

Cover Picture



Many diseases are still neglected: not only genetic diseases, but especially infectious ones, caused by parasites, microbes and viruses. They are often concentrated in the tropical regions. In a world in which the mobility of individuals has greatly increased the probability of a local outbreak becoming a major global disease, countries like Brazil have both a unique opportunity and a unique responsibility. Thus, this issue becomes peculiar and special to the scientific community, both Brazilian and international.

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Editorial

- 1755 The beginning: global responsibility in healthcare - with a focus on tropical disease
George M. Whitesides

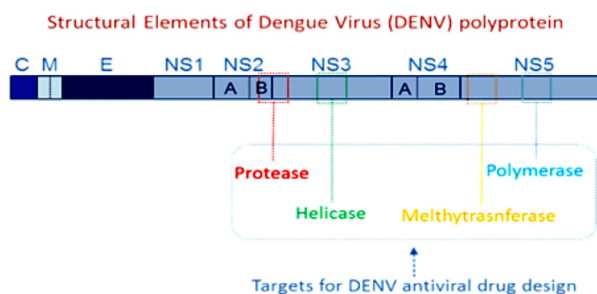
Reviews

1759 NS3 and NS5 Proteins: Important Targets for Anti-Dengue Drug Design

André S. de Oliveira, Milene L. da Silva, Ana Flávia C. S. Oliveira, Cynthia C. da Silva, Róbson R. Teixeira and Sérgio O. De Paula

Graphical Abstract

Dengue virus enzymes are important targets for antiviral drug design

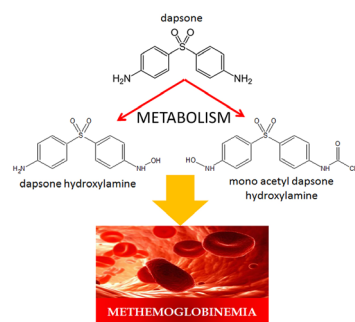


1770 Clinical Applications and Methemoglobinemia Induced by Dapsone

Fábio R. Oliveira, Mariely C. Pessoa, Rosyana F. V. Albuquerque, Taysa R. Schalcher and Marta C. Monteiro

Graphical Abstract

This review summarizes the chemical structure of dapsone, a drug used mainly in the treatment of leprosy and dermatitis, and its metabolism leads to the formation of toxic metabolites that cause adverse reactions, such as methemoglobinemia, which occurs because of the inability of methemoglobin to bind oxygen, causing a state of functional anemia

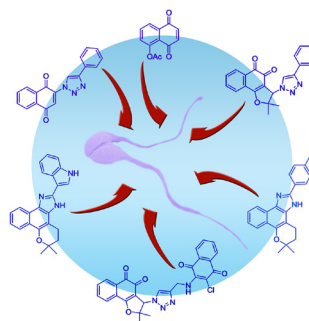


1780 Anti-*Trypanosoma cruzi* Compounds: Our Contribution for the Evaluation and Insights on the Mode of Action of Naphthoquinones and Derivatives

Eufrânio N. da Silva Júnior, Guilherme A. M. Jardim, Rubem F. S. Menna-Barreto and Solange L. de Castro

Graphical Abstract

The present review describes the synthesis of naphthoquinoidal compounds and their derivatives, their activities and mechanisms of action against *Trypanosoma cruzi*, the causative agent of Chagas disease

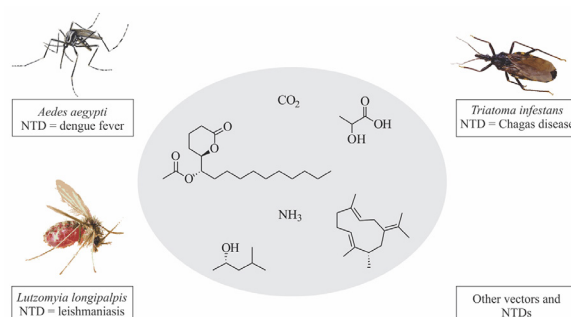


1799 Control of Neglected Disease Insect Vectors: Future Prospects for the Use of Tools Based on Behavior Manipulation-Interference

Marcelo G. Lorenzo, Diogo M. Vidal and Paulo H. G. Zarbin

Graphical Abstract

The present review describes avenues recently explored for the search of behavior modifying compounds by means of high throughput methodologies. Specifically, examples of how such methodologies mediate the search for new repellents and attractants are described

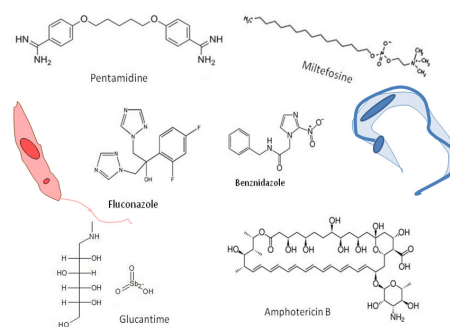


1810 Leishmaniasis and Chagas Disease Chemotherapy: a Critical Review

Izaltina Silva-Jardim, Otavio H. Thiemann and
Fernanda F. Anibal

Graphical Abstract

The main form of treatment for leishmaniasis and Chagas disease is still chemotherapy. There is no effective vaccine available and the search for new drugs is a priority. This review outlines the current understanding of different drugs against leishmaniasis and Chagas disease and the search for new drugs



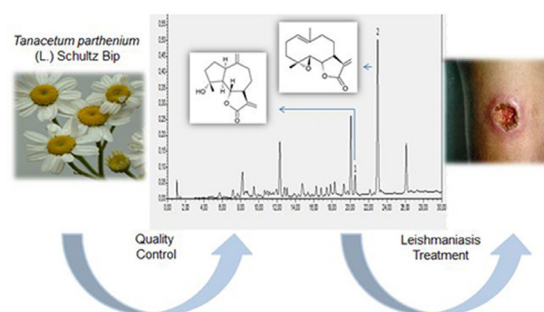
Articles

1824 Development and Validation of a Method for Simultaneous Determination of Bioactive Compounds of *Tanacetum parthenium* (L.) Schultz-Bip

Mirela F. Rabito, Mariana B. Almeida, Amanda L. Moreira,
Amadeu H. Iglesias, Fernando de Paula, Bruna P. da Silva,
Diógenes A. Cortez, Suzana L. Nixdorf and
Izabel C. P. Ferreira

Graphical Abstract

This study aimed to develop and validate a liquid chromatographic method for simultaneous determination of two sesquiterpene lactones from *Tanacetum parthenium*. A potential tool for quality control of this medicinal plant with *in vitro* and *in vivo* antileishmaniasis activities

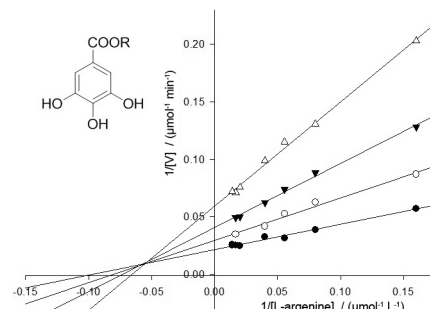


1832 Leishmanicidal Galloylquinic Acids are Noncompetitive Inhibitors of Arginase

Lorena R. F. de Sousa, Suelem D. Ramalho, João B. Fernandes,
Maria Fátima das G. F. da Silva, Mônica R. da C. Iemma,
Caroindes J. Corrêa, Dulce H. F. de Souza, Maria I. S. Lima
and Paulo C. Vieira

Graphical Abstract

Leishmanicidal galloylquinic acids from *B. coccolobifolia* showed as novel noncompetitive and mixed inhibitors of arginase from *L. amazonensis*

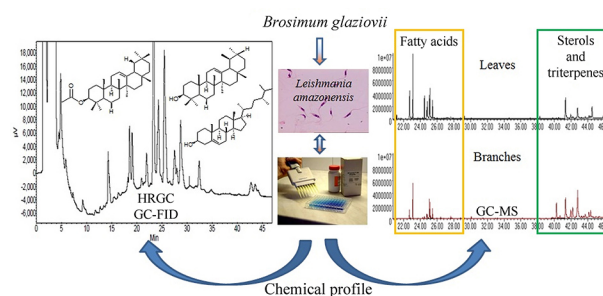


1839 Leishmanicidal Activity of *Brosimum glaziovii* (Moraceae) and Chemical Composition of the Bioactive Fractions by Using High-Resolution Gas Chromatography and GC-MS

Aline Coqueiro, Luis O. Regasini, Gabriel M. Leme,
Luciana Polese, Camila T. Nogueira, Mayara L. Del Cistia,
Marcia A. S. Graminha and Vanderlan da S. Bolzani

Graphical Abstract

Chemical composition of the hexane fractions from the leaves and branches of *B. glaziovii* that exhibited activity in the leishmanicidal tests as evaluated by high-resolution gas chromatography (HRGC) and GC-MS



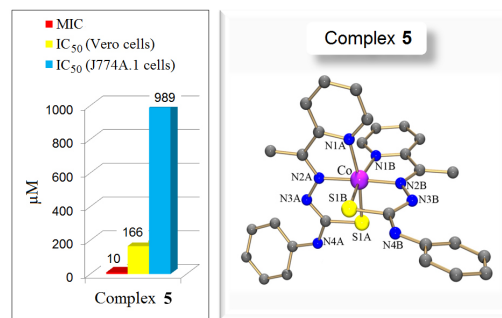
1848 Cobalt(III) Complexes with Thiosemicarbazones as Potential anti-*Mycobacterium tuberculosis* Agents

Carolina G. Oliveira, Pedro Ivo da S. Maia, Marcelo Miyata, Fernando R. Pavan, Clarice Q. F. Leite, Eduardo Tonon de Almeida and Victor M. Defflon

SI online

Graphical Abstract

Co^{III} complexes with a family of thiosemicarbazones were evaluated for their anti-*Mycobacterium tuberculosis* effect. Complex 5 exhibited good activity with high selectivity index

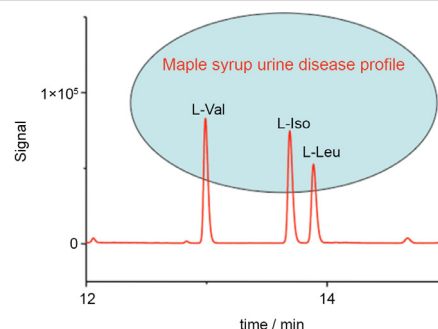


1857 Potential Diagnostic of Branched-Chain Ketoaciduria by HPLC-DAD

Maíra Magalhães Trintinalia, Atecla Nunciata Lopes Alves, Lilian Fernandes, Etelvino Jose Henriques Bechara and Nilson Antonio Assunção

Graphical Abstract

HPLC profile of three amino acids representative of the biochemical alterations found in maple syrup urine disease, a metabolic disorder



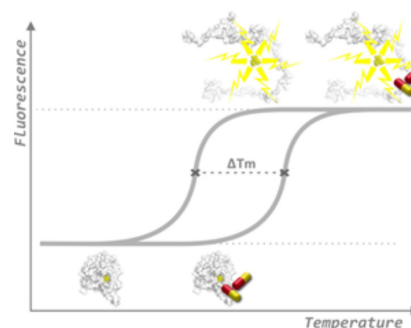
1864 ThermoFMN - A ThermoFluor Assay Developed for Ligand-Screening as an Alternative Strategy for Drug Discovery

Ricardo A. P. Pádua, Giovanni P. Tomaleri, Renata A. G. Reis, Juliana S. David, Valeria C. Silva, Matheus P. Pinheiro and Maria Cristina Nonato

SI online

Graphical Abstract

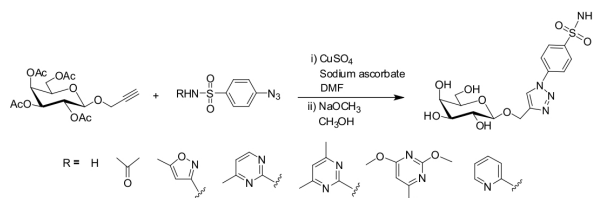
Monitoring of flavin mononucleotide fluorescence when exposed to solvent upon protein unfolding was used to determine flavoprotein melting temperature (T_m). Interaction of ligands to flavoproteins induces a shift in T_m and this phenomenon can be used on the screening of compounds as a tool for hit identification during the process of drug development



1872 Synthesis and *in vitro* Evaluation of Novel Galactosyl-triazolo-benzenesulfonamides Against *Trypanosoma cruzi*

Getúlio G. Junqueira, Marcelo R. Carvalho, Peterson de Andrade, Carla D. Lopes, Zumira A. Carneiro, Renata Sesti-Costa, João S. Silva and Ivone Carvalho

SI online



Graphical Abstract

Synthesis of galactose-containing triazol-arylsulfonamides and evaluation of *Trypanosoma cruzi* trans-sialidase inhibition, antitrypanosomal and cytotoxicity activities

1885 The Semisynthetic Landscape of Aphidicolin: Inspiration Towards Leishmanicidal Compounds

SI online  **Gabriela B. Santos, Marília O. Almeida, Iara A. Cardoso, Viviane Manfrim, Fernanda O. Chagas, Juliano S. Toledo, Camila C. Pinzan, Alexandre Suman de Araujo, Angela K. Cruz, Monica T. Pupo and Flavio S. Emery**

Graphical Abstract

Preliminary evaluation demonstrated high leishmanicidal activity for aphidicolin and a new oxime derivative with selectivity for the *L. braziliensis* species

N. sphaerica

2

1

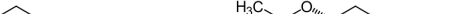
FGI

1900 Antimalarial Activity of Piperidine Alkaloids from *Senna spectabilis* and Semisynthetic Derivatives

 **ISI** *Specials and Semisynthetic Derivatives*
 Marcos Pivatto, Luciene R. Baccini, Abhinay Sharma,
 Myna Nakabashi, Amanda Danuello, Claudio Viegas Júnior,
 Celia R. S. Garcia and Vanderlan S. Bolzani
 **ISI** *SI online*

Graphical Abstract

Piperidine alkaloids (-)-cassine and (-)-spectaline isolated from the flowers of *Senna spectabilis* and semisynthetic derivatives (-)-3-*O*-acetylcassine and (-)-3-*O*-acetylspectaline were assessed for their antimalarial inhibitory activity by means of flow cytometry screening assay.



(-)-Cassine n = 7
 (-)-Spectaline n = 9

(-)-3-O-Acetylcassine n = 7
 (-)-3-O-Acetylspectaline n = 9

1907 Application of the Negishi Reaction in the Synthesis of Thiophene-Based Lignans Analogues with Leishmanicidal Effects

SI online *Mônica F. Z. J. Amaral, Daniel R. Callejon, Thalita B. Riul, Marcelo D. Baruffi, Fabiano T. Toledo, Norberto P. Lopes and Giuliano C. Clossoski*

Graphical Abstract

Thiophene derivatives obtained by Negishi reaction induced cell death on *Leishmania braziliensis* without inducing toxicity on macrophage

The figure illustrates the synthesis and application of thienothiopyran derivatives. On the left, a chemical reaction scheme shows the Negishi reaction of thiophene (a five-membered ring with one sulfur atom) under microwave (MW) irradiation to produce a substituted thiophene with two aryl groups, Ar and Ar', attached to the 2 and 5 positions. The Ar group is colored green and the Ar' group is colored blue. Two arrows branch from the product to two panels on the right. The top panel shows a microscopic view of *Leishmania brasiliensis* parasites, which are elongated, flagellated organisms. The bottom panel shows a microscopic view of macrophages, which are larger, more rounded cells. Both panels show the thienothiopyran derivatives (represented by small chemical structures) interacting with the organisms.

1914 Inborn Errors of Metabolism, an Important Group of Orphan Neglected Diseases: Investigation of 8,000 Patients in Rio de Janeiro, Brazil

*Fernanda B. Scalco, Maria Lúcia C. Oliveira, Ruth E. Simoni
and Francisco R. Aquino Neto*

Graphical Abstract

The survey presents the results obtained after diagnostic investigation of inborn errors of metabolism (IEM) in 8,000 patients from the state of Rio de Janeiro by qualitative and quantitative methods and the distribution of the diagnosed case

Diagnosed cases / %

- Lysosomal storage disease (LSD)
- Amino acid metabolism
- Organic acid metabolism
- Carbohydrate metabolism
- Transport defects
- Other (Smith-Lemli-Opitz syndrome, Lowe syndrome, vitamin E deficiency)

45.1

22.8

9.2

8.6

8.1

8.1

100 cases

1918 Bioanalytical Studies of Porphyrinic Disorders Using HPLC with Fluorescence Detection

Michele G. S. C. Cypriani, Atecla N. L. Alves,
Etelvino J. H. Bechara and Nilson A. Assunção

Graphical Abstract

High-performance liquid chromatography (HPLC)/fluorescence detection of porphyrins in a standard mixture of six porphyrinogens (black trace) and in the urine of a symptomatic carrier of acute intermittent porphyria (or porphyria cutanea tarda) (red trace). The excitation and emission wavelengths used were 400 and 620 nm, respectively

