



Mini Curso - 004

# Planejamento de candidatos a novos fármacos

Parte 4

*Eliezer J. Barreiro*

Professor Titular - UFRJ



## Ementa

Breve introdução histórica da Química Medicinal; O papel dos pioneiros; Os fármacos e os produtos naturais; Estratégias de desenho molecular de novos candidatos a fármacos; Considerações finais.

64ª Reunião Anual da SBPC

22 a 27 de Julho de 2012 | UFMA | São Luís, MA

CIÊNCIA, CULTURA E SABERES TRADICIONAIS PARA ENFRENTAR A POBREZA.

SB  
PC



Universidade Federal do Rio de Janeiro

# Considerações finais



Química  
e Medicinal



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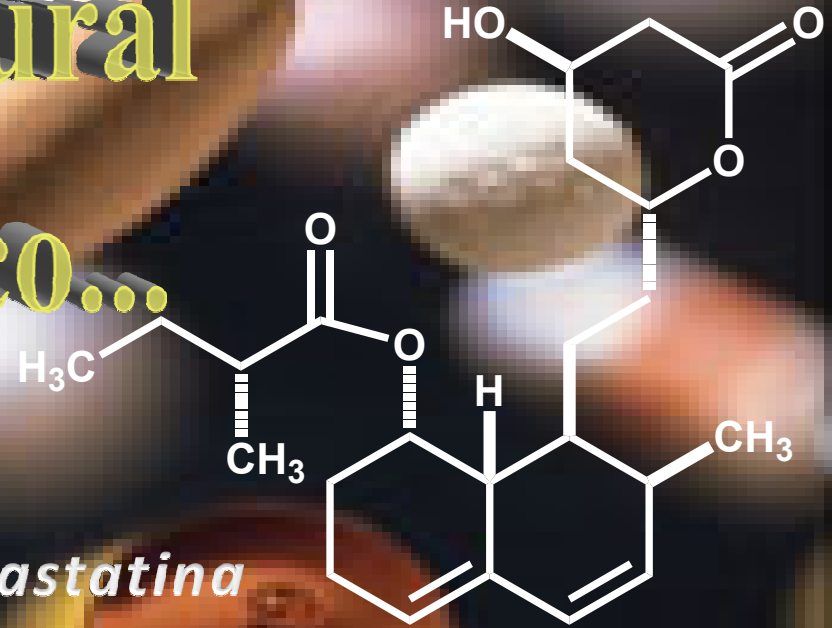
# Do protótipo natural ao Super-fármaco...



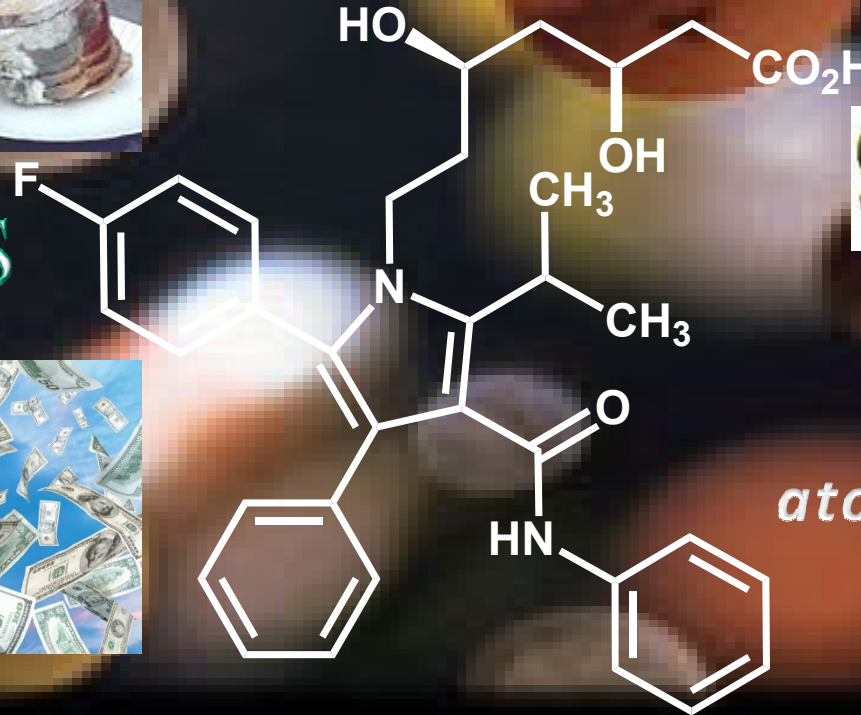
## Fungos



*mevastatina*



*atorvastatina*





Universidade Federal do Rio de Janeiro



Akira Endo, Sankyo Co

# Metabólito de Fungo

## Protótipo natural

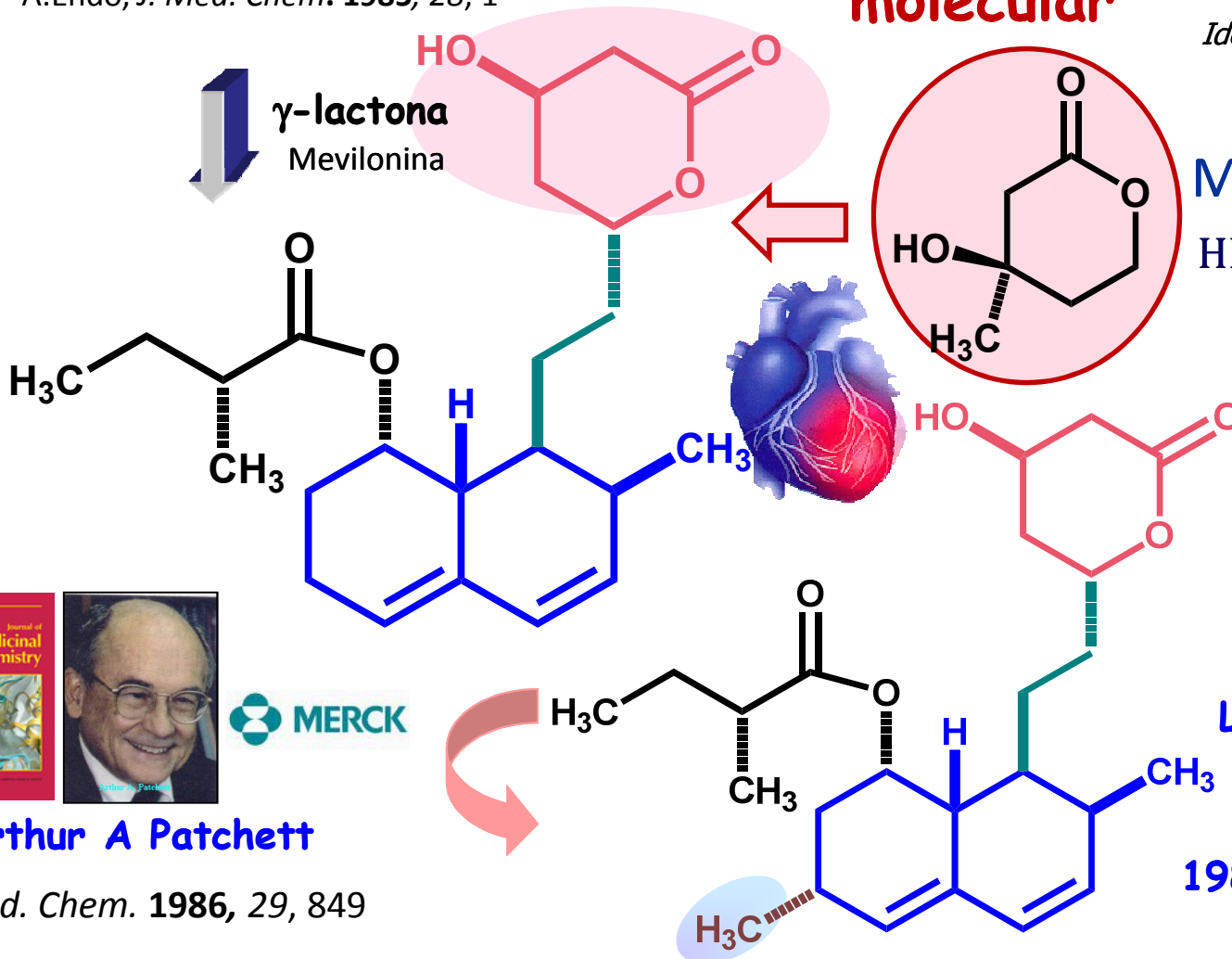


A.Endo, *J. Antibiot.*  
**1976**, 29, 1346  
*Penicillium citrinum*  
*Idem, Ibid*, **1979**, 32, 852  
*Monascus ruber*  
(compactina)

1975 – Mevastatina (ML-263b)

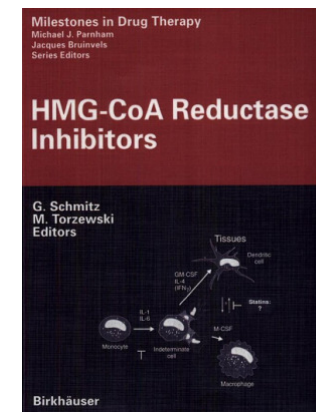
A.Endo, *J. Med. Chem.* **1985**, 28, 1

### Similaridade molecular



### Mevalolactona

HMG-CoA redutase



### Lovastatin (MK-803)

1980 – Merck & Co.  
*Aspergillus terreus*

1987 – MS&D (Mevacor<sup>®</sup>)



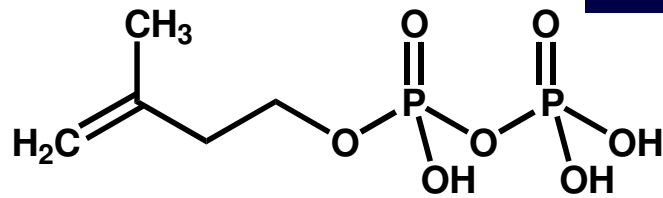
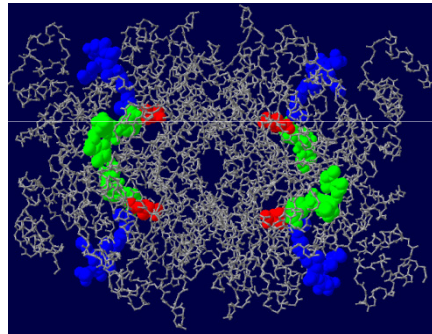
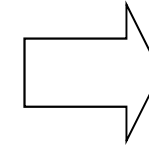
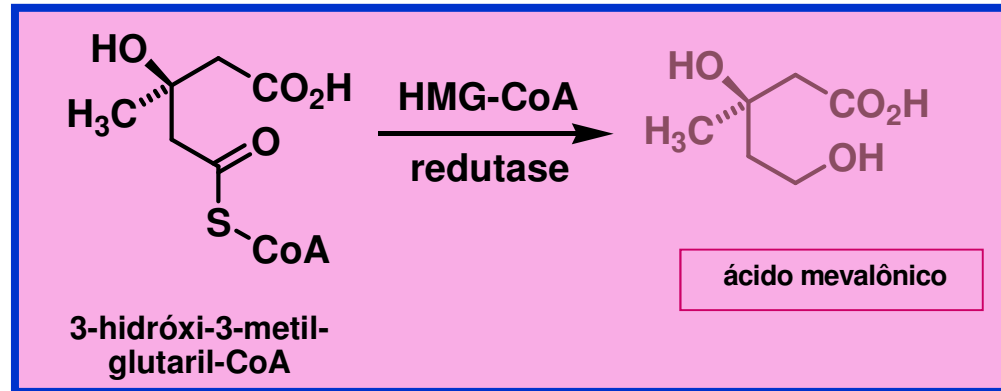
Arthur A Patchett

*J. Med. Chem.* **1986**, 29, 849

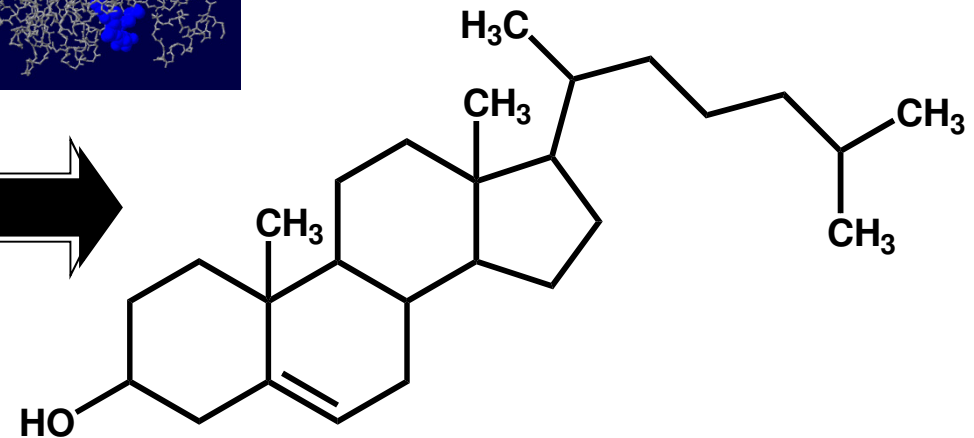
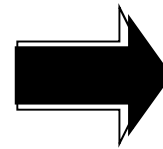




# Biossíntese do colesterol



pirofosfato de isopentenila



colesterol

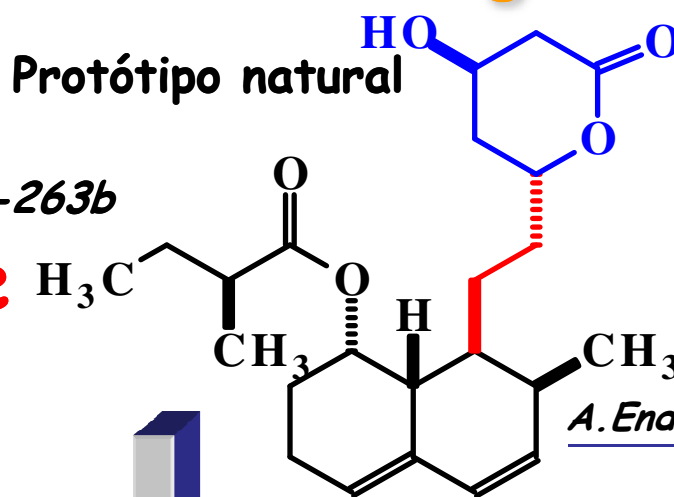


Akira Endo, Sankyo Co

1975 - Mevastatina (ML-263b)

# Similaridade molecular

## Metabólito de Fungo



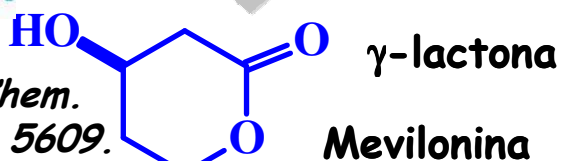
A.Endo, *J. Antibiot.*  
1976, 29, 1346  
*Penicillium citrinum*  
Idem, *Ibid*, 1979, 32, 852  
*Monascus ruber*  
(*compactina*)

A.Endo, *J. Med. Chem.* 1985, 28, 01

Arthur A. Patchett

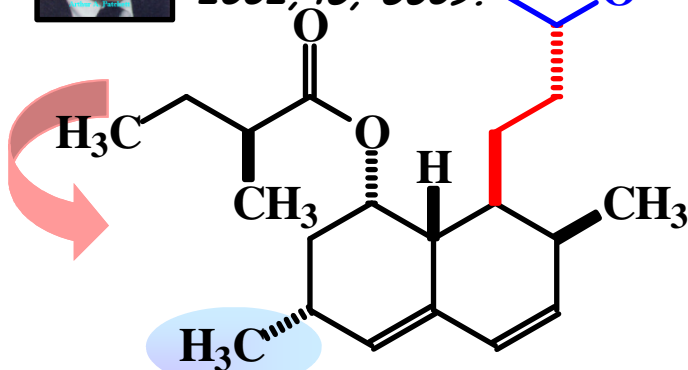


*J. Med. Chem.*  
2002, 45, 5609.



US\$ 5,5 bi  
(2007)

Pró-fármaco



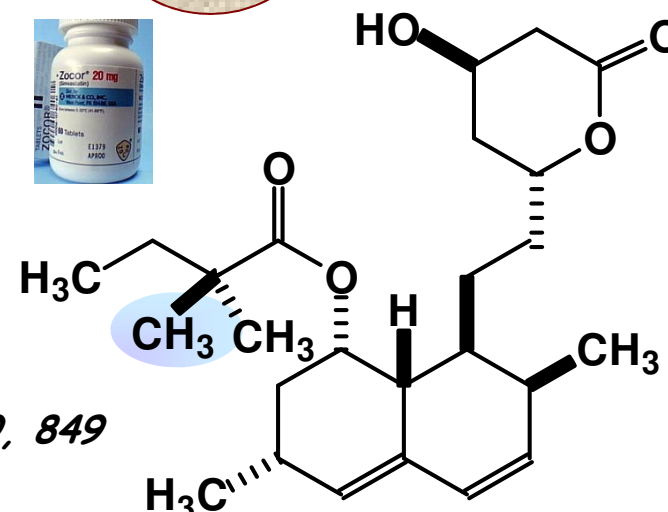
Lovastatin (MK-803)

1980 - Merck & Co.

*Aspergillus terreus*

1987 - MS&D (Mevacor<sup>®</sup>)

*Simvastatin*  
(Zoccor<sup>®</sup>)  
MK-733  
1988



IC<sub>50</sub> = 11,2 nM

*J. Med. Chem.* 1986, 29, 849





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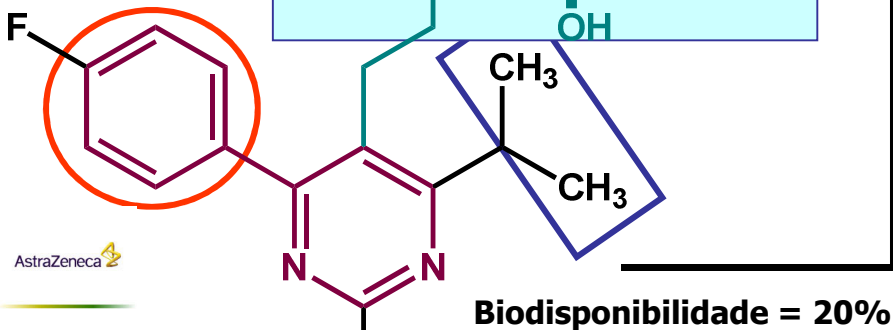
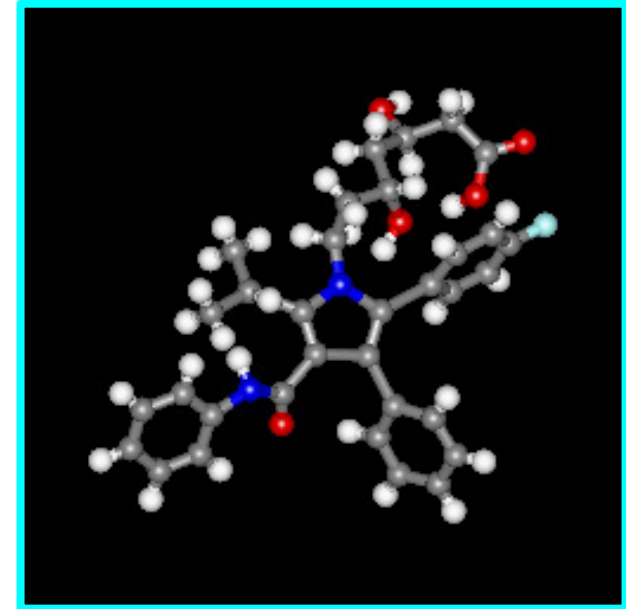
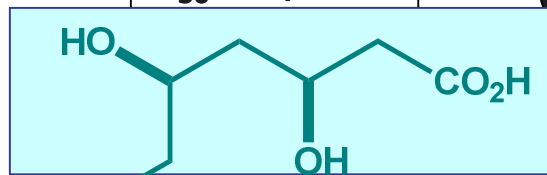
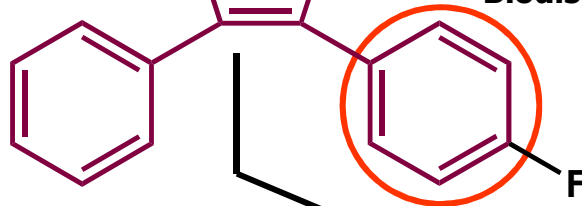
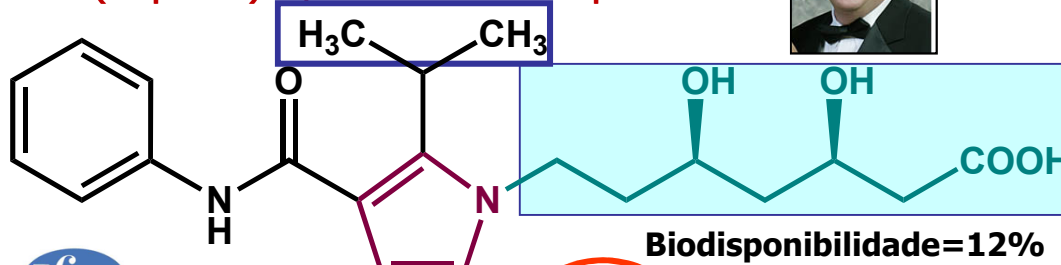
# Estatinas

ácido (*N*-pirrol)-3,5-di-hidróxi-heptanóico

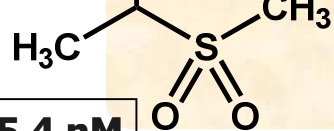
Bruce Roth



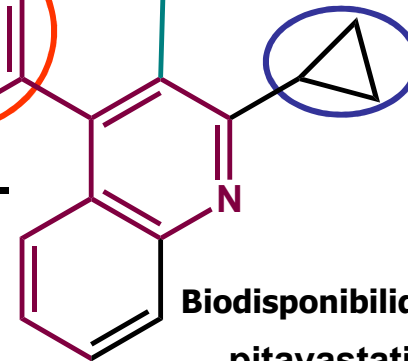
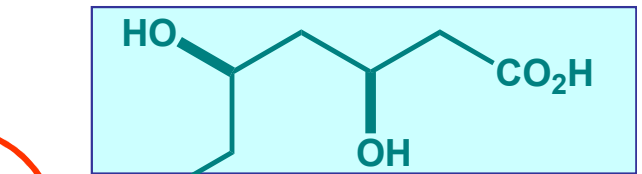
## Similaridade Molecular



rosuvastatina



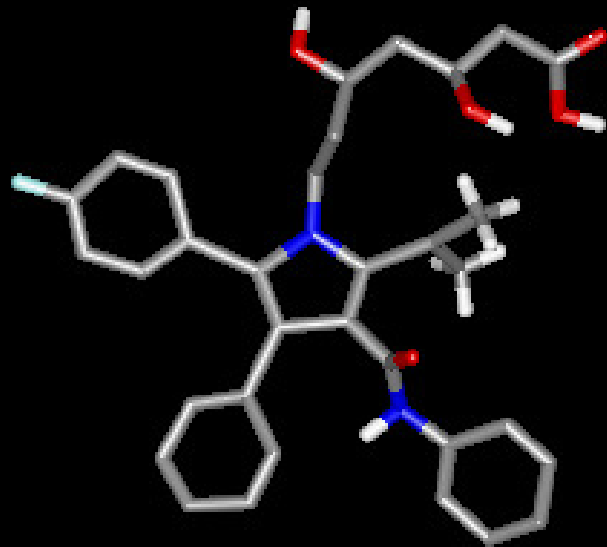
(pitavastatin) tablets  
 Kowa Pharmaceuticals



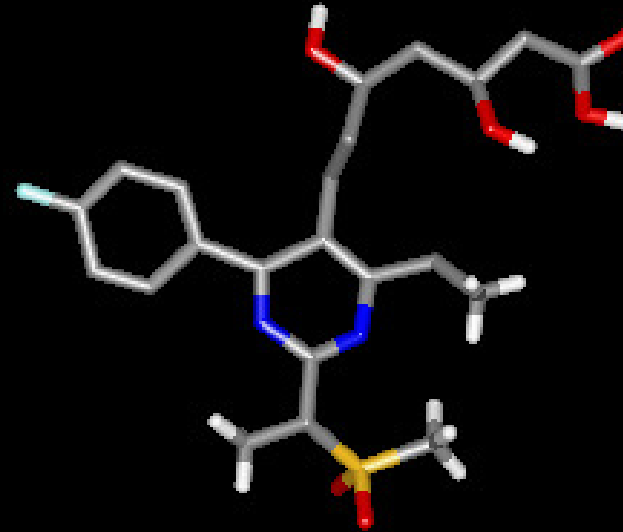
$IC_{50} = 3,4 \text{ nM}$



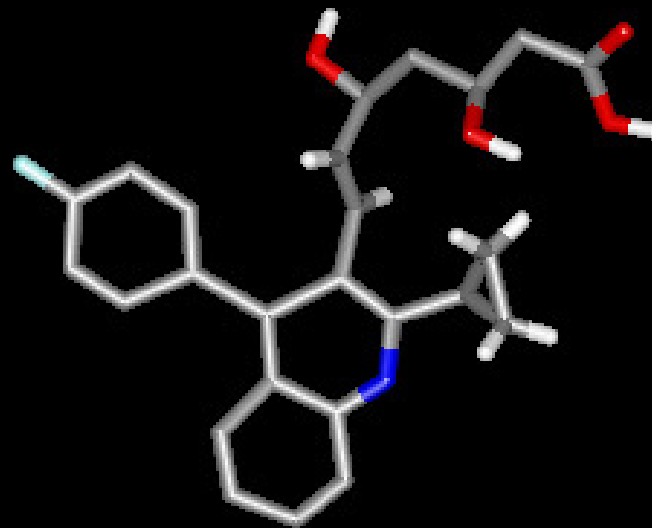




atorvastatina



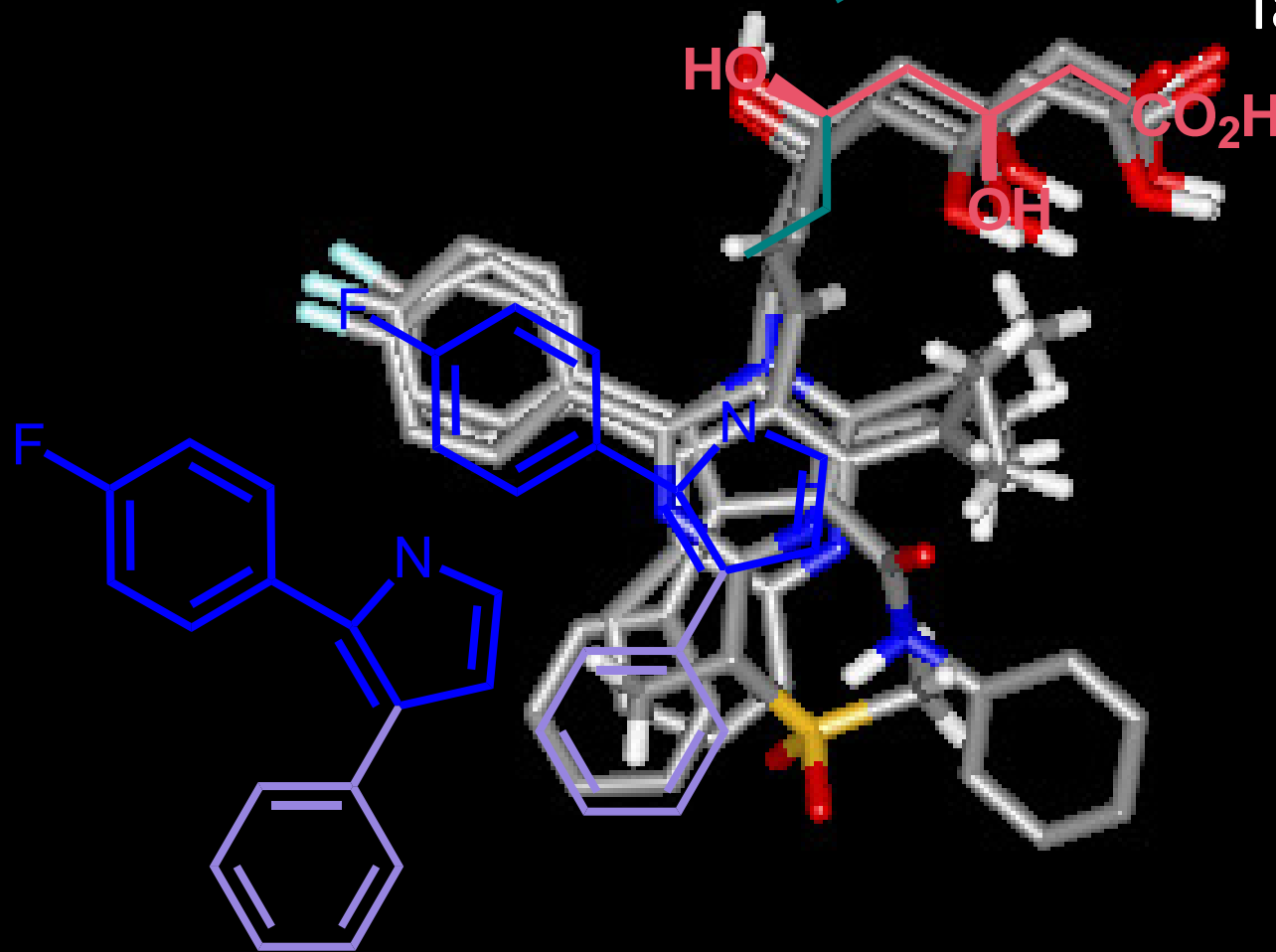
rosuvastatina



pitavastatina

Grupamento farmacofórico

Pontos farmacofóricos



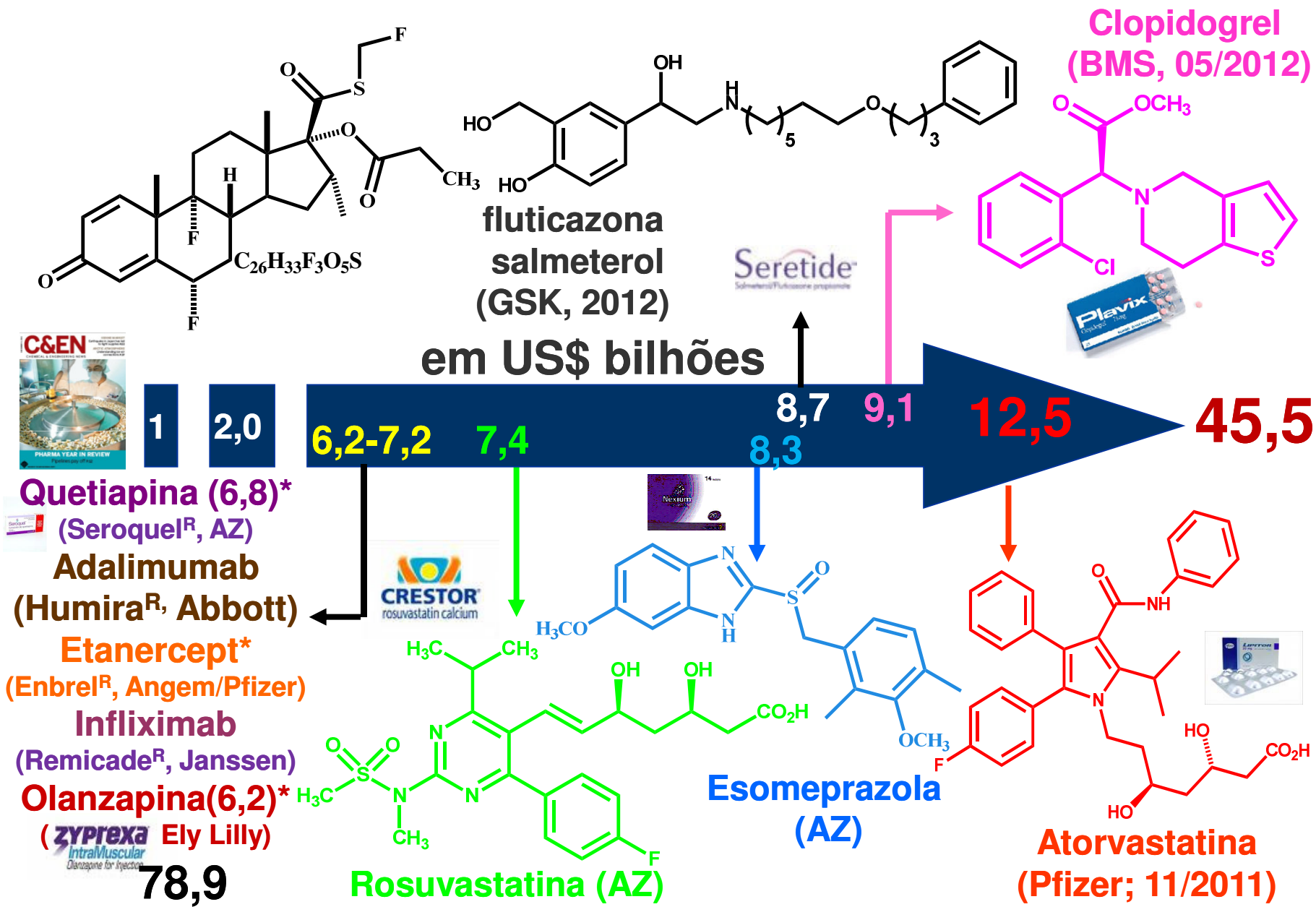
Grupamento auxofórico

Bióforos



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# Os fármacos *best-seller* em 2011\*



**1** **2,0**

**Quetiapina (6,8)\***  
(Seroquel<sup>®</sup>, AZ)

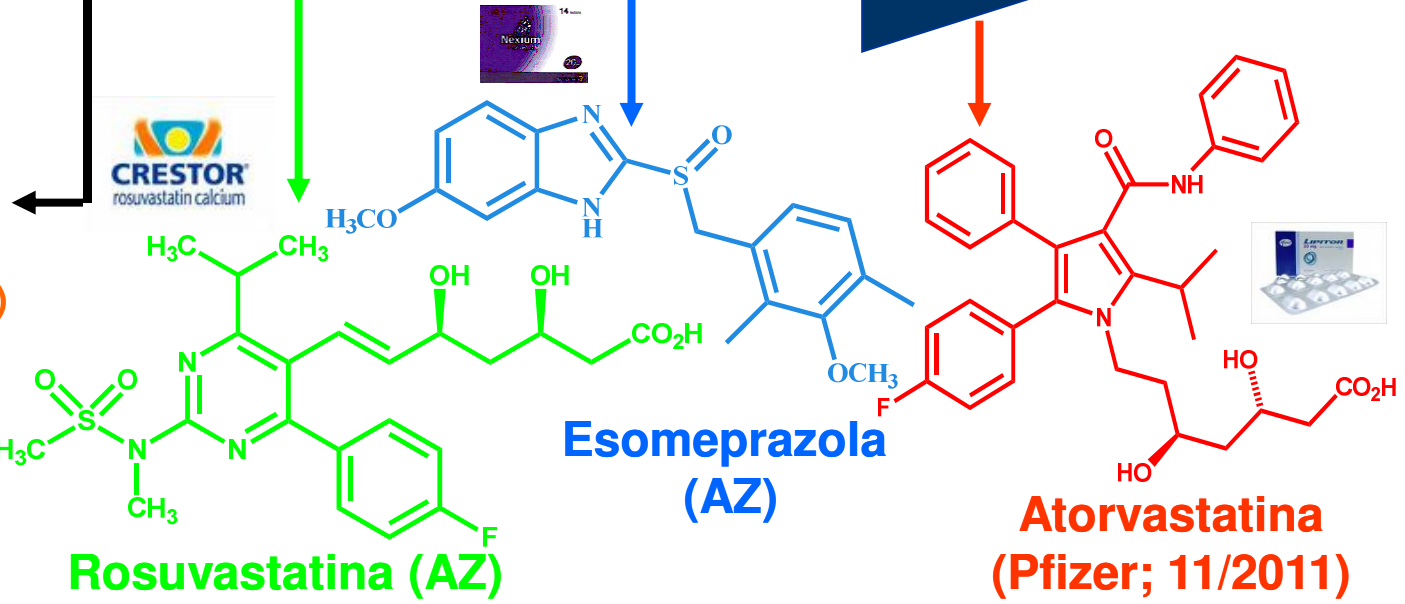
**Adalimumab**  
(Humira<sup>®</sup>, Abbott)

**Etanercept\***  
(Enbrel<sup>®</sup>, Amgen/Pfizer)

**Infliximab**  
(Remicade<sup>®</sup>, Janssen)

**Olanzapina (6,2)\***  
(ZYPREXA Ely Lilly)

**78,9**  
(3,9%)



\* R Mullin, *C&EN* 2011 (05/12) 12-18



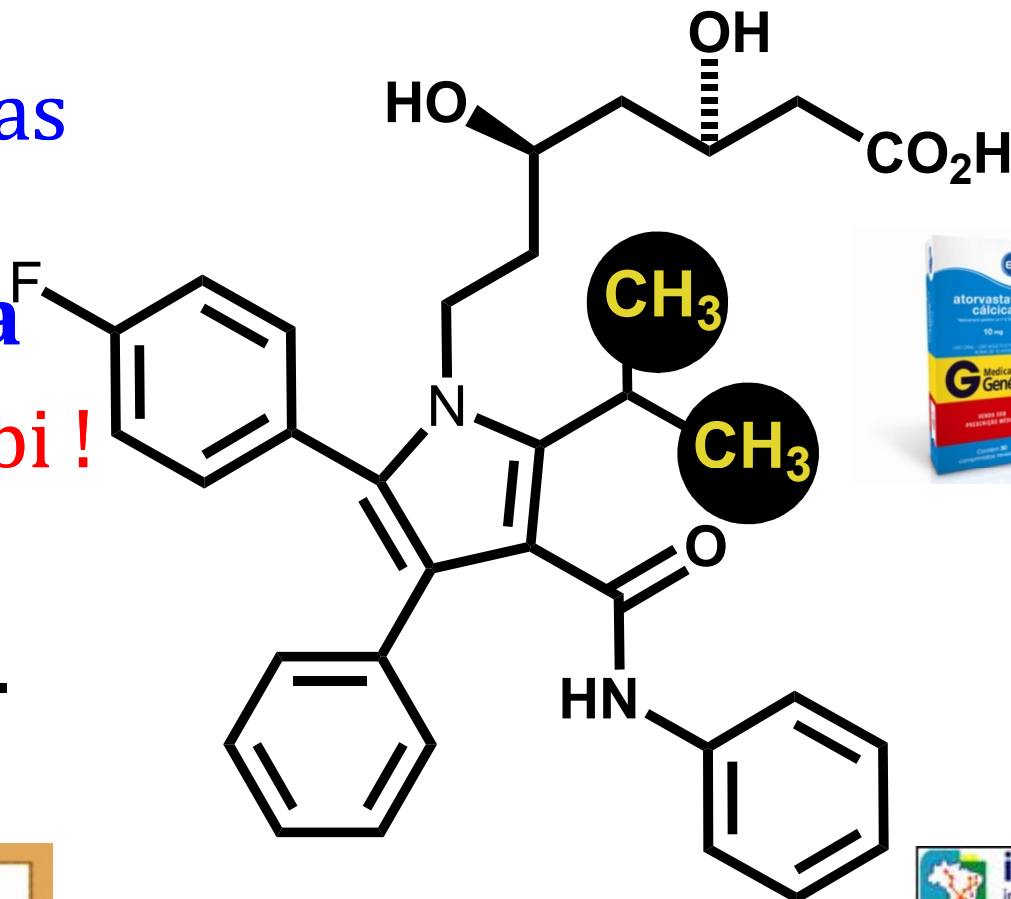
# As metilinhas mais valiosas da história... ...cada = US\$ 3,6 bi!

1991-2011

➤ Total de vendas mundiais da atorvastatina

**ca. >US\$ 120 bi!**

➤ 41 milhões de pessoas.



1985 - Bruce D Roth, Parke Davis Co

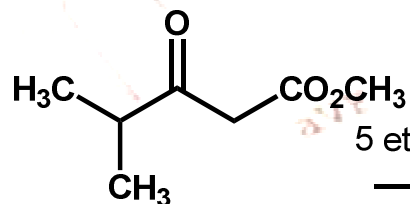
Escala de 5g  
11 etapas = 19,3%



2010



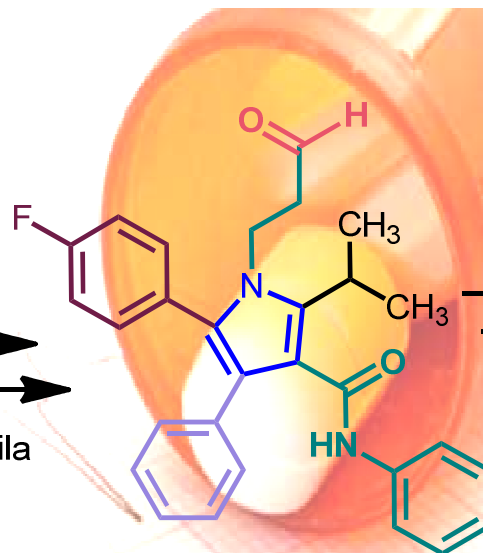
Universidade Federal do Rio de Janeiro



5 etapas

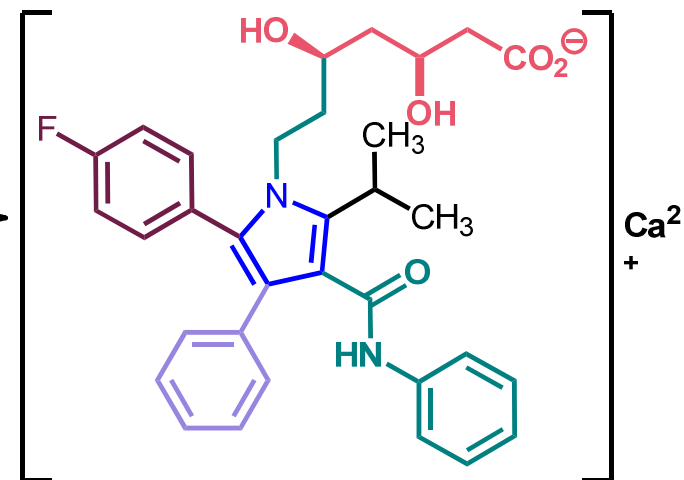
4-metil-3-oxo pentanoato de metila

US Patent Number 5,273,995



intermediário-chave

7 etapas



atorvastatina cálcica

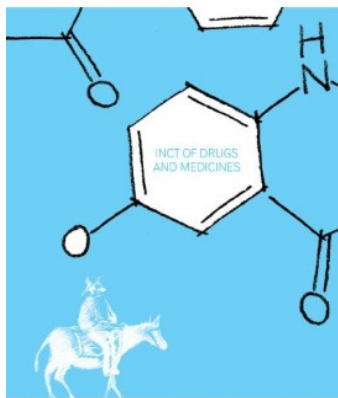
12 etapas  
Y = 4,2 %

INCT-INOVAR  
11 etapas  
Y = 19,3%

LC Dias, AS Vieira, EJ Barreiro,  
Processo de obtenção de atorvastatina cálcica utilizando novos intermediários

PI 018110015039 (INPI, em  
25/04/2011)

PCT dezembro de 2011



2010 ANNUAL ACTIVITIES REPORT

[www.inct-inofar.ccs.ufrj.br/download/aar/2010.pdf](http://www.inct-inofar.ccs.ufrj.br/download/aar/2010.pdf)



Universidade Federal do Rio de Janeiro

**inovar**  
**inofar**

**INOVAÇÃO RADICAL**  
Inovação de produtos em fase de pesquisa de alto impacto, com potencial de gerar produtos inéditos que revolucionam a terapêutica medicamentosa.

**INOVAÇÃO INCREMENTAL**  
Desenvolvimento de novos fármacos para melhorar ou complementar os existentes, quanto aos efeitos, efeitos secundários, palatabilidade e preço.

**DIVULGAÇÃO CIENTÍFICA**  
Atividade científica e divulgação de resultados de pesquisas em áreas relacionadas à saúde humana, promovendo a interação entre pesquisadores e a sociedade em geral.

**EDUCAÇÃO CONTINUADA**  
Atividades educativas para atualização dos profissionais de saúde em temas relacionados à pesquisa e desenvolvimento de fármacos e medicamentos, promovendo a interação entre pesquisadores e a sociedade em geral.

**EDUCAÇÃO EM SAÚDE**  
Atividades educativas para a população em geral, promovendo a interação entre pesquisadores e a sociedade em geral.

**instituto nacional de ciência e tecnologia de**  
**Fármacos e Medicamentos**  
[www.inct-inofar.ccs.ufrj.br](http://www.inct-inofar.ccs.ufrj.br)

**COLÓQUIO INCT-INOVAR:**  
21/08 das 14h às 16h  
Agende-se aqui.

**REDE DE PESQUISA**

**LASSBio**  
Laboratório de Avaliação e Síntese de Substâncias Bioativas



Universidade Federal do Rio de Janeiro

# O uso de produtos naturais abundantes como biofóforos

química nova

Volume 32, Número 3, 2009

Recursos Naturais:

Oportunidades na Academia e na Indústria



## LASSBio

Laboratório de Avaliação e Síntese de Substâncias Bioativas

EJ Barreiro & VS Bolzani, Biodiversidade: fonte potencial para a descoberta de fármacos, *Química Nova* 2009, 3, 679



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**LASSBio**  
Laboratório de Avaliação e Síntese de Substâncias Bioativas

Química Medicinal



**Eleição do alvo-terapêutico**



Química Computacional



Produtos Naturais

Síntese Orgânica Medicinal



Protótipo

Bioensaios



Ensaio clínico

Otimização

Novo fármaco



Quimioteca com 1745 compostos originais





# Óleo de Sapucaíinha

1980



Ácido hidnocárpico

Cole & Cardoso, 1938

**Sapucainha**, Papo de anjo, Pau de cachimbo, Canudo de pito, Fruta de cotia, Fruta de Macaco.



*Carpotroche brasiliensis*, Endl  
Flacourtiácea



AS Oliveira, JA Lima, CM Rezende, AC Pinto, Ácidos ciclopentênicos do óleo da Sapucainha (*Carpotroche brasiliensis* Endl, Flacourtiaceae): o primeiro antileprótico usado no Brasil, *Quim. Nova* **2009**, 32, 139-145.



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# Produtos naturais como blocos moleculares

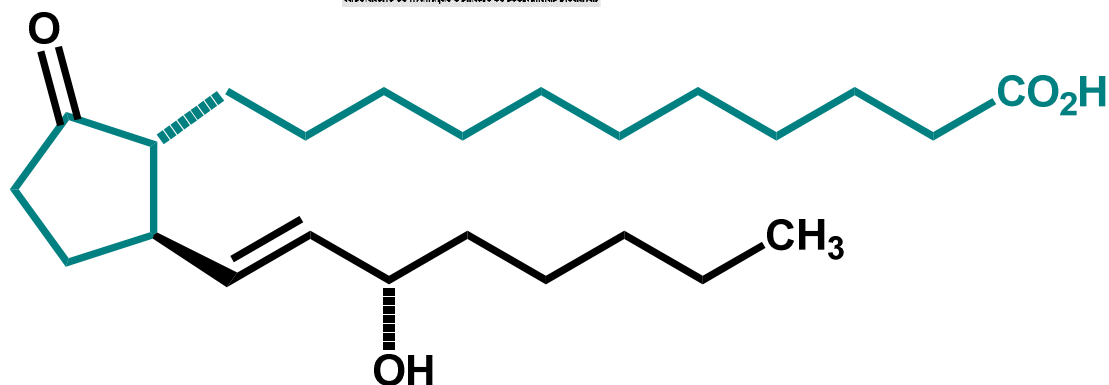


Óleo de sapucainha  
*Carpotroche brasiliensis* Endl.

1982



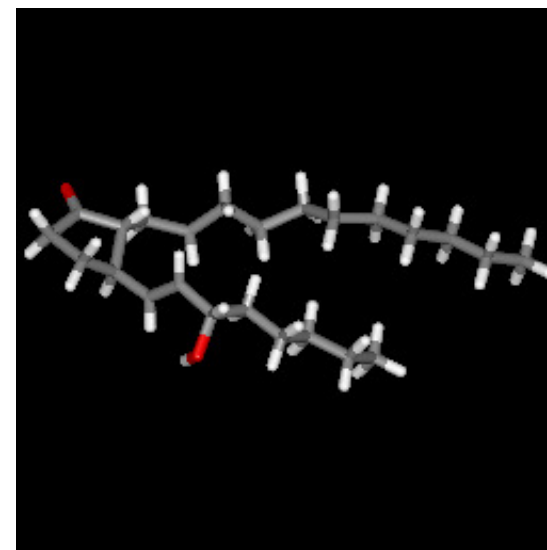
Coronel  
Fabriciano, MG



11-desoxi-tetrahomopGE<sub>1</sub>\*

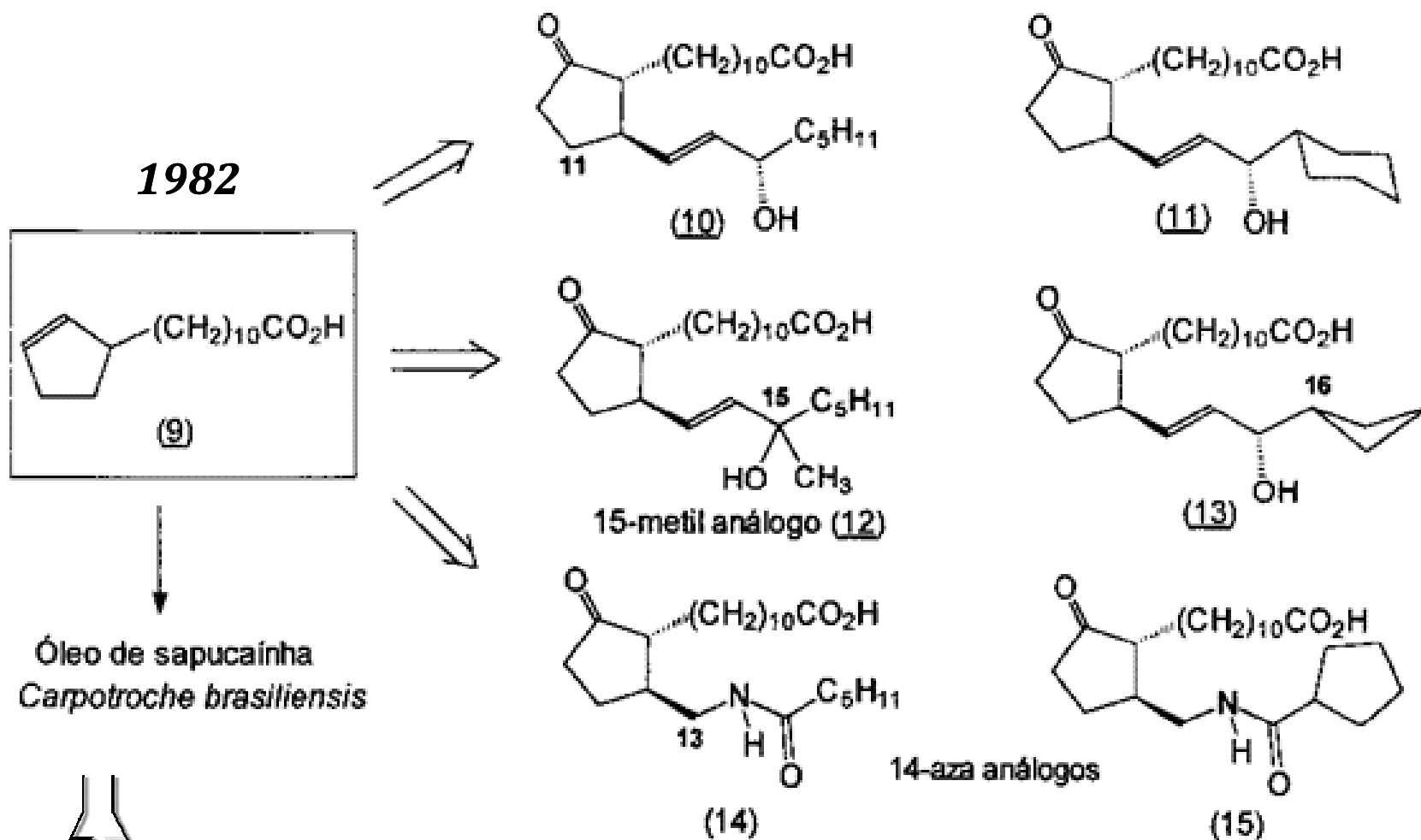
EJ Barreiro, LNLFGomes, Prostaglandin Analogues. Synthesis of Tetrahomoprostaglandin Derivatives From Natural Hydnocarpic Acid Isolated From Sapucainha Oil, *J. Chem. Res.* **1983**, 2701;

\*EJ Barreiro, LNLFGomes, Novo Método de Síntese de Prostaglandinas Modificadas da Série 11-desoxi PG E1". INPI, PI 38201866, 02/04/1982 ; *Chem. Abstr.*, **100**, 17452lu (1984)





# Primeiras prostaglandinas brasileiras\*





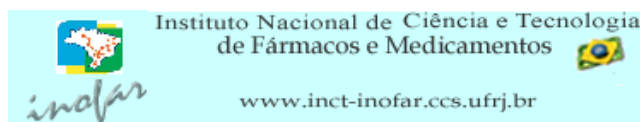
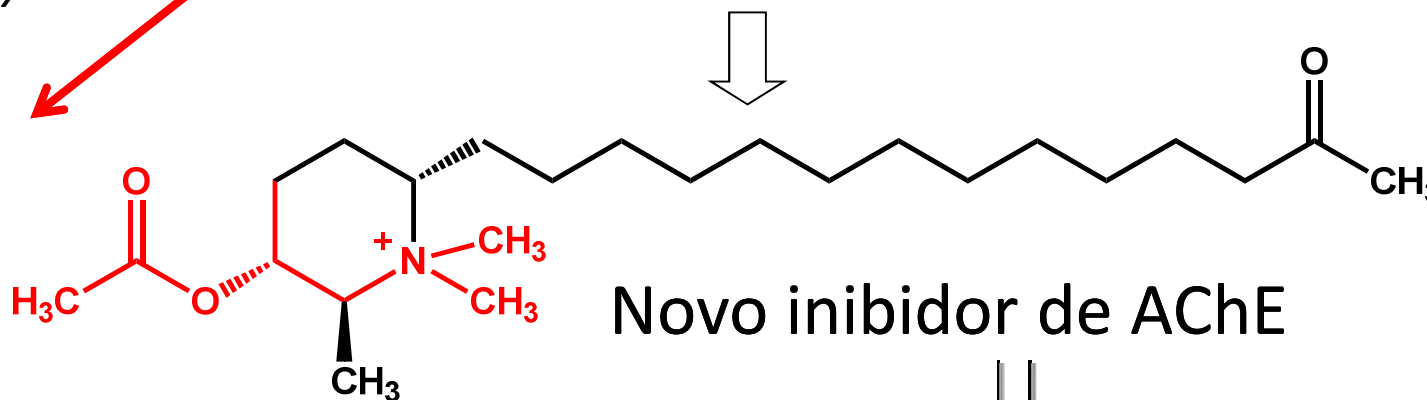
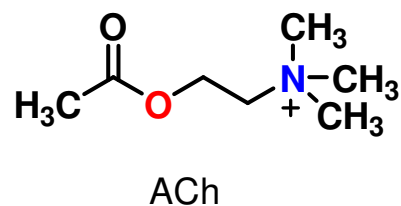
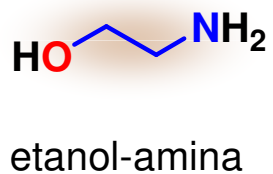
2003

# Novos inibidores de AChE\*



*Cassia leptophylla*  
Leguminosa

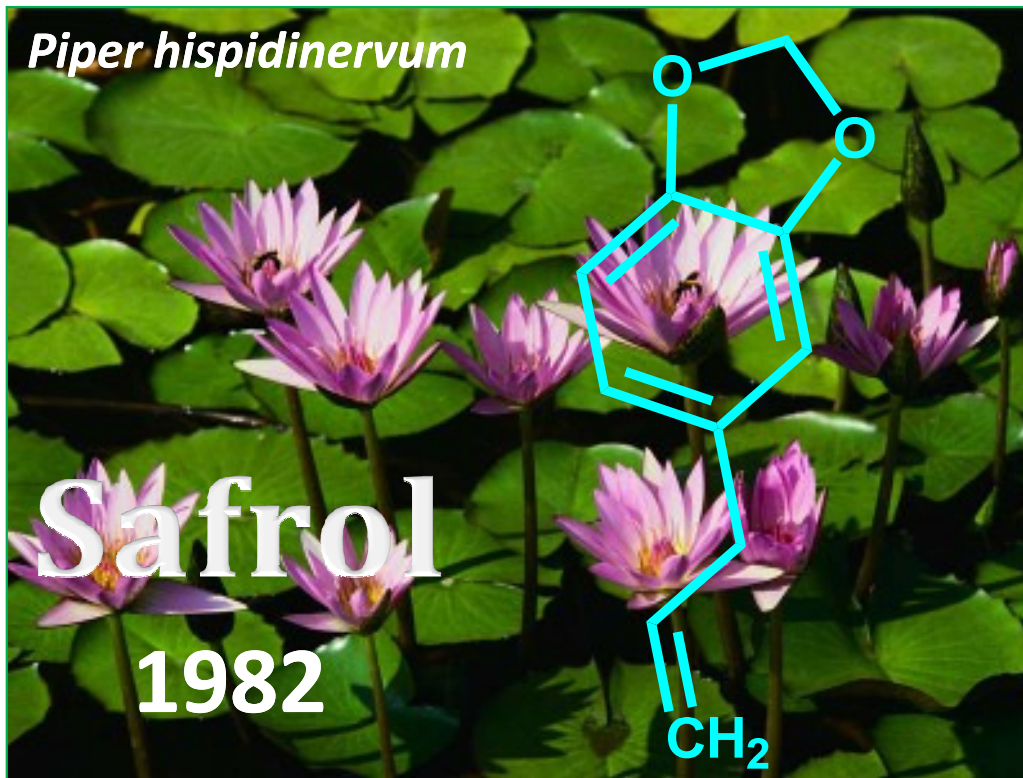
Protótipo natural



\* Patent NZ554392 (15/10/2004)

\* INPI PI 0305690-2 08/10/2003





*Piper hispidinervum*

Safrol

1982

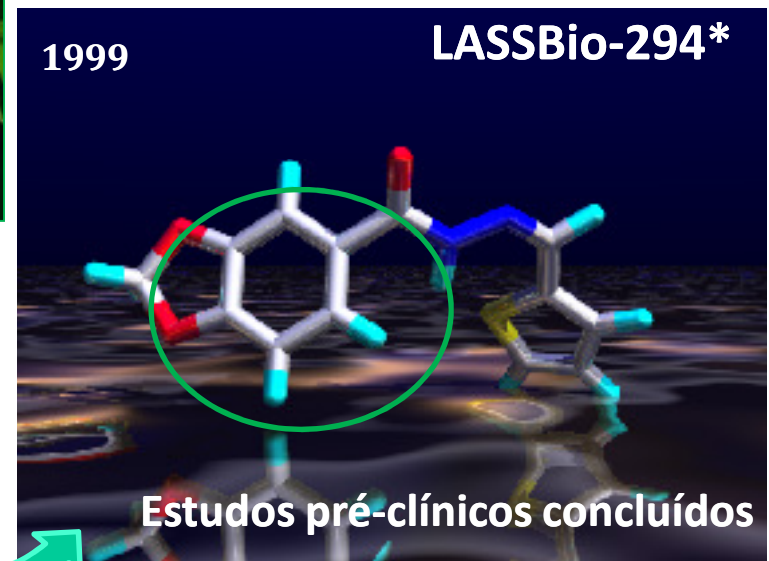
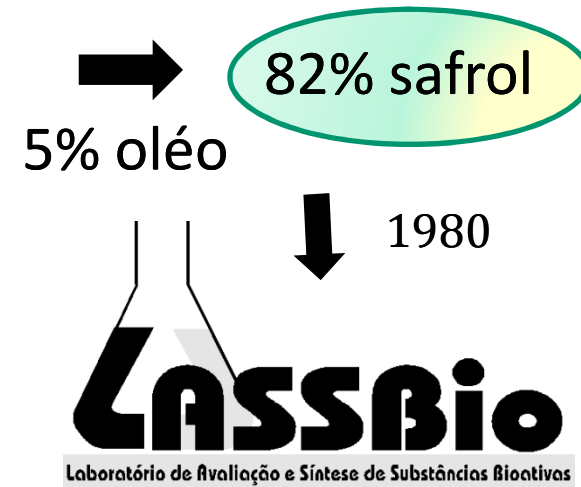
CH<sub>2</sub>

D Riva *et al.*, *Acta Amazonica* 2011, 41, 297

## Óleo de Sassafrás *Ocotea pretiosa*

E. J. Barreiro, P. R. R. Costa, P. R. V. R. Barros e W. M. Queiroz, "An Improved Synthesis of Indole Derivatives Related to Indomethacin from Natural Safrole", *Journal of Chemical Research (S)*, 102-103; (M) 1142-1165, (1982)

E. J. Barreiro & C. A. M. Fraga, "A Utilização do Safrol, Principal Componente Químico do Óleo de Sassafrás, na Síntese de Substâncias Bioativas na Cascata do Ácido Araquidônico: Anti-inflamatórios, Analgésicos e Anti-trombóticos", *Química Nova*, 22, 744-759 (1999)



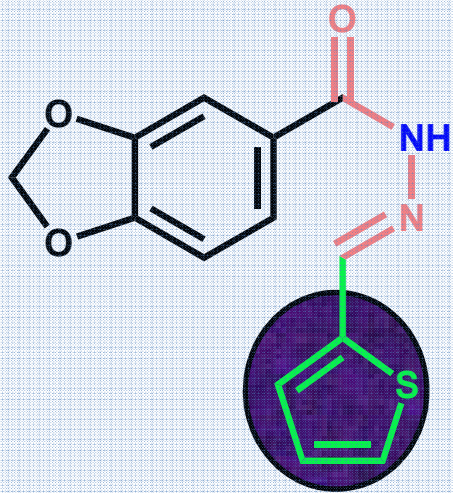
## Novo protótipo de fármaco cardioativo

\*US Patent US7091238-15/08/2006

European Patent EP1532140; WO-0078754



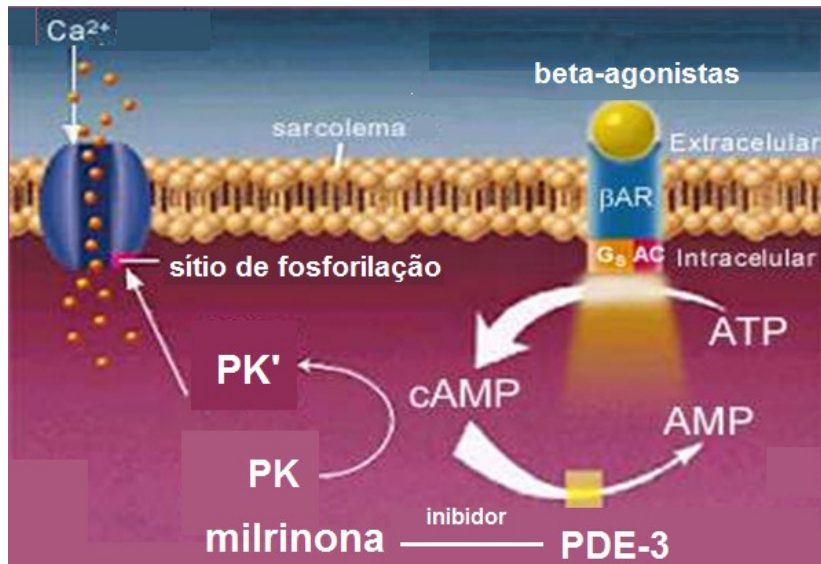
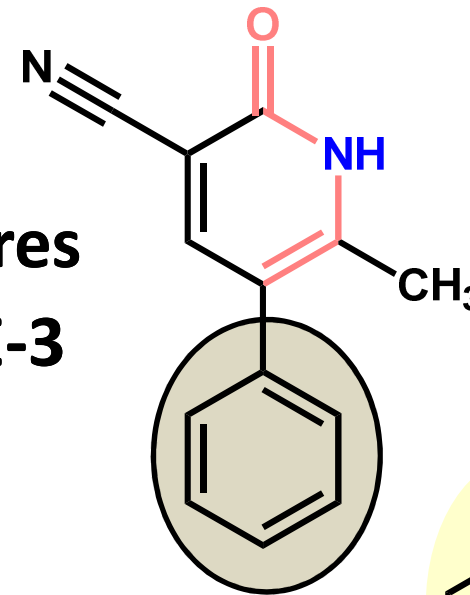
# A gênese do LASSBio-294...



LASSBio-294

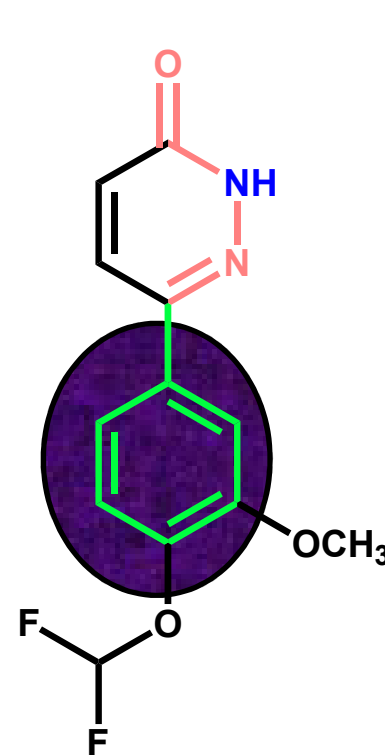
Química Medicinal

## Inibidores de PDE-3

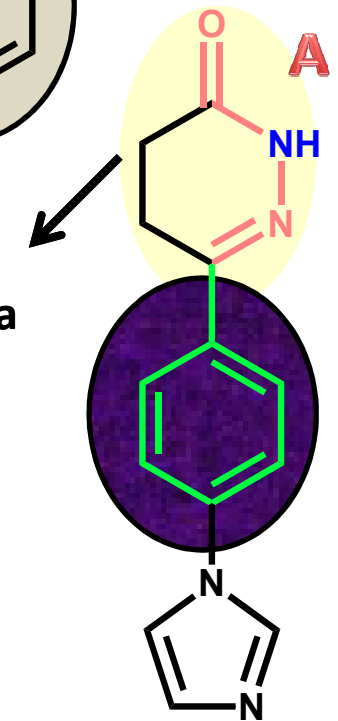


Propriedades inotrópicas, vasodilatadoras (arritmias ventriculares)

Sistema piridazina



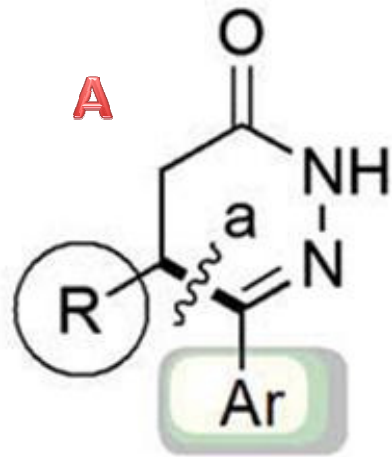
zardaverina



imazodana

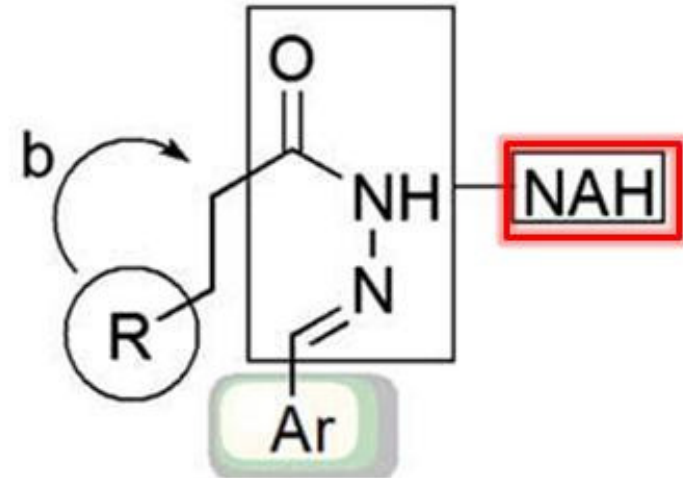
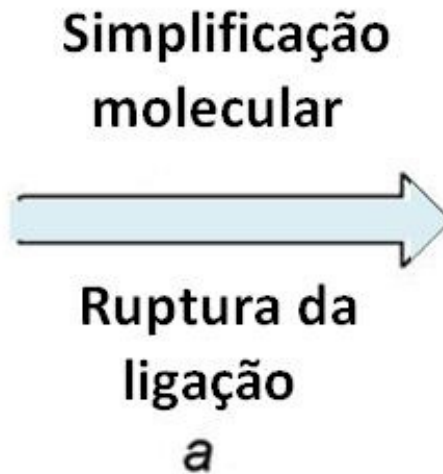


# A gênese do LASSBio-294...



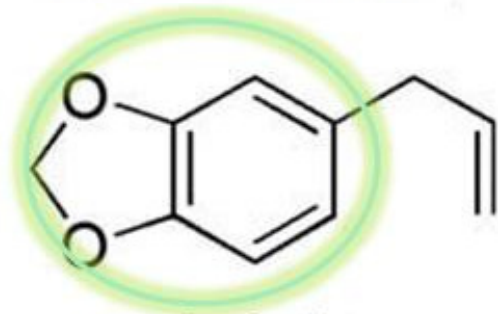
Sistema  
piridazinônico

Química  
Medicinal

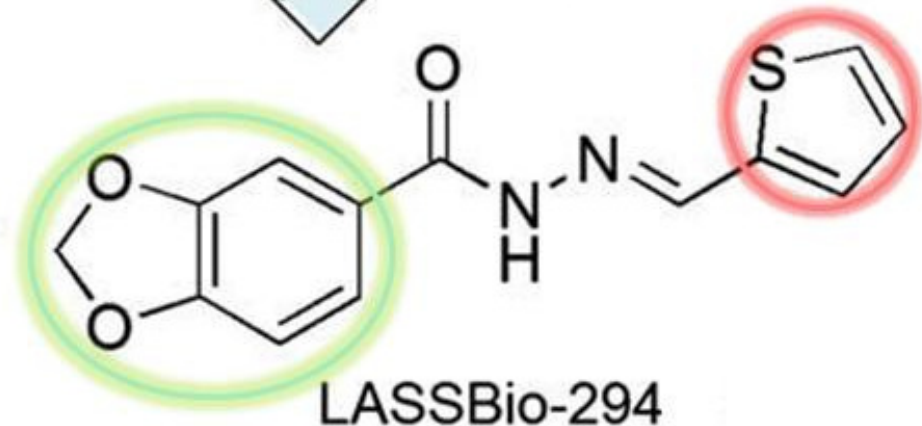


*N*-acilidrazona

Inclusão de anel  
*b*



Safrol

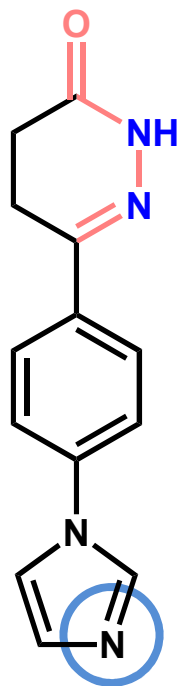


LASSBio-294





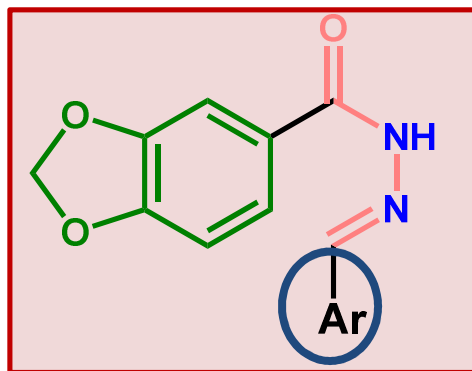
# A série congênere



Imazodana

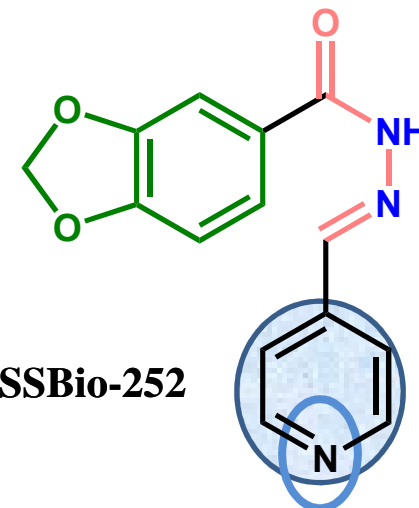


NAH

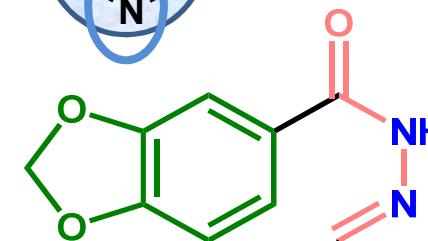


benzodioxola  
(safrol)

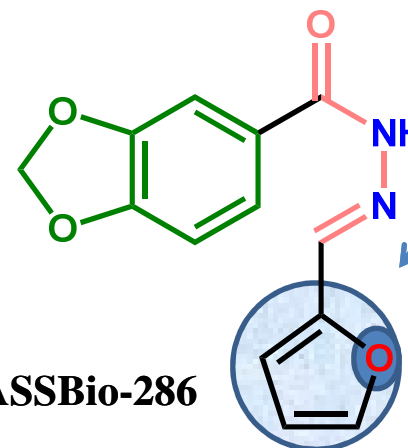
Química  
Medicinal



LASSBio-252



LASSBio-294

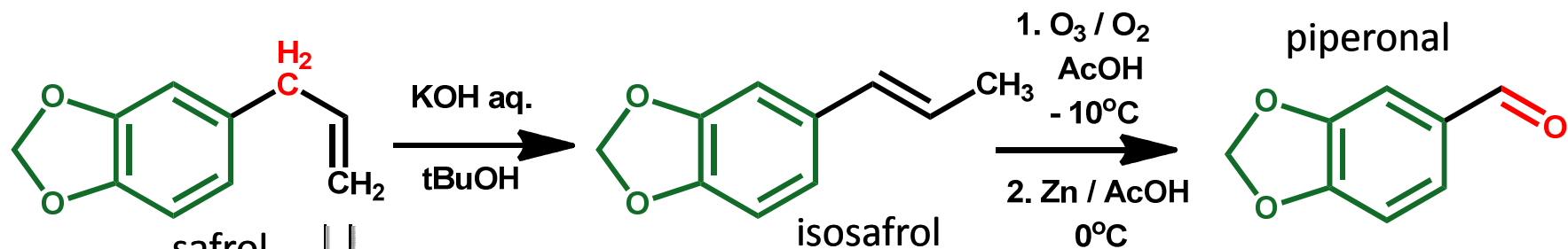


LASSBio-286

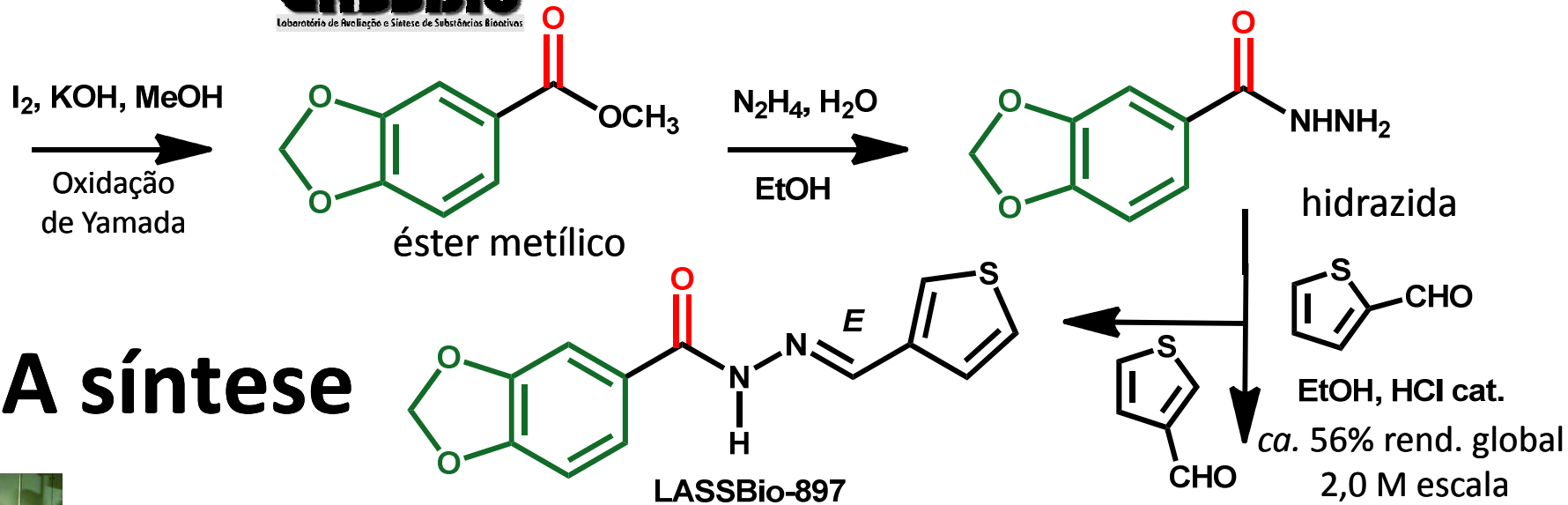
isosterismo



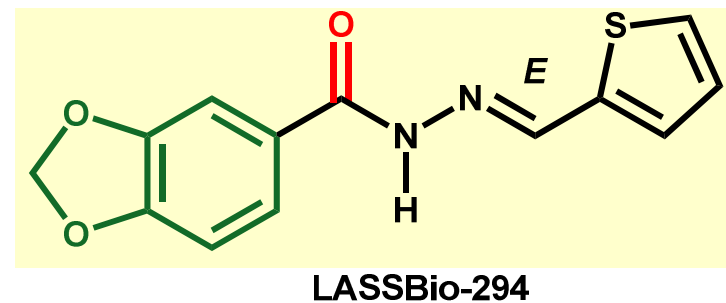
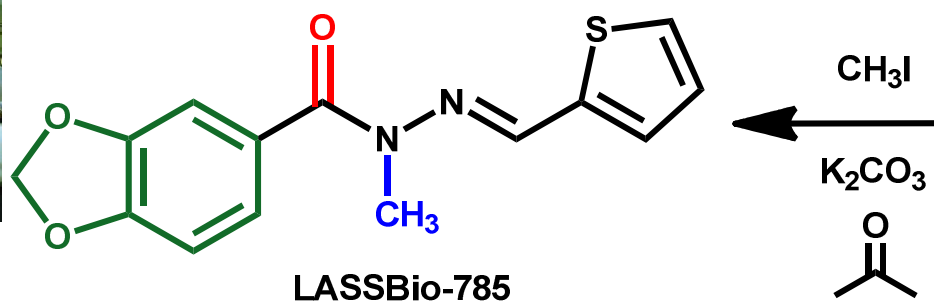




MEF Lima & EJ Barreiro, *J. Pharm. Sci.* **1992**, *81*, 1219



# A síntese



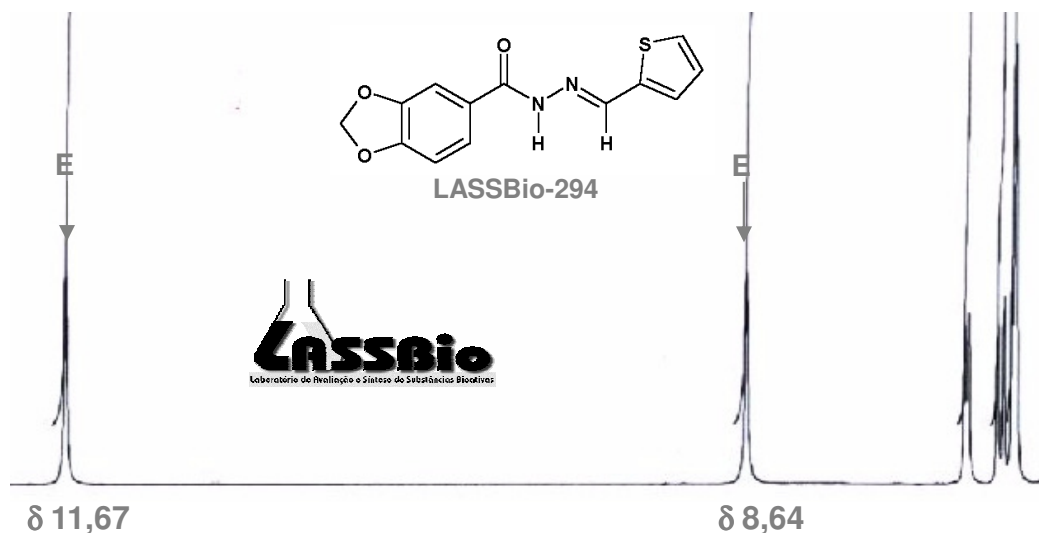
P. C. Lima, L. M. Lima, K. C. M. da Silva, P. H. O. Léda, A. L. P. Miranda, C. A. M. Fraga & E. J. Barreiro, "Synthesis and Non-addictive Analgesic Activity of Novel *N*-acylarylhydrazones and Isosters, Derived from Natural Safrole", *Eur. J. Med. Chem.*, **35**, 187 (2000).



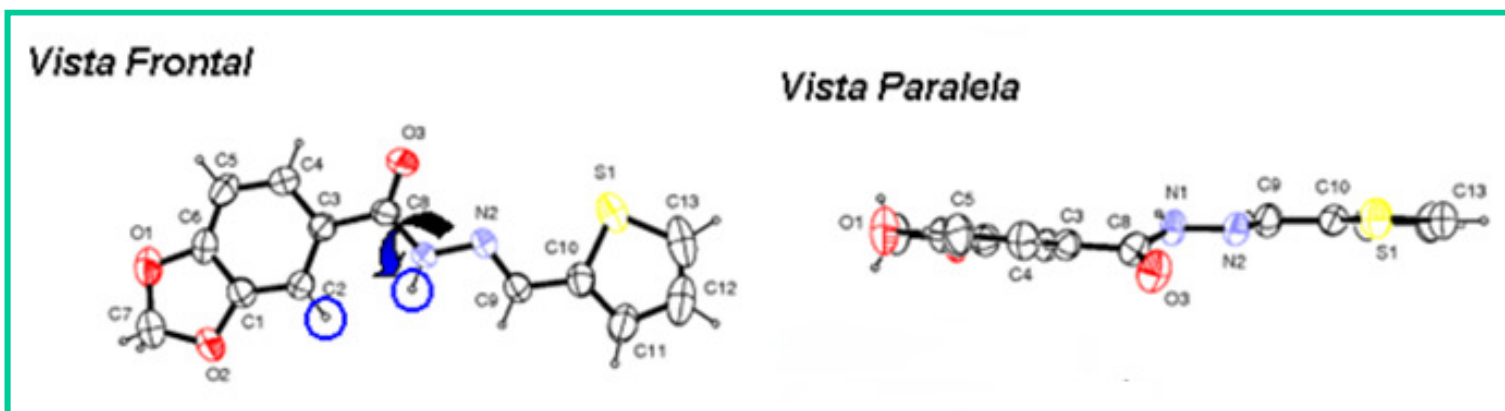


# Análise espectroscópica e raios X

Composto	X	R	$\delta^1H$
LASSBio-129	O	H	8,32
LASSBio-294	S	H	8,64
LASSBio-787	S	CH <sub>3</sub>	8,58
LASSBio-789	S	Br	8,55
LASSBio-790	S	NO <sub>2</sub>	8,81 / 8,09
LASSBio-1028	NH	H	8,28



Karabatsos, G.J., *et al.* (1964) *J. Am. Chem. Soc.*, 86, 3351; Karabatsos, G.J., *et al.* (1967) *Tetrahedron*, 24, 3907; *ibid* (1967) *Tetrahedron*, 24, 3361.



Kummerle, A. E.; Raimundo, J. M.; Leal, C. M.; Silva, G. S.; Balliano, T. A.; Pereira, M. A.; DeSimone, C. A.; Sudo, R. T.; Zapata-Sudo, G.; Fraga, C. A. M.; Barreiro, E. J., *Eur. J. Med. Chem.* 2009, 44, 4004-4009

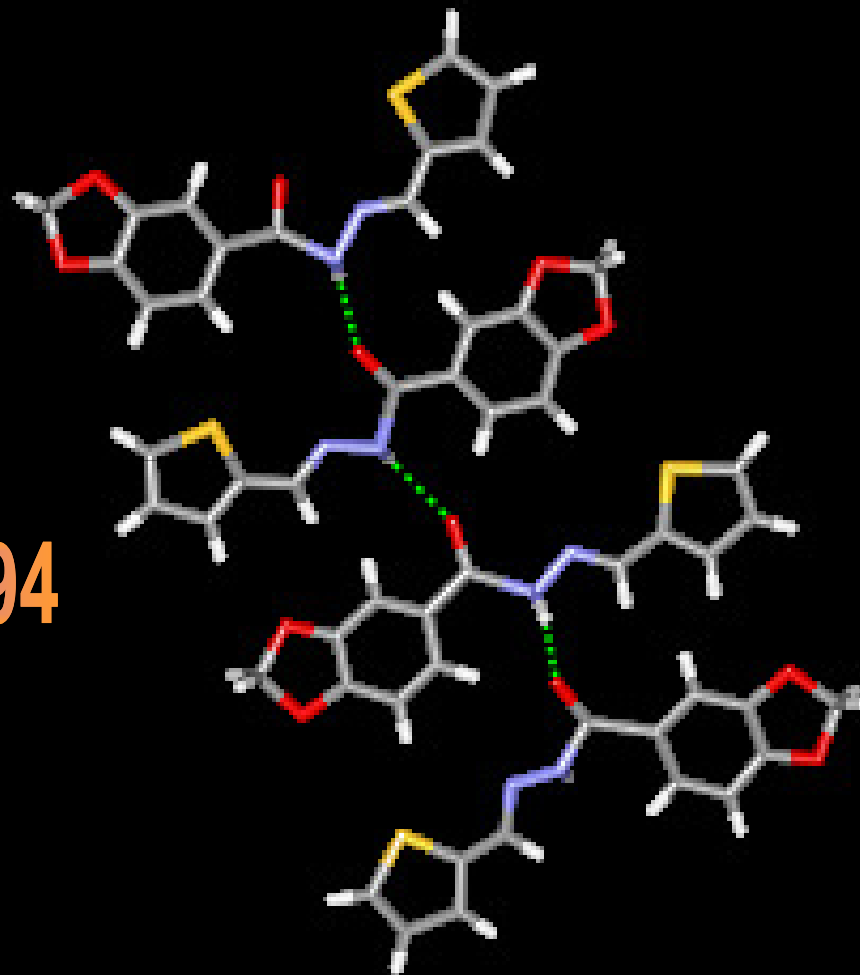


Universidade Federal do Rio de Janeiro

# Cristalografia de Raios-X

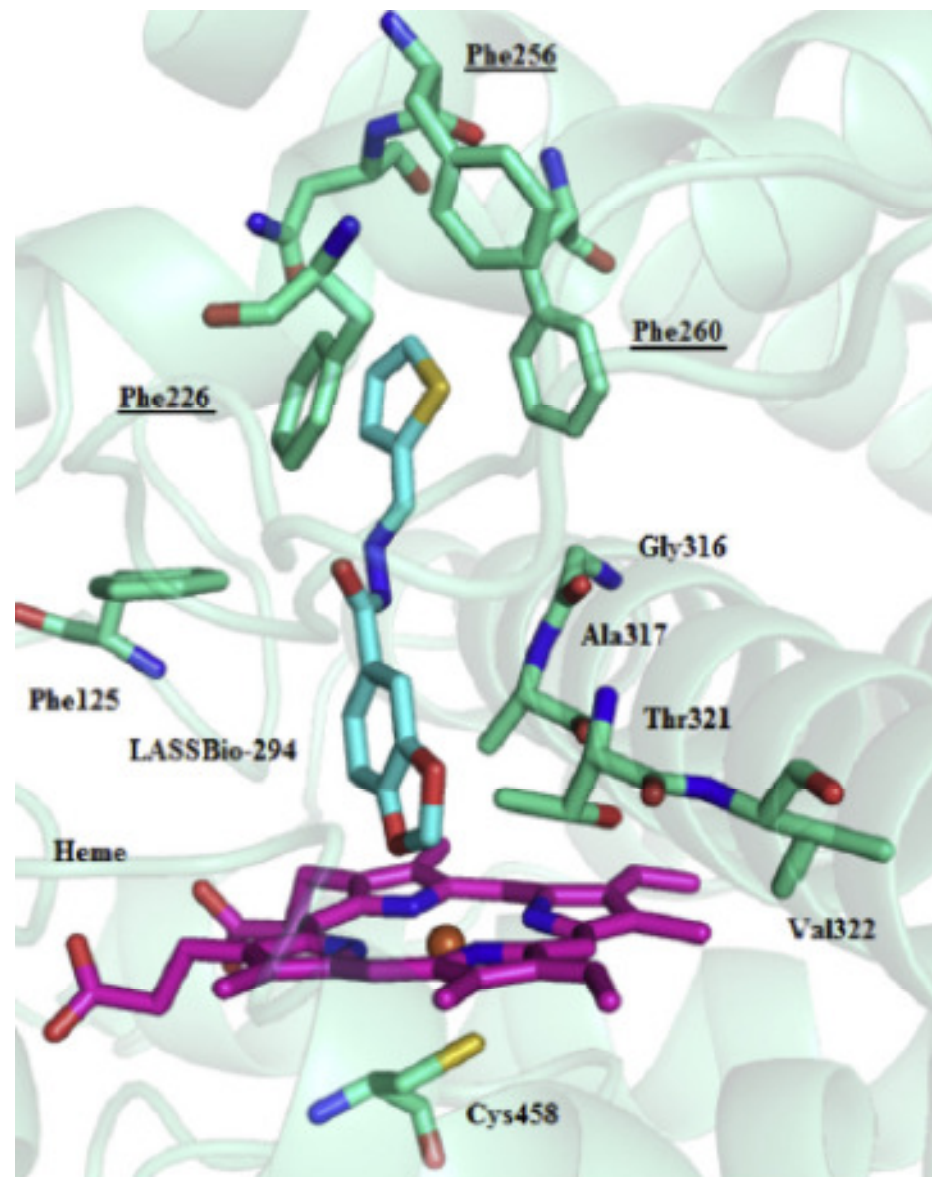
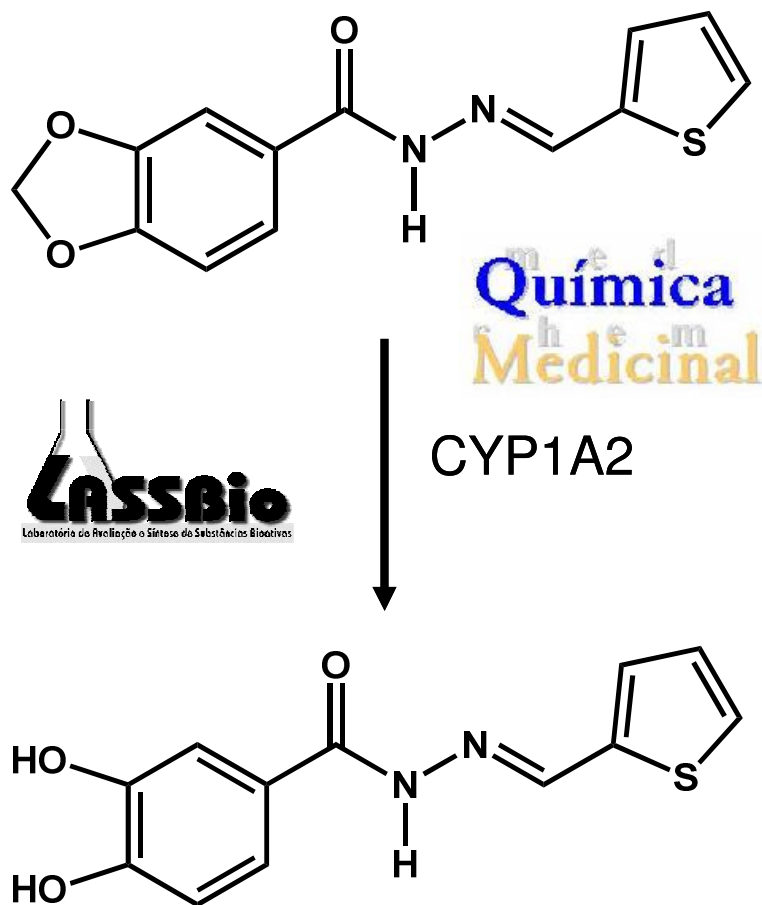
## LASSBio-294

$C_{13}H_{10}N_2O_3S$





# Metabolismo de LASSBio-294

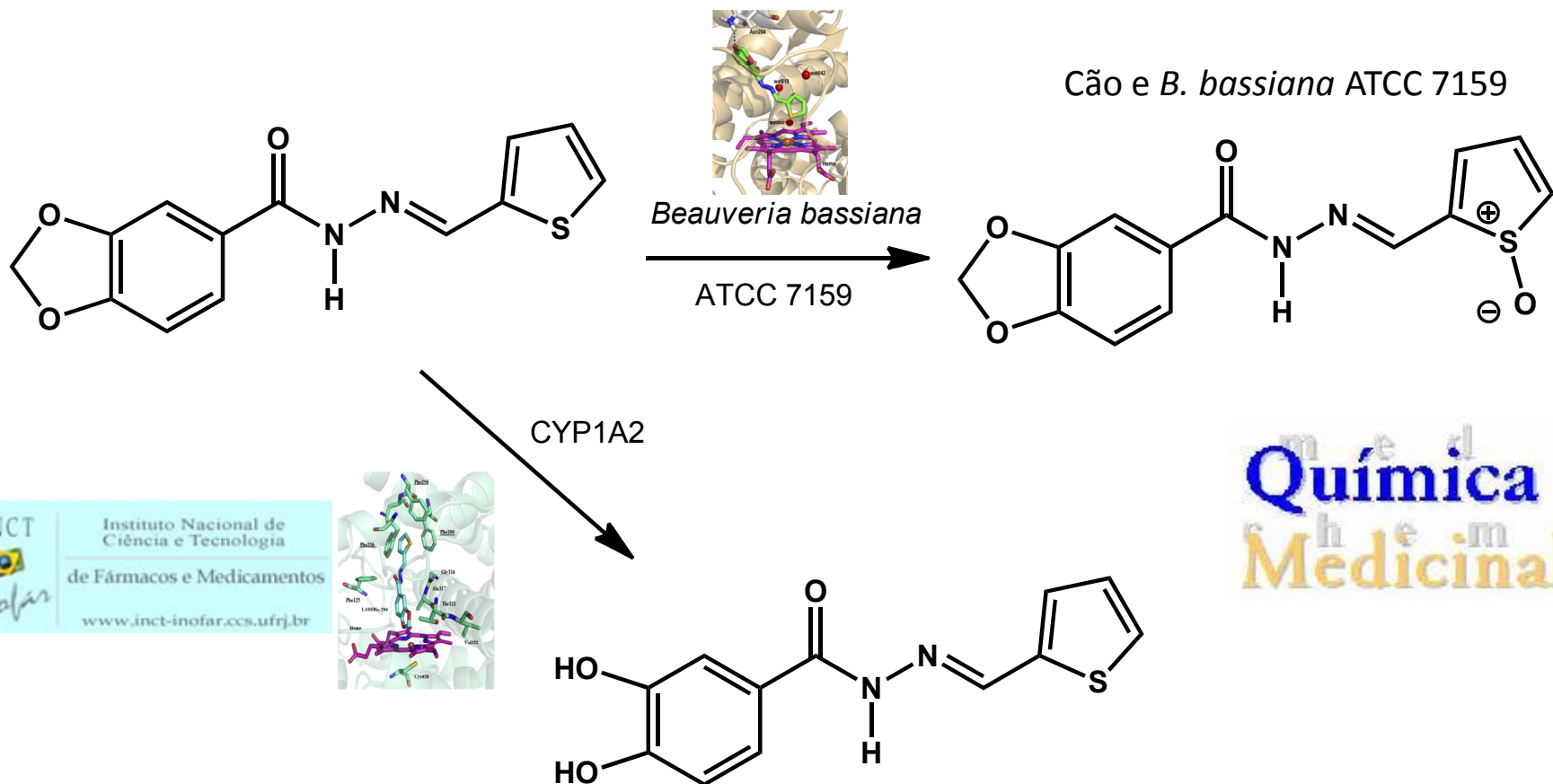


A. G. M. Fraga *et al.*, "CYP1A2-mediated biotransformation of cardioactive 2-thienylidene-3,4-methylenedioxybenzoylhydrazine (LASSBio-294) by rat liver microsomes and human recombinant CYP enzymes", *Eur J. Med Chem.*, **46**, 349 (2011);





# Metabolismo de LASSBio-294



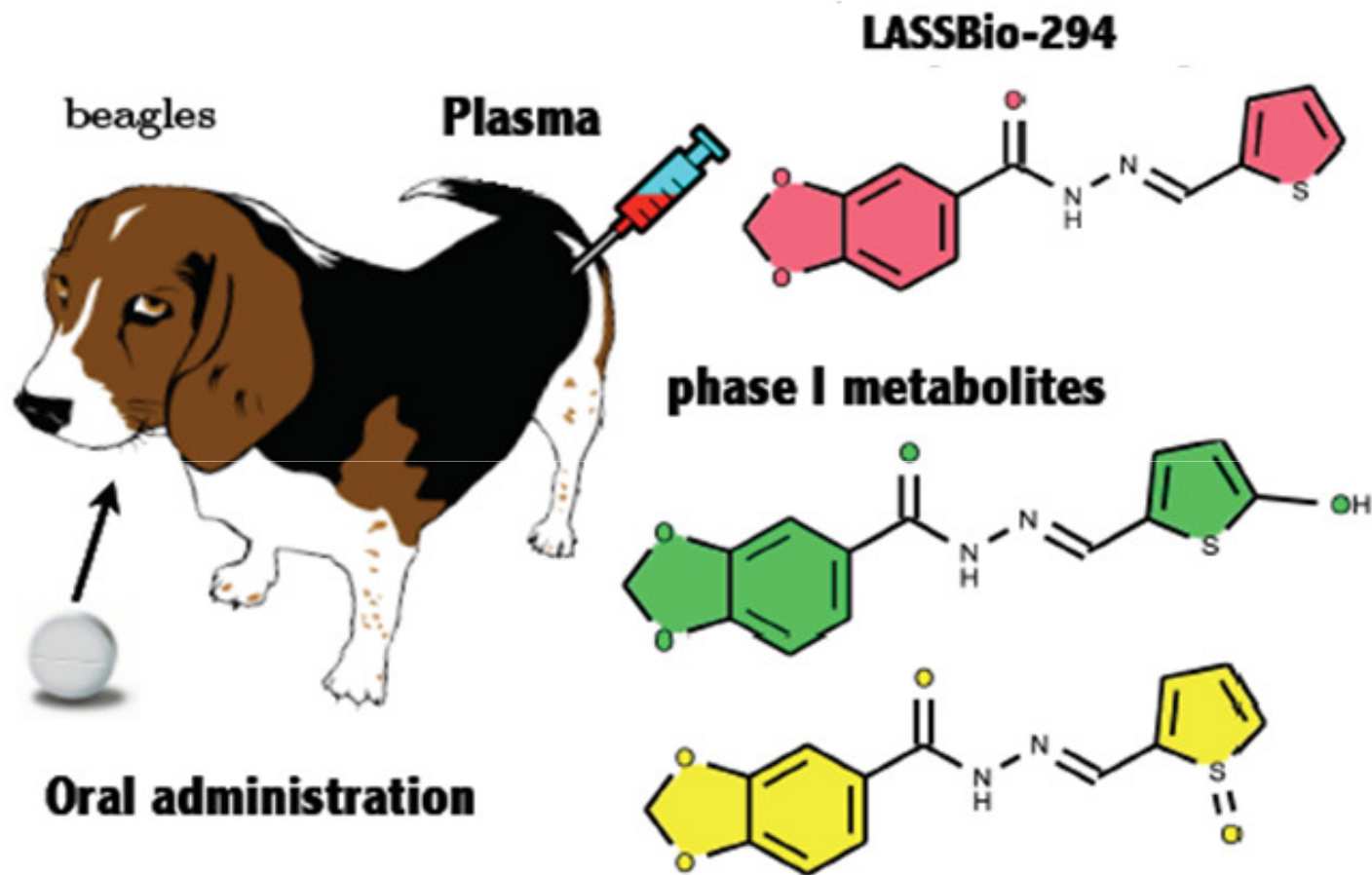
Química  
e Farmácia  
Medicinal

Microsomas de fígado de rato e CYPs recombinantes<sup>&</sup>

- E. O. Carneiro, C. H. Andrade, R. C. Braga, *et al.*, Structure-based prediction and biosynthesis of the major mammalian metabolite of the cardioactive prototype LASSBio-294, *Bioorg. Med. Chem. Lett.*, **20**, 3734 (2010); R. C. Braga *et al.*, "Determination of cardioactive prototype LASSBio-294 and its metabolites in dog plasma by LC-MS/MS: application for a pharmacokinetic studies", *J. Pharm. Biomed. Analysis*, **55**, 1024 (2011);
- & AGM Fraga *et al.* *Eur. J. Med. Chem.*, **46**, 349-355, 2011



# Metabolismo de LASSBio-294



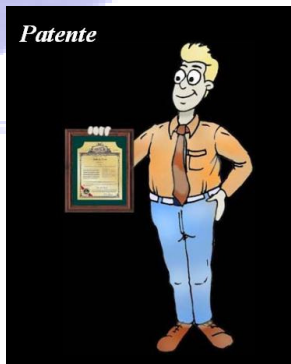


# LASSBio-294

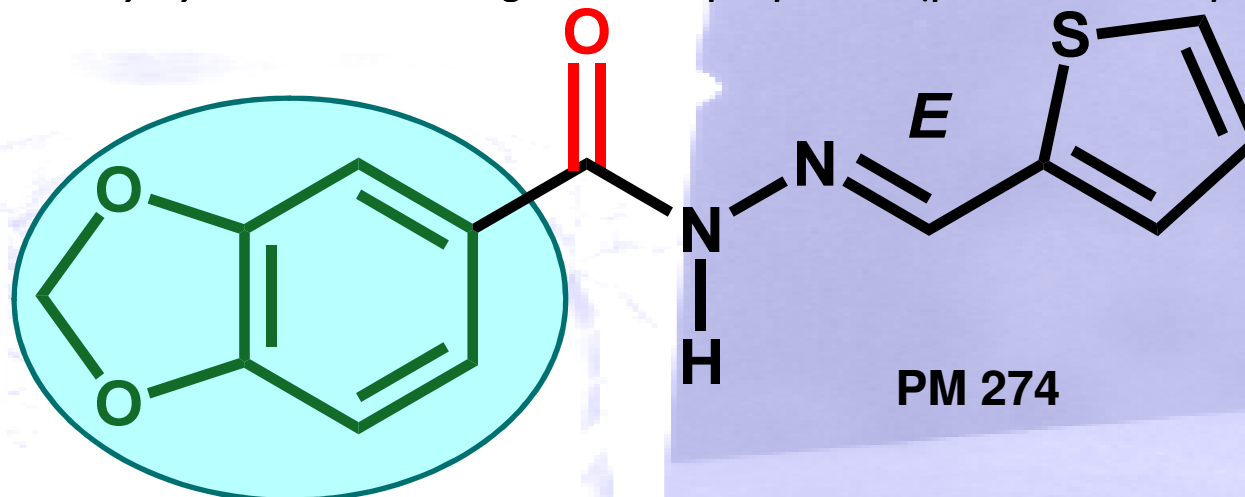
## Novo protótipo de fármaco cardioativo\*

\*US Patent US7091238-15/08/2006

\*European Patent EP1532140; WO-0078754



*Thienylhydrazone with digitalis-like properties (positive inotropic effects)*



- ✓ Estruturalmente simples, com rota de síntese com > 55% de rendimento global, na escala 2,0, 5,0, 10, 20M (ca. 5 kg), empregando matéria-prima acessível;
- ✓ Potentes propriedades inotrópicas positivas, vasodilatadoras e neuroprotetoras, administrado por via oral;
- ✓ Novo mecanismo farmacológico de ação: ligante de receptores adenosinérgicos;
- ✓ Sem citotoxicidade, nem genotoxicidade, sem toxicidade sistêmica (aguda e sub-aguda) em duas vias de administração (*p.o.* e *i.p.*\*) em doses **1000  $\mu\text{M}/\text{kg}$**  e **73  $\mu\text{M}/\text{kg}$** , respectivamente.

\**i.p.*, administrando-se 2 vezes ao dia, durante 15 dias seguidos: ~**100 vezes  $\text{ED}_{50}$  *in vivo***).

Química  
e  
Medicinal



# Patente obtida

Patent (USPTO) 7.091.238 (15/08/2006) → *Cardiotônicos vasoativos*

Sudo, R.T. *et al.* (2006) US Pat. 7,091,238 (15 de Agosto de 2006)



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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
106700328	Aug. 15, 2006	7,091,238	33385-179643	9691
VENABLE LLP P.O. BOX 34385 WASHINGTON, DC 20043-9998				

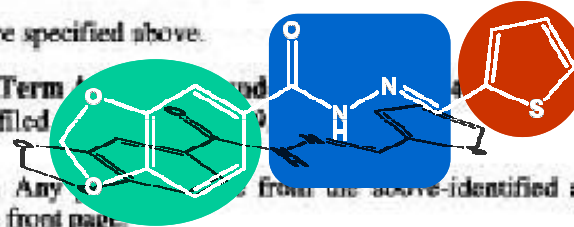
Thienylhydrazone with Digitalis-like properties (positive inotropic effects)

## LASSBio-294

### ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Adjustment (PTA) and  
(application filed)



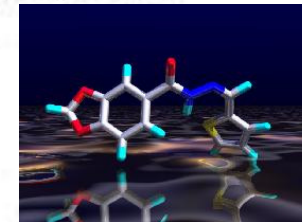
The Patent Term Adjustment is 109 day(s). Any ... from the above-identified application include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571) 272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

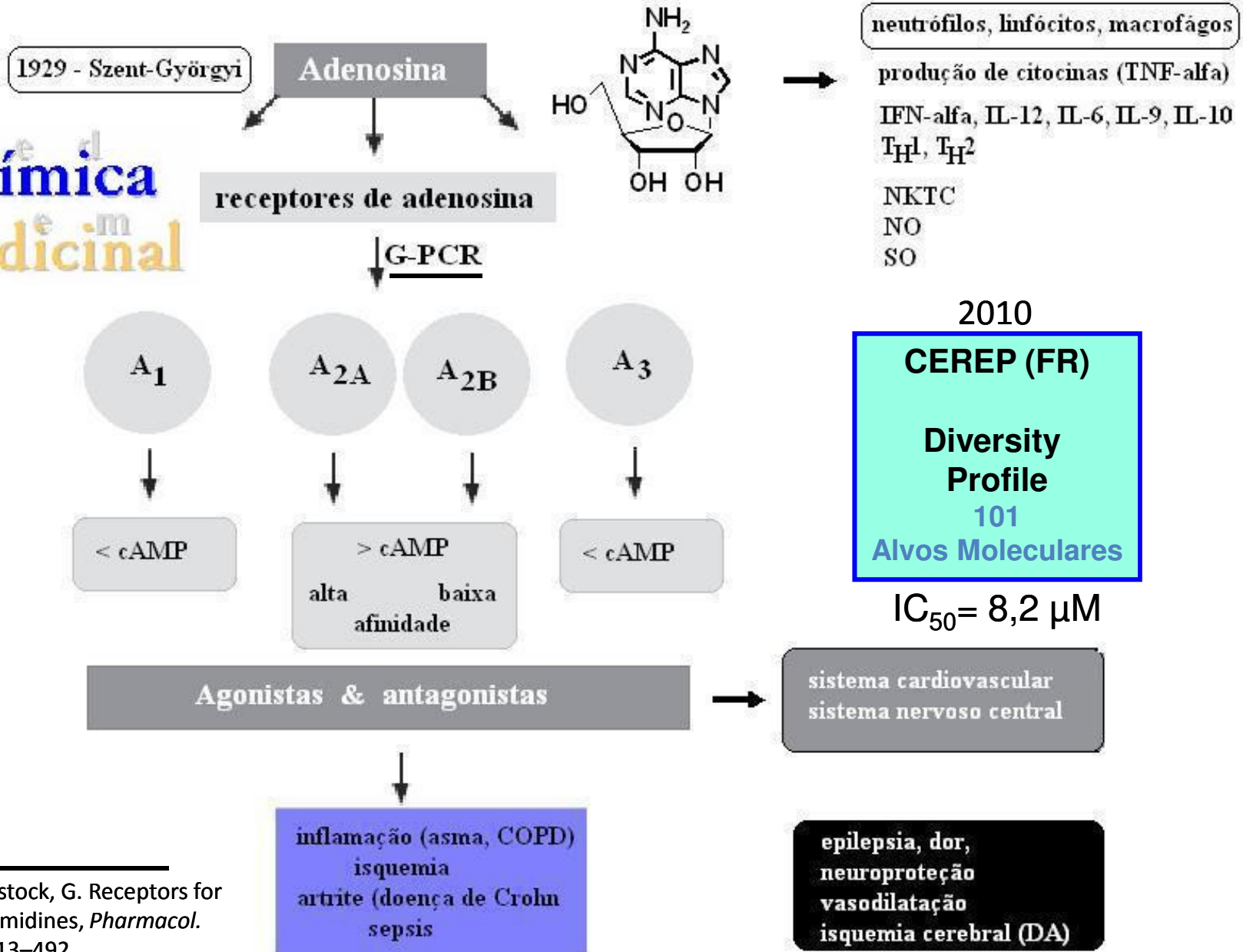
Roberto Takashi Sudo, Rio de Janeiro, BRAZIL;  
Edson X. Albuquerque, Baltimore, MD;  
Eliane J. Barreiro, Rio de Janeiro, MD;  
Carlos Alberto Manssour Fraga, Rio de Janeiro, BRAZIL;  
Ana Luiza Palhares De Miranda, Petropolis, BRAZIL;







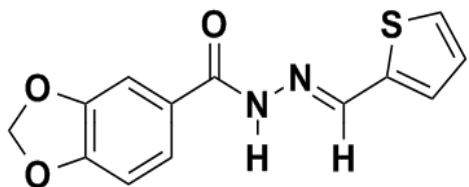
# Estudo do mecanismo de ação



Ralevic, V.; Burnstock, G. Receptors for purines and pyrimidines, *Pharmacol. Rev.* 1998, 50, 413–492.

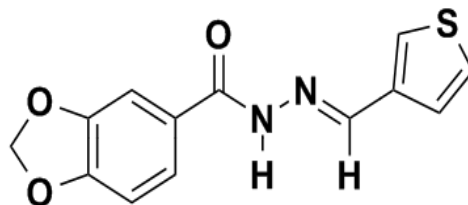


# Estudo do mecanismo de ação



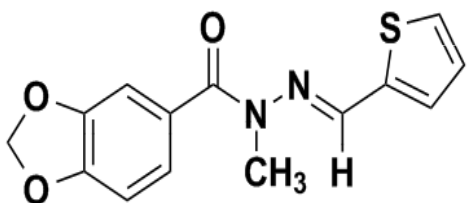
LASSBio-294

$$IC_{50}A_{2A} = 8,2 \mu M$$



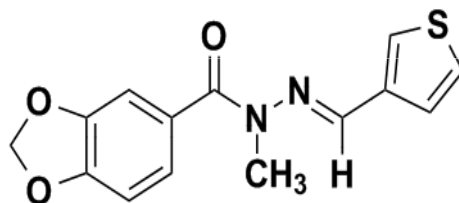
LASSBio-897

$$IC_{50}A_{2A} = 9,9 \mu M$$



LASSBio-785

$$IC_{50}A_{2A} = 22 \mu M$$



LASSBio-1289

$$IC_{50}A_{2A} = 17 \mu M$$

Efeito inotrópico positivo

Efeito vasodilatador

Química  
e  
Medicinal

SUDO, R. T.; ZAPATA-SUDO, G.; BARREIRO, E. J. *British Journal of Pharmacology*. 2001,134,603-613.

DUARTE, C. D.; BARREIRO, E. J.; FRAGA, C. A. M. *Mini Reviews in Medicinal Chemistry*. 2007, 7, 1108-1119.

ZAPATA-SUDO, G. *et al. American Journal of Hypertension*. 2010,23,135-141.

PCT Int. Appl. (2000) WO 2000078754

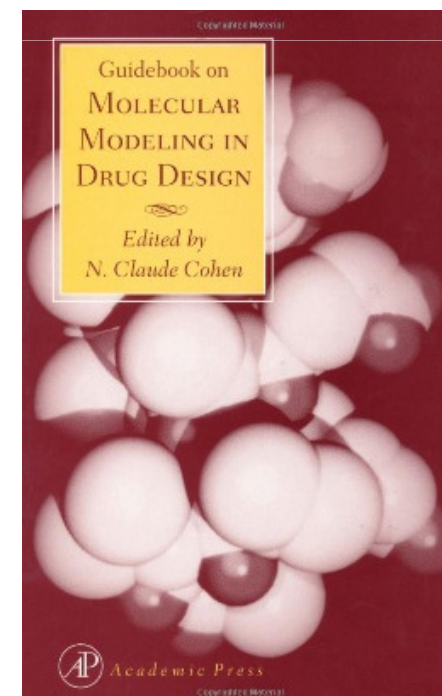
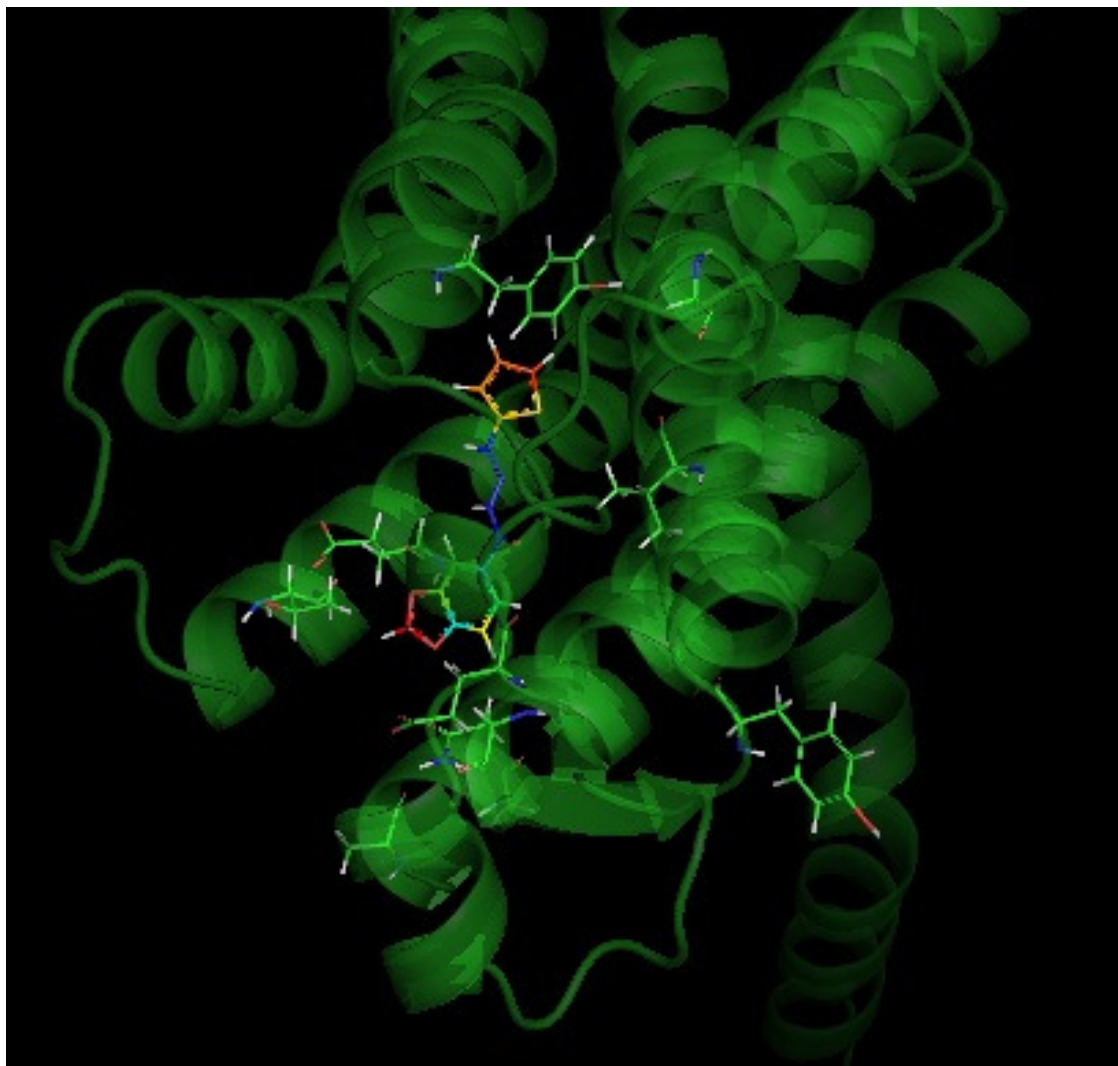
PCT Int. Appl. (2010) WO 2010043010





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# Química Computacional



Química  
e  
Medicinal

**LASSBio**  
Laboratório de Avaliação e Síntese de Substâncias Bioativas



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```

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ftp_derived	Derived data directory within ftp archive Aproximately 134 MB ( /pub/pdb/derived_data )
ftp_doc	Doc directory within ftp archive Aproximately 234 MB ( /pub/pdb/doc )

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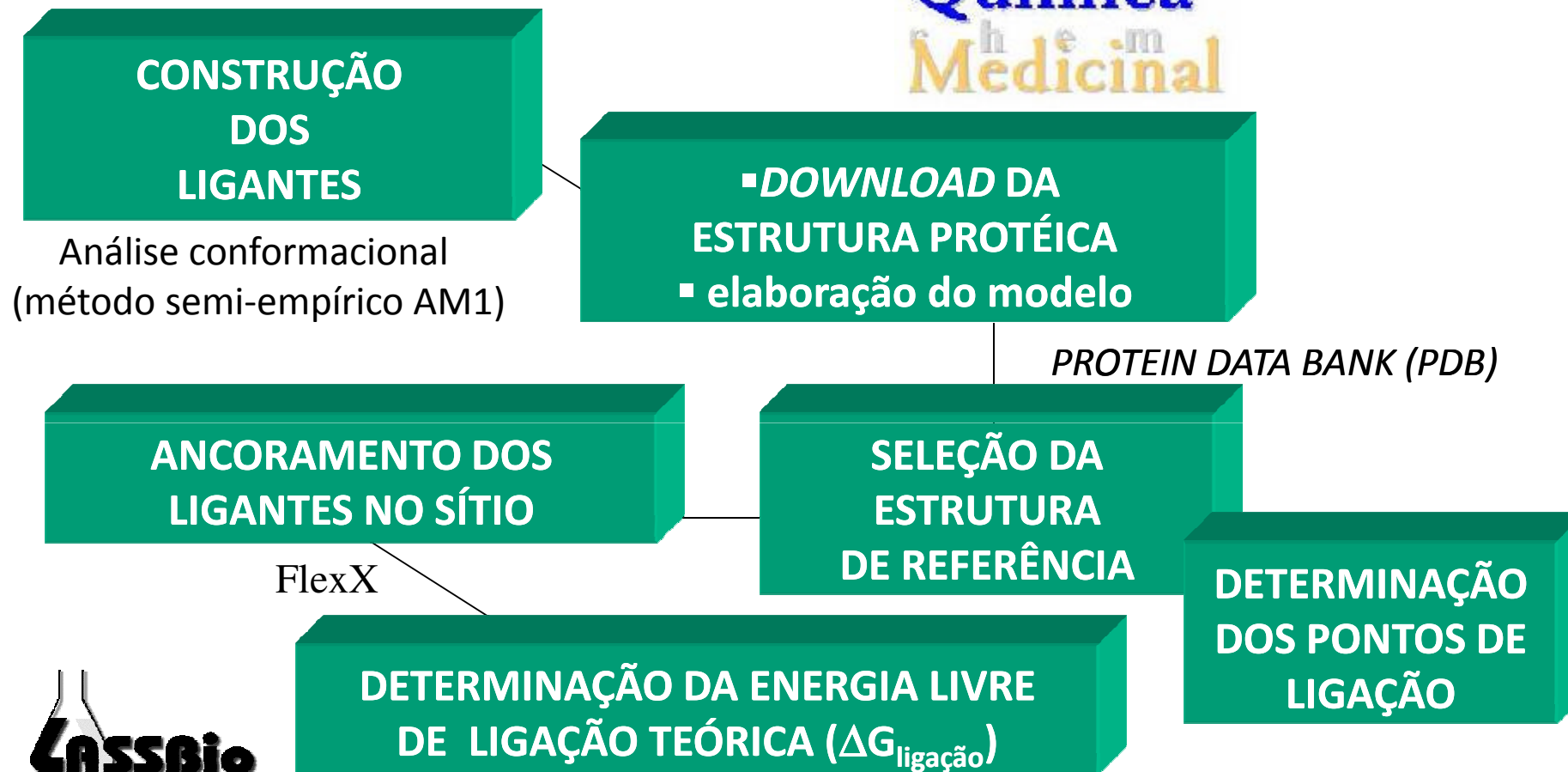
```
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rsync.wwpdb.org::ftp_data/structures/divided/mmCIF/ ./mmCIF
```

**Downloading coordinate files in PDBML Format (xml):** To download the entry files in PDBML format the following rsync command may be used:



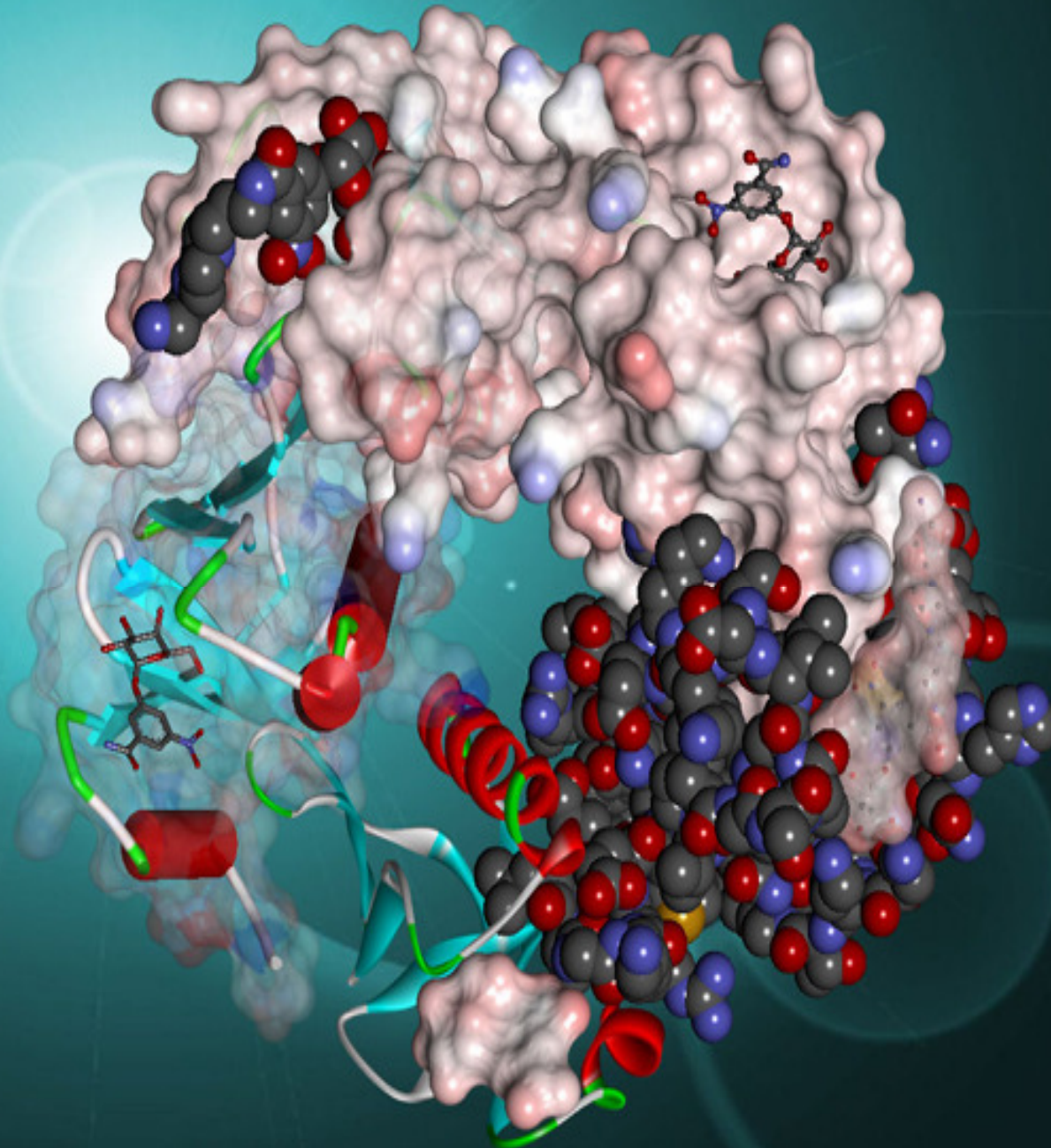
# Métodos computacionais

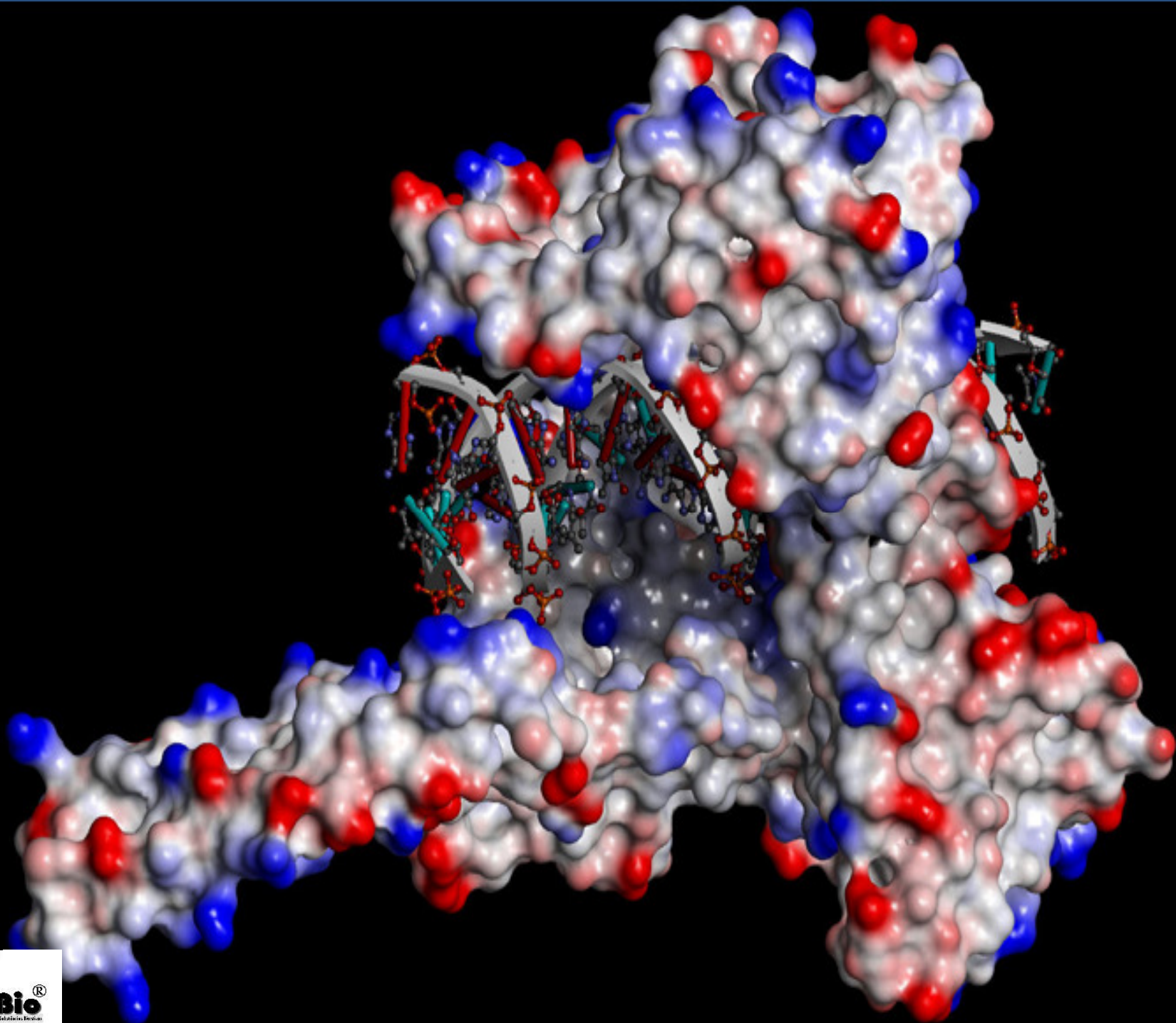
Química  
Medicinal

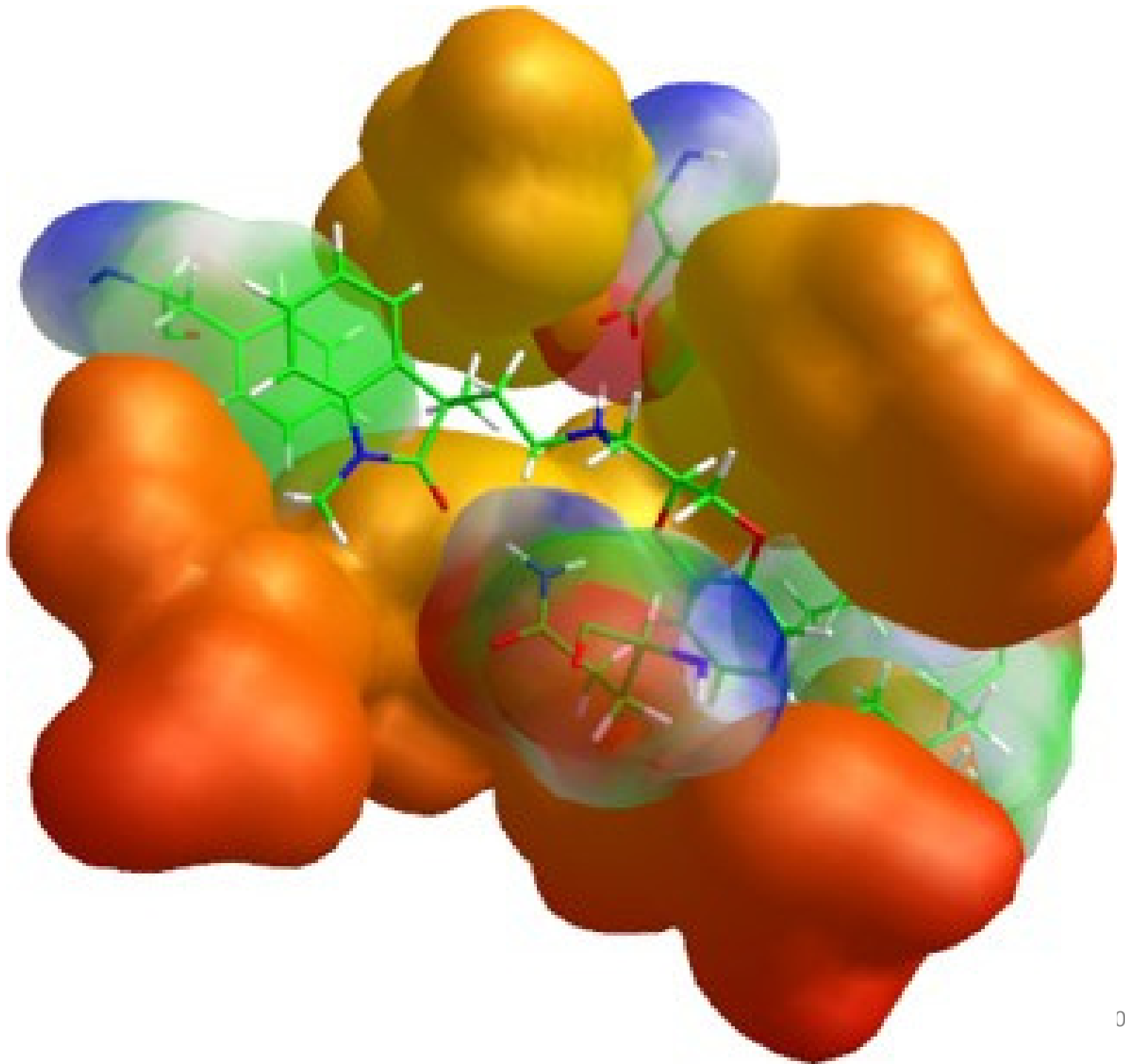


Sybyl, Version 8.0, Tripos Associates: St. Louis, MO, 2007 (Licença # 7512)

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





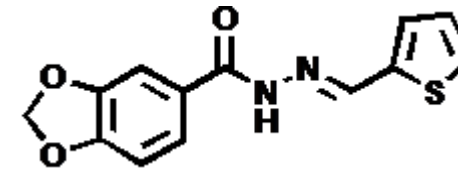






# Mecanismo de ação in silico

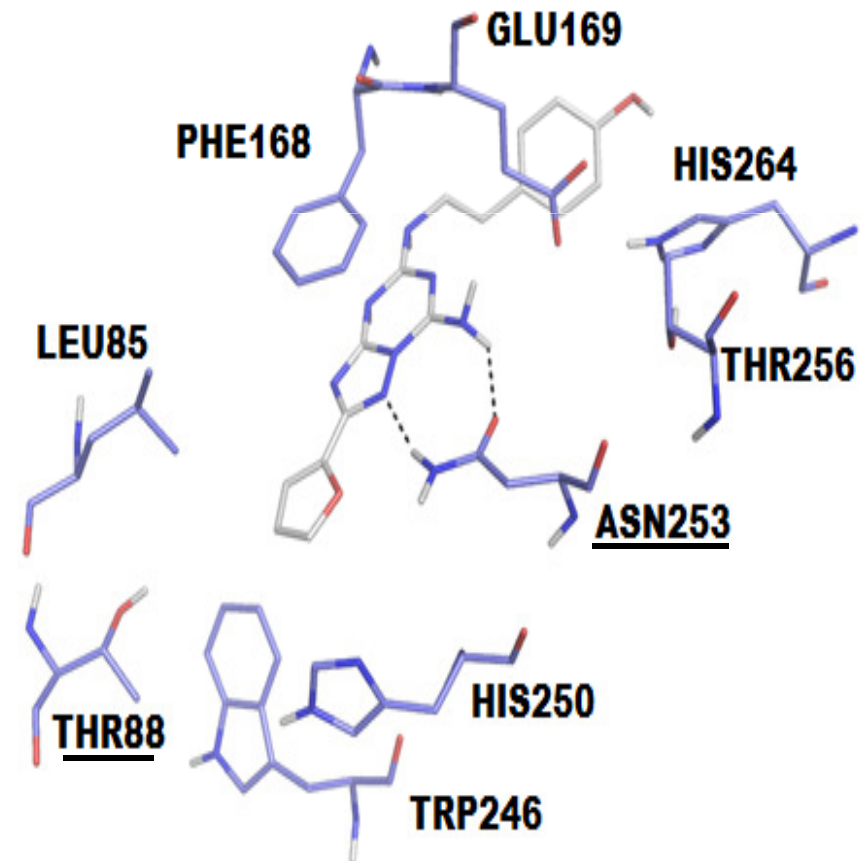
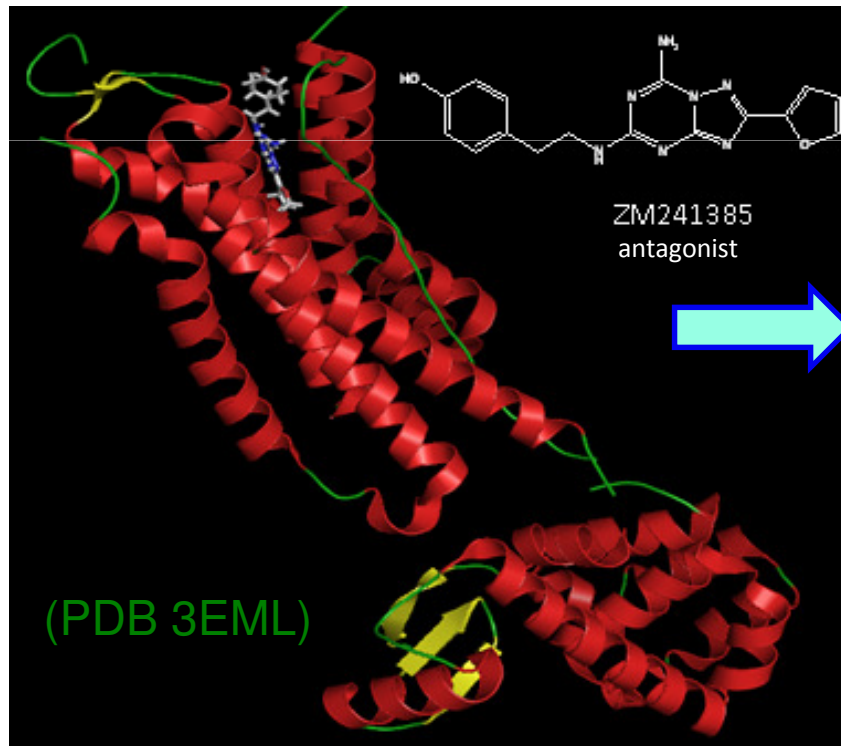
Receptores de Adenosina A<sub>2A</sub>

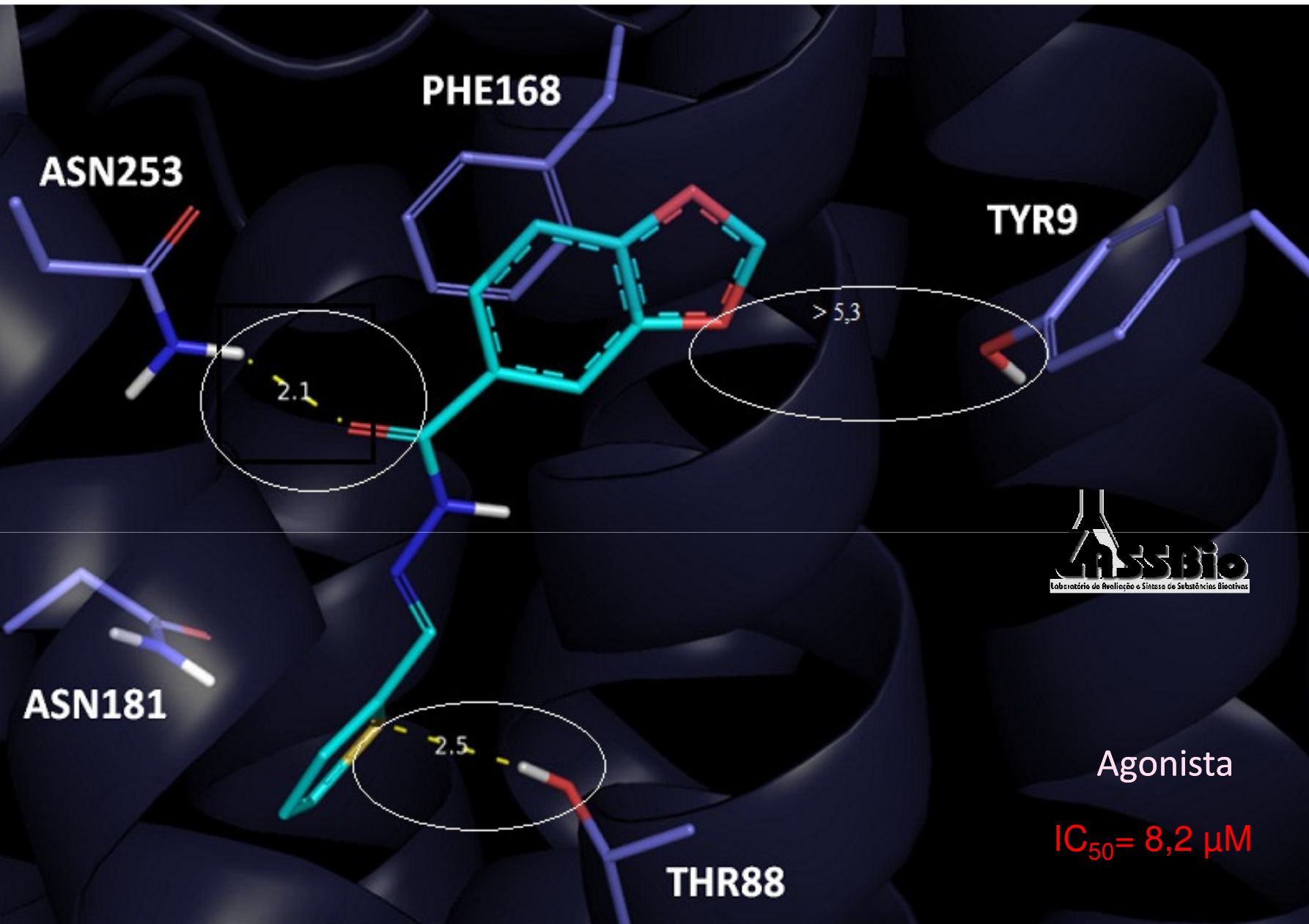


LASSBio-294

Química  
Farmacológica  
Medicinal

LASSBio  
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LASSBio-294 docked no cristal 3QAK do receptor adenosinérgico A2A  
Programa GOLD 5.1. (CCDC) (nº de registro 8588); Função: ASP

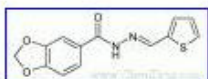


# Patentes de ligantes de receptores de adenosina

Patent number(s)	Assignee(s)	Subject
WO 2007136817	Adenosine Therapeutics	Describes substituted aryl piperidinylalkynyl adenosines; useful for treating diseases that provoke inflammation, also useful for treating sepsis.
WO 2007120972 US 20080009460	Adenosine Therapeutics <i>et al.</i>	These describe the use of A <sub>2A</sub> receptor agonists that do not have undesirable side effects; useful for treating acute inflammatory events such as cerebrovascular accident.
US 2007299089	CV Therapeutics	Describes the use of A <sub>2A</sub> agonists — especially CVT-3146 and CVT-3033 — in treating ischaemia.
WO 2008063712 US 20070299089	CV Therapeutics	These describes the use of A <sub>2A</sub> agonists, such as methylcarboxamide derivatives, for treating ischaemia.
US 2007207978 US 2007203090	CV Therapeutics	These describe C-pyrazole and N-pyrazole A <sub>2A</sub> agonists that are vasodilatory agents; useful in heart imaging and as therapeutics for coronary artery disease.
US 2008132526	GlaxoSmithKline	Describes new purine derivatives; useful for treating inflammatory diseases such as asthma and <u>chronic obstructive pulmonary disease</u> .
EP 1904512	GlaxoSmithKline	Describes new substituted purine derivatives that are potent A <sub>2A</sub> agonists that are safer alternatives to corticosteroids; useful for treating inflammatory disease.
WO 2008031875 EP 1861412	Novartis	These describe adenosine derivatives; useful for <u>treating inflammatory conditions or obstructive airway diseases</u> .
WO 2007121923 and others	Novartis	These describe purine derivatives that are useful for treating inflammatory or obstructive airway diseases, and <u>eosinophil-related disorders of the airways</u> .
WO 2007121920 WO 2007121918	Novartis	These describe organic compounds that act as A <sub>2A</sub> agonists; useful for treating inflammatory or obstructive airway diseases.
WO 2007121921	Novartis	Describes the use of a substituted purinylamine compound to treat cystic fibrosis, pulmonary hypertension, <u>pulmonary fibrosis</u> , inflammatory bowel syndrome and wounds.
WO 2007107598	J. Schrader & C. E. Mueller	Describes a phosphorylated compound that comprises a ribosyl moiety and a purine moiety that has agonist properties on the A <sub>2A</sub> receptor after dephosphorylation.
US 2007232559	University of Virginia	Describes new 2-propynyl adenosine analogues and methods of their use for treating inflammatory activity due to pathological agents or trauma.
US 20080064653	University of Virginia	Describes compounds that are selective modulators of A <sub>2A</sub> receptors; useful for preventing and treating central nervous system injury in spinal-cord cells.
JP 2008508360	University of Virginia <i>et al.</i>	Describes new 2-propynyl adenosine analogues with modified 5'-ribose groups; useful for treating inflammatory response, autoimmune disease, and allergic and infectious disease.

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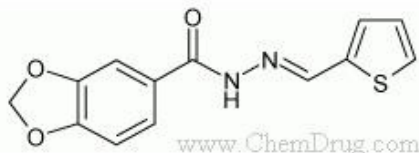
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您现在的位置: >> [专业资料首页](#) >> [药物合成数据库](#) >> [L-294, LASSBio-294,314021-07-3,C13-H10-N2-O3-S,\(E\)-N'-\(Thien-2-ylmethylene\)-1,3-benzodioxole-5-carbohydrazide-药物合成数据库](#)**【药物名称】** L-294, LASSBio-294**【化学名】** (E)-N'-(Thien-2-ylmethylene)-1,3-benzodioxole-5-carbohydrazide**【CAS登记号】** 314021-07-3**【结构式】****【分子式】** C13-H10-N2-O3-S**【分子量】** 274.299**【原研厂家】** LASSBio (Originator), University of Maryland (Originator)**【作用类别】** CARDIOVASCULAR DRUGS, Cerebrovascular Diseases, Treatment of, Heart Failure Therapy, NEUROLOGIC DRUGS, Positive Inotropic Agents, Phosphodiesterase III Inhibitors

AD-8717,181821-99-8,N-(2,6-DMP-802,,3-[2-[3-(4-Amidino) Zonampanel, YM-872,21024 SB-221284,196965-14-7,5-(0

## 推荐专业资料

ZINC00145813,ST5197865,	Oprea1_826548,MLS000122
ZINC00151021	IUPAC Name: 3-(2-chlorophe
ZINC00257502	MLS000716050,BAS 078671
STK138182,ZINC00302421,	IUPAC Name: (3E)-3-[(4-etho
Oprea1_091018,ST031273,	ZINC00104509
ZINC00084075	IUPAC Name: (2R)-1-(4-mett
IUPAC Name: (1R,,6R)-6-[(2-	Oprea1_406105
IUPAC Name: 6-hydroxy-1-(2-	ZINC00081150
STOCK2S-20570,ZINC0026f	ZINC00214910
ZINC00230690	Oprea1_042214,CBDivE_01

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DE SISTEMAS BIOLÓGICOS  
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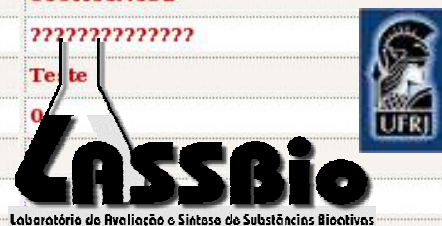
# Banco de dados de moléculas =

## Novos protótipos




**Medichem Database:**  
Chemical, Biological and Pharmacological Applications

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



A quimioteca do LASSBio tem 1745 compostos originais e ativos



Jmol

Wireframe Ball-and-Stick Space Fill

To return for initial orientation

Rotacionar



Universidade Federal do Rio de Janeiro



Lídia Moreira Lima  
Carlos Alberto Manssour Fraga  
Eliezer J. Barreiro

# Química na Saúde

<http://quimica2011.org.br/images/stories/6-CotidianoSaude.pdf>



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

## 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.

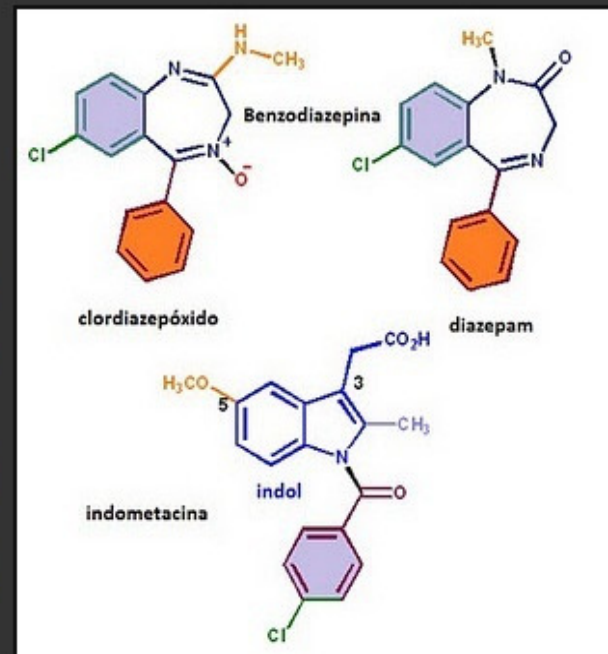
SÁBADO, 26 DE NOVEMBRO DE 2011

### A Linha do Tempo da Química Medicinal: assim nascem os fármacos (IV)



Nesta etapa da Linha do Tempo da Química Medicinal: assim nascem os fármacos

atingimos a década de 50, a partir de quando surgiram inúmeras inovações terapêuticas significativas, resultado dos avanços importantes observados em várias disciplinas relacionadas à Química ou à Biologia.



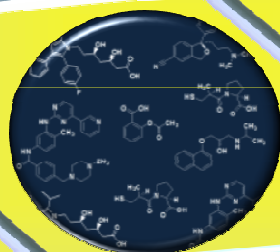
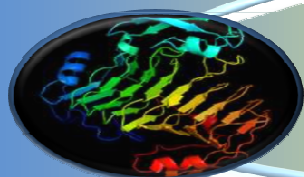
<http://ejb-eliezer.blogspot.com>



**XIX Escola**  
de **Verão**  
em Química Farmacêutica  
e Medicinal

De 28 de janeiro  
a 01 de fevereiro  
de 2013

Química  
e Medicinal



**Inscrições em setembro/2012**

<http://www.farmacia.ufrj.br/lasbio>

Realização:



Parceria:



instituto nacional  
de ciência e tecnologia de Fármacos e Medicamentos

[www.inct-inofar.ccs.ufrj.br](http://www.inct-inofar.ccs.ufrj.br)





**"Meditai se só as nações  
fortes podem fazer Ciência  
ou se é a Ciência  
que as fazem fortes"**



**Oswaldo Cruz**



Universidade Federal do Rio de Janeiro

## Epílogo

“...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).*



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