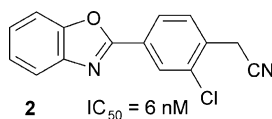


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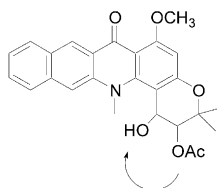
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### ARTICLES

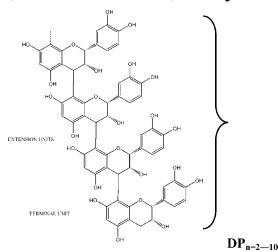
<b>Discovery of novel modulators of metabotropic glutamate receptor subtype-5</b>	pp 17–21
Bowe Wang,* Jean-Michel Vernier, Sara Rao, Janice Chung, Jeffery J. Anderson, Jesse D. Brodtkin, Xiaohui Jiang, Michael F. Gardner, Xiaoqing Yang and Benito Munoz*	



<b>A transesterification reaction is implicated in the covalent binding of benzo[b]acronycine anticancer agents with DNA and glutathione</b>	pp 23–29
Marie-Hélène David-Cordonnier, William Laine, Mostafa Kouach, Gilbert Briand, Hervé Vezin, Thomas Gaslonde, Sylvie Michel, Huong Doan Thi Mai, Francois Tillequin, Michel Koch, Stéphane Léonce, Alain Pierré and Christian Bailly*	



<b>Occurrence of antioxidant and radical scavenging proanthocyanidins from the Indian minor spice nagkesar (<i>Mammea longifolia</i> planch and triana syn)</b>	pp 31–36
Lingamallu Jagan Mohan Rao,* Hiroshi Yada, Hiroshi Ono, Mayumi Ohnishi-Kameyama and Mitsuru Yoshida	

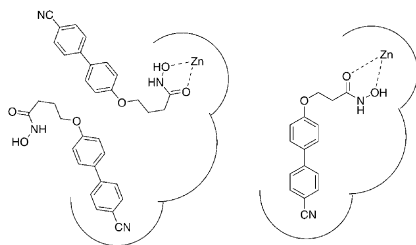


Antioxidant and radical scavenging oligomeric proanthocyanidins are isolated and identified with the help of spectral data and chemical degradation, from the methanol extract of the buds of *Mammea longifolia*.

**Structure–activity relationships by mass spectrometry: identification of novel MMP-3 inhibitors**

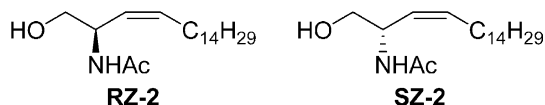
pp 37–44

Denise A. Ockey,\* Jenna L. Dotson, Martin E. Struble, John T. Stults, James H. Bourell, Kevin R. Clark and Thomas R. Gadek

**(3Z)-2-Acetylamino-3-octadecen-1-ol as a potent apoptotic agent against HL-60 cells**

pp 45–51

Hayato Niiro, Hideki Azuma,\* Shinsuke Tanago, Kiyohiro Matsumura, Keiji Shikata, Taro Tachibana and Kenji Ogino\*



(2*R*,3*Z*)- and (2*S*,3*Z*)-2-Acetylamino-3-octadecen-1-ol were prepared and their antileukemic activities were examined against HL-60 cells.

**DNA sequence-specific recognition of peptides incorporating the HPRK and polyamide motifs**

pp 53–61

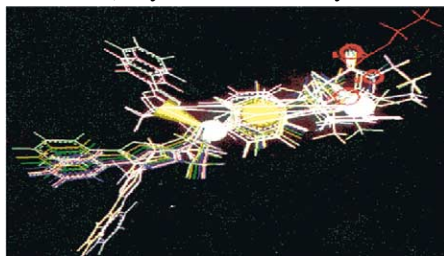
Jung-Cheng Chang, Chia-Hung Yang, Ping-Yen Chou, Wan-Hsu Yang, I.-Chun Chou, Ching-Tai Lu, Pei-Hsuan Lin, Rolis Chien-Wei Hou, Kee-Ching G. Jeng, Chien-Chung Cheng and Leung Sheh\*

Three peptide amides, HPRK(Py)<sub>4</sub>HPRK-NH<sub>2</sub> (PyH-12), HPRK(Py)<sub>3</sub>HPRK-NH<sub>2</sub> (PyH-11) and HPRK(Py)<sub>2</sub>HPRK-NH<sub>2</sub> (PyH-10), were synthesized. On a 5'-<sup>32</sup>P-labeled 158-mer Watson strand, the most distinctive DNase I footprinting blockages seen with all three peptides occur around sequences 5'-GAGAAAAT-3' and 5'-CGGT-3'. On the complementary 5'-<sup>32</sup>P-labeled Crick strand, only PyH-12 strongly discriminates the 5'-TTT-3' site. Possible interactions of the amino acid side chains of these peptides with DNA bases are discussed.

**Pharmacophore identification and 3D-QSAR studies in *N*-(2-benzoyl phenyl)-*L*-tyrosines as PPAR $\gamma$  agonists**

pp 63–69

Lalit Rathi, Sushil K. Kashaw, Anshuman Dixit, Gyanendra Pandey and Anil K. Saxena\*

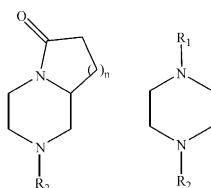


The identification of pharmacophore and three dimensional quantitative structure–activity studies have been performed on a set of *N*-(2-benzoylphenyl)-*L*-tyrosine for their PPAR $\gamma$  agonist activity by using the logico-structural based method which describe the properties and distribution of primary and secondary biophore sites in the three dimensional space

**Structure–activity relationship studies on unifiram (DM232) and sunifiram (DM235), two novel and potent cognition enhancing drugs**

pp 71–85

Serena Scapecchi,\* Elisabetta Martini, Dina Manetti, Carla Ghelardini, Cecilia Martelli, Silvia Dei, Nicoletta Galeotti, Luca Guandalini, Maria Novella Romanelli and Elisabetta Teodori

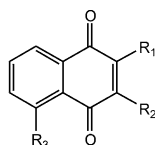


Structure–activity relationships on two novel potent cognition enhancing drugs, unifiram (DM232, **1**) and sunifiram (DM235, **2**), are reported. Although none of the compounds synthesised reached the potency of the parent drugs, some fairly active compounds have been identified that may represent new leads to develop other cognition enhancing drugs.

**Quantitative structure–activity relationship in aziridinyl-1,4-naphthoquinone antimalarials: study of theoretical correlations by the PM3 method**

pp 87–93

Elizabeth V. M. dos Santos, José W. de M. Carneiro\* and Vitor F. Ferreira



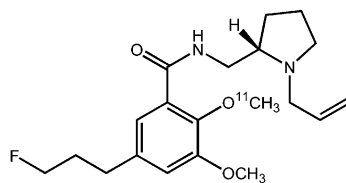
$R_1$  = alkyl, ether, ester or sulfonic ester  
 $R_2$  = and/or aziridinyl or amines  
 $R_3$  = and/or aziridinyl or amines

Several molecular parameters for 1,4-naphthoquinones and 2,3-aziridinyl-1,4-naphthoquinones with antimalarial activities were obtained with the semi-empirical PM3 method. The descriptor related to the Gibbs free energy of an isodesmic equation defining the reduction of the naphthoquinones was found to have high correlation with activity.

 **$^{11}\text{C}$ -Fallypride: radiosynthesis and preliminary evaluation of a novel dopamine D2/D3 receptor PET radiotracer in non-human primate brain**

pp 95–102

Jogeshwar Mukherjee,\* Bingzhi Shi, Bradley T. Christian, Sankha Chattopadhyay and Tanjore K. Narayanan



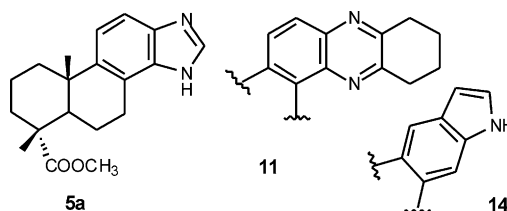
$^{11}\text{C}$ -Fallypride

Development of  $^{11}\text{C}$ -fallypride, a new radiopharmaceutical suitable for PET imaging studies of extrastriatal dopamine D2/D3 receptors is reported.

**Synthesis and antiviral evaluation of benzimidazoles, quinoxalines and indoles from dehydroabiatic acid**

pp 103–112

Tatiana Fonseca, Bárbara Gigante,\* M. Matilde Marques, Thomas L. Gilchrist and Erik De Clercq

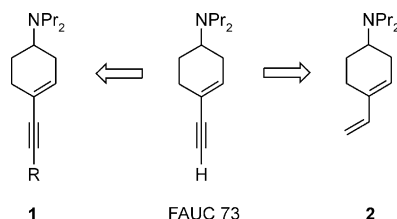


Several benzimidazoles, quinoxalines and indoles with a hydrophenanthrene-based skeleton, such as **5a**, **11** and **14**, were synthesized from dehydroabiatic acid. Some of the new heterocycles showed activity against human cytomegalovirus and varicella-zoster virus.

### Analogues of FAUC 73 revealing new insights into the structural requirements of nonaromatic dopamine D3 receptor agonists

pp 113–117

Carola Lenz, Frank Boeckler, Harald Hübner and Peter Gmeiner\*

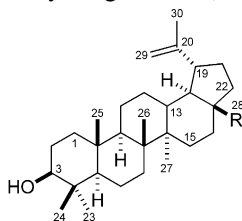


Employing the D3 agonist FAUC 73 as a lead compound, novel nonaromatic bioisosteres were synthesized via palladium-catalyzed cross-coupling and investigated for their binding properties.

### Erythrocyte membrane modifying agents and the inhibition of *Plasmodium falciparum* growth: structure–activity relationships for betulinic acid analogues

pp 119–127

Hanne L. Ziegler, Henrik Franzyk, Majid Sairafianpour, Mehrnosh Tabatabai, Mahboubeh D. Tehrani, Karim Bagherzadeh, Henry Hägerstrand, Dan Stærk and Jerzy W. Jaroszewski\*

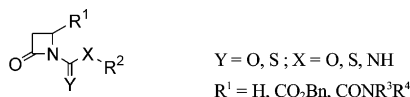


Several betulinic acid analogues were synthesized and shown to modify erythrocyte membrane according to their hydrogen bonding properties; the presence of the compounds in the erythrocyte membrane inhibited invasion and growth of malaria parasites.

### Synthesis and evaluation of N1/C4-substituted $\beta$ -lactams as PPE and HLE inhibitors

pp 129–138

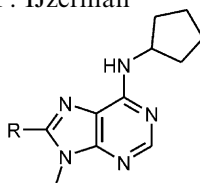
Stéphane Gérard, Moreno Galleni, Georges Dive and Jacqueline Marchand-Brynaert\*



### Synthesis and biological evaluation of disubstituted $N^6$ -cyclopentyladenine analogues: the search for a neutral antagonist with high affinity for the adenosine $A_1$ receptor

pp 139–149

Rianne A. F. de Ligt, Pieter A. M. van der Klein, Jacobien K. von Frijtag Drabbe Künzel, Anna Lorenzen, Fatna Ait El Maate, Shelly Fujikawa, Rosemarijn van Westhoven, Thijs van den Hoven, Johannes Brussee and Ad P. IJzerman\*

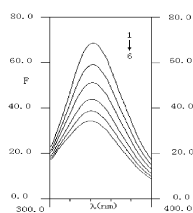


Derivatives of the above general structure were synthesized and tested as ligands for adenosine  $A_1$  receptors. Several compounds showed nanomolar affinity, some of them behaving as neutral antagonists, whereas others proved to be inverse agonists with varying degrees of (negative) intrinsic activity.

### Interactions between 1-benzoyl-4-*p*-chlorophenyl thiosemicarbazide and serum albumin: investigation by fluorescence spectroscopy

pp 151–157

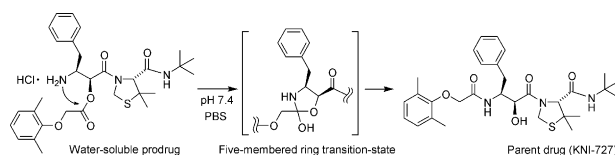
Feng-Ling Cui, Jing Fan, Jian-Ping Li and Zhi-De Hu\*



### Water-soluble prodrugs of dipeptide HIV protease inhibitors based on *O*→*N* intramolecular acyl migration: design, synthesis and kinetic study

pp 159–170

Yoshio Hamada, Hikaru Matsumoto, Satoshi Yamaguchi, Tooru Kimura, Yoshio Hayashi and Yoshiaki Kiso\*

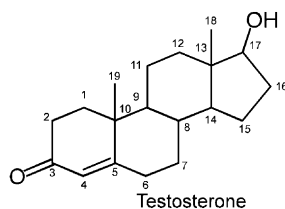


Based on the *O*→*N* acyl migration strategy, water-soluble prodrugs of small-sized dipeptide HIV protease inhibitors were designed and synthesized.

### DFT-based QSAR study of testosterone and its derivatives

pp 171–177

P. P. Singh,\* H. K. Srivastava and F. A. Pasha

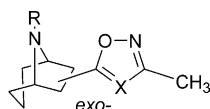


Testosterone is primarily male sex hormone. The Density Functional Theory (DFT)-based QSAR study of 75 derivatives of Testosterone is presented with PM3 calculations on WinMopac 7.21 software.

### Homoepiboxidines: further potent agonists for nicotinic receptors

pp 179–190

Richard W. Fitch, Xue-Feng Pei, Yumika Kaneko, Tara Gupta, Dan Shi, Irina Federova and John W. Daly\*

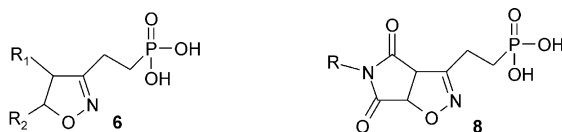


Homoepiboxidine (R=H, X=CH), its *N*-methyl and *N*-benzyl derivatives, as well as two oxadiazole (R=H, CH<sub>3</sub>, X=N) analogues were prepared. In vitro binding and functional activities at several nicotinic acetylcholine receptor subtypes were evaluated as well as in vivo analgesia and toxicities.

### One-pot synthesis of functionalized 4,5-dihydroisoxazole derivatives via nitrile oxides and biological evaluation with plant cells

pp 191–197

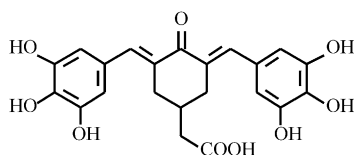
Zoia Mincheva, Martine Courtois, Joël Crèche, Marc Rideau and Marie-Claude Viaud-Massuard\*



### 2,6-Bis(3,4,5-trihydroxybenzylidene) derivatives of cyclohexanone: novel potent HIV-1 integrase inhibitors that prevent HIV-1 multiplication in cell-based assays

pp 199–215

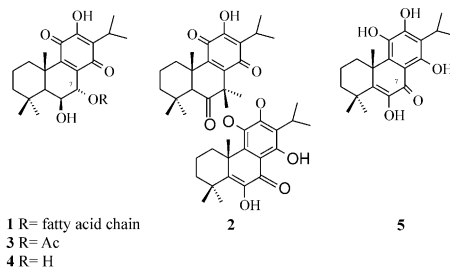
Roberta Costi, Roberto Di Santo, Marino Artico,\* Silvio Massa, Rino Ragno, Roberta Loddo, Massimiliano La Colla, Enzo Tramontano, Paolo La Colla\* and Alessandra Pani



### Effect of abietane diterpenes from *Plectranthus grandidentatus* on T- and B-lymphocyte proliferation

pp 217–223

F. Cerqueira, A. Cordeiro-Da-Silva, C. Gaspar-Marques, F. Simões, M. M. M. Pinto and M. S. J. Nascimento\*

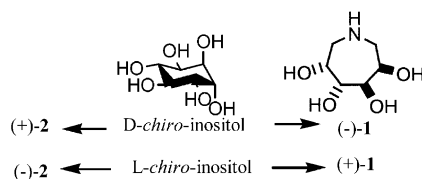


The effect of natural abietane diterpenes of the royleanone and coleon type on the proliferation of human lymphocytes and mouse splenocytes proliferation induced by different mitogens is described. Their effect on the CD69 expression and apoptosis is also reported.

### Syntheses of tetrahydroxyazepanes from *chiro*-inositols and their evaluation as glycosidase inhibitors

pp 225–232

Gavin F. Painter,\* Paul J. Eldridge and Andrew Falshaw

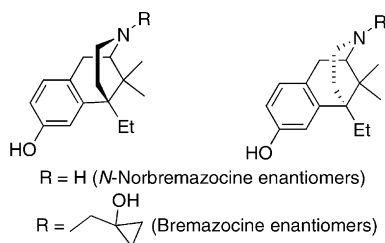


Synthesis and enzyme inhibition properties of four C<sub>2</sub> symmetric tetrahydroxyazepanes.

### A novel and facile preparation of bremazocine enantiomers through optically pure *N*-norbremazocines

pp 233–238

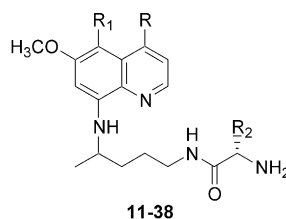
Elisabeth Greiner, John E. Folk, Arthur E. Jacobson and Kenner C. Rice\*



### 8-Quinolinamines conjugated with amino acids are exhibiting potent blood-schizontocidal antimalarial activities

pp 239–247

Suryanarayana Vangapandu, Sandeep Sachdeva, Meenakshi Jain, Savita Singh, Prati Pal Singh, Chaman Lal Kaul and Rahul Jain\*

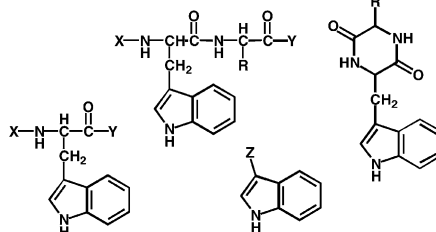


Synthesis and potent in vivo antimalarial activities of a series of L-amino acid conjugates of *N*<sup>8</sup>-(4-amino-1-methylbutyl)-5-alkoxy-4-ethyl-6-methoxy-8-quinolinamines and primaquine against drug-sensitive and multi-drug resistant strain of *Plasmodium* are described.

### Relationship between structure and permeability of dipeptide derivatives containing tryptophan and related compounds across human intestinal epithelial (Caco-2) cells

pp 249–255

Rieko Ano, Yukitaka Kimura, Machiko Urakami, Motohiro Shima, Ryuichi Matsuno, Tamio Ueno and Miki Akamatsu\*

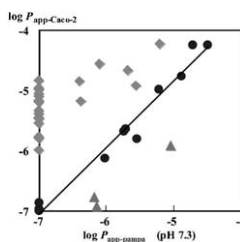


The permeability of dipeptide derivatives containing tryptophans and indole derivatives through Caco-2 cells was used as an in vitro intestinal absorption model in order to clarify structural factors which influence their intestinal epithelial permeation and metabolism.

### Relationships between structure and high-throughput screening permeability of peptide derivatives and related compounds with artificial membranes: application to prediction of Caco-2 cell permeability

pp 257–264

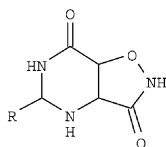
Rieko Ano, Yukitaka Kimura, Motohiro Shima, Ryuichi Matsuno, Tamio Ueno and Miki Akamatsu\*



To evaluate absorption of compounds across the membrane via a transcellular route, the permeability of peptide derivatives and related compounds was measured by the parallel artificial membrane permeation assay (PAMPA). The relationship between Caco-2 cell permeability and artificial lipid membrane permeability was then determined.

**Synthesis and pharmacological assessment of derivatives of isoxazolo[4,5-*d*]pyrimidine****pp 265–272**

Edwin Wagner,\* Lilianna Becan and Elżbieta Nowakowska

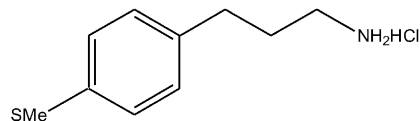


A series of new 5-alkyl and 5-arylisoxazolo[4,5-*d*]pyrimidinones were prepared from 4-amino-3-oxo-isoxazolidine-5-carboxylic acid amide. Some of the aryl derivatives of isoxazolo[4,5-*d*]pyrimidine were tested.

**Synthesis of 4-methyl-thio-phenyl-propylamine and the evaluation of its interaction with different amine oxidases****pp 273–279**

Alejandra Gallardo-Godoy, Mar Hernandez, Elisenda Sanz and Mercedes Unzeta\*

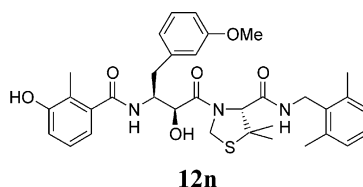
A new molecule, the 4-methyl-thio-phenyl-propylamine, was synthesized and its biological interaction with different amine oxidases such as semicarbazide sensitive amine oxidase (SSAO) [E.C.1.4.3.6], and Monoamine Oxidase [E.C.1.4.3.4] under its two isoforms, MAO A and MAO B, has been assessed. The substrate specificities of MAO and SSAO overlap to some extent. In this context the search for new molecules, able to discriminate between these different amine oxidases is very important as it will allow greater elucidation of the role of SSAO in physiological and pathological conditions. We report for the first time, the synthesis and evaluation of a new molecule which has a high affinity towards the SSAO family of enzymes, more so than previously described and furthermore an ability to discriminate between the different amine oxidases.



4-Methyl-thio-phenyl-propylamine

**Structure–activity and structure–metabolism relationships of HIV protease inhibitors containing the 3-hydroxy-2-methylbenzoyl-allophenylnorstatine structure****pp 281–293**

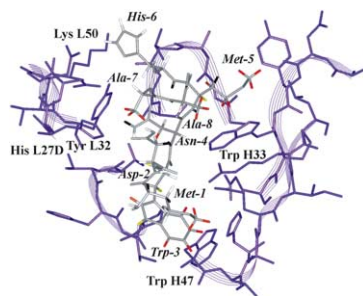
Tsutomu Mimoto,\* Keisuke Terashima, Satoshi Nojima, Haruo Takaku, Mitsunobu Nakayama, Makoto Shintani, Takashi Yamaoka and Hideya Hayashi



SM-322377 (**12n**) had potent antiviral activity against not only wild type HIV-1 but also the multi-drug-resistant HIV-1.

**Saturation-transfer difference NMR studies for the epitope mapping of a carbohydrate-mimetic peptide recognized by an anti-carbohydrate antibody****pp 295–300**

Margaret A. Johnson and B. Mario Pinto\*





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Contributors to this issue  
Instructions to contributors

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\*Corresponding author

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**COVER**

2004: Overlaps of the eight known aldolase alpha-beta barrels in 2-Deoxyribose-5-phosphate aldolase (DERA). Ribbon model for DERA is shown in green, with key Lys residues capable of Schiff base formation highlighted in stick figure. Reactive Lys167 is shown in yellow. DeSantis, G.; Liu, J.; Clark, D. P.; Heine, A.; Wilson, I. A.; and Wong, C.-H. *Bioorganic & Medical Chemistry* **2003**, *11*, 43–52.



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