

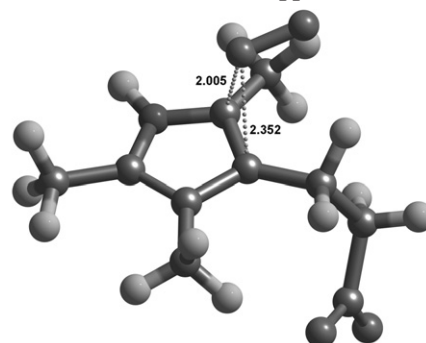
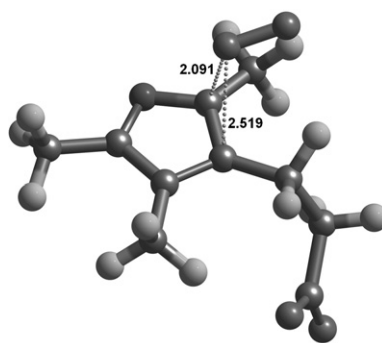
Contents

ARTICLES

A comparative density-functional study of the reaction mechanism of the O₂-dependent coproporphyrinogen III oxidase

Pedro J. Silva and Maria João Ramos*

DFT calculations on several reaction mechanisms proposed for coproporphyrinogen oxidase allow the rejection of a direct electron abstraction from the *protonated* substrate and favor direct dioxygen addition.

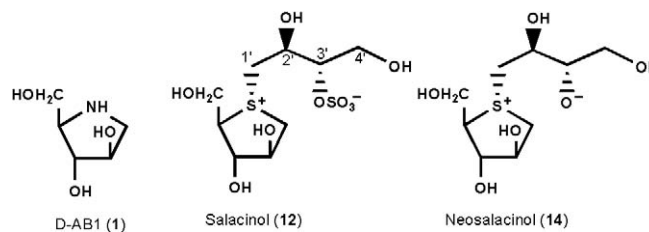


pp 2726–2733

Effect of five-membered sugar mimics on mammalian glycogen-degrading enzymes and various glucosidases

Yasuhiro Minami, Chinami Kuriyama, Kyoko Ikeda, Atsushi Kato, Kenji Takebayashi, Isao Adachi, George W. J. Fleet, Aikkarach Kettawan, Tadashi Okamoto and Naoki Asano*

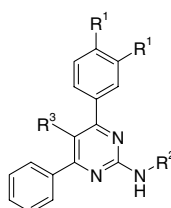
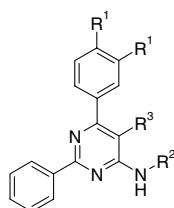
Anti-hyperglycemic effect of D-AB 1 on oh/oh mice reported maybe due to a combination of glycogen phosphorylase and amylo-1,6-glucosidase inhibition. The sulfate in the side chain of salacinol plays an important role in the specificity of enzyme inhibition.



pp 2734–2740

A new generation of adenosine receptor antagonists: From di- to trisubstituted aminopyrimidines

Jacobus P. D. van Veldhoven, Lisa C. W. Chang, Jacobien K. von Frijtag Drabbe Künzel, Thea Mulder-Krieger, Regina Struensee-Link, Margot W. Beukers, Johannes Brussee and Adriaan P. IJzerman*



R¹ = H, OCH₂O
R² = H, COR⁴, R⁴ = alkyl, cycloalkyl, aryl
R³ = H, CN

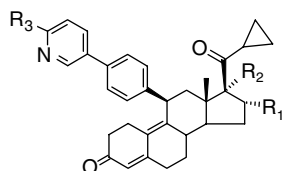
pp 2741–2752

Di- and trisubstituted aminopyrimidines as adenosine receptor antagonists.

11-(Pyridinylphenyl)steroids—A new class of mixed-profile progesterone agonists/antagonists

pp 2753–2763

Jos Rewinkel,* Mark Enthoven, Irene Golstein, Marcel van der Rijst, André Scholten, Martin van Tilborg, Dirk de Weys, Jeffrey Wisse and Hans Hamersma



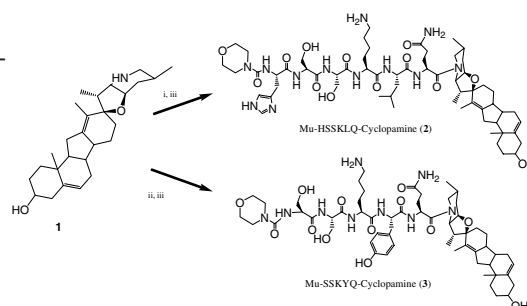
11-(Pyridinylphenyl)steroids and a series of heteroaryl analogs were prepared which show a remarkable mixed progesterone agonist/antagonist profile, wherein the efficacies for both activities range from 40% to 60%.

Targeted inhibition of hedgehog signaling by cyclopamine prodrugs for advanced prostate cancer

pp 2764–2768

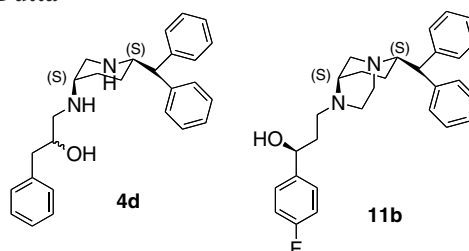
Srinivas K. Kumar, Indrajit Roy, Ravi K. Anchoori, Sarah Fazli, Anirban Maitra, Philip A. Beachy and Saeed R. Khan*

Novel peptide-cyclopamine conjugates as prostate-specific antigen (PSA)-activated prodrugs for use against prostate cancer.

**Further structural optimization of *cis*-(6-benzhydryl-piperidin-3-yl)-benzylamine and 1,4-diazabicyclo[3.3.1]nonane derivatives by introducing an exocyclic hydroxyl group: Interaction with dopamine, serotonin, and norepinephrine transporters**

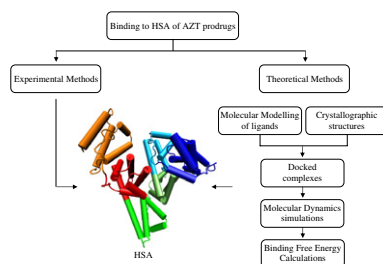
pp 2769–2778

Manoj Mishra, Rohit Kolhatkar, Juan Zhen, Ingrid Parrington, Maarten E. A. Reith and Alope K. Dutta*

**Binding to human serum albumin of zidovudine (AZT) and novel AZT derivatives. Experimental and theoretical analyses**

pp 2779–2790

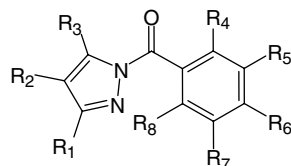
Mario A. Quevedo, Sergio R. Ribone, Guillermo N. Moroni and Margarita C. Briñón*




Structure–activity relationship analysis of *N*-benzoylpyrazoles for elastase inhibitory activity: A simplified approach using atom pair descriptors

pp 2791–2802

Andrei I. Khlebnikov,* Igor A. Schepetkin and Mark T. Quinn*



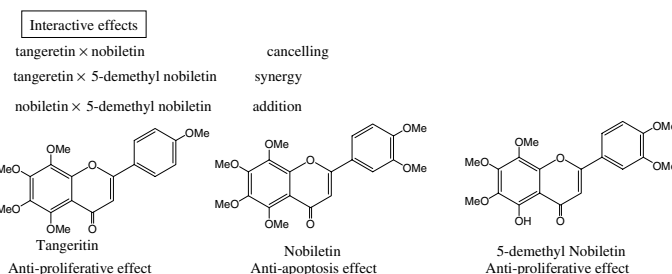
SAR analysis of 53 *N*-benzoylpyrazoles using atom pair descriptors and 2-dimensional molecular descriptors represents a simplified approach to predict inhibitors of human neutrophil elastase. 

Interactive effects of polymethoxy flavones from *Citrus* on cell growth inhibition in human neuroblastoma SH-SY5Y cells

pp 2803–2810

Yukihiro Akao,* Tomohiro itoh, Kenji Ohguchi, Munekazu Iinuma and Yoshinori Nozawa

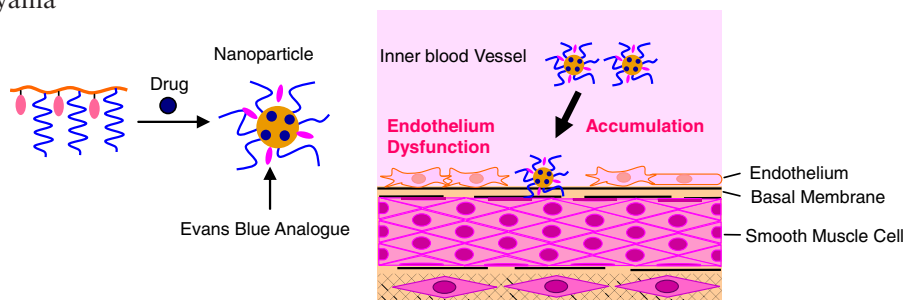
Nobiletin, a typical polymethoxy flavone from *Citrus*, had a preventive effect on H₂O₂-induced apoptosis at 20–30 mM in human neuroblastoma SH-SY5Y cells. Nobiletin acted as a signal modulator to attenuate the activation of intrinsic pathway in the apoptosis induced by H₂O₂ exposure. Tangeretin and 5-demethyl nobiletin, which are also polymethoxy flavones from *Citrus*, were shown to have a growth inhibitory effect. We found that tangeretin, nobiletin, and 5-demethyl nobiletin exhibited a cancelling, synergistic, or addition effect in various combinations of two compounds.



Development of polymeric drug delivery system for recognizing vascular endothelial dysfunction

pp 2811–2818

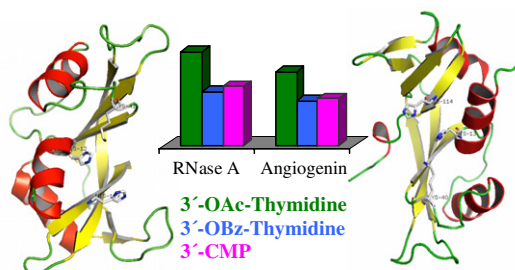
Kenjiro Ikuta, Takeshi Mori, Tatsurhiro Yamamoto, Takuro Niidome, Hiroaki Shimokawa and Yoshiki Katayama*



Exploring the potential of 3'-*O*-carboxy esters of thymidine as inhibitors of ribonuclease A and angiogenin

pp 2819–2828

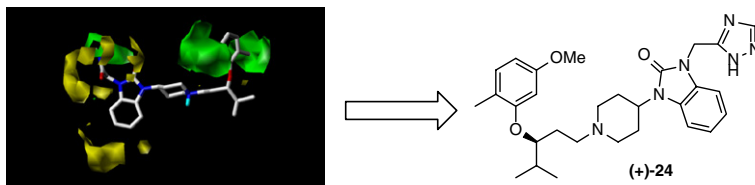
Kalyan S. Ghosh, Joy Debnath, Palash Dutta, Bijaya K. Sahoo and Swagata Dasgupta*



Structure–activity relationships and CoMFA of N-3 substituted phenoxypropyl piperidine benzimidazol-2-one analogues as NOP receptor agonists with analgesic properties

pp 2829–2851

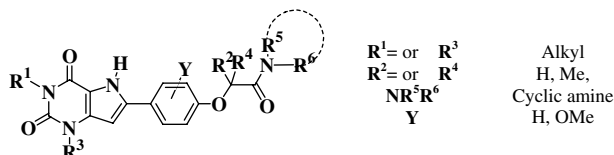
Ronald Palin,* John K. Clark, Louise Evans, Andrea K. Houghton, Philip S. Jones, Alan Prosser, Grant Wishart and Kazuya Yoshiizumi



1-, 3- and 8-substituted-9-deazaxanthines as potent and selective antagonists at the human A_{2B} adenosine receptor

pp 2852–2869

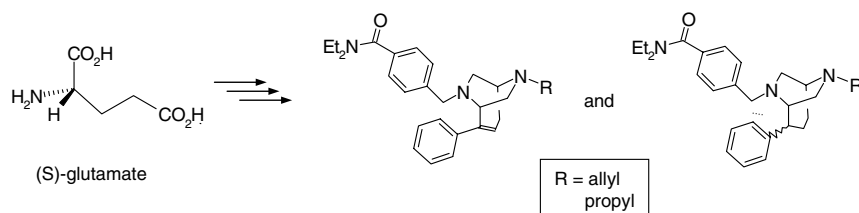
Angela Stefanachi, Jose Manuel Brea, Maria Isabel Cadavid, Nuria B. Centeno, Cristina Esteve, Maria Isabel Loza, Ana Martinez, Rosa Nieto, Enrique Raviña, Ferran Sanz, Victor Segarra, Eddy Sotelo, Bernat Vidal and Angelo Carotti*



Synthesis and pharmacological evaluation of bicyclic SNC80 analogues with separated benzhydryl moiety

pp 2870–2885

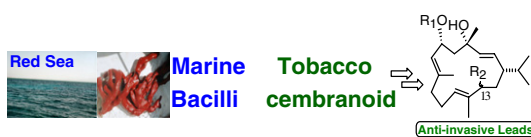
Bettina Jung, Werner Englberger, Roland Fröhlich, Dirk Schepmann, Kirstin Lehmkuhl and Bernhard Wünsch*



Biocatalytic and semisynthetic optimization of the anti-invasive tobacco (1S,2E,4R,6R,7E,11E)-2,7,11-cembratriene-4,6-diol

pp 2886–2893

Khalid A. El Sayed,* Surat Laphookhieo, Hany N. Baraka, Muhammad Yousaf, Anne Hebert, Danielle Bagaley, Frederick A. Rainey, A. Muralidharan, Shibu Thomas and Girish V. Shah



pp 2894–2902

$R = O, NH, N-Ar$

$R1 = H$
 $= 4-OH$
 $= 4-OH, 3-OCH_3$

pp 2903–2911

[illegible]

pp 2912–2920

Figure 1 Chemical structures of **1** and **2**. **1** is a steroid with a complex sugar chain at C-3. **2** is a steroid with a complex sugar chain at C-3. **3** is a steroid with a complex sugar chain at C-3. **4** is a steroid with a complex sugar chain at C-3.

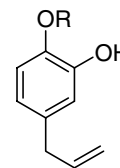
pp 2921–2931

5-Fluorouridine-SPIONs were characterized and evaluated as anti-cancer agents using human melanoma cells. The 5-fluorouridine-SPION **6S** with an optimized ester linker was taken up by cells and proved to be efficient anti-tumor agent.

Inhibitory property of the *Piper betel* phenolics against photosensitization-induced biological damages pp 2932–2938

Soumyaditya Mula, Debashish Banerjee, Birija S. Patro, Sayanti Bhattacharya, Atanu Barik, Sandip K. Bandyopadhyay and Subrata Chattopadhyay*

APC and CHV prevented the photosensitized-induced lipid peroxidation of rat liver mitochondria. The better efficacy of APC correlated with its higher reactivity with $^1\text{O}_2$. APC was also found to protect the mouse fibroblast L929 cells against photo-toxicity of methylene blue + UVA light.



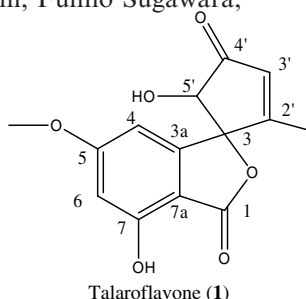
APC: R = H; CHV: R = Me

1-Deoxyrubralactone, a novel specific inhibitor of families X and Y of eukaryotic DNA polymerases from a fungal strain derived from sea algae

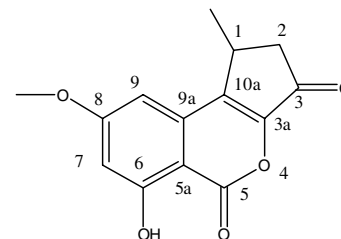
pp 2939–2944

Mitsuki Naganuma, Masayuki Nishida, Kouji Kuramochi, Fumio Sugawara, Hiromi Yoshida and Yoshiyuki Mizushima*

Talaroflavone (1) and 1-deoxyrubralactone[6-hydroxy-8-methoxy-1-methyl-1,2,3a,9b-tetrahydrocyclopenta[*c*]isochromene-3,5-dione] (2), known and novel polyketide family compounds, respectively, were isolated from fungal strain derived from sea algae, and selectively inhibited the activity of families X and Y of eukaryotic DNA polymerases.



Talaroflavone (1)

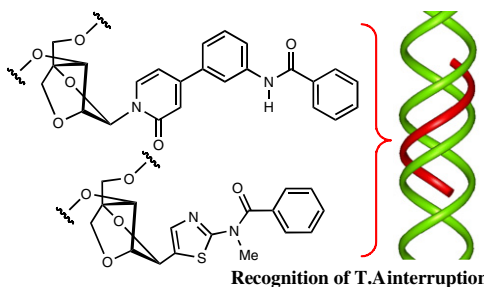


1-Deoxyrubralactone (2)

Recognition of T·A interruption by 2',4'-BNAs bearing heteroaromatic nucleobases through parallel motif triplex formation

pp 2945–2954

Satoshi Obika, Hiroyasu Inohara, Yoshiyuki Hari and Takeshi Imanishi*

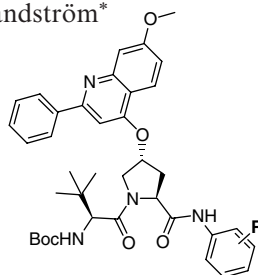


Recognition of T·A interruption

Hepatitis C virus NS3 protease inhibitors comprising a novel aromatic P_1 moiety

pp 2955–2967

Robert Rönn, Anna Lampa, Shane D. Peterson, Thomas Gossas, Eva Åkerblom, U. Helena Danielson, Anders Karlén and Anja Sandström*



R = COOH, CONHSO₂R'



Lead identification of acetylcholinesterase inhibitors–histamine H₃ receptor antagonists from molecular modeling

pp 2968–2973

Scott D. Bembenek,* John M. Keith, Michael A. Letavic, Richard Apodaca, Ann J. Barbier, Lisa Dvorak, Leah Aluisio, Kirsten L. Miller, Timothy W. Lovenberg and Nicholas I. Carruthers

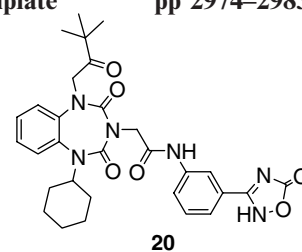
The proposed binding mode for a novel acetylcholinesterase inhibitor–histamine H₃ receptor antagonist is shown in the active site of acetylcholinesterase.

**Achiral, selective CCK₂ receptor antagonists based on a 1,3,5-benzotriazepine-2,4-dione template**

pp 2974–2983

John Spencer, John Gaffen, Eric Griffin, Elaine A. Harper, Ian D. Linney, Iain M. McDonald,* Sonia P. Roberts, Mark E. Shaxted, Trushar Adatia and Alan Bashall

Novel, achiral 1*H*-1,3,5-benzotriazepine-2,4(3*H*,5*H*)-diones have been prepared and structurally characterized. These compounds are potent CCK₂ receptor antagonists that display a high degree of selectivity over CCK₁ receptors.

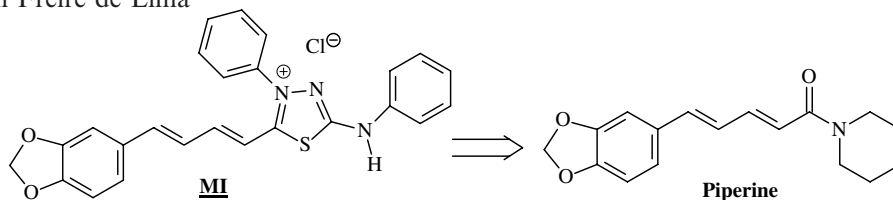


pK_i = 8.92 (hCCK₂)
pK_i = 6.50 (hCCK₁)

**Novel 1,3,4-thiadiazolium-2-phenylamine chlorides derived from natural piperine as trypanocidal agents: Chemical and biological studies**

pp 2984–2991

Welisson da Silva Ferreira, Leonardo Freire-de-Lima, Víctor Barbosa Saraiva, Frederico Alisson-Silva, Lucia Mendonça-Previato, José Osvaldo Previato, Aurea Echevarria and Marco Edilson Freire de Lima*

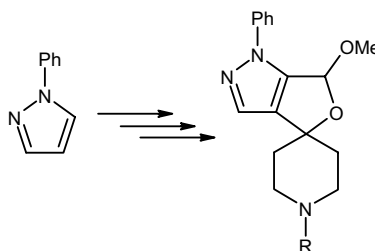


Synthesis and evaluation of trypanocidal activity of nine new 1,3,4-thiadiazolium-2-phenylamine chlorides derived from natural amide piperine are reported. Among them **MI** showed potent trypanocidal activity with reduced toxicity to macrophages.

Synthesis and structure–affinity relationships of novel spirocyclic σ receptor ligands with fuopyrazole structure

pp 2992–3001

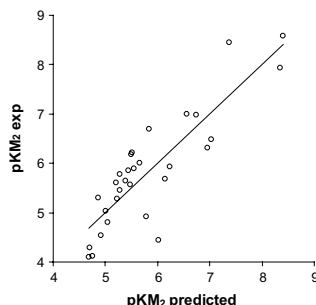
Torsten Schläger, Dirk Schepmann, Ernst-Ulrich Würthwein and Bernhard Wunsch*



Docking analyses on human muscarinic receptors: Unveiling the subtypes peculiarities in agonists binding

pp 3049–3058

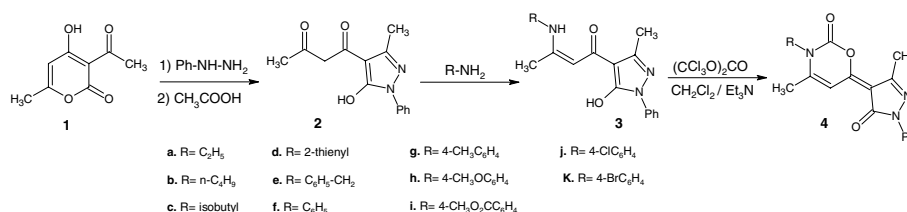
Giulio Vistoli,* Alessandro Pedretti, Silvia Dei, Serena Scapecchi, Cristina Marconi and Maria Novella Romanelli



Synthesis and in silico biological activity evaluation of new N-substituted pyrazolo-oxazin-2-one systems

pp 3059–3066

Nora Benaamane, Bellara Nedjar-Kolli,* Yamina Bentarzi, Lamouri Hammal, Athina Geronikaki,* Phaedra Eleftheriou and Alexey Lagunin

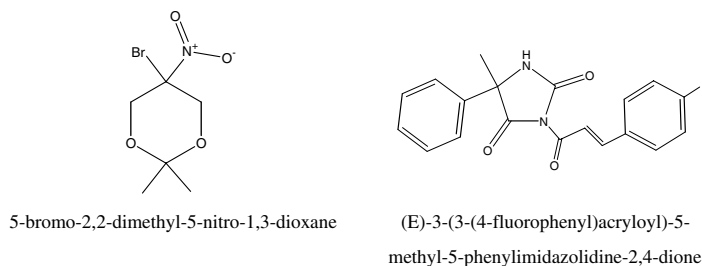


Eleven N-substituted pyrazolo-1,3-oxazin-2-ones were synthesised and their biological activity spectra were predicted by computer program PASS. COX-1 inhibitory activity of the compounds was confirmed by experimental data.

Disruption of Kv1.1 N-type inactivation by novel small molecule inhibitors (disinactivators)

pp 3067–3075

Qiang Lu, Joseph Peevey, Flora Jow, Michael M. Monaghan, Grace Mendoza, Howard Zhang, Jerome Wu, Callain Y. Kim, James Bicksler, Lynn Greenblatt, Stephen S. Lin, Wayne Childers and Mark R. Bowlby*



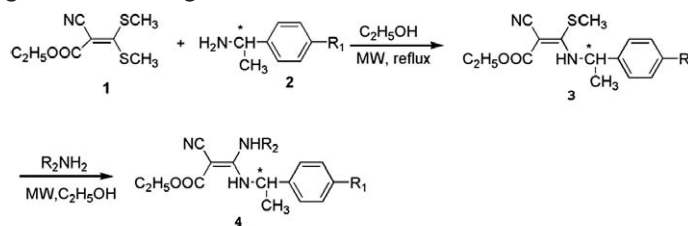
Representatives of two series that directly disrupt inactivation of the Kv1.1/β1 complex.

Synthesis and antiviral activities of novel chiral cyanoacrylate derivatives with (E) configuration

pp 3076–3083

Zhuo Chen, Xianyou Wang, Baoan Song,* Hua Wang, Pinaki S. Bhadury, Kai Yan, Huiping Zhang, Song Yang, Linhong Jin, Deyu Hu, Wei Xue, Song Zeng and Jun Wang

Nucleophilic attack of the appropriate amine under microwave irradiation on 3 generates the chiral (E) isomers of title compound 4 exhibiting weak to good anti-TMV bioactivity, (R)-4p showing significant enhancement of disease resistance in tobacco leaves.



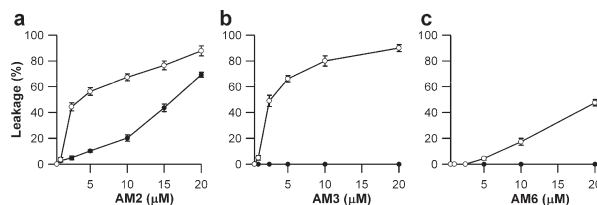
R₁: F, Br, H; R₂ = benzylamino; 2-nitrophenylamino; 3-nitrophenylamino; 2, 4-dinitrophenylamino; 4-trifluoromethylphenylamino; 6-nitrobenzothiazol-2-amino; 4-methylbenzothiazole-2-amino.



Effects of lipid constituents on membrane-permeabilizing activity of amphidinols

pp 3084–3090

Nagy Morsy, Toshihiro Houdai, Keiichi Konoki, Nobuaki Matsumori,
Tohru Oishi and Michio Murata*

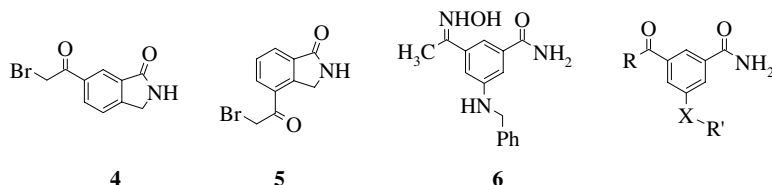


Among amphidinols tested, only AM2 revealed membrane-permeabilizing activity to unsaturated lipid membrane.

**New anti-viral drugs for the treatment of the common cold**

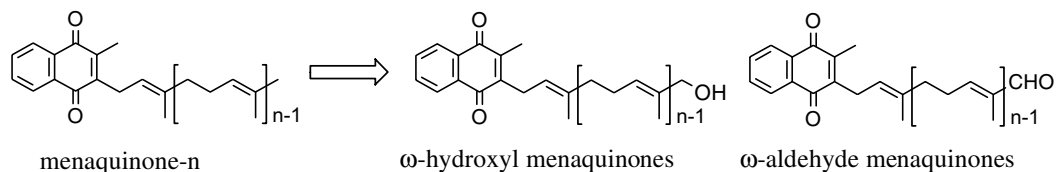
pp 3091–3107

Caterina Maugeri,* Maria A. Alisi, Claudia Apicella, Luciano Cellai, Patrizia Dragone,
Elena Fioravanzo, Saverio Florio, Guido Furlotti, Giorgina Mangano, Rosella Ombrato,
Renzo Luisi, Raffaello Pompei, Vito Rincicotti, Vincenzo Russo, Marco Vitiello and Nicola Cazzolla

**Design and synthesis of biologically active analogues of vitamin K₂: Evaluation of their biological activities with cultured human cell lines**

pp 3108–3117

Yoshitomo Suhara, Yoshihisa Hirota, Kimie Nakagawa, Maya Kamao,
Naoko Tsugawa and Toshio Okano*

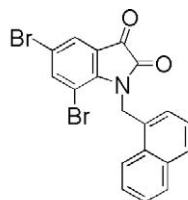


Novel ω-oxygenated vitamin K₂ analogues were efficiently synthesized and their biological activities were evaluated.

**N-Phenethyl and N-naphthylmethyl isatins and analogues as in vitro cytotoxic agents**

pp 3118–3124

Lidia Matesic,* Julie M. Locke, John B. Bremner, Stephen G. Pyne,
Danielle Skropeta, Marie Ranson and Kara L. Vine

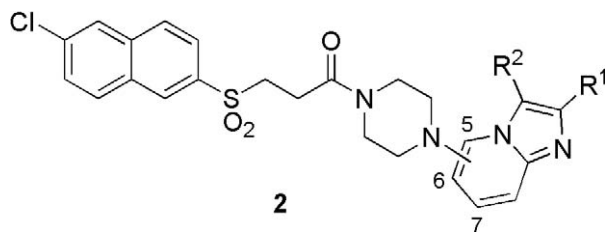


IC₅₀ = 0.19 μM (U937 human lymphoma cells)

Discovery of piperazinylimidazo[1,2-*a*]pyridines as novel S4 binding elements for orally active Factor Xa inhibitors

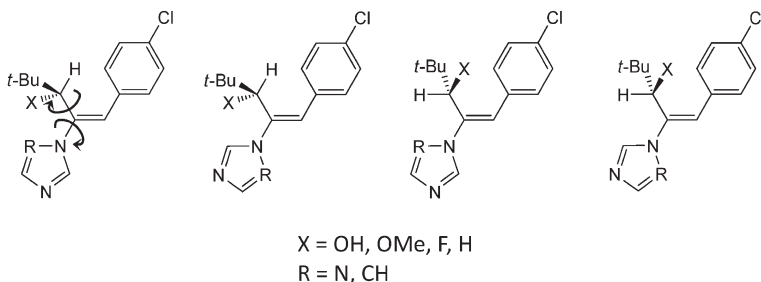
pp 3125–3140

Yasuhiro Imaeda,* Tetsuji Kawamoto, Mamoru Tobisu, Noriko Konishi, Katsuhiko Hiroe, Masaki Kawamura, Toshimasa Tanaka and Keiji Kubo

A new series of piperazinylimidazo[1,2-*a*]pyridines **2** as orally active FXa inhibitors are reported.**Structure–activity relationship of uniconazole, a potent inhibitor of ABA 8'-hydroxylase, with a focus on hydrophilic functional groups and conformation**

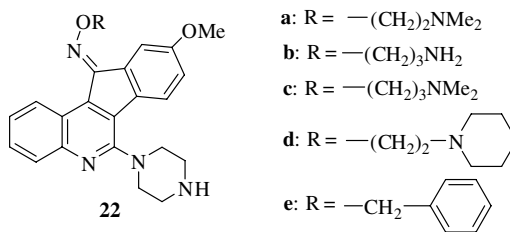
pp 3141–3152

Yasushi Todoroki,* Kyotaro Kobayashi, Hidetaka Yoneyama, Saori Hiramatsu, Mei-Hong Jin, Bunta Watanabe, Masaharu Mizutani and Nobuhiro Hirai

**Synthesis and antiproliferative evaluation of certain indeno[1,2-*c*]quinoline derivatives**

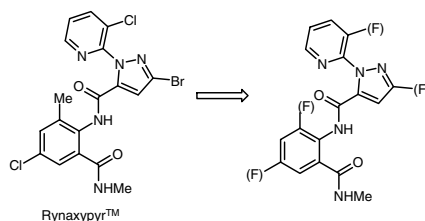
pp 3153–3162

Chih-Hua Tseng, Yeh-Long Chen, Pei-Jung Lu,* Chia-Ning Yang and Cherng-Chyi Tzeng*

**Synthesis of insecticidal fluorinated anthranilic diamides**

pp 3163–3170

David A. Clark,* George P. Lahm, Ben K. Smith, James D. Barry and Don G. Clagg

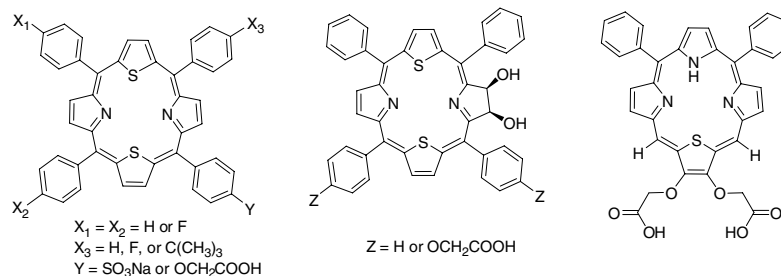


Fluorinated analogs of Rynaxypyr™ have been prepared in a search for plant-systemic insecticides for the control of Hemiptera.

Core-modified porphyrins. Part 6: Effects of lipophilicity and core structures on physicochemical and biological properties in vitro

pp 3171–3183

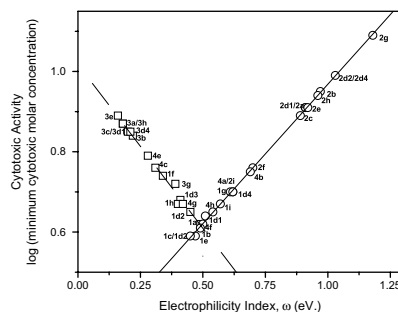
Ethel J. Ngen, Thalia S. Daniels, Rajesh S. Murthy, Michael R. Detty and Youngjae You*



Structure–reactivity relationships for electrophilic sugars in interaction with nucleophilic biological targets

pp 3184–3190

Paola R. Campodónico* and Renato Contreras*

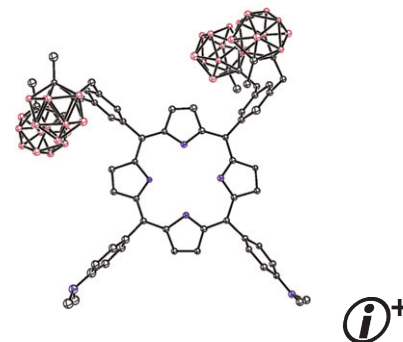


Synthesis and in vitro properties of trimethylamine- and phosphonate-substituted carboranylporphyrins for application in BNCT

pp 3191–3208

Michael W. Easson, Frank R. Fronczek,* Timothy J. Jensen and M. Graça H. Vicente*

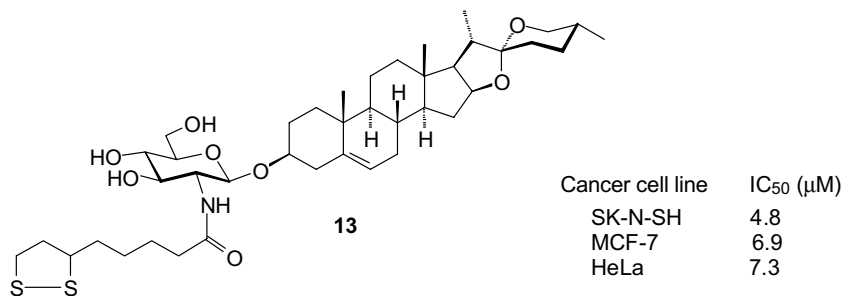
The synthesis of *closo*-carboranylporphyrins containing either amine or phosphonic acid functionalities is described. These compounds show no dark cytotoxicity up to 100 μM , are readily taken up by human glioma T98G cells, deliver therapeutic amounts of boron to these cells, and localize preferentially within the lysosomes.



Synthesis and cytotoxic activity of diosgenyl saponin analogues

pp 3209–3217

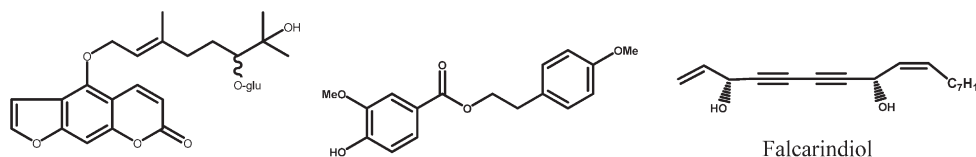
Matthew J. Kaskiw, Mary Lynn Tassotto, John Th'ng and Zi-Hua Jiang*



Novel coumarin glycoside and phenethyl vanillate from *Notopterygium forbesii* and their binding affinities for opioid and dopamine receptors

pp 3218–3223

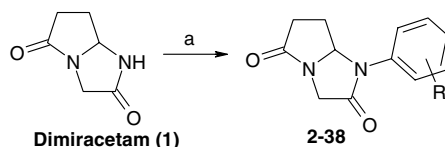
Zhongze Ma, Wei Xu, Lee-Yuan Liu-Chen and David Y. W. Lee*



New coumarin glycoside and phenethyl vanillate, along with 17 known compounds, were isolated from *Notopterygium forbesii*. Falcarindiol showed the highest binding affinities to the opioid and dopamine receptors.

Synthesis and biological evaluation of novel dimiracetam derivatives useful for the treatment of neuropathic pain

pp 3224–3232

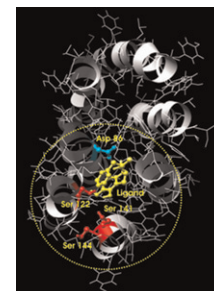
Carlo Farina, Stefania Gagliardi, Carla Ghelardini, Marisa Martinelli,*
Monica Norcini, Carlo Parini, Paola Petrillo and Silvano Ronzoni

Synthesis, dopaminergic profile, and molecular dynamics calculations of *N*-aralkyl substituted 2-aminoindans

pp 3233–3244

Sebastian A. Andujar, Biagina Migliore de Angel, Jaime E. Charris, Anita Israel, Heberto Suárez-Roca, Simon E. López, Maria R. Garrido, Elvia Victoria Cabrera, Gonzalo Visbal, Cecire Rosales, Fernando D. Suvire, Ricardo D. Enriz* and Jorge E. Angel-Guío*

N-[2-(4,5-Dihydroxyphenyl)-methyl-ethyl]-4,5-dihydroxy-2-aminoindan hydrobromide (**3**) demonstrated an inhibitory effect on dopaminergic-induced behavior and renal action. In contrast *N*-[2-(-methyl-ethyl)]-4,5-dihydroxy-2-aminoindan hydrobromide (**4**) produces an agonistic response. To better understand the experimental results we performed molecular dynamics simulations of two complexes: compound **3**/D₂DAR (dopamine receptor) and compound **4**/D₂DAR.

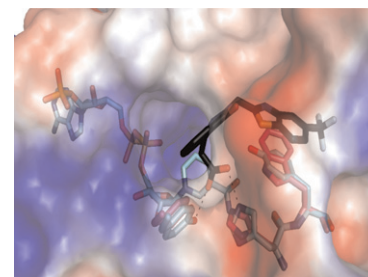


Inhibition of 3(17) α -hydroxysteroid dehydrogenase (AKR1C21) by aldose reductase inhibitors

pp 3245–3254

Urmi Dhagat, Satoshi Endo, Akira Hara and Ossama El-Kabbani*

Aldose reductase (AR) inhibitors were evaluated against 3(17) α -hydroxysteroid dehydrogenase (AKR1C21). Compounds that showed competitive inhibition patterns were modelled into the active site of AKR1C21 and the inhibitor-binding sites of the two enzymes were compared.

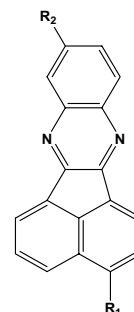


Novel nitroheterocyclic hypoxic markers for solid tumor: Synthesis and biological evaluation

pp 3255–3260

Weiping Zhu, Min Dai, Yufang Xu* and Xuhong Qian*

Several novel nitroheterocyclic compounds without 2-nitroimidazole as potential hypoxic markers were prepared and evaluated.



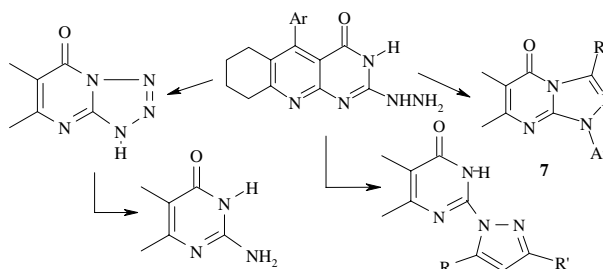
A1: R₁:NO₂, R₂:NO₂;
A2: R₁:NO₂, R₂:H;
A3: R₁:H, R₂:NO₂;

A4: R₁:N(CH₂CH₂)₂NCH₃, R₂:NO₂
A5: R₁:NHCH₂CH₂N(CH₃)₂, R₂:NO₂
A6: R₁:NH₂, R₂:NO₂

Synthesis, analgesic, anti-inflammatory, and antimicrobial activity of some novel pyrimido[4,5-*b*]quinolin-4-ones

pp 3261–3273

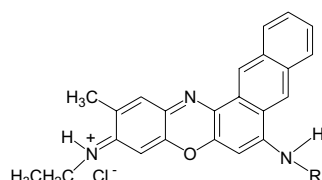
Abdel-Rahman B. A. El-Gazzar,* Mervat M. El-Enany and Mahmoud N. Mahmoud



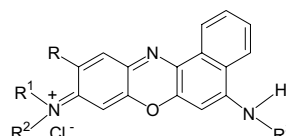
Synthesis of naphtho[2,3-*a*]phenoxazinium chlorides: Structure–activity relationships of these heterocycles and benzo[*a*]phenoxazinium chlorides as new antimicrobials

pp 3274–3282

Vânia H. J. Frade, Maria J. Sousa, João C. V. P. Moura and M. Sameiro T. Gonçalves*



R = H, (CH₂)₂Me, (CH₂)₃CO₂Et,
(CH₂)₃OH, (CH₂)₃NH₂, (CH₂)₃Cl

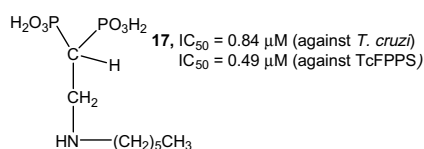


R, R¹, R² = H, Me, Et; R³ = H, (CH₂)_nCO₂Et, (CH₂)_nOH,
(CH₂)_nNH₂, (CH₂)_nCl; n = 2, 3

Synthesis and biological evaluation of 2-alkylaminoethyl-1,1-bisphosphonic acids against *Trypanosoma cruzi* and *Toxoplasma gondii* targeting farnesyl diphosphate synthase

pp 3283–3290

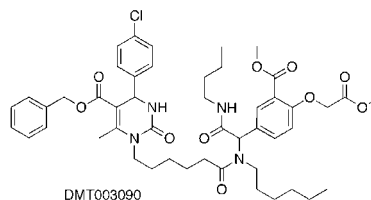
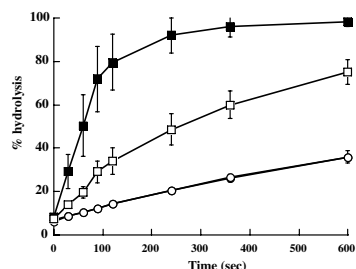
Sergio H. Szajnman, Guadalupe E. García Liñares, Zhu-Hong Li, Cuiying Jiang, Melina Galizzi, Esteban J. Bontempi, Marcela Ferella, Silvia N. J. Moreno, Roberto Docampo and Juan B. Rodriguez*



Pyrimidinone-peptoid hybrid molecules with distinct effects on molecular chaperone function and cell proliferation

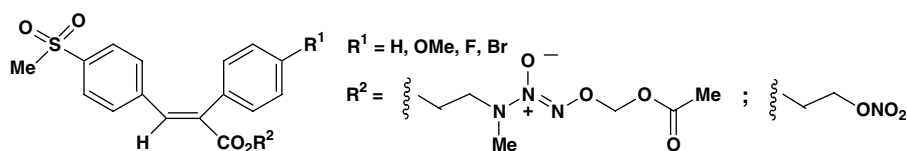
pp 3291–3301

Christine M. Wright, Raj J. Chovatiya, Nora E. Jameson, David M. Turner, Guangyu Zhu, Stefan Werner, Donna M. Huryn, James M. Pipas, Billy W. Day, Peter Wipf and Jeffrey L. Brodsky*

**Diazen-1-ium-1,2-diylated and nitrooxyethyl nitric oxide donor ester prodrugs of anti-inflammatory (*E*)-2-(aryl)-3-(4-methanesulfonylphenyl)acrylic acids: Synthesis, cyclooxygenase inhibition, and nitric oxide release studies**

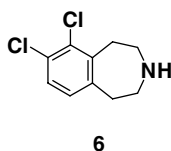
pp 3302–3308

Khaled R. A. Abdellatif, Morshed Alam Chowdhury, Ying Dong, Qiao-Hong Chen and Edward E. Knaus*

**Synthesis and structure–activity relationships of a series of benzazepine derivatives as 5-HT_{2C} receptor agonists**

pp 3309–3320

Itsuro Shimada,* Kyoichi Maeno, Yutaka Kondoh, Hidetaka Kaku, Keizo Sugawara, Yasuharu Kimura, Ken-ichi Hatanaka, Yuki Naitou, Fumikazu Wanibuchi, Shuichi Sakamoto and Shin-ichi Tsukamoto

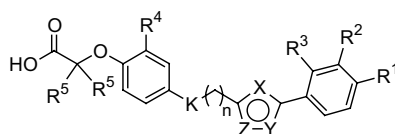


A novel series of benzazepine derivatives was prepared, and their binding affinities for 5-HT_{2C}, 5-HT_{2A}, and 5-HT_{2B} receptors were evaluated. Synthesis and structure–activity relationships, including in vivo evaluation, are discussed.

Synthesis and structure–activity relationships of thiadiazole-derivatives as potent and orally active peroxisome proliferator-activated receptors α/δ dual agonists

pp 3321–3341

Lan Shen, Yan Zhang, Aihua Wang, Ellen Sieber-McMaster, Xiaoli Chen, Patricia Pelton, June Z. Xu, Maria Yang, Peifang Zhu, Lubing Zhou, Michael Reuman, Zhiyong Hu, Ronald Russell, Alan C. Gibbs, Hamish Ross, Keith Demarest, William V. Murray and Gee-Hong Kuo*

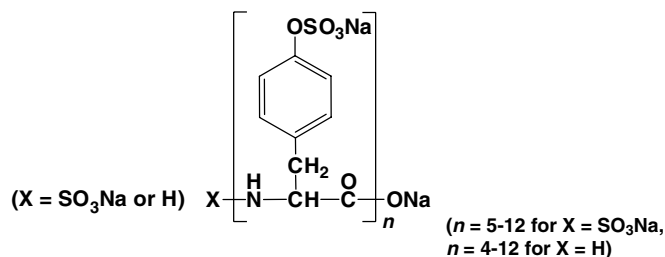


Using PPAR δ selective agonist (GW501516) as the lead, we conducted the structure–activity relationship study and identified the [1,2,4]thiadiazole-derivatives as potent and orally active peroxisome proliferators-activated receptors α/δ dual agonists.

Oligo(tyrosine sulfate)s as heparin pentasaccharide mimic: Evaluation by surface noncovalent affinity mass spectrometry

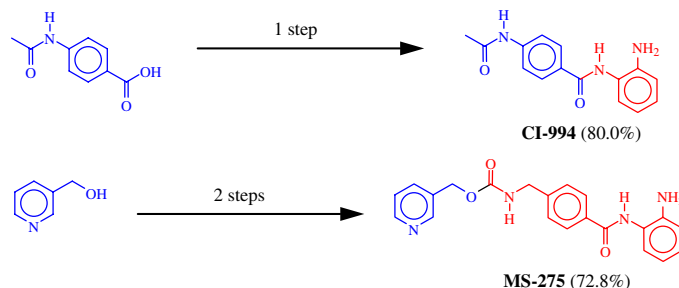
pp 3342–3351

Miyuki Yamaguchi, Tsukasa Ohmori, Yoichi Sakata and Masaaki Ueki*


Improved synthesis of histone deacetylase inhibitors (HDIs) (MS-275 and CI-994) and inhibitory effects of HDIs alone or in combination with RAMBAs or retinoids on growth of human LNCaP prostate cancer cells and tumor xenografts

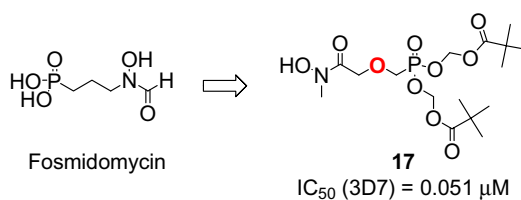
pp 3352–3360

Lalji K. Gediya, Aashvini Belosay, Aakanksha Khandelwal, Puranik Purushottamachar and Vincent C. O. Njar*


Synthesis of β - and γ -oxa isosteres of fosmidomycin and FR900098 as antimalarial candidates

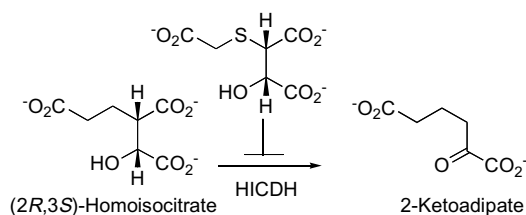
pp 3361–3371

Timothy Haemers, Jochen Wiesner, Dirk Gießmann, Thomas Verbrugghen, Ulrik Hillaert, Regina Ortmann, Hassan Jomaa, Andreas Link, Martin Schlitzer and Serge Van Calenbergh*


Thiahomoisocitrate: A highly potent inhibitor of homoisocitrate dehydrogenase involved in the α -amino adipate pathway

pp 3372–3376

Takashi Yamamoto and Tadashi Eguchi*

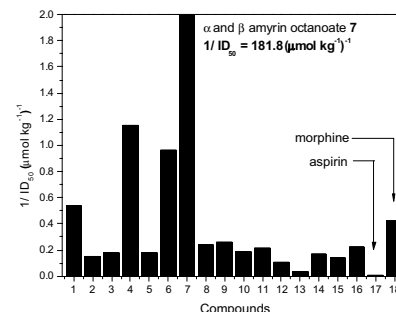
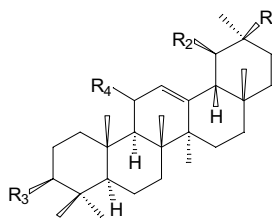


Synthetic derivatives of the α - and β -amyrin triterpenes and their antinociceptive properties

pp 3377–3386

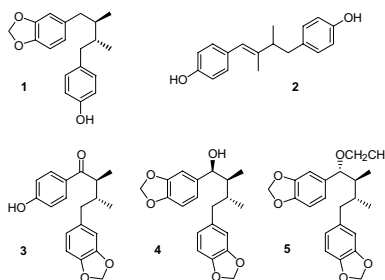
Cristian Soldi, Moacir Geraldo Pizzolatti,* Ana Paula Luiz, Rodrigo Marcon, Flavia Carla Meotti, Leticia Adelia Miotto and Adair R. S. Santos

A series of α - and β -amyrin triterpene derivatives were prepared and screened for antinociceptive activity using the acetic acid pain model. The α - and β -amyrin octanoate **7** derivatives were the most active substance showing an effect **427** times more potent than the well-known drug morphine in the pain model tested.

**Structure and estrogenic activity of new lignans from *Iryanthera lancifolia***

pp 3387–3394

Dulce Mesa-Siverio, Rubén P. Machín, Ana Estévez-Braun,* Ángel. G. Ravelo* and Olga Lock

**QSAR modeling of the rodent carcinogenicity of nitrocompounds**

pp 3395–3407

Aliuska Morales Helguera, M. Natália D. S. Cordeiro, Miguel Ángel Cabrera Pérez, Robert D. Combes and Maykel Pérez González*

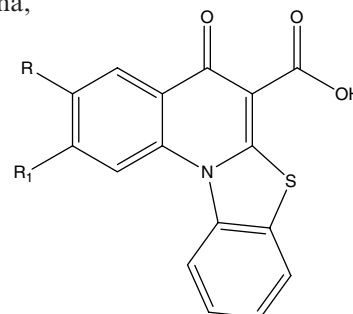
Chemical carcinogenicity is of primary interest, because it drives much of the current regulatory actions regarding new and existing chemicals. This paper reports a QSAR study for predicting carcinogenic potency of nitrocompounds. Several different theoretical molecular descriptors, calculated only on the basis of knowledge of the molecular structure and an efficient variable selection procedure led to models with satisfactory predictive ability.

**Antimycobacterial activities of novel 2-(sub)-3-fluoro/nitro-5,12-dihydro-5-oxobenzothiazolo[3,2-a]quinoline-6-carboxylic acid**

pp 3408–3418

Murugesan Dinakaran, Palaniappan Senthilkumar, Perumal Yogeeswari, Arnab China, Valakunja Nagaraja and Dharmarajan Sriram*

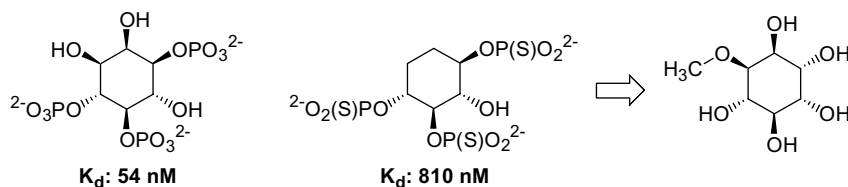
Various 2-(sub)-3-fluoro/nitro-5,12-dihydro-5-oxobenzothiazolo[3,2-a]quinoline-6-carboxylic acid derivatives were synthesized from 2-aminothiophenol by a five-step reaction, and evaluated for in-vitro and in-vivo antimycobacterial activities. Compound **7I** was found to be the most active compound in vitro with MIC of 0.18 and 0.08 μ M against MTB and MTR-TB, respectively, and **7I** decreased the bacterial load in lung and spleen tissues with 2.78 and 3.12 – log 10 protections, respectively, at the dose of 50 mg/kg body weight.



Deoxygenated phosphorothioate inositol phosphate analogs: Synthesis, phosphatase stability, and binding affinity

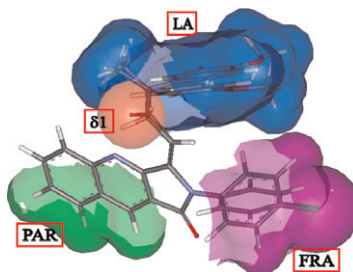
pp 3419–3427

Xiaodan Liu, Emily C. Moody, Stephen S. Hecht and Shana J. Sturla*


Synthesis and structure–activity relationship studies in peripheral benzodiazepine receptor ligands related to alpidem

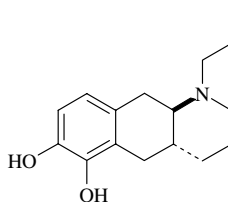
pp 3428–3437

Andrea Cappelli,* Germano Giuliani, Salvatore Valenti, Maurizio Anzini, Salvatore Vomero, Gianluca Giorgi, Cristiana Sogliano, Elisabetta Maciocco, Giovanni Biggio and Alessandra Concas


A novel synthesis and pharmacological evaluation of a potential dopamine D₁/D₂ agonist: 1-Propyl-1,2,3,4,4a,5,10,10a-octahydrobenzo[g]quinoline-6,7-diol

pp 3438–3444

Danyang Liu, Durk Dijkstra,* Jan B. de Vries and Håkan V. Wikström

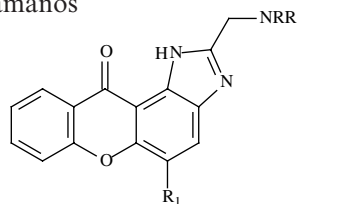


1-Propyl-1,2,3,4,4a,5,10,10a-octahydrobenzo[g]quinoline-6,7-diol is an extremely potent dopamine receptor agonist. As a catecholamine, this compound is comparable to apomorphine for the treatment of Parkinson's disease.

Design, synthesis and cell growth inhibitory activity of a series of novel aminosubstituted xantheno[1,2-d]imidazoles in breast cancer cells

pp 3445–3455

Ioannis K. Kostakis, Nicole Pouli, Panagiotis Marakos,* Olga Ch. Kousidou, Andreas Roussidis, George N. Tzanakakis and Nikos K. Karamanos



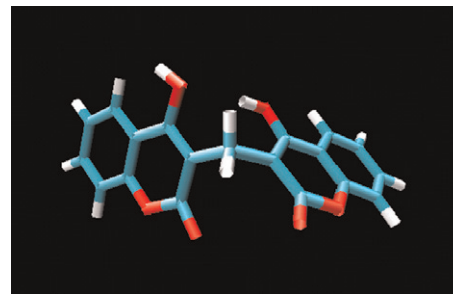
R₁ = H, NO₂, NHCOCH₂NRR
 NRR = N(CH₃)₂, N(C₂H₅)₂, N(CH₂)₄, N(CH₂)₅

**3D-QSAR CoMFA studies on bis-coumarine analogues as urease inhibitors:
A strategic design in anti-urease agents**

pp 3456–3461

Zaheer-ul-Haq, M. Arif Lodhi, Sarfraz Ahmad Nawaz, Sajid Iqbal, Khalid Mohammed Khan, Bernd M. Rode, Atta-ur-Rahman and M. Iqbal Choudhary*

A 3D-QSAR study has been performed on thirty (30) bis-coumarine derivatives to correlate their chemical structures with their observed urease inhibitory activity. To generate the 3D-QSAR model, comparative molecular field analysis (CoMFA) method was applied. Significant q^2 (0.558) and r^2 (0.992) values were obtained and are discussed in the manuscript.


**OTHER CONTENTS****Corrigendum**

p3462

Summary of instructions to authors

p I

*Corresponding author

 Supplementary data available via ScienceDirect

COVER

A deoxygenated phosphorothioate inositol phosphate analog binds to the inositol 1,4,5-trisphosphate [Ins(1,4,5)P₃] receptor and is resistant to metabolism. Figure was created using X-ray data downloaded from the protein data bank from the following publication: Bosanac, I., Alattia, J. R., Mal, T. K., Chan, J., Talarico, S., Tong, F. K., Tong, K. I., Yoshikawa, F., Furuichi, T., Iwai, M., Michikawa, T., Mikoshiba, K., Ikura, M. (2002) Structure of the inositol 1,4,5-trisphosphate receptor binding core in complex with its ligand. *Nature* 420: 696–700 [Liu, X.; Moody, E. C.; Hecht, S. S.; Sturla, S. J. *Bioorg. Med. Chem.* **2008**, 16, 3429–3429].

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