

European Journal of Medicinal Chemistry Vol 43, No 11, 2008

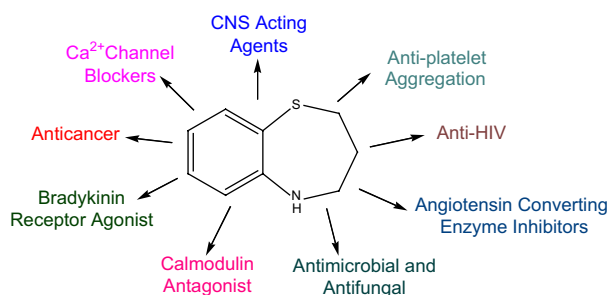
Contents

INVITED REVIEWS

1,5-Benzothiazepine, a versatile pharmacophore: A review

pp. 2279–2290

Jitender B. Bariwal, Kuldip D. Upadhyay, Atul T. Manvar, Jalpa C. Trivedi,
Jyoti S. Singh, Kishor S. Jain and Anamik K. Shah*

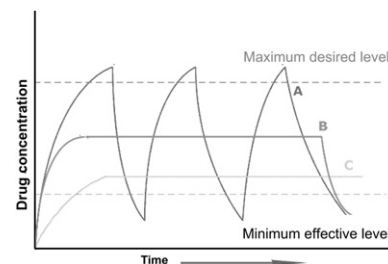


The effect of dendrimers on the pharmacodynamic and pharmacokinetic behaviors of non-covalently or covalently attached drugs

pp. 2291–2297

Yiyun Cheng* and Tongwen Xu**

Potential pharmacokinetic profiles of (A) traditional dosing, (B) formulations of drug–dendrimer complexes, and (C) drug–dendrimer conjugates.

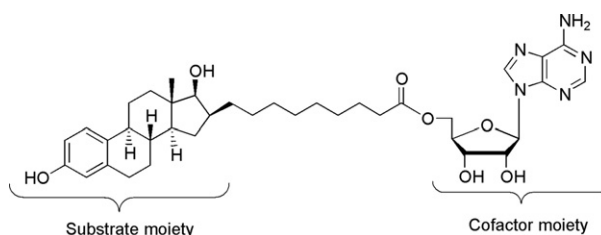


MINI-REVIEWS

Design and synthesis of bisubstrate inhibitors of type 1 17 β -hydroxysteroid dehydrogenase: Overview and perspectives

pp. 2298–2306

D. Fournier, D. Poirier*, M. Mazumdar and S.-X. Lin

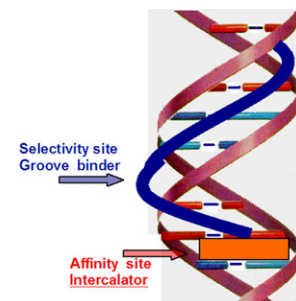


Ligand binding to nucleic acids and proteins: Does selectivity increase with strength?

pp. 2307–2315

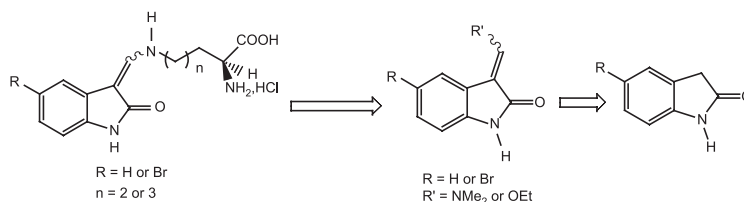
Hans-Jörg Schneider*

Linear correlation between selectivity and affinity may be expected on the basis of thermodynamic principles, but are often not observed. Apart from statistical problems this is mostly due to interactions which may remain constant at sites responsible for selectivity, but can differ significantly at affinity-dominating sites.

**ORIGINAL ARTICLES****Synthesis and biological evaluation of diversely substituted indolin-2-ones**

pp. 2316–2322

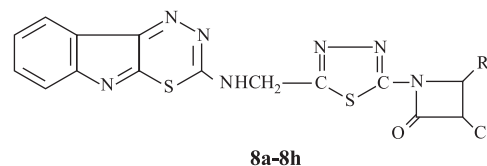
Fadoua Bouchikhi, Emilie Rossignol, Martine Sancelme, Bettina Aboab, Fabrice Anizon, Dorian Fabbro, Michelle Prudhomme and Pascale Moreau*

**Synthesis of new substituted azetidinoyl and thiazolidinoyl-1,3,4-thiadiazino (6,5-b) indoles as promising anti-inflammatory agents**

pp. 2323–2330

Sudhir Kumar Bhati and Ashok Kumar*

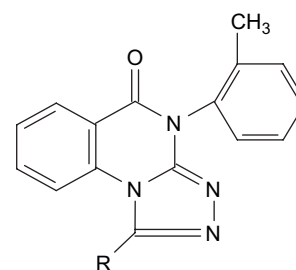
Synthesis and characterization of some indole derivatives have been found to possess anti-inflammatory and analgesic activities. The most active compound is **8g**. It showed better anti-inflammatory and analgesic activities at the dose of 100 mg/kg p.o.

**Synthesis and pharmacological investigation of novel 4-(2-methylphenyl)-1-substituted-4H-[1,2,4]triazolo[4,3-a]quinazolin-5-ones as new class of H₁-antihistaminic agents**

pp. 2331–2337

V. Alagarsamy*, M. Rupeshkumar, K. Kavitha, S. Meena, D. Shankar, A.A. Siddiqui and R. Rajesh

In the present study, new series of 1-substituted-4-(2-methylphenyl)-4H-[1,2,4]triazolo[4,3-a]quinazolin-5-ones were synthesized by the cyclization of 2-hydrazino-3-(2-methylphenyl)-3H-quinazolin-4-one with various one carbon donors and tested for their *in vivo* H₁-antihistaminic activity.

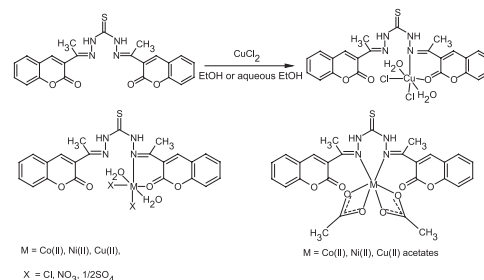


Synthesis and antitumor studies on novel Co(II), Ni(II) and Cu(II) metal complexes of bis(3-acetylcoumarin)thiocarbohydrazone

pp. 2338–2346

M.P. Sathisha, Ullas N. Shetti, V.K. Revankar* and K.S.R. Pai

Complexes of cobalt(II), nickel(II) and copper(II) with potential biologically active Schiff base ligand, bis(3-acetylcoumarin)thiocarbohydrazone synthesized and characterized. Their cytotoxic activity has been determined.

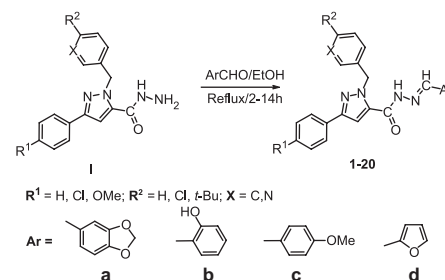


Synthesis and structure–activity relationships of novel 1-arylmethyl-3-aryl-1H-pyrazole-5-carbohydrazone hydrazone derivatives as potential agents against A549 lung cancer cells

pp. 2347–2353

Yong Xia, Chuan-Dong Fan, Bao-Xiang Zhao*, Jing Zhao, Dong-Soo Shin* and Jun-Ying Miao*

A series of novel 1-arylmethyl-3-aryl-1H-pyrazole-5-carbohydrazone hydrazone derivatives were synthesized and the effects of all the compounds on A549 cell growth were investigated. The study on structure–activity relationships and prediction of lipophilicities of compounds showed that compounds with Log *P* values in the range of 4.12–6.80 had inhibitory effects on the growth of A549 cells.

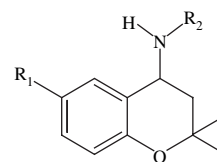


QSAR study about ATP-sensitive potassium channel activation of cromakalim analogues using CP-MLR approach

pp. 2354–2360

Susheela Sharma, Yenamandra S. Prabhakar, Prithvi Singh and Brij Kishore Sharma*

The structure–activity models of the myorelaxant activity of the cromakalim analogues have been investigated with topological descriptors using Combinatorial Protocol in Multiple Linear Regression (CP-MLR). The models developed and the participating descriptors suggest that the substituent groups hold scope for further modification in the optimization of activity.

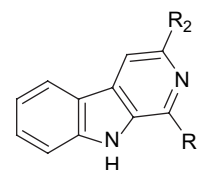


3D and quantum QSAR of non-benzodiazepine compounds

pp. 2361–2372

F.A. Pasha, M. Muddassar, Seung Joo Cho*, Kaleem Ahmad and Yakub Beg

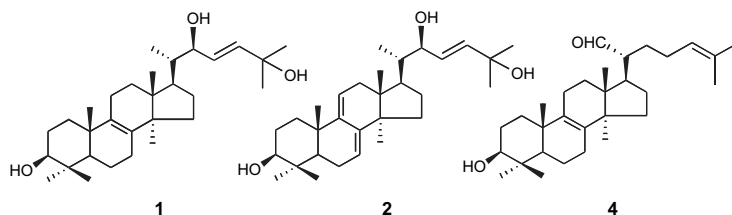
A combined physicochemical and 3D technique is used to establish the QSAR of four series of non-benzodiazepines towards BzR.



Lanostane-type triterpenoids from the sclerotia of *Inonotus obliquus* possessing anti-tumor promoting activity pp. 2373–2379

Sayaka Taji, Takeshi Yamada, Shun-ichi Wada, Harukuni Tokuda, Kazuo Sakuma and Reiko Tanaka*

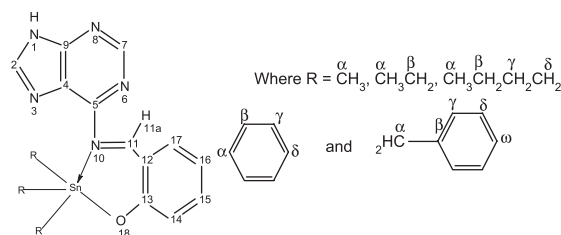
New triterpenoids **1** and **2** were isolated and their structures were determined to be **1** and **2**. Compound **4** showed strong anti-tumor promoting activity in the in vivo carcinogenesis test.



Synthesis, spectral characterization and bio-analysis of some organotin(IV) complexes pp. 2380–2385

Wajid Rehman*, Musa Kaleem Baloch and Amin Badshah

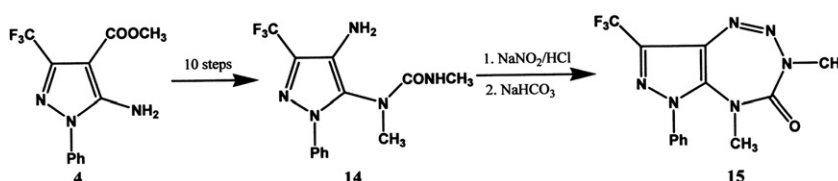
Five novel organotin(IV) derivatives have been synthesized by refluxing trimethyl, triethyl, tributyl, and triphenyl and tribenzyltin chloride with Schiff base derived from salicylaldehyde and adenine. These compounds were characterized by spectroscopic (IR, ^1H , ^{13}C , ^{119}Sn -NMR, $^{119\text{m}}\text{Sn}$ Mössbauer) techniques and elemental analysis. Based on these results trigonal bipyramidal geometry is suggested. The synthesized compounds were also treated with various microorganisms and found to be active.



Proposed structure of trialkyltin (IV) complexes of the ligand.

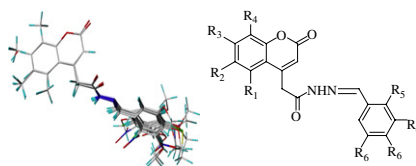
Synthesis and induction of G0–G1 phase arrest with apoptosis of 3,5-dimethyl-6-phenyl-8-(trifluoromethyl)-5,6-dihydropyrazolo[3,4-f][1,2,3,5]tetrazepin-4(3H)-one pp. 2386–2394

Benedetta Maggio, Demetrio Raffa, Maria Valeria Raimondi, Stella Cascioferro, Fabiana Plescia, Manlio Tolomeo, Eleonora Barbusca, Giuliana Cannizzo, Salvatrice Mancuso and Giuseppe Daidone*



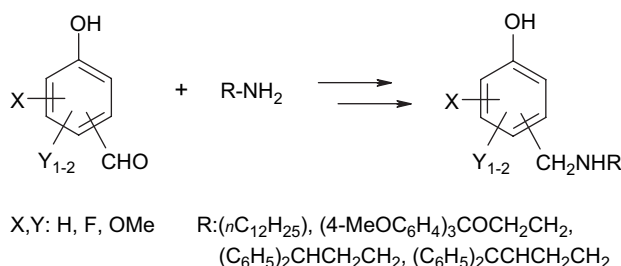
Synthesis, anti-tubercular activity and 3D-QSAR study of coumarin-4-acetic acid benzylidene hydrazides pp. 2395–2403

Atul Manvar, Alpeshkumar Malde, Jitender Verma, Vijay Virsodia, Arun Mishra, Kuldip Upadhyay, Hrishikesh Acharya, Evans Coutinho** and Anamik Shah*



Synthesis and biological evaluation of aminomethylphenol derivatives as inhibitors of the murine GABA transporters mGAT1–mGAT4 pp. 2404–2411

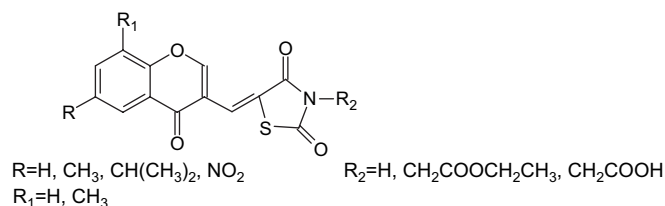
Andrea Kragler, Georg Höfner and Klaus T. Wanner*



Synthesis and aldose reductase inhibitory activity of some new chromonyl-2,4-thiazolidinediones pp. 2412–2417

Oya Bozdağ-Dündar*, Begüm Evranos, Net Daş-Evcimen, Mutlu Sarıkaya and Rahmiye Ertan

A series of chromonyl-2,4-thiazolidinediones (**Ia–e**, **IIa–e**, **IIIa–e**) were prepared by Knoevenagel reaction. The prepared compounds were tested for their aldose reductase inhibitory activities.



Synthesis and testing of peptides for anti-prion activity pp. 2418–2427

Shane Sellarajah, Cyrille Boussard, Tamuna Lekishvili, David R. Brown and Ian H. Gilbert*

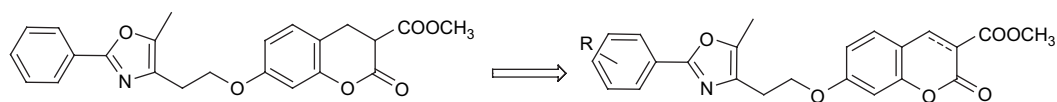
This paper describes the design, synthesis and evaluation of small peptides designed to interfere with interaction between PrP-res and PrP^C.

Gly-Ala-Ala-Ala-Pro-Gly

Synthesis and evaluation of a series of benzopyran derivatives as PPAR α/γ agonists pp. 2428–2435

Juanhong Yu, Lei Tang, Yushe Yang* and Ruyun Ji

A new series of benzopyran derivatives were synthesized as continuing work of compound **5**. Their PPAR agonist activities were evaluated and most of the compounds exhibit reasonable PPAR α and PPAR γ agonist activities. In particular, compounds **7b**, **8b**, **8e** and **8h** with remarkable PPAR γ EC₅₀ values of 0.001 μM are excellent full PPAR γ agonists.

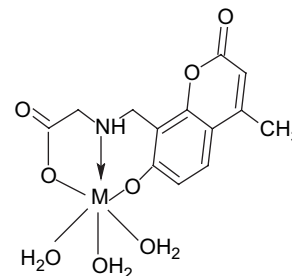


Synthesis, characterization of copper(II), cobalt(II), nickel(II), zinc(II) and cadmium(II) complexes of [7-hydroxy-4-methyl-8-coumarinyl]glycine and a comparative study of their microbial activities

pp. 2436–2441

Kalagouda B. Gudasi*, Manjula S. Patil and Ramesh S. Vadavi

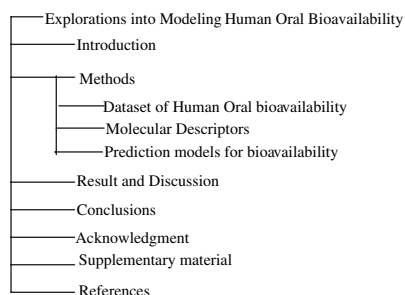
The metal salts, ligand and the corresponding complexes were screened simultaneously for their antimicrobial activity. As a synergic effect the metal complexes have shown enhanced activity against both the bacteria and fungi used.



Explorations into modeling human oral bioavailability

pp. 2442–2452

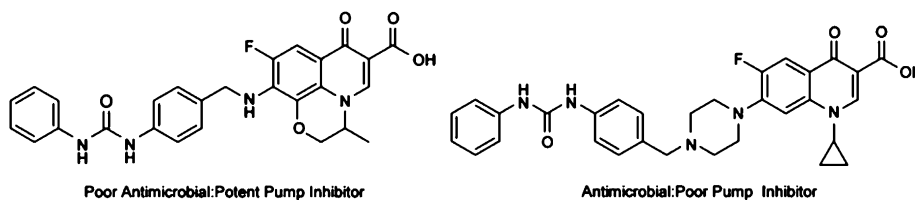
Zhi Wang, Aixia Yan*, Qipeng Yuan and Johann Gasteiger



Synthesis and evaluation of fluoroquinolone derivatives as substrate-based inhibitors of bacterial efflux pumps

pp. 2453–2463

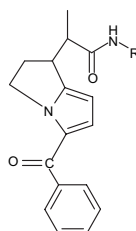
Nadezhda German, Peng Wei, Glenn W. Kaatz and Robert J. Kerns*



Synthesis, characterization and pharmacological evaluation of amide prodrugs of ketorolac

pp. 2464–2472

Ashutosh Mishra, Ravichandran Veerasamy, Prateek Kumar Jain, Vinod Kumar Dixit and Ram Kishor Agrawal*



Chemotherapy of leishmaniasis part-VIII: Synthesis and bioevaluation of novel chalcones

pp. 2473–2478

S.N. Suryawanshi*, Naveen Chandra, Pawan Kumar, Jyoti Porwal and Suman Gupta

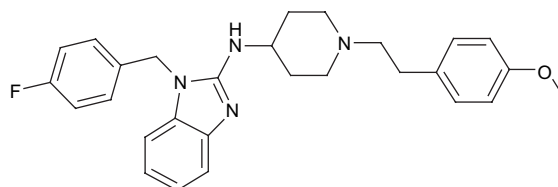
Some novel dihydro- α -ionone based chalcones have been synthesized and evaluated for their in vitro antileishmanial activity in promastigote and amastigote model. Some of the compounds showed 100% inhibition at 5 and 2 μ m/ml concentration.

**Identification of “toxicophoric” features for predicting drug-induced QT interval prolongation**

pp. 2479–2488

Alessio Coi, Ilaria Massarelli, Lara Testai, Vincenzo Calderone and Anna Maria Bianucci*

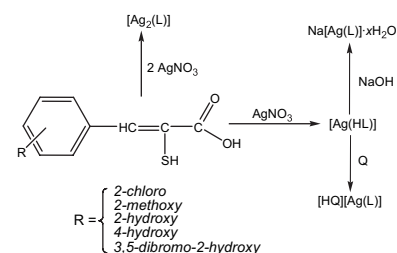
QT-prolonging drugs (like astemizole, in figure) were experimentally tested and computationally analyzed in order to evidence minimal features responsible for this undesired cardiotoxicity.

**Synthesis and antimicrobial activities of silver(I) 3-(substituted phenyl)sulfanylpropenoates**

pp. 2489–2497

Elena Barreiro, José S. Casas, María D. Couce, Agustín Sánchez, Rafael Seoane, José Sordo*, José M. Varela and Ezequiel M. Vázquez-López

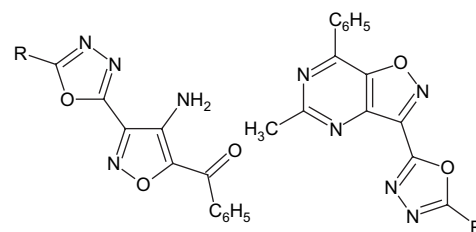
The reaction of 3-(aryl)-2-sulfanylpropenoic acids (H_2L) with silver nitrate afforded complexes of the type $[Ag(HL)]$, $[Ag_2(L)]$, $[HQ][Ag(L)]$ (HQ = diisopropylammonium) and $Na[Ag(L)] \cdot xH_2O$. The antimicrobial activities of the complexes against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Candida albicans*, *Pseudomonas aeruginosa* and carbapenem-resistant *P. aeruginosa* were evaluated.

**Synthesis and pharmacological screening of derivatives of isoxazolo[4,5-d]pyrimidine**

pp. 2498–2504

Edwin Wagner*, Kamal Al-Kadasi, Michał Zimecki and Wanda Sawka-Dobrowolska

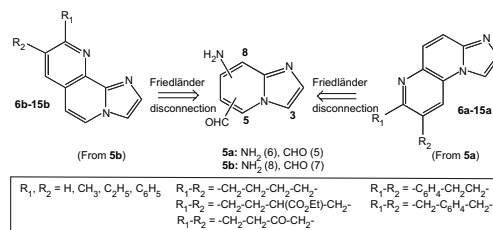
Derivative [4-amino-3-(1,3,4-oxiadiazol-2-yl)(phenyl)metanone showed interesting activity as cytostatic agent. Derivatives of isoxazolo[4,5-d]pyrimidine showed immunosuppressed activity. This effect was even stronger than that of Cephalosporin A.



Novel imidazo[1,2-*a*]naphthyridinic systems (part 1): Synthesis, antiproliferative and DNA-intercalating activities

pp. 2505–2517

Mounir Andaloussi, Emmanuel Moreau*, Nicolas Masurier, Jacques Lacroix, René C. Gaudreault, Jean-Michel Chezal, Anas El Laghdach, Damien Canitrot, Eric Debiton, Jean-Claude Teulade and Olivier Chavignon**

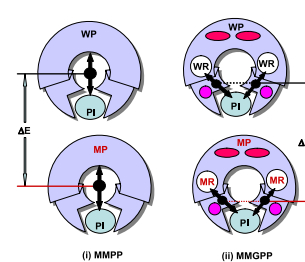
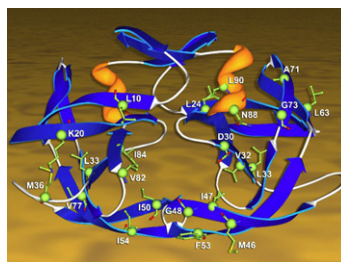


Prediction of HIV-1 protease inhibitor resistance by Molecular Modeling Protocols (MMPs) using GenMol™ software

pp. 2518–2534

G. Pèpe*, J. Courcambeck, R. Perbost, P. Jouanna and P. Halfon

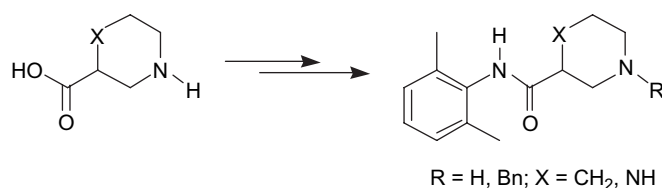
GenMol™ software is used for predicting HIV-1 Protease Inhibitor (PI) resistance. (i) The Molecular Modeling Phenotype Protocol (MMPP) considers the difference ΔE between (PI + wild protease WP) and (PI + mutated protease MP) binding energies. (ii) The Molecular Modeling Genotype–Phenotype Protocol (MMGPP) considers the difference ΔIE between (PI + wild residue WR) and (PI + mutated residue MR) interaction energies.



Constrained analogues of tocainide as potent skeletal muscle sodium channel blockers towards the development of antimyotonic agents

pp. 2535–2540

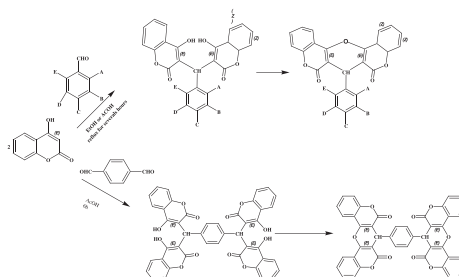
Alessia Catalano, Alessia Carocci, Filomena Corbo, Carlo Franchini*, Marilena Muraglia, Antonio Scilimati, Michela De Bellis, Annamaria De Luca, Diana Conte Camerino, Maria Stefania Sinicropi and Vincenzo Tortorella



Synthesis, structure, antimicrobial and antioxidant investigations of dicoumarol and related compounds

pp. 2541–2548

Naceur Hamdi*, M. Carmen Puerta and Pedro Valerga

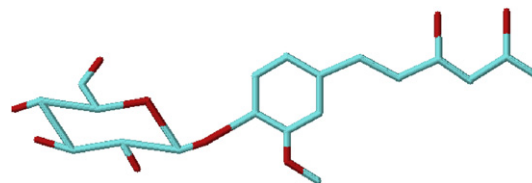


Synthesis, chemical and biological studies on new Fe^{3+} -glycosilated β -diketo complexes for the treatment of iron deficiency

pp. 2549–2556

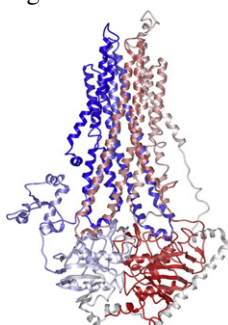
Beatrice Arezzini, Marco Ferrali, Erika Ferrari, Chiara Frassinetti, Sandra Lazzari, Gaetano Marverti, Ferdinando Spagnolo and Monica Saladini*

New glycosylated β -diketo compounds are synthesized and tested as potential oral iron supplements in treatment of anaemia. They show low cytotoxicity, form stable complexes and demonstrate poor affinity for Ca^{2+} .



A molecular model of a putative substrate releasing conformation of multidrug resistance protein 5 (MRP5) pp. 2557–2567

Aina Westrheim Ravna, Ingebrigt Sylte* and Georg Sager



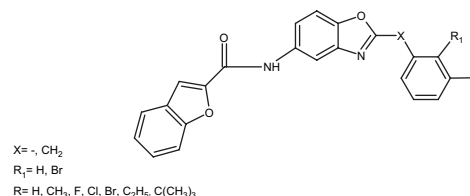
SHORT COMMUNICATIONS

Synthesis, antimicrobial activity, pharmacophore analysis of some new 2-(substitutedphenyl/benzyl)-5-[(2-benzofuryl)carboxamido]benzoxazoles

pp. 2568–2578

Sabiha Alper-Hayta, Mustafa Arisoy, Özlem Temiz-Arpaci, Ilkay Yildiz*, Esin Aki, Semiha Özkan and Fatma Kaynak

New 2-(substitutedphenyl/benzyl)-5-[(2-benzofuryl)carboxamido]benzoxazole derivatives were synthesized and antimicrobial activity of the compounds was investigated. The *in vitro* antimicrobial activity of the compounds was determined against some Gram-positive, Gram-negative bacteria and *Candida albicans*, *Candida krusei* and their drug-resistant isolates in comparison with standard drugs. Antimicrobial results indicated that the synthesized compounds possessed a broad spectrum of activity with MIC values 500–15.125 $\mu\text{g}/\text{ml}$. In the series, the most active compound against *C. krusei* and *C. albicans* isolates is **8** with MIC value 31.25 $\mu\text{g}/\text{ml}$. However, it is one dilution less potent than the compared fluconazole. Some of the screened compounds exhibit significant activity, having MIC value as 31.25 $\mu\text{g}/\text{ml}$ in *Pseudomonas aeruginosa* having same activity as Rifampicin. Furthermore, considering the worth of developing new antibacterial agents against drug-resistant *P. aeruginosa* the present study explores the structure–activity relationship analysis of 2-(substitutedphenyl/benzyl)-5-[(2-benzofuryl)carboxamido]benzoxazoles using 3D-common features pharmacophore hypotheses approach.

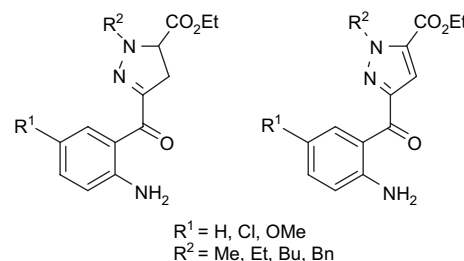


Pyrazoles and pyrazolines as neural and inducible nitric oxide synthase (nNOS and iNOS) potential inhibitors (III)

pp. 2579–2591

M. Dora Carrión, Luisa C. López Cara, M. Encarnación Camacho, Víctor Tapias, Germaine Escames, Darío Acuña-Castroviejo, Antonio Espinosa, Miguel A. Gallo and Antonio Entrena*

The synthesis and preliminary evaluation of a series of 1-alkyl-3-benzoyl-4,5-dihydro-1*H*-pyrazole and 1-alkyl-3-benzoyl-1*H*-pyrazole as potential inhibitors of both neuronal and inducible nitric oxide synthases (nNOS and iNOS) are described.

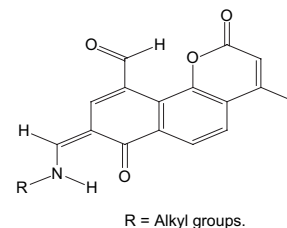


Novel keto-enamine Schiff's bases from 7-hydroxy-4-methyl-2-oxo-2H-benzo[h]chromene-8,10-dicarbaldehyde as potential antidyslipidemic and antioxidant agents

pp. 2592–2596

Koeni V. Sashidhara*, Jammikuntla N. Rosaiah, Gitika Bhatia and J.K. Saxena

A series of keto-enamine Schiff bases have been synthesized and evaluated for antidyslipidemic and anti-oxidant activity.



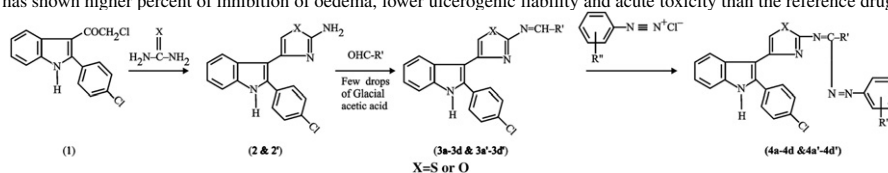
PRELIMINARY COMMUNICATIONS

Thiazolyl/oxazolyl formazanyl indoles as potent anti-inflammatory agents

pp. 2597–2609

Nisha Singh, Sudhir Kumar Bhati and Ashok Kumar*

A series of 3-(2'-substituted indolidene aminothiazol-4'-yl)-2-(4-chlorophenyl) indoles (**3a–3d**), 3-(2'-substituted indolidene amino oxazol-4'-yl)-2-(4-chlorophenyl) indoles (**3a'–3d'**) and 3-[2'-(1'-substituted phenyl-3'-substituted indolyl formazan-4'-yl)-thiazol-4'-yl]-2-(4-chlorophenyl) indoles (**4a–4h**), 3-[2'-(1'-substituted phenyl-3'-substituted indolyl formazan-4'-yl) oxazol-4'-yl]-2-(4-chlorophenyl) indoles (**4a'–4h'**) were synthesized and evaluated for their anti-inflammatory activity against carrageenan induced oedema in albino rats at a dose of 50 mg/kg p.o. The structure of all these compounds were established on the basis of elemental and spectral (IR, ¹H NMR and mass spectral data) studies. All the compounds of this series show moderate to good activity. The most active compound of this series 3-(2'-methyl indolidene aminothiazol-4'-yl)-2-(4-chlorophenyl) indole (**3b**) is found to be the most potent and has shown higher percent of inhibition of oedema, lower ulcerogenic liability and acute toxicity than the reference drug phenyl butazone.

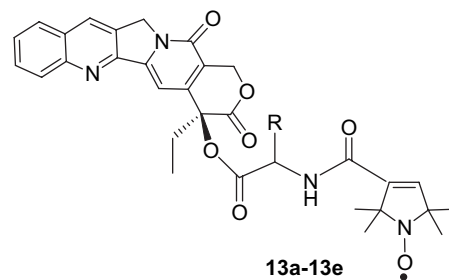


First synthesis of novel spin-labeled derivatives of camptothecin as potential antineoplastic agents

pp. 2610–2614

Ying-Qian Liu*, Xuan Tian**, Liu Yang and Zong-Cheng Zhan

Five novel spin-labeled camptothecin derivatives were synthesized and the *in vitro* pharmacokinetic determination of the lactones of representative compound **13a** showed that the biological life span of their lactone forms in human and mouse plasma significantly increased when compared with their mother compound camptothecin. Also, the *in vitro* cytotoxicity of compounds **13a–13e** against human bladder cancer T-24 showed either similar or better activity than that of the parent drug, camptothecin, and clinically available drug, irinotecan.



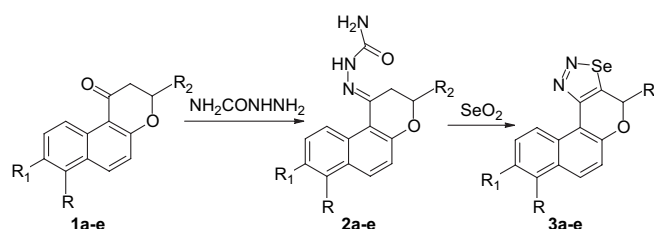
LABORATORY NOTES

Synthesis and *in vitro* anti-bacterial evaluation of tetracyclic-ortho-fused 4H-naphtho [1',2'–5,6]pyrano[3,4-d](1,2,3)selenadiazole and its derivatives

pp. 2615–2617

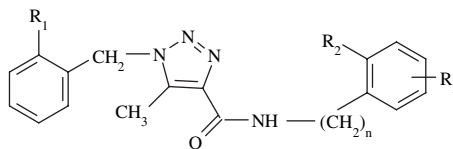
A.V. Karnik*, A.M. Kulkarni, N.J. Malviya, B.R. Mourya and B.L. Jadhav

Synthesis of naphthopyran fused 1,2,3-selenadiazole derivatives **3a–e** is achieved using high yielding synthetic protocol. These molecules **3a–e** have exhibited moderate antibacterial activity



1,2,3-Triazol-carboxanilides and 1,2,3-triazol-(N-benzyl)-carboxamides as BK-potassium channel activators. XII**pp. 2618–2626**

Vincenzo Calderone*, Francesca Lidia Fiamingo, Gabriella Amato, Irene Giorgi, Oreste Livi, Alma Martelli and Enrica Martinotti



n = 0 : Triazolcarboxanilides ; n = 1 : Triazol-N-benzylamide

COVER

Overlay of the experimental and docked conformations of the ligand fluorescein in complex with an anti-fluorescein 4-4-20 Fab fragment (PDB code 1flr, 1.85 Å). The top-scoring conformation (purple) selected by the HINT force field, among the 255 poses generated by AutoDock, nearly overlays the crystallographic structure (yellow), while the conformation selected by the AutoDock scoring function (green) reverses the positions of the carbonyl and hydroxyl groups.

Image provided by Francesca Spyraakis, Alessio Amadasi, Micaela Fornabaio, Donald J. Abraham, Andrea Mozzarelli, Glen E. Kellogg, Pietro Cozzini. © 2008. Published by Elsevier Masson SAS

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