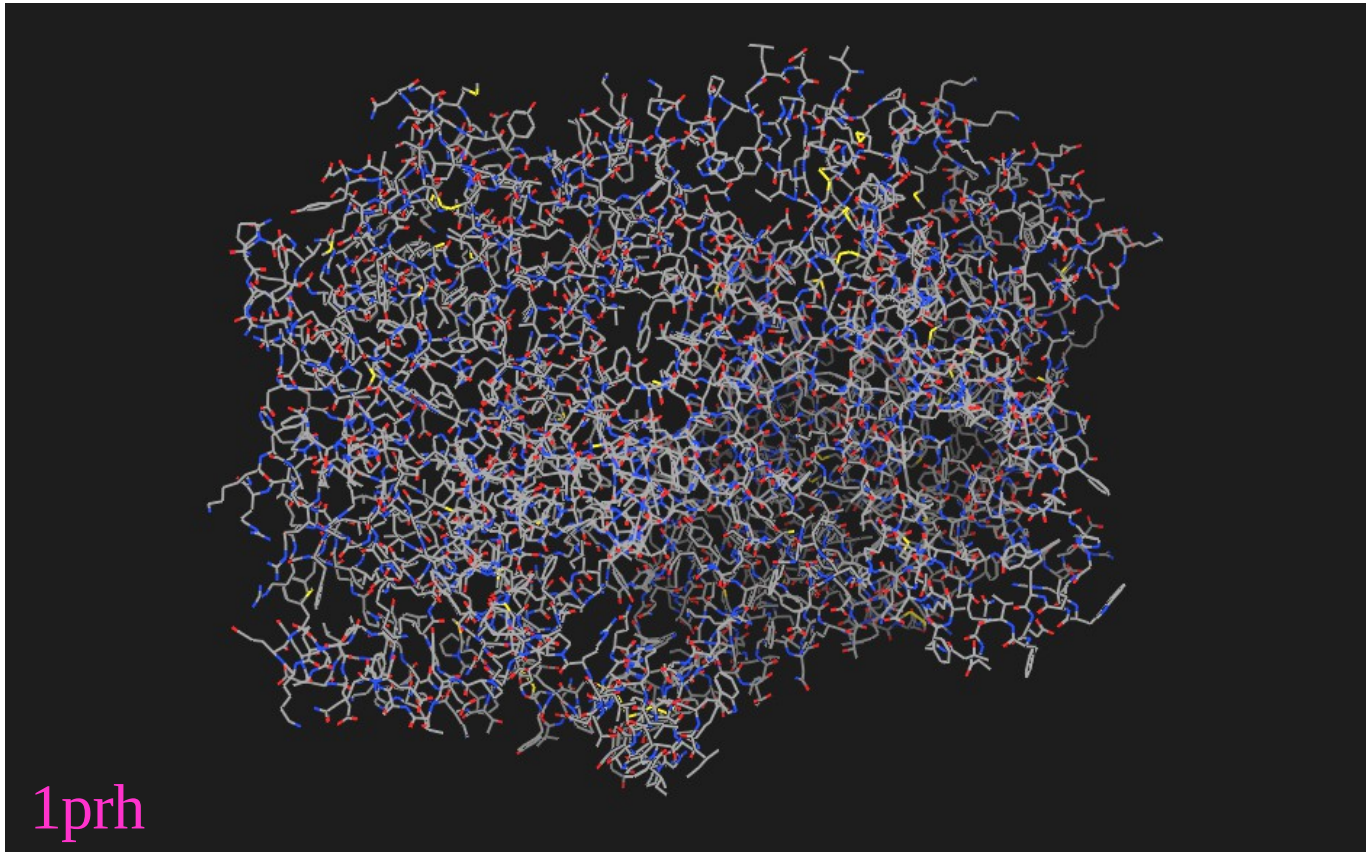


N Engl J Med, Vol. 345, No. 25 · December 20, 2001 · www.nejm.org


http://www.rcsb.org/pdb/home/home.do
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RCSB PDB-101
Health & Disease
Molecule of the Month
Ricin
Ricin is one of the most deadly toxins that has been discovered. A single molecule can kill an entire cell. It's also a very common toxin. It's made by the castor bean plant, which can be found in gardens and wild areas around the world and is widely grown for the oil it produces. The seeds are laced
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New PDB-101 Features
Updated Version of MAXIT Available
Rutgers Day (April 27)

Raggi X e biochimica: n*uove frontiere*

- Se posso vedere una piccola molecola perché non provare con quelle grandi?



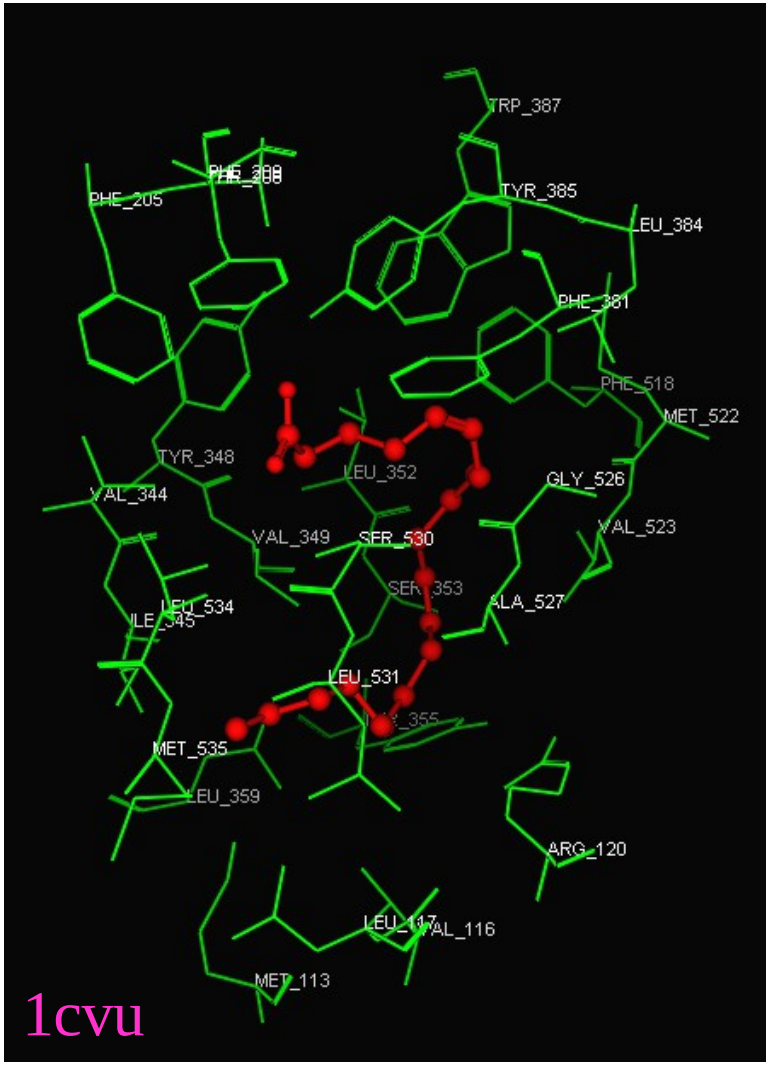
Raggi X e biochimica: *l'enzima cicloossigenasi*

- Questo è finalmente l'enzima cicloossigenasi responsabile della trasformazione dell'acido arachidonico

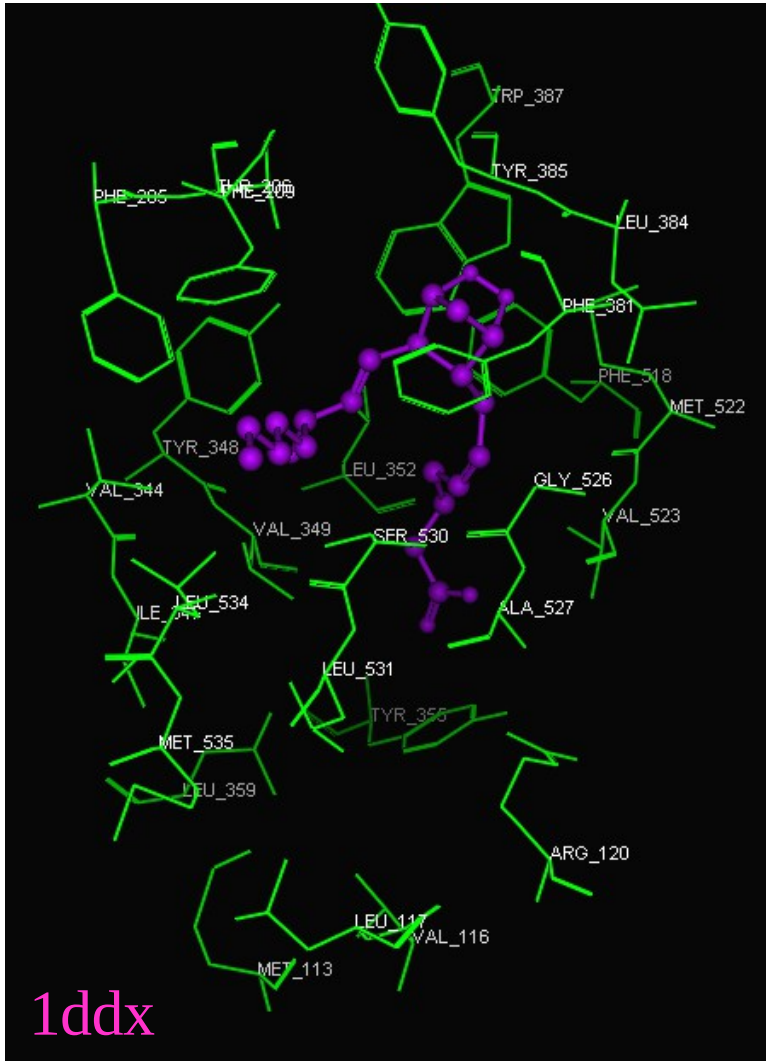


…. gli inibitori delle cicloossigenasi

Ac. arachidonico

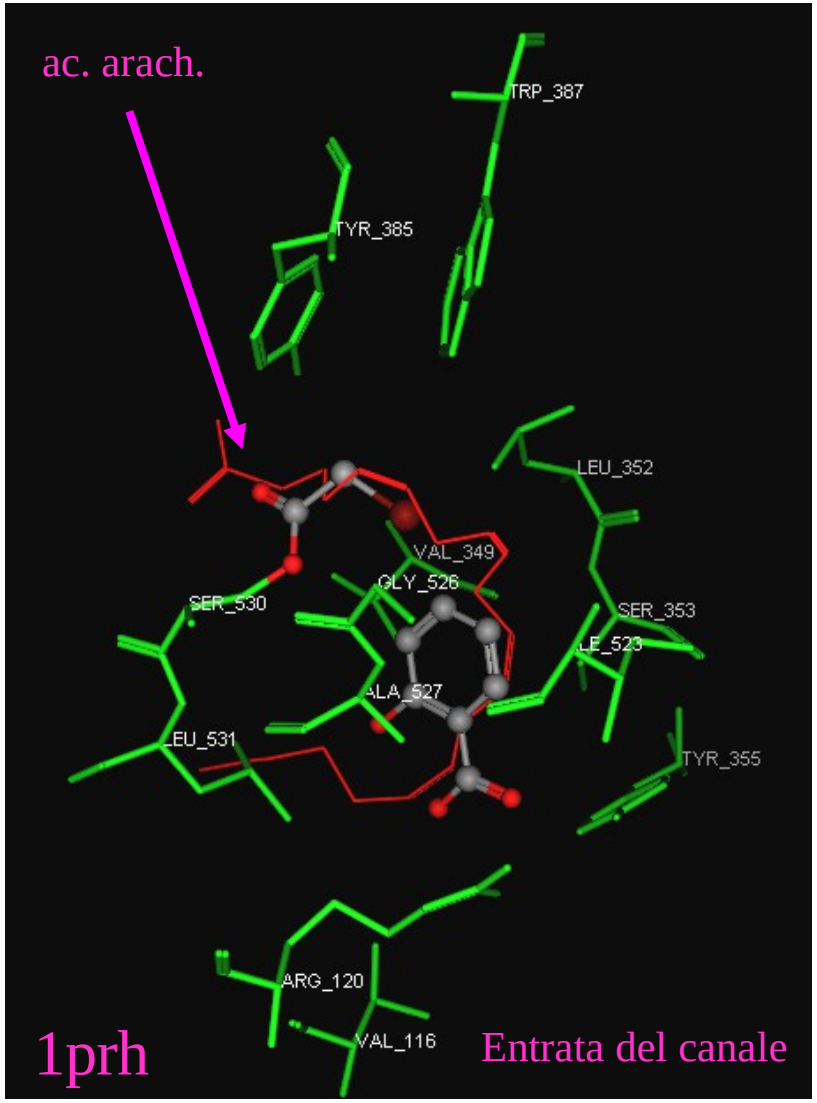


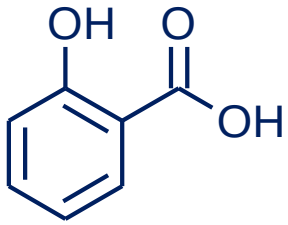
Prostaglandina



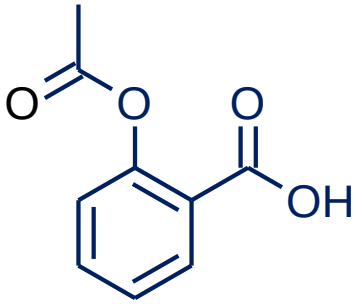
Fine della storia …

finalmente "vediamo" l'aspirina in azione





Acido salicilico



Acido acetilsalicilico

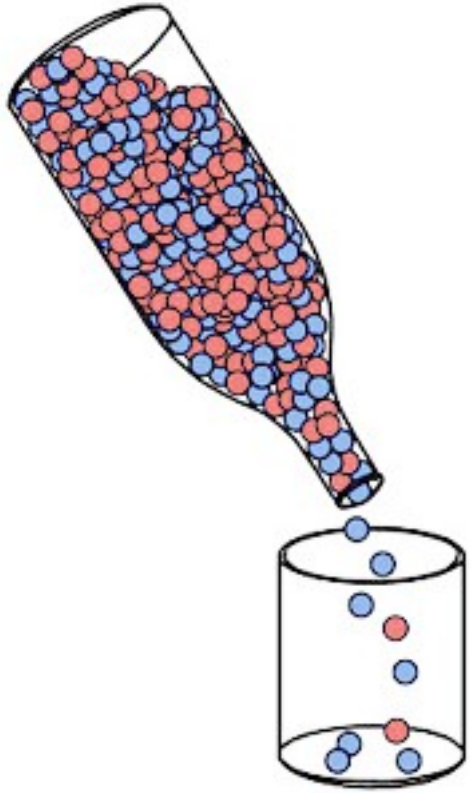




Ricerca di nuovi lead compounds: la forza bruta...

Sintesi combinatoriale

Possibile sintetizzare molte molecole caratterizzate da alta diversità strutturale

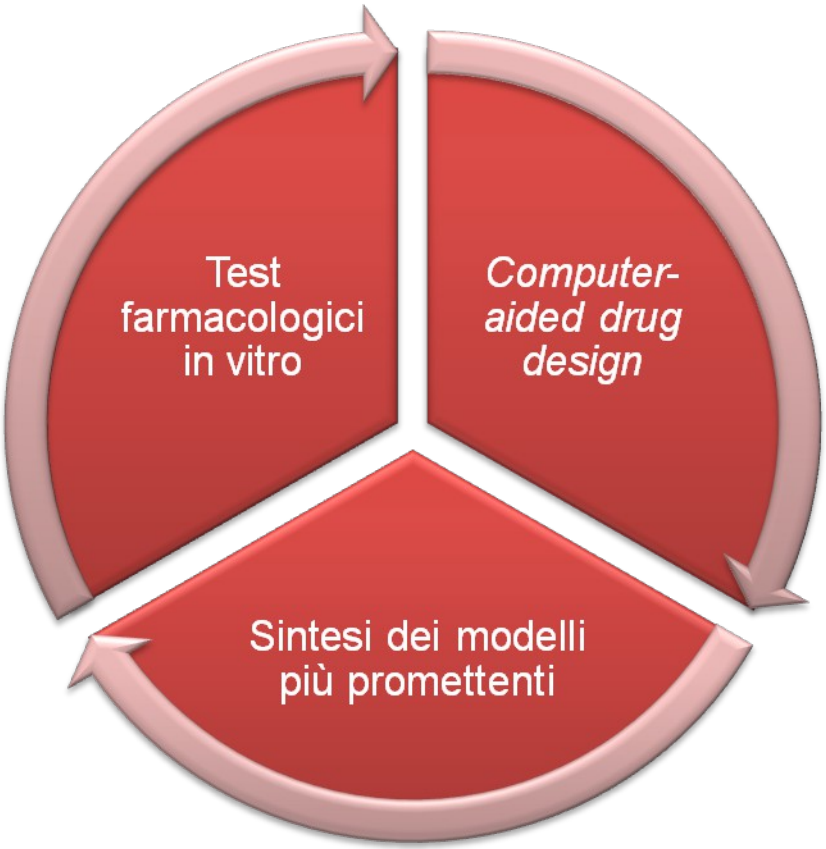


High-throughput screening

Possibile effettuare un elevato numero di test biologici *in vitro* in breve tempo

...e la progettazione razionale

- Ottimizzazione dei modelli sulla base dei risultati dei test in vitro



- *Virtual screening* di grandi librerie di composti su un determinato target di struttura 3D nota
- *Rational drug design*

La sintesi è limitata ai modelli più promettenti