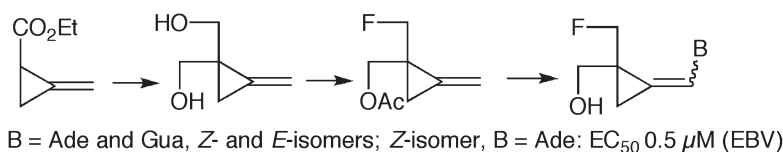


## Contents

### ARTICLES

- Fluorinated methylenecyclopropane analogues of nucleosides. Synthesis and antiviral activity of (*Z*)- and (*E*)-9-[(2-fluoromethyl-2-hydroxymethyl)cyclopropylidene]methyl}adenine and -guanine**  
Chengwei Li, Mark N. Prichard, Brent E. Korba, John C. Drach and Jiri Zemlicka\*

pp 2148–2155

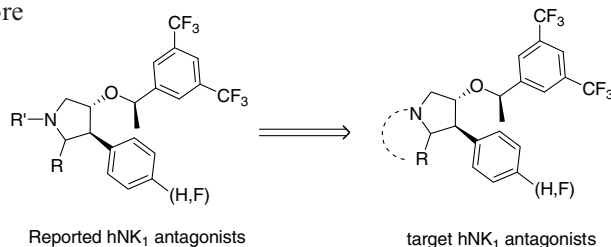


- Fused bicyclic pyrrolizinones as new scaffolds for human NK<sub>1</sub> antagonists**

pp 2156–2170

Gregori J. Morriello,\* Robert J. DeVita, Sander G. Mills, Jonathan R. Young, Peter Lin, George Doss, Gary G. Chicchi, Julie DeMartino, Marc M. Kurtz, Kwei-Lan C. Tsao, Emma Carlson, Karen Townson, Alan Wheeldon, Susan Boyce, Neil Collinson, Nadia Rupniak and Stephen Moore

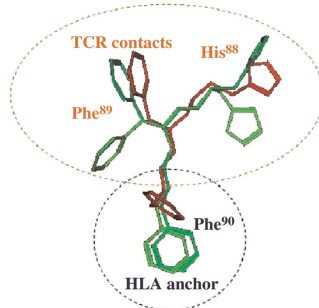
A novel 5,5-fused pyrrolidine scaffold has been discovered which exhibits superior brain penetration and maintains excellent binding affinity, as well as, functional IP activity versus previously reported hNK<sub>1</sub> antagonist.



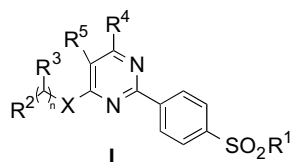
- A combined NMR and molecular dynamics simulation study to determine the conformational properties of agonists and antagonists against experimental autoimmune encephalomyelitis**

pp 2171–2182

Efthimia D. Mantzourani, Klemen Blokar, Theodore V. Tselios, John M. Matsoukas, James A. Platts, Thomas M. Mavromoustakos and Simona Golič Grdadolnik\*



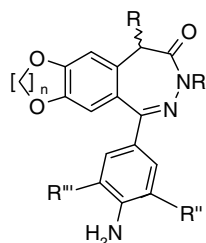
**Novel 2-(4-methylsulfonylphenyl)pyrimidine derivatives as highly potent and specific COX-2 inhibitors** pp 2183–2199

 Aurelio Orjales,\* Ramón Mosquera, Beatriz López, Roberto Olivera,  
 Luis Labeaga and M. Teresa Núñez


New series of pyrimidines **I** were synthesized and evaluated as cyclooxygenase-2 (COX-2) inhibitors. Compounds **8**, **67**, **69**, **71**, **82** and **83** were highly potent and specific COX-2 inhibitors (HWB COX-2 IC<sub>50</sub> = 2.4–0.3 nM and 80- to 780-fold more selective than rofecoxib).

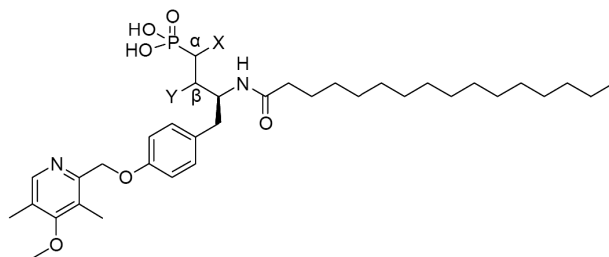

**Structure–activity study of 2,3-benzodiazepin-4-ones noncompetitive AMPAR antagonists: Identification of the 1-(4-amino-3-methylphenyl)-3,5-dihydro-7,8-ethylenedioxy-4*H*-2,3-benzodiazepin-4-one as neuroprotective agent**

pp 2200–2211

 Nicola Micale,\* Simona Colleoni, Giovanna Postorino, Alessia Pellicanò, Maria Zappalà,  
 John Lazzaro, Valentina Diana, Alfredo Cagnotto, Tiziana Mennini and Silvana Grasso

**α- and β-Substituted phosphonate analogs of LPA as autotaxin inhibitors**

pp 2212–2225

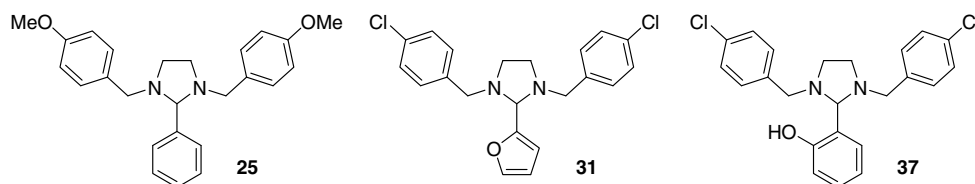
Peng Cui,\* William F. McCalmont, Jose L. Tomsig, Kevin R. Lynch and Timothy L. Macdonald



A series of α- and β-substituted phosphonate analogs of LPA were synthesized and evaluated for ATX inhibitory activity.

**Imidazolidines as new anti-*Trypanosoma cruzi* agents: Biological evaluation and structure–activity relationships**

pp 2226–2234

 M. Cristina Caterina, Isabel A. Perillo,\* Lucía Boiani, Horacio Pezaroglo, Hugo Cerecetto,  
 Mercedes González\* and Alejandra Salerno


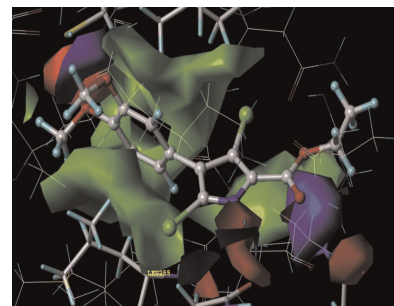
A series of imidazolidines with relevant in vitro activity against *Trypanosoma cruzi* are described. Activity is related to imidazolidines' lipophilicity.

**Docking and hydrophobic scoring of polysubstituted pyrrole compounds with antitubulin activity**

pp 2235–2242

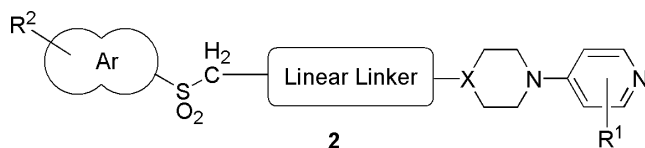
Ashutosh Tripathi, Micaela Fornabaio, Glen E. Kellogg,\* John T. Gupton, David A. Gewirtz, W. Andrew Yeudall, Nina E. Vega and Susan L. Mooberry

HINT Interaction maps of JG-03-14 bound at the colchicine site of tubulin. Blue contours: favorable polar (H-bond); red: unfavorable polar; green: hydrophobic.

**Discovery of sulfonylalkylamides: A new class of orally active factor Xa inhibitors**

pp 2243–2260

Yasuhiro Imaeda,\* Toshio Miyawaki, Hiroki Sakamoto, Fumio Itoh, Noriko Konishi, Katsuhiko Hiroe, Masaki Kawamura, Toshimasa Tanaka and Keiji Kubo

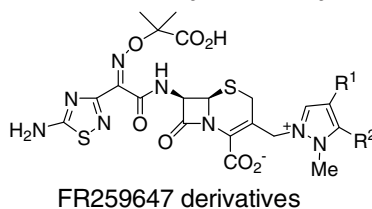


Synthesis, structure–activity relationships, ex vivo anticoagulant activities, selectivity, and pharmacokinetics of sulfonylalkylamides 2 as novel non-amidine FXa inhibitors are reported.

**Structural requirements for the stability of novel cephalosporins to AmpC  $\beta$ -lactamase based on 3D-structure**

pp 2261–2275

Kenji Murano,\* Toshio Yamanaka, Ayako Toda, Hidenori Ohki,\* Shinya Okuda, Kohji Kawabata, Kazuo Hatano, Shinobu Takeda, Hisashi Akamatsu, Kenji Itoh, Keiji Misumi, Satoshi Inoue and Tatsuya Takagi



FR259647 derivatives

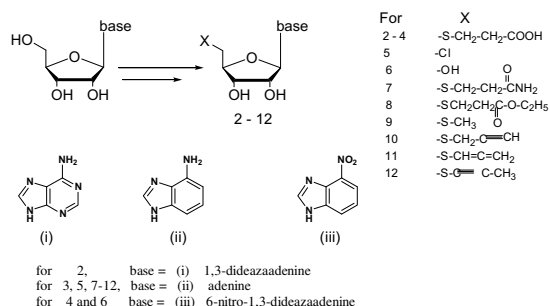
We propose novel structural requirements that FR259647 derivatives with lower probability of entry into the binding pocket of AmpC  $\beta$ -lactamase are more stable to the enzyme.

**Activation and inhibition of DNA methyltransferases by *S*-adenosyl-L-homocysteine analogues**

pp 2276–2285

Ritesh Kumar, Richa Srivastava, Ramendra Kumar Singh, Avadhesh Suroliya and Desirazu N. Rao\*

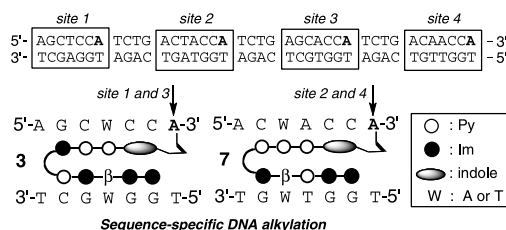
A series of 11 AdoHcy analogues were synthesized and evaluated for their modulating effects on DNA methylation catalyzed by DNA methyltransferases.



### Requirement of $\beta$ -alanine components in sequence-specific DNA alkylation by pyrrole-imidazole conjugates with seven-base pair recognition

pp 2286–2291

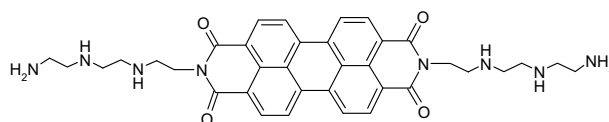
Toshikazu Bando,\* Masafumi Minoshima, Gengo Kashiwazaki, Ken-ichi Shinohara, Shunta Sasaki, Jun Fujimoto, Akimichi Ohtsuki, Masataka Murakami, Satomi Nakazono and Hiroshi Sugiyama\*



### The number and distances of positive charges of polyamine side chains in a series of perylene diimides significantly influence their ability to induce G-quadruplex structures and inhibit human telomerase

pp 2292–2304

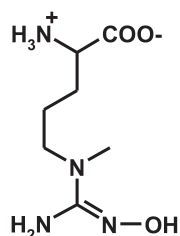
Marco Franceschin,\* Caterina Maria Lombardo, Emanuela Pascucci, Danilo D'Ambrosio, Emanuela Micheli, Armandodoriano Bianco, Giancarlo Ortaggi and Maria Savino



### $N^{\delta}$ -Methylated L-arginine derivatives and their effects on the nitric oxide generating system

pp 2305–2312

Jürke Kotthaus, Dennis Schade, Katrin Töpker-Lehmann, Eric Beitz and Bernd Clement\*



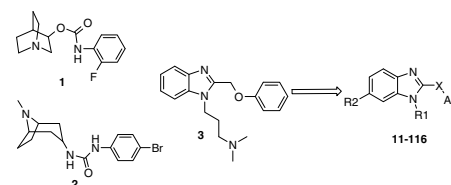
The influence of  $N^{\delta}$ -methyl-L-arginine and its presumed metabolites by NOS catalysis was investigated on the whole nitric oxide generating system including NOSs, arginase and DDAH.  $N^{\omega}$ -Hydroxy- $N^{\delta}$ -methyl-L-arginine presents a strong inhibitor of arginase with a  $K_i$  of 17  $\mu$ M.

### Parallel synthesis of a series of potentially brain penetrant aminoalkyl benzimidazoles

pp 2313–2328

Iolanda Micco,\* Arianna Nencini,\* Joanna Quinn,\* Hendrick Bothmann, Chiara Ghiron, Alessandro Padova and Silvia Papini

Alpha7 agonists were identified via GOLD (CCDC) docking in the putative agonist binding site of an alpha7 homology model and a series of aminoalkyl benzimidazoles was synthesised to obtain potentially brain penetrant drugs. The array was prepared starting from the reaction of *ortho*-fluoronitrobenzenes with a selection of diamines, followed by reduction of the nitro group to obtain a series of monoalkylated phenylene diamines. *N,N'*-Carbonyldiimidazole (CDI) mediated acylation, followed by a parallel automated work-up procedure, afforded the monoacylated phenylenediamines which were cyclised under acidic conditions. Parallel work-up and purification afforded the array products in good yields and purities with a robust parallel methodology which will be useful for other libraries. Screening for alpha7 activity revealed compounds with agonistic activity for the receptor.

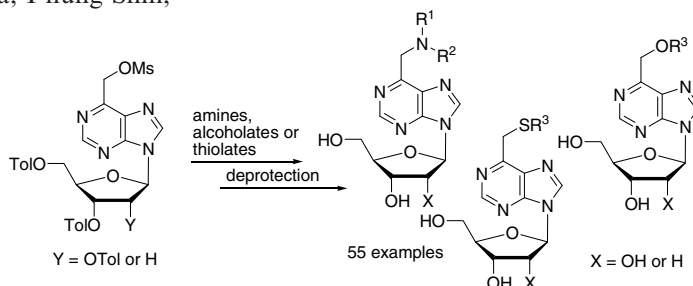


**Synthesis, cytostatic and anti-HCV activity of 6-(*N*-substituted aminomethyl)-, 6-(*O*-substituted hydroxymethyl)- and 6-(*S*-substituted sulfanylmethyl)purine nucleosides**

pp 2329–2366

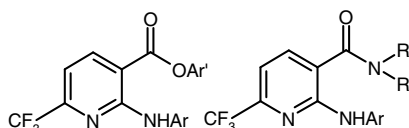
Peter Šilhár, Michal Hocek,\* Radek Pohl, Ivan Votruba, I-hung Shih, Eric Mabery and Richard Mackman

An efficient synthesis of a large series of 6-(*N*-substituted aminomethyl)-, 6-(*O*-substituted hydroxymethyl)- and 6-(*S*-substituted sulfanylmethyl)purine nucleosides was developed.

**Synthesis and evaluation of antitumoral activity of ester and amide derivatives of 2-aryl-amino-6-trifluoromethyl-3-pyridinecarboxylic acids**

pp 2367–2378

Valentina Onnis,\* Maria T. Cocco, Valentina Lilliu and Cenzo Congiu

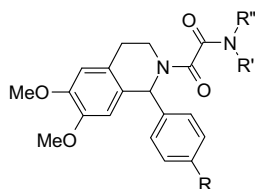


Ester and amide derivatives of 2-aryl-amino-6-trifluoromethyl-3-pyridinecarboxylic acids demonstrated inhibitory effects on the growth of a wide range of cancer cell lines in the low micromolar to nanomolar concentration range.

**Synthesis and anticonvulsant evaluation of *N*-substituted isoquinoline AMPA receptor antagonists**

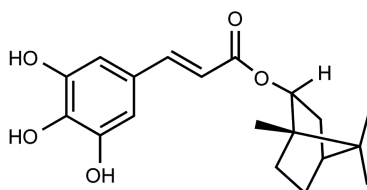
pp 2379–2384

Rosaria Gitto, Laura De Luca, Benedetta Pagano, Rita Citraro, Giovanbattista De Sarro, Lara Costa, Lucia Ciranna and Alba Chimirri\*

**Bornyl (3,4,5-trihydroxy)-cinnamate - An optimized human neutrophil elastase inhibitor designed by free energy calculations**

pp 2385–2390

Thomas Steinbrecher, Andrea Hrenn, Korinna L. Dormann, Irmgard Merfort\* and Andreas Labahn\*

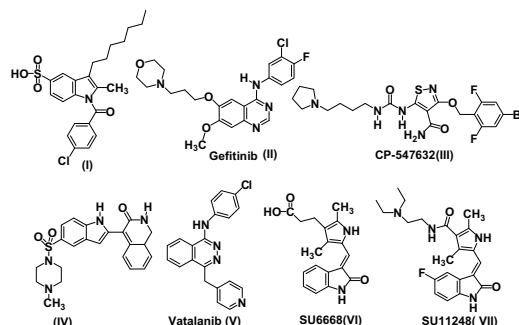


The binding affinity of bornyl (3,4,5-trihydroxy)-cinnamate was predicted by thermodynamic integration calculations. A synthesis protocol was developed for the ligand and its inhibitory effect was tested against the isolated enzyme.

### Molecular modeling study and synthesis of novel pyrrolo[2,3-*d*]pyrimidines and pyrrolotriazolopyrimidines of expected antitumor and radioprotective activities

pp 2391–2402

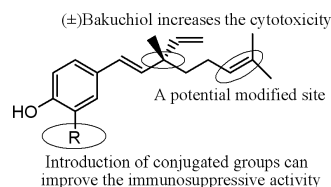
Dalal A. Abou El Ella, Mostafa M. Ghorab,\* Eman Noaman, Helmy I. Heiba and Amira I. Khalil



### Synthesis and structure–immunosuppressive activity relationships of bakuchiol and its derivatives

pp 2403–2411

Hongli Chen, Xiaolong Du, Wei Tang, Yu Zhou, Jianping Zuo, Huijin Feng and Yuanchao Li\*



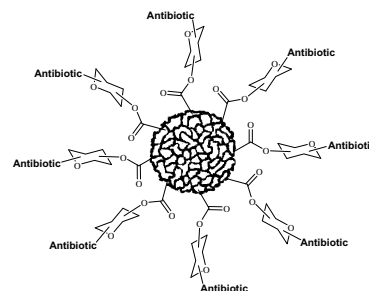
A series of derivatives of bakuchiol were synthesized and tested in vitro for their cytotoxicity, and inhibition of T cell proliferation and B cell proliferation. The data obtained provided preliminary structure–activity relationships of the compounds as immunosuppressive activity.

### Glyconanobiotics: Novel carbohydrate nanoparticle antibiotics for MRSA and *Bacillus anthracis*

pp 2412–2418

Sampath C. Abeylath, Edward Turos,\* Sonja Dickey and Daniel V. Lim

The synthesis and biological activity of carbohydrate-derivatized polyacrylate nanoparticles (right) against methicillin-resistant *Staphylococcus aureus* and *Bacillus anthracis* is described.

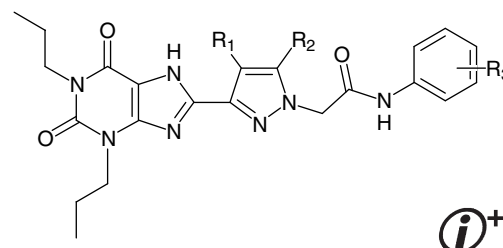


### 1,3-Dipropyl-8-(1-phenylacetamide-1*H*-pyrazol-3-yl)-xanthine derivatives as highly potent and selective human A<sub>2B</sub> adenosine receptor antagonists

pp 2419–2430

Mojgan Aghazadeh Tabrizi, Pier Giovanni Baraldi,\* Delia Preti, Romeo Romagnoli, Giulia Saponaro, Stefania Baraldi, Allan R. Moorman, Abdel Naser Zaid, Katia Varani and Pier Andrea Borea

In the present study, synthesis of a new series of 1,3-dipropyl-8-(1-phenylacetamide-1*H*-pyrazol-3-yl)-xanthine derivatives and evaluation of their biological activity as A<sub>2B</sub> adenosine receptor antagonists are described.

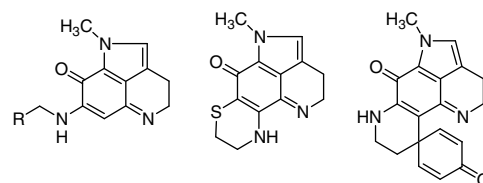


**Synthesis and biological evaluation of pyrroloiminoquinone derivatives**

pp 2431–2438

Daniele Passarella,\* Francesca Belinghieri, Michele Scarpellini, Graziella Pratesi, Franco Zunino, Ornella Maria Gia, Lisa Dalla Via, Giuseppe Santoro and Bruno Danieli

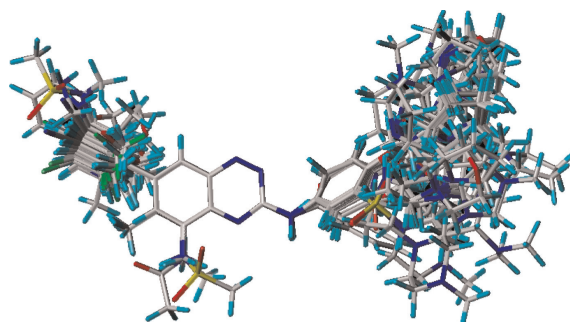
A series of pyrroloiminoquinone derivatives has been synthesized and tested for their antiproliferative activity toward NCI-H460, HeLa and HL-60. The capacity of selected compounds to affect the enzymatic activity of topoisomerase II and the interaction with DNA extracted from HeLa cells is discussed. An effective inhibitory effect on topoisomerase II is demonstrated.

**Three-dimensional quantitative structure–activity relationship studies on novel series of benzotriazine based compounds acting as Src inhibitors using CoMFA and CoMSIA**

pp 2439–2447

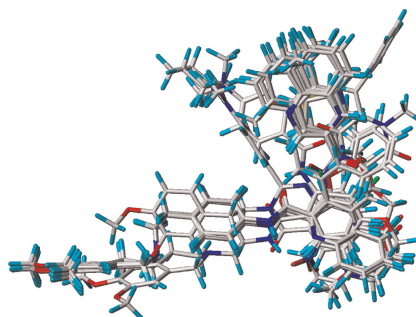
Carlos Gueto, José L. Ruiz, Juan E. Torres, Jefferson Méndez and Ricardo Vivas-Reyes\*

3D-view of aligned molecules (training and test sets).

**Functional assay and structure–activity relationships of new third-generation P-glycoprotein inhibitors**

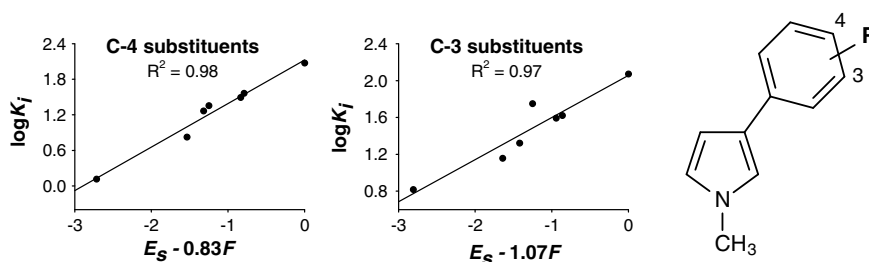
pp 2448–2462

Henrik Müller, Ilza K. Pajeva, Christoph Globisch and Michael Wiese\*

**Structure–activity relationships in the inhibition of monoamine oxidase B by 1-methyl-3-phenylpyrroles**

pp 2463–2472

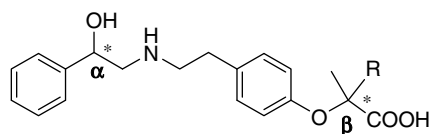
Modupe O. Ogunrombi, Sarel F. Malan, Gisella Terre'Blanche, Neal Castagnoli, Jr., Jacobus J. Bergh and Jacobus P. Petzer\*



**Stereospecific synthesis and bio-activity of novel  $\beta_3$ -adrenoceptor agonists and inverse agonists**

pp 2473–2488

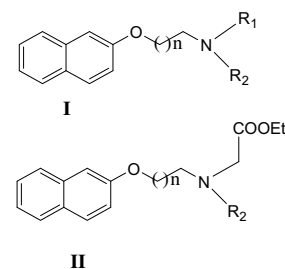
Maria Grazia Perrone, Ernesto Santandrea, Laura Bleve, Paola Vitale, Nicola Antonio Colabufo, Ralf Jockers, Ferdinando Maria Milazzo, Anna Floriana Sciarroni and Antonio Scilimati\*

 **$\omega$ -(2-Naphthyloxy) amino alkanes as a novel class of anti-hyperglycemic and lipid lowering agents**

pp 2489–2498

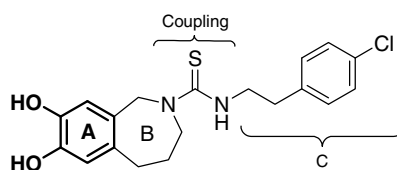
Devdutt Chaturvedi,\* Suprabhat Ray, Arvind K. Srivastava and Ramesh Chander

$\omega$ -(2-Naphthyloxy) amino alkanes, obtained as major by-product during course of synthesis of carbamate esters from  $\omega$ -(2-naphthyloxy) alkyl halides and amines, showed significant anti-hyperglycemic and lipid lowering activities in various test models as a novel class of compounds. Compounds were tested in rat GLM, SLM, STZ, and STZ-S models at 100 mg/kg dose. Of these compound **13** was found to be the most active which caused lowering of sugar by 33.6%, 31.0%, 28.5%, and 73.8% in GLM, SLM, STZ, STZ-S, and db/db mice models, respectively. It also significantly effected lowering of LDL in rat model and also in hamster model without reducing HDL. Most of the compounds showing anti-diabetic and lipid lowering activity have shown promising PPAR- $\alpha/\gamma/\delta$ -agonistic activity. Compounds **6**, **13**, and **19** have shown very good PPAR- $\alpha/\gamma/\delta$ -agonistic activity.

**SAR studies of capsazepinoid bronchodilators. Part 1: The importance of the catechol moiety and aspects of the B-ring structure**

pp 2499–2512

Maria F. Dalence-Guzmán, Magnus Berglund, Staffan Skogvall and Olov Sterner\*

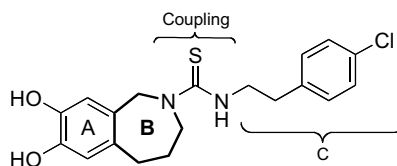


A series of capsazepinoids with different number/position of hydroxyl groups in the A-ring and B-ring size/substitution were prepared, and assayed for bronchorelaxing activity in human small airway preparations.

**SAR studies of capsazepinoid bronchodilators. Part 2: Chlorination and catechol replacement in the A-ring**

pp 2513–2528

Magnus Berglund, María F. Dalence-Guzmán, Staffan Skogvall and Olov Sterner\*



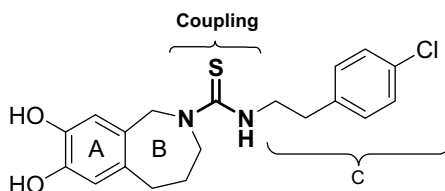
The dependence of the bronchodilating activity in human small airways of capsazepine derivatives on the chlorination of the A-ring and the replacement of the catechol moiety with bioisosteric groups has been investigated.



### SAR studies of capsazepinoid bronchodilators 3: The thiourea part (coupling region) and the 2-(4-chlorophenyl)ethyl moiety (C-region)

pp 2529–2540

Magnus Berglund, María F. Dalence-Guzmán, Staffan Skogvall and Olov Sterner\*

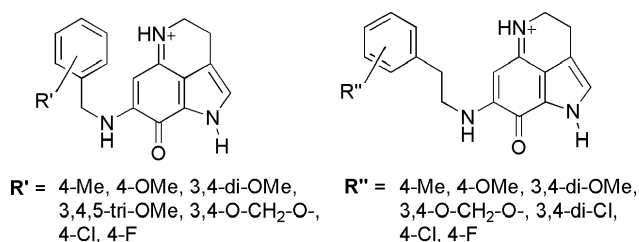


Capsazepine derivatives with various coupling- and C-regions were synthesized and assayed as part of a SAR study of the bronchorelaxing activity in human small airways.

### Synthesis and antiproliferative activity of benzyl and phenethyl analogs of makaluvamines

pp 2541–2549

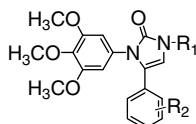
Bidhan A. Shinkre, Kevin P. Raisch, Liming Fan and Sadanandan E. Velu\*



### Synthesis and biological evaluation of imidazol-2-one derivatives as potential antitumor agents

pp 2550–2557

Na Xue, Xiaochun Yang, Rui Wu, Jing Chen, Qiaojun He, Bo Yang, Xiuyang Lu and Yongzhou Hu\*



$R_1 = \text{H}, \text{COCH}_3, \text{NHCOR}$   
 $R_2 = \text{H}, 4\text{-Br}, 4\text{-Cl}, 4\text{-NO}_2, 4\text{-OCH}_3, 2,4\text{-2F}, 3,4\text{-(OCH}_3)_2, 3\text{-NO}_2\text{-4-OCH}_3, 3\text{-NH}_2\text{-4-OCH}_3, 3\text{-OH-4-OCH}_3$

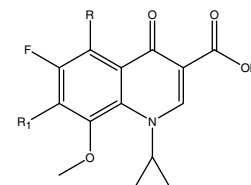
A new series of imidazol-2-one derivatives were prepared and investigated as anticancer agents.

### Synthesis and antimycobacterial evaluation of newer 1-cyclopropyl-1,4-dihydro-6-fluoro-7-(substituted secondary amino)-8-methoxy-5-(sub)-4-oxoquinoline-3-carboxylic acids

pp 2558–2569

Palaniappan Senthilkumar, Murugesan Dinakaran, Debjani Banerjee, Ruth Vandana Devakaram, Perumal Yogeeswari, Arnab China, Valakunja Nagaraja and Dharmarajan Sriram\*

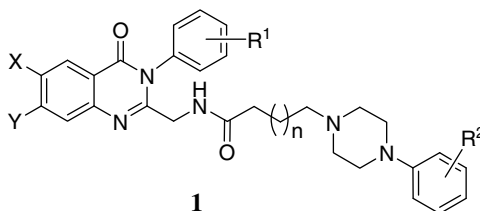
Thirty-four newer 1-cyclopropyl-1,4-dihydro-6-fluoro-7-(substituted secondary amino)-8-methoxy-5-(sub)-4-oxoquinoline-3-carboxylic acids were synthesized and its in vitro and in vivo antimycobacterial activities against *Mycobacterium tuberculosis* H37Rv (MTB), multi-drug resistant *M. tuberculosis* (MDR-TB) and *Mycobacterium smegmatis* (MC<sup>2</sup>) and its ability to inhibit the supercoiling activity of DNA gyrase were reported.



**Novel quinazolinone derivatives as 5-HT<sub>7</sub> receptor ligands**

pp 2570–2578

Yong Ho Na, Sung Ho Hong, Jung Hyang Lee, Woo-Kyu Park, Du-Jong Baek, Hun Yeong Koh, Yong Seo Cho, Hyunah Choo\* and Ae Nim Pae\*



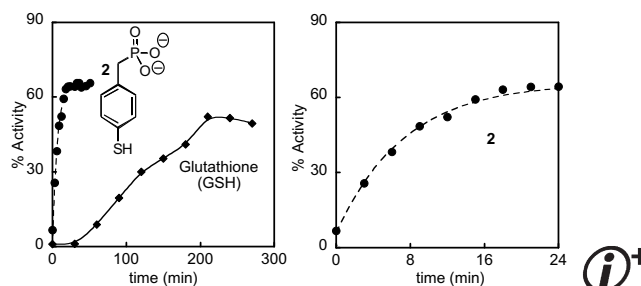
A small molecule library of quinazolinone derivatives **1** was synthesized and biologically evaluated to estimate binding affinity to the 5-HT<sub>7</sub> receptor.

**Rate enhancement of the oxidative folding of lysozyme by the use of aromatic thiol containing redox buffers**

pp 2579–2590

Minakshi C. Gurbhele-Tupkar, Lissette R. Perez, Yenya Silva and Watson J. Lees\*

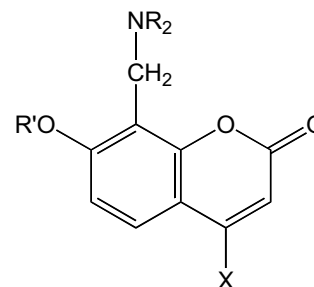
The folding rate of reduced lysozyme to native protein was enhanced by a factor of 10 at pH 7 when the standard redox buffer component glutathione was replaced by an aromatic thiol.

**Activity of Mannich bases of 7-hydroxycoumarin against Flaviviridae**

pp 2591–2605

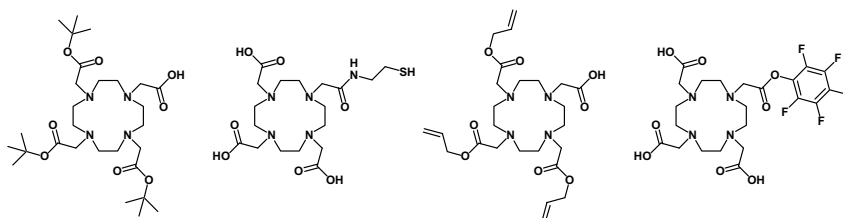
Mauro Mazzei,\* Erika Nieddu, Mariangela Miele, Alessandro Balbi, Marco Ferrone, Maurizio Fermeglia, Marco T. Mazzei, Sabrina Priol, Paolo La Colla, Fabio Marongiu, Cristina Ibba and Roberta Loddo

Some Mannich bases of 7-hydroxycoumarin were prepared and tested against viruses containing single-stranded, positive-sense RNA genomes (ssRNA<sup>+</sup>). When position 7 was propylated, the resulting 7-propyloxy derivatives were in some cases endowed with an interesting activity against BVDV. Therefore, 7-propyloxy derivatives were submitted to a molecular modeling study using DNA polymerase of HCV as a target. The good correlation between calculated molecular modeling IC<sub>50</sub> and experimental EC<sub>50</sub> is reasonable proof that DNA polymerase is potentially involved in the inhibition of surrogate HCV viruses.

**Improved syntheses and applicability of different DOTA building blocks for multiply derivatized scaffolds**

pp 2606–2616

C. Wängler, B. Wängler, M. Eisenhut, U. Haberkorn and W. Mier\*

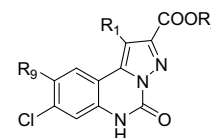


Improved synthesis protocols for several DOTA derivatives. The utility of these and other DOTA derivatives for multimerization reactions is studied with PAMAM dendrimers.

### Novel AMPA and kainate receptor antagonists containing the pyrazolo[1,5-*c*]quinazoline ring system: pp 2617–2626 Synthesis and structure–activity relationships

Flavia Varano,\* Daniela Catarzi, Vittoria Colotta, Ombretta Lenzi, Guido Filacchioni, Alessandro Galli and Chiara Costagli

The synthesis and Gly/NMDA, AMPA and KA receptor binding activities of a new set of 1,9-disubstituted-8-chloro-pyrazolo[1,5-*c*]quinazoline-2-carboxylates designed as AMPA and KA receptor antagonists are described.



R<sub>1</sub> = Cl, NO<sub>2</sub>, COOEt, COOH  
R<sub>2</sub> = Et, H  
R<sub>9</sub> = NO<sub>2</sub>, heterocycles, NHCONHR, NHCO(2-COOHC<sub>6</sub>H<sub>4</sub>)

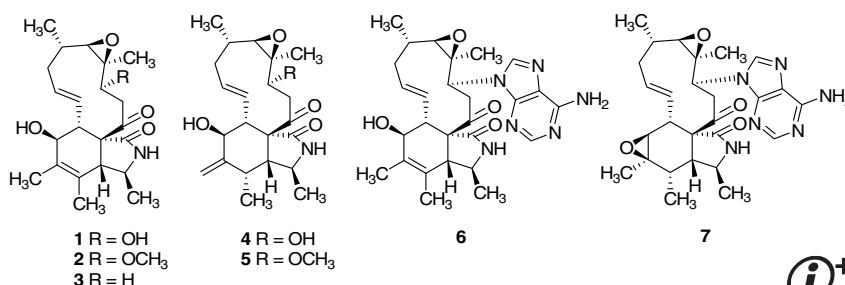


### Alachalasins A–G, new cytochalasins from the fungus *Stachybotrys charatum*

pp 2627–2634

Yonggang Zhang, Renrong Tian, Shuchun Liu, Xulin Chen, Xingzhong Liu and Yongsheng Che\*

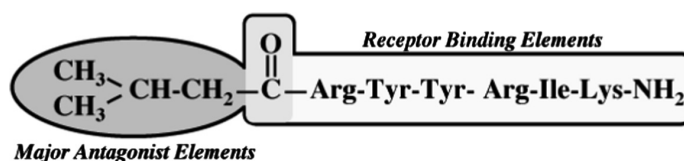
Alachalasins A–G (1–7), seven new cytochalasins, have been isolated from cultures of an isolate of *Stachybotrys charatum*. The structures of these compounds were determined mainly by analysis of their NMR spectroscopic data.



### Designed modification of partial agonist of ORL1 nociceptin receptor for conversion into highly potent antagonist

pp 2635–2644

Jinglan Li, Kaname Isozaki, Kazushi Okada, Ayami Matsushima, Takeru Nose, Tommaso Costa and Yasuyuki Shimohigashi\*



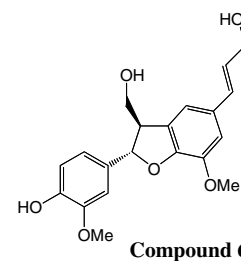
Ac-RYYRIK-NH<sub>2</sub> isolated from the peptide library is a partial agonist of the nociceptin/ORL1 ligand–receptor system. We explored that its isovaleryl derivative functions as a pure antagonist.

### Low molecular weight lignin suppresses activation of NF-κB and HIV-1 promoter

pp 2645–2650

Shinya Mitsuhashi, Takao Kishimoto, Yasumitsu Uraki, Takashi Okamoto and Makoto Ubukata\*

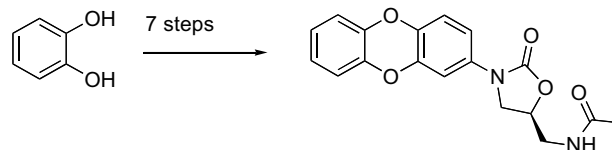
Low molecular weight lignin (less than 0.5 kDa) suppresses activation of NF-κB induced by TNF-α and HIV-1 gene expression. Among six lignin dimer-like compounds, compound 6 containing β-5 bond has more potent inhibitory activity than compounds 1, 2, 3, 4, and 5, which contain β-1, β-O-4, 5-5, and β–β structural units. These results suggested that the small molecule of lignin inhibits HIV-1 replication through suppression of HIV-1 transcription from LTR via NF-κB activation.



**Synthesis of novel oxazolidinone antimicrobial agents**

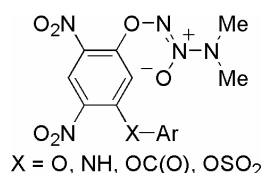
pp 2651–2656

David C. Ebner, Jeffrey C. Culhane, Tyler N. Winkelman, Mitchell D. Haustein, Jayna L. Ditty and J. Thomas Ippoliti\*

**Synthesis, nitric oxide release, and anti-leukemic activity of glutathione-activated nitric oxide prodrugs: Structural analogues of PABA/NO, an anti-cancer lead compound**

pp 2657–2664

Harinath Chakrapani,\* Thomas C. Wilde, Michael L. Citro, Michael M. Goodblatt, Larry K. Keefer and Joseph E. Saavedra\*

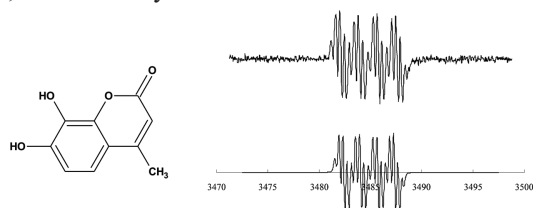


A number of structural analogues of PABA/NO, an anti-cancer lead compound, were synthesized; their nitric oxide release patterns and anti-leukemic activity are reported.

**Structural insights into hydroxycoumarin-induced apoptosis in U-937 cells**

pp 2665–2675

Maria E. Riveiro, Albertina Moglioni, Ramiro Vazquez, Natalia Gomez, Graciela Facorro, Lidia Piehl, Emilio Rubin de Celis, Carina Shayo and Carlos Davio\*



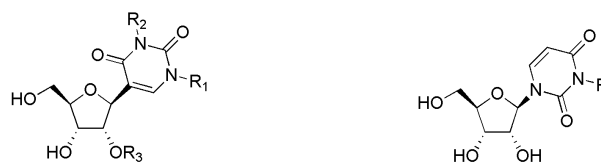
ESR signal of the 7,8-dihydroxy-4-methylcoumarin radical

The present work evaluates the structural requirements of related hydroxycoumarins to induce apoptosis in a leukemic cell line, suggesting that reactive oxygen species generation plays a critical role in dihydroxycoumarin-induced apoptosis in U-937 cells.

**Synthesis and solution conformation studies of 3-substituted uridine and pseudouridine derivatives**

pp 2676–2686

Yu-Cheng Chang, Jayatilake Herath, Tony H.-H. Wang and Christine S. Chow\*



R<sub>1</sub> = H, R<sub>2</sub> = H, R<sub>3</sub> = H  
 R<sub>1</sub> = CH<sub>3</sub>, R<sub>2</sub> = H, R<sub>3</sub> = H  
 R<sub>1</sub> = CH<sub>3</sub>, R<sub>2</sub> = CH<sub>2</sub>CH<sub>2</sub>CH(NH<sub>2</sub>)(COOH), R<sub>3</sub> = H  
 R<sub>1</sub> = CH<sub>3</sub>, R<sub>2</sub> = CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>OH, R<sub>3</sub> = H  
 R<sub>1</sub> = H, R<sub>2</sub> = H, R<sub>3</sub> = CH<sub>3</sub>

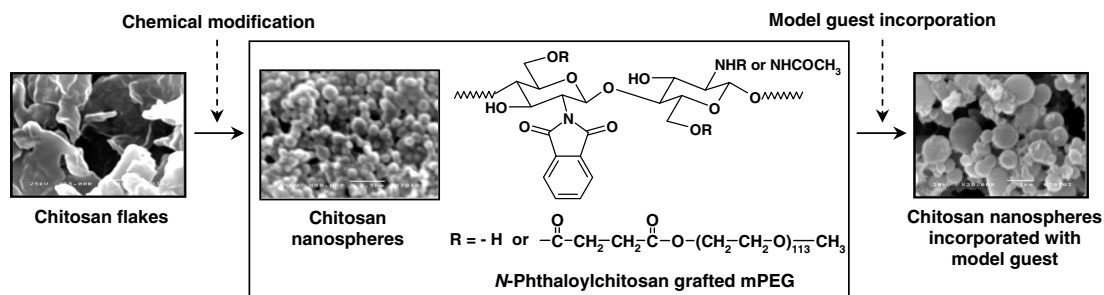
R = CH<sub>2</sub>CH<sub>2</sub>CH(NH<sub>2</sub>)(COOH)  
 R = CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH(NH<sub>2</sub>)(COOH)  
 R = CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>COOH  
 R = CH<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>CH<sub>2</sub>OH



**Amphiphilic chitosan nanosphere: Studies on formation, toxicity, and guest molecule incorporation**

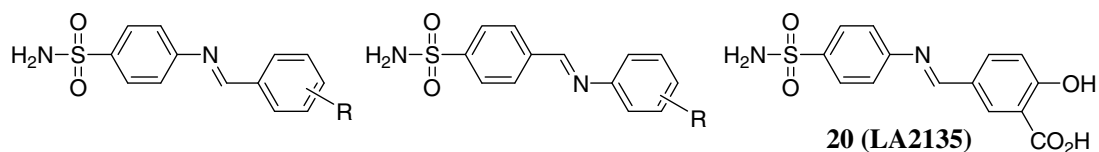
pp 2687–2696

Rangrong Yoksan\* and Suwabun Chirachanchai\*

**Selective COX-2 inhibitors. Part 2: Synthesis and biological evaluation of 4-benzylideneamino- and 4-phenyliminomethyl-benzenesulfonamides**

pp 2697–2706

Shwu-Jiuan Lin, Wei-Jern Tsai, Wen-Fei Chiou, Tsang-Hsiung Yang and Li-Ming Yang\*



The synthesis, evaluation, and structure–activity relationships of two series of benzenesulfonamides as potent and selective COX-2 inhibitors are described.

**OTHER CONTENTS****Summary of instructions to authors**

p I

\*Corresponding author

i+ Supplementary data available via ScienceDirect

**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, *102*, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, *61*(6), 355–360].

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