



## European Journal of Medicinal Chemistry Vol 45, No 7, 2010

## Contents

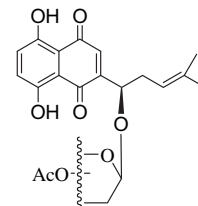
## ORIGINAL ARTICLES

**Synthesis and antitumor activity of new shikonin glycosides**

pp. 2713–2718

Yehua Su, Jiansheng Xie, Yanguang Wang\*, Xun Hu\* and Xianfu Lin

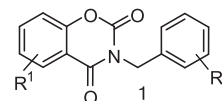
Eleven shikonin glycosides were synthesized and evaluated for their antitumor activity in vitro. Some of them were found to exhibit cytotoxic activities against both drug-sensitive and drug-resistant cell lines.

**A note to the biological activity of benzoxazine derivatives containing the thioxo group**

pp. 2719–2725

Karel Waisser\*, Eva Petřílková, Milan Perina, Věra Klimešová, Jiří Kuneš, Karel Palát, Jr., Jarmila Kaustová, Hans-Martin Dahse and Ute Möllmann

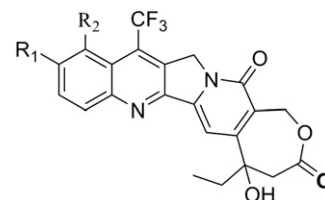
The replacement of the oxo group by the thioxo group in 3-benzyl-2*H*-1,3-benzoxazine-2,4(3*H*)-diones increases antimycobacterial activity. The most active derivatives are more active than isonicotinhydrazide (INH).

**Trifluoromethyl-promoted homocamptothecins: Synthesis and biological activity**

pp. 2726–2732

Lingjian Zhu, Zhenyuan Miao\*, Chunquan Sheng, Wei Guo, Jianzhong Yao, Wenfeng Liu, Xiaoying Che, Wenya Wang, Pengfei Cheng and Wannian Zhang\*\*

Seven new 7-trifluoromethylated homocamptothecin derivatives were prepared firstly by proline-catalyzed Friedländer annulation. Several of these fluorinated derivatives possessed higher antitumor activities than Topotecan (TPT).

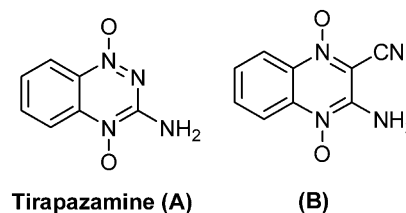


## New quinoxaline 1, 4-di-N-oxides: Anticancer and hypoxia-selective therapeutic agents

pp. 2733–2738

Magda M.F. Ismail\*, Kamelia M. Amin, Eman Noaman, Dalia H. Soliman and Yousry A. Ammar

A new series of quinoxaline 1,4-di-*N*-oxides was synthesized and evaluated for antitumor and hypoxic-selective cytotoxic activities compared to standards A and B respectively. Antitumor activity against liver carcinoma (Hepg2) and brain tumor (U251) human cell lines were evaluated, among the tested compounds, **5b** and **9b** exhibited potential cytotoxic effect against Hepg2 with IC50 values of 0.77 and 0.50 µg/mL respectively, whereas, all the tested compounds lack antitumor activity against U251 human cell line. Moreover, compound **4** was the most potent hypoxia selective-cytotoxin on EAC cell line; IC50 2.5 µg/mL, potency 22 µg/mL, and was approximately 5.4-times more selective cytotoxin (HCR > 40) than 3-amino-2-quinoxalinecarbonitrile-1,4-dioxide (standard B, HCR > 7.4). Compounds **8b** and **9b** were more selective than the standard.

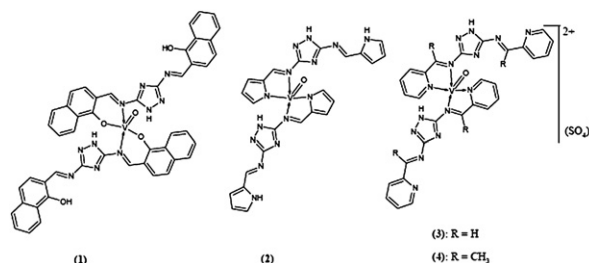


## Metal based biologically active compounds: Design, synthesis, and antibacterial/antifungal/cytotoxic properties of triazole-derived Schiff bases and their oxovanadium(IV) complexes

pp. 2739–2747

Zahid H. Chohan\*, Sajjad H. Sumrra, Moulay H. Youssoufi and Taibi B. Hadda\*\*

The simple Schiff bases showed weaker to significant activity against one or more bacterial and fungal strains. In most of the cases higher activity was exhibited upon coordination with vanadium(IV) metal. Brine shrimp bioassay was also carried out for *in vitro* cytotoxic properties against *Artemia salina*.

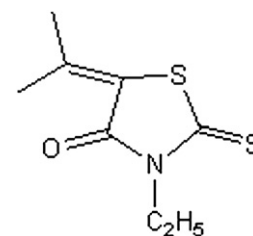


## 5-Isopropylidene-3-ethyl rhodanine induce growth inhibition followed by apoptosis in leukemia cells

pp. 2748–2752

Subban Ravi\*, Kishore K. Chiruvella, K. Rajesh, V. Prabhu and Sathees C. Raghavan

Microwave assisted synthesis of 5-isopropylidene-3-ethyl rhodanine **II** and its cytotoxic activity and induction of apoptosis in CEM.

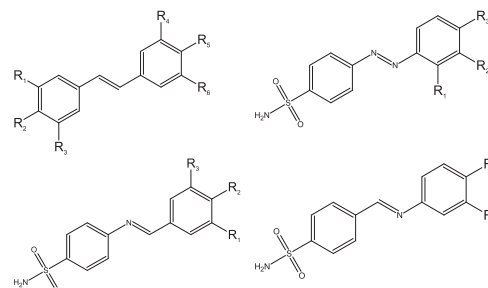


## QSAR analysis of diaryl COX-2 inhibitors: Comparison of feature selection and train-test data selection methods

pp. 2753–2760

Somaieh Soltani, Hoda Abolhasani, Afshin Zarghi and Abolghasem Jouyban\*

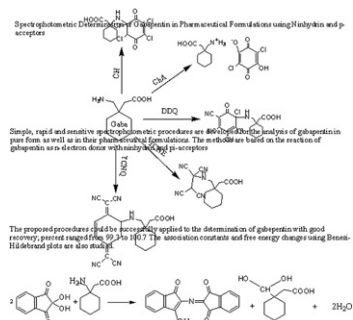
A QSAR study was developed in order to model the COX-2 inhibitory activity of a series of trans-stilbenoid diaryl compounds.



**Spectrophotometric determination of gabapentin in pharmaceutical formulations using ninhydrin and  $\pi$ -acceptors**

pp. 2761–2767

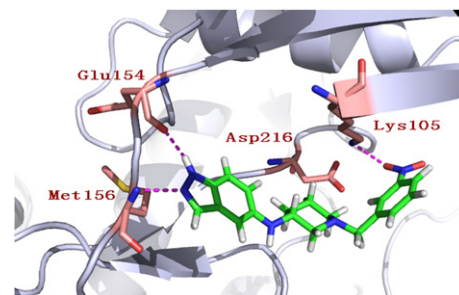
Farhan Ahmed Siddiqui\*, M. Saeed Arayne, Najma Sultana, Faiza Qureshi, Agha Zeeshan Mirza, M. Hashim Zuberi, Saima Sher Bahadur, Nawab Sher Afridi, Hina Shamshad and Nadia Rehman

**Molecular modeling studies of Rho kinase inhibitors using molecular docking and 3D-QSAR analysis**

pp. 2768–2776

Jin Qin, Beilei Lei, Lili Xi, Huanxiang Liu and Xiaojun Yao\*

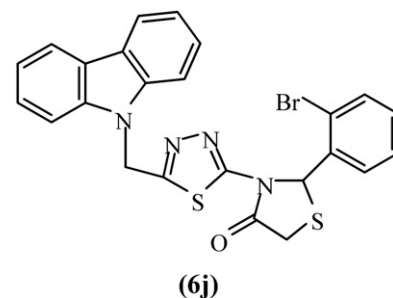
The interactions between the active site and compound 36 produced using the PyMol program [38]. Key hydrogen bonds to the protein backbone are highlighted in magenta.

**Synthesis and antipsychotic and anticonvulsant activity of some new substituted oxa/thiadiazolylazetidinonyl/thiazolidinonylcarbazoles**

pp. 2777–2783

Hemlata Kaur, Sunil Kumar, Pinki Vishwakarma, Monica Sharma, K.K. Saxena and Ashok Kumar\*

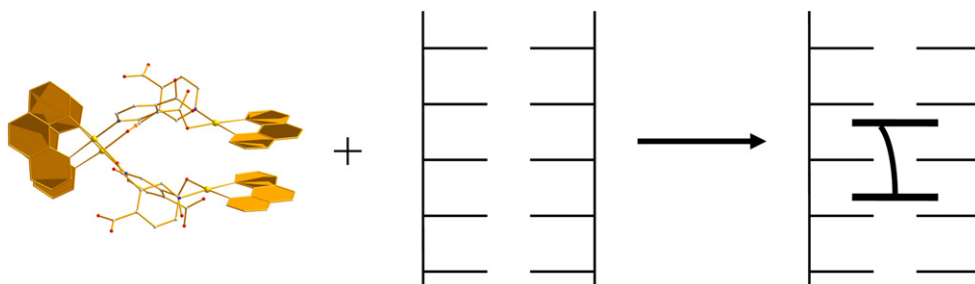
Synthesis and anticonvulsant activity of new oxa/thiadiazolylazetidinonyl/ thiazolidinonylcarbazole derivatives were reported here in. The compound **6j** exhibited promising antipsychotic and anticonvulsant activity.

**Hairpin-shaped tetranuclear palladium(II) complex: Synthesis, crystal structure, DNA binding and cytotoxicity activity studies**

pp. 2784–2790

En-Jun Gao\*, Ke-Hua Wang, Ming-Chang Zhu and Lei Liu

A tetranuclear complex with dipalladated phenanthroline rings bisintercalate to the base pairs of DNA.

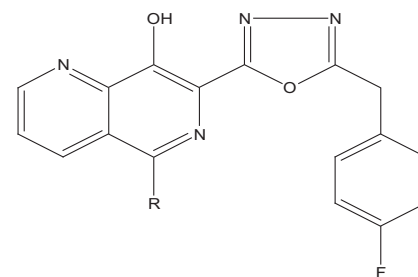


**QSAR study of substituted 1,3,4-oxadiazole naphthyridines as HIV-1 integrase inhibitors**

pp. 2791–2797

Veerasamy Ravichandran\*, Sivadasan Shalini, Karupiah Sundram and Arumugam Dhanaraj Sokkalingam

QSAR model indicates that valence connectivity index order 1, low unoccupied molecular orbital and dielectric energy are playing an important role in the HIV-1 integrase inhibitory activities of 1,3,4-oxadiazole substituted naphthyridine derivatives.

**Synthesis and preliminary biological evaluation of novel taspine derivatives as anticancer agents**

pp. 2798–2805

Jie Zhang, Yanmin Zhang, Yuanyuan Shan, Na Li, Wei Ma and Langchong He\*

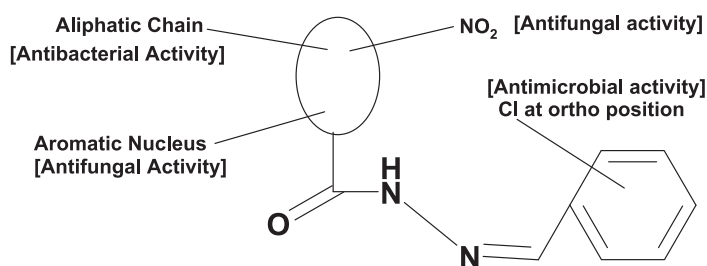
The compound **28** was built and docked into the active site of bFGFR-1 (PDB ID: 3C4F) using Sybyl 7.0. The docking result was showed by PyMOL.

**Benzylidene/2-chlorobenzylidene hydrazides: Synthesis, antimicrobial activity, QSAR studies and antiviral evaluation**

pp. 2806–2816

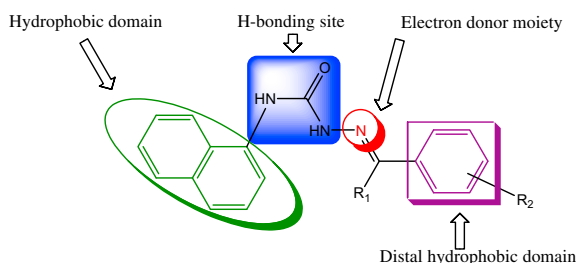
Davinder Kumar, Vikramjeet Judge, Rakesh Narang, Sonia Sangwan, Erik De Clercq, Jan Balzarini and Balasubramanian Narasimhan\*

Multi-target QSAR models developed for the antimicrobial activity of synthesized substituted hydrazides indicated the importance of topological parameters in demonstrating antimicrobial activity.

**Combating oxidative stress in epilepsy: Design, synthesis, quantum chemical studies and anticonvulsant evaluation of 1-(substituted benzylidene/ethylidene)-4-(naphthalen-1-yl)semicarbazides**

pp. 2817–2826

Faizul Azam\*, Bashir A. El-gnidi and Ismail A. Alkskas

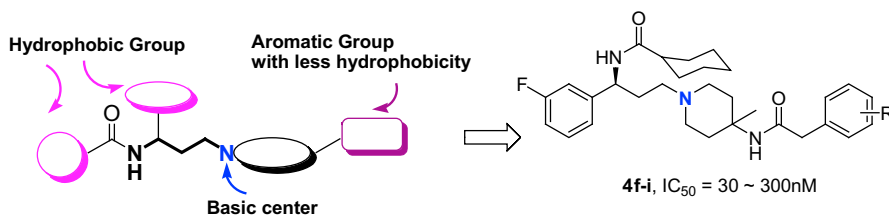


## Efficient synthesis and identification of novel propane-1,3-diamino bridged CCR5 antagonists with variation on the basic center carrier

pp. 2827–2840

Xing Fan, Hu-Shan Zhang, Li Chen and Ya-Qiu Long\*

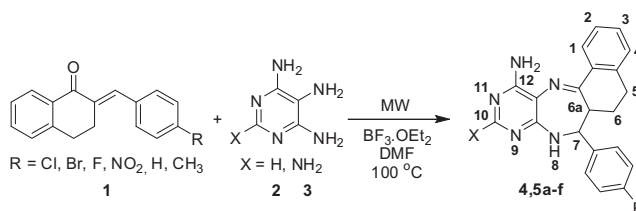
Based on the putative 3-domain pharmacophore model for CCR5 inhibition, piperidine-/tropane-/piperazine-bridged 1-acyl-1,3-propanediamine compounds were designed and synthesized, focused on the basic center carrier structure. Thus 4-methyl-4-aminopiperidine containing analogs were identified as new scaffold CCR5 antagonists with nanomolar  $IC_{50}$  values.



## Synthesis of novel 6,6a,7,8-tetrahydro-5H-naphtho[1,2-e]pyrimido[4,5-b][1,4]diazepines under microwave irradiation as potential anti-tumor agents

pp. 2841–2846

Braulio Insuasty\*, Angélica García, Jairo Quiroga, Rodrigo Abonia, Manuel Nogueras and Justo Cobo

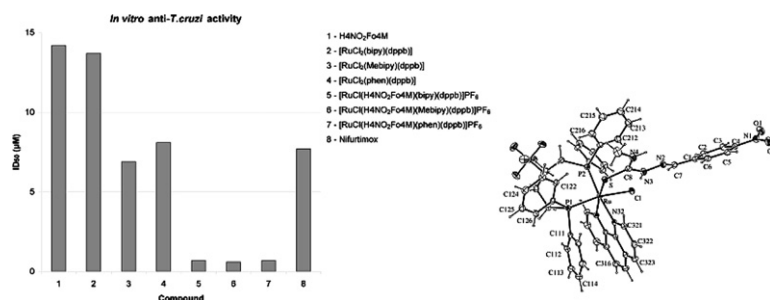


## Coordination of nitro-thiosemicarbazones to ruthenium(II) as a strategy for anti-trypanosomal activity improvement

pp. 2847–2853

Claudia Rodrigues, Alzir A. Batista, Javier Ellena, Eduardo E. Castellano, Diego Benítez, Hugo Cerecetto, Mercedes González, Leticia R. Teixeira\* and Heloisa Beraldo

The association of a nitro-thiosemicarbazone with ruthenium(II), dppb = 1,4-bis(diphenylphosphine)butane and bipyridine (bipy) or phenanthroline (phen) in one same complex proved to be an excellent strategy of anti-*T. cruzi* activity improvement.

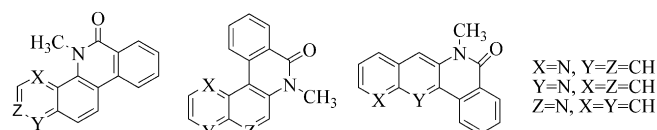


## Design and preparation of aza-analogues of benzo[c]phenanthridine framework with cytotoxic and antiplasmodial activities

pp. 2854–2859

Ange-Désiré Yapi, Nicolas Desbois, Jean-Michel Chezal, Olivier Chavignon, Jean-Claude Teulade, Alexis Valentin and Yves Blache\*

A novel library of aza-analogs of benzo[c]phenanthroline framework derivatives was designed and prepared. All compounds were tested for *in vitro* antiplasmodial activities against both chloroquino-sensitive and chloroquino-resistant lines. In addition, some of them displayed good *in vitro* activities against two cancer lines.

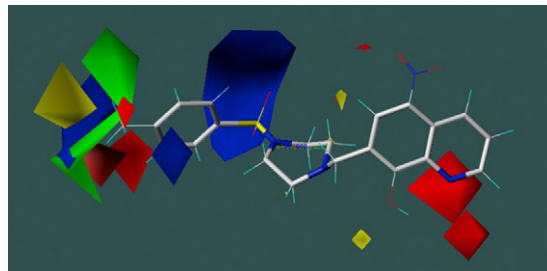


**Synthesis and structure-activity relationship study of 8-hydroxyquinoline-derived Mannich bases as anticancer agents**

pp. 2860–2867

Arthur Y. Shaw\*, Chun-Yi Chang, Mei-Yuan Hsu, Pei-Jung Lu, Chia-Ning Yang,  
Hui-Ling Chen, Cheng-Wei Lo, Chung-Wai Shiau and Ming-Kai Chern

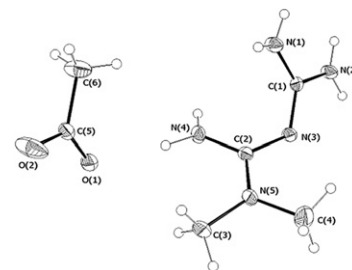
Synthesis of clioquinol-derived Mannich bases and SAR study for their anticancer activity are reported.

**Prospects for new antimicrobials based on N,N-dimethylbiguanide complexes as effective agents on both planktonic and adhered microbial strains**

pp. 2868–2875

Rodica Olar\*, Mihaela Badea, Dana Marinescu, Carmen-Mariana Chifiriuc, Coralia Bleotu,  
Maria Nicoleta Grecu, Emilia Elena Iorgulescu, Marcela Bucur, Veronica Lazar and Adriana Finaru

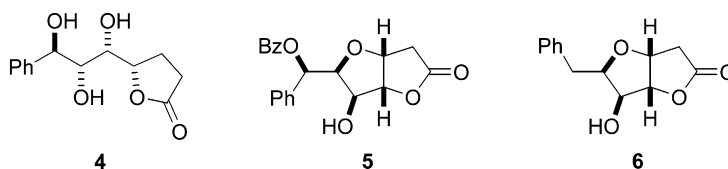
A series of new complexes  $M(\text{DMBG})_2(\text{CH}_3\text{COO})_2 \cdot n\text{H}_2\text{O}$  ( $M$ : Mn, Ni, Cu and Zn; DMBG: N,N-dimethylbiguanide) as well as the derivative  $(\text{HDMBG})(\text{CH}_3\text{COO})$  have been synthesised and evaluated for their antimicrobial, antibiofilm as well as cytostatic activity.

**Design, synthesis and antiproliferative activity of styryl lactones related to (+)-goniofufurone**

pp. 2876–2883

Velimir Popsavin\*, Bojana Srećo, Goran Benedeković, Jovana Francuz, Mirjana Popsavin, Vesna Kojić and Gordana Bogdanović

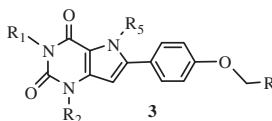
(+)-Goniofufurone analogues **4–6** have been synthesized starting from D-xylose. Their in vitro antitumour activities were recorded and compared with those observed for the parent natural product.

**Synthesis and pharmacological evaluation of novel substituted 9-deazaxanthines as A<sub>2B</sub> receptor antagonists**

pp. 2884–2892

María Isabel Nieto, María Carmen Balo, José Brea, Olga Caamaño\*, Franco Fernández\*, Xerardo García-Mera, Carmen López, María Isabel Loza, José Enrique Rodríguez-Borges and Bernat Vidal

A new series of 9-deazaxanthine derivatives with various substituents in the ring were synthesized and evaluated for their binding affinities for the four human recombinant adenosine receptors.



$R_1$  = H, methyl, propyl

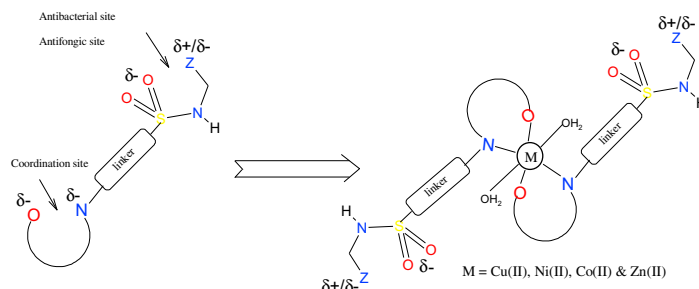
$R_2$  = H, methyl, propyl

$R_5$  = H, methyl

$R$  = phenylaminocarbonyl, bromophenylaminocarbonyl, fluorophenylaminocarbonyl, 4-phenylpiperazylincarbonyl, 3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl, 3,4-dihydroisquinolin-2(1H)-ylcarbonyl

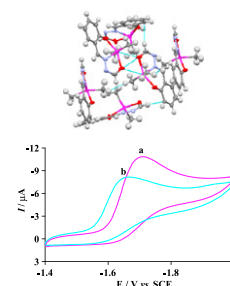
## pp. 2893–2901

Our real challenge is not to prepare new attractive molecular edifice but to know how to combine pharmacophore sites and to be able to improve the adequate antimicrobial activity of organic drugs against various microorganisms via metal coordination approach without losing control of selectivity.



## pp. 2902–2911

Six new diorganotin(IV) derivatives of N'-(2-hydroxybenzylidene)formohydrazide (H<sub>2</sub>L) have been synthesised and characterized. These compounds have good DNA binding ability.

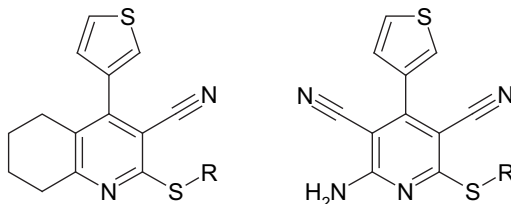


## pp. 2912–2918

$R1 = \alpha \text{ OH}, R2 = \text{OH}$   
 $R1 = \beta \text{ OH}, R2 = \text{H}$   
 $R1 = \alpha \text{ OH}, R2 = \text{H}$

pp. 2919–2927

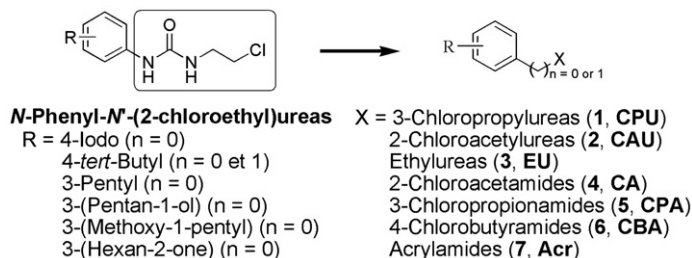
The title compounds were developed as inhibitors of the cancer-related tyrosine kinase RET and tested for antiproliferative activity against cancer cell lines.



### Synthesis, antiproliferative activity evaluation and structure–activity relationships of novel aromatic urea and amide analogues of *N*-phenyl-*N'*-(2-chloroethyl)ureas

pp. 2928–2937

Sébastien Fortin\*, Emmanuel Moreau, Jacques Lacroix, Marie-France Côté, Éric Petitclerc and René C.-Gaudreault\*\*

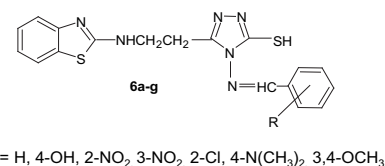


### Synthesis and evaluation of some new benzothiazole derivatives as potential antimicrobial agents

pp. 2938–2942

Balram Soni\*, Mahendra Singh Ranawat, Rambabu Sharma, Anil Bhandari and Sanjay Sharma

A novel series of 5-[2-(1,3-benzothiazol-2-yl-amino) ethyl]-4-(arylideneamino)-3-mercapto-(4*H*)-1,2,4-triazoles **6a–g** were synthesized and evaluated for their antimicrobial activity to identify potential compounds.

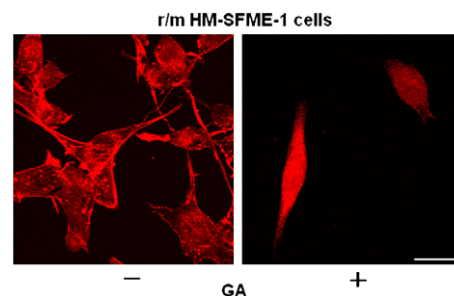


### Novel effects of glycyrrhetic acid on the central nervous system tumorigenic progenitor cells: Induction of actin disruption and tumor cell-selective toxicity

pp. 2943–2948

Hideaki Yamaguchi\*, Toshiro Noshita, Tao Yu, Yumi Kidachi, Katsuyoshi Kamiie, Hironori Umetsu and Kazuo Ryoyama

GA disrupts actin cytoskeleton and shows selective toxicity against the CNS tumorigenic progenitor cells.

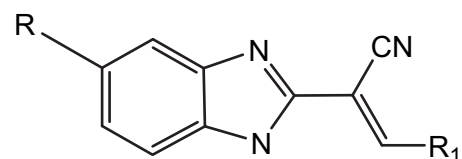


### Synthesis and anticancer activity of some novel 2-substituted benzimidazole derivatives

pp. 2949–2956

Hanan M. Refaat\*

Synthesis and in vitro anticancer evaluation of various series of 2-substituted benzimidazoles.



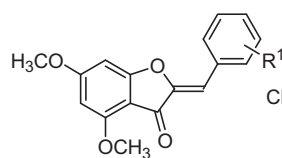


**Functionalized aurones as inducers of NAD(P)H:quinone oxidoreductase 1 that activate AhR/XRE and Nrf2/ARE signaling pathways: Synthesis, evaluation and SAR**

pp. 2957–2971

Chong-Yew Lee, Eng-Hui Chew and Mei-Lin Go\*

The design, synthesis and biological evaluation of a series of functionalized aurones as potential chemopreventive agents is described. Several active compounds were identified.

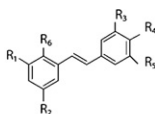
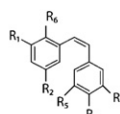


CD: Concentration to double NQO1 activity

R<sup>1</sup> = 2'-OH CD = 0.18 μMR<sup>1</sup> = 2'-F CD = 0.16 μMR<sup>1</sup> = 3'-F CD = 0.15 μM**Structural determinants of resveratrol for cell proliferation inhibition potency: Experimental and docking studies of new analogs**

pp. 2972–2980

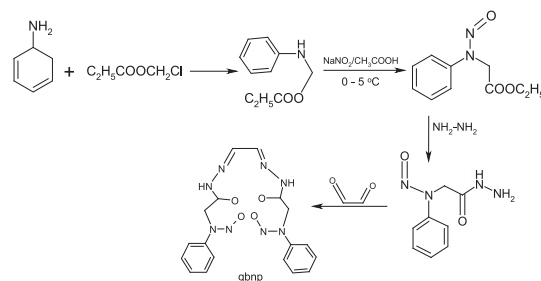
Frédéric Mazué, Colin Didier, Jessica Gobbo, Maria Wegner, Antonio Rescifina, Carmela Spatafora, Dominique Fasseur, Dominique Delmas, Philippe Meunier, Corrado Tringali and Norbert Latruffe\*

**1** R<sub>1</sub> = R<sub>2</sub> = R<sub>4</sub> = OH; R<sub>3</sub> = R<sub>5</sub> = R<sub>6</sub> = H**3** R<sub>1</sub> = R<sub>2</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>3</sub> = R<sub>5</sub> = R<sub>6</sub> = H**5** R<sub>1</sub> = R<sub>2</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>3</sub> = R<sub>5</sub> = H; R<sub>6</sub> = OH**7** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>5</sub> = OCH<sub>3</sub>; R<sub>4</sub> = R<sub>6</sub> = H**9** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>5</sub> = OCH<sub>3</sub>; R<sub>4</sub> = H; R<sub>6</sub> = OH**11** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>5</sub> = R<sub>6</sub> = H**13** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>5</sub> = H; R<sub>6</sub> = OH**2** R<sub>1</sub> = R<sub>2</sub> = R<sub>4</sub> = OH; R<sub>3</sub> = R<sub>5</sub> = R<sub>6</sub> = H**4** R<sub>1</sub> = R<sub>2</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>3</sub> = R<sub>5</sub> = R<sub>6</sub> = H**6** R<sub>1</sub> = R<sub>2</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>3</sub> = R<sub>5</sub> = H; R<sub>6</sub> = OH**8** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>5</sub> = OCH<sub>3</sub>; R<sub>4</sub> = R<sub>6</sub> = H**10** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>5</sub> = OCH<sub>3</sub>; R<sub>4</sub> = H; R<sub>6</sub> = OH**12** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>5</sub> = R<sub>6</sub> = H**14** R<sub>1</sub> = R<sub>2</sub> = R<sub>3</sub> = R<sub>4</sub> = OCH<sub>3</sub>; R<sub>5</sub> = H; R<sub>6</sub> = OH**Transition metal complexes of a new hexadentate macrocyclic N<sub>2</sub>O<sub>4</sub>-donor Schiff base: Inhibitory activity against bacteria and fungi**

pp. 2981–2986

Manjula Patil, Rekha Hunoor and Kalagouda Gudasi\*

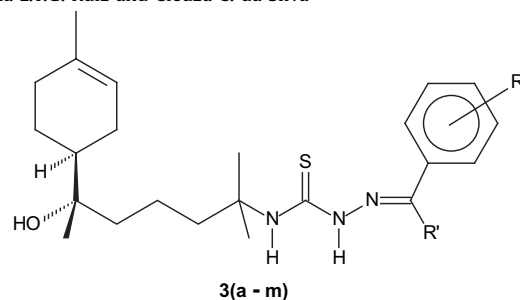
The new macrocyclic hexadentate ligand has potential binding sites towards metal ions, coordinating through two azomethine nitrogens, two amide carbonyl oxygens and two nitroso oxygens in N<sub>2</sub>O<sub>4</sub> fashion.

**Antitumor activity of (–)-α-bisabolol-based thiosemicarbazones against human tumor cell lines**

pp. 2987–2993

Alan P. da Silva, Manuele V. Martini, Cecília M.A. de Oliveira, Silvio Cunha, João E. de Carvalho, Ana L.T.G. Ruiz and Cleuza C. da Silva\*

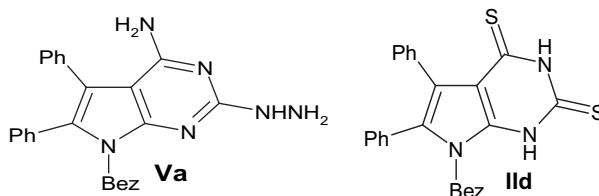
A new series of thiosemicarbazone derivatives based on the natural product α-(–)-bisabolol was synthesized and the *in vitro* anti-cancer activity of these compounds was evaluated against eight human tumor cell lines.



### Synthesis and biological evaluation of some thio containing pyrrolo [2,3-d]Pyrimidine derivatives for their anti-inflammatory and anti-microbial activities

pp. 2994–3004

Mosaad S. Mohamed\*, Rehab Kamel and Samar S. Fatahala

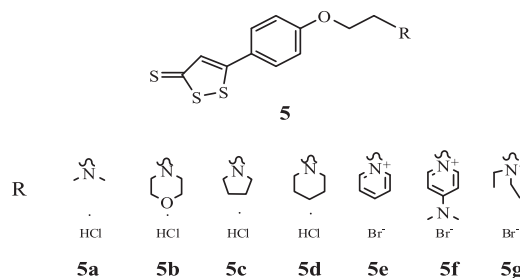


### Design, synthesis, and pharmacological evaluation of the aqueous prodrugs of desmethyl anethole trithione with hepatoprotective activity

pp. 3005–3010

Pei Chen, Yu Luo, Li Hai, Shan Qian and Yong Wu\*

The water-soluble prodrug **5a** exhibited the best hepatoprotective activity equal to the reference drug anethole trithione. Their main metabolite was the same desmethyl anethole trithione found in mice.

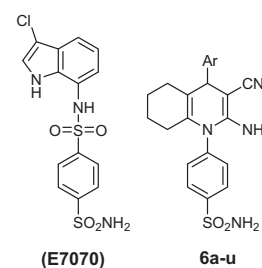


### Synthesis and *in vitro* anticancer screening of some novel 4-[2-amino-3-cyano-4-substituted-5,6,7,8-tetrahydroquinolin-1-(4H)-yl]benzenesulfonamides

pp. 3011–3018

Mansour S. Al-Said, Mostafa M. Ghorab\*, Saleh I. Al-qasoumi, Ebba M. El-Hossary and Eman Noaman

A series of some new 4-(quinolin-1-yl)benzenesulfonamide derivatives **6a–u** was synthesized, and evaluated for their *in vitro* anticancer activity.

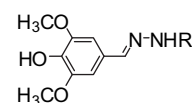


### Synthesis and antioxidant activity evaluation of a syringic hydrazones family

pp. 3019–3026

Nadji Belkheiri, Benaissa Bouguerne, Florence Bedos-Belval, Hubert Duran, Corinne Bernis, Robert Salvayre, Anne Nègre-Salvayre\* and Michel Baltas\*\*

A series of syringic hydrazones has been synthesized. Their antioxidant properties and their carbonyl scavenger efficiency have been explored suggesting a new class of agents.

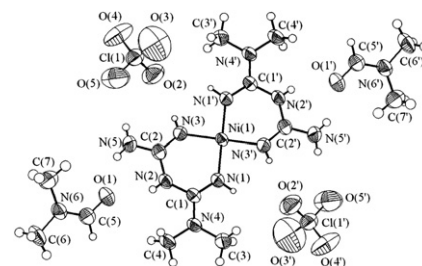


***N,N*-dimethylbiguanide complexes displaying low cytotoxicity as potential large spectrum antimicrobial agents**

pp. 3027–3034

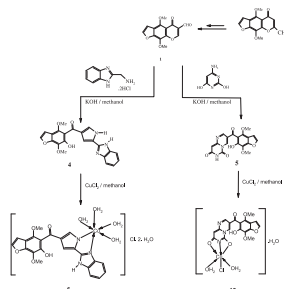
Rodica Olar\*, Mihaela Badea, Dana Marinescu, Mariana-Carmen Chifiriuc, Coralia Bleotu, Maria Nicoleta Grecu, Emilia-Elena Iorgulescu and Veronica Lazar

A series of new complexes  $M(\text{DMBG})_2(\text{ClO}_4)_2$  ( $M$ : Mn, Ni, Cu and Zn; DMBG: *N,N*-dimethylbiguanide) have been synthesised and evaluated for their antimicrobial, antibiofilm as well as cytostatic activity.

**Novel antiviral benzofuran-transition metal complexes**

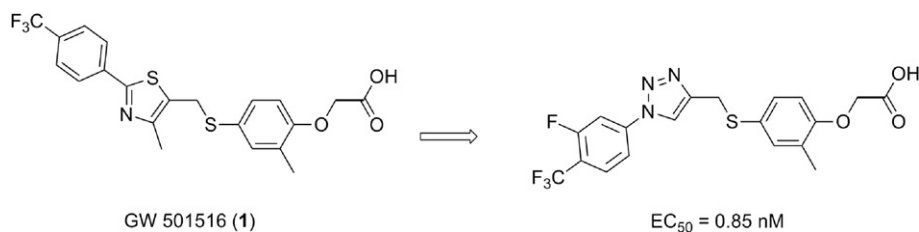
pp. 3035–3046

Shadia A. Galal\*, Amira S. Abd El-All, Khaled H. Hegab, Asmaa A. Magd-El-Din, Nabil S. Youssef and Hoda I. El-Diwani

**Synthesis and dual PPAR $\alpha/\delta$  agonist effects of 1,4-disubstituted 1,2,3-triazole analogues of GW 501516**

pp. 3047–3055

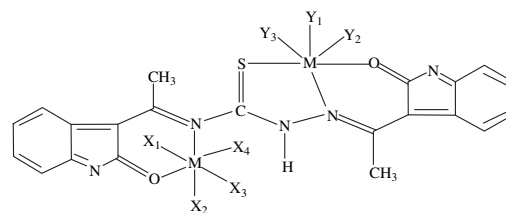
Calin C. Ciocoiu, Nataša Nikolić, Huyen Hoa Nguyen, G. Hege Thoresen, Arne J. Aasen and Trond Vidar Hansen\*

**Synthesis, spectral characterization and antimicrobial evaluation of Schiff base Cu (II), Ni (II) and Co (II) complexes**

pp. 3056–3062

Gajendra Kumar, Dharmendra Kumar, Shoma Devi, Rajeev Johari and C.P. Singh\*

Schiff base  $M$  (II) complexes were synthesized and evaluated for antimicrobial activity. Complex 4  $[\text{HLNi}_2(\text{OC}(\text{O})\text{CH}_3)_4(\text{H}_2\text{O})_3]$  exhibited best antimicrobial activity.

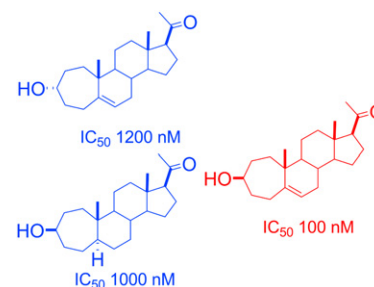


### Synthesis and GABA<sub>A</sub> receptor activity of A-homo analogues of neuroactive steroids

pp. 3063–3069

María V. Dansey, Pablo H. Di Chenna, Adriana S. Veleiro, Zdena Krístofiková, Hana Chodounska, Alexander Kasal and Gerardo Burton\*

A-homo steroids were synthesized by acid catalyzed rearrangement of a cyclopropylpregnane. The unsaturated 3 $\beta$ -hydroxy steroid was as active as allopregnanolone in the inhibition of TBPS binding to GABA<sub>A</sub> receptors.

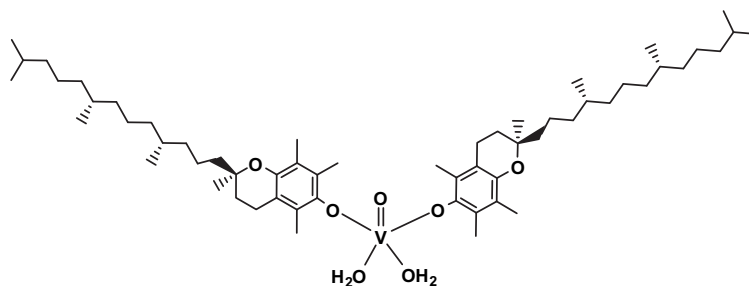


### Identification of a new anti-diabetic agent by combining VOSO<sub>4</sub> and vitamin E in a single molecule: Studies on its spectral, thermal and pharmacological properties

pp. 3070–3079

Moamen S. Refat\* and Samir A. El-Shazly

Structure of [VO(Vit E)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>]<sub>2</sub>H<sub>2</sub>O complex.

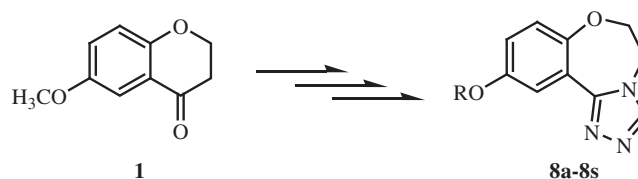


### Design and synthesis of 10-alkoxy-5, 6-dihydro-triazolo[4,3-d]benzo[f][1,4]oxazepine derivatives with anticonvulsant activity

pp. 3080–3086

Xian-Qing Deng, Cheng-Xi Wei, Fu-Nan Li, Zhi-Gang Sun\*\* and Zhe-Shan Quan\*

A series of novel triazolo[4,3-d]benzo[f][1,4]oxazepine derivatives was synthesized and their anticonvulsant effects on mice were assessed. The mechanism of action of compound 8f was GABA-mediated.

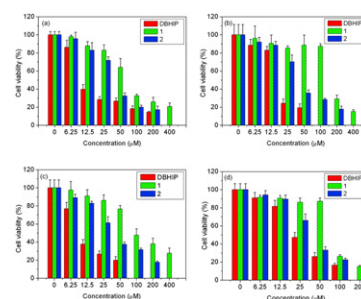


### Synthesis of ruthenium(II) complexes and characterization of their cytotoxicity in vitro, apoptosis, DNA-binding and antioxidant activity

pp. 3087–3095

Yun-Jun Liu\*, Cheng-Hui Zeng, Zhen-Hua Liang, Jun-Hua Yao, Hong-Liang Huang, Zheng-Zheng Li and Fu-Hai Wu

The DNA-binding properties of complexes [Ru(bpy)<sub>2</sub>(DBHIP)]<sup>2+</sup> and [Ru(phen)<sub>2</sub>(DBHIP)]<sup>2+</sup> were investigated. The cytotoxicity was evaluated by MTT assay. The apoptosis assay was performed with acridine orange/ethidium bromide (AO/EB) staining methods.

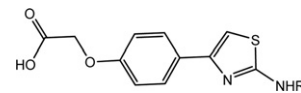


**Synthesis and hypolipidemic activity of novel 2-(4-(2-substituted aminothiazole-4-yl) phenoxy) acetic acid derivatives**

pp. 3096–3100

Santosh N. Mokale, Priyanka T. Sanap and Devanand B. Shinde\*

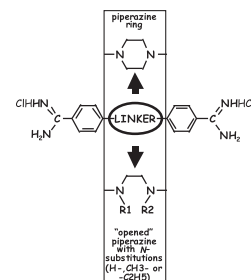
A novel series of aminothiazole compounds possessing phenoxy acetic acid moiety were synthesized. The synthesized compounds were evaluated for their hypolipidemic activity.

**1,2-Ethane bis-1-amino-4-benzamidine is active against several brain insult and seizure challenges through anti-NMDA mechanisms targeting the <sup>3</sup>H-TCP binding site and antioxidant action**

pp. 3101–3110

Joseph Vamecq\*, Pierre Maurois, Nicole Pages, Pierre Bac, James P. Stables, Pierre Gressens, Dimitri Stanicki and Jean Jacques Vanden Eynde

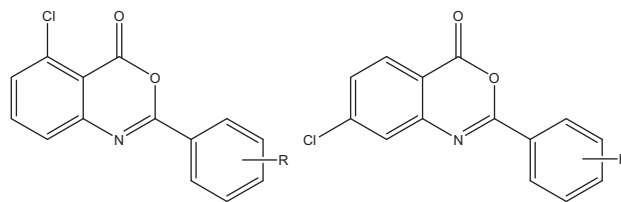
1,2-Ethane bis-1-amino-4-benzamidine [EBAB] (R1 = R2 = H) presented with efficacy against various types of seizures and brain wounds, along with inhibitory properties towards <sup>3</sup>H-TCP binding to NMDA receptor (IC<sub>50</sub> = 1.4 mM).

**Synthesis and evaluation of benzoxazinone derivatives on activity of human neutrophil elastase and on hemorrhagic shock-induced lung injury in rats**

pp. 3111–3115

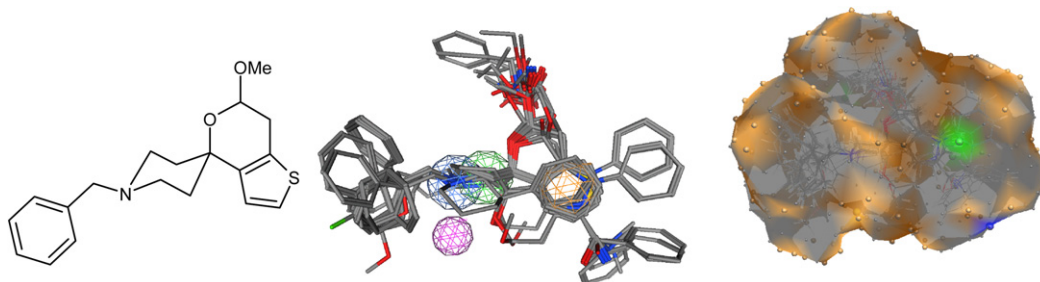
Pei-Wen Hsieh\*, Huang-Ping Yu, Yi-Ju Chang and Tsong-Long Hwang\*\*

Series new 5-/ or 7-chloro benzoxazinone analogs were synthesized. These compounds showed directly inhibited elastase activity.

R = F, Cl, Br, CH<sub>3</sub>, OCH<sub>3</sub>**5D-QSAR for spirocyclic  $\sigma_1$  receptor ligands by Quasar receptor surface modeling**

pp. 3116–3124

Christoph Oberdorf, Thomas J. Schmidt\* and Bernhard Wünsch\*\*

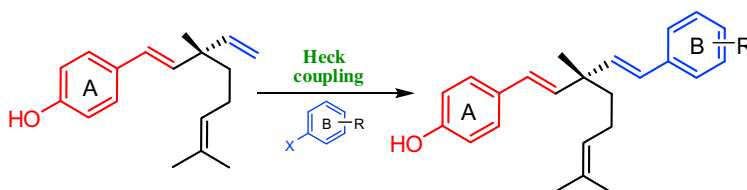


### Novel bisstyryl derivatives of bakuchiol: Targeting oral cavity pathogens

pp. 3125–3134

Mallepally V. Reddy, Niranjana Thota, Payare L. Sangwan, Pankaj Malhotra, Furqan Ali, Inshad A. Khan, Swapandeep S. Chimni and Surrinder Koul\*

Novel bisstyryls derived via Heck coupling reaction of (*S*)-bakuchiol as oral antimicrobial agents along with their mode of action and SAR is described.

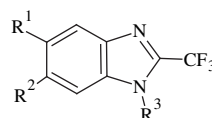


### Synthesis and biological activity of 2-(trifluoromethyl)-1*H*-benzimidazole derivatives against some protozoa and *Trichinella spiralis*

pp. 3135–3141

Francisco Hernández-Luis, Alicia Hernández-Campos, Rafael Castillo, Gabriel Navarrete-Vázquez, Olivia Soria-Arteche, Manuel Hernández-Hernández and Lilián Yépez-Mulia\*

2-(Trifluoromethyl)-1*H*-benzimidazole derivatives **1b**, **1c** and **1e** showed the most desirable *in vitro* antiparasitic profile against *Giardia intestinalis*, *Entamoeba histolytica*, *Trichomonas vaginalis* and *Trichinella spiralis*.



**1b**: R<sup>1</sup> = 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>O, R<sup>2</sup> = H, R<sup>3</sup> = CH<sub>3</sub>

**1c**: R<sup>1</sup> = H, R<sup>2</sup> = 2,3-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>O, R<sup>3</sup> = CH<sub>3</sub>

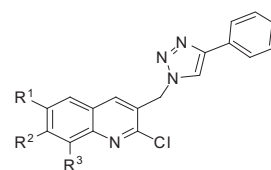
**1e**: R<sup>1</sup> = C<sub>10</sub>H<sub>7</sub>O, R<sup>2</sup> = Cl, R<sup>3</sup> = H

### Synthesis and biological evaluation of new 2-chloro-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)quinoline derivatives via click chemistry approach

pp. 3142–3146

Amol H. Kategaonkar, Pravin V. Shinde, Atul H. Kategaonkar, Sharad K. Pasale, Bapurao B. Shingate and Murlidhar S. Shingare\*

A series of new 2-chloro-3-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)quinoline derivatives have been synthesized for the first time and screened for antimicrobial activity.



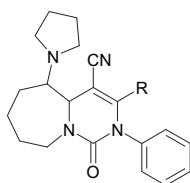
(4a–h)

- a) R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = H; b) R<sup>2</sup> = R<sup>3</sup> = H; R<sup>1</sup> = Me;  
 c) R<sup>1</sup> = R<sup>3</sup> = H; R<sup>2</sup> = Me; d) R<sup>1</sup> = R<sup>2</sup> = H; R<sup>3</sup> = Me;  
 e) R<sup>2</sup> = R<sup>3</sup> = H; R<sup>1</sup> = OMe; f) R<sup>1</sup> = R<sup>3</sup> = H; R<sup>2</sup> = OMe;  
 g) R<sup>2</sup> = R<sup>3</sup> = H; R<sup>1</sup> = OEt; h) R<sup>1</sup> = R<sup>2</sup> = H; R<sup>3</sup> = Et.

### Synthesis, anti-inflammatory and ulcerogenicity studies of some substituted pyrimido[1,6-*a*]azepine derivatives

pp. 3147–3154

Nehad A. El-Sayed, Fadi M. Awadallah\*, Nashwa A. Ibrahim and Mohammed T. El-Saadi



**4** R = -NH<sub>2</sub>

**5 a-c** R = -NH-CH<sub>2</sub>-N

**7 a-c** R = -N=CH-NH-Ar

**8 a-c** R = -N=CH-Ar'

**10 a-c** R = -NH-CH<sub>2</sub>-CON

**9,11** R = -NH-CH<sub>2</sub>-COOR'

**12 a,b** R = -NH-CO-COOR''

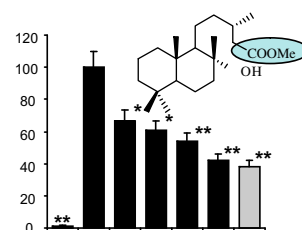
**13 a,b** R = -NH-CO-Ar''

**Evaluation of labdane derivatives as potential anti-inflammatory agents**

pp. 3155–3161

Natalia Girón, Elisa Pérez-Sacau, Raquel López-Fontal, Juan M. Amaro-Luis, Sonsoles Hortelano\*\*, Ana Estevez-Braun\*\*\* and Beatriz de las Heras\*

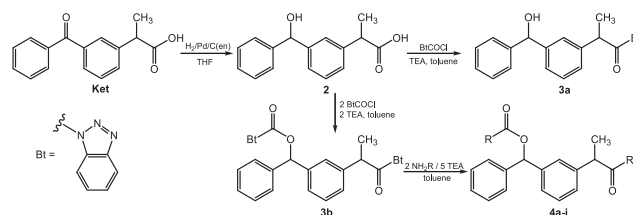
Several labdane derivatives resulted be potent inhibitors of LPS induced NO and PGE<sub>2</sub> production in macrophage cells.

**PGE<sub>2</sub> release (%)****Synthesis and biological screening of some novel amidocarbamate derivatives of ketoprofen**

pp. 3162–3168

Prasanta Kumar Sahoo\* and Pritishova Behera

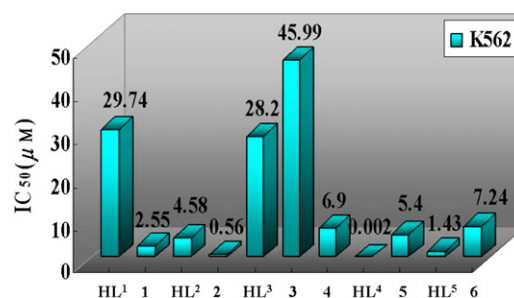
A series of novel ketoprofen derivatives **4a–j** bearing both amide and carbamate functionalities were prepared using benzotriazole. Selective reduction of ketoprofen produced hydroxy derivative **2**, which reacts with one or 2 mol of 1-benzotriazole carboxylic acid chloride (**1**) gave benzotriazole derivatives **3a** and **3b** respectively. Antioxidative screenings revealed that the prepared compounds **3b** and **4a–j** possess excellent lipid peroxidation inhibition at 0.1 mM concentration. Two of the compounds **3b** and **4g** also showed high soybean lipoxygenase inhibition activity, where as the amidocarbamate derivatives of ketoprofen showed only weak reducing activity against 1,1-diphenyl-2-picrylhydrazyl radicals. No selective antiviral effects were noted for the tested compounds against a broad variety of DNA and RNA viruses.

**Mn(II), Co(II) and Zn(II) complexes with heterocyclic substituted thiosemicarbazones: Synthesis, characterization, X-ray crystal structures and antitumor comparison**

pp. 3169–3177

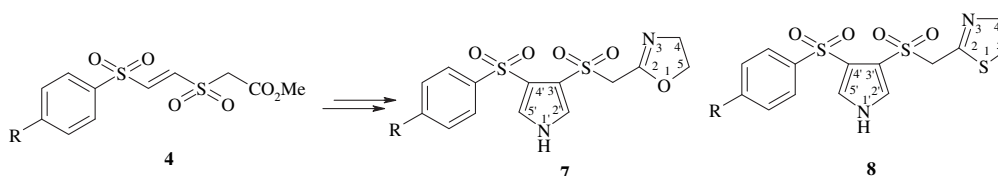
Ming Xue Li, Chun Ling Chen, Dong Zhang, Jing Yang Niu\* and Bian Sheng Ji

Preliminary *in vitro* screening indicated that all the tested compounds showed significant antitumor activity against K562 leucocythemia cell line.

**Synthesis and bioassay of pyrrolyl oxazolines and thiazolines**

pp. 3178–3183

V. Padmavathi\*, K. Mahesh, G. Dinneswara Reddy and A. Padmaja



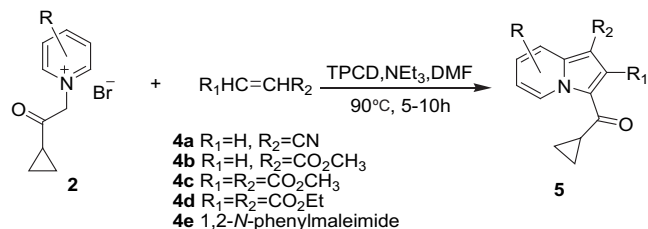
## SHORT COMMUNICATIONS

**Synthesis and antiproliferative activity of indolizine derivatives incorporating a cyclopropylcarbonyl group against Hep-G2 cancer cell line**

pp. 3184–3190

Yong-Miao Shen, Peng-Cheng Lv, Peng-Gang Liu, Ming-Zhu Zhang and Hai-Liang Zhu\*

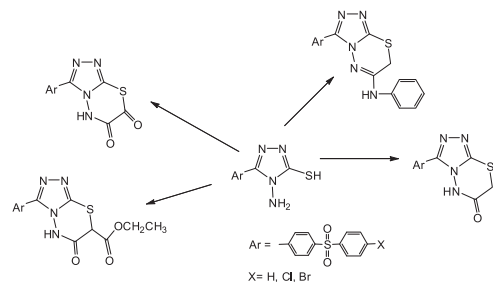
Indolizine and annulated indolizine derivatives incorporating a cyclopropylcarbonyl group were synthesized by the tandem reactions of [3 + 2] cycloaddition of the corresponding *N*-ylide with electron deficient alkene.

**New 6-amino-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazines and [1,2,4]triazolo[3,4-b][1,3,4]thiadiazin-6-ones: Synthesis, characterization and antibacterial activity evaluation**

pp. 3191–3195

Gabriela Laura Almajan\*, Stefania-Felicia Barbuceanu, Ioana Saramet and Constantin Draghici

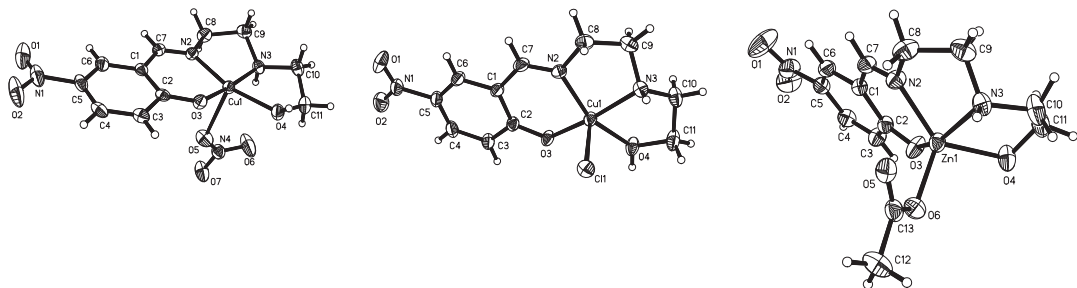
A new series of heterocyclic condensed systems with bridgehead nitrogen obtained by ring formation of 1,3,4-thiadiazine fused with 1,2,4-triazole were synthesized and characterized on the basis of IR, NMR and elemental analysis and potential antibacterial effects were investigated.

**Synthesis, structures, and urease inhibitory activities of three copper(II) and zinc(II) complexes with 2-[[2-(2-hydroxyethylamino)ethylimino]methyl]-4-nitrophenol**

pp. 3196–3199

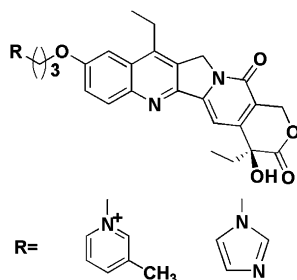
Zhong-Lu You\*, Li-Li Ni, Da-Hua Shi and Shun Bai

Three mononuclear complexes of Cu(II) and Zn(II) with Schiff base 2-[[2-(2-hydroxyethylamino)ethylimino]methyl]-4-nitrophenol have been prepared and structurally characterized. The two Cu(II) complexes may serve as potential urease inhibitors.

**Cytotoxicity and Topo I targeting activity of substituted 10-nitrogenous heterocyclic aromatic group derivatives of SN-38**

pp. 3200–3206

Qing-yong Li\*, Xiao-qiu Deng, Yuan-gang Zu\*, Hongyan Lv, Lin Su, Liping Yao, Yu Zhang and Lei Li



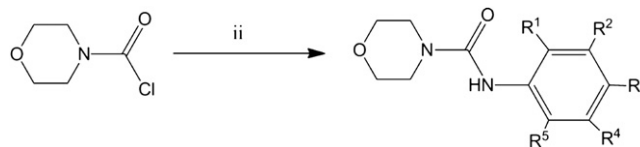


**Synthesis of some N-alkyl substituted urea derivatives as antibacterial and antifungal agents**

pp. 3207–3212

Qing-Zhong Zheng, Kui Cheng, Xiao-Min Zhang, Kai Liu, Qing-Cai Jiao\* and Hai-Liang Zhu\*

A series of N-alkyl substituted urea derivatives were synthesized and evaluated for their in vitro antibacterial and antifungal activities. Mono fluoro substituted compounds with morpholine ring exhibited potent antimicrobial activities

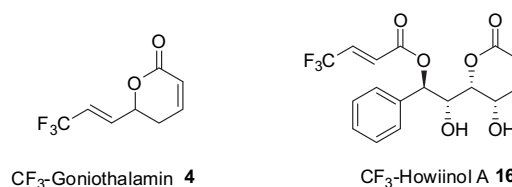
**Synthesis and cytotoxic activity of fluorinated analogues of Goniiothalamus lactones.**

pp. 3213–3218

**Impact of fluorine on oxidative processes**

Lidia Dumitrescu, Doan Thi Mai Huong, Nguyen Van Hung, Benoit Crousse and Danièle Bonnet-Delpon \*

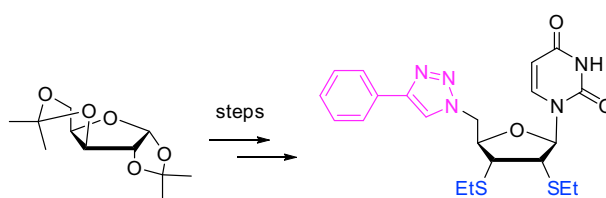
Novel trifluoromethyl analogues of goniiothalamine and howiino A have been prepared and exhibited slightly lower or similar cytotoxicity towards various cancer cell lines. The CF<sub>3</sub> group prevented from biomimetic oxidative processes all sites of molecules **4** and **16**.

**Synthesis and antitumor activity of novel 2',3'-diethanethio-2',3',5'-trideoxy-5'-triazolonucleoside analogues**

pp. 3219–3222

Jin-Lan Yu, Qin-Pei Wu\*, Qing-Shan Zhang, Xiao-Dong Xi, Ning-Ning Liu, Yun-Zheng Li, Yan-Hong Liu and Hong-Quan Yin

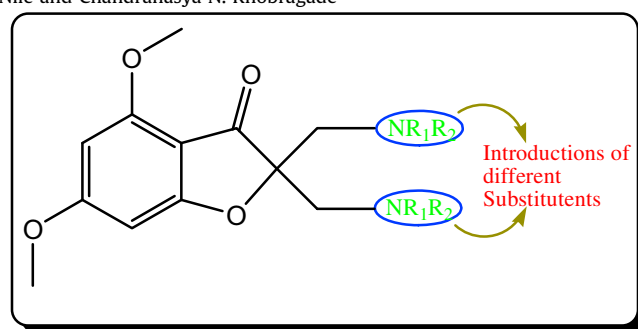
A series of novel 2', 3'-di ethanethio-2', 3',5'-trideoxy-5'-triazoloribonucleosides was synthesized in excellent yields and their antitumor activity was evaluated.

**Synthesis and biological evaluation of a novel series of 2,2-bisaminomethylated aurone analogues as anti-inflammatory and antimicrobial agents**

pp. 3223–3227

Babasaheb P. Bandgar\*, Sachin A. Patil, Balaji L. Korbadi, Satish C. Biradar, Shivraj N. Nile and Chandrasaya N. Khobragade

A novel series of 2,2-bisaminomethylated aurone analogues have been synthesized by Mannich reaction. The compounds were evaluated for their anti-inflammatory activity (against TNF- $\alpha$  and IL-6) and antimicrobial activity.

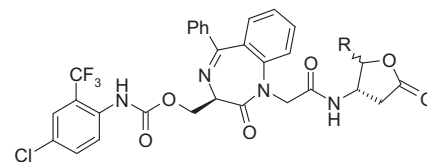


**Synthesis of novel peptidomimetics as inhibitors of protozoan cysteine proteases falcipain-2 and rhodesain**

pp. 3228–3233

Roberta Ettari\*, Maria Zappalà, Nicola Micale, Tanja Schirmeister, Christoph Gelhaus, Matthias Leippe, Astrid Evers and Silvana Grasso

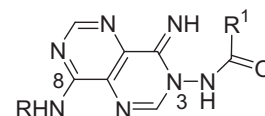
This paper describes the synthesis and the biological evaluation towards protozoan cysteine proteases of novel peptidomimetics bearing a protected aspartyl aldehyde warhead.

**PRELIMINARY COMMUNICATIONS****Synthesis and in vitro evaluation of substituted pyrimido[5,4-*d*]pyrimidines as a novel class of *Antimycobacterium tuberculosis* agents**

pp. 3234–3239

Ana H. Bacelar, M. Alice Carvalho\* and M. Fernanda Proença

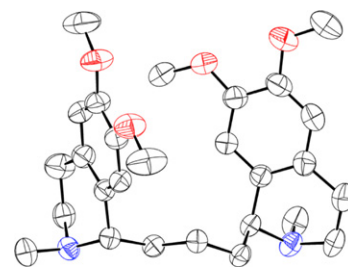
Novel 3,8-disubstituted-pyrimido[5,4-*d*]pyrimidines were synthesized and evaluated against *Mycobacterium tuberculosis* strain H<sub>37</sub>Rv. The new compounds showed activity against the bacilli that depends on the substituents present in N-3 and C-8.

**LABORATORY NOTE****Bis-tetrahydroisoquinoline derivatives: Structure analysis of the three stereoisomers of 1,1'-(propane-1,3-diyl)-bis-(6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline)**

pp. 3240–3244

Johan Wouters\*, Kossay Elasaad, Bernadette Norberg, Amaury Graulich and Jean-François Liégeois\*

Crystal structure of the three stereoisomers of 1,1'-(propane-1,3-diyl)-bis-(6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline) hydrochloride after resolution by semi-preparative chiral HPLC establishes the absolute configuration and conformation.



**COVER**

Image of Antibacterial activities of urea and thiourea derivatives of 15-membered azalides in comparison to sulfonylurea analogs. 44/9, P3459–3470 by Mirjana Bukvić Krajačić, Predrag Novak, Miljenko Dumić, Mario Cindrić, Hana Čipčić Paljetak and Nedjeljko Kujundžić © 2009 Published by Elsevier Masson SAS

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