



Bioorganic & Medicinal Chemistry Volume 19, Issue 18, 2011

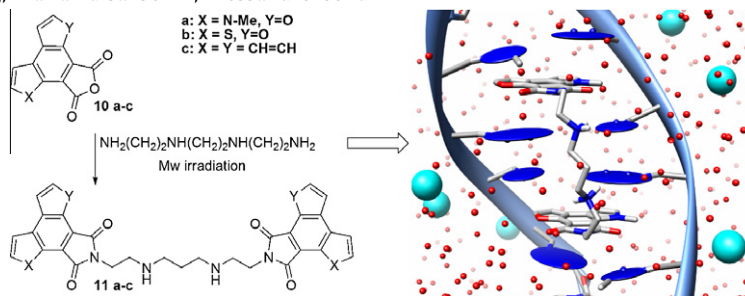
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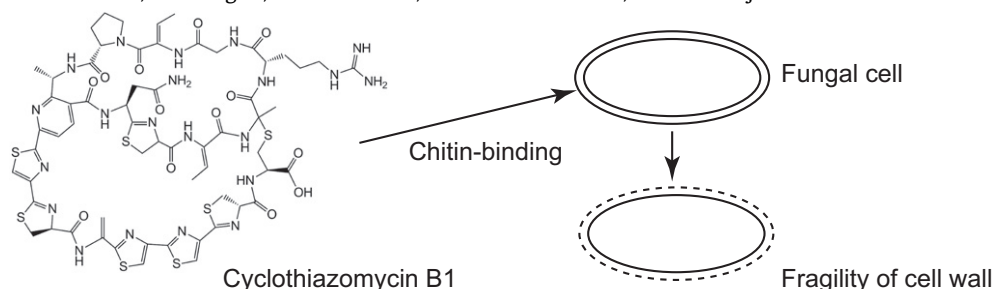
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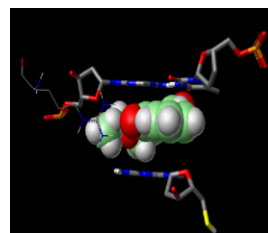
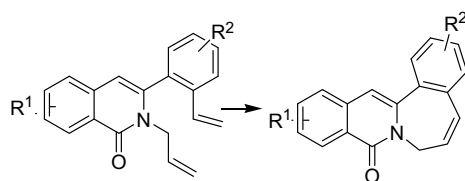
Naoko Mizuhara, Manabu Kuroda, Akira Ogita, Toshio Tanaka, Yoshinosuke Usuki*, Ken-ichi Fujita*



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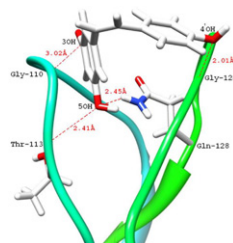
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Chemical modifications of resveratrol for improved protein kinase C alpha activity

pp 5321–5333

Joydip Das*, Satyabrata Pany, Anjoy Majhi

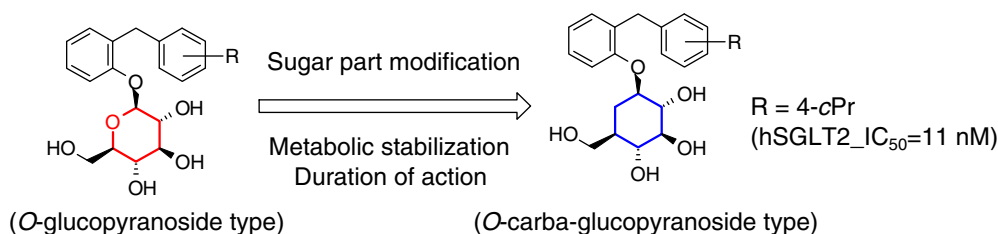


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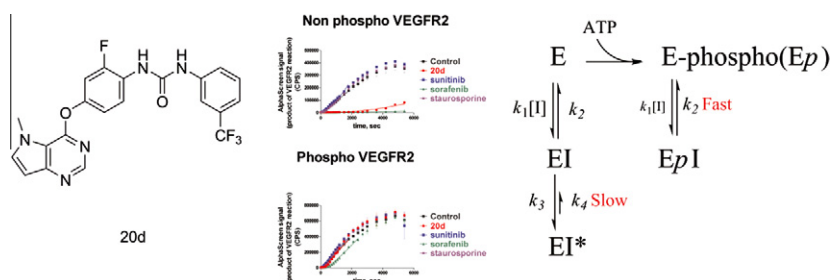
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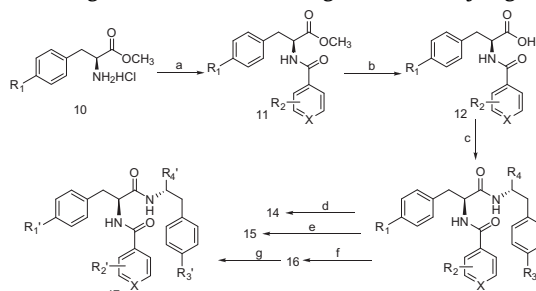
Hidehisa Iwata, Shinichi Imamura, Akira Hori, Mark S. Hixon*, Hiroyuki Kimura, Hiroshi Miki*



Synthesis and biological evaluation of Matijing-Su derivatives as potent anti-HBV agents

pp 5352–5360

Jingying Qiu, Bixue Xu, Zhengming Huang, Weidong Pan, Peixue Cao, Changxiao Liu, Xiaojiang Hao, Baoan Song, Guangyi Liang*

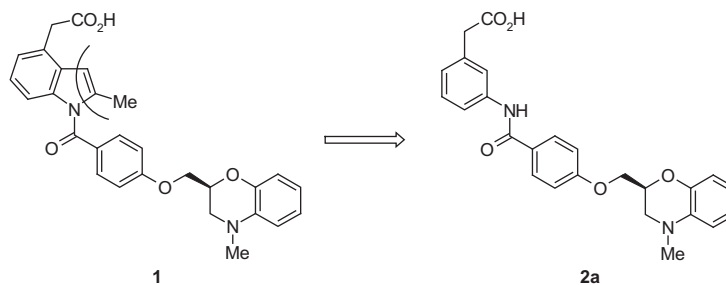


A series of Matijing-Su (MTS, *N*-(*N*-benzoyl-L-phenylalanyl)-*O*-acetyl-L-phenylalanol) derivatives were synthesized and evaluated for their anti-hepatitis B virus (HBV) activity in 2.2.15 cells.

Design and synthesis of new prostaglandin D₂ receptor antagonists

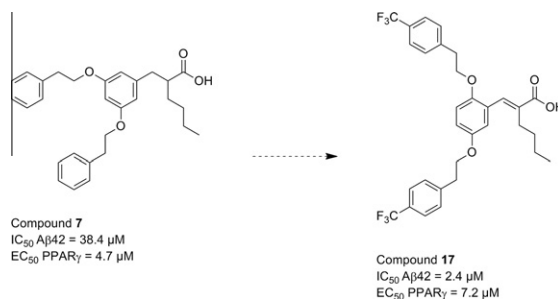
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Maki Iwahashi*, Eiji Takahashi, Motoyuki Tanaka, Yoko Matsunaga, Yutaka Okada, Ryoji Matsumoto, Fumio Nambu, Hisao Nakai, Masaaki Toda

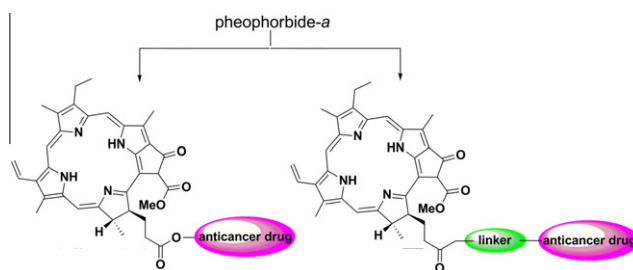
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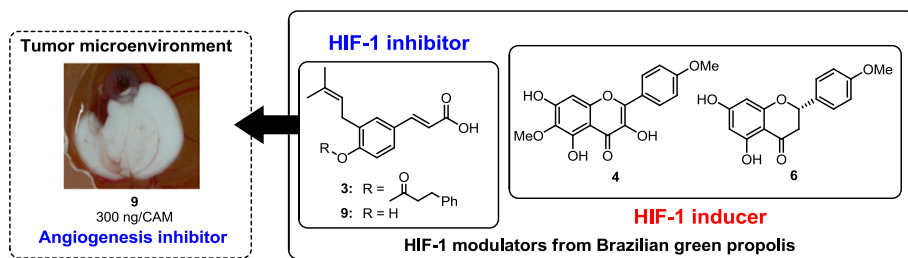
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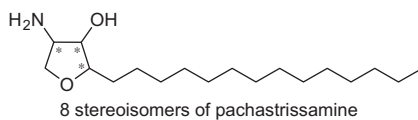
Hisanori Hattori, Kensuke Okuda, Tetsuji Murase, Yuki Shigetsura, Kosuke Narise, Gregg L. Semenza, Hideko Nagasawa*



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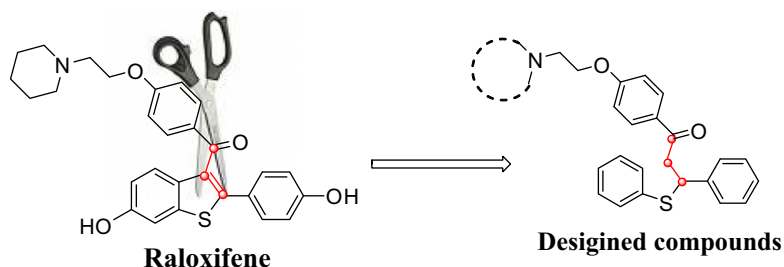
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Yuji Yoshimitsu, Shinya Oishi*, Jun Miyagaki, Shinsuke Inuki, Hiroaki Ohno, Nobutaka Fujii*

**Design and synthesis of 1,3-biarylsulfanyl derivatives as new anti-breast cancer agents**

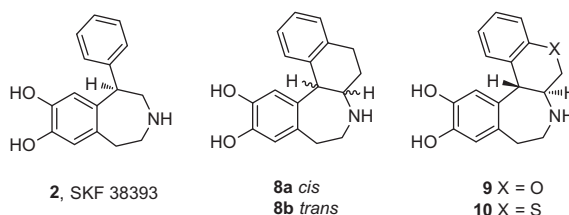
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Atul Kumar*, Vishwa Deepak Tripathi, Promod Kumar, Lalit Prakash Gupta, Akanksha, Ritu Trivedi, Hemant Bid, V. L. Nayak, Jawed A. Siddiqui, Bandana Chakravarti, Ruchi Saxena, Anila Dwivedi, M. I. Siddiquee, U. Siddiqui, Rituraj Konwar, Naibedya Chattopadhyay

**Assessment of dopamine D₁ receptor affinity and efficacy of three tetracyclic conformationally-restricted analogs of SKF38393**

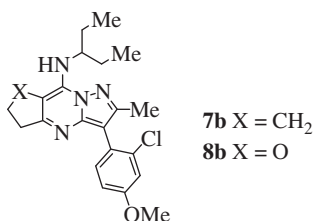
pp 5420–5431

Alia H. Clark, John D. McCorvy, Val J. Watts, David E. Nichols*

**6,7-Dihydro-5H-cyclopenta[d]pyrazolo[1,5-a]pyrimidines and their derivatives as novel corticotropin-releasing factor 1 receptor antagonists**

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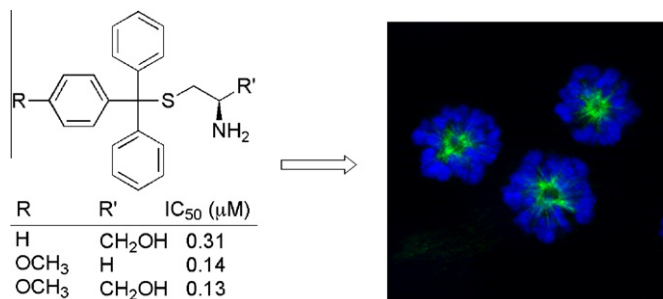
Tetsuji Saito*, Tetsuo Obitsu, Takashi Kondo, Toshiaki Matsui, Yuuki Nagao, Kensuke Kusumi, Naoya Matsumura, Sonoko Ueno, Akihiro Kishi, Seishi Katsumata, Yoshifumi Kagamiishi, Hisao Nakai, Masaaki Toda



Synthesis and characterization of tritylthioethanamine derivatives with potent KSP inhibitory activity

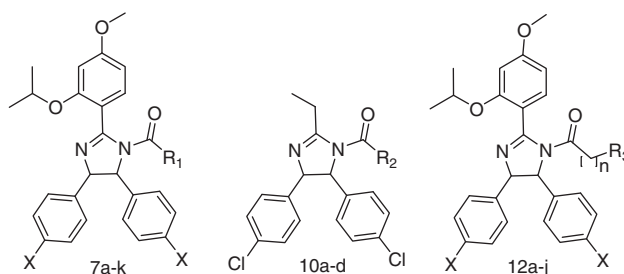
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Delany Rodriguez, Chinnasamy Ramesh, Lauren H. Henson, Lori Wilmeth, Bj K. Bryant, Samuel Kadavakollu, Rebecca Hirsch, Johnelle Montoya, Porsha R. Howell, Jon M. George, David Alexander, Dennis L. Johnson, Jeffrey B. Arterburn, Charles B. Shuster*

**Design, synthesis, and biological evaluation of imidazoline derivatives as p53–MDM2 binding inhibitors**

pp 5454–5461

Chunqi Hu, Xin Li, Weisi Wang, Lei Zhang, Lulu Tao, Xiaowu Dong, Rong Sheng, Bo Yang, Yongzhou Hu*

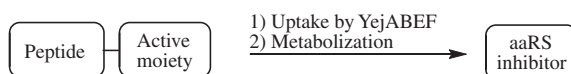


Three series of novel Nutlin analogs were designed, synthesized as p53–MDM2 binding inhibitors. Compound **7c** showed a promising inhibitory activity and induced cell cycle arrest in A549 cells.

Extended targeting potential and improved synthesis of Microcin C analogs as antibacterials

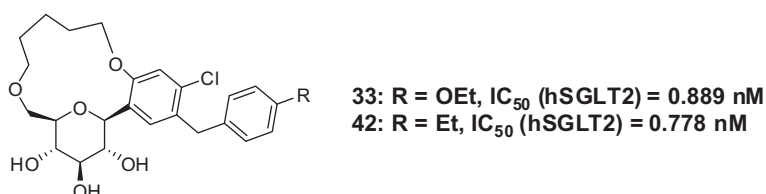
pp 5462–5467

Gaston H. M. Vondenhoff, Svetlana Dubiley, Konstantin Severinov, Eveline Lescrinier, Jef Rozenski, Arthur Van Aerschot*

**Novel macrocyclic C-aryl glucoside SGLT2 inhibitors as potential antidiabetic agents**

pp 5468–5479

Min Ju Kim, Suk Ho Lee, So Ok Park, Hyunku Kang, Jun Sung Lee, Ki Nam Lee, Myung Eun Jung, Jeongmin Kim, Jinhwa Lee*

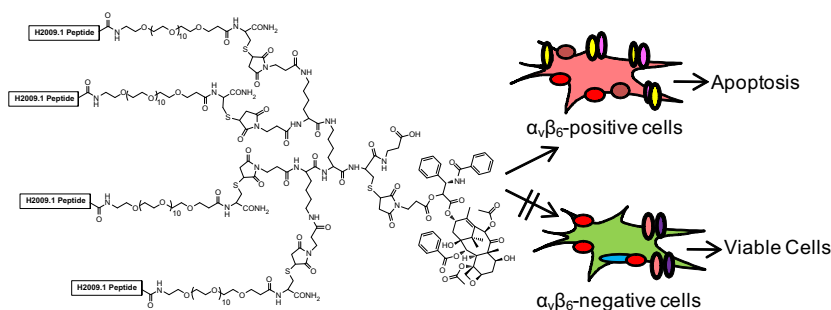


Novel macrocyclic C-aryl glucoside SGLT2 inhibitors were designed and synthesized. Two different synthetic routes of macrocyclization were adopted to prepare novel macrocyclic SGLT2 inhibitors. Among the compounds tested, [1,7]dioxacyclopentadecine macrocycles possessing ethylphenyl at the distal ring **42** or ethoxyphenyl at the distal ring **33** showed the best in vitro inhibitory activity in this series to date (**42**, IC_{50} = 0.778 nM and **33**, IC_{50} = 0.899 nM) against hSGLT2.

Synthesis and biological evaluation of a peptide–paclitaxel conjugate which targets the integrin $\alpha_v\beta_6$

pp 5480–5489

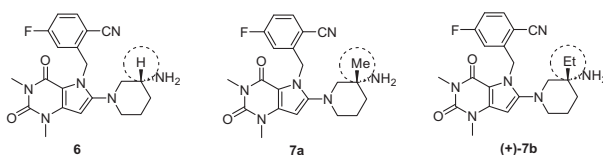
Shunzi Li, Bethany Powell Gray, Michael J. McGuire, Kathlynn C. Brown*



2-({6-[(3R)-3-amino-3-methylpiperidine-1-yl]-1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-5H-pyrrolo[3,2-d]pyrimidine-5-yl)methyl)-4-fluorobenzonitrile (DSR-12727): A potent, orally active dipeptidyl peptidase IV inhibitor without mechanism-based inactivation of CYP3A

pp 5490–5499

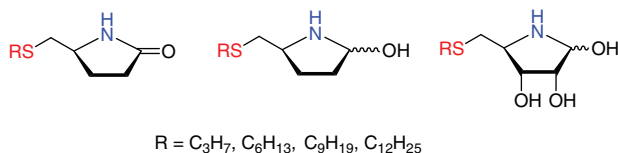
Yukihiro Nishio*, Hidenori Kimura, Naoyuki Sawada, Eiji Sugaru, Masakuni Horiguchi, Michiko Ono, Yudai Furuta, Mutsuko Sakai, Yumi Masui, Misato Otani, Takahiko Hashizuka, Yayoi Honda, Jiro Deguchi, Tsutomu Nakagawa, Hiroyuki Nakahira



Substituted lactam and cyclic azahemiacetals modulate *Pseudomonas aeruginosa* quorum sensing

pp 5500–5506

Venkata L. A. Malladi, Adam J. Sobczak, Natalie Maricic, Senthil Kumar Murugapiran, Lisa Schneper, John Makemson, Kalai Mathee, Stanislaw F. Wnuk*



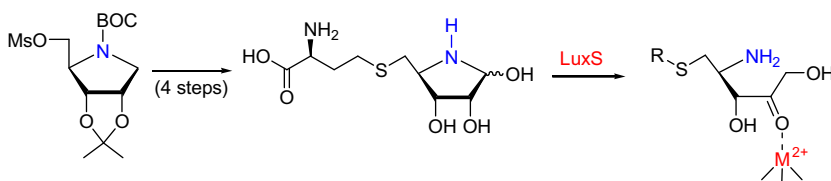
The cyclic azahemiacetals with propylthio or hexylthio substituent strongly inhibit both *las* and *rhl* signaling at higher concentrations while the propylthio analogue stimulates the *las* QS system at lower concentrations.



Inhibition of LuxS by S-ribosylhomocysteine analogues containing a [4-aza]ribose ring

pp 5507–5519

Venkata L. A. Malladi, Adam J. Sobczak, Tiffany M. Meyer, Dehua Pei, Stanislaw F. Wnuk*

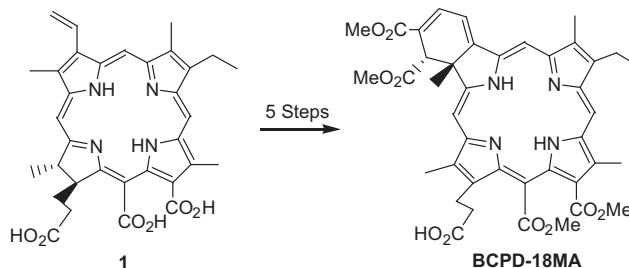


The [4-aza] S-ribosylhomocysteine analogue exhibited time-dependent inhibition of LuxS consistent with the enzyme-catalyzed ring opening and generation of 2- and/or 3-ketone intermediates.

Synthesis and photobiological study of a novel chlorin photosensitizer BCPD-18MA for photodynamic therapy

pp 5520–5528

Jialiang Zhang, Li Deng, Jianzhong Yao*, Peng Gu, Feng Yang, Xiuxin Wang, Wei Liu, Yingying Zhang, Xingfa Ke, Xiaolong Jing, Jianming Chen*

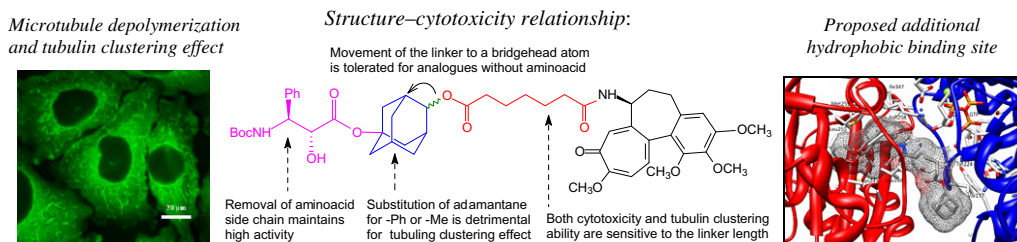


We describe the synthesis and biological properties of a novel chlorin photosensitizer benzochlorophyllin monoacid derivative BCPD-18MA which is promising candidate for applications in PDT.

Synthesis and SAR requirements of adamantane–colchicine conjugates with both microtubule depolymerizing and tubulin clustering activities

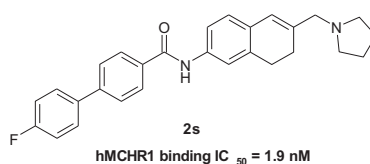
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Olga N. Zefirova*, Evgeniya V. Nurieva, Dmitrii V. Shishov, Igor I. Baskin, Fabian Fuchs, Heiko Lemcke, Fabian Schröder, Dieter G. Weiss, Nikolay S. Zefirov, Sergei A. Kuznetsov

**Discovery, synthesis, and structure–activity relationship of 6-aminomethyl-7,8-dihydronaphthalenes as human melanin-concentrating hormone receptor 1 antagonists**

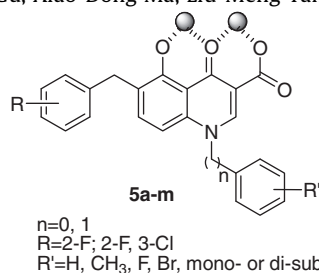
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Makoto Kamata*, Toshiro Yamashita, Toshihiro Imaeda, Toshio Tanaka, Jun Terauchi, Maki Miyamoto, Taiichi Ora, Michiko Tawada, Satoshi Endo, Shiro Takekawa, Asano Asami, Nobuhiro Suzuki, Yasutaka Nagisa, Yoshihide Nakano, Kaoru Watanabe, Hitomi Ogino, Koki Kato, Kaneyoshi Kato, Yuji Ishihara

**Synthesis and biological evaluation of HQCAs with aryl or benzyl substituents on N-1 position as potential HIV-1 integrase inhibitors**

pp 5553–5558

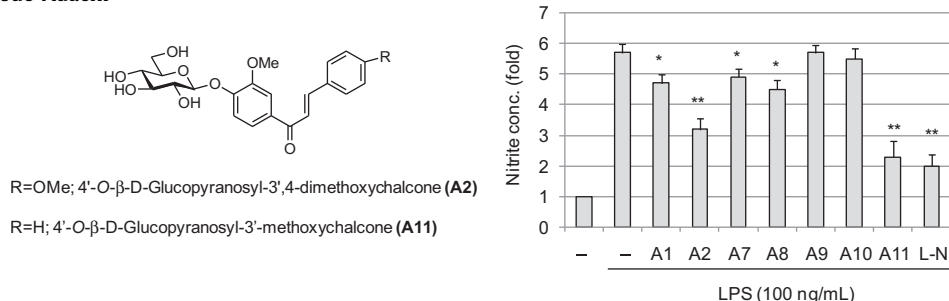
Qiu-Qin He, Xuan Zhang, Hai-Qiu Wu, Shuang-Xi Gu, Xiao-Dong Ma, Liu-Meng Yang, Yong-Tang Zheng, Fen-Er Chen*



A series of new 5-hydroxyquinolone-3-carboxylic acids (HQCAs) with various aryl or benzyl substituents on N-1 position were synthesized with the aim of contributing to a better understanding of the structure–activity relationships of HQCAs.

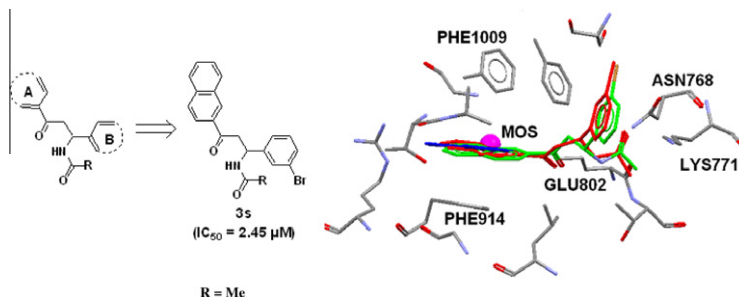
Inhibitory effects of chalcone glycosides isolated from *Brassica rapa* L. 'hidabeni' and their synthetic derivatives on LPS-induced NO production in microglia pp 5559–5568

Hirokazu Hara*, Yoko Nakamura, Masayuki Ninomiya, Ryosuke Mochizuki, Tetsuro Kamiya, Elias Aizenman, Mamoru Koketsu, Tetsuo Adachi



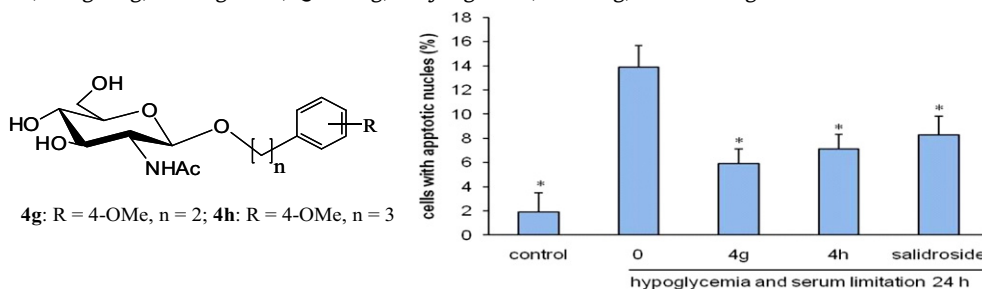
N-(1,3-Diaryl-3-oxopropyl)amides as a new template for xanthine oxidase inhibitors pp 5569–5576

Kunal Nepali, Amit Agarwal, Sameer Sapra, Vineet Mittal, Raj Kumar*, Uttam C. Banerjee, Manish K. Gupta, Naresh K. Satti, Om P. Suri, Kanaya L. Dhar



Synthesis and protective effects of aralkyl alcoholic 2-acetamido-2-deoxy-β-D-pyranosides on hypoglycemia and serum limitation induced apoptosis in PC12 cell pp 5577–5584

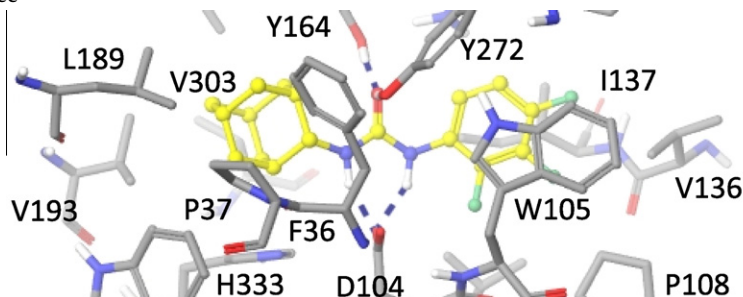
Ying Meng, Yibing Guo, Yong Ling, Yahong Zhao, Qi Zhang, Xinyang Zhou, Fei Ding, Yumin Yang*



Most compounds showed strong neuroprotective effects, especially for **4g** and **4h**, which attenuated cell viability loss and apoptotic cell death in cultured PC12 cells.

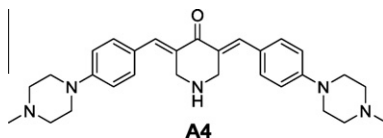
The structure–activity relationship of urea derivatives as anti-tuberculosis agents pp 5585–5595

Joshua R. Brown, Elton J. North, Julian G. Hurdle, Christophe Morisseau, Jerrod S. Scarborough, Dianqing Sun, Jana Korduláková, Michael S. Scherman, Victoria Jones, Anna Grzegorzewicz, Rebecca M. Crew, Mary Jackson, Michael R. McNeil, Richard E. Lee*



Design, synthesis, and biological evaluation of curcumin analogues as multifunctional agents for the treatment of Alzheimer's disease pp 5596–5604

Shang-Ying Chen, Yuan Chen, Yan-Ping Li, Shu-Han Chen, Jia-Heng Tan*, Tian-Miao Ou, Lian-Quan Gu, Zhi-Shu Huang*



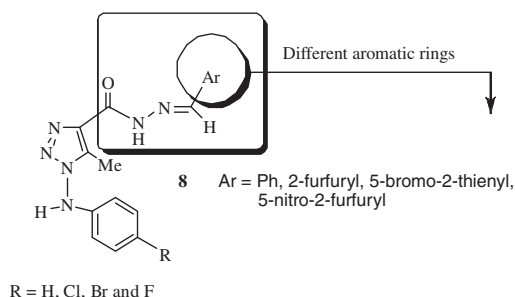
A series of novel curcumin analogues were designed, synthesized, and biologically evaluated as multifunctional agents targeting β -amyloid, oxidative stress, and redox-active metal ions. Compound **A4** was found to have the most potent $A\beta$ aggregation inhibitory activity ($IC_{50} = 2.5 \mu M$).



Synthesis, antitubercular activity, and SAR study of N-substituted-phenylamino-5-methyl-1H-1,2,3-triazole-4-carbohydrazides pp 5605–5611

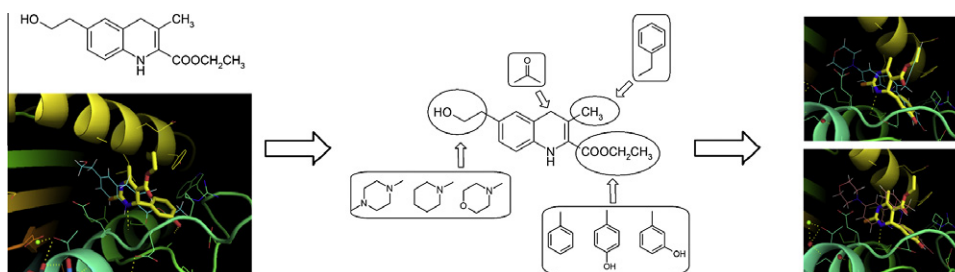
Alessandro K. Jordão, Plínio C. Sathler, Vitor F. Ferreira, Vinícius R. Campos, Maria C. B. V. de Souza, Helena C. Castro, Andressa Lannes, André Lourenco, Carlos R. Rodrigues, Murilo L. Bello, Maria C. S. Lourenco, Guilherme S. L. Carvalho, Maria C. B. Almeida, Anna C. Cunha*

This paper describes the synthesis, experimental evaluation for antitubercular activity and theoretical analysis of the N-substituted-phenylamino-5-methyl-1H-1,2,3-triazole-4-carbohydrazides **8**.



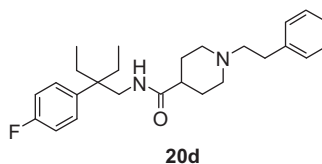
De novo design, synthesis and biological evaluation of 1,4-dihydroquinolin-4-ones and 1,2,3,4-tetrahydroquinazolin-4-ones as potent kinesin spindle protein (KSP) inhibitors pp 5612–5627

Cheng Jiang, Lei Yang, Wu-Tong Wu, Qing-Long Guo, Qi-Dong You*



Synthesis and pharmacological evaluation of 1-alkyl-N-[2-ethyl-2-(4-fluorophenyl)butyl]piperidine-4-carboxamide derivatives as novel antihypertensive agents pp 5628–5638

Susumu Watanuki*, Keisuke Matsuura, Yuichi Tomura, Minoru Okada, Toshio Okazaki, Mitsuaki Ohta, Shin-ichi Tsukamoto

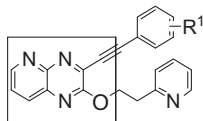


1-Alkyl-N-[2-ethyl-2-(4-fluorophenyl)butyl]piperidine-4-carboxamide derivatives were synthesized and evaluated for their T-type Ca^{2+} channel inhibitory activity.

A novel 3-arylethynyl-substituted pyrido[2,3-*b*]pyrazine derivatives and pharmacophore model as Wnt2/ β -catenin pathway inhibitors in non-small-cell lung cancer cell lines

pp 5639–5647

Young-Dae Gong*, Mi-Sook Dong*, Sang-Bum Lee, Nayeon Kim, Mi-Seon Bae, Nam-Sook Kang



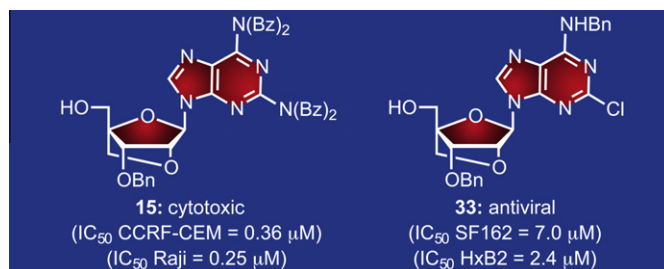
One hundred pyrido[2,3-*b*]pyrazine derivatives were synthesized that were able to inhibit the Wnt/ β -catenin signal pathway and a novel lead compound **954** ($<0.2 \mu\text{M}$) was identified by cell proliferation screening.



Synthesis and biological evaluation of 2',4'- and 3',4'-bridged nucleoside analogues

pp 5648–5669

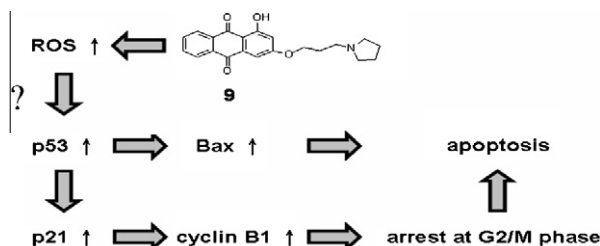
K. C. Nicolaou*, Shelby P. Ellery, Fatima Rivas, Karen Saye, Eric Rogers, Tyler J. Workinger, Mark Schallenberger, Rommel Tawatao, Ana Montero, Ann Hessel, Floyd Romesberg, Dennis Carson, Dennis Burton



Anthraquinone derivatives induce G2/M cell cycle arrest and apoptosis in NTUB1 cells

pp 5670–5678

Huang-Yao Tu, A-Mei Huang, Chi-Huang Teng, Tzyh-Chyuan Hour, Shyh-Chyun Yang*, Yeong-Shiau Pu, Chun-Nan Lin*

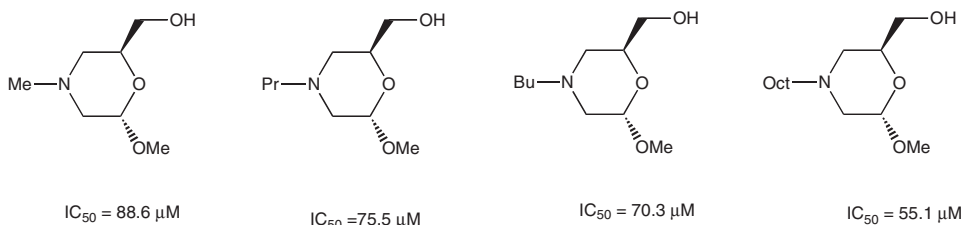


Thirteen anthraquinone derivatives **5–17** including two 3-(3-alkylaminopropoxy)-9,10-anthraquinone derivatives **5** and **6** and eleven 1-hydroxy-3-(3-alkylaminopropoxy)-9,10-anthraquinone derivatives **7–17** were synthesized. Compound **9** induced up-regulation of cyclin B1 and p21 expressions. Biological results suggested that the induction of G2/M arrest, apoptosis, and cell death by **9** may associate with increased expression of p21 and cyclin B1, elevation of Bax and p53 levels, and generation of ROS in the cell.

Synthesis and glycosidase inhibitory profiles of functionalised morpholines and oxazepanes

pp 5679–5692

Peter A. Burland, Helen M. I. Osborn*, Andrea Turkson



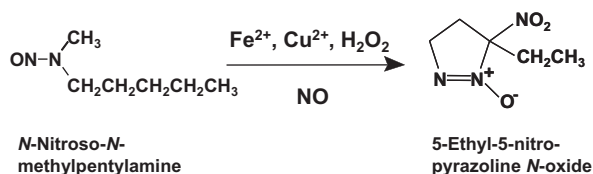
In this work libraries of morpholines and oxazepanes have been prepared via the reductive amination reaction between dialdehydes, derived from carbohydrates, and a range of amines. The inhibitory profiles of these targets against a range of glycosidase enzymes have been assessed. Good inhibition of the β -D-galactosidase enzyme derived from Bovine kidney was obtained for a range of the morpholine targets.



Isolation and structural identification of a direct-acting mutagen derived from *N*-nitroso-*N*-methylpentylamine and Fenton's reagent with copper ion

pp 5693–5697

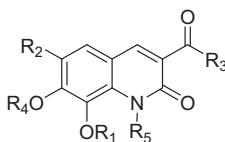
Motofumi Miura, Keiko Inami, Masafumi Yoshida, Kentaro Yamaguchi, Tadahiko Mashino, Masataka Mochizuki*



Fluorinated cannabinoid CB2 receptor ligands: Synthesis and in vitro binding characteristics of 2-oxoquinoline derivatives

pp 5698–5707

Nashaat Turkman, Aleksander Shavrin, Roman A. Ivanov, Brian Rabinovich, Andrei Volgin, Juri G. Gelovani, Mian M. Alauddin*



A series of fluorinated 2-oxo-quinoline derivatives were synthesized and their in vitro assay was performed against [^3H]CP-55,940, using the human cancer cell line U87, genetically engineered to express human CB2 or CB1 receptors. Of all the synthesized compounds, six compounds displayed inhibition constant (K_i) value at the level of nanomolar and sub-nanomolar concentrations. Preliminary in vitro results suggest that these six compounds may be useful for therapeutic application to neuropathic pain, neuroinflammatory diseases and immune disorders.

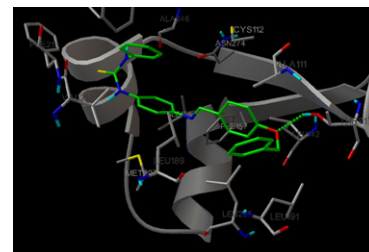


Synthesis, antibacterial activities and molecular docking studies of Schiff bases derived from *N*-(2/4-benzaldehyde-amino) phenyl-*N'*-phenyl-thiourea

pp 5708–5715

Hong-Jia Zhang, Xuan Qin, Kai Liu, Di-Di Zhu, Xiao-Ming Wang*, Hai-Liang Zhu*

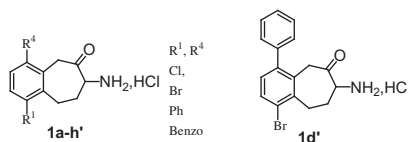
A series of novel Schiff base derivatives have been designed and synthesized, and their biological activities were also evaluated as potential inhibitors of FabH. These compounds were assayed for antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Staphylococcus aureus*. Compounds with potent antibacterial activities were tested for their *E. coli* FabH inhibitory activity. Compound **3v** showed the most potent antibacterial activity with MIC of 1.56–6.25 $\mu\text{g/mL}$ against the tested bacterial strains and exhibited the most potent *E. coli* FabH inhibitory activity with IC_{50} of 4.3 μM . Docking simulation was performed to position compound **3v** into the *E. coli* FabH active site to determine the probable binding conformation.



A novel amino-benzosuberone derivative is a picomolar inhibitor of mammalian aminopeptidase N/CD13

pp 5716–5733

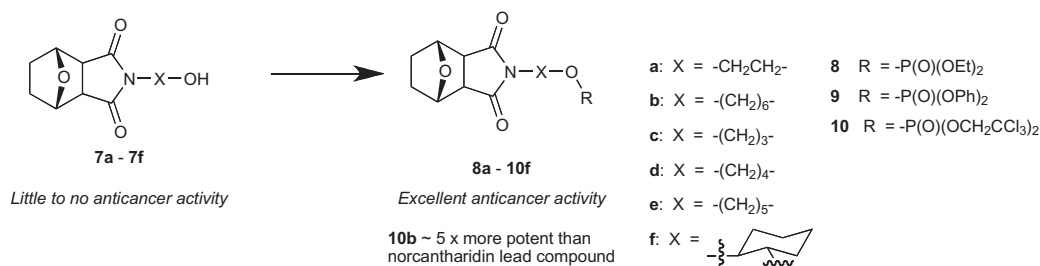
Carmen Maieranu, Céline Schmitt, Nadège Schifano-Faux, Didier Le Nouën, Albert Defoin*, Céline Tarnus*



Some racemic amino-benzosuberones **1a-h'**, were synthesised and evaluated as inhibitors of four representative members of zinc-dependent amino-peptidases. K_i values in the nanomolar to picomolar range were obtained selectively against the 'one zinc' aminopeptidase AP-N/CD13. The bromo-phenyl derivative **1d'** belongs to the most potent and selective non-peptidic known inhibitor ($K_i = 60 \text{ pM}$).

Norcantharimide analogues possessing terminal phosphate esters and their anti-cancer activity**pp 5734–5741**

Mark J. Robertson, Christopher P. Gordon, Jayne Gilbert, Adam McCluskey*, Jennette A. Sakoff

**OTHER CONTENT****Corrigendum****p 5742**

*Corresponding author

Supplementary data available via SciVerse ScienceDirect

COVER

The known veterinary anthelmintic and proton ionophore, closantel, was recently discovered to also exhibit potent chitinase inhibition activity and inhibit molting in the parasitic nematode, *Onchocerca volvulus*, the causative agent of the neglected tropical disease onchocerciasis. [C. Gloeckner, A. L. Garner, F. Mersha, Y. Oksov, N. Tricoche, L. M. Eubanks, S. Lustigman, G. F. Kaufmann, K. D. Janda, Repositioning of an existing drug for the neglected tropical disease Onchocerciasis, *Proc. Natl. Acad. Sci., U.S.A.* **2010**, 107, 3424.]

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