

PRINCÍPIOS & FUNDAMENTOS

da Química Medicinal

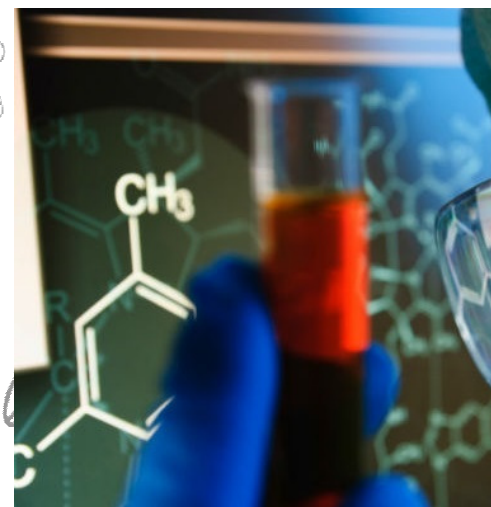
Eliezer J. Barreiro

Professor Titular

Universidade Federal do Rio de Janeiro



instituto de química
Universidade Federal do Rio de Janeiro



A painting of a seascape. The sky is filled with large, textured clouds in shades of brown, orange, and white. The sea is a deep blue with white-capped waves. In the foreground, several large, rounded rocks or buoys are scattered across the water. One rock in the center has a person standing on it, looking out at the sea. The rocks are in various colors: white, red, orange, and purple. The overall style is expressive and somewhat abstract.

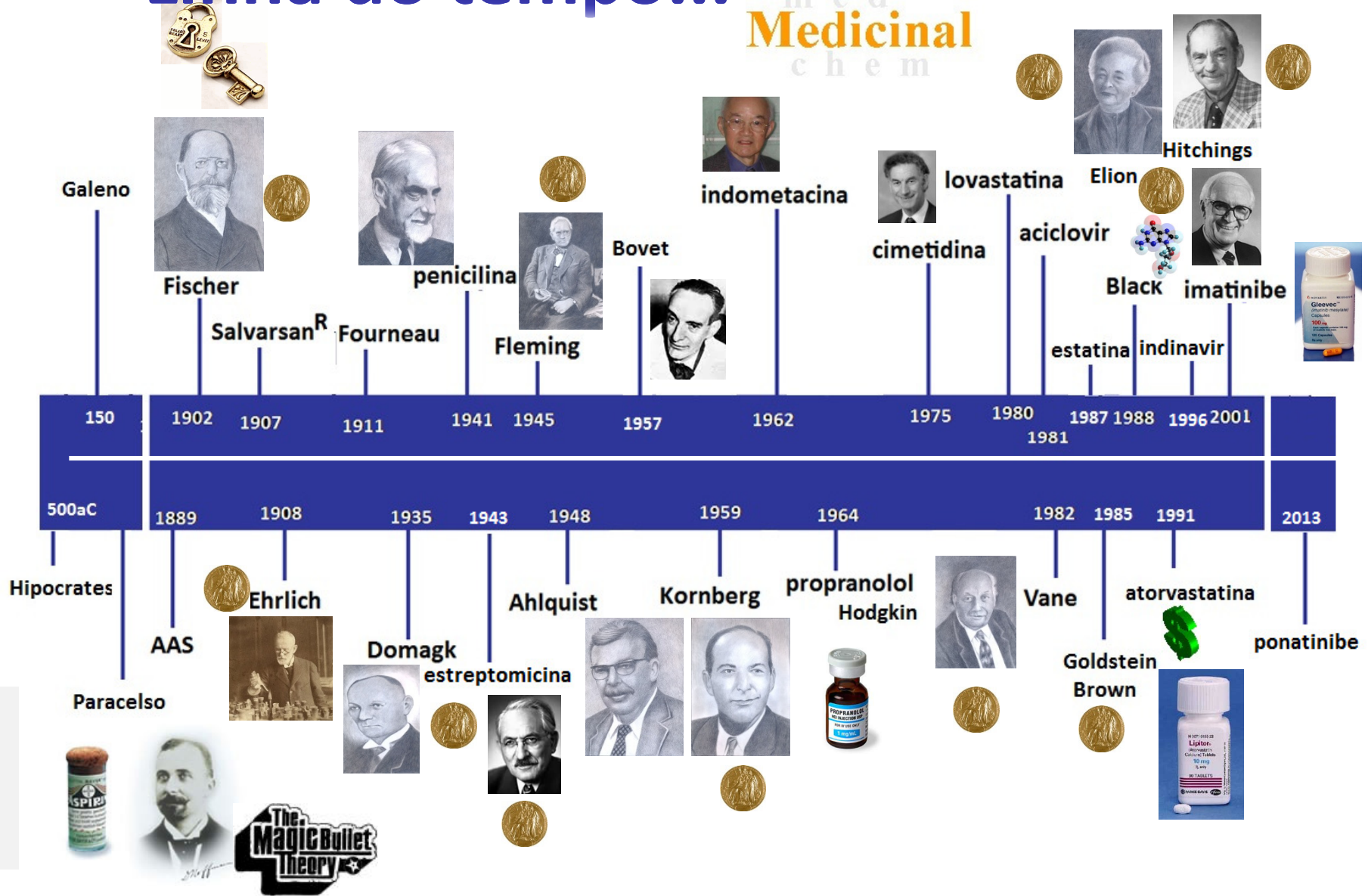
Obrigado

pelo convite

& pela presença!

Linha do tempo...

Química med Medicinal chem



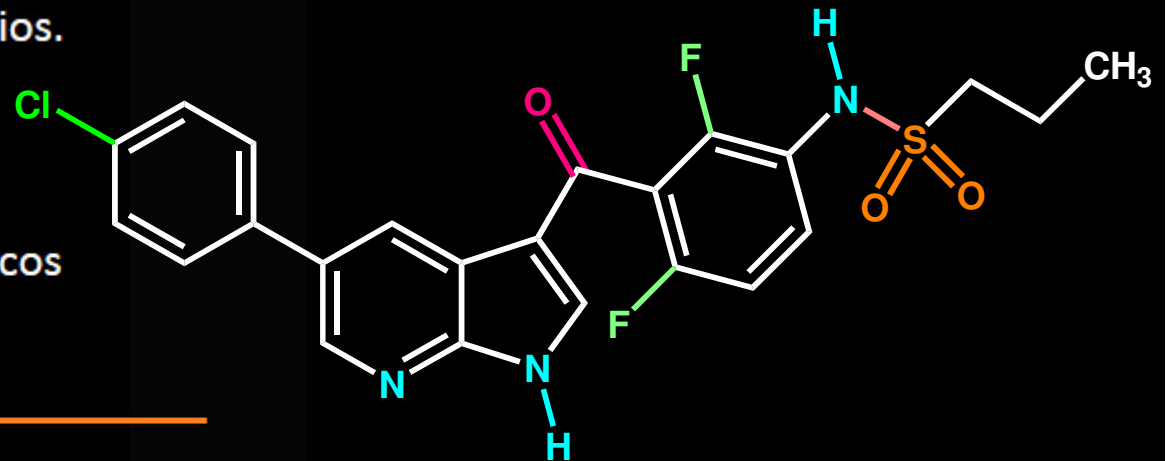
Blog com histórias & fofocas sobre fármacos

De fármacos e suas descobertas

Pretende-se tratar de temas, opiniões, comentários sobre a Ciência dos Fármacos, seu uso seguro e benefícios. História da descoberta/invenção de fármacos e aspectos da formação qualificada de universitários e pós-graduandos nas Ciências dos Fármacos também são de interesse.

sexta-feira, 27 de dezembro de 2013

A descoberta do vemurafenibe, primeiro fármaco para o tratamento do melanoma metastático



<http://ejb-eliezer.blogspot.com>

Química Medicinal

...medicinal chemists today **live** in exciting times...

their work can have a beneficial effect on millions of suffering patients – surely an important motivating factor for any scientist...

med
Química
Farmacêutica
chem
Medicinal



Joseph G. Lombardino & John A. Lowe, III

The Role of the Medicinal Chemist in Drug Discovery – Then and Now,

Nature Rev. Drug Disc. **2004**, 3, 853.

[doi:10.1038/nrd1523]



Como nascem os fármacos





Como inventar uma molécula?

Bioativa....(?)

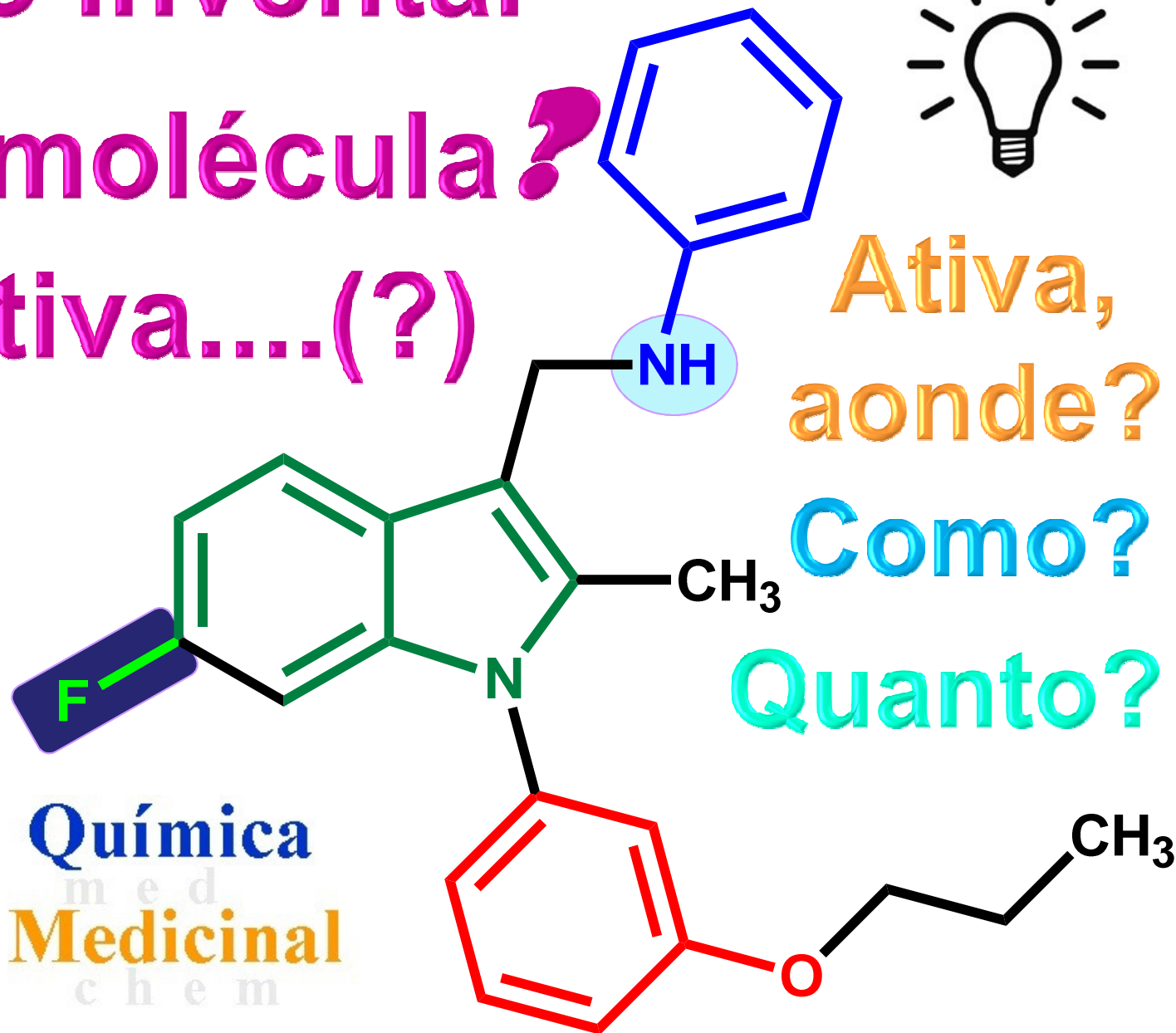


Ativa,
aonde?

Como?

Quanto?

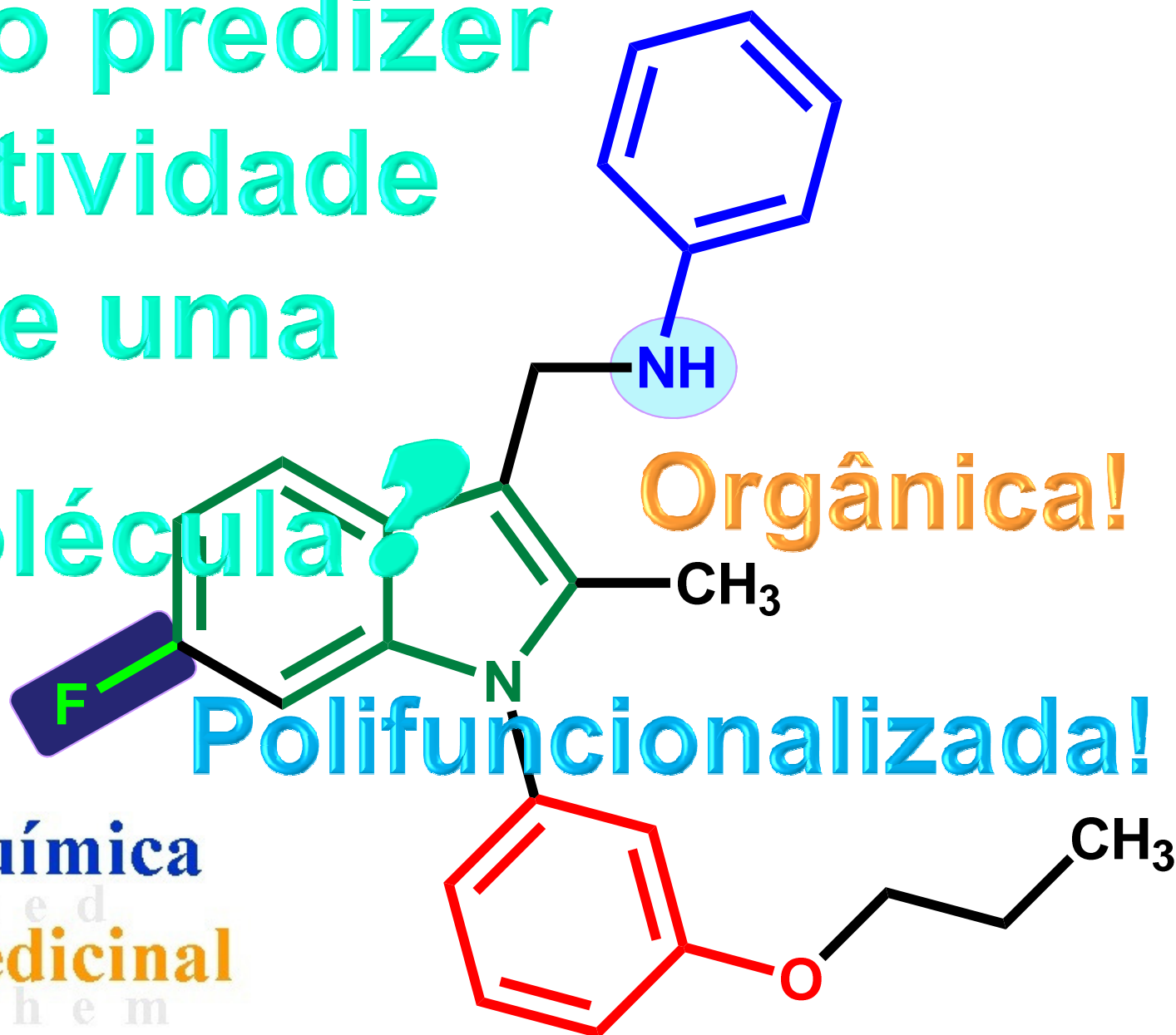
S
O
C
N
X
H



Química
med
Medicinal
chem

Como predirer
a atividade
de uma

molécula?

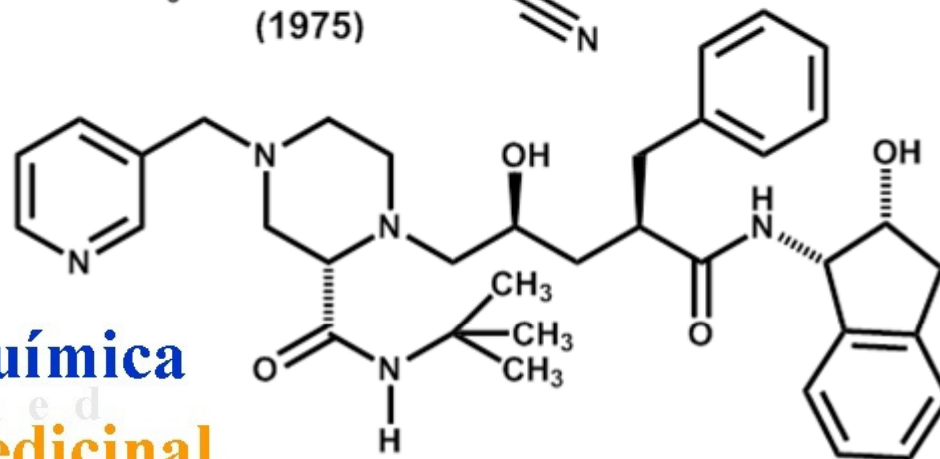
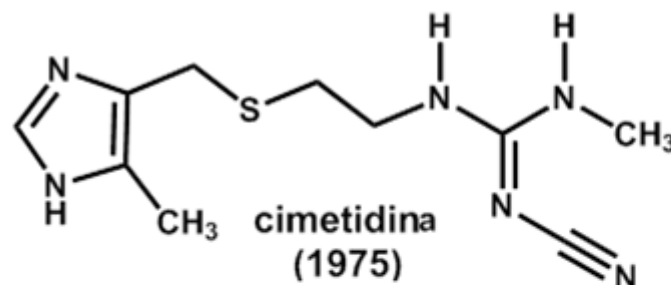
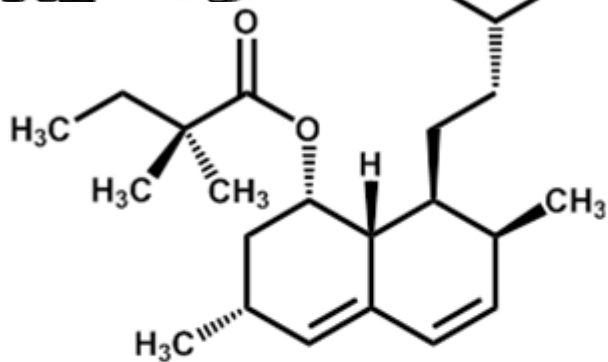
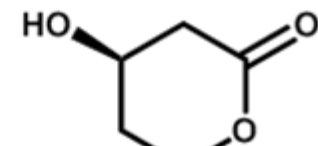
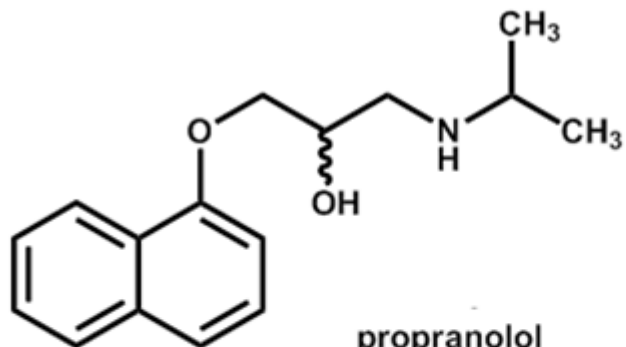


Química
m e d
Medicinal
c h e m

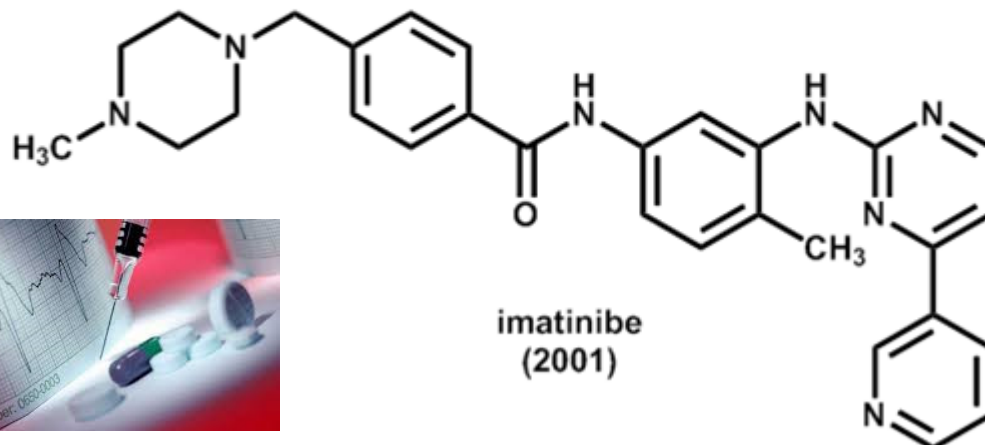


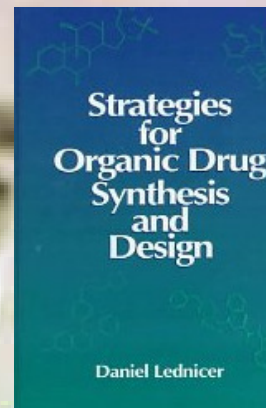
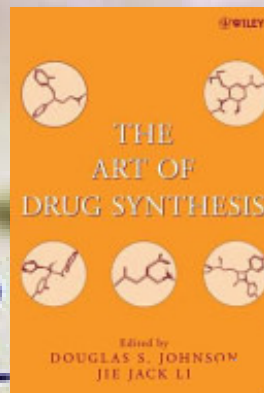
Os medicamentos foram uma das principais invenções do século 20

Universidade Federal do Rio de Janeiro



Química
med
Medicinal
chem





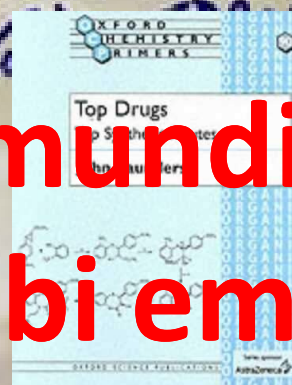
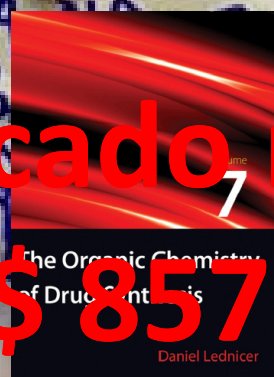
>> 85% do ar\$enal terapêutico

\$ão fármaco\$ \$intético\$

& \$ub\$tância\$ orgânica\$

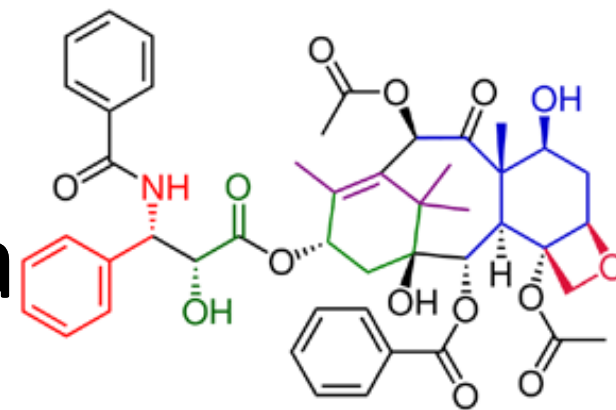


O mercado mundial foi de



US\$ 857 bi em 2013

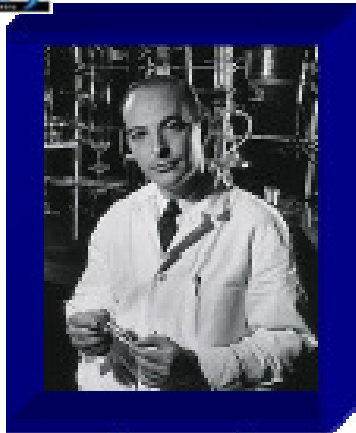
A valia da síntese orgânica



The collage consists of several images: a laboratory setting with a scientist working at a bench; a molecular model of a complex organic molecule; a chessboard with chemical structures and names of reactions (Cignard, Wittig, Diels-Alder, Brown) on the squares; and portraits of chemists with chemical structures overlaid.

US\$ 728,5 bi em 2013

As moléculas que mudaram a história da Síntese Orgânica



Arthur Kornberg
1918-2007

Nobel Prize, 1959



The Two Cultures: Chemistry and Biology¹

Arthur Kornberg

Department of Biochemistry, Stanford University, Stanford, California 94305

Received July 14, 1987

“Much of life can be understood in rational terms if expressed in the language of chemistry... the

historical roots of chemistry and biology are intertwined in many places...

Pharmaceutical chemistry was until recently the bastion of organic chemistry... in the search for alternative or superior drugs for the treatment of various diseases...”

**Pharmacology
for Chemists**

SECOND EDITION

JOSEPH G. CANNON



A. Kornberg, Science and medicine at the millennium, *Braz J Med Biol Res*, 1997, 30, 1379



Biochemistry 1987, 26, 6888-6891

IUPAC - Subcommittee Medicinal Chemistry & Drug Development

Definição: **Química Medicinal** é a disciplina que estuda os aspectos relacionados à descoberta ou invenção dos fármacos, OS aspectos moleculares envolvidos em seu mecanismo de ação e aqueles que governam a **absorção**, **distribuição**, **metabolismo**, **eliminação** e **toxicidade** (ADME/T), incluindo a compreensão da relação entre a estrutura química e a atividade terapêutica (REA=SAR).

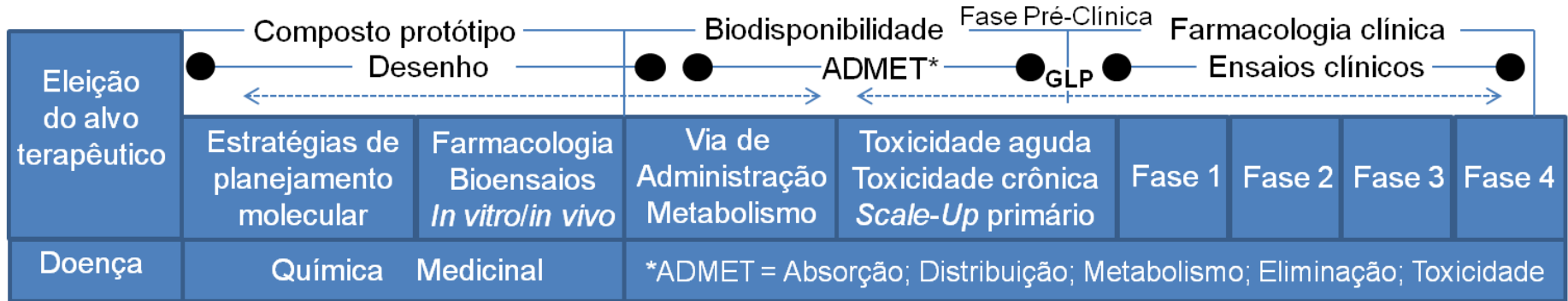


Química
m e d
Medicinal
c h e m

IUPAC

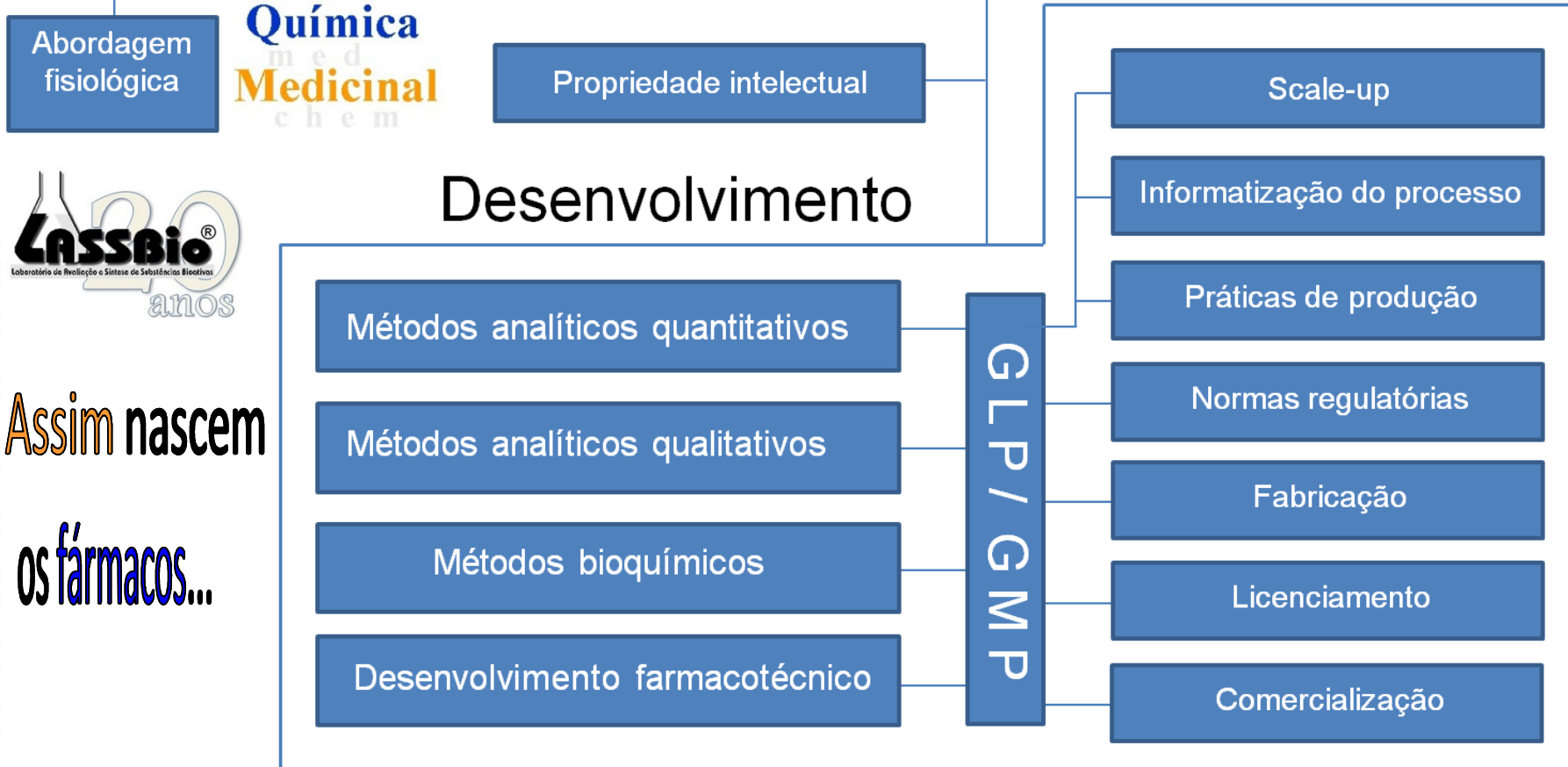
Pure & Appl. Chem., Vol. 70, No. 5, pp. 1129–1143, 1998.
Printed in Great Britain.
© 1998 IUPAC

Eur. J. Med. Chem., 31, 747 (1996)



Pesquisa

Modelo Linear



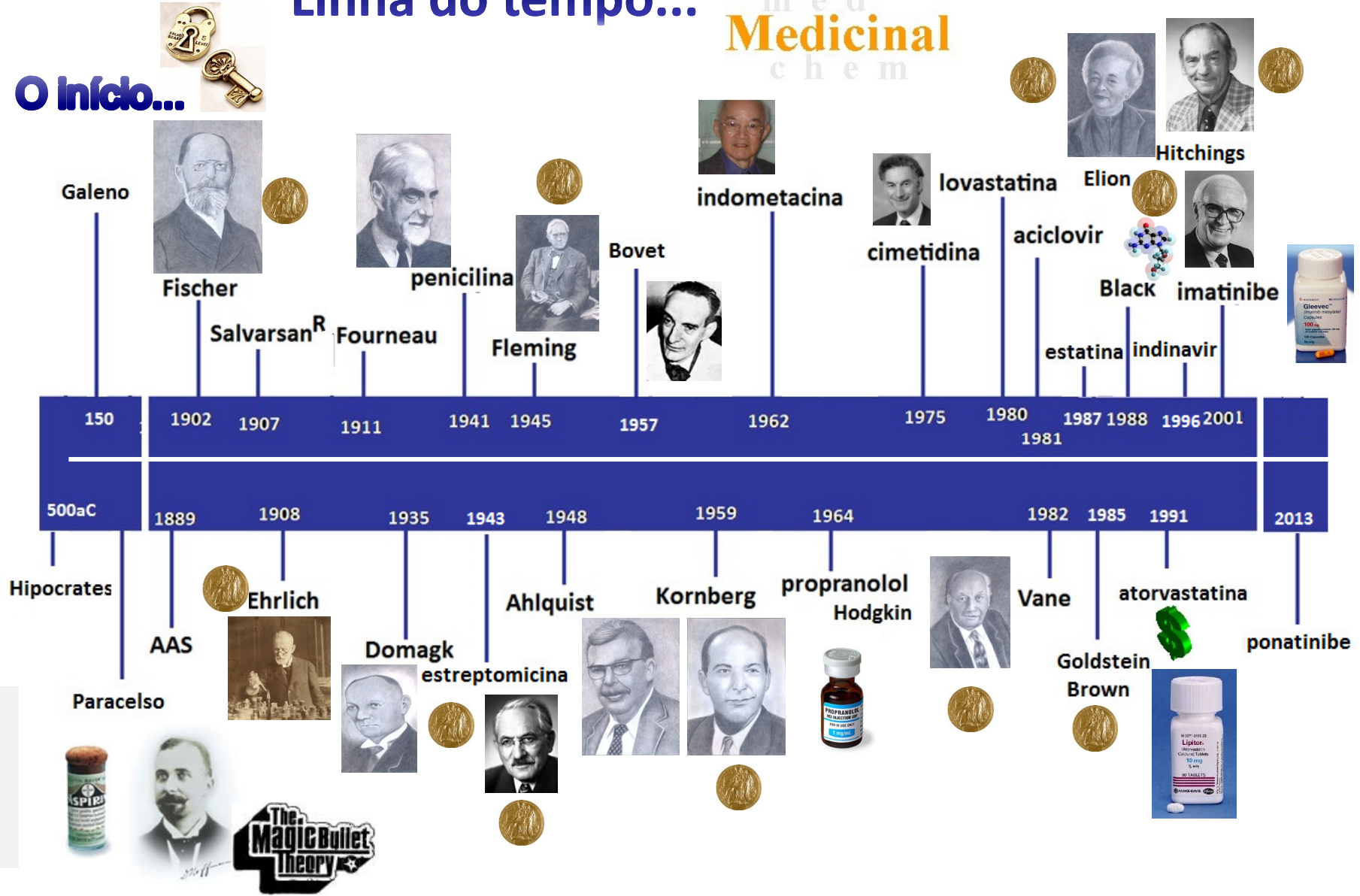
Assim nascem

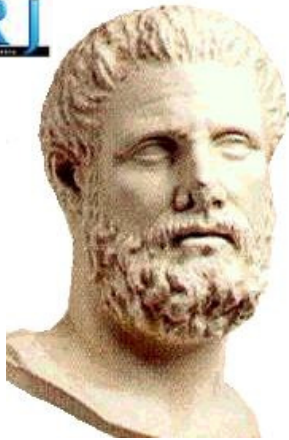
os fármacos...

Química Medicinal

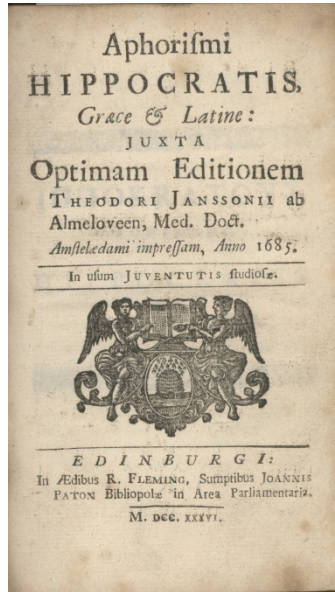
Linha do tempo...

O Início...





Hippocrates
500aC

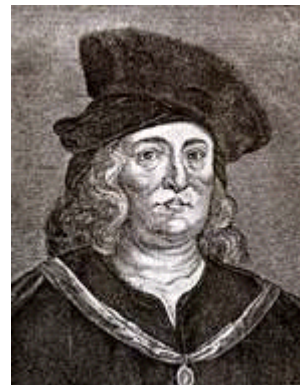


O início



Galen!

Galeno
(129-199)



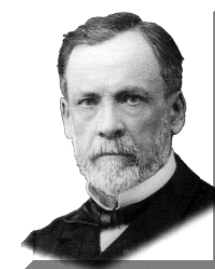
Paracelso
(1493-1541)



A Vesalius
(1514 - 1564)

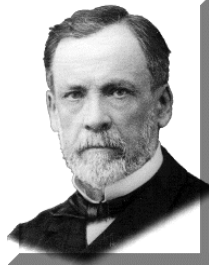


W Harvey
(1578 - 1657)



L Pasteur
(1822 - 1895)

O início



L Pasteur
(1822 - 1895)



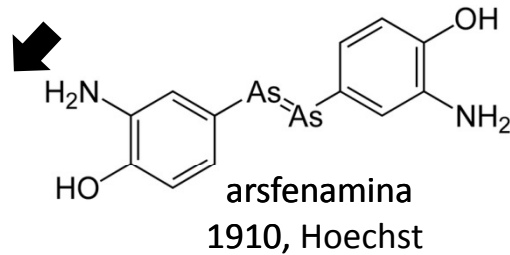
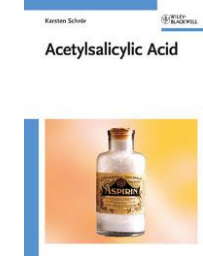
P Ehrlich
(1854 - 1915)



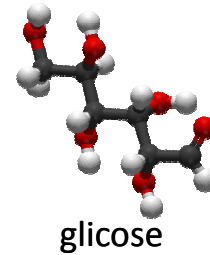
E Fischer
(1852 - 1919)



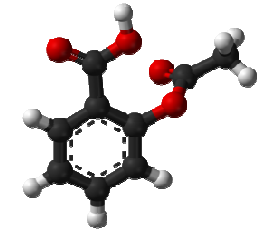
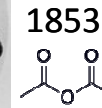
F Hoffmann 1899
(1868 - 1946)



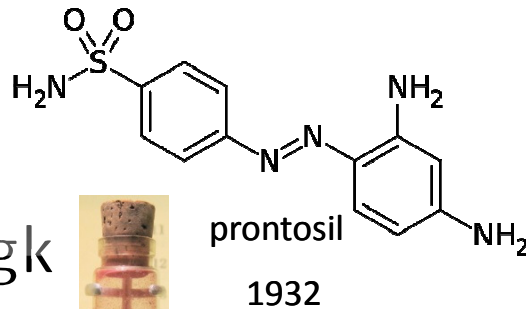
NC Loyd et al., *Angew. Chem. Int. Ed.* **2005**, *44*, 941



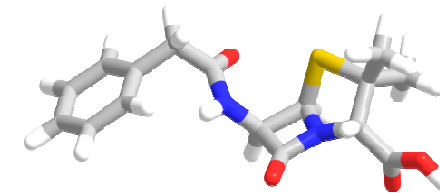
C F Gerhardt
(1816 - 1856)



GHP Domagk
(1895 - 1964)



A Fleming
(1881 - 1955)



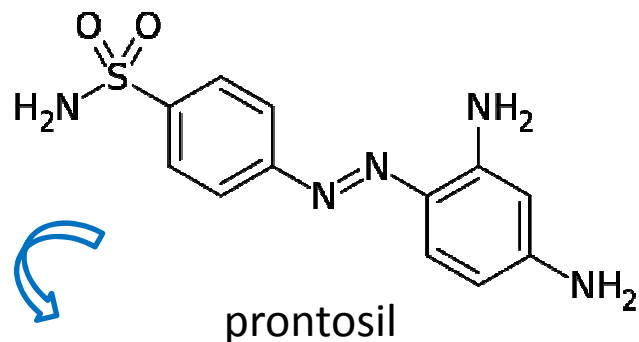
penicilina

1928



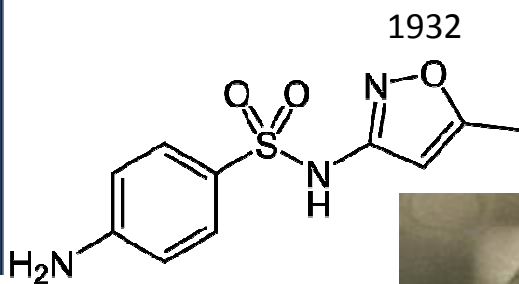
1943

O início



Thérèse Tréfouël
(1892-1978)

Jacques Tréfouël
(1897-1977)



Germaine Benoit
(1901-1983)



Daniel Bovet
(1907-1992)



Federico Nitti
(1903-1947)

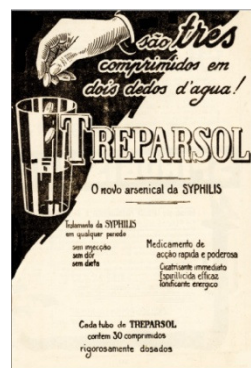
sulfaisoxazola

“Services des recherches et des fabrications de chimie organique à usage thérapeutique” (1899)
Établissements Poulenc

O berço da Química Medicinal

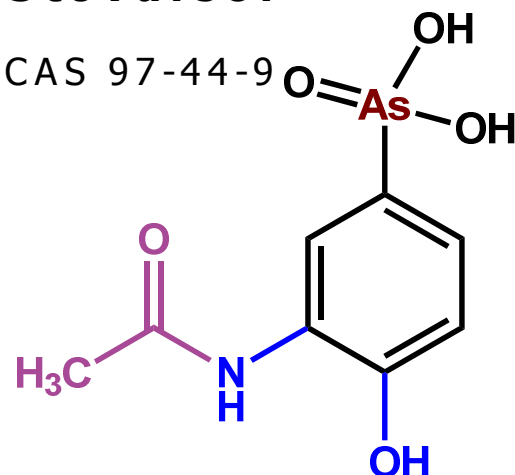


Ernest Fourneau
1872-1949
[Biografia de Fourneau](#)

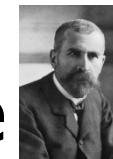


Stovarsol

CAS 97-44-9



Institut Pasteur (1887)



1911- Laboratoire de Chimie Thérapeutique

Institut Pasteur (Pierre Paul Emile Roux)

1^o *paper* sobre **SAR**
Curare and Curare-like Agents.

Prêmio Nobel de
Fisiologia/Medicina
1957



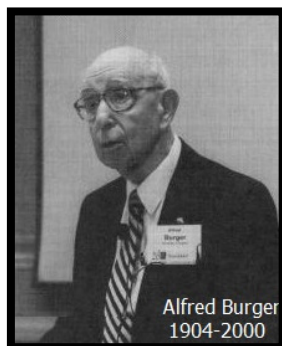
Daniel Bovet
1907-1992 *
Sulfonamidas,
anti-histamínicos.



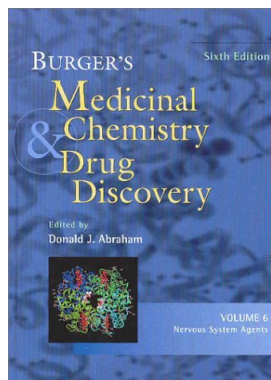
Chimie des médicaments, 1966

O início ...

Quelques Aspects de la Chimie des Médicaments. By ALBERT and CHARLES LESPAGNOL, DENISE BAR, and MICHEL DAUTREVAUX. Masson et Cie., Editors, Paris. 1966. viii + 268 pp. 16 X 24 cm. Paperback, 78 Francs.



Alfred Burger *



2

J. Med. Chem. 1991, 34, 2-6

Química Medicinal

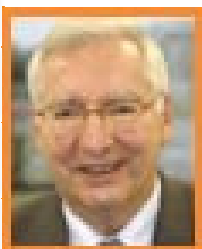
An Editor's Commentary on the Birth of a Journal

Alfred Burger†

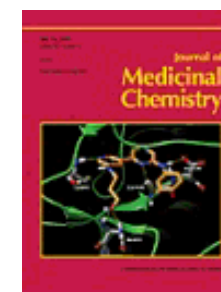
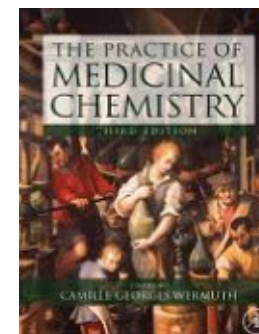
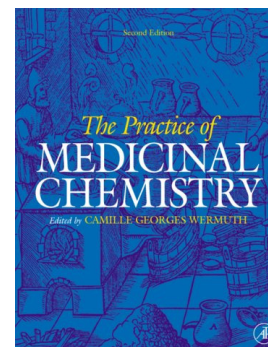
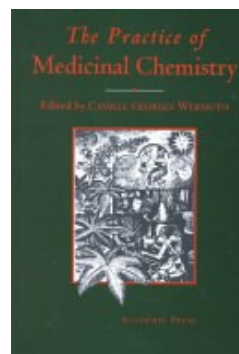
Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901



* 1978 - Congresso Brasileiro de Farmacologia e Terapêutica Experimental, São Paulo, SP
 Conferência Plenária: "Highlight in Medicinal Chemistry"



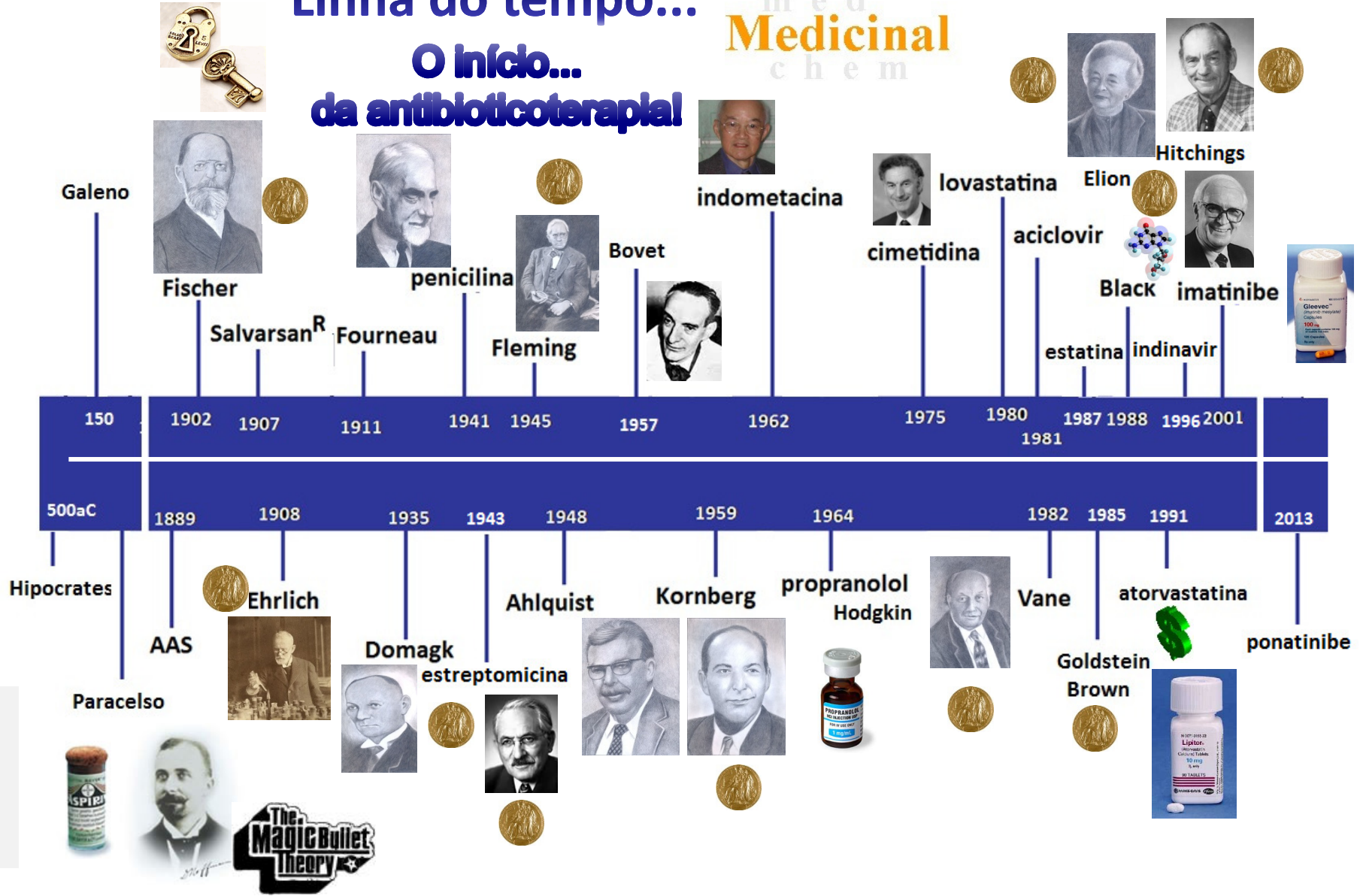
Camille G. Wermuth
 Université Louis Pasteur



Química Medicinal

Linha do tempo... O início... da antibioticoterapia

Química
med
Medicinal
chem

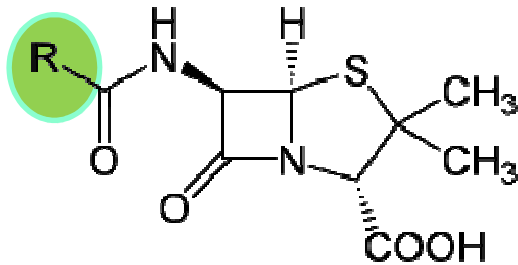


Molécula salva-vidas...

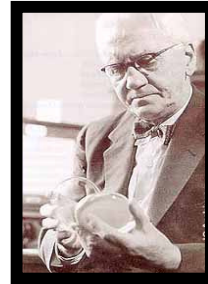
Antibióticos β-lactâmicos



- 1877 – L. Pasteur
- 1897 - Ernest Duchesne, Lyon
- 1928 – A Fleming, Londres
- 1939 – Florey & Chain
- 1943 – RB Woodward, R Robinson
- 1945 - Dorothy C. Hodgkin
- 1948 – Patente de processo
- 1957 – John Sheehan, MIT



Penicilina



Alexander Fleming
1881-1955



Howard W. Florey
1898-1968



E. Boris Chain
1906-1979



FUNGOS



1945



Dorothy C. Hodgkin
1910-1994



MD Vargas, *Rev Virtual Quim* **2012**, 4, 85

antibioticoterapia

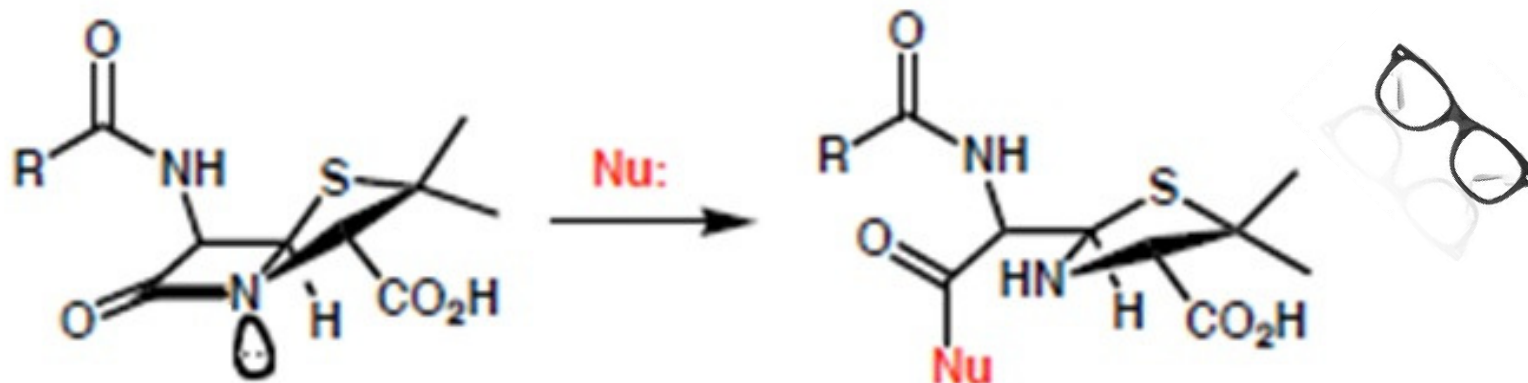
O acaso ajuda a sorte



EB Chain *et al.*,
Lancet **1940**, 2, 226

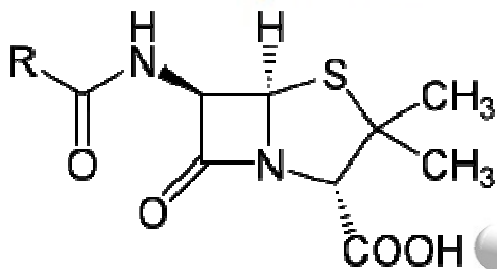


O sistema β -lactâmico

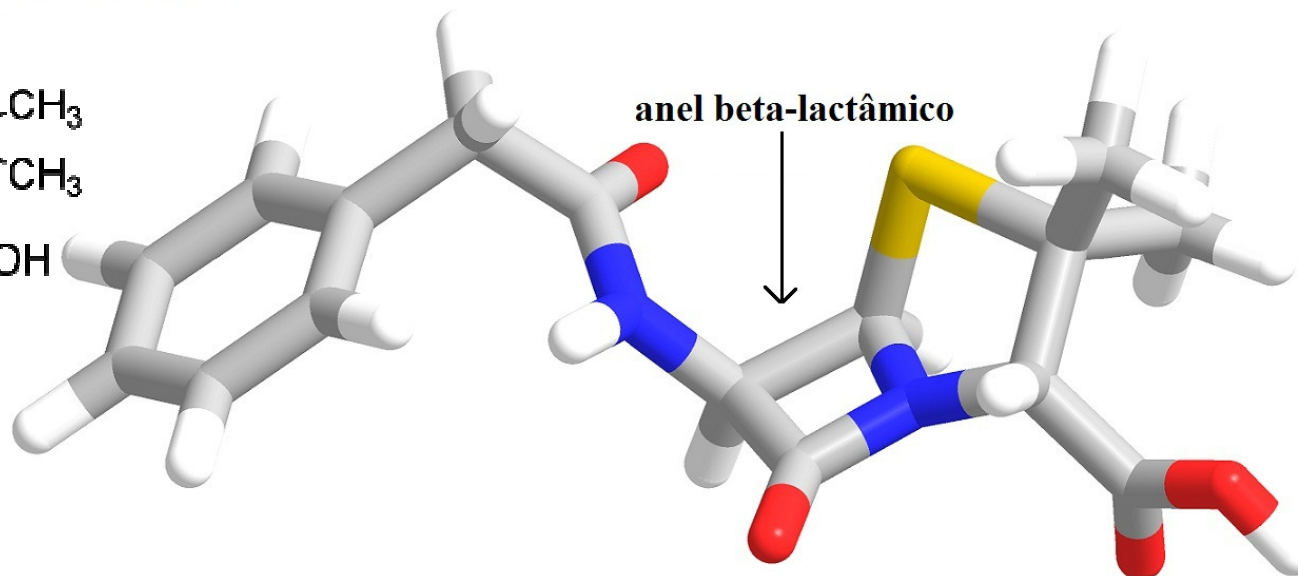


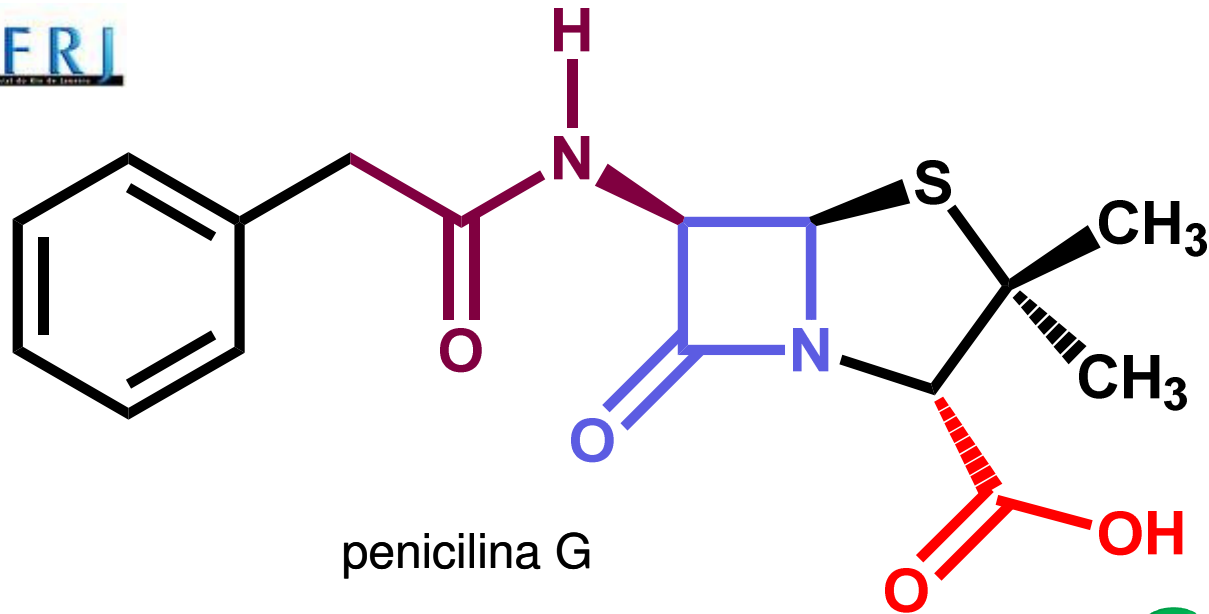
anel beta-lactâmico
de conformação
piramidal definida

Importância dos aspectos conformacionais

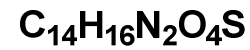


Química
m e d
Medicinal
c h e m



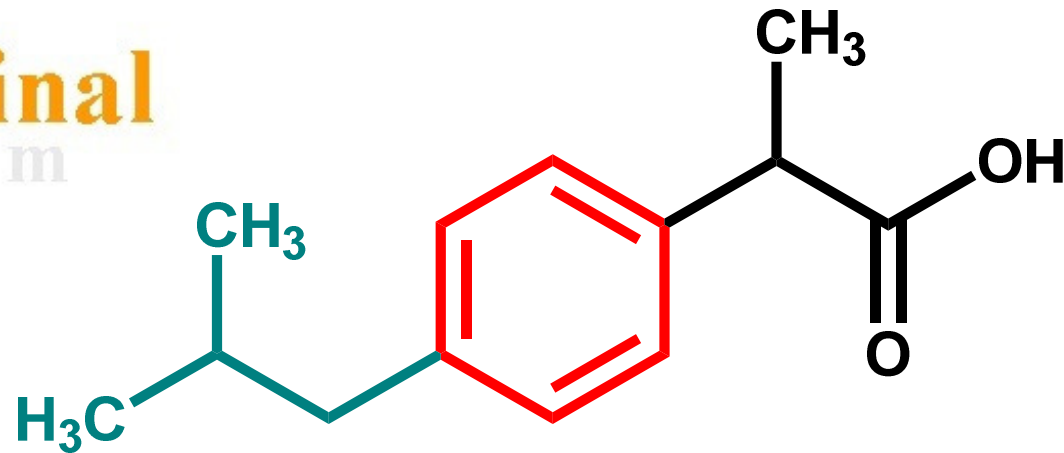


penicilina G

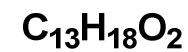


O quê têm
em comum?

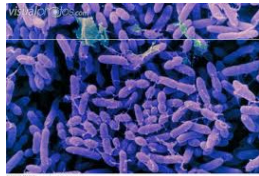
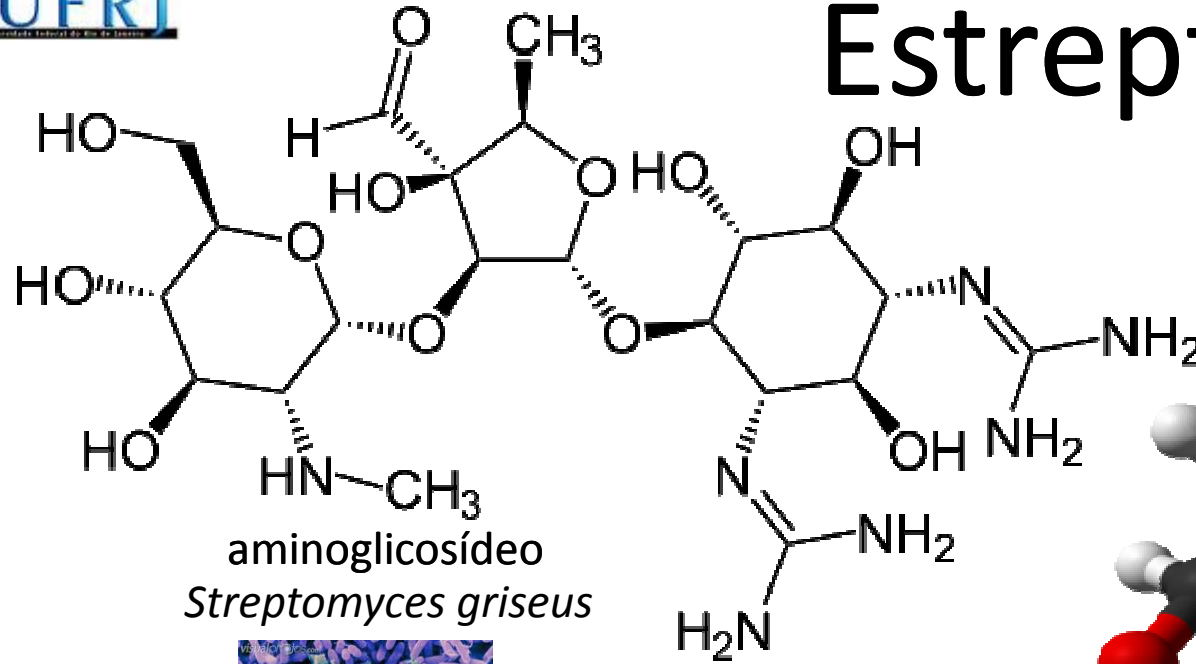
Química
m e d
Medicinal
c h e m



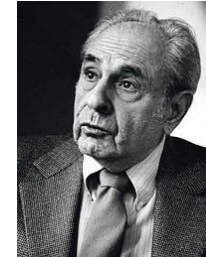
naproxeno



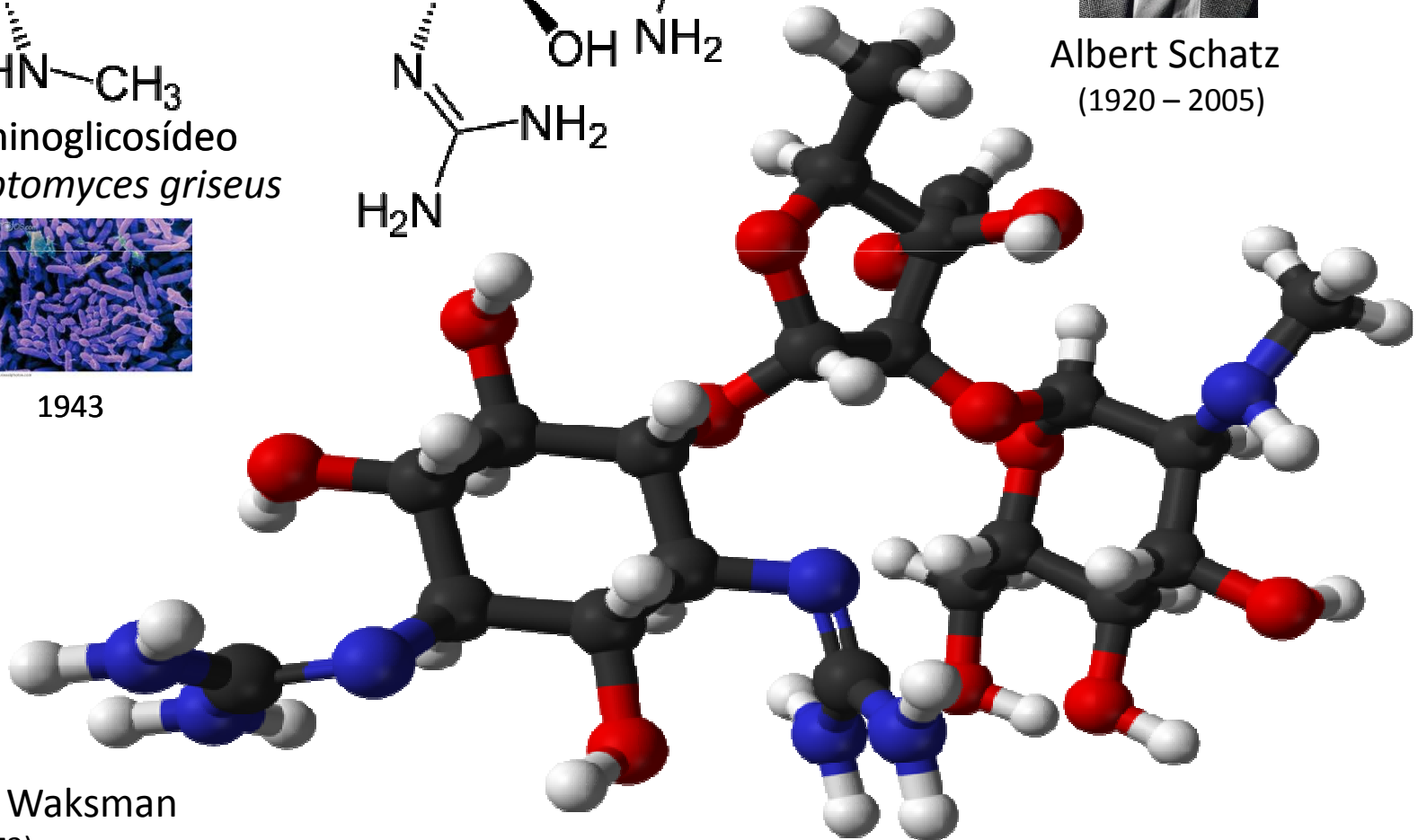
Estreptomicina



1943



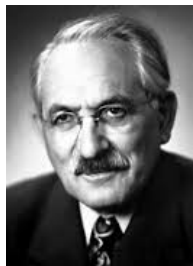
Albert Schatz
(1920 – 2005)

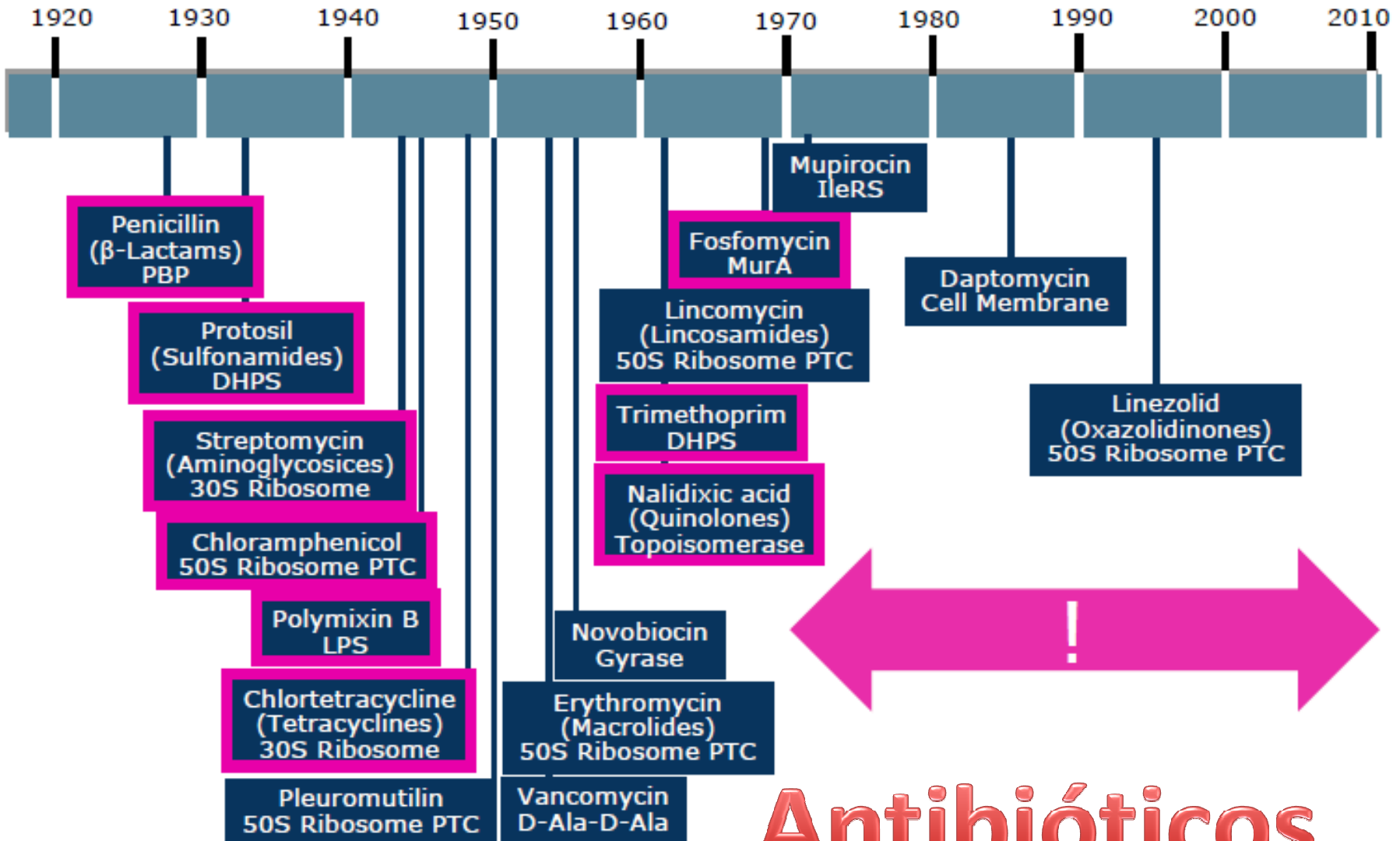


1952

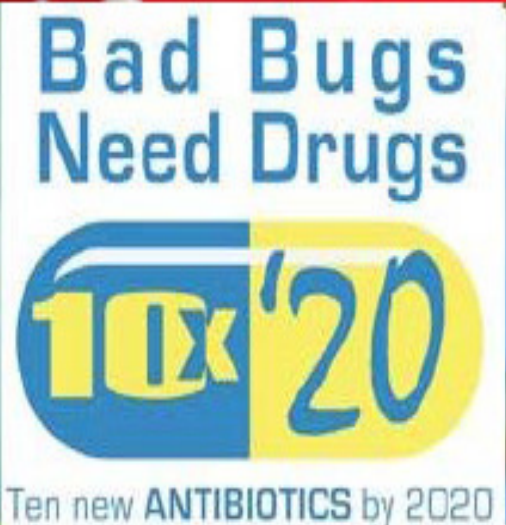
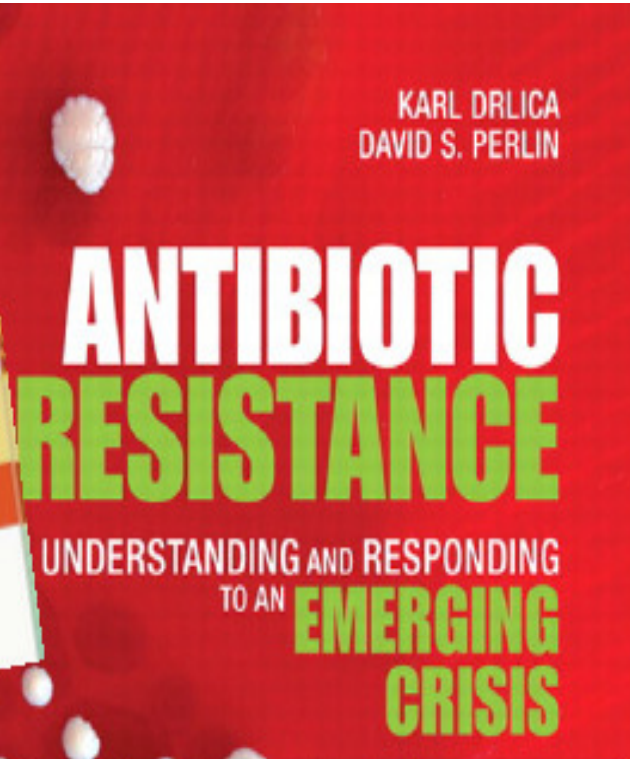
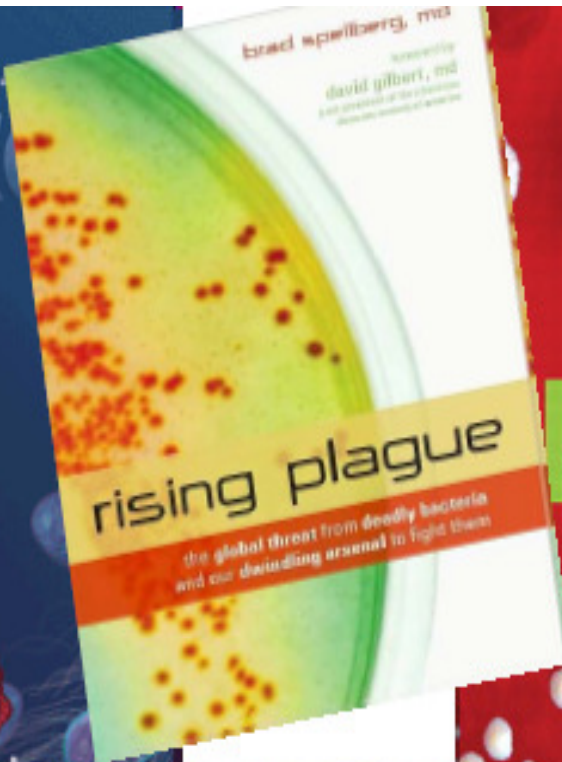
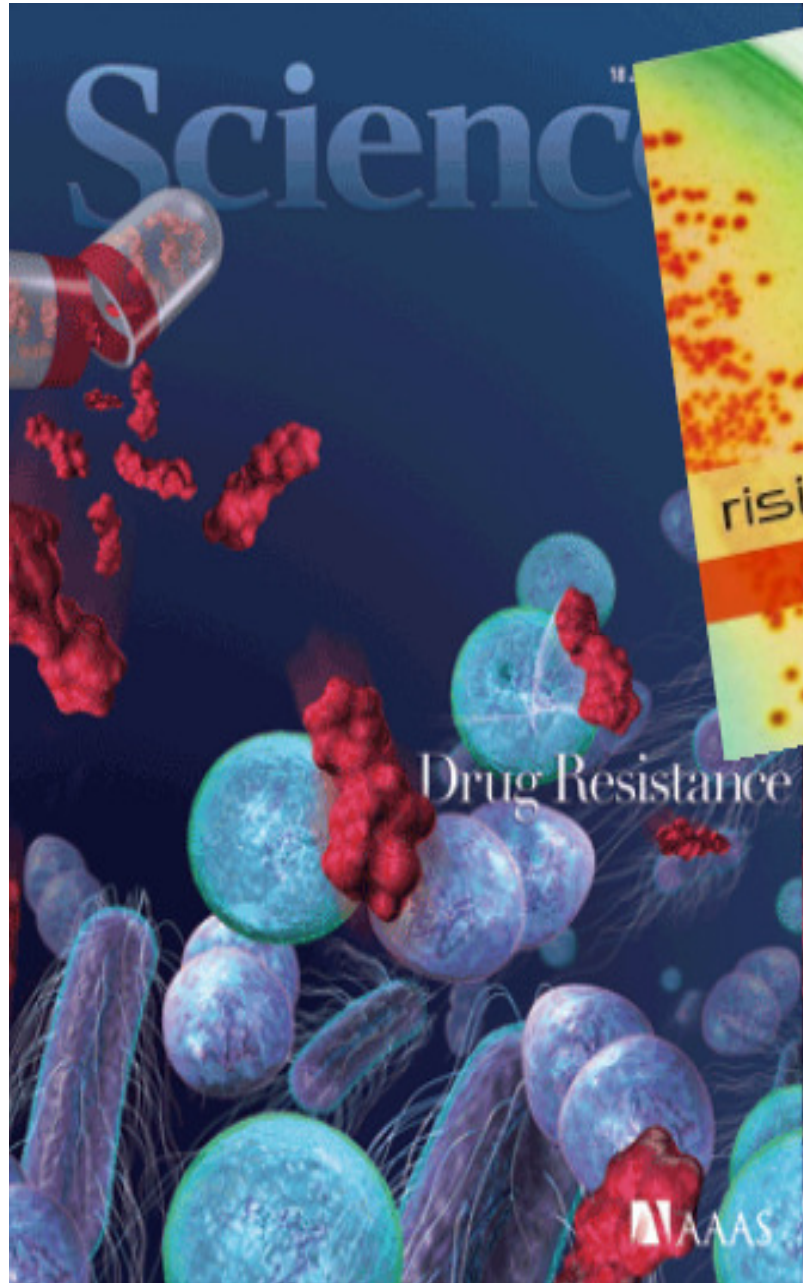
Selman Abraham Waksman
(1888 – 1973)

1939



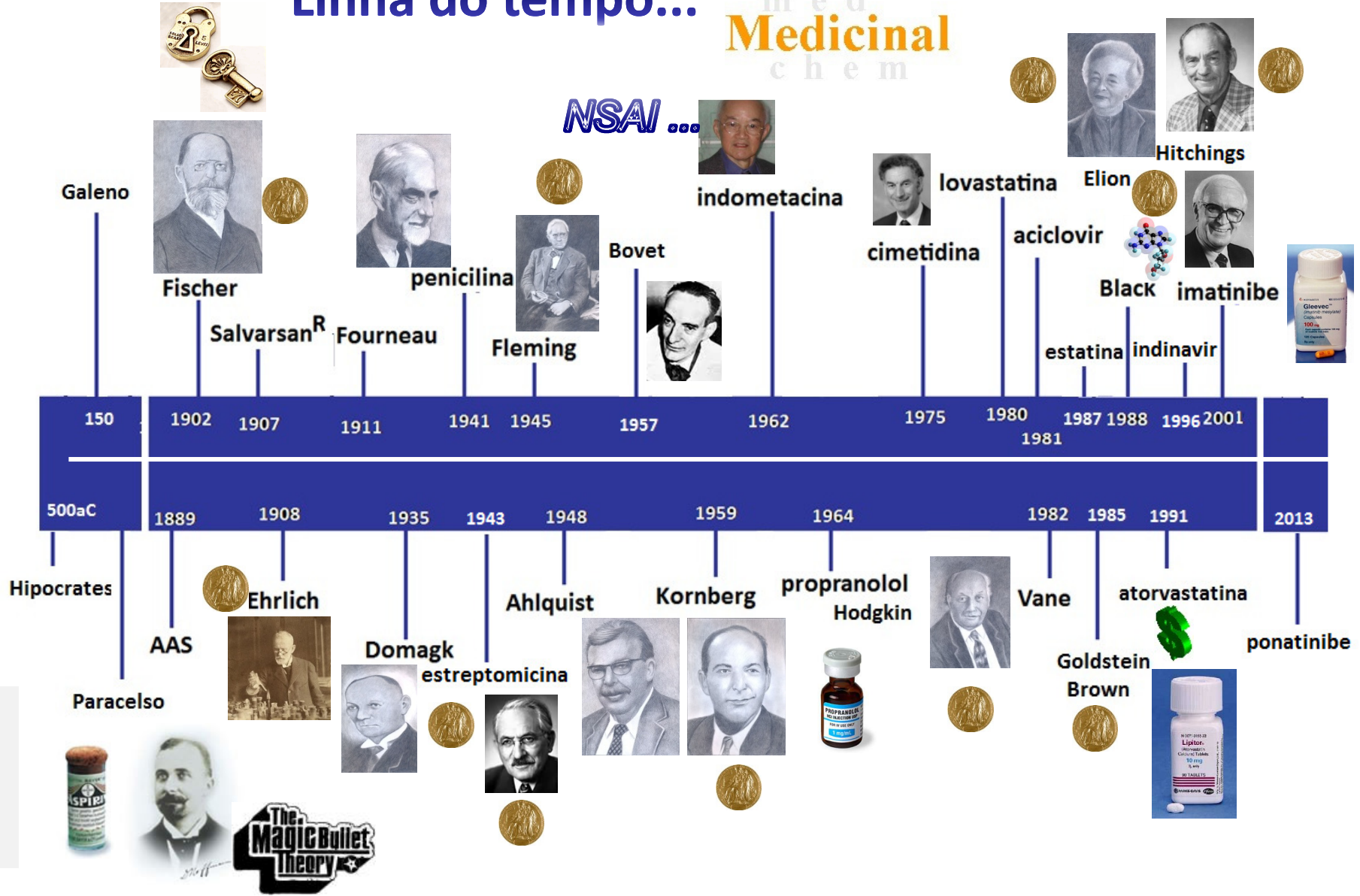


Antibióticos...



Química Medicinal

Linha do tempo...



Os AINE's (NSAI's)

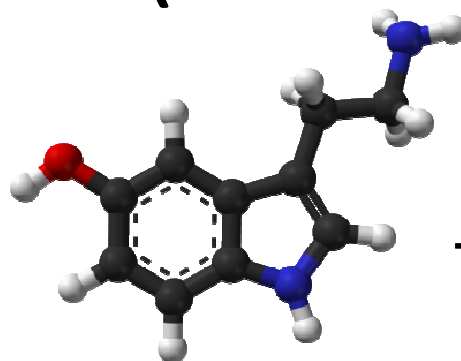


Tsung Y. Shen

(1924 -)

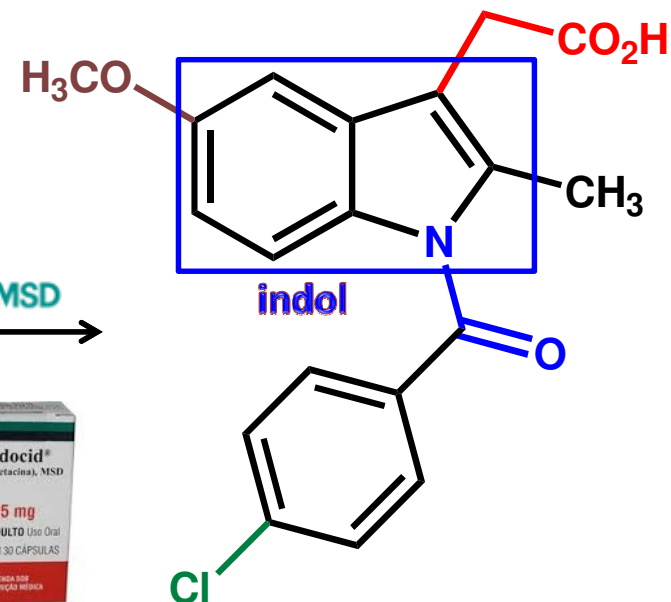
Charles Allen Winter

(1903 – 1999)



serotonina

1958



indometacina

Journal of the
American
Chemical
Society

T. Y. Shen et al., *J. Am. Chem. Soc.* **1963**, *85*, 488 [JA|C|S](#)

T. Y. Shen, Toward more selective antiarthritic therapy, *J. Med. Chem.*, **1981**, *24*, 1

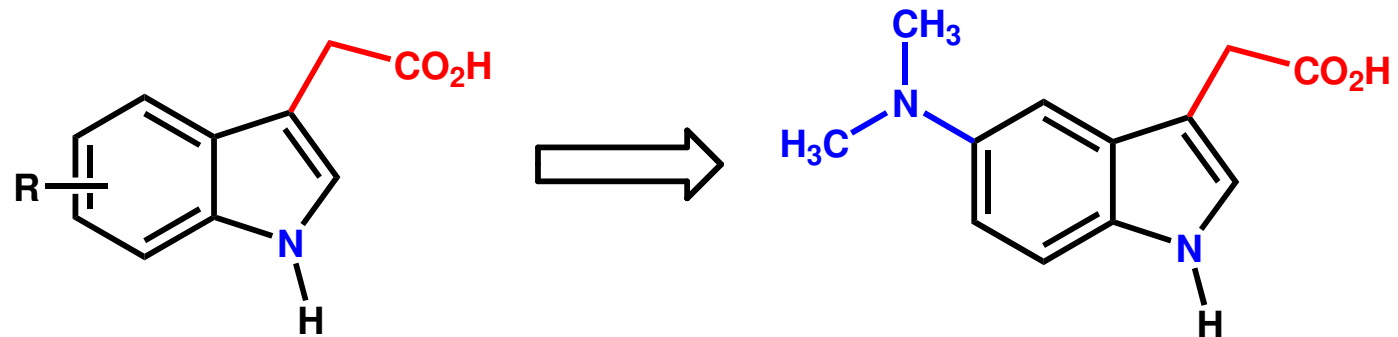
- American Chemical Society Division of Medicinal Chemistry Hall of Fame
- First winner of the GlaxoSmithKline Alfred Burger Award



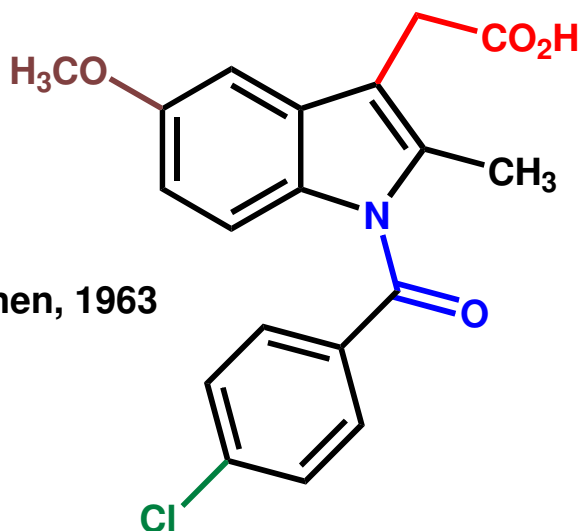
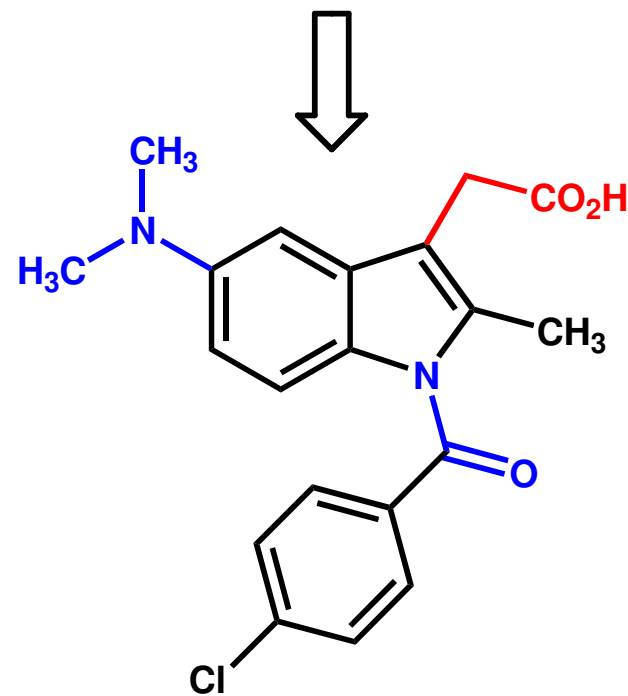
American Chemical Society
Division of Medicinal Chemistry
Hall of Fame

[ACS Hall of Fame](#)

Gênese da indometacina



ácidos indolil-acéticos



TY Shen, 1963

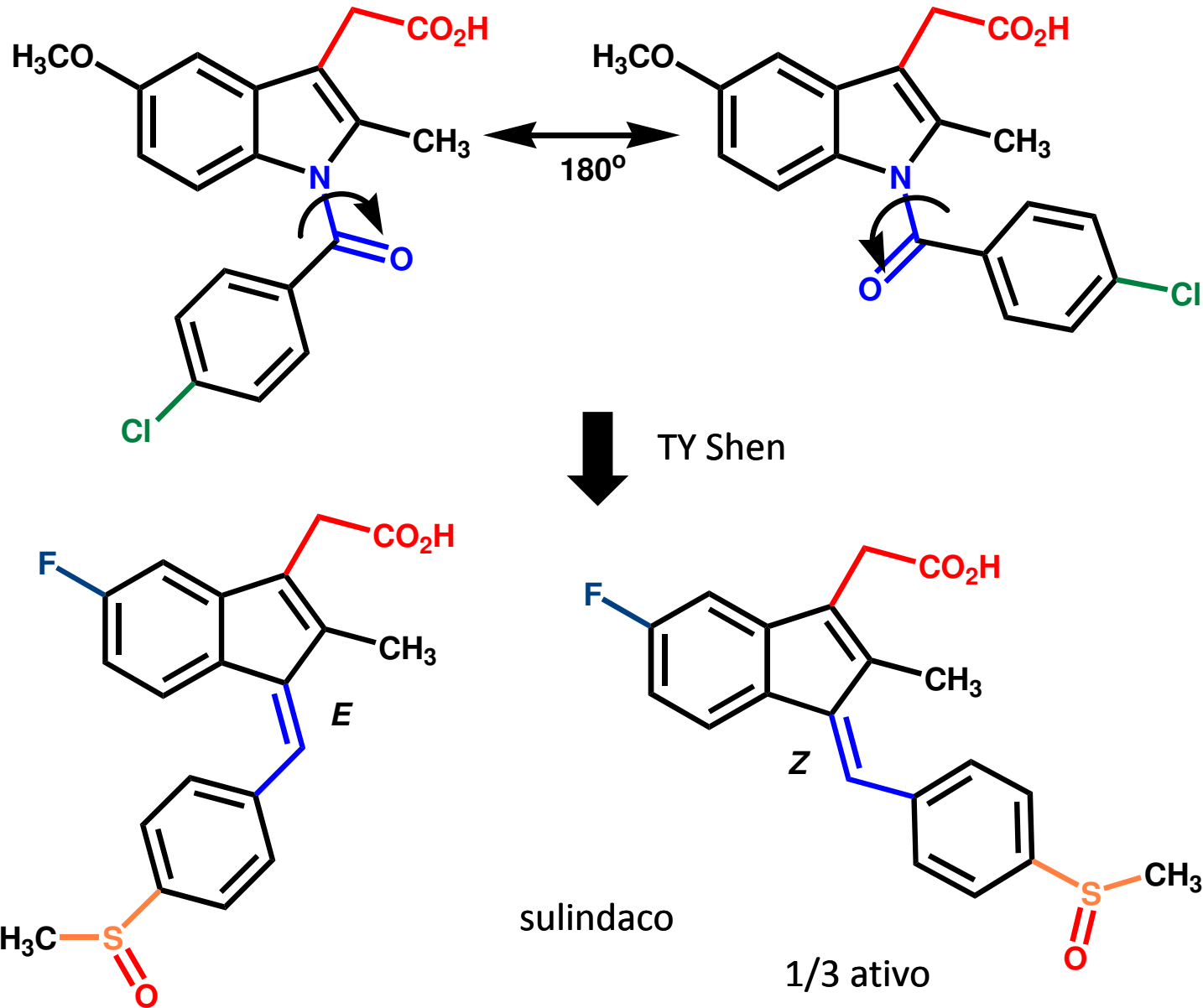
indometacina

ca. 300 compostos

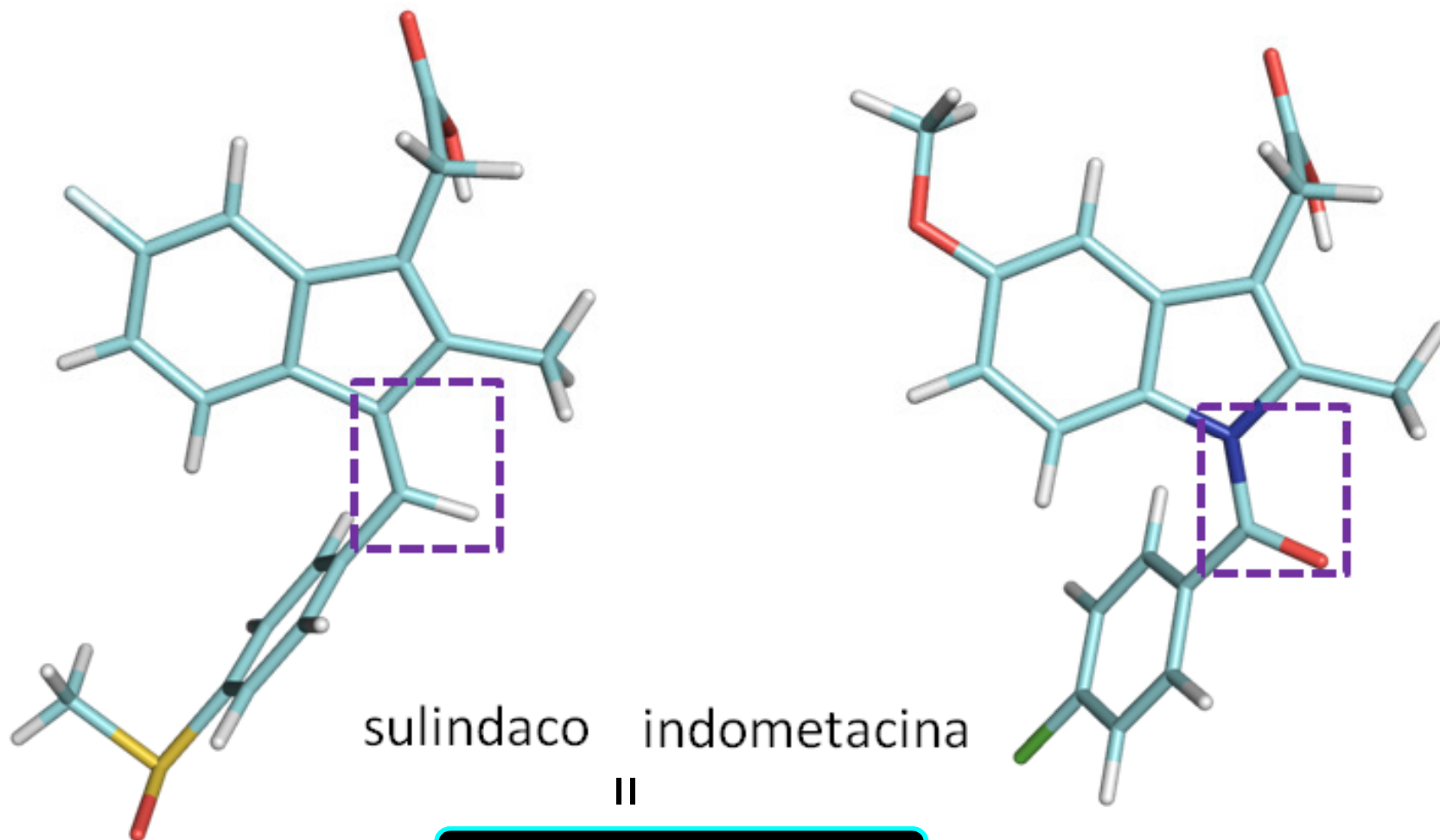
Charles A Winter
Cg ind r.p.e.
MSD

MT-587

Conformação Bioativa



Similaridade molecular



sulindaco indometacina

||

iso-conformacionais

O uso do safrol como bióforo natural no

