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REVIEW

Antituberculosis drugs: Ten years of research

Yves L. Janin*

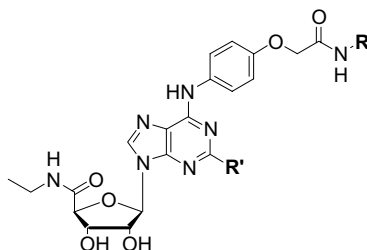
pp 2479–2513

Death of Frédéric Chopin; 1810–1849 (after a painting of Félix Barrias; Bibliothèque Nationale de France; <http://ark.bnf.fr/ConsulterElementNum?O=IFN-7720446&E=JPEG&Deb=38&Fin=38&Param=C>).

ARTICLES

N⁶-(Hetero)aryl(cyclo)alkyl-carbamoyl-methoxy-phenyl]-(2-chloro)-5'-N-ethylcarboxamido-adenosines: pp 2514–2527 The first example of adenosine-related structures with potent agonist activity at the human A_{2B} adenosine receptor

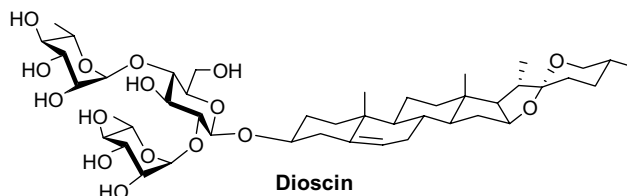
Pier Giovanni Baraldi,* Delia Preti, Mojgan Aghazadeh Tabrizi, Francesca Fruttarolo, Giulia Saponaro, Stefania Baraldi, Romeo Romagnoli, Allan R. Moorman, Stefania Gessi, Katia Varani and Pier Andrea Borea



Exploration of the correlation between the structure, hemolytic activity, and cytotoxicity of steroid saponins

Yibing Wang, Yichun Zhang, Ziyang Zhu, Shilei Zhu, Yingxia Li, Ming Li and Biao Yu*

pp 2528–2532

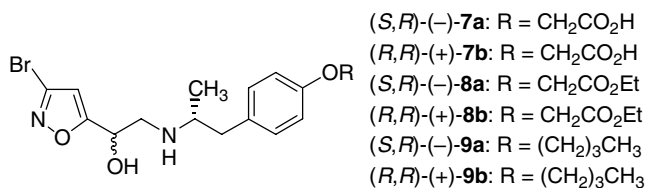


The hemolytic activity of a collection of 63 steroid saponins, mostly congeners of dioscin, was determined, which is highly dependent on their structures and has no correlation with their cytotoxicity.

Novel chiral isoxazole derivatives: Synthesis and pharmacological characterization at human β -adrenergic receptor subtypes

pp 2533–2543

Clelia Dallanocce, Fabio Frigerio, Marco De Amici,* Sandra Dorsch, Karl-Norbert Klotz* and Carlo De Micheli



A set of new enantiopure isoxazole derivatives has been prepared and tested for their affinity and efficacy at human β_1 -, β_2 -, and β_3 -adrenergic receptor subtypes.

On the applicability of QSAR for recognition of miRNA bioorganic structures at early stages of organism and cell development: Embryo and stem cells

pp 2544–2550

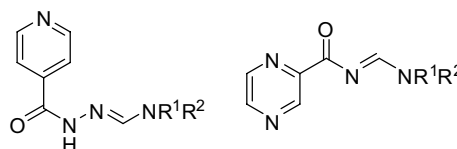
Humberto González-Díaz,* Santiago Vilar, Lourdes Santana, Gianni Podda and Eugenio Uriarte



A new modification of anti-tubercular active molecules

pp 2551–2559

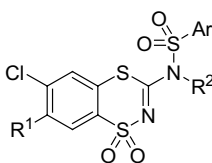
Aleš Imramovský,* Slovenko Polanc,* Jarmila Vinšová, Marijan Kočevár, Josef Jampílek, Zuzana Rečková and Jarmila Kaustová



Synthesis, structural characterization, and in vitro antitumor activity of novel *N*-(6-chloro-1,1-dioxo-1,4,2-benzodithiazin-3-yl)arylsulfonamides

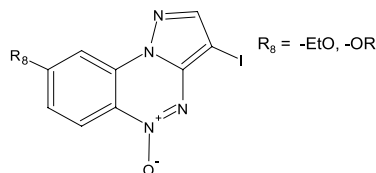
pp 2560–2572

Zdzisław Brzozowski, Franciszek Sączewski,* Jarosław Sławiński, Patrick J. Bednarski, Renate Grünert and Maria Gdaniec



Novel 3-iodo-8-ethoxypyrazolo[5,1-*c*][1,2,4]benzotriazine 5-oxide as promising lead for design of $\alpha 5$ -inverse agonist useful tools for therapy of mnemonic damage pp 2573–2586

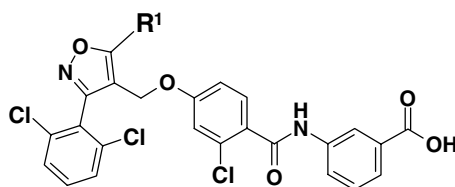
Gabriella Guerrini,* Giovanna Ciciani, Giovanni Cambi, Fabrizio Bruni, Silvia Selleri, François Besnard, Marina Montali, Claudia Martini, Carla Ghelardini, Nicoletta Galeotti and Annarella Costanzo



The synthesis, biological, and pharmacological investigation on new 3-iodo-8-alkyloxy pyrazolo[5,1-*c*][1,2,4]benzotriazine 5-oxide are reported. The structure–activity relationships for these compounds are discussed. Compounds **5c** and **5'e** emerge for their pro-mnemonic activity from in vivo tests.

Design, synthesis, and evaluation of non-steroidal farnesoid X receptor (FXR) antagonist pp 2587–2600

Masahiko Kainuma, Makoto Makishima, Yuichi Hashimoto and Hiroyuki Miyachi*



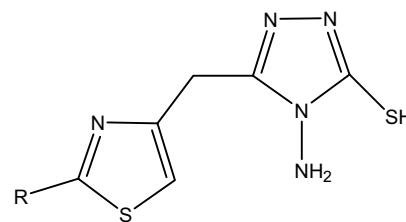
R¹ = 2-naphthyl, 4-biphenyl

A series of substituted-isoxazole derivatives was prepared as candidate farnesoid X receptor (FXR) antagonists, based on our previously proposed ligand superfamily concept.

Clubbed thiazoles by MAOS: A novel approach to cyclin-dependent kinase 5/p25 inhibitors as a potential treatment for Alzheimer's disease pp 2601–2610

Mahendra Ramesh Shiradkar,* Kalyan Chakravarthy Akula, Varaprasad Dasari, Vijayakumar Baru, Bhoomeshwar Chiningiri, Santosh Gandhi and Ranjit Kaur

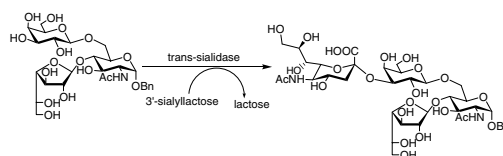
The synthesis of a new series of triazolyl-thiazole derivatives under microwave assisted organic synthesis is described. They were tested as cdk5/p25 inhibitors. It was also observed that **8b** possesses 17-fold selectivity for cdk5/cdk2. Compounds **8a** and **8c** have shown appreciable cdk5/p25 inhibitory potency. Few compounds were good inhibitors while others were inactive.



Comparative rates of sialylation by recombinant *trans*-sialidase and inhibitor properties of synthetic oligosaccharides from *Trypanosoma cruzi* mucins-containing galactofuranose and galactopyranose pp 2611–2616

Rosalía Agustí, M. Eugenia Giorgi, Verónica M. Mendoza, Carola Gallo-Rodriguez and Rosa M. de Lederkremer*

The presence of galactofuranose in the oligosaccharides from mucins of *Trypanosoma cruzi* does not impair their acceptor properties. The oligosaccharides inhibit sialylation of *N*-acetylglucosamine with IC₅₀ values between 0.6 and 4 mM. A representative reaction is shown:



Amphipathic benzoic acid derivatives: Synthesis and binding in the hydrophobic tunnel of the zinc deacetylase LpxC

pp 2617–2623

Hyunshun Shin, Heather A. Gennadios, Douglas A. Whittington and David W. Christianson*

Benzoic acid derivatives bearing aliphatic substituents bind to LpxC with micromolar affinity. Surprisingly, the X-ray crystal structure of the complex with 3-(heptyloxy)-benzoate reveals a 'backward' binding mode.

Actions between neonicotinoids and key residues of insect nAChR based on an ab initio quantum chemistry study: Hydrogen bonding and cooperative π - π interaction

pp 2624–2630

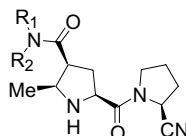
Yanli Wang, Jiagao Cheng, Xuhong Qian* and Zhong Li*

The alternative binding model between neonicotinoids and nAChR.

Design and synthesis of new potent dipeptidyl peptidase IV inhibitors with enhanced ex vivo duration

pp 2631–2650

Takashi Kondo,* Takahiro Nekado, Isamu Sugimoto, Kenya Ochi, Shigeyuki Takai, Atsushi Kinoshita, Yohei Tajima, Susumu Yamamoto, Kazuhito Kawabata, Hisao Nakai and Masaaki Toda

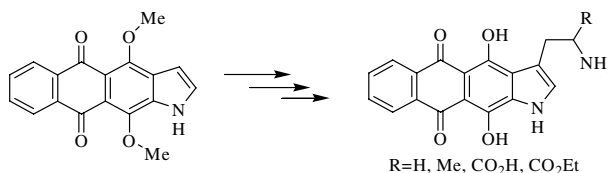


A series of 5 β -methylprolyl-2-cyanopyrrolidine analogs were synthesized and identified as long-acting DPP-IV inhibitors. The mode of binding and the effect on the plasma glucose level were evaluated.

Naphthoindole-based analogues of tryptophan and tryptamine: Synthesis and cytotoxic properties

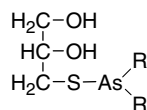
pp 2651–2659

Andrey E. Shchekotikhin,* Lyubov G. Dezhenkova, Olga Yu. Susova, Valeria A. Glazunova, Yuri N. Luzikov, Yuri B. Sinkevich, Vladimir N. Buyanov, Alexander A. Shtil and Maria N. Preobrazhenskaya

R=H, Me, CO₂H, CO₂Et

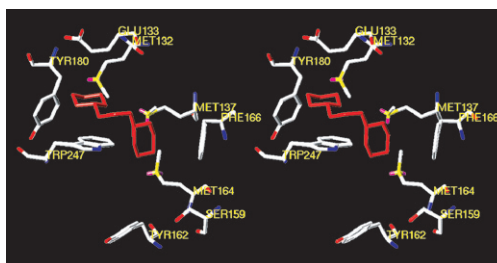
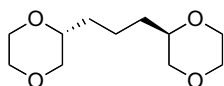
Naphtho[2,3-*f*]indole-5,10-dione-based analogues of tryptophan and tryptamine suppress topoisomerase I and circumvent resistance mediated by P-glycoprotein and p53 dysfunction of tumor cells.

Synthesis of *S*-dialkylarsino-3-mercapto-1,2-propanediols and evaluation of their anticancer activity pp 2660–2666
 Mingzhang Gao, Songde Tan, Yiwen Chen and Ralph A. Zingaro*



Some *S*-dialkylarsenic compounds have been synthesized and most of them display anticancer activity and especially towards leukemia, renal cancer and prostate cancer cell lines.

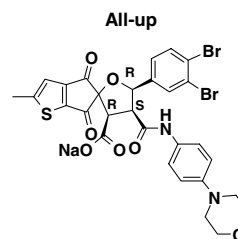
Synthesis of dioxane-based antiviral agents and evaluation of their biological activities as inhibitors of Sindbis virus replication pp 2667–2679
 Ha Young Kim, Richard J. Kuhn, Chinmay Patkar, Ranjit Warriar and Mark Cushman*



QSAR analysis for heterocyclic antifungals pp 2680–2689
 Pablo R. Duchowicz,* Martín G. Vitale, Eduardo A. Castro, Michael Fernández and Julio Caballero

Linear and non-linear QSAR for the antifungal potency of 96 heterocyclic ring derivatives, using Forward Stepwise Regression and the Replacement Method. Different parallelisms are argued between the activities and the molecular descriptors involved. Antifungal activity = function (molecular structural descriptors).

Optimization and determination of the absolute configuration of a series of potent inhibitors of human papillomavirus type-11 E1–E2 protein–protein interaction: A combined medicinal chemistry, NMR and computational chemistry approach pp 2690–2700
 Nathalie Goudreau,* Dale R. Cameron, Robert Déziel, Bruno Haché, Araz Jakalian, Eric Malenfant, Julie Naud, William W. Ogilvie, Jeff O'Meara, Peter W. White and Christiane Yoakim



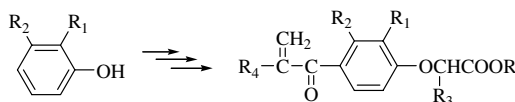
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HPV11 E1/E2/DNA IC₅₀ = 0.006 μM

The synthesis of α,β -unsaturated carbonyl derivatives with the ability to inhibit both glutathione *S*-transferase P1-1 activity and the proliferation of leukemia cells

pp 2701–2707

Guisen Zhao, Chuan Liu, Rui Wang, Dandan Song, Xiaobing Wang, Hongxiang Lou* and Yongkui Jing*

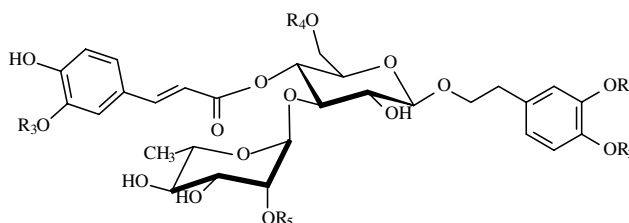


Twenty-one novel ethacrynic acid (EA) derivatives are synthesized and their inhibitory effects on GSTP1-1 activity and growth of HL-60 cells are determined.

Identification of tyrosinase inhibitors from *Marrubium velutinum* and *Marrubium cylleneum*

pp 2708–2714

Anastasia Karioti, Anastasia Protopappa, Nikolaos Megoulas and Helen Skaltsa*

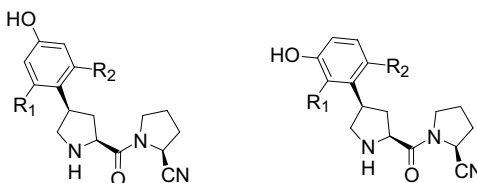


Forty-five secondary metabolites isolated from *Marrubium velutinum* and *Marrubium cylleneum* belonging to the classes of flavonoids, phenylethanoid glycosides, phenolic acids and lignan glycosides were screened for their inhibitory activity against mushroom tyrosinase, a key enzyme in the production of melanins in plants and animals.

Design and synthesis of long-acting inhibitors of dipeptidyl peptidase IV

pp 2715–2735

Takashi Kondo,* Isamu Sugimoto, Takahiro Nekado, Kenya Ochi, Tazumi Ohtani, Yohei Tajima, Susumu Yamamoto, Kazuhito Kawabata, Hisao Nakai and Masaaki Toda

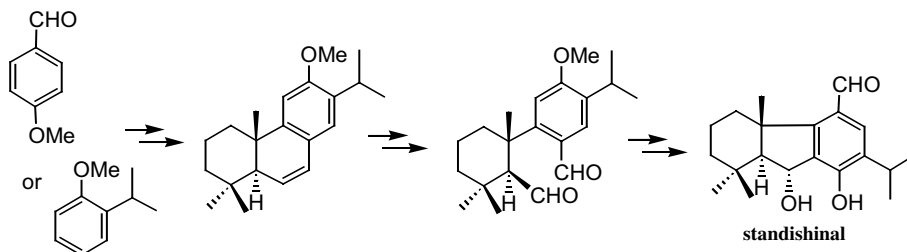


The 4β-[4-(hydroxyphenyl)prolyl]prolinenitriles were synthesized and evaluated as inhibitors of dipeptidylpeptidase IV (DPP-IV). Metabolic formation of the corresponding phenol glucuronates was found to contribute to their long duration of action.

Synthesis of DL-standishinal and its related compounds for the studies on structure–activity relationship of inhibitory activity against aromatase

pp 2736–2748

Takahiro Katoh, Taichi Akagi, Chie Noguchi, Tetsuya Kajimoto, Manabu Node,* Reiko Tanaka, Manabu Nishizawa (née Iwamoto), Hironori Ohtsu, Noriyuki Suzuki and Koichi Saito



Design, synthesis, inhibitory activity, and SAR studies of pyrrolidine derivatives as neuraminidase inhibitors

pp 2749–2758

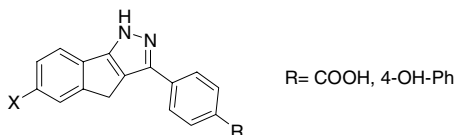
Jie Zhang, Qiang Wang, Hao Fang, Wenfang Xu,* Ailin Liu and Guanhua Du

Structure-based design has led to the synthesis of a series of influenza neuraminidase (NA) inhibitors containing pyrrolidine core. Several compounds exhibit some specific activity against influenza A (H3N2).

Discovery of 1,4-dihydroindeno[1,2-c]pyrazoles as a novel class of potent and selective checkpoint kinase 1 inhibitors

pp 2759–2767

Yunsong Tong,* Akiyo Claiborne, Kent D. Stewart, Chang Park, Peter Kovar, Zehan Chen, Robert B. Credo, Wen-Zhen Gu, Stephen L. Gwaltney, II, Russell A. Judge, Haiying Zhang, Saul H. Rosenberg, Hing L. Sham, Thomas J. Sowin and Nan-horng Lin



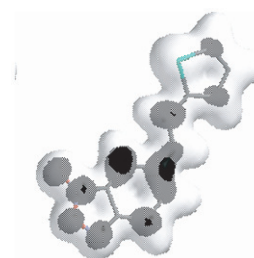
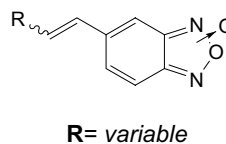
A new class of checkpoint kinase 1 inhibitors was developed after initial hits from high throughput screening. The efficient hit-to-lead process was facilitated by X-ray crystallography and led to potent inhibitors. Compounds were capable of potentiating DNA-damaging agents in cell proliferation assays and abrogating G2/M checkpoint.

**Second generation of 5-ethenylbenzofuroxan derivatives as inhibitors of *Trypanosoma cruzi* growth: Synthesis, biological evaluation, and structure–activity relationships**

pp 2768–2781

Williams Porcal, Paola Hernández, Gabriela Aguirre, Lucía Boiani, Mariana Boiani, Alicia Merlino, Ana Ferreira, Rossanna Di Maio, Ana Castro, Mercedes González* and Hugo Cerecetto*

Second generation of 5-ethenylbenzofuroxan derivatives as anti-trypanosomal compounds are synthesized using Wittig methodology. The compounds are evaluated in three different strains of *Trypanosoma cruzi* and human macrophages. SAR studies are performed.

**Synthesis and antiplasmodial activity of new *N*-[3-(4-{3-[(7-chloroquinolin-4-yl)amino]propyl}piperazin-1-yl)propyl]carboxamides**

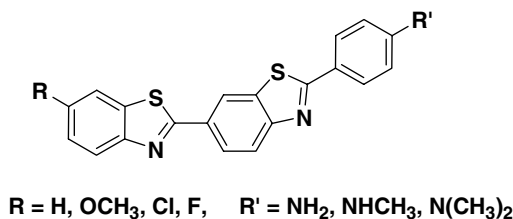
pp 2782–2788

Marcus Freitag, Marcel Kaiser, Tim Larsen, Vida Zohrabi-Kalantari, Philipp Heidler and Andreas Link*

Dibenzothiazoles as novel amyloid-imaging agents

pp 2789–2796

Chunying Wu, Jingjun Wei, Kuanqiang Gao and Yanming Wang*

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*Corresponding author

i⁺ Supplementary data available via ScienceDirect**COVER**

Death of Frédéric Chopin; 1810–1849 (after a painting of Félix Barrias; Bibliothèque Nationale de France; 38641706) [Janin, Y. L. *Bioorg. Med. Chem.* **2007**, 15, 2479–2513].

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