

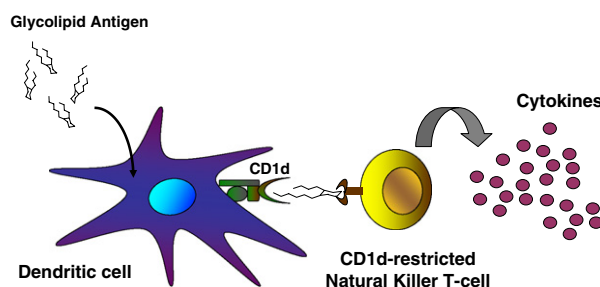
Contents

REVIEW

Glycolipids as immunostimulating agents

Douglass Wu, Masakazu Fujio and Chi-Huey Wong*

pp 1073–1083

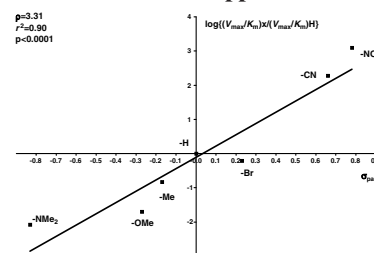
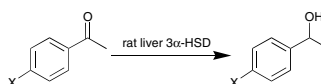


ARTICLES

Electronic effects of *para*-substitution on acetophenones in the reaction of rat liver 3 α -hydroxysteroid dehydrogenase

Koji Uwai,* Noboru Konno, Yuka Yasuta and Mitsuhiro Takeshita*

pp 1084–1089



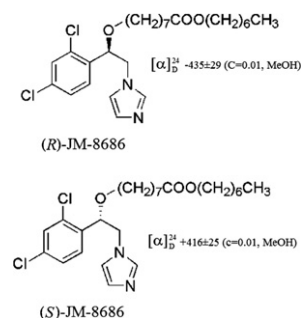
We report the substituent effects on the mechanism of reduction of acetophenone derivatives that were contained in the number of the structure of the drug, using rat liver 3 α -HSD.

Asymmetric synthesis and stereochemical structure–activity relationship of (*R*)- and (*S*)-8-[1-(2,4-dichlorophenyl)-2-imidazol-1-yl-ethoxy] octanoic acid heptyl ester, a potent inhibitor of allene oxide synthase

Keimei Oh,* Yoichiro Shimura, Kyoko Ishikawa, Yudai Ito, Tadao Asami, Noboru Murofushi and Yuko Yoshizawa

pp 1090–1095

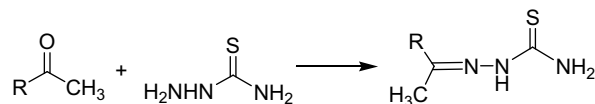
The preparation of both enantiomers of 8-[1-(2,4-dichlorophenyl)-2-imidazol-1-yl-ethoxy] octanoic acid heptyl ester (JM-8686) has been achieved. The inhibitory activity and binding affinity of both enantiomers toward allene oxide synthase are described.



1-(1-Arylethylidene)thiosemicarbazide derivatives: A new class of tyrosinase inhibitors

pp 1096–1102

Jinbing Liu, Wei Yi, Yiqian Wan, Lin Ma and Huacan Song*

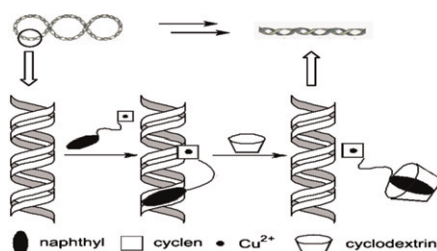


A series of 1-(1-arylethylidene)thiosemicarbazide compounds and their analogues were synthesized and characterized by ^1H NMR, MS. Their tyrosinase inhibitory activities were investigated by an assay based on the catalyzing ability of tyrosinase for the oxidation of L-DOPA, comparing with 4-methoxycinnamic acid and arbutin.

DNA cleavage by novel copper (II) complex and the role of β -cyclodextrin in promoting cleavage

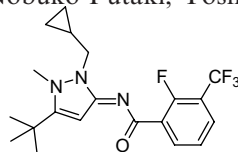
pp 1103–1110

Yu Huang, Qiao-Sen Lu, Ji Zhang, Zhong-Wei Zhang, Yu Zhang, Shan-Yong Chen, Kun Li, Xin-Yu Tan, Hong-Hui Lin* and Xiao-Qi Yu*

**Imine derivatives as new potent and selective CB₂ cannabinoid receptor agonists with an analgesic action**

pp 1111–1124

Hiroshi Ohta,* Tomoko Ishizaka, Makoto Tatsuzuki, Mitsukane Yoshinaga, Izumi Iida, Tomomi Yamaguchi, Yasumitsu Tomishima, Nobuko Futaki, Yoshihisa Toda and Shuji Saito

**6b** CB₂ IC₅₀ = 2.9 nM

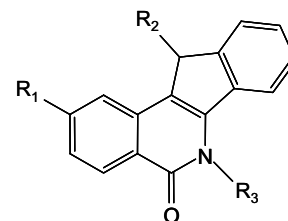
Compound **6b** (CBS0550) had high affinity for the human CB₂ receptor (CB₂ IC₅₀ = 2.9 nM, EC₅₀ = 1.8 nM, E_{max} = 85%), and orally administered compound **6b** significantly reversed mechanical hyperalgesia in the Randall–Selitto model of inflammatory pain in rats.

Indeno[1,2-*c*]isoquinolines as enhancing agents on all-*trans* retinoic acid-mediated differentiation of human myeloid leukemia cells

pp 1125–1132

Seung Hyun Kim, Sang Mi Oh, Ju Han Song, Daeho Cho, Quynh Manh Le, Suh-Hee Lee, Won-Jea Cho and Tae Sung Kim*

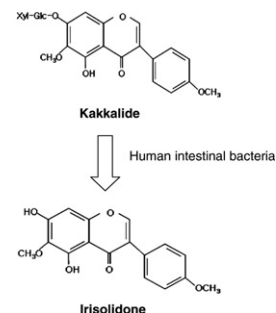
Acute myelocytic leukemia may eventually be treated with agents that induce terminal differentiation. In this study we investigated a possible enhancement of indeno[1,2-*c*]isoquinolines on all-*trans* retinoic acid-induced differentiation of human myeloid leukemia cells.



Protective effect of irisolidone, a metabolite of kakkalide, against hydrogen peroxide induced cell damage via antioxidant effect

Kyoung Ah Kang, Rui Zhang, Mei Jing Piao, Dong Ok Ko, Zhi Hong Wang, Bum Joon Kim, Jae Woo Park, Hee Sun Kim, Dong Hyun Kim and Jin Won Hyun*

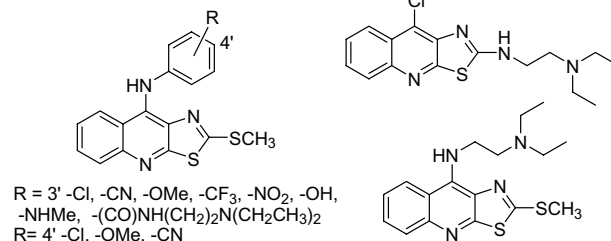
Irisolidone (a metabolite of kakkalide by intestinal bacteria) protected V79-4 cells against hydrogen peroxide induced damage via the activation of the ERK and AP-1 pathway.



Synthesis, cytotoxic evaluation, and DNA binding of novel thiazolo[5,4-*b*]quinoline derivatives

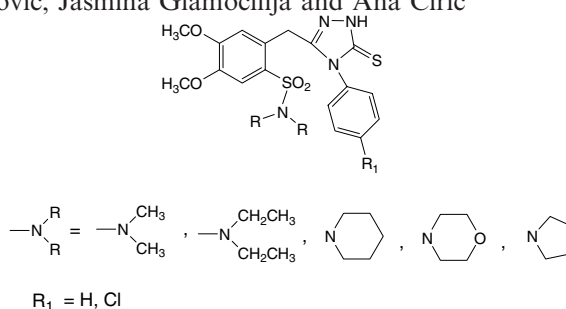
Marco A. Loza-Mejía, Karina Maldonado-Hernández, Fernando Rodríguez-Hernández, Rogelio Rodríguez-Sotres, Ignacio González-Sánchez, Angelina Quintero, José D. Solano and Alfonso Lira-Rocha*

Electron-withdrawing/electron-releasing substituents attached at 3' and 4'-position of anilino ring or alkylamino residues were relevant to the cytotoxicity and DNA intercalation of several novel thiazolo[5,4-*b*]quinoline derivatives.



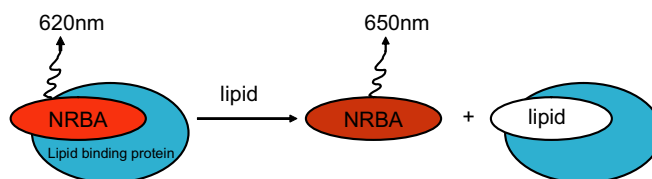
Sulfonamide-1,2,4-triazole derivatives as antifungal and antibacterial agents: Synthesis, biological evaluation, lipophilicity, and conformational studies

Iraj Rahavi Ezabadi, Charalabos Camoutsis,* Panagiotis Zoumpoulakis, Athina Geronikaki, Marina Soković, Jasmina Glamočilić and Ana Ćirić



Probing lipid- and drug-binding domains with fluorescent dyes

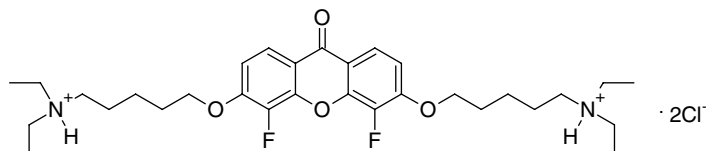
Shannon L. Black, Will A. Stanley, Fabian V. Filipp, Michelle Bhairo, Ashwani Verma, Oliver Wichmann, Michael Sattler, Matthias Wilmanns and Carsten Schultz*



Synthesis and heme-binding correlation with antimalarial activity of 3,6-bis-(ω -*N,N*-diethylaminoamyloxy)-4,5-difluoroxanthone

pp 1174–1183

Rozalia A. Dodean, Jane X. Kelly, David Peyton, Gary L. Gard, Michael K. Riscoe and Rolf W. Winter*

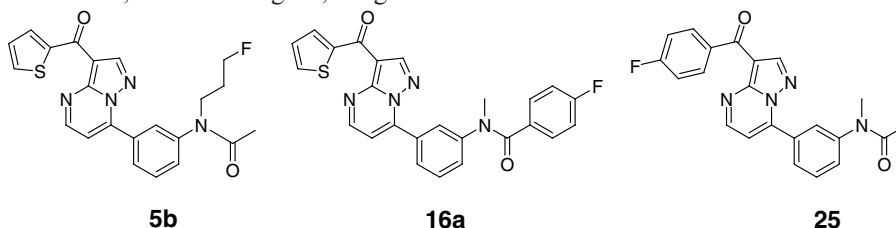


In this study, the synthesis and the heme-binding ability of a fluorine-containing xanthone are presented. 3,6-Bis-(ω -*N,N*-diethylaminoamyloxy)-4,5-difluoroxanthone was designed to have enhanced affinity to heme and increased antimalarial potency.

Synthesis of fluorine substituted pyrazolopyrimidines as potential leads for the development of PET-imaging agents for the GABA_A receptors

pp 1184–1194

Alexander Hoepping,* Michael Diekers, Winnie Deuther-Conrad, Matthias Scheunemann, Steffen Fischer, Achim Hiller, Florian Wegner, Jörg Steinbach and Peter Brust

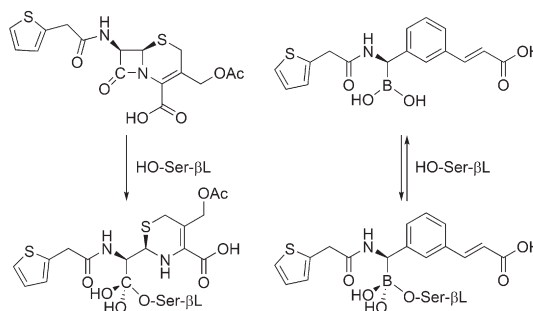


A series of potent fluorinated analogues of the pyrazolopyrimidine Indiplon has been synthesized and evaluated in vitro as potential agents for imaging the GABA_A receptor by means of positron emission tomography (PET).

Structure-based optimization of cephalothin-analogue boronic acids as β -lactamase inhibitors

pp 1195–1205

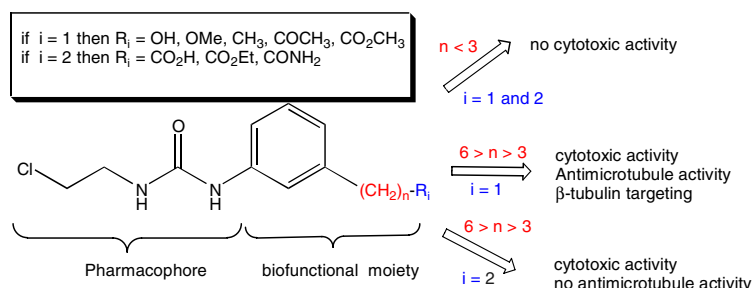
Stefania Morandi, Federica Morandi, Emilia Caselli, Brian K. Shoichet and Fabio Prati*



N-Phenyl-*N'*-(2-chloroethyl)ureas (CEUs) as potential antineoplastic agents. Part 3: Role of carbonyl groups in the covalent binding to the colchicine-binding site

pp 1206–1217

Emmanuel Moreau,* Sébastien Fortin, Jacques Lacroix, Alexandre Patenaude, Jean L. C. Rousseau and René C-Gaudreault*

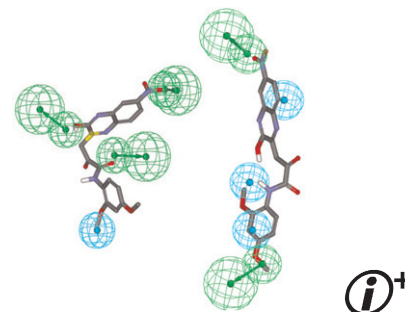


Discovery of new MurF inhibitors via pharmacophore modeling and QSAR analysis followed by in-silico screening

pp 1218–1235

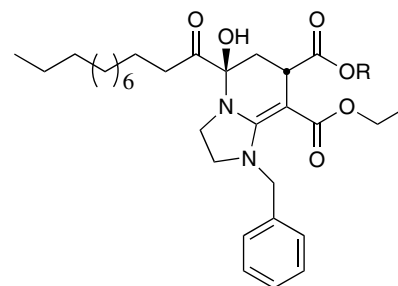
Mutasem O. Taha,* Naji Atallah, Amal G. Al-Bakri, Catherine Paradis-Bleau, Hiba Zalloum, Khaled S. Younis and Roger C. Levesque

In-silico-based discovery of new promising MurF inhibitors is reported.

**Imidazo[1,2-*a*]pyridine derivatives as inhibitors of TNF- α expression in T cells**

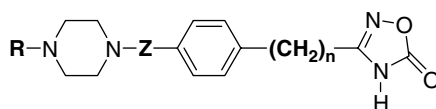
pp 1236–1241

Jan Rether, Gerhard Erkel, Timm Anke, Johan Bajtner and Olov Sterner*

A set of imidazo[1,2-*a*]pyridine derivatives prepared from the fungal metabolite podoscyphic acid have been evaluated for their ability to inhibit the inducible TNF- α promoter activity in T cells.**Design of new potent and selective secretory phospholipase A₂ inhibitors. Part 5: Synthesis and biological activity of 1-alkyl-4-[4,5-dihydro-1,2,4-[4*H*]-oxadiazol-5-one-3-ylmethylbenz-4'-yl(oil)] piperazines**

pp 1242–1253

Latifa Boukli, Mohamed Touaibia, Nadia Meddad-Belhabich, Atimé Djimdé, Chang-Ha Park, Jung-Joo Kim, Joo-Hyoung Yoon, Aazdine Lamouri and Françoise Heymans*

Z = CO, CH₂, deleted.

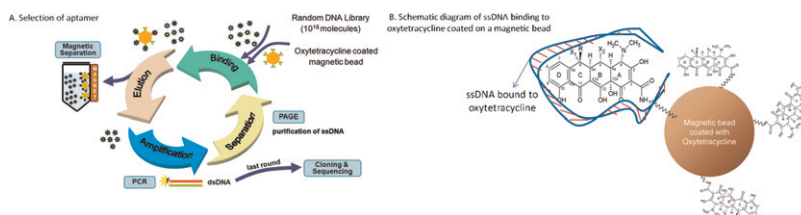
n = 0, 1, 2, 3.

R = alkyl chain.

ssDNA aptamers that selectively bind oxytetracycline

pp 1254–1261

Javed H. Niazi, Su Jin Lee, Yeon Seok Kim and Man Bock Gu*

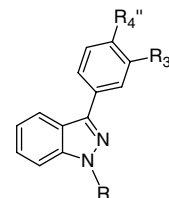


Synthesis and antiplatelet activity of ethyl 4-(1-benzyl-1*H*-indazol-3-yl)benzoate (YD-3) derivatives

pp 1262–1278

Hua-Sin Chen, Sheng-Chu Kuo, Che-Ming Teng, Fang-Yu Lee, Jih-Pyang Wang, Yu-Chun Lee, Chiung-Wen Kuo, Ching-Che Huang, Chin-Chung Wu* and Li-Jiau Huang*

YD-3 was used as a lead compound and a series of its derivatives were synthesized and evaluated for their selective anti-PAR4 activity. Through structure–activity relationship (SAR) study, we identified the important functional groups contributing to anti-PAR4 activity. Among them, compound **33** showed the most potent inhibitory effect on PAR4-mediated platelet aggregation, ATP release, and P-selectin expression. On the other hand, compound **83** exhibited dual inhibitory effects on PAR4 and thromboxane formation from arachidonic acid. The above findings can be used as guidelines for development of novel antiplatelet drug candidates.

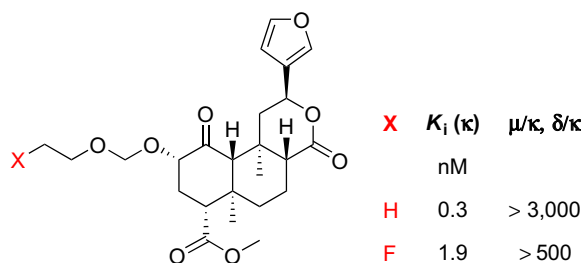


33: R₃'=H, R₄'=COOEt, R= 3-Cl-C₆H₄
83: R₃'=H, R₄'=COOEt, R=C₆H₅

Standard protecting groups create potent and selective κ opioids: Salvinorin B alkoxymethyl ethers

pp 1279–1286

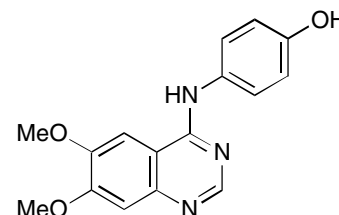
Thomas A. Munro,* Katharine K. Duncan, Wei Xu, Yulin Wang, Lee-Yuan Liu-Chen, William A. Carlezon, Jr., Bruce M. Cohen and Cécile Béguin

**Anti-inflammatory activity profile of JANEX-1 in preclinical animal models**

pp 1287–1298

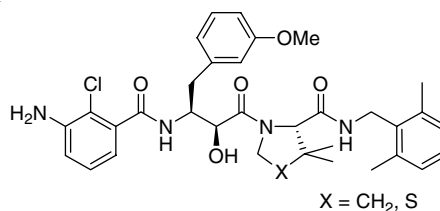
Fatih M. Uckun,* Heather Tibbles, Zahide Ozer, Sanjive Qazi and Alexei Vassilev

We examined the biologic activity of the rationally designed JAK3 inhibitor, JANEX-1, in several cellular and animal models of inflammation. Notably, JANEX-1 exhibited potent anti-inflammatory activity in each of these preclinical models, including mouse models of peritonitis, colitis, cellulitis, and systemic inflammatory response syndrome. Therefore, JANEX-1 may prove useful as a broad-spectrum anti-inflammatory agent. The present study may provide the basis for new and effective treatment as well as prevention programs for inflammatory disorders.

**JANEX - 1****Structure–activity relationships of novel HIV-1 protease inhibitors containing the 3-amino-2-chlorobenzoyl-allophenylnorstatine structure**

pp 1299–1308

Tsutomu Mimoto,* Satoshi Nojima, Keisuke Terashima, Haruo Takaku, Makoto Shintani and Hideya Hayashi

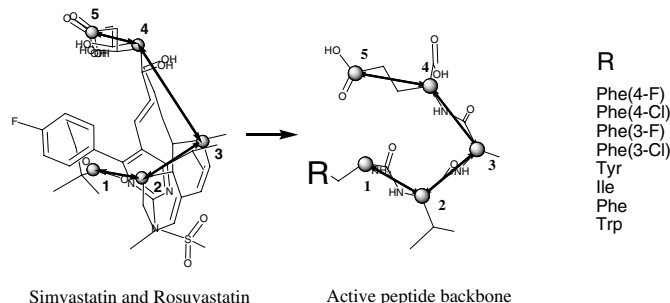


HIV protease inhibitors containing the 3-amino-2-chlorobenzoyl-allophenylnorstatine structure were designed and synthesized. These compounds exhibited excellent pharmacokinetic profile and potent antiviral activity against wild-type and resistant HIV-1s.

Binding effect and design of a competitive inhibitory peptide for HMG-CoA reductase through modeling of an active peptide backbone

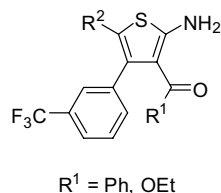
pp 1309–1318

Valeriy Viktorovich Pak,* Minseon Koo, Min Jung Kim, Lyubov Yun and Dae Young Kwon

**5-Substituted 2-aminothiophenes as A₁ adenosine receptor allosteric enhancers**

pp 1319–1327

Luigi Aurelio, Heidi Figler, Bernard L. Flynn, Joel Linden and Peter J. Scammells*

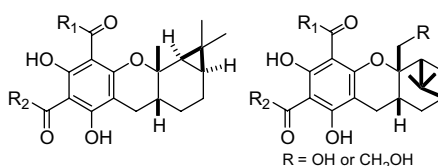


Two series of 5-substituted 2-amino-4-(3-trifluoromethylphenyl)thiophenes were prepared and evaluated as allosteric enhancers at the A₁ adenosine receptor. More specifically, the structure–activity relationships of the 5-position were explored in series of 2-amino-4-(3-trifluoromethylphenyl)thiophenes with 3-benzoyl and 3-ethoxycarbonyl functionality.

S-Euglobals: Biomimetic synthesis, antileishmanial, antimalarial, and antimicrobial activities

pp 1328–1336

Sandip B. Bharate, Shabana I. Khan, Babu L. Tekwani, Melissa Jacob, Ikhlas A. Khan and Inder Pal Singh*



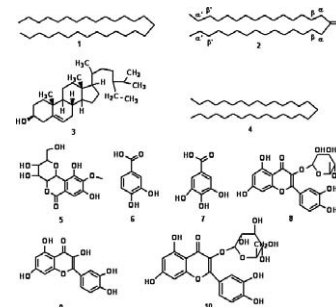
Several new *S*-euglobals were synthesized from suitably substituted phloroglucinol and different monoterpenes via a three-component reaction involving Knoevenagel condensation followed by [4+2] cycloaddition. Out of 16, nine analogues were found to exhibit antileishmanial activity. Robustadials also showed moderate antileishmanial activity and weak antimalarial activity against *Plasmodium falciparum*. Few analogues also showed antibacterial activity.

Studies on the chemical constituents and anticancer activity of *Saxifraga stolonifera* (L) Meeb

pp 1337–1344

Zhuo Chen, Yu-Mei Liu, Song Yang, Bao-An Song,* Guang-Fang Xu, Pinaki S. Bhadury, Lin-Hong Jin, De-Yu Hu, Fang Liu, Wei Xue and Xia Zhou

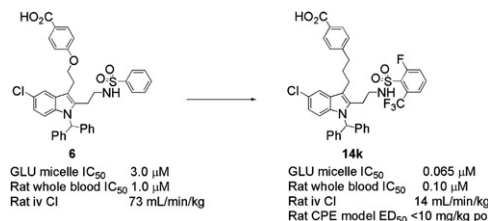
Ten compounds were isolated from ethanol extracts of *Saxifraga stolonifera* plant and were identified as *n*-C₃₁H₆₄ (1), (*n*-C₁₇H₃₅)₂CO (2), β-sitosterol (3), *n*-C₂₉H₆₀ (4), Bergenin (5), Protocatechuic acid (6), Gallic acid (7), Quercitrin 3-*O*-α-L-rhamnoside (8), Quercetin (9), and Quercetin 3-*O*-β-D-glucopyranoside (10). Among them, *n*-C₃₁H₆₄ (1), (*n*-C₁₇H₃₅)₂CO (2), β-sitosterol (3), and *n*-C₂₉H₆₀ (4) were isolated from this plant for the first time. The anticancer activities of *S. stolonifera* constituents on human gastric carcinoma cell line BGC-823 were evaluated by MTT assay and microscopic observation, DNA fragmentation, and flow cytometry analysis assay. It was found that quercetin from *S. stolonifera* is a potential agent capable of inducing apoptosis in BGC-823 cells.



Benzenesulfonamide indole inhibitors of cytosolic phospholipase A₂α: Optimization of in vitro potency and rat pharmacokinetics for oral efficacy

pp 1345–1358

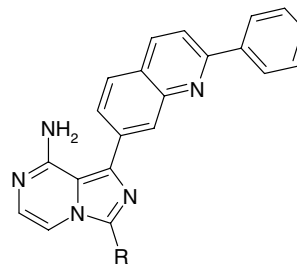
Katherine L. Lee,* Mark L. Behnke, Megan A. Foley, Lihren Chen, Weiheng Wang, Richard Vargas, Jill Nunez, Steve Tam, Nevena Mollova, Xin Xu, Marina W. H. Shen, Manjunath K. Ramarao, Debra G. Goodwin, Cheryl L. Nickerson-Nutter, William M. Abraham, Cara Williams, James D. Clark and John C. McKew



Novel 2-phenylquinolin-7-yl-derived imidazo[1,5-a]pyrazines as potent insulin-like growth factor-I receptor (IGF-IR) inhibitors

pp 1359–1375

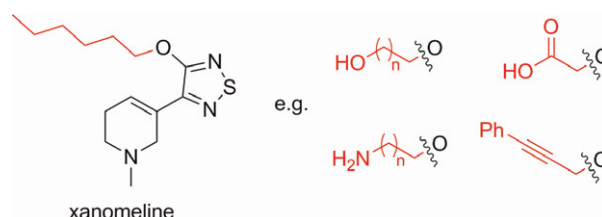
Mark J. Mulvihill,* Qun-Sheng Ji, Heather R. Coate, Andrew Cooke, Hanqing Dong, Lixin Feng, Kenneth Foreman, Maryland Rosenfeld-Franklin, Ayako Honda, Gilda Mak, Kristen M. Mulvihill, Anthony I. Nigro, Matthew O'Connor, Caroline Pirrit, Arno G. Steinig, Kam Siu, Kathryn M. Stolz, Yingchuan Sun, Paula A. R. Tavares, Yan Yao and Neil W. Gibson



Synthesis and evaluation of xanomeline analogs—Probing the wash-resistant phenomenon at the M₁ muscarinic acetylcholine receptor

pp 1376–1392

Brian E. Kane, Marianne K. O. Grant, Esam E. El-Fakahany and David M. Ferguson*

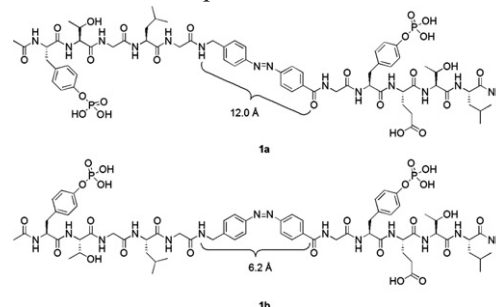


A photoswitchable ITAM peptidomimetic: Synthesis and real time surface plasmon resonance (SPR) analysis of the effects of *cis-trans* isomerization on binding

pp 1393–1399

Joeri Kuil, Loek T. M. van Wandelen, Nico J. de Mol* and Rob M. J. Liskamp

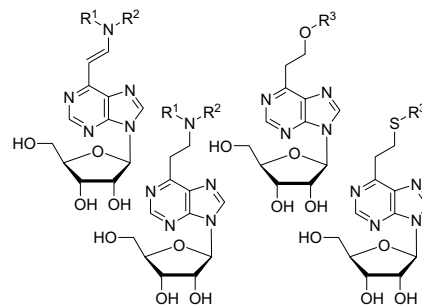
The native γ-ITAM peptide and the photoswitchable ITAM mimics. The indicated distances are between the SH2 binding epitopes.



Synthesis, cytostatic, and antiviral activity of novel 6-[2-(dialkylamino)ethyl]-, 6-(2-alkoxyethyl)-, 6-[2-(alkylsulfanyl)ethyl]-, and 6-[2-(dialkylamino)vinyl]purine nucleosides

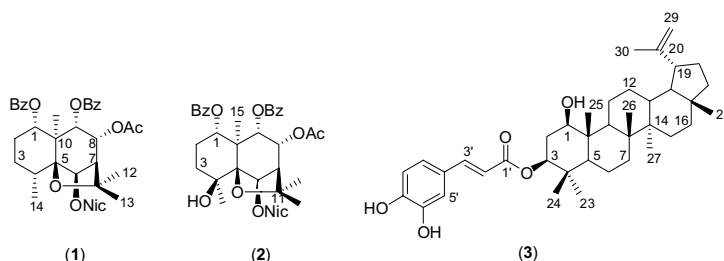
pp 1400–1424

Martin Kuchař, Michal Hocek,* Radek Pohl, Ivan Votruba, I-hung Shih, Eric Mabery and Richard Mackman

**New terpenoids from *Maytenus apurimacensis* as MDR reversal agents in the parasite *Leishmania***

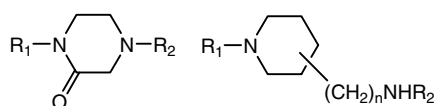
pp 1425–1430

Paulino Delgado-Méndez, Nora Herrera, Haydee Chávez, Ana Estévez-Braun,* Ángel G. Ravelo,* Fernando Cortes, Santiago Castanys and Francisco Gamarro

**Design, synthesis and preliminary pharmacological evaluation of new piperidine and piperazine derivatives as cognition-enhancers**

pp 1431–1443

Elisabetta Martini, Carla Ghelardini, Silvia Dei, Luca Guandalini, Dina Manetti, Michele Melchiorre, Monica Norcini, Serena Scapecchi, Elisabetta Teodori and Maria Novella Romanelli*

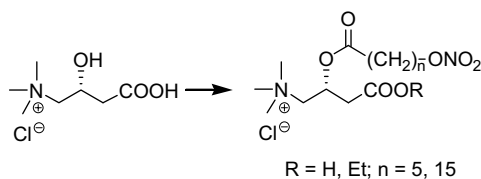


A series of 2-oxopiperazine, 4-aminomethyl-, 3-amino- and 3-aminomethylpiperidine have been synthesized and tested in the mouse passive-avoidance test. The compounds display minimal effective doses in the range 0.3–10 mg/kg.

**Synthesis and characterization of carnitine nitro-derivatives**

pp 1444–1451

Oriana Piermatti, Francesco Fringuelli, Lorena Pochini, Cesare Indiveri and Carlo A. Palmerini*

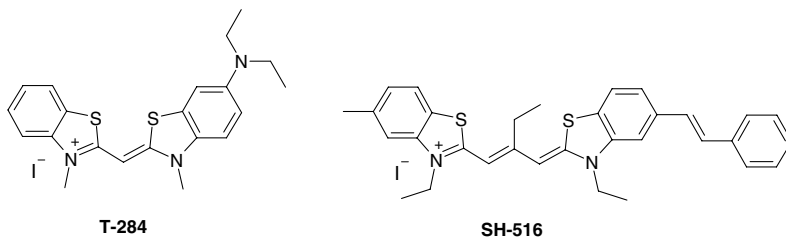


The synthesis of carnitine nitro-derivatives, their biotransformation in biological fluids and in red blood cells and the interaction of carnitine nitrates with the plasma membrane carnitine transporter has been described.

Specific fluorescent detection of fibrillar α -synuclein using mono- and trimethine cyanine dyes

pp 1452–1459

K. D. Volkova, V. B. Kovalska, A. O. Balanda, M. Yu Losytskyy, A. G. Golub, R. J. Vermeij, V. Subramaniam, O. I. Tolmachev and S. M. Yarmoluk*

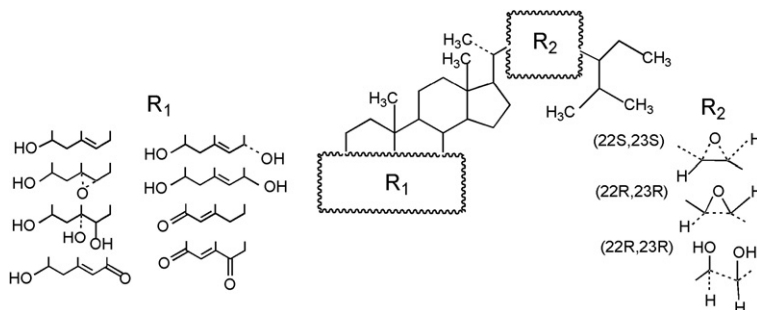


Firstly, fluorescent cyanine dyes (monomethine T-284 and trimethine SH-516) are proposed for selective fluorescent detection of fibrillar α -synuclein. Studies of interaction mode of dyes with aggregated protein are presented.

Synthesis and cytotoxicity evaluation of 22,23-oxygenated stigmasterane derivatives

pp 1460–1473

Alexander Yu. Misharin, Arif R. Mehtiev, Galina E. Morozevich, Yaroslav V. Tkachev and Vladimir P. Timofeev*

**New 7,8-benzoflavanones as potent aromatase inhibitors: Synthesis and biological evaluation**

pp 1474–1480

Samir Yahiaoui, Catherine Fagnere, Christelle Pouget, Jacques Buxeraud and Albert-José Chulia*

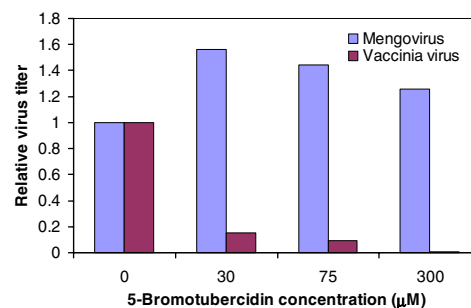
Flavonoids are known to possess a moderate inhibitory activity against aromatase, this enzyme being an interesting target for hormone-dependent breast cancer treatment. In this paper, new 7,8-benzoflavanones were synthesized and tested for their activity toward aromatase inhibition. 7,8-Benzoflavanones were found to exhibit high inhibitory potency against aromatase.

Biochemical and biological properties of 5-bromotubercidin: Differential effects on cellular DNA-directed and viral RNA-directed RNA synthesis

pp 1481–1482

Branko Brdar* and Edward Reich

The growth and RNA synthesis of mengovirus were completely resistant to concentrations of 5-bromotubercidin which strongly inhibited the growth of the host cell, of DNA virus vaccinia and of the DNA-dependent RNA synthesis of uninfected cells.

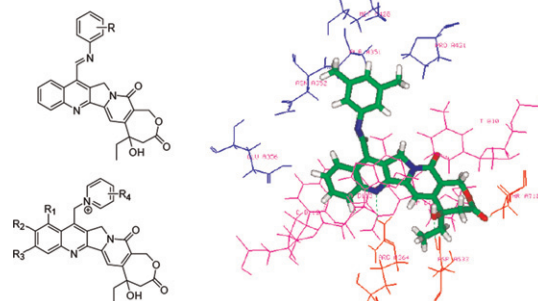


New homocamptothecins: Synthesis, antitumor activity, and molecular modeling

pp 1493–1510

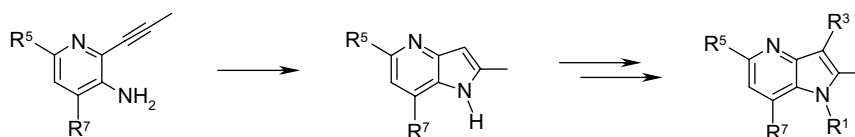
Zhenyuan Miao, Chunquan Sheng, Wannian Zhang,* Haitao Ji, Jing Zhang, Lücheng Shao, Liang You, Min Zhang, Jianzhong Yao and Xiaoyin Che

A series of novel 7-substituted homocamptothecins were designed and synthesized. The binding mode was clarified by molecular docking.

**5-Substituted 1H-pyrrolo[3,2-b]pyridines as inhibitors of gastric acid secretion**

pp 1511–1530

Andreas Marc Palmer,* Gabriela Münch, Christof Brehm, Peter Jan Zimmermann, Wilm Buhr, Martin Philipp Feth and Wolfgang Alexander Simon

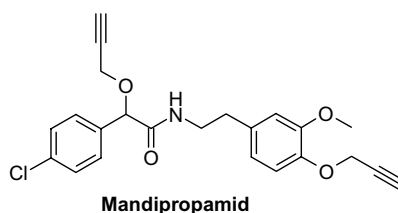


A new series of 1H-pyrrolo[3,2-b]pyridines was prepared by copper(I) iodide mediated cyclization of 2-prop-1-ynyl-pyridin-3-amines and their inhibiting effect on the gastric proton pump enzyme (H^+/K^+ ATPase) was assessed.

Multicomponent reactions in fungicide research: The discovery of mandipropamid

pp 1531–1545

Clemens Lamberth,* Andre Jeanguenat, Fredrik Cederbaum, Alain De Mesmaeker, Martin Zeller, Hans-Joachim Kempf and Ronald Zeun



Mandipropamid is a highly efficient new fungicide against the agronomically important oomycetes diseases *Phytophthora infestans* (potato and tomato late blight) and *Plasmopara viticola* (grape downy mildew).

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Summary of instructions to authors

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*Corresponding author

Supplementary data available via ScienceDirect

COVER

The transport reactions of the gastric H^+/K^+ -ATPase comprise the binding of Mg^{2+} -ATP and H^+ or hydronium (H_3O^+) ions to the pump, which is then phosphorylated and protons or hydronium ions are exported out of the cell. During this phosphorylation reaction, K^+ binds to the outward conformation of the pump, and is channeled into the cell. The binding of potassium-competitive acid blockers (P-CABs) to the gastric H^+/K^+ -ATPase results in an effective inhibition of acid secretion. P-CABs are currently evaluated as a new therapeutic class for the treatment of acid-related diseases [Palmer, A. M.; Münch, G.; Brehm, C.; Zimmerman, P. J.; Buhr, W.; Feth, M. P.; Simon, W. A. *Bioorg. Med. Chem.* **2008**, *16*, 1511–1530].

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