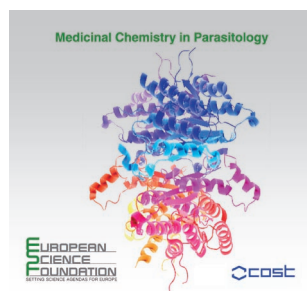


## COVER PICTURE



The cover picture shows the structure of the *Leishmania major* pteridine reductase, which is part of the folate biosynthesis pathway in this parasite. It is a parasite-specific co-target for the treatment of leishmaniasis. For details on other specific targets for the treatment of parasitic diseases, please refer to the articles in this issue that discuss research results pertinent to the *Medicinal Chemistry in Parasitology* meeting held last year in Modena, Italy under the COST action B22, which is focused on target identification and drug development for parasitic diseases; these articles are marked with the COST logo.

## NEWS

Spotlights on our sister journals

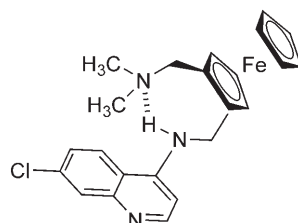
380 – 381

## MINIREVIEWS

D. Dive, C. Biot\*

383 – 391

**Ferrocene Conjugates of Chloroquine and other Antimalarials: the Development of Ferroquine, a New Antimalarial**



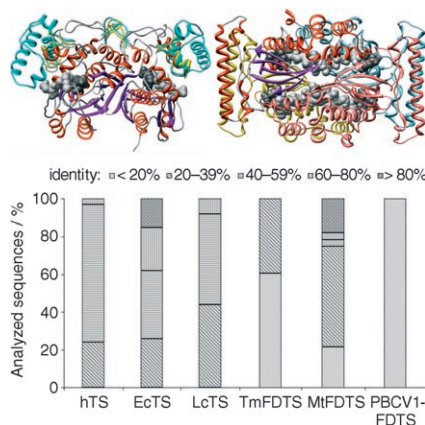
A convenient approach to antimalarial drug discovery is the use of the organic scaffold of a known antimalarial drug and an organometallic moiety to alter its unwanted properties and/or to optimize its initial effects. This minireview focuses mainly on the discovery of ferroquine, which has emerged from a collaborative French discovery project, and efforts to understand its mechanism of action and resistance.

S. Ferrari,\* V. Losasso, M. P. Costi\*

392 – 401

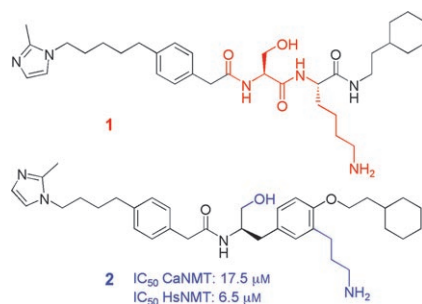


**Sequence-Based Identification of Specific Drug Target Regions in the Thymidylate Synthase Enzyme Family**



**Thymidylate synthases from pathogenic organisms:** Sequence analysis and knowledge-based grouping have provided a step forward in the identification of potential drug target regions in thymidylate synthases. This provides a unique approach toward blocking the growth of pathogenic organisms.

**Parasite specific:** The inhibition of myristoyl-CoA:protein *N*-myristoyltransferase (NMT) can lead to parasite death in culture. Herein we review recent work that supports the suitability of NMT as a parasite-specific drug target. The example shown illustrates the peptidomimetic compound **2**, which is more stable, yet retains the Ser and Lys functional groups of compound **1** that are necessary for NMT inhibition.



*P. W. Bowyer, E. W. Tate,  
R. J. Leatherbarrow, A. A. Holder,  
D. F. Smith, K. A. Brown\**

402 – 408

***N*-Myristoyltransferase: a Prospective Drug Target for Protozoan Parasites**



## CONFERENCE REPORTS

**Medicinal Chemistry in Parasitology: New Avenues in Drug Discovery**

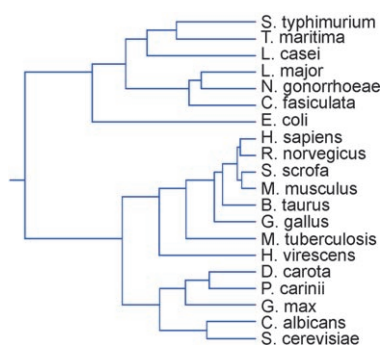
*A. Tait\**

409 – 411



## COMMUNICATIONS

**Predicting proteins.** PIPSA (Protein Interaction Property Similarity Analysis) provides a means to detect similarities and differences in the interaction fields of structurally related proteins and can therefore assist in identification of regions of proteins to target for selective ligand design. Herein, this is illustrated by application of PIPSA to dihydrofolate reductase, an important drug target.



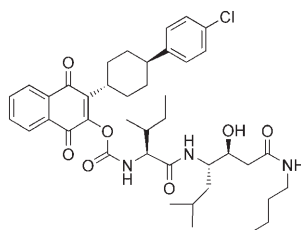
*S. Henrich,\* S. Richter, R. C. Wade\**

413 – 417

**On the use of PIPSA to Guide Target-Selective Drug Design**



**Combining chemicals.** Malaria is one of the most widespread parasitic infections in the world, however, the unavailability of a vaccine and the spread and intensification of drug resistance over the past 15–20 years have led to a dramatic decline in the efficacy of the most affordable antimalarial drugs. Herein, the development of “double-drugs” to tackle inhibition of *P. falciparum* growth is discussed.



*S. Romeo,\* S. Parapini, M. Dell'Agli,  
N. Vaiana, P. Magrone, G. Galli,  
A. Sparatore, D. Taramelli, E. Bosisio*

418 – 420

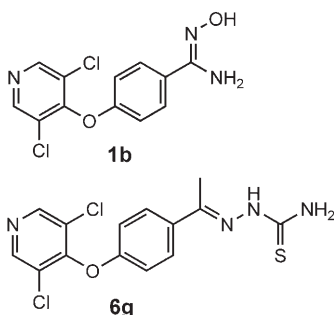
**Atovaquone-Statine “Double-Drugs” with High Antiplasmodial Activity**



T. Rossi, A. Coppi, E. Bruni, M. Sgobba,  
G. Degliesposti, G. Rastelli\*

421 – 424

## In vitro Effects of *Plasmodium falciparum* Dihydrofolate Reductase Inhibitors on Normal and Cancer Cell Proliferation

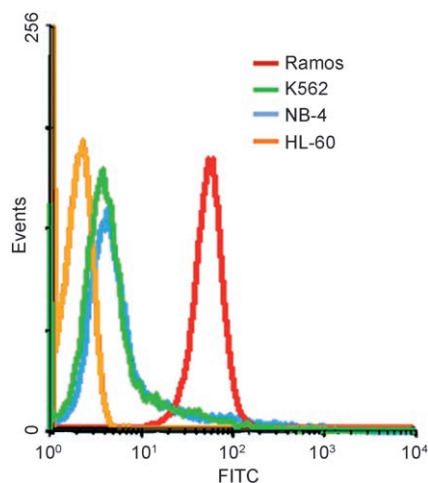


**Toxicological evaluations** were performed on two novel *Plasmodium falciparum* dihydrofolate reductase inhibitors and other known antimalarial drugs. Cytotoxicity tests were performed on Vero and MCF-7 cells and apoptotic and/or proliferative markers p21 and p53 and A, B1, D1, and D2 cyclins. The results are discussed and show that this molecule can be considered an interesting new candidate for further development.

P. Mallikaratchy, Z. Tang, W. Tan\*

425 – 428

## Cell Specific Aptamer-Photosensitizer Conjugates as a Molecular Tool in Photodynamic Therapy



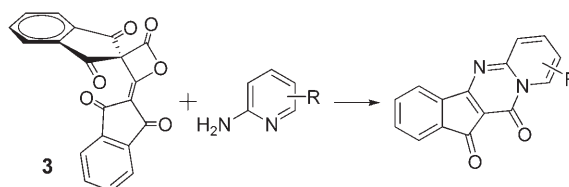
### Photodynamic therapy for tumors.

This paper describes the application of a molecular construct of a photosensitizer and an aptamer for phototherapeutically targeting tumor cells. Coupled with the advantages of the cell-SELEX in generating multiple effective aptamers for diseased cell recognition, we will be able to develop highly efficient photosensitizer-based therapeutic reagents for clinical applications.

M. Tsanakopoulou, T. Cottin, A. Büttner,  
V. Sarli, E. Malamidou-Xenikaki,\*  
S. Spyridis,\* A. Giannis\*

429 – 433

## Indeno[1,2-d]pyrido[1,2-a]pyrimidines: A New Class of Receptor Tyrosine Kinase Inhibitors



**Indanedione ketene dimer 3**, obtained in quantitative yield from the thermal decomposition of the phenyliodonium ylide of 2-hydroxy-1,4-naphthoquinone, reacts readily with 2-aminopyridines

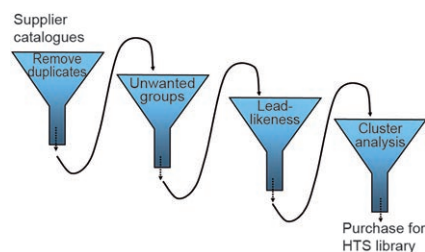
and 2-aminopyrimidines to afford the title compounds. They represent a new class of cell-permeable inhibitors for receptor tyrosine kinases implicated in angiogenesis and cancer cell proliferation.

## FULL PAPERS

R. Brenk,\* A. Schipani, D. James,  
A. Krasowski, I. H. Gilbert, J. Frearson,  
P. G. Wyatt

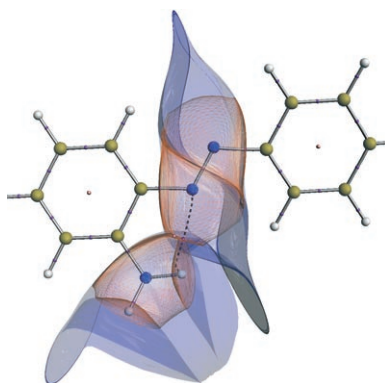
435 – 444

## Lessons Learnt from Assembling Screening Libraries for Drug Discovery for Neglected Diseases



**Drug discovery on a low budget:** To enable a drug discovery operation for neglected diseases, a small but diverse high-throughput library was assembled. The selected compounds span a broad range of lead-like space, show a high degree of structural integrity and purity, and demonstrate appropriate solubility for the purposes of biochemical screening.

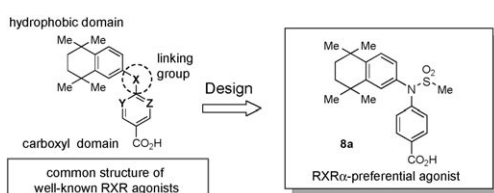
**Using QCT for drug design.** A newly developed method to calculate the polar surface areas based on quantum chemical topology is described and the results compared with standard methods. Differences between methods showed how the calculation of the PSA depends on the method used, and therefore, judicious application of the upper limits used in the prediction of oral bioavailability is warranted.



*I. Bytheway,\* M. G. Darley,  
P. L. A. Popelier\**

445 – 453

**The Calculation of Polar Surface Area from First Principles: An Application of Quantum Chemical Topology to Drug Design**



**Improving RXR subtype specificity.** Although RXR agonists are interesting candidates for the treatment of cancers or obesity, they possess a strong lipophilic character and no subtype selectivity. In this study, we aimed to produce

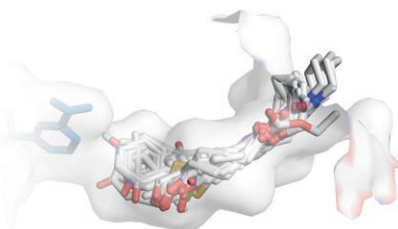
less-lipophilic and subtype-selective RXR agonists. Our results indicated that the reduction of lipophilicity at the hydrophobic-interaction region of RXR agonists enables production of RXR subtype preference.

*K. Takamatsu, A. Takano, N. Yakushiji,  
K.-i. Morishita, N. Matsuura,  
M. Makishima, H. I. Ali, E. Akaho, A. Tai,  
K. Sasaki, H. Kakuta\**

454 – 460

**Reduction of Lipophilicity at the Lipophilic Domain of RXR Agonists Enables Production of Subtype Preference: RXRα-Preferential Agonist Possessing a Sulfonamide Moiety**

**The binding of 17β-HSD1 inhibitors** based on a thieno[2,3-*d*]pyrimidin-4(3*H*)-one core was studied using molecular dynamics simulations and ligand–protein docking. The alignment and biological activities were employed to generate a 3D QSAR model with good predictive power.

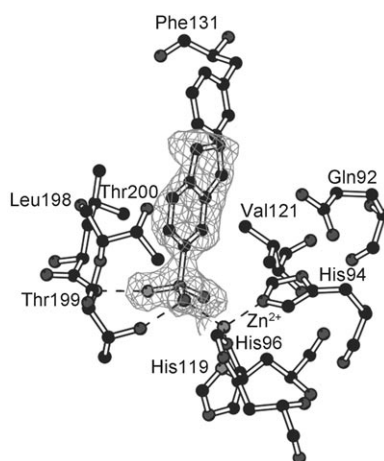


*S. Karkola, A. Lilienkampf, K. Wähälä\**

461 – 472

**A 3D QSAR Model of 17β-HSD1 Inhibitors Based on a Thieno[2,3-*d*]pyrimidin-4(3*H*)-one Core Applying Molecular Dynamics Simulations and Ligand–Protein Docking**

**An X-ray crystallographic study** of the adducts of two indanesulfonamide derivatives with human Carbonic Anhydrase II is reported. These studies suggest that the introduction of bulky moieties on the indane-sulfonamide scaffold may represent a powerful strategy to induce a desired physicochemical property to an aromatic sulfonamide scaffold or to obtain inhibitors with diverse inhibition profiles and selectivity for various mammalian CAs.



*K. D'Ambrosio, B. Masereel, A. Thiry,  
A. Scozzafava, C. T. Supuran,\*  
G. De Simone\**

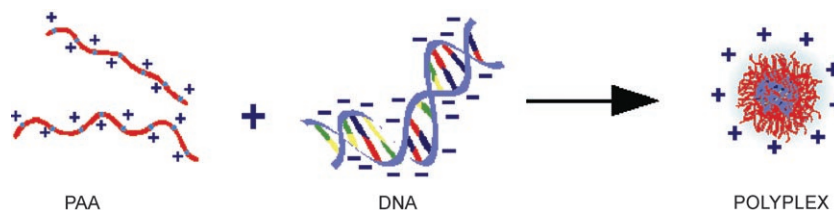
473 – 477

**Carbonic Anhydrase Inhibitors: Binding of Indanesulfonamides to the Human Isoform II**

M. A. Mateos-Timoneda, M. C. Lok,  
W. E. Hennink, J. Feijen, J. F. J. Engbersen\*

478 – 486

## Poly(amido amine)s as Gene Delivery Vectors: Effects of Quaternary Nicotinamide Moieties in the Side Chains



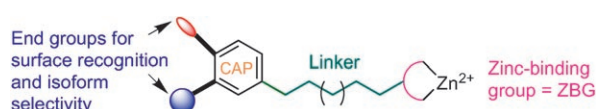
**Developing gene delivery vectors.** A novel class of poly(amido amine)s with pendant quaternary nicotinamide groups were synthesized and evaluated as gene delivery vectors. The quaternary nicotinamide groups in the polymer

promote the formation of small and stable nanoparticles with DNA by both electrostatic and intercalate interactions and lead to increased transfection efficiencies.

A. P. Kozikowski,\* Y. Chen, A. M. Gaysin,  
D. N. Savoy, D. D. Billadeau, K. H. Kim

487 – 501

## Chemistry, Biology, and QSAR Studies of Substituted Biaryl Hydroxamates and Mercaptoacetamides as HDAC Inhibitors—Nanomolar-Potency Inhibitors of Pancreatic Cancer Cell Growth



**Isoform selectivity:** structurally unique HDAC inhibitors are equipped with an amino acid residue that serves as a potential isoform-differentiating, surface-recognition element. The surface-recog-

nition group is connected through the usual carbon linker to either a hydroxamate or a mercaptoacetamide group that chelates the catalytic site zinc ion.

Supporting information on the WWW (see article for access details).

A video clip is available as Supporting Information on the WWW (see article for access details).

\* Author to whom correspondence should be addressed.

Participant at the Medicinal Chemistry in Parasitology meeting, February 2007.

## BOOKS

- |   |                          |
|---|--------------------------|
| MALDI MS: A Practical Guide to Instrumentation, Methods, and Applications ·<br>F. Hillenkamp, J. Peter-Katalinić (Eds.) | J. Falkenhagen ..... 502 |
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