Métodos Químicos para o estudo de Produtos Naturais

Prof. Marcelo J. Pena Ferreira
marcelopena@ib.usp.br

1

Quem são os componentes bioativos?

- ✓ Macromoléculas biológicas
- ✓ Substâncias oriundas de síntese orgânica (Produtos Sintéticos)
- ✓ Substâncias de origem natural (Produtos Naturais)

Quais são as fontes?

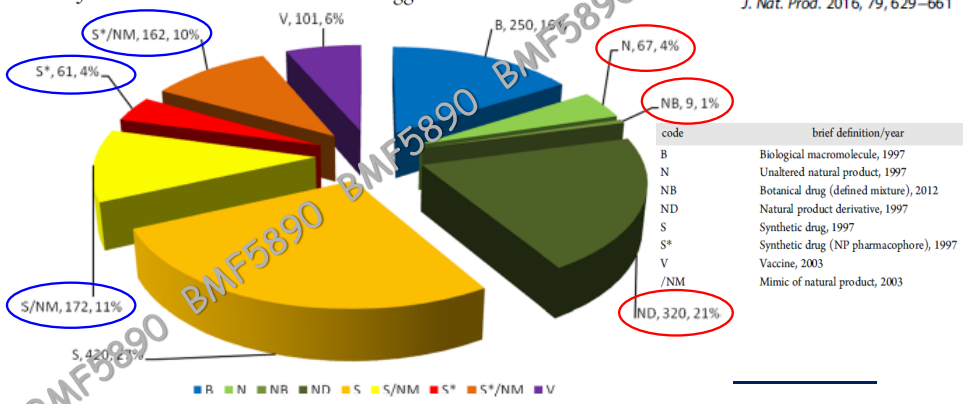
2

JOURNAL OF NATURAL PRODUCTS
Review
pubs.acs.org/jnp

Natural Products as Sources of New Drugs from 1981 to 2014

David J. Newman*,† and Gordon M. Cragg‡

DOI: 10.1021/acs.jnatprod.5b01055
J. Nat. Prod. 2016, 79, 629−661



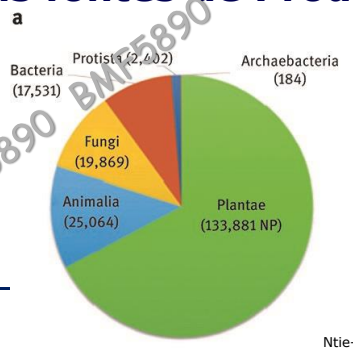
code	brief definition/year
B	Biological macromolecule, 1997
N	Unaltered natural product, 1997
NB	Botanical drug (defined mixture), 2012
ND	Natural product derivative, 1997
S	Synthetic drug, 1997
S*	Synthetic drug (NP pharmacophore), 1997
V	Vaccine, 2003
/NM	Mimic of natural product, 2003

Figure 1. All new approved drugs 1981−2014; $n = 1562$.

Quem são os componentes bioativos?

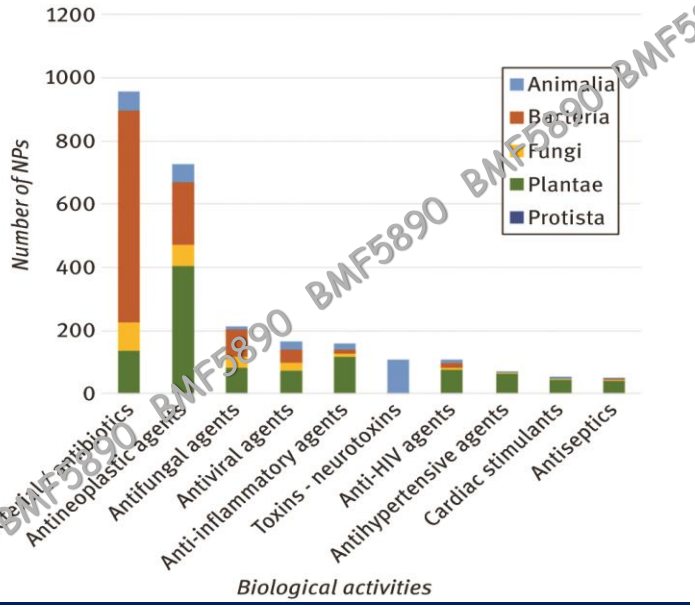
- ✓ Macromoléculas biológicas
- ✓ Substâncias oriundas de síntese orgânica (Produtos Sintéticos)
- ✓ Substâncias de origem natural (Produtos Naturais)

Quais são as fontes de Produtos Naturais?



Ntie-Kang & Svozil, *Phys. Sci. Rev.* 2019: 20180121

5



Ntie-Kang & Svozil, *Phys. Sci. Rev.* 2019: 20180121

6

Available online at www.sciencedirect.com
ScienceDirect
Current Opinion in Chemical Biology

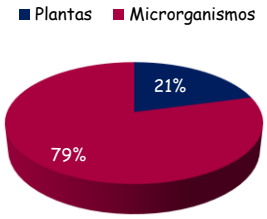
The impact of natural products upon modern drug discovery

A Ganesan

Current Opinion in Chemical Biology 2008, 12:306–317

The 24 natural products discovered since 1970 that led to an approved drug in 1981–2006

Lead, year, and structural class	Origin	Discoverer	Drug, year	Route	Sales
Validamycin, 1970 Oligosaccharide	Actinomycete	Takeda (JAP)	Acarbose, 1990 Voglibose, 1994	po po	857
Midecamycin, 1971 Macrolide	Actinomycete	Meiji (JAP)	Miocamycin, 1985	po	
Pseudomonic acid, 1971 Polyketide	Bacteria	Beecham (UK)	Mupirocin, 1995	top	436
Taxol, 1971 Diterpene	Plant	Res Triangle Inst/NIH (USA)	Paclitaxel, 1993 Docetaxel, 1995	iv iv	81 123
Cephamycin C, 1971 β-lactam	Actinomycete	Lilly (USA)	Moxalactam, 1982 Cefotetan, 1984 Cefbuperazone, 1985	iv iv iv	
Coformycin, 1974 Nucleoside	Actinomycete	Inst Microbial Chem (JAP)	Pentostatin, 1992	iv	
Echinocandin B, 1974 Cyclopeptide	Fungus	Ciba-Geigy (SWI)	Caspofungin, 2001 Micafungin, 2002 Anidulafungin, 2006	iv iv iv	293
Mizoribine, 1974 Nucleoside	Fungus	Tokyo (JAP)	Mizoribine, 1984	po	
Rapamycin, 1974 Polyketide	Actinomycete	Ayerst (CAN)	Sirolimus, 1999 Everolimus, 2004 Zotarolimus, 2005	po po po	434
Compactin, 1975 Polyketide	Fungus	Sankyo (JAP)	Lovastatin, 1984 Simvastatin, 1988 Pravastatin, 1989 Fluvastatin, 1994 Atorvastatin, 1997 Cerivastatin, 1997 Pitavastatin, 2003 Rosuvastatin, 2003	po po po po po po po po	264 2 41 195 1 71
Cyclosporine A, 1975 Cyclopeptide	Fungus	Sandoz (SWI)	Ciclosporin, 1983	po	122



7

JOURNAL OF NATURAL PRODUCTS
ARTICLE
pubs.acs.org/jnp
J. Nat. Prod. 2011, 74, 983–988

High-Throughput Profiling of Microbial Extracts

Tatsuya Ito,* Takamichi Odake, Hideyuki Katoh, Yuichi Yamaguchi, and Masahiro Aoki

Table 1. Analytical Results of 16 025 Samples

group	microbe	number of samples	number of peaks	number of peaks/sample	peak identifiers (PIs)	accumulation of PIs	group-specific PIs	group-specific PIs/sample
A	fungi	5924	255 094	43.1	24 235	24 235	10 257	1.73
B	fungi	1376	47 342	34.4	9654	27 864	2120	1.54
C	fungi	1624	56 254	34.6	9759	30 892	1850	1.14
D	fungi	1587	46 356	29.2	9013	33 620	2190	1.38
E	actinomycete	854	24 480	28.7	2025	34 302	379	0.44
F	fungi	2474	70 749	28.6	11 858	37 013	2575	1.04
G	actinomycete	2186	52 320	23.9	5063	38 753	1740	0.80
total		16 025	552 619	34.5	71 607	38 753	21 111	1.15[a]

[a] Average of group-specific PIs/sample.

✓ ~13.000 extratos de microrganismos: 1,04-1,73 componentes únicos

8

ESTIMATIVAS RELEVANTES PARA ANÁLISE

✓ ~ 20.000 metabólitos fúngicos na literatura

✓ Número de metabólitos secundários: ~2 componentes por cepa estudada

✓ Número de fungos: 1,5 – 5,1 milhões

ONDE ESTÃO OS DEMAIS 3-10 MILHÕES DE METABÓLITOS ?

9

E NO BRASIL ??

NPR

REVIEW View Article Online View Journal

Cite this: DOI: 10.1039/c3np70112c

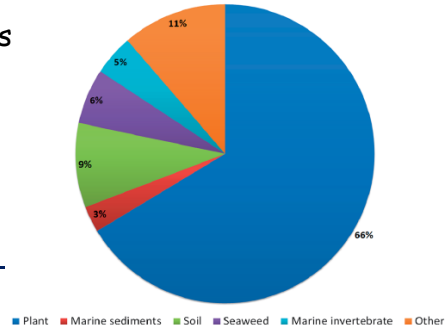
Thinking big about small beings – the (yet) underdeveloped microbial natural products chemistry in Brazil

Laura P. Ióca, Pierre-Marie Allard and Roberto G. S. Berlinck

✓ 280 Metabólitos microrganismos

✓ 235 Metabólitos fúngicos

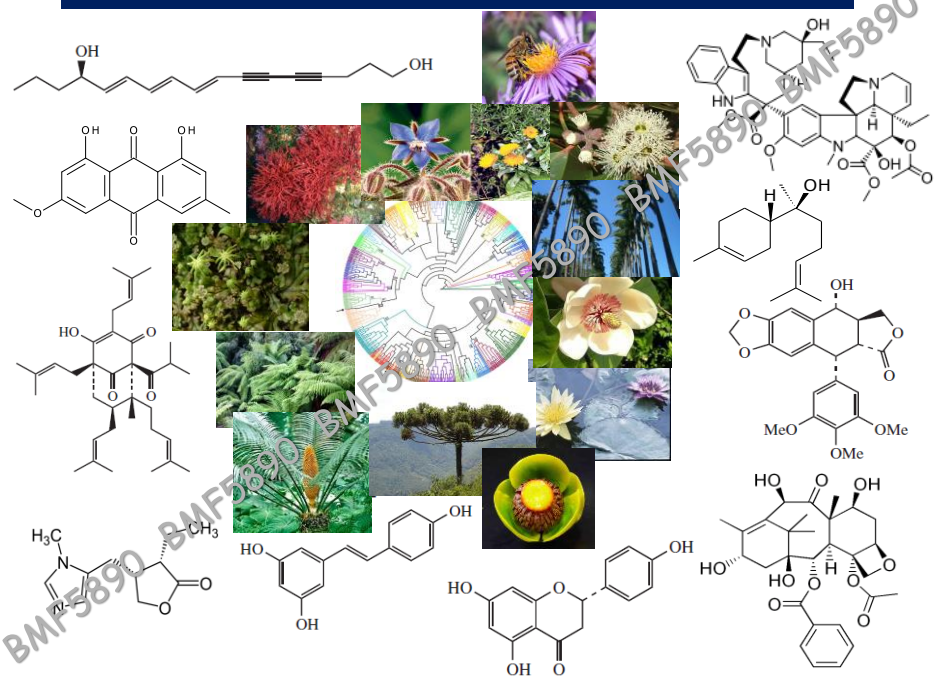
BIOTA+10



10

Por quê plantas e microrganismos são tão prolíficos produtores de componentes bioativos?

11

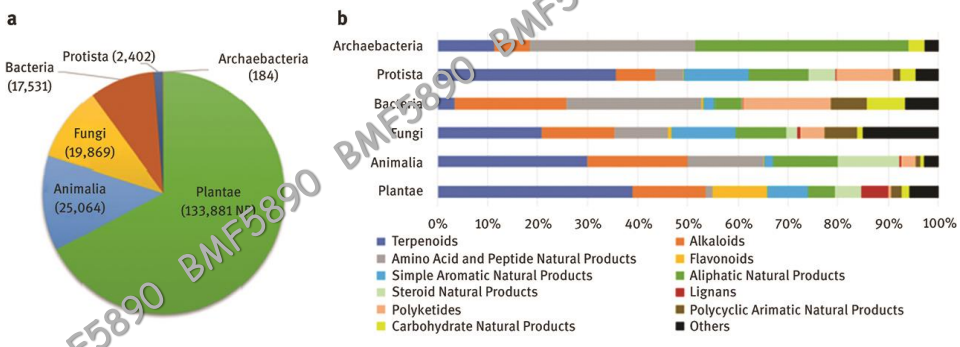


12

Quem são os componentes bioativos?

Quais são as fontes?

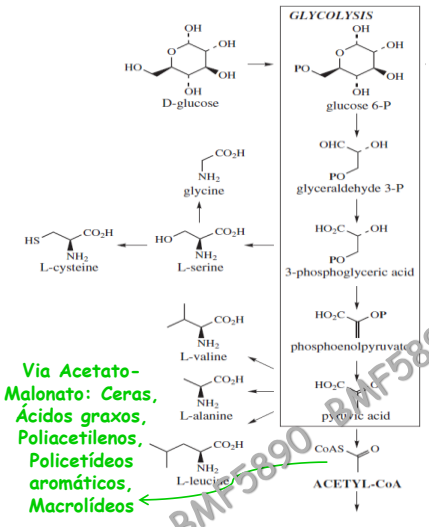
Quais são as classes de metabólitos?



Ntie-Kang & Svozil, *Phys. Sci. Rev.* 2019: 20180121

13

Como são formados?



14

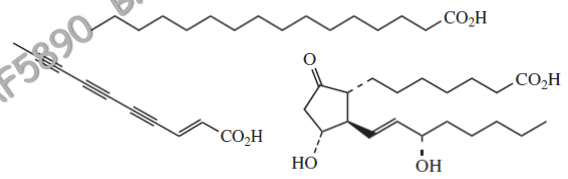
Via do acetato-malonato

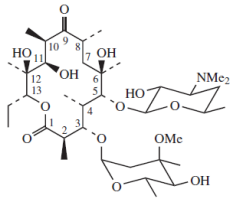
- Precursora de policetídeos: cadeias poli-β-ceto

$$n CH_3CO_2H \rightarrow —[CH_2CO]_n—$$

- Compreende as seguintes classes de metabólitos:
  - Ácidos graxos;
  - Poliacetilenos;
  - Prostaglandinas;
  - Antibióticos macrolídeos;
  - Várias substâncias aromáticas:

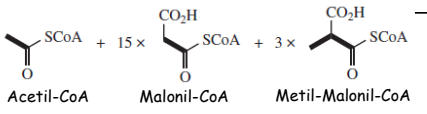
xantonas, antraquinonas, tetraciclinas..

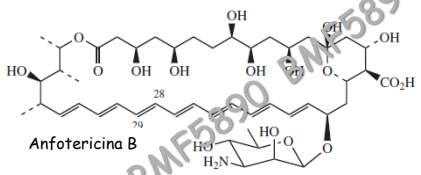


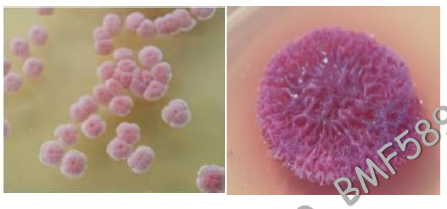


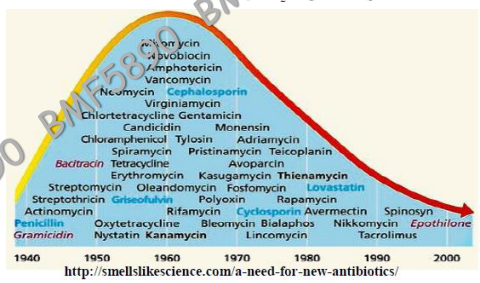
15

Macrolídeos



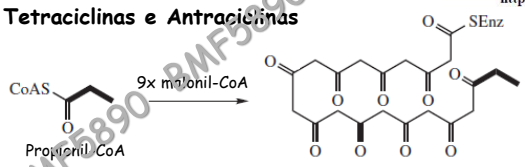


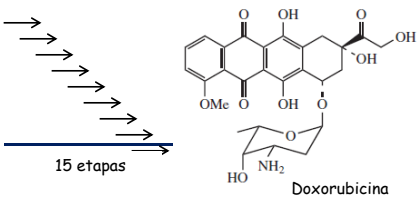




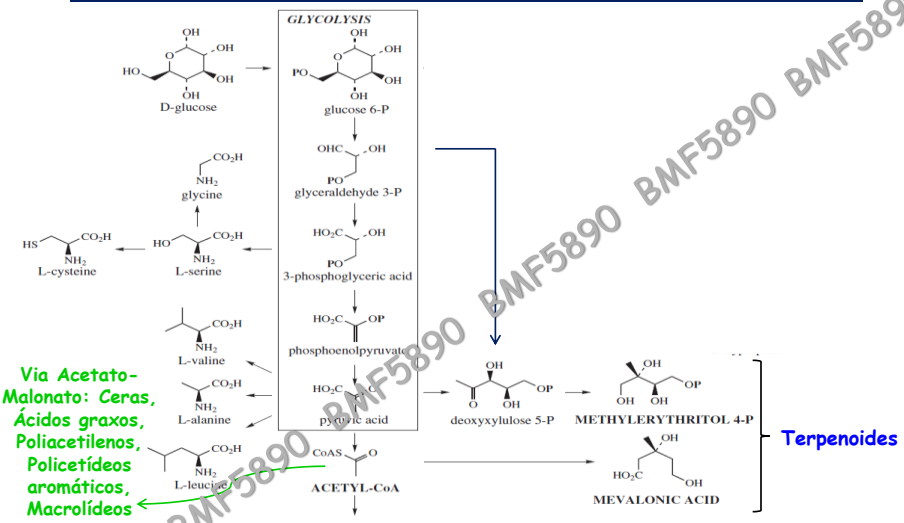
http://smellslikescience.com/a-need-for-new-antibiotics/

Tetraciclinas e Antraciclinas



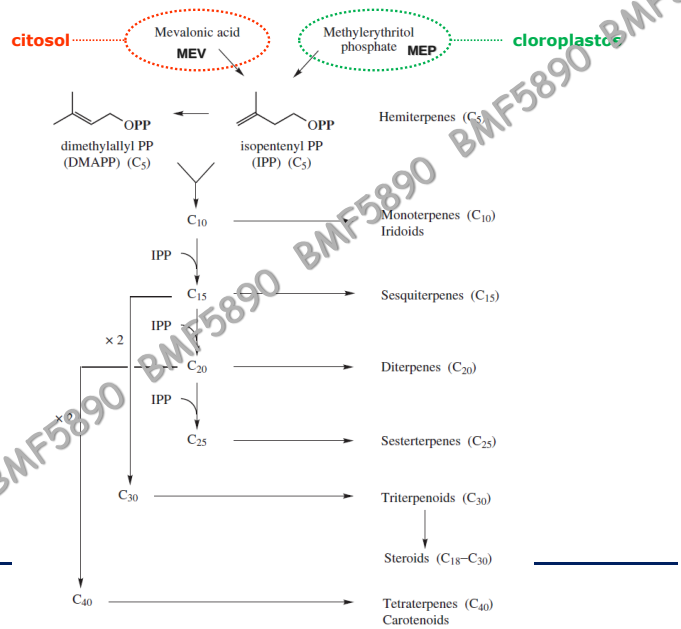


16



17

SUBSTÂNCIAS TERPENOÍDICAS



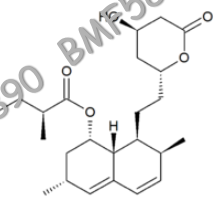
18

EXPRESSÃO DAS VIAS MEV E MEP NOS ORGANISMOS

✓ Animais e fungos: exclusivamente via MEV

✓ Bactérias, algas e plantas: apresentam e empregam as vias MEP e MEV

Aspergillus terreus

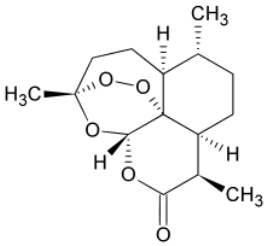


Lovastatina

✓ Enzimas da via MEP são alvos atrativos no desenvolvimento de novos antimicrobianos → via MEP usada pelo patógeno e ausente em humanos

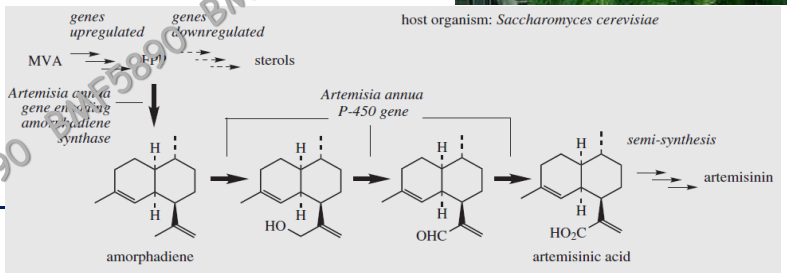
19

SESQUITERPENOIDES (C_{15})



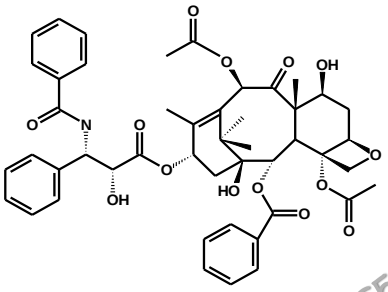
Artemisinina

Componente de *Artemisia annua* (Asteraceae). Possui atividade contra *Plasmodium falciparum*, causador da malária.



20

DITERPENOIDES (C_{20})



Taxus brevifolia – Taxaceae
Gymnospermae

Paclitaxel (Taxol)
isolado das cascas de *Taxus brevifolia*
e usado na quimioterapia do câncer.

21

FUNGOS ENDOFÍTICOS: O CASO DO TAXOL

Journal of Natural Products 1315
Vol. 58, No. 9, pp. 1315-1324, September 1995

THE SEARCH FOR A TAXOL-PRODUCING MICROORGANISM AMONG THE ENDOPHYTIC FUNGI OF THE PACIFIC YEW, *TAXUS BREVIFOLIA*[1]

Taxol – *Taxus brevifolia*

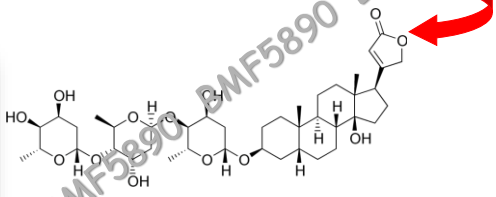
1993 – *Taxomyces andreanae*

1995 - *Pestalotiopsis versicolor* (478µg.L^{-1})

22

ESTEROIDES (C_{27-32})

As folhas fornecem glicosídeos cardioativos

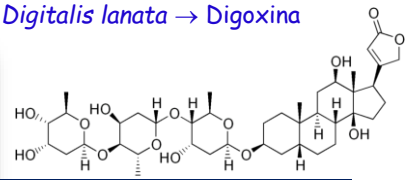


Digitoxina

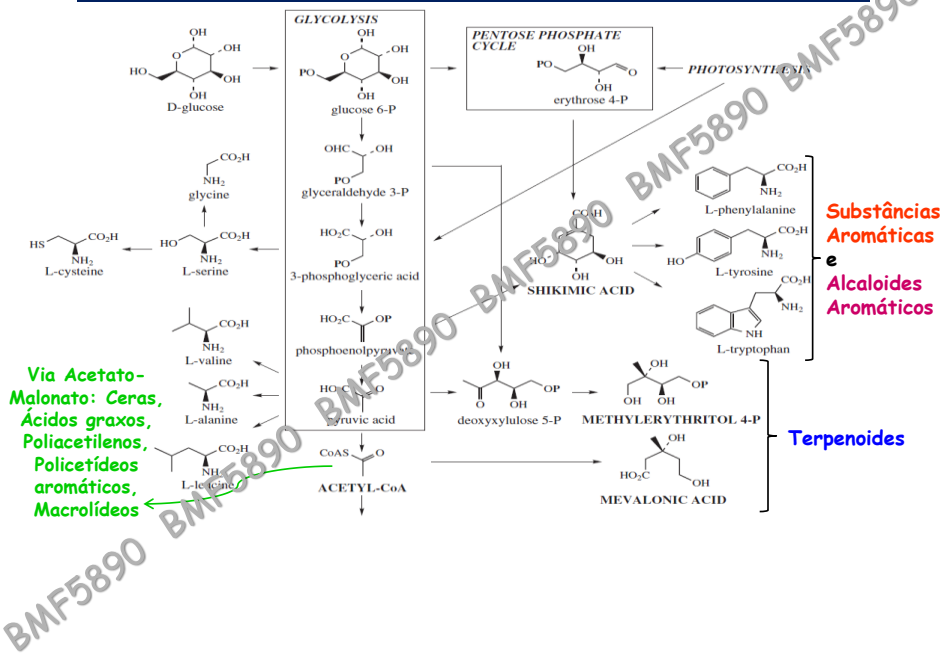
Núcleo esteroidal tetracíclico e três resíduos de açúcar.

Digitalis purpurea
Plantaginaceae
Dedaleira

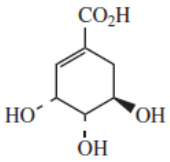
Digitalis lanata → Digoxina



23



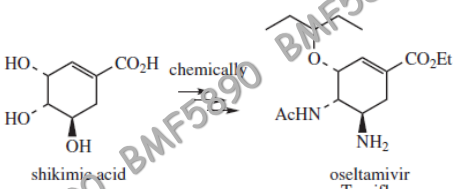
24



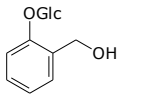
Ácido chiquímico

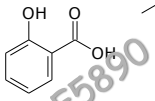
Illicium verum (Schisandraceae)

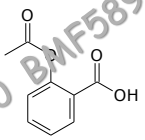
Anis-estrelado - "Shikimi"



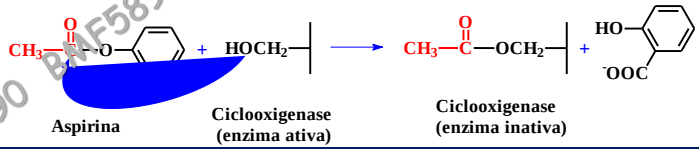
25







Salicina; Aspirina: inibe a atividade da COX, por transferência de um grupo acetil para o grupo hidroxílico do aa. serina da enzima. A aspirina reduz o processo inflamatório e inibe a síntese de prostaglandinas.

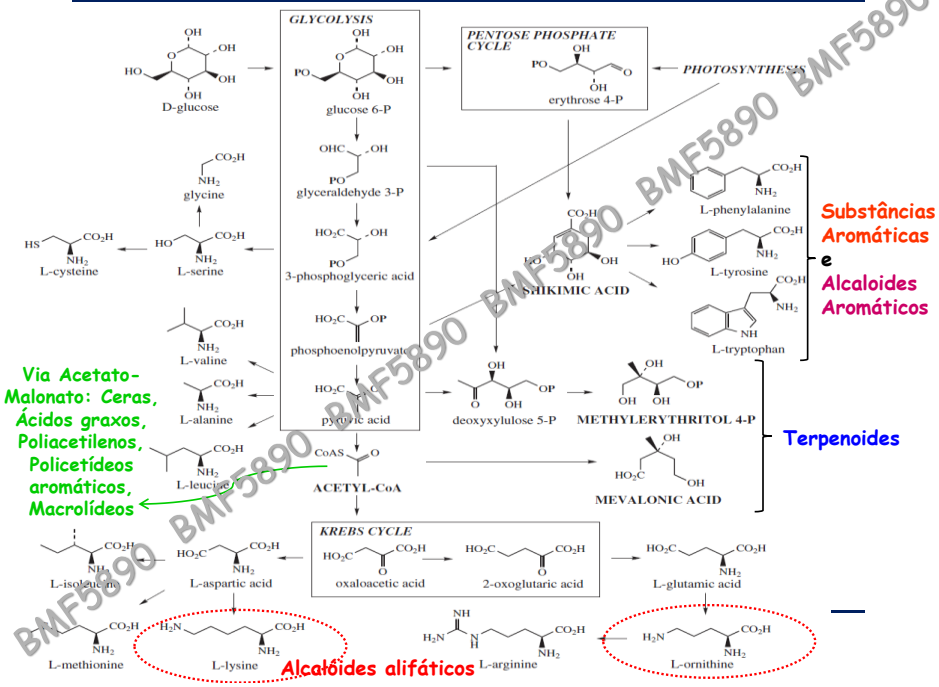


Aspirina

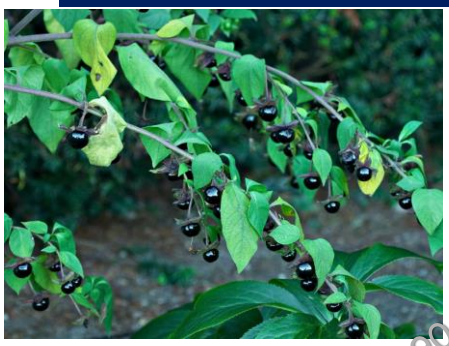
Ciclooxigenase (enzima ativa)

Ciclooxigenase (enzima inativa)

26

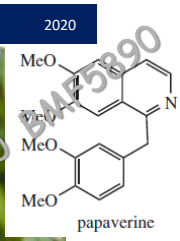


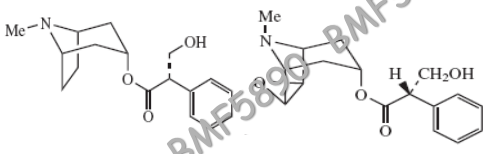
27



Atropa belladona – Solanaceae

Papaver somniferum – Papaveraceae



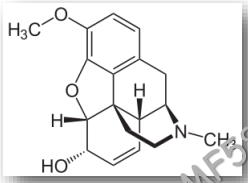


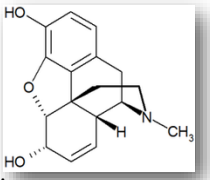
Atropina e Escopolamina: relaxante musculatura lisa, alívio cólicas intestinais e menstruais, anti-espasmódico.

Papaverina: vasodilatador na insuficiência circulatória cerebral e relaxante musculatura lisa.

28

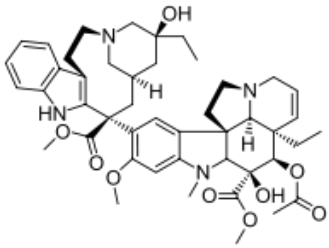
Papaver somniferum – Papaveraceae
papoula





Codeína: analgésico e antitússico.
Morfina: usada mundialmente como analgésico.

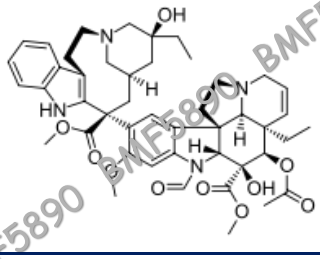
29



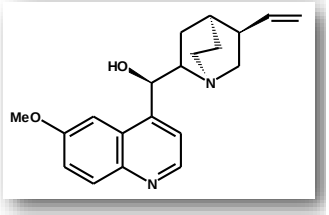
Vimblastina: doença de Hodgkin

Catharanthus roseus – Apocynaceae

Vincristina: antitumoral variado

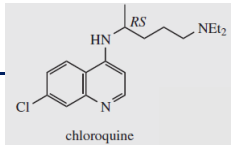


30



Cinchona sp. – Rubiaceae

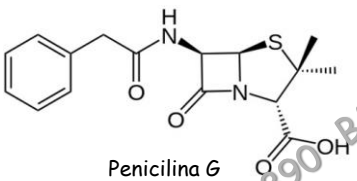
Quinino usada como antimalárico.
Derivado: cloroquina



chloroquine

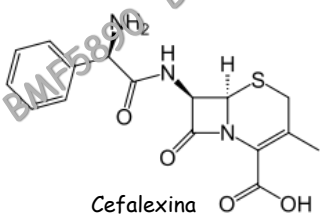
31

Penicillium chrysogenum



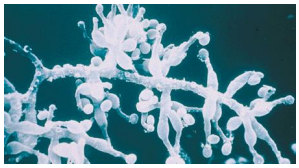
Penicilina G

Cephalosporium acremonium

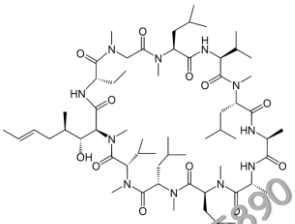


Cefalexina

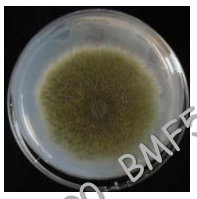
32



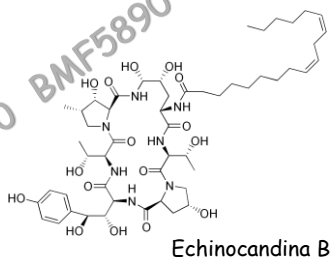
Tolypocladium inflatum



Ciclosporina



Aspergillus nidulans



Echinocandina B

33

Como são obtidos (extraídos)?

EXTRAÇÃO: obtenção de substâncias a partir de matrizes [vegetais (raízes, caules, folhas, flores e frutos), organismos marinhos ou microrganismos]

extração sólido-líquido

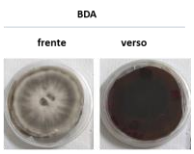
↓ eficiência

DIVISÃO E RIGIDEZ DO MATERIAL

34

Como são obtidos (extraídos)?

FUNGO 931 - *Botryocladia occidentalis*



Arroz

Meios líquidos

Bioensaios
Caracterização química

DEPENDENTE DA:

POLARIDADE DO SOLVENTE

35

SOLVENTE — *seletivo*

POLARIDADE

Hexano
Éter de petróleo
Cicloexano
Tolueno
Diclorometano
Clorofórmio
Éter etílico
Acetato de etila
Acetona
Etanol
Metanol
Água

Extração fracionada

OUTROS FATORES: Agitação; Temperatura; Tempo

MÉTODOS DE EXTRAÇÃO A FRIO: Maceração; entre outros

MÉTODOS DE EXTRAÇÃO A QUENTE: Infusão; Refluxo

36

Como são obtidos (extraídos)?

37

Fracionamento, isolamento e purificação:

- ✓ Partição por solventes: dissolução seletiva e distribuição entre as fases de dois solventes imiscíveis

- ✓ Métodos cromatográficos: .....

38

Cromatografia

A Cromatografia é um método físico-químico de separação.

Fundamentado na migração diferencial de componentes de uma mistura, que ocorre devido a diferentes interações entre duas fases imiscíveis:

- Fase móvel
- Fase estacionária

39

- *Cromatografia planar*
  - cromatografia em papel (CP)
  - cromatografia em camada delgada (CCD)

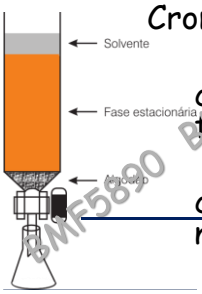
- *cromatografia em coluna – Classificada em função da fase móvel*

  Cromatografia à gás (CG)

  Cromatografia líquida

  cromatografia líquida clássica (CLC) apenas pela força da gravidade

  cromatografia líquida de alta eficiência (CLAE) necessário o uso de uma bomba de alta pressão



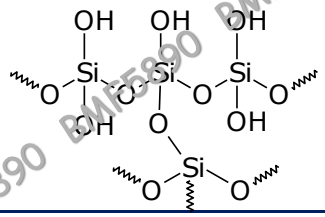
40

Parâmetros para se utilizar a cromatografia

Natureza das substâncias a serem separadas.

Escolha da fases estacionárias

As mais usadas (menor custo) são a sílica e a alumina (ambas com caráter polar) – **fase normal** (mais polar que a fase móvel)



Sílica

Al_2O_3

Alumina

41

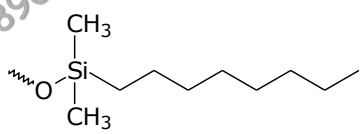
Escolha da fases estacionárias

fase reversa – sílica modificada (ou fase quimicamente ligada) : sílica C_8, C_{18}

(menos polar que a fase móvel)

Vantagens:

- substâncias iônicas, não-iônicas e ionizáveis
- força de atração superfície-soluto é fraca
- adsorção irreversível é rara



Sílica modificada – C_8

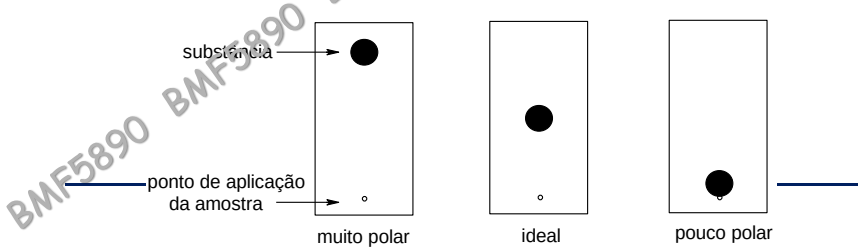
42

CROMATOGRAFIA EM CAMADA DELGADA (CCD)

- A cromatografia em camada delgada (CCD) é uma técnica de adsorção líquido-sólido.

- Separação pela diferença de afinidade dos componentes de uma mistura pela fase estacionária.

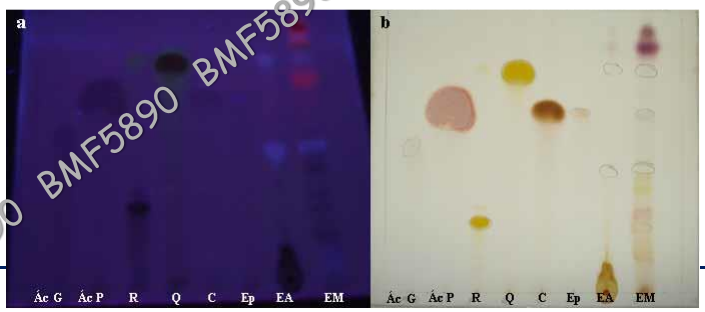
Escolha da fase móvel



43

REVELAÇÃO

- Visual : Se as substâncias são coloridas.
- Luz ultravioleta: Muitos compostos se tornam fluorescentes quando excitados por luz UV
- Reveladores específicos: $AlCl_3$; Dragendorff

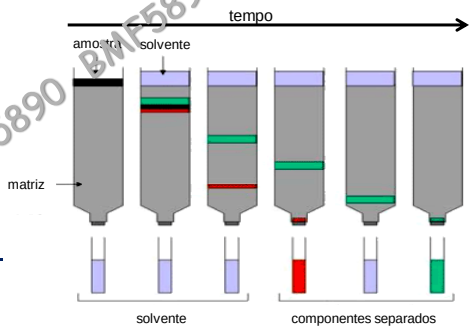


44

CROMATOGRAFIA LÍQUIDA EM COLUNA (CC)

Fase Móvel: A escolha do eluente (solvente) pode ser mudada durante o processo cromatográfico.

Em fase normal: menos polares > eluição que mais polares



45

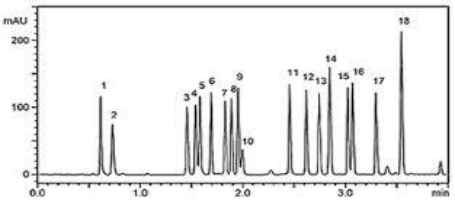
CROMATOGRAFIA LÍQUIDA DE ALTA EFICIÊNCIA (CLAE)

Coluna metálica: fase reversa (+ comum C_{18})

Equipamento: Cromatógrafo

Fase móvel:

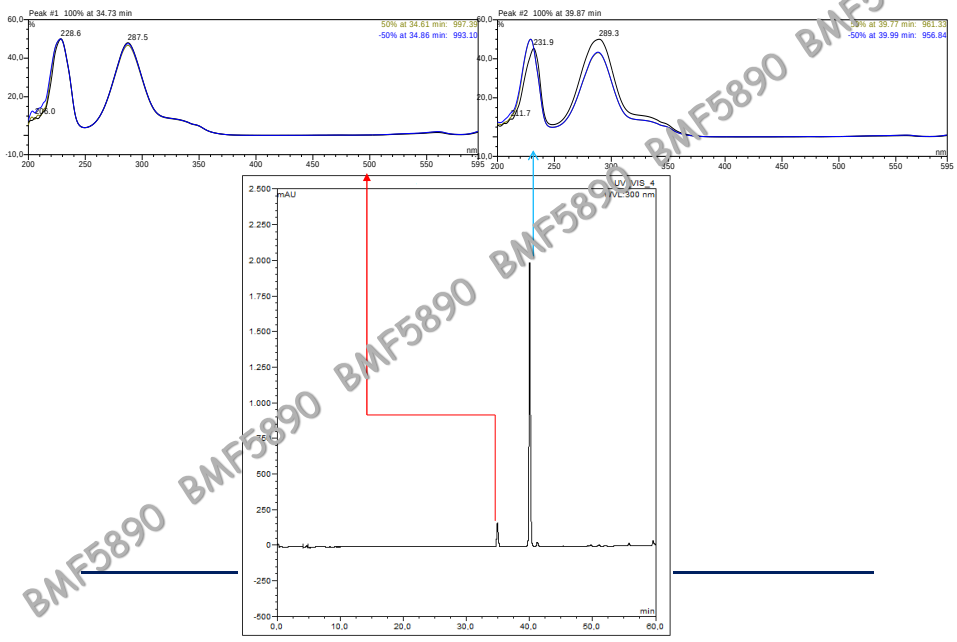
Detectores: UV-Vis, UV-EM, RMN, IR



46

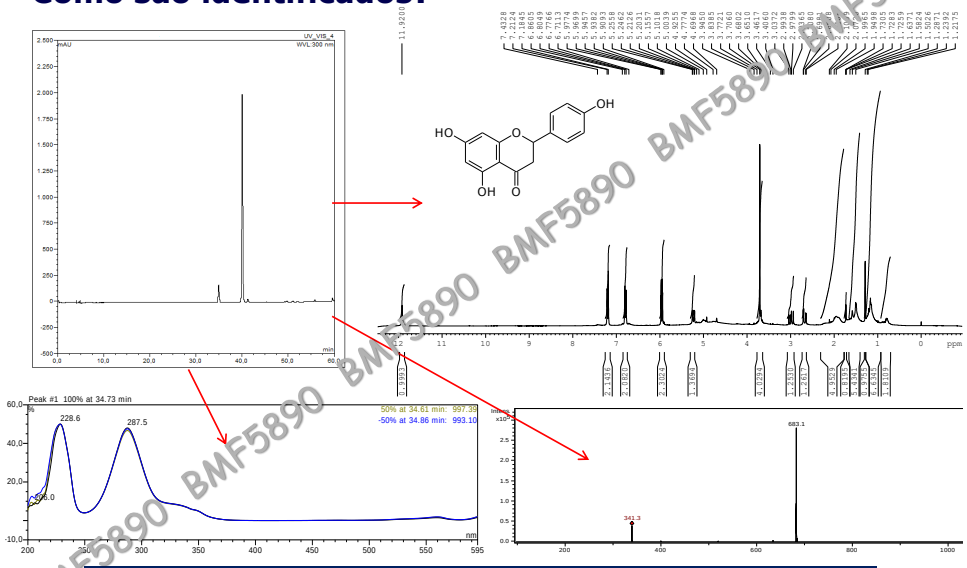
47

CLAE - UV



48

Como são identificados?



49

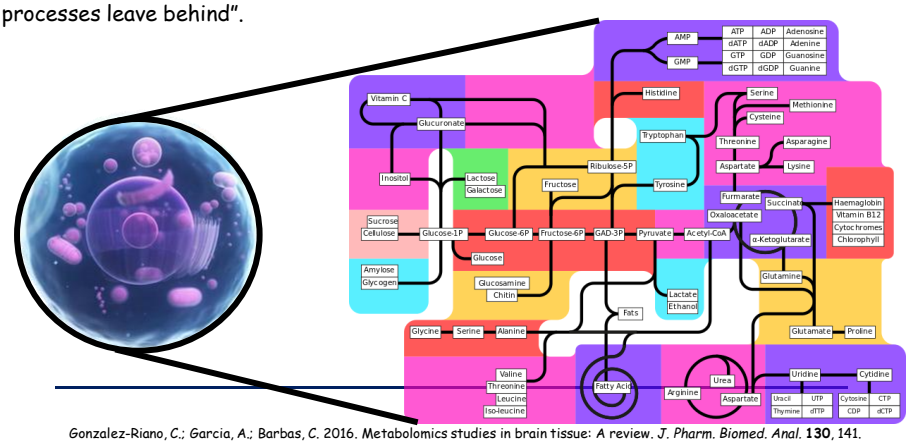
Como analisar o conjunto de metabólitos produzidos por um organismo e obter um novo componente bioativo?

50

What are metabolomic studies ?

1998 → emergence of the word "Metabolome"

"Complete set of low-molecular weight molecules (< 1500 Da) or metabolites synthesized by a cell, whose shifts give the unique chemical fingerprints that specific cellular processes leave behind".

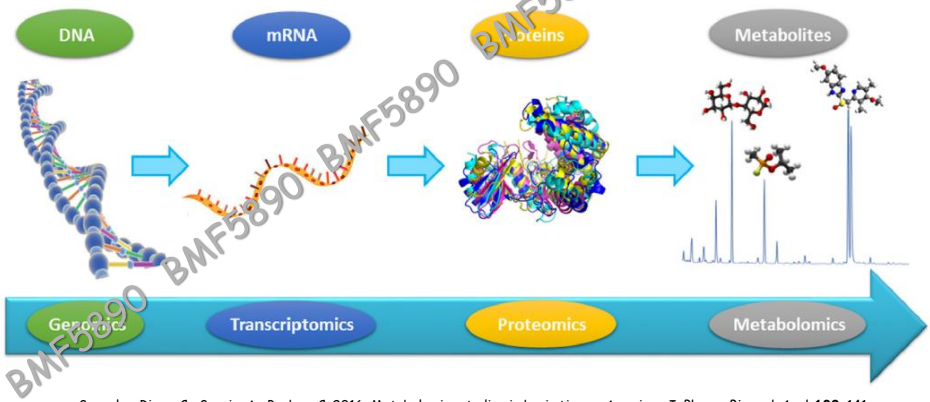


Gonzalez-Riano, C.; Garcia, A.; Barbas, C. 2016. Metabolomics studies in brain tissue: A review. *J. Pharm. Biomed. Anal.* **130**, 141.

51

Metabolomic studies

- Metabolomics has joined genomics, proteomics and transcriptomics as one of the new "omics", all of them employed to understand the global systems biology.
- Systems biology → holistic approaches to inspect the dynamic collection of proteins, genes, transcripts and metabolites present in the living organism.



Gonzalez-Riano, C.; Garcia, A.; Barbas, C. 2016. Metabolomics studies in brain tissue: A review. *J. Pharm. Biomed. Anal.* **130**, 141.

52

Metabolome

How to access and analyze the metabolome ?

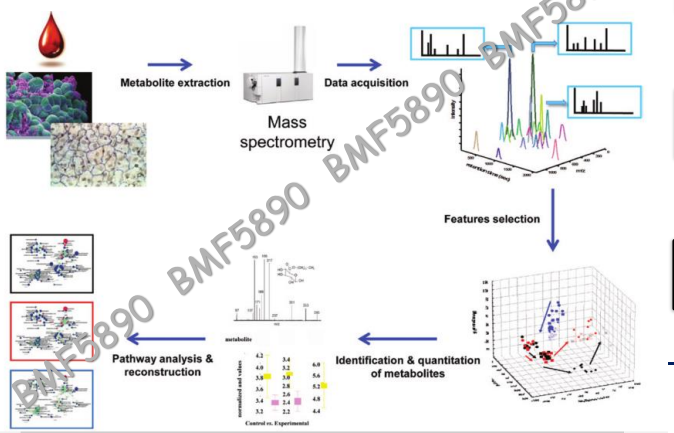
Analytical techniques → **Small sample amounts** → **Rapid detection and identification of hundreds of metabolites**

Which analytical technique to use ?

53

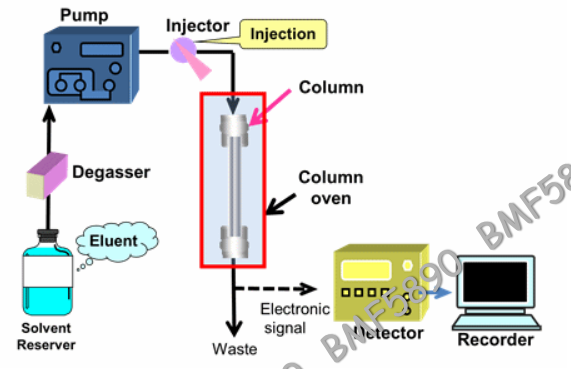
Metabolomic studies – Analytical techniques

- Samples
- Analyses:
  - ✓ Chromatography
  - ✓ UV
  - ✓ Mass spectrometry
  - ✓ NMR
- Data acquisition
- Detection & Identification
- Data processing (Bioinformatics)

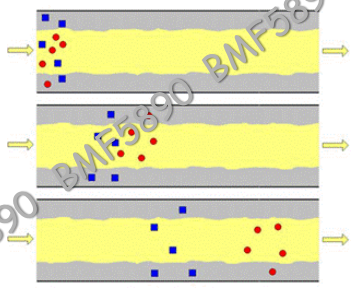


54

CHROMATOGRAPHIC ANALYSIS : HPLC



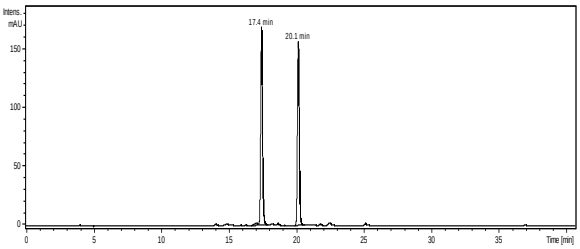
HPLC system



Compounds elution

Obtained data:

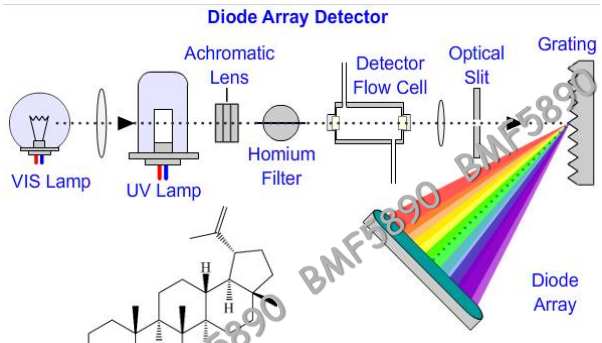
- Retention times
- Abundance of components

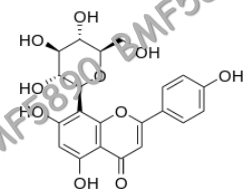


55

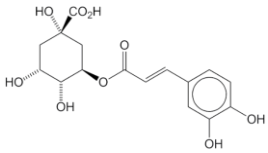
DETECTION: PDA

- PDA – Photo Diode Array Detector



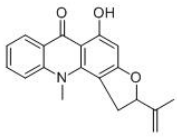


Vitexin

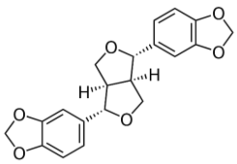


Chlorogenic acid

Lupeol



Rutacridone



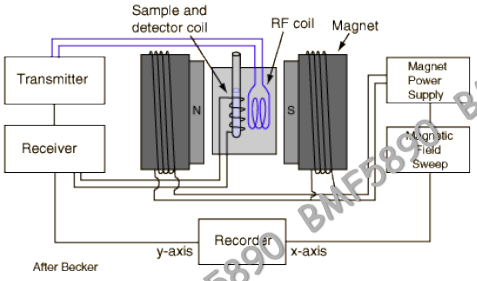
Sesamin

Obtained data: NP class (sometimes)

56

DETECTION: NMR

- NMR – Nuclear Magnetic Resonance



Obtained data: Chemical structure

DETECTION: MS

Mass Spectrometry

Low Resolution

MM_{Oxygen} = 16 a.m.u.
$MM_{Nitrogen}$ = 14 a.m.u.
$MM_{Hydrogen}$ = 1 a.m.u.

MM H_2O = 18 g.mol^{-1}
MM NH_4^+ = 18 g.mol^{-1}

High Resolution

MM_{Oxygen} = 15.9994 a.m.u.
$MM_{Nitrogen}$ = 14.0067 a.m.u.
$MM_{Hydrogen}$ = 1.0079 a.m.u.

MM H_2O = 18.0152 g.mol^{-1}
MM NH_4^+ = 18.0384 g.mol^{-1}

Obtained data: Molecular Mass

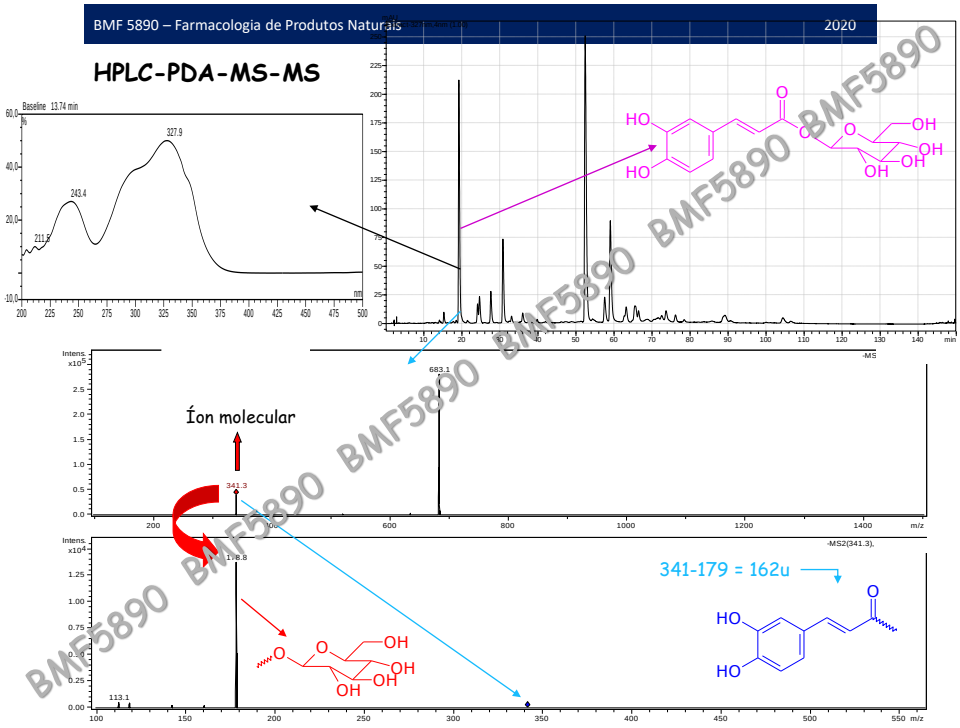
HYPHENATED TECHNIQUES IN METABOLOMIC APPROACHES

- Hyphenated technique is a combination or coupling of two different techniques with the help of proper interface.
- The term was introduced by Hirschfield (1980).
- The hyphenated technique is developed from the coupling of a separation technique and an online spectroscopic detection technology.

Examples:

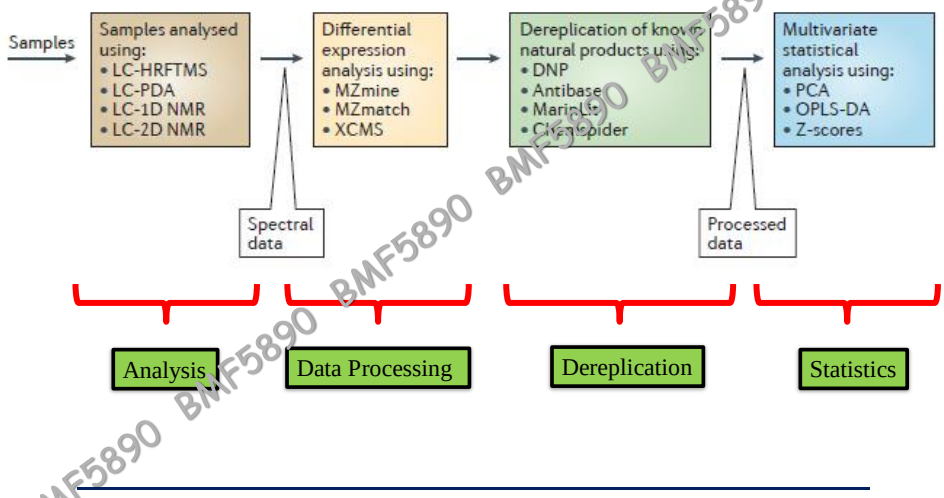
59

HPLC-PDA-MS-MS



60

Metabolomic studies – Work flowchart



61

Metabolomic studies – Work flowchart

- Data Processing

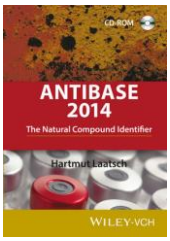
	Compound 1	Compound 2	Compound 3	Compound 4	Compound 5	Compound 6	Compound 7
row retention time	0.66	0.67	0.68	1.45	1.46	1.53	1.60
row m/z	218.09842	201.10237	204.08280	239.13658	249.12092	202.08458	243.13393
RKMT_176_ASW-Am_01.cdf peak area	0	0	0	0	0	0	0
RKMT_176_ASW-Am_02.cdf peak area	0	0	0	0	0	0	0
RKMT_176_BFM-11m_01.cdf peak area	0	0	0	0	0	408987.958	0
RKMT_176_BFM-11m_02.cdf peak area	0	0	0	0	0	390879.16	0
RKMT_176_BFM-1m_01.cdf peak area	0	0	0	0	0	0	0
RKMT_176_BFM-1m_02.cdf peak area	0	0	0	0	0	0	0
RKMT_176_BFM-2m_01.cdf peak area	0	0	0	0	0	0	0
RKMT_176_BFM-2m_02.cdf peak area	0	0	0	0	0	0	0
RKMT_176_BFM-3m_01.cdf peak area	0	349595.572	279225.725	0	0	2686404.16	0
RKMT_176_BFM-3m_02.cdf peak area	137704.533	366920.773	257520.333	252988.906	0	2994991.34	212050.828
RKMT_176_BFM-4m_01.cdf peak area	0	0	0	0	0	0	0
RKMT_176_BFM-4m_02.cdf peak area	0	0	0	0	0	0	0
RKMT_176_BFM-5m_01.cdf peak area	0	187033.675	233374.013	287729.615	0	2126167.22	0
RKMT_176_BFM-5m_02.cdf peak area	0	182821.874	230427.035	0	0	2173357.33	248352.875
RKMT_176_ISP3m_01.cdf peak area	0	0	0	0	0	0	0
RKMT_176_ISP3m_02.cdf peak area	0	0	0	0	0	0	0
RKMT_176_MB_01.cdf peak area	0	0	0	0	448014.57	0	0
RKMT_176_MB_02.cdf peak area	0	0	0	0	446484.049	0	0

62

Metabolomic studies – Work flowchart

- Dereplication Process

The Urine Metabolome database is a freely available electronic database containing detailed information about ~3100 small molecule metabolites found in human urine along with ~3900 concentration values.

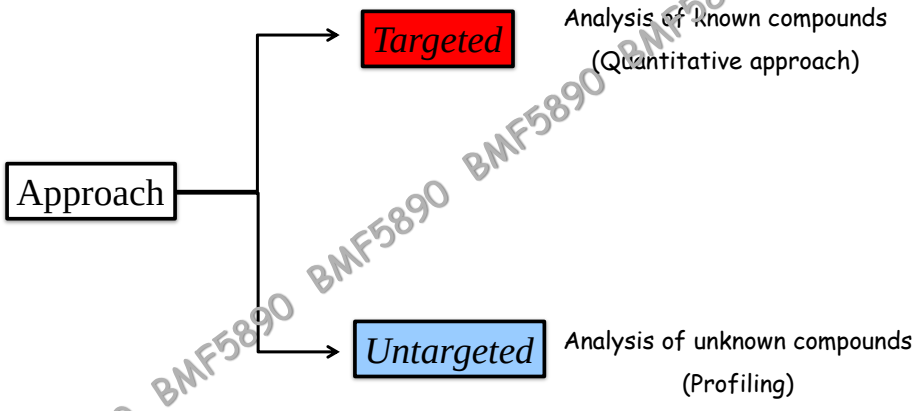


MarinLit
A database of the marine natural products literature

LIPID Metabolites and Pathways Strategy (LIPID MAPS®)
Lipidomics Gateway

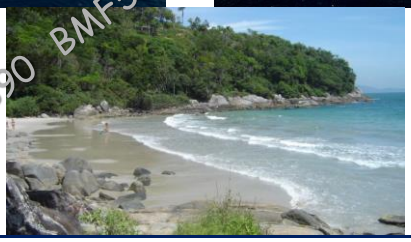
63

Metabolomic studies – Work flowchart



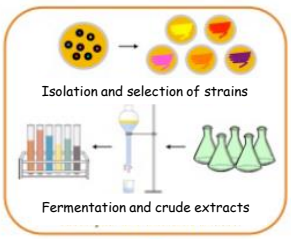
64

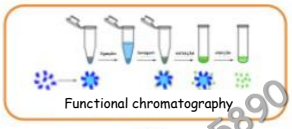
METABOLITES FROM MARINE MICROORGANISMS

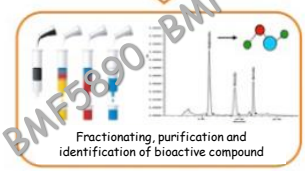


65

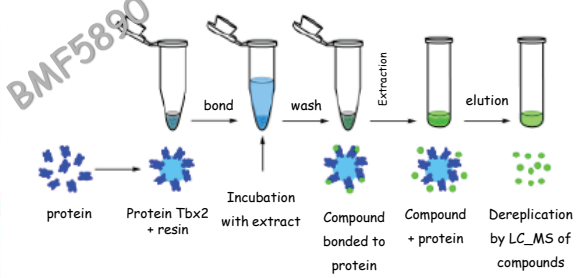
METABOLOMIC STUDIES – TARGET APPROACH







Araçá Beach São Sebastião - SP



66

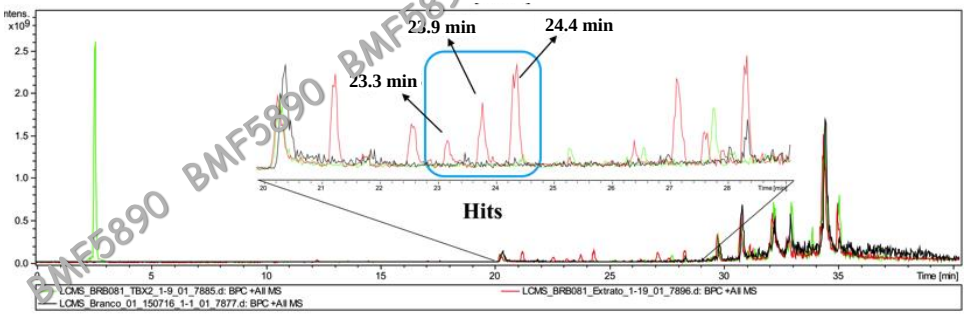
Araçá Beach
São Sebastião - SP

Metabolomic studies – Targeted approach

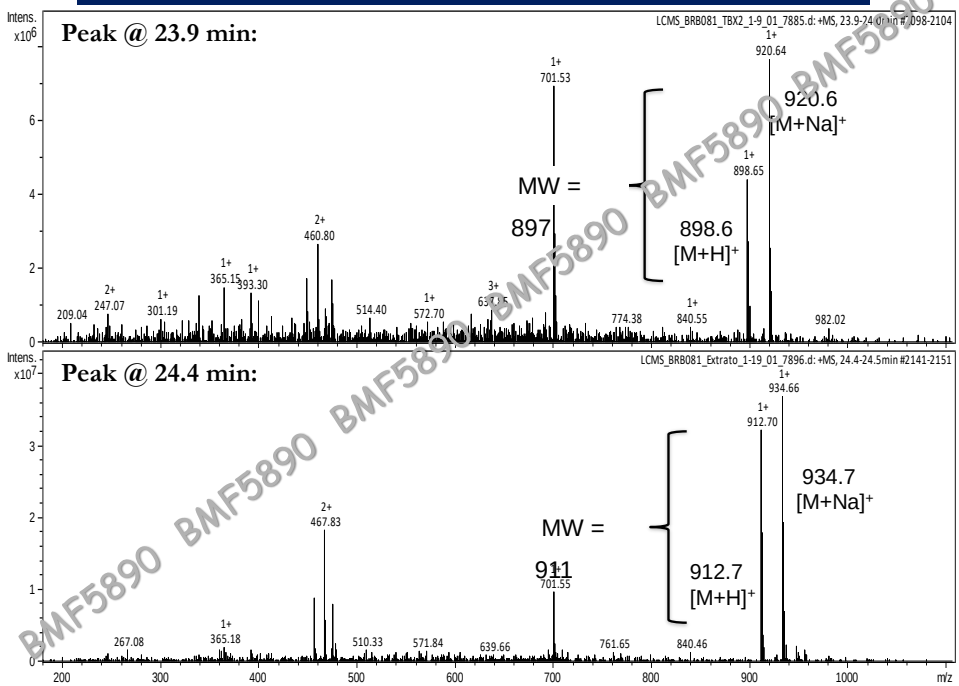
BRB-081

Functional chromatography

- Protein control
- Crude extract (pre-FC)
- Extract (post-FC)



67

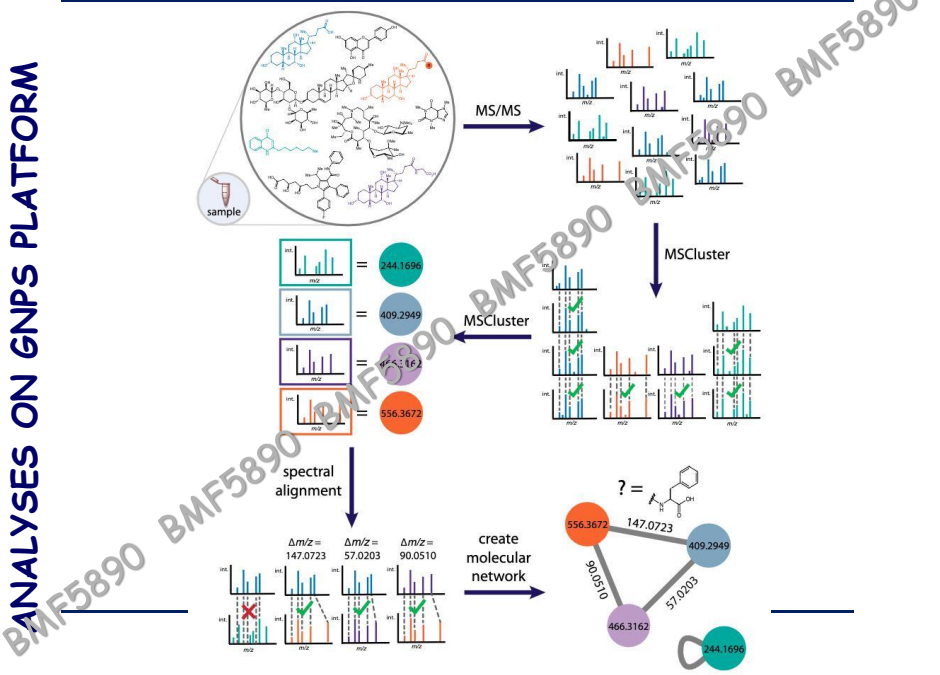


68

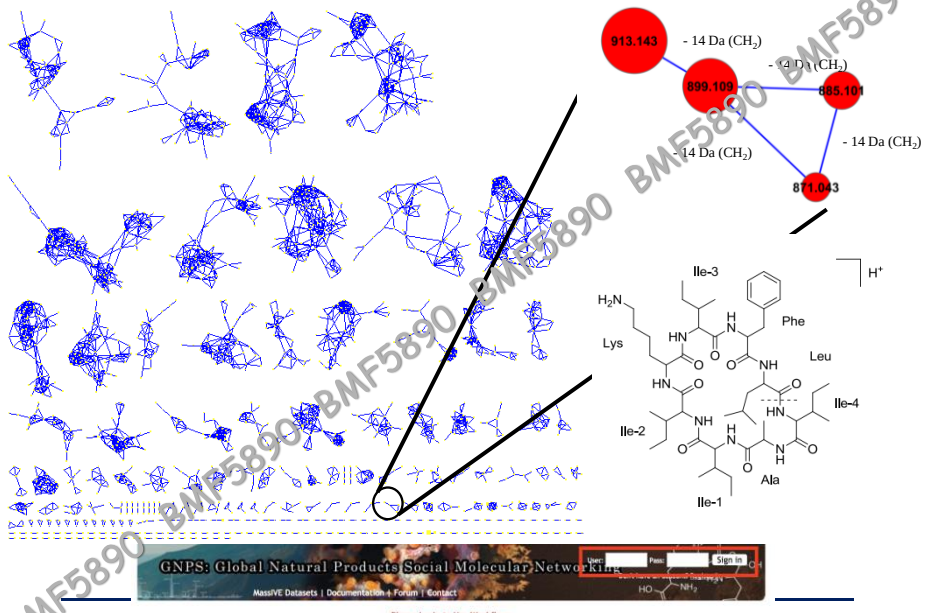
ANALYSES ON GNPS PLATFORM

69

ANALYSES ON GNPS PLATFORM



70



The Future of Natural Products Research and Mass Spectrometry

71

BRB-081

Mass-guided Fractionation

Araçá Beach

BRB-081 (2L) – A1
1.40 g

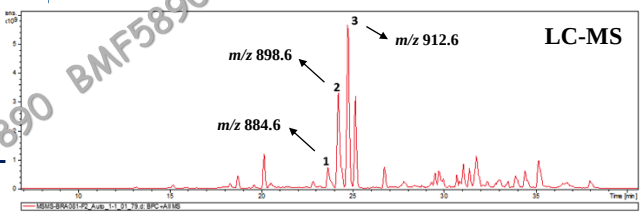
BRB-081 Hex
0.51 g

BRB-081 $CHCl_3$
0.47 g

BRB-081 MeOH
0.42 g

Sephadex LH-20

C1 C2 C3 C4 C5 C6 C7 C8 C9 C10 C11



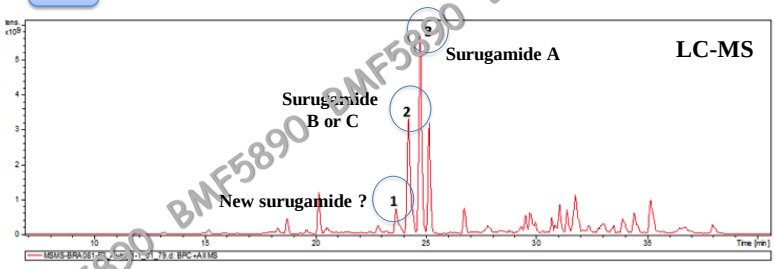
72

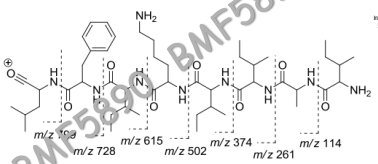
BRB-081

Mass-guided Fractionation

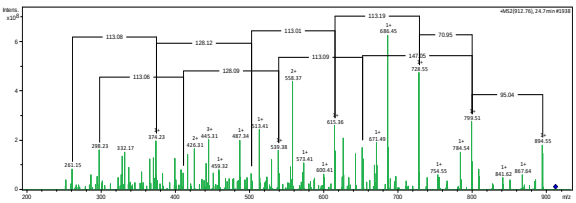
Araçá Beach

C2





Surugamide A



73

BRB-081

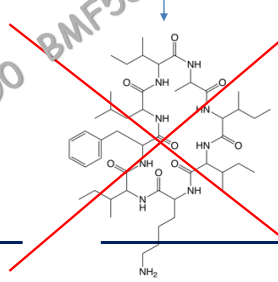
Araçá Beach

BRB-081 (20L)
7.40 g

BRB-081 Hex
2.91 g

BRB-081 $CHCl_3$
2.17 g

BRB-081 MeOH
2.32 g



74

BRB-081- *Streptomyces* sp.

Where are surugamides ?

... and the challenge goes on .....

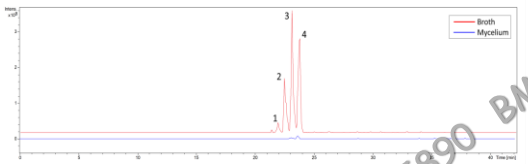
OSMAC approach : One Strain Many Compounds

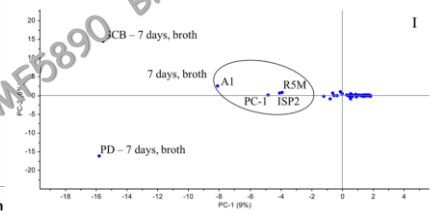
75

BRB-081- *Streptomyces* sp.

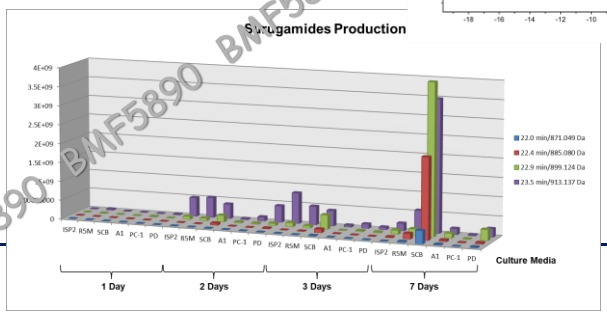
OSMAC approach

Araçá Beach



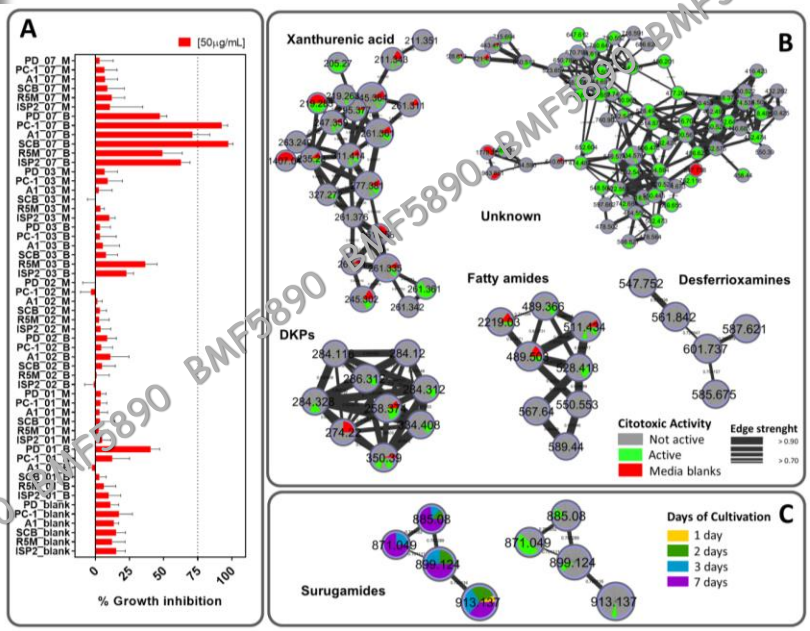


Surugamides Production



76

BRB-081
Streptomyces sp.



77

Metabolomic studies – Untargeted approach

Atol das Rocas – Brazil
Bacteria

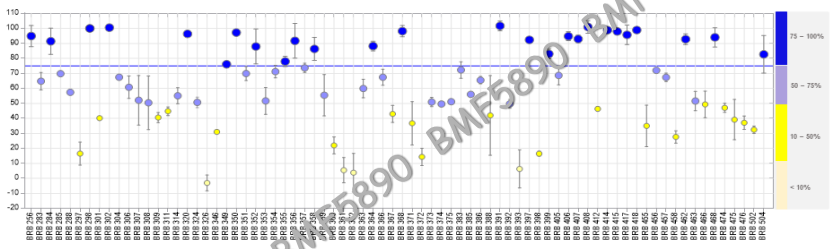
78

Article

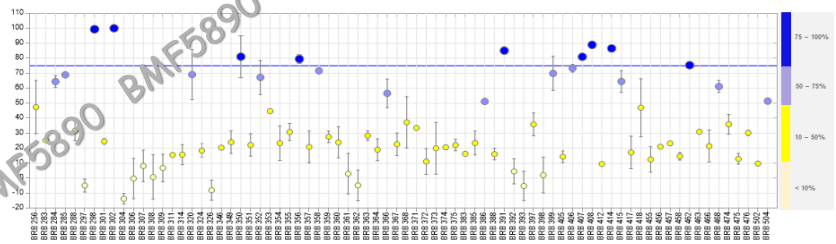
Marine Bacteria from Rocas Atoll as a Rich Source of Pharmacologically Active Compounds

Mar. Drugs **2019**, *17*, 671; doi:10.3390/md17120671

a) 50 µg/mL



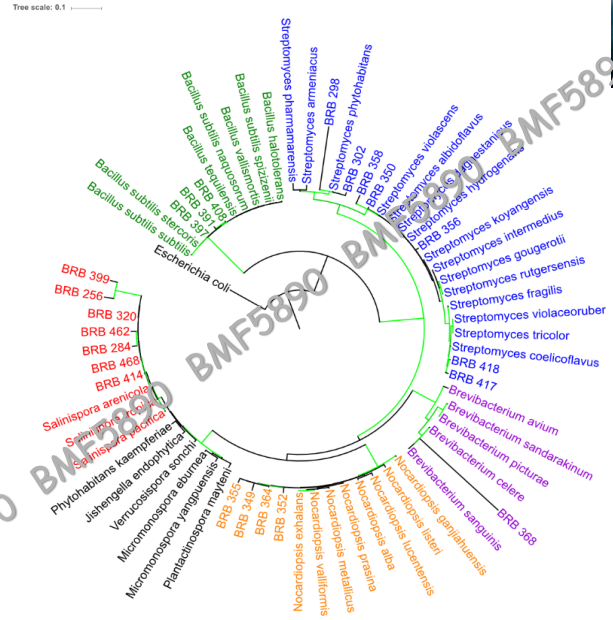
b) 5 µg/mL



79

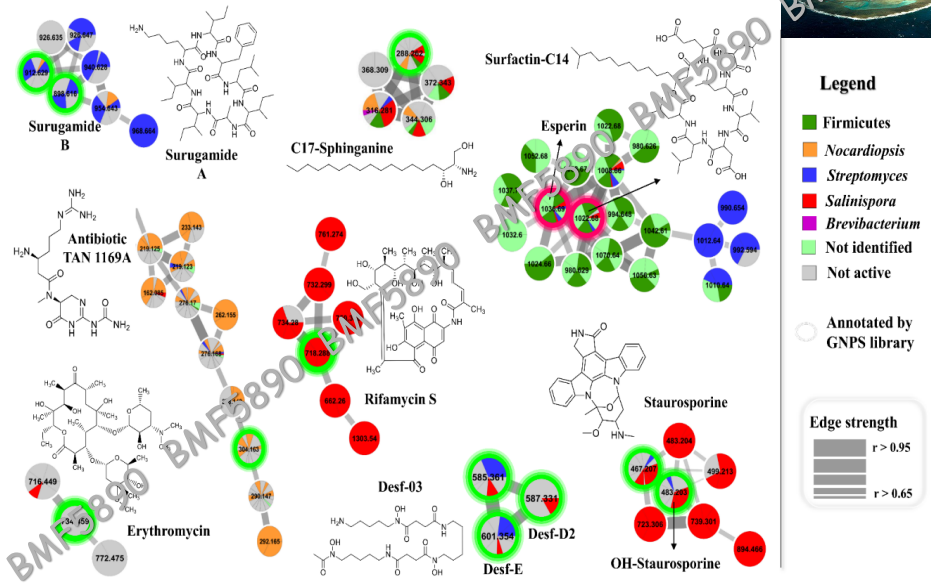
Marine bacteria from Rocas Atoll

Cytotoxic crude extracts



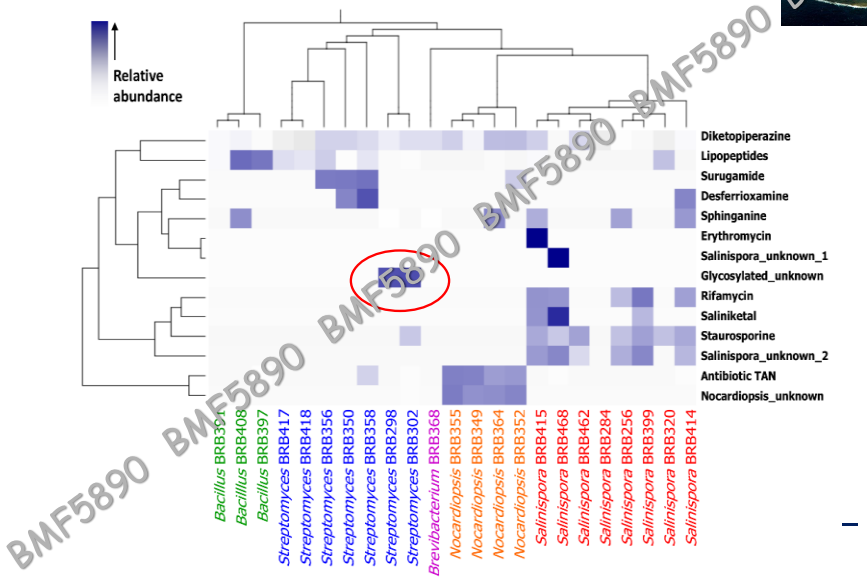
80

MOLECULAR NETWORKING OF MARINE BACTERIA FROM ROCAS ATOLL

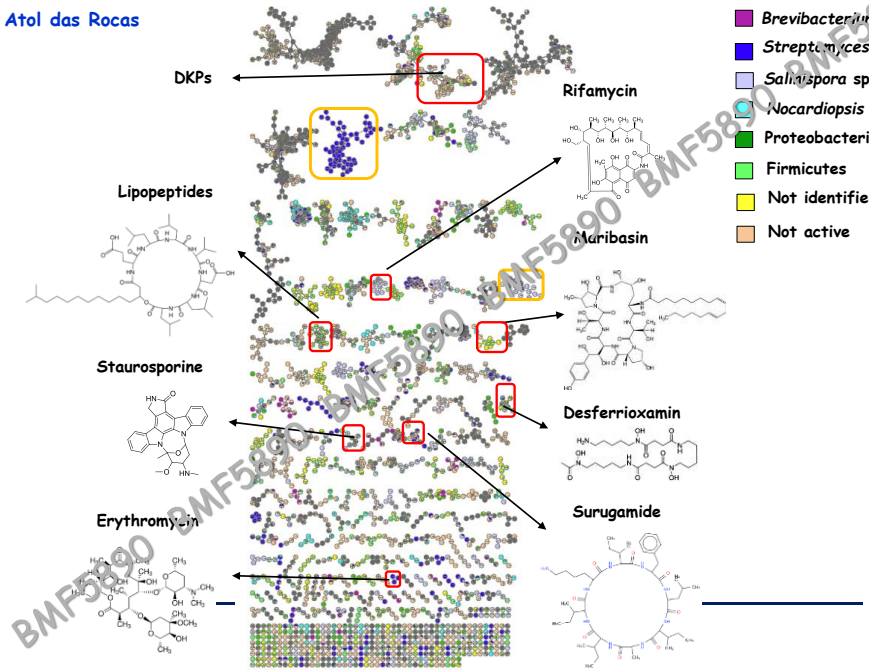


81

CHEMICAL CLASSES FOUND IN ACTIVE EXTRACTS OF MARINE BACTERIA FROM ROCAS ATOLL

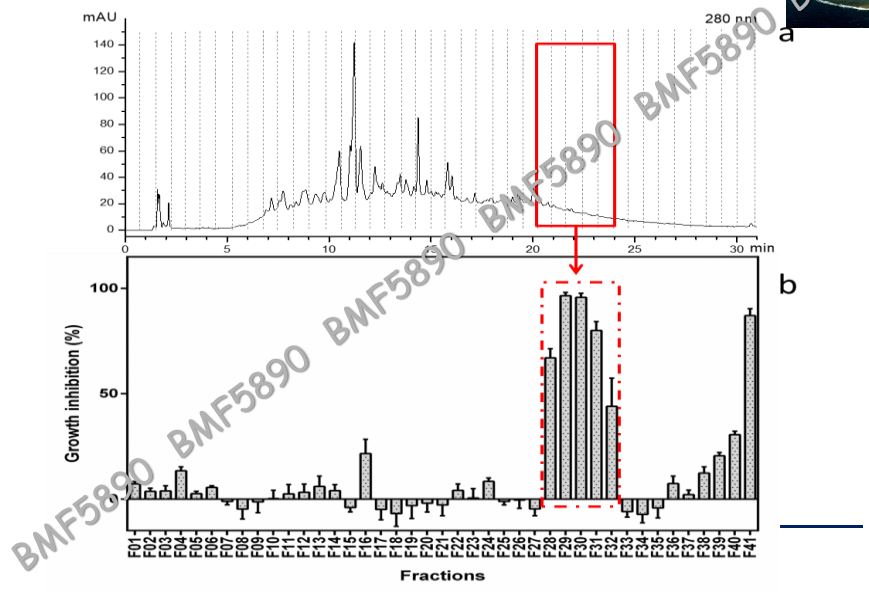


82



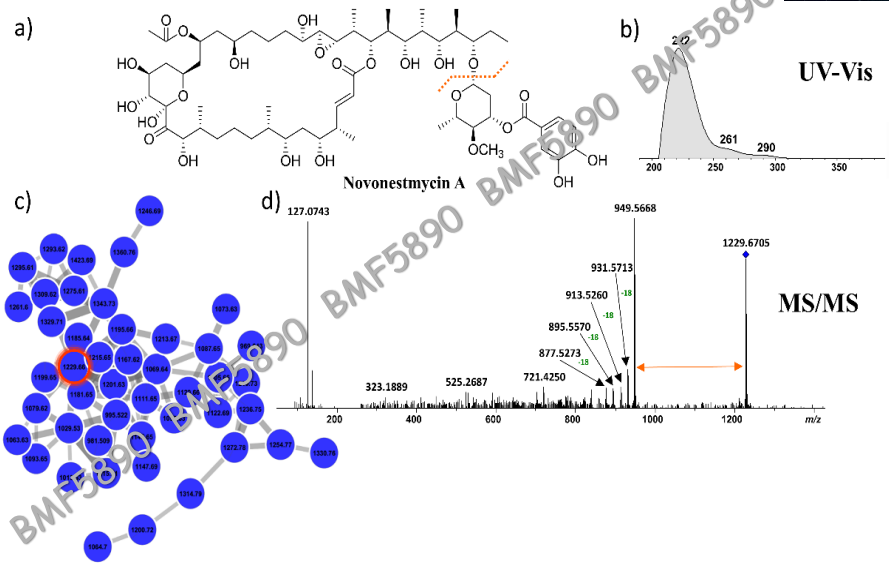
83

CHROMATOGRAPHIC FRACTIONATION OF *Streptomyces* sp. (BRB-302) FROM ROCAS ATOLL



84

IDENTIFICATION OF COMPOUNDS – *Streptomyces* sp. (BRB-302)



85

- ✓ Ambas as abordagens (targeted or untargeted) permitem obter o componente bioativo
- ✓ Estratégia pode ser aplicada a qualquer extrato, oriundo de um organismo
- ✓ Permite guiar o isolamento por atividade biológica e/ou por novos componentes

Dúvidas ????

Obrigado pela atenção !!!

86