



Núcleo de Bioensaios  
Biossíntese e Ecofisiologia  
de Produtos Naturais

10 anos

## III WORKSHOP

CONSERVAÇÃO E USO SUSTENTÁVEL DA DIVERSIDADE  
DE PLANTAS DO CERRADO E MATA ATLÂNTICA:  
DIVERSIDADE QUÍMICA E PROSPECÇÃO DE BIOPRODUTOS



### Mesa Redonda

## ***NuBBE 10 anos: Impactos e Perspectivas***

07 E 08 DE JULHO  
INSTITUTO DE QUÍMICA  
UNESP - ARARAQUARA

Coordenador: Profa. Dra. Vanderlan da S. Bolzani, IQ - UNESP

Prof. Dr. Marcos Macari (Reitor-UNESP)

Prof. Dr. Carlos H. Brito Cruz (Diretor Científico – FAPESP, São Paulo, SP)

Prof. Dr. Ângelo da Cunha Pinto (IQ – UFRJ, Rio de Janeiro, RJ)

Prof. Dr. Carlos Joly (IB-INICAMP, Campinas, SP)

Prof. Dr. **Eliezer J. Barreiro** (LASSBio, Faculdade de Farmácia, UFRJ, Rio de Janeiro, RJ)

Prof. Dr. Manoel Odorico de Moraes Filho (Faculdade de Medicina, UFC, Fortaleza, CE)

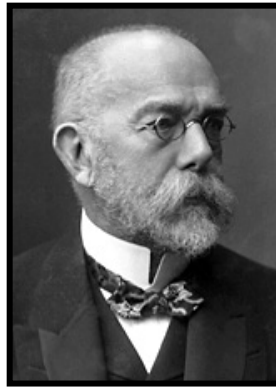




**Louis Pasteur**

1822-1895

“La vie empeche  
la vie”



**Robert Koch**

1843-1910

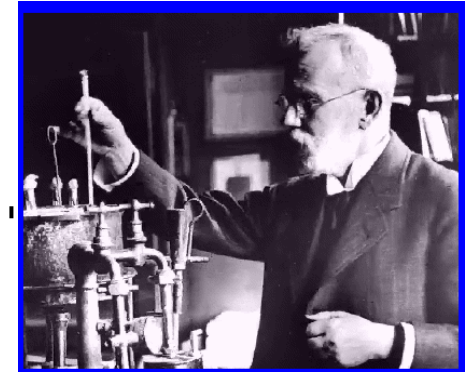
**1905**



**Emil Fisher**

1852-1919

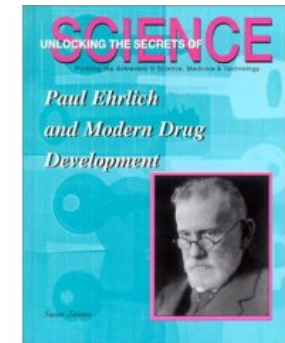
**1902**



**Paul Ehrlich**

1854-1915

**1908**



Química  
Medicinal

**Transdisciplinaridade**

## Quimiodiversidade

A estrutura química & fármacos

Peso molecular ~ 500 Da

< sete ciclos (anéis)



65 quatrilhões de estruturas  
possíveis \*



\* **Tudor I. Oprea**  
(University of New Mexico,  
School of Medicine  
Albuquerque, USA)



MM Hann & TI Oprea,  
*Curr. Opin. Chem. Biol.* 2004, **8**, 255



f á r m a c o s  
f á r m a c o s

**C** **Diversidade**

**+C** **Molecular**

**C-C** **C<sub>6</sub>H<sub>14</sub>**

**+C**

**C-C-C**

**C<sub>6</sub>H<sub>12</sub>**

**+C**

**C-C-C-C**

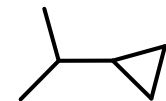
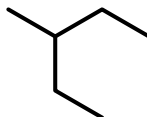
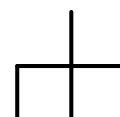
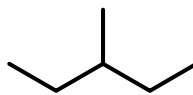
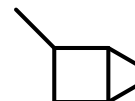
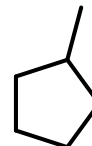
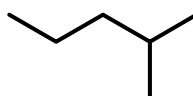
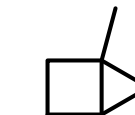
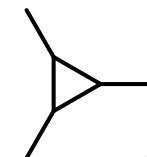
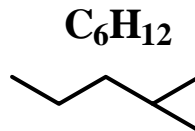
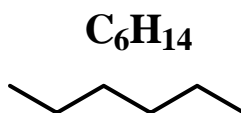
**C<sub>6</sub>H<sub>10</sub>**

**+C**

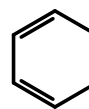
**C-C-C-C-C**

**C<sub>6</sub>H<sub>8</sub>**

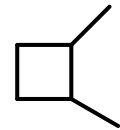
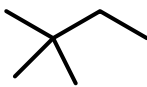
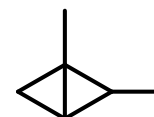
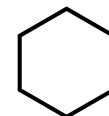
**+C**



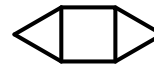
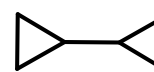
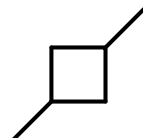
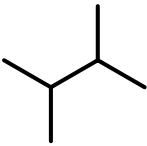
**C<sub>6</sub>H<sub>6</sub>**



**C<sub>6</sub>H<sub>10</sub>**



**C<sub>6</sub>H<sub>8</sub>**



**24 compostos**

**Quimiodiversidade**





## A quimiodiversidade dos produtos naturais

camptotecina

compactina

domesticacão molecular

artemisinina

Morfina

beta-carbolina

galantamina

Quinina

atropina

monocrotalina

lipstatina

antibióticos

vincristina

Digitálicos

safrol

ácido hidnocárpico

Penicilina

escopolamina

indolizidina

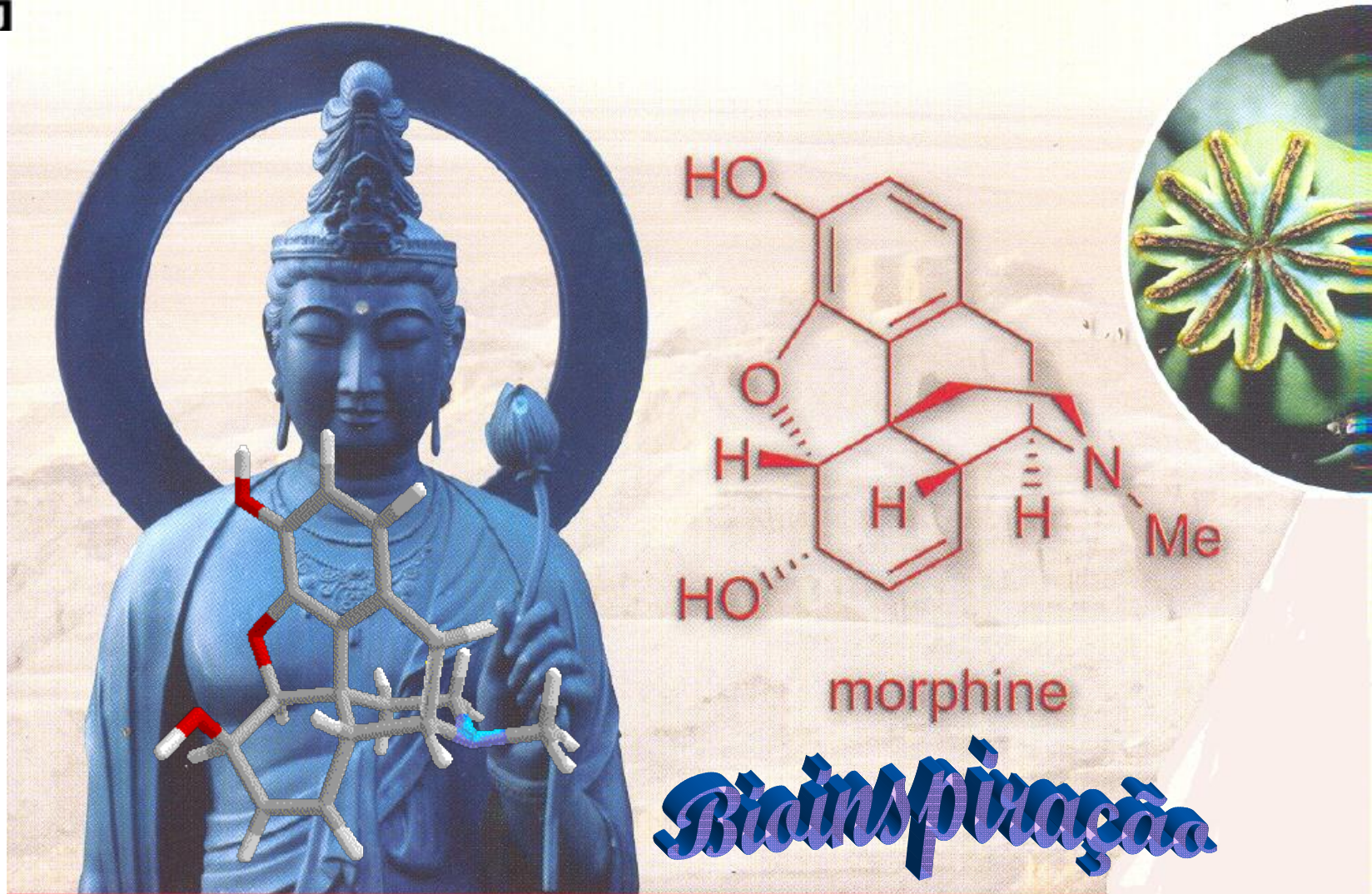
papaverina

epibatidina

caféina

### SMALL-MOLECULE PROBES

Colony-stimulating factor receptor (CSF-R) is a tyrosine kinase receptor used to discover the protein 5-lipoxygenase (5-LOX) family of protein kinases; pargoline, a tryptamine derivative; MK-564, used to discover the protein 5-lipoxygenase (5-LOX) family of protein kinases; 506BD, a probe of immunophilin action; dimerizer, an inactive variant of rapamycin, by chemical modification, gained the ability to control proximal proteins in cells and animals; a probe of the rapid response signaling network, one of the proteins FRAP; K<sub>252a</sub> affinity reagent (lysine variant of trapoxin) used to discover FRAP.

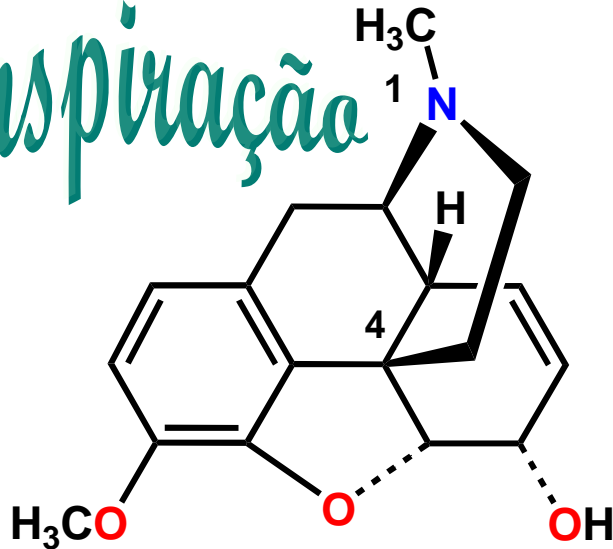


Alcalóides → *inter-alia*: morfina, quinina → Fármacos



*Bioinspiração*

## Hipno-analgésicos



morfina

*Molécula selvagem*

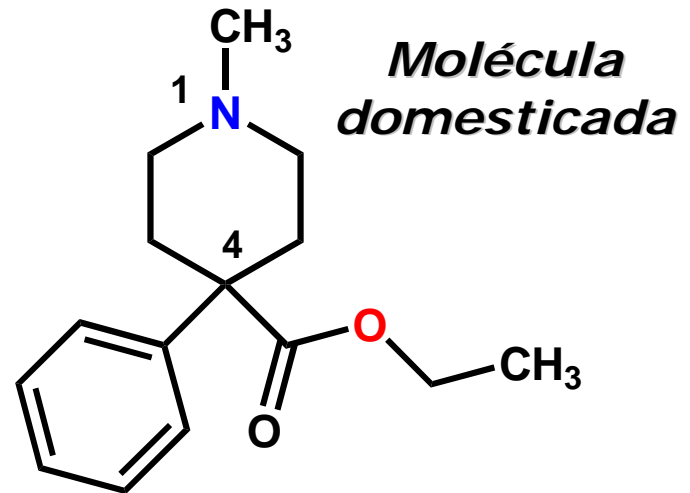
PM = 299.3

C<sub>18</sub>H<sub>21</sub>NO<sub>3</sub>

Quimiotipo:  
4-fenilpiperidina

streptase

molecular



meperidina

*Molécula domesticada*

PM = 247.3

C<sub>15</sub>H<sub>21</sub>NO<sub>2</sub>

*Protótipo natural*

*Fármaco*

“... **A NATUREZA INTERESSADA**  
**NA PRESERVAÇÃO DA**  
**ESPÉCIE HUMANA,**  
**INSPIRA A COMPOSIÇÃO**  
**DOS REMÉDIOS ...”**

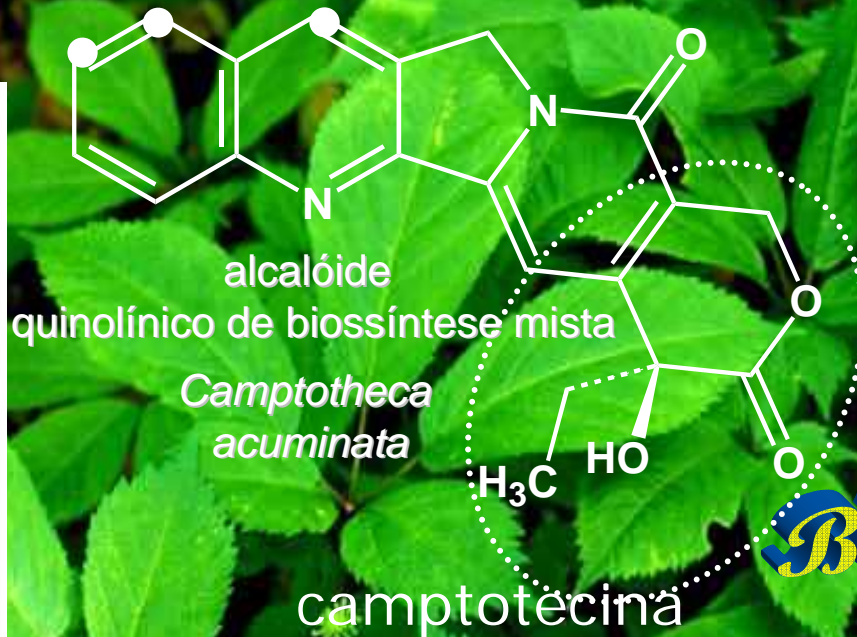
***“Porque os remédios morrem ?***

**Joaquim Maria Machado de Assis**  
(1839-1908)

em “A Semana” de 19/11/1893



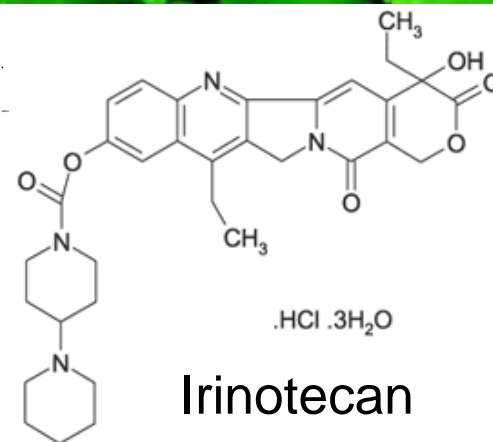
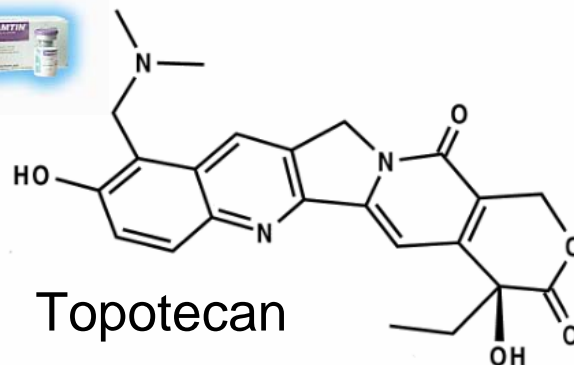




Inibidor de  
topoisomerase-1



*Bioinspiração*



Drugs

*moléculas domesticadas*

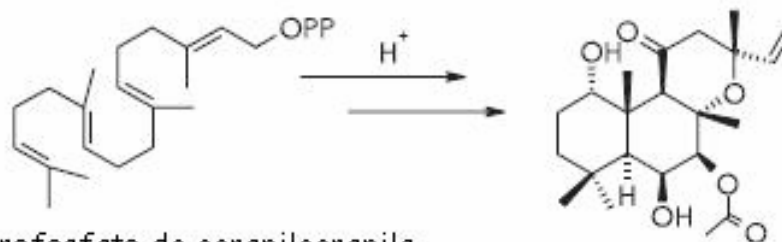
Wall, ME & Wani, MC "Camptothecin: Discovery to Clinic"  
*Annals of the New York Academy of Sciences* 1996, 803, 1



## Bioinspiração

**biodiversidade**

Labdanos



Pirofosfato de geranilgeranila

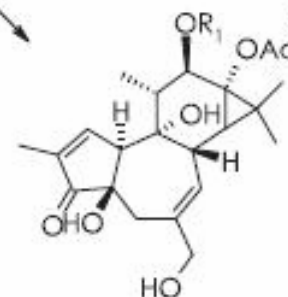
Colforsina

### Ativador PKA (c-AMP)



*Coleus forskoholii*

**Tiglian**



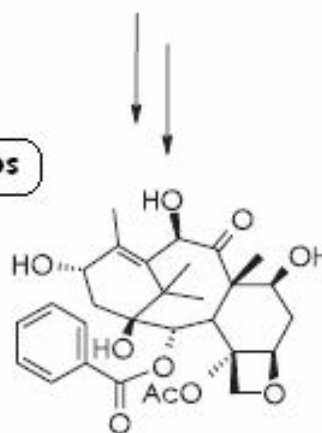
Forbol

### Ativador PKC



*Daphne* sp  
*Cratan* sp

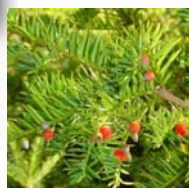
## Taxanos



## Inibidor tubulinas

10-Desacetylbaconina

*Taxus brevifolia*



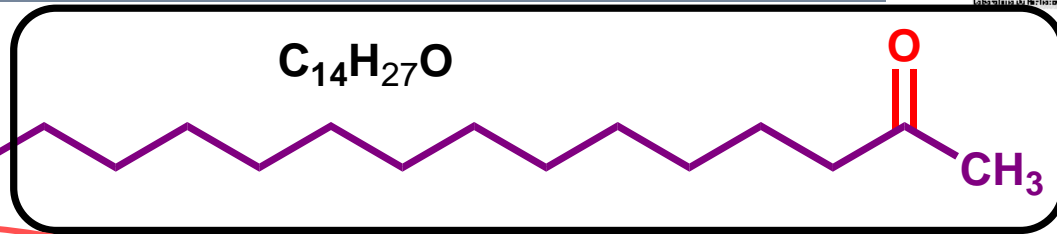
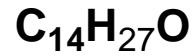
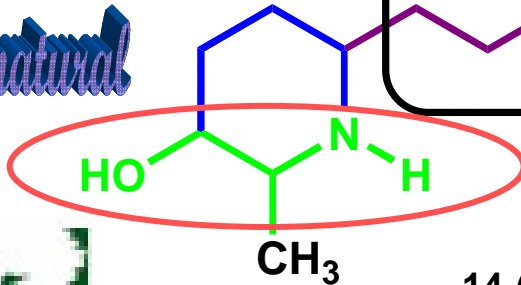
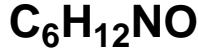
**TAXOL®**  
*Science and  
Applications*

*Edited by*  
S. S. S. S.





*Protótipo natural*



Alcalóide piperidínico

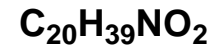
14-(5-hidróxi-6-metil-piperidin-2-il)-tetradecan-2-ona



*Bioinspiração*



Espectalina



Fórmula molecular

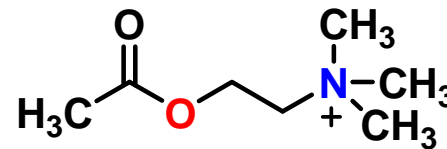
Peso molecular: 325,5



Cassia spectabilis



etanol-amina



ACh

Química Medicinal

## Antinociceptive Profile of 2,3,6-Trisubstituted Piperidine Alkaloids: 3-*O*-Acetyl-spectaline and Semi-synthetic Derivatives of (–)-Spectaline

Cláudio VIEGAS, Jr.<sup>a</sup> Magna Suzana ALEXANDRE-MOREIRA,<sup>b</sup> Carlos Alberto Manssour FRAGA,<sup>c</sup> Eliezer Jesus BARREIRO,<sup>c</sup> Vanderlan da Silva BOLZANI,<sup>d</sup> and Ana Luísa Palhares de MIRANDA<sup>\*,c</sup>

<sup>a</sup>Laboratório de Fitoquímica e Química Medicinal, Departamento de Ciências Exatas, Universidade Federal de Alfenas; 37130-000, Alfenas, MG, Brazil; <sup>b</sup>Laboratório de Farmacologia e Imunidade, Departamento de Fisiologia, Centro de Ciências Biológicas, Universidade Federal de Alagoas; Maceió, Al, Brazil; <sup>c</sup>Laboratório de Avaliação e Síntese de Substâncias Bioativas, Departamento de Fármacos, Faculdade de Farmácia, Universidade Federal do Rio de Janeiro; 21941-902, Rio de Janeiro, RJ, Brazil; and <sup>d</sup>Núcleo de Bioensaios, Biossíntese e Ecofisiologia de Produtos Naturais, Instituto de Química, Universidade Estadual Paulista; 14800-900, Araraquara, SP, Brazil.

Received July 2, 2007; accepted January 24, 2008; published online January 28, 2008

*European Journal of Pharmacology* 2008, 580, 339

## CNS-selective noncompetitive cholinesterase inhibitors derived from the natural piperidine alkaloid (–)-spectaline

Newton G. Castro<sup>a,\*</sup>, Rodrigo S. Costa<sup>a</sup>, Luisa S.B. Pimentel<sup>a</sup>, Amanda Danuello<sup>b</sup>, Nelilma C. Romeiro<sup>c</sup>, Cláudio Viegas Jr.<sup>d</sup>, Eliezer J. Barreiro<sup>c</sup>, Carlos A.M. Fraga<sup>c</sup>, Vanderlan S. Bolzani<sup>b</sup>, Monica S. Rocha<sup>a</sup>

<sup>a</sup>Departamento de Farmacologia Básica e Clínica, Instituto de Ciências Biomédicas, Universidade Federal do Rio de Janeiro, CCS Bloco J Sala J1-029, 21941-902, Rio de Janeiro, RJ, Brazil

<sup>b</sup>Núcleo de Bioensaios, Biossíntese e Ecofisiologia de Produtos Naturais (NuBBE), Instituto de Química, Universidade Estadual Paulista Júlio de Mesquita Filho, CP 355, 14801-970, Araraquara, SP, Brazil

<sup>c</sup>Laboratório de Avaliação e Síntese de Substâncias Bioativas (LASSBio), Faculdade de Farmácia, Universidade Federal do Rio de Janeiro, CP 68023, 21944-910, Rio de Janeiro, RJ, Brazil

<sup>d</sup>Laboratório de Fitoquímica e Química Medicinal (LFQM) Departamento de Ciências Exatas, Universidade Federal de Alfenas, 37130-000, Alfenas, MG, Brazil





Bioorganic & Medicinal Chemistry 13 (2005) 4184–4190

## New selective acetylcholinesterase inhibitors designed from natural piperidine alkaloids

Cláudio Viegas, Jr.,<sup>a,b</sup> Vanderlan S. Bolzani,<sup>b</sup> Luísa S. B. Pimentel,<sup>c</sup> Newton G. Castro,<sup>c</sup> Rafael F. Cabral,<sup>c</sup> Rodrigo S. Costa,<sup>c</sup> Corinne Floyd,<sup>c</sup> Mônica S. Rocha,<sup>c</sup> Maria C. M. Young,<sup>d</sup> Eliezer J. Barreiro<sup>a</sup> and Carlos A. M. Fraga<sup>a,\*</sup>

<sup>a</sup>Laboratório de Avaliação e Síntese, de Substâncias Bioativas (LASSBio), Faculdade de Farmácia, Universidade Federal do Rio de Janeiro, CP 68023, 21944-910, Rio de Janeiro, Brazil

<sup>b</sup>Núcleo de Bioensaios, Biossíntese e Ecofisiologia, de Produtos Naturais (NuBBE), Instituto de Química, Universidade Estadual Paulista 'Julio de Mesquita Filho', CP 355, 14801-970, Araraquara, Brazil

<sup>c</sup>Departamento de Farmacologia Básica e Clínica, Instituto de Ciências Biomédicas, Centro de Ciências da Saúde, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

<sup>d</sup>Seção de Bioquímica e Fisiologia de Plantas, Instituto de Botânica, São Paulo, Brazil

*J. Nat. Prod.* 2004, 67, 908–910

## Further Bioactive Piperidine Alkaloids from the Flowers and Green Fruits of *Cassia spectabilis*

Claudio Viegas, Jr.,<sup>†</sup> Vanderlan da S. Bolzani,<sup>\*,†</sup> Maysa Furlan,<sup>†</sup> Eliezer J. Barreiro,<sup>‡</sup> Maria Claudia M. Young,<sup>§</sup> Daniela Tomazela,<sup>‡</sup> and Marcos N. Eberlin<sup>‡</sup>

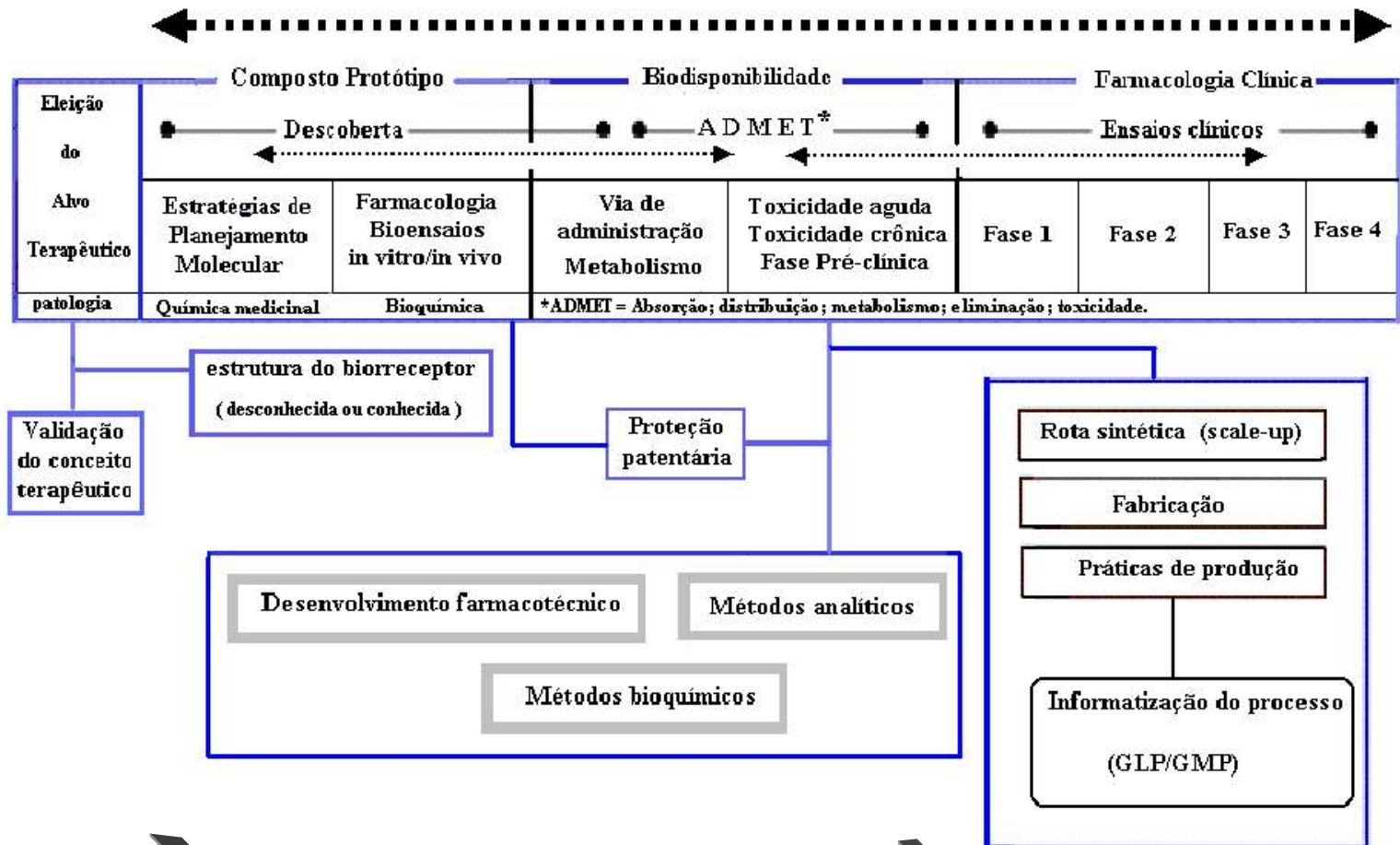
Instituto de Química, Universidade Estadual Paulista (UNESP), CP 359, 14800-900, Araraquara, SP, Brazil, Faculdade de Farmácia, Universidade Federal do Rio de Janeiro (UFRJ), 21944-190, Rio de Janeiro, RJ, Brazil, Seção de Fisiologia e Bioquímica de Plantas, Instituto de Botânica (IBt), 01061-970, São Paulo, SP, Brazil, and Instituto de Química, Universidade Estadual de Campinas (UNICAMP), 13083-970, Campinas, SP, Brazil

Received August 26, 2003

Alexandre-Moreira, M. S.; Viegas, C., Jr.; Miranda, A. L. P.; Bolzani, V. S.; Barreiro, E. J. *Planta Med.* 2003, 69, 795.

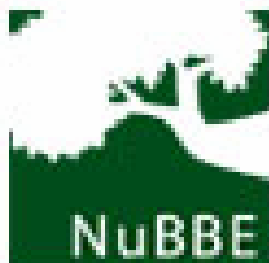


## Visão esquemática do processo de descoberta racional de fármacos.



# Interdisciplinaridade

## Profa. Dra Vanderlan Bolzani



# Parabéns!