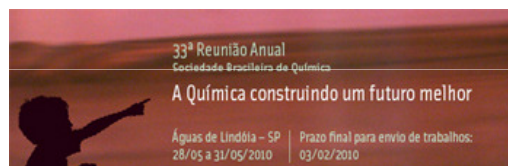




Universidade Federal do Rio de Janeiro

# Interfaces entre a química e a biologia nas áreas de produtos naturais e química medicinal – Salão Real

Coordenadores: Profs. Adriano D. Andricopolo & Maria da Conceição F. de Oliveira



*Eliezer J. Barreiro*  
Professor Titular



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

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

&

**Programa de Desenvolvimento de Fármacos  
ICB - UFRJ**



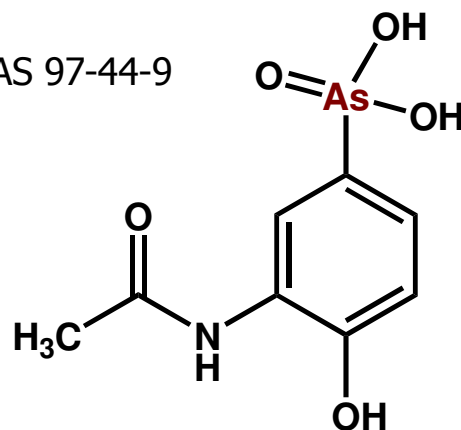
# O berço da Química Medicinal



Ernest Fourneau  
1872-1949

## Stovarsol

CAS 97-44-9



Institut Pasteur (1887)

## 1911- Laboratoire de Chimie Thérapeutique

Institut Pasteur (Emile Roux)

1911-1944 – J. Tréfouël, Th. Tréfouël,  
G. Benoit, D. Bovet, F. Nitti

Prontosil rubrum  
(sulfonamidas)

Curare: SAR



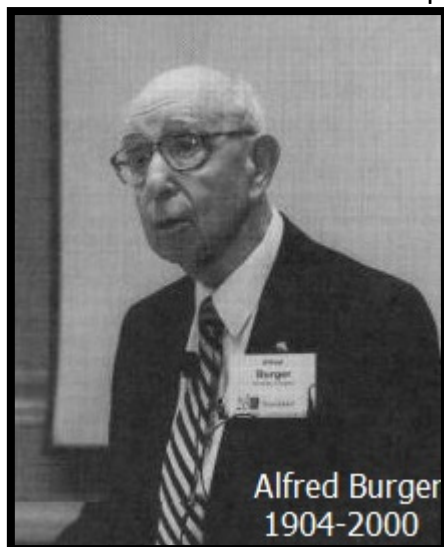
Daniel Bovet  
1907-1992

Prêmio Nobel de  
Fisiologia/Medicina

1957



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



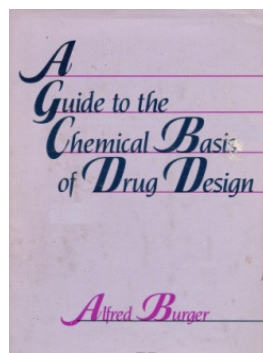
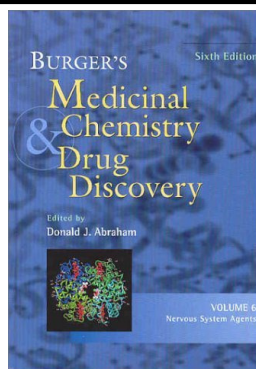
# Química Medicinal

## 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



Interfaces entre a química e a biologia nas áreas de produtos naturais e química medicinal

# Journal of Medicinal Chemistry

Química Medicinal  
Farmacologia

© Copyright 1980 by the American Chemical Society

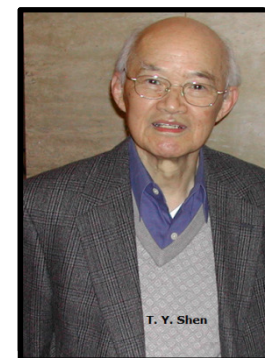
Volume 24, Number 1

January 1981

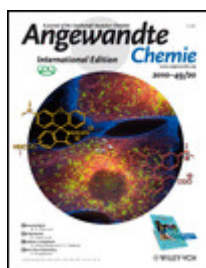
BURGER AWARD ADDRESS

## Toward More Selective Antiarthritic Therapy<sup>1</sup>

T. Y. Shen



Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey 07065. Received October 22, 1980

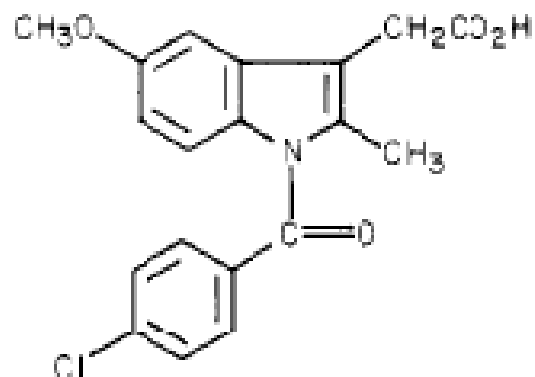


1963

CAS 53-86-1

indomethacin

C<sub>19</sub>H<sub>16</sub>ClNO<sub>4</sub>

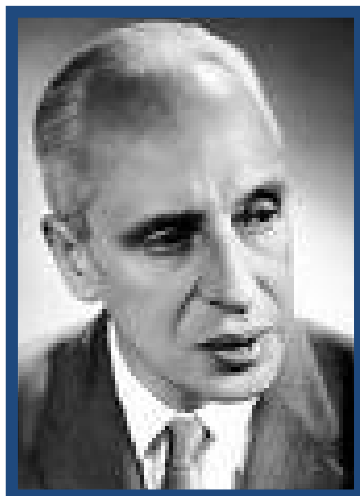


Charles A. Winter & T. Y. Shen  
Merck Research Laboratories

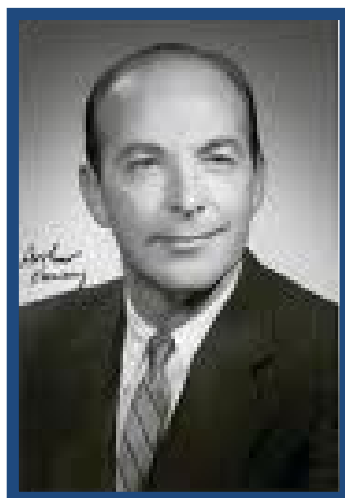
2-{1-[(4-chlorophenyl)carbonyl]-5-methoxy-2-methyl-1H-indol-3-yl}acetic acid

SH Ferreira, S Monçada, JR Vane "Indomethacin and aspirin abolish prostaglandin release from the spleen". *Nat New Biol* 1971, 231, 237





Severo Ochoa  
1905-1993



Arthur Kornberg  
1918-2007

# Prêmio Nobel de Fisiologia/Medicina 1959



“for their discovery of the mechanisms in the biological synthesis of RNA and DNA”

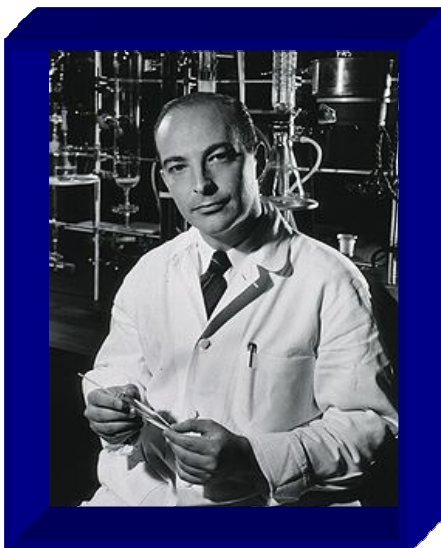


ARTHUR KORNBERG

The biologic synthesis of deoxyribonucleic acid

*Nobel Lecture, December 11, 1959*

**Interdisciplinaridade**

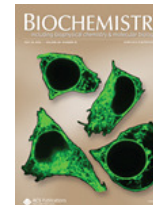


# Prêmio Nobel, 1959



FORUM

## The Two Cultures: Chemistry and Biology<sup>1</sup>

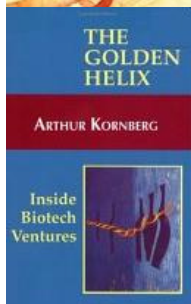
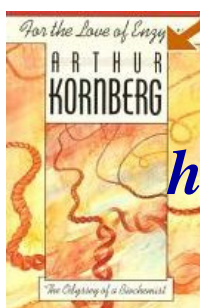


Arthur Kornberg

Department of Biochemistry, Stanford University, Stanford, California 94305

Received July 14, 1987

Arthur Kornberg  
1918-2007



University of Stanford



*“Much of life can be understood in rational terms if expressed in the language of chemistry... the historical roots of chemistry and biology are intertwined in many places...*

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

Química Medicinal

Biochemistry 1987, 26, 6888-6891

## Slide 6

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### EJB2

Kornberg definiu as bases da interdisciplinaridade das ciências dos fármacos quando antecipou a necessidade de aproximar-se a Química e a Biologia.

Eliezer J. Barreiro; 04/03/2010



# Molécula Salva-vidas



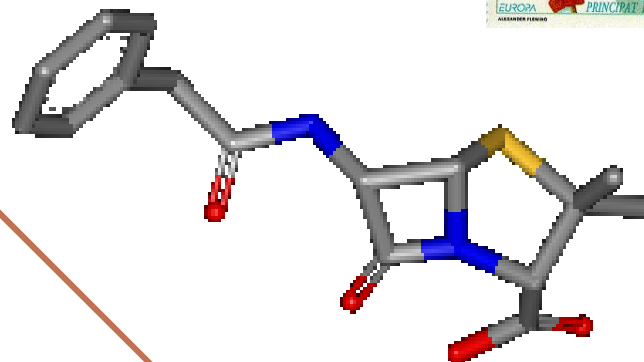
1928



Alexander Fleming  
1881-1955



Howard Walter Florey  
1898-1968

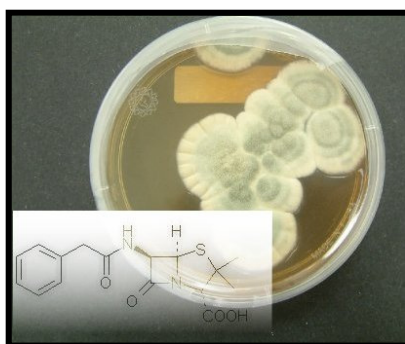


Penicilina

1941



Ernst Boris Chain  
1906-1999



195 pesquisadores ganharam o Prêmio Nobel de Medicina desde 1901



<http://nobelprize.org>

Prêmio Nobel de Fisiologia/Medicina  
1945







# O planejamento racional

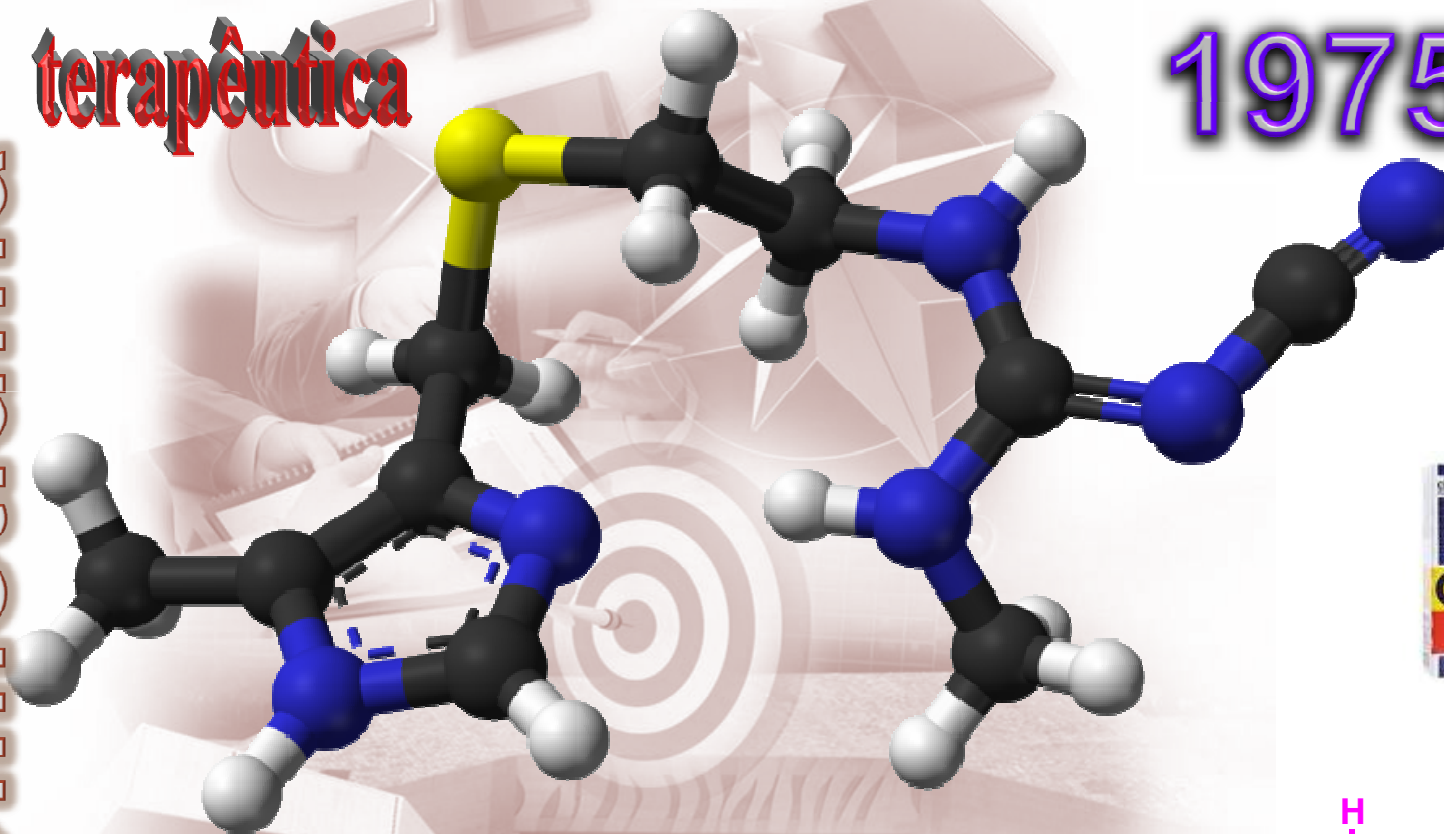
Inovação

Química Medicinal

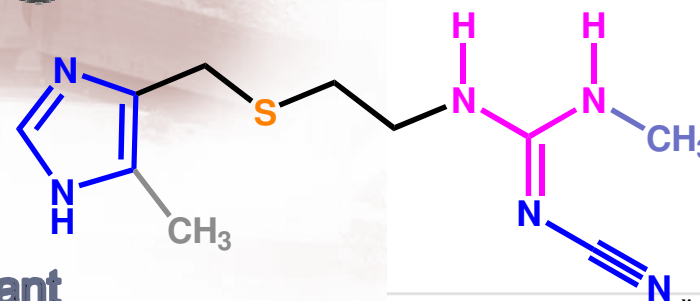
terapêutica

1975

Cimetidina



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



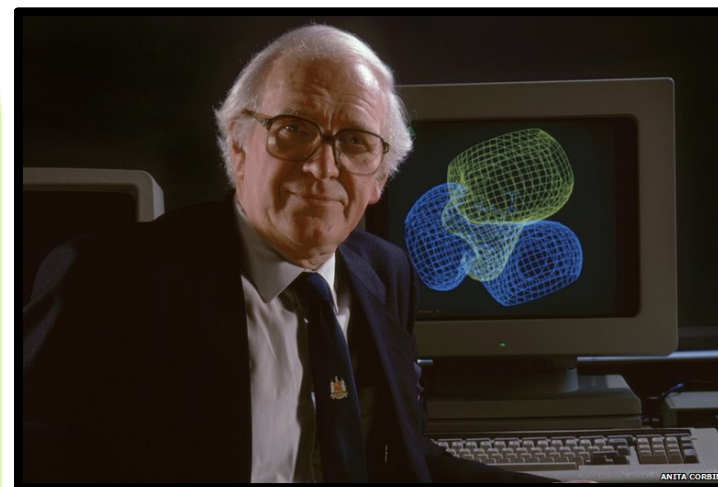
James Black, Robin Ganellin, Emmett, Durant



# Sir James W. Black: *drug hunter*

Química & Biologia

“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”<sup>12</sup>.



James Whyte Black

1924-2010

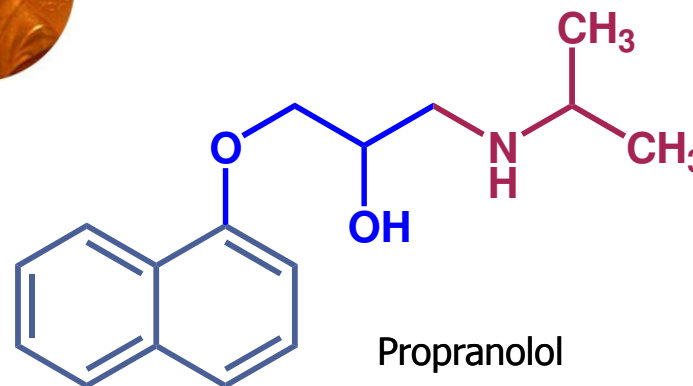
[R Ganellin & W Duncan, *Nature* **2010**, 464, 1292]



Prêmio Nobel de Medicina  
1988

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

Química Medicinal







Universidade Federal do Rio de Janeiro



# LASSBio

Laboratório de Avaliação e Síntese de Substâncias Bioativas

Cidade Universitária, ilha do Fundão

Química Medicinal

19/04/1994 → 19/04/2009

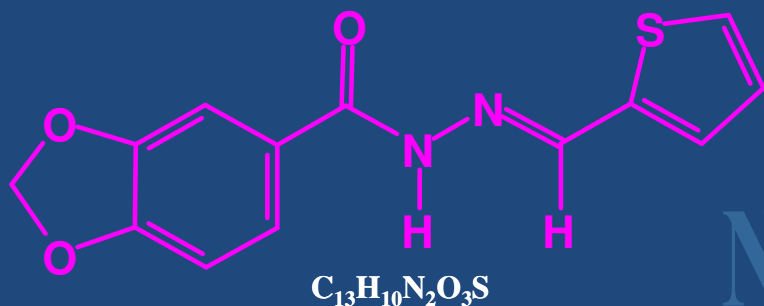
Laboratório de Avaliação e Síntese de Substâncias Bioativas



Pharmacology  
Farmacologia



# Novo Protótipo de Fármaco Cardioativo



## LASSBio-294

Estruturalmente simples;  
Sinteticamente acessível  
em ótimos rendimentos;  
Matéria-prima disponível  
(produto natural abundante).

Novo agente cardioativo, seletivo,  
não-digitalico, não-adrenérgico,  
**Sulfonol**  
com potentes propriedades  
inotrópicas & vasodilatadoras;  
Ativo por via oral;  
Sem toxicidade aguda.



**Patente US 7.091.238 (ag. 2006)**

**“Novel, Non-toxic Chronotropic Stimulator  
of Cardiac and Skeletal Muscle”**

EX Albuquerque, EJ Barreiro, RT Sudo, "LASSBio294 A Novel Digitalis-like Compound with Potential Anti-fatigue Activity"  
US Patent Office Provisorial Number 60-525,352 (1999); Patent US # 7091238 (2006).





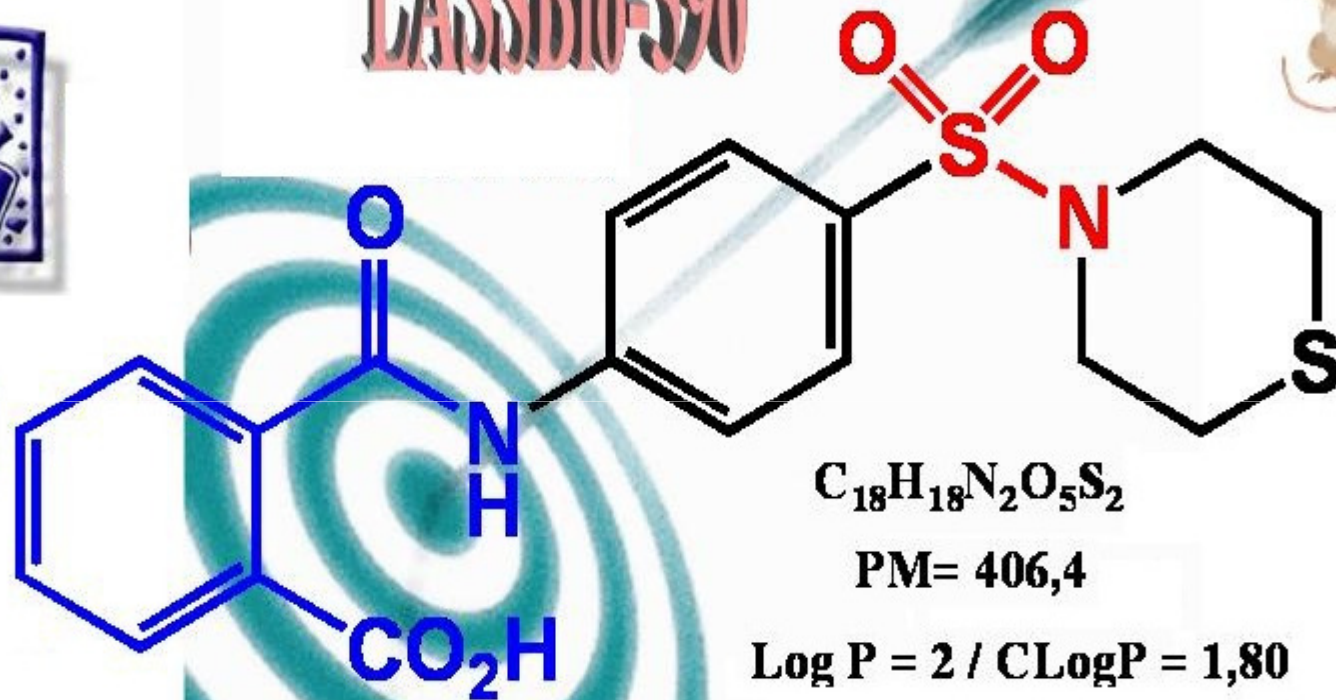
## Novo protótipo de fármaco anti-asmático



### LASSBio-596



anti-asmático



Fase Pré-clínica

PIBR 0208767-7 - 08/11/2002



instituto nacional de ciência e tecnologia

de Fármacos e Medicamentos

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





Dept. of Medicinal Chemistry  
and Molecular Pharmacology  
School of Pharmacy and Pharmaceutical Sciences



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8

Pharmacy School Rankings		
1	<b>University of California--San Francisco</b>   San Francisco, CA	4.7
2	<b>University of North Carolina--Chapel Hill</b>   Chapel Hill, NC	4.4
3	<b>University of Minnesota</b>   Minneapolis, MN	4.3
4	<b>University of Texas--Austin</b>   Austin, TX	4.2
5	<b>Purdue University</b>   West Lafayette, IN	4.1

Contato →

Cursos →

Disciplinas →

Editais de Seleção →

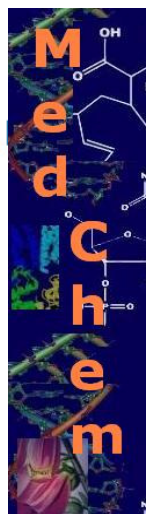
Informações Gerais →

Orientadores e Linhas de Pesquisa →

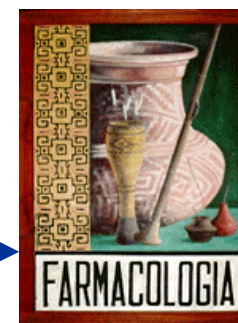
## Programa de Pós Graduação em Farmacologia e Química Medicinal

29 de abril de 2008

O Instituto de Ciências Biomédicas (ICB) da Universidade Federal do Rio de Janeiro mantém o Programa de Pós-Graduação na modalidade *stricto sensu* que permite obter graus de Mestre e Doutor em Ciências (Farmacologia e Química Medicinal). Os cursos de Mestrado e Doutorado são reconhecidos pela CAPES com conceito 4 e credenciados pelo Conselho Federal de Educação, tendo participações significativas na formação de recursos humanos. O Mestrado e o Doutorado recebem alunos novos regularmente duas vezes ao ano, através de seleções realizadas em fevereiro/março ou julho/agosto.



# Interdisciplinaridade



Único programa de pós-graduação  
(M/D) da América Latina

## Slide 14

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**EJB3**

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





Universidade Federal do Rio de Janeiro



Obrigado

