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Bioorganic & Medicinal Chemistry Vol. 17, No. 8, 2009

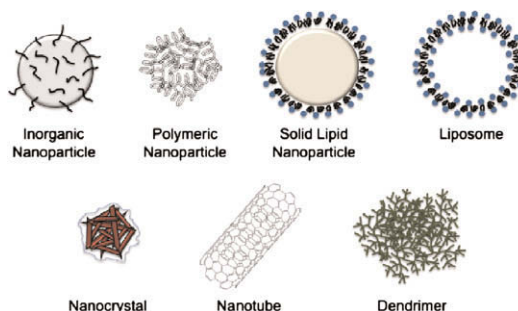
Contents

REVIEW

Nanoparticles in cellular drug delivery

pp 2950–2962

Amir H. Faraji, Peter Wipf*

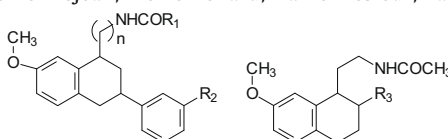


Nanoparticles exploit biological pathways to achieve payload delivery of small molecules to cellular and intracellular targets. Synthetic strategies, including surface, porosity, stealthing, and size modifications, can be utilized to refine the pharmacokinetic properties of nanoparticles and allow for efficient delivery.

ARTICLES

Design and synthesis of 3-phenyltetrahydronaphthalenic derivatives as new selective MT₂ melatoninergic ligands. Part II pp 2963–2974

Sophie Durieux, Angéline Chanu, Christophe Bochu, Valérie Audinot, Sophie Coumilleau, Jean A. Boutin, Philippe Delagrangé, Daniel H. Caignard, Caroline Bennejean, Pierre Renard, Daniel Lesieur, Pascal Berthelot, Saïd Yous*



R₁ = CH₃, C₂H₅, n-C₃H₇, c-C₄H₇, CH₂Br, CH₂I, C₃H₆Cl, CH=CH₂, CH₂CH=CH₂,

NHCOR₁ = pyrrolidinone

R₂ = H, NHCOCH₃, CF₃, OCH₃

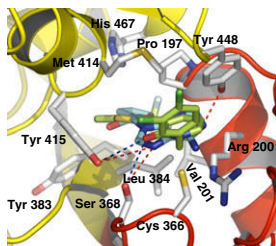
R₃ = C₆H₅, CH₂C₆H₅

n = 1, 2

Identification of novel inhibitors of HCV RNA-dependent RNA polymerase by pharmacophore-based virtual screening and in vitro evaluation

pp 2975–2982

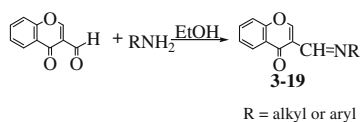
Kisun Ryu, Nam Doo Kim, Seong Il Choi, Cheol Kyu Han, Jeong Hyeok Yoon, Kyoung Tai No, Kyun-Hwan Kim*, Baik L. Seong*



Schiff bases of 3-formylchromone as thymidine phosphorylase inhibitors

pp 2983–2988

Khalid Mohammed Khan*, Nida Ambreen, Sajjad Hussain, Shahnaz Perveen, M. Iqbal Choudhary

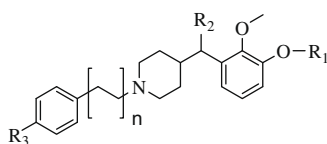


A series of substituted Schiff bases of 3-formylchromone have been synthesized and screened against thymidine phosphorylase enzyme. Results were astounding and several leads were obtained for further optimization.

Synthesis and in vitro affinities of various MDL 100907 derivatives as potential ¹⁸F-radioligands for 5-HT_{2A} receptor imaging with PET

pp 2989–3002

Matthias M. Herth*, Vasko Kramer, Markus Piel, Mikael Palner, Patrick J. Riss, Gitte M. Knudsen, Frank Rösch

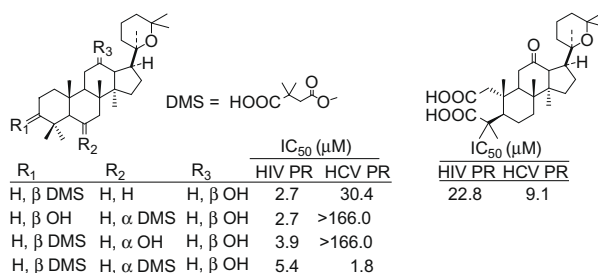


Synthesis of various MDL 100907 derivatives as potential ¹⁸F-radioligands for PET molecular imaging.

Synthesis of dammarane-type triterpene derivatives and their ability to inhibit HIV and HCV proteases

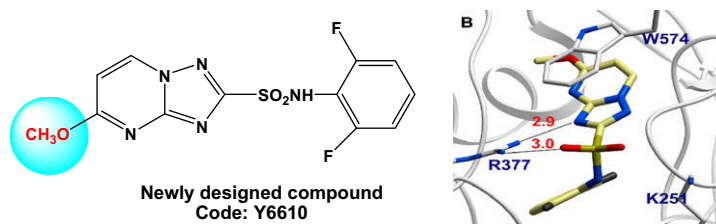
pp 3003–3010

Ying Wei, Chao-Mei Ma, Masao Hattori*

**Design and synthesis of N-2,6-difluorophenyl-5-methoxyl-1,2,4-triazolo[1,5-a]-pyrimidine-2-sulfonamide as acetohydroxyacid synthase inhibitor**

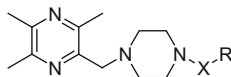
pp 3011–3017

Chao-Nan Chen, Li-Li Lv, Feng-Qin Ji, Qiong Chen, Hui Xu*, Cong-Wei Niu, Zhen Xi, Guang-Fu Yang*



Ligustrazine derivatives. Part 3: Design, synthesis and evaluation of novel acylpiperazinyl derivatives as potential cerebrocardiac vascular agents pp 3018–3024

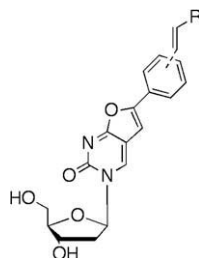
Xian-Chao Cheng, Xin-Yong Liu^{*}, Wen-Fang Xu, Xiu-Li Guo, Ning Zhang, Yu-Ning Song



A series of novel acylpiperazinyl Ligustrazine derivatives was designed and synthesized. Their protective effects on damaged ECV-304 cells and antiplatelet aggregation activities were reported.

Alkenyl substituted bicyclic nucleoside analogues retain nanomolar potency against Varicella Zoster Virus pp 3025–3027

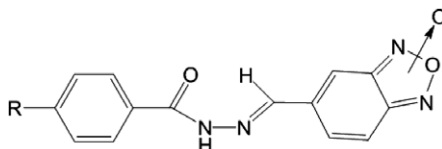
Christopher McGuigan^{*}, Olivier Bidet, Marco Derudas, Graciela Andrei, Robert Snoeck, Jan Balzarini



Nanomolar potency versus VZV for *para* systems only. *Ortho* and *meta* poorly active.

Design, synthesis, antimicrobial activity and molecular modeling studies of novel benzofuroxan derivatives against *Staphylococcus aureus* pp 3028–3036

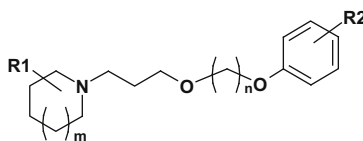
Salomão Dória Jorge^{*}, Andrea Masunari, Carlota Oliveira Rangel-Yagui, Kerly Fernanda Mesquita Pasqualoto, Leoberto Costa Tavares



A new series of 14 4-substituted [*N'*-(benzofuroxan-5-yl)methylene] benzohydrazides with structure analogous of nifuroxazide were synthesized and tested against standard and multidrug-resistant *Staphylococcus aureus* strains.

Diether derivatives of homo- or substituted piperidines as non-imidazole histamine H₃ receptor ligands pp 3037–3042

Dorota Łażewska, Kamil Kuder, Xavier Ligneau, Jean-Claude Camelin, Walter Schunack, Holger Stark, Katarzyna Kieć-Kononowicz^{*}

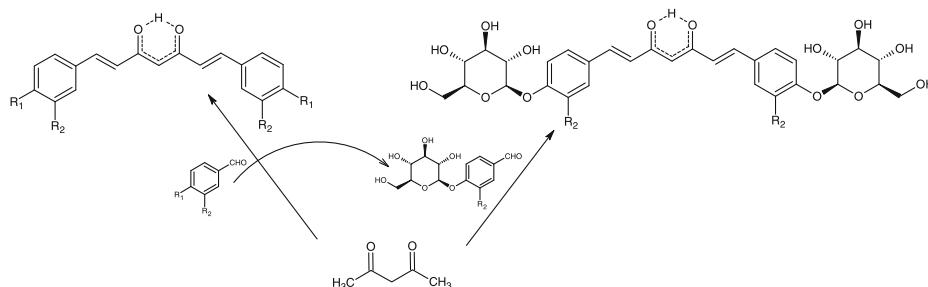


New diethers **4–16** were prepared and evaluated for their *in vitro* binding affinities at human histamine H₃ receptor. The 3-methylpiperidine derivative **11** ($R^1 = 3\text{-CH}_3$, $m = 1$, $n = 3$, $R^2 = 4\text{-Cl}$) is the most potent compound (K_i value of 3.2 nM) in this series.

Synthesis, cytotoxic and combined cDDP activity of new stable curcumin derivatives

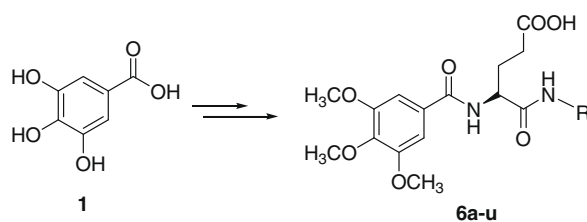
pp 3043–3052

Erika Ferrari, Sandra Lazzari, Gaetano Marverti, Francesca Pignedoli, Ferdinando Spagnolo, Monica Saladini *

**Novel aminopeptidase N inhibitors derived from antineoplaston AS2-5 (Part I)**

pp 3053–3060

Xun Li, Junli Wang, Jinpei Li, Jifeng Wu, Yonggang Li, Huawei Zhu, Ruifang Fan, Wenfang Xu *

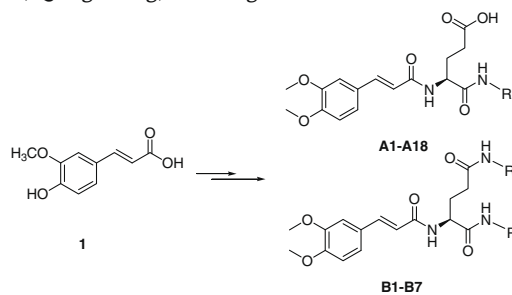


A series of novel *L*-iso-glutamine derivatives (**6a–u**) based on the antineoplaston AS2-5 scaffold were synthesized and evaluated for their *in vitro* enzymatic inhibitory activities against aminopeptidase N (APN) and MMP-2.

Novel aminopeptidase N inhibitors derived from antineoplaston AS2-5 (Part II)

pp 3061–3071

Xun Li, Yazhou Wang, Jifeng Wu, Yonggang Li, Qiang Wang, Wenfang Xu *

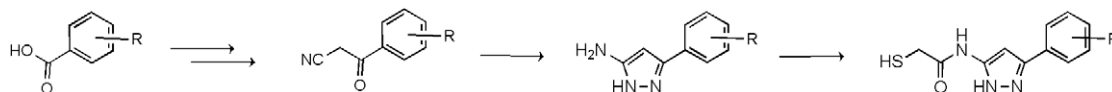


A series of novel *L*-iso-glutamine derivatives (**A1–A18** and **B1–B7**) based on the antineoplaston AS2-5 scaffold were synthesized and evaluated for their *in vitro* enzymatic inhibitory activities against aminopeptidase N (APN, CD13) and MMP-2.

Botulinum neurotoxin serotype A inhibitors: Small-molecule mercaptoacetamide analogs

pp 3072–3079

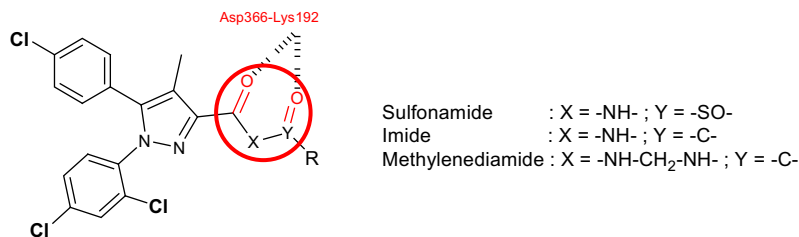
Scott T. Moe, Andrew B. Thompson, Genessa M. Smith, Ross A. Fredenburg, Ross L. Stein, Alan R. Jacobson *



Botulinum neurotoxin serotype A, interferes with neurotransmitter release via a metalloprotease-mediated process. We designed a novel series of inhibitors active against the enzyme. SAR studies revealed components essential for low micromolar activity.

Synthesis and structure–activity relationship of novel diarylpyrazole imide analogues as CB1 cannabinoid receptor ligands pp 3080–3092

Kwang-Seop Song, Min Ju Kim, Hee Jeong Seo, Sung-Han Lee, Myung Eun Jung, Soo-Un Kim, Jeongmin Kim, Jinhwa Lee*

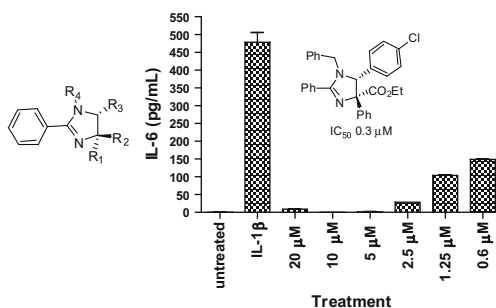


Novel CB1 receptor antagonists, including diketone group as hydrogen bonding acceptor, were identified and the classical QSAR study was performed to search for the compound with an optimized CB1 binding affinity.



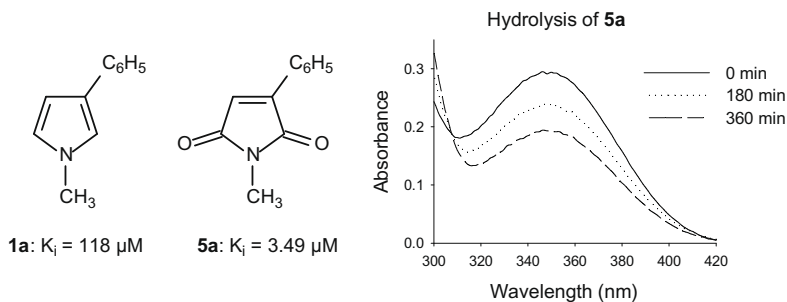
Structural–activity relationship study of highly-functionalized imidazolines as potent inhibitors of nuclear transcription factor-κB mediated IL-6 production pp 3093–3103

Daljinder K. Kahlon, Theresa A. Lansdell, Jason S. Fisk, Jetze J. Tepe*



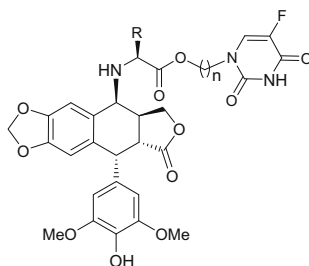
Inhibition of monoamine oxidase B by *N*-methyl-2-phenylmaleimides pp 3104–3110

Clarina I. Manley-King, Gisella Terre'Blanche, Neal Castagnoli Jr., Jacobus J. Bergh, Jacobus P. Petzer*



Synthesis and biological evaluation of novel conjugates of podophyllotoxin and 5-FU as antineoplastic agents pp 3111–3117

Shi-Wu Chen*, Rong Xiang, Jian Liu, Xuan Tian*



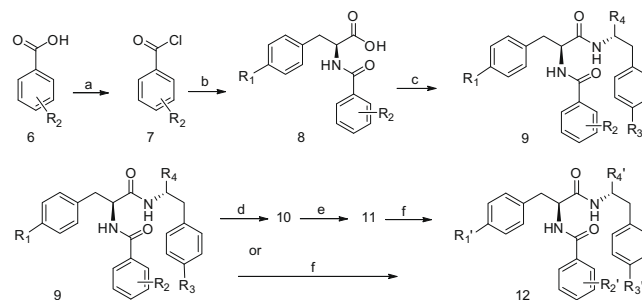
The novel conjugates **10–21** showed superior or comparable inhibitions against HL-60, K562, A-549 and AGS to VP-16, and better water solubility. Compound **21** also showed interaction with calf thymus DNA, and was stable in human plasma.

Synthesis and anti-hepatitis B virus activities of Matijing-Su derivatives

pp 3118–3125

Bixue Xu, Zhengming Huang, Changxiao Liu, Zegui Cai, Weidong Pan, Peixue Cao, Xiaojiang Hao, Guangyi Liang*

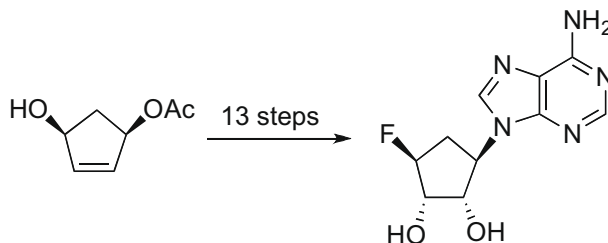
A series of derivatives of Matijing-Su (MTS, *N*-(*N*-benzoyl-L-phenylalanyl)-*O*-acetyl-L-phenylalanol) was synthesized and evaluated for their anti-hepatitis B virus (HBV) activities in 2.2.15 cells.



A new synthesis and an antiviral assessment of the 4'-fluoro derivative of 4'-deoxy-5'-noraristeromycin

pp 3126–3129

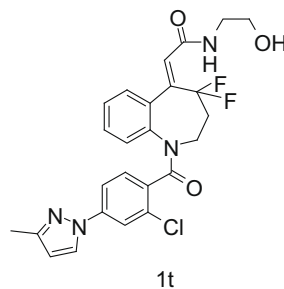
Xue-qiang Yin, Wei-kuan Li, Minmin Yang, Stewart W. Schneller*



Synthesis and structure–activity relationships of amide derivatives of (4,4-difluoro-1,2,3,4-tetrahydro-5H-1-benzazepin-5-ylidene)acetic acid as selective arginine vasopressin V₂ receptor agonists

pp 3130–3141

Issei Tsukamoto*, Hiroyuki Koshio, Takahiro Kuramochi, Chikashi Saitoh, Hiroko Yanai-Inamura, Chika Kitada-Nozawa, Eisaku Yamamoto, Takeyuki Yatsu, Yoshiaki Shimada, Shuichi Sakamoto, Shin-ichi Tsukamoto

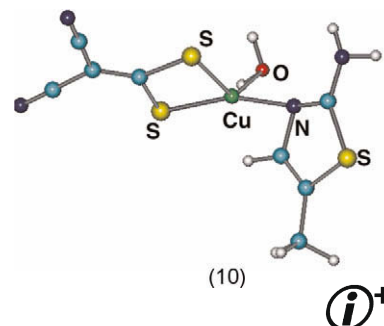


Synthesis, characterization, toxicity, cytogenetic and in vivo antitumor studies of 1,1-dithiolate Cu(II) complexes with di-, tri-, tetra- amines and 1,3-thiazoles. Structure–activity correlation

pp 3142–3151

C. A. Bolos*, A. T. Chaviara, D. Mourelatos, Z. Iakovidou, E. Mioglou, E. Chrysogelou, A. Papageorgiou

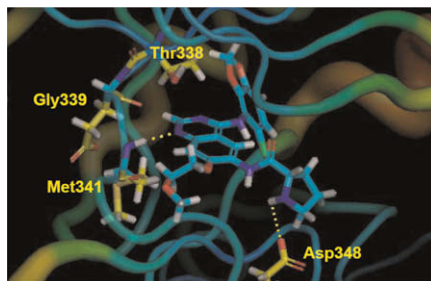
A series of mixed-ligand neutral Cu(II) complexes with dithiolates, amines or thiazole ligands have been synthesized and the acute toxicity, cytogenetic and in vivo antitumor effects can be related to their chemical and physicochemical properties. The tests showed that the compound **10** can be used as lead compound.



Structure-based virtual screening of Src kinase inhibitors

pp 3152–3161

Kyungik Lee, Jongwoo Kim, Ki-Woong Jeong, Ki Won Lee, Yeonjoo Lee, Ji Yeon Song, Maeng Sup Kim, Gwan Sun Lee, Yangmee Kim*

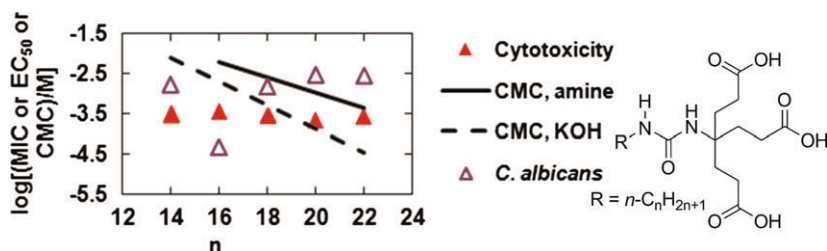


Here, selective candidate Src inhibitors were screened by structure-based virtual screening.

Comparing anti-HIV, antibacterial, antifungal, micellar, and cytotoxic properties of tricarboxylate dendritic amphiphiles

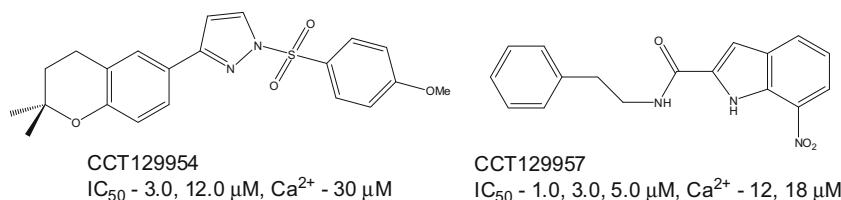
pp 3162–3168

Richard V. Macri, Janka Karlovská, Gustavo F. Doncel, Xiaosong Du, Bhadreshkumar B. Maisuria, André A. Williams, Eko W. Sugandhi, Joseph O. Falkinham III, Alan R. Esker, Richard D. Gandour*

**The identification of novel PLC- γ inhibitors using virtual high throughput screening**

pp 3169–3176

Jóhannes Reynisson*, William Court, Ciaran O'Neill, James Day, Lisa Patterson, Edward McDonald, Paul Workman, Matilda Katan, Suzanne A. Eccles*

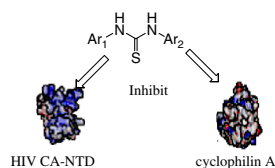


Phospholipase C- γ (PLC- γ) is as a potential biological target for anticancer drug therapy. Virtual high throughput screening was performed using $\sim 5.3 \times 10^5$ compounds to identify hits. The most potent compounds according to a biochemical assay were in the low single digit micro-molar range which translated into a GC_{50} of $\sim 15 \mu\text{M}$ for a functional assay in cells. About 30% of the compounds tested were active ($IC_{50} < 50 \mu\text{M}$) and were structurally diverse.

Discovery of dual inhibitors targeting both HIV-1 capsid and human cyclophilin A to inhibit the assembly and uncoating of the viral capsid

pp 3177–3188

Jiebo Li, Zhiwu Tan, Shixing Tang, Indira Hewlett, Ruifang Pang, Meizi He, Shanshan He, Baohe Tian, Kan Chen, Ming Yang*



A series of compounds were prepared to inhibit viral replication by delaying the capsid assembly rate in vitro, and inhibiting PPlase activity of cyclophilin A to disrupt the uncoating process of viral life cycle.

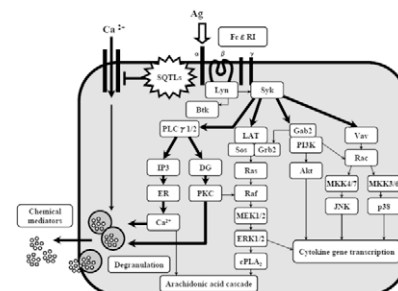
Inhibitory effects of sesquiterpene lactones isolated from *Eupatorium chinense* L. on IgE-mediated degranulation in rat basophilic leukemia RBL-2H3 cells and passive cutaneous anaphylaxis reaction in mice

pp 3189–3197

Tomohiro Itoh*, Masayoshi Oyama, Norihiko Takimoto, Chihiro Kato, Yoshinori Nozawa, Yukihiro Akao, Munekazu Iinuma

Sesquiterpene lactones (SQTs) isolated from *Eupatorium chinense* L. suppressed the antigen-induced degranulation in rat basophilic leukemia RBL-2H3 cells. Suppression of Ag-stimulated degranulation by these SQTs is mainly due to the decreased Ca^{2+} influx.

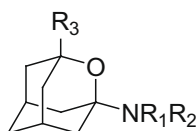
Furthermore, in order to clarify the in vivo effect of SQT-rich extract, we administered SQT-rich extract to the type I allergic model mice. The SQTs remarkably suppressed PCA reaction in a dose-dependent manner. Thus, it was suggested that SQTs would be a candidate as an anti-allergic agent.



Synthesis and pharmacological evaluation of (2-oxaadmant-1-yl)amines

pp 3198–3206

María D. Duque, Pelayo Camps, Lenuta Profire, Silvia Montaner, Santiago Vázquez*, Francesc X. Sureda, Jordi Mallol, Marta López-Querol, Lieve Naesens, Erik De Clercq, S. Radhika Prathalingam, John M. Kelly

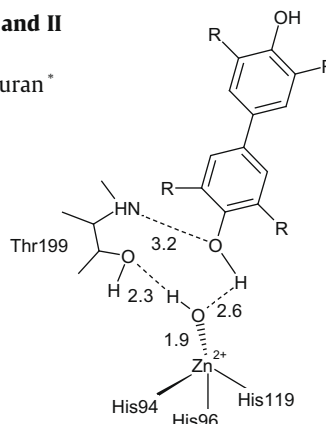


Several (2-oxaadmant-1-yl)amines have been synthesized and their antiviral, NMDA receptor antagonist, and trypanocidal activities have been studied.

Carbonic anhydrase inhibitors. Inhibition of human erythrocyte isozymes I and II with a series of antioxidant phenols

pp 3207–3211

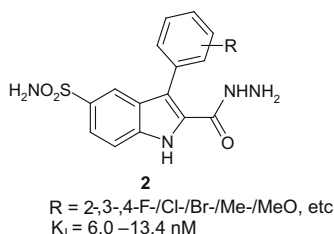
Murat Şentürk, İlhami Gülçin*, Arif Daştan, Ö. İrfan Küfrevioğlu, Claudiu T. Supuran*



Carbonic anhydrase inhibitors. The nematode α -carbonic anhydrase of *Caenorhabditis elegans* CAH-4b is highly inhibited by 2-(hydrazinocarbonyl)-3-substituted-phenyl-1H-indole-5-sulfonamides

pp 3212–3215


Özlen Güzel, Alessio Innocenti, Rebecca A. Hall, Andrea Scozzafava, Fritz A. Mühlischlegel, Claudiu T. Supuran*



OTHER CONTENTS

Erratum	pp 3216–3217
Bioorganic & Medicinal Chemistry Reviews and Perspectives	pp 3218–3220
Instructions to contributors	p I

*Corresponding author

+ Supplementary data available via ScienceDirect

COVER

Binding of two sulfonamides to carbonic anhydrase II (CA). Adduct in magenta shows 2-(hydrazinocarbonyl)-3-phenyl-1*H*-indole-5-sulfonamides and the one in gold a thiabendazole-5-sulfonamide which strongly inhibit *Caenorhabditis elegans* CAH-4b, with the possibility of leading to new antihelmintics [Güzel, Ö.; Innocenti, A.; Hall, R. A.; Scozzafava, A.; Mühlischlegel, F. A.; Supuran, C. T. *Bioorg. Med. Chem.* **2009**, *17*, 3212–3215].

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