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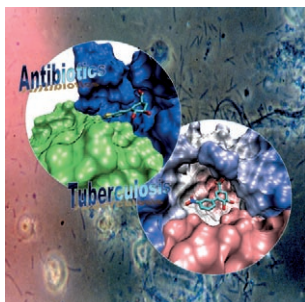
Full text:



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Some articles in this issue have already appeared online in Wiley InterScience. See [www.chemmedchem.org](http://www.chemmedchem.org) under EarlyView®

## COVER PICTURE



The cover picture shows two representations of two potent competitive inhibitors of *Mycobacterium tuberculosis* and *Streptomyces coelicolor* dehydroquinase with a bacterial culture in the background. These enzymes operate in the shikimic acid pathway, which is an important target for the development of new antibiotics. On the right, the bioactive conformation of the 3-nitrophenyl derivative as bound to the *Mycobacterium tuberculosis* active site, obtained from NMR spectroscopy, is highlighted. On the left, the picture depicts the proposed binding mode for the most potent inhibitor reported to date against any dehydroquinase, a 6-benzothio-phenyl derivative (4 nM). For more details, see the Full Paper by C. González-Bello et al. on p. 194 ff.

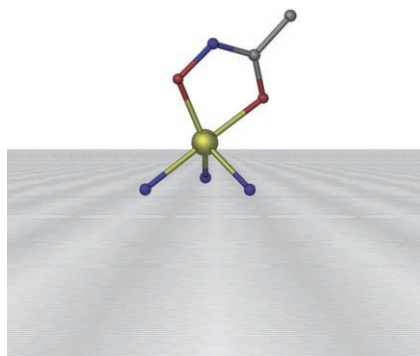
## NEWS

From our sister journals

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## REVIEWS

**Metalloproteins play important roles** in the propagation of human disease. Understanding the bioinorganic coordination chemistry of these proteins is essential to the development of effective inhibitors. This review highlights several target metalloproteins and the drug-discovery approaches that have been used to develop inhibitors of these systems.



F. E. Jacobsen, J. A. Lewis, S. M. Cohen\*

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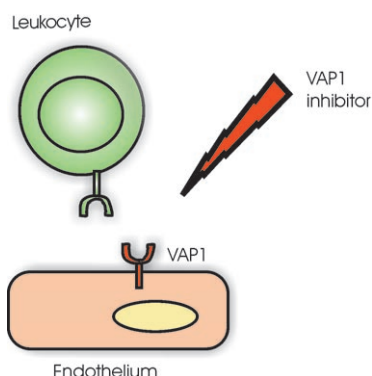
**The Design of Inhibitors for Medically Relevant Metalloproteins**

## HIGHLIGHTS

F. Yraola, F. Albericio, M. Royo\*

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## Inhibition of VAP1: Quickly Gaining Ground as an Anti-Inflammatory Therapy



## VAP1 as anti-inflammatory target:

Over the last two years, small-molecule design in SSAO/VAP1 inhibitors has rapidly gained ground as an anti-inflammatory therapy. Small-molecule VAP1 inhibitors block SSAO enzymatic activity, thereby preventing leukocyte internalization through the endothelium. Thus, novel anti-adhesive molecules will allow the development of new anti-inflammatory compounds.

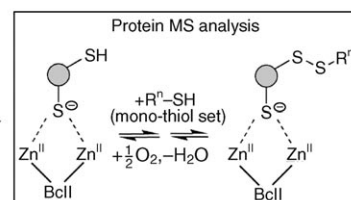
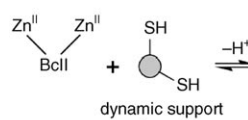
## COMMUNICATIONS

B. M. R. Liénard, N. Selevsek,  
N. J. Oldham, C. J. Schofield\*

175 – 179



## Combined Mass Spectrometry and Dynamic Chemistry Approach to Identify Metalloenzyme Inhibitors



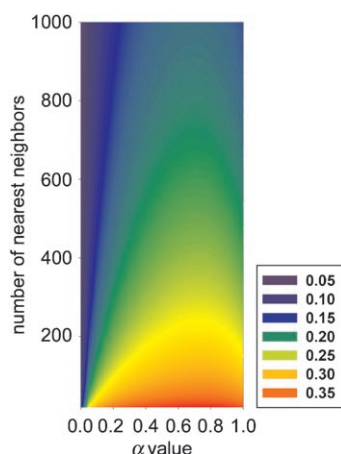
An approach combining thiol based dynamic chemistry and MS was used to explore the SAR of a metallo- $\beta$ -lactamase.

Analogues of preferentially binding disulfides were synthesized and shown to be potent inhibitors.

X. Chen,\* F. K. Brown

180 – 182

## Asymmetry of Chemical Similarity



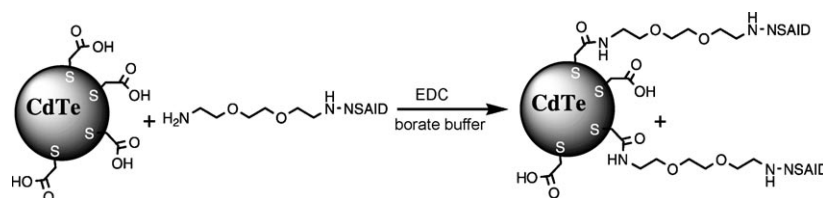
**The power of asymmetry:** Although symmetry is conceptually more beautiful, asymmetry can be more powerful in practice owing to the imperfectness of available information. We present evidence of asymmetry in pairwise chemical similarity measures by an empirical simulated similarity search based on two large pharmaceutical databases.

S. J. Byrne, B. le Bon, S. A. Corr,  
M. Stefanko, C. O'Connor, Y. K. Gun'ko,\*  
Y. P. Rakovich, J. F. Donegan, Y. Williams,  
Y. Volkov, P. Evans

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## Synthesis, Characterisation, and Biological Studies of CdTe Quantum Dot-Naproxen Conjugates

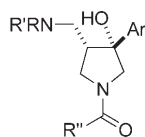


**The first naproxen-QD conjugates** have been synthesised and investigated. These conjugates demonstrated interesting photophysical properties, good stability in an aggressive enzymatic

medium, and cellular localisation in macrophage (THP-1) cells. These nanocomposites might have the potential to act as drug delivery and cellular imaging agents.

## FULL PAPERS

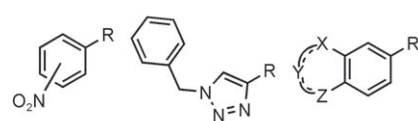
**A 1,3,3,4-tetrasubstituted pyrrolidine** containing CCR5 receptor antagonist, with potent inhibition of the replication of seven genetically diverse R5 HIV-1 strains and good oral bioavailabilities, is described.



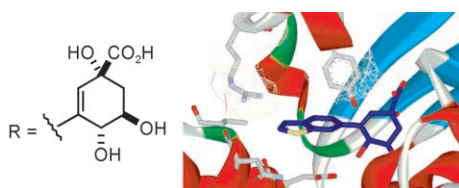
D. Ma,\* S. Yu, B. Li, L. Chen, R. Chen, K. Yu, L. Zhang, Z. Chen, D. Zhong, Z. Gong, R. Wang, H. Jiang, G. Pei

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**Synthesis and Biological Evaluation of 1,3,3,4-Tetrasubstituted Pyrrolidine CCR5 Receptor Antagonists. Discovery of a Potent and Orally Bioavailable Anti-HIV Agent**



**Isomeric nitrophenyl and heterocyclic analogues** of the known inhibitor (1*S*,3*R*,4*R*)-1,3,4-trihydroxy-5-cyclohexene-1-carboxylic acid were synthesized. Inhibition studies with *M. tuberculosis* and *S. coelicolor* type II dehydroquinase



revealed highly potent and selective competitive inhibitors against *S. coelicolor* dehydroquinase. These derivatives are also competitive inhibitors against the *M. tuberculosis* enzyme, but with lower affinities.

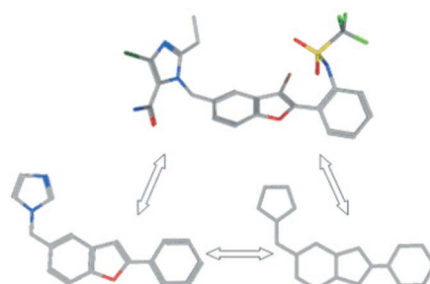
V. F. V. Prazeres, C. Sánchez-Sixto, L. Castedo, H. Lamb, A. R. Hawkins, A. Riboldi-Tunnicliffe, J. R. Coggins, A. J. Laphorn, C. González-Bello\*

194 – 207

**Nanomolar Competitive Inhibitors of *Mycobacterium tuberculosis* and *Streptomyces coelicolor* Type II Dehydroquinase**



**Systematic similarity search calculations** using different 2D fingerprints, multiple reference structures, and specially designed sets of active compounds revealed superior performance of a novel fingerprint type with inherent training potential. In many cases, nearest-neighbor search strategies increased compound recovery over fingerprint-averaging techniques, but decreased the structural diversity of hits (shown is an angiotensin-II antagonist, its core structure, and the corresponding cyclic carbon scaffold).

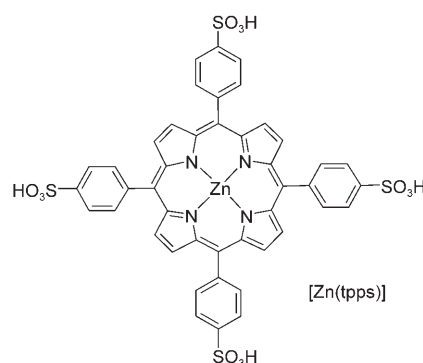


A. Tovar, H. Eckert, J. Bajorath\*

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**Comparison of 2D Fingerprint Methods for Multiple-Template Similarity Searching on Compound Activity Classes of Increasing Structural Diversity**

**A zinc(II)-porphyrin complex** has been shown to be an effective insulin mimetic, as observed in both in vitro and in vivo assays. [Zn(tpps)] is the first example of an orally active Zn<sup>II</sup>-porphyrin complex with a Zn(N<sub>4</sub>) coordination environment that is efficacious in the treatment of type 2 diabetes in mice; it and also has promise for combating a range of other metabolic disorders.



T. K. Saha,\* Y. Yoshikawa, H. Sakurai

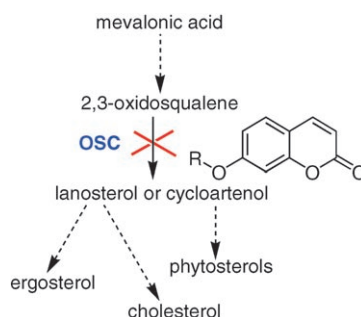
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**A [meso-Tetrakis(4-sulfonato-phenyl)porphyrinato]zinc(II) Complex As an Oral Therapeutic for the Treatment of Type 2 Diabetic KKA<sup>y</sup> Mice**

S. Oliaro-Bosso, F. Viola, S. Taramino,  
S. Tagliapietra, A. Barge, G. Cravotto,  
G. Balliano\*

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**Inhibitory Effect of Umbelliferone  
Aminoalkyl Derivatives on  
Oxidosqualene Cyclases from  
*S. cerevisiae*, *T. cruzi*, *P. carinii*,  
*H. sapiens*, and *A. thaliana*: a  
Structure–Activity Study**



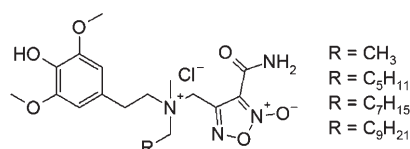
**Five different oxidosqualene cyclases (OSCs)** expressed in yeast, two of which from the pathogens *Trypanosoma cruzi* and *Pneumocystis carinii*, were studied as targets of 18 coumarin derivatives prepared by unconventional synthetic procedures. Results show that this family of compounds has promise for the development of novel antiparasitic agents.

K. Chegaev, L. Lazzarato, B. Rolando,  
E. Marini, G. V. Lopez, M. Bertinaria,  
A. Di Stilo, R. Fruttero, A. Gasco\*

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**Amphiphilic NO-Donor Antioxidants**



**Models of amphiphilic NO-donor anti-oxidants** were synthesized and studied for their antioxidant and vasodilator properties. Their ability to interact with phospholipid layers was investigated by NMR techniques. These compounds could be useful tools for pharmacological investigations.

## BOOKS

**Medicinal Chemistry of Bioactive Natural Products** · X.-T. Liang, W.-S. Fang (Eds.)  
**The Interferons: Characterization and Application** · A. Meager (Ed.)  
**Sodium Channels, Pain, and Analgesia** · K. Coward, M. D. Baker (Eds.)  
**Exploiting Chemical Diversity for Drug Discovery** · P. A. Bartlett, M. Entzeroth (Eds.)

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