



Química Medicinal / Química Médica

Eliezer J. Barreiro

Professor Titular



Simpósio de Integração Universitária à Indústria (I SIUIN)



Laboratório de Avaliação e Síntese de Substâncias Bioativas

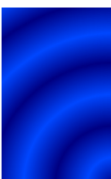
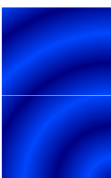
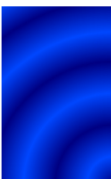
www.farmacia.ufrj.br/lassbio

Instituto Nacional de Ciência e Tecnologia de Fármacos e Medicamentos



INCT-INO FAR

www.inct-inofar.ccs.ufrj.br



QUÍMICA MEDICINAL

AS BASES MOLECULARES DA AÇÃO DOS FÁRMACOS

ELIEZER J. BARREIRO
CARLOS ALBERTO MANSSOUR FRAGA

2ª EDIÇÃO





DEFINIÇÃO; HISTÓRICO; os Pioneiros; Ernest forneau; Alfred Burger; a EVOLUÇÃO da QUÍMICA Medicinal; *a linha do TeMPO* da Química Medicinal; moléculas *pioneiras*; os FÁRMACOS e o **Nobel**; Emil Fischer; Paul Ehrlich; Robert KOCH; Alexander Fleming; **Ernest** Chain; Howard FLOREY; bent *Samuelsson*; SUNE bergstron; John VANE; George Hitchings; Gertrude Belle ELION; Arthur Kornberg; a INTERDISCIPLINARIDADE; os FÁRMACOS e os medicamentos; características estrutrais dos FÁRMACOS; o processo de *descoberta*; o mercado farmacêutico mundial & do BRASIL; novos fármacos; as *fases DA ação* dos FÁRMACOS; as razões moleculares DA ação dos fármacos; o PARADIGMA de *Ehrlich & Fischer*; BIORRECEPTORES; modelo chave-fechadura; AS ligações frágeis; TIPOS de interações FÁRMACOS-biorreceptores; reconhecimento MOLECULAR; Topografia 3D dos BIORRECEPTORES; bioinformática & QUÍMICA COMPUTACIONAL; dissecação molecular; QUEM são OS BIORRECEPTORES; a quiralidade; SIMILARIDADE e dissimilaridade MOLECULAR; FASE farmacocinética; *metabolismo* dos fármacos; CYP450; RATO transgênico; *origem* dos FÁRMACOS; os produtos NATURAIS; os índios e os indóis; **curare**; BLOQUEADORES ganglionares; decano dos fÁRMACOS; teoria das assinaturas; *domesticando* moléculas; STREPTASE molecular; MORFINA; analgésicos SINTÉTICOS; quinina; *anti-maláricos*; alcalóides da VINCA; Taxol[®]; camptotecina; FÁRMACOS anti-câncer; o MAR como *fonte* de fármacos; HIV; FÁRMACOS *e serpentes*; sistema RENINA-ANGIOTENSINA; MOLÉCULAS e comportamento; fármacos sintéticos; CONCEITO de composto-PROTÓTIPO; grupamentos farmacofóricos, *auxofóricos* e toxicofóricos; MOLÉCULAS inteligentes; Planejamento RACIONAL; antagonistas de biorreceptores; inibidores enzimáticos; bióforos *naturais*; PRODUTOS NATURAIS como PROTÓTIPOS; abordagem fisiológica; LASSBio; considerações finais; SCIELO; *bibliografia*; EPÍLOGO; agradecimentos.



Definição:

Química Medicinal

Chemistry and Human Health Division (VII)
Subcommittee on Medicinal Chemistry and Drug Development.



é a disciplina que estuda os aspectos relacionados à descoberta, invenção e preparação dos fármacos, princípio-ativo dos medicamentos.

Estuda os fatores moleculares do seu modo de ação, incluindo a compreensão da relação entre a estrutura química e atividade (SAR/QSAR), absorção, distribuição, metabolismo, eliminação e toxicidade.

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



A **Química Medicinal** é a disciplina chave, de vital importância para a indústria farmacêutica. Os **Químicos Medicinais** participam do processo da descoberta de novos fármacos e solucionam problemas relacionados à otimização das propriedades farmacológicas das moléculas.

<http://www.iupac.org>

C. R. Ganellin *et al.*, *Eur. J. Med. Chem.* 2000, **35**, 163
Monge *et al.*, *Eur. J. Med. Chem.* 2000, **35**, 1121

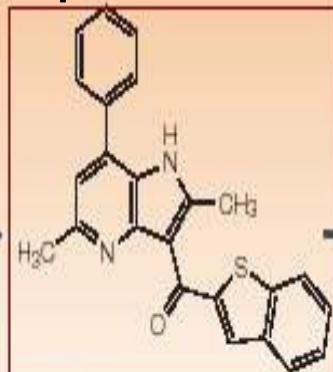


Preclinical studies

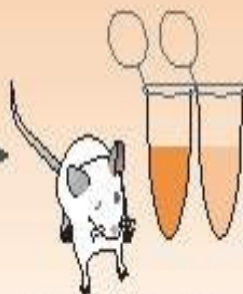
O processo da descoberta de novos fármacos é complexo...



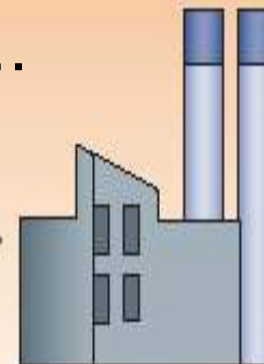
Research team formed and objectives set



Novel chemicals synthesized



Chemicals tested for efficacy and safety in test tubes and animals. Results used to choose drug candidate.



Formulation, stability scale-up synthesis, chronic safety in animals



Company files Investigational New Drug (IND) application with FDA

Clinical studies

Química Medicinal



Drug is approved for marketing

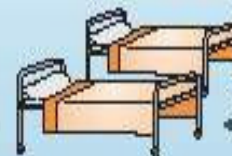
ANVISA

FDA

FDA reviews NDA



Company files New Drug Application (NDA)



Phase III: large clinical trials in many patients



Phase II: studies in patients (efficacy)



Phase I: studies in healthy humans (toleration)





O fármaco...

Princípio ativo



Forma farmacêutica



cristalização

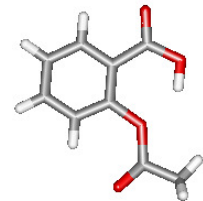


cristalização

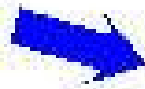


Medicamento

Fármaco



ácido acetilsalicílico



É o fármaco formulado galenicamente...



O que é um fármaco ?

• **Fármaco...**

- É uma substância orgânica (> 99%) com propriedades farmacoterapêuticas para uso médico, capaz de recuperar, promover, manter ou preservar o estado de Saúde;
- Tem elevada eficácia para o alvo terapêutico (PD);
- Não tóxico;
- Potente *in vivo* com boa biodisponibilidade: ativo em doses baixas, usado por oral em dose-única ao dia;
- Bem absorvido e estável metabolicamente (PK):
 - Propriedades físico-químicas críticas para a atividade do fármaco por via oral: solubilidade, boa partição passiva membrana/água, peso molecular, ligações-H;
- Proteção intelectual (*i.e.* patenteável = conteúdo inventivo);
- Acessível sinteticamente em custos aceitáveis (*scale-up*);
- Tem aplicação médica segura & inovadora (?);

- **... as propriedades moleculares dos fármacos são objeto do estudo da**

Química Medicinal



Química
Medicinal

**Histórico do planejamento
racional de fármacos e a
Química Medicinal:
*Os pioneiros***



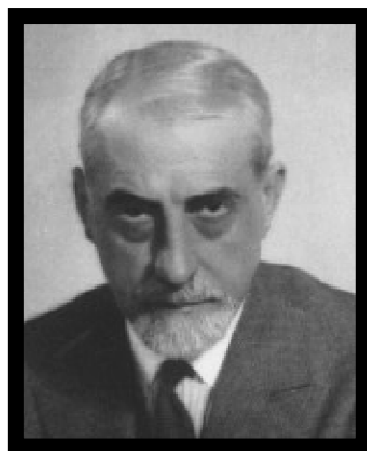
De fármacos e suas descobertas

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

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



O berço da Química Medicinal

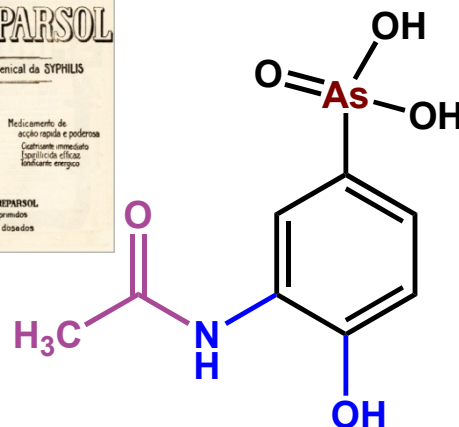


Ernest Fourneau
1872-1949



Stovarsol

CAS 97-44-9



Institut Pasteur (1887)

1911- Laboratoire de Chimie Thérapeutique

Institut Pasteur (Emile Roux)

- 1911-1944 – Jacques Tréfouël (1897-1977)
 Thérèze Tréfouël (1892-1978)
 Germaine Benoit (1901-1983)
 Federico Nitti (1903-1947)



Daniel Bovet
1907-1992 *

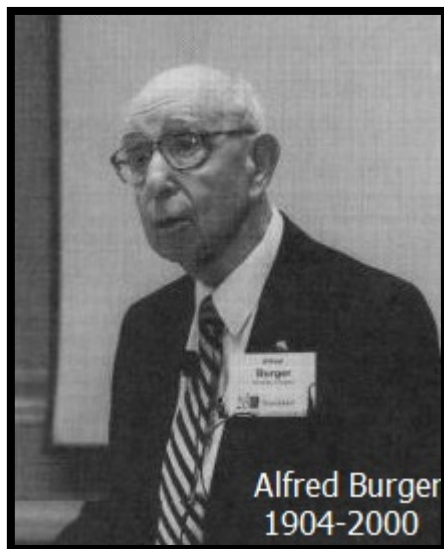
* Farmacêutico suíço
Doutor *h.c.* UFRJ

Prêmio Nobel de
Fisiologia/Medicina
1957



Sulfonamidas,
anti-histamínicos.
Curare: SAR

J-P Fourneau, « Ernest Fourneau fondateur de la Chimie Pharmaceutique française », *Revue de l'Histoire de la Pharmacie*, t.XXXIV, n° 275, 335-355

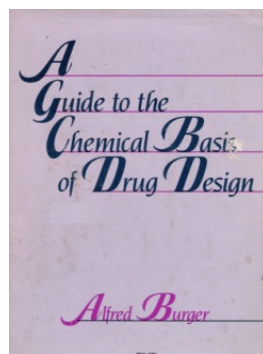
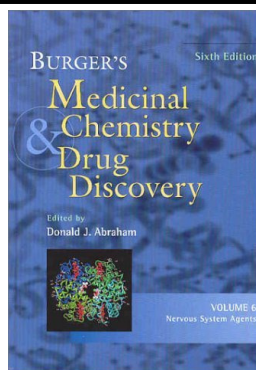


Química Medicinal

Prof. Alfred Burger

(1904-2000)

University of Virginia
EUA



1958 – cria o Journal of the Medicinal and Pharmaceutical Chemistry → depois Journal of Medicinal Chemistry

“An Editor’s Commentary on the Birth of a Journal”
J. Med. Chem. **1991**, 34, 2-6

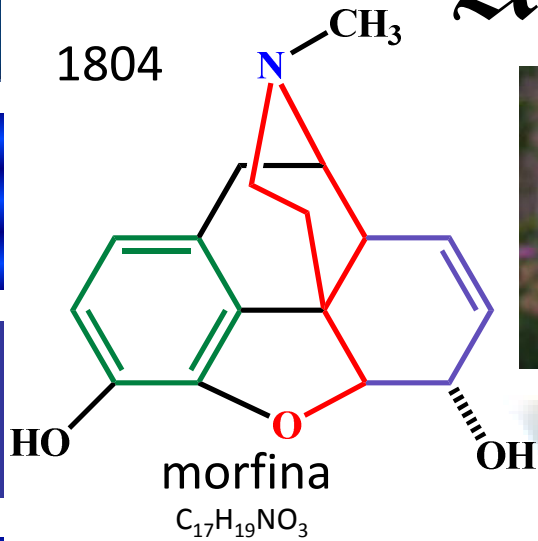


1978 - GlaxoSmithKline cria com ACS o “Alfred Burger Award” em Química Medicinal
T. Y. Shen - inventor da indometacina



As moléculas pioneiras...

1804

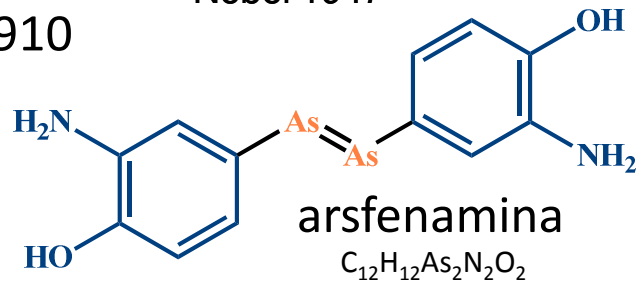


Friedrich W. A. Sertürner
1783- 1841

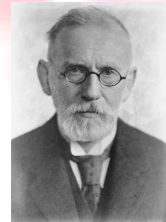


Sir Robert Robinson
1886-1975
Nobel 1947

1910



Paul Ehrlich
1854-1915
Nobel 1908

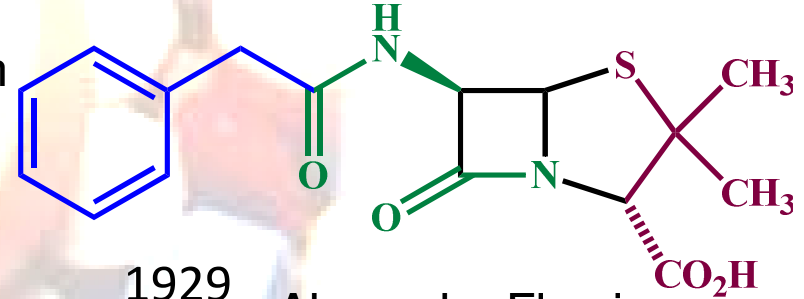


Library of Congress

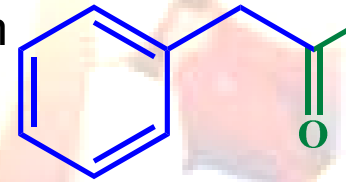


1929

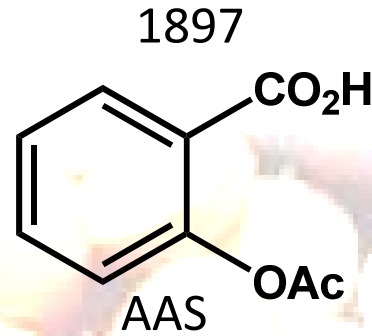
Alexander Fleming
1881-1955
Nobel 1945



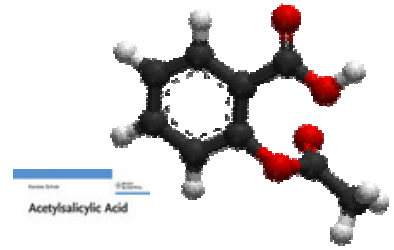
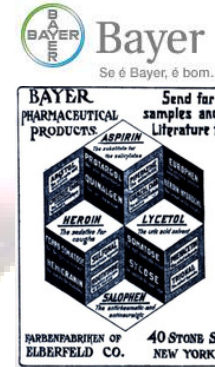
Felix Hoffman
1868- 1946

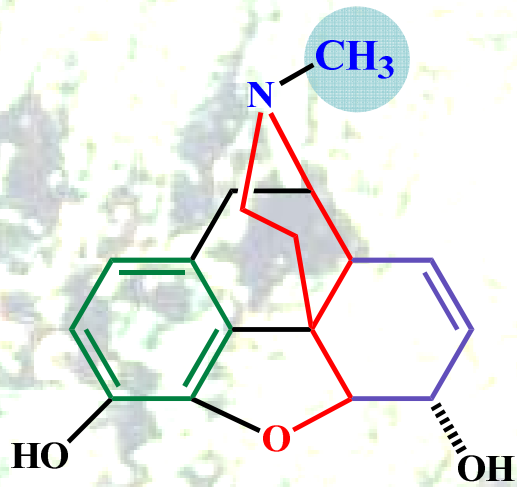


C₉H₈O₄



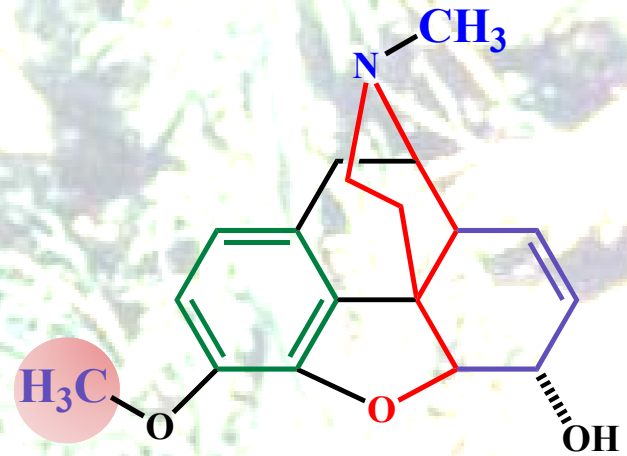
1897





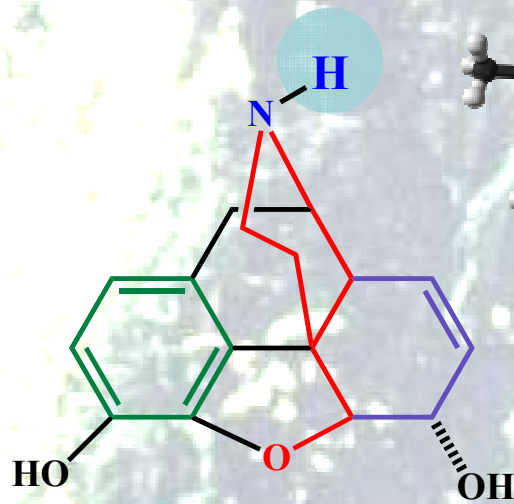
morfina

1853 - Henry How
Un Glasgow
1º derivado sal 4^{ario}

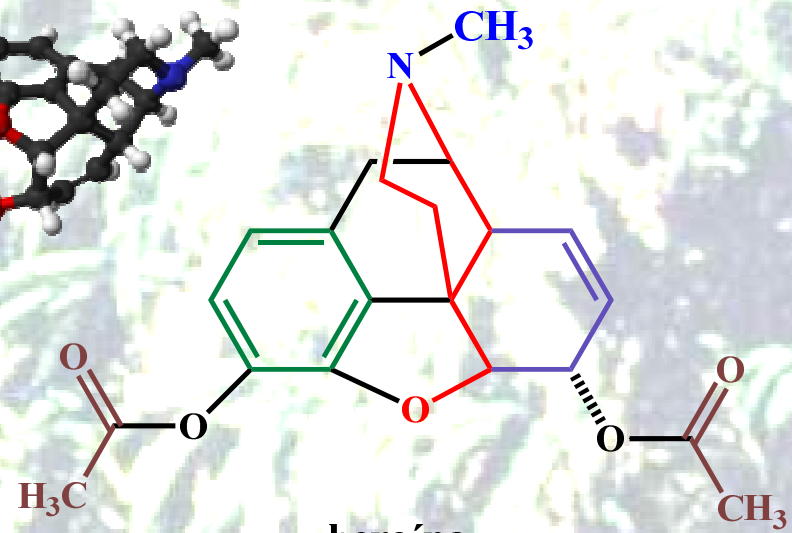
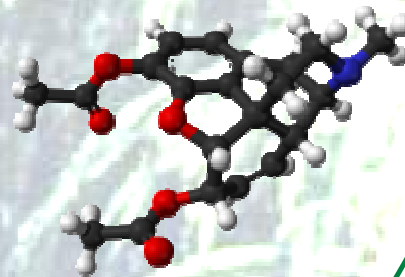


codeína

O-metil morfina

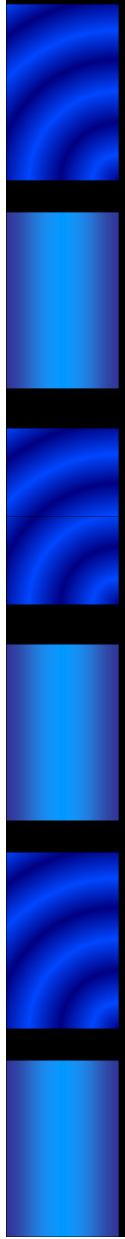
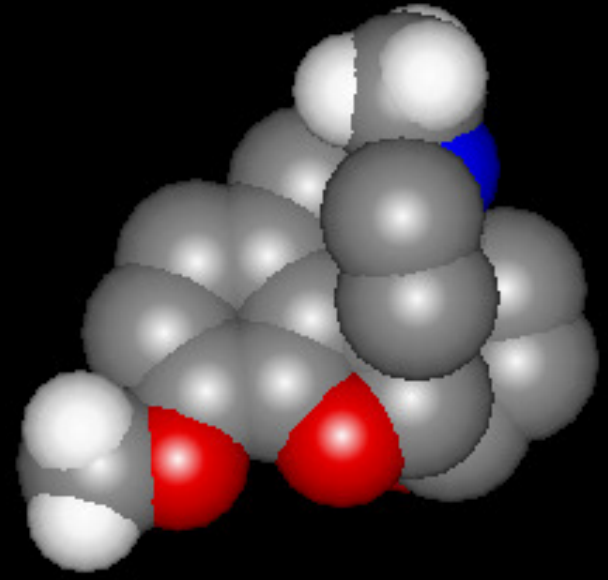
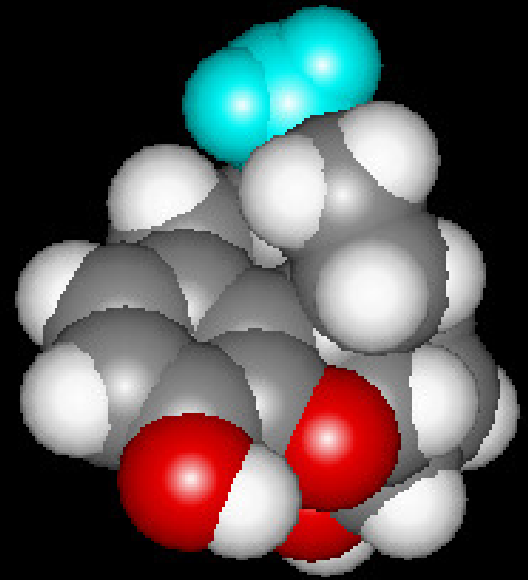
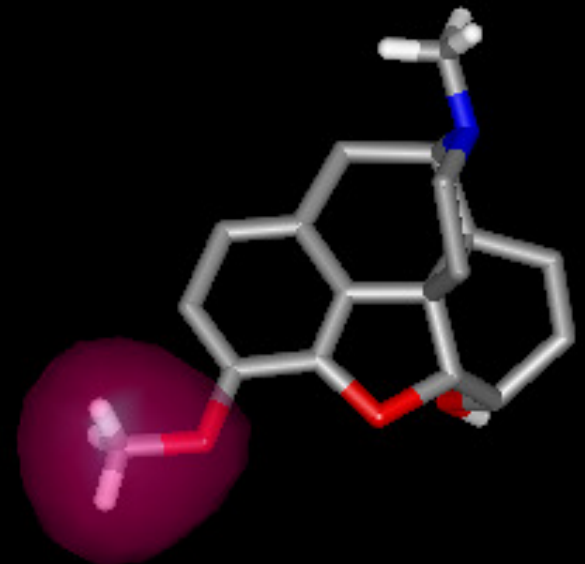
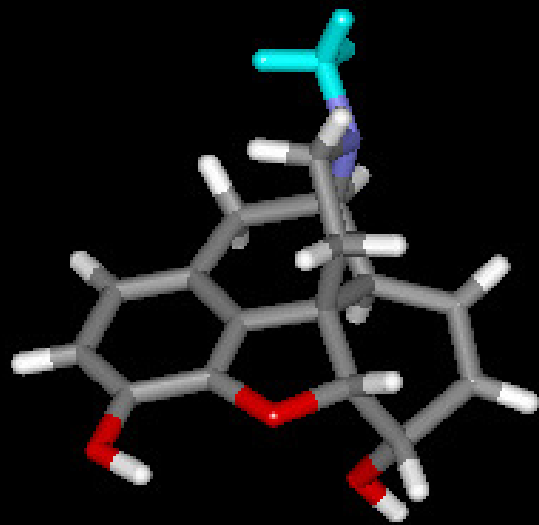


nor-morfina



heroína

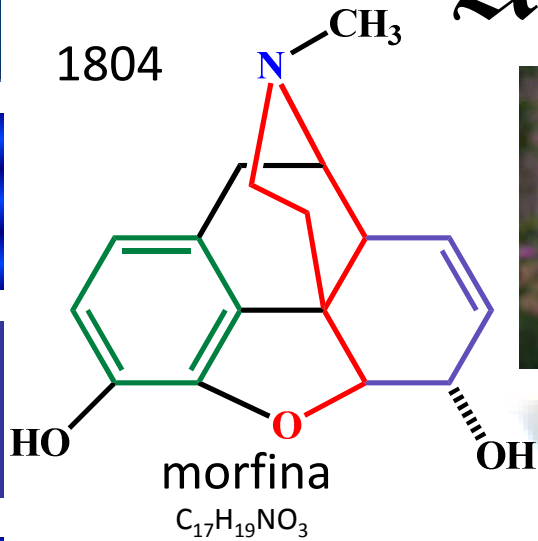
Diacetil-morfina





As moléculas pioneiras...

1804

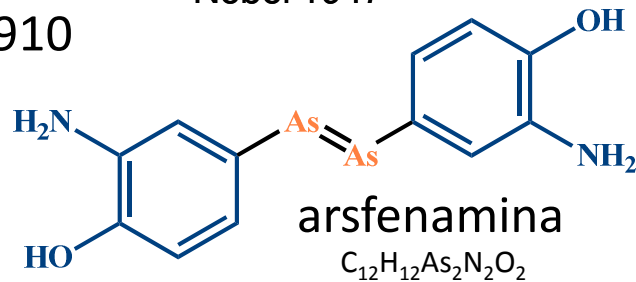


Friedrich W. A. Sertürner
1783- 1841

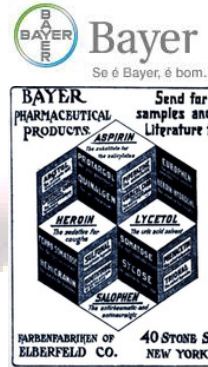
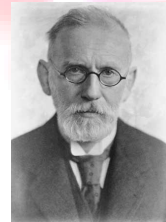


Sir Robert Robinson
1886-1975
Nobel 1947

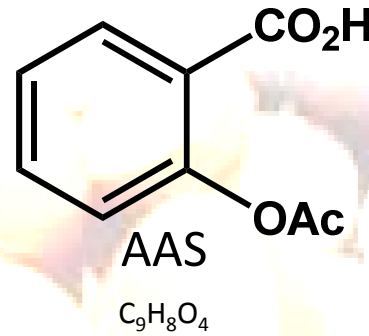
1910



Paul Ehrlich
1854-1915
Nobel 1908



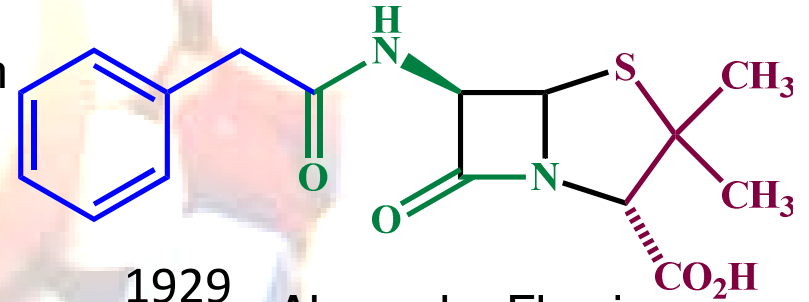
1897



Felix Hoffman
1868- 1946



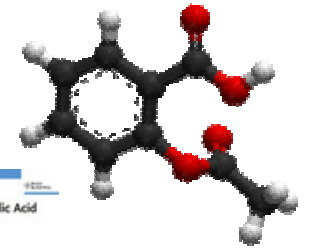
1929



Alexander Fleming
1881-1955
Nobel 1945

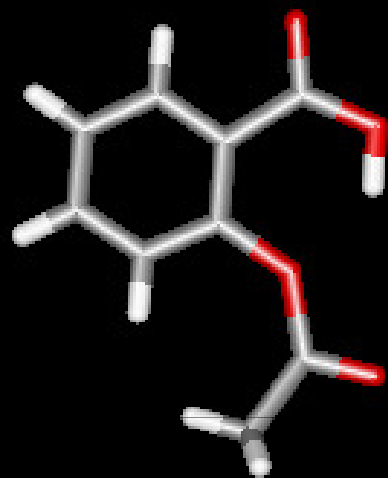


Library of Congress





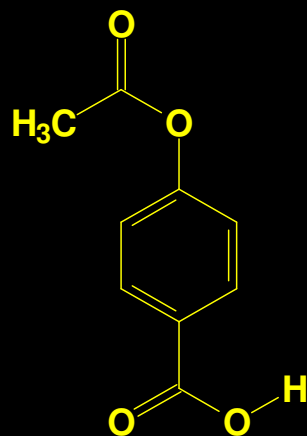
Isomêros do ácido acetil salicílico (AAS)



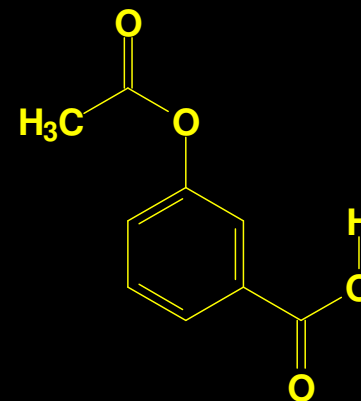
orto



para



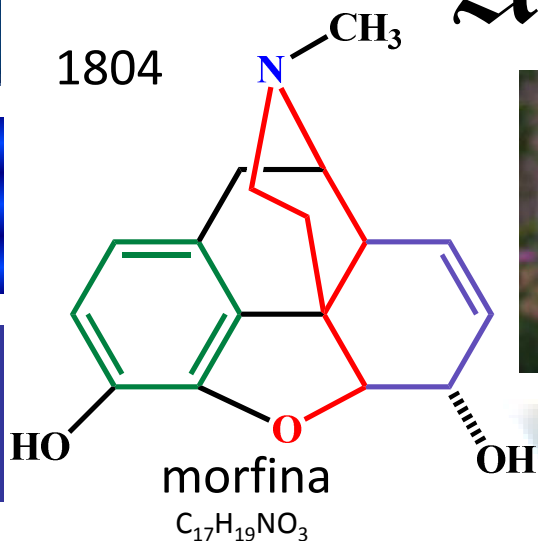
meta





As moléculas pioneiras...

1804



Friedrich W. A. Sertürner
1783- 1841

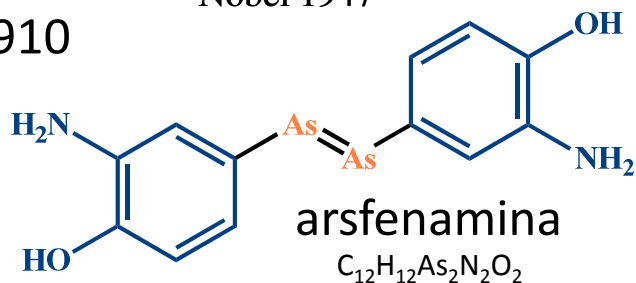


Felix Hoffman
1868- 1946

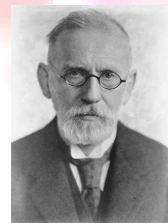


Sir Robert Robinson
1886-1975
Nobel 1947

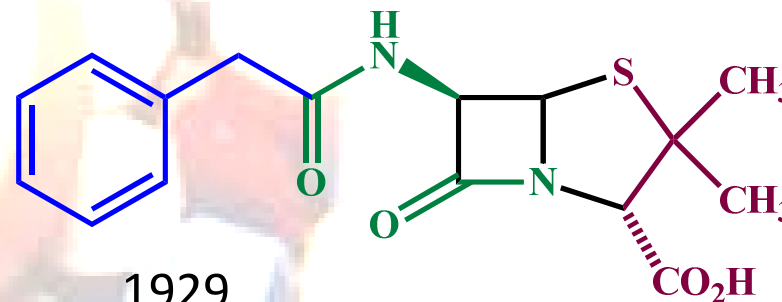
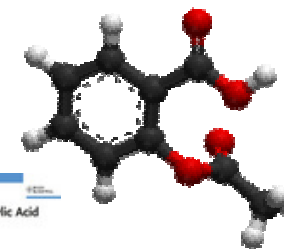
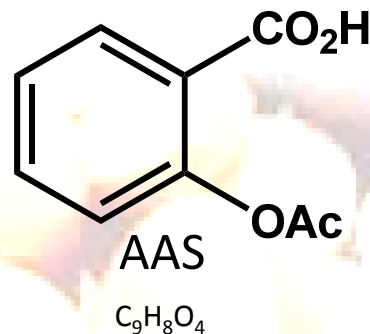
1910



Paul Ehrlich
1854-1915
Nobel 1908

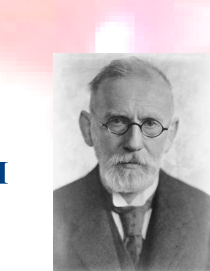


1897



1929

Alexander Fleming
1881-1955
Nobel 1945



Library of Congress



Med
Chem



Paul Ehrlich

1854-1915

Nobel 1908

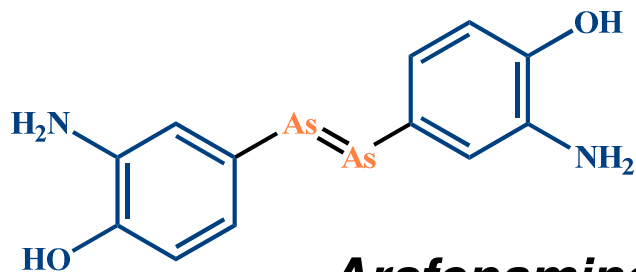


Patente 10 de junho de 1909;
Farbwerk Hoeschst 1910

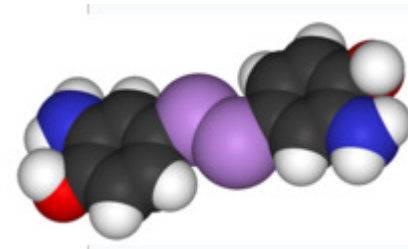
Ber. 1912, 45, 756

Berichte der
Deutschen
Chemischen
Gesellschaft

Deutsche
Chemische
Gesellschaft, ...

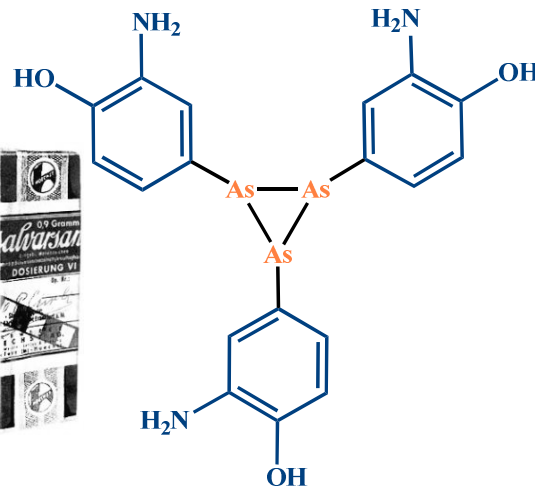


Arsfenamina

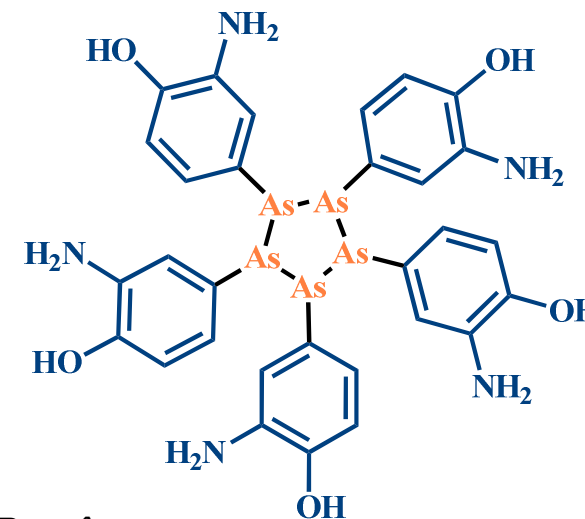
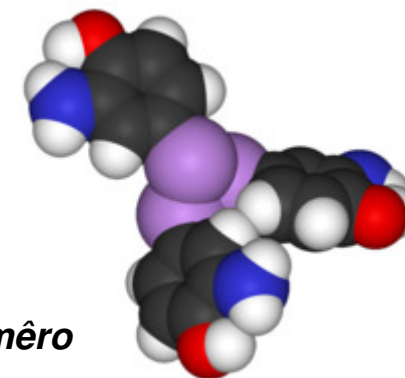


Salvarsan^R

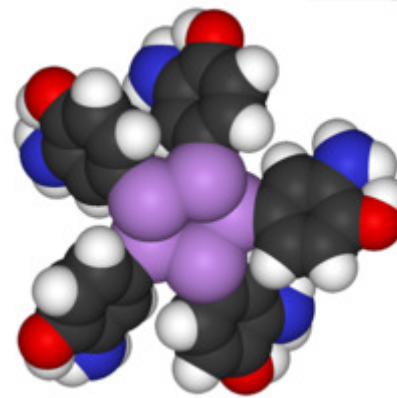
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Trimêro



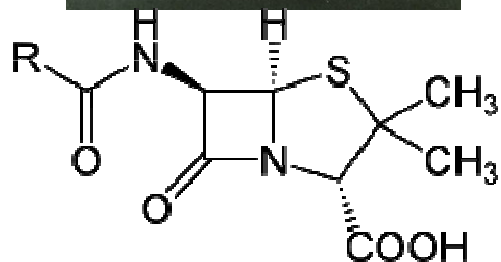
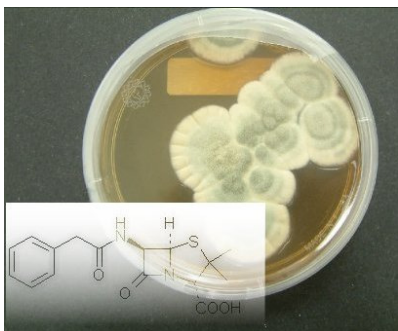
Pentâmero



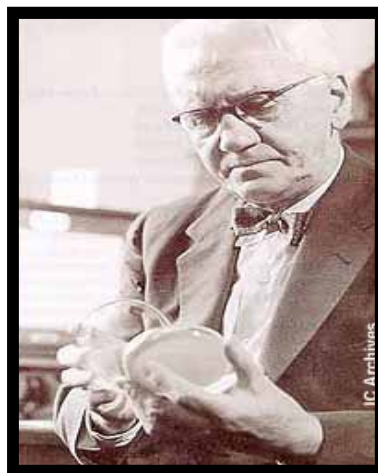
NC Lloyd, HW Morgan, BK Nicholson, RS Ronimus "The composition of Ehrlich's salvarsan: resolution of a century-old debate". *Angew. Chem. Int. Ed. Engl.* 2005, 44, 941.



Fármaco Salva-vidas

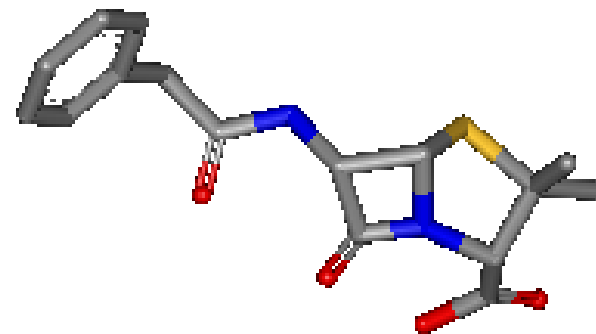


- 1896 - Robert Duchesne
- 1928 – A Fleming
- 1939 – Florey & Chain
- 1943 - Andrew J Moyer
- 1945 - Dorothy C. Hodgkin
- 1948 - Patente
- 1957 –John Sheehan



Alexander Fleming

1881-1955



Penicilina



Howard W. Florey

1898-1968



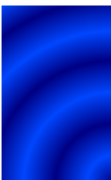
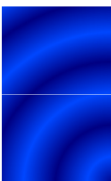
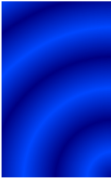
<http://nobelprize.org>

1945



Ernest B. Chain

1906-1979



Os fármacos
e o Prêmio
Nobel

Química
Medicinal

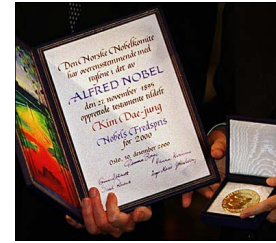




Os fármacos e o Nobel !



1982



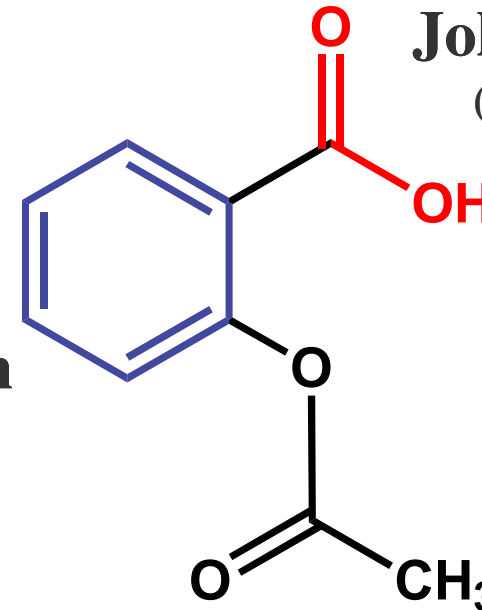
John R. Vane
(1927-2004)



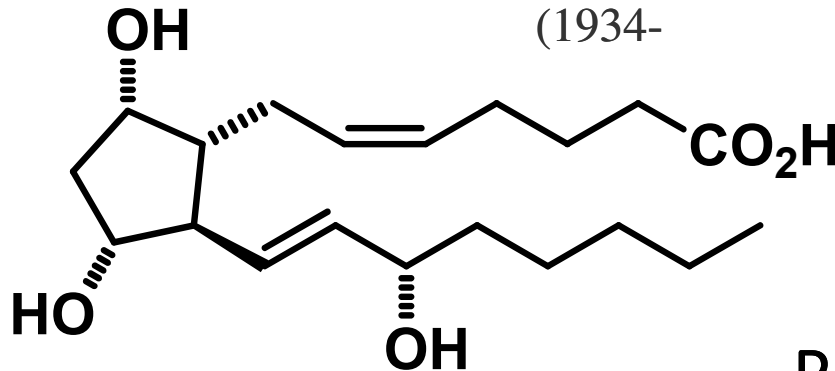
Sune K. Bergström
(1916-2004)



Bengt I. Samuelsson
(1934-



1982 – AAS



$C_9H_8O_4$

Prostaglandina F_{2α}

■ 196 pesquisadores

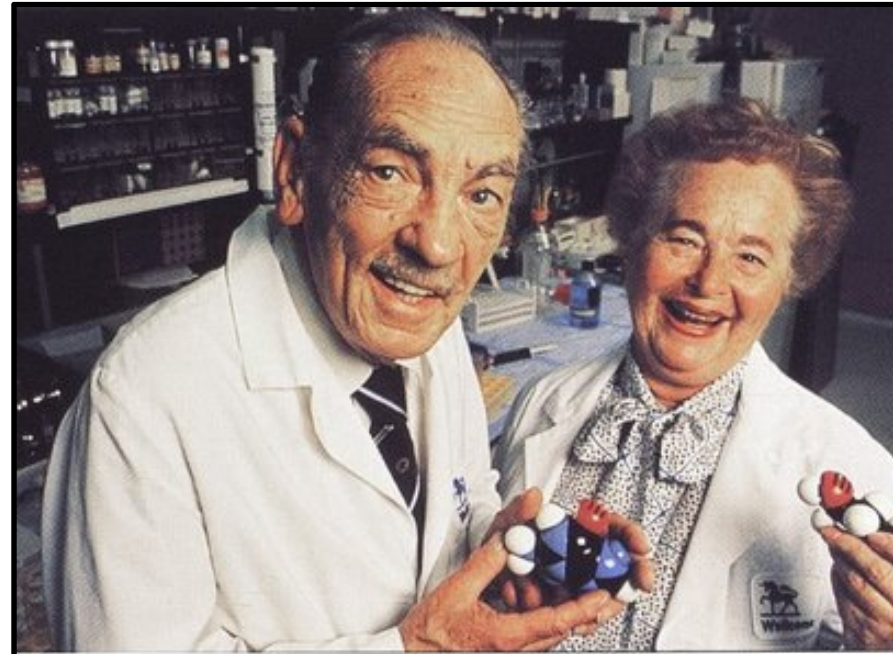
ganharam o Prêmio Nobel de Medicina
(1901-2010)



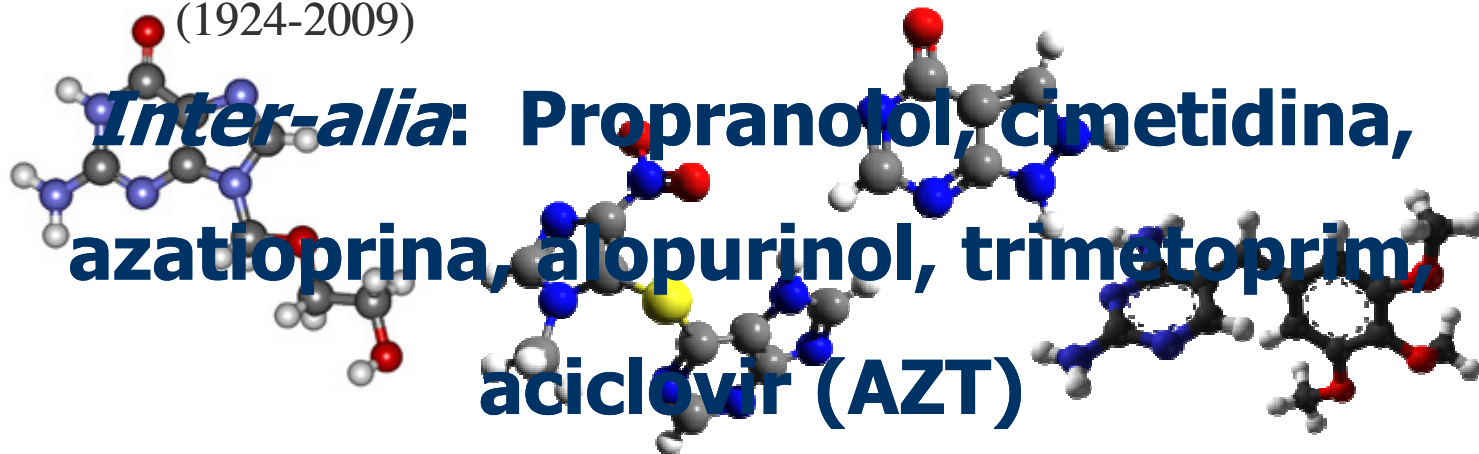
“for their discoveries of important principles for drug treatment”



James W. Black
(1924-2009)



George Hitchings **Gertrude B. Elion**
(1905-1998) (1918-1999)

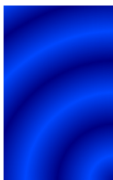
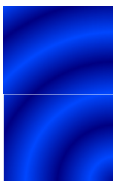
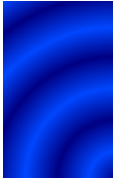


1988



Química
Medicinal

O processo ...
(O Paradigma
de Ehrlich &
Fischer)



Emil Fischer
 1852-1919
1902
 E. Fischer, Ber. Dtsch.
 Chem. Ges. 1890, 23, 799

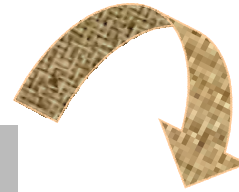


Paul Ehrlich
 1854-1915
1908

O paradigma de Ehrlich & Fischer



LOCK & KEY
 CONCEPT



Biorreceptor

macrobíomolécula
 baseado no sítio de
 reconhecimento



**Planejamento
 racional**

BSRM

BL-AA



Fármaco

micromolécula

baseado no ligante
 / análogo-ativo



THE LANCET

Physiologic
A abordagem
 approach
fisiológica

"In patients with locally advanced or high-risk local prostate cancer, addition of local radiotherapy to endocrine treatment halved 10-year prostate-cancer-specific mortality."

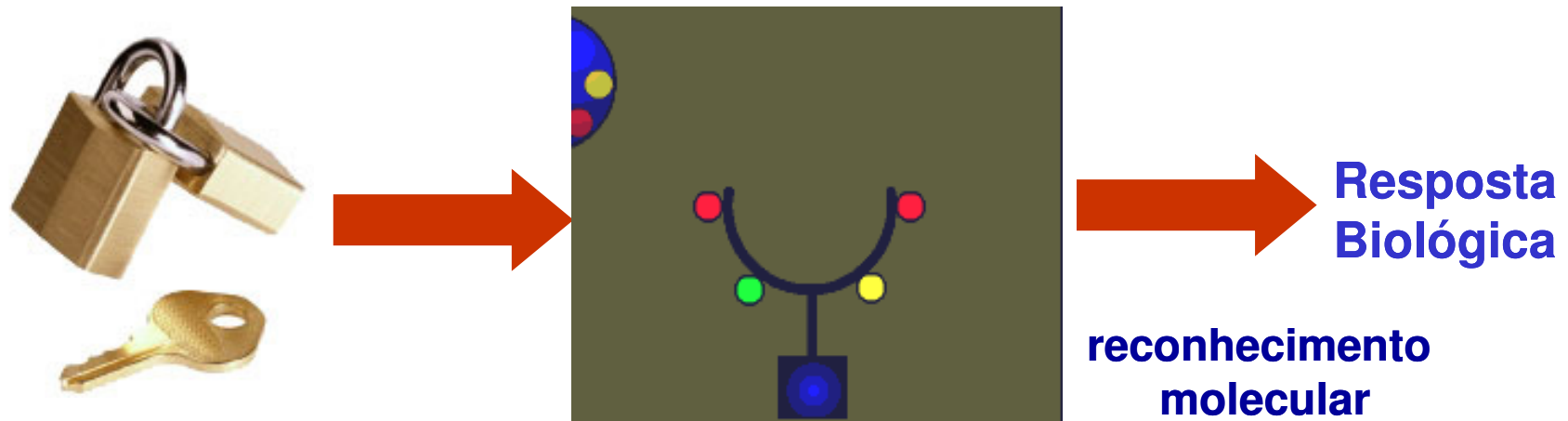
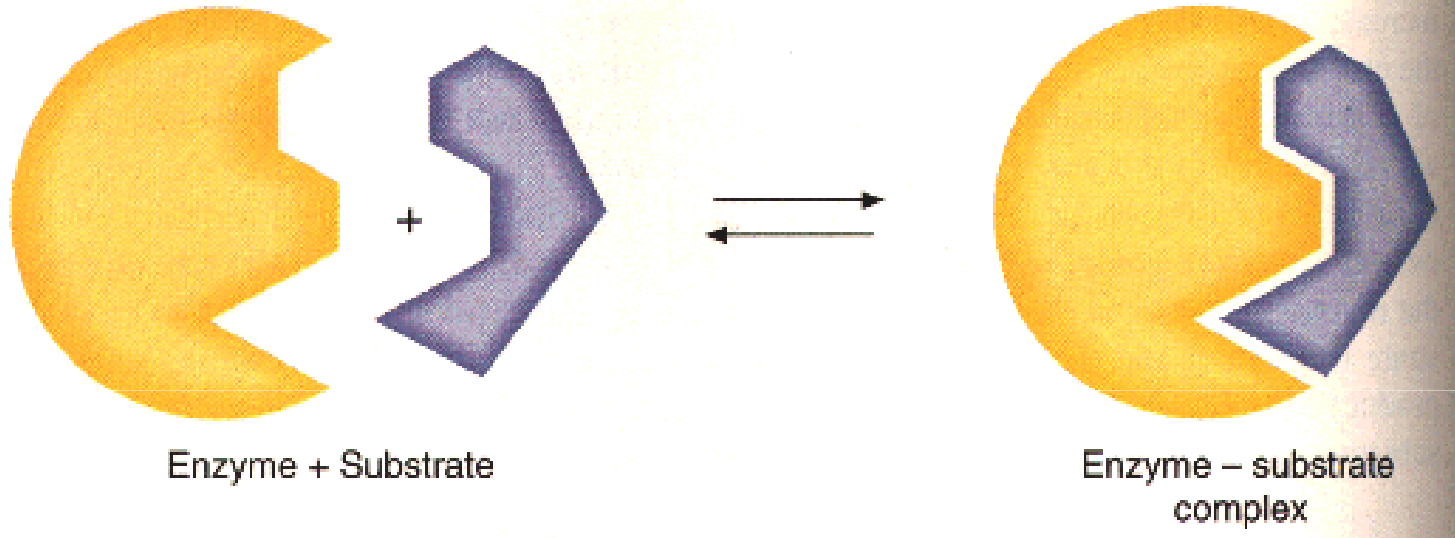


P. Ehrlich, *Chemotherapeutics: scientific principles, methods and results.* Lancet 1913, 2, 445



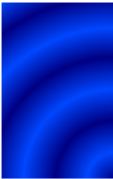
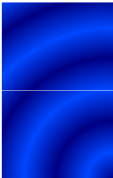
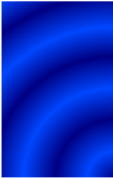
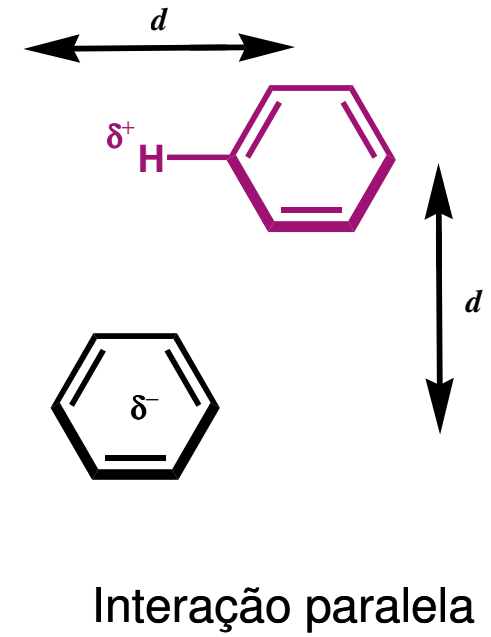
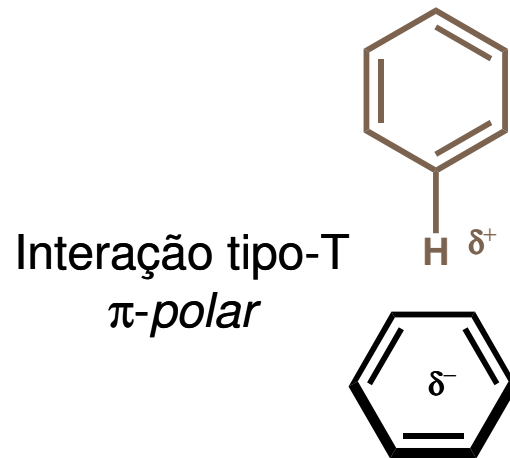
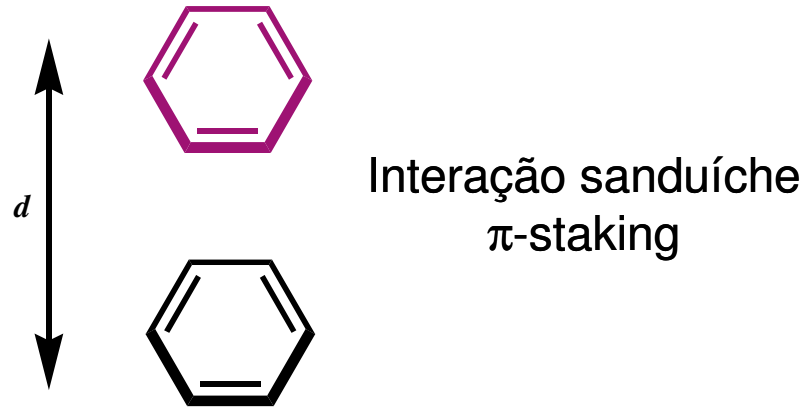
Modelo Chave-Fechadura

Enzyme Catalysis



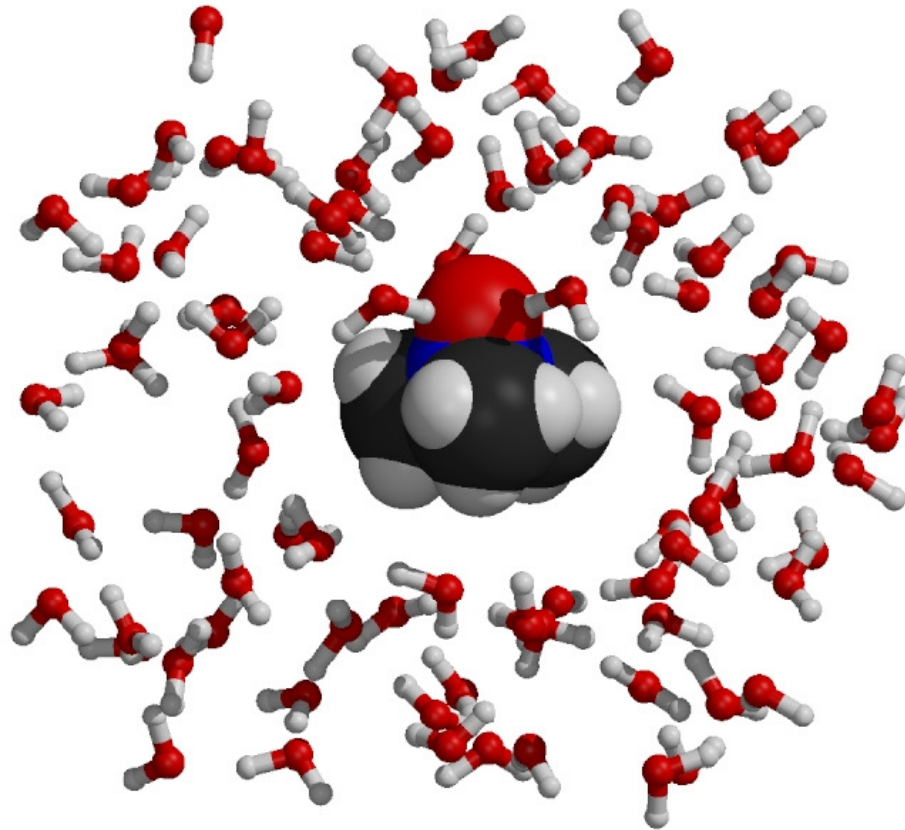
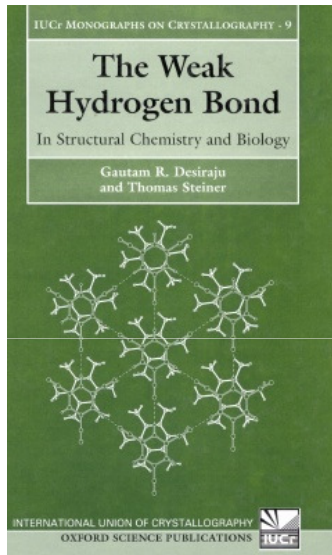
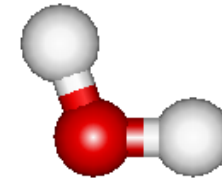


Interações π - π

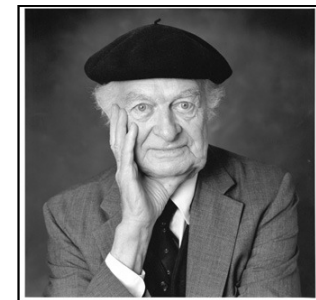




A importância das “*ligações*” frágeis...



“*ligações*”
de hidrogênio ...



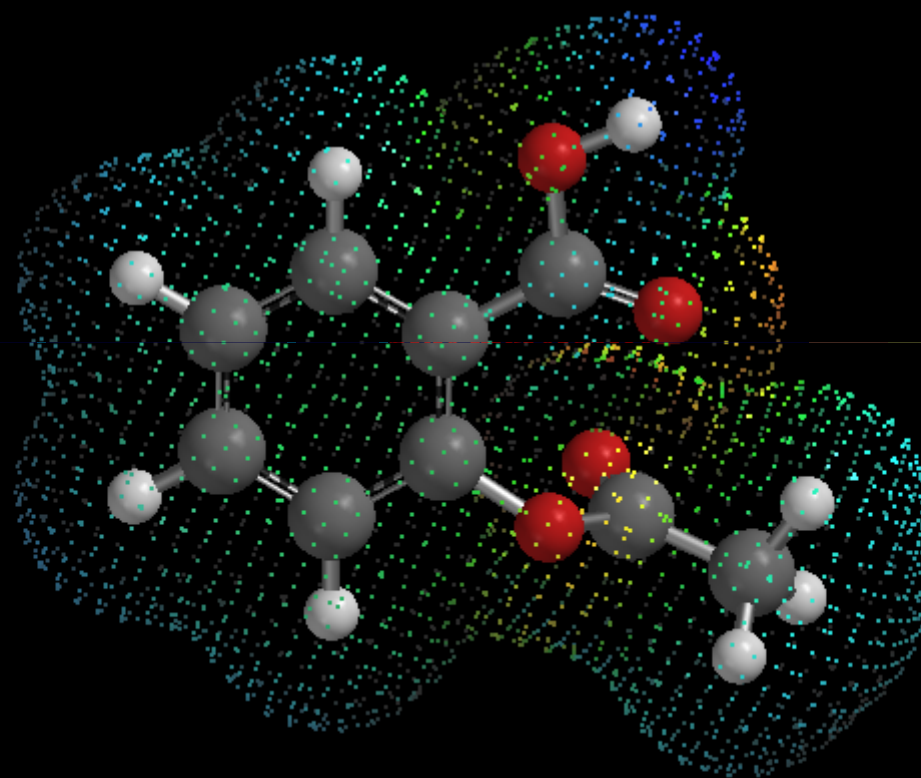
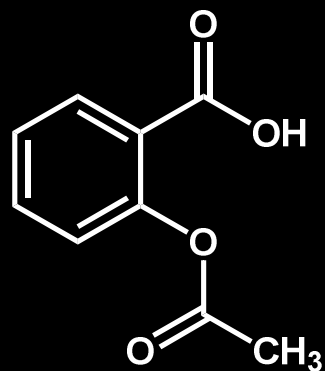
Linus Pauling
1901-1994

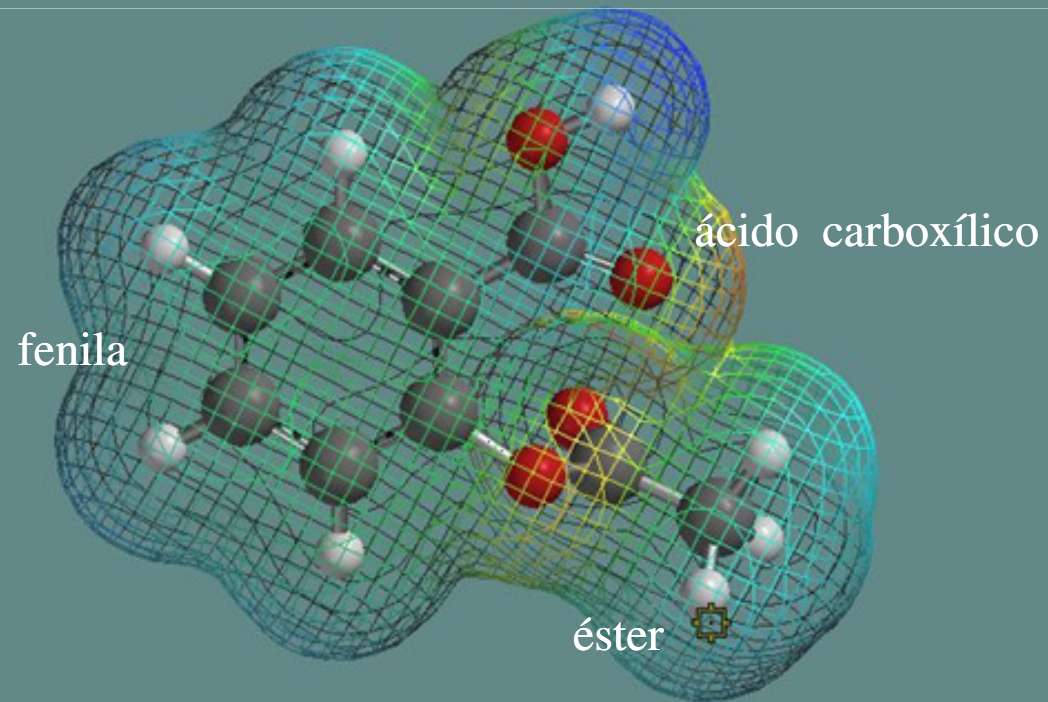
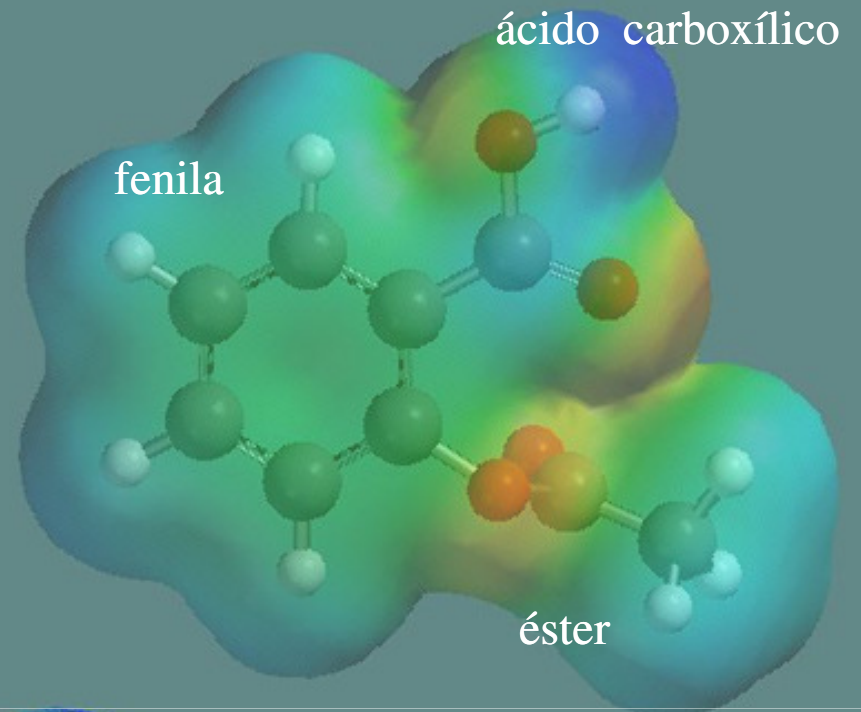
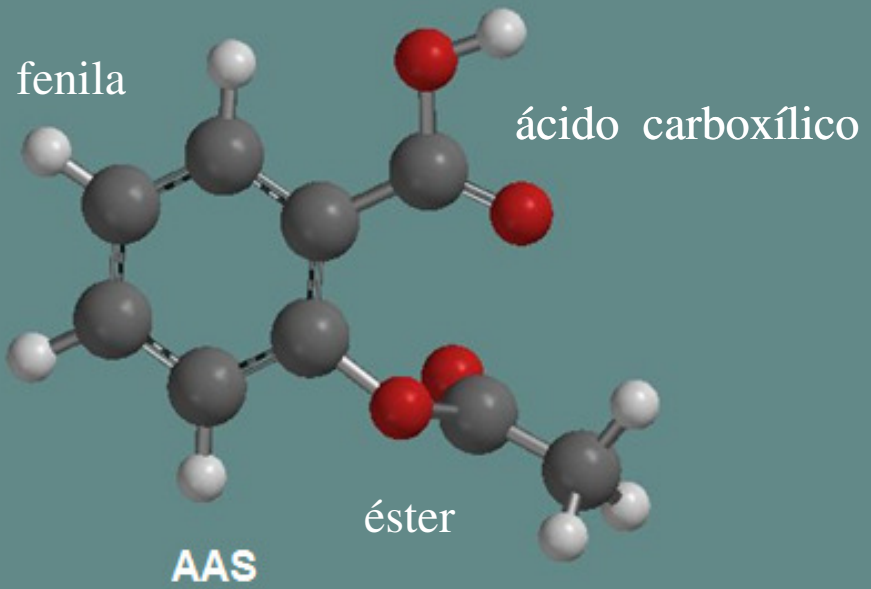
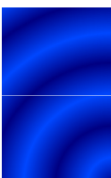
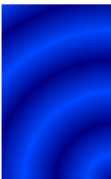


1954 & 1962



O Centenário Modelo "Chave-Fechadura"







Como as chaves
acham as
fechaduras ?

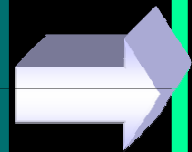
Como os fármacos
chegam aos
alvos terapêuticos ?



Medicamento

F
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O



Química Medicinal

Fase farmacêutica

Excreção

Eliminação renal

Bile, fezes, pulmão

Biofase

Agente de depósito

Bioinativação

tóxico

Complexo tissular

Bioativação

Distribuição

Hepática, plasmática, entérica

Absorção

Metabolismo

F-R

E.T.

Polimorfismo, idade, raça, sexo

PQF

P
pKa
D

Complexo plasmático

Indução / inibição enzimática

Agente de deslocamento

Afinidade
Potência
Eficácia
Sinergismo

Vida-média

Agente de co-solubilidade

Fármaco

Fase farmacocinética (ADME)

Fase farmacodinâmica



Biofase

Absorção

Concentração

Meia-vida

Posologia

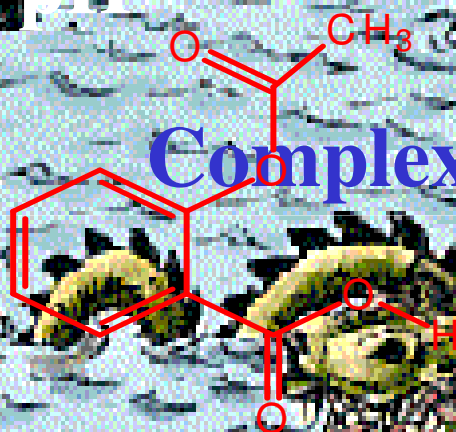
pH

Complexação plasmática

Deposito tissular

Metabolismo

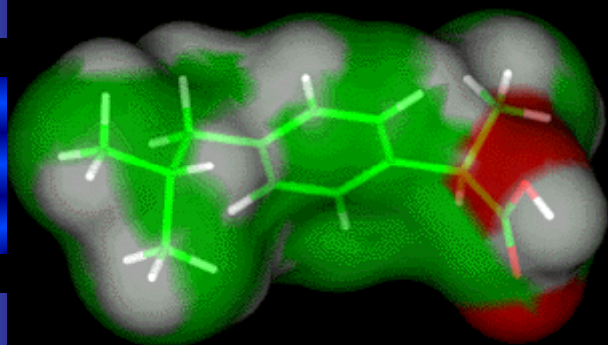
Eliminação



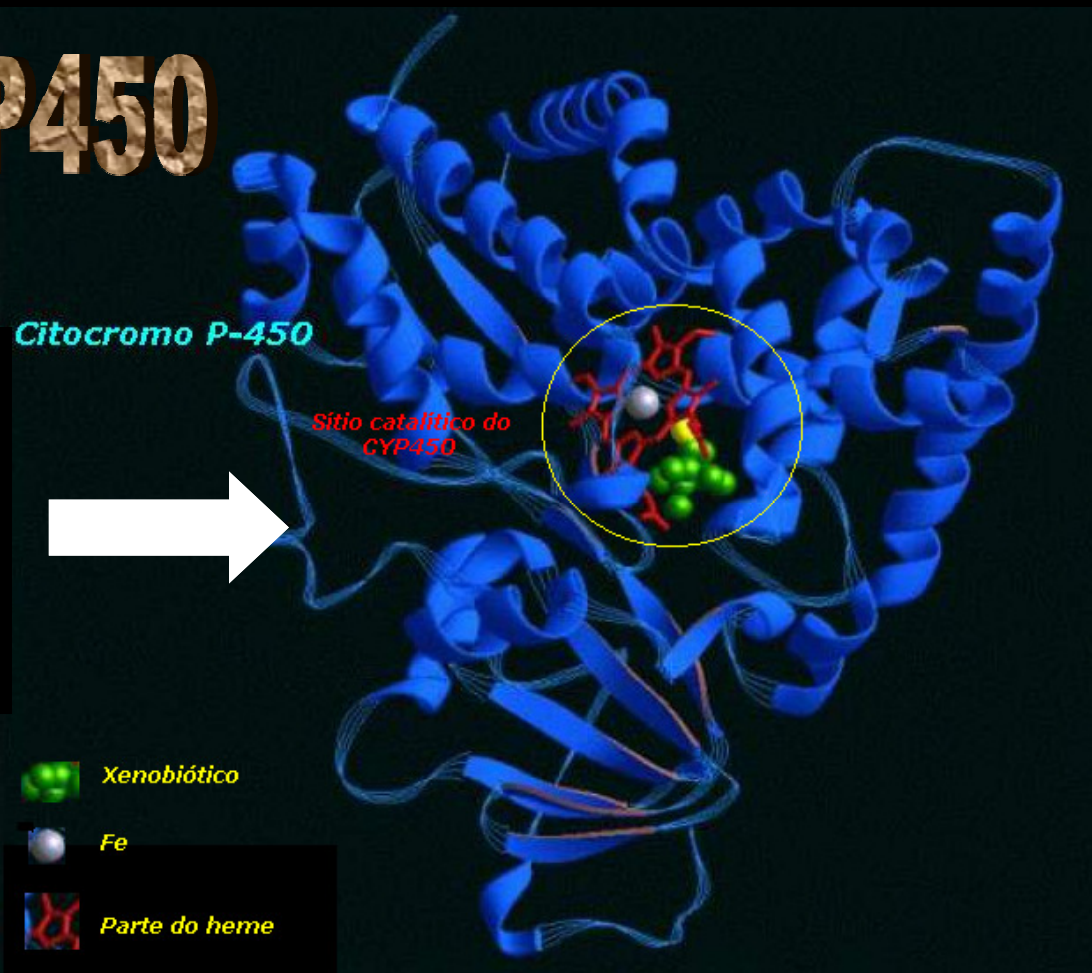


Enzimas oxidativas: fase 1

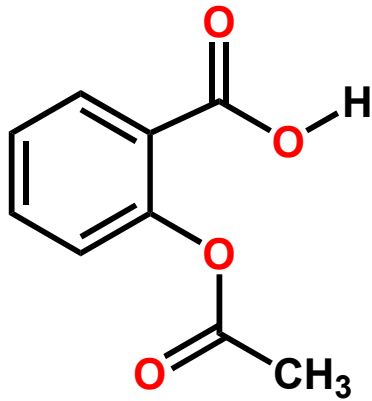
Citocromo P450



Fármaco



Retículo microssomal hepático



$C_9H_8O_4$

PM = 180 g



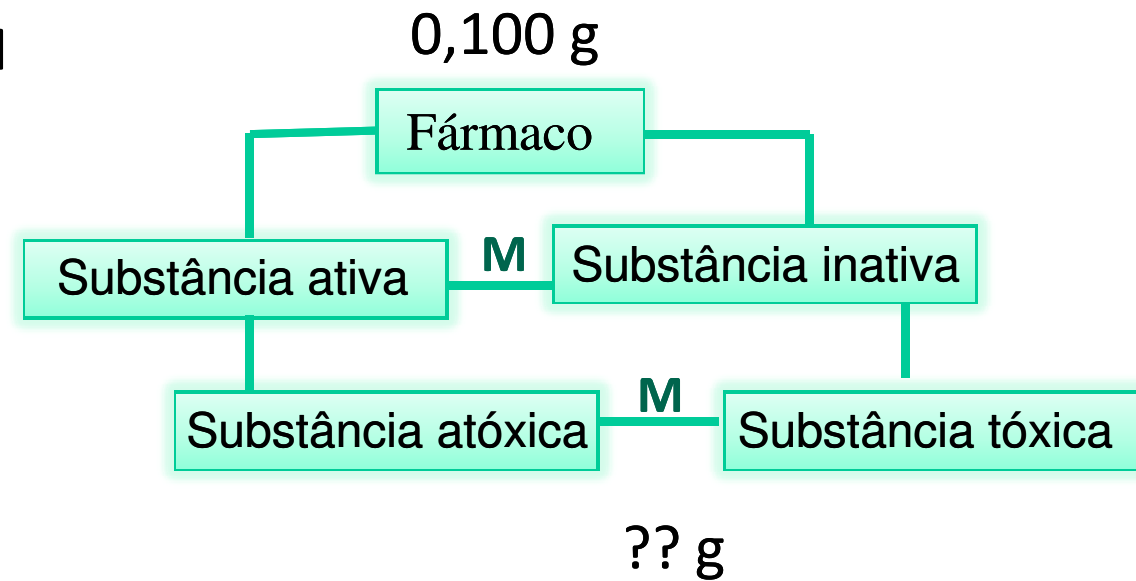
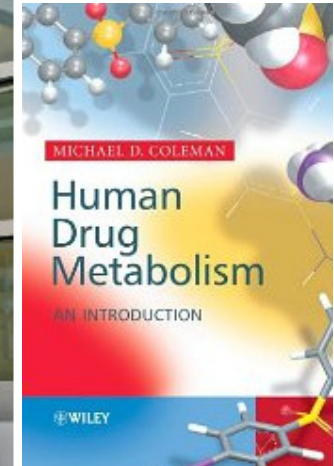
0,100 g ~ 0,5 M

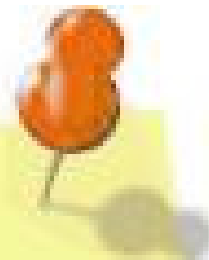
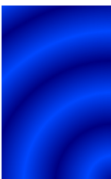
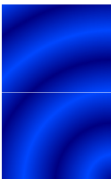
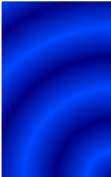


70 kg



VERTICAL PATH
Time-of-flight mass spectrometers, such as the one shown here, can now achieve high levels of resolving power.





^{m e d}
Química
^{c h e m}
Medicinal

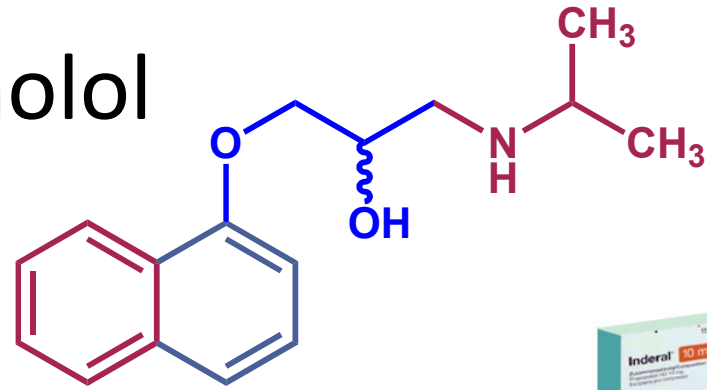
O processo ...

A invenção do
propranolol



A invenção do propranolol

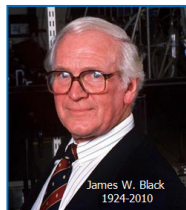
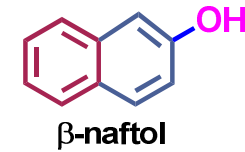
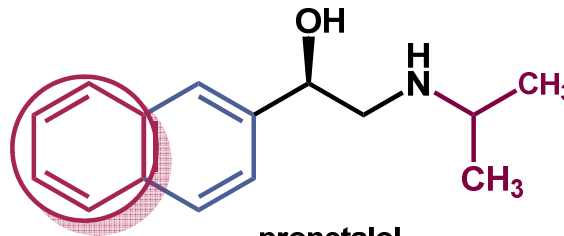
m e d
Química
Farmacêutica
chem
Medicinal



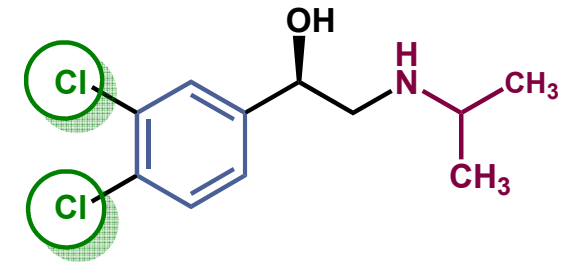
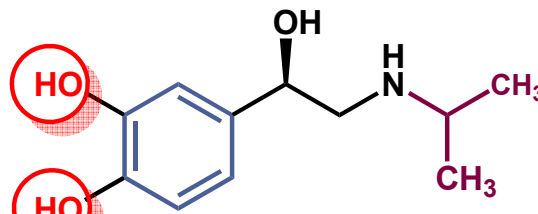
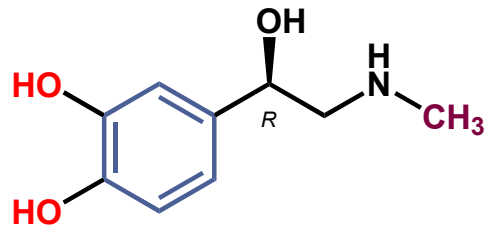
propranolol
1964

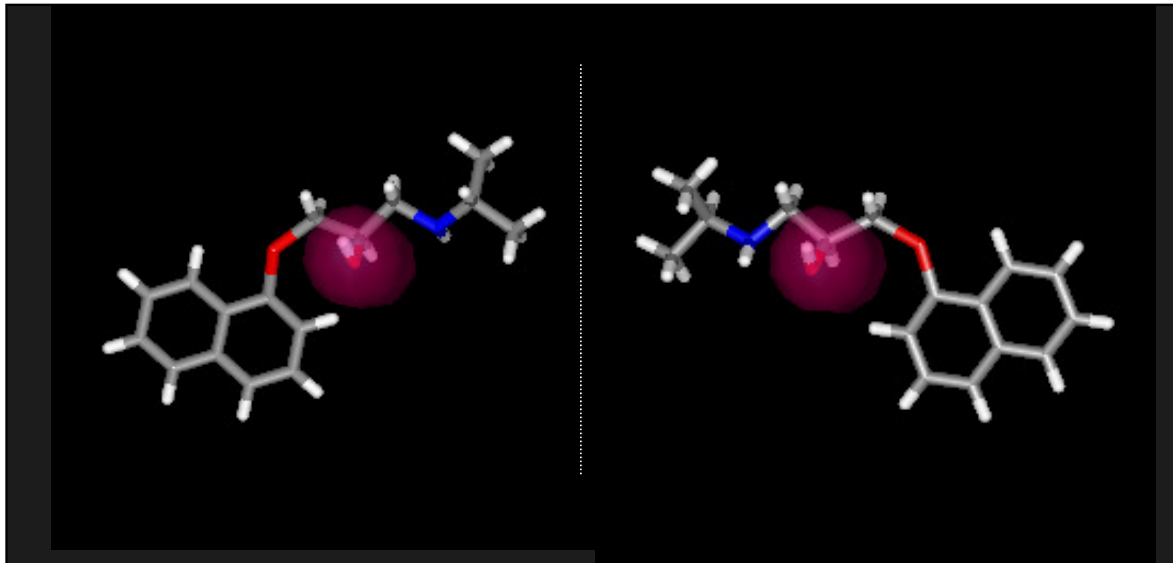


J. Black et al., *Br. J. Pharmacol. Chemother.* **1965**, 25, 577



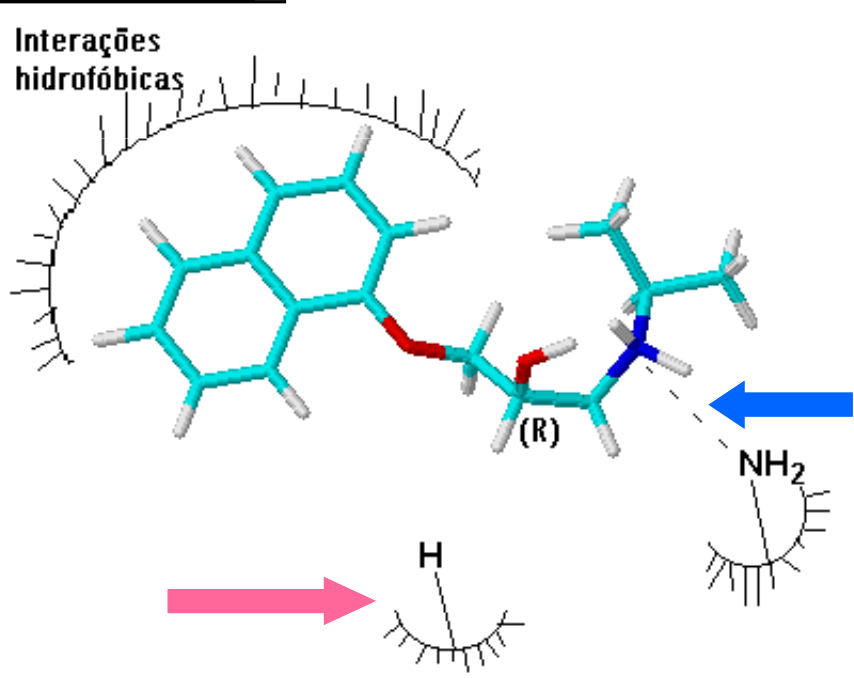
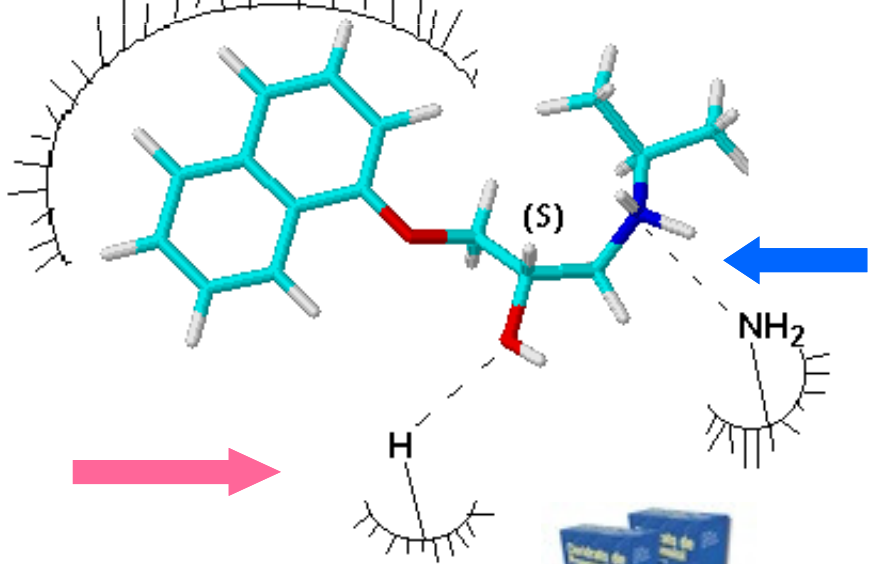
James W. Black, 1988 - "Pronethalol always seemed to us to be a prototype drug, good enough to answer questions of principle, but not good enough to be marketable"





Eutômero
Distômero

Interações hidrofóbicas
Propranolol (18)



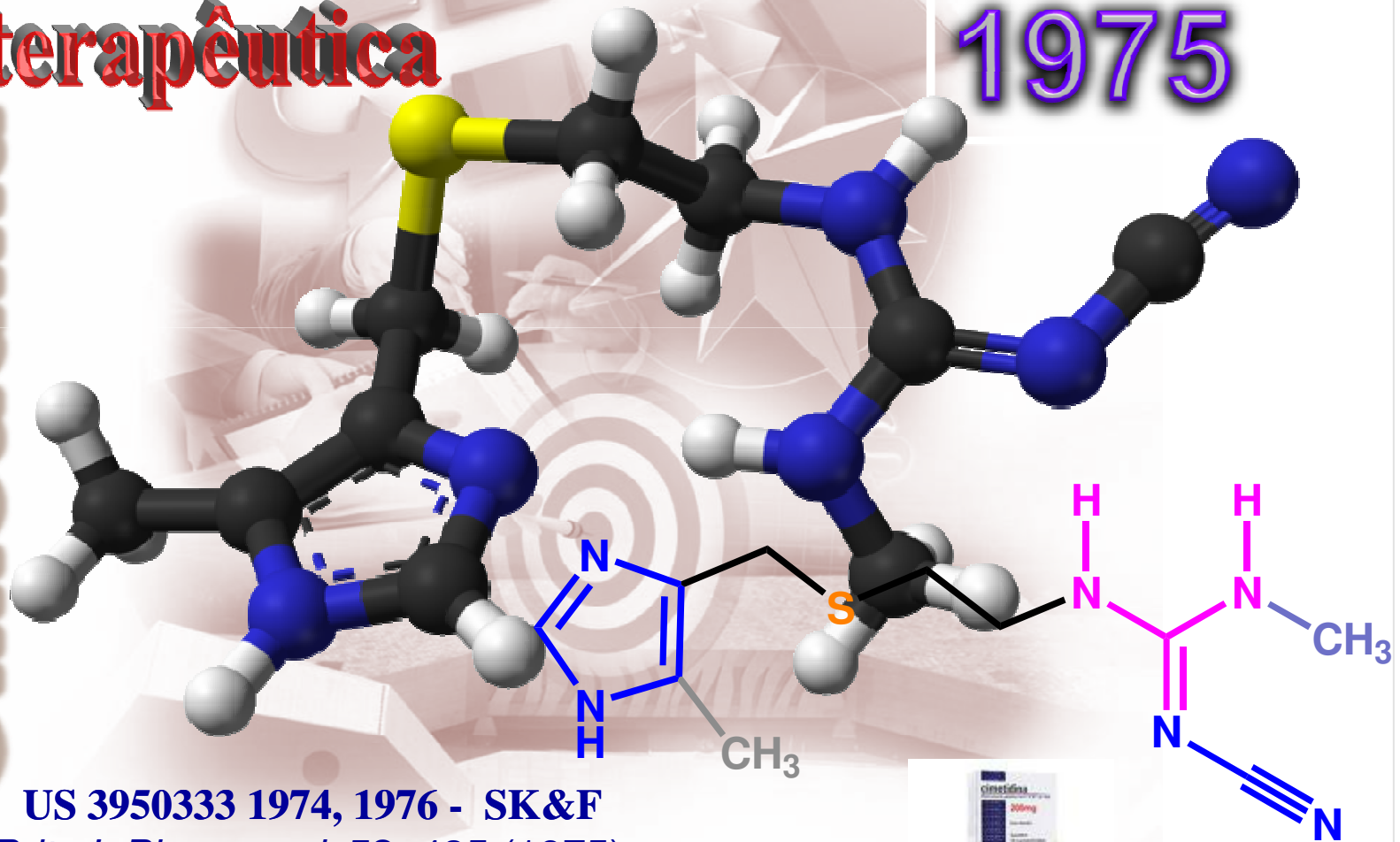


O desenvolvimento racional

Inovação
terapêutica

1975

Cimetidina



US 3950333 1974, 1976 - SK&F
Brit. J. Pharmacol. **53**, 435 (1975).

James Black, Robin Ganellin, Emmett, Durant





Sir James W. Black: *drug hunter*

Química Medicinal

"During the last forty years I have seen the tremendous success that the pharmaceutical industry has achieved by basing its drug strategy around the naturally occurring molecules, hormone and substrates, etc. These native molecules were the leads. Close analogues and derivatives were then designed around these leads. Classical bioassays and biochemistry were able to select-in those compounds that competed with the native molecule for the same active site. Compounds with a high degree of selectivity were regularly produced. The new strategy (ie, combinatorial chemistry and HTS) may not be so lucky. Proteins are inherently 'sticky' molecules. There may well be a danger that the binding reactions used in the high-throughput screening that is used in conjunction with combinatorial chemistry will select-in nonspecific molecules. Non-selectivity may not become visible until the development stage involving intact animals is reached. Too much combinatorial chemistry might well come to be seen as a risk factor to the corporate health"¹².



James Whyte Black

1924-2010

[R Ganellin & W Duncan, *Nature* **2010**, 464, 1292]



Prêmio Nobel de Medicina
1988

J. Black, Future perspectives in pharmaceutical research.
Pharm. Policy Law. 1, 85-92 (1999).



Inventor de moléculas mágicas & inovadoras

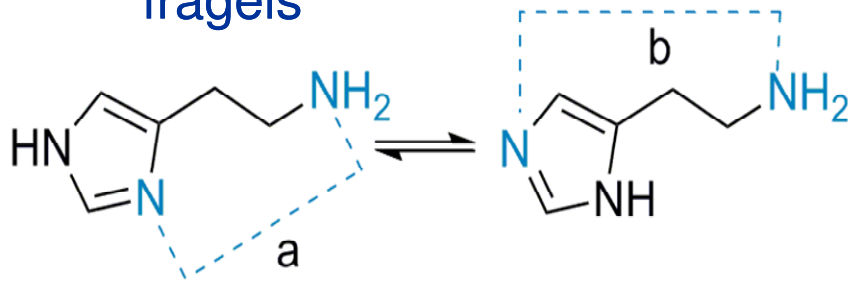
Cimetidina



Abordagem Fisiológica

Química Medicinal

Interações frágeis



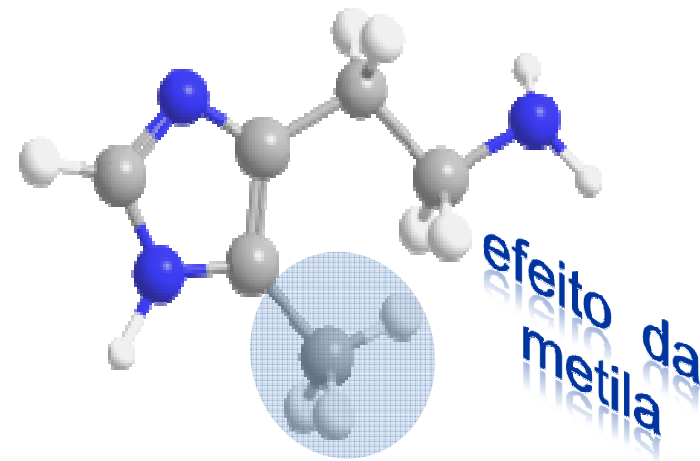
Forma A

$a = 4,83 \text{ \AA}$
 $b = 5,52 \text{ \AA}$

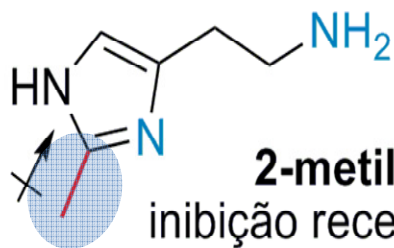
Forma B

tautomêros

Propriedades estruturais

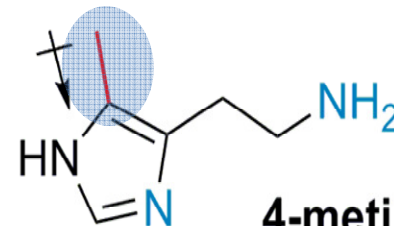


4-metil-histamina



2-metil-histamina

inibição receptores $H_1 = 17\%$
inibição receptores $H_2 = < 2\%$



Análogo ativo

4-metil-histamina

inibição receptores $H_1 = 0,2\%$
inibição receptores $H_2 = 50\%$

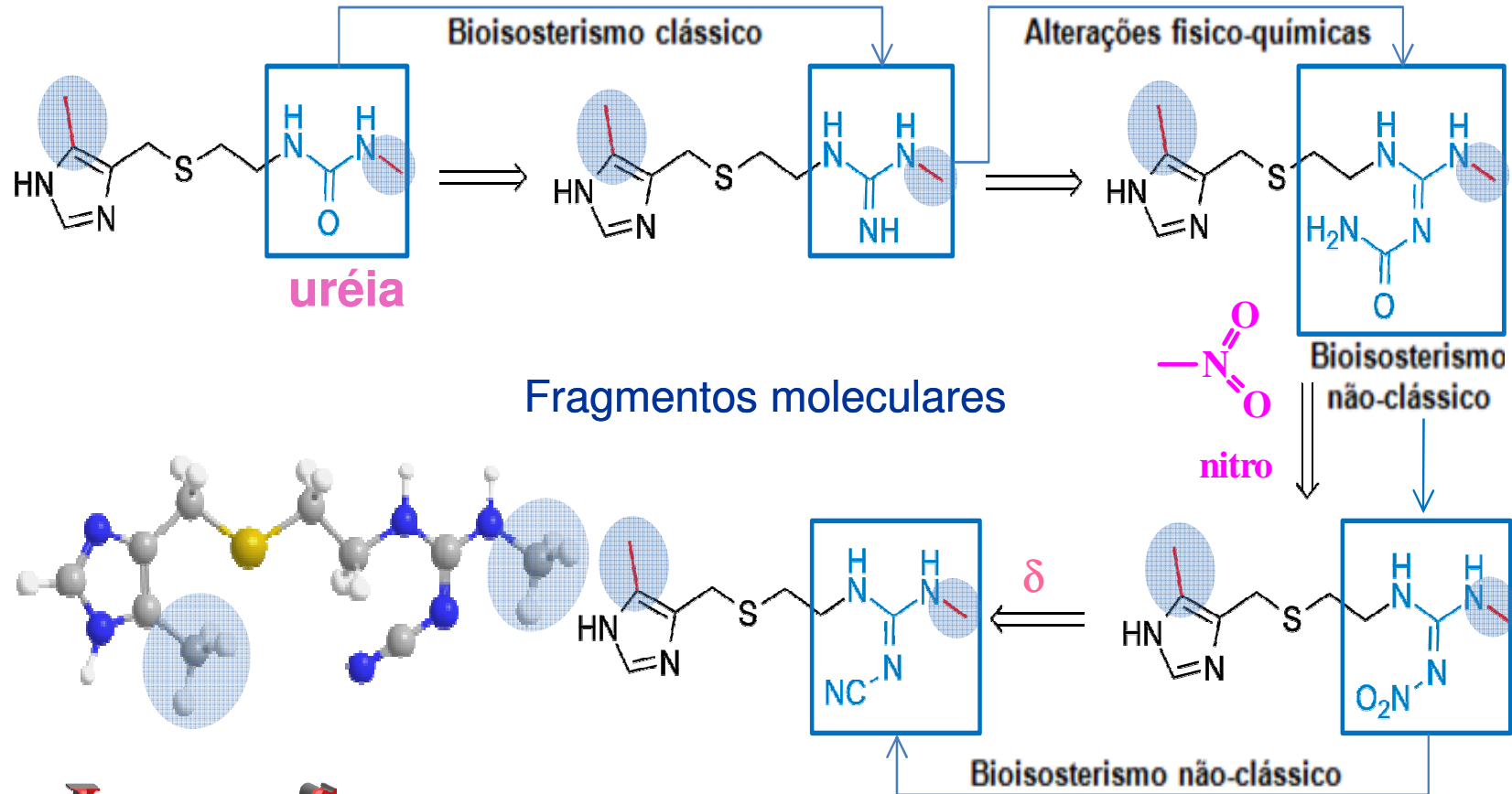
Dois sub-tipos de H_R

Desenho estrutural baseado no substrato



Gênese da cimetidina

Química Medicinal



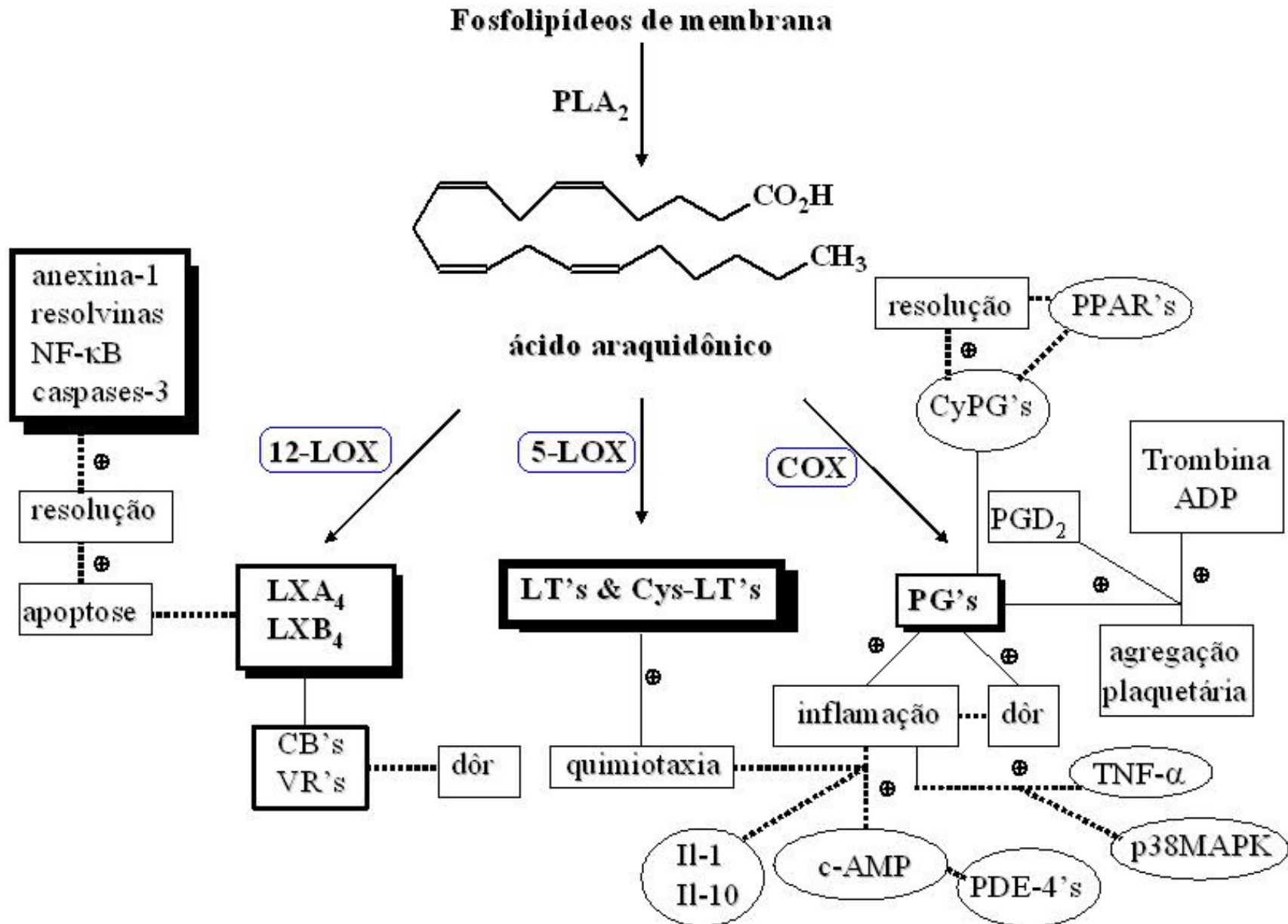
Inovação
terapêutica

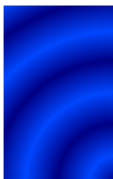
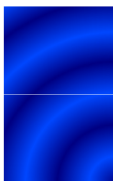
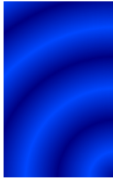
cimetidina

$C_{10}H_{16}N_6S$
PM: 252,1

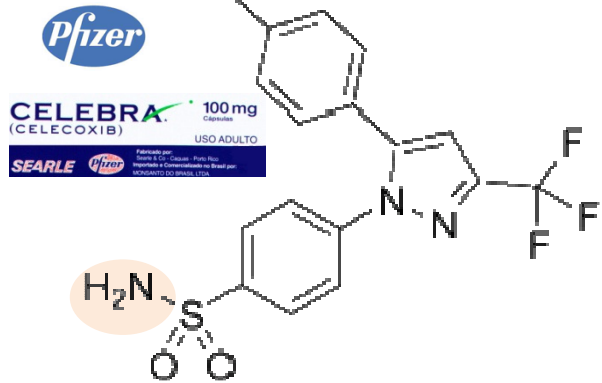


A fisiopatologia do processo

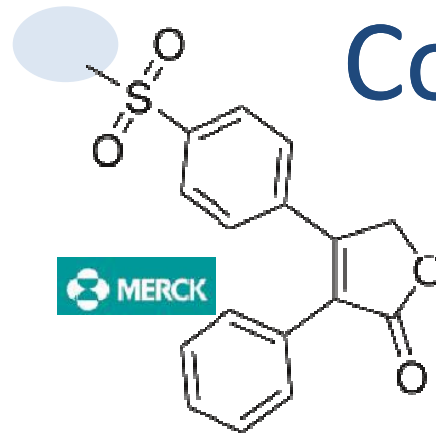




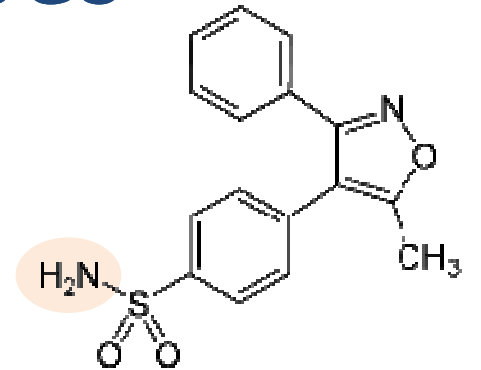
Coxibes



1999 (Pfizer US\$ 30 bi)

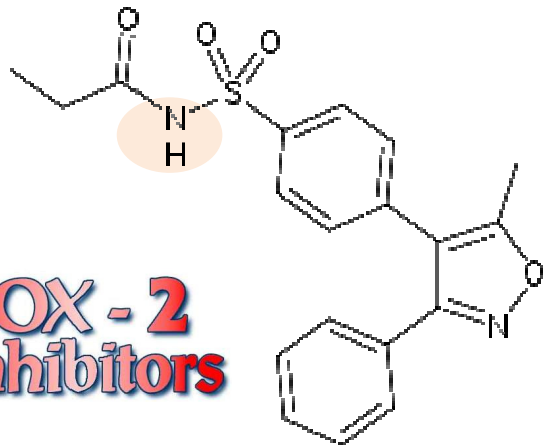


1999 - 2006



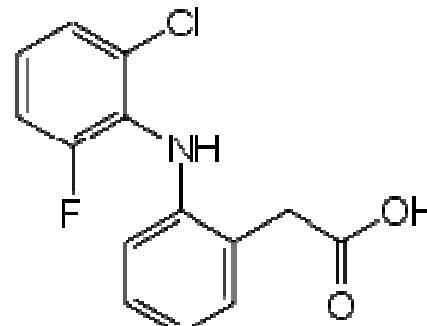
2004- 2006

COX-2 Inhibitors

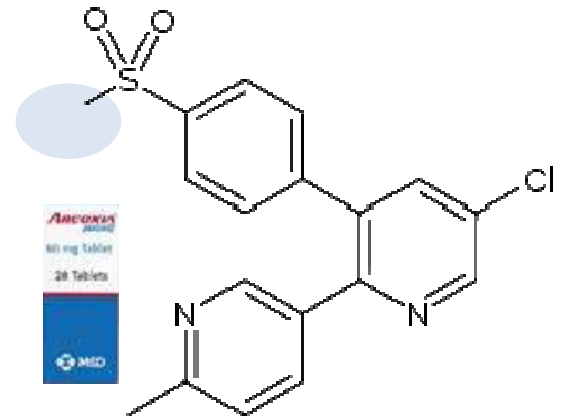


2005- 2006

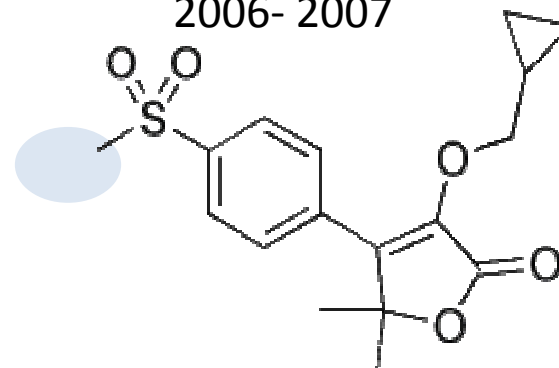
Firocoxibe (Equioxx^R)
2007
(FDA - cavalos)



2006- 2007



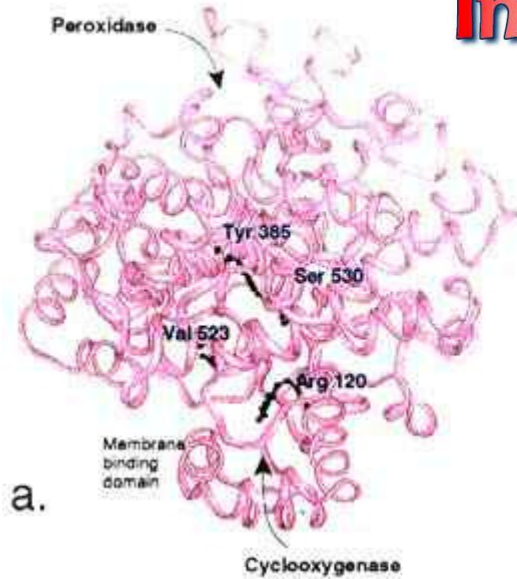
2007- 2008



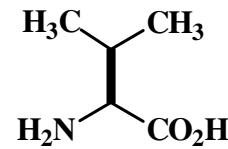
Cimicoxibe, Timacoxibe



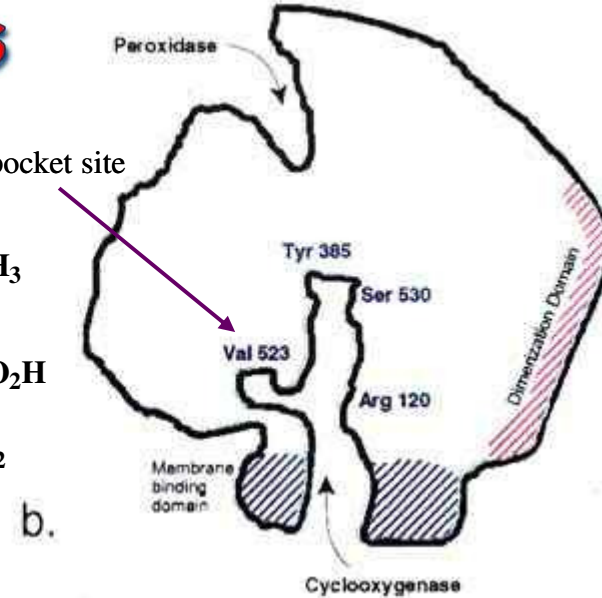
COX-2 Inhibitors



Secondary pocket site



$C_5H_{11}NO_2$
Valina



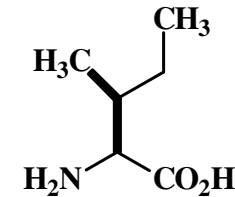
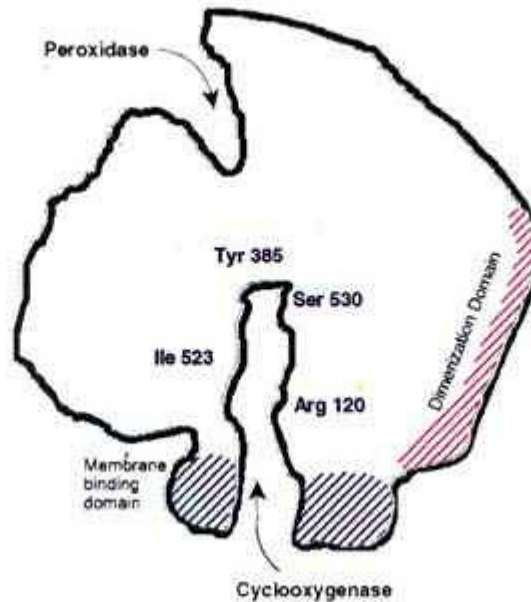
COX-2

Inflamação,
Câncer
Endotélio
vascular
Rins
Cérebro

COX-1

Plaquetas,
Estômago,
Rins

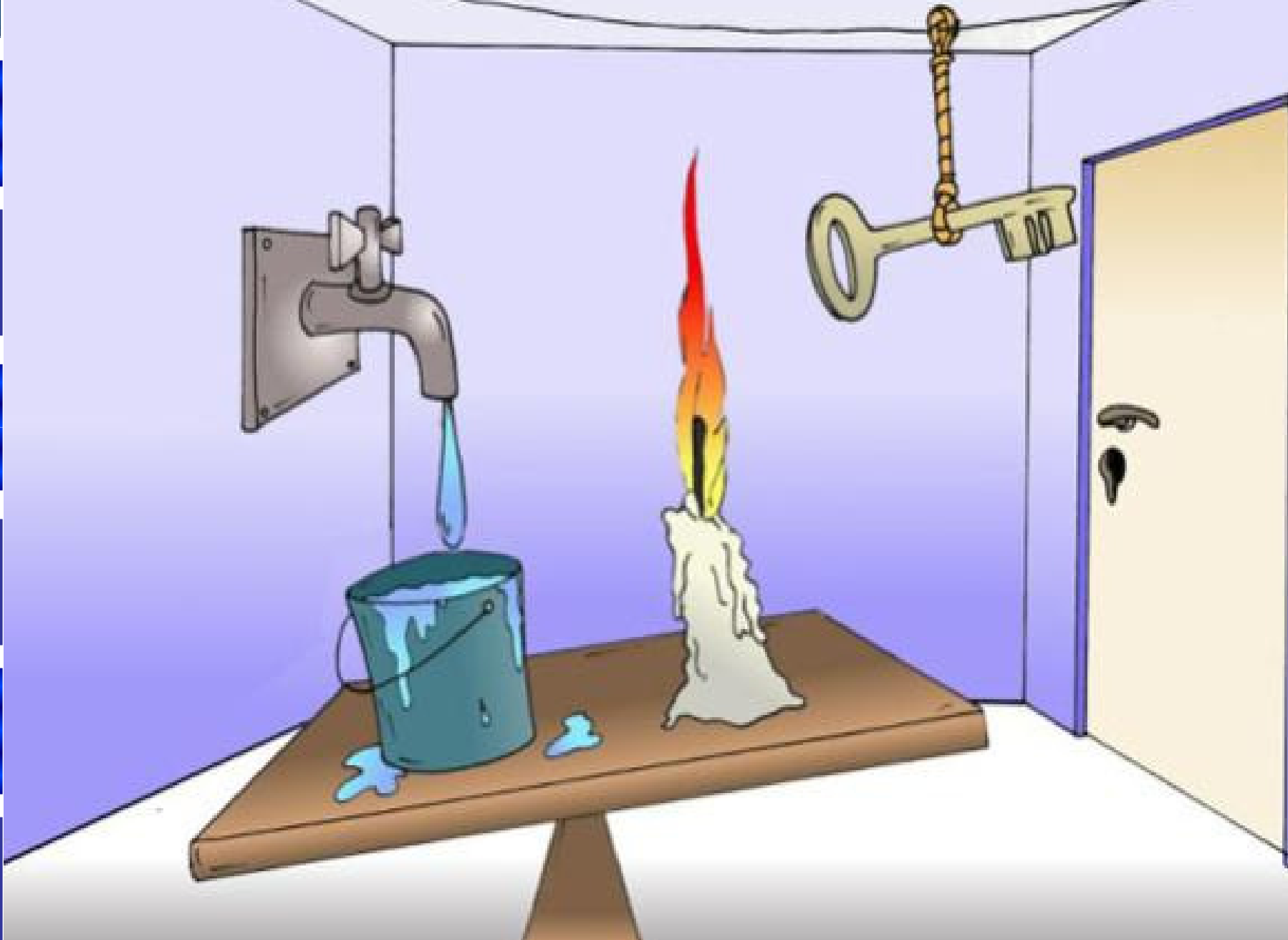
c.



$C_6H_{13}NO_2$
Isoleucina



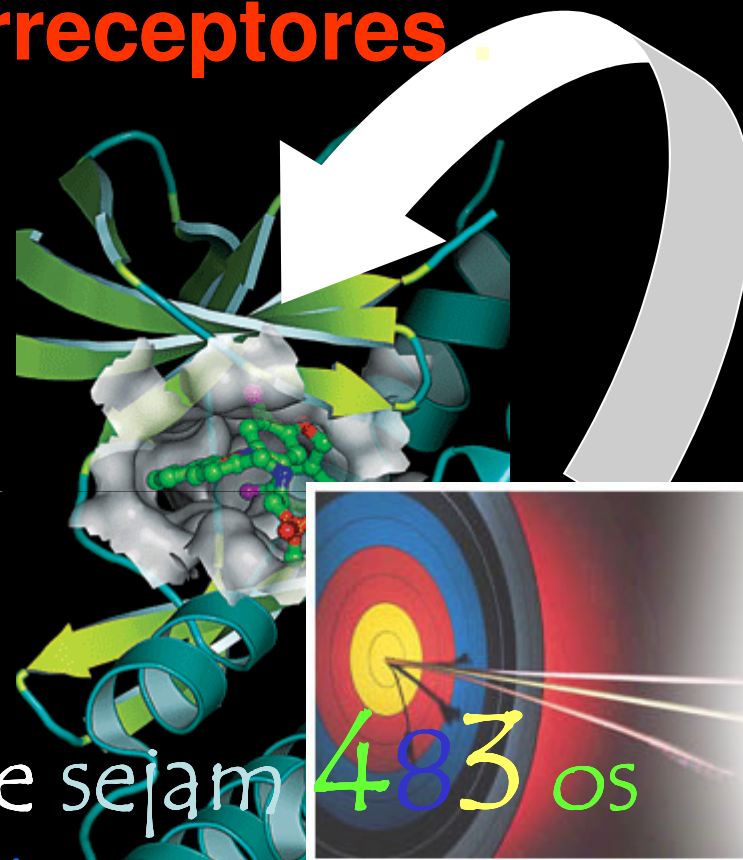
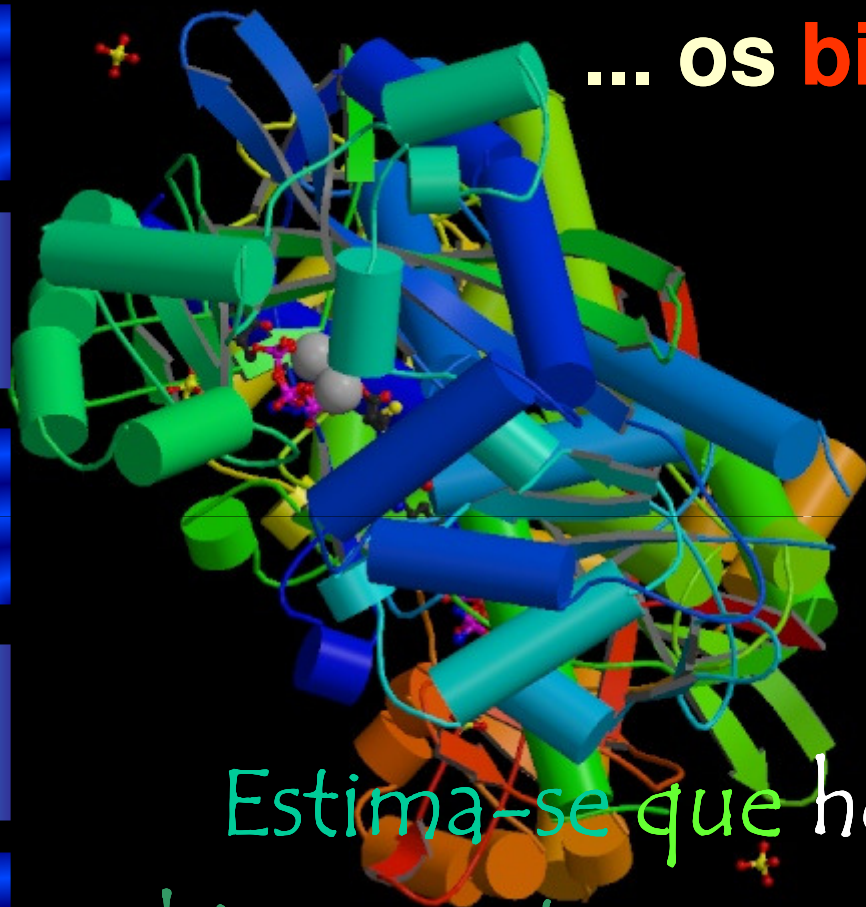
O processo racional da descoberta de fármacos





Os fármacos atuam em alvos terapêuticos...

... os **bioreceptores**.



Estima-se que hoje sejam **483** os bioreceptores envolvidos na resposta terapêutica de todos os fármacos contemporâneos.



Biorreceptor

Estrutura 3D do alvo terapêutico

homologia

Sítio de reconhecimento molecular

In silico

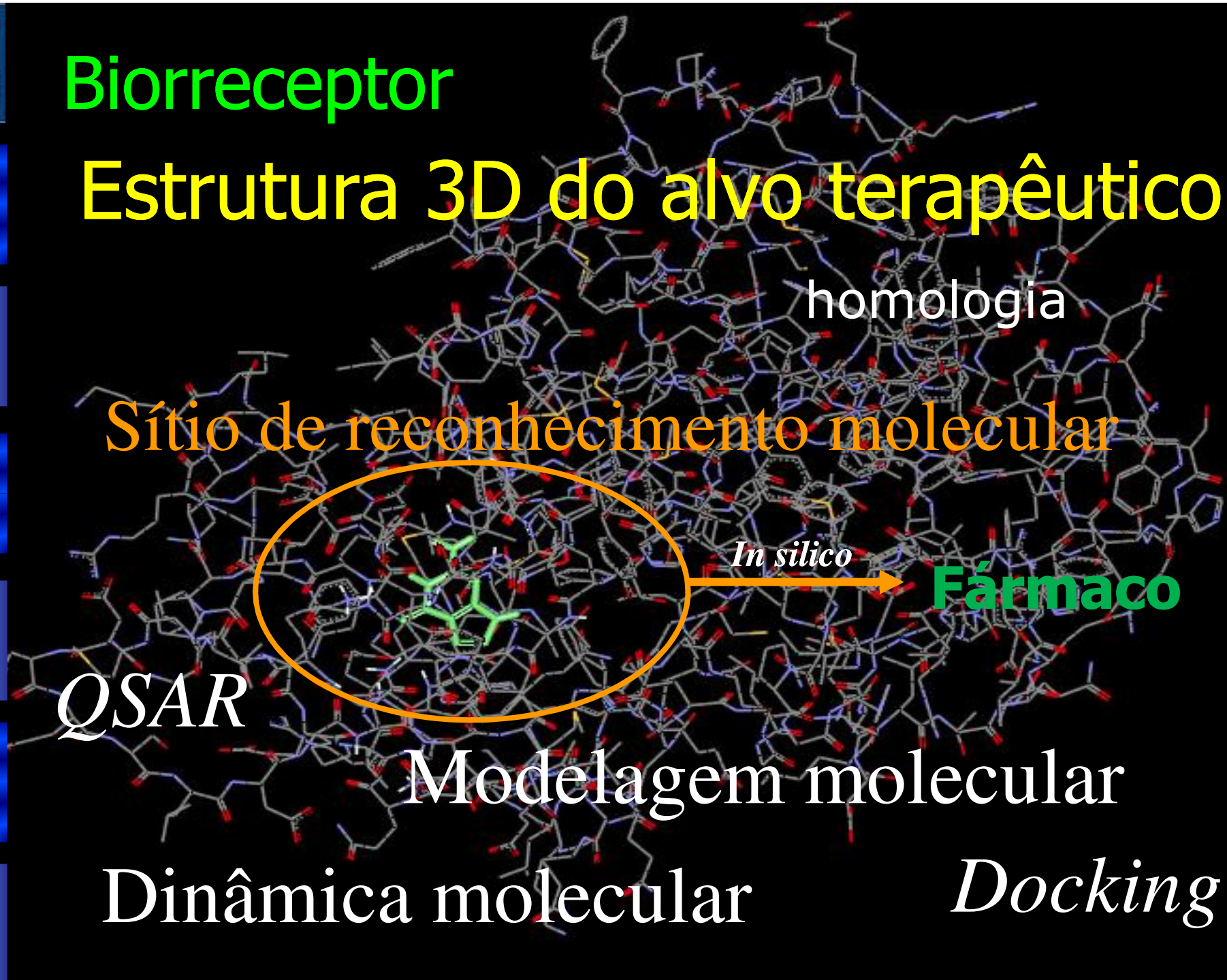
Fármaco

QSAR

Modelagem molecular

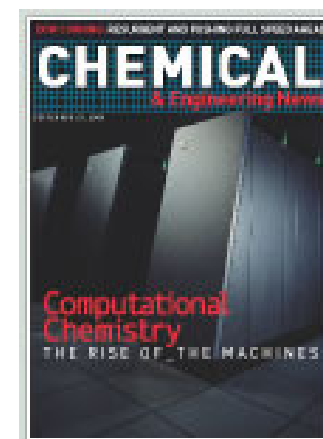
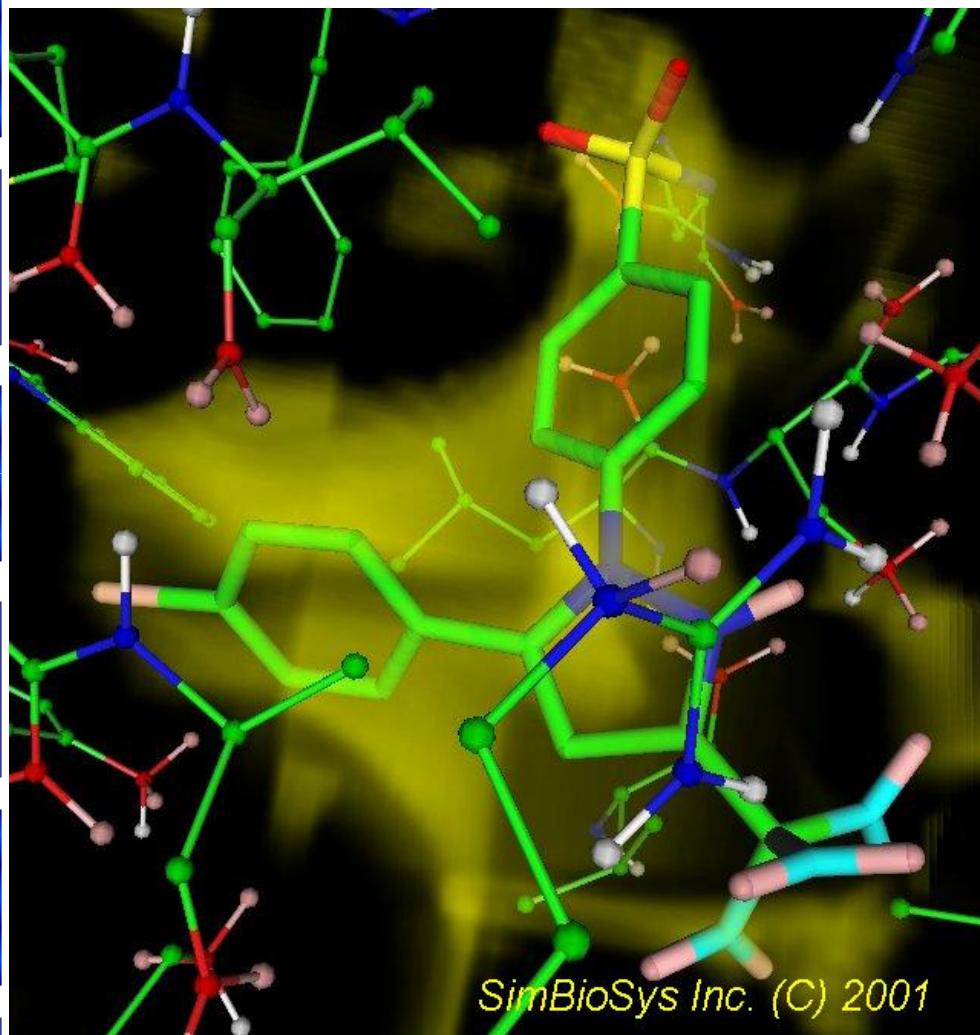
Dinâmica molecular

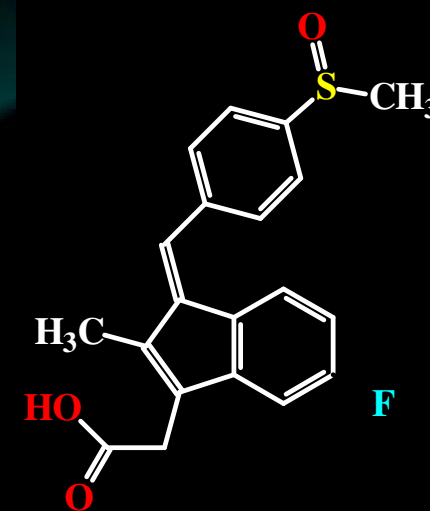
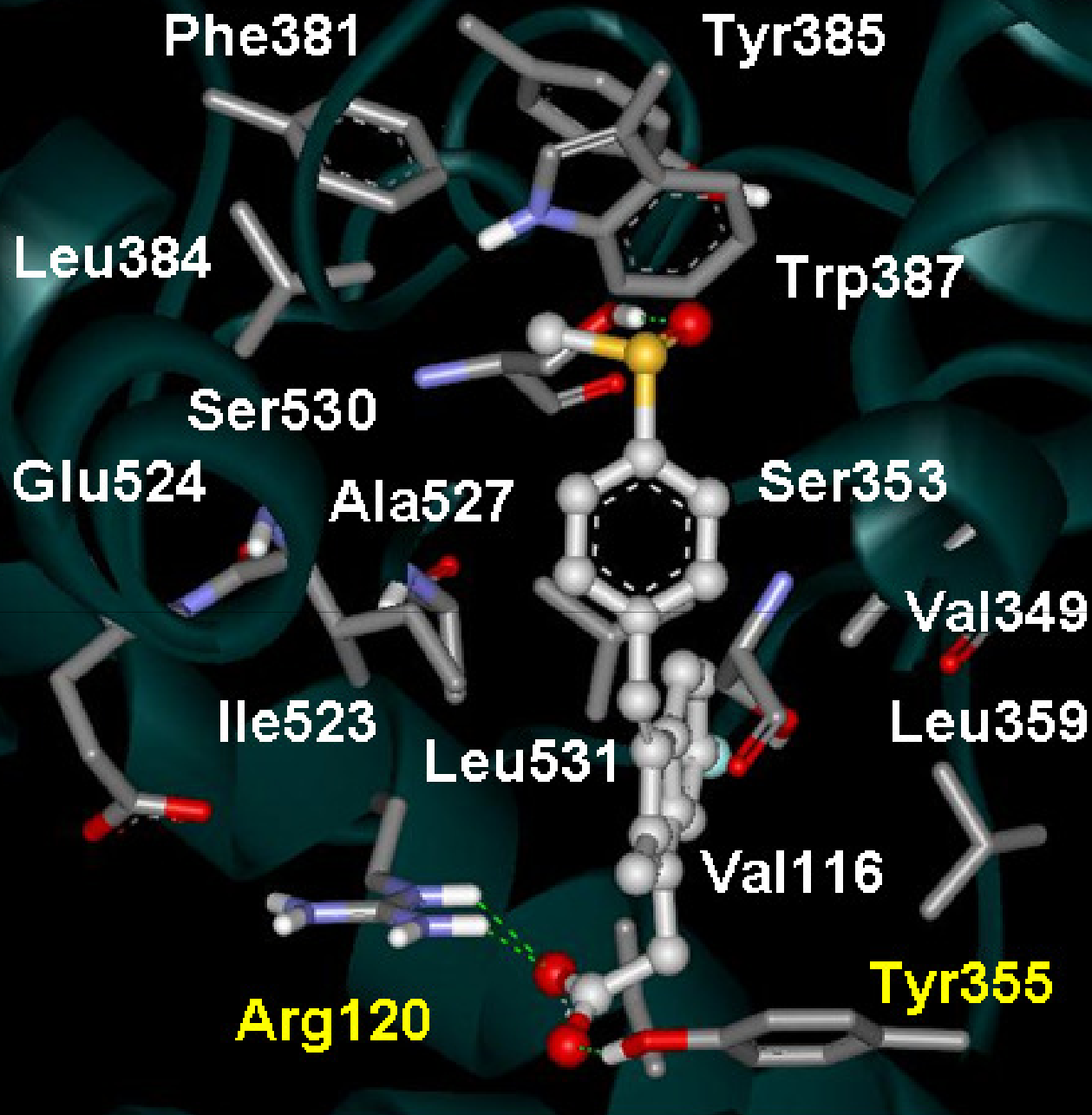
Docking



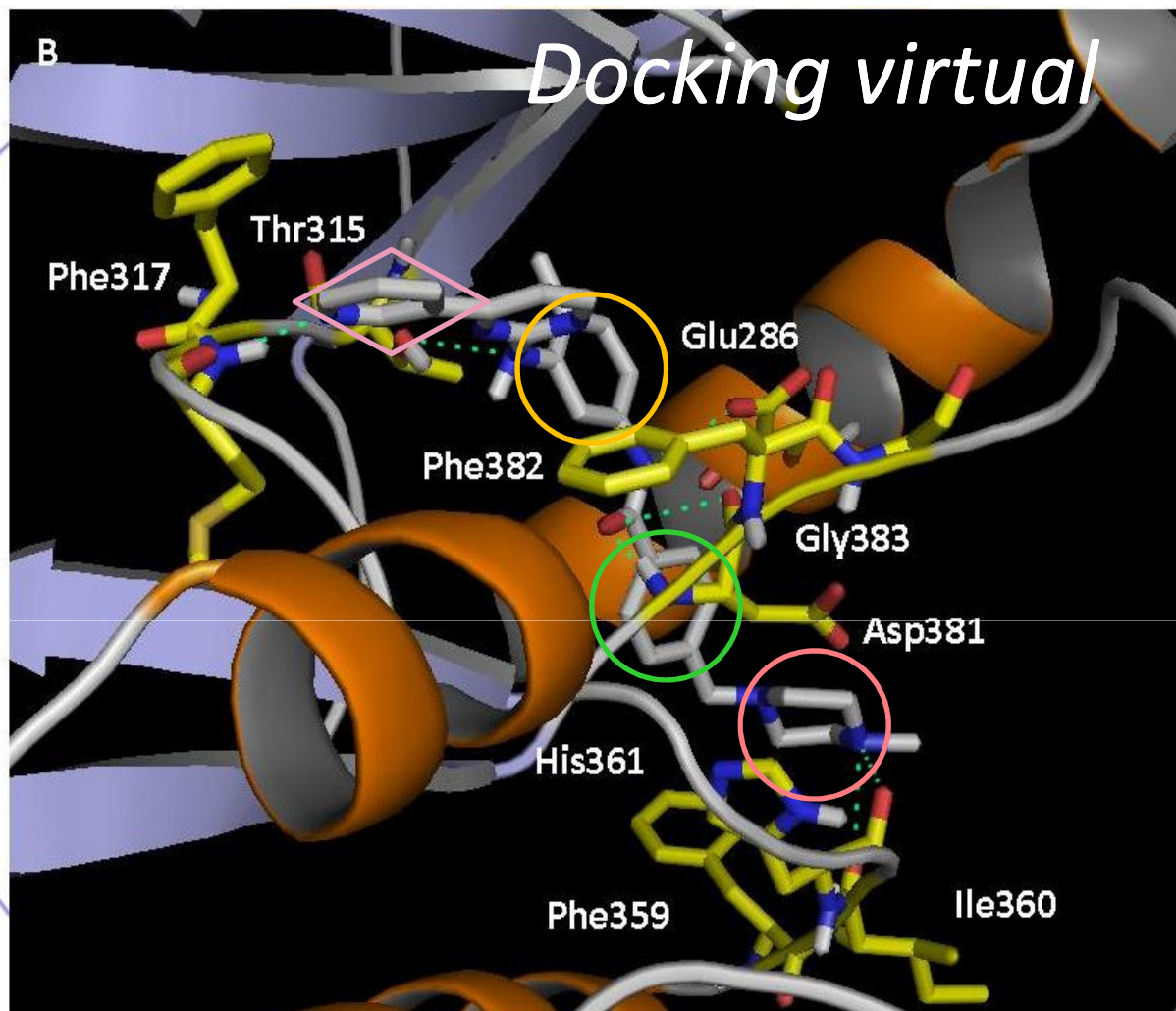
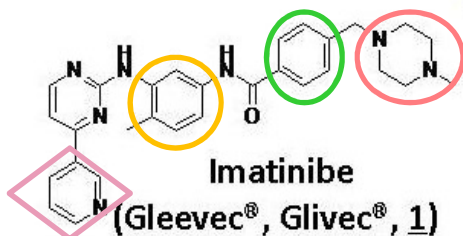
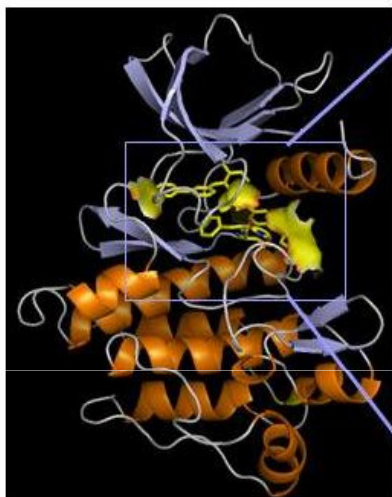


Química Computacional





Interações do sulindaco com COX-1



Modos de ligação do imatinibe com a ABL. Os átomos de hidrogênio foram eliminados para facilitar a visualização. Ligações-H estão representadas por linhas pontilhadas verdes.

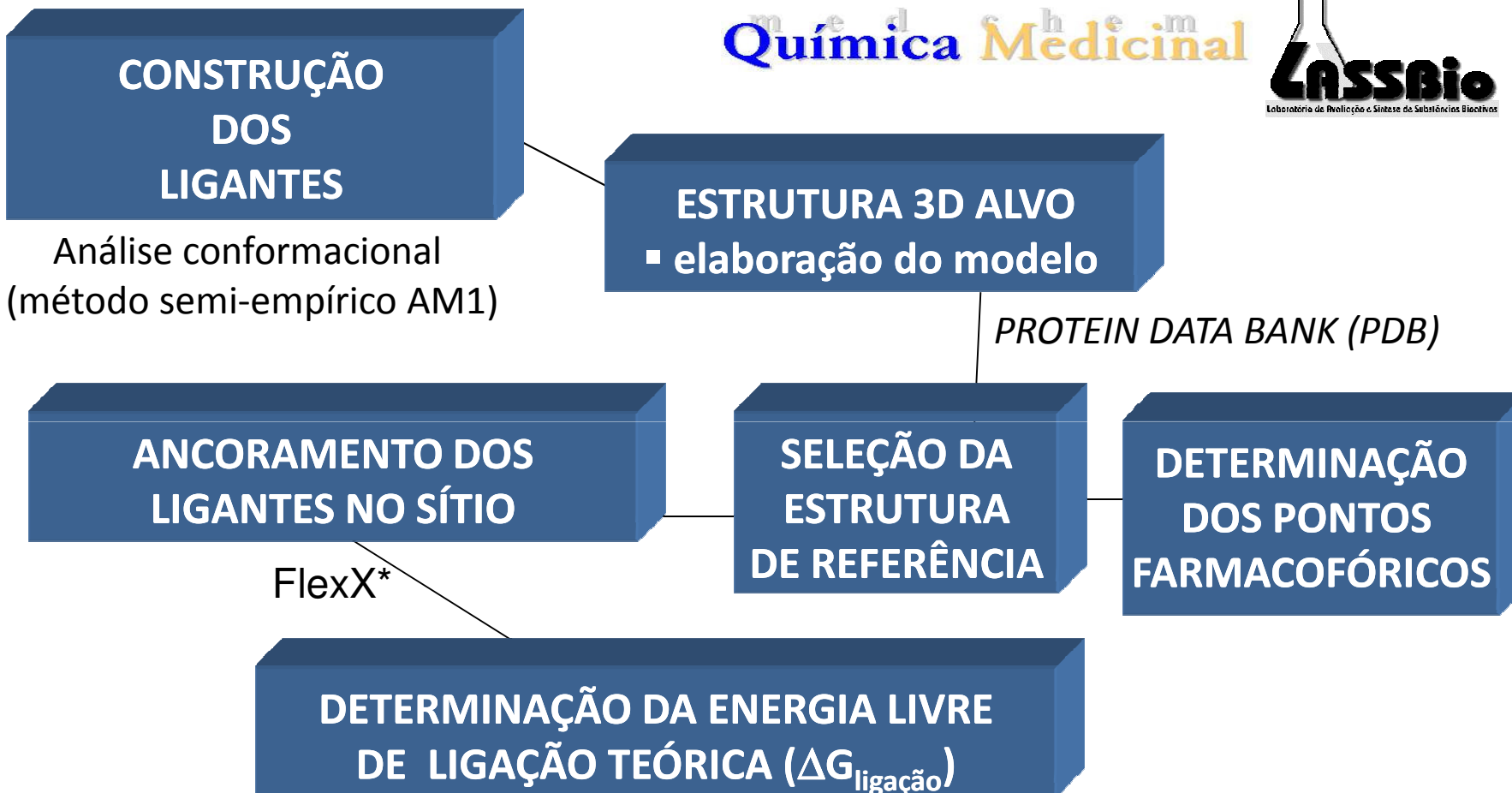
C.M. Avila, N. C. Romeiro, *Revista Virtual de Química* 2010, 2, 59

Novos inibidores de tirosina quinase



Metodologia: Estudos de *docking*

Química Medicinal



* FlexX one of the most cited commercial docking software

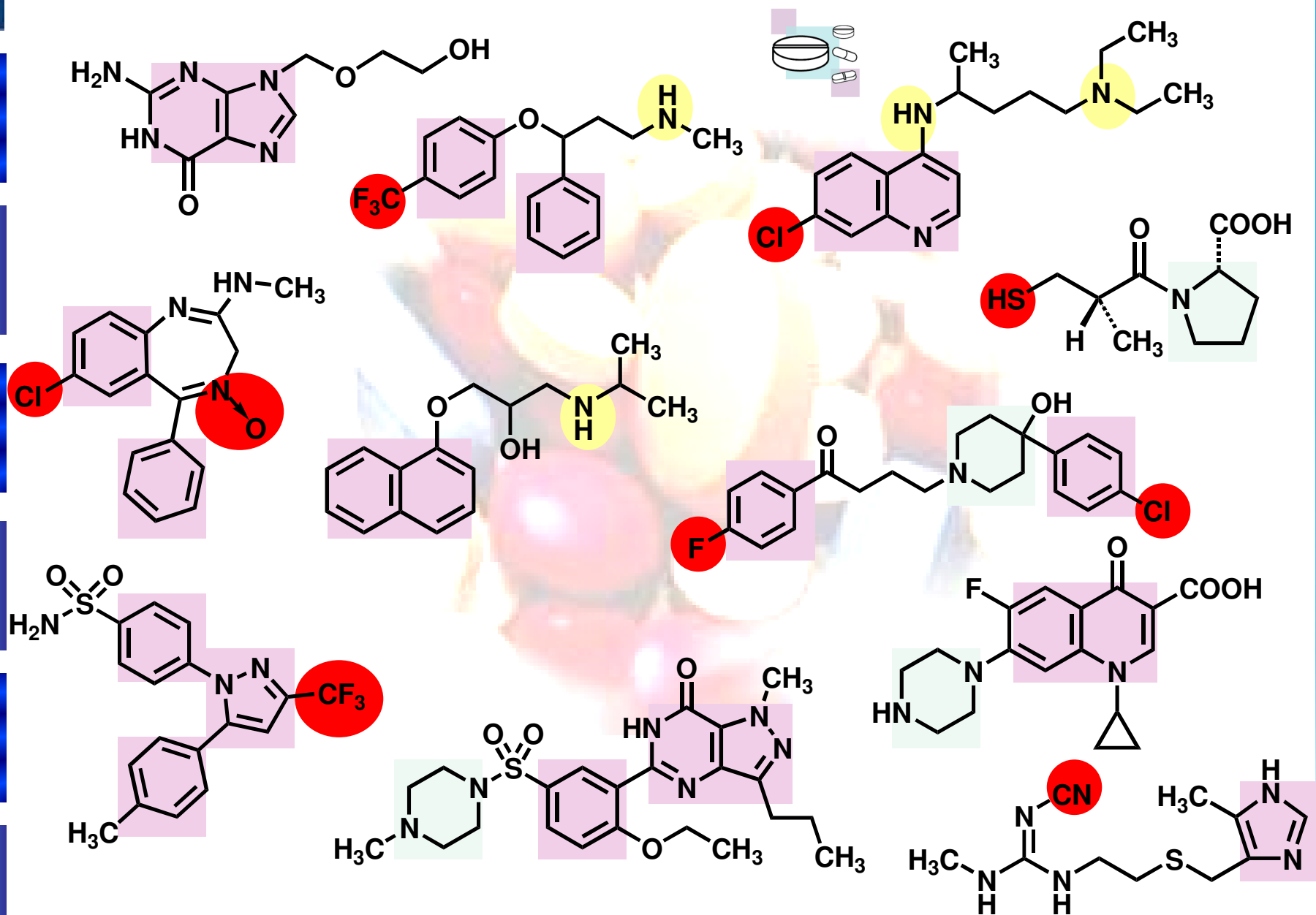
Sybyl, Version 8.0, Tripos Associates: St. Louis, MO, 2007 (Licença # 7512)

Spartan Pro; Wavefunction, Inc. 18401 Von Karman Avenue, Suite 370. Irvine, California 92612, USA (Licença # 1-001259)

FlexiDock; GLIDE; Gold; AutoDock (GNU) General Public License;



A quimiodiversidade dos fármacos...é singela!





Universidade Federal do Rio de Janeiro

Considerações

finais



Química
Medicinal



Universidade Federal do Rio de Janeiro

Química Medicinal



LASSBio

Laboratório de Avaliação e Síntese de Substâncias Bioativas

Cidade Universitária, ilha do Fundão,
Rio de Janeiro, RJ

Criado em 19/04/1994 Laboratório de Avaliação e Síntese de Substâncias Bioativas



inct



inofar

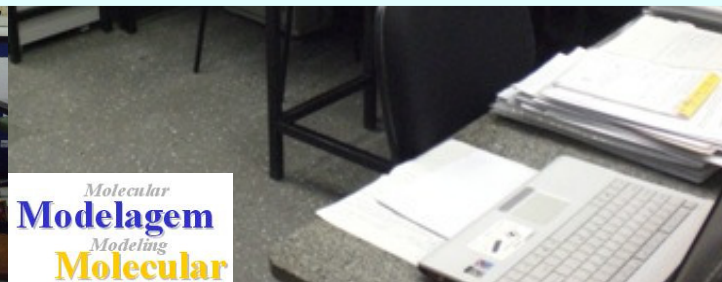
Instituto nacional de ciência e tecnologia

de Fármacos e Medicamentos

www.inct-inofar.ccs.ufrj.br



Pharmacology
Farmacologia



Molecular
Modelagem
Modeling
Molecular



© 2010



Abordagem Fisiológica



Síntese orgânica medicinal

Princípio de Price

Química Medicinal

Pharmacology
Farmacologia

Efeito porta-ao-lado

Molecular
Modelagem
Modeling
Molecular

Química
Medicinal

Química

computacional

modelagem molecular



Bioensaios



in vivo / in vitro

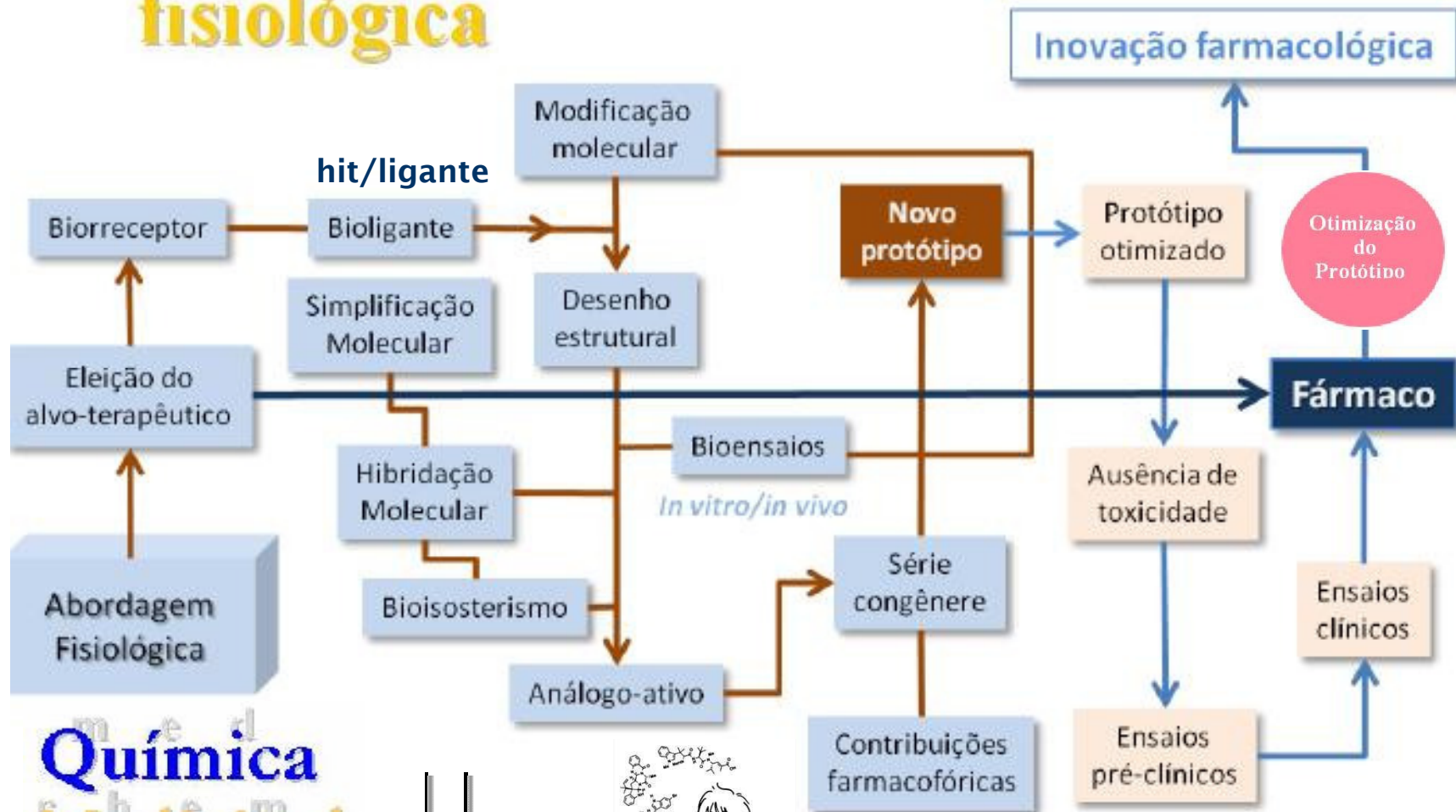
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Physiologic A abordagem

approach
fisiológica

Estratégias de desenho molecular



Química
Medicinal

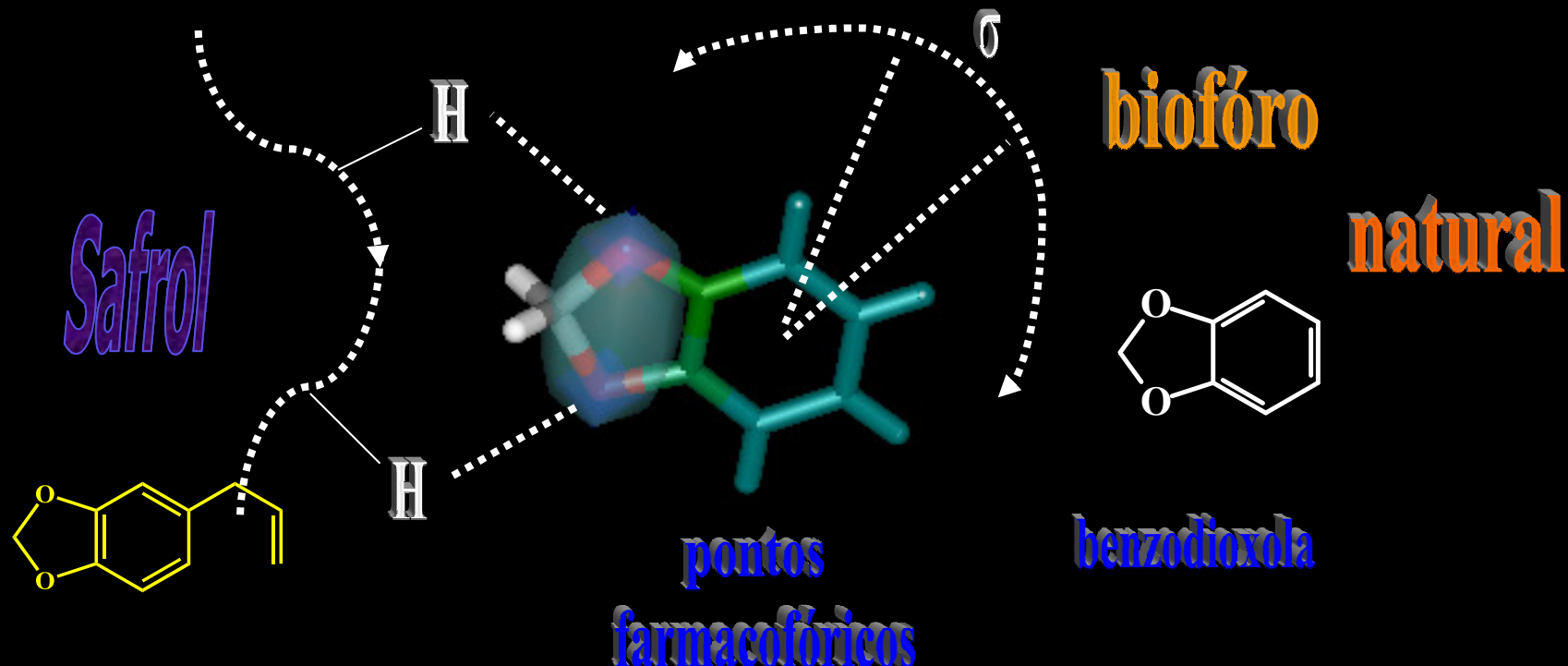
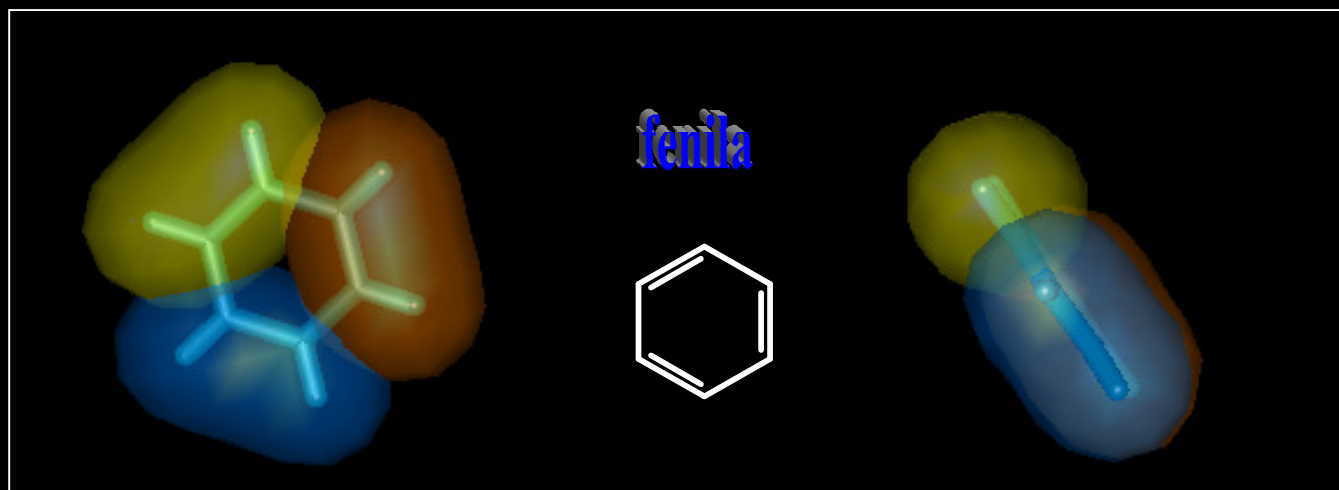


Laboratório de Avaliação e Síntese de Substâncias Bioativas

validação precoce do
alvo-terapêutico

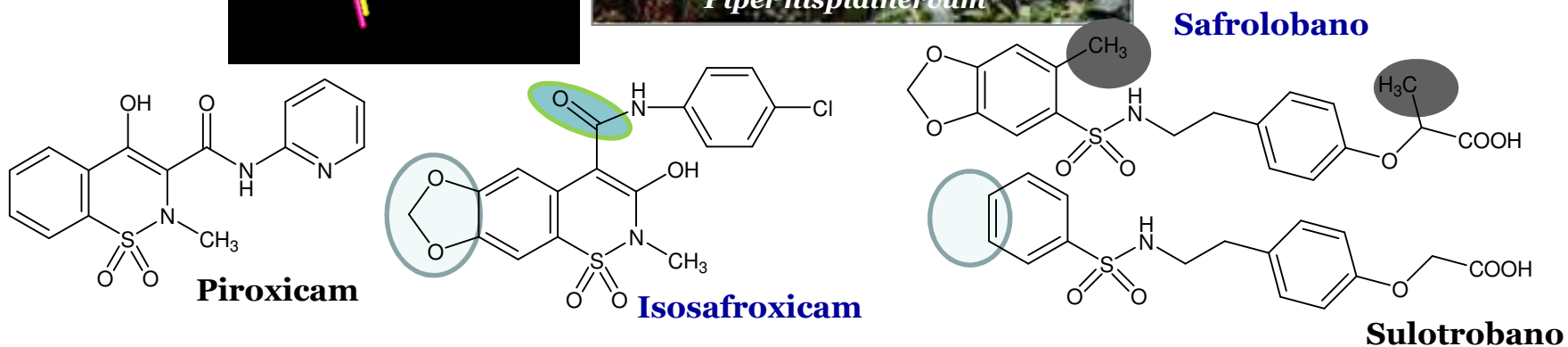
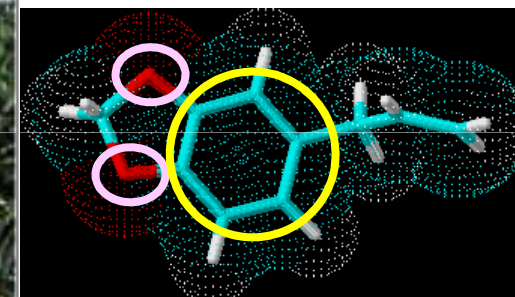
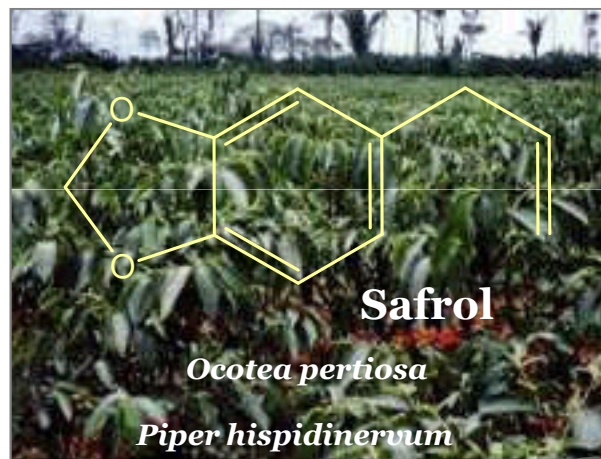
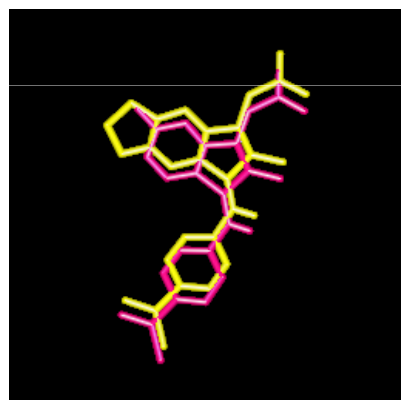
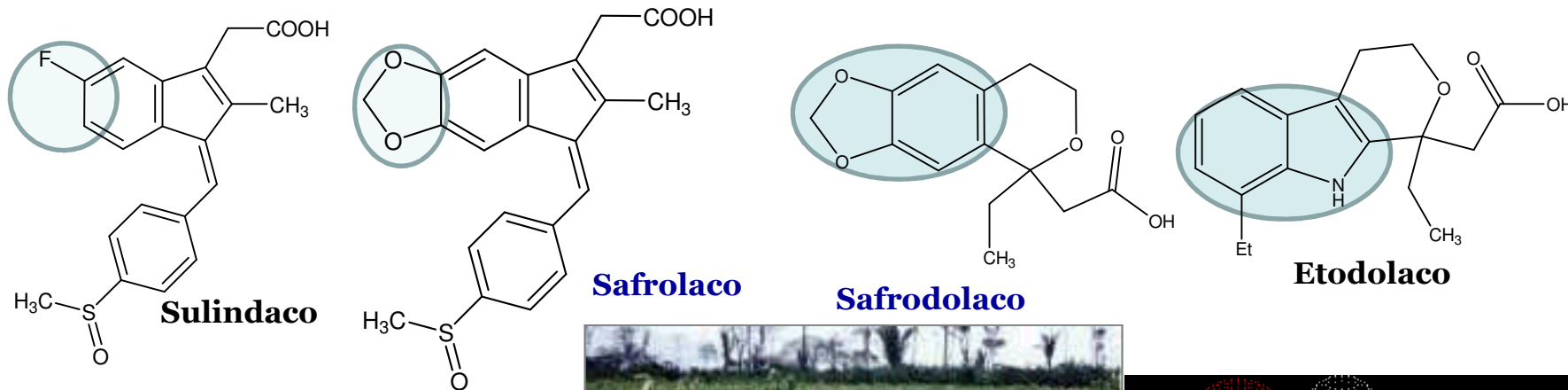


Fragmentos moleculares naturais





O uso do safrol como bióforo natural no





Métodos farmacológicos

Química Medicinal

- Ensaio de contorção abdominal induzida por ácido acético (COLLIER et



Tratamento i.p.

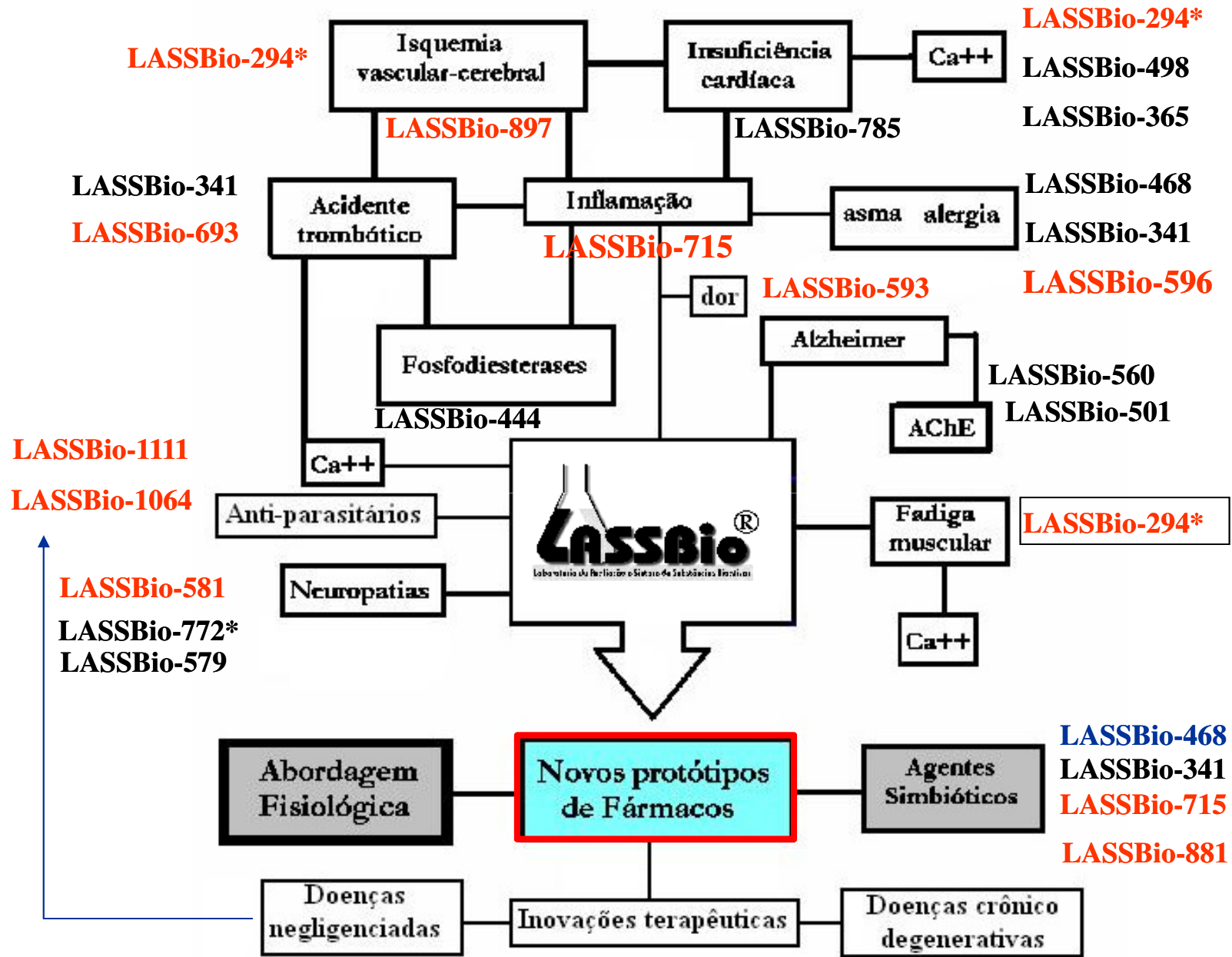
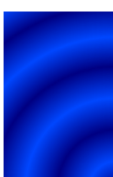
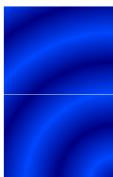
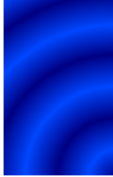
40 min

Administração i.p. Ác. Acético 0,6%

10 min

Contagem por 20 min

Liberação de mediadores endógenos da dor (bradicinina, serotonina, histamina, citocinas, PG's...)





Resultado da pesquisa pelo c... Tabelas em HTML - Extensões - T... php PHP: print_r - Manual

LASSBio LLDB LIGAND DATA BANK

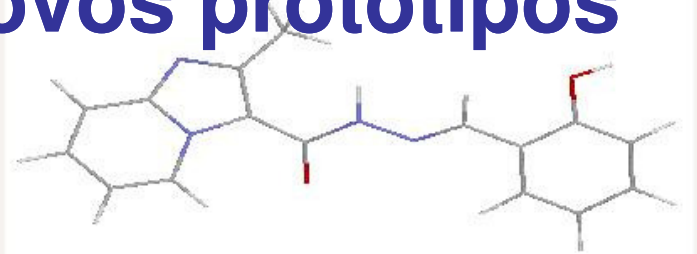
L. E. Dardenne, LNCC
GRUPO DE MODELAGEM MOLECULAR
DE SISTEMAS BIOLÓGICOS
LNCC/MCT

LNCC UFRJ

Search Register Ligand Help Logout

Banco de dados de moléculas =

Novos protótipos



Molecular Form:	C16H14N4O2
IUPAC Nomenclature :	???????????????
Fantasy Name :	Te te
Number of Quiral Centers :	0
Number of H-Bond Donors	
Number of H-Bond Acceptors	
Number of Free Bonds	4
Log P	2.0
Fusion Point	100
Functional Group:	Acylhydrazone



Medicchem Database:
Chemical, Biological and Pharmacological Applications

A quimioteca do
LASSBio tem
1735 compostos
originais

Jmol

Wireframe Ball-and-Stick Space Fill
To return for initial orientation
Rotacionar



ICB Instituto
de Ciências
Biomédicas

Anúncio

Da molécula ao corpo

Revista BIO ICB

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Orientadores e Lir

Pesquisa →

Programa de Pós Graduação em Farmacologia e Química Medicinal **2006**

29 de abril de 2008

“Medicinal chemistry or pharmaceutical chemistry is a discipline at the intersection of chemistry and pharmacology involved with designing, synthesizing and developing drugs.”

Interface Química-Biologia em Química Medicinal

Farmacologia
Química
Medicinal

Interdisciplinaridade



FARMACOLOGIA

M
e
d
C
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e
m

CASSBio
Laboratório de Pesquisa e Síntese de Substâncias Biológicas

Único programa de pós-graduação (M/D)
com este perfil na América Latina

Slide 62

EJB6

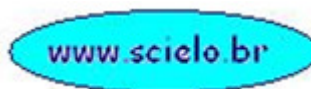
A recente criação da PG (M&D) em Farmacologia e Química Medicinal ilustra nova perspectiva de horizonte na PG da UFRJ, pois é a primeira com o perfil desta proposta interdisciplinar na AL.I

Eliezer J. Barreiro; 04/03/2010



Bibliografia

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- L. M. LIMA, **Química Medicinal moderna: desafios e contribuição brasileira**
Quím. Nova **2007**, 30, 1456-1468

Química Medicinal

- Journal of Medicinal Chemistry

<http://pubs.acs.org/journals/jmcmar/index.html>

- ACS Medicinal Chemistry Letters

<http://pubs.acs.org/toc/amclct>

- Bioorganic Medicinal Chemistry

<http://www.elsevier.com/inca/publications/store/1/2/9/>

- Bioorganic Medicinal Chemistry Letters

<http://www.elsevier.com/inca/publications/store/9/7/2/>

- Current Medicinal Chemistry

<http://www.bscipubl.demon.co.uk/cmci/index.html>

- MedChemComm

<http://www.rsc.org/Publishing/Journals/MD/Index.asp>

- Current Topics in Medicinal Chemistry e outros

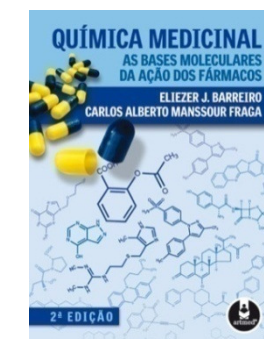
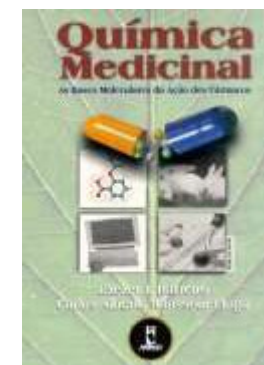
<http://www.bentham.org/>

- Livro "Química Medicinal: As Bases Moleculares da Ação dos Fármacos"

<http://www.artmed.com.br/>

- Glossário de termos de Química Medicinal

<http://www.chem.qmw.ac.uk/iupac/medchem/>





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“...Para achar água é preciso
descer terra adentro,
Encharcar-se no lodo.

Mas há os que preferem
olhar os céus,
E esperar pelas chuvas...”

Oduvaldo Vianna Filho

*(em “Cúmplice da Paixão”, Dênis de Moraes
Ed. Nórdica, RJ, 1991).*