



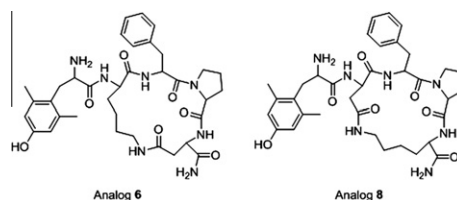
## Bioorganic & Medicinal Chemistry Volume 19, Issue 23, 2011

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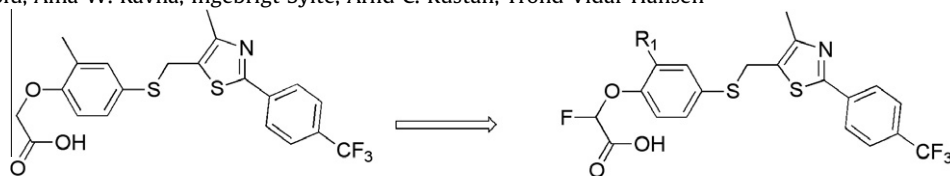
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Jakub Fichna, Renata Perlikowska, Anna Wyreńska, Katarzyna Gach, Justyna Piekłna, Jean Claude do-Rego, Geza Toth, Alicja Kluczyk, Tomasz Janecki, Anna Janecka\*



##### Synthesis, molecular modeling studies and biological evaluation of fluorine substituted analogs of GW 501516 pp 6982–6988

Calin C. Ciocoiu, Aina W. Ravna, Ingebrigt Sylte, Arild C. Rustan, Trond Vidar Hansen\*

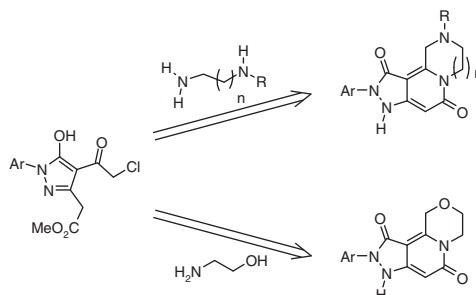


GW 501516

(±)-**2a**: R<sub>1</sub> = Methyl EC<sub>50</sub> = 55 nM against PPARδ  
 (±)-**2b**: R<sub>1</sub> = Ethyl EC<sub>50</sub> = 290 nM against PPARδ  
 (±)-**2c**: R<sub>1</sub> = *Is*o-propyl EC<sub>50</sub> = 580 nM against PPARδ

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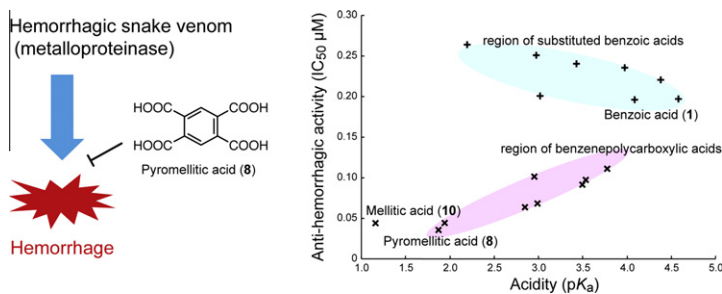
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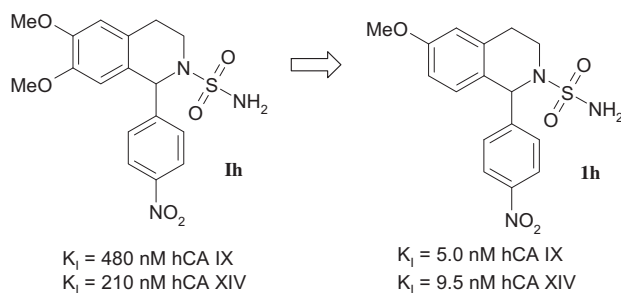
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Hnin Thanda Aung, Toshiaki Nikai, Masatake Niwa, Yoshiaki Takaya\*

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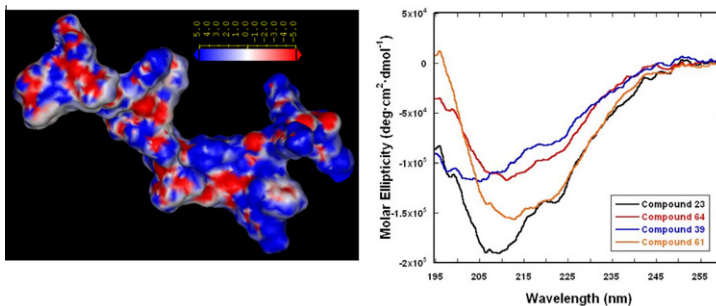
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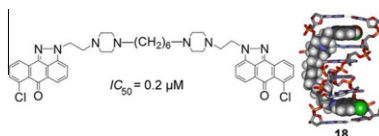
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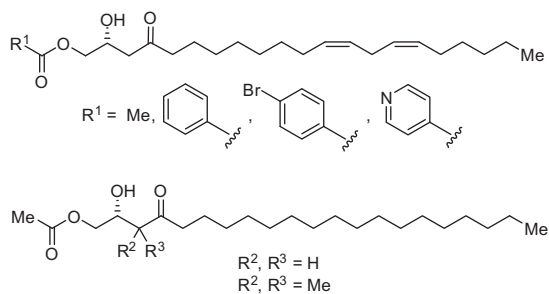
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Rui Zhang, Xing Wu, Jack C. Yalowich, Brian B. Hasinoff\*



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Darby G. Brooke\*, Elizabeth J. Shelley, Caroline G. Roberts, William A. Denny, Robert L. Sutherland, Alison J. Butt

**Trace amine-associated receptor 1 is a stereoselective binding site for compounds in the amphetamine class**

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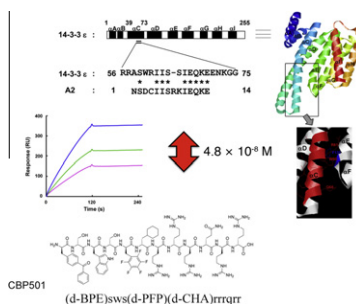
Anita H. Lewin\*, Gregory M. Miller, Brian Gilmour



TAAR1 stereoselectivity for (*S*)- versus (*R*)-configuration for compounds in the amphetamine class supports a role for TAAR1 in the psychostimulant properties of this class of compounds and is consistent with TAAR1 as a stereoselective binding site for amphetamine.

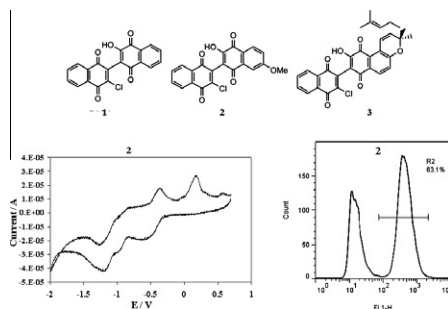
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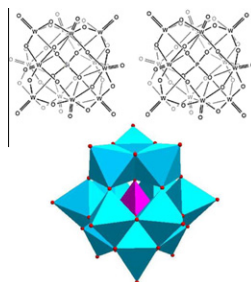
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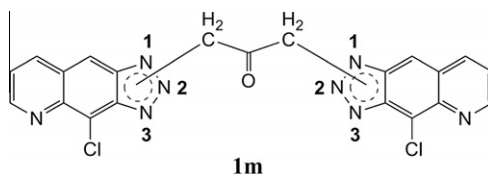
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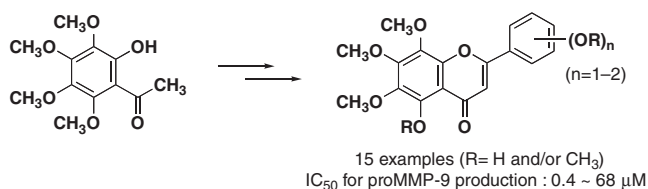
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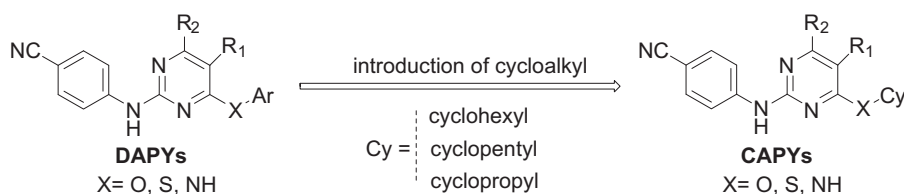
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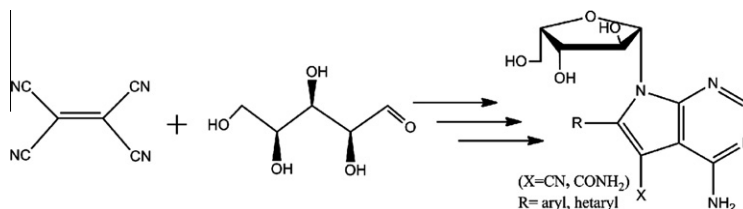
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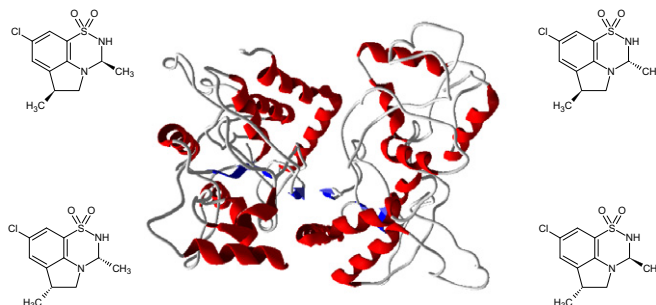


**Synthesis of 6-(het) ary Xylocyidine analogues and evaluating their inhibitory activities of CDK1 and CDK2 in vitro** pp 7100–7110

Chuan Xiao, Chao Sun, Weiwei Han, Feng Pan, Zhu Dan, Yu Li, Zhi-Guang Song\*, Ying-Hua Jin\*

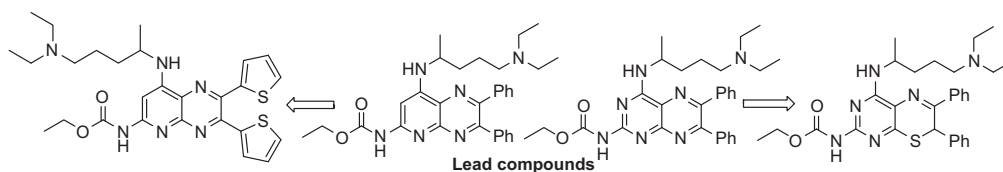
**Molecular modeling studies, synthesis, configurational stability and biological activity of 8-chloro-2,3,5,6-tetrahydro-3,6-dimethyl-pyrrolo[1,2,3-de]-1,2,4-benzothiadiazine 1,1-dioxide** pp 7111–7119

Umberto M. Battisti, Marina M. Carrozzo, Giuseppe Cannazza\*, Giulia Puia, Luigino Troisi, Daniela Braghiroli, Carlo Parenti, Krzysztof Jozwiak

**Novel pyridopyrazine and pyrimidothiazine derivatives as FtsZ inhibitors**

pp 7120–7128

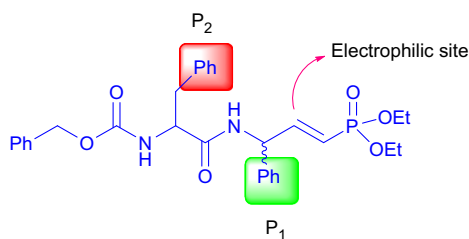
Bini Mathew, Shefali Srivastava, Larry J. Ross, William J. Suling, E. Lucile White, Lisa K. Woolhiser, Anne J. Lenaerts, Robert C. Reynolds\*



Eighteen new pyridopyrazine and pyrimidothiazine derivatives were synthesized and tested against FtsZ from *Mycobacterium tuberculosis* (Mtb) and in vitro antibacterial activity against Mtb H<sub>37</sub>Ra and Mtb H<sub>37</sub>Rv. Two compounds were studied in vivo in a murine Mtb model.

**Design, synthesis and biological evaluation of peptidyl-vinylaminophosphonates as novel cysteine protease inhibitors** pp 7129–7135

Asish K. Bhattacharya\*, Kalpeshkumar C. Rana

IC<sub>50</sub> = 30 μM (one of the most active compound)

Peptidyl-vinylaminophosphonates, a new class of cysteine protease inhibitors have been designed and synthesized. Some of the synthesized molecules have shown inhibition against papain, a model cysteine protease with IC<sub>50</sub> values in the range of 30–54 μM.

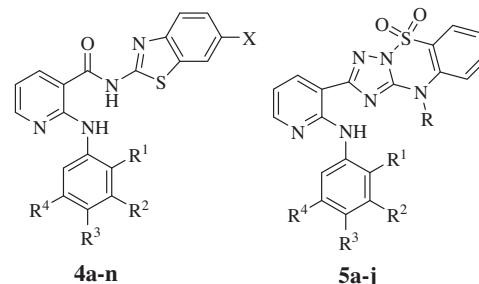


## 2-Anilinonicotinyl linked 2-aminobenzothiazoles and [1,2,4]triazolo[1,5-b] [1,2,4]benzothiadiazine conjugates as potential mitochondrial apoptotic inducers

pp 7136–7150

Ahmed Kamal\*, Y.V.V. Srikanth, M. Naseer Ahmed Khan, Md. Ashraf, M. Kashi Reddy, Farheen Sultana, Tandeep Kaur, Gousia Chashoo, Nitasha Suri, Irum Sehar, Zahoor A. Wani, Arpita Saxena, Parduman R. Sharma, Shashi Bhushan, Dilip M. Mondhe, Ajit K. Saxena

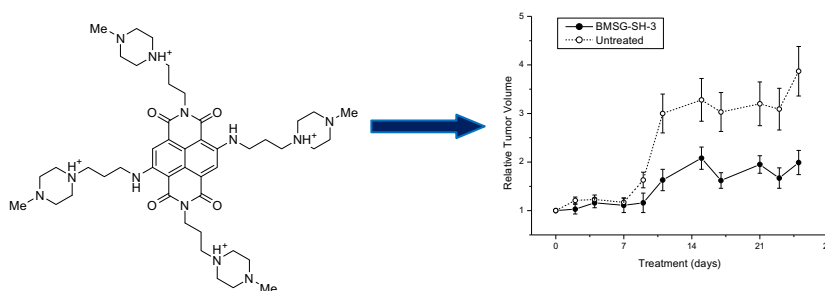
A series of *N*-(2-anilino-pyridyl) linked 2-amino benzothiazoles (**4a–n**) and [1,2,4]triazolo [1,5-*b*]benzothiadiazine conjugates (**5a–j**) have been designed, synthesized and evaluated for their antiproliferative activity. The active compounds were tested for their effects on the cell cycle perturbations and induction of apoptosis.



## Targeting pancreatic cancer with a G-quadruplex ligand

pp 7151–7157

Mekala Gunaratnam, Maria de la Fuente, Sonja M. Hampel, Alan K. Todd, Anthony P. Reszka, Andreas Schätzlein, Stephen Neidle\*

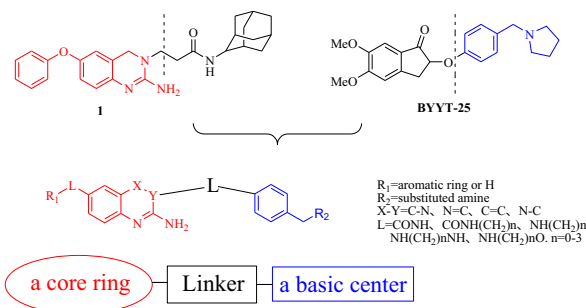


## Searching for the Multi-Target-Directed Ligands against Alzheimer's disease: Discovery of quinoxaline-based hybrid compounds with AChE, H<sub>3</sub>R and BACE 1 inhibitory activities

pp 7158–7167

Wenhai Huang, Li Tang, Ying Shi, Shufang Huang, Lei Xu, Rong Sheng, Peng Wu, Jia Li, Naiming Zhou, Yongzhou Hu\*

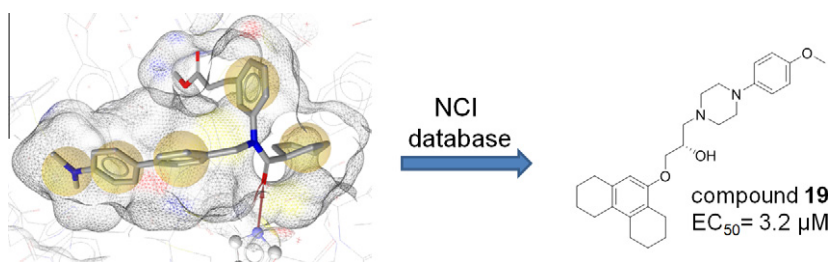
A novel series of quinoxaline derivatives were designed by lending the core structural elements required for H<sub>3</sub>R antagonists and hybridizing BACE 1 inhibitor **1** with AChE inhibitor BYYT-25 as Multi-Target-Directed Ligands (MTDLs) for AD treatment.



## Pharmacophore-based discovery of FXR agonists. Part I: Model development and experimental validation

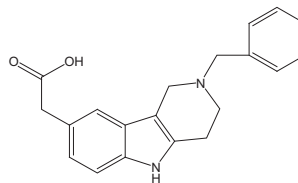
pp 7168–7180

Daniela Schuster\*, Patrick Markt, Ulrike Grienke, Judit Mihaly-Bison, Markus Binder, Stefan M. Noha, Judith M. Rollinger, Hermann Stuppner, Valery N. Bochkov, Gerhard Wolber

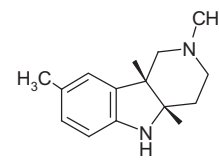


**(2-Benzyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indol-8-yl)-acetic acid: An aldose reductase inhibitor and antioxidant of zwitterionic nature** pp 7181–7185

Milan Stefek\*, Anna Tsantili-Kakoulidou, Ivana Milackova, Maria Juskova, Vladimir Snirc, Nikos Triantos



(1)



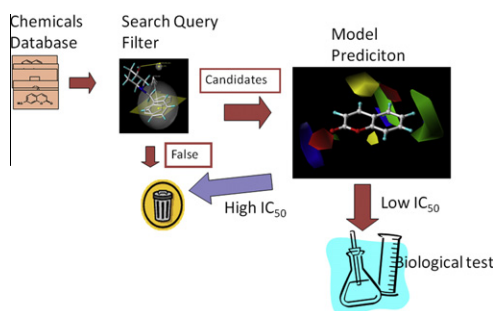
Stobadine (2)

Chemical structure of (2-benzyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indol-8-yl)-acetic acid (1) and stobadine [(–)-cis-2,8-dimethyl-2,3,4,4a,5,9b-hexahydro-1H-pyrido[4,3-b]indole] (2).

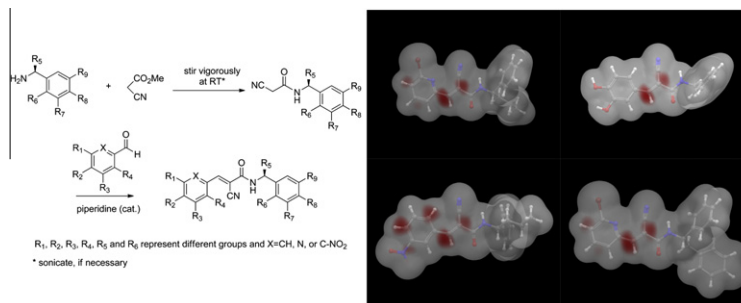
**Identification of novel CYP2A6 inhibitors by virtual screening**

pp 7186–7193

Minna K. Rahnasto\*, Hannu A. Raunio, Carsten Wittekindt, Kaisa A. Salminen, Jukka Leppänen, Risto O. Juvonen, Antti Poso, Maija K. Lahtela-Kakkonen

**Tyrphostin-like compounds with ubiquitin modulatory activity as possible therapeutic agents for multiple myeloma** pp 7194–7204

Zhenghong Peng, Ashutosh Pal, Dongmei Han, Shimei Wang, David Maxwell, Alexander Levitzki, Moshe Talpaz, Nicholas J. Donato, William Bornmann\*

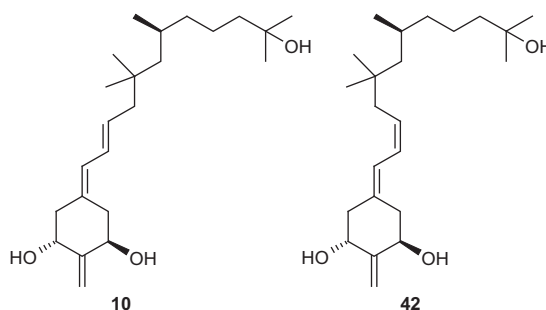


$R_1, R_2, R_3, R_4, R_5$  and  $R_6$  represent different groups and  $X = CH, N$ , or  $C-NO_2$  \* sonicate, if necessary.

**13,13-Dimethyl-*des*-C,D analogues of (20S)-1 $\alpha$ ,25-dihydroxy-2-methylene-19-norvitamin D<sub>3</sub> (2MD): Total synthesis, docking to the VDR, and biological evaluation**

pp 7205–7220

Katarzyna Plonska-Ocypa, Izabela Sibilska, Rafal R. Sicinski, Wanda Sicinska, Lori A. Plum, Hector F. DeLuca\*



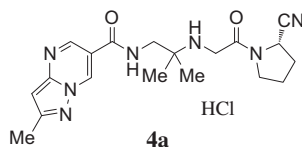
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### Discovery and pharmacological characterization of *N*-[2-({2-[(2*S*)-2-cyanopyrrolidin-1-yl]-2-oxoethyl}amino)-2-methylpropyl]-2-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxamide hydrochloride (anagliptin hydrochloride salt) as a potent and selective DPP-IV inhibitor

pp 7221–7227

Noriyasu Kato\*, Mitsuru Oka, Takayo Murase, Masahiro Yoshida, Masao Sakairi, Satoko Yamashita, Yoshika Yasuda, Aya Yoshikawa, Yuuji Hayashi, Mitsuhiro Makino, Motohiro Takeda, Yakufu Mirensa, Takuji Kakigami



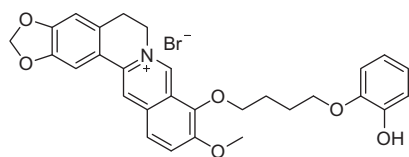
Synthesis and evaluation of a series of pyrazolo[1,5-*a*]pyrimidine derivatives have led to the discovery of *N*-[2-({2-[(2*S*)-2-cyanopyrrolidin-1-yl]-2-oxoethyl}amino)-2-methylpropyl]-2-methylpyrazolo[1,5-*a*]pyrimidine-6-carboxamide hydrochloride (anagliptin hydrochloride salt: **4a**) as a highly selective, potent inhibitor of DPP-IV.



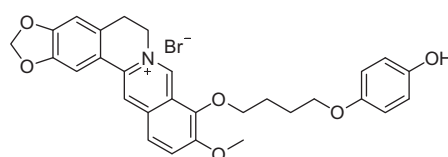
### Benzenediol-berberine hybrids: Multifunctional agents for Alzheimer's disease

pp 7228–7235

Huailei Jiang, Xu Wang, Ling Huang, Zonghua Luo, Tao Su, Ke Ding\*, Xingshu Li\*



**8:** IC<sub>50</sub> of 0.123 μM for AChE; 84.5% for Aβ<sub>1-42</sub> at 20 μM; ORAC-FL value of 3.54



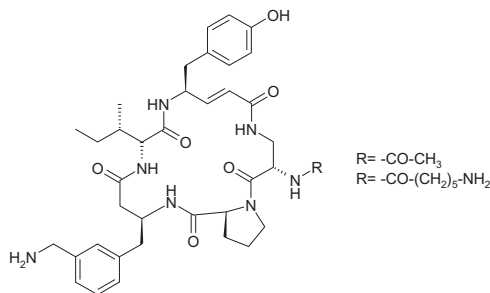
**12:** IC<sub>50</sub> of 0.460 μM for AChE; 92% for Aβ<sub>1-42</sub> at 20 μM; ORAC-FL value of 9.54

A series of hybrid molecules, by reacting berberine with benzenediol, melatonin, or ferulic acid, were designed and synthesized. These compounds were evaluated for: (i) the ability to inhibit multiple cholinesterases (ChEs); (ii) the capacity to prevent amyloid β (Aβ) aggregation; and (iii) antioxidant potential.

### The arginine mimicking β-amino acid β<sup>3</sup>hPhe(3-H<sub>2</sub>N-CH<sub>2</sub>) as S1 ligand in cyclotheonamide-based β-tryptase inhibitors

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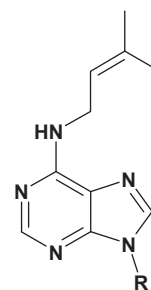
Dennis Janke, Christian P. Sommerhoff, Norbert Schaschke\*



### N9-Substituted *N*<sup>6</sup>-[(3-methylbut-2-en-1-yl)amino]purine derivatives and their biological activity in selected cytokinin bioassays

pp 7244–7251

Václav Mik, Lucie Szüčová\*, Lukáš Spíchal, Ondřej Plíhal, Jaroslav Nisler, Lenka Zahajská, Karel Doležal, Miroslav Strnad



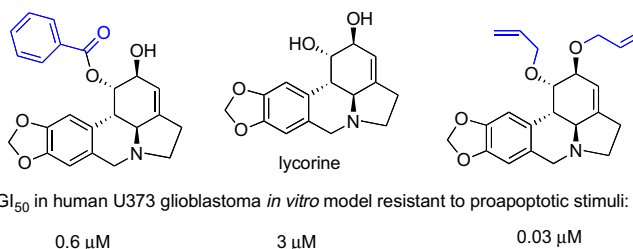
Synthesis of N9-substituted derivatives of *N*<sup>6</sup>-[(3-methylbut-2-en-1-yl)amino]purine (iP), their characterization by C, H, N elemental analyses, thin layer chromatography, high performance liquid chromatography, <sup>1</sup>H NMR, and CI+ MS spectrometry as well as their cytokinin activity in vitro in three classical cytokinin bioassays (tobacco callus, wheat leaf senescence, and *Amaranthus* bioassay), and perception by cytokinin receptors CRE1/AHK4, ZmHK1, and ZmHK3a are described.



**In search of a cytostatic agent derived from the alkaloid lycorine: Synthesis and growth inhibitory properties of lycorine derivatives**

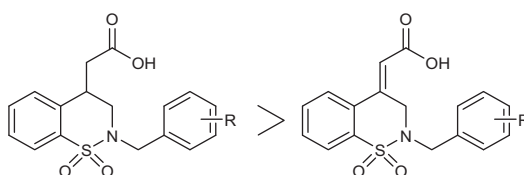
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Nikolai M. Evdokimov, Delphine Lamoral-Theys, Véronique Mathieu, Anna Andolfi, Liliya V. Frolova, Stephen C. Pelly, Willem A. L. van Otterlo, Igor V. Magedov, Robert Kiss, Antonio Evidente, Alexander Kornienko\*

**1,2-Benzothiazine 1,1-dioxide carboxylate derivatives as novel potent inhibitors of aldose reductase**

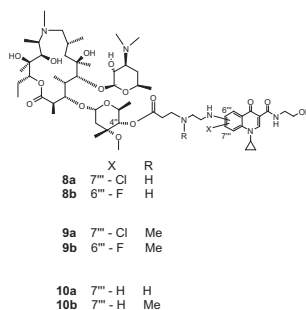
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Xin Chen, Shuzhen Zhang, Yanchun Yang, Saghir Hussain, Minlan He, Dequan Gui, Bing Ma, Chaojun Jing, Zhixin Qiao, Changjin Zhu\*, Qun Yu\*

**Synthesis and activity of new macrolones: Conjugates between 6(7)-(2'-aminoethyl)-amino-1-cyclopropyl-3-carboxylic acid (2'-hydroxyethyl) amides and 4"-propenoyl-azithromycin**

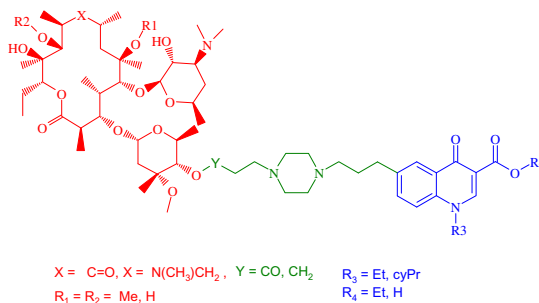
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Samra Kapić\*, Andrea Fajdetić, Sanja Koštrun, Ana Čikoš, Hana Čipčić Paljetak, Roberto Antolović, David J. Holmes, Sulejman Alihodžić

**Synthesis of macrolones with central piperazine ring in the linker and its influence on antibacterial activity**

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Samra Kapić\*, Hana Čipčić Paljetak, Ivana Palej Jakopović, Andrea Fajdetić, Marina Ilijaš, Vlado Štimac, Karmen Brajša, David J. Holmes, John Berge, Sulejman Alihodžić



\*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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