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# Bioorganic & Medicinal Chemistry Letters

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## Bioorganic & Medicinal Chemistry Letters Volume 21, Issue 3, 2011

### Contents

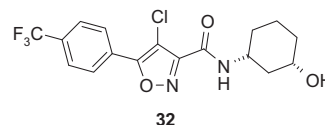
#### ARTICLES

##### Structure–activity studies of a novel series of isoxazole-3-carboxamide derivatives as TRPV1 antagonists

pp 892–898

Ronald Palin\*, Lynn Abernethy, Nasrin Ansari, Kenneth Cameron, Tom Clarkson, Maureen Dempster, David Dunn, Anna-Marie Easson, Darren Edwards, John Maclean, Katy Everett, Helen Feilden, Koc-Kan Ho, Steve Kultgen, Peter Littlewood, Duncan McArthur, Deborah McGregor, Hazel McLuskey, Irina Neagu, Stuart Neale, Lesley-Anne Nisbet, Michael Ohlmeyer, Quynhchi Pham, Paul Ratcliffe, Yajing Rong, Andrew Roughton, Melanie Sammons, Robert Swanson, Heather Tracey, Glenn Walker

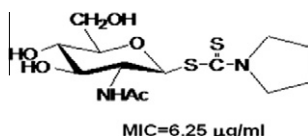
Optimisation of a screening hit incorporating both TRPV1 activity and solubility was conducted. Substitution of the isoxazole-3-carboxamide with the bespoke 1*S*, 3*R*-3-aminocyclohexanol motif afforded the requisite balance of potency and solubility. Compounds **32** and **40** were found to have antihyperalgesic effects in the rat CFA Hg assay and induce a mechanism based hyperthermia.



##### Synthesis and evaluation of anti-tubercular activity of new dithiocarbamate sugar derivatives

pp 899–903

Yasuhiro Horita, Takemasa Takii\*, Ryuji Kuroishi, Taku Chiba, Kenji Ogawa, Laurent Kremer, Yasuo Sato, YooSa Lee, Tomohiro Hasegawa, Kikuo Onozaki



A series of dithiocarbamate sugar derivatives were synthesized and determined anti-tubercular activity.

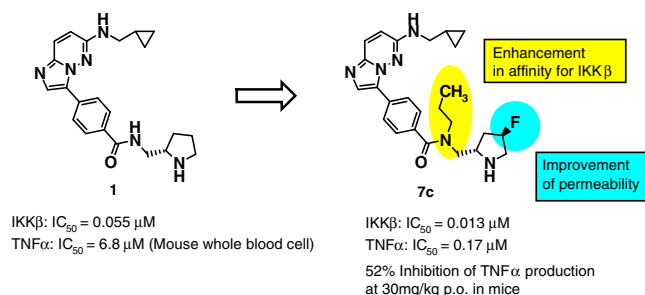


##### Discovery of imidazo[1,2-*b*]pyridazines as IKKβ inhibitors. Part 2: Improvement of potency in vitro and in vivo

pp 904–908

Hiroki Shimizu\*, Isao Yasumatsu, Tomoaki Hamada, Yoshiyuki Yoneda, Tomonori Yamasaki, Shinji Tanaka, Tadashi Toki, Mika Yokoyama, Kaoru Morishita, Shin Iimura

We have increased the potency of imidazo[1,2-*b*]pyridazine derivatives as IKKβ inhibitors with two strategies. One is to enhance the activity in cell-based assay by adjusting the polarity of molecules to improve permeability. Another is to increase the affinity for IKKβ by the introduction of additional substituents based on the hypothesis derived from an interaction model study. These improved compounds such as **7c** showed inhibitory activity of TNFα production in mice.

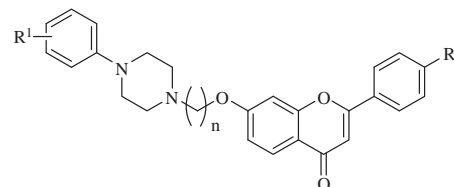


### Design, synthesis and biological evaluation of new arylpiperazine derivatives bearing a flavone moiety as $\alpha_1$ -adrenoceptor antagonists

pp 909–911

Jing Jin, Xiao-Bing Wang, Ling-Yi Kong\*

Eighteen new phenylpiperazine derivatives have been synthesized and evaluated on the basis of their  $\alpha_1$ -adrenoceptor antagonistic activities. Compounds **1**, **4**, **10**, **13** and **15** demonstrated activities close to the reference compound (Prazosin).

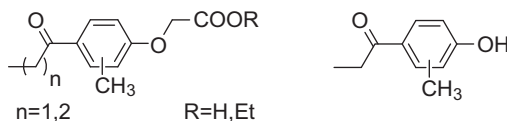


- 1**  $n=2$ ,  $R^1=H$ ,  $R^2=H$   
**4**  $n=2$ ,  $R^1=p\text{-CH}_3$ ,  $R^2=H$   
**10**  $n=2$ ,  $R^1=H$ ,  $R^2=Cl$   
**13**  $n=2$ ,  $R^1=p\text{-CH}_3$ ,  $R^2=Cl$   
**15**  $n=4$ ,  $R^1=p\text{-CH}_3$ ,  $R^2=Cl$

### Inhibitory effects of ethacrynic acid analogues lacking the $\alpha,\beta$ -unsaturated carbonyl unit and *para*-acylated phenols on human cancer cells

pp 912–915

Zack E. Bryant, Romy F. J. Janser, Medina Jabarkhail, Melissa S. Candelaria-Lyons, Brittini B. Romero, Severine Van slambrouck, Wim F. A. Steelant, Ingo Janser\*

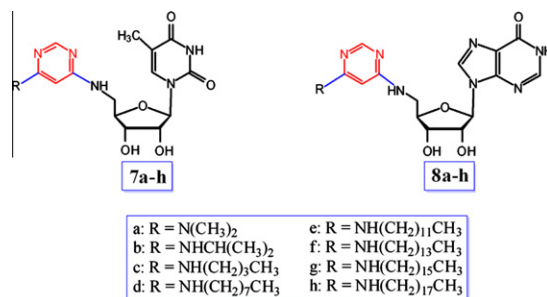


Analogues of ethacrynic acid, lacking the  $\alpha,\beta$ -unsaturated carbonyl unit, and their synthetic precursors, *para*-acylated phenols were designed, synthesized, and subsequently evaluated for their cytotoxicity and inhibitory effects against human prostate cancer cells, C4-2B and human breast cancer cells, Hs578T(i)8.

### Synthesis and antitumor activity of novel ribonucleosides with C-5 OH replaced by a diaminopyrimidinyl group

pp 916–919

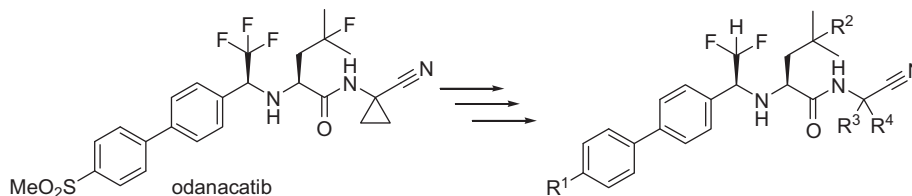
Kerang Wang, Ling Wu, Zhanbin Qin, Xinhao Yan, Xiaoliu Li\*, Hua Chen, Pingzhu Zhang, Jinchao Zhang



### Difluoroethylamines as an amide isostere in inhibitors of cathepsin K

pp 920–923

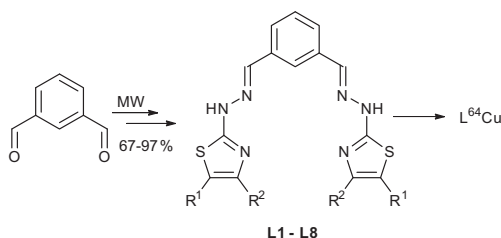
Elise Isabel\*, Christophe Mellon, Michael J. Boyd, Nathalie Chauret, Denis Deschênes, Sylvie Desmarais, Jean-Pierre Falguyret, Jacques Yves Gauthier, Karine Khougaz, Cheuk K. Lau, Serge Léger, Dorothy A. Levorse, Chun Sing Li, Frédéric Massé, M. David Percival, Bruno Roy, John Scheigetz, Michel Thérien, Vouy Linh Truong, Gregg Wesolowski, Robert N. Young, Robert Zamboni, W. Cameron Black



**Efficient synthesis of new tetradentate ligands with potential applications for  $^{64}\text{Cu}$  PET-imaging**

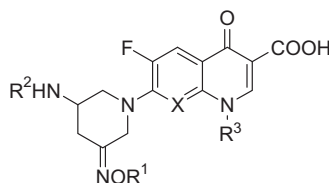
pp 924–927

Ewen Bodio, Karine Julienne, Sébastien G. Gouin, Alain Faivre-Chauvet, David Deniaud\*

**Synthesis and in vitro antibacterial activity of 7-(3-alkoxyimino-5-amino/methylaminopiperidin-1-yl)fluoroquinolone derivatives**

pp 928–931

Yibin Zhang, Guoqing Li, Mingliang Liu\*, Xuefu You, Lianshun Feng, Kai Lv, Jue Cao, Huiyuan Guo



A series of novel 7-(3-alkoxyimino-5-amino/methylaminopiperidin-1-yl)fluoroquinolone derivatives were designed, synthesized and evaluated for their in vitro antibacterial activity compared with gemifloxacin, ciprofloxacin and levofloxacin. All of the target compounds **10–27** have good activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, and *Escherichia coli*. In particular, some compounds showed useful activity against several fluoroquinolone-resistant strains, and the most active compound **15** was found to be 16–128, 2–32, and 4–8-fold more potent than the three reference drugs against fluoroquinolone-resistant MSSA, MRSA, and MRSE.

**1H-Imidazo[4,5-c]pyridine-4-carbonitrile as cathepsin S inhibitors: Separation of desired cellular activity from undesired tissue accumulation through optimization of basic nitrogen  $pK_a$** 

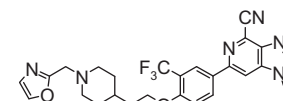
pp 932–935

Wullie Arbuckle, Mark Baugh, Simone Belshaw, D. Jonathan Bennett, John Bruin, Jiaqiang Cai\*, Kenneth S. Cameron, Chris Claxton, Maureen Dempster, Kathryn Everett, Xavier Fradera, William Hamilton, Philip S. Jones, Emma Kinghorn, Clive Long, Iain Martin, John Robinson, Paul Westwood

Based on the theoretical understanding of the in vivo lysosomotropism, by manipulating the  $pK_a$  of the cathepsin S inhibitors, a set of compounds with  $pK_a$  6–8 were identified to have excellent cell based Lip10 activity, yet avoiding undesired sequestration in spleen.

Quantitative description of unbound compound lysosomotropism:

$$f = \frac{10^{pH_M}}{10^{pH_L}} \times \frac{10^{pK_a} + 10^{pH_L}}{10^{pK_a} + 10^{pH_M}} = \frac{10^{7.4}}{10^{4.8}} \times \frac{10^{pK_a} + 10^{4.8}}{10^{pK_a} + 10^{7.4}}$$

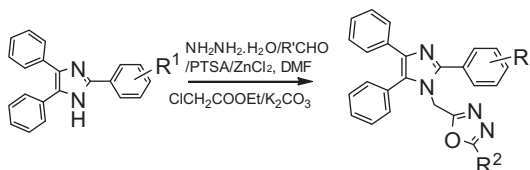


hCatS  $IC_{50}$ : 7.9nM  
Lip10  $IC_{50}$ : 39nM  
F%: 112 (C57 mice)  
 $pK_a$ : 6.3  
Spleen/Plasma ratio: 1.9

**Substituted imidazole derivatives as novel cardiovascular agents**

pp 936–939

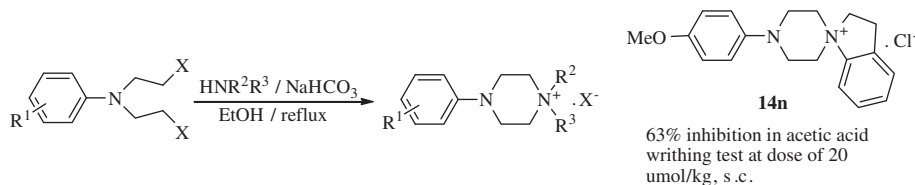
Vineet Malhotra, Seema R. Pathak\*, Rajendra Nath, Devashish Mukherjee, K. Shanker



### Synthesis and structure–analgesic activity relationships of a novel series of monospirocyclopiperazinium salts (MSPZ)

pp 940–943

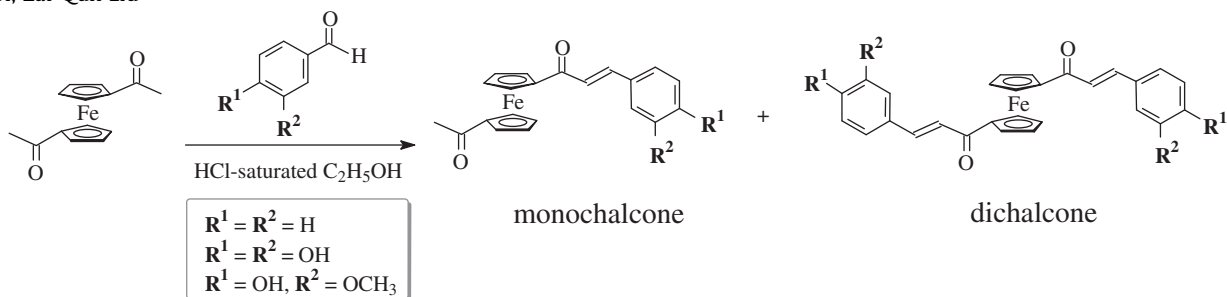
Song-Wen Lin, Qi Sun, Ze-Mei Ge, Xin Wang, Jia Ye\*, Run-Tao Li\*



### Radical-scavenging properties of ferrocenyl chalcones

pp 944–946

Gul Nabi, Zai-Qun Liu\*



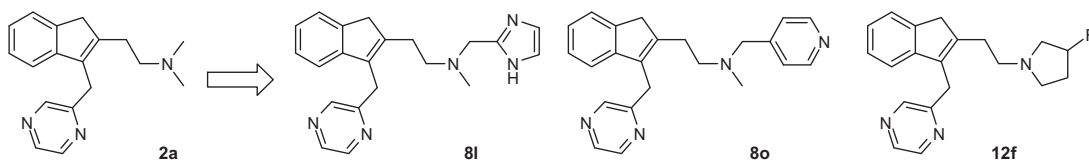
ABTS<sup>+</sup>, DPPH, and galvinoxyl radical-scavenging evaluations revealed that both Fe(II) in ferrocene and hydroxyl groups in ferrocenyl chalcones played radical-scavenging role.



### Influence of pK<sub>a</sub> on the biotransformation of indene H<sub>1</sub>-antihistamines by CYP2D6

pp 947–951

Charles Huang, Wilna J. Moree\*, Said Zamani-Kord, Bin-Feng Li, Fabio C. Tucci, Siobhan Malany, Jianyun Wen, Hua Wang, Samuel R. J. Hoare, Chun Yang, Ajay Madan, Paul D. Crowe, Graham Beaton\*

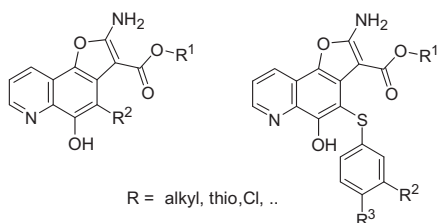


Near exclusive CYP2D6 metabolism in early lead **2a** was addressed by reduction in pK<sub>a</sub> of the basic amine. Incorporation of a heteroaryl moiety or a β-fluoro substituent led to the identification of **8l**, **8o**, and **12f**, with promising primary in vitro profiles and reduced biotransformation via CYP2D6.

### Synthesis and antifungal activity of furo[2,3-*f*]quinolin-5-ols

pp 952–955

Chung-Kyu Ryu\*, Yang Hui Kim, Ji-Hee Nho, Jung An Hong, Joo Hee Yoon, Aram Kim

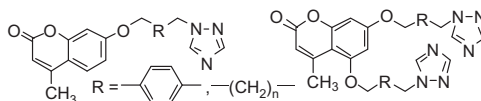


Furo[2,3-*f*]quinolin-5-ols were synthesized and tested for in vitro antifungal activity against pathogenic fungi. Among them tested, many of furo[2,3-*f*]quinolin-5-ols exhibited potent antifungal activity.

**Synthesis and evaluation of a class of new coumarin triazole derivatives as potential antimicrobial agents**

pp 956–960

Yuan Shi, Cheng-He Zhou\*

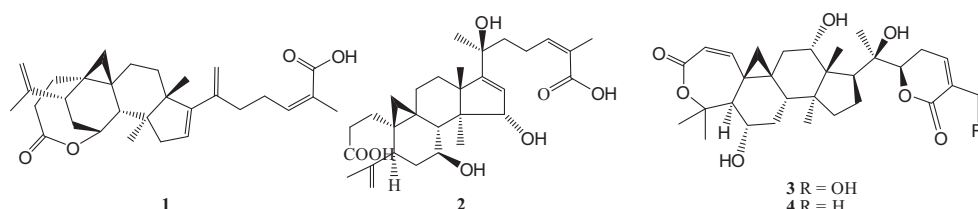


A series of new coumarin-based 1,2,4-triazoles were synthesized and some of them displayed comparable or even better antibacterial and antifungal efficacy compared to reference drugs Enoxacin, Chloromycin and Fluconazole.

**Compounds from *Kadsura angustifolia* with anti-HIV activity**

pp 961–965

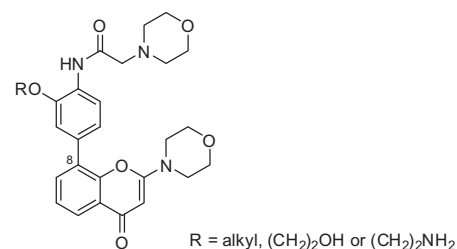
Rong Sun, Hong-Chuan Song, Chun-Ren Wang, Kai-Ze Shen, Yao-Bo Xu, Yan-Xiu Gao, Ye-Gao Chen\*, Jin-Yan Dong\*

**DNA-dependent protein kinase (DNA-PK) inhibitors: Structure–activity relationships for *O*-alkoxyphenylchromen-4-one probes of the ATP-binding domain**

pp 966–970

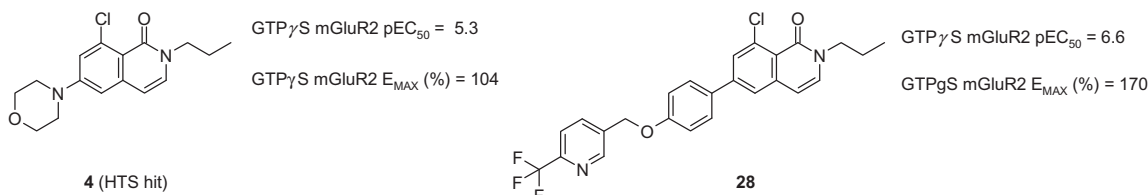
Kate M. Clapham, Julia Bardos, M. Raymond V. Finlay, Bernard T. Golding, Edward J. Griffen, Roger J. Griffin, Ian R. Hardcastle, Keith A. Menear, Attila Ting, Paul Turner, Gail L. Young, Céline Cano\*

Introduction of an *O*-alkoxyphenyl substituent at the 8-position of the 2-morpholino-4*H*-chromen-4-one pharmacophore enabled regions of the ATP-binding site of DNA-dependent protein kinase (DNA-PK) to be probed further.

**New positive allosteric modulators of the metabotropic glutamate receptor 2 (mGluR2): Identification and synthesis of *N*-propyl-8-chloro-6-substituted isoquinolones**

pp 971–976

Andrés A. Trabanco\*, Guillaume Duvey, José María Cid, Gregor J. Macdonald, Philippe Cluzeau, Vanthea Nhem, Rocco Furnari, Nadia Behaj, Géraldine Poulain, Terry Finn, Hilde Lavreysen, Sonia Poli, Alexandre Raux, Yves Thollon, Nicolas Poirier, David D'Addona, José Ignacio Andrés, Robert Lutjens, Emmanuel Le Poul, Hassan Imogai, Jean-Philippe Rocher

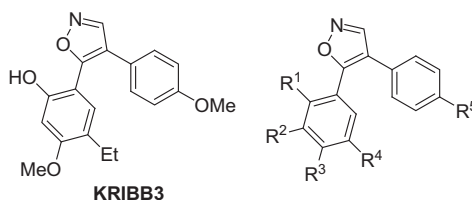


A series of *N*-propyl-8-chloro-6-substituted isoquinolones was identified as positive allosteric modulators of metabotropic glutamate receptor 2 (mGluR2 PAM) via high throughput screening (HTS). The subsequent synthesis and initial SAR exploration that led to the identification of compound **28** is described.

**Biological evaluation of KRIBB3 analogs as a microtubule polymerization inhibitor**

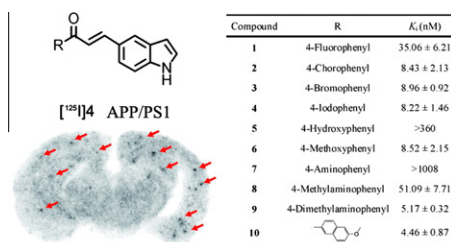
pp 977–979

Sangku Lee\*, Jae Nyoung Kim, Hyeong Kyu Lee, Kab Seog Yoon, Ki Deok Shin, Byoung-Mog Kwon, Dong Cho Han\*

**Synthesis and biological evaluation of indole-chalcone derivatives as  $\beta$ -amyloid imaging probe**

pp 980–982

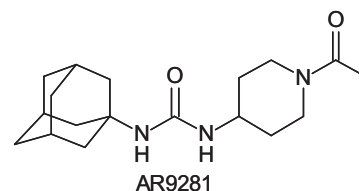
Mengchao Cui, Masahiro Ono\*, Hiroyuki Kimura, Bo Li Liu, Hideo Saji\*

A series of novel indole-chalcone derivatives were synthesized and evaluated as  $A\beta$  imaging probes.**1-(1-Acetyl-piperidin-4-yl)-3-adamantan-1-yl-urea (AR9281) as a potent, selective, and orally available soluble epoxide hydrolase inhibitor with efficacy in rodent models of hypertension and dysglycemia**

pp 983–988

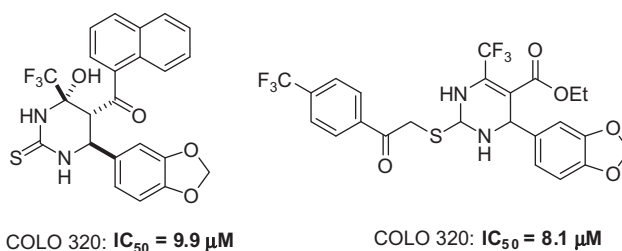
Sampath-Kumar Anandan\*, Heather Kay Webb, Dawn Chen, Yi-Xin (Jim) Wang, Basker R. Aavula, Sylvaine Cases, Ying Cheng, Zung N. Do, Upasana Mehra, Vinh Tran, Jon Vincelette, Joanna Waszczuk, Kathy White, Kenneth R. Wong, Le-Ning Zhang, Paul D. Jones, Bruce D. Hammock, Dinesh V. Patel, Randall Whitcomb, D. Euan MacIntyre, James Sabry, Richard Gless

1-(1-Acetyl-piperidin-4-yl)-3-adamantan-1-yl-urea (AR9281) attenuated the enhanced glucose excursion following an intraperitoneal glucose tolerance test and the increase in blood pressure in angiotensin-II-induced hypertension in rats. These effects were dose-dependent and well correlated with inhibition of the soluble epoxide hydrolase (sEH) activity in whole blood.

**Synthesis and in vitro cytotoxicity evaluation of some fluorinated hexahydropyrimidine derivatives**

pp 989–992

Oluropo C. Agbaje, Olugbeminiyi O. Fadeyi, S. Adamson Fadeyi, Lewis. E. Myles, Cosmas O. Okoro\*

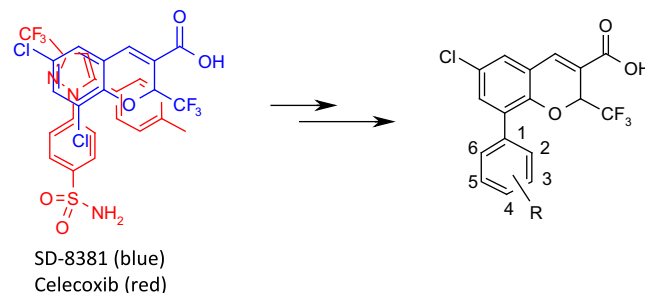


## Structure-based parallel medicinal chemistry approach to improve metabolic stability of benzopyran COX-2 inhibitors

pp 993–996

Li Xing, Bruce C. Hamper, Theresa R. Fletcher, Jay M. Wendling, Jeffery Carter, James K. Gierse, Subo Liao\*

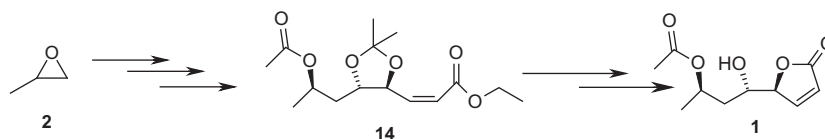
Based on the understanding on the binding structures of two lead COX-2 inhibitor, **SD-8381** and **Celecoxib**, the combination of structure-based design and solid-phase parallel synthesis provided an integrated approach to rapidly establish the structure–activity/property relationship of benzopyran COX-2 inhibitors and identify potent and selective new lead compounds with improved metabolic properties. Free energy perturbation prediction yielded insights into binding free energies that guide inhibitor design.



## Stereoselective first total synthesis, confirmation of the absolute configuration and bioevaluation of botryolide-E

pp 997–1000

D. Kumar Reddy, V. Shekhar, P. Prabhakar, D. Chanti Babu, D. Ramesh, B. Siddhardha, U. S. N. Murthy, Y. Venkateswarlu\*

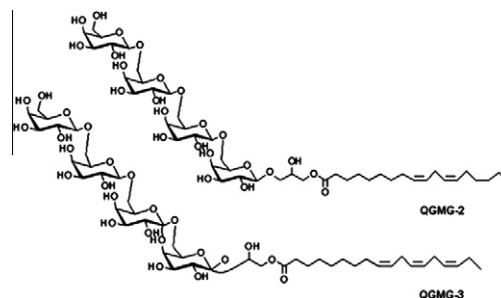


## Glucose-lowering activity of novel tetrasaccharide glyceroglycolipids from the fruits of *Cucurbita moschata*

pp 1001–1003

Zhiguo Jiang, Qizhen Du\*

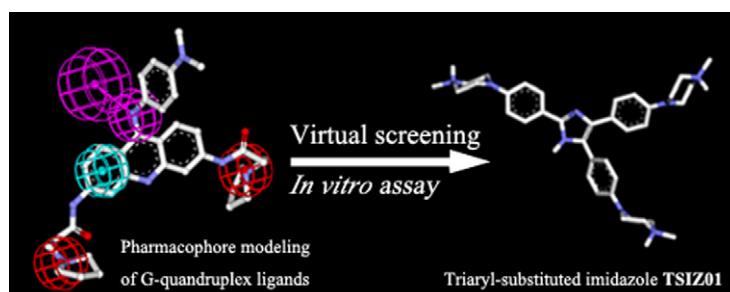
Phytochemical investigation resulted in the isolation of two new tetrasaccharide glyceroglycolipids (**QGMG-3** and **QGMG-2**) from the fruit of *Cucurbita moschata*. The two compounds significantly lowered blood glucose level of the streptozotocin- and high-fat diet-induced diabetic mouse.



## Pharmacophore-based discovery of triaryl-substituted imidazole as new telomeric G-quadruplex ligand

pp 1004–1009

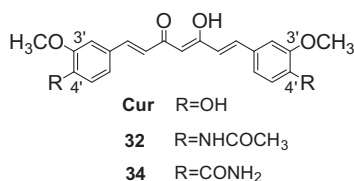
Shuo-Bin Chen, Jia-Heng Tan\*, Tian-Miao Ou, Shi-Liang Huang, Lin-Kun An, Hai-Bin Luo, Ding Li, Lian-Quan Gu, Zhi-Shu Huang\*



**Synthesis and preliminary evaluation of curcumin analogues as cytotoxic agents**

pp 1010–1014

Qin Zhang, Ying Zhong, Lin-Na Yan, Xun Sun, Tao Gong, Zhi-Rong Zhang\*

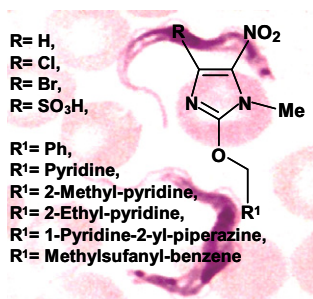


Several synthetic curcumin analogues, especially **32** and **34**, exhibited highly selective cytotoxicity against human epidermoid carcinoma cell line A-431 and human glioblastoma cell line U-251, suggesting their specific potential in the chemoprevention and chemotherapy of skin cancer and glioma.

**Compounds containing 2-substituted imidazole ring for treatment against human African trypanosomiasis**

pp 1015–1018

Bhupesh S. Samant\*, Mugdha G. Sukhthankar

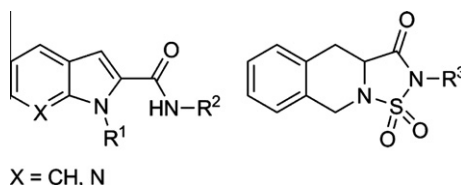


A series of compounds containing a 2-substituted imidazole ring has been synthesized from imidazole and tested for its biological activity against human African trypanosomiasis (HAT) along with its cytotoxicity and solubility.

**Design, synthesis and biological evaluation of new thalidomide analogues as TNF- $\alpha$  and IL-6 production inhibitors**

pp 1019–1022

Charlotte Chaulet, Cécile Croix, David Alagille, Sylvain Normand, Adriana Delwail, Laure Favot, Jean-Claude Lecron, Marie-Claude Viaud-Massuard\*

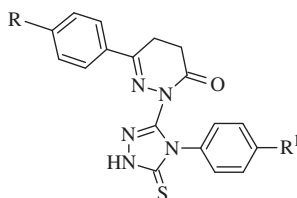


Several thalidomide analogues were synthesized and compared to thalidomide and its more active analogue, lenalidomide, for their ability to inhibit the production of the pro-inflammatory cytokine tumour necrosis factor (TNF)- $\alpha$  and interleukin (IL)-6 by LPS-activated peripheral blood mononuclear cells (PBMCs).

**Triazole incorporated pyridazinones as a new class of antihypertensive agents: Design, synthesis and in vivo screening**

pp 1023–1026

Anees A. Siddiqui, Ravinesh Mishra\*, Mohammad Shaharyar, Asif Husain, Mohd. Rashid, Palash Pal



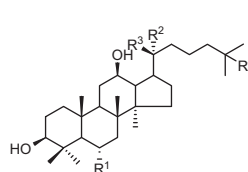
The current work describes the design and synthesis of novel triazole incorporated pyridazinones derivatives with encouraging in vivo antihypertensive activity by non-invasive method using Tail Cuff method.

**Novel dammarane-type sapogenins from *Panax ginseng* berry and their biological activities**

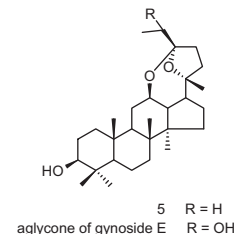
pp 1027–1031

Jun-Ming Zhao, Ning Li, Hong Zhang, Chun-fu Wu, Hu-Ri Piao<sup>\*\*</sup>, Yu-Qing Zhao<sup>\*</sup>

Three new dammarane-type sapogenins (**1**, **3**, and **5**) together with two known ones (**2** and **4**) were isolated and identified from the total hydrolyzed saponins extracted from the fruits of *Panax ginseng* based on physicochemical characteristics and NMR data. Their antitumor activities were evaluated in six human cancer cell lines (MCF-7, HepG2, Du145, Colon205, A549, and HL-60). The novel compounds **1** and **3** showed significant cytotoxic activity against six cell lines and the IC<sub>50</sub> values of **3** to HepG2, Colon205, A549, and HL-60 were much lower. These findings suggest a structure–activity relationship among dammarane-type sapogenins: the antitumor effects of compounds which have monomethoxyl group were more significant than those of compounds with no or two methoxyl groups.



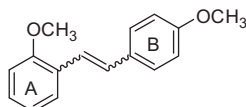
1	R <sup>1</sup> = H	R <sup>2</sup> = OH	R <sup>3</sup> = H	R <sup>4</sup> = OCH <sub>3</sub>
2	R <sup>1</sup> = OH	R <sup>2</sup> = OH	R <sup>3</sup> = H	R <sup>4</sup> = OCH <sub>3</sub>
3	R <sup>1</sup> = H	R <sup>2</sup> = OCH <sub>3</sub>	R <sup>3</sup> = H	R <sup>4</sup> = OH
4	R <sup>1</sup> = H	R <sup>2</sup> = H	R <sup>3</sup> = OCH <sub>3</sub>	R <sup>4</sup> = OCH <sub>3</sub>
20 (S)-25-OCH <sub>3</sub> -PPD	R <sup>1</sup> = H	R <sup>2</sup> = H	R <sup>3</sup> = OH	R <sup>4</sup> = OCH <sub>3</sub>



**5** R = H  
aglycone of gynoside E R = OH

**Methoxylation of resveratrol: Effects on induction of NAD(P)H Quinone-oxidoreductase 1 (NQO1) activity and growth inhibitory properties**

pp 1032–1035

Wei Zhang, Mei Lin Go<sup>\*</sup>

**3E** : IC<sub>50</sub> NQO1 induction: 0.85 μM

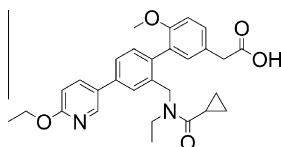
**3Z** : IC<sub>50</sub> (growth inhibition MCF7) 5.1 μM

Different structural features of resveratrol are required for induction of NQO1 and growth inhibition of human cancer cell lines.

**Sodium [2'-[(cyclopropanecarbonyl-ethyl-amino)-methyl]-4'-(6-ethoxy-pyridin-3-yl)-6-methoxy-biphenyl-3-yl]-acetate (AM432): A potent, selective prostaglandin D<sub>2</sub> receptor antagonist**

pp 1036–1040

Nicholas Stock<sup>\*</sup>, Deborah Volkots, Karin Stebbins, Alex Broadhead, Brian Stearns, Jeffrey Roppe, Timothy Parr, Christopher Baccei, Gretchen Bain, Charles Chapman, Lucia Correa, Janice Darlington, Christopher King, Catherine Lee, Daniel S. Lorrain, Pat Prodanovich, Angelina Santini, Jilly F. Evans, John H. Hutchinson, Peppi Prasit



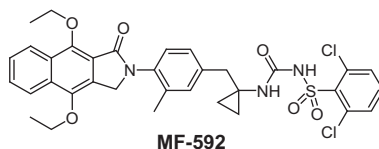
**21** (AM432)

Compound **21** (AM432) was identified as a potent and selective antagonist of the DP<sub>2</sub> receptor (CRTH2). Modification of a bi-aryl core identified a series of tri-aryl antagonists of which compound **21** proved a viable clinical candidate.

**Naphthalene/quinoline amides and sulfonylureas as potent and selective antagonists of the EP<sub>4</sub> receptor**

pp 1041–1046

Jason D. Burch, Julie Farand, John Colucci, Claudio Sturino, Yves Ducharme, Richard W. Friesen, Jean-François Lévesque, Sébastien Gagné, Mark Wrona, Alex G. Therien, Marie-Claude Mathieu, Danielle Denis, Erika Vigneault, Daigen Xu, Patsy Clark, Steve Rowland, Yongxin Han<sup>\*</sup>



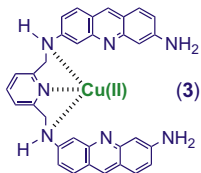
**MF-592**

K<sub>i</sub> = 0.3 nM; IC<sub>50</sub> = 3 nM; HWB IC<sub>50</sub> = 78 nM

### Synthesis and DNA photocleavage by a pyridine-linked bis-acridine chromophore in the presence of copper(II): Ionic strength effects

pp 1047–1051

Kathryn B. Grant\*, Carla A. Terry, Lourdes Gude, María-José Fernández, Antonio Lorente\*



10 to 30  $\mu\text{M}$  of **3**, 1 mol equiv **Cu(II)**, 150 mM NaCl and 260 mM KCl, 419 nm

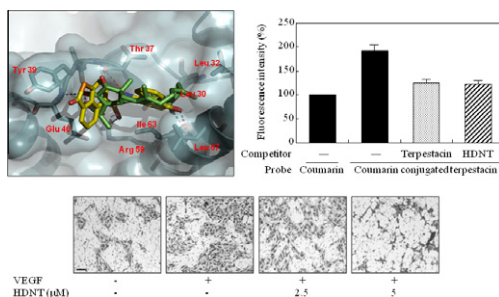
Copper(II) chloride enhances DNA photocleavage by bis-acridine **3** in the presence of physiological concentrations of salt.



### Identification of a novel small molecule targeting UQCRB of mitochondrial complex III and its anti-angiogenic activity

pp 1052–1056

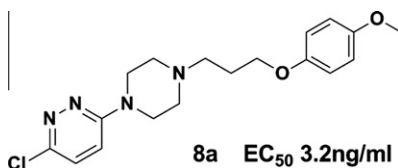
Hye Jin Jung, Ki Hyun Kim, Nam Doo Kim, Gyoonee Han, Ho Jeong Kwon\*



### Pharmacophore-based design, synthesis, and biological evaluation of novel chloro-pyridazine piperazines as human rhinovirus (HRV-3) inhibitors

pp 1057–1059

Hongliang Wang, Junhai Xiao\*, Dapeng Gao, Xian Zhang, Hui Yan, Zehui Gong, Tinmin Sun\*, Song Li



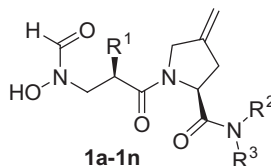
A new series of chloro-pyridazine piperazines (i.e., **8a**) are described as potent HRV-3 inhibitors.



### Design, synthesis and antibacterial activity of 3-methylenepyrrolidine formyl hydroxyamino derivatives as novel peptide deformylase inhibitors

pp 1060–1063

Wei Shi, Haikun Ma, Yuejiao Duan, Kelly Aubart, Yuhong Fang, Rimma Zonis, Liping Yang, Wenhao Hu\*

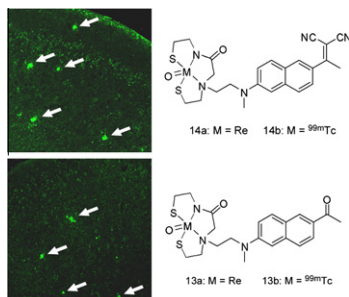


Design and synthesis of 3-methylenepyrrolidine formyl hydroxyamino derivatives as novel peptide deformylase inhibitors, and their antibacterial activities against susceptible and resistant clinical isolates including Gram-positive bacterial strains and Gram-negative ones have been reported.

**<sup>99m</sup>Tc- and Re-labeled 6-dialkylamino-2-naphthylethylidene derivatives as imaging probes for  $\beta$ -amyloid plaques**

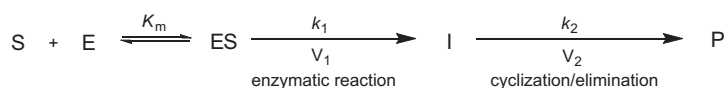
pp 1064–1068

Mengchao Cui, Ruikun Tang, Zijing Li, Huiying Ren, Boli Liu\*

**Kinetic delay of cyclization/elimination-coupled enzyme assays: Analysis and solution**

pp 1069–1071

Fengtian Xue\*, Christopher T. Seto



\*Corresponding author

Supplementary data available via ScienceDirect

**COVER**

Botulinum neurotoxins are the most deadly toxins known to man, approximately 10 million times more deadly than cyanide. Botulinum neurotoxins are classified by the US Centers for Disease Control (CDC) as bioterrorism agents. The etiological agent responsible for botulinum intoxication is a metalloprotease; as such this is a key therapeutic target. Currently, there are no approved pharmacological treatments for botulinum intoxication. Discovering molecules that could be used as a path forward for therapeutic development as botulinum protease inhibitors is tantamount. A benzylidene cyclopentenedione-based inhibitor was found to be the first affinity reagent to covalently modify the active site of botulinum neurotoxin A light chain metalloprotease. Its kinetic parameters are reported and such an approach for inhibition of this deadly neurotoxin. [Capková, K.; Hixon, M. S.; Pellett, S.; Barbieri, J. T.; Johnson, E. A.; Janda, K. D. *Bioorg. Med. Chem. Lett.* **2010**, 20, 206.]

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