

FUNDAMENTOS DE QUÍMICA

MedChem

Parte 1

MEDICINAL - COMO NASCEM OS FÁRMACOS

26ª Semana da Química do Instituto de Química da UFRJ
09-13 de abril de 2018



Eliezer J. Barreiro

Professor Titular



Resumo

Universidade Federal do Rio de Janeiro

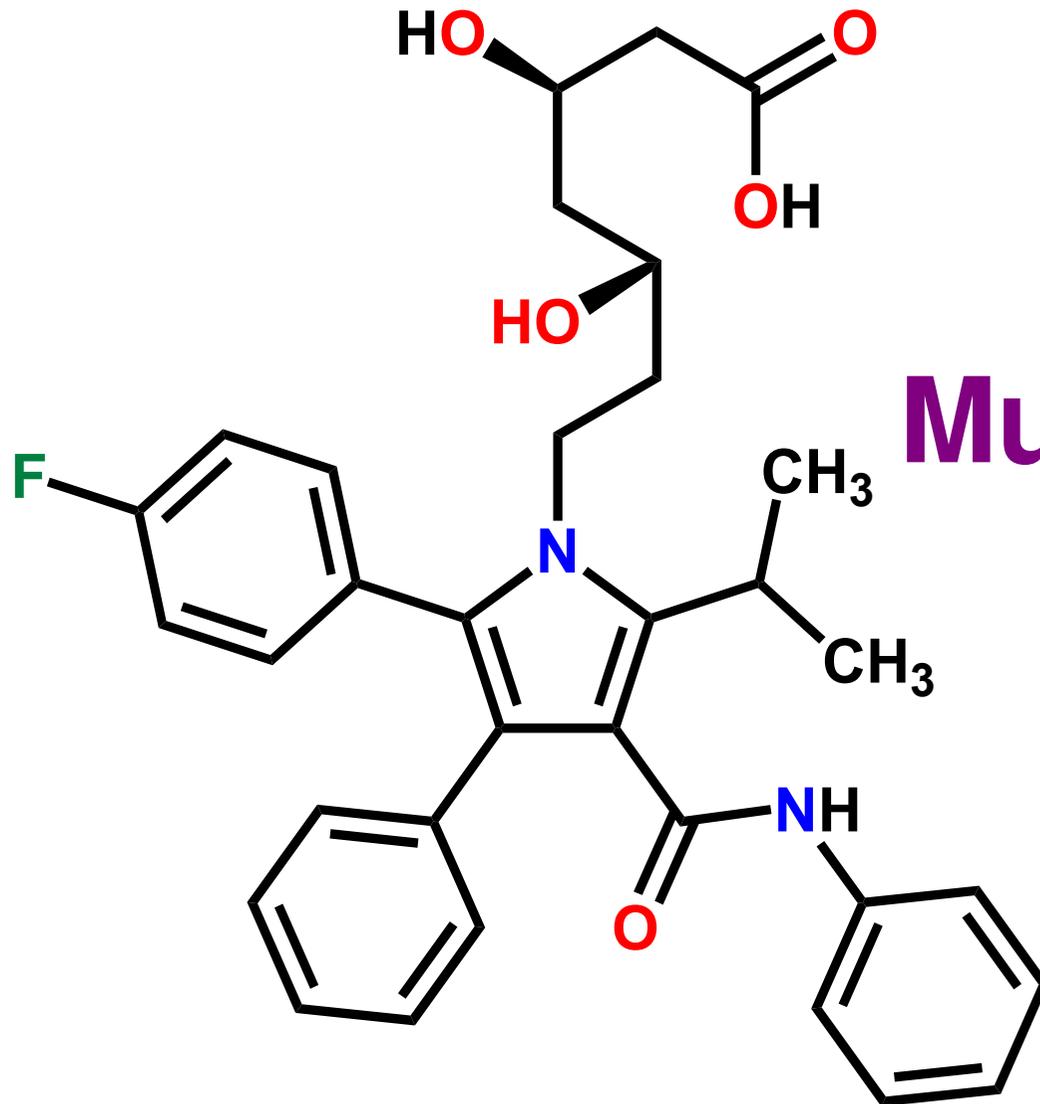
Neste curso-curto apresentaremos os fundamentos da **Química Medicinal**, para o desenho molecular de novos candidatos a fármacos. A introdução abordará o histórico e a cronologia da disciplina, com ênfase ao seu caráter interdisciplinar. O processo de descoberta de fármacos ilustrará como “nascem” os fármacos. Apresentaremos alguns aspectos da inovação farmacêutica radical, em especial para os fármacos sintéticos. Em conclusão, alguns exemplos selecionados do trabalho realizado no Laboratório de Avaliação e Síntese de Substâncias Bioativas (LASSBio) do ICB da UFRJ, criado e coordenado pelo apresentador, serão apresentados.



Pendências

Atorvastatina

AAS



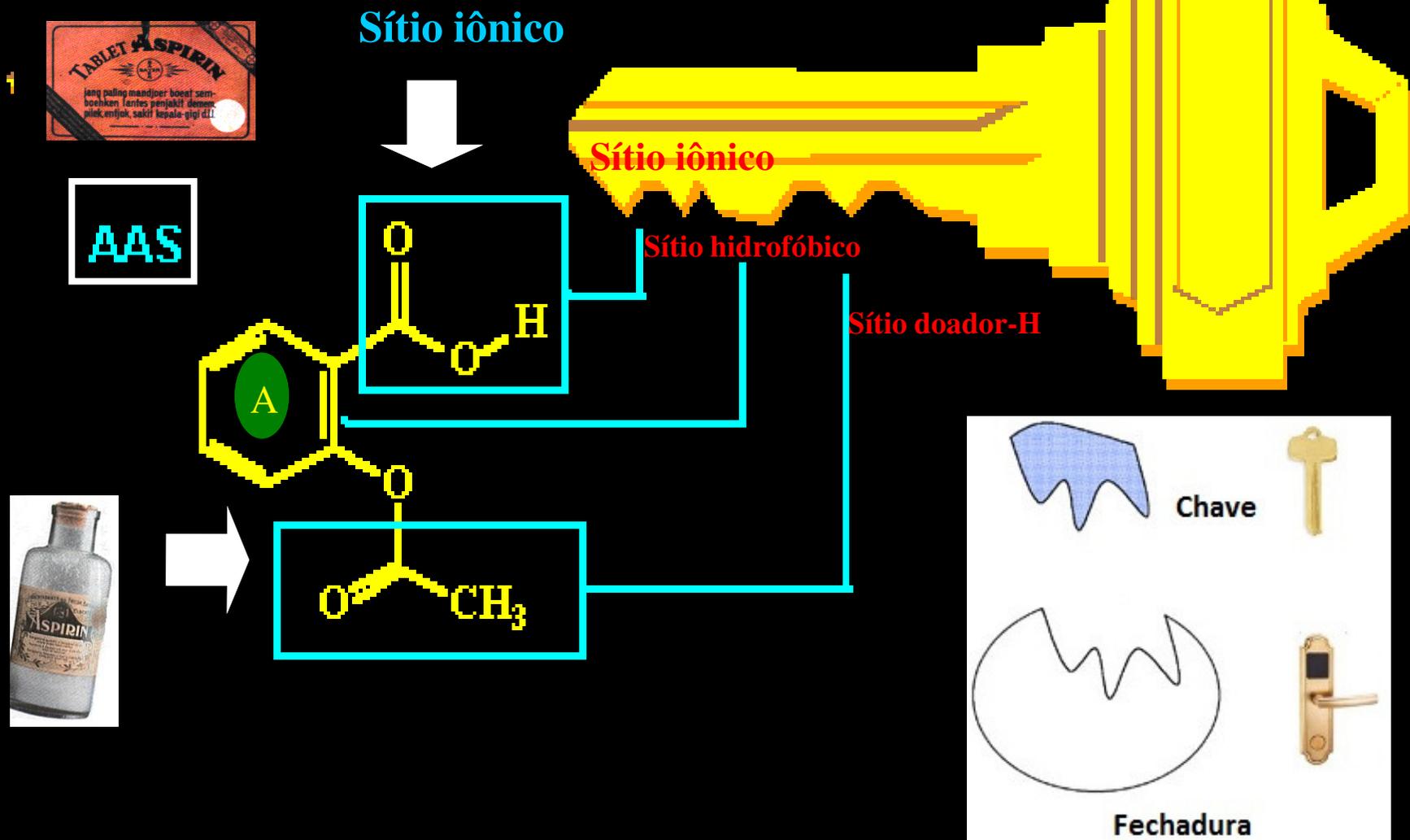
**Molécula
Multifuncional
=
Fármacos**

atorvastatina



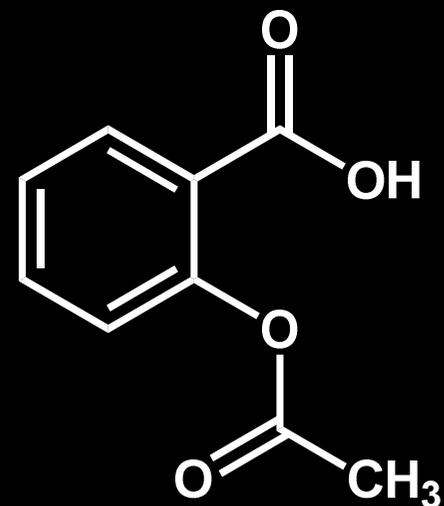
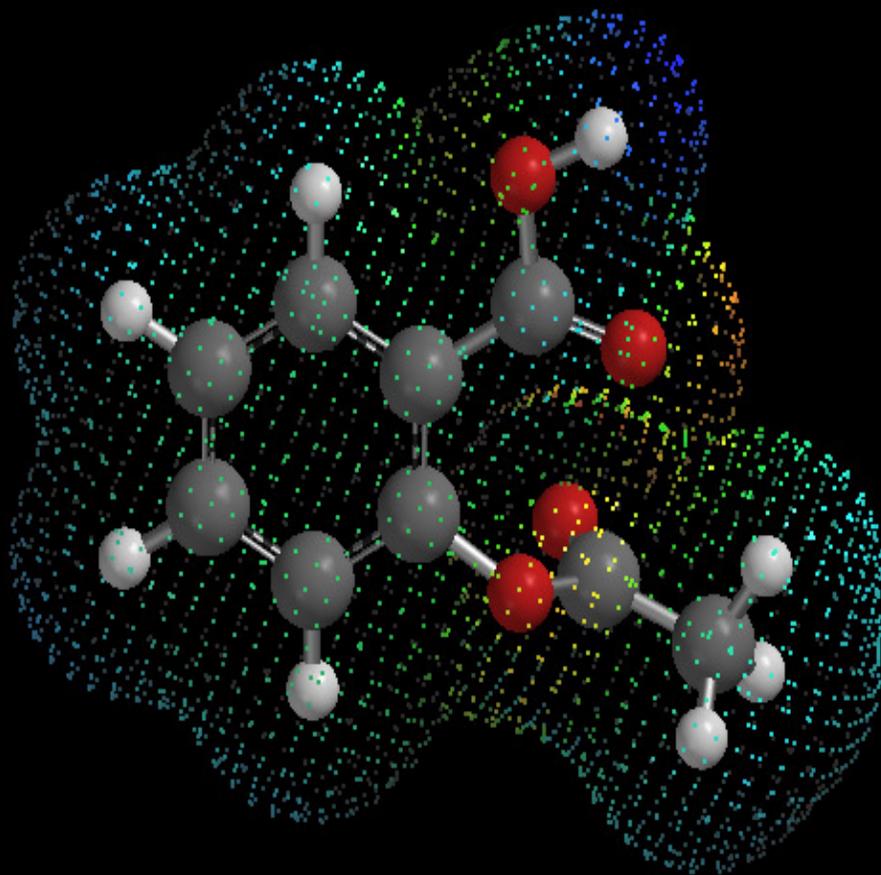
O Centenário Modelo "Chave-Fechadura"

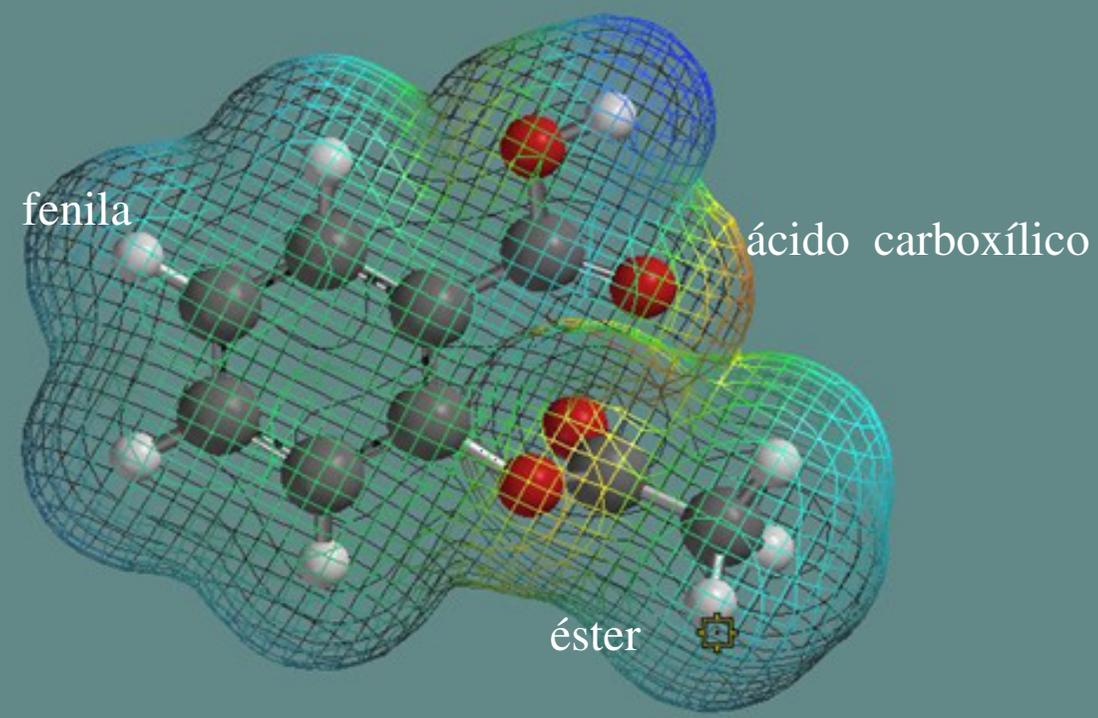
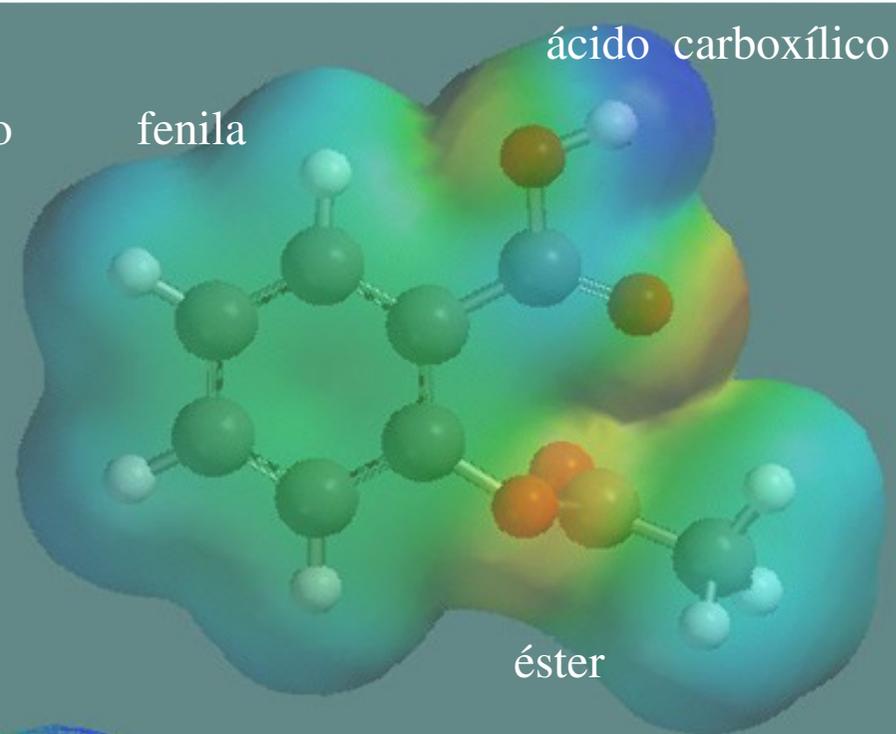
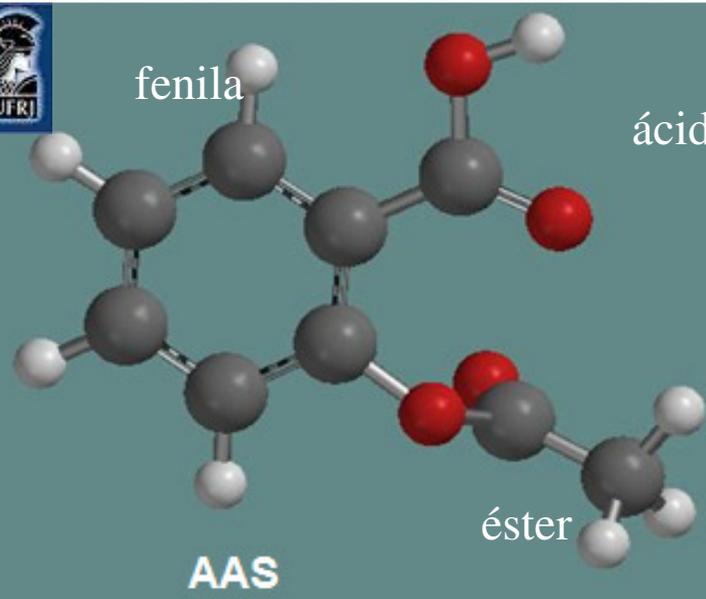
Complementaridade do modelo Chave-fechadura





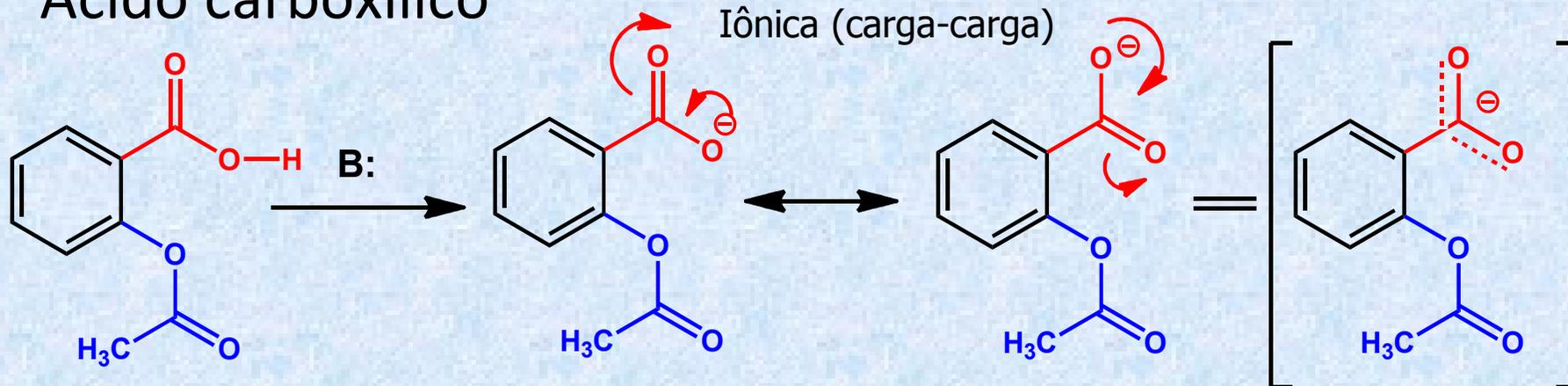
Ácido acetil salicílico



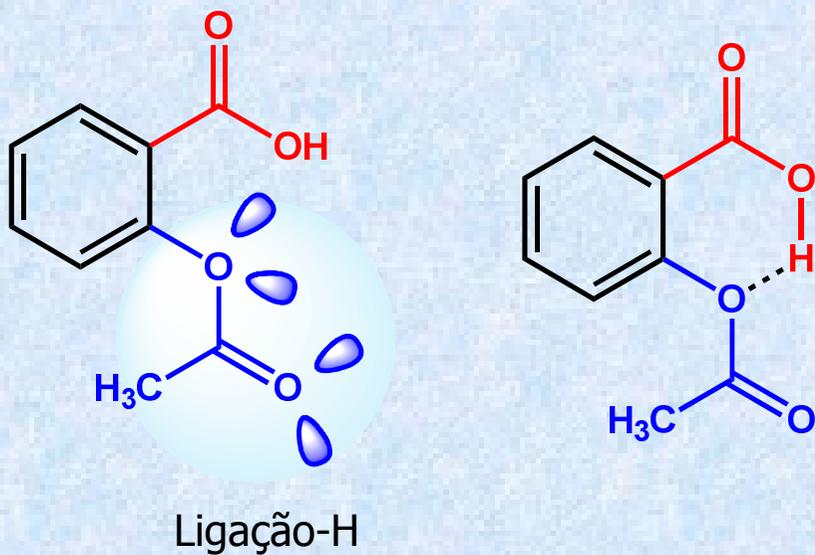




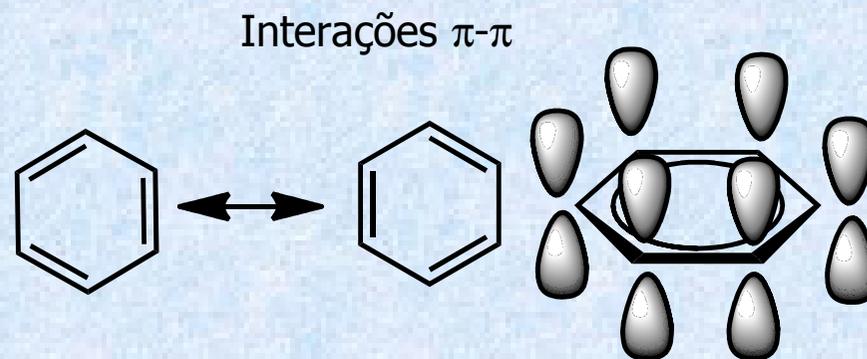
Ácido carboxílico



Éster



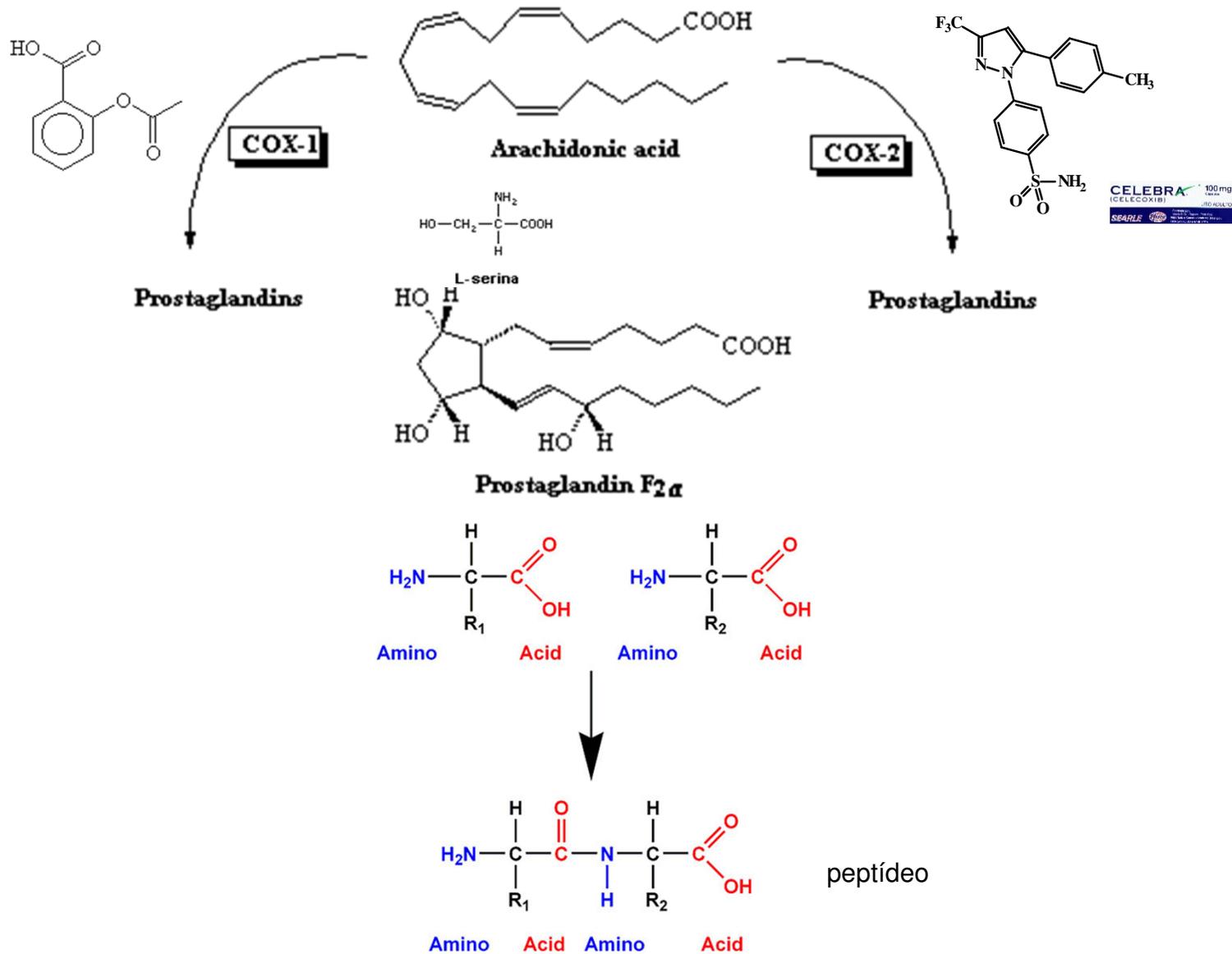
Fenila



Grupos funcionais

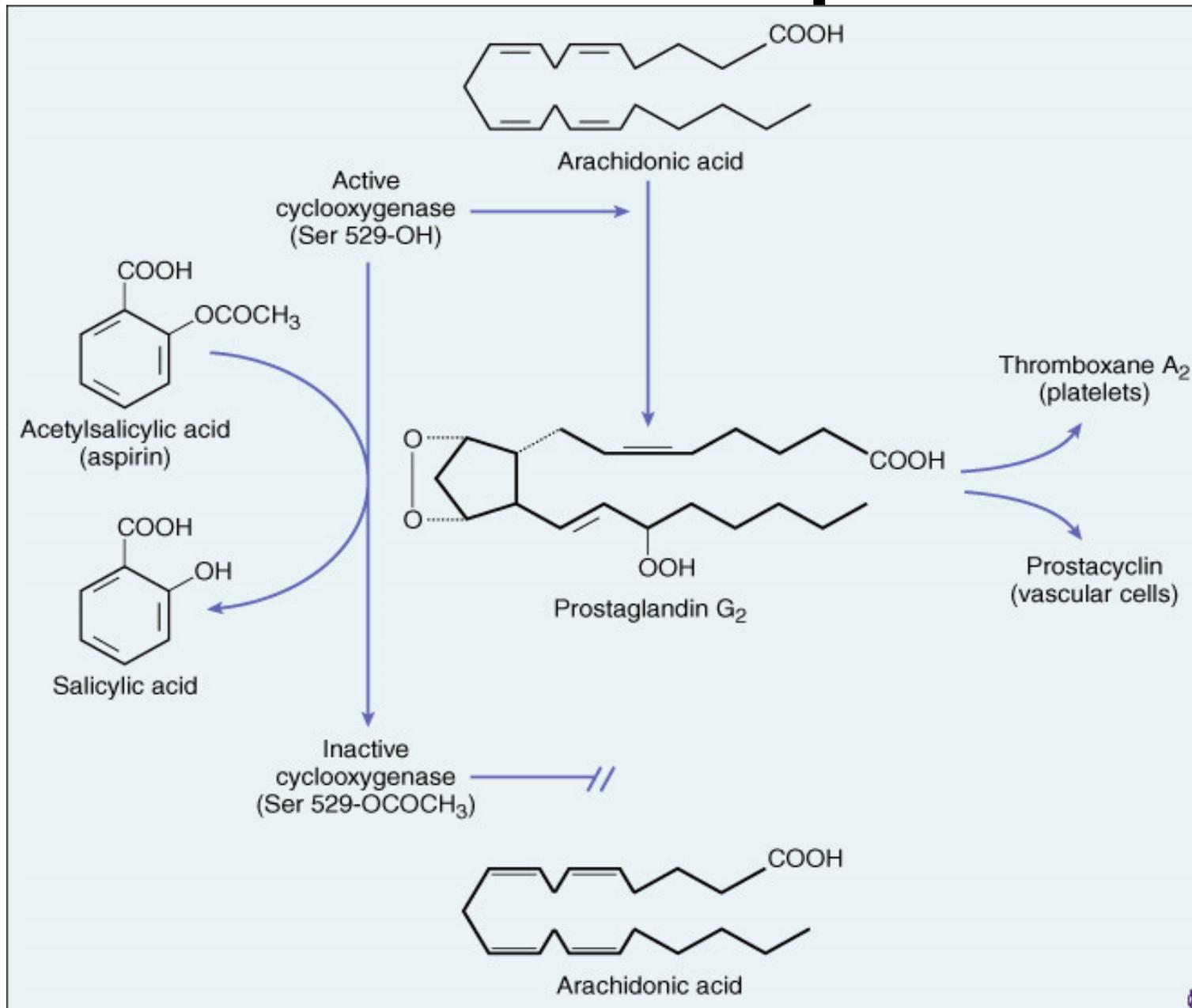


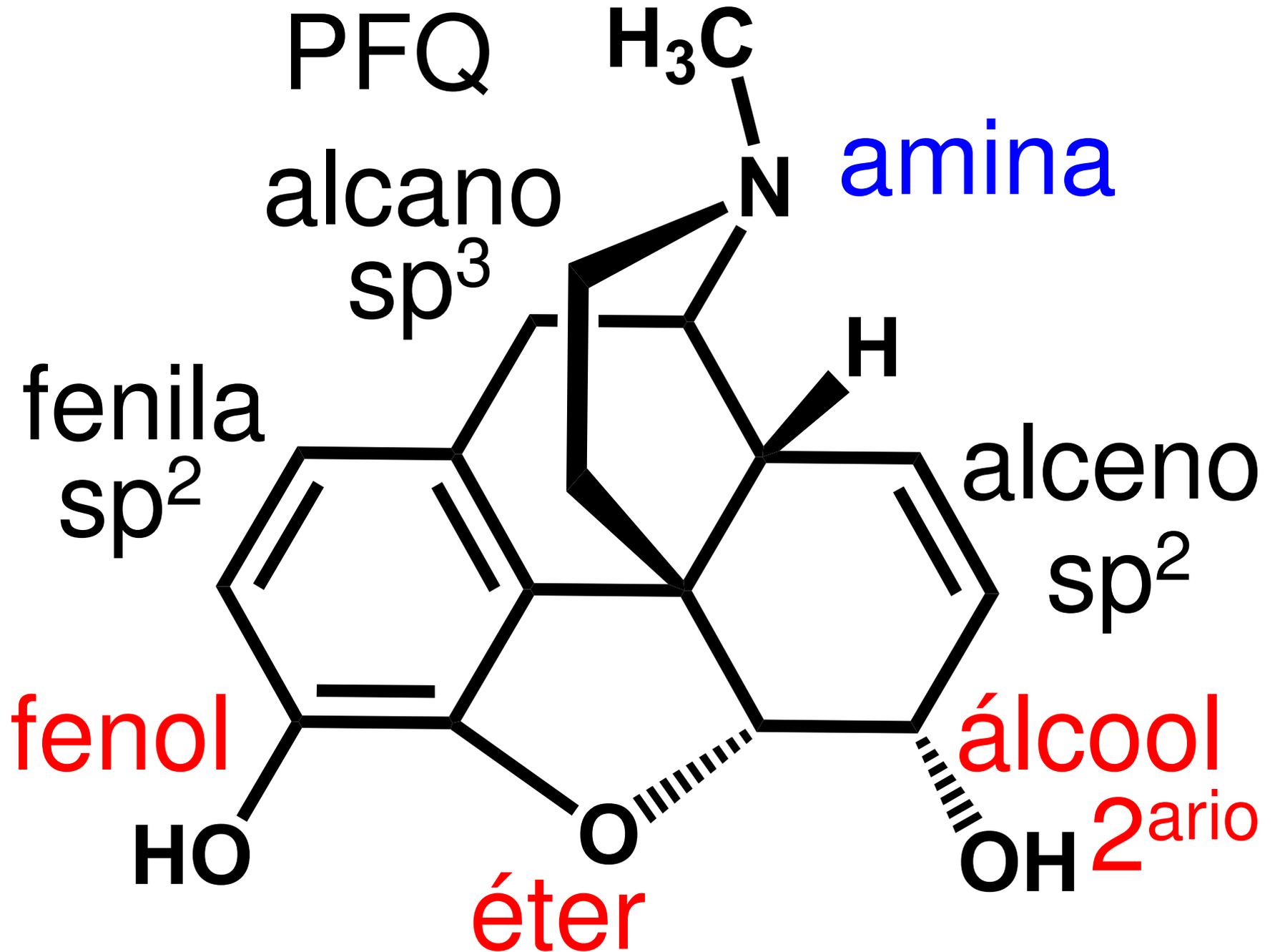
Cascata do Ácido Araquidônico





Cascata do Ácido Araquidônico





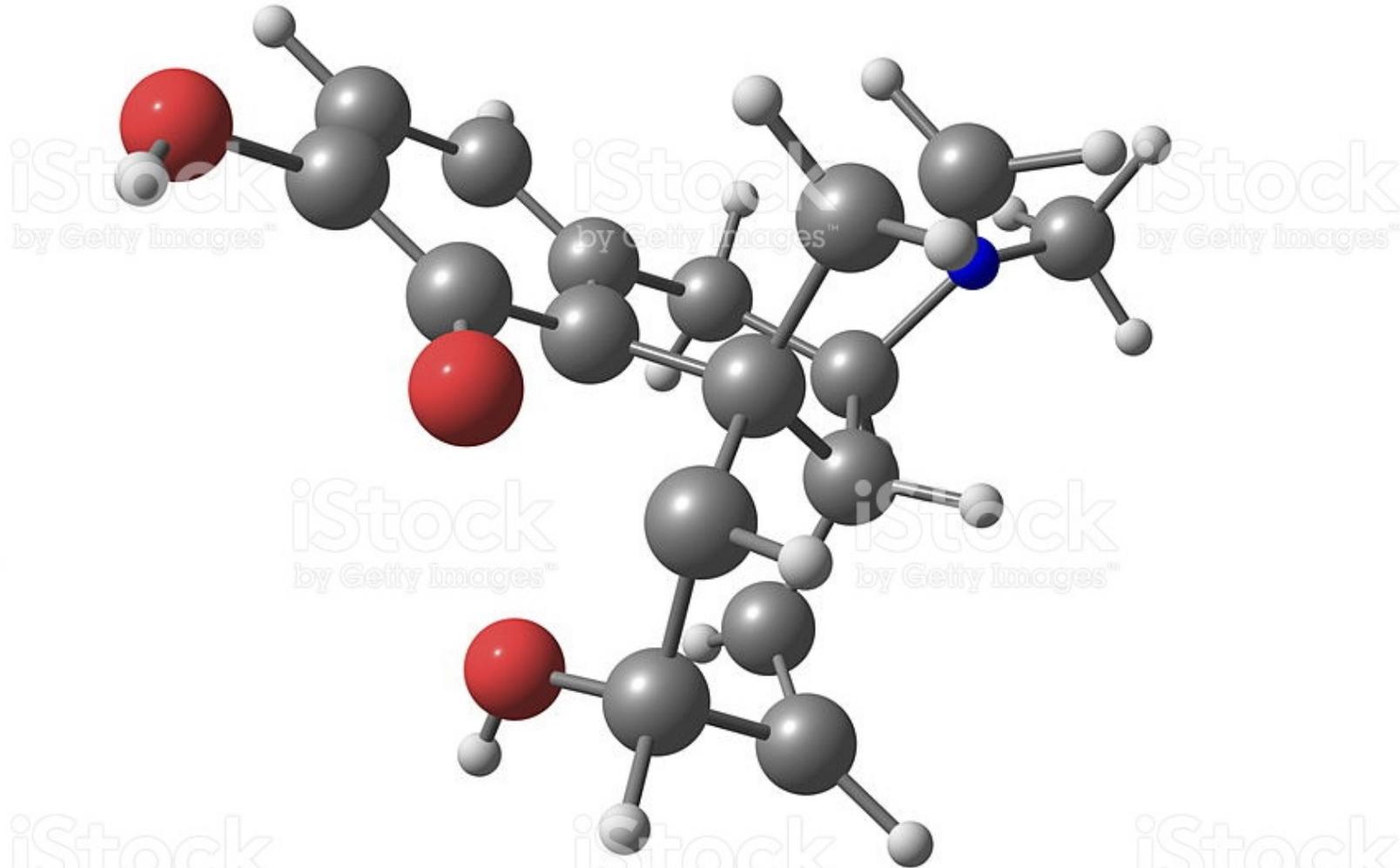


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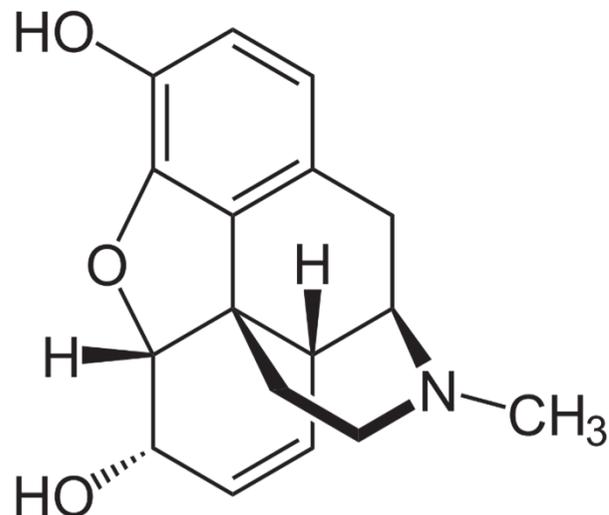
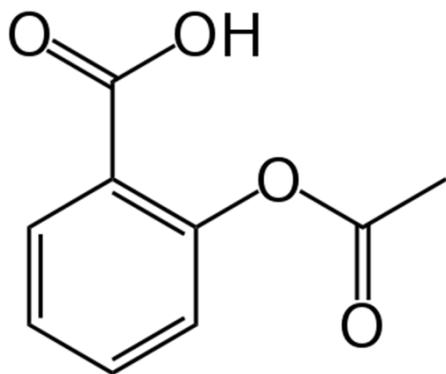
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chaves



Ambas moléculas
são analgésicas



chave

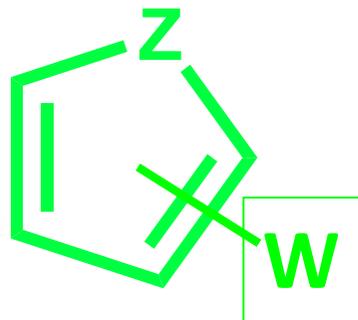


fechadura

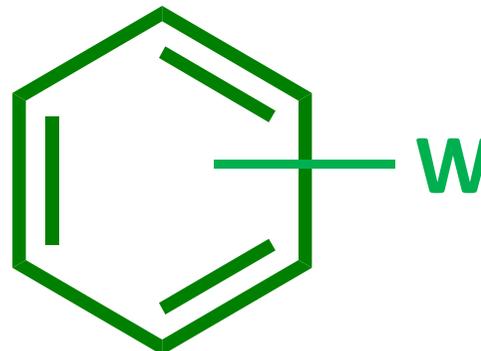




A estrutura química e a atividade



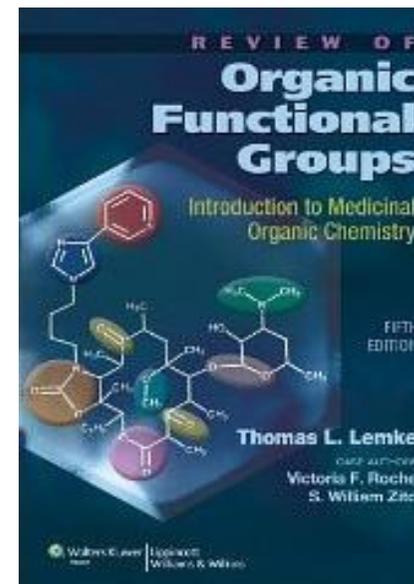
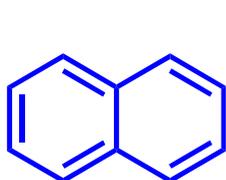
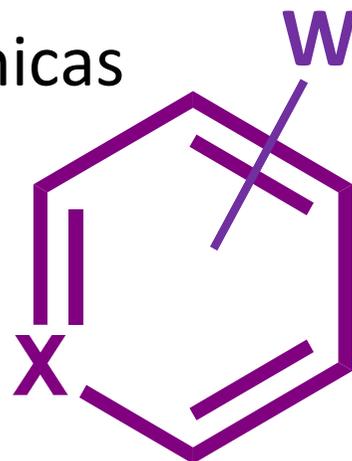
$Z = \text{NH, O, S}$



Propriedades eletrônicas

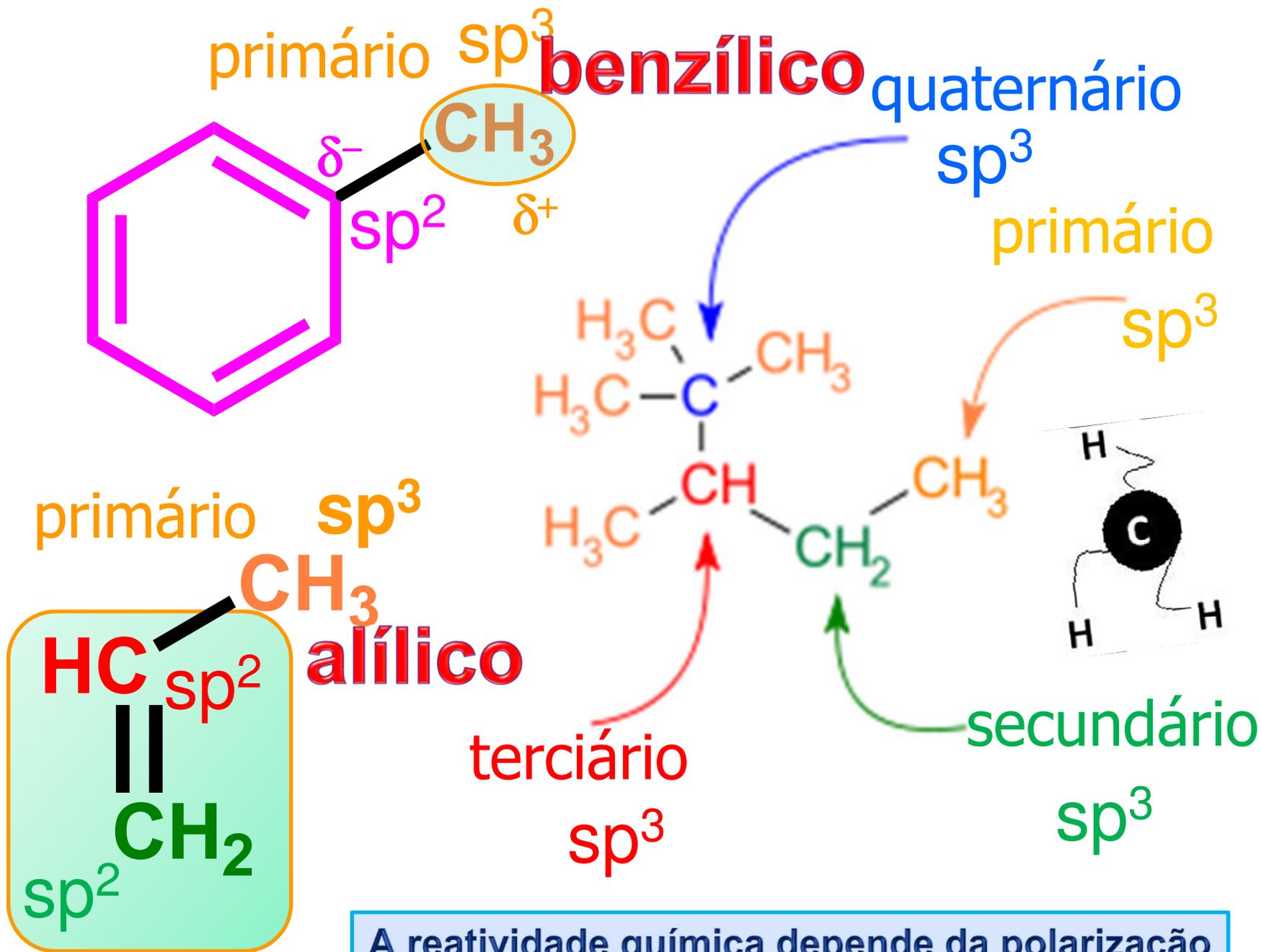
$X = \text{N}$

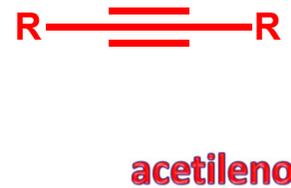
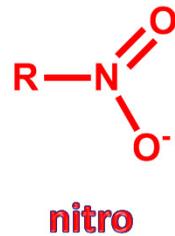
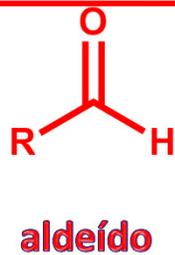
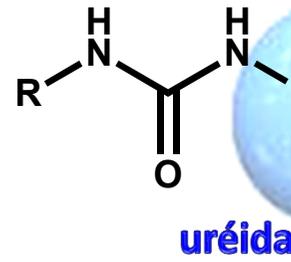
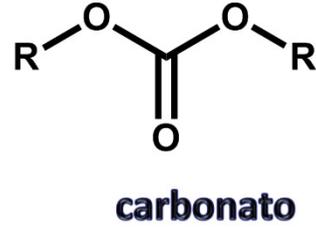
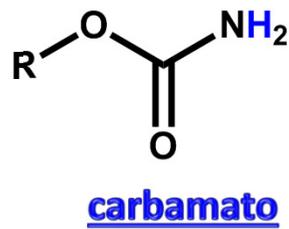
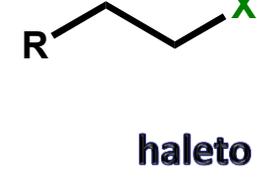
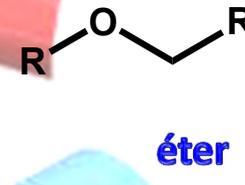
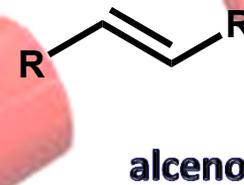
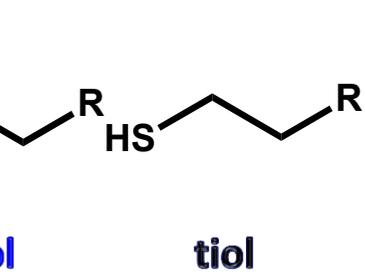
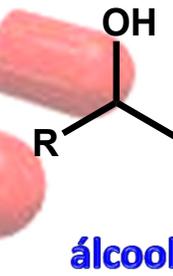
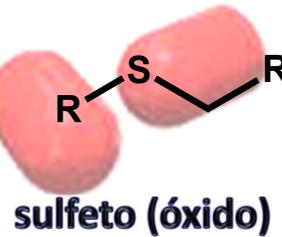
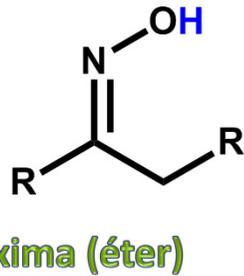
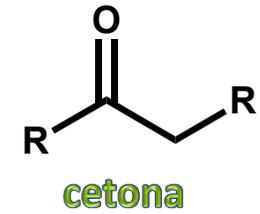
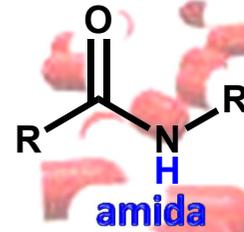
6, 10, 14, 18 π



> 50% dos fármacos
contêm pelo menos *um*
anel aromático, capaz de
sofrer substituições!

Os grupos funcionais mais frequentes nos fármacos





Grupos reativos

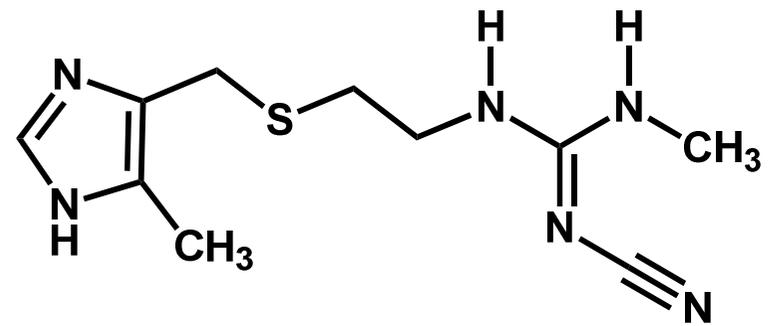
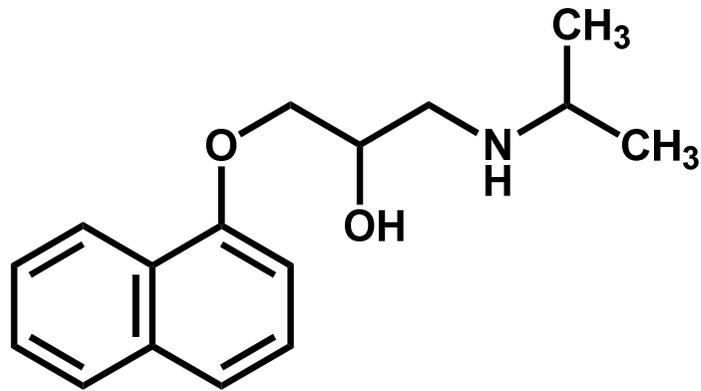
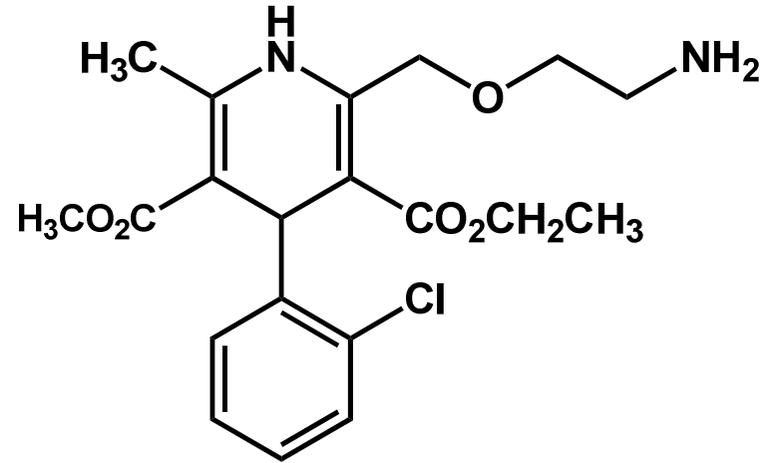
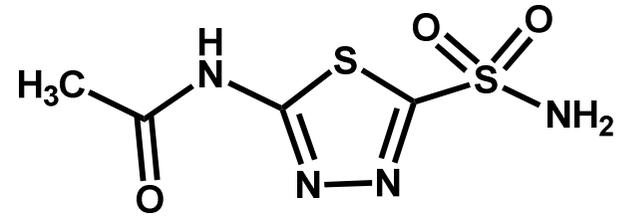
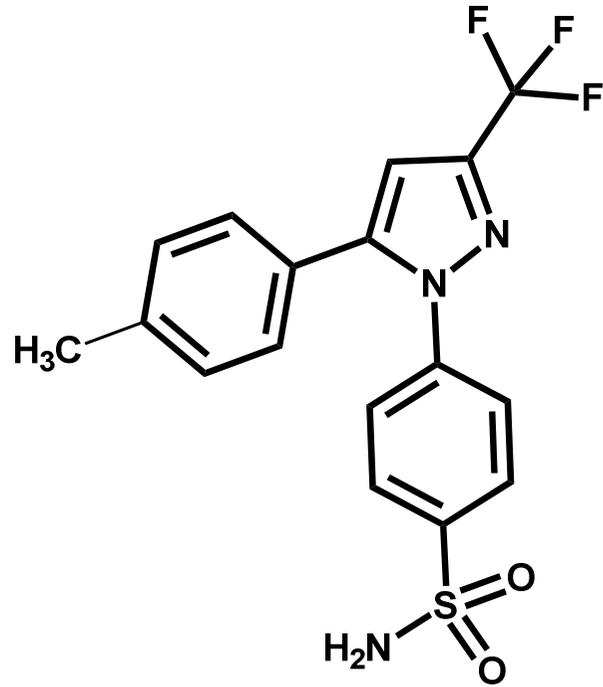


Chemical Abstracts Service ([CAS](#); ACS)
= 139 milhões de compostos (2016)

Chemical space

Espaço químico

Quantos podem ser fármacos?

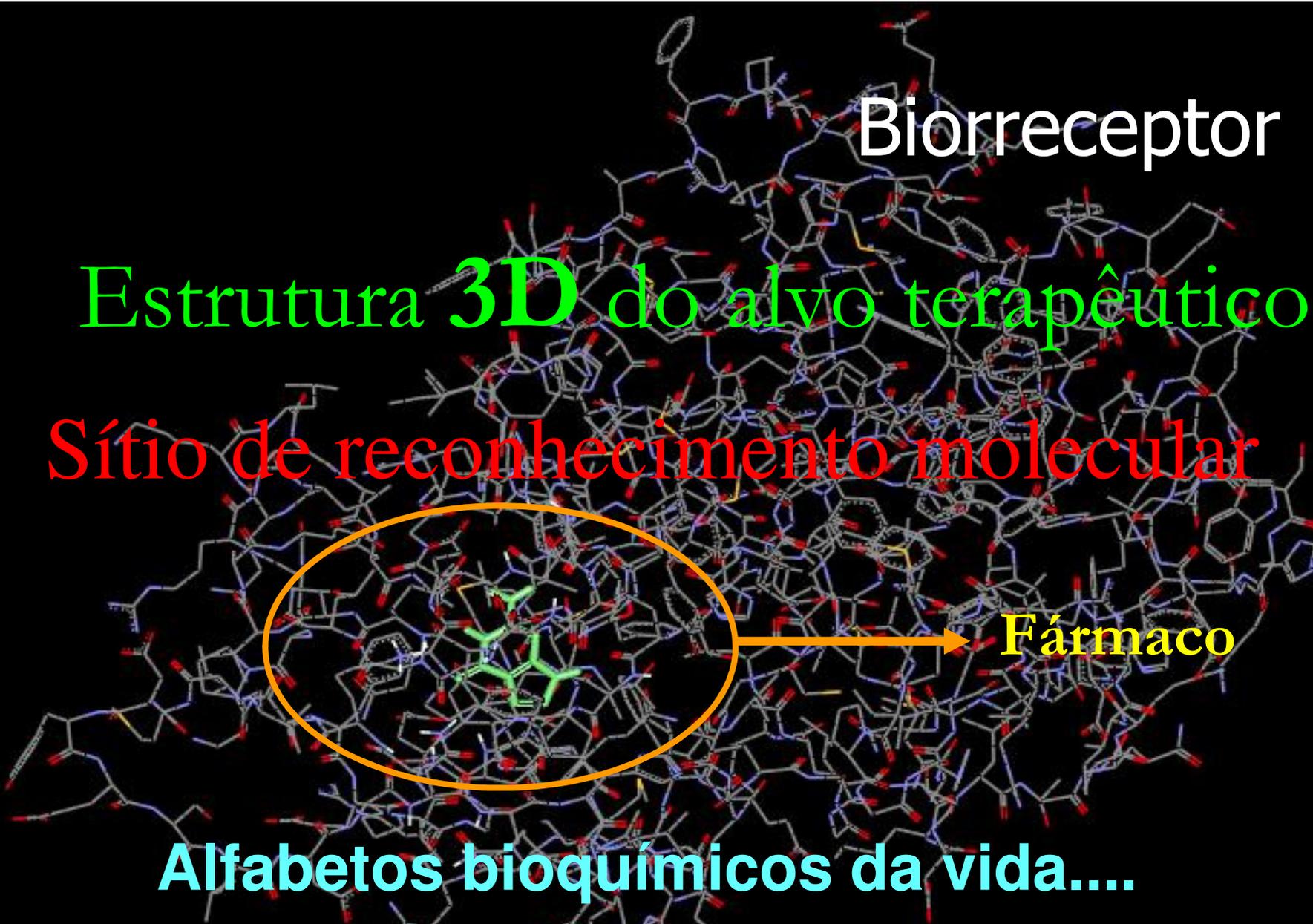




Biorreceptor

Estrutura 3D do alvo terapêutico

Sítio de reconhecimento molecular



Fármaco

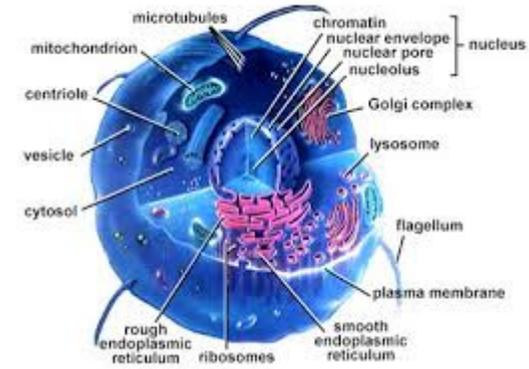
Alfabetos bioquímicos da vida....

483 são os alvos-terapêuticos

dos fármacos contemporâneos!



A maioria dos biorreceptores dos fármacos contemporâneos são enzimas ...



receptores nucleares

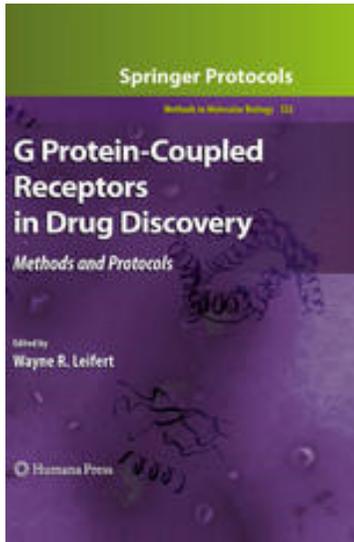
150

receptores acoplados a proteína G (GPCR)

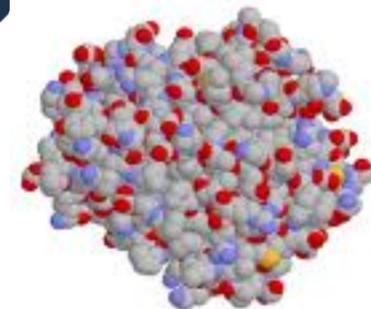
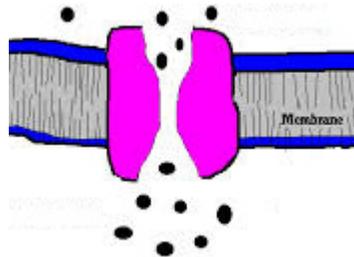
2000

82%

enzimas
3500



canais iônicos
1000



www.nature.com/reviews/drugdisc
Hopkins, A. L. & Groom, C. R. The druggable genome. *Nature Rev. Drug Discov.* 1, 727-30 (2002).