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Bioorganic & Medicinal Chemistry Volume 20, Issue 3, 2012

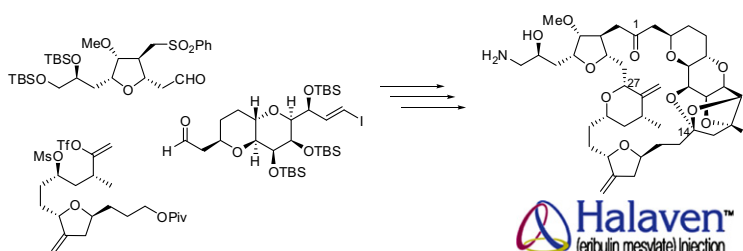
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Synthetic approaches to the 2010 new drugs

pp 1155–1174

Kevin K.-C. Liu, Subas M. Sakya, Christopher J. O'Donnell*, Andrew C. Flick, Hong X. Ding

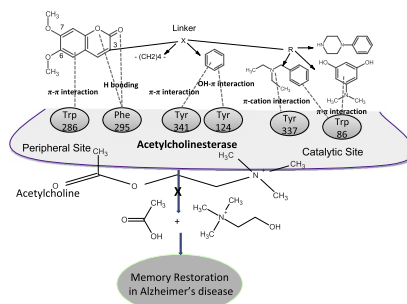


Plus the 14 other new drugs marketed in 2010.

A review on coumarins as acetylcholinesterase inhibitors for Alzheimer's disease

pp 1175–1180

Preet Anand, Baldev Singh*, Nirmal Singh



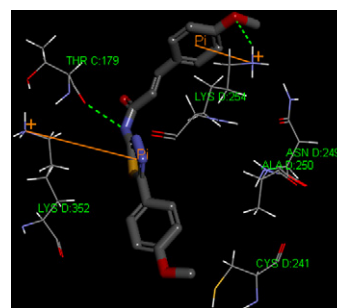
ARTICLES

Synthesis, biological evaluation, and molecular docking studies of cinnamic acyl 1,3,4-thiadiazole amide derivatives as novel antitubulin agents

pp 1181–1187

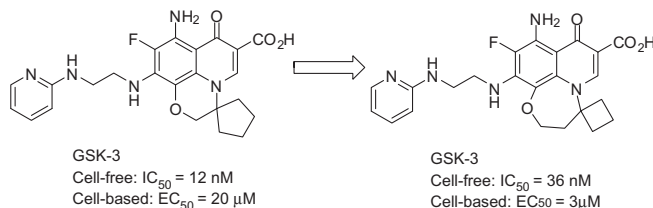
Xian-Hui Yang, Qing Wen, Ting-Ting Zhao, Jian Sun, Xi Li, Man Xing, Xiang Lu*, Hai-Liang Zhu*

A series of cinnamic acyl 1,3,4-thiadiazole amide derivatives have been designed and synthesized, and their biological activities were also evaluated as potential antiproliferation and tubulin polymerization inhibitors. Compound **10e** possessed the most potent tubulin polymerization inhibitory activity ($IC_{50} = 1.16 \mu\text{g/mL}$) and anticancer activities ($IC_{50} = 0.28 \mu\text{g/mL}$ for MCF-7 and $IC_{50} = 0.52 \mu\text{g/mL}$ for A549). Docking simulation was performed to insert compound **10e** into the crystal structure of tubulin to determine the probable binding model.



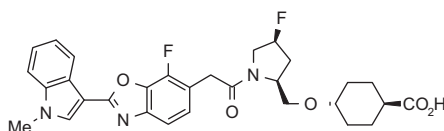
Quinolone derivatives containing strained spirocycle as orally active glycogen synthase kinase 3 β (GSK-3 β) inhibitors for type 2 diabetics pp 1188–1200

Shigeki Seto*, Kazuhiko Yumoto, Kyoko Okada, Yoshikazu Asahina, Aya Iwane, Maki Iwago, Reiko Terasawa, Kevin R. Shreder, Koji Murakami, Yasushi Kohno



Identification of *trans*-4-[1-[[7-fluoro-2-(1-methyl-3-indolyl)-6-benzoxazolyl]acetyl]-(4*S*)-fluoro-(2*S*)-pyrrolidinylmethoxy]cyclohexanecarboxylic acid as a potent, orally active VLA-4 antagonist pp 1201–1212

Masaki Setoguchi*, Shin Iimura, Yuuichi Sugimoto, Yoshiyuki Yoneda, Jun Chiba, Toshiyuki Watanabe, Fumihito Muro, Yutaka Iigo, Gensuke Takayama, Mika Yokoyama, Tomoe Taira, Misato Aonuma, Tohru Takashi, Atsushi Nakayama, Nobuo Machinaga

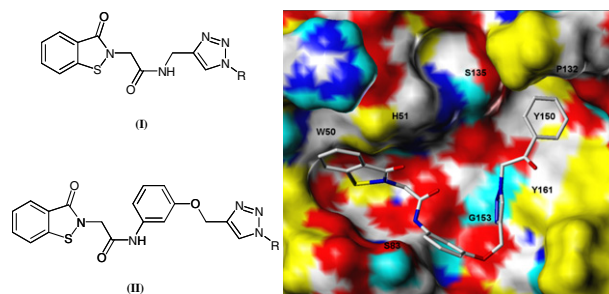


7e: VLA-4/VCAM-1 binding assay, IC₅₀ = 4.7 nM

Compound **7e** with 7-fluoro-2-(1-methyl-1*H*-indol-3-yl)-1,3-benzoxazolyl group significantly inhibited eosinophil infiltration into bronchoalveolar lavage fluid at 15 mg/kg in an *Ascaris*-antigen-induced murine bronchial inflammatory model.

Inhibition of Dengue virus and West Nile virus proteases by click chemistry-derived benz[d]isothiazol-3(2*H*)-one derivatives pp 1213–1221

Kok-Chuan Tiew, Dengfeng Dou, Tadahisa Teramoto, Huiguo Lai, Kevin R. Alliston, Gerald H. Lushington, R. Padmanabhan, William C. Groutas*

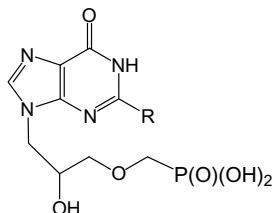


Two click chemistry-derived focused libraries based on the benz[d]isothiazol-3(2*H*)-one scaffold were synthesized and screened against Dengue virus and West Nile virus NS2B-NS3 proteases. Several compounds (**4l**, **7j–n**) displayed noteworthy inhibitory activity toward Dengue virus NS2B-NS3 protease in the absence and presence of added detergent.

Synthesis of purine *N*⁹-[2-hydroxy-3-*O*-(phosphonmethoxy)propyl] derivatives and their side-chain modified analogs as potential antimalarial agents pp 1222–1230

Marcela Krečmerová*, Martin Dračinský, Dana Hocková, Antonín Holý, Dianne T. Keough, Luke W. Guddat

Inhibition of hypoxanthine-guanine-(xanthine)-phosphoribosyltransferase:



iso-HPMPHx (R = H)

K_i (*Pf*) HGXPRT: 1.9 μ M

K_i (*human*) HGPRT: no inhibition

iso-HPMPG (R = NH₂)

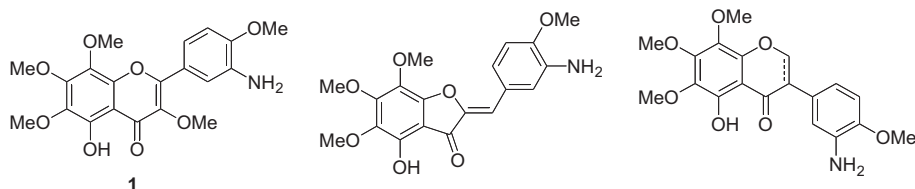
K_i (*Pf*) HGXPRT: 1.4 μ M

K_i (*human*) HGPRT: 8 μ M

Influence of the skeleton on the cytotoxicity of flavonoids

pp 1231–1239

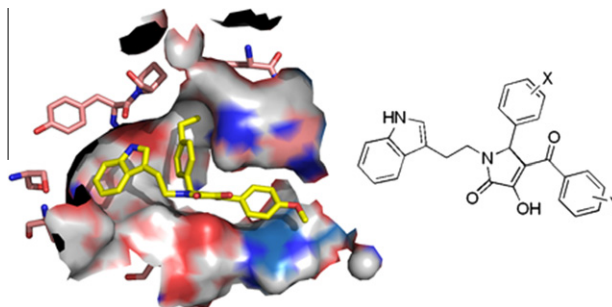
Guy Lewin*, Geneviève Aubert, Sylviane Thoret, Joëlle Dubois, Thierry Cresteil



Aurone, isoflavone and isoflavanone analogs of the cytotoxic flavone **1** were synthesized. Cytotoxicity of these new compounds (and fifteen other ones) was evaluated, and SARs discussed.

**Identification of *Trypanosoma brucei* leucyl-tRNA synthetase inhibitors by pharmacophore- and docking-based virtual screening and synthesis** pp 1240–1250

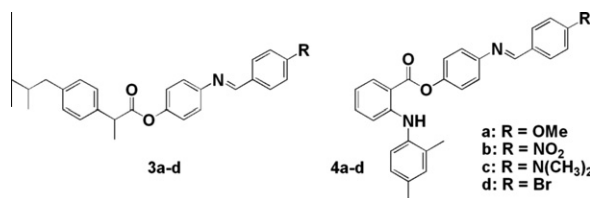
Yaxue Zhao, Qing Wang, Qingqing Meng, Dazhong Ding, Huaiyu Yang, Guangwei Gao, Dawei Li, Weiliang Zhu, Huchen Zhou*

**Construction of an Indonesian herbal constituents database and its use in Random Forest modelling in a search for inhibitors of aldose reductase** pp 1251–1258

Sadaf Naeem, Peter Hylands, David Barlow*

**Design, synthesis, biological evaluation, and comparative Cox1 and Cox2 docking of *p*-substituted benzylidenamino phenyl esters of ibuprofenic and mefenamic acids** pp 1259–1270

Gehan H. Hegazy, Hamed I. Ali*

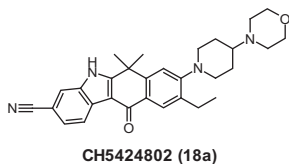


The ibuprofenic acid and mefenamic acid esters coupled with [4-(4-substituted benzylidene amino)phenols] Schiff's bases revealed remarkable analgesic anti-inflammatory activities with surprising non-ulcerogenic effects. A correlation between their biological activities and AutoDock binding free energies was obtained by comparative docking into Cox1 and Cox2.

Design and synthesis of a highly selective, orally active and potent anaplastic lymphoma kinase inhibitor (CH5424802)

pp 1271–1280

Kazutomo Kinoshita*, Kohsuke Asoh, Noriyuki Furuichi, Toshiya Ito, Hatsuo Kawada, Sousuke Hara, Jun Ohwada, Takuho Miyagi, Takamitsu Kobayashi, Kenji Takanashi, Toshiyuki Tsukaguchi, Hiroshi Sakamoto, Takuo Tsukuda, Nobuhiro Oikawa



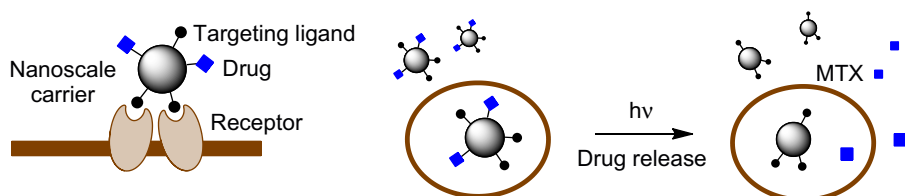
ALK IC_{50} = 1.9 nM
 MET IC_{50} >5000 nM
 KARPAS-299 IC_{50} = 3.0 nM
 F (monkey) = 50.4%



A photochemical approach for controlled drug release in targeted drug delivery

pp 1281–1290

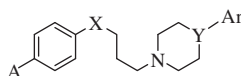
Seok Ki Choi*, Manisha Verma, Justin Silpe, Ryan E. Moody, Kenny Tang, Jeffrey J. Hanson, James R. Baker Jr.*



Multi-receptor drug design: Haloperidol as a scaffold for the design and synthesis of atypical antipsychotic agents

pp 1291–1297

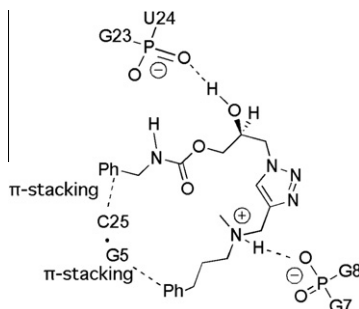
Kwakye Peprah, Xue Y. Zhu, Suresh V. K. Eyunni, Vincent Setola, Bryan L. Roth, Seth Y. Ablordepey*



Characterization of a 1,4-disubstituted 1,2,3-triazole binding to T box antiterminator RNA

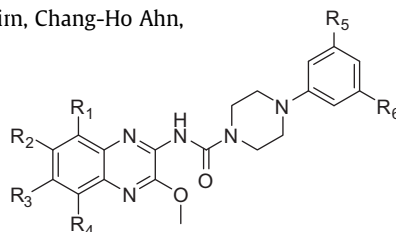
pp 1298–1302

S. Zhou, J. A. Means, G. Acquaaah-Harrison, S. C. Bergmeier, J. V. Hines*



Synthesis, anticancer activity and pharmacokinetic analysis of 1-[(substituted 2-alkoxyquinoxalin-3-yl)aminocarbonyl]-4-(hetero)arylpiperazine derivatives pp 1303–1309

Young Bok Lee*, Young-Dae Gong*, Deog Joong Kim, Chang-Ho Ahn, Jae-Yang Kong, Nam-Sook Kang

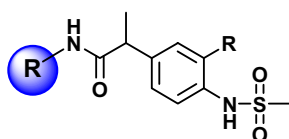


A series of novel 7 or 8-substituted compounds on the quinoxaline ring of 1-[(2-alkoxyquinoxalin-3-yl)aminocarbonyl]-4-(hetero)arylpiperazine derivatives were newly synthesized and tested as a prominent anticancer agent in various types of human cancer cell lines. Among representative compounds substituted on the quinoxaline ring, in vitro cell line and pharmacokinetic studies suggest that compound **6k** has a strong anticancer efficacy and desirable pharmacokinetic properties. These data support further development of compound **6k** to achieve an orally available anticancer drug.



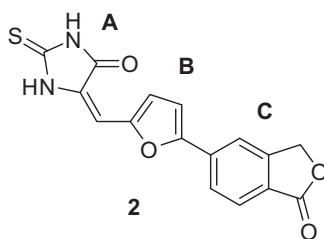
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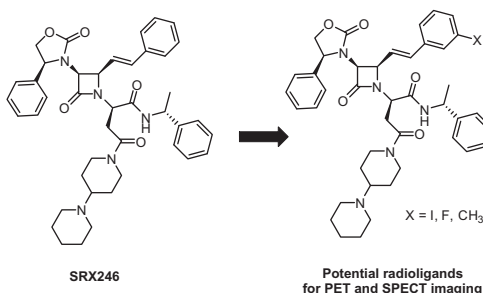
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Julie A. Spicer*, Kristiina M. Huttunen, Christian K. Miller, William A. Denny, Annette Ciccone, Kylie A. Browne, Joseph A. Trapani



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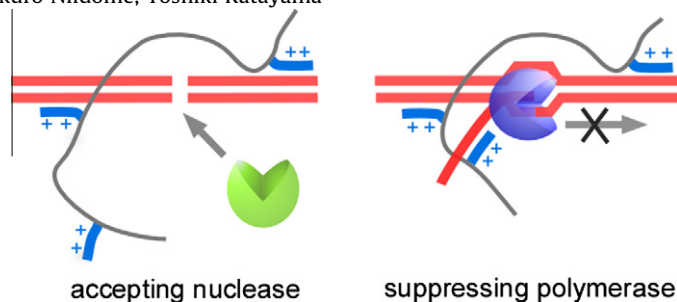
Karine Fabio, Christophe Guillon*, Carl J. Lacey, Shi-fang Lu, Ned D. Heindel, Craig F. Ferris, Michael Placzek, Graham Jones, Michael J. Brownstein, Neal G. Simon



Creating a unique environment for selecting reactive enzymes with DNA: 'Sticky' binding of oligocation-grafted polymers to DNA

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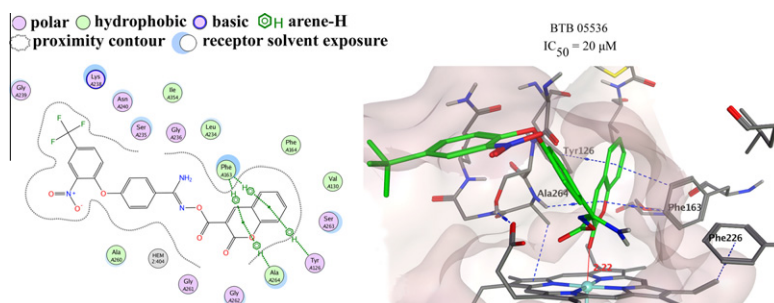
Hiroyuki Tanaka, Takeshi Mori*, Takuro Niidome, Yoshiki Katayama*



Novel indoleamine 2,3-dioxygenase-1 inhibitors from a multistep in silico screen

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Jason R. Smith, Krystal J. Evans, Adam Wright, Robert D. Willows, Joanne F. Jamie*, Renate Griffith



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*Corresponding author

i+ Supplementary data available via SciVerse ScienceDirect

COVER

Formulating a new basis for the treatment against botulinum neurotoxin intoxication: 3,4-Diaminopyridine prodrug design and characterization. [Zakhari, J.S.; Kinoyama, I.; Hixon, M.S.; Di Mola, A.; Globisch, D.; Janda, K.D.; *Bioorg. Med. Chem.* **2011**, *19*, 6203–6209.]

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