



Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry

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Bioorganic & Medicinal Chemistry Volume 18, Issue 3, 2010

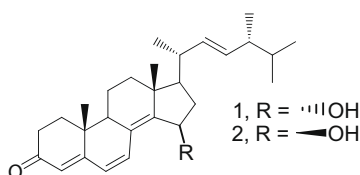
Contents

ARTICLES

Ganodermasides A and B, two novel anti-aging ergosterols from spores of a medicinal mushroom *Ganoderma lucidum* on yeast via *UTH1* gene

pp 999–1002

Yufang Weng, Lan Xiang, Akira Matsuura, Yang Zhang, Qianming Huang, Jianhua Qi*

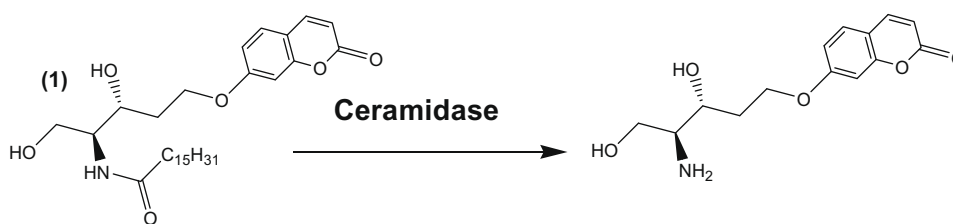


Two novel ergosterol derivatives, ganodermasides A (1) and B (2), were isolated from spores of a medicinal mushroom, *Ganoderma lucidum*. They exhibited remarkable activity on extending replicative lifespan of a yeast strain via *UTH1* gene.

Improved synthesis of a fluorogenic ceramidase substrate

pp 1003–1009

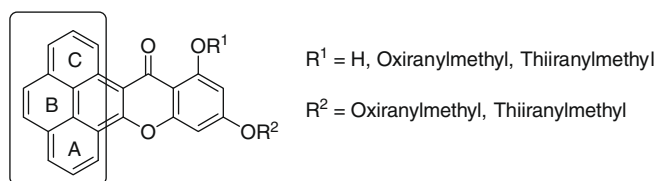
Zuping Xia, Jeremiah M. Draper, Charles D. Smith*



New benzoxanthone derivatives as topoisomerase inhibitors and DNA cross-linkers

pp 1010–1017

Hee-Ju Cho, Mi-Ja Jung, Sangwook Woo, Jungsook Kim, Eung-Seok Lee, Youngjoo Kwon*, Younghwa Na*

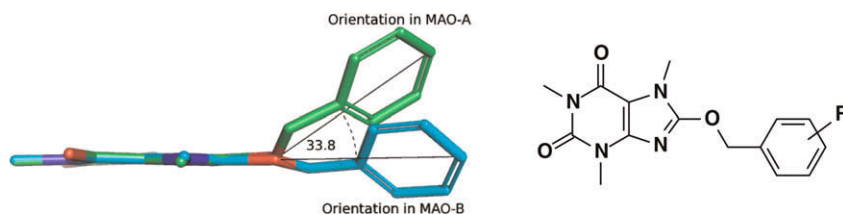


Target structures

Inhibition of monoamine oxidase by 8-benzyloxycaffeine analogues

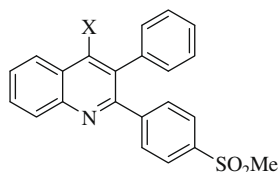
pp 1018–1028

Belinda Strydom, Sarel F. Malan, Neal Castagnoli Jr., Jacobus J. Bergh, Jacobus P. Petzer*

**Design, synthesis and biological evaluation of new 2,3-diarylquinoline derivatives as selective cyclooxygenase-2 inhibitors**

pp 1029–1033

Razieh Ghodsi, Afshin Zarghi*, Bahram Daraei, Mehdi Hedayati

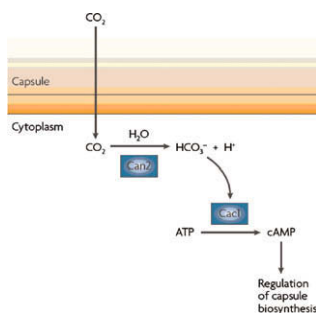


A new group of 2,3-diarylquinoline derivatives possessing a methylsulfonyl COX-2 pharmacophore at the *para*-position of the C-2 phenyl ring were designed and synthesized as selective COX-2 inhibitors. In vitro COX-1/COX-2 structure–activity relationships were determined by varying the substituents on the C-4 quinoline ring.

Carbonic anhydrase activators: Activation of the β -carbonic anhydrases from the pathogenic fungi *Candida albicans* and *Cryptococcus neoformans* with amines and amino acids

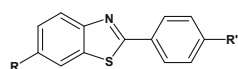
pp 1034–1037

Alessio Innocenti, Rebecca A. Hall, Andrea Scozzafava, Fritz A. Mühlischlegel, Claudiu T. Supuran*

**Novel amidino substituted 2-phenylbenzothiazoles: Synthesis, antitumor evaluation in vitro and acute toxicity testing in vivo**

pp 1038–1044

Livio Racané, Marijeta Kralj, Lidija Šuman, Ranko Stojković, Vesna Tralić-Kulenović, Grace Karminski-Zamola*



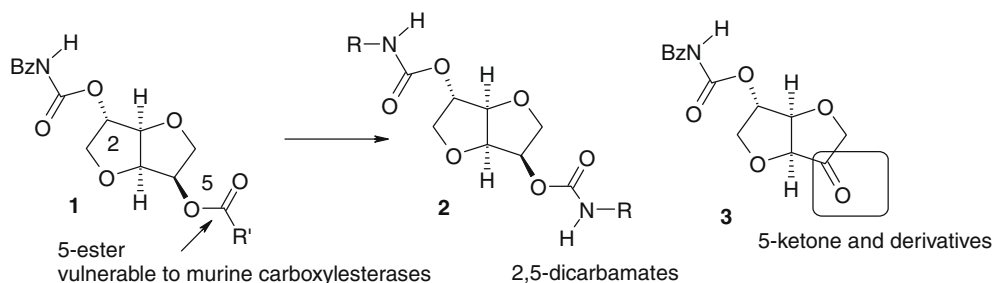
- 9a** R=R'= amidino x HCl
9b R=R'=imidazoliny x HCl
10a R=NO₂, R'= amidino x HCl
10b R= NO₂, R'=imidazoliny x HCl
11a R= amidino x HCl, R'= NO₂
11b R=imidazoliny, R'= NO₂
12a R=amino, R'= amidino x HCl
12b R=amino, R'=imidazoliny x HCl
13a R= amidino x HCl, R'=amino
13b R=imidazoliny x HCl, R'=amino

The series of new nitro–amidino, amino–amidino and diamidino-substituted 2-phenylbenzothiazoles were prepared. All compounds except diamidino-substituted 2-phenylbenzothiazole **9a** show exceptionally prominent tumor cell-growth inhibitory activity.

Isosorbide-based cholinesterase inhibitors; replacement of 5-ester groups leading to increased stability

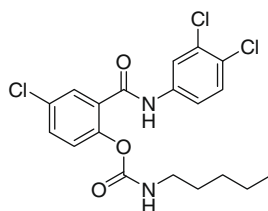
pp 1045–1053

Gerald P. Dillon, Joanne M. Gaynor, Denise Khan, Ciaran G. Carolan, Sheila A. Ryder, Juan F. Marquez, Sean Reidy, John F. Gilmer*

**Salicylanilide carbamates: Antitubercular agents active against multidrug-resistant *Mycobacterium tuberculosis* strains**

pp 1054–1061

Juana M. Ferriz, Kateřina Vávrová, Filip Kunc, Aleš Imramovský, Jiřina Stolaříková, Eva Vavříková, Jarmila Vinšová*

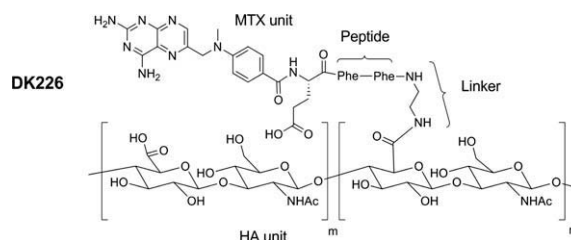


MIC = 0.5–1 $\mu\text{mol/L}$ against MDR-Tuberculosis strains
 EC_{50} = 40 $\mu\text{mol/L}$
 SI = 40–80

Synthesis and optimization of hyaluronic acid–methotrexate conjugates to maximize benefit in the treatment of osteoarthritis

pp 1062–1075

Akie Homma*, Haruhiko Sato*, Tatsuya Tamura, Akira Okamachi, Takashi Emura, Takenori Ishizawa, Tatsuya Kato, Tetsu Matsuura, Shigeo Sato, Yoshinobu Higuchi, Tomoyuki Watanabe, Hidetomo Kitamura, Kentaro Asanuma, Tadao Yamazaki, Masahisa Ikemi, Hironoshin Kitagawa, Tadashi Morikawa, Hitoshi Ikeya, Kazuaki Maeda, Koichi Takahashi, Kenji Nohmi, Noriyuki Izutani, Makoto Kanda, Ryohchi Suzuki

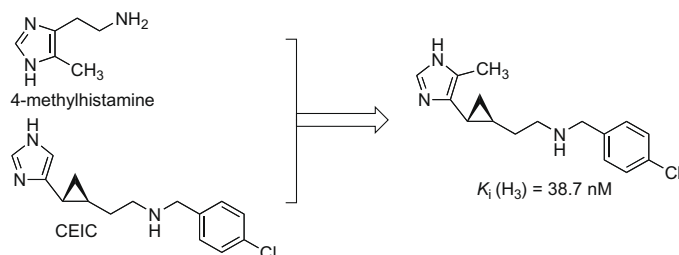


We found **DK226** to be a candidate drug for the treatment of osteoarthritis. Among several hyaluronic acid and methotrexate conjugates, **DK226** showed remarkable inhibition of the proliferation of human synovial fibroblasts in vitro and knee swelling in rat antigen-induced monoarthritis in vivo.

Synthesis and structural and pharmacological properties of cyclopropane-based conformationally restricted analogs of 4-methylhistamine as histamine H_3/H_4 receptor ligands

pp 1076–1082

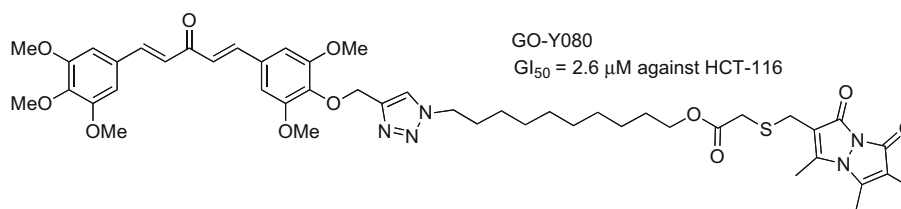
Takaaki Kobayashi, Mizuki Watanabe, Akira Yoshida, Shizuo Yamada, Mika Ito, Hiroshi Abe, Yoshihiro Ito, Mituhiro Arisawa, Satoshi Shuto*



Structure–activity relationship of C₅-curcuminoids and synthesis of their molecular probes thereof

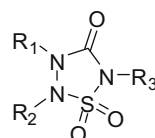
pp 1083–1092

Hiroyuki Yamakoshi, Hisatsugu Ohori, Chieko Kudo, Atsuko Sato, Naoki Kanoh, Chikashi Ishioka, Hiroyuki Shibata, Yoshiharu Iwabuchi*

**Utilization of the 1,2,3,5-thiatriazolidin-3-one 1,1-dioxide scaffold in the design of potential inhibitors of human neutrophil proteinase 3**

pp 1093–1102

Dengfeng Dou, Guijia He, Yi Li, Zhong Lai, Liuqing Wei, Kevin R. Alliston, Gerald H. Lushington, David M. Eichhorn, William C. Groutas*

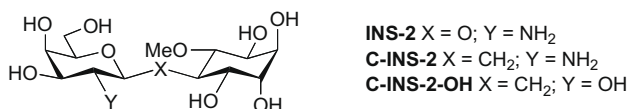


A series of 1,2,3,5-thiatriazolidin-3-one 1,1-dioxide derivatives were synthesized and used to probe the S' subsites of human neutrophil proteinase 3.

Synthesis of C-glycoside analogues of β-galactosamine-(1→4)-3-O-methyl-*D*-chiro-inositol and assay as activator of protein phosphatases PDHP and PP2Cα

pp 1103–1110

Sunej K. Hans, Fatoumata Camara, Ahmad Altiti, Alejandro Martín-Montalvo, David L. Brautigan, Douglas Heimark, Joseph Larner, Scott Grindrod, Milton L. Brown, David R. Mootoo*

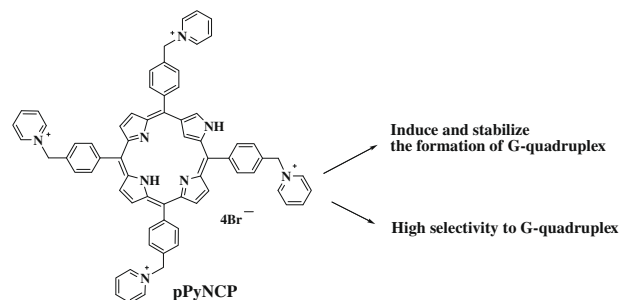


C-INS-2 and C-INS-2-OH, two C-glycoside analogs of INS-2, a putative second messenger–modulator for insulin, were synthesized. C-INS-2 was found to activate pyruvate dehydrogenase phosphatase comparable to INS-2, but failed to activate protein phosphatase 2Cα. C-INS-2-OH was inactive in affecting either phosphatase.

Cationic N-confused porphyrin derivative as a better molecule scaffold for G-quadruplex recognition

pp 1111–1116

Yuhao Du, Dan Zhang, Wei Chen, Ming Zhang, Yangyang Zhou, Xiang Zhou*



One N-confused porphyrin derivative was prepared and its first observation that it could stabilize G-quadruplex and possessed high selectivity over duplex DNA was made.

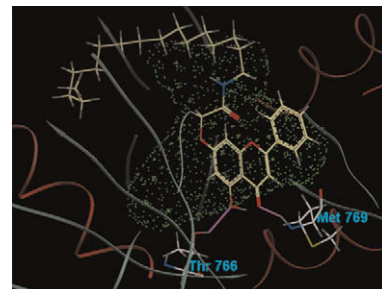


Design, synthesis and biological evaluation of chrysin long-chain derivatives as potential anticancer agents

pp 1117–1123

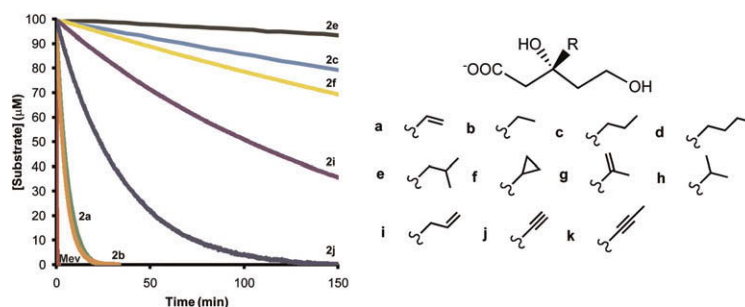
Peng-Cheng Lv, Kai-Rui Wang, Qing-Shan Li, Jin Chen, Juan Sun, Hai-Liang Zhu*

A series of long-chain derivatives of chrysin (compounds **3–22**) were synthesized to evaluate for their antiproliferative activities against the human liver cancer cell line HT-29 and EGFR inhibitory activity. Compounds **10** and **20** displayed potent EGFR inhibitory activity with IC_{50} values of 0.048 μ M and 0.035 μ M, comparable to the positive control erlotinib.

**Mevalonate analogues as substrates of enzymes in the isoprenoid biosynthetic pathway of *Streptococcus pneumoniae***

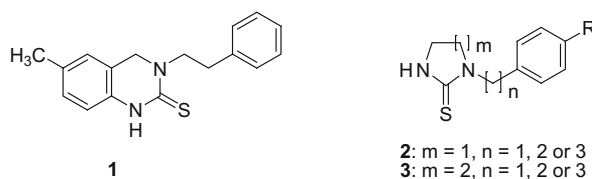
pp 1124–1134

Takashi Kudoh, Chan Sun Park, Scott T. Lefurgy, Meihao Sun, Theodore Michels, Thomas S. Leyh*, Richard B. Silverman*

**Inhibitory effect of novel tetrahydropyrimidine-2(1H)-thiones on melanogenesis**

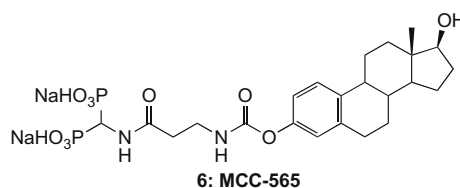
pp 1135–1142

P. Thanigaimalai, Ki-Cheul Lee, Seong-Cheol Bang, Jee-Hyun Lee, Cheong-Yong Yun, Eunmiri Roh, Bang-Yeon Hwang, Youngsoo Kim, Sang-Hun Jung*

**Design, synthesis, and biological evaluation of novel estradiol–bisphosphonate conjugates as bone-specific estrogens**

pp 1143–1148

Masahiko Morioka, Akihito Kamizono, Hirosato Takikawa, Akihisa Mori, Hiroaki Ueno, Shu-ichiro Kadowaki, Yoshihide Nakao, Kuniki Kato, Kazuo Umezawa*

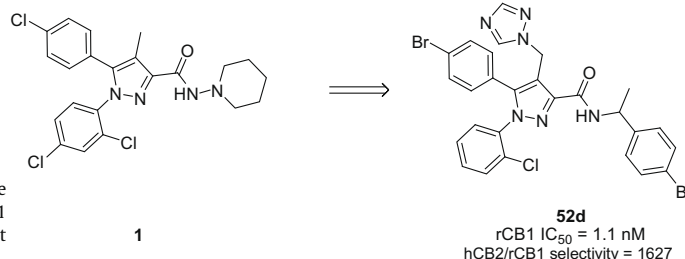


Synthesis of new estradiol–bisphosphonate conjugates (E_2 -BPs) was accomplished and their in vivo activity as bone-specific estrogens examined. Among them, MCC-565 showed selective estrogenic activity in bones; but it showed little estrogenic activity in the uterus.

Synthesis and structure–activity relationship of 1,2,4-triazole-containing diarylpyrazolyl carboxamide as CB1 cannabinoid receptor–ligand

pp 1149–1162

Hee Jeong Seo, Min Ju Kim, Suk Ho Lee, Sung-Han Lee, Myung Eun Jung, Mi-Soon Kim, Kwangwoo Ahn, Jeongmin Kim, Jinhwa Lee*



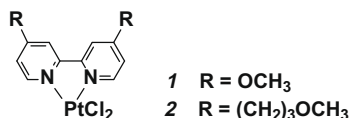
We have identified novel 1,2,4-triazole-containing diarylpyrazolyl carboxamide series of small molecule cannabinoid-1 ligands that show improvement for CB1 receptor binding affinity. Importantly, these analogues also exhibited excellent selectivity for CB1 receptor over CB2 receptor.



Novel 4,4'-diether-2,2'-bipyridine cisplatin analogues are more effective than cisplatin at inducing apoptosis in cancer cell lines

pp 1163–1170

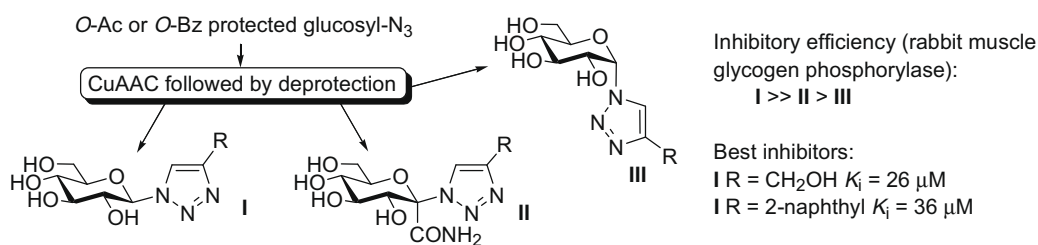
Van Vo, Zeynep G. Kabuloglu-Karayusuf, Stephen W. Carper, Byron L. Bennett*, Caryn Evilia



Synthesis of 1-(*D*-glucopyranosyl)-1,2,3-triazoles and their evaluation as glycogen phosphorylase inhibitors

pp 1171–1180

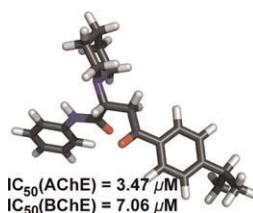
Éva Bokor, Tibor Docsa, Pál Gergely, László Somsák*



4-Aryl-4-oxo-*N*-phenyl-2-aminybutyramides as acetyl- and butyrylcholinesterase inhibitors. Preparation, anticholinesterase activity, docking study, and 3D structure–activity relationship based on molecular interaction fields

pp 1181–1193

Maja D. Vitorović-Todorović*, Ivan O. Juranić, Ljuba M. Mandić, Branko J. Drakulić



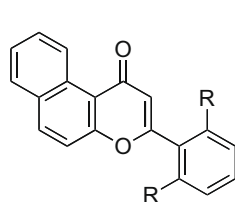
Synthesis and anticholinesterase activity of 4-aryl-4-oxo-*N*-phenyl-2-aminybutyramides, novel class of reversible, moderately potent cholinesterase inhibitors, are reported. Simple substituent variation on aryl moiety changes anti-AChE activity for two orders of magnitude; also substitution and type of hetero(ali)cycle in position 2 of butanoic moiety govern AChE/BChE selectivity.



β -Naphthoflavone analogs as potent and soluble aryl hydrocarbon receptor agonists: Improvement of solubility by disruption of molecular planarity

pp 1194–1203

Yuji Fujita, Mitsuhiro Yonehara, Masashi Tetsushashi, Tomomi Noguchi-Yachide, Yuichi Hashimoto, Minoru Ishikawa*

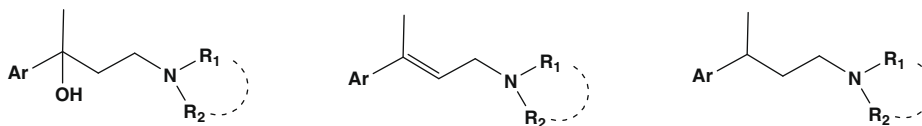


R	<i>ortho</i> -substitution to bicyclic molecule \Rightarrow planarity \Rightarrow crystal packing \Rightarrow solubility	AhR agonistic activity		
	dihedral angle (°)	melting point (°C)	solubility (μg/mL)	EROD EC ₅₀ (μM)
H	17.8	166	84.6	1.4
F	40.5	150	248	0.20

Design, synthesis and SAR analysis of novel selective σ_1 ligands (Part 2)

pp 1204–1212

Daniela Rossi, Mariangela Urbano, Alice Pedrali, Massimo Serra, Daniele Zampieri, Maria Grazia Mamolo, Christian Laggner, Caterina Zanette, Chiara Florio, Dirk Schepmann, Bernard Wuensch, Ornella Azzolina, Simona Collina*

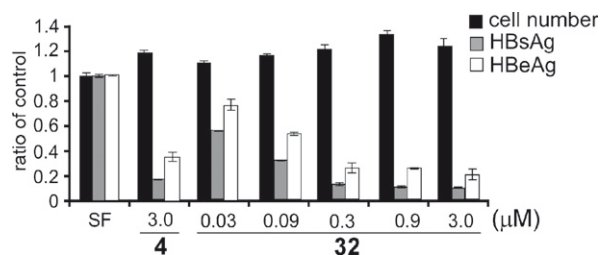
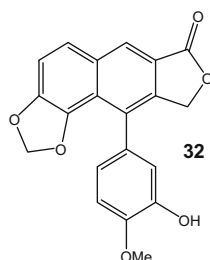


Preparation and SAR results of novel σ ligands are herein presented. Among the most σ_1 -active compounds, (*R/S*)-**1d** showed noticeable selectivity towards σ_2 subtype and excellent selectivity against opioid receptors.

**Synthesis and the biological evaluation of arynaphthalene lignans as anti-hepatitis B virus agents**

pp 1213–1226

Damodar Janmanchi, Ya Ping Tseng, Kuei-Chen Wang, Ray Ling Huang, Chih Hsiu Lin*, Sheau Farn Yeh*



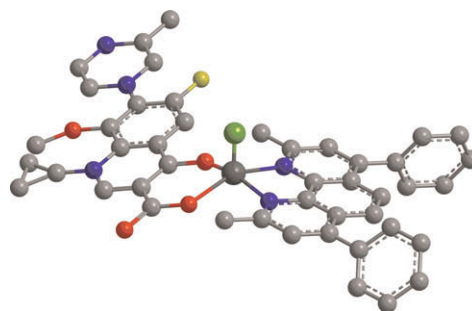
In a series of synthetic helioxanthin (**4**) derivative, compound **32** showed the most effective suppression on hepatitis B virus surface antigen (HBsAg) and e antigen (HBeAg) production in HepA2 cells with EC₅₀ values of 0.06 and 0.14 μM, respectively.

**Square pyramidal copper(II) complexes with forth generation fluoroquinolone and neutral bidentate ligand: Structure, antibacterial, SOD mimic and DNA-interaction studies**

pp 1227–1235

Mohan N. Patel*, Pradhuman A. Parmar, Deepen S. Gandhi

Formulation of copper complexes using drug and some NN/NO donor ligands resulting in efficiency compounds that can act as DNA gyrase and exhibit SOD resemblance.

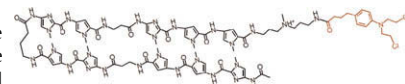


Comparative analysis of DNA alkylation by conjugates between pyrrole–imidazole hairpin polyamides and chlorambucil or *seco*-CBI

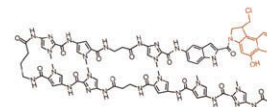
pp 1236–1243

Masafumi Minoshima, Toshikazu Bando, Ken-ichi Shinohara, Gengo Kashiwazaki, Shigeki Nishijima, Hiroshi Sugiyama*

We investigated sequence-specific DNA alkylation using conjugates between the *N*-methylpyrrole (Py)-*N*-methylimidazole (Im) polyamide and the DNA alkylating agent, chlorambucil, or 1-(chloromethyl)-5-hydroxy-1,2-dihydro-3Hbenz[e]indole (*seco*-CBI). Polyamide–chlorambucil conjugates **1–4** differed in the position at which the DNA alkylating chlorambucil moiety was bound to the Py–Im polyamide. High-resolution denaturing polyacrylamide gel electrophoresis (PAGE) revealed that chlorambucil conjugates **1–4** alkylated DNA at the sequences recognized by the Py–Im polyamide core moiety. Reactivity and sequence specificity were greatly affected by the conjugation position, which reflects the geometry of the alkylating agent in the DNA minor groove. Polyamide–*seco*-CBI conjugate **5** was synthesized to compare the efficacy of chlorambucil with that of *seco*-CBI as an alkylating moiety for Py–Im polyamides. Denaturing PAGE analysis revealed that DNA alkylation activity of polyamide–*seco*-CBI conjugate **5** was similar to that of polyamide–chlorambucil conjugates **1** and **2**. In contrast, the cytotoxicity of conjugate **5** was superior to that of conjugates **1–4**. These results suggest that the *seco*-CBI conjugate was distinctly active in cells compared to the chlorambucil conjugates. These results may contribute toward the development of more specific and active DNA alkylating agents.



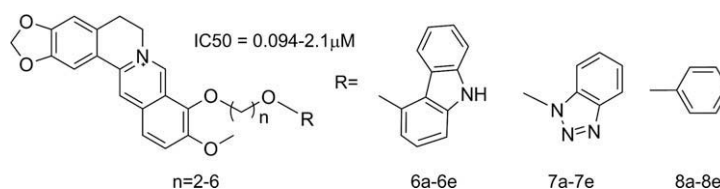
Py-Im polyamide–chlorambucil conjugate

Py-Im polyamide–*seco*-CBI conjugate

Synthesis, biological evaluation, and molecular modeling of berberine derivatives as potent acetylcholinesterase inhibitors

pp 1244–1251

Ling Huang, Anding Shi, Feng He*, Xingshu Li*

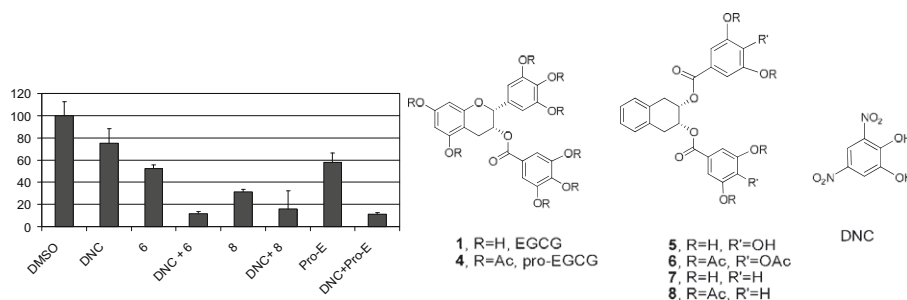


A new series of berberine derivatives was designed, synthesized, and evaluated as AChE inhibitors. Most of the derivatives inhibited AChE in the sub-micromolar range.

Proteasome inhibition in human breast cancer cells with high catechol-*O*-methyltransferase activity by green tea polyphenol EGCG analogs

pp 1252–1258

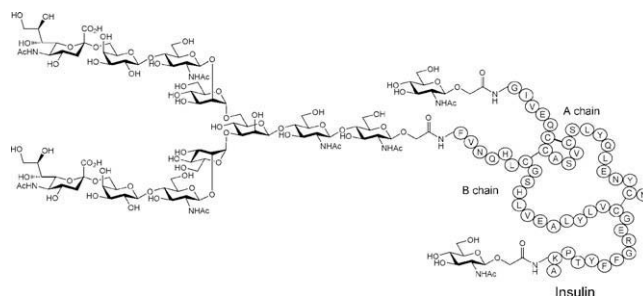
Congde Huo, Huanjie Yang, Qiuzhi Cindy Cui, Q. Ping Dou*, Tak Hang Chan*



Chemo-enzymatic synthesis of glycosylated insulin using a GlcNAc tag

pp 1259–1264

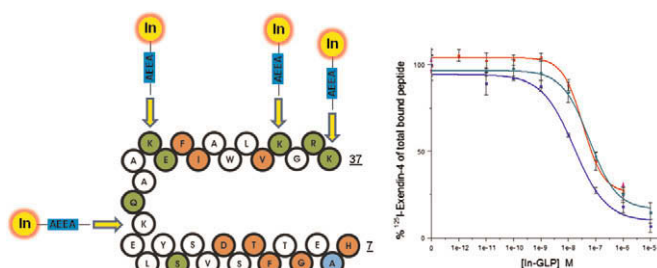
Yusuke Tomabechi, Rena Suzuki, Katsuji Haneda, Toshiyuki Inazu*



Design, synthesis and in vitro characterization of Glucagon-Like Peptide-1 derivatives for pancreatic beta cell imaging by SPECT

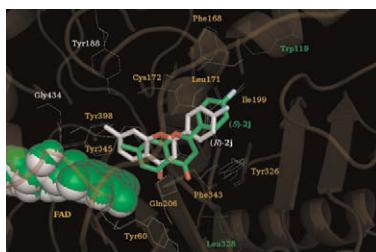
pp 1265–1272

Babak Behnam Azad, Vanessa A. Rota, Daniel Breadner, Savita Dhanvantari, Leonard G. Luyt*

**A new series of flavones, thioflavones, and flavanones as selective monoamine oxidase-B inhibitors**

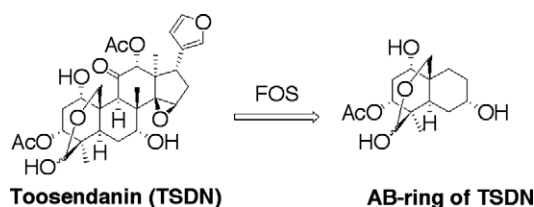
pp 1273–1279

Franco Chimenti, Rossella Fioravanti*, Adriana Bolasco, Paola Chimenti, Daniela Secci, Francesca Rossi, Matilde Yáñez, Francisco Orallo, Francesco Ortuso, Stefano Alcaro, Roberto Cirilli, Rosella Ferretti, M. Luisa Sanna

**Toosendanin: Synthesis of the AB-ring and investigations of its anti-botulinum properties (Part II)**

pp 1280–1287

Yuya Nakai, Sabine Pellett, William H. Tepp, Eric A. Johnson, Kim D. Janda*

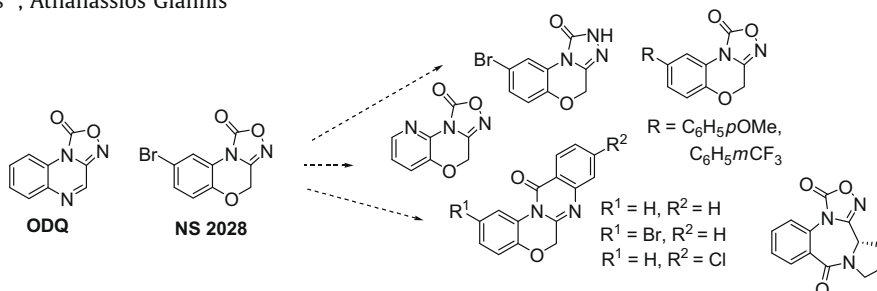


Toosendanin, a limonoid, inhibits the biological activity of BoNT/A. With the concept of function-oriented synthesis as a goal, the AB-ring of toosendanin was prepared and examined for anti-botulinum properties.

Synthesis and biological evaluation of oxadiazole derivatives as inhibitors of soluble guanylyl cyclase

pp 1288–1296

Margarete von Wantoch Rekowski, Anastasia Pyriochou, Nektarios Papapetropoulos, Anne Stößel, Andreas Papapetropoulos*, Athanassios Giannis*

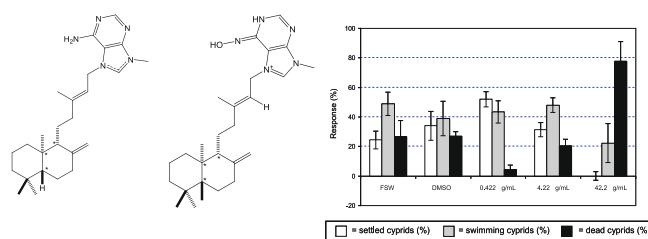


Herein, we report an expeditious synthesis of the known sGC inhibitors ODQ and NS 2028, as well as the preparation and biological evaluation of a small library of analogues.

From anti-fouling to biofilm inhibition: New cytotoxic secondary metabolites from two Indonesian *Agelas* sponges

pp 1297–1311

Triana Hertiani, RuAngelie Edrada-Ebel^{*}, Sofia Ortlepp, Rob W. M. van Soest, Nicole J. de Voogd, Victor Wray, Ute Hentschel, Svetlana Kozytska, Werner E. G. Müller, Peter Proksch^{*}

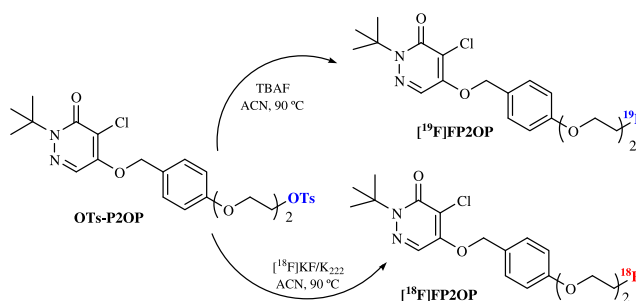


Preparation and biodistribution of [¹⁸F]FP2OP as myocardial perfusion imaging agent for positron emission tomography

pp 1312–1320

Tiantian Mou, Huihui Jing, Wenjiang Yang, Wei Fang, Cheng Peng, Feng Guo, Xianzhong Zhang^{*}, Yan Pang, Yunchuan Ma

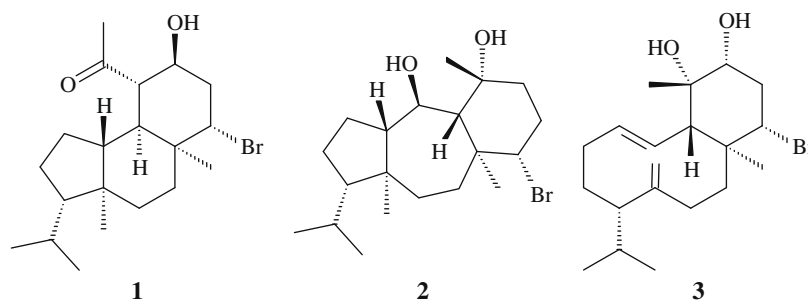
A pyridaben analogue as mitochondria complex I inhibitor was synthesized and radiolabeled with ¹⁸F ([¹⁸F]FP2OP) by one-step synthesis, then it was evaluated as a potential PET myocardial perfusion imaging agent.



Structure and in vitro antitumor activity evaluation of brominated diterpenes from the red alga *Sphaerococcus coronopifolius*

pp 1321–1330

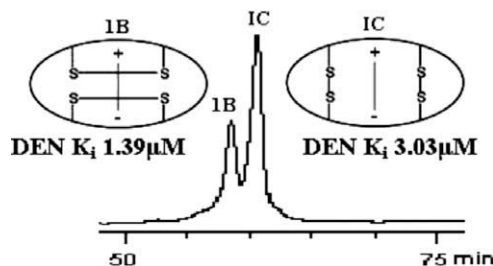
Vangelis Smyrniotopoulos, Constantinos Vagias, Céline Bruyère, Delphine Lamoral-Theys, Robert Kiss, Vassilios Roussis^{*}



Synthesis and disulfide bond connectivity–activity studies of a kalata B1-inspired cyclopeptide against dengue NS2B–NS3 protease

pp 1331–1336

Yaojun Gao, Taian Cui^{*}, Yulin Lam^{*}



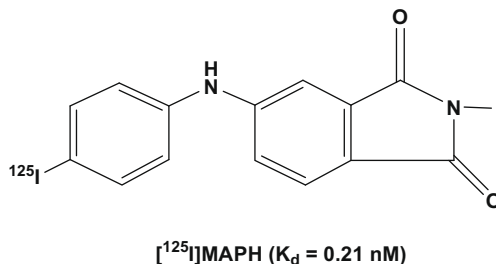
Two isomers of an oxidized kalata B1 analogue were found to possess potent inhibition against dengue NS2B–NS3 protease. This reveals the importance of disulfide bond connectivity in substrate-competitive inhibitory activity.



Novel anilinophthalimide derivatives as potential probes for β -amyloid plaque in the brain

pp 1337–1343

Xin-Hong Duan, Jin-Ping Qiao, Yang Yang, Meng-Chao Cui, Jiang-Ning Zhou, Bo-Li Liu*

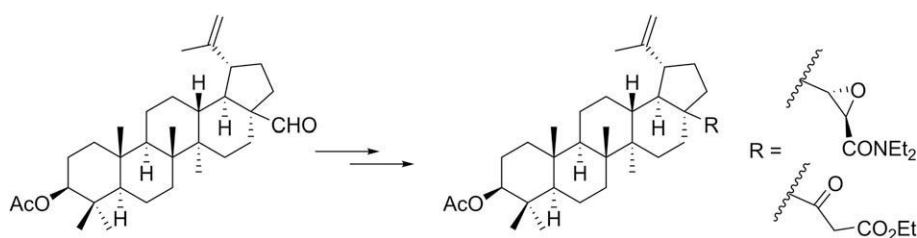


A novel anilinophthalimide derivative of $[^{125}\text{I}]\text{MAPH}$ is a promising candidate probe for SPECT imaging in the brain.

Synthesis and biological evaluation of antitumour-active betulin derivatives

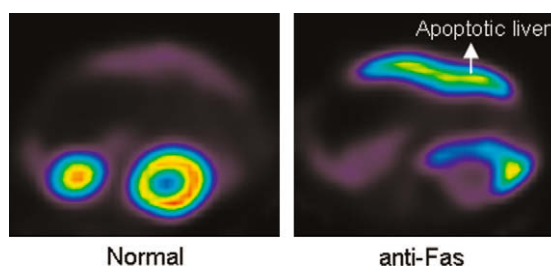
pp 1344–1355

René Csuk*, Alexander Barthel, Ralph Kluge, Dieter Ströhl, Harish Kommera, Reinhard Paschke

**Site-specific labeling of ‘second generation’ annexin V with $^{99\text{m}}\text{Tc}(\text{CO})_3$ for improved imaging of apoptosis in vivo**

pp 1356–1363

Marijke De Saint-Hubert, Felix M. Mottaghy, Kathleen Vunckx, Johan Nuyts, Humphrey Fonge, Kristof Prinsen, Sigrid Stroobants, Luc Mortelmans, Niko Deckers, Leo Hofstra, Chris P. M. Reutelingsperger, Alfons Verbruggen*, Dirk Rattat

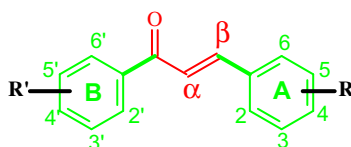


μSPECT images of $^{99\text{m}}\text{Tc}(\text{CO})_3\text{-HIS-cys-AnxV}$ before (normal) and after treatment with anti-Fas.

Synthesis and biological evaluation of simple methoxylated chalcones as anticancer, anti-inflammatory and antioxidant agents


pp 1364–1370

Babasaheb P. Bandgar*, Shrikant S. Gawande, Ragini G. Bodade, Jalinder V. Totre, Chandahas N. Khobragade



Here, we describe a series of methoxylated chalcones. The most active derivative act as promising anticancer, anti-inflammatory and antioxidant agent.

*Corresponding author

 Supplementary data available via ScienceDirect

COVER

When investigating a natural product besides determining its biological activity, it is also critical to consider its origin, molecular structure, and ultimately if possible structure activity relationships. The major limonoid constituent found in *M. toosendan* is toosendanin, a tetranortriterpene. We have confirmed toosendanin's gross molecular structure/stereochemistry via crystallographic analysis and its anti-botulinum properties both in a cellular and animal model. To gain a deeper understanding of toosendanin's remarkable anti-botulinum properties, the AB-ring of toosendanin was synthesized and used to dissect its importance in botulinum intoxication. [Nakai, Y.; Pellett, S.; Tepp, W.H.; Johnson, E.A.; Janda, K.D. *Bioorg. Med. Chem.* **2010**, 18, 1280–1287].

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ISSN 0968-0896