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Bioorganic & Medicinal Chemistry Volume 20, Issue 9, 2012

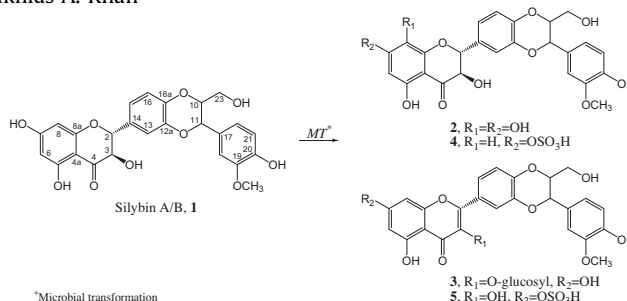
Contents

ARTICLES

Bioconversion of silybin to phase I and II microbial metabolites with retained antioxidant activity

pp 2784–2788

Ehab A. Abourashed*, Julie R. Mikell, Ikhlas A. Khan

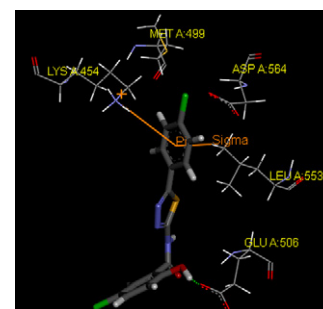


Synthesis, biological evaluation, and molecular docking studies of 1,3,4-thiadiazol-2-amide derivatives as novel anticancer agents

pp 2789–2795

Xian-Hui Yang, Lu Xiang, Xi Li, Ting-Ting Zhao, Hui Zhang, Wen-Ping Zhou, Xiao-Ming Wang*, Hai-Bin Gong*, Hai-Liang Zhu*

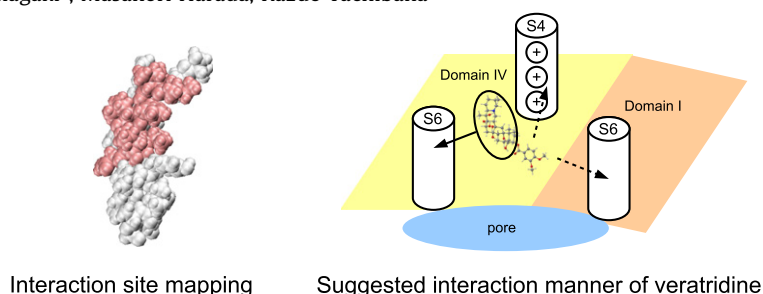
A series of 1,3,4-thiadiazol-2-amide derivatives have been designed and synthesized, and their biological activities were also evaluated as potential antiproliferation and FAK inhibitors. Compound **5h** possessed the most potent FAK inhibitory activity ($IC_{50} = 5.32 \mu M$) and anticancer activities ($IC_{50} = 0.45 \mu M$ for MCF-7 and $IC_{50} = 0.31 \mu M$ for B16-F10). Docking simulation was performed to insert compound **5h** into the crystal structure of FAK to determine the probable binding model.



Solution NMR analysis of the binding mechanism of DIVS6 model peptides of voltage-gated sodium channels and the lipid soluble alkaloid veratridine

pp 2796–2802

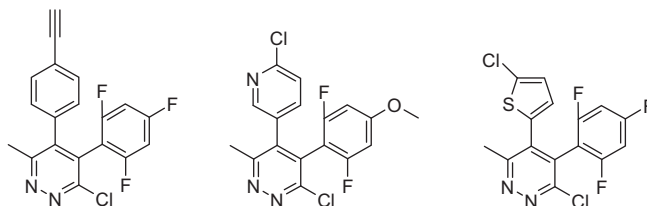
Ai Yoshinaka-Niitsu, Tohru Yamagaki*, Masanori Harada, Kazuo Tachibana



Synthesis and fungicidal activity of tubulin polymerisation promoters. Part 2: Pyridazines

pp 2803–2810

Clemens Lamberth*, Stephan Trah, Sebastian Wendeborn, Raphael Dumeunier, Mikael Courbot, Jeremy Godwin, Peter Schneider

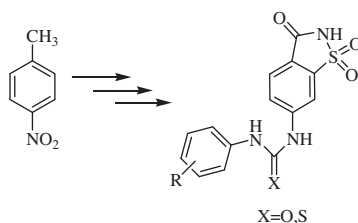


Highly active against *Botrytis cinerea* (grey mould), *Mycosphaerella graminicola* (wheat leaf blotch) and *Alternaria solani* (potato and tomato early blight).

New saccharin derivatives as tyrosinase inhibitors

pp 2811–2821

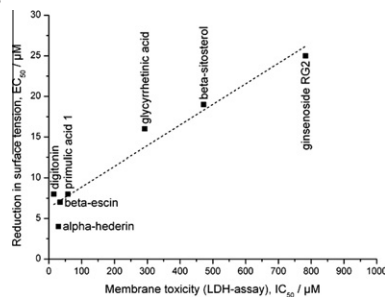
Nahit Gençer*, Dudu Demir, Fatih Sonmez, Mustafa Kucukislamoglu



Saponins can perturb biologic membranes and reduce the surface tension of aqueous solutions: A correlation?

pp 2822–2828

Stefan Böttger, Katja Hofmann, Matthias F. Melzig*

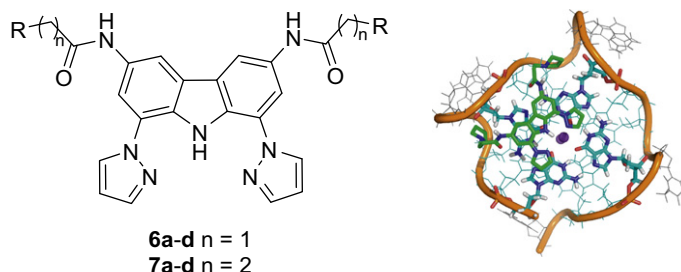


The attempt is undertaken to find a correlation between the cytotoxic effects and the physico-chemical properties of saponins.

Disubstituted 1,8-dipyrzolo-carbazole derivatives as a new type of c-myc G-quadruplex binding ligands

pp 2829–2836

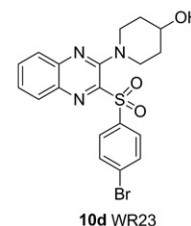
Wei-Jia Chen, Chen-Xi Zhou, Pei-Fen Yao, Xiao-Xiao Wang, Jia-Heng Tan, Ding Li, Tian-Miao Ou, Lian-Quan Gu, Zhi-Shu Huang*



A series of 1,8-dipyrzolo-carbazole derivatives were synthesized, and found to be a new type of selective binding ligands for c-myc G-quadruplex over duplex DNA.



pp 2837–2844




The design and synthesis of potent, selective benzodiazepine sulfonamide bombesin receptor subtype 3 (BRS-3) agonists with an increased barrier of atropisomerization

pp 2845–2849

Cc1c2c(c3c1c(c4c3c5c(c2n5)C(F)(F)F)C(F)(F)F)C(F)(F)F

Synthesis and biological evaluation of truncated α -galactosylceramide derivatives focusing on cytokine induction profile pp 2850–2859



$A = O, CH_2$
 $Y = (CH_2)_mCH_3, OR, Ar, etc.$

Design and synthesis of 4-O-methylhonokiol analogs as inhibitors of cyclooxygenase-2 (COX-2) and PGF₁ production pp 2860–2868

Phenol substituents

ortho-Position modification

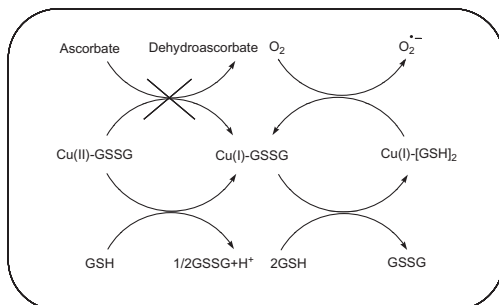
Olefin modification

Azole analogs



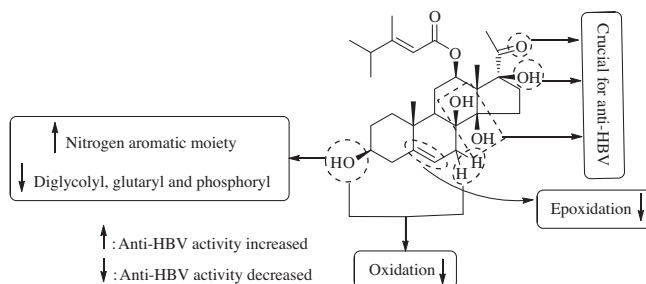
Redox-changes associated with the glutathione-dependent ability of the Cu(II)–GSSG complex to generate superoxide pp 2869–2876

Margarita E. Aliaga*, Camilo López-Alarcón, Luis García-Río, Manuel Martín-Pastor, Hernán Speisky

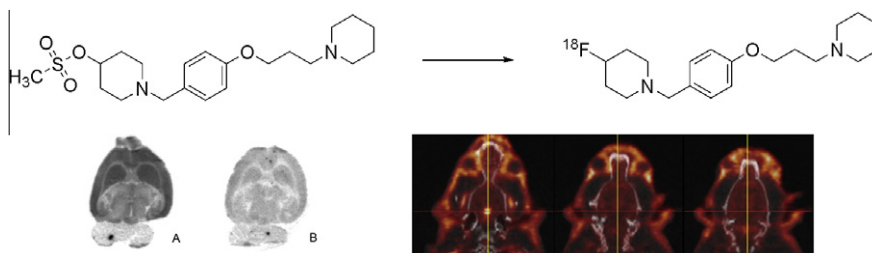
**Synthesis, structure–activity relationships and biological evaluation of caudatin derivatives as novel anti-hepatitis B virus agents** pp 2877–2888

Li-Jun Wang, Chang-An Geng, Yun-Bao Ma, Xiao-Yan Huang, Jie Luo, Hao Chen, Rui-Hua Guo, Xue-Mei Zhang, Ji-Jun Chen*

A series of caudatin derivatives were synthesized, and their anti-hepatitis B virus (HBV) activity was evaluated in HepG 2.2.15 cells. Most of the 3-O-substituted caudatin derivatives showed effective anti-HBV activity. Two compounds (**2e**, **2f**) had potent activity inhibiting not only the secretion of HBsAg, HBeAg, but also HBV DNA replication. The structure–activity relationships (SARs) of caudatin derivatives had been discussed.

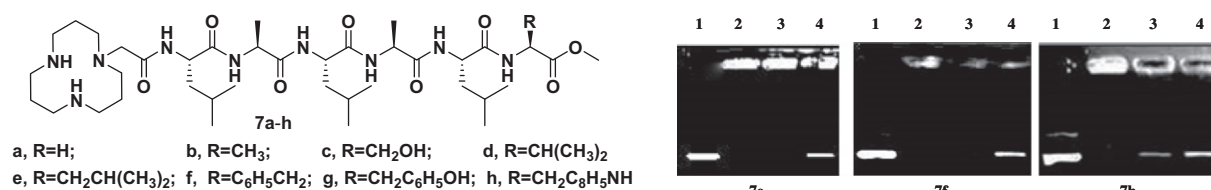
**Radiofluorinated histamine H₃ receptor antagonist as a potential probe for in vivo PET imaging: Radiosynthesis and pharmacological evaluation** pp 2889–2896

Svetlana V. Selivanova*, Michael Honer, Francine Combe, Kathleen Isensee, Holger Stark, Stefanie D. Krämer, P. August Schubiger, Simon M. Ametamey

**Syntheses of [12]aneN₃–oligopeptide conjugates as effective DNA condensation agents**

pp 2897–2904

Zhi-Fen Li, Zhi-Fo Guo, Hao Yan, Zhong-Lin Lu*, Da-Yong Wu*



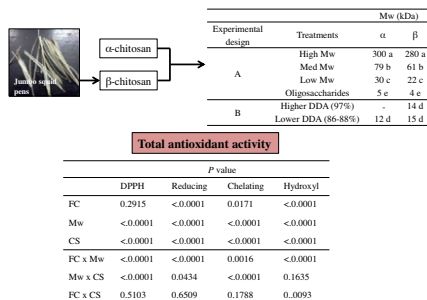
A series of oligopeptide derived macrocyclic polyamine [12]aneN₃ conjugates **7a–h**·3HCl have been synthesized and showed reversible DNA condensation ability.



Comparison in antioxidant action between α -chitosan and β -chitosan at a wide range of molecular weight and chitosan concentration

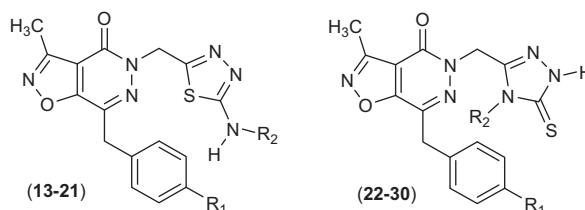
pp 2905–2911

Jooyeoun Jung, Yanyun Zhao*

**Synthesis and biological evaluation of isoxazolo[4,5-d]pyridazin-4-(5H)-one analogues as potent anti-inflammatory agents**

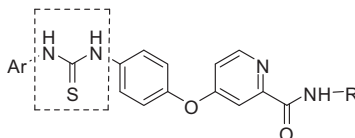
pp 2912–2922

Keriman Özadalı, Fügen Özkanlı, Sarthak Jain, Praveen P. N. Rao, Carlos A. Velázquez-Martínez*

**Design, synthesis and biological activities of thiourea containing sorafenib analogs as antitumor agents**

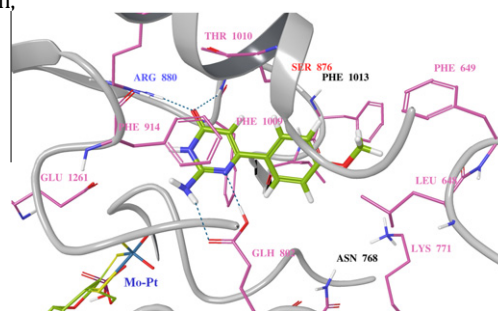
pp 2923–2929

Jianwen Yao, Jing Chen, Zuopeng He, Wei Sun, Wenfang Xu*

Twenty new diaryl thiourea containing sorafenib derivatives **9a–t** have been prepared and evaluated for their anticancer activity.**Identification of novel isocytosine derivatives as xanthine oxidase inhibitors from a set of virtual screening hits**

pp 2930–2939

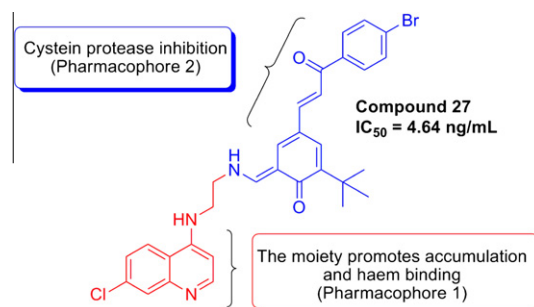
Chandrika B-Rao*, Asha Kulkarni-Almeida, Kamlesh V. Katkar, Smriti Khanna, Usha Ghosh, Ashish Keche, Pranay Shah, Ankita Srivastava, Vaidehi Korde, Kumar V. S. Nemmani, Nitin J. Deshmukh, Amol Dixit, Manoja K. Brahma, Umakant Bahirat, Lalit Doshi, Rajiv Sharma, H. Sivaramakrishnan



Antiplasmodial activity of novel keto-enamine chalcone-chloroquine based hybrid pharmacophores

pp 2971–2981

Koneni V. Sashidhara*, Manoj Kumar, Ram K. Modukuri, Rajeev Kumar Srivastava, Awakash Soni, Kumkum Srivastava, Shiv Vardan Singh, J. K. Saxena, Harsh M. Gauniyal, Sunil K. Puri

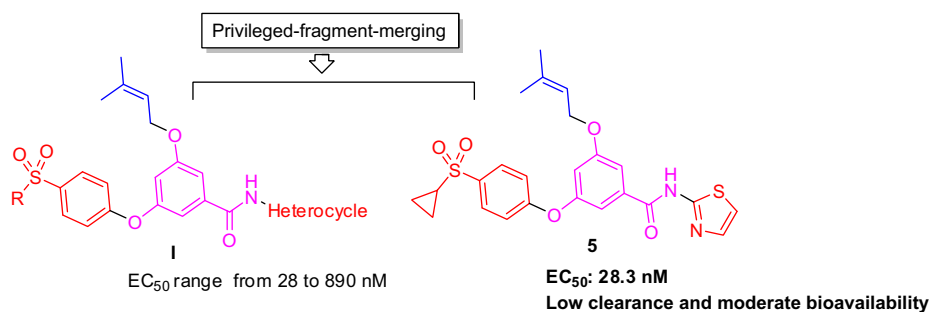


Synthesis and antimalarial evaluation of novel chalcone-chloroquine hybrids is reported.

**Design, synthesis, and pharmacological evaluation of benzamide derivatives as glucokinase activators**

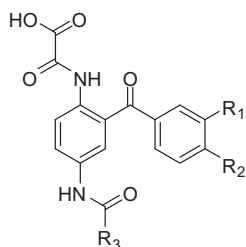
pp 2982–2991

Weiwei Mao, Mengmeng Ning, Zhiqing Liu, Qingzhang Zhu, Ying Leng*, Ao Zhang*

**Synthesis and biological evaluation of novel human Pin1 inhibitors with benzophenone skeleton**

pp 2992–2999

Chang Liu, Jing Jin, Liang Chen, Jie Zhou, Xiaoguang Chen, Decai Fu, Hongrui Song, Bailing Xu*

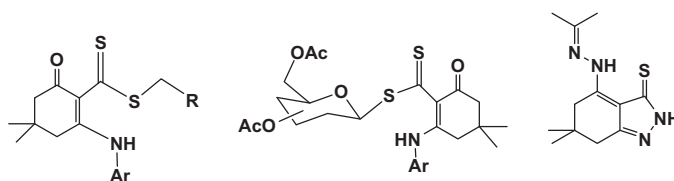


A series of novel benzophenone derivatives were prepared and their inhibitory activities were evaluated on hPin1. Of all the synthesized compounds, the most active compound displayed inhibitory activities with IC_{50} value of 5.99 $\mu\text{mol/L}$. Preliminary structure–activity relationships were analyzed in details and the binding mode of the titled compounds was predicted using FlexX algorithm.

Synthesis, biological evaluation, and molecular docking studies of benzyl, alkyl and glycosyl [2-(arylamino)-4,4-dimethyl-6-oxo-cyclohex-1-ene]carbodithioates, as potential immunomodulatory and immunosuppressive agents

pp 3000–3008

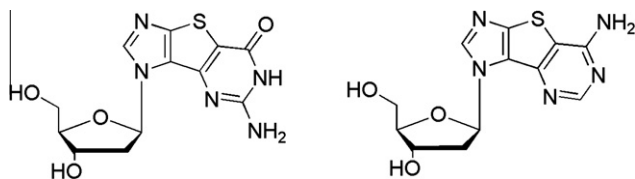
El Sayed H. El Ashry*, Mohammad R. Amer, Omer M. Abdalla, Aly A. Aly, Samreen Soomro, Almas Jabeen, Sobia Ahsan Halim, M. Ahmed Mesaik, Zaheer Ul-Haq



Synthesis and biological evaluation of a series of thieno-expanded tricyclic purine 2'-deoxy nucleoside analogues

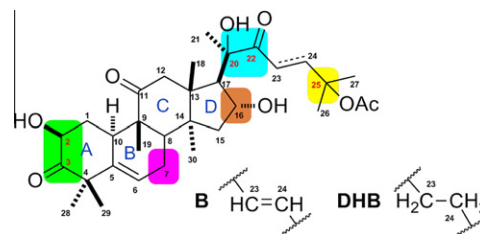
pp 3009–3015

Orrette R. Wauchope, Cameron Johnson, Pasupathy Krishnamoorthy, Graciela Andrei, Robert Snoeck, Jan Balzarini, Katherine L. Seley-Radtke*

**Synthesis and cytotoxic activity evaluation of dihydrocucurbitacin B and cucurbitacin B derivatives**

pp 3016–3030

Karen Luise Lang*, Izabella Thaís Silva, Lara Almida Zimmermann, Vanessa Rocha Machado, Marina Rodrigues Teixeira, María Ivana Lapuh, Mariana Alejandra Galetti, Jorge Alejandro Palermo, Gabriela Myriam Cabrera, Lílían Sibelle Campos Bernardes, Cláudia Maria Oliveira Simões, Eloi Paulo Schenkel, Miguel Soriano Balparda Caro, Fernando Javier Durán

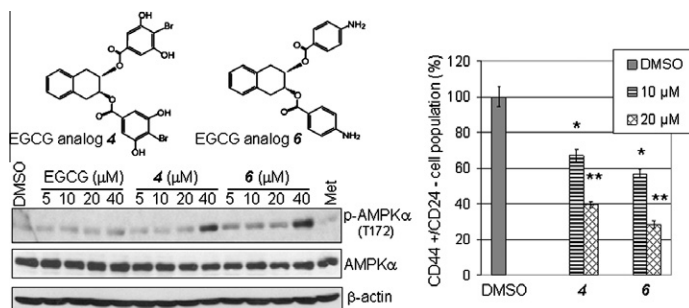


Semi-synthetic transformations were performed at positions 2, 3, 7, 16, 20, 22, and 25 on dihydrocucurbitacin B (**1**) and cucurbitacin B (**2**). Novel twenty-nine semisynthetic compounds, as well as **1** and **2** were tested in vitro for their cytotoxic effects on non-small-cell lung cancer cells (A549 cells).

**Novel epigallocatechin gallate (EGCG) analogs activate AMP-activated protein kinase pathway and target cancer stem cells**

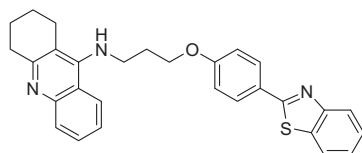
pp 3031–3037

Di Chen, Sreedhar Pamu, Qiuzhi Cui, Tak Hang Chan*, Q. Ping Dou*

**Inhibition of cholinesterase activity and amyloid aggregation by berberine-phenyl-benzoheterocyclic and tacrine-phenyl-benzoheterocyclic hybrids**

pp 3038–3048

Ling Huang, Tao Su, Wenjun Shan, Zonghua Luo, Yang Sun, Feng He*, Xingshu Li*



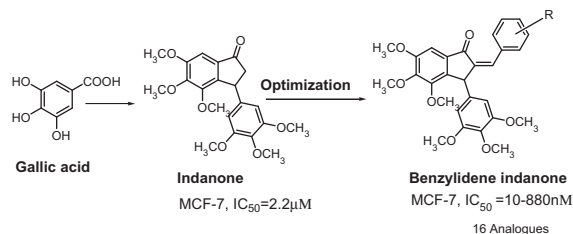
44b: IC₅₀ of 0.017 μM for AChE;
51.8% for Aβ₁₋₄₂ at 20 μM

A series of berberine-phenyl-benzoheterocyclic and tacrine-phenyl-benzoheterocyclic hybrids were synthesised and evaluated as multifunctional anti-Alzheimer's disease agents. Compound **44b**, was the most potent AChE inhibitor with an IC₅₀ value of 0.017 μM. This compound demonstrated similar Aβ aggregation inhibitory activity with curcumin (51.8% vs 52.1% at 20 μM, respectively).

Synthesis and anticancer activity of 2-benzylidene indanones through inhibiting tubulin polymerization

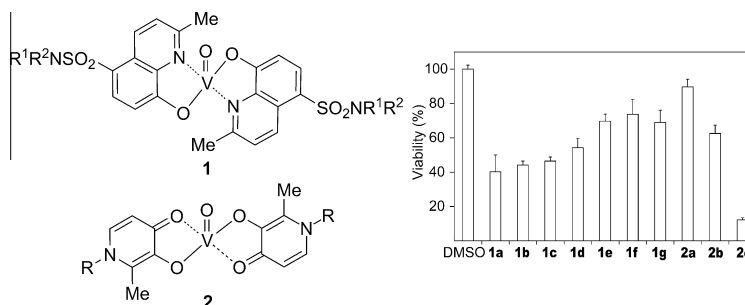
pp 3049–3057

A. P. Prakasham, A. K. Saxena, Suaib Luqman, Debabrata Chanda, Tandeep Kaur, Atul Gupta, D. K. Yadav, C. S. Chanotiya, Karuna Shanker, F. Khan, Arvind S. Negi*

Gallic acid has been modified to 2-benzylidene indanones. Three of the analogues exhibited potent anticancer activity (IC_{50} in nM) through tubulin polymerization inhibition.**Oxovanadium complexes with quinoline and pyridinone ligands: Syntheses of the complexes and effect of alkyl chains on their apoptosis-inducing activity in leukemia cells**

pp 3058–3064

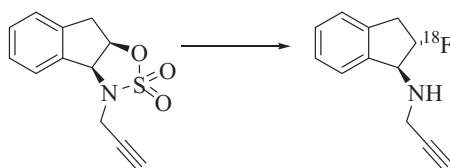
Tomoko Yamaguchi, Shinya Watanabe, Yuriko Matsumura, Yoshikazu Tokuoka, Akihiro Yokoyama*

**Synthesis and evaluation of [^{18}F]fluororasagiline, a novel positron emission tomography (PET) radioligand for monoamine oxidase B (MAO-B)**

pp 3065–3071

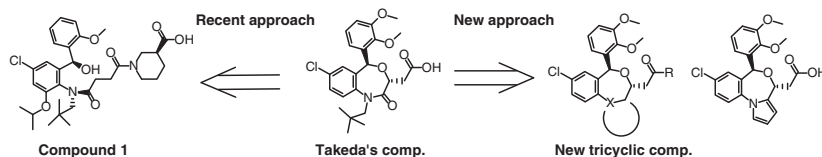
S. Nag*, L. Lehmann, G. Kettschau, T. Heinrich, A. Thiele, A. Varrone, B. Gulyas, C. Halldin

Development of novel PET radioligand for MAO-B

**Discovery of novel tricyclic compounds as squalene synthase inhibitors**

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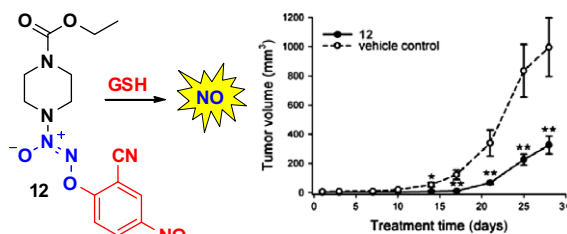
Masanori Ichikawa*, Masami Ohtsuka, Hitoshi Ohki, Noriyasu Haginoya, Masao Itoh, Kazuyuki Sugita, Hiroyuki Usui, Makoto Suzuki, Koji Terayama, Akira Kanda



Structural modifications modulate stability of glutathione-activated arylated diazeniumdiolate prodrugs

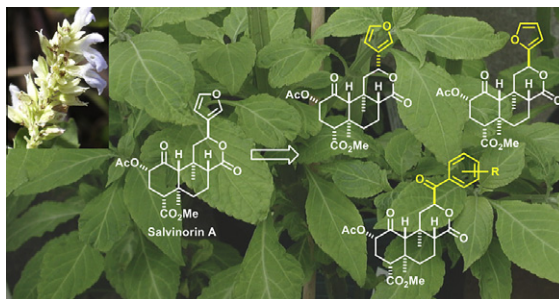
pp 3094–3099

Rahul S. Nandurdikar*, Anna E. Maciag, Ryan J. Holland, Zhao Cao, Paul J. Shami, Lucy M. Anderson, Larry K. Keefer, Joseph E. Saavedra*

**Semisynthetic neoclerodanes as kappa opioid receptor probes**

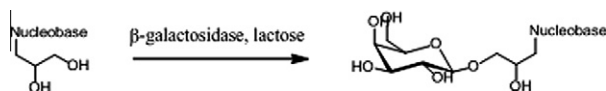
pp 3100–3110

Kimberly M. Lovell, Tamara Vasiljevik, Juan J. Araya, Anthony Lozama, Katherine M. Prevatt-Smith, Victor W. Day, Christina M. Dersch, Richard B. Rothman, Eduardo R. Butelman, Mary Jeanne Kreek, Thomas E. Prisinzano*

**An enzymatic glycosylation of nucleoside analogues using β -galactosidase from *Escherichia coli***

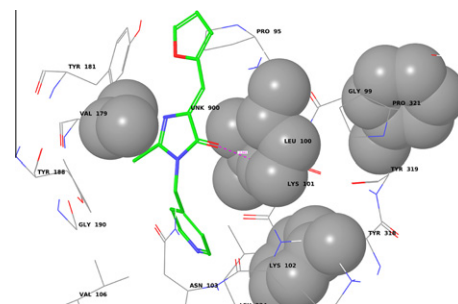
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Jiří Blažek*, Petr Jansa, Ondřej Baszczyński, Martin Maxmilian Kaiser, Miroslav Otmar, Marcela Krečmerová, Martin Drančinský, Antonín Holý, Blanka Králová

**Synthesis, biological activity and docking study of imidazol-5-one as novel non-nucleoside HIV-1 reverse transcriptase inhibitors**

pp 3119–3127

Santosh N. Mokale, Deepak Lokwani, Devanand B. Shinde*

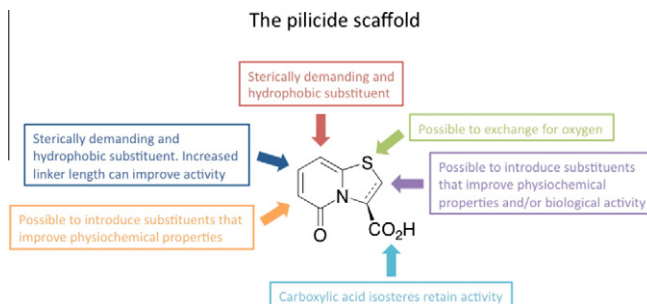


A novel series of substituted imidazol-5-ones were designed, synthesized and evaluated for reverse transcriptase inhibition activity using reverse transcriptase (RT) assay kit (Roche, Colorimetric). Docking study was performed to study the binding orientation and affinity of synthesized compounds for RT enzyme.

Mapping pilicide anti-virulence effect in *Escherichia coli*, a comprehensive structure–activity study

pp 3128–3142

Erik Chorell, Jerome S. Pinkner, Christoffer Bengtsson, Thomas Sainte-Luce Banchelin, Sofie Edvinsson, Anna Linusson, Scott J. Hultgren*, Fredrik Almqvist*



*Corresponding author

* Supplementary data available via SciVerse ScienceDirect

COVER

Dipyrone (metamizol) is a common antipyretic drug and the most popular non-opioid analgesic in many countries. In spite of its long and widespread use, molecular details of its fate in the body are not fully known. Two unknown metabolites were now found, viz. arachidonoyl amides, and positively tested for cannabis receptor binding (CB1 and CB2) and cyclooxygenase inhibition. Two more puzzle pieces of the dipyrone story found! (Rogosch, T.; Sinning, C.; Podlewski, A.; Watzer, B.; Schlosburg, J.; Lichtman, A.H.; Cascio, M.G.; Bisogno, T.; Di Marzo, V.; Nüsing, R.; Imming, P. *Bioorg. Med. Chem.* **2012**, 20, 103–109.)

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