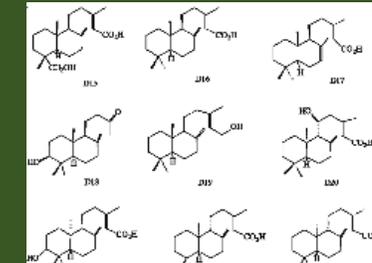
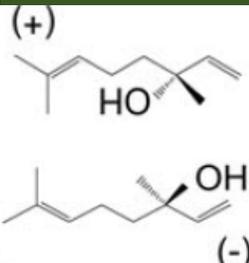
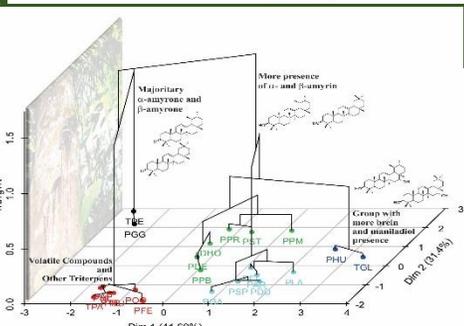
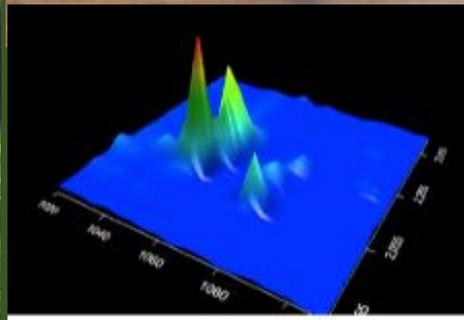
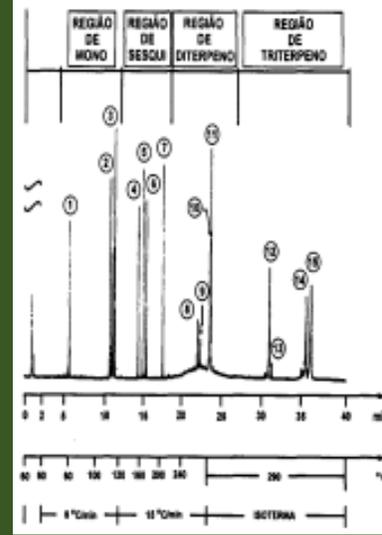


Mesa Redonda:

A química e a biodiversidade amazônica

Valdir Florêncio da Veiga Junior

Belém, 9 de novembro de 2016



1ª Questão: Como valorizar os bioprodutos Amazônicos tradicionais?

- Usos tradicionais
- Novos usos
- Resíduos da bioindústria

2ª Questão: Como aumentar a qualidade dos bioprodutos Amazônicos?

- DOC
- Valorizar diferenças regionais

3ª Questão: Como conhecer e valorizar a biodiversidade ainda desconhecida?

- Animais
- Microorganismos
- Aproveitamentos transdisciplinares

4ª Questão: Qual o trabalho do fitoquímico no século XXI?

- Isolar
- Aumento de Escala
- Identificar em misturas
- Padronizar extratos e frações ativos

1ª Questão:

- Como valorizar os bioprodutos Amazônicos tradicionais?

- Usos tradicionais**
- Novos usos**
- Resíduos da bioindústria**

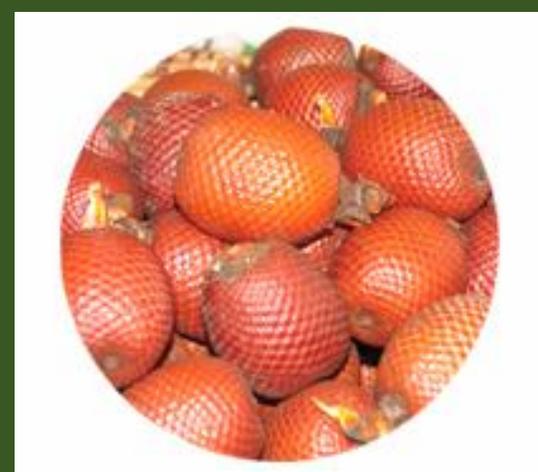
Buriti– *Mauritia flexuosa*





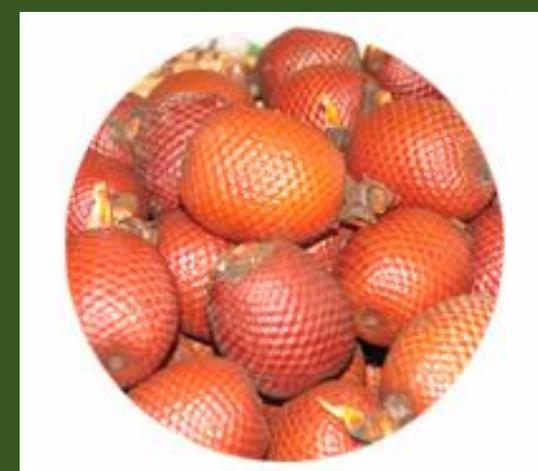
Pracaxí– *Pentaclethra macroloba*





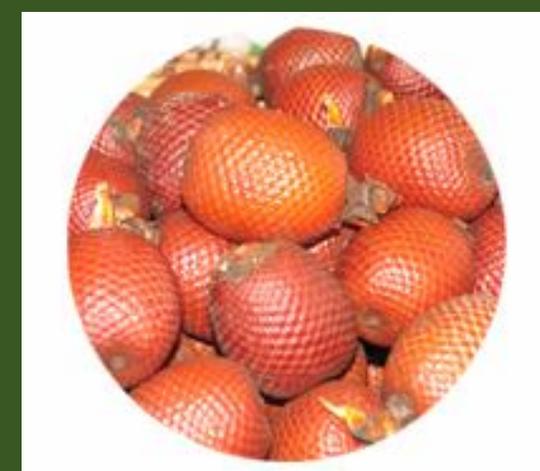
Pimenta-de-macaco – *Piper aduncum*





Jambú – *Spilanthes acmella*





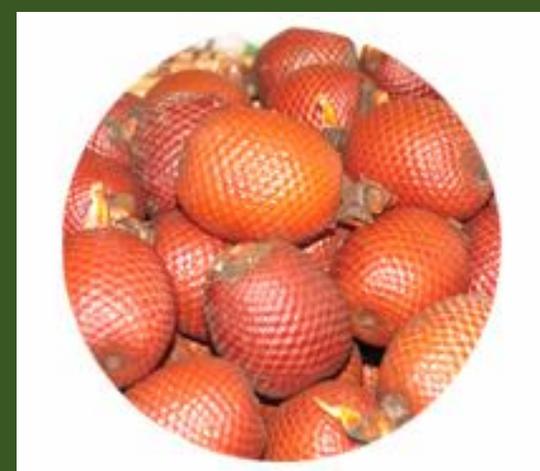
Castanha do Brasil - *Bertholletia excelsa*





Ucuúba– *Virola sebifera*



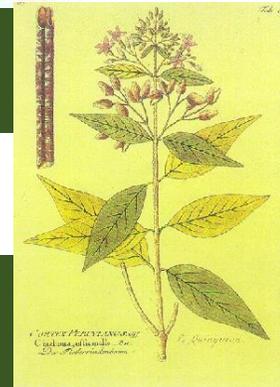


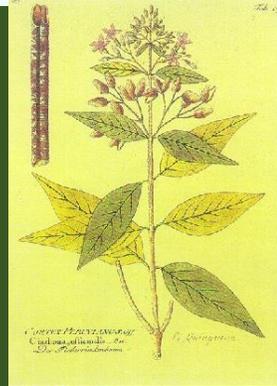
Guaraná – *Paullinia cupana*





Quina – *Cinchona officinalis*



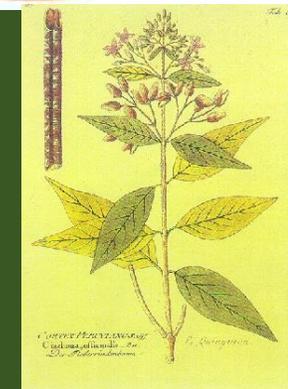


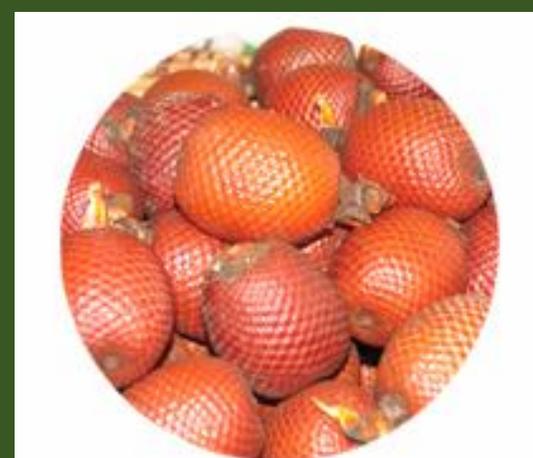
Murumuru— *Arstrocaryum murumuru*



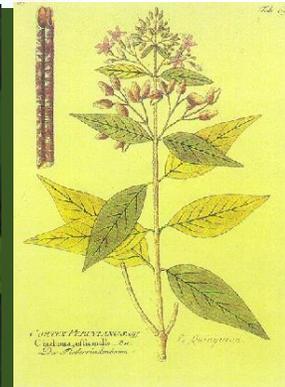


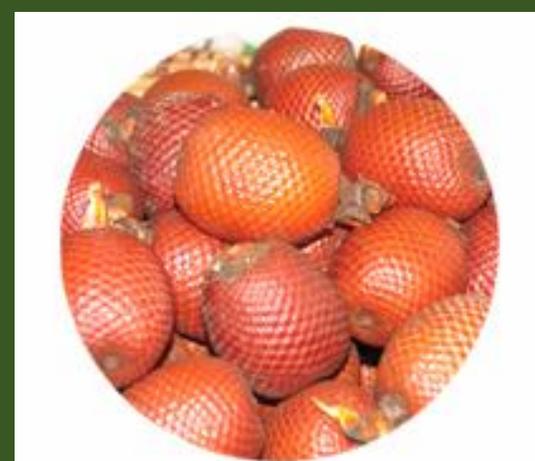
Ipecacuanha – *Psychotria ipecacuanha*



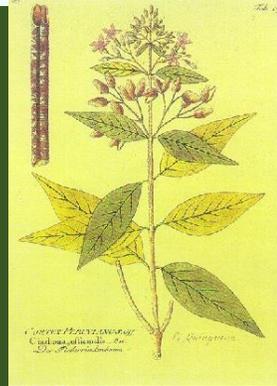


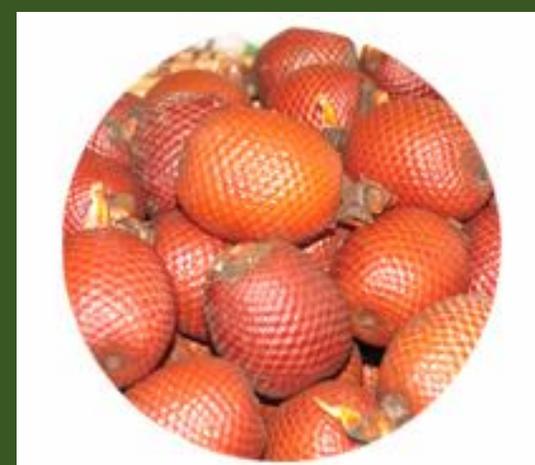
Sacaca – *Croton cajucara*



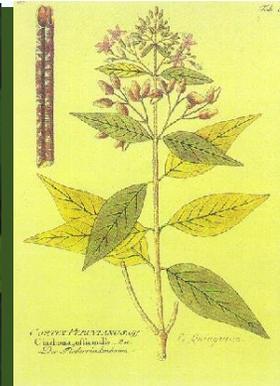


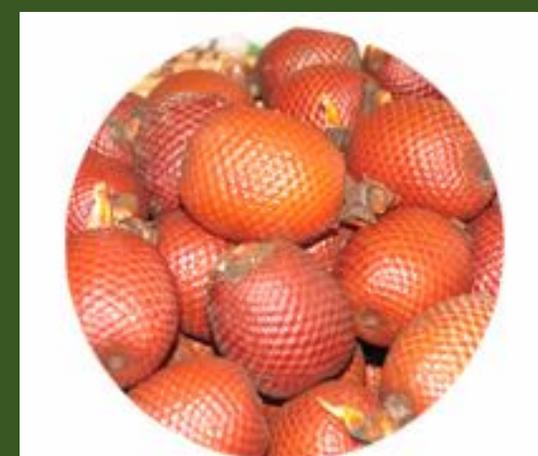
Quassia - *Quassia amara*



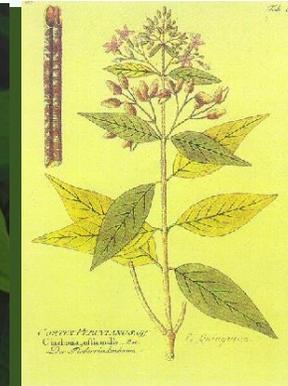


Saracura-mirá
Ampelozizyphus amazonicus





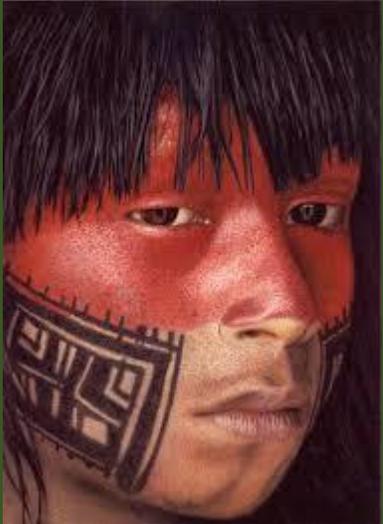
- Do puxuri à pimenta-longa
- Da seringueira ao açaí
- Da copaíba ao cipó-titica
- Do cumarú ao paricá
- Do cupuaçu à sorva
- Do tucumã ao bacuri
- Da mandioca à casca-preciosa
- Do pau-rosa ao taperebá
- Do piquiá à macacaporanga
- Da unha-de-gato ao babaçu
- Da priprioca ao patchouli
- Da pataqueira à catinga de mulata
- Da sálvia-do-marajó ao breu...



No início: de frente para o mar..
...a busca por especiarias.

“...e os mesmos eram
cheios de grãos vermelhos,
pequenos, que,
esmagando-os entre os dedos,
faziam tintura muito vermelha, da
qual eles andavam tintos...”



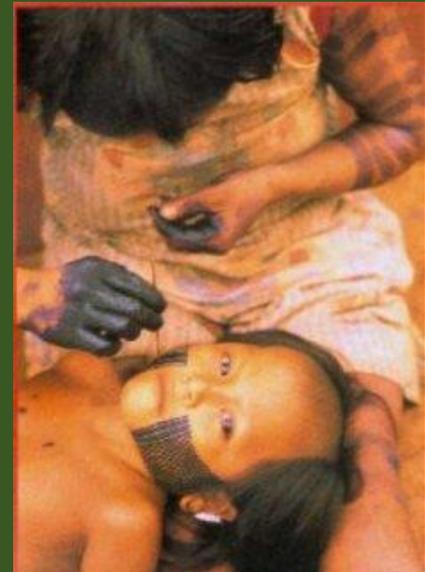


Urucum
Bixa orellana
Bixaceae



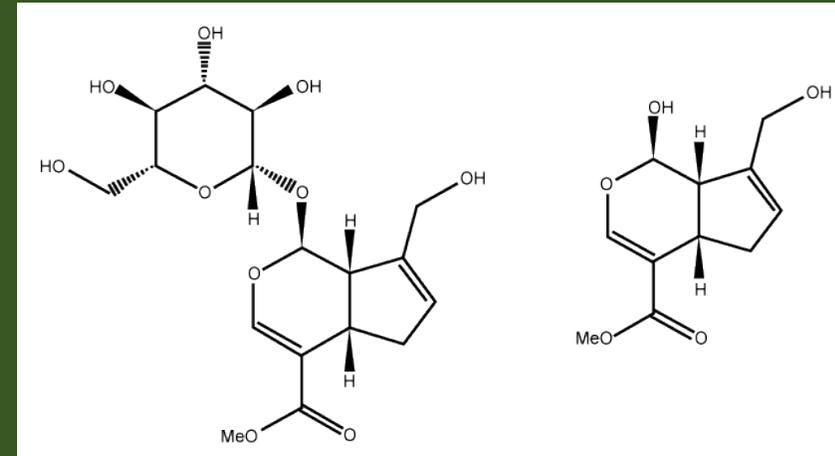
"...mascam essa fruta e espremem o suco dentro de um vaso. Com ele é que se pintam. Quando esfregam o suco sobre a pele, no início parece água. Mas depois de algum tempo a pele fica tão preta como se fosse tinta. Isso perdura até o nono dia. Depois a cor desaparece, mas não antes desse prazo, mesmo quando eles se lavam muitas vezes".

Jenipapo
Genipa americana
Rubiaceae

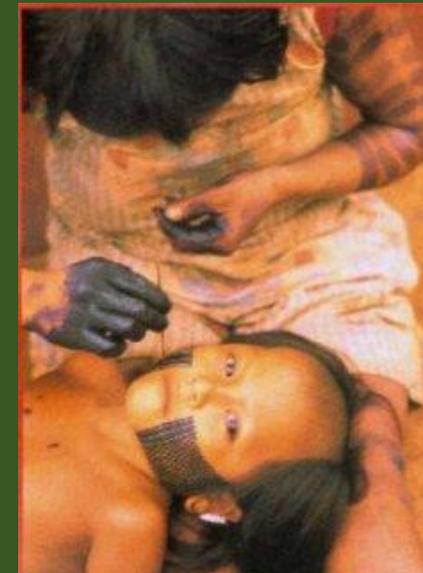


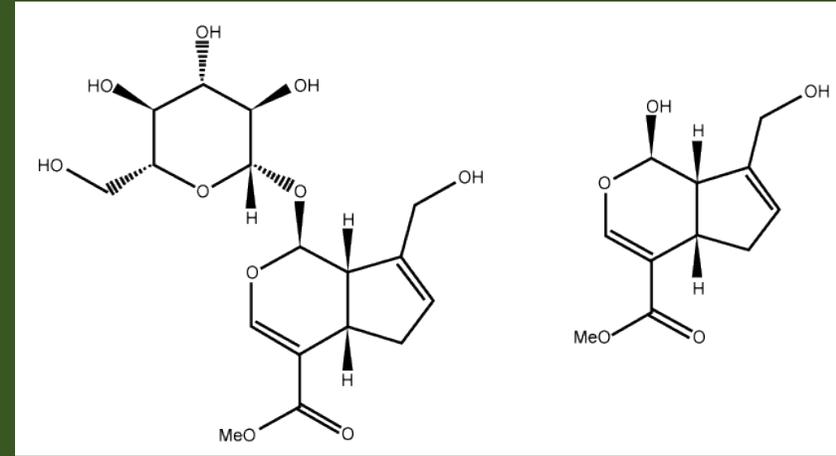


Urucum
Bixa orellana
Bixaceae



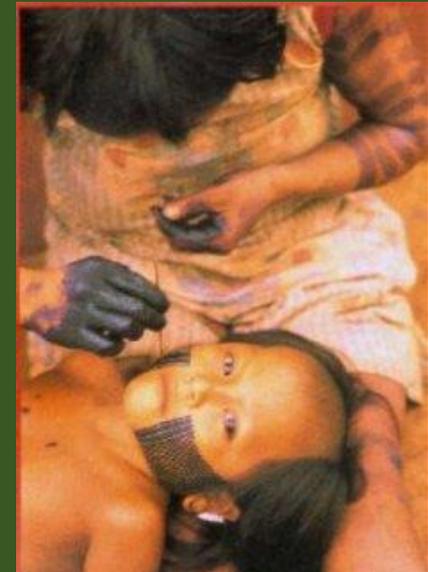
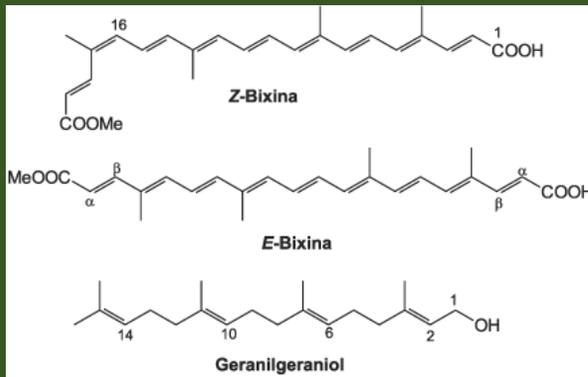
Jenipapo
Genipa americana
Rubiaceae

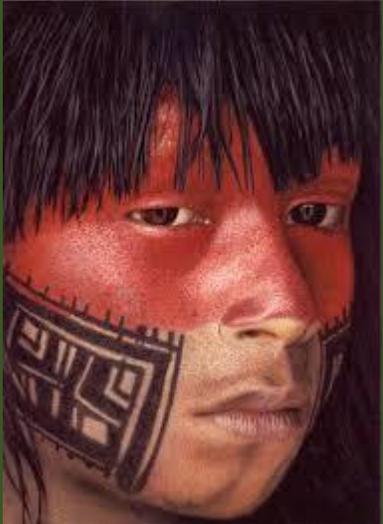




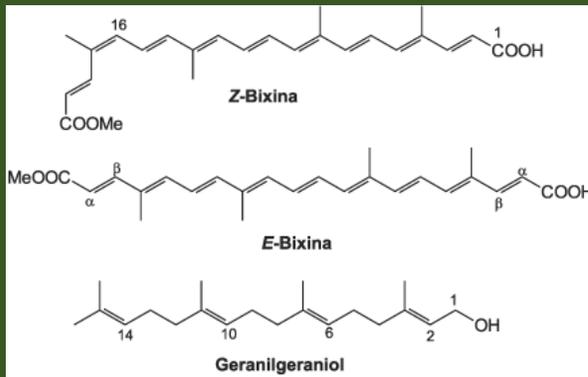
Jenipapo
Genipa americana
Rubiaceae

Urucum
Bixa orellana
Bixaceae





Urucum
Bixa orellana
Bixaceae



J Biomed Mater Res B Appl Biomater. 2016 Jun 13. doi: 10.1002/jbm.b.33724. [Epub ahead of print]

Efficient cutaneous wound healing using bixin-loaded PCL nanofibers in diabetic mice.

Pinzón-García AD¹, Cassini-Vieira P², Ribeiro CC¹, de Matos Jensen CE³, Barcelos LS², Cortes ME⁴, Sinisterra RD¹.

Journal of
Biomedical Materials Research
PART B APPLIED BIOMATERIALS

Efficient cutaneous wound healing using bixin-loaded PCL nanofibers in diabetic mice

Ana Delia Pinzón-García,¹ Puebla Cassini-Vieira,² Cyntia Cabral Ribeiro,¹ Carlos Eduardo de Matos Jensen,³ Luciola Silva Barcelos,² Maria Esperanza Cortes,⁴ Ruben Dario Sinisterra¹



Free Radical Biology and Medicine

Volume 89, December 2015, Pages 690–700



Original Contribution

Systemic administration of the apocarotenoid bixin protects skin against solar UV-induced damage through activation of NRF2

Shasha Tao, Sophia L. Park, Montserrat Rojo de la Vega, Donna D. Zhang, Georg T. Wondrak

Int J Pharm. 2014 Oct 1;473(1-2):485-92. doi: 10.1016/j.ijpharm.2014.07.027. Epub 2014 Jul 24.

Bixin loaded solid lipid nanoparticles for enhanced hepatoprotection-preparation, characterisation and in vivo evaluation.

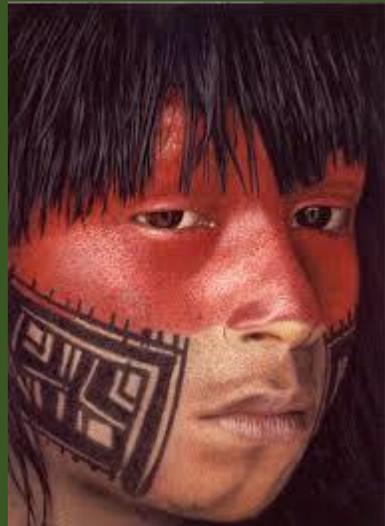
Rao MP¹, Manjunath K², Bhagawati ST³, Thippeswamy BS¹.

Arq. Bras. Med. Vet. Zootec., v.68, n.1, 104-112, 2016

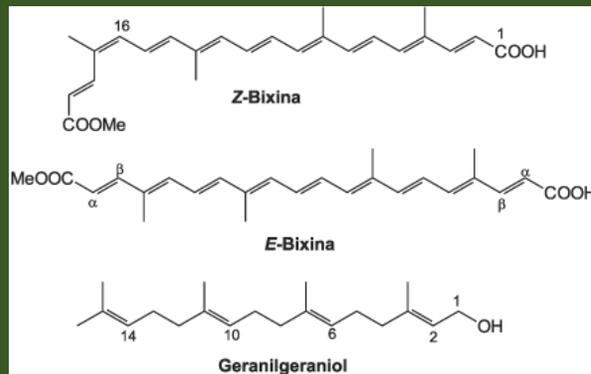
Potencial cicatricial da *Bixa orellana* L. em feridas cutâneas: estudo em modelo experimental

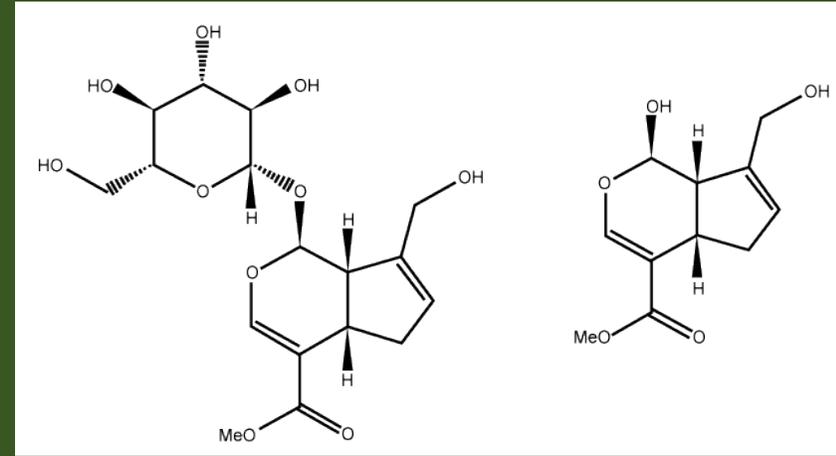
[Therapeutic potential of *Bixa orellana* L. in skin wounds: a study in the rat model of open wound healing]

S.O. Capella¹, M.T. Tillmann¹, A.O.C. Félix², E.G. Fontoura¹, C.G. Fernandes², R.A. Freitag³, M.A.Z. Santos³, S.R. Félix¹, M.O. Nobre²

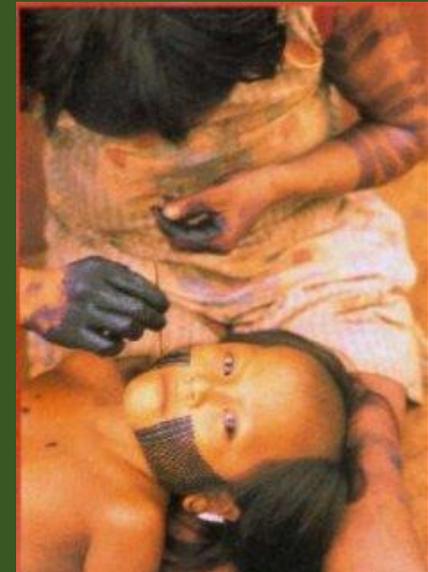


Urucum
Bixa orellana
Bixaceae





Jenipapo
Genipa americana
Rubiaceae

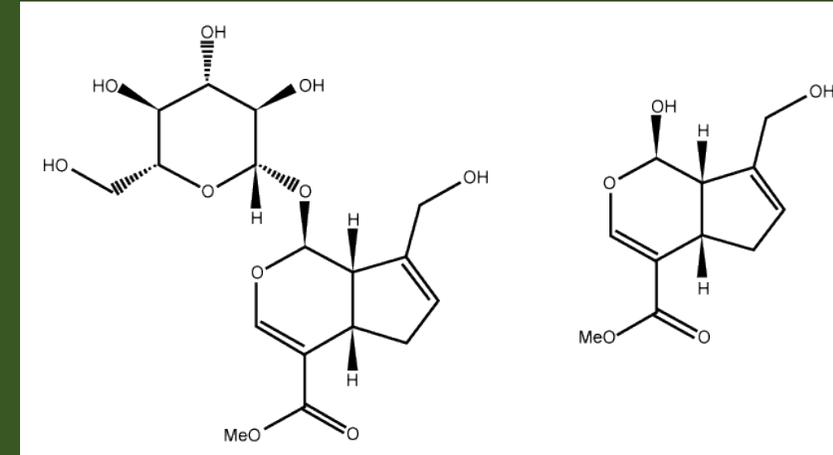


J Bacteriol Virol. 2016 Jun;46(2):108-113. Korean.
Published online June 28, 2016. <https://doi.org/10.4167/jbv.2016.46.2.108>

Copyright © 2016 The Korean Society for Microbiology and The Korean Society of Virology

Antitumor Effects of Genipin: New and Emerging Insights from Recent Studies

Yu Su Shin,¹ Miyeon Cho,² Gyu Hwan Park,² Hyosun Cho,³ and Hyojeung Kang²



Molecules. 2016 Jul 16;21(7). pii: E923. doi: 10.3390/molecules21070923.

Evaluation of the Antidepressant Activity, Hepatotoxicity and Blood Brain Barrier Permeability of Methyl Genipin.

Che X^{1,2,3}, Wang M^{4,5,6}, Wang T^{7,8,9}, Fan H^{10,11,12}, Yang M^{13,14,15}, Wang W^{16,17,18}, Xu H^{19,20,21}.

Jenipapo
Genipa americana
Rubiaceae



Alternative and Integrative Medicine

Meng et al., *Altern Integ Med* 2013, 2:4
<http://dx.doi.org/10.4172/2327-5162.1000117>

Review Article

Open Access

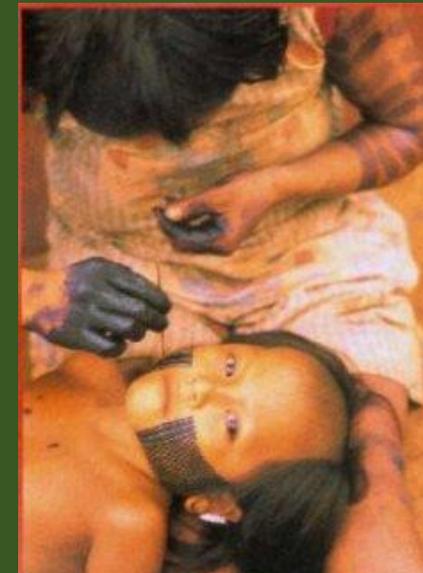
The Role of Genipin and Geniposide in Liver Diseases: A Review

Sheng-xi Meng^{1,2}, Jing-hua Peng^{1,2,5}, Qin Feng^{1,2}, Jian-mei Cao⁴ and Yi-yang Hu^{1-3*}

Drug Metab Lett. 2016 Oct 20. [Epub ahead of print]

Genipin inhibits the induction of inducible nitric oxide synthase through the inhibition of NF-κB activation in rat hepatocytes.

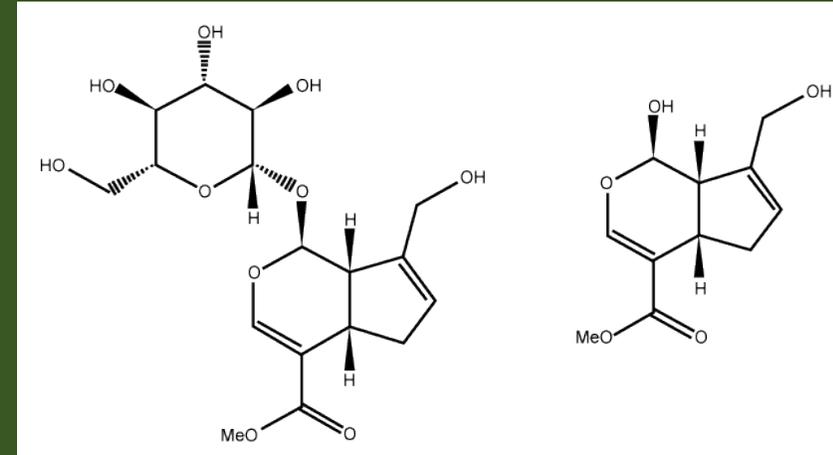
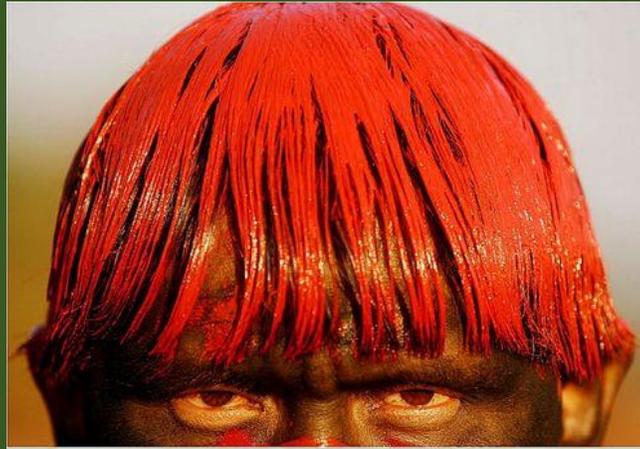
Nakatake R, Tsuda T, Matsuura T, Miki H, Hishikawa H, Matsushima H, Ishizaki M, Matsui K, Kaibori M, Nishizawa M, Okumura T¹, Kon M.



RESEARCH ARTICLE

Genipin Enhances Kaposi's Sarcoma-Associated Herpesvirus Genome Maintenance

Miyeon Cho¹, Seok Won Jung¹, Soomin Lee¹, Kuwon Son¹, Gyu Hwan Park¹, Jong-Wha Jung¹, Yu Su Shin², Taegun Seo², Hyosun Cho^{1*}, Hyojeung Kang^{1*}



Genipin
Genipa americana
Rubiaceae

Mater Sci Eng C Mater Biol Appl. 2016 Dec 1;69:967-76. doi: 10.1016/j.msec.2016.08.011. Epub 2016 Aug 5.

Novel genipin crosslinked atorvastatin loaded sericin nanoparticles for their enhanced antihyperlipidemic activity.

[Kanoujia J¹](#), [Singh M¹](#), [Singh P¹](#), [Saraf SA²](#).

Colloids Surf B Biointerfaces. 2016 Dec 1;148:607-614. doi: 10.1016/j.colsurfb.2016.09.031. Epub 2016 Sep 22.

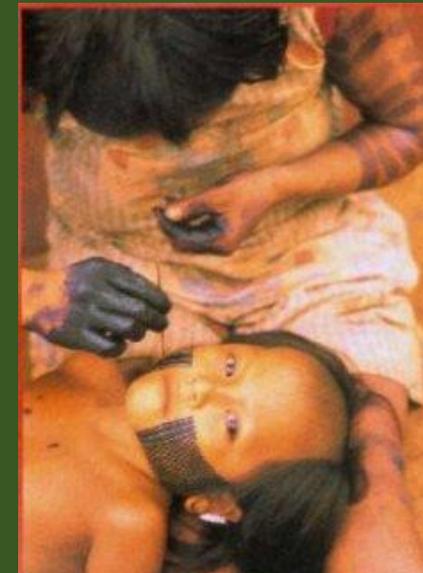
Biopolymeric hydrogels - nanostructured TiO₂ hybrid materials as potential injectable scaffolds for bone regeneration.

[Zazakowny K¹](#), [Lewandowska-Łańcucka J²](#), [Mastalska-Popławska J¹](#), [Kamiński K³](#), [Kusior A¹](#), [Radecka M¹](#), [Nowakowska M³](#).

[+ Author information](#)

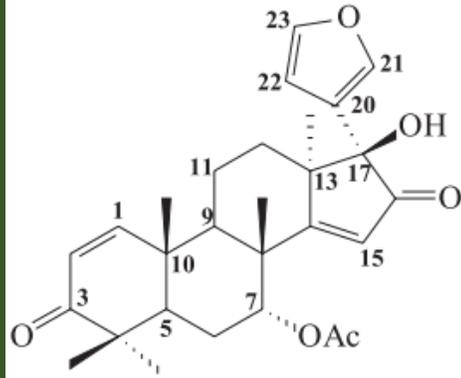
Abstract

The present work aims at development of novel hybrid materials from **genipin** crosslinked collagen or collagen/chitosan hydrogels containing various types of TiO₂ nanoparticles

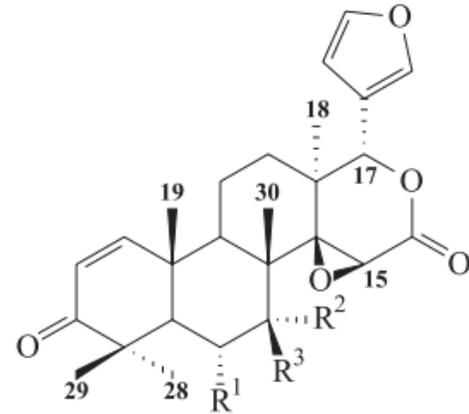




Andiroba
Carapa guianensis
 Meliaceae



1

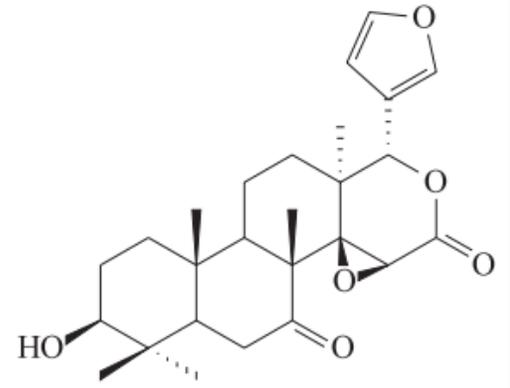


2: $R^1 = R^3 = H; R^2 = OAc$

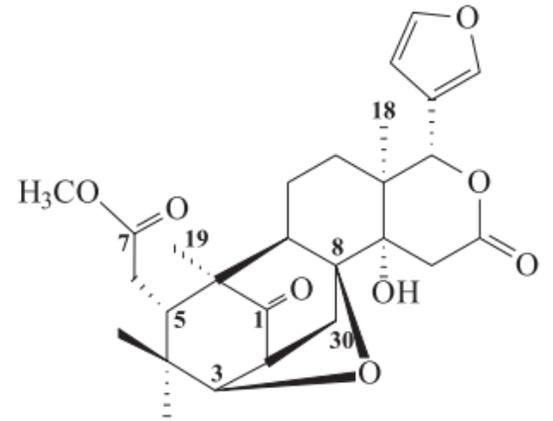
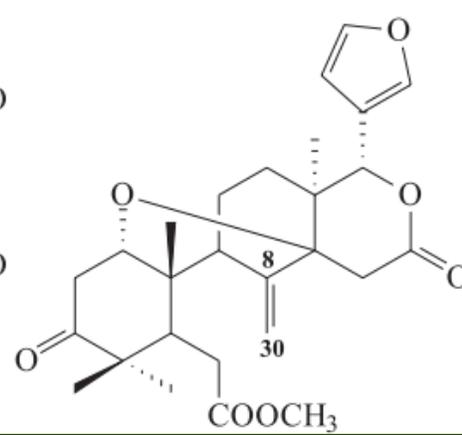
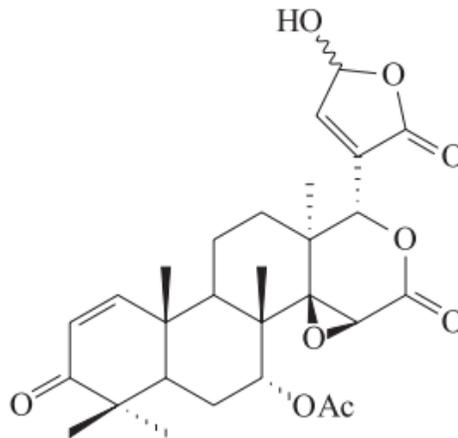
3: $R^1 = R^2 = OAc, R^3 = H$

4: $R^1 = H; R^2 = R^3 = O$

6: $R^1 = R^3 = H, R^2 = OH$



5





Andiroba
Carapa guianensis
Meliaceae

Curr Pharm Des. 2014;20(6):850-6.

The therapeutic properties of *Carapa guianensis*.

Henriques Md, Penido C¹.



Genetics and Molecular Biology, 39, 2, 248-256 (2016)
Copyright © 2016, Sociedade Brasileira de Genética. Printed in Brazil
DOI: <http://dx.doi.org/10.1590/1678-4685-GMB-2015-0098>

Research Article

The lipidome, genotoxicity, hematotoxicity and antioxidant properties of andiroba oil from the Brazilian Amazon

Susana Suely Rodrigues Milhomem-Paixão¹, Maria Luiza Fascineli², Mariana Matos Roll³, João Paulo Figueiró Longo², Ricardo Bentes Azevedo², Julio Cesar Pieczarka¹, Hugo Leonardo Crisóstomo Salgado⁴, Alberdan Silva Santos⁴ and Cesar Koppe Grisolia³

Malar J. 2014 Aug 13;13:317. doi: 10.1186/1475-2875-13-317.

In vitro and in vivo anti-malarial activity of limonoids isolated from the residual seed biomass from *Carapa guianensis* (andiroba) oil production.

Pereira TB, Rocha E Silva LF, Amorim RC, Melo MR, Zacardi de Souza RC, Eberlin MN, Lima ES, Vasconcellos MC, Pohlit AM¹.

J Ethnopharmacol. 2012 Aug 1;142(3):679-83. doi: 10.1016/j.jep.2012.05.037. Epub 2012 May 31.

Antiplasmodial activity of the andiroba (*Carapa guianensis* Aubl., Meliaceae) oil and its limonoid-rich fraction.

Miranda Júnior RN¹, Dolabela MF, da Silva MN, Póvoa MM, Maia JG.

Efeito da *Carapa guianensis* Aublet (Andiroba) e *Orbignya phalerata* (Babaçu) na cicatrização de colorrafias em ratos

Effect of Carapa guianensis Aublet (Andiroba) and Orbignya phalerata (Babassu) in colonic healing in rats

CICERO EVANDRO SOARES SILVA^{1,2}, ORLANDO JOSE DOS SANTOS², JURANDIR MARCONDES RIBAS-FILHO¹; FERNANDO ISSAMU TABUSHI¹; MARCIO HIROAKI KUME¹; LEANDRO BRESSIANINI JUKONIS¹; IGOR FURLAN CELLA¹

Rev. Col. Bras. Cir. 2015; 42(6): 399-406

Molecules 2014, 19(11), 17130-17140;
doi:10.3390/molecules191117130

Open Access Article

Carapanolides J–L from the Seeds of *Carapa guianensis* (Andiroba) and Their Effects on LPS-Activated NO Production

Yuuki Matsui¹, Takashi Kikuchi¹, Takanobu Inoue¹, Osamu Muraoka², Takeshi Yamada¹ and Reiko Tanaka^{1,*} 



Tetrahedron

Volume 71, Issue 18, 6 May 2015, Pages 2753–2760



Carapanolides M–S from seeds of andiroba (*Carapa guianensis*, Meliaceae) and triglyceride metabolism-promoting activity in high glucose-pretreated HepG2 cells

Takanobu Inoue^a, Yuuki Matsui^a, Takashi Kikuchi^a, Takeshi Yamada^a, Yasuko In^a, Osamu Muraoka^a, Chie Sakai^a, Kiyofumi Ninomiya^a, Toshio Morikawa^a, Reiko Tanaka^a  

Fitoterapia, 2014 Jul;96:56-64. doi: 10.1016/j.fitote.2014.04.006. Epub 2014 Apr 15.

Carapanolides C–I from the seeds of andiroba (*Carapa guianensis*, Meliaceae).

Inoue T¹, Matsui Y¹, Kikuchi T¹, In Y¹, Muraoka O², Yamada T¹, Tanaka R³.

Molecules 2015, 20(11), 20955-20966; doi:10.3390/molecules201119737

Open Access

Article

Carapanolides T–X from *Carapa guianensis* (Andiroba) Seeds

Tepei Miyake¹, Sari Ishimoto¹, Naoko Ishimatsu¹, Keiichiro Higuchi¹, Katsuhiko Minoura¹, Takashi Kikuchi¹, Takeshi Yamada¹, Osamu Muraoka² and Reiko Tanaka^{1,*}

Fitoterapia, 2013 Oct;90:20-9. doi: 10.1016/j.fitote.2013.07.001. Epub 2013 Jul 10.

Andirolides Q–V from the flower of andiroba (*Carapa guianensis*, Meliaceae).

Sakamoto A¹, Tanaka Y, Inoue T, Kikuchi T, Kajimoto T, Muraoka O, Yamada T, Tanaka R.



Fitoterapia

Volume 100, January 2015, Pages 81–87



Andirolides W–Y from the flower oil of andiroba (*Carapa guianensis*, Meliaceae)

Asami Sakamoto^a, Yuji Tanaka^a, Takeshi Yamada^a, Takashi Kikuchi^a, Osamu Muraoka^b, Kiyofumi Ninomiya^c, Toshio Morikawa^c  , Reiko Tanaka^a  

Int. J. Mol. Sci. 2016, 17(4), 591; doi:10.3390/ijms17040591

Open Access

Article

Hepatoprotective Limonoids from Andiroba (*Carapa guianensis*)

Kiyofumi Ninomiya^{1,2}, Seiya Miyazawa¹, Kaiten Ozeki¹, Natsuko Matsuo¹, Osamu Muraoka^{1,2,3}, Takashi Kikuchi⁴, Takeshi Yamada⁴, Reiko Tanaka^{4,*} and Toshio Morikawa^{1,2,*}

Andiroba
Carapa guianensis
Meliaceae



Caça

O Curare

“...Os curares constituem talvez o exemplo mais perfeito da argúcia, do engenho, da perspicácia do índio sul-americano.

Em quase todos os recônditos do grande vale, descobriu ele aquelas plantas que embora botanicamente diversas, podiam fornecer-lhe o veneno, inócuo por via oral, do qual uma gota, injetada, permitia prostrar a caça em fração de segundos”.

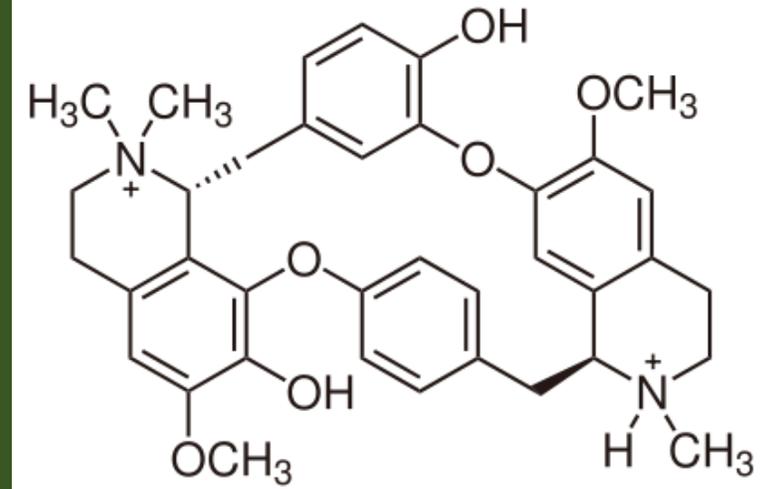
Gottlieb, O.R e Mors, W.B. Interciência, 252, 1978.



Caça

O Curare

- Mais de 70 espécies são utilizadas para a produção do curare nos gêneros:
 - *Strychnos*
 - *Chondodendrom*



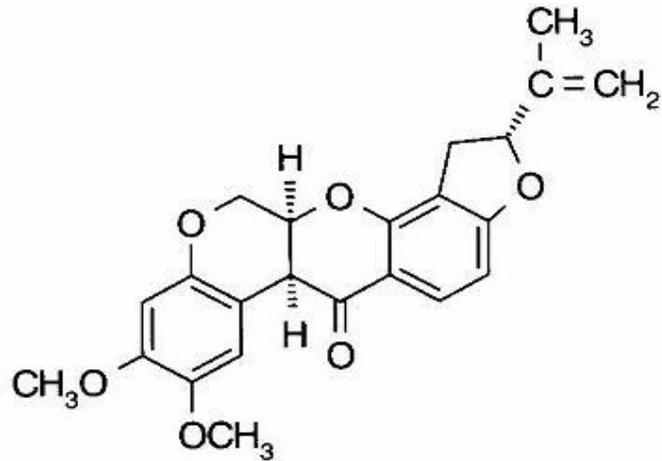
Tubocurarina

Pesca

O Timbó

- Princípios ativos encontrados nas cascas das raízes de Leguminosas dos gêneros:

- *Derris*
- *Lonchocarpus*



Rotenonas: Deguelina, tefrosina

2ª Questão:

- Como aumentar a qualidade dos bioprodutos Amazônicos?

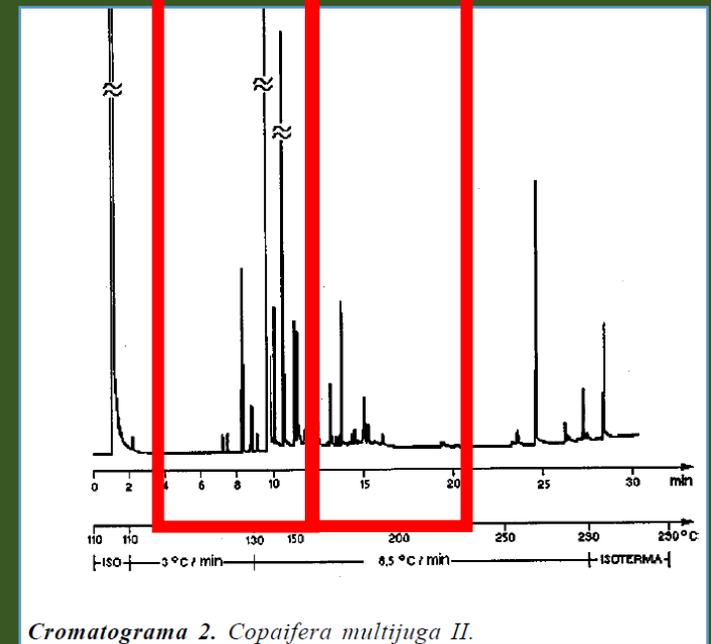
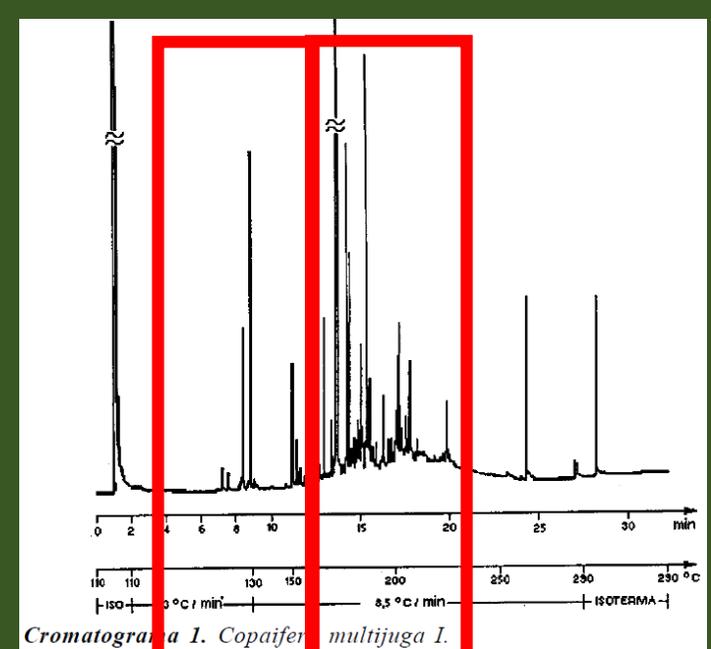
- DOC
- Valorizar diferenças regionais

Óleos de copaíba apresentam grande variação em sua composição química

Sesquiterpenos não oxigenados

Sesquiterpenos oxigenados

Commodities *versus* DOC



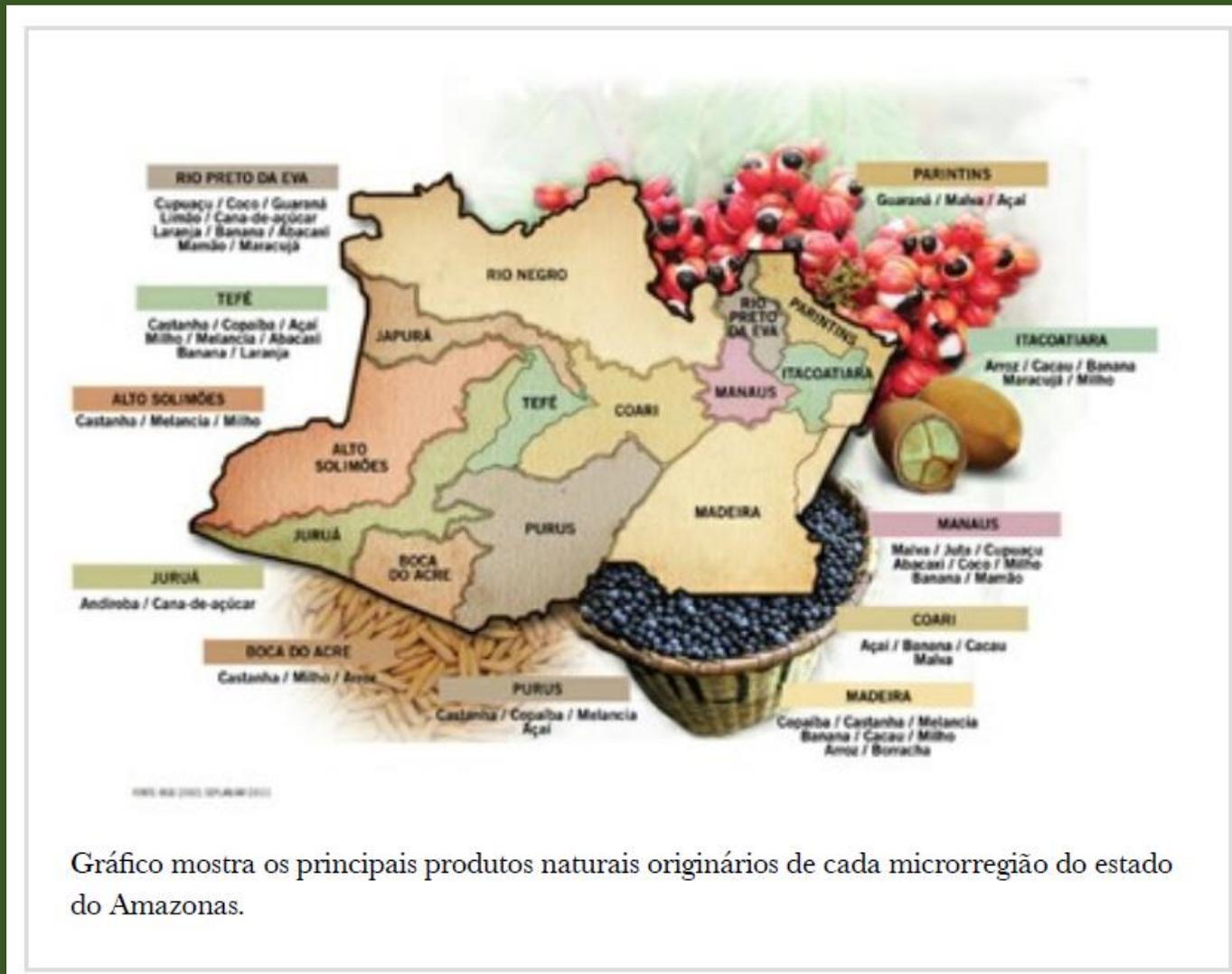
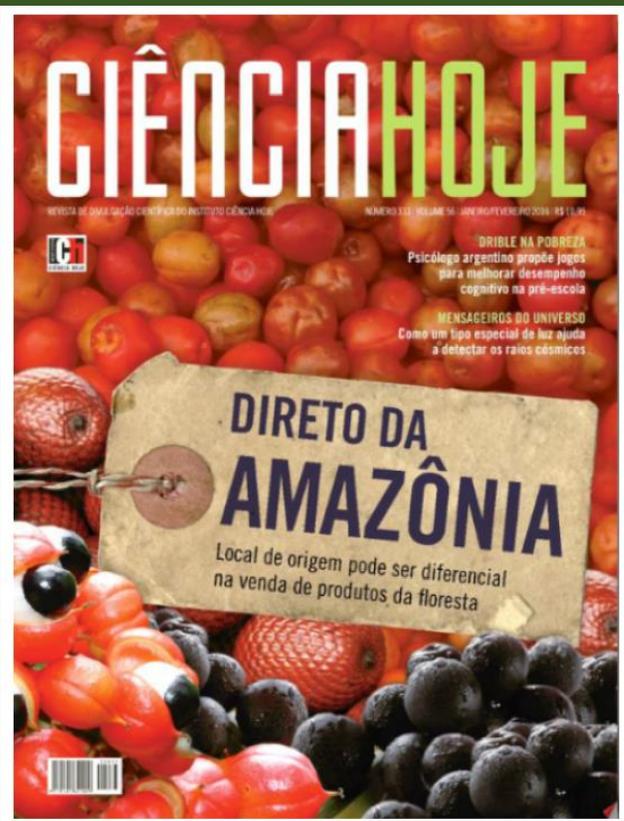


Gráfico mostra os principais produtos naturais originários de cada microrregião do estado do Amazonas.

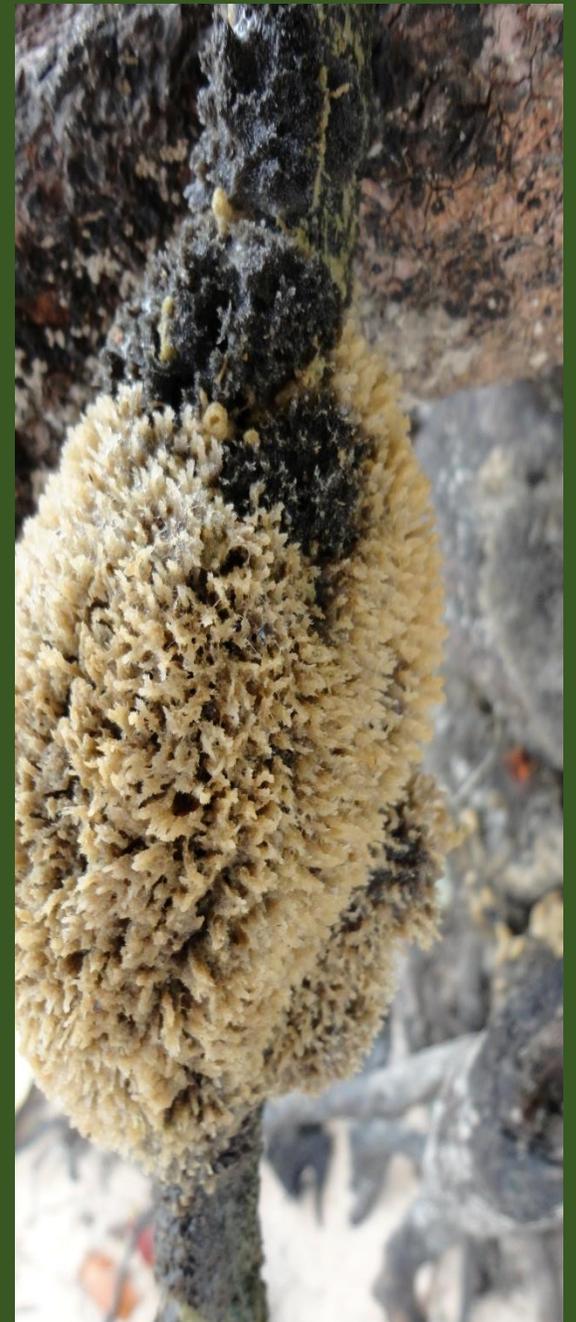
Commodities *versus* DOC

3ª Questão:

- Como conhecer e valorizar a biodiversidade ainda desconhecida?

- Animais**
- Microorganismos**
- Aproveitamentos transdisciplinares**

Esponjas de água-doce: Cauixí





Elemental Composition of *Drulia browni* Collected in Negro River (Amazonas, Brazil)

Iuri Bezerra de Barros^{1,3}, Cecília Volkmer-Ribeiro⁴, Cláudia Cândida Silva^{1*} and Valdir Florêncio da Veiga Junior³

¹Grupo Crowfoot de Métodos de Raios-X, Escola Superior de Tecnologia, Universidade do Estado do Amazonas, Av. Darcy Vargas 1200, 69065-020 Manaus – AM, Brazil

²Instituto Politécnico do Rio de Janeiro, Universidade do Estado do Rio de Janeiro, R. Bonfim, 25, CEP 28625-570 Nova Friburgo – RJ, Brazil

³Departamento de Química, Instituto de Ciências Exatas, Universidade Federal do Amazonas, Av. Rodrigo Octávio, 6200, CEP 69077-000 Manaus – AM, Brazil

⁴Museu de Ciências Naturais, Fundação Zoobotânica do Rio Grande do Sul, Cx.P. 1188, 900001-970 Porto Alegre – RS, Brazil

OCORRÊNCIA DE ESPONJAS DE ÁGUA DOCE (PORIFERA, DEMOSPONGIAE) NA BAÍA DO MALHEIROS, PANTANAL MATO-GROSSENSE

Occurrence of freshwater sponges (Porifera, demospongiae) in the Bay of Malheiros, Pantanal Mato-Grossense

MAROSTEGA, T. N.

MORINI, A. A. E. T.

RODRIGUES, F. A. C.

ARAÚJO, L. M.

BARROS, I. B.

DA VEIGA J. V. F.



Extraction of High Purity Silica from Amazonian Sponges

Iuri Bezerra de Barros^{1,2}, Cecília Volkmer-Ribeiro², Valdir Florêncio da Veiga Junior² and Cláudia Cândida Silva^{3,4*}

Elemental composition of freshwater sponges *Drulia uruguayensis* and *Drulia cristata* collected in the Tapajós River

Iuri Bezerra de Barros,^a Emily Silva Gomes dos Santos,^b
Desirée Emelly Dantas Gomes,^b Cecília Volkmer-Ribeiro,^c
Cláudia Cândida Silva^{b*} and Valdir Florêncio da Veiga Junior^a



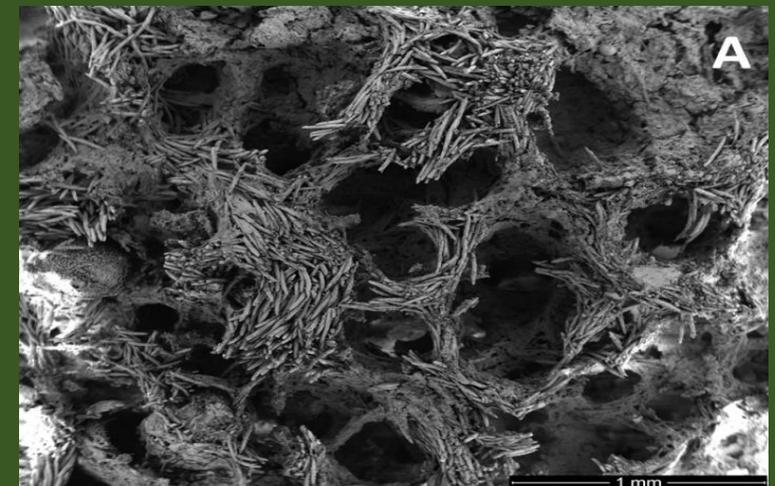
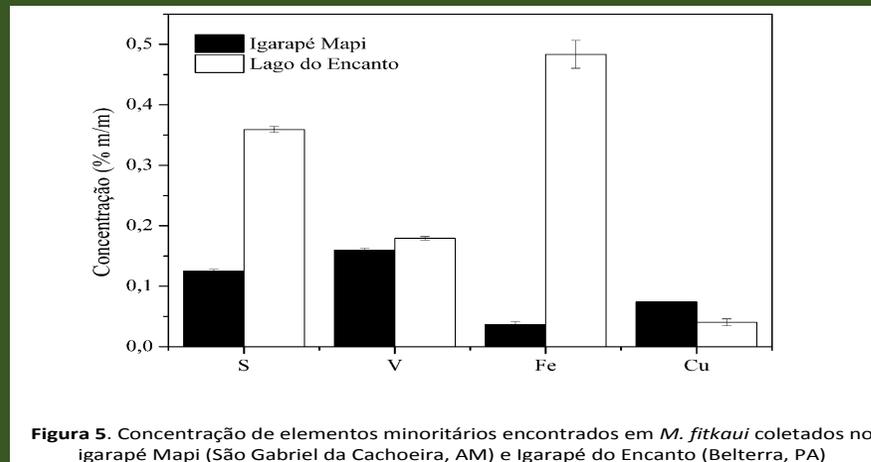
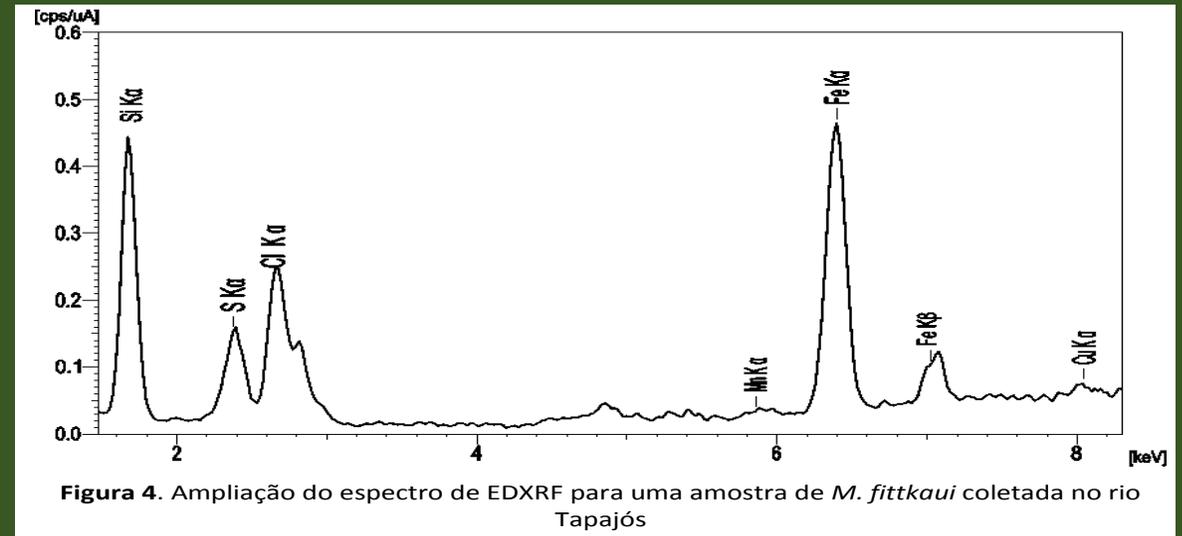
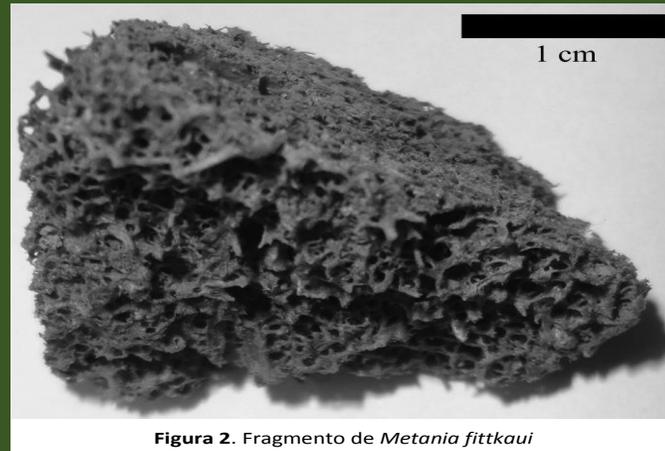
Composição Elementar da Esponja Dulcícola *Metania fittkaui* Volkmer-Ribeiro

de Barros, I. B.; Volkmer-Ribeiro, C.; Silva, C. C.; Veiga Junior, V. F.*

Rev. Virtual Quim., 2014, 6 (5), 1380-1390. Data de publicação na Web: 25 de julho de 2014

<http://www.uff.br/rvq>

Composição inorgânica e usos de esponjas dulcícolas





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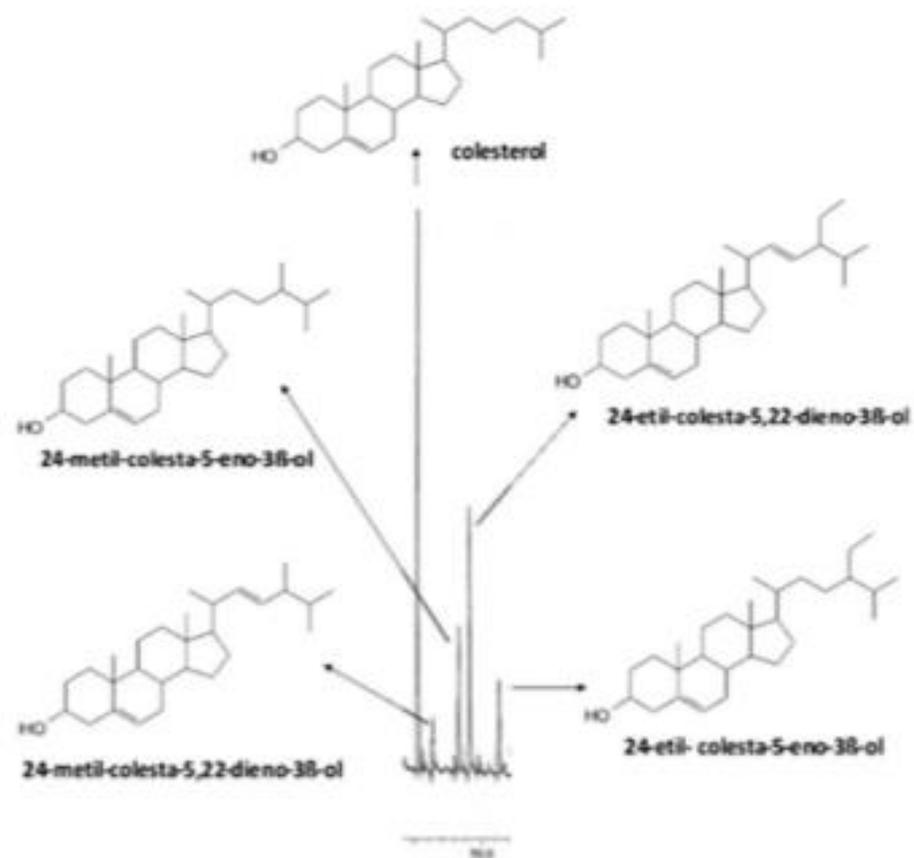
Sterols from sponges of Anavilhanas

Iuri Bezerra de Barros^a, Cecília Volkmer-Ribeiro^b,
Valdir Florêncio da Veiga Junior^{a,*}<http://dx.doi.org/10.5935/0100-4042.20150134>

Quim. Nova, Vol. 38, No. 9, 1192-1195, 2015

ESTERÓIS E CONSTITUINTES VOLÁTEIS DA ESPONJA DULCÍCOLA *Trochospongilla paulula* (BOWERBANK)Iuri B. de Barros^{a,b}, Cecília Volkmer Ribeiro^c e Valdir F. da Veiga Junior^{b,*}Tabela 1. Composição da fração volátil de *Trochospongilla paulula*.

| Substância | Índice de retenção | | Percentual (%) |
|----------------------|--------------------|-------------------------|----------------|
| | experimental | literatura ⁷ | |
| Tetradecanol | 1675 | 1671 | 6,28 |
| Pentadecanal | 1712 | | 1,30 |
| Pentadecanol | 1775 | | 14,22 |
| Hexadecanal | 1813 | 1819 | 2,15 |
| Ácido pentadecanóico | 1865 | | 5,02 |
| Hexadecanol | 1879 | 1874 | 31,15 |
| Ácido hexadecanóico | 1960 | 1959 | 9,30 |

Figura 1. Perfil cromatográfico dos esteróis da esponja *Trochospongilla paulula*

SÍNTESE DO MATERIAL MESOPOROSO MCM-41 USANDO ESPONJA DE ÁGUA-DOCE COMO FONTE DE SÍLICA

Orivaldo da Silva Lacerda Júnior, Rodrigo Marinho Cavalcanti, Thaisa Moreira de Matos, Jocilândia de Brito Venâncio, Iuri Bezerra de Barros, Valdir Florêncio da Veiga-Júnior e Ivoneide de Carvalho Lopes Barros*

Departamento de Química, Instituto de Ciências Exatas, Universidade Federal do Amazonas, Avenida General Rodrigo Octávio, Coroado, 6200, 69077-000 Manaus – AM, Brasil

Recebido em 14/3/13; aceito em 11/7/13; publicado na web em 9/8/13

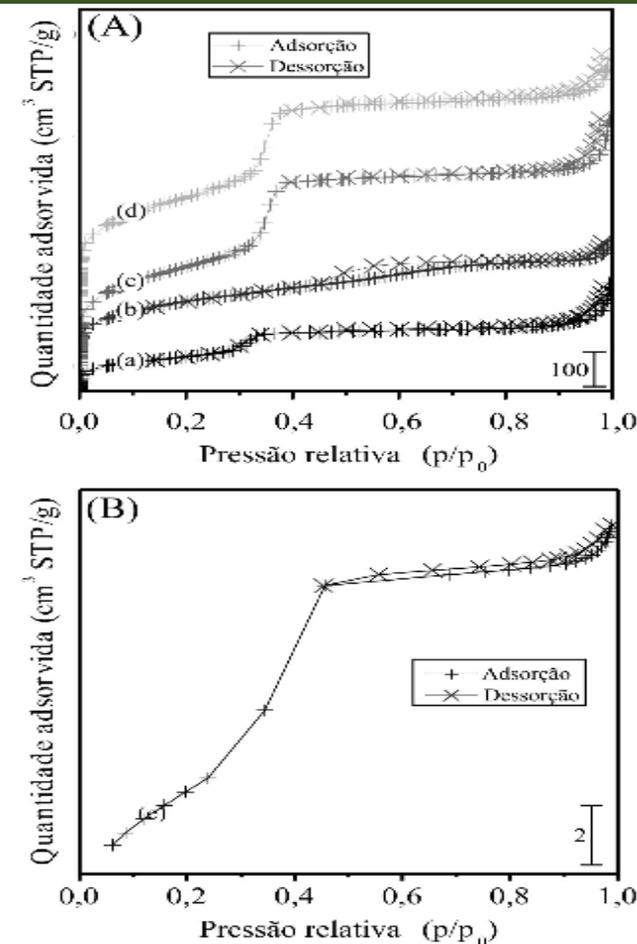
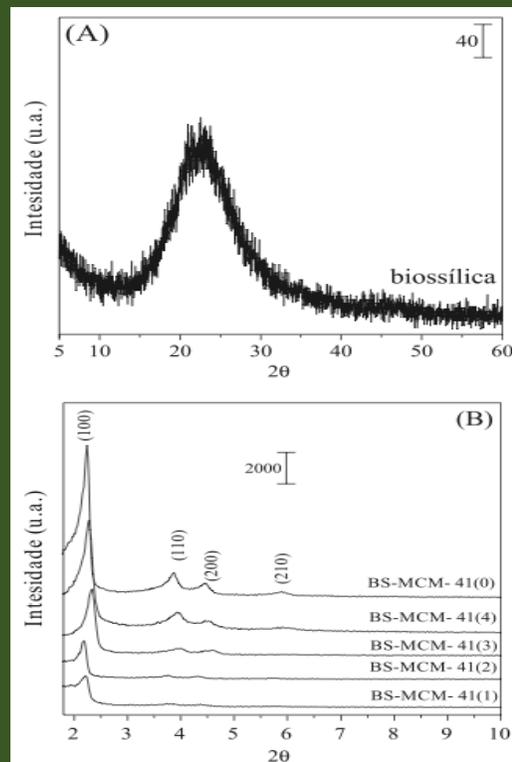


Figura 5. Isothermas de adsorção-dessorção de N₂ das amostras: (

Uso da sílica como suporte de catalizadores

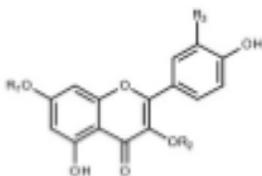


Kambô



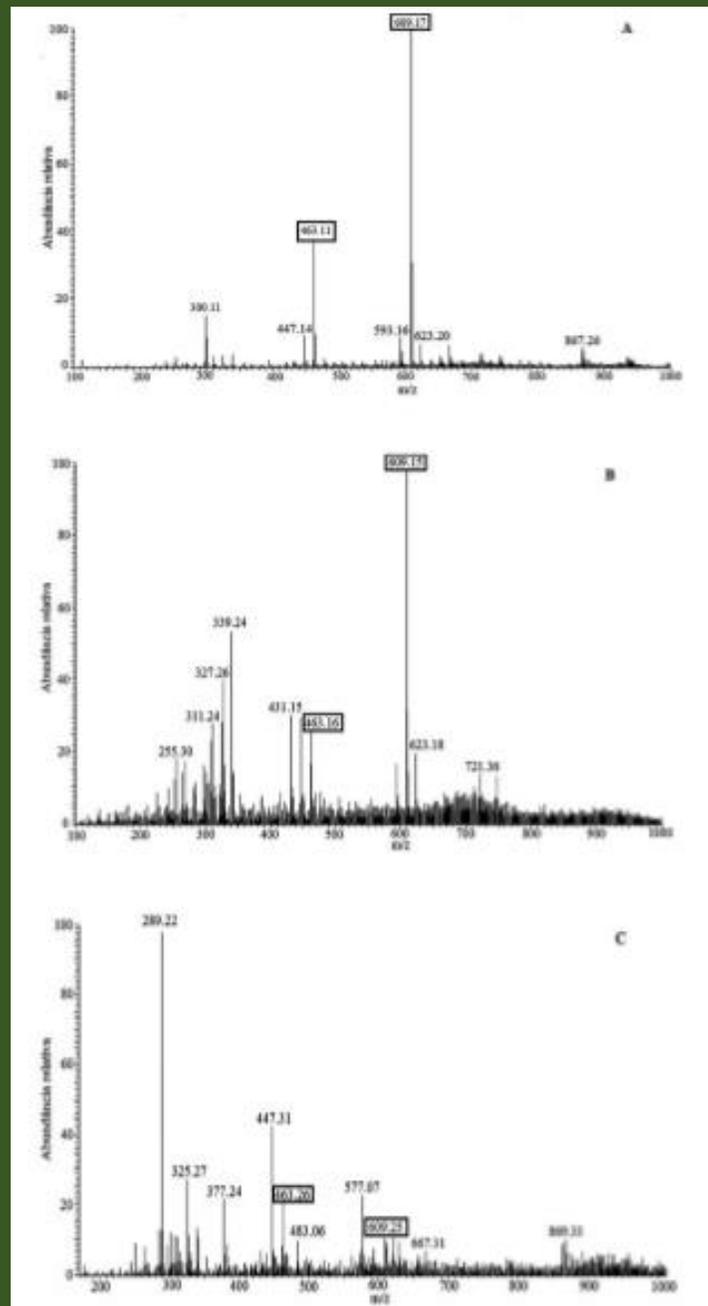
PERFIL DE FLAVONOIDES E AVALIAÇÃO DO POTENCIAL ANTIOXIDANTE E CITOTÓXICO DE *Bauhinia purpurea* (Fabaceae) DA REGIÃO AMAZÔNICA

Priscila Moraes dos Santos^a, Patrícia Danielle Oliveira de Almeida^b, Emerson Silva Lima^b, Manoel Odorico de Moraes^c, Patrícia Marçal da Costa^c, Assuero Silva Meira^c, Cláudia do Ó Pessoa^c, Ligia Maria Marino Valente^d e Valdir Florêncio da Veiga Junior^{a,*}



- 1 - R₁=R₂= α-Ramnose, R₃ = H
- 2 - R₁ = H, R₂= β-Glicose, R₃ = OH
- 3 - R₁ = H, R₂= α-Ramosil(1→6)β-Glicose, R₃ = OH

Figura 1. Estrutura dos flavonoides glicosilados presentes em espécies de *Bauhinia* usados como substâncias de referência: (1) kaempferitrin; (2) isoquercitrina; (3) rutina



The inhibitory action of *Bauhinia purpurea* extracts on the corrosion of carbon steel in sulfuric acid medium

Iuri Bezerra de Barros^a, Marco André Abud Kappel^a, Priscila Moraes dos Santos^b,
Valdir Florêncio da Veiga Junior^b, Eliane D'Elia^a, Ivan Napoleão Bastos^{a*}

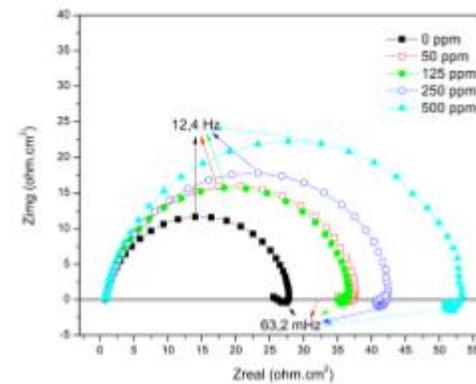
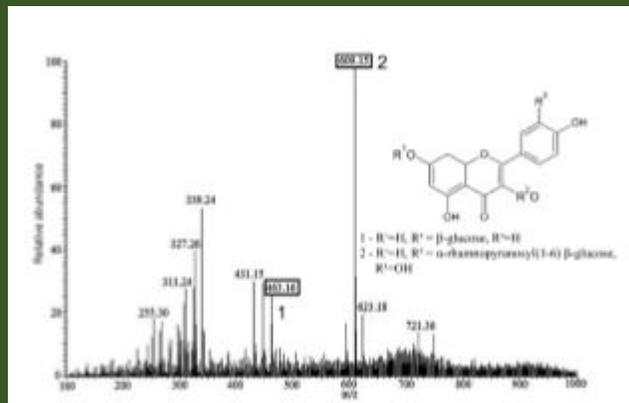


Figure 4: Nyquist plots obtained at the OCP for C-steel in 1.0 mol·L⁻¹ H₂SO₄ with and without of methanolic *Bauhinia purpurea* extract at the following concentrations: 50, 125, 250 and 500 mg·L⁻¹ at 25 °C.

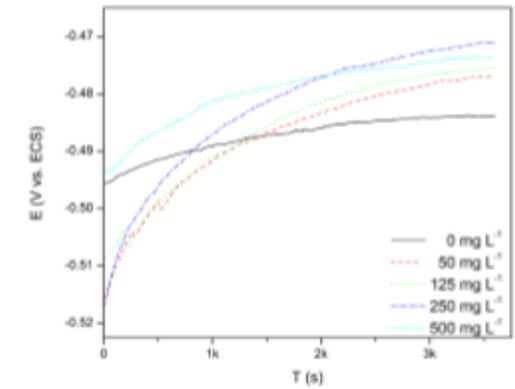


Figure 2: Open circuit potential (OCP) of C-steel in 1.0 mol·L⁻¹ H₂SO₄ with and without methanolic *Bauhinia purpurea* extract at the following concentrations: 50, 125, 250 and 500 mg·L⁻¹ at 25 °C.

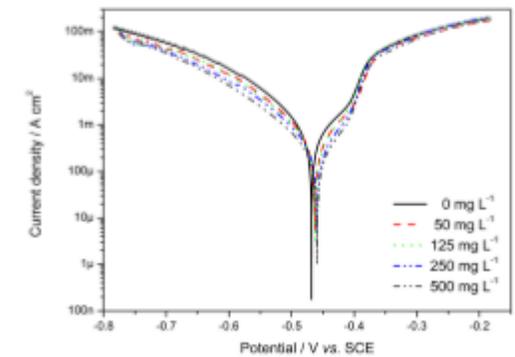


Figure 3: Polarization curve of C-steel in 1.0 mol·L⁻¹ H₂SO₄ with and without methanolic *Bauhinia purpurea* extract at the following concentrations: 50, 125, 250 and 500 mg·L⁻¹ at 25 °C.

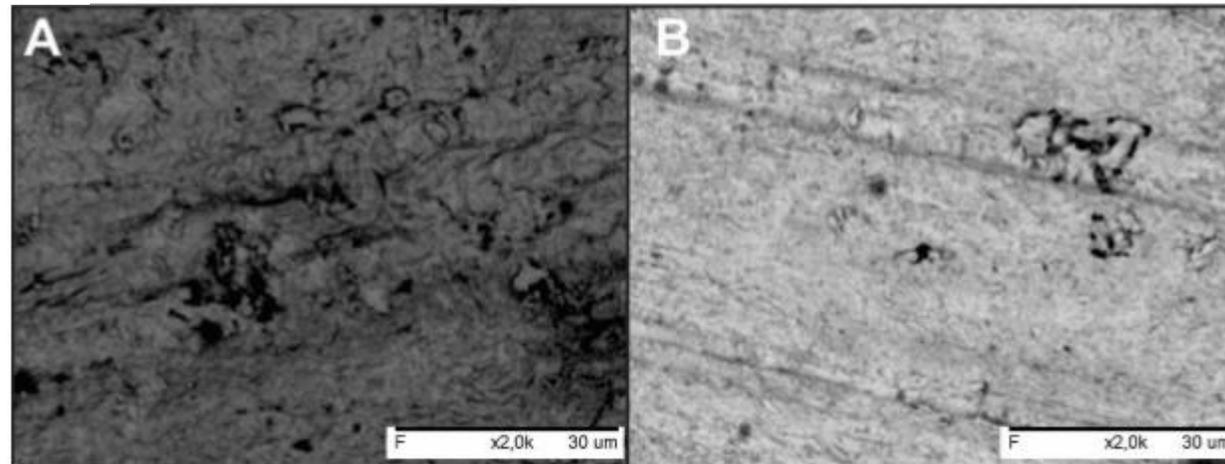
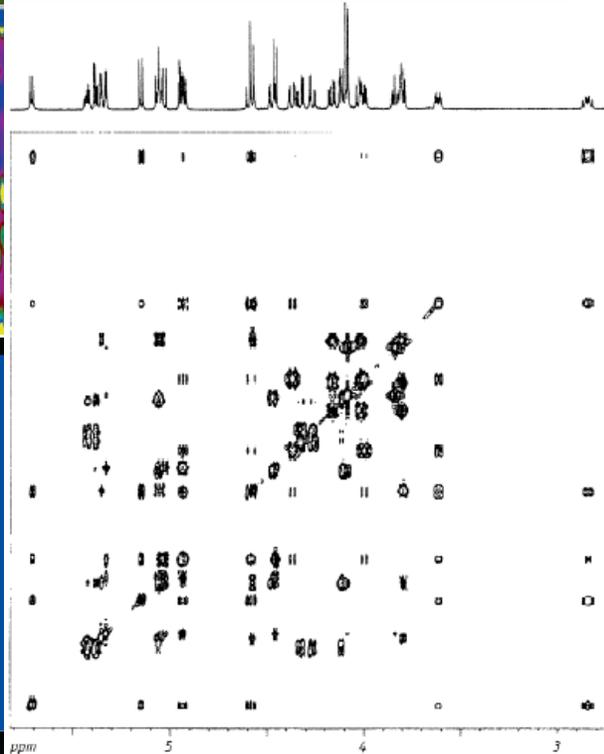
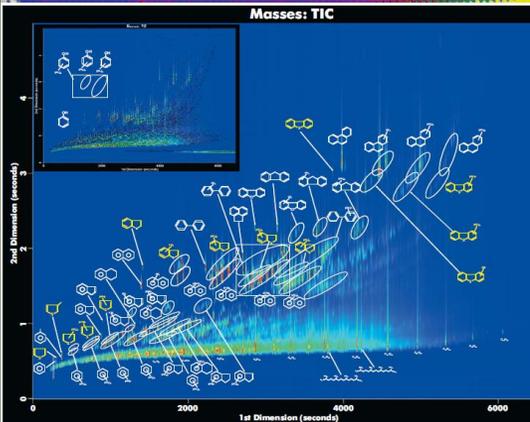
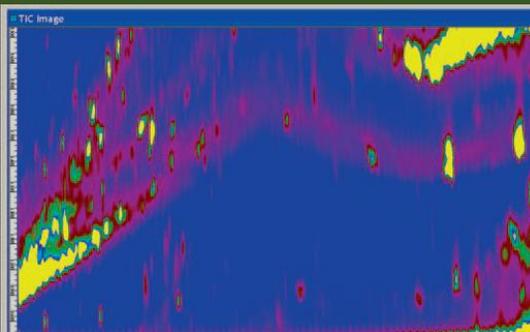
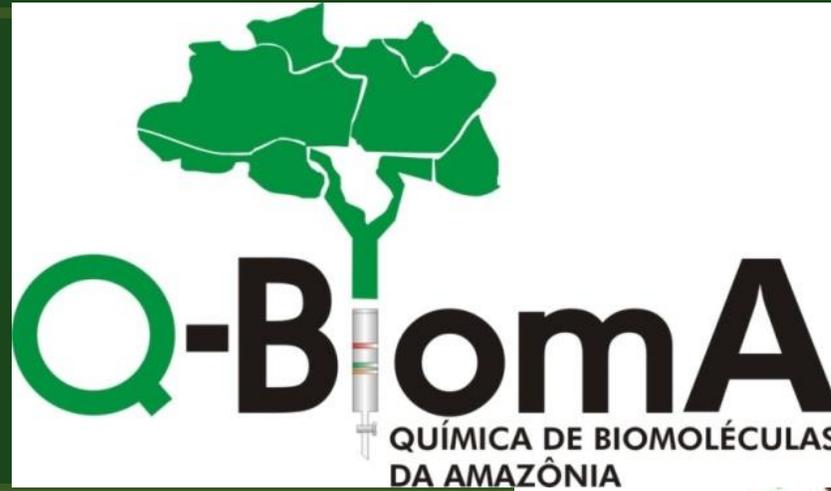


Figure 7: SEM micrograph (2000x) of C-steel immersed in 1.0 mol·L⁻¹ H₂SO₄ in the absence (A) and presence of 250 mg·L⁻¹ of methanolic *Bauhinia purpurea* extract (B).

O trabalho do fitoquímico

- Tecnologia
- Criatividade
- Estatística
- Aumento de Escala



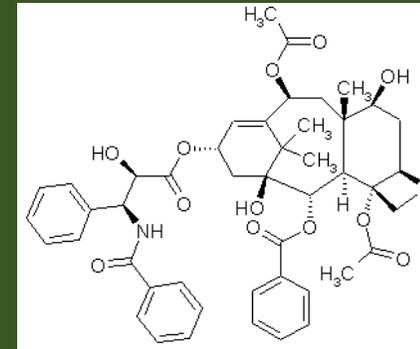
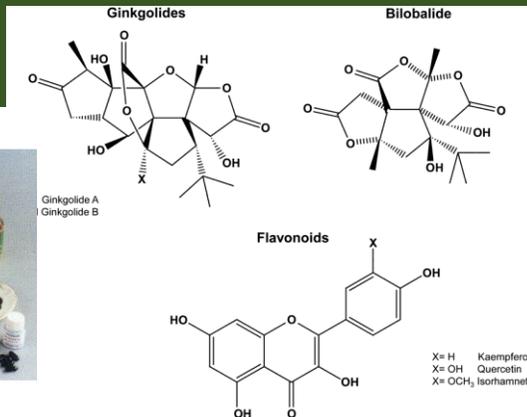
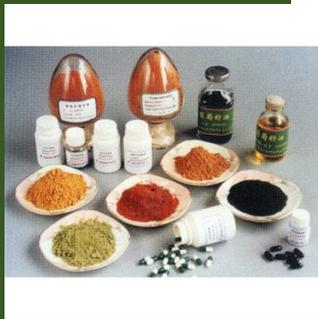
4ª Questão: Qual o trabalho do fitoquímico no século XXI?



Analisar em mistura ou isolar?



Sinergismo ou pureza?



Permanecem os paradigmas do século XX ?

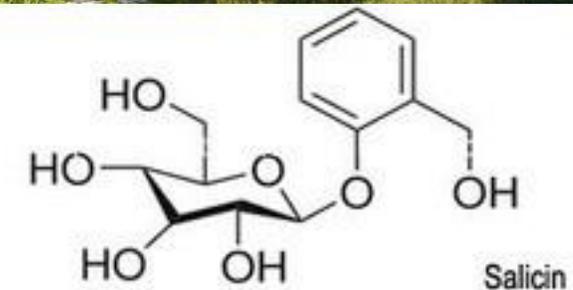
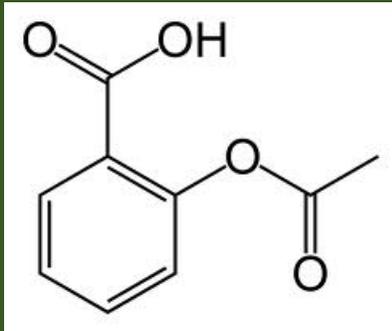
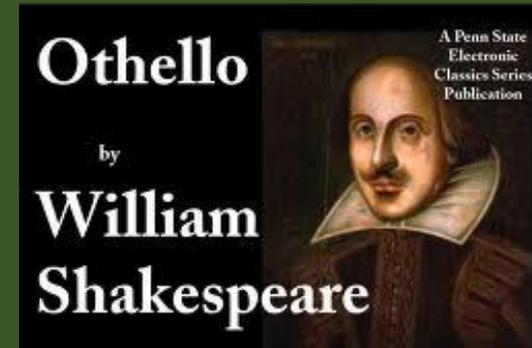


Isolar ainda é necessário ?



Substâncias purificadas de produtos naturais

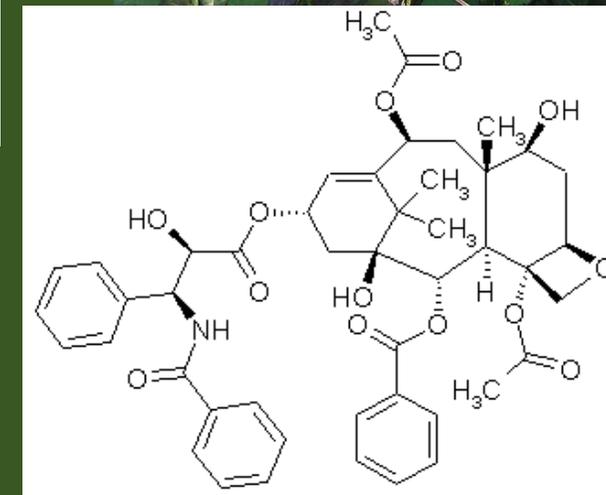
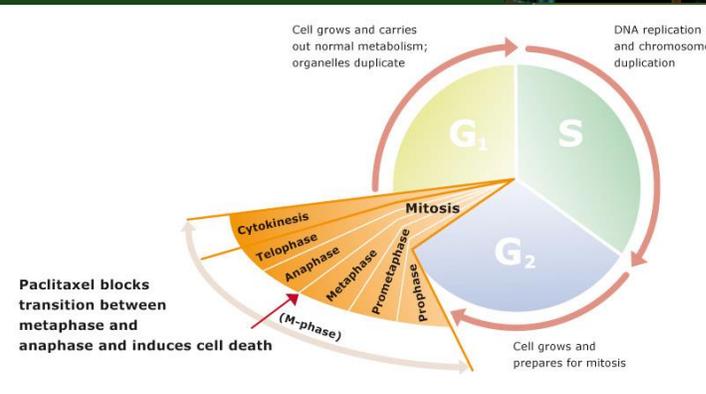
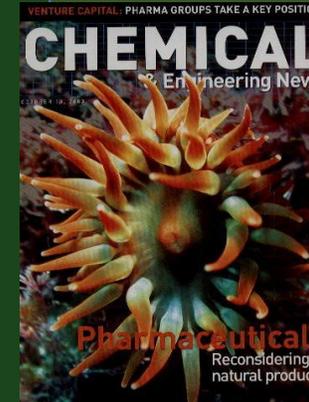
“...A suspirar cantava a coitadinha à sombra do salgueiro.
Canto de dor coração lhe vinha: Oh salgueiro! salgueiro!
Triste, ouvia-a o regato todo o dia: Oh salgueiro!
salgueiro! O pranto a pedra dura amolecia...”,
Desdêmona cantava apaixonada.



Taxol

- Primeira coleta em 1962 (*Taxus brevifolia*)
- Isolamento publicado em 1971
- Ensaios clínicos: 1983
- Comercializado em 1994 (Paclitaxel)
- *Taxus baccata*

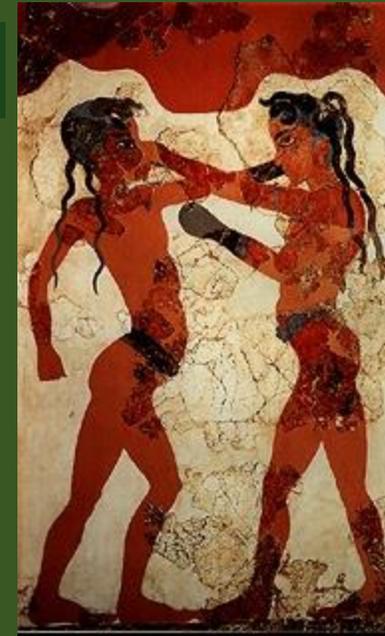
Substâncias purificadas de produtos naturais



Efeito sinérgico de produtos naturais

Linimento Negro dos Vencedores Olímpicos

- Nos Jogos Olímpicos da Antiguidade, os vencedores recebiam remédios especiais para curar suas feridas e aliviar suas dores:
- O linimento utilizava Mirra, Frankincense, Acácia e Ópio



Reduz o inchaço e alivia a dor de forma 25% mais efetiva que os modernos emplastos utilizados para este fim.

Efeito sinérgico de produtos naturais

Cinco ervas mais utilizadas na medicina nos EUA

- **Echinaceae**
- Alho
- **Ginkgo biloba**
- Saw Palmetto
- **Ginseng**

São comercializadas como extratos, ação pelo efeito sinérgico da combinação de seus constituintes



GINKGO BILOBA
EFICIENTE CONTRA A PERDA DE MEMÓRIA

Efeito sinérgico de produtos naturais

Dores de cabeça, enxaquecas, vertigens, zumbidos, insuficiência circulatória periférica.

Mal de Alzheimer

Demências e doenças degenerativas

EGb761

Ginkgo-flavonaglicosídeos (24%) e terpenoides (6%)

4-6% de Lactonas terpênicas

2,8–3,4% ginkgolídeos A, B e C

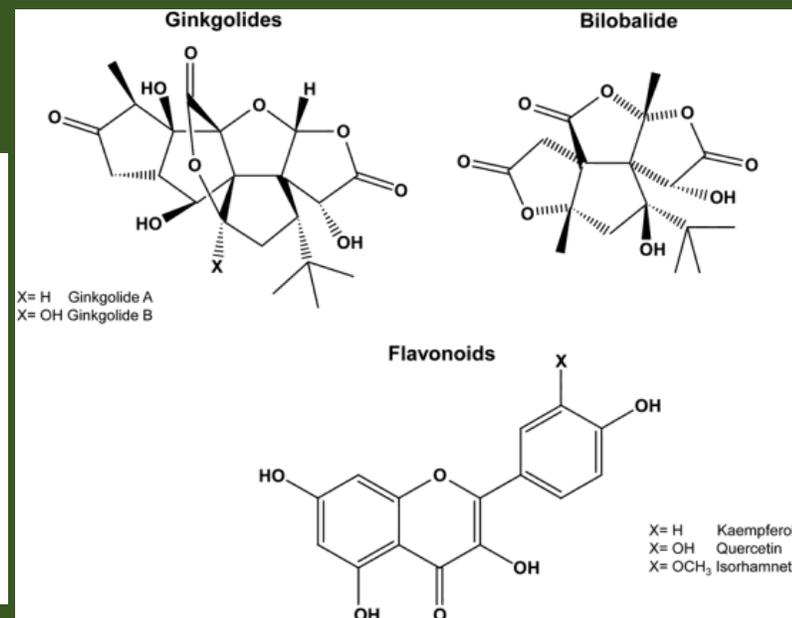
2,6–3,2% bilobalídeos

24,40% de glicosídeos flavonoídicos

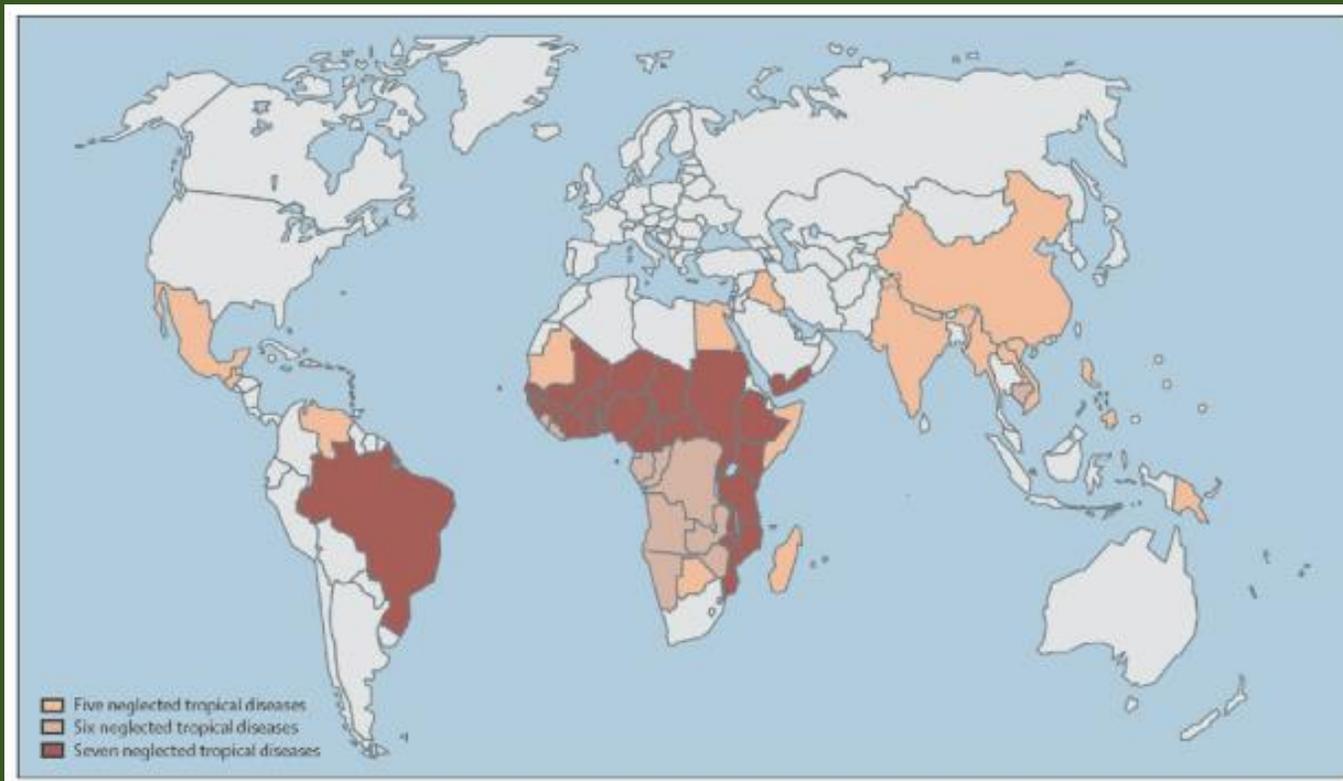
10,85% quercetina glicosilada

11,80% kaempferol glicosilado

1,75% isorhamnetina glicosilada



Necessidade de Estudos de Fármacos para Doenças Negligenciadas

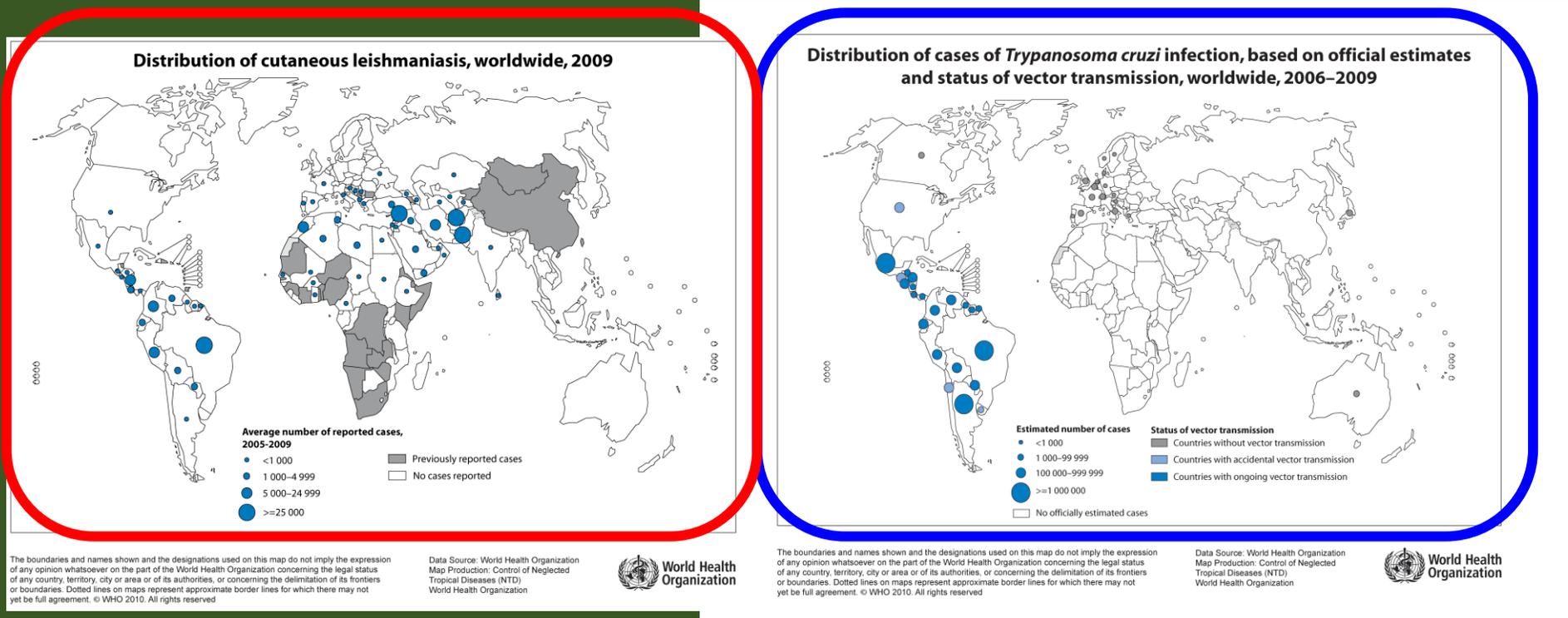


Elevada Incidência

Presença das nove principais doenças negligenciadas na Amazônia

Fig. 2 - Map of Brazil showing the geographic overlap and distribution of the main neglected tropical diseases (A) according to the health surveillance service (Ministry of Health) and the distribution of human development index (B) according to the Brazilian Institute of Geography and Statistics (IBGE).

Necessidade de Estudos de Fármacos para Doenças Negligenciadas



Distribution of Neglected Tropical Diseases according to categories. (Based on panel from the TDR/World Health Organization)

Category 1.
Emerging and uncontrolled disease

Leishmaniasis
African trypanosomiasis
Dengue fever

Category 2.
Control strategy available
Disease burden persists

Malaria
Schistosomiasis
Tuberculosis

Category 3.
Control strategy effective
Disease burden falling
Elimination planned

Chagas' Disease
Leprosy
Lymphatic filariasis
Onchocerciasis

NPR

Cite this: *Nat. Prod. Rep.*, 2011, **28**, 809

www.rsc.org/npr

REVIEW

Natural products and Chagas' disease: a review of plant compounds studied for activity against *Trypanosoma cruzi*

Erika Izumi,^a Tânia Ueda-Nakamura,^b Benedito Prado Dias Filho,^{ab} Valdir Florêncio Veiga Júnior^c and Celso Vataru Nakamura^{*ab}

Received 31st May 2010

DOI: 10.1039/c0np00069h

Covering: 1995 to 2010



Erika Izumi

Erika Izumi obtained her BSc degree in Biological Sciences in 2004 from the Universidade Estadual de Londrina, Brazil. Currently she is a microbiology PhD student under the supervision of Professor Nakamura at the same university, where she is studying the biological activity of medicinal plants from the Amazon rainforest against protozoan parasites. Her research interests are natural products and their application to neglected diseases.



Tânia Ueda-Nakamura

Tânia Ueda-Nakamura obtained her BSc degree in Pharmacy and Biochemistry in 1980 from the Universidade Estadual de Maringá, Brazil. In 2001 she received her PhD degree in Biophysics from the Universidade Federal do Rio de Janeiro, and currently she is an Associate Professor of the Universidade Estadual de Maringá. Her research interests are antiviral and antiprotozoal activities of natural products.



Benedito Prado Dias Filho

Benedito Prado Dias Filho received his BSc degree in Pharmacy and Biochemistry in 1973 from the Universidade Estadual de Ponta Grossa, Brazil, and in 1992 he obtained his PhD degree in Microbiology from the Universidade Federal do Rio de Janeiro. Currently he is a Full Professor of the Universidade Estadual de Maringá and Pro-rector of the Postgraduate Program and Research. His main interests are nanotechnology and antimicrobial activity of natural products, focusing on dermatophytes.



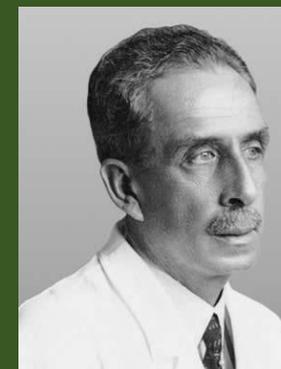
Valdir Florêncio Veiga Júnior

Valdir Florêncio Veiga Júnior obtained his BSc degree in Chemical Engineering in 1995 and the PhD degree in Chemistry in 2004 from the Universidade Federal do Rio de Janeiro, Brazil. Currently he is an Associate Professor of the Universidade Federal do Amazonas. His research interests are the chemistry of natural products, focusing on medicinal plants of the families Fabaceae, Burseraceae, and Lauraceae.

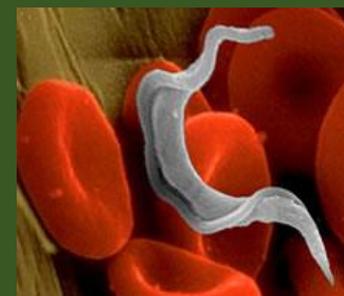


Celso Vataru Nakamura

Celso Vataru Nakamura graduated in Pharmacy and Biochemistry at the Universidade Estadual de Maringá, Brazil, in 1979. He obtained his PhD degree in Microbiology at the Universidade Federal do Rio de Janeiro in 1992, and he undertook postdoctoral research on Biophysics, working with ultrastructural analysis of cellular organelles from parasitic protozoa. Currently he is an Associate Professor at the Universidade Estadual de Maringá, and his research interests are the development of new drugs from natural sources, focusing on antimicrobial, antiprotozoal, and melanogenic activities.



Adult *Rhodnius prolixus*, a kissing bug. WHO/TDR/Stammers



Terpenes from *Copaifera* Demonstrated in Vitro Antiparasitic and Synergic Activity

Erika Izumi,[†] Tânia Ueda-Nakamura,[‡] Valdir F. Veiga, Jr.,[§] Angelo C. Pinto,^{||}
and Celso Vataru Nakamura^{*,†,‡}

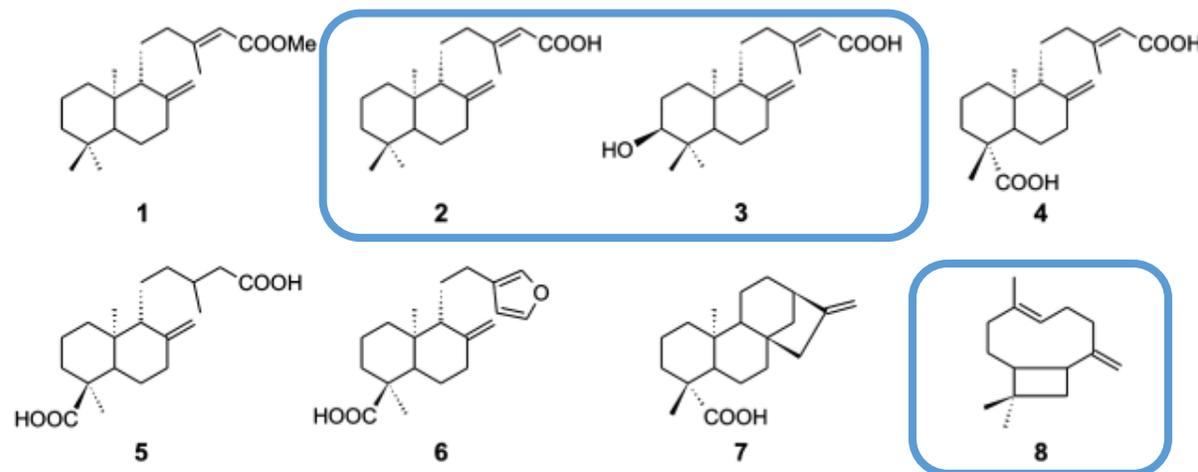


Figure 1. Terpenes evaluated for antitrypanosomal activity. Methyl copalate (1), copalic acid (2), 3 β -hydroxycopalic acid (3), agathic acid (4), pinifolic acid (5), polyaltic acid (6), kaurenoic acid (7), and β -caryophyllene (8).

Table 1. Inhibition of *T. cruzi* Life Stages and Cytotoxicity on Mammalian Cells^a

| compd | epimastigotes | trypomastigotes | amastigotes | LLCMK ₂ | erythrocytes | SI |
|-------|------------------------|------------------------|------------------------|------------------------|-----------------------|--|
| | IC ₅₀ /96 h | EC ₅₀ /24 h | IC ₅₀ /96 h | CC ₅₀ /96 h | HC ₅₀ /3 h | CC ₅₀ /IC ₅₀ ama |
| 1 | 83.3 ± 2.2 | 377.3 ± 88 | 2.5 ± 0.06 | 69.1 ± 4.4 | 1597 ± 9.4 | 27.6 |
| 2 | 42.7 ± 6.5 | 444 ± 161.1 | 1.3 ± 0.06 | 39.4 ± 4.6 | 65.7 ± 0.2 | 30.3 |
| 3 | 41.2 ± 0.9 | 453.1 ± 109.3 | 1.8 ± 0.06 | 31.2 ± 6.5 | 125 ± 7.5 | 17.3 |
| 4 | 86.8 ± 14.9 | 823.3 ± 104.7 | 14.9 ± 2.9 | 56.8 ± 6.2 | 1047 ± 10.4 | 3.8 |
| 5 | 854 ± 108.6 | 1630 ± 108.6 | 18.6 ± 3.1 | 251.5 ± 13 | >1552 | 13.5 |
| 6 | 167.7 ± 6.3 | 965.1 ± 66.4 | 28.4 ± 6.3 | 60.1 ± 8.8 | >1582 | 2.1 |
| 7 | 167.2 ± 2.3 | 596 ± 92.7 | 16.5 ± 3.3 | 76.1 ± 4.6 | 463.5 ± 56.5 | 4.6 |
| 8 | 78.4 ± 4.9 | 1593 ± 171.5 | 63.7 ± 9.8 | 1,715 ± 171.5 | >2451 | 26.9 |
| BZ | 6.5 ± 0.7 | 34.5 ± 7.6 | 19.2 ± 3.0 | 614.7 ± 115.2 | >1,921 | 32.0 |

^aValues of concentration are represented in μM . IC₅₀, inhibitory concentration of 50%; EC₅₀, effective concentration of 50%; CC₅₀, cytotoxic concentration of 50%; HC₅₀, hemolytic concentration of 50%; SI, selectivity index between host cell LLCMK₂ and amastigote forms; ama, amastigotes; \pm , standard deviation; >, above; and BZ, standard drug benznidazole. Significant differences between compound's activity and control cell growth, ANOVA ($p < 0.0001$).

Estudos de atividade biológica dos óleos de Copaíba

| | | | | | | |
|-------|------------------------|------------------------|------------------------|------------------------|-----------------------|--|
| 5 | 854 ± 108.6 | 1630 ± 108.6 | 18.6 ± 3.1 | 251.5 ± 13 | >1552 | 13.5 |
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| 8 | 78.4 ± 4.9 | 1593 ± 171.5 | 63.7 ± 9.8 | 1,715 ± 171.5 | >2451 | 26.9 |
| B7 | 166.5 ± 0.7 | 594.5 ± 2.6 | 19.2 ± 3.0 | 614.7 ± 115.2 | >1921 | 32.0 |
| 7 | 167.2 ± 2.3 | 596 ± 92.7 | 16.5 ± 3.3 | 76.1 ± 4.6 | 463.5 ± 56.5 | 4.6 |
| compd | IC ₅₀ /96 h | EC ₅₀ /24 h | IC ₅₀ /96 h | CC ₅₀ /96 h | HC ₅₀ /3 h | CC ₅₀ /IC ₅₀ ama |

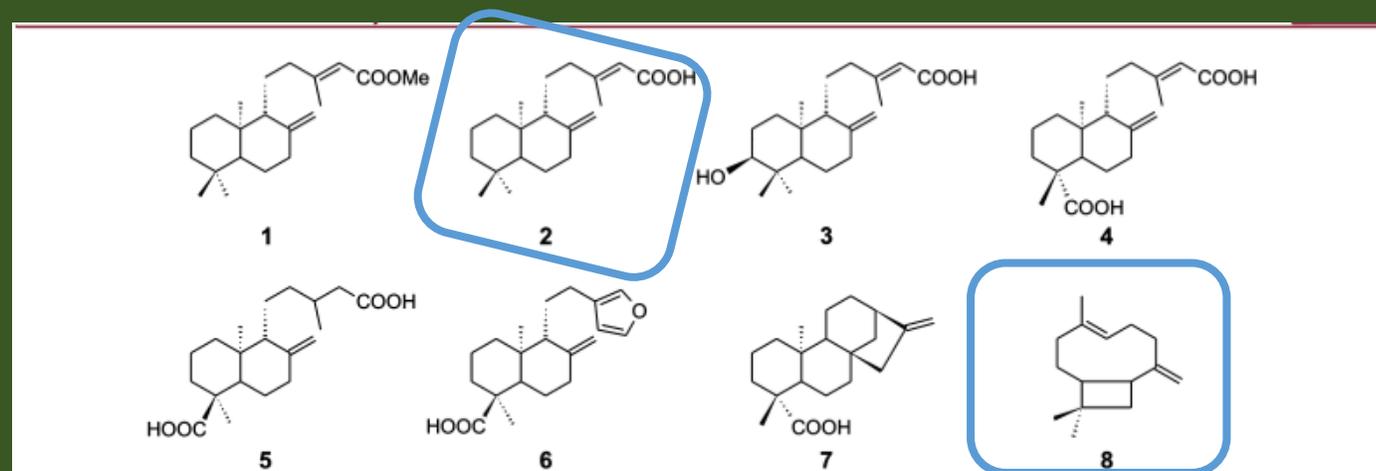
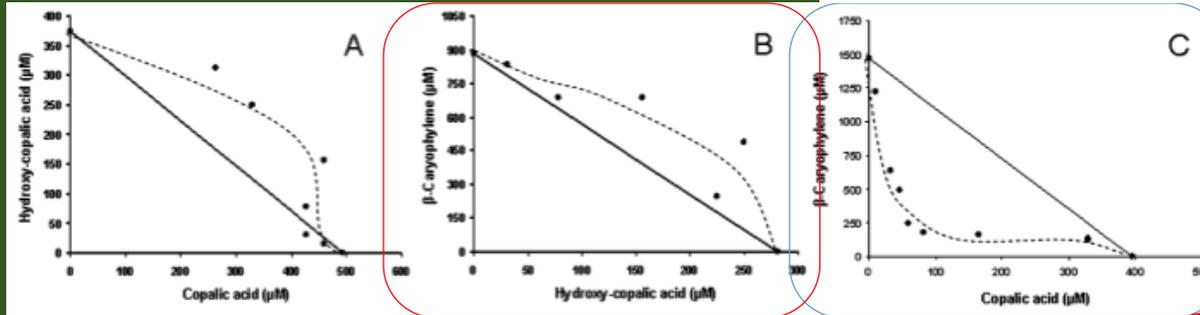


Figure 1. Terpenes evaluated for antitrypanosomal activity. Methyl copalate (1), copalic acid (2), 3β-hydroxycopalic acid (3), agathic acid (4), pinifolic acid (5), polyaltic acid (6), kaurenoic acid (7), and β-caryophyllene (8).

Estudos de atividade biológica dos óleos de Copaíba

$$1 + 1 < 2!$$

$$1 + 1 > 2!$$



Efeito Sinérgico
comprovado entre o cariofileno e o ácido copálico

Redução da DL50 da ordem de 25 vezes.

Efeito Negativo
provocado pela presença da hidroxila

Menor atividade.

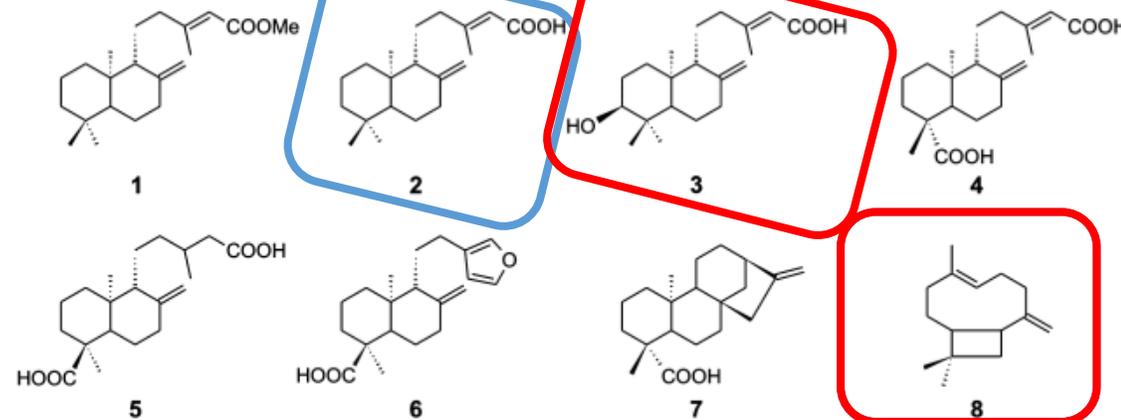


Figure 1. Terpenes evaluated for antitrypanosomal activity. Methyl copalate (1), copalic acid (2), 3β-hydroxycopalic acid (3), agathic acid (4), pinifolic acid (5), polyaltic acid (6), kaurenoic acid (7), and β-caryophyllene (8).

Terpenes from *Copaifera* Demonstrated in Vitro Antiparasitic and Synergic Activity

Erika Izumi,[†] Tânia Ueda-Nakamura,[‡] Valdir F. Veiga, Jr.,[§] Angelo C. Pinto,^{||} and Celso Vataru Nakamura^{*,†,‡}

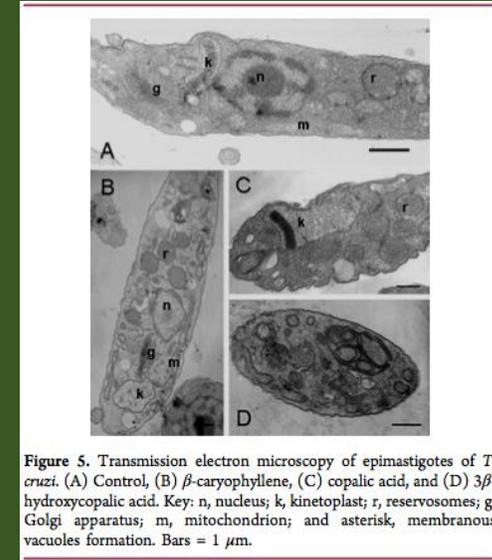


Figure 5. Transmission electron microscopy of epimastigotes of *T. cruzi*. (A) Control, (B) β -caryophyllene, (C) copalic acid, and (D) 3β -hydroxycopalic acid. Key: n, nucleus; k, kinetoplast; r, reservosomes; g, Golgi apparatus; m, mitochondrion; and asterisk, membranous vacuoles formation. Bars = 1 μ m.

- Doses letais ao parasita são muito menores que as doses tóxicas ao hospedeiro
- Efeito sinérgico entre terpenos de copaíba pela primeira vez
- Mecanismo de ação identificado com aumento do stress oxidativo, alteração da membrana celular, desorganização do cinetoplasto, formação de vacúolos membranosos com possível autofagia

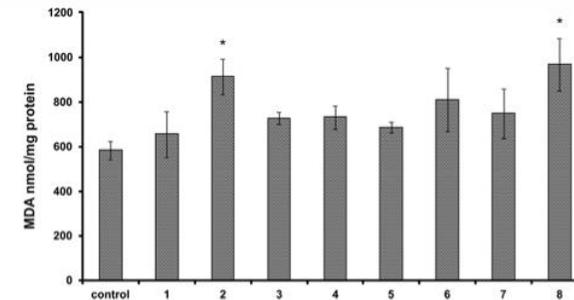


Figure 3. Evaluation of lipid peroxidation caused by terpenes on epimastigote forms. Treatment with 400 μ M for 6 h. ANOVA–Dunnett (* p = 0.02).

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Effect of Brazilian copaiba oils on *Leishmania amazonensis*

Adriana O. Santos^a, Tânia Ueda-Nakamura^b, Benedito P. Dias Filho^{a,b}, Valdir E. Veiga Junior^{c,d}, Angelo C. Pinto^d, Celso Vataru Nakamura^{a,b,*}

Table 1
Correlation of values of IC₅₀ for promastigotes of *Leishmania amazonensis* with the percentage of sesquiterpene and diterpene content in copaiba oils from different species of *Copaifera*

| Oleoresins | IC ₅₀ (μg/mL)* | Main sesquiterpenes | % | Total sesquiterpene content (%) | Main acid diterpenes | % | Total diterpene content (%) |
|------------------------------------|---------------------------|---|--------------------|---------------------------------|-------------------------------------|--------------------|-----------------------------|
| <i>Copaifera reticulata</i> (Pará) | 5.0 ± 0.8 | α-Copaene Bergamotene β-Caryophyllene | 3.0 4.1 40.9 | 78.2 | Copalic Kaurenoic | 2.4 3.9 | 21.8 |
| <i>Copaifera reticulata</i> (Acre) | 22.0 ± 0.0 | α-Copaene β-Caryophyllene | 25.1 13.1 | 68.2 | Copalic Kaurenoic Hardwickiic | 7.7 7.5 6.9 | 31.8 |
| <i>Copaifera martii</i> | 14.0 ± 0.9 | β-Bisabolene Zingiberene | 10.7 7.2 | 37.7 | Kaurenoic Kovalenic | 7.9 29.0 | 62.3 |
| <i>Copaifera cearensis</i> | 18.0 ± 0.0 | β-Caryophyllene α-Copaene | 19.7 8.2 | 76.5 | Hardwickiic Copalic | 6.2 2.1 | 23.5 |
| <i>Copaifera paupera</i> | 11.0 ± 0.4 | β-Bisabolene α-Zingiberene | 20.2 19.4 | 45.5 | Kaurenoic Copalic | 13.3 6.1 | 54.5 |
| <i>Copaifera langsdorfii</i> | 20.0 ± 0.8 | β-Caryophyllene | 32.8 | 40.4 | Kaurenoic Copalic Hardwickiic | 44.3 5.6 8.2 | 59.6 |
| <i>Copaifera officinalis</i> | 20.0 ± 0.4 | β-Caryophyllene | 8.5 | 22.7 | Hardwickiic Copalic | 30.7 13.9 | 77.3 |
| <i>Copaifera multijuga</i> | 10.0 ± 0.8 | β-Caryophyllene | 57.5 | 85.5 | Copalic | 6.2 | 14.5 |
| <i>Copaifera lucens</i> | 20.0 ± 0.9 | β-Caryophyllene | 1.8 | 18.6 | Polyalthic Copalic | 69.8 11.1 | 81.4 |
| Amphotericin B | 0.05 ± 0.0 | | | | | | |

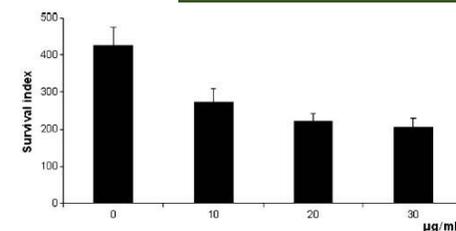


Fig. 2. Effect of *Copaifera reticulata* (collected at Pará) on *Leishmania amazonensis*-cell interaction. Peritoneal macrophage cells were infected with promastigotes of *Leishmania amazonensis* and then treated with 10, 20 or 30 μg/mL of copaiba oil. The survival index was calculated by multiplying the percentage of macrophages cells with parasites and the mean number of internalized parasites per cell. Each bar represents the mean ± standard error of at least three independent experiments, which were performed in duplicate.

Atividade leishmanicida também varia com o local de coleta e a espécie



Leishmania amazonensis: Effects of oral treatment with copaiba oil in mice

Adriana Oliveira dos Santos^a, Marco Antonio Costa^b, Tânia Ueda-Nakamura^b, Benedito Prado Dias-Filho^{a,b}, Valdir Florêncio da Veiga-Júnior^c, Marli Miriam de Souza Lima^b, Celso Vataru Nakamura^{a,b,*}

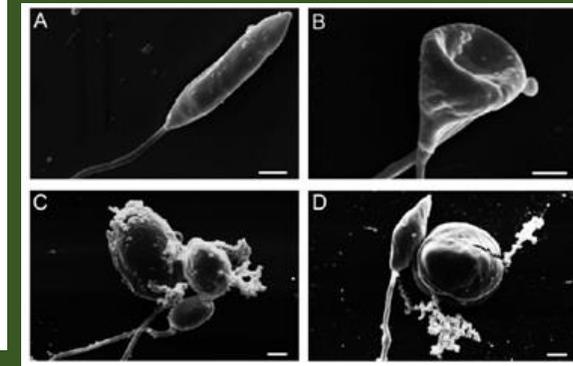


Table 1

Effects of copaiba oil on lesion development in mice infected with *L. amazonensis* promastigotes. Results are shown as the mean \pm SD for the four mice in each group.

| Treatment | Average lesion size (mm) (mean \pm SD) |
|--|--|
| Group I C(–): Infected and untreated | 4.4 \pm 1.3 |
| Group II (C+): Glucantime [®] | 0.9 \pm 0.3 ^a |
| Group III: C.O. Subcutaneous route | 3.0 \pm 1.0 ^b |
| Group IV: C.O. Oral route | 1.1 \pm 0.4 ^a |
| Group V: C.O. Topical | 4.9 \pm 0.3 ^b |
| Group VI: C.O. Oral route and topical | 1.2 \pm 0.2 ^a |

C(–): negative control; C(+): positive control; C.O.: copaiba oil; SD: standard deviation.



Atividade leishmanicida de
Copaifera reticulata

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Volume 2012, Article ID 898419, 7 pages
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Research Article

Copaiba Oil: An Alternative to Development of New Drugs against Leishmaniasis

Adriana Oliveira dos Santos,¹ Tânia Ueda-Nakamura,² Benedito Prado Dias Filho,^{1,2} Valdir Florêncio da Veiga Junior,³ and Celso Vataru Nakamura^{1,2}

Atividade leishmanicida do óleo de copaiba de *Copaifera reticulata* em formas promastigotas e axênicas amastigotas

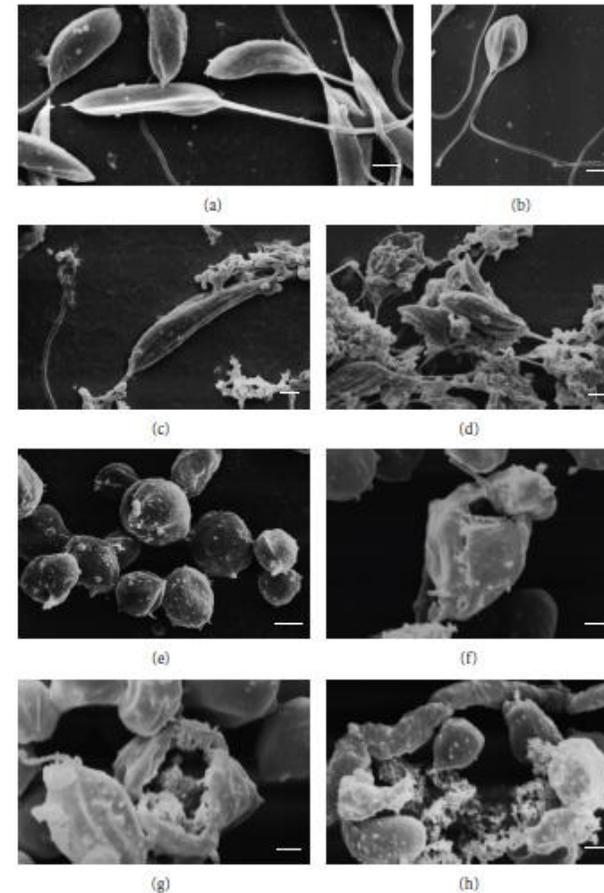


FIGURE 1: Scanning electron micrographs of promastigote and axenic amastigote forms of *L. amazonensis* treated with copaiba oil for 72 h. (a) promastigote, control; (b) promastigote after treatment with IC_{50} of copaiba oil; (c and d) promastigote after treatment with IC_{50} of copaiba oil; (e) amastigote, control; (f) amastigote after treatment with IC_{20} of copaiba oil; (g and h) amastigote after treatment with IC_{90} of copaiba oil. Bars = 1 μ m.

Antileishmanial activity of diterpene acids in copaiba oil

Adriana Oliveira dos Santos¹, Erika Izumi¹, Tânia Ueda-Nakamura², Benedito Prado Dias-Filho^{1,2}, Valdir Florêncio da Veiga-Júnior³, Celso Vataru Nakamura^{1,2/+}

TABLE

Antileishmanial and cytotoxic activity of diterpenes from copaiba oil

| Compounds | µg/mL | | | |
|----------------------------|------------------------------|-------------------------------|-------------------|--|
| | IC ₅₀ | | CC ₅₀ | IS |
| | Promastigote | Amastigote | Erythrocytes | CC ₅₀ /IC ₅₀ ama |
| Agathic acid | 28.0 ± 1.5 ^b | 17.0 ± 2.0 ^b | 350.0 ± 3.4 | 20.6 |
| Hydroxycopalic acid | 2.5 ± 0.4^a | 18.0 ± 1.5^b | 40.0 ± 2.4 | 2.2 |
| Kaurenoic acid | 28.0 ± 0.7 ^b | 3.5 ± 0.5 ^a | 140.0 ± 17.0 | 40.0 |
| Methyl copalate | 6.0 ± 0.9 ^a | 14.0 ± 1.0 ^b | 500.0 ± 3.0 | 35.7 |
| Pinifolic acid | 70.0 ± 8.0 ^b | 4.0 ± 0.4 ^a | > 500.0 | > 125.0 |
| Polyaltic acid | 35.0 ± 2.0 ^b | 15.0 ± 1.0 ^b | > 500.0 | > 33.3 |
| Amphotericin B | 0.06 ± 0.0 | 0.23 ± 0.0 | ND | ND |

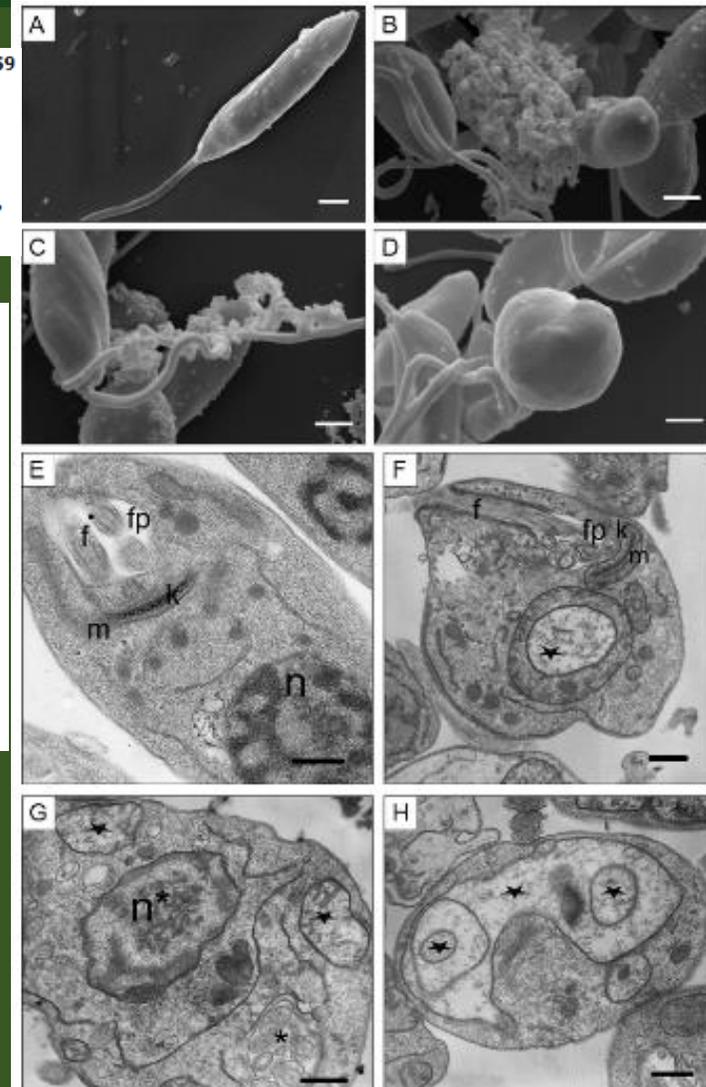
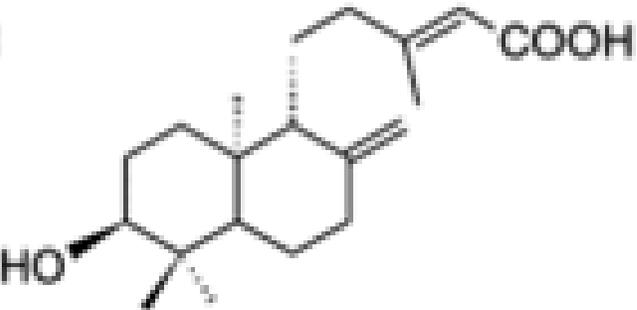


Fig. 1: scanning (SEM) and transmission (TEM) electron micrographs of promastigote forms of *Leishmania amazonensis* treated with 2.5 µg/mL hydroxycopalic acid for 72 h. A: control (SEM); B-D: treated parasites; E: control (TEM); F, G: treated parasites. The hydroxyco-

Atividade leishmanicida dos ácidos isolados, mostrando potencial especialmente para o **ácido 3-hidróxi-copálico**



1ª Questão: Como valorizar os bioprodutos Amazônicos?

- Usos tradicionais
- Novos usos
- Resíduos da bioindústria

2ª Questão: Como aumentar a qualidade dos bioprodutos Amazônicos?

- DOC
- Valorizar diferenças regionais

3ª Questão: Como conhecer e valorizar a biodiversidade ainda desconhecida?

- Animais
- Microorganismos
- Aproveitamentos transdisciplinares

4ª Questão: Qual o trabalho do fitoquímico no século XXI?

- Isolar
- Aumento de Escala
- Identificar em misturas
- Padronizar extratos e frações ativos

Questão Fundamental:

Químicos e a biodiversidade Amazônica, pra quem?

- **Academia...?**
- **Para atender requisitos da CAPES...?**

ou

- **Para entregar à Indústria Bioprodutos ativos e padronizados, de comercialização viável e que promovam o Desenvolvimento Regional?**



22 anos de pesquisas na Amazônia

Obrigado

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