

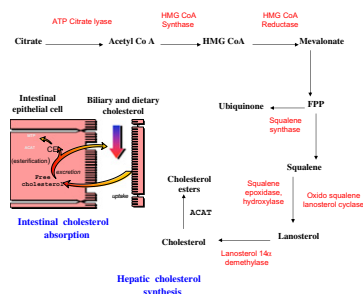
Contents

REVIEW

The biology and chemistry of hyperlipidemia

pp 4674–4699

Kishor S. Jain,* M. K. Kathiravan, Rahul S. Somani and Chamanlal J. Shishoo

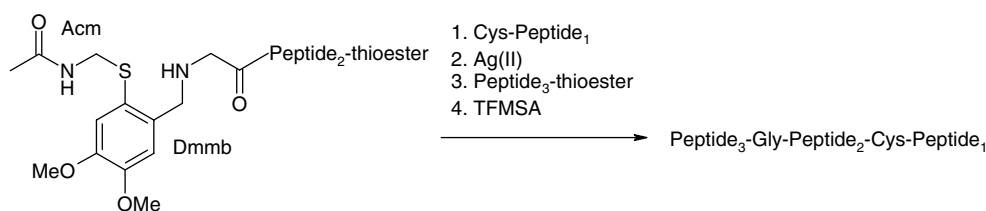


ARTICLES

Tandem ligation at X-Cys and Gly-Gly positions via an orthogonally protected auxiliary group

pp 4700–4704

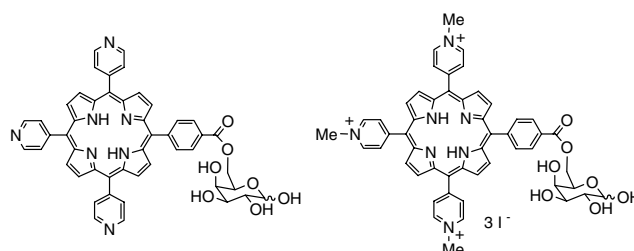
Jane C. Spetzler and Thomas Hoeg-Jensen*



Synthesis of neutral and cationic tripyridylporphyrin-D-galactose conjugates and the photoinactivation of HSV-1

pp 4705–4713

João P. C. Tomé, Eduarda M. P. Silva, Ana M. V. M. Pereira, Cristina M. A. Alonso, Maria A. F. Faustino, Maria G. P. M. S. Neves, Augusto C. Tomé, José A. S. Cavaleiro,* Sabina A. P. Tavares, Ricardo R. Duarte, Maria F. Caeiro and Maria L. Valdeira

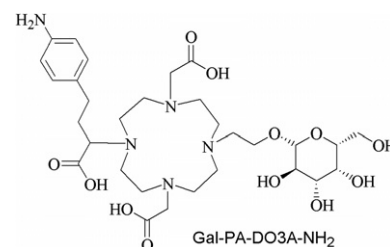


Synthesis of a novel ‘smart’ bifunctional chelating agent 1-(2-[β ,D-galactopyranosyloxy]ethyl)-7-(1-carboxy-3-[4-aminophenyl]propyl)-4,10-bis(carboxymethyl)-1,4,7,10-tetraazacyclododecane (Gal-PA-DO3A-NH₂) and its Gd(III) complex

pp 4714–4721

Nick J. Wardle, Amy H. Herlihy, Po-Wah So, Jimmy D. Bell and S. W. Annie Bligh*

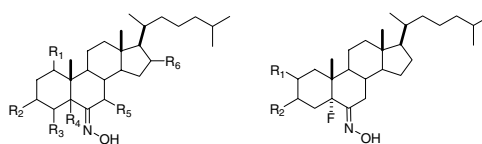
A novel synthesis of Gal-PA-DO3A-NH₂ was developed, and the relaxivity of its Gd(III) complex and its responsiveness to β -galactosidase was comparable to the reported ‘smart’ MRI contrast agent, Gd(III) Gal-DO3A complex.



Synthesis and evaluation of new 6-hydroximinosteroid analogs as cytotoxic agents

pp 4722–4740

Javier Poza, Miriam Rega, Vanessa Paz, Beatriz Alonso, Jaime Rodríguez,*
Nélida Salvador, Antonio Fernández and Carlos Jiménez*



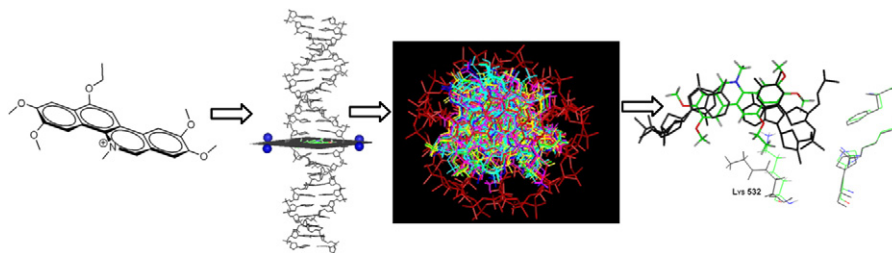
R₁, R₂, R₃, R₄, R₅, R₆ = different oxygenated positions

Several new 6-hydroximinosteroid derivatives have been prepared and evaluated for their cytotoxic activity against A-549, H116, PSN1 and T98G cultured tumor cell lines. They showed an important selectivity toward colon tumor line (HCT-116).

Exploring DNA topoisomerase I inhibition by the benzo[c]phenanthridines fagaronine and ethoxidine using steered molecular dynamics

pp 4741–4752

Rachel L. Clark, Fiona M. Deane, Nahoum G. Anthony, Blair F. Johnston,
Florence O. McCarthy and Simon P. Mackay*

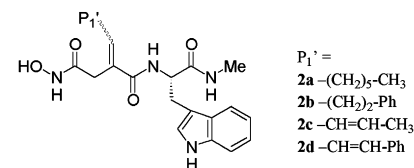


Simultaneous presence of unsaturation and long alkyl chain at P₁' of Ilomastat confers selectivity for gelatinase A (MMP-2) over gelatinase B (MMP-9) inhibition as shown by molecular modelling studies

pp 4753–4766

Gautier Moroy, Clément Denhez, Haquima El Mourabit, Alix Toribio, Alexandra Dassonville,
Martine Decarme, Jean-Hugues Renault, Catherine Mirand, Georges Bellon, Janos Sapi,
Alain J. P. Alix, William Hornebeck and Erika Bourguet*

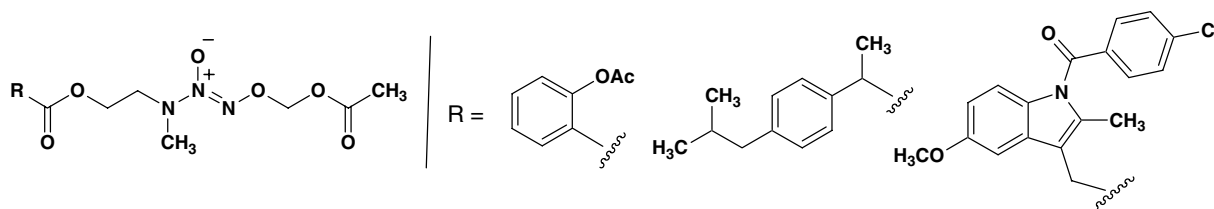
The synthesis and centrifugal partition chromatography (CPC) purification, molecular modelling, as well as the biological activities of structural analogues of Ilomastat as MMPs inhibitors are reported. The modifications of P₁' sites have demonstrated potent inhibitory and selective activities against either MMP-2 or MMP-9.



***O*²-Acetoxymethyl-protected diazeniumdiolate-based NSAIDs (NONO-NSAIDs):
Synthesis, nitric oxide release, and biological evaluation studies**

pp 4767–4774

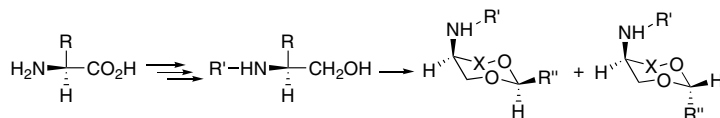
Carlos A. Velázquez, P. N. Praveen Rao, Michael L. Citro, Larry K. Keefer and Edward E. Knaus*



**Toward the development of chemoprevention agents. Part 1: Design, synthesis,
and anti-inflammatory activities of a new class of 2,5-disubstituted-dioxacycloalkanes**

pp 4775–4799

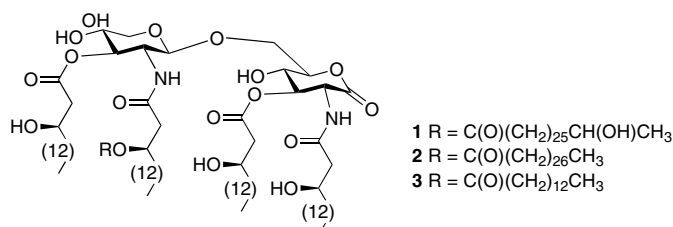
Keli Gu, Lanrong Bi, Ming Zhao,* Chao Wang, Jingfang Ju* and Shiqi Peng*



**The influence of the long chain fatty acid on the antagonistic activities of
Rhizobium sin-1 lipid A**

pp 4800–4812

Yanghui Zhang, Margreet A. Wolfert and Geert-Jan Boons*

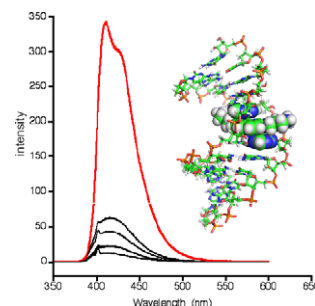


Synthesis of *Rhizobium sin-1* lipid A analogues and evaluation of their ability to antagonize the production of TNF- α by human monocytic cells induced by enteric LPS are described.

**Emission of characteristic fluorescence from the ligand–cytosine complex in U_A/ACU
bulged RNA duplex**

pp 4813–4817

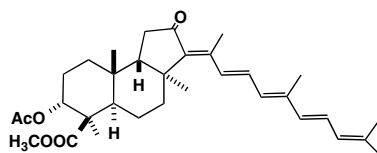
Jinhua Zhang, Fumie Takei and Kazuhiko Nakatani*

DANP binds to C-bulge in U_A/ACU RNA duplex and emits characteristic fluorescence.

Novel isommarabarian triterpenes, exhibiting selective anti-proliferative activity against vascular endothelial cells, from marine sponge *Rhabdastrella globostellata*

pp 4818–4828

Shunji Aoki, Mami Sanagawa, Yasuo Watanabe, Andi Setiawan, Masayoshi Arai and Motomasa Kobayashi*



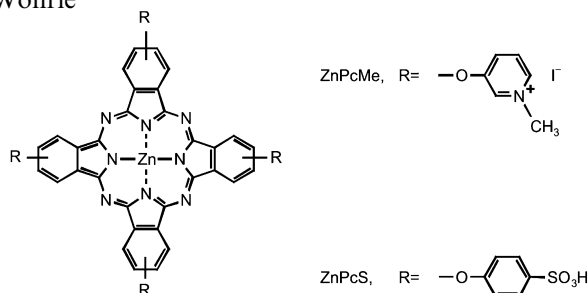
13E,17E-Globostellatic acid X methyl ester

Four novel isommarabarian triterpenes named globostellatic acid methyl esters and the related compounds were isolated from the marine sponge *Rhabdastrella globostellata*. Their chemical structures and in vitro antiangiogenic activities were examined.

Photodynamic activity of water-soluble phthalocyanine zinc(II) complexes against pathogenic microorganisms

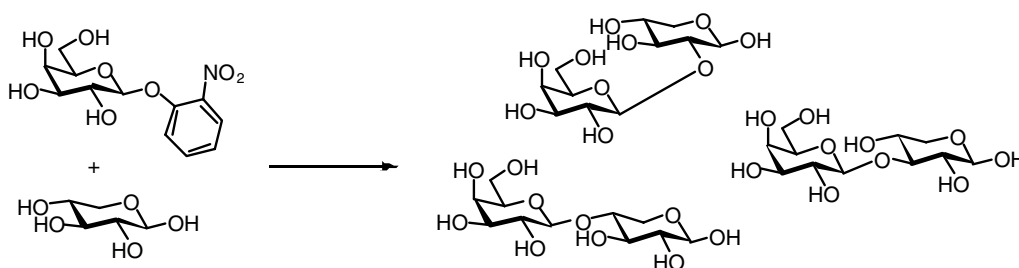
pp 4829–4835

Vanya Mantareva,* Veselin Kussovski, Ivan Angelov, Ekaterina Borisova, Latchezar Avramov, Günter Schnurpfeil and Dieter Wöhrle


Optimizing the enzymatic synthesis of β -D-galactopyranosyl-D-xyloses for their use in the evaluation of lactase activity in vivo

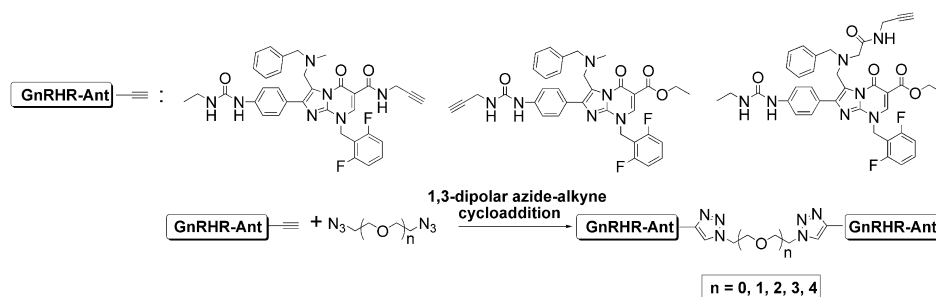
pp 4836–4840

Carmen Hermida, Guillermo Corrales, Francisco J. Cañada, Juan J. Aragón* and Alfonso Fernández-Mayoralas*


Synthesis and evaluation of homo-bivalent GnRHR ligands

pp 4841–4856

Kimberly M. Bongers, Richard J. B. H. N. van den Berg, Laura H. Heitman, Ad P. IJzerman, Julia Oosterom, Cornelis M. Timmers, Herman S. Overkleeft* and Gijsbert A. van der Marel*

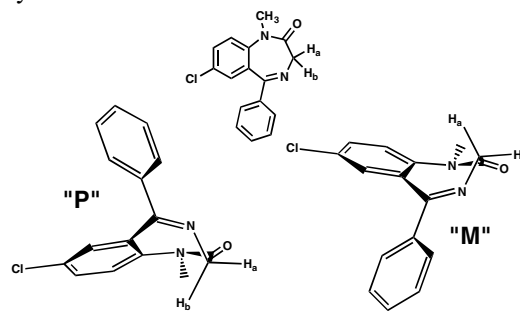


Conformation selectivity in the binding of diazepam and analogues to α_1 -acid glycoprotein

pp 4857–4862

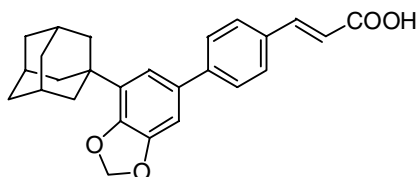
Ilona Fitos,* Júlia Visy, Ferenc Zsila, György Mády and Miklós Simonyi

Diazepam forms an equimolar mixture of two chiral conformers. Induced CD spectra in serum protein solutions proved the P-conformer to be preferred by α_1 -acid glycoprotein binding, contrary to albumin.

**Synthesis and structure–activity relationships of new antiproliferative and proapoptotic retinoid-related biphenyl-4-yl-acrylic acids**

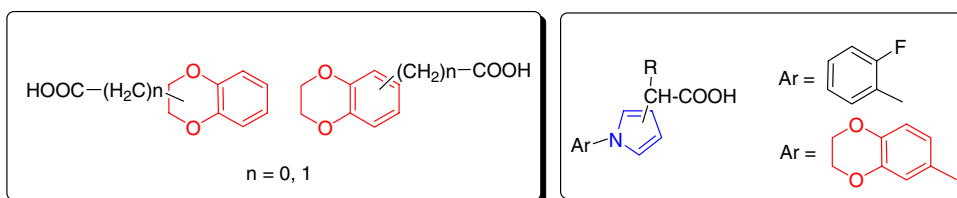
pp 4863–4875

Raffaella Cincinelli, Sabrina Dallavalle,* Raffaella Nannei, Lucio Merlini, Sergio Penco, Giuseppe Giannini, Claudio Pisano, Loredana Vesci, Fabiana Fosca Ferrara, Valentina Zuco, Chiara Zanchi and Franco Zunino

**Synthesis and biological activity of new anti-inflammatory compounds containing the 1,4-benzodioxine and/or pyrrole system**

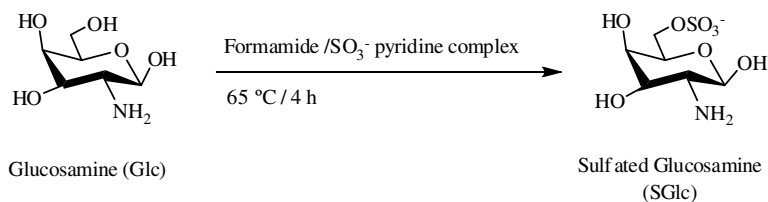
pp 4876–4890

Y. Harrak, G. Rosell, G. Daidone, S. Plescia, D. Schillaci and M. D. Pujol*

**Sulfated glucosamine inhibits MMP-2 and MMP-9 expressions in human fibrosarcoma cells**

pp 4891–4896

Niranjan Rajapakse, Eresha Mendis, Moon-Moo Kim and Se-Kwon Kim*

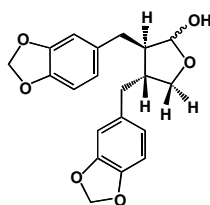


Sulfated glucosamine (SGlc) was prepared from glucosamine (Glc) and studied for its inhibitory effects on MMP-2 and MMP-9 in human fibrosarcoma (HT1080) cells. SGlc inhibited both MMP-2 and MMP-9 expressions by down-regulating their transcription factor NF- κ B.

Mechanism of the melanogenesis stimulation activity of (–)-cubebin in murine B16 melanoma cells

pp 4897–4902

Noriko Hirata, Shunsuke Naruto, Kenji Ohguchi, Yukihiro Akao, Yoshinori Nozawa, Munekazu Iinuma and Hideaki Matsuda*



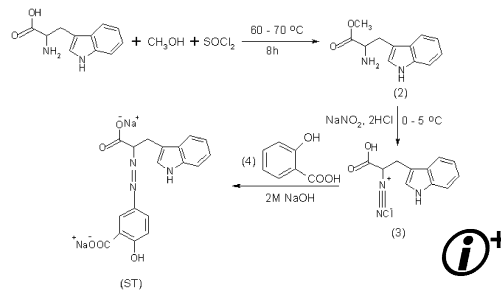
(–)-Cubebin increased melanogenesis in B16 cells through the enhancement of tyrosinase expression mediated by activation of p38 MAPK.

Colon-specific, mutual azo prodrug of 5-aminosalicylic acid with L-tryptophan:
Synthesis, kinetic studies and evaluation of its mitigating effect
in trinitrobenzenesulfonic acid-induced colitis in rats

pp 4903–4909

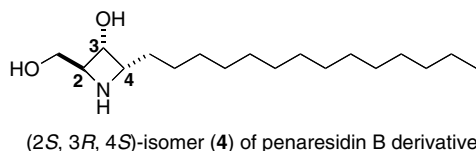
Suneela S. Dhaneshwar,* Neha Gairola, Mini Kandpal, Gaurav Vadnerkar and Lokesh Bhatt

Mutual azo prodrug of 5-aminosalicylic acid with L-tryptophan was synthesized by coupling L-tryptophan with salicylic acid, for targeted drug delivery to the inflamed gut tissue in inflammatory bowel disease.

**Synthesis of penaresidin derivatives and its biological activity**

pp 4910–4916

Kengo Ohshita, Haruaki Ishiyama, Yohei Takahashi, Junji Ito, Yuzuru Mikami and Jun'ichi Kobayashi*

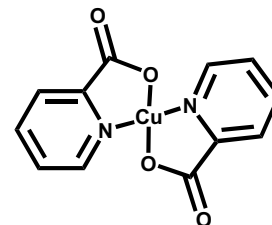


Antidiabetic copper(II)-picolinate: Impact of the first transition metal in the
metallopicolinate complexes

pp 4917–4922

Naoko Yasumatsu, Yutaka Yoshikawa,* Yusuke Adachi and Hiromu Sakurai*

Bis(picolinato)copper(II) complex, Cu(pa)₂, was found to exhibit the most potent insulinomimetic and hypoglycemic effects among the bis or Tris(picolinato) first transition metal complexes examined in this study.



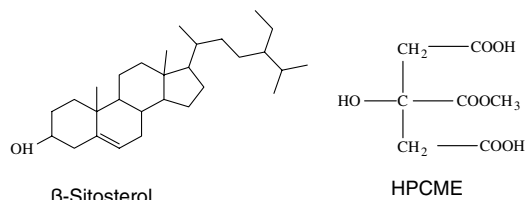
bis(picolinato)copper(II) complex

Inhibition of colon cancer cell growth and antioxidant activity of bioactive compounds from *Poncirus trifoliata* (L.) Raf.

pp 4923–4932

G. K. Jayaprakasha, K. K. Mandadi, Shibu M. Poullose, Y. Jadegoud, G. A. Nagana Gowda and Bhimanagouda S. Patil*

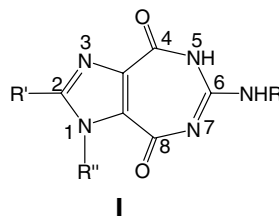
β -Sitosterol and 2-hydroxy-1,2,3-propanetricarboxylic acid 2-methyl ester (HPCME) were isolated and identified from *Poncirus trifoliata* for the first time. These compounds have been tested for their antioxidant capacity and inhibition of cancer cell proliferation and apoptosis using human colon cancer cell line (HT-29). The results were compared with activity on non-cancerous cells (COS-1 fibroblast cells). Significant arrest of cell growth was observed with β -sitosterol even at concentration as low as 0.63 μ M in 48 h.



Chemical and biological effects of substitution of the 2-position of ring-expanded ('fat') nucleosides containing the imidazo[4,5-e][1,3]diazepine-4,8-dione ring system: The role of electronic and steric factors on glycosidic bond stability and anti-HCV activity

pp 4933–4945

Peng Zhang, Ning Zhang, Victor E. Buckwold and Ramachandra S. Hosmane*



Effects of substitution at the 2-position of ring-expanded nucleosides containing the title ring system on their chemical as well as biological activity have been reported.

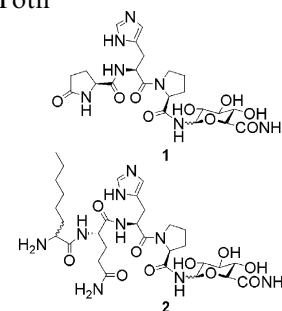


Caco-2 cell permeability and stability of two D-glucopyranuronamide conjugates of thyrotropin-releasing hormone

pp 4946–4950

Susanne T. Wessling, Benjamin P. Ross, Yasuko Koda, Joanne T. Blanchfield and Istvan Toth*

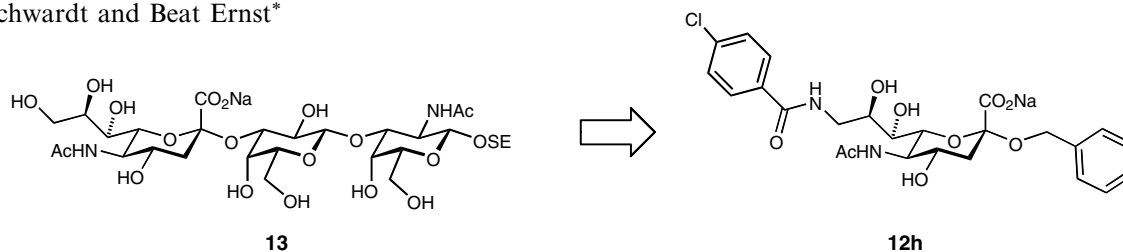
Caco-2 cell permeability and stability assays were used as an in vitro model to study the intestinal epithelial transport and stability of two analogues of thyrotropin-releasing hormone (TRH; Pyr-His-Pro-NH₂).



Synthesis of sialic acid derivatives as ligands for the myelin-associated glycoprotein (MAG)

pp 4951–4965

Sachin V. Shelke, Gan-Pan Gao, Stefanie Mesch, Heiko Gäthje, Soerge Kelm, Oliver Schwardt and Beat Ernst*

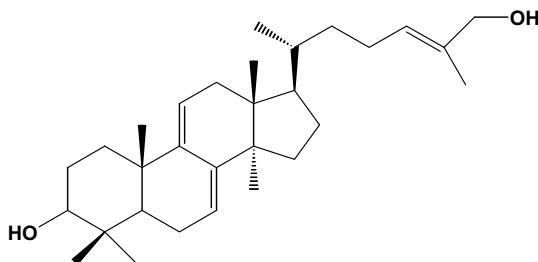


Simplified mimics of trisaccharide **13**, where the core disaccharide Gal β (1–3)GalNAc was replaced with a benzyl group, and the non-reducing end substituted with a *para*-chloro-benzamide, were synthesized and biologically evaluated to produce a 1000-fold more active inhibitor of the myelin-associated glycoprotein (MAG).

The anti-androgen effect of ganoderol B isolated from the fruiting body of *Ganoderma lucidum*

pp 4966–4972

Jie Liu, Kuniyoshi Shimizu, Fumiko Konishi, Shoichiro Kumamoto and Ryuichiro Kondo*

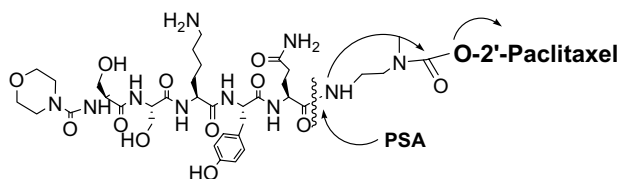


Ganoderol B has been isolated from the ethanol extract of the fruiting body of *Ganoderma lucidum*. This compound exhibited the anti-androgen effect in vitro and in vivo.

Modulating paclitaxel bioavailability for targeting prostate cancer

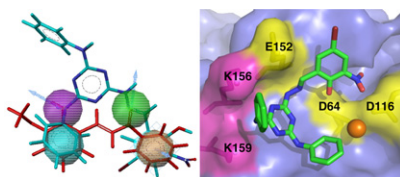
pp 4973–4984

Srinivas K. Kumar, Simon A. Williams, John T. Isaacs, Samuel R. Denmeade and Saeed R. Khan*

2'-[Mu-Ser-Ser-Lys-Tyr-Gln--NH-(CH₂)₂-N(CH₃)]-Paclitaxel**Discovery of structurally diverse HIV-1 integrase inhibitors based on a chalcone pharmacophore**

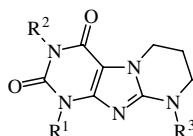
pp 4985–5002

Jinxia Deng, Tino Sanchez, Laith Q. Al-Mawsawi, Raveendra Dayam, Rosendo A. Yunes, Antonio Garofalo, Michael B. Bolger and Nouri Neamati*

**N9-Benzyl-substituted 1,3-dimethyl- and 1,3-dipropyl-pyrimido[2,1-f]purinediones: Synthesis and structure–activity relationships at adenosine A₁ and A_{2A} receptors**

pp 5003–5017

Anna Drabczyńska, Christa E. Müller, Janina Karolak-Wojciechowska, Britta Schumacher, Anke Schiedel, Olga Yuzlenko and Katarzyna Kieć-Kononowicz*

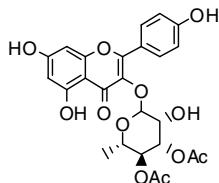


New 1,3-dimethyl and 1,3-dipropyl pyrimido [2,1-f]purinediones were obtained and evaluated in vitro for their affinity to A₁ and A_{2A} adenosine receptors. Physicochemical properties of the compounds were examined by means of calculations. The obtained compounds showed affinity and A₁ or A_{2A} AR selectivity. SAR studies have revealed dependence between A₁ AR affinity and log *P* value. Pharmacophore model for A₁ R ligands has been created.



Structural basis for the activity of the RSK-specific inhibitor, SL0101**pp 5018–5034**

Jeffrey A. Smith, David J. Maloney, Sidney M. Hecht* and Deborah A. Lannigan*



Through the preparation and study of a number of analogues of SL0101, the structural elements essential for its activity and selectivity in vitro and in cells has been defined.

OTHER CONTENTS**Bioorganic & Medicinal Chemistry Reviews and Perspectives****pp 5035–5037****Summary of instructions to authors****p I**

*Corresponding author

①⁺ Supplementary data available via ScienceDirect**COVER**

Terfenadine (an antihistamine pulled from the market in 1997) bound to a model of an open form of the homo-tetrameric pore domain of hERG, produced using Schrödinger's "Induced Fit Docking" technology [Farid, R.; Day, T.; Friesner, R. A.; Pearlstein, R. A. *Bioorg. Med. Chem.* **2006**, *14*, 3160–3173].

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