

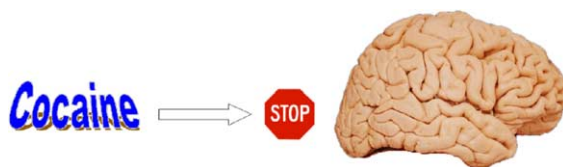
## Contents

### REVIEW

**Cocaine pharmacology and current pharmacotherapies for its abuse**

pp 5019–5030

M. Rocío A. Carrera, Michael M. Meijler and Kim D. Janda\*

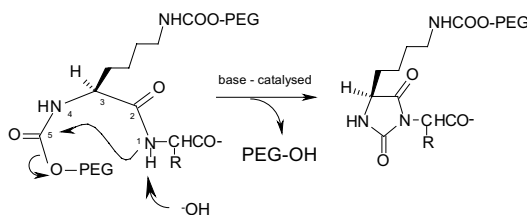


### ARTICLES

**Anchimeric assistance effect on regioselective hydrolysis of branched PEGs:  
a mechanistic investigation**

pp 5031–5037

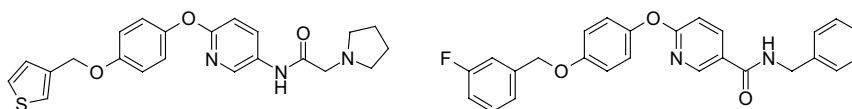
Andrea Guiotto, Mirta Canevari, Michela Pozzobon, Stefano Moro, Piero Orsolini  
and Francesco M. Veronese\*



**Synthesis and structure–activity relationships of phenoxy pyridine derivatives as novel  
inhibitors of the sodium–calcium exchanger**

pp 5039–5056

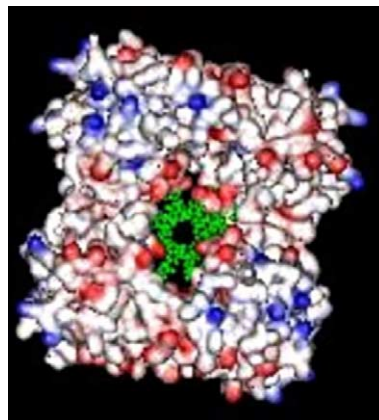
Takahiro Kuramochi,\* Akio Kakefuda, Hiroyoshi Yamada, Ippei Sato,  
Taku Taguchi and Shuichi Sakamoto



A series of 2-phenoxy pyridine derivatives were prepared and evaluated for their inhibitory activity against the reverse and forward modes of the sodium–calcium exchanger (NCX). The structure–activity relationships of these compounds on the inhibitory activity for the sodium–calcium exchanger are discussed.

### Designed calix[8]arene-based ligands for selective tryptase surface recognition

Tommaso Mecca, Grazia M. L. Consoli, Corrada Geraci and Francesca Cunsolo\*

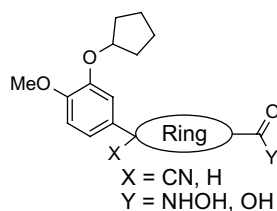


pp 5057–5062

### Design, synthesis, and biological evaluation of new phosphodiesterase type 4 inhibitors

pp 5063–5078

Hiroshi Ochiai, Yoshihiko Odagaki, Tazumi Ohtani, Akiharu Ishida, Kensuke Kusumi, Katuya Kishikawa, Susumu Yamamoto, Hiroshi Takeda, Takaaki Obata, Kaoru Kobayashi, Hisao Nakai\* and Masaaki Toda

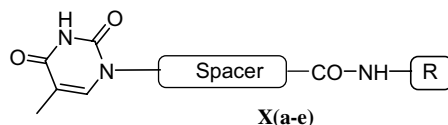


The mode of interaction with enzyme is hypothesized based on the SAR data.

### Synthesis and evaluation of thymine-derived carboxamides against mitochondrial thymidine kinase (TK-2) and related enzymes

pp 5079–5090

Eva-María Priego, Jan Balzarini, Anna Karlsson, María-José Camarasa and María-Jesús Pérez-Pérez\*

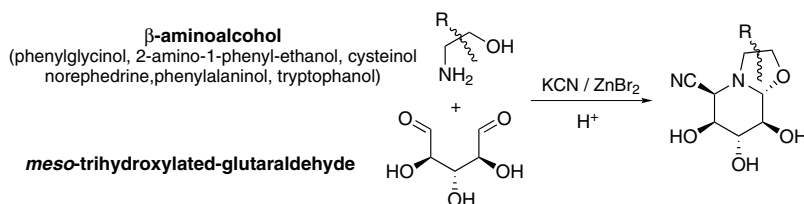


Three series of thymine-derived carboxamides **X(a–e)** have been prepared by a solution-phase parallel synthesis based on the coupling of thymine-derived acids [4-(thymine-1-yl)butyric acid (**I**), 4-(thymine-1-yl)-butyrylamino]acetic acid (**II**) and 6-(thymine-1-yl)hexanoic acid (**III**)] with different commercially available primary amines that carry cyano and/or phenyl groups. The resulting carboxamides have been tested against TK-2 and related enzymes.

### Synthesis of polyhydroxylated piperidines and evaluation as glycosidase inhibitors

pp 5091–5097

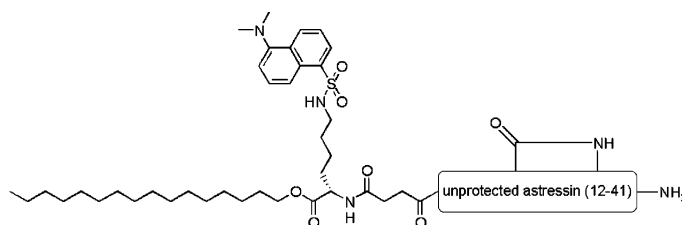
Tony Tite, Marie-Christine Lallemand,\* Erwan Poupon, Nicole Kunesch, François Tillequin, Christine Gravier-Pelletier, Yves Le Merrer and Henri-Philippe Husson\*



**Synthesis and biological activity of N-terminal lipidated and/or fluorescently labeled conjugates of astressin as corticotropin releasing factor antagonists**

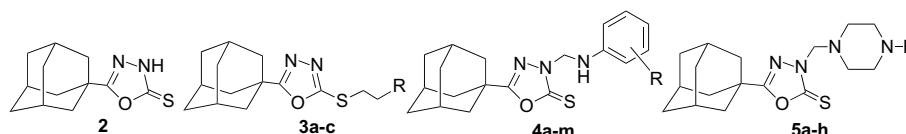
pp 5099–5106

Dirk T. S. Rijkers,\* Jack A. J. den Hartog and Rob M. J. Liskamp

unprotected astressin: ~D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Glu\*-Ala-His-Lys\*-Asn-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH<sub>2</sub>, (Glu\*/Lys\* form the lactam bridge)**Synthesis, antimicrobial, and anti-HIV-1 activity of certain 5-(1-adamantyl)-2-substituted thio-1,3,4-oxadiazoles and 5-(1-adamantyl)-3-substituted aminomethyl-1,3,4-oxadiazoline-2-thiones**

pp 5107–5113

Ali A. El-Emam,\* Omar A. Al-Deeb, Mohamed Al-Omar and Jochen Lehmann

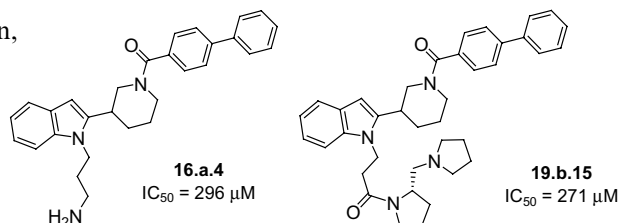


Derivatives of the above structures were synthesized and tested for their in vitro antimicrobial and anti-HIV-1 activity.

**Combinatorial synthesis of substituted 3-(2-indolyl)piperidines and 2-phenyl indoles as inhibitors of ZipA–FtsZ interaction**

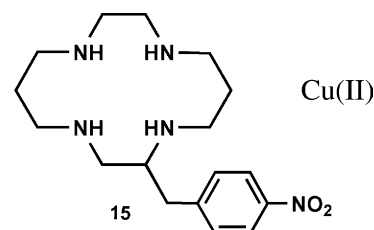
pp 5115–5131

Lee D. Jennings,\* Kenneth W. Foreman, Thomas S. Rush, III, Desiree H. H. Tsao, Lidia Mosyak, Scott L. Kincaid, Mohani N. Sukhdeo, Alan G. Sutherland, Weidong Ding, Cynthia Hess Kenny, Chantel L. Sabus, Hanlan Liu, Elizabeth G. Dushin, Soraya L. Moghazeh, Pornpen Labthavikul, Peter J. Petersen, Margareta Tuckman and Alexey V. Ruzin

**Evaluation of chelating agents as anti-angiogenic therapy through copper chelation**

pp 5133–5140

Kevin Camphausen, Mary Sproull, Steve Tantama, Vincent Venditto, Sandeep Sankineni, Tamalee Scott and Martin W. Brechbiel\*



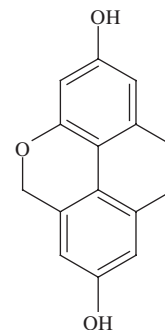
A set of novel polyamine hexadentate *cis,cis*-1,3,5,-triaminocyclohexane (tach) chelating agents were synthesized and evaluated in conjunction with a selection of both linear and macrocyclic polyamines as copper chelators for novel anti-angiogenic therapy in an in vitro endothelial cell proliferation assay to assess their cytotoxicity and selectivity. Macrocyclic polyamine 15 exhibited the greatest selective activity in this assay while the tach based ligands exhibited cytotoxicity, but no selectivity.

**Antioxidant activities of flavidin in different in vitro model systems**

pp 5141–5146

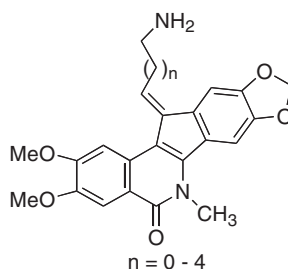
Guddadarangavvanahally K. Jayaprakasha,\* Lingamallu Jaganmohan Rao and Kunnumpurath K. Sakariah

Flavidin was isolated from *Orchidaceae* species and purified by silica gel column chromatography. The structure was identified using spectral studies. Antioxidant potency of flavidin was investigated employing various established in vitro model systems viz.,  $\beta$ -carotene-linoleate, 1,1-diphenyl-2-picryl hydrazyl (DPPH), phosphomolybdenum method, and scavenging of hydrogen peroxide methods. Flavidin showed very good antioxidant activity in all the tested in vitro methods. This is the first report on antioxidant activity of 9,10-dihydro-5H-phenanthro-(4,5 bcd)-pyrans/flavidin type of compounds.

**Design, synthesis, and biological evaluation of cytotoxic 11-aminoalkenylindenoisoquinoline and 11-diaminoalkenylindenoisoquinoline topoisomerase I inhibitors**

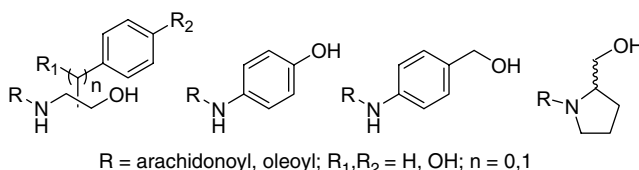
pp 5147–5160

Xiangshu Xiao, Smitha Antony, Glenda Kohlhagen, Yves Pommier and Mark Cushman\*

**The anandamide membrane transporter. Structure–activity relationships of anandamide and oleylethanolamine analogs with phenyl rings in the polar head group region**

pp 5161–5169

Vincenzo Di Marzo, Alessia Ligresti, Enrico Morera, Marianna Nalli and Giorgio Ortar\*

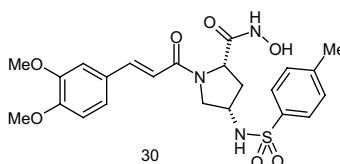


A new series of arachidonic and oleic acids derivatives, most of which with aromatic moieties in the head group region, has been synthesized and evaluated as inhibitors of anandamide uptake.

**Design, synthesis, and activity of caffeoyl pyrrolidine derivatives as potential gelatinase inhibitors**

pp 5171–5180

Ya-Lin Li and Wen-Fang Xu\*

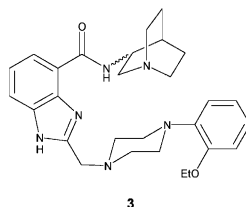


A group of caffeoyl pyrrolidine derivatives has been developed to act as potential gelatinase inhibitors.

**Benzimidazole derivatives. Part 5: Design and synthesis of new benzimidazole–arylpiperazine derivatives acting as mixed 5-HT<sub>1A</sub>/5-HT<sub>3</sub> ligands**

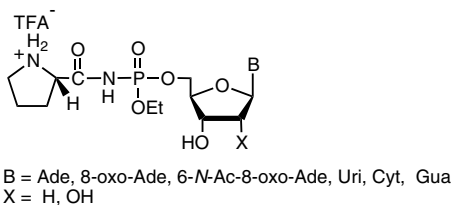
pp 5181–5191

María L. López-Rodríguez,\* Bellinda Benhamú, M<sup>a</sup> José Morcillo, Ignacio Tejada, David Avila, Isabel Marco, Lucio Schiapparelli, Diana Frechilla and Joaquín Del Río

**Structure–activity relationship of phosmidosine: importance of the 7,8-dihydro-8-oxoadenosine residue for antitumor activity**

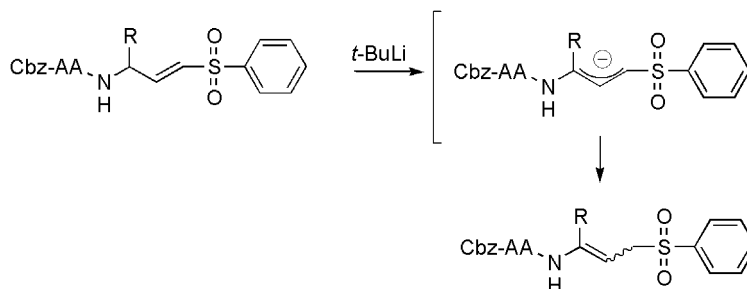
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Mitsuo Sekine,\* Kazuhisa Okada, Kohji Seio, Hideaki Kakeya, Hiroyuki Osada and Takuma Sasaki

**Peptidyl allyl sulfones: a new class of inhibitors for clan CA cysteine proteases**

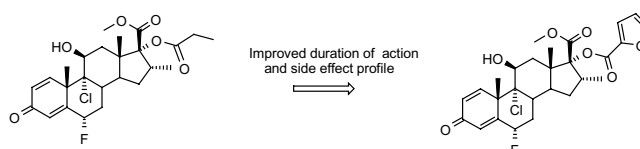
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Marion G. Götz, Conor R. Caffrey, Elizabeth Hansell, James H. McKerrow and James C. Powers\*

**Synthesis and biological properties of novel glucocorticoid androstene C-17 furoate esters**

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David A. Sandham,\* Lucy Barker, David Beattie, David Beer, Louise Bidlake, David Bentley, Keith D. Butler, Sarah Craig, David Farr, Claire Ffoulkes-Jones, John R. Fozard, Sandra Habberthuer, Colin Howes, Deborah Hynx, Sarah Jeffers, Thomas H. Keller, Paul A. Kirkham, Janet C. Maas, Lazzaro Mazzoni, Andrew Nicholls, Gaynor E. Pilgrim, Elisabeth Schaebulin, Gillian M. Spooner, Rowan Stringer, Pamela Tranter, Katharine L. Turner, Morris F. Tweed, Christoph Walker, Simon J. Watson and Bernard M. Cuenoud\*

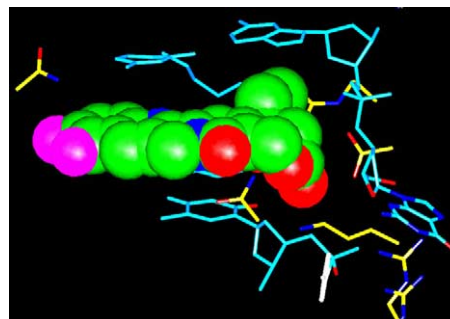


**Analysis of human topoisomerase I inhibition and interaction with the cleavage site +1 deoxyguanosine, via in vitro experiments and molecular modeling studies**

pp 5225–5235

Gary S. Laco, Wu Du, Glenda Kohlhausen, Jane M. Sayer,  
Donald M. Jerina, Thomas G. Burke, Dennis P. Curran  
and Yves Pommier\*

Human topoisomerase I Tyr723 (white) in covalent complex with DNA (light blue) via the –1 deoxythymidine (bottom), while the +1 deoxyguanosine with a free 5'-OH is rotated out of the helix (right). Homocamptothecin 9,10 diF (green) is docked in the active site (A–E rings, left to right). Active-site residues (yellow) that make H-bond/electrostatic contacts with either inhibitor, or the rotated +1 deoxyguanosine, are shown. Oxygen, red; nitrogen, blue; fluorine, magenta.

**OTHER CONTENTS****Corrigendum**

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**Bioorganic & Medicinal Chemistry Reviews and Perspectives**

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**Contributors to this issue**

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**Instructions to contributors**

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\*Corresponding author

**COVER**

The cover image illustrates some of the therapeutical and immunological strategies that have been explored recently to block the effects of cocaine on the brain. Details can be found in *Bioorganic & Medicinal Chemistry* **2004**, 12, 5019–5030.  
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