



## Bioorganic & Medicinal Chemistry Volume 18, Issue 1, 2010

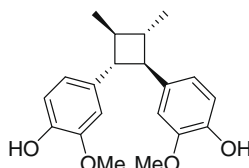
### Contents

#### ARTICLES

**Carbonic anhydrase inhibitors. Identification of selective inhibitors of the human mitochondrial isozymes VA and VB over the cytosolic isozymes I and II from a natural product-based phenolic library**

pp 14–18

Rohan A. Davis, Alessio Innocenti, Sally-Ann Poulsen, Claudiu T. Supuran \*

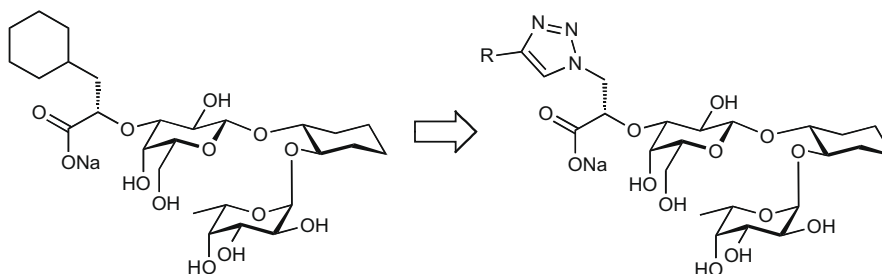


$K_i = 368 \mu\text{M}$  (CA I);  $K_i = 11.7 \mu\text{M}$  (CA II);  $K_i = 91 \text{ nM}$  (CA VA);  $K_i = 69 \text{ nM}$  (CA VB).

**Probing the carbohydrate recognition domain of E-selectin: The importance of the acid orientation in sLe<sup>x</sup> mimetics**

pp 19–27

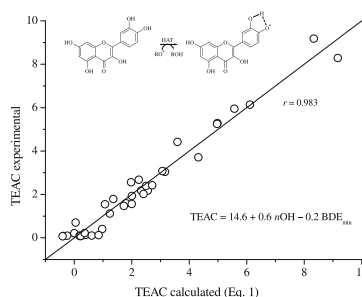
Alexander Titz, John Patton, Martin Smiesko, Zorana Radic, Oliver Schwardt, John L. Magnani, Beat Ernst \*



**Reliability of bond dissociation enthalpy calculated by the PM6 method and experimental TEAC values in antiradical QSAR of flavonoids**

pp 28–35

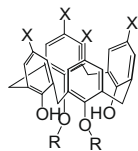
Dragan Amić \*, Bono Lučić



**Synthesis and anti-HIV evaluation of water-soluble calixarene-based bithiazolyl podands**

pp 36–45

Maxime Mourer, Nicolas Psychogios, Géraldine Laumond, Anne-Marie Aubertin, Jean-Bernard Regnouf-de-Vains \*

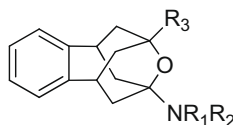
X = SO<sub>3</sub>Na, CH<sub>2</sub>P(O)(OH)(ONa), CH<sub>2</sub>COONa

R = H; Y = H, COONa

**New oxapolycyclic cage amines with NMDA receptor antagonist and trypanocidal activities**

pp 46–57

María D. Duque, Pelayo Camps, Eva Torres, Elena Valverde, Francesc X. Sureda, Marta López-Querol, Antoni Camins, S. Radhika Prathalingam, John M. Kelly, Santiago Vázquez \*

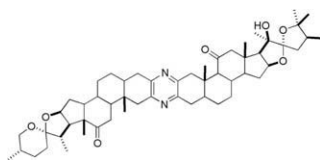


Several benzopolycyclic amines have been synthesized and their NMDA receptor antagonist and trypanocidal activities have been studied. Four of them displayed similar activity to memantine as NMDA receptor antagonists and several derivatives showed a significant level of trypanocidal activity.

**Synthesis of a new cytotoxic cephalostatin/ritterazine analogue from hecogenin and 22-*epi*-hippuristanol**

pp 58–63

Javier Jesús Poza, Jaime Rodríguez \*, Carlos Jiménez \*

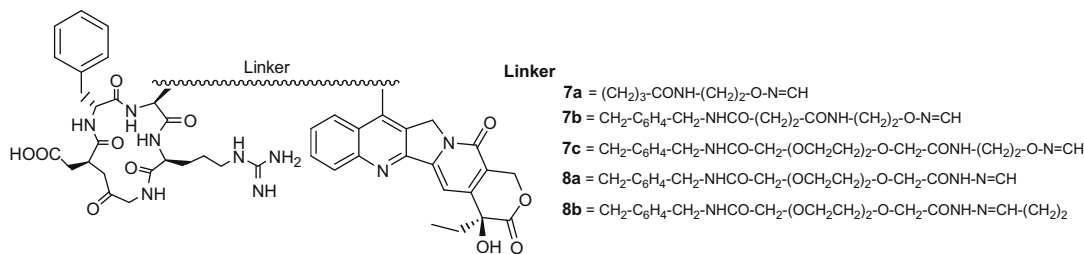


A new cephalostatin/ritterazine analogue was prepared from the commercially available hecogenin acetate and the natural cytotoxic steroid 22-*epi*-hippuristanol. The method involved the reductive dimerization of enaminoketones (condensation of  $\alpha$ -aminoketones) and condensation between an enaminoketone and an  $\alpha$ -hydroxyketone. The new analogue showed higher cytotoxic activity than the cytotoxic 22-*epi*-hippuristanol against MDA-MB-231, A-549 and HT-29 cultured tumor cell lines.

**Novel tumor-targeted RGD peptide–camptothecin conjugates: Synthesis and biological evaluation**

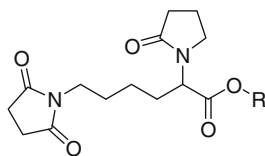
pp 64–72

Alma Dal Pozzo \*, Ming-Hong Ni, Emiliano Esposito, Sabrina Dallavalle, Loana Musso, Alberto Bargiotti, Claudio Pisano, Loredana Vesci, Federica Bucci, Massimo Castorina, Rosanna Foderà, Giuseppe Giannini, Concetta Aulicino, Sergio Penco



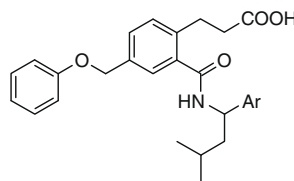
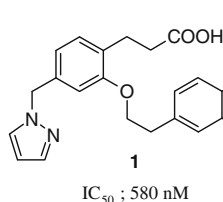
### Synthesis, physico-chemical properties and penetration activity of alkyl-6-(2,5-dioxopyrrolidin-1-yl)-2-(2-oxopyrrolidin-1-yl)hexanoates as potential transdermal penetration enhancers

pp 73–79

Katerina Brychtova<sup>\*</sup>, Josef Jampilek, Radka Opatrilova, Ivan Raich, Oldrich Farsa, Jozef CsolleiR = C<sub>2</sub>H<sub>5</sub>, C<sub>6</sub>H<sub>13</sub>, C<sub>7</sub>H<sub>15</sub>, C<sub>8</sub>H<sub>17</sub>, C<sub>9</sub>H<sub>19</sub>, C<sub>10</sub>H<sub>21</sub>, C<sub>11</sub>H<sub>23</sub>, C<sub>12</sub>H<sub>25</sub>

### 3-(2-Aminocarbonylphenyl)propanoic acid analogs as potent and selective EP3 receptor antagonists. Part 1: Discovery and exploration of the carboxamide side chain

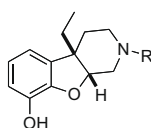
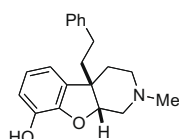
pp 80–90

Masaki Asada<sup>\*</sup>, Tetsuo Obitsu, Toshihiko Nagase, Motoyuki Tanaka, Yoshiyuki Yamaura, Hiroya Takizawa, Ken Yoshikawa, Kazutoyo Sato, Masami Narita, Shuichi Ohuchida, Hisao Nakai, Masaaki Toda

No.	Ar	IC <sub>50</sub>
8		68 nM
14		2.0 nM

### Probes for narcotic receptor mediated phenomena. 40. N-Substituted cis-4a-ethyl-1,2,3,4,4a,9a-hexahydrobenzofuro[2,3-c]pyridin-8-ols

pp 91–99

Malliga R. Iyer, Yong Sok Lee, Jeffrey R. Deschamps, Richard B. Rothman, Christina M. Dersch, Arthur E. Jacobson, Kenner C. Rice<sup>\*</sup>

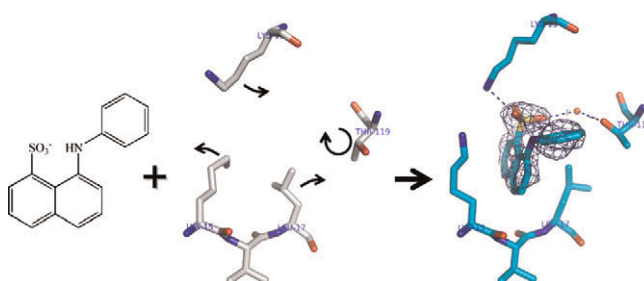
R = Me  
 CH<sub>2</sub>CH<sub>2</sub>Ph  
*p*-NO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>Ph  
 CH<sub>2</sub>Cyclopropyl  
*p*-FCH<sub>2</sub>Ph  
*p*-FCH<sub>2</sub>CH<sub>2</sub>Ph

*rac*-Pyridin-8-ols, compounds with an aromatic hydroxy moiety situated *ortho* to the dihydrofuran's oxygen atom, do not interact as well with opioid receptors as comparable *para*-oriented phenolic compounds (the pyridin-6-ols).



### Identification of a novel ligand binding motif in the transthyretin channel

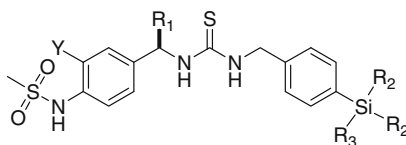
pp 100–110

Luis Mauricio T.R. Lima<sup>\*</sup>, Vivian de Almeida Silva, Leonardo de Castro Palmieri, Maria Clara B.R. Oliveira, Débora Foguel, Igor Polikarpov<sup>\*</sup>

**Silicon switch approach in TRPV1 antagonist MK-056 and its analogues**

pp 111–116

Minsun Chang, Seol-Rin Park, Juhyun Kim, Mijung Jang, Jeong Hyun Park, Ji Eun Park, Hyeung-Geun Park, Young-Ger Suh, Yeon Su Jeong, Young-Ho Park, Hee-Doo Kim

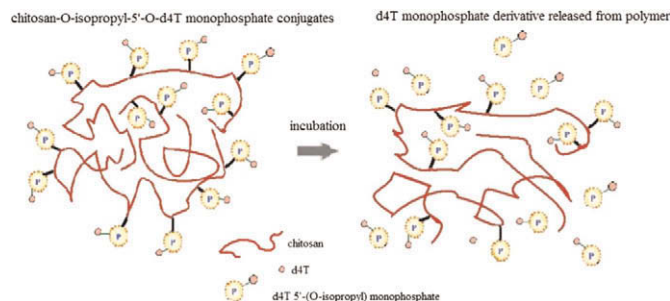


A series of silicon analogues of the MK-056 were designed and synthesized by silicon switch approach to search for new TRPV1 antagonist. *tert*-Butyl on MK-056 can be replaced to trimethylsilyl without loss of activity.

**Synthesis, nanosizing and in vitro drug release of a novel anti-HIV polymeric prodrug: Chitosan-O-isopropyl-5'-O-d4T monophosphate conjugate**

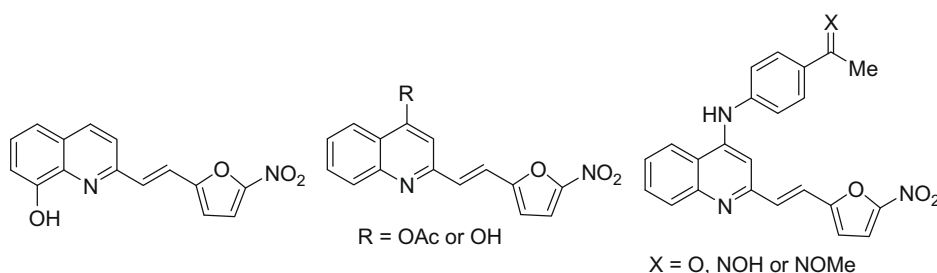
pp 117–123

Lin Yang, Liqiang Chen, Rong Zeng \*, Chao Li, Renzhong Qiao \*, Liming Hu, Zelin Li

**Synthesis and antiproliferative evaluations of certain 2-phenylvinylquinoline (2-styrylquinoline) and 2-furanylvinylquinoline derivatives**

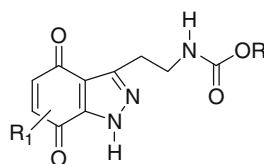
pp 124–133

Feng-Shuo Chang, Weichung Chen, Chihuei Wang \*, Cherng-Chyi Tzeng, Yeh-Long Chen \*

**Synthesis of 3-[(N-carboalkoxy)ethylamino]-indazole-dione derivatives and their biological activities on human liver carbonyl reductase**

pp 134–141

Solomon Berhe, Andrew Slupe, Choice Luster, Henry A. Charlier Jr., Don L. Warner, Leon H. Zalkow, Edward M. Burgess, Nkechi M. Enwerem, Oladapo Bakare \*



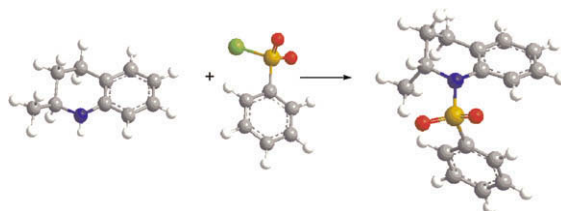
R<sub>1</sub> = Phenylamino, phenyl, methyl, methoxy, chloro  
R = CH<sub>3</sub>, PhCH<sub>2</sub>

A series of indazole-dione derivatives were synthesized and their biological activities on human carbonyl reductase are studied.

## Synthesis, stereoelectronic characterization and antiparasitic activity of new 1-benzenesulfonyl-2-methyl-1,2,3,4-tetrahydroquinolines

pp 142–150

Romina J. Pagliero, Sabrina Lusvarghi, Adriana B. Pierini, Reto Brun, María R. Mazzieri \*



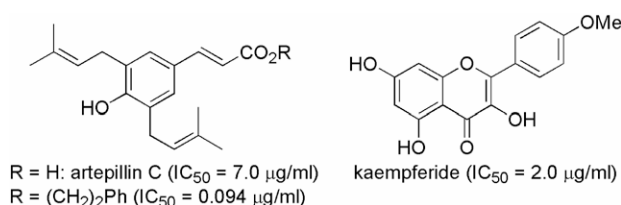
New *N*-benzenesulfonyl derivatives of 2-methyl-1,2,3,4-tetrahydroquinoline with antiparasitic activity were synthesized. Some derivatives demonstrated interesting activity against *Trypanosoma cruzi* and *Plasmodium falciparum* with low cytotoxicity, and can be considered as lead scaffolds for further optimization.



## Inhibitory activity of Brazilian green propolis components and their derivatives on the release of cys-leukotrienes

pp 151–157

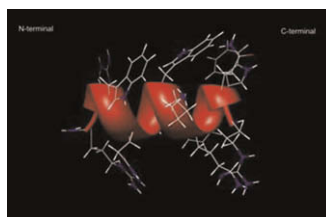
Hiroko Tani \*, Keiko Hasumi, Tomoki Tatefuji, Ken Hashimoto, Hiroyuki Koshino, Shunya Takahashi \*



## New small-size peptides possessing antifungal activity

pp 158–167

Francisco M. Garibotto, Adriana D. Garro, Marcelo F. Masman, Ana M. Rodríguez, Paul G. M. Luiten, Marcela Raimondi, Susana A. Zacchino, Csaba Somlai, Botond Penke, Ricardo D. Enriz \*



We designed, synthesized, and tested new small-size peptides possessing antifungal activity against *Cryptococcus neoformans* and *Candida albicans*. These compounds were obtained from a molecular modeling study.

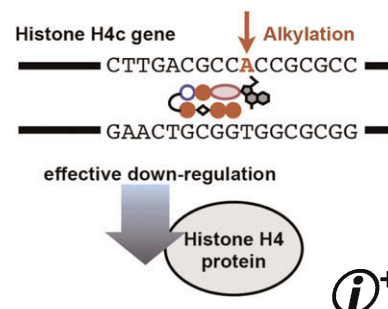


## Potent activity against K562 cells by polyamide–seco-CBI conjugates targeting histone H4 genes

pp 168–174

Masafumi Minoshima, James C. Chou, Sophie Lefebvre, Toshikazu Bando, Ken-ichi Shinohara, Joel M. Gottesfeld \*, Hiroshi Sugiyama \*

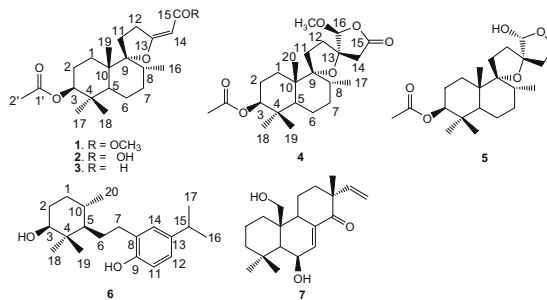
We designed and synthesized conjugates between pyrrole–imidazole polyamides and *seco*-CBI that alkylate within the coding regions of the histone H4 genes. DNA alkylating activity on the histone H4 fragment and cellular effects against K562 chronic myelogenous leukemia cells were investigated. One of the conjugates, **5-CBI**, showed strong DNA alkylation activity and good sequence specificity on a histone H4 gene fragment. K562 cells treated with **5-CBI** down-regulated the histone H4 gene and induced apoptosis efficiently. Global gene expression data revealed that a number of histone H4 genes were down-regulated by **5-CBI** treatment. These results suggest that sequence-specific DNA alkylating agents may have the potential of targeting specific genes for cancer chemotherapy.



**Anti-inflammatory diterpenes from the seeds of *Vitex negundo***

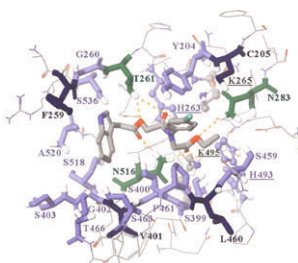
pp 175–181

Cheng-Jian Zheng, Bao-Kang Huang, Yang Wang, Qi Ye, Ting Han, Qiao-Yan Zhang, Hong Zhang, Lu-Ping Qin \*

Anti-inflammatory activity and identification of seven new diterpenes negundoin A–G (**1–7**) from the seeds of *Vitex negundo* are reported.**Inhibitors of human tyrosyl-DNA phosphodiesterase (hTdp1) developed by virtual screening using ligand-based pharmacophores**

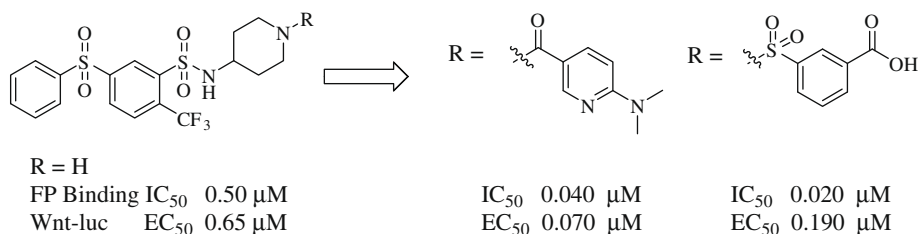
pp 182–189

Iwona E. Weidlich, Thomas Dexheimer, Christophe Marchand, Smitha Antony, Yves Pommier, Marc C. Nicklaus \*

Compound **15** found as an inhibitor of Tdp1.**Modulation of Wnt signaling through inhibition of secreted frizzled-related protein I (sFRP-1) with N-substituted piperidinyl diphenylsulfonyl sulfonamides: Part II**

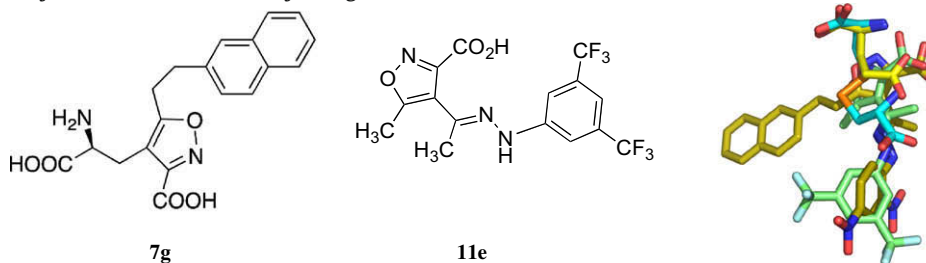
pp 190–201

William J. Moore \*, Jeffrey C. Kern, Ramesh Bhat, Peter V. N. Bodine, Shoichi Fukuyama, Girija Krishnamurthy, Ronald L. Magolda, Keith Pitts, Barb Stauffer, Eugene J. Trybulski

**Isoxazole analogues bind the System x<sub>c</sub><sup>-</sup> transporter: Structure–activity relationship and pharmacophore model**

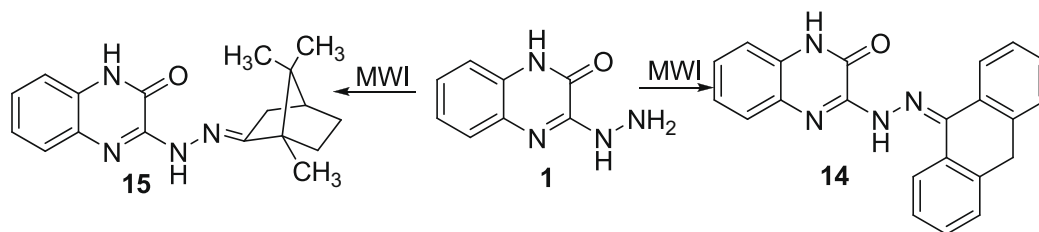
pp 202–213

Sarjubhai A. Patel, Trideep Rajale, Erin O'Brien, David J. Burkhardt, Jared K. Nelson, Brendan Twamley, Alex Blumenfeld, Monika I. Szabon-Watola, John M. Gerdes, Richard J. Bridges, Nicholas R. Natale \*

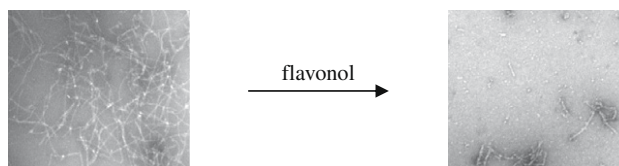
Isoxazole amino acid **7g** and hydrazone **11e** were found to possess System x<sub>c</sub><sup>-</sup> binding affinity comparable to the endogenous substrate cystine, and using these observations a pharmacophore model had been developed.

**Microwave assisted synthesis and antimicrobial activity of 2-quinoxalinone-3-hydrazone derivatives**

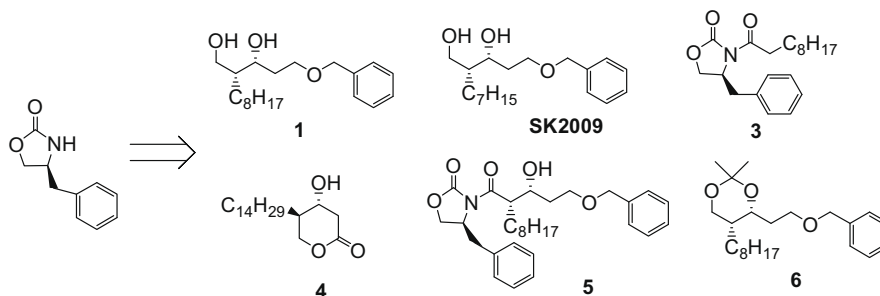
pp 214–221

Olayinka O. Ajani <sup>\*</sup>, Craig A. Obafemi, Obinna C. Nwinyi, David A. Akinpelu**Carboxymethylated-κ-casein: A convenient tool for the identification of polyphenolic inhibitors of amyloid fibril formation**

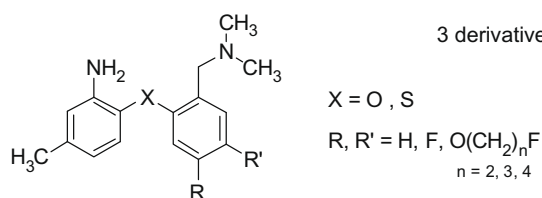
pp 222–228

John A. Carver, Peter J. Duggan <sup>\*</sup>, Heath Ecroyd, Yanqin Liu, Adam G. Meyer, C. Elisabet Tranberg**Inhibition of IκB kinase and NF-κB by a novel synthetic compound SK 2009**

pp 229–235

Ravi Kumar Anchoori, Kuzhuvilil B. Harikumar, Venkateswara Rao Batchu, Bharat B. Aggarwal, Saeed R. Khan <sup>\*</sup>**Synthesis and in vitro evaluation of fluorinated diphenyloxide derivatives and sulfur analogs as serotonin transporter ligands**

pp 236–241

Sylvie Mavel <sup>\*</sup>, Nathalie Meheux, Denis Guilloteau, Patrick Emond

3 derivatives present good in vitro affinity for the SERT

$$K_{i_{\text{SERT}}} = 7-8 \text{ nM}$$

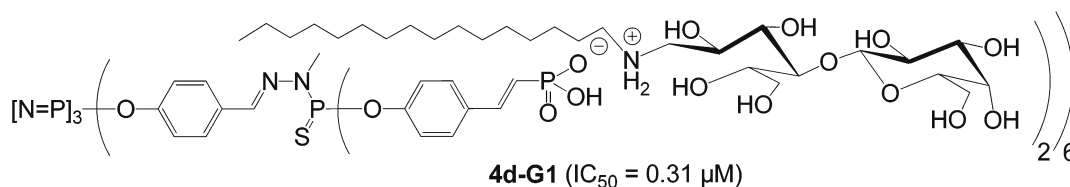
X = O, S

R, R' = H, F, O(CH<sub>2</sub>)<sub>n</sub>F  
n = 2, 3, 4

**Multivalent cationic GalCer analogs derived from first generation dendrimeric phosphonic acids**

pp 242–248

Alexandra Pérez-Anes, Cristina Stefaniu, Christine Moog, Jean-Pierre Majoral, Muriel Blanzat <sup>\*</sup>, Cédric-Olivier Turrin <sup>\*</sup>, Anne-Marie Caminade, Isabelle Rico-Lattes

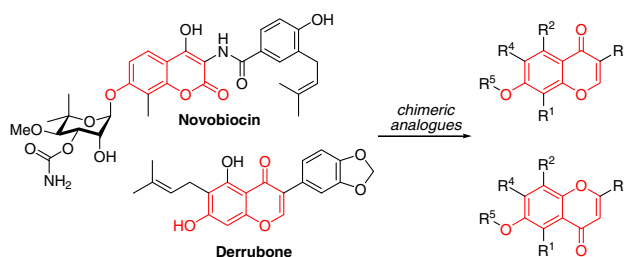


A new series of cationic multivalent analogs of GalCer based on phosphonic acid terminated dendrimers and *N*-hexadecylamino lactitol moieties is described. Oppositely to their corresponding sodium salts, the anti-HIV properties of these cationic systems is hardly influenced by the phosphonic acids vicinity.

**The synthesis and evaluation of flavone and isoflavone chimeras of novobiocin and derrubone**

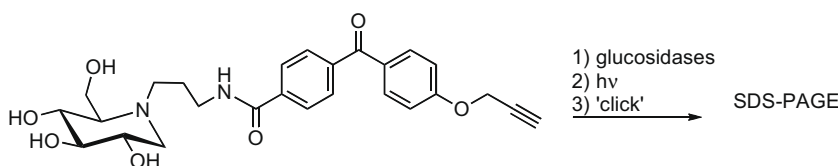
pp 249–266

Jared R. Mays, Stephanie A. Hill, Justin T. Moyers, Brian S. J. Blagg <sup>\*</sup>

**Nanomolar affinity, iminosugar-based chemical probes for specific labeling of lysosomal glucocerebrosidase**

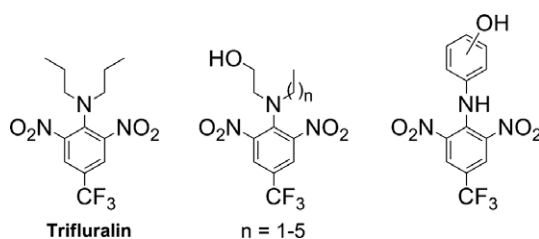
pp 267–273

Monique van Scherpenzeel, Richard J. B. H. N. van den Berg, Wilma E. Donker-Koopman, Rob M. J. Liskamp, Johannes M. F. G. Aerts, Herman S. Overkleeft, Roland J. Pieters <sup>\*</sup>

**Synthesis and biological evaluation of trifluralin analogues as antileishmanial agents**

pp 274–281

M. A. Esteves, I. Fragiadaki, R. Lopes, E. Scoulica, M. E. M. Cruz <sup>\*</sup>

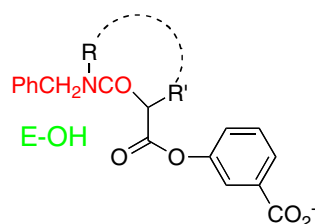




**Substituted aryl malonamates as new serine  $\beta$ -lactamase substrates: Structure–activity studies**

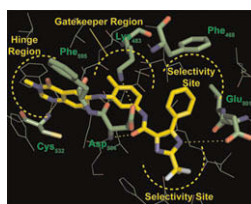
pp 282–291

S. A. Adediran, D. Cabaret, J. -F. Lohier, M. Wakselman, R. F. Pratt \*

**Application of a novel [3+2] cycloaddition reaction to prepare substituted imidazoles and their use in the design of potent DFG-out allosteric B-Raf inhibitors**

pp 292–304

Justin Dietrich, Vijay Gokhale, Xiadong Wang, Laurence H. Hurley, Gary A. Flynn \*

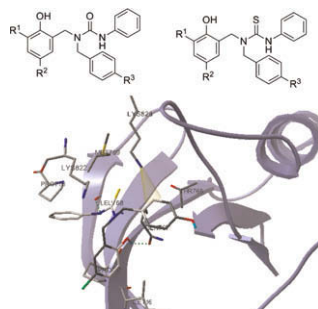


We report the de novo design of a potent series of imidazole based inhibitors of B-Raf V600E, a novel [3+2] cycloaddition route to obtain tri-substituted imidazoles, the biochemical evaluation of a series of analogues, and unique kinase inhibition profiles of three selected molecules.

**Synthesis and structure–activity relationships of *N*-benzyl-*N*-(*X*-2-hydroxybenzyl)-*N'*-phenylureas and thioureas as antitumor agents**

pp 305–313

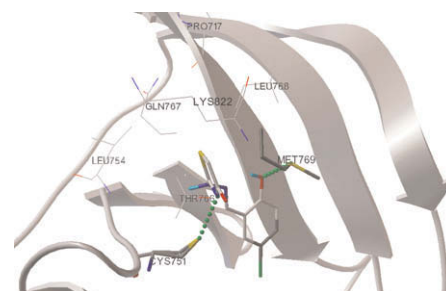
Huan-Qiu Li, Tao Yan, Ying Yang, Lei Shi, Chang-Fang Zhou \*, Hai-Liang Zhu \*

**Design, synthesis and biological evaluation of thiazolidinone derivatives as potential EGFR and HER-2 kinase inhibitors**

pp 314–319

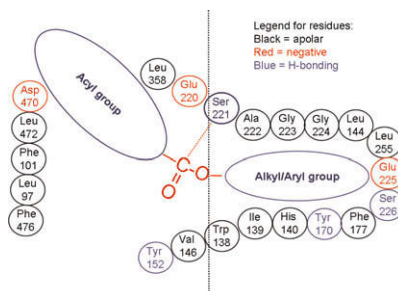
Peng-Cheng Lv, Chang-Fang Zhou, Jin Chen, Peng-Gang Liu, Kai-Rui Wang, Wen-Jun Mao, Huan-Qiu Li, Ying Yang, Jing Xiong, Hai-Liang Zhu \*

Compound **12** displayed the most potent inhibitory activity ( $IC_{50} = 0.09 \mu M$  for EGFR and  $IC_{50} = 0.42 \mu M$  for HER-2), comparable to the positive control erlotinib. Docking simulation was performed to position compound **12** into the EGFR active site to determine the probable binding model and antiproliferative assay results indicating that some of the thiazolidinone derivatives own high antiproliferative activity against MCF-7. Compound **12** with potent inhibitory activity in tumor growth inhibition would be a potential anticancer agent.



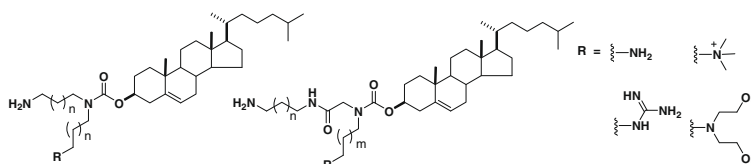
## In silico prediction of human carboxylesterase-1 (hCES1) metabolism combining docking analyses and MD simulations

pp 320–329

Giulio Vistoli<sup>\*</sup>, Alessandro Pedretti, Angelica Mazzolari, Bernard Testa

## Solid phase synthesis of novel asymmetric hydrophilic head cholesterol-based cationic lipids with potential DNA delivery

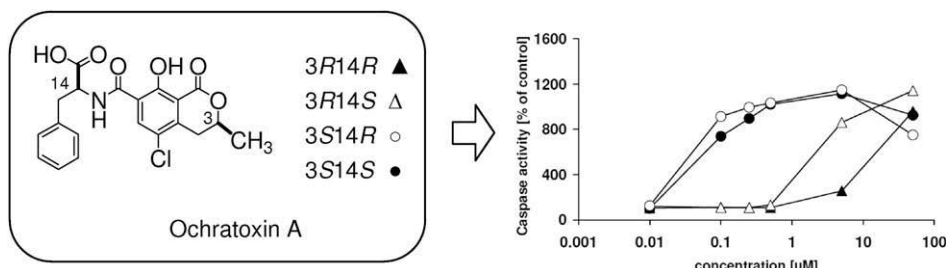
pp 330–342

Widchaya Radchatawedchakoon, Ramida Watanapokasin, Aungkana Krajarng, Boon-ek Yingyongnarongkul<sup>\*</sup>

Asymmetric hydrophilic head cholesterol-based cationic lipids with equal and unequal chain length were synthesized. The in vitro transfection efficiency of these cationic lipids when formulated as liposome was investigated. Some of them exhibited higher transfection efficiency than the commercially available gene delivery reagent Effectene™, DOTAP and DC-Chol.

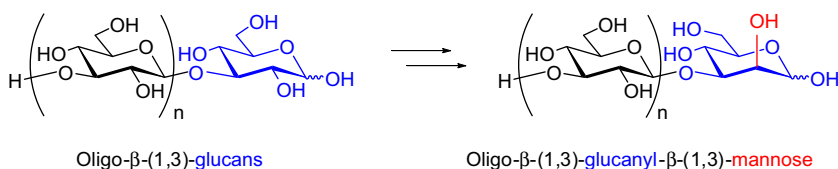
## Total synthesis and cytotoxicity evaluation of all ochratoxin A stereoisomers

pp 343–347

Benedikt Cramer, Henning Harrer, Kazuhiko Nakamura, Daisuke Uemura, Hans-Ulrich Humpf<sup>\*</sup>

## New oligo-β-(1,3)-glucan derivatives as immunostimulating agents

pp 348–357

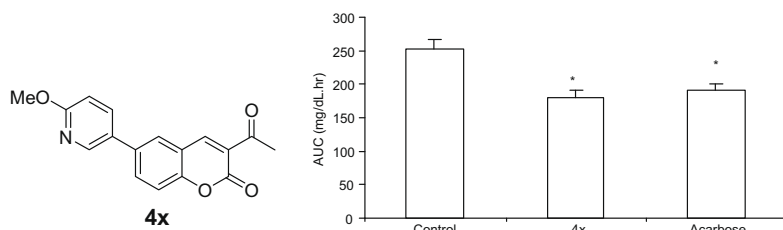
Karine Descroix, Vaclav Větvíčka<sup>\*</sup>, Isabelle Laurent, Frank Jamois, Jean-Claude Yvin, Vincent Ferrières<sup>\*</sup>

New β-(1,3)-glucanyl-mannose conjugates were synthesized. The resulting small linear oligosaccharides indeed stimulate the immune defence in murine model even if they are not able to adopt helical arrangements.



**$\alpha$ -Glucosidase inhibitory antihyperglycemic activity of substituted chromenone derivatives**

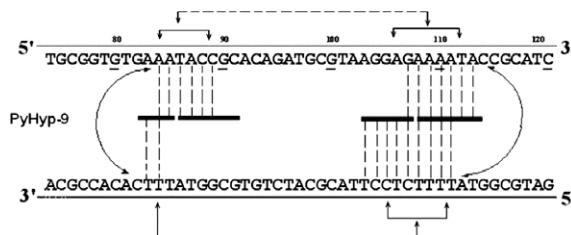
pp 358–365

B. China Raju <sup>\*</sup>, Ashok K. Tiwari <sup>\*</sup>, J. Ashok Kumar, A. Zehra Ali, Sachin B. Agawane, G. Saidachary, K. Madhusudana

Series of chromenone derivatives were synthesized, among them compound **4x** is new and being reported in this study to possess intestinal  $\alpha$ -glucosidase inhibitory as well as antihyperglycemic activity for the first time to serve as a model compound for design and development of therapeutic based on  $\alpha$ -glucosidase inhibitory antihyperglycemic activity.

**Detection of multiple network-based allosteric interactions between peptides and arrays of DNA binding sites**

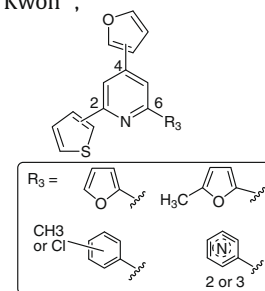
pp 366–376

Karen K. L. Kao, Jonathan C. T. Huang, Chi-Kai Yang, Kee-Ching G. Jeng, Jung-Cheng Chang, Wen-Chen Yao, S. C. Hsien, Michael J. Waring, Ming-Hua Chen, Lin Ma, Leung Sheh <sup>\*</sup>

Three different types of network-based allosteric communication in DNA-peptide sequence-selective interactions are reported.

**2-Thienyl-4-furyl-6-aryl pyridine derivatives: Synthesis, topoisomerase I and II inhibitory activity, cytotoxicity, and structure–activity relationship study**

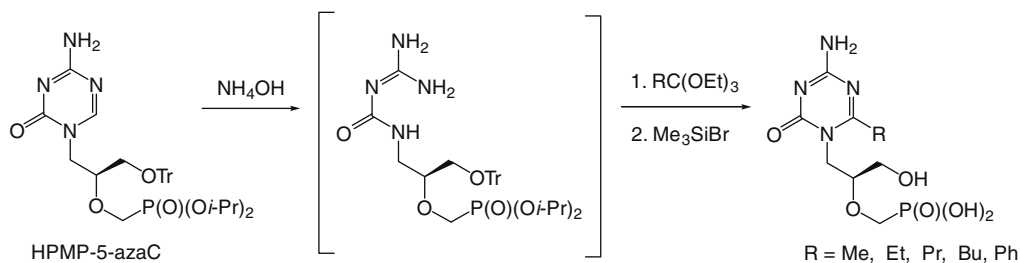
pp 377–386

Pritam Thapa, Radha Karki, Uttam Thapa, Yurngdong Jahng, Mi-Ja Jung, Jung Min Nam, Younghwa Na, Youngjoo Kwon <sup>\*</sup>, Eung-Seok Lee <sup>\*</sup>

A series of 2-thienyl-4-furyl-6-aryl pyridine derivatives were designed and synthesized and evaluated for their topoisomerase I and II inhibitory activities and cytotoxicity against several human cancer cell lines.

**Acyclic nucleoside phosphonates with 5-azacytosine base moiety substituted in C-6 position**

pp 387–395

Marcela Krečmerová <sup>\*</sup>, Milena Masojídková, Antonín Holý

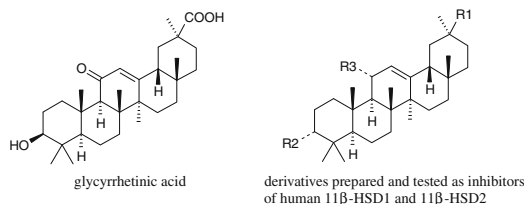
Introduction of substituents to C-6 position of 1-(S)-[3-hydroxy-2-(phosphonomethoxy)propyl]-5-azacytosine (HPMP-5-azaC).



**Synthesis of glycyrrhetic acid derivatives for the treatment of metabolic diseases**

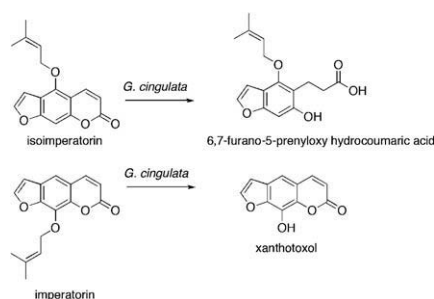
pp 433–454

Igor Beseda, Laszlo Czollner, Priti S. Shah, Rupesh Khunt, Rawindra Gaware, Paul Kosma, Christian Stanetty, Maria Carmen del Ruiz-Ruiz, Hassan Amer, Kurt Mereiter, Thierry Da Cunha, Alex Odermatt, Dirk Claßen-Houben, Ulrich Jordis \*

**Biotransformation of isoimperatorin and imperatorin by *Glomerella cingulata* and  $\beta$ -secretase inhibitory activity**

pp 455–459

Shinsuke Marumoto, Mitsuo Miyazawa \*

**OTHER CONTENTS****Corrigenda**

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\*Corresponding author

Supplementary data available via ScienceDirect

**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, 102, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, 61(6), 355–360].

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