



European Journal of Medicinal Chemistry Vol 45, No 10, 2010

Contents

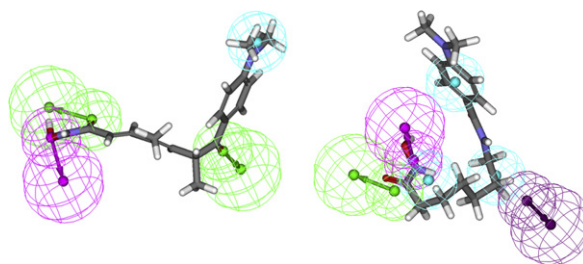
ORIGINAL ARTICLES

Ligand and structure based pharmacophore modeling to facilitate novel histone deacetylase 8 inhibitor design

pp. 4409–4417

Sundarapandian Thangapandian, Shalini John, Sugunadevi Sakkiah and Keun Woo Lee*

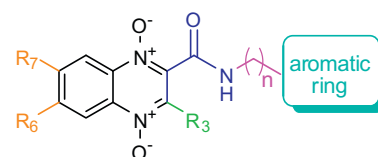
Ligand and structure based pharmacophore methodologies were successfully applied to identify three virtual hits that can act as potential leads in novel HDAC8 inhibitor design.

**Synthesis and antimycobacterial activity of new quinoxaline-2-carboxamide 1,4-di-*N*-oxide derivatives**

pp. 4418–4426

Elsa Moreno, Saioa Ancizu, Silvia Pérez-Silanes*, Enrique Torres, Ignacio Aldana and Antonio Monge

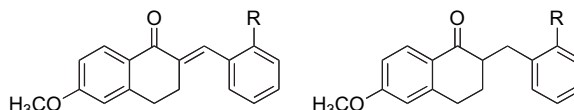
Forty-three new amide quinoxaline-1,4-di-*N*-oxide derivatives have been synthesized and evaluated as potential anti-tubercular agents by the TAACF. The obtained results allowed us to establish structural requirements for the design of new anti-tuberculosis drugs.

**Synthesis and CYP24A1 inhibitory activity of (*E*)-2-(2-substituted benzylidene)- and 2-(2-substituted benzyl)-6-methoxy-tetralones**

pp. 4427–4434

Ahmed S. Aboraia, Bart Makowski, Alba Bahja, David Prosser, Andrea Brancale, Glenville Jones and Claire Simons*

A series of (*E*)-2-(2-substituted benzylidene)- and 2-(2-substituted benzyl)-6-methoxy-tetralones were prepared and evaluated for their inhibitory activity against cytochrome CYP24A1, CYP27A1 and CYP24A1 mutant strains.



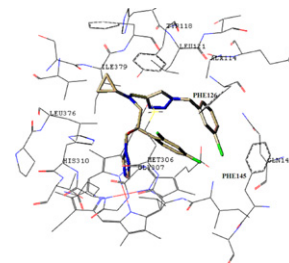
R = alkyl, aryl, bromide

Synthesis and antifungal evaluation of novel triazole derivatives as inhibitors of cytochrome P450 14 α -demethylase

pp. 4435–4445

Shichong Yu, Xiaoyun Chai, Honggang Hu, Yongzheng Yan, Zhongjun Guan, Yan Zou, Qingyan Sun and Qiuye Wu*

A number of novel triazole derivatives have been designed, synthesized by click reaction. And their antifungal activities have been evaluated against eight human pathogenic fungi.

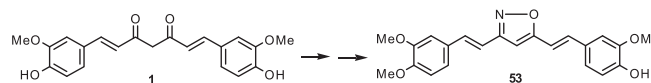


Isoxazole analogs of curcuminoids with highly potent multidrug-resistant antimycobacterial activity

pp. 4446–4457

Chatchawan Changtam, Poonpilas Hongmanee and Apichart Suksamrarn*

The MIC of the most active analog **53** was 0.09 $\mu\text{g/mL}$, which was 1131-fold more active than curcumin (**1**), and was 18 and 2-fold more active than the drugs kanamycin and isoniazid.

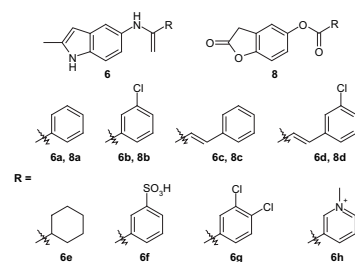


Inhibition of monoamine oxidase by indole and benzofuran derivatives

pp. 4458–4466

Louis H.A. Prins, Jacobus P. Petzer and Sarel F. Malan*

A series of indole and benzofuran derivatives were synthesised and evaluated for their ability to inhibit monoamine oxidase (MAO) A and B.

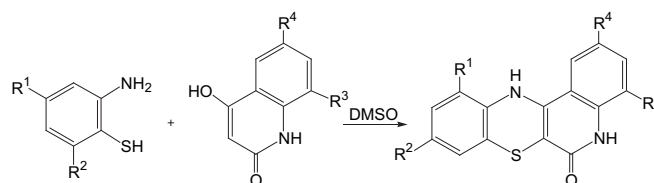


Synthesis and antioxidant activity of quinolinobenzothiazinones

pp. 4467–4472

M. Kumar*, Kshitija Sharma, R.M. Samarth and A. Kumar

Structurally diverse quinolinobenzothiazinones have been synthesized and evaluated for their antioxidant activity.

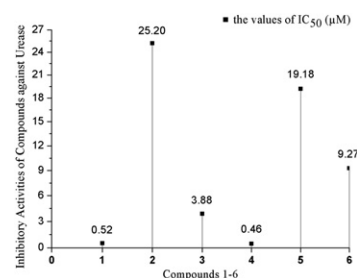


Synthesis, molecular docking and biological evaluation of Schiff base transition metal complexes as potential urease inhibitors

pp. 4473–4478

Wu Chen, Yuguang Li, Yongming Cui, Xian Zhang, Hai-Liang Zhu* and Qingfu Zeng*

Schiff base transition metal compounds **1–6** were evaluated for the inhibitory activities on the *jack bean* urease ($IC_{50} = 0.46–25.20 \mu\text{M}$). A docking analysis using the AUTODOCK 4.0 program could explain the inhibitory activities of compound **1** and **4** against urease.

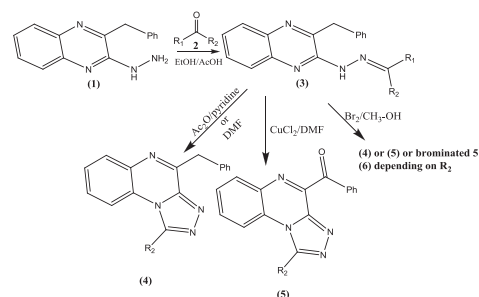


Synthesis of new series of quinoxaline based MAO-inhibitors and docking studies

pp. 4479–4489

Sherine N. Khattab, Seham Y. Hassan, Adnan A. Bekhit, Abdel Moneim El Massry, Vratislav Langer and Adel Amer*

A series of 2-benzyl-3-(2-arylidenehydrazinyl)quinoxalines **3**, 4-benzyl-1-aryl-[1,2,4]triazolo[4,3-a]quinoxalines **4** and phenyl(1-aryl-[1,2,4]triazolo[4,3-a]quinoxalin-4-yl)methanones **5** analogues were synthesized and investigated for their monoamine oxidase (MAO) inhibitory property. The inhibition profile was found to be competitive for compounds **3k**, **3m**, **5f** and **5n** with MAO-A selectivity. Observation of the docked positions of these compounds revealed interactions with many residues previously reported to have an effect on the inhibition of the enzyme. The structural features of the new compounds have been determined from the microanalytical, IR, ^1H , ^{13}C NMR spectral studies and X-ray crystallography.

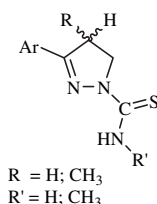


Synthesis of new 3-aryl-4,5-dihydropyrazole-1-carbothioamide derivatives. An investigation on their ability to inhibit monoamine oxidase

pp. 4490–4498

E. Maccioni, S. Alcaro*, F. Orallo, M.C. Cardia, S. Distinto, G. Costa, M. Yanez, M.L. Sanna, S. Vigo, R. Meleddu and D. Secci

All the active compounds showed a selective activity towards the B isoform of the enzyme, regardless of the substitution on the heterocyclic ring. 3-(4-methoxyphenyl) substituted pyrazolines were the most active within the tested compounds.

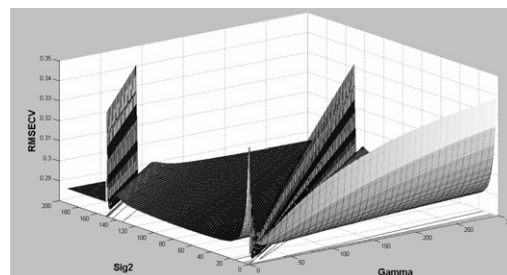


QSAR study of anthranilic acid sulfonamides as inhibitors of methionine aminopeptidase-2 using LS-SVM and GRNN based on principal components

pp. 4499–4508

Mohsen Shahlai, Razieh Sabet, Maryam Bahman Ziari, Behzad Moeinifard, Afshin Fassihi* and Reza Karbakhsh

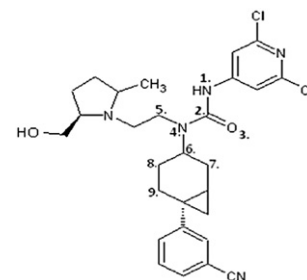
PC-GRNN and PC-LS-SVM as regression methods were investigated for building quantitative structure–activity relationships for the prediction of inhibitory activity of methionine aminopeptidase-2 antagonists.



Three-dimensional quantitative structure–activity relationship CoMSIA/CoMFA and LeapFrog studies on novel series of bicyclo[4.1.0] heptanes derivatives as melanin-concentrating hormone receptor R1 antagonists pp. 4509–4522

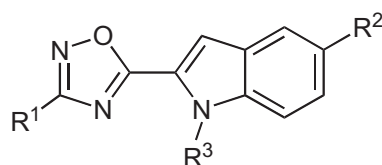
Alejandro Morales-Bayuelo, Hernan Ayazo and Ricardo Vivas-Reyes*

Structure of compound **53** and its atoms used for superposition are labeled.



Design, synthesis and pro-apoptotic antitumour properties of indole-based 3,5-disubstituted oxadiazoles pp. 4523–4530

Noha I. Ziedan, Fabio Stefanelli, Stefano Fogli* and Andrew D. Westwell

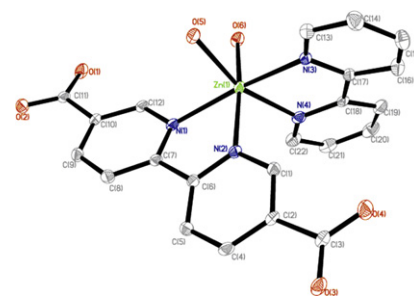


pro-apoptotic antitumour agents

Synthesis, characterization, interaction with DNA and cytotoxicity in vitro of novel pyridine complexes with Zn(II) pp. 4531–4538

En-jun Gao*, Tie-dong Sun, Shi-hua Liu, Shuang Ma, Zheng Wen, Ying Wang, Ming-chang Zhu, Lei Wang, Xia-nan Gao, Feng Guan, Mei-jun Guo and Fu-chun Liu

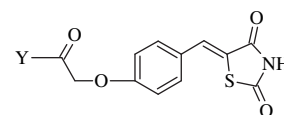
In the complex, Zn(II) is six coordinated by four nitrogen atoms from bipy and 2,2'-bipyridine-5,5'-dicarboxylic acid ligand and two oxygen atoms from H₂O, with the axial Zn–N(1) distance (2.204 Å) and Zn–N(3) distance (2.161 Å) elongated in comparison to Zn–N(2) distance (2.171 Å) and Zn–N(4) distance (2.179 Å).



Synthesis and primary cytotoxicity evaluation of new 5-benzylidene-2, 4-thiazolidinedione derivatives pp. 4539–4544

Vijay Patil, Kalpana Tilekar, Sonali Mehendale-Munj, Rhea Mohan and C.S. Ramaa*

In this communication, a series of ten (**3a–3j**) novel 5-benzylidene-2,4-thiazolidinedione derivatives were synthesized and evaluated in vitro against different human cancer cell lines



Y=R–NH for 3b, 3c, 3e, 3f, 3g, 3i and 3j

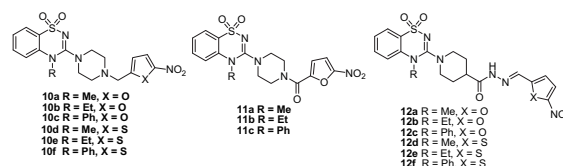
Y= R for 3a, 3d and 3h

Anti-tubercular agents. Part 5: Synthesis and biological evaluation of benzothiadiazine 1,1-dioxide based congeners

pp. 4545–4553

Ahmed Kamal*, Rajesh V.C.R.N.C. Shetti, Shaik Azeeda, S. Kaleem Ahmed, P. Swapna, A. Malla Reddy, Inshad Ali Khan, Sandeep Sharma and Sheikh Tasduq Abdullah

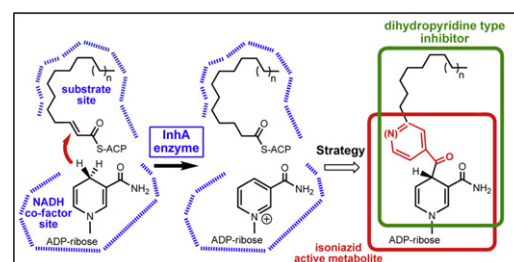
A new series of benzothiadiazine 1,1-dioxide based congeners was synthesized and evaluated against *Mycobacterium tuberculosis*, Gram-positive, Gram-negative bacteria and fungi. Further, *in vivo* activity of earlier potent molecule of this series is also discussed.

**Development of isoniazid–NAD truncated adducts embedding a lipophilic fragment as potential bi-substrate InhA inhibitors and antimycobacterial agents**

pp. 4554–4561

Tamara Delaine, Vania Bernardes-Génisson*, Annaik Quémard, Patricia Constant, Bernard Meunier and Jean Bernadou*

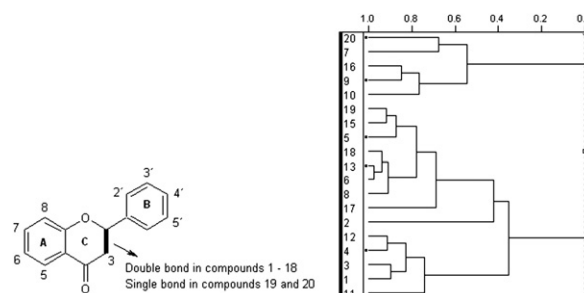
Mimicking the active metabolite of isoniazid: a way to antimycobacterial agents.

**Multivariate QSAR study on the antimutagenic activity of flavonoids against 3-NFA on *Salmonella typhimurium* TA98**

pp. 4562–4569

Eduardo Borges de Melo, João Paulo Ataíde Martins, Teresa Cristina Marinho Jorge, Marcelo Couto Friozi and Márcia Miguel Castro Ferreira*

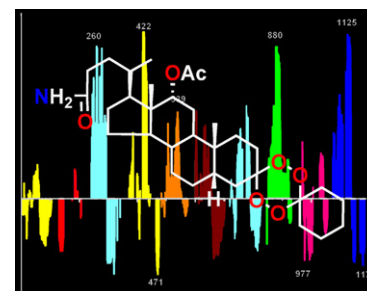
QSAR model for twenty antimutagenic flavonoids was built using four topological descriptors, fully validated and chemically interpreted. Biological activity depends on molecular size, shape and Sanderson electronegativity.

**An alignment independent 3D QSAR study of the antiproliferative activity of 1,2,4,5-tetraoxanes**

pp. 4570–4577

Ilija N. Cvijetić, Željko P. Žižak, Tatjana P. Stanojković, Zorica D. Juranić, Nataša Terzić, Igor M. Opsenica, Dejan M. Opsenica, Ivan O. Juranić and Branko J. Drakulić*

The pharmacophoric points common for high antiproliferative potency of tetraoxane derivatives are outlined, by using alignment-independent descriptors derived from molecular interaction fields.

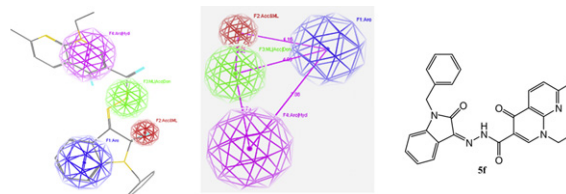


Schiff bases of indoline-2,3-dione (isatin) derivatives and nalidixic acid carbohydrazide, synthesis, antitubercular activity and pharmacophoric model building

pp. 4578–4586

Tarek Aboul-Fadl*, Fayzah A.S. Bin-Jubair and Omima Aboul-Wafa

Potent anti-TB activity was observed with a Schiff base of 1-benzylisatin and nalidixic acid carbohydrazide (**5f**) which is consistent with the hypothetical pharmacophore model built using Molecular Operating Environment (MOE).

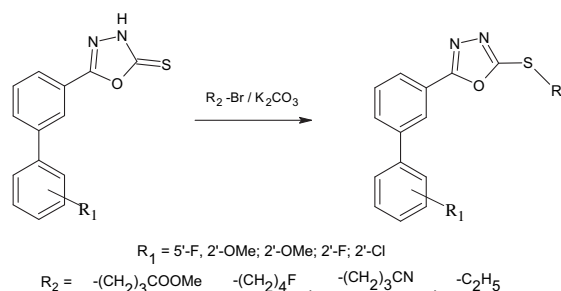


Synthesis and biological property of some novel 1,3,4-oxadiazoles

pp. 4587–4593

G.C. Ramaprasad, Balakrishna Kalluraya*, B. Sunil Kumar and Ravindra K. Hunnur

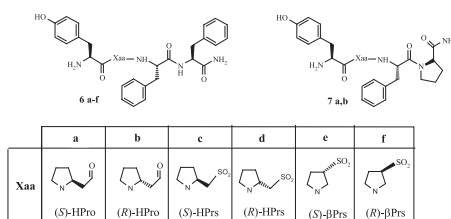
A novel series of 5-[substituted-(1,1'-biphenyl)-3-yl]-1,3,4-oxadiazole-2(3H)-thiones and their S-alkylated derivatives have been prepared through a multi step organic synthesis involving palladium catalyzed Suzuki-Miyaura coupling. The new compounds have been screened for their antibacterial, antifungal and analgesic activity.



Synthesis and activity of endomorphin-2 and morphiceptin analogues with proline surrogates in position 2

pp. 4594–4600

Cesare Giordano*, Anna Sansone, Annalisa Masi, Gino Lucente, Pasqualina Punzi, Adriano Mollica, Francesco Pinnen, Federica Feliciani, Ivana Cacciatore, Peg Davis, Josephine Lai, Shou-Wu Ma, Frank Porreca and Victor Hruby

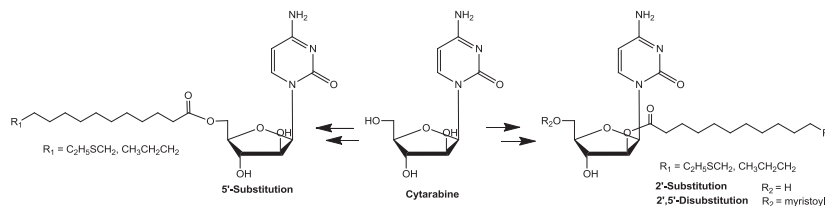


Synthesis and evaluation of fatty acyl ester derivatives of cytarabine as anti-leukemia agents

pp. 4601–4608

Bhupender S. Chhikara, Deendayal Mandal and Keykavous Parang*

Cytarabine is an anti-leukemia agent with a short plasma half-life. Three classes of 5'-O-substituted, 2'-O-substituted, and 2',5'-disubstituted fatty acyl derivatives of cytarabine were synthesized and their anti-leukemia activities were evaluated.

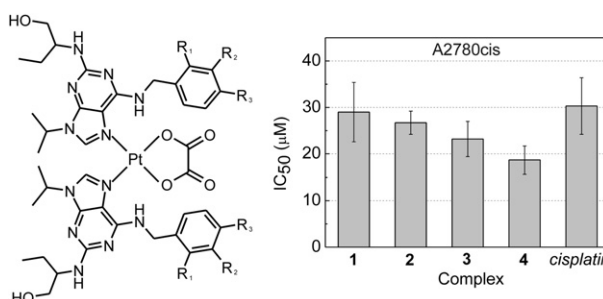


Roscovitine-based CDK inhibitors acting as N-donor ligands in the platinum(II) oxalato complexes: Preparation, characterization and *in vitro* cytotoxicity

pp. 4609–4614

Zdeněk Trávníček*, Pavel Štarha, Igor Popa, Radim Vrzal and Zdeněk Dvořák

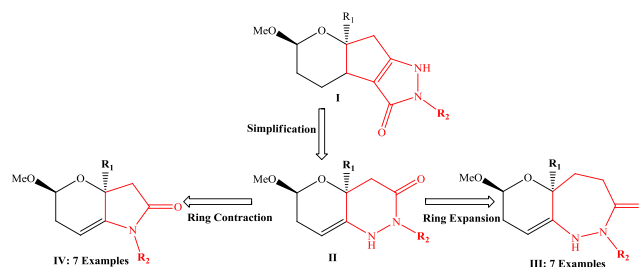
The platinum(II) oxalato complexes involving *Roscovitine* or its benzyl-substituted analogues are reported, together with their *in vitro* cytotoxicity against A2780, A2780cis, G-361, A549, HeLa, MCF7 and HOS human cancer cell lines, and primary cultures of human hepatocytes.

**Design, synthesis and qualitative structure–activity evaluations of novel hexahydropyrano[3,2-c][1,2]diazepin-3(4H)-one and tetrahydropyrano[3,2-b]pyrrol-2(1H)-one derivatives as anticancer agents**

pp. 4615–4621

Taleb H. Al-Tel*

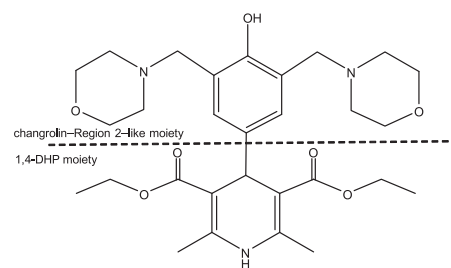
Polysubstituted hexahydropyrano[3,2-c][1,2]diazepin-3(4H)-one and tetrahydropyrano[3,2-b]pyrrol-2(1H)-one derivatives were synthesized and biologically evaluated as novel anticancer agents.

**Antihypertensive and antiarrhythmic properties of a *para*-hydroxy[bis(*ortho*-morpholinylmethyl)]phenyl-1,4-DHP compound: Comparison with other compounds of the same kind and relationship with $\log P$ values**

pp. 4622–4630

Victor H. Abrego, Beatriz Martínez-Pérez, Luis A. Torres, Enrique Ángeles*, Luisa Martínez, J. Lorena Marroquín-Pascual, Rosario Moya-Hernández, Héctor Adrián Amaro-Recillas, Juan Carlos Rueda-Jackson, Damaris Rodríguez-Barrientos and Alberto Rojas-Hernández*

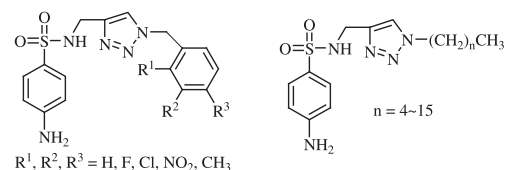
A new *para*-hydroxy[bis(*ortho*-morpholinylmethyl)]phenyl-1,4-DHP substituted compound has been synthesized. The antihypertensive and antiarrhythmic efficacies as well as the $\log P$ values have been compared with other compounds of the same kind.

**Synthesis of novel sulfanilamide-derived 1,2,3-triazoles and their evaluation for antibacterial and antifungal activities**

pp. 4631–4639

Xian-Long Wang, Kun Wan and Cheng-He Zhou*

A series of novel sulfanilamide-derived 1,2,3-triazoles were synthesized and evaluated for their antibacterial and antifungal activities *in vitro*.

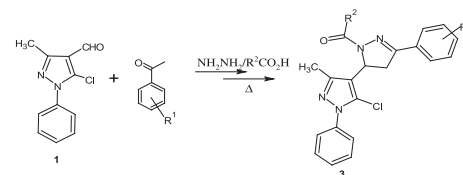


Synthesis and pharmacological study of 1-acetyl/propyl-3-aryl-5-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)-2-pyrazoline

pp. 4640–4644

K.S. Girisha, Balakrishna Kalluraya*, Vijaya Narayana and Padmashree

A series of pyrazolines were synthesized in one pot reaction by condensing propenones, hydrazine and acetic/propionic acid. The newly synthesized compounds were screened for analgesic and anti-inflammatory activities.

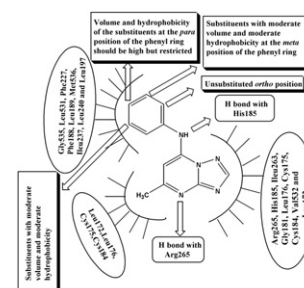


Chemometric modeling, docking and *in silico* design of triazolopyrimidine-based dihydroorotate dehydrogenase inhibitors as antimalarials

pp. 4645–4656

Probir Kumar Ojha and Kunal Roy*

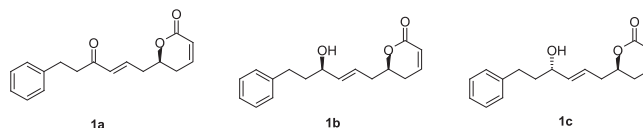
In the present work, QSAR and molecular docking studies have been performed on triazolopyrimidine-based dihydroorotate dehydrogenase (DHODH) inhibitors as antimalarial agents.



Stereoselective synthesis and biological evaluation of (*R*)-rugulactone, (*6R*)-((*4R*)-hydroxy-6-phenyl-hex-2-enyl)-5,6-dihydro-pyran-2-one and its *4S* epimer

pp. 4657–4663

D. Kumar Reddy, V. Shekhar, P. Prabhakar, B. Chinna Babu, B. Siddhardha, U.S.N. Murthy and Y. Venkateswarlu*



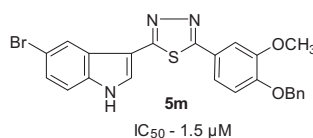
SHORT COMMUNICATIONS

Synthesis and anticancer activity of 5-(3-indolyl)-1,3,4-thiadiazoles

pp. 4664–4668

Dalip Kumar*, N. Maruthi Kumar, Kuei-Hua Chang and Kavita Shah

A series of 5-(3-indolyl)-1,3,4-thiadiazole were synthesized and the compound 5m showed considerable cytotoxicity against PaCa2 cancer cell line with an IC_{50} value of 1.5 μ M.

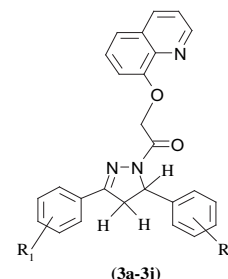


Synthesis, characterization, antiamoebic activity and cytotoxicity of novel series of pyrazoline derivatives bearing quinoline tail

pp. 4669–4675

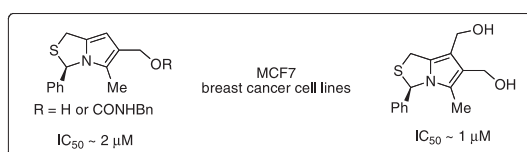
Faisal Hayat, Attar Salahuddin, Sadiq Umar and Amir Azam*

Novel pyrazoline derivatives (**3a–3j**) were synthesized. Compounds **3d**, **3g**, **3h** and **3j** exhibited better antiamoebic activity and screened for cytotoxicity.

**Chiral 6-hydroxymethyl-1*H*,3*H*-pyrrolo[1,2-*c*]thiazoles: Novel antitumor DNA monoalkylating agents**

pp. 4676–4681

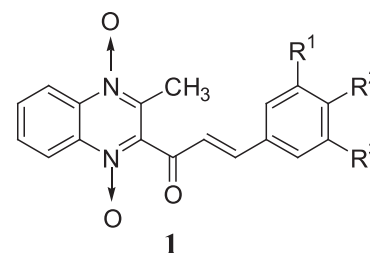
Maria I.L. Soares, Ana Filipa Brito, Mafalda Laranjo, Ana Margarida Abrantes, M. Filomena Botelho, José A. Paixão, Ana Matos Beja, Manuela Ramos Silva and Teresa M.V.D. Pinho e Melo*

***E*-2-[3-(3,4-Dichlorophenyl)-1-oxo-2-propenyl]-3-methylquinoxaline-1,4-dioxide: A lead antitubercular agent which alters mitochondrial respiration in rat liver**

pp. 4682–4686

Umashankar Das*, Swagatika Das, Brian Bandy, Dennis K.J. Gorecki and Jonathan R. Dimmock

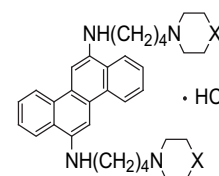
A number of substituted quinoxaline-1,4-dioxides **1** display excellent potency towards *Mycobacterium tuberculosis* from which a lead compound **1h** ($R^1 = R^2 = \text{Cl}$; $R^3 = \text{H}$) having IC₅₀ and IC₉₀ values of 1.03 μM and 1.53 μM, respectively, was identified.

**Novel 6,12-disubstituted chrysene as potent anticancer agent: Synthesis, *in vitro* and *in vivo* study**

pp. 4687–4691

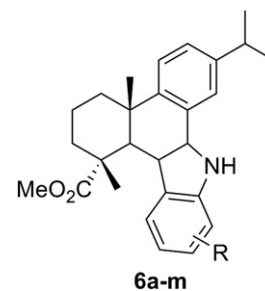
Bimal K. Banik* and Frederick F. Becker

We have synthesized a few new derivatives derived from chrysene. Structure–activity studies have identified compounds with anticancer activities *in vitro* and also *in vivo*.



Synthesis and antimicrobial activities of novel 1*H*-dibenzo[*a,c*]carbazoles from dehydroabietic acid**pp. 4692–4696**Wen Gu^{*} and Shifa Wang

A series of new 1*H*-dibenzo[*a,c*]carbazole derivatives (**6a–m**) were synthesized and evaluated for their antimicrobial activity against several bacterial and fungal strains.



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

* Corresponding authors.



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