



European Journal of Medicinal Chemistry Vol 48, 2012

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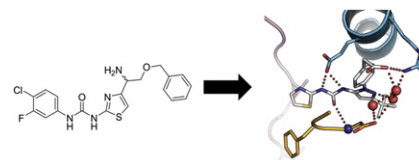
ORIGINAL ARTICLES

Structure-based design, synthesis and biological evaluation of *N*-pyrazole, *N'*-thiazole urea inhibitors of MAP kinase p38 α

pp. 1–15

Matthäus Getlik, Christian Grütter, Jeffrey R. Simard, Hoang D. Nguyen, Armin Robubi, Beate Aust, Willem A.L. van Otterlo** and Daniel Rauh*

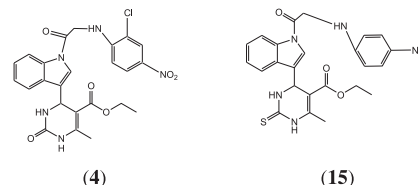
The SAR of a series of *N*-pyrazole, *N'*-thiazole-ureas was explored systematically and resulted in ethyl [4-(3-*tert*-butyl-5-[[[(1,3-thiazol-2-ylamino)carbonyl]amino]-1*H*-pyrazol-1-yl]phenyl]acetate (**18b**) with potent cellular activity against p38 α .

**Synthesis, antimicrobial, anticancer evaluation and QSAR studies of 6-methyl-4-[1-(2-substituted-phenylamino)-acetyl]-1*H*-indol-3-yl]-2-oxo/thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid ethyl esters**

pp. 16–25

Sandeep Kumar Sharma, Pradeep Kumar, Balasubramanian Narasimhan*, Kalavathy Ramasamy, Vasudevan Mani, Rakesh Kumar Mishra and Abu Bakar Abdul Majeed

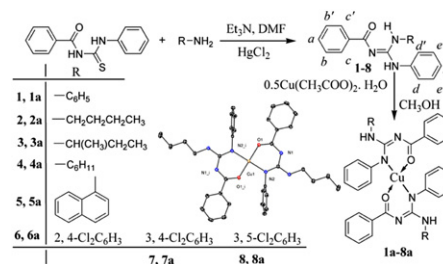
The biological screening results indicated that 6-methyl-4-[1-[2-(4-nitro-phenylamino)-acetyl]-1*H*-indol-3-yl]-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid ethyl ester (**15**) and 4-[1-[2-(2-chloro-4-nitro-phenylamino)-acetyl]-1*H*-indol-3-yl]-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylic acid ethyl ester (**4**) were found to be the most effective antimicrobial and anticancer agents respectively.

**Synthesis, structural characterization and *in vitro* biological screening of some homoleptic copper(II) complexes with substituted guanidines**

pp. 26–35

Ghulam Murtaza, Muhammad Khawar Rauf, Amin Badshah*, Masahiro Ebihara, Muhammad Said, Marcel Gielen, Dick de Vos, Erum Dilshad and Bushra Mirza

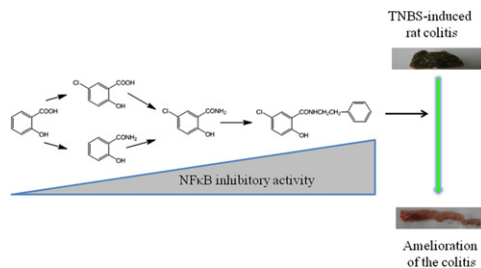
A series of homoleptic copper(II) complexes (1a–8a) with *N,N',N''*-trisubstituted guanidines (1–8), have been synthesized, characterized and screened for *in vitro* cytotoxicity activity in human cell lines carcinomas A498 (Renal), EVSAT (Breast), H226 (Lung), IGROV (Ovarian), M19 (Melanoma-Skin), MCF-7 (Breast) and WIDR (Colon), showing a moderate level of cytotoxicity against these cancer cell lines as compared with standard chemotherapeutic drugs.



Structure–activity relationship of salicylic acid derivatives on inhibition of TNF- α dependent NF κ B activity: Implication on anti-inflammatory effect of N-(5-chlorosalicyloyl)phenethylamine against experimental colitis

pp. 36–44

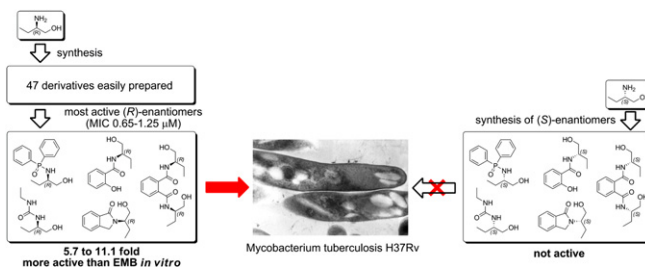
Jihye Kim, Sookjin Kang, Sungchae Hong, Soowhan Yum, Young Mi Kim and Yunjin Jung*



Synthesis and *in vitro* antimycobacterial activity of compounds derived from (*R*)- and (*S*)-2-amino-1-butanol – The crucial role of the configuration

pp. 45–56

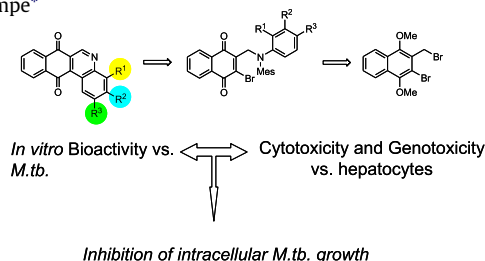
Georgi M. Dobrikov*, Violeta Valcheva, Margarita Stoilova-Disheva, Georgi Momekov, Pavleta Tzvetkova, Angel Chimov and Vladimir Dimitrov*



Straightforward palladium-mediated synthesis and biological evaluation of benzo[*j*]phenanthridine-7,12-diones as anti-tuberculosis agents

pp. 57–68

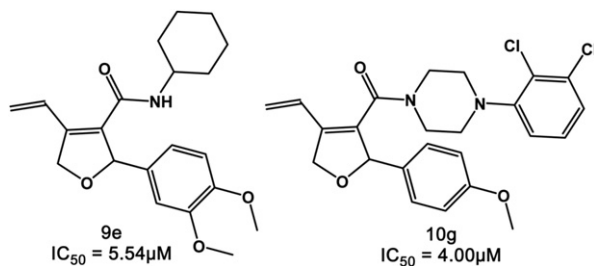
Davie Cappoen, Jan Jacobs, Tuyen Nguyen Van, Sven Claessens, Gaston Diels, Roel Anthonissen, Thorbjorg Einarsdottir, Maryse Fauville, Luc Verschaeve, Kris Huygen** and Norbert De Kimpe*



Synthesis of novel 2, 5-dihydrofuran derivatives and evaluation of their anticancer activity

pp. 69–80

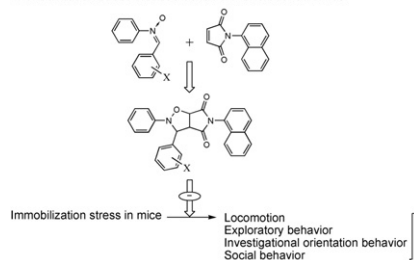
Yikai Zhang, Hanyu Zhong, Tiantian Wang, Dongping Geng, Mingfeng Zhang and Ke Li*



Synthesis and evaluation of hexahydropyrrolo[3,4-*d*]isoxazole-4,6-diones as anti-stress agents

pp. 81–91

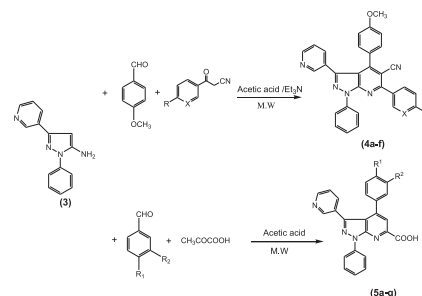
Rahul Badru, Preet Anand and Baldev Singh*

Anti-stress effect of Hexahydropyrrolo[3,4-*d*]isoxazole-4,6-dione derivatives in immobilization stress induced behavioral alterations in mice**Synthesis of pyrazolo[3,4-*b*]pyridines under microwave irradiation in multi-component reactions and their antitumor and antimicrobial activities – Part 1**

pp. 92–96

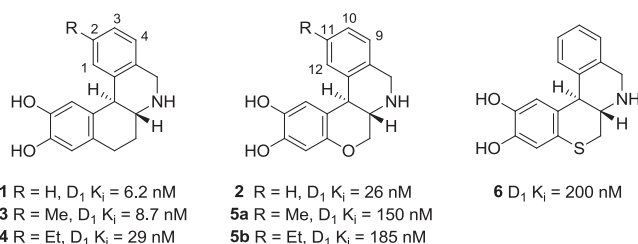
M.A. El-borai, H.F. Rizk*, M.F. Abd-Aal and I.Y. El-Deeb

Synthesis of some new pyrazolo[3,4-*b*]pyridine derivatives were reported. The reactions were carried out by conventional heating and microwave irradiation. Most of the synthesized compounds were screened for antimicrobial and antitumor activities.

**Analogues of doxanthrine reveal differences between the dopamine D₁ receptor binding properties of chromanoisoquinolines and hexahydrobenzo[*a*]phenanthridines**

pp. 97–107

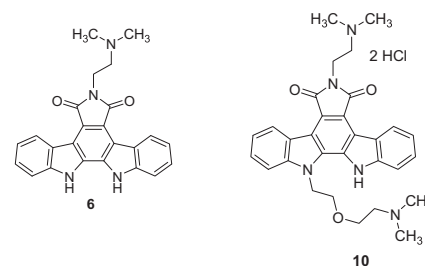
Juan Pablo Cueva, Benjamin R. Chemel, Jose I. Juncosa, Jr., Markus A. Lill, Val J. Watts and David E. Nichols*

**Synthesis and biological evaluation of novel indolocarbazoles with anti-angiogenic activity**

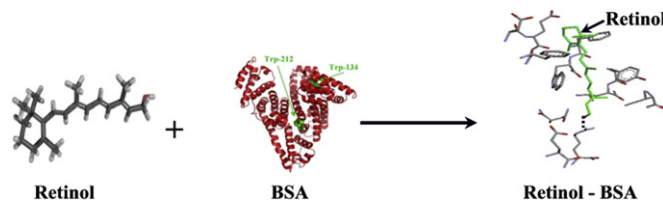
pp. 108–113

Nuria Acero*, Miguel F. Braña**, Loreto Añorbe, Gema Domínguez, Dolores Muñoz-Mingarro, Francesc Mitjans and Jaume Piulats

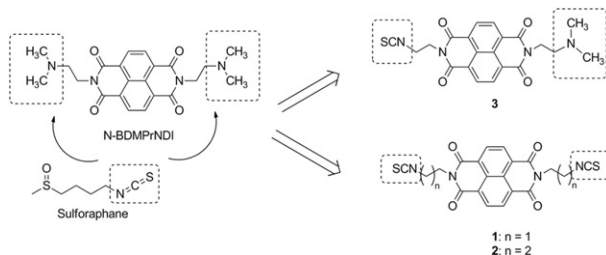
A new series of indolocarbazoles related to staurosporine were synthesized and their antiproliferative and anti-angiogenic activity were evaluated. **6** and **10** were the most promising compounds.



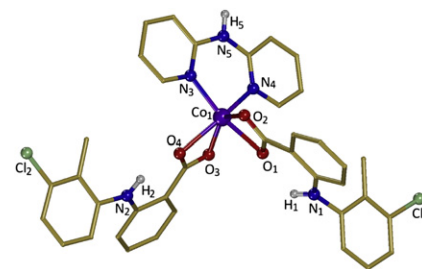
pp. 114–123



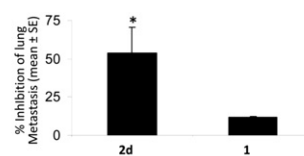
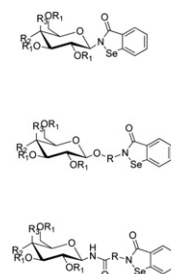
pp. 124–131



pp. 132–142



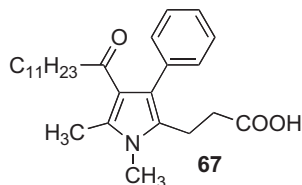
pp. 143–152



Pyrrole alkanolic acid derivatives as nuisance inhibitors of microsomal prostaglandin E₂ synthase-1

pp. 153–163

Andrea Wiegard, Walburga Hanekamp, Klaus Griessbach, Jörg Fabian and Matthias Lehr*



Inhibition of human recombinant mPGES-1

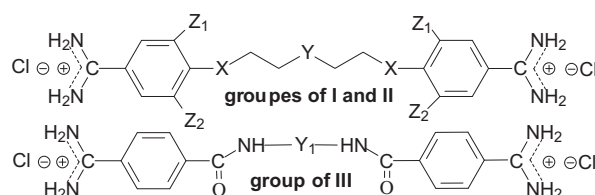
- in absence of Triton X-100: IC₅₀ = 0.14 μM
- in presence of Triton X-100: not active at 10 μM

Analogs of pentamidine as potential anti-*Pneumocystis* chemotherapeutics

pp. 164–173

Dorota Maciejewska*, Jerzy Żabinski, Paweł Kaźmierczak, Mateusz Rezler, Barbara Krassowska-Świebocka, Margaret S. Collins and Melanie T. Cushion**

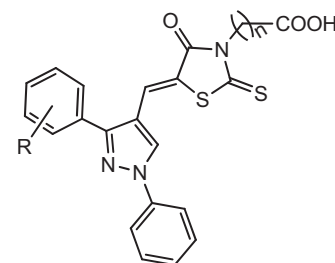
Pentamidine analogs were prepared and analyzed for efficacy against *Pneumocystis carinii*. In ATP bioassay they showed marked or moderate activity. Most of them had no cytotoxicity in mammalian cell cultures.

**Synthesis of novel 1,3-diaryl pyrazole derivatives bearing rhodanine-3-fatty acid moieties as potential antibacterial agents**

pp. 174–178

Li-Li Xu, Chang-Ji Zheng, Liang-Peng Sun, Jing Miao and Hu-Ri Piao*

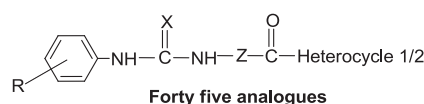
A series of 4-functionalized-pyrazoles were synthesized and evaluated for their antibacterial activity.

**Synthesis of uriedo and thiouriedo derivatives of peptide conjugated heterocycles – A new class of promising antimicrobials**

pp. 179–191

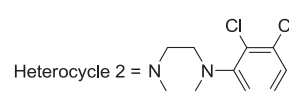
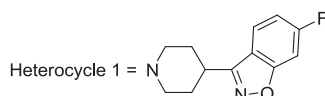
R. Suhas, S. Chandrashekar and D. Channe Gowda*

The title compounds were synthesized and evaluated for their possibility to arrest the growth of pathogenic bacteria and fungi. All the synthesized derivatives were potentially active.



R = 2F, 4Cl, 4OMe; X = O, S; Z = Trp, GGIP, GGFP, GVGVP, GFGFP, GEGFPGVGVPVGVPVGVPVGFPFGFGFP,

GEGFPGVGVPVGVPFGFGFPVGVPVGFP

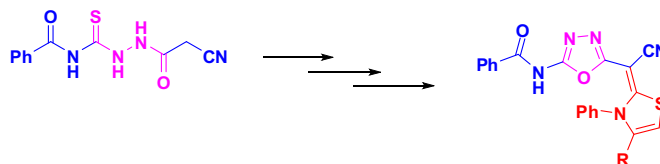


Synthesis and antitumor evaluation of some new 1,3,4-oxadiazole-based heterocycles

pp. 192–199

Samir Bondock*, Shymaa Adel, Hassan A. Etman and Farid A. Badria

A novel series of 1,3,4-oxadiazole-based heterocycles were synthesized to evaluate their antitumor activity.

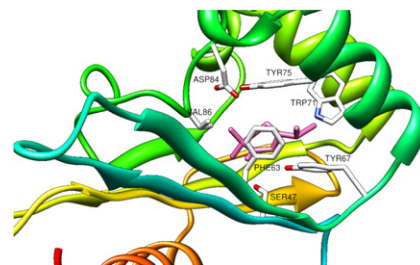


Structure-based virtual screening for plant-derived SdiA-selective ligands as potential antivirulent agents against uropathogenic *Escherichia coli*

pp. 200–205

Vinothkannan Ravichandiran, Karthi Shanmugam, K. Anupama, Sabu Thomas and Adline Princy*

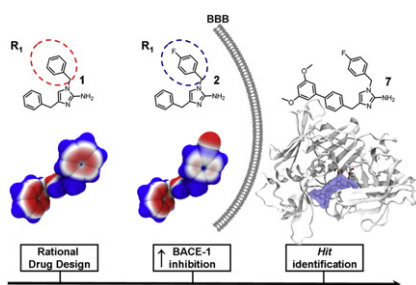
The interaction between SdiA, a transcriptional regulator of *Escherichia coli* quorum sensing, and the ligand derived from *Melia dubia* bark (BL39R1) shows the maximum binding potential.



A small chemical library of 2-aminoimidazole derivatives as BACE-1 inhibitors: Structure-based design, synthesis, and biological evaluation

pp. 206–213

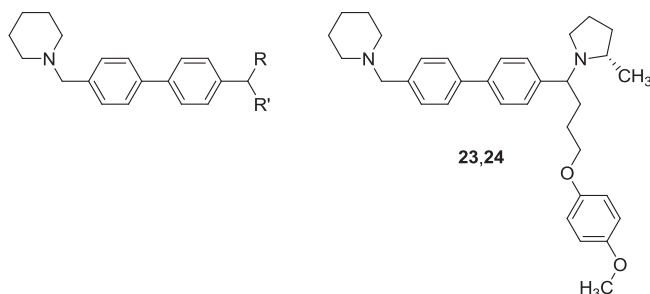
Gianpaolo Chiriano, Angela De Simone, Francesca Mancini, Daniel I. Perez, Andrea Cavalli, Maria Laura Bolognesi, Giuseppe Legname, Ana Martinez, Vincenza Andrisano, Paolo Carloni and Marinella Roberti*



Dibasic biphenyl H₃ receptor antagonists: Steric tolerance for a lipophilic side chain

pp. 214–230

Fabrizio Bordi, Silvia Rivara*, Elisa Dallaturca, Caterina Carmi, Daniele Pala, Alessio Lodola, Federica Vacondio, Lisa Flammini, Simona Bertoni, Vigilio Ballabeni, Elisabetta Barocelli and Marco Mor

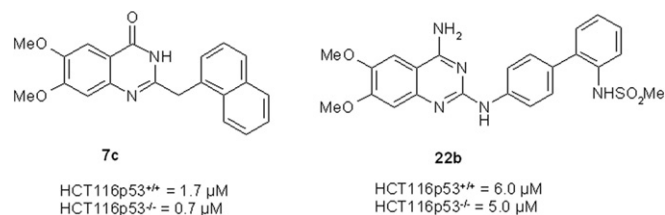


Cytotoxic potential of novel 6,7-dimethoxyquinazolines

pp. 231–243

Mange R. Yadav*, Fedora Grande, Bishram S. Chouhan, Prashant P. Naik, Rajani Giridhar, Antonio Garofalo and Nouri Neamati

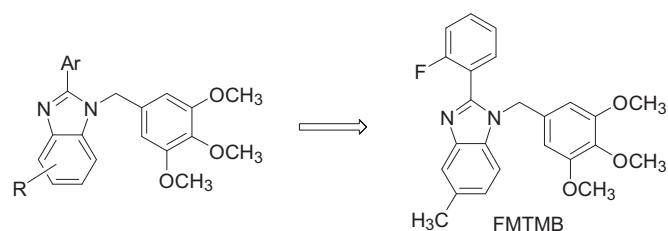
The synthesis and cytotoxicity activity of a series of variously substituted 6,7-dimethoxyquinazoline derivatives is reported. Nine of the tested compounds showed remarkable cytotoxicity in all cell lines.

**Synthesis and bioevaluation of novel 3,4,5-trimethoxybenzylbenzimidazole derivatives that inhibit *Helicobacter pylori*-induced pathogenesis in human gastric epithelial cells**

pp. 244–254

Chih-Shiang Chang, Ju-Fang Liu, Hwai-Jeng Lin, Chia-Der Lin, Chih-Hsin Tang, Dah-Yuu Lu, Yu-Ting Sing, Li-Yu Chen, Min-Chuan Kao, Sheng-Chu Kuo and Chih-Ho Lai*

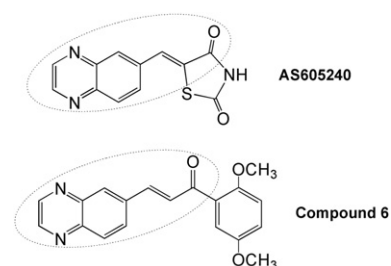
A series of 3,4,5-trimethoxybenzylbenzimidazole derivatives were synthesized. 2-Fluorophenyl-5-methyl-1-(3,4,5-trimethoxybenzyl)benzimidazole (FMTMB) was determined as the most potent in the inhibition of *Helicobacter pylori* growth and pathogenesis of host cells.

**Activity of novel quinoxaline-derived chalcones on *in vitro* glioma cell proliferation**

pp. 255–264

Tânia R. Mielcke, Alessandra Mascarello, Eduardo Filippi-Chiela, Rafael F. Zanin, Guido Lenz, Paulo César Leal, Louise D. Chirardia, Rosendo A. Yunes, Ricardo J. Nunes, Ana M.O. Battastini, Fernanda B. Morrone and Maria M. Campos*

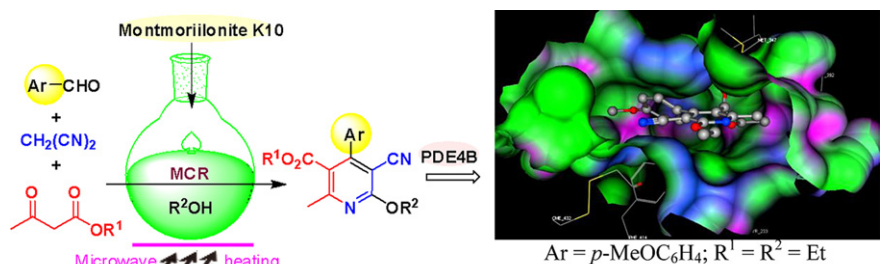
Chalcones derived from quinoxaline-6-carbaldehyde, structurally based on the selective PI3K γ inhibitor AS605240, were assayed in glioma cell lines from human and rat origin (U-138 MG and C6, respectively), and compound **6** presented the best activity (2.64 μ M for U-138 MG cells and 1.35 μ M for C6 cells).

**Montmorillonite K-10 mediated green synthesis of cyano pyridines: Their evaluation as potential inhibitors of PDE4**

pp. 265–274

T. Ram Reddy, G. Rajeshwar Reddy, L. Srinivasula Reddy, Subbarao Jammula, Y. Lingappa, Ravikumar Kapavarapu, Chandana Lakshmi T. Meda, Kishore V.L. Parsa and Manojit Pal*

Functionalized cyano pyridines synthesized via montmorillonite K-10 mediated multi-component reaction have been identified as a new class of PDE4 inhibitors.

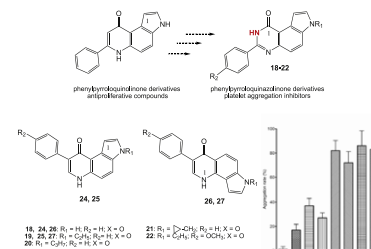


Synthesis and evaluation of platelet aggregation inhibitory activity of some 3-phenyl-pyrroloquinazolinones

pp. 275–283

Maria Grazia Ferlin*, Christian Borgo and Renzo Deana

The present results indicate that 3-PPyQZ structure, with the quite potent inhibitor of platelet aggregation compound **18** acting by an interesting mixed action-mechanism, might constitute a starting point for the synthesis of potential anti-thrombosis agents.

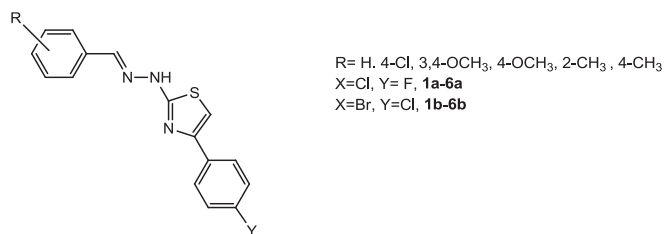


Synthesis and biological assessment of novel 2-thiazolylhydrazones and computational analysis of their recognition by monoamine oxidase B

pp. 284–295

Simona Distinto, Matilde Yáñez, Stefano Alcaro*, M. Cristina Cardia, Marco Gaspari, M. Luisa Sanna, Rita Meleddu, Francesco Ortuso, Johannes Kirchmair, Patrick Markt, Adriana Bolasco, Gerhard Wolber, Daniela Secci and Elias Maccioni

A series of novel 2-thiazolylhydrazones derivatives were synthesized. Some compounds showed interesting activity and selectivity toward MAO-B isoform. Induced fit docking, molecular dynamics simulations and FEP analysis were applied in order to gain insight about SAR.

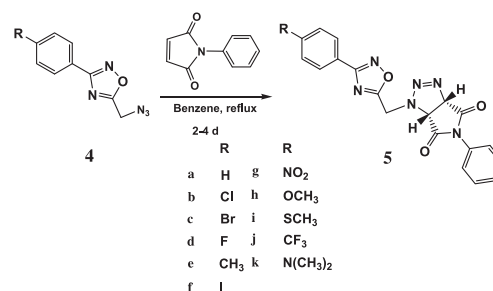


Synthesis and anti-protozoal activity of novel dihydropyrrolo[3,4-d][1,2,3]triazoles

pp. 296–304

Yaşar Dürüst*, Hamza Karakuş, Marcel Kaiser and Deniz Tasdemir**

A series of novel dihydropyrrolo[3,4-d][1,2,3]triazoles (**5a-k**) were designed and synthesized. The title compounds were assayed for their anti-protozoal activity against *Trypanosoma brucei rhodesiense*, *Trypanosoma cruzi*, *Leishmania donovani*, *Plasmodium falciparum* and cytotoxicity against L6 cells.

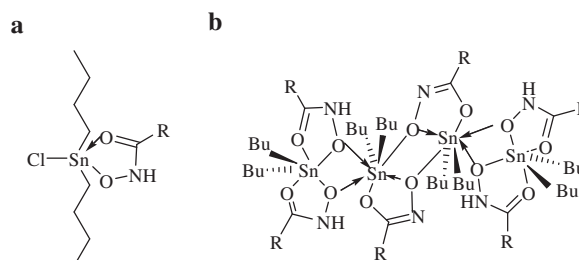


Novel di-n-butyltin(IV) derivatives: Synthesis, high levels of cytotoxicity in tumor cells and the induction of apoptosis in KB cancer cells

pp. 305–312

Xianmei Shang*, Nan Ding and Guangya Xiang*

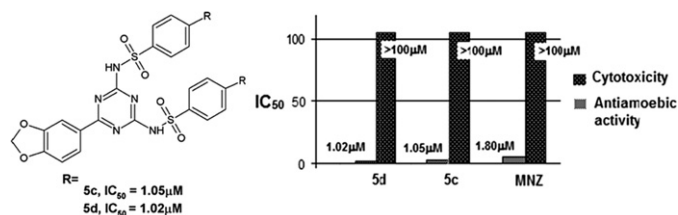
Two classes of dibutyltin(IV) hydroxamates complexes were prepared and evaluated for *in vitro* antitumor activities. Annexin V FITC-PI assay and cell cycle assay was consistent with the MTT results.



Probing the antiamoebic and cytotoxicity potency of novel tetrazole and triazine derivatives

pp. 313–320

Mohammad Younus Wani, Abdul Rooof Bhat, Amir Azam, Inho Choi and Fareeda Athar*

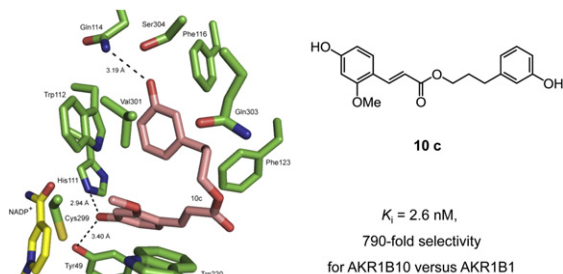


Two new compounds 5c and 5d were found as least cytotoxic and excellent *Entamoeba histolytica* inhibitors in a series of compounds synthesized and screened.

Design, synthesis and evaluation of caffeic acid phenethyl ester-based inhibitors targeting a selectivity pocket in the active site of human Aldo-Keto reductase 1B10

pp. 321–329

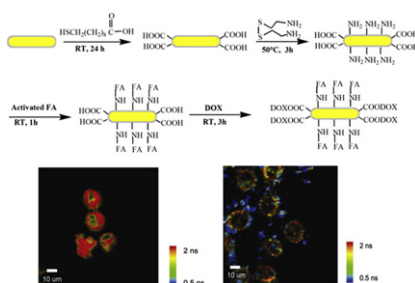
Midori Soda, Dawei Hu, Satoshi Endo, Mayuko Takemura, Jie Li, Ryogo Wada, Syohei Ifuku, Hai-Tao Zhao, Ossama El-Kabbani, Shozo Ohta, Keiko Yamamura, Naoki Toyooka, Akira Hara and Toshiyuki Matsunaga*



Multifunctional gold nanorod theragnostics probed by multi-photon imaging

pp. 330–337

Britanny Book Newell, Yuling Wang and Joseph Irudayaraj*

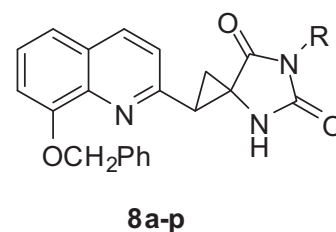


Synthesis and anticonvulsant activity of 1-(8-(benzyloxy)quinolin-2-yl)-6-substituted-4,6-diazaspiro[2,4]heptane-5,7-diones

pp. 338–346

Xianran He, Min Zhong, Tao Zhang, Jin Yang, Zhongyuan Wu, Yuling Xiao, Hao Guo, Guofu Qiu and Xianming Hu*

A series of 1-(8-(benzyloxy)quinolin-2-yl)-6-substituted-4,6-diazaspiro[2,4]heptanes-5,7-diones (**8a–p**) were synthesized. Their anticonvulsant activity was evaluated by MES and scPTZ test, and their neurotoxicity was evaluated by the rotarod neurotoxicity test.



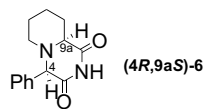
SHORT COMMUNICATIONS

Synthesis and anticonvulsant activity of novel 2,6-diketopiperazine derivatives. Part 2: Perhydropyrido[1,2-*a*]pyrazines

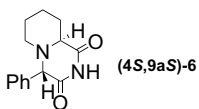
pp. 347–353

Maciej Dawidowski*, Franciszek Herold, Andrzej Chodkowski and Jerzy Kleps

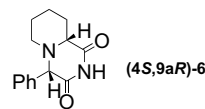
A series of chiral pyrido[1,2-*a*]pyrazine derivatives was evaluated as potential anticonvulsant agents. A very pronounced influence of stereochemistry on the *in vivo* anti-seizure activity was observed.



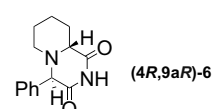
MES/scMET: **inactive**
6 Hz: **inactive**
TOX: **inactive**



MES/scMET: **active**
6 Hz: **active**
TOX: **active**



MES/scMET: moderate activity
6 Hz: **active**
TOX: moderate neurotoxicity



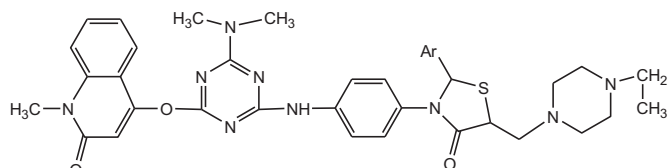
MES/scMET: **inactive**
6 Hz: **active**
TOX: **inactive**

Synthesis and biological evaluation of some thiazolidinones as antimicrobial agents

pp. 354–362

Divyesh Patel, Premalata Kumari* and Navin Patel

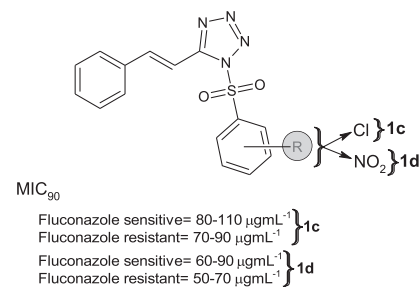
Synthesis, characterization, antibacterial and antifungal properties of some novel *s*-triazine analogs comprise of quinoline, thiazolidinone and piperazine nucleus.

**Proton-pumping-ATPase-targeted antifungal activity of cinnamaldehyde based sulfonyl tetrazoles**

pp. 363–370

Sheikh Shreaz, Mohammad Younus Wani, Rayees A. Sheikh, Sheikh Imran Ahmad, Rimple Bhatia, Fareeda Athar, Manzoor Nikhat and Luqman A. Khan*

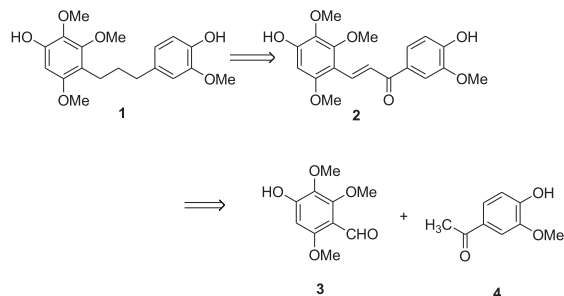
A series of cinnamaldehyde based sulfonyl tetrazoles were designed and subjected to antifungal screening. Compound **1c** and **1d** showed promising plasma membrane H^+ -ATPase targeted antifungal activity.

**A concise synthesis of viscolin, and its anti-inflammatory effects through the suppression of iNOS, COX-2, ERK phosphorylation and proinflammatory cytokines expressions**

pp. 371–378

Guan-Jhong Huang, M. Vijaya Bhaskar Reddy, Ping-Chung Kuo, Chieh-Hung Huang, Hung-Cheng Shih, E-Jian Lee, Mei-Lin Yang, Yann-Lii Leu and Tian-Shung Wu*

In the present report, a concise synthesis of viscolin (**1**) has been achieved. The anti-inflammatory effect of viscolin was investigated and the anti-inflammatory mechanisms were elucidated.

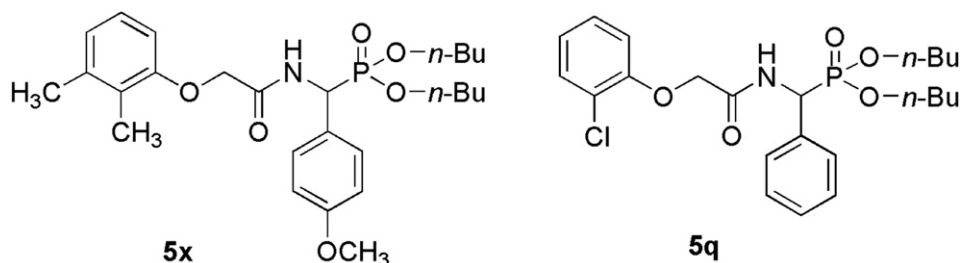


Synthesis and cytotoxicity of *O,O'*-dialkyl {[2-(substituted phenoxy)acetamido](substituted phenyl)methyl} phosphonates

pp. 379–384

Lihong Ning, Wei Wang, Yongju Liang, Hao Peng, Liwu Fu* and Hongwu He*

A series of *O,O'*-dialkyl {[2-(substituted phenoxy)acetamido](substituted phenyl)methyl}phosphonates was synthesized and the compounds **5x** and **5q** exhibited the best cytotoxicity against KB and CNE2 cells, respectively.

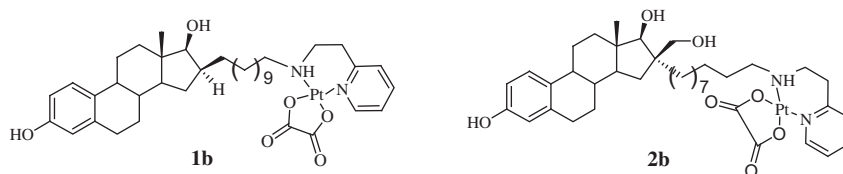


Synthesis, antiproliferative activity and estrogen receptor α affinity of novel estradiol-linked platinum(II) complex analogs to carboplatin and oxaliplatin. Potential vector complexes to target estrogen-dependent tissues

pp. 385–390

Pijus Saha, Caroline Descôteaux, Kevin Brasseur, Sébastien Fortin, Valérie Leblanc, Sophie Parent, Éric Asselin and Gervais Bérubé*

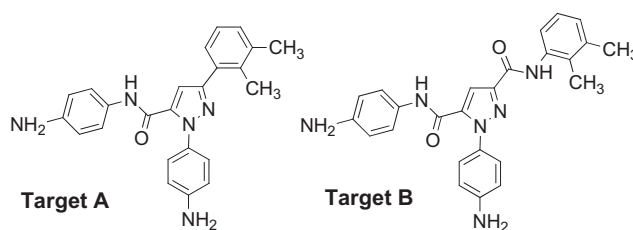
Six novel estradiol-linked platinum(II) complexes analog to carboplatin (**1a–3a**) and oxaliplatin (**1b–3b**) were prepared and biologically evaluated. Compounds **1b** and **2b** show antiproliferative activity in micromolar range and good affinity for estrogen receptor α suggesting these molecules potentially be promising alternatives vector complexes to target estrogen-dependent tissues.



Design, synthesis and biological evaluation of pyrazole derivatives as potential multi-kinase inhibitors in hepatocellular carcinoma

pp. 391–401

Elena Strocchi, Francesca Fornari, Manuela Minguzzi, Laura Gramantieri, Maddalena Milazzo, Valentina Rebutini, Simone Breviglieri, Carlo Maurizio Camaggi, Erica Locatelli, Luigi Bolondi and Mauro Comes-Franchini*



COVER

This picture is taken from the review published in: European Journal of Medicinal Chemistry, 2010, Volume 45, Pages 2095–2116. The review is focused on the binding of inhibitors to the catalytic site of histone deacetylase © 2010 Published by Elsevier Masson SAS

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ISSN 0223-5234