

Contents

COMMUNICATIONS

In vitro monitoring of nanogram levels of puerarin in human urine using flow injection chemiluminescence

pp 4127–4130

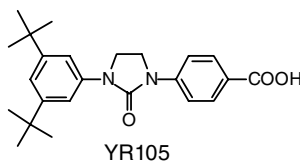
Changna Wang and Zhenghua Song*

A rapid and sensitive method for the determination of sub-nanogram amounts of puerarin in pharmaceutical injections and human urine samples is described, based on the increased effect of puerarin on chemiluminescence reaction between luminol and periodate. Combined with the flow-injection technique, the method supplies a throughput of 180 h^{-1} and linear ranges over puerarin concentration of $0.3\text{--}100\text{ ng mL}^{-1}$ with a detection limit as low as 0.1 ng mL^{-1} (3σ).

Design and synthesis of cyclic urea compounds: a pharmacological study for retinoidal activity

pp 4131–4134

Masaaki Kurihara,* Abu Shara Shamsur Rouf, Hisao Kansui, Hiroyuki Kagechika, Haruhiro Okuda and Naoki Miyata

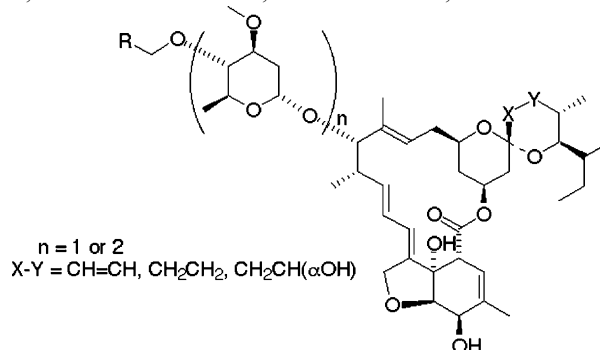


YR105 exhibited potent differentiation-inducing ability toward human promyelocytic leukemia HL-60 cells at the concentration of 10^{-9} M : its potency was almost equal to that of the native ligand, all-*trans* retinoic acid.

Synthesis and biological evaluation of novel 4''-alkoxy avermectin derivatives

pp 4135–4139

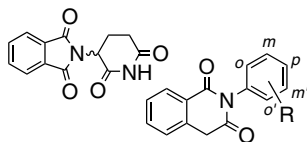
Kenichiro Nagai, Kazuro Shiomi, Toshiaki Sunazuka, Achim Harder, Andreas Turberg and Satoshi Ōmura*



Phenylhomophthalimide-type NOS inhibitors derived from thalidomide

pp 4141–4145

Tomomi Noguchi, Hiroko Sano, Rumiko Shimazawa, Aya Tanatani, Hiroyuki Miyachi and Yuichi Hashimoto*

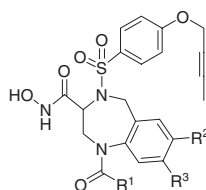


Thalidomide shows moderate inhibitory activity nNOS and iNOS, but not toward eNOS. Structural development studies of thalidomide yielded novel phenylhomophthalimide-type NOS inhibitors.

Benzodiazepine inhibitors of the MMPs and TACE. Part 2

pp 4147–4151

Jeremy I. Levin,* Frances C. Nelson, Efren Delos Santos, Mila T. Du, Gloria MacEwan, James M. Chen, Semiramis Ayral-Kaloustian, Jun Xu, Guixian Jin, Terri Cummons and Dauphine Barone



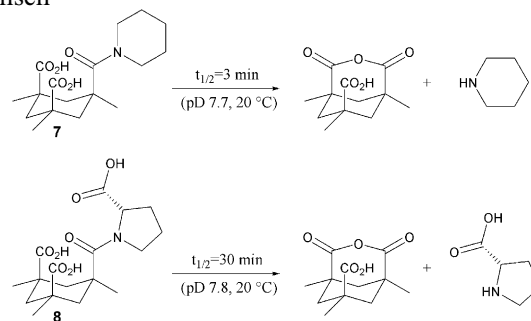
A series of benzodiazepine MMP/TACE inhibitors bearing polar moieties has been synthesized in an effort to optimize inhibitory activity in cells and in vivo.

Rapid cleavage of cyclic tertiary amides of Kemp's triacid: effects of ring structure

pp 4153–4156

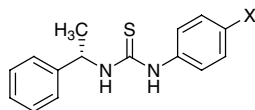
Michael L. Dougan, Jonathan L. Chin, Ken Solt and David E. Hansen*

The rate of amide cleavage of the Kemp's triacid piperidyl derivative **7** and prolyl derivative **8** is extraordinarily rapid and is comparable to that previously reported for the corresponding pyrrolidyl and methylphenethyl amide derivatives. The Kemp's triacid scaffolding thus provides a general means of activating tertiary amide derivatives.

**Thiourea inhibitors of herpesviruses. Part 3: Inhibitors of varicella zoster virus**

pp 4157–4160

Martin J. Di Grandi,* Kevin J. Curran, Gregg Feigelson, Amar Prashad, Adma A. Ross, Robert Visalli, Jeanette Fairhurst, Boris Feld and Jonathan D. Bloom

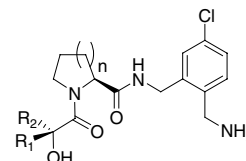


The preparation of α -methylbenzyl thioureas and their biological activity against varicella zoster virus is described. Several analogs demonstrated IC_{50} s $< 0.1 \mu M$ and their SAR are discussed. These compounds represent a novel class of potent and selective nonnucleoside inhibitors of varicella zoster virus.

Low molecular weight thrombin inhibitors with excellent potency, metabolic stability, and oral bioavailability

pp 4161–4164

Matthew M. Morrisette,* Kenneth J. Stauffer, Peter D. Williams, Terry A. Lyle, Joseph P. Vacca, Julie A. Krueger, S. Dale Lewis, Bobby J. Lucas, Bradley K. Wong, Rebecca B. White, Cynthia Miller-Stein, Elizabeth A. Lyle, Audrey A. Wallace, Yvonne M. Leonard, Denise C. Welsh, Joseph J. Lynch and Daniel R. McMasters

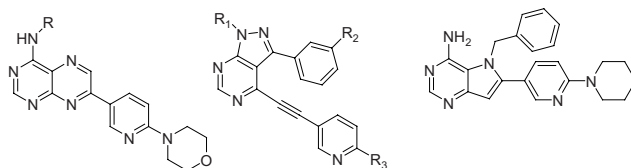


In order to overcome several limitations of our lead compound, which possessed a fluorenyl side chain in P3, we synthesized a series of analogs where we systematically truncated this fluorenyl side chain. This resulted in a series of compounds with progressively smaller aliphatic side chains inhabiting P3. These changes dialed out the undesired properties of the fluorenyl side chain while maintaining thrombin inhibition and desired pharmacokinetics. Subsequent elaboration of the proline P2 unit with an azetidine unit maintained these effects while increasing metabolic stability.

Synthesis and biological evaluation of pteridine and pyrazolopyrimidine based adenosine kinase inhibitors

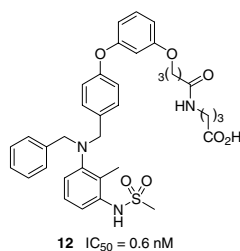
pp 4165–4168

Arthur Gomtsyan,* Stanley Didomenico, Chih-Hung Lee, Andrew O. Stewart, Shripad S. Bhagwat, Elizabeth A. Kowaluk and Michael F. Jarvis

**Optimization and metabolic stabilization of a class of nonsteroidal glucocorticoid modulators**

pp 4169–4172

J. T. Link,* Bryan K. Sorensen, Jyoti Patel, David Arendsen, Gaoquan Li, Susan Swanson, Bach Nguyen, Maurice Emery, Marlena Grynfarb and Annika Goos-Nilsson

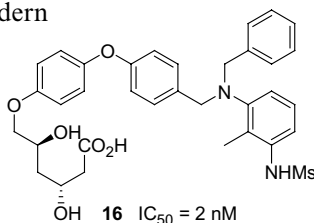


The synthesis and biochemical profile of the potent glucocorticoid receptor modulator **12** (h-GR binding IC_{50} = 0.6 nM) is reported.

Synthesis, activity, metabolic stability, and pharmacokinetics of glucocorticoid receptor modulator–statin hybrids

pp 4173–4178

J. T. Link,* Bryan K. Sorensen, Chunqiu Lai, Jiahong Wang, Steven Fung, Daisy Deng, Maurice Emery, Sherry Carroll, Marlena Grynfarb, Annika Goos-Nilsson and Thomas von Geldern



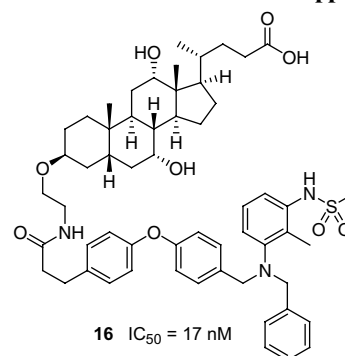
The synthesis and hepatic selectivity of steroidal and nonsteroidal glucocorticoid receptor modulator–statin hybrids (e.g., **16** h-GR binding IC_{50} = 2 nM) is reported.

Bile acid conjugates of a nonsteroidal glucocorticoid receptor modulator

pp 4179–4183

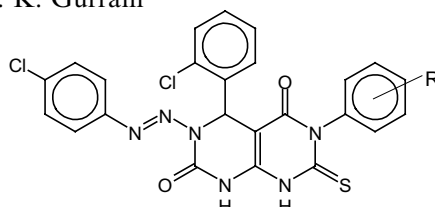
Noah Tu, J. T. Link,* Bryan K. Sorensen, Maurice Emery,
Marlena Grynfarb, Annika Goos-Nilsson and Bach Nguyen

The synthesis and profile of the selective nonsteroidal glucocorticoid receptor modulator bile acid conjugate **16** (h-GR binding IC_{50} =17 nM) is reported.

**Synthesis and QSAR studies of pyrimido[4,5-*d*]pyrimidine-2,5-dione derivatives as potential antimicrobial agents**

pp 4185–4190

Pratibha Sharma,* Nilesh Rane and V. K. Gurram

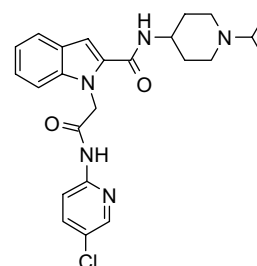


A number of pyrimido[4,5-*d*]pyrimidine-2,5-dione derivatives were synthesized and screened for their in vitro antibacterial and antifungal activities. All the compounds under investigation showed the potent antimicrobial activity. To establish a correlation between the structural features of the synthesized compounds and biological activity, quantitative structure–activity relationship investigations have also been carried out.

Factor Xa inhibitors based on a 2-carboxyindole scaffold: SAR of neutral P1 substituents

pp 4191–4195

Marc Nazaré,* Melanie Essrich, David W. Will, Hans Matter, Kurt Ritter,
Matthias Urmann, Armin Bauer, Herman Schreuder, Angela Dudda,
Jörg Czech, Martin Lorenz, Volker Laux and Volkmar Wehner

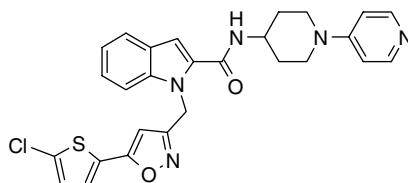


A series of novel, highly potent 2-carboxyindole-based factor Xa inhibitors is described. Structural requirements for neutral ligands, which bind in the S1 pocket of factor Xa were investigated with the 2-carboxyindole scaffold yielding a set of equipotent, selective inhibitors with structurally diverse neutral P1 substituents. The compound shown was found to be the most active in a number of antithrombotic secondary assays.

Novel factor Xa inhibitors based on a 2-carboxyindole scaffold: SAR of P4 substituents in combination with a neutral P1 ligand

pp 4197–4201

Marc Nazaré,* Melanie Essrich, David W. Will, Hans Matter, Kurt Ritter, Matthias Urmann,
Armin Bauer, Herman Schreuder, Jörg Czech, Martin Lorenz, Volker Laux and Volkmar Wehner

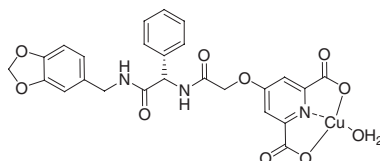


A series of novel, highly potent 2-carboxyindole-based factor Xa inhibitors is described. Structural requirements for P4 ligands in combination with a neutral biaryl P1 ligand were investigated with the 2-carboxyindole scaffold. A diverse set of P4 substituents was identified, leading to highly potent and selective factor Xa inhibitors, efficacious in various antithrombotic secondary assays.

Copper dipicolinates as peptidomimetic ligands for the Src SH2 domain

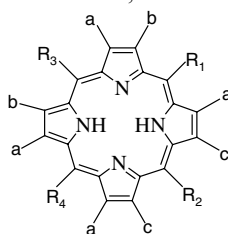
pp 4203–4206

Boris Schmidt,* Jan Jiricek, Alexander Titz, Guofeng Ye and Keykavous Parang

**Amino porphyrins as photoinhibitors of Gram-positive and -negative bacteria**

pp 4207–4211

V. Sol,* P. Branland, V. Chaleix, R. Granet, M. Guilloton, F. Lamarche, B. Verneuil and P. Krausz

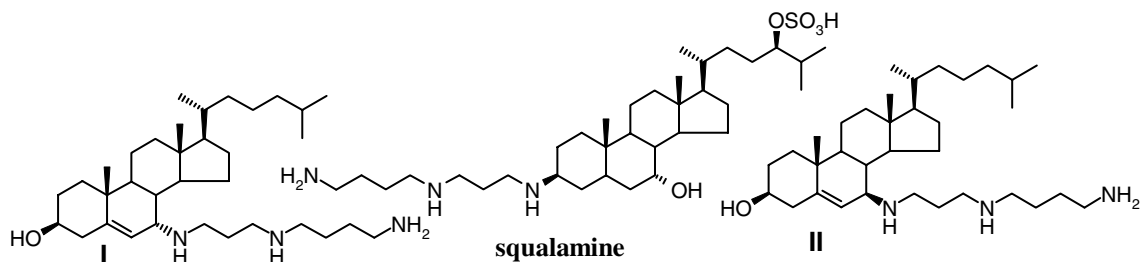


Twenty four aminoporphyrin derivatives have been tested in vitro for their antibacterial photoactivity against *Escherichia coli* and *Staphylococcus aureus*. Two of these compounds, bearing polyamine units (**17–18**) exhibited a significant activity especially against Gram-negative bacteria. For **17**, **18**: $R_1=R_2=R_3=R_4=H$, $a=CH_3$, $b=CH=CH_2$ and $c=(CH_2)_2COspermidine$ for **17**, $c=(CH_2)_2COspermine$ for **18**.

Synthesis of 7 α - and 7 β -spermidinylcholesterol, squalamine analogues

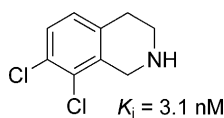
pp 4213–4216

B. Choucair, M. Dherbomez, C. Roussakis and L. El kihel*

**Phenylethanolamine N-methyltransferase inhibition: re-evaluation of kinetic data**

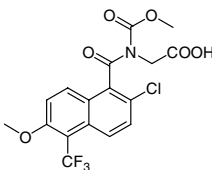
pp 4217–4220

Qian Wu, Kevin R. Criscione, Gary L. Grunewald and Michael J. McLeish*



Identification of [(naphthalene-1-carbonyl)-amino]-acetic acid derivatives as nonnucleoside inhibitors of HCV NS5B RNA dependent RNA polymerase pp 4221–4224

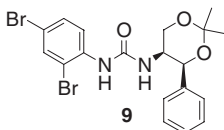
Ariamala Gopalsamy,* Kitae Lim, John W. Ellingboe, Girija Krishnamurthy, Mark Orlowski, Boris Feld, Marja van Zeijl and Anita Y. M. Howe



A novel series of HCV NS5B RNA dependent RNA polymerase inhibitors containing a naphthalene carboxamide scaffold and the structure–activity relationship studies to improve potency are described.

Novel substituted 4-phenyl-[1,3]dioxanes: potent and selective orexin receptor 2 (OX₂R) antagonists pp 4225–4229

Laura C. McAtee, Steven W. Sutton,* Dale A. Rudolph, Xiaobing Li, Leah E. Aluisio, Victor K. Phuong, Curt A. Dvorak, Timothy W. Lovenberg, Nicholas I. Carruthers and Todd K. Jones

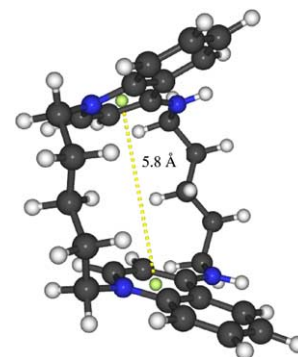


A series of novel, selective orexin receptor 2 antagonists consisting of substituted 4-phenyl-[1,3]dioxanes is reported (e.g. 9).

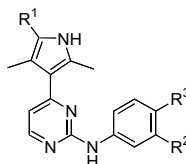
Bis-quinolinium cyclophanes: toward a pharmacophore model for the blockade of apamin-sensitive SK_{Ca} channels in sympathetic neurons pp 4231–4235

Dimitrios Galanakis,* C. Robin Ganellin, Jian-Quing Chen, Diyan Gunasekera and Philip M. Dunn

Two important elements of the pharmacophore are a distance of ca. 5.8 Å between the centroids of the pyridinium rings and a high population of synperiplanar conformations.

**Synthesis and biological activity of 2-anilino-4-(1H-pyrrol-3-yl) pyrimidine CDK inhibitors** pp 4237–4240

Shudong Wang,* Gavin Wood, Christopher Meades, Gary Griffiths, Carol Midgley, Iain McNae, Campbell McInnes, Sian Anderson, Wayne Jackson, Mokdad Mezna, Rhoda Yuill, Malcolm Walkinshaw and Peter M. Fischer

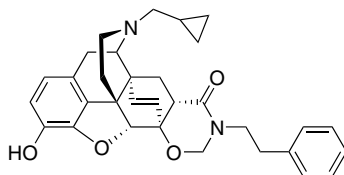


A series of 2-anilino-4-(1H-pyrrol-3-yl) pyrimidines were prepared and evaluated for their ability to inhibit cyclin-dependent kinases (CDKs). These inhibitors also exhibit potent anti-proliferative activity against human tumour cell lines. Structure–activity relationships and biochemical characterization are discussed.

Rational drug design and synthesis of a selective ϵ opioid receptor antagonist on the basis of the accessory site concept

pp 4241–4243

Hideaki Fujii,* Minoru Narita, Hirokazu Mizoguchi, Junichi Hirokawa, Koji Kawai, Toshiaki Tanaka, Leon F. Tseng and Hiroshi Nagase*

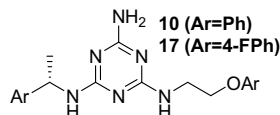


The rational drug design of a selective ϵ opioid receptor antagonist from an agonist for putative ϵ opioid receptor on the basis of the accessory site concept was described.

Aminotriazine 5-HT₇ antagonists

pp 4245–4248

Ronald J. Mattson,* Derek J. Denhart, John D. Catt, Michael F. Dee, Jeffrey A. Deskus, Jonathan L. Ditta, James Epperson, H. Dalton King, Aiming Gao, Michael A. Poss, Ashok Purandare, David Tortolani, Yufen Zhao, Hua Yang, Suresh Yeola, Jane Palmer, John Torrente, Arlene Stark and Graham Johnson

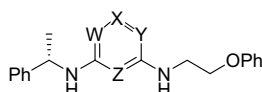


A series of aminotriazines as novel 5-HT₇ receptor antagonists are discussed. Compounds **10** and **17** have high affinity for the 5-HT₇ receptor, produce no agonist effects by themselves, and shift the dose–response curve of 5-CT to the right in the manner of an antagonist.

Diaminopyrimidine and diaminopyridine 5-HT₇ ligands

pp 4249–4252

Derek J. Denhart,* Ashok V. Purandare,* John D. Catt, H. Dalton King, Aiming Gao, Jeffrey A. Deskus, Michael A. Poss, Arlene D. Stark, John R. Torrente, Graham Johnson and Ronald J. Mattson

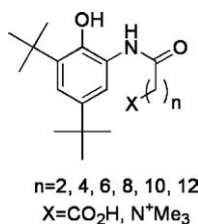


The present studies have identified a series of diaminopyrimidines and diaminopyridines as novel 5-HT₇ receptor ligands. Three regioisomeric classes of pyrimidines and four regioisomeric classes of pyridines were synthesized and analyzed for binding to the 5-HT₇ receptor. The 5-HT₇ binding affinities of different regioisomers show clearly the structure–activity relationship with position of ring nitrogens.

Novel (3,5-di-*tert*-butyl-2-hydroxy-phenylcarbamoyl)-alkanoic acids as potent antioxidants

pp 4253–4256

Vladimir I. Lodyato, Irina L. Yurkova, Viktor L. Sorokin, Oleg I. Shadyro, Vladimir I. Dolgopalets and Mikhail A. Kisel*

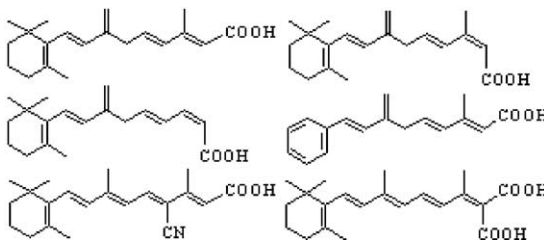


Synthesis and structure–antioxidant activity relationships of novel membrane-addressed antioxidants are reported.

Structure–activity relationships of methylene or terminal side chain modified retinoids on the differentiation and cell death signaling in NB4 promyelocytic leukemia cells

pp 4257–4261

Diana Ivanova, Aurélie Rossin, Hinrich Gronemeyer,* Alain Valla, Dominique Cartier, Régis Le Guillou and Roger Labia

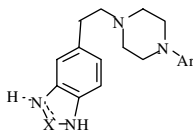


New structure–activity relationships of a series of methylene or side chain modified retinoids are investigated on the basis of their selective RAR/RXR binding profile.

Pharmacological evaluation of selected arylpiperazines with atypical antipsychotic potential

pp 4263–4266

Mirko Tomić,* Marija Kundaković, Biljana Butorović, Branka Janać, Deana Andrić, Goran Roglić, Djurdjica Ignjatović and Sladjana Kostić-Rajačić

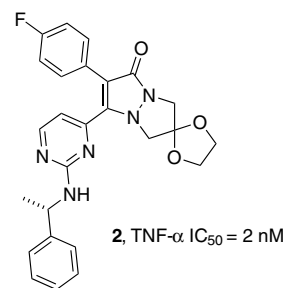


Six previously synthesized aryl piperazines were evaluated in vitro and one in vivo for atypical antipsychotic potential.

The development of novel inhibitors of tumor necrosis factor- α (TNF- α) production based on substituted [5,5]-bicyclic pyrazolones

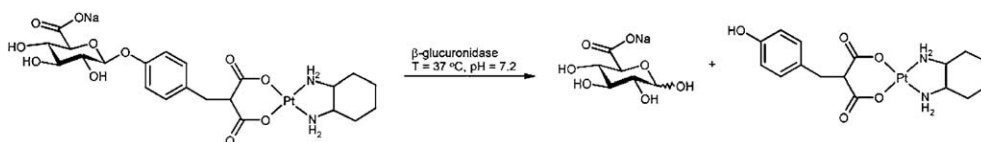
pp 4267–4272

Matthew J. Lauferweiler,* Todd A. Brugel, Michael P. Clark, Adam Golebiowski, Roger G. Bookland, Steven K. Laughlin, Mark P. Sabat, Jennifer A. Townes, John C. VanRens, Biswanath De, Lily C. Hsieh, Sandra A. Heitmeyer, Karen Juergens, Kimberly K. Brown, Marlene J. Mekel, Richard L. Walter and Michael J. Janusz


The β -glucuronyl-based prodrug strategy allows for its application on β -glucuronyl-platinum conjugates

pp 4273–4276

Reynier A. Tromp, Stella S. G. E. van Boom, C. Marco Timmers, Steven van Zutphen, Gijsbert A. van der Marel, Herman S. Overkleeft, Jacques H. van Boom and Jan Reedijk*

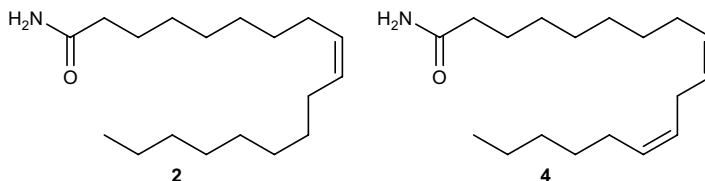


A β -glucuronyl-platinum conjugate was synthesised to test the compatibility of platinum compounds with the β -glucuronidase-based prodrug therapy.

Acyl-CoA: cholesterol acyltransferase inhibitory activities of fatty acid amides isolated from *Mylabris phalerate* Pallas

pp 4277–4280

Ming-Zhe Xu, Woo Song Lee, Mi Jeong Kim, Doo-Sang Park, Hana Yu, Guan-Rong Tian, Tae-Sook Jeong* and Ho-Yong Park*

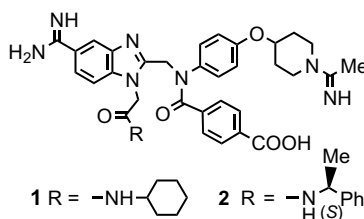


Unsaturated fatty acid amides **2** and **4**, isolated from *Mylabris phalerate* Pallas, inhibited rat liver microsomal ACAT, hACAT-1, and -2 activities.

Structure–activity relationships of potent and selective factor Xa inhibitors: benzimidazole derivatives with the side chain oriented to the prime site of factor Xa

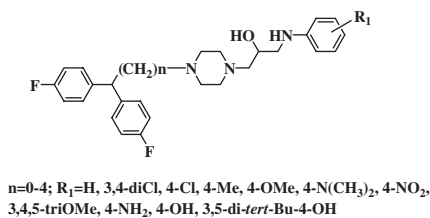
pp 4281–4286

Hiroshi Ueno, Susumu Katoh, Katsuyuki Yokota, Jun-ichi Hoshi, Mikio Hayashi, Itsuo Uchida, Kazuo Aisaka, Yasunori Hase and Hidetsura Cho*

**Antioxidative activities of novel diphenylalkyl piperazine derivatives with high affinities for the dopamine transporter**

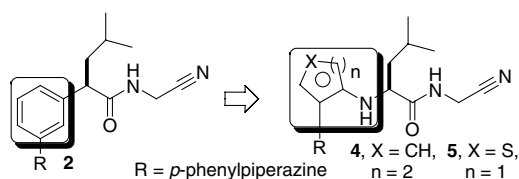
pp 4287–4290

Makoto Kimura,* Tomoko Masuda, Koji Yamada, Nobuyuki Kawakatsu, Nobuo Kubota, Masaki Mitani, Kenichi Kishii, Masato Inazu, Yuji Kiuchi, Katsuji Oguchi and Takayuki Namiki*

**Rational design of potent and selective NH-linked aryl/heteroaryl cathepsin K inhibitors**

pp 4291–4295

Joël Robichaud,* Christopher Bayly,* Renata Oballa, Peppi Prasit, Christophe Mellon, Jean-Pierre Falgueyret, M. David Percival, Gregg Wesolowski and Sevgi B. Rodan



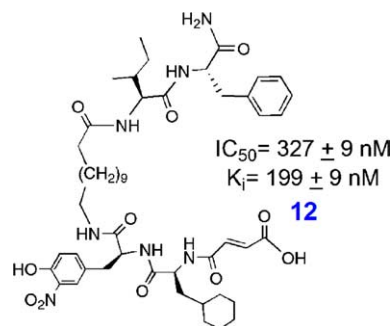
Modelling studies suggested that the introduction of a NH linker between the P3 aryl and P2 leucinamide moieties of our previously reported inhibitor **2** would allow the formation of an H-bond with the Gly66 residue of Cat K. Aniline **4** and thiophene **5** were prepared and confirmed this hypothesis by showing increased potency against Cat K and good selectivity.

A unidirectional crosslinking strategy for HIV-1 protease dimerization inhibitors

pp 4297–4300

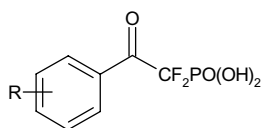
You Seok Hwang and Jean Chmielewski*

A unidirectional crosslinking strategy to identify potent HIV-1 protease dimerization inhibitors was developed using 12-aminododecanoic acid as a tether. The terminal amine of the southern peptide and side chains were further diversified to find essential functional groups for potent dimerization inhibition.

 **α,α -Difluoro- β -ketophosphonates as potent inhibitors of protein tyrosine phosphatase 1B**

pp 4301–4306

Xianfeng Li,* Ashok Bhandari, Christopher P. Holmes and Anna K. Szardenings

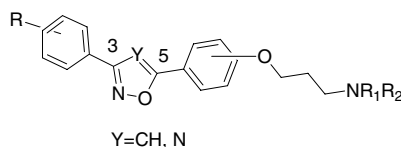


A novel series of inhibitors that contain an aryl α,α -difluoro- β -ketophosphonate group has been synthesized and evaluated against PTP1B. These compounds exhibit strong inhibitory activity, the best of which has a K_i value of 0.17 μ M.

Synthesis and structure–activity relationships of 3,5-diarylisoxazoles and 3,5-diaryl-1,2,4-oxadiazoles, novel classes of small molecule interleukin-8 (IL-8) receptor antagonists

pp 4307–4311

Michele A. Weidner-Wells,* Todd C. Henninger, Stephanie A. Fraga-Spano, Christine M. Boggs, Michele Matheis, David M. Ritchie, Dennis C. Argentieri, Michael P. Wachter and Dennis J. Hlasta



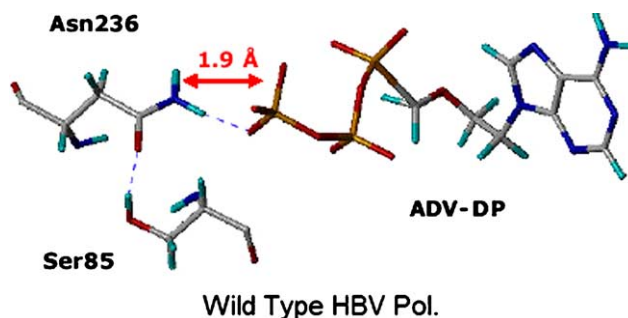
A novel series of 3,5-diarylisoxazole and 3,5-diaryl-1,2,4-oxadiazole IL-8 antagonists has been identified. These compounds also are active in a functional elastase assay. One of the compounds exhibits oral activity in a rat adjuvant arthritis model.

Molecular mechanisms of adefovir sensitivity and resistance in HBV polymerase mutants: a molecular dynamics study

pp 4313–4317

Vikas Yadav and Chung K. Chu*

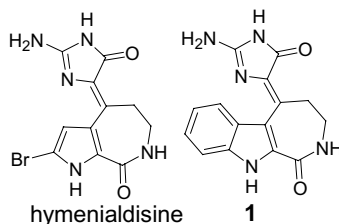
Molecular mechanisms determining adefovir diphosphate efficacy against wild type and drug-resistant HBV polymerase mutants has been studied by energy minimization and molecular dynamics simulation.



Potent inhibition of checkpoint kinase activity by a hymenialdisine-derived indoloazepine

pp 4319–4321

Vasudha Sharma and Jetze J. Tepe*

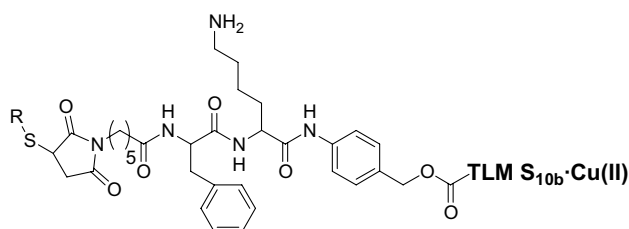


The inhibition of kinase activity by a hymenialdisine-derived indoloazepine is reported. Compound **1** was found to be a potent inhibitor of Chk2 ($IC_{50} = 8 \text{ nM}$).

**Monoclonal antibody mediated intracellular targeting of tallysomycin S_{10b}**

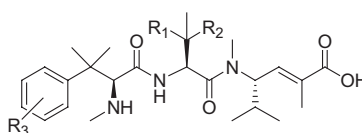
pp 4323–4327

Michael A. Walker,* H. Dalton King, Richard A. Dalterio, Pamela Trail, Raymond Firestone and Gene M. Dubowchik

**Tubulin inhibitors. Synthesis and biological activity of HTI-286 analogs with B-segment heterosubstituents**

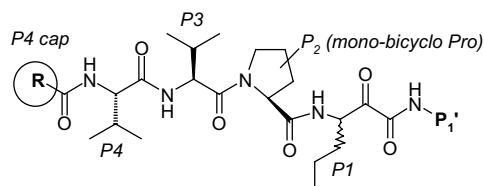
pp 4329–4332

Chuan Niu,* Daniel Smith, Arie Zask, Frank Loganzo, Carolyn Discafani, Carl Beyer, Lee Greenberger and Semiramis Ayril-Kaloustian

**P4 cap modified tetrapeptidyl α -ketoamides as potent HCV NS3 protease inhibitors**

pp 4333–4338

David X. Sun, Lifei Liu, Beverly Heinz, Alexander Kolykhalov, Jason Lamar, Robert B. Johnson, Q. May Wang, Yvonne Yip and Shu-Hui Chen*

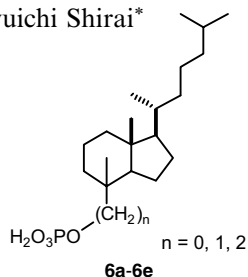


The design, syntheses, and biological evaluation of new series of P4 tetrazole, adipic acid, ester, amide capped tetrapeptidyl α -ketoamide based HCV NS3 protease inhibitors are discussed.

Design and synthesis of novel Cdc25A-inhibitors having phosphate group as a hydrophilic residue

pp 4339–4342

Rumiko Shimazawa, Mika Gochomori and Ryuichi Shirai*

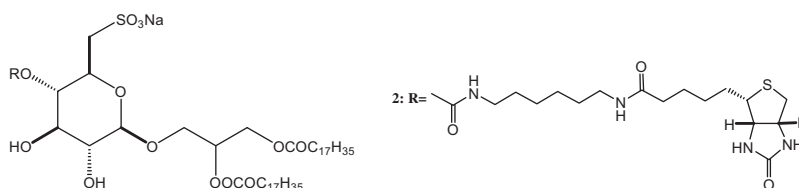


Compounds (**6a–e**) were synthesized by phosphorylation of hydrophobic perhydroindan derivatives derived from vitamin D₃, and were found to show strong inhibitory activity towards dual-specificity phosphatase Cdc25A (IC₅₀=0.7–24.5 μM).

Synthesis of an immunosuppressant SQAG9 and determination of the binding peptide by T7 phage display

pp 4343–4346

Takayuki Yamazaki, Satoko Aoki, Keisuke Ohta, Shinji Hyuma, Kengo Sakaguchi and Fumio Sugawara*

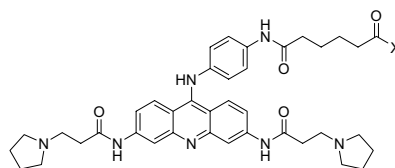


The synthesis of the biotinylated immunosuppressant and the determination of its binding peptide are reported.

Synthesis, biophysical and biological evaluation of 3,6-bis-amidoacridines with extended 9-anilino substituents as potent G-quadruplex-binding telomerase inhibitors

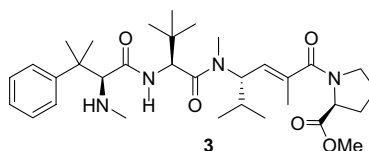
pp 4347–4351

Christoph M. Schultes, Bérangère Guyen, Javier Cuesta and Stephen Neidle*


D-piece modifications of the hemiasterlin analog HTI-286 produce potent tubulin inhibitors

pp 4353–4358

Arie Zask,* Gary Birnberg, Katherine Cheung, Joshua Kaplan, Chuan Niu, Emily Norton, Ayako Yamashita, Carl Beyer, Girija Krishnamurthy, Lee M. Greenberger, Frank Loganzo and Semiramis Ayral-Kaloustian



Modifications of the D-piece carboxylic acid group of HTI-286 gave tubulin inhibitors that were potent cytotoxic agents. For example, the amide analog derived from L-proline (**3**) had an IC₅₀ = 1.5 nM in KB-3-1 cells and was effective in a human xenograft model in athymic mice.

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*Corresponding author

①⁺ Supplementary data available via ScienceDirect

COVER

Cover figure provided by **Indraneel Ghosh**, Department of Chemistry, University of Arizona. The cover depicts the **Dual Surface Selection** methodology developed by the author: the blue helix of htBI (center) allows structural selection with the Fc portion of Immunoglobulin (left), while the residues randomized on the red sheet of htBI (center) allows for functional selection against thrombin (right) [Rajagopal, S.; Meza-Romero, R.; Ghosh, I. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1389].



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