



Contents lists available at ScienceDirect

# Bioorganic & Medicinal Chemistry

journal homepage: [www.elsevier.com/locate/bmc](http://www.elsevier.com/locate/bmc)



## Bioorganic & Medicinal Chemistry Vol. 16, No. 21, 2008

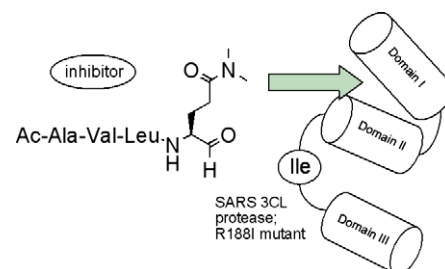
### Contents

#### ARTICLES

##### Evaluation of peptide-aldehyde inhibitors using R188I mutant of SARS 3CL protease as a proteolysis-resistant mutant

Kenichi Akaji\*, Hiroyuki Konno, Mari Onozuka, Ayumi Makino, Hiroyuki Saito, Kazuto Nosaka

pp 9400–9408

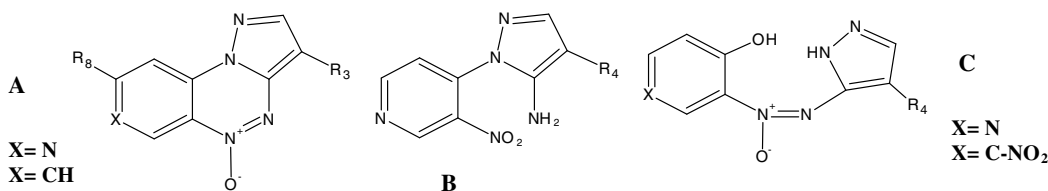


The mature SARS 3CL protease is subject to degradation at 188Arg/189Gln. The tetrapeptide sequence is enough for inhibitory activities of peptide-aldehyde inhibitor of the protease.

##### Synthesis of new pyrazolo[5,1-c][1,2,4] benzotriazines, pyrazolo[5,1-c]pyrido[4,3-e][1,2,4] triazines and their open analogues as cytotoxic agents in normoxic and hypoxic conditions

pp 9409–9419

Giovanna Ciciani\*, Marcella Coronello, Gabriella Guerrini, Silvia Selleri, Miriam Cantore, Paola Failli, Enrico Mini, Annarella Costanzo



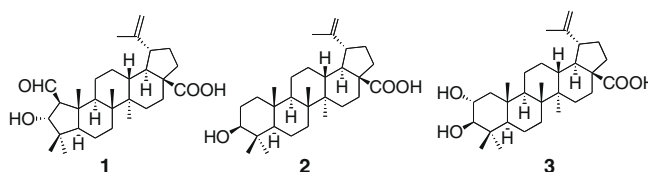
The synthesis and antitumor activity in normoxic and hypoxic conditions of a series of pyrazolo[5,1-c][1,2,4]benzotriazine and related analogues are reported. All compounds were tested on human colorectal adenocarcinoma cell line HCT-8; ROS production, cell cycle, and DNA fragmentation were also measured.



##### Hedgehog/GLI-mediated transcriptional inhibitors from *Zizyphus cambodiana*

pp 9420–9424

Midori A. Arai, Chikashi Tateno, Takahiro Hosoya, Takashi Koyano, Thaworn Kowithayakorn, Masami Ishibashi\*

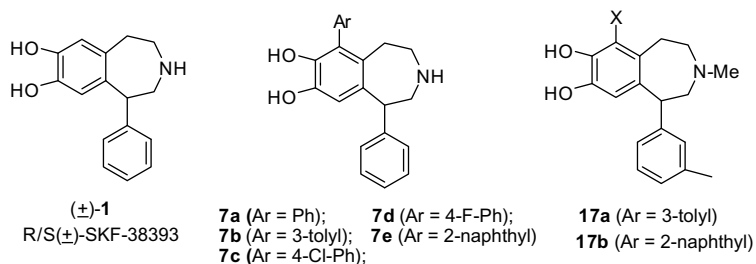


By using our constructed cell-based screening system, three pentacyclic triterpenes, colubrinic acid (1), betulinic acid (2) and alphitolic acid (3), were identified from *Zizyphus cambodiana* as potent hedgehog (Hh)/GLI signaling pathway inhibitors.

### Synthesis of 6-substituted 1-phenylbenzazepines and their dopamine D<sub>1</sub> receptor activities

pp 9425–9431

Jing Zhang, Xuetao Chen, Leiping Yu, Xuechu Zhen\*, Ao Zhang\*



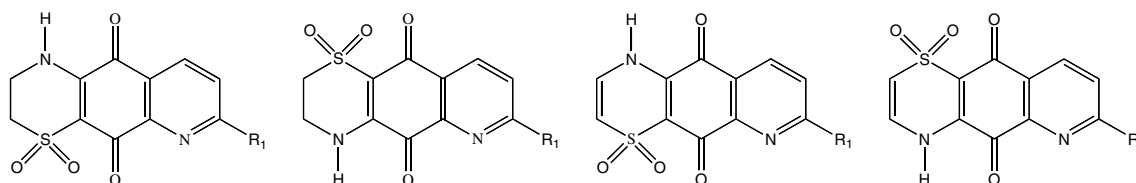
A series of 6-substituted analogs of (±)-SKF-38393 ((±)-1) was synthesized, and their binding affinity for dopamine receptors (D<sub>1</sub>, D<sub>2</sub>) and serotonin receptors (5-HT<sub>1A</sub>, 5-HT<sub>2A</sub>) were evaluated.



### Synthesis and anti-inflammatory structure–activity relationships of thiazine–quinoline–quinones: Inhibitors of the neutrophil respiratory burst in a model of acute gouty arthritis

pp 9432–9442

Elizabeth W. Chia, A. Norrie Pearce, Michael V. Berridge, Lesley Larsen, Nigel B. Perry, Catherine E. Sansom, Colette A. Godfrey, Lyall R. Hanton, Guo-Liang (Leon) Lu, Michaela Walton, William A. Denny, Victoria L. Webb, Brent R. Copp, Jacquie L. Harper\*



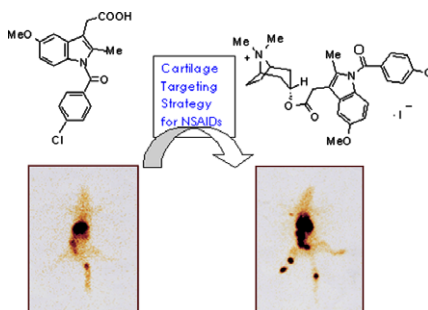
Synthesised thiazine–quinoline–quinones were assayed for inhibition of superoxide production in vitro. Analogues were tested in vivo for inhibition of neutrophil superoxide production and infiltration induced by monosodium urate crystals.



### Site specific chemical delivery of NSAIDs to inflamed joints: Synthesis, biological activity and $\gamma$ -imaging studies of quaternary ammonium salts of tropinol esters of some NSAIDs or their active metabolites

pp 9443–9449

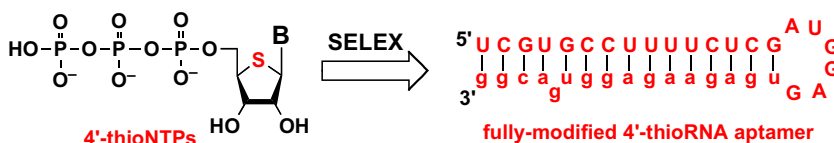
Mange Ram Yadav\*, Vijay P. Pawar, Sejal M. Marvaniya, Parmeshwari K. Halen, Rajani Giridhar, Anil K. Mishra



### Investigations toward the selection of fully-modified 4'-thioRNA aptamers: Optimization of in vitro transcription steps in the presence of 4'-thioNTPs

pp 9450–9456

Noriaki Minakawa\*, Mioko Sanji, Yuka Kato, Akira Matsuda\*



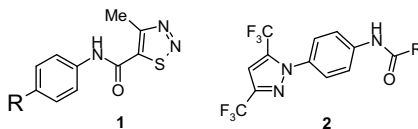
Investigation of in vitro transcription using four kinds of 4'-thioNTPs was examined. As a result, we succeeded to isolate fully-modified 4'-thioRNA aptamer.



### Novel potent and selective Ca<sup>2+</sup> release-activated Ca<sup>2+</sup> (CRAC) channel inhibitors. Part 3: Synthesis and CRAC channel inhibitory activity of 4'-[(trifluoromethyl)pyrazol-1-yl]carboxanilides

pp 9457–9466

Yasuhiro Yonetoku\*, Hirokazu Kubota, Yoji Miyazaki, Yoshinori Okamoto, Masashi Funatsu, Noriko Yoshimura-Ishikawa, Jun Ishikawa, Taiji Yoshino, Makoto Takeuchi, Mitsuaki Ohta



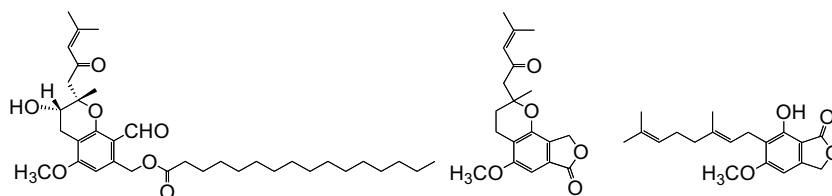
4-Methyl-1,2,3-thiadiazole-5-carboxanilide (1) and 4'-[3,5-bis(trifluoromethyl)pyrazol-1-yl]carboxanilide (2) derivatives were prepared and evaluated for their CRAC channel inhibitory activity.

### An endoplasmic reticulum (ER) stress-suppressive compound and its analogues from the mushroom

pp 9467–9470

#### *Hericium erinaceum*

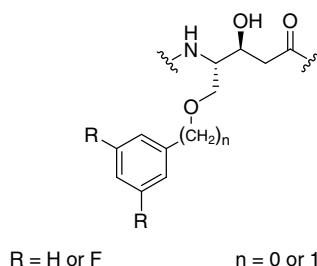
Keiko Ueda, Megumi Tsujimori, Shinya Kodani, Akiko Chiba, Masakazu Kubo, Kazuhiko Masuno, Atsushi Sekiya, Kaoru Nagai\*, Hirokazu Kawagishi\*



### Design, synthesis and SAR of potent statine-based BACE-1 inhibitors: Exploration of P1 phenoxy and benzyloxy residues

pp 9471–9486

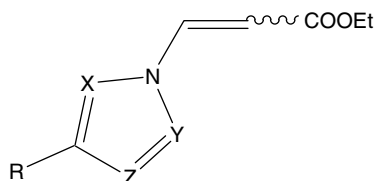
Marcus Bäck, Jonas Nyhlén, Ingemar Kvarnström, Sara Appeltgren, Neera Borkakoti, Katarina Jansson, Jimmy Lindberg, Susanne Nyström, Anders Hallberg, Åsa Rosenquist\*, Bertil Samuelsson\*



### Inhibition of the CRM1-mediated nucleocytoplasmic transport by N-azolylacrylates: Structure–activity relationship and mechanism of action

pp 9487–9497

Tine Van Neck, Christophe Pannecouque, Els Vanstreels, Miguel Stevens, Wim Dehaen, Dirk Daelemaans\*

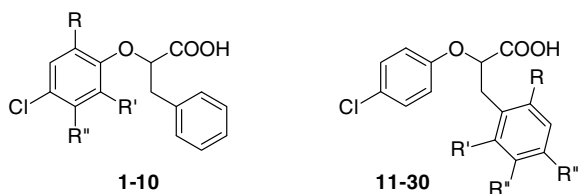


Structural analogs of the low-molecular weight compound PKF50-638 were synthesized and evaluated for their inhibitory effect on the nuclear export of RevM5-GFP with the aim to develop HIV inhibitors.

**Synthesis, biological evaluation, and molecular modeling investigation of chiral 2-(4-chloro-phenoxy)-3-phenyl-propanoic acid derivatives with PPAR $\alpha$  and PPAR $\gamma$  agonist activity**

pp 9498–9510

Giuseppe Fracchiolla, Antonio Lavecchia\*, Antonio Laghezza, Luca Piemontese, Raffaella Trisolini, Giuseppe Carbonara, Paolo Tortorella, Ettore Novellino, Fulvio Liodice\*

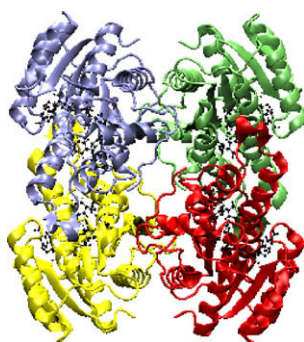


R, R', R'', R''' = H, alkyl, aryl, halogen, CF<sub>3</sub> or PhO


**Molecular dynamics simulations of the amyloid-beta binding alcohol dehydrogenase (ABAD) enzyme**

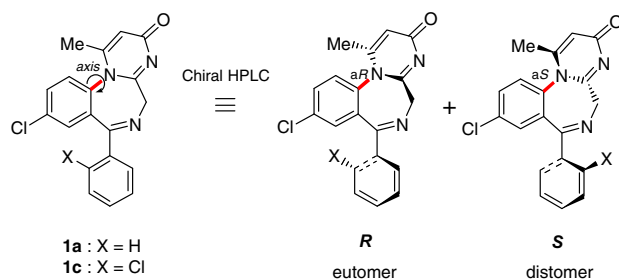
pp 9511–9518

Alexandra T. Marques, Pedro A. Fernandes, Maria João Ramos\*


**Axial chirality and affinity at the GABA<sub>A</sub> receptor of pyrimido[1,2-a][1,4]benzodiazepines and related compounds**

pp 9519–9523

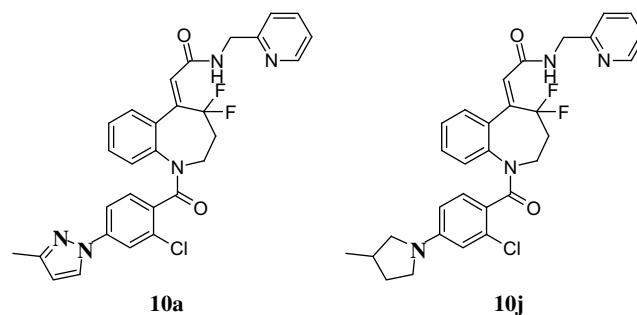
Shoukou Lee, Tomonori Kamide, Hidetsugu Tabata, Hideyo Takahashi, Motoo Shiro, Hideaki Natsugari\*


**Preparation of (4,4-difluoro-1,2,3,4-tetrahydro-5H-1-benzazepin-5-ylidene)acetamide derivatives as novel arginine vasopressin V<sub>2</sub> receptor agonists**

pp 9524–9535

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

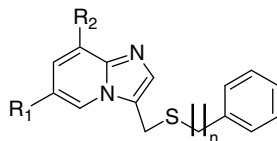
A novel series of (4,4-difluoro-1,2,3,4-tetrahydro-5H-1-benzazepine-5-ylidene)acetamide derivatives were prepared, and their binding affinity for V<sub>2</sub> receptor and intrinsic activity were evaluated. Synthesis and structure–activity relationships including in vivo evaluation are described.



### Influence of 6- or 8-substitution on the antiviral activity of 3-arylalkylthiomethylimidazo[1,2-*a*]pyridine against human cytomegalovirus (CMV) and varicella-zoster virus (VZV): Part II

pp 9536–9545

Jean-Baptiste Véron, Hassan Allouchi, Cécile Enguehard-Gueiffier, Robert Snoeck, Graciela Andrei, Erik De Clercq, Alain Gueiffier\*



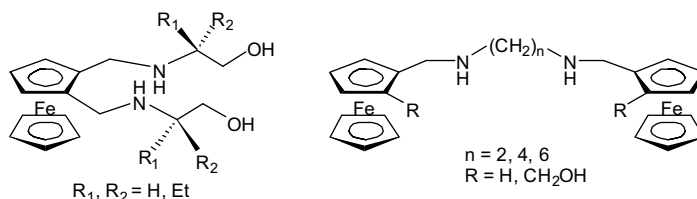
R<sub>1</sub>, R<sub>2</sub> = heteroaryl, azole, alicyclic amine, lactam, cyano, phenylthio

The imidazo[1,2-*a*]pyridines bearing a 5 membered heterocycle (thiophene, furane or pyrrole) in the 6 position or a phenylthio group in the 6 or 8 position were the most potent against human cytomegalovirus (CMV) and varicella-zoster virus (VZV). These compounds showed similar activity against thymidine kinase competent (TK<sup>+</sup>) and deficient (TK<sup>-</sup>) VZV strains, demonstrating a mechanism of action independent of the viral thymidine kinase.

### Synthesis and antitubercular activity of ferrocenyl diaminoalcohols and diamines

pp 9546–9553

Dimby Andrianina Ralambomanana, Dorothée Razafimahefa-Ramilison, Andry Clément Rakotohova, Jeanne Maugein, Lydie Péliniski\*

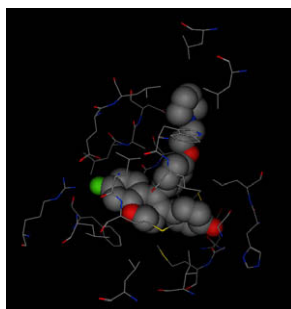


Ferrocenyl and benzyl diaminoalcohols and diamines were synthesized and evaluated against *Mycobacterium tuberculosis* H37Rv.

### Synthesis, biological evaluation, structural–activity relationship, and docking study for a series of benzoxepin-derived estrogen receptor modulators

pp 9554–9573

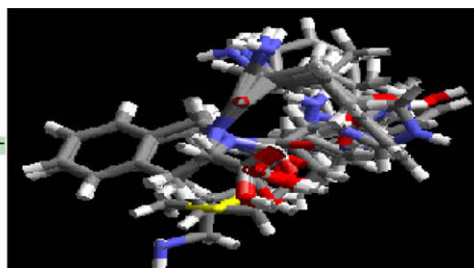
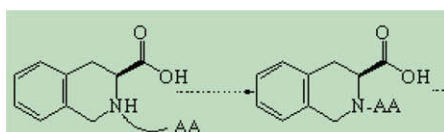
Irene Barrett, Mary J. Meegan\*, Rosario B. Hughes, Miriam Carr, Andrew J. S. Knox, Natalia Artemenko, Georgia Golfis, Daniela M. Zisterer, David G. Lloyd



### (3*S*)-*N*-(*L*-Aminoacyl)-1,2,3,4-tetrahydroisoquinolines, a class of novel antithrombotic agents: Synthesis, bioassay, 3D QSAR, and ADME analysis

pp 9574–9587

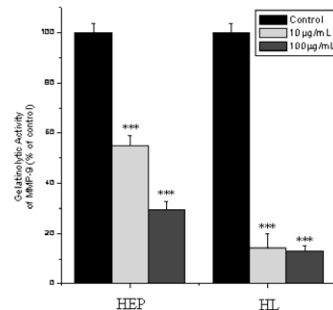
Meiqing Zheng, Xiaoyi Zhang, Ming Zhao\*, Heng Wei Chang\*, Wei Wang, Yuji Wang, Shiqi Peng\*



### Anti-inflammatory properties of a heparin-like glycosaminoglycan with reduced anti-coagulant activity isolated from a marine shrimp

pp 9588–9595

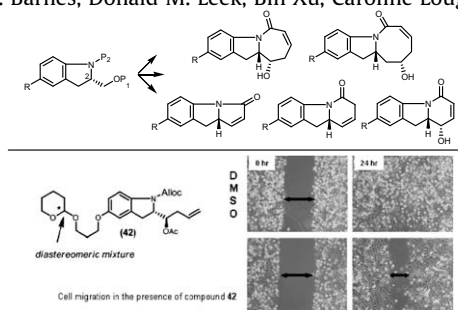
Adriana S. Brito, Dayse S. Arimatéia, Lucilla R. Souza, Marcelo A. Lima, Vanessa O. Santos, Valquíria P. Medeiros, Paula A. Ferreira, Rodrigo A. Silva, Carmen V. Ferreira, Giselle Z. Justo, Edda L. Leite, Julianna P. V. Andrade, Fernanda W. Oliveira, Helena B. Nader, Suely F. Chavante \*



### Building skeletally diverse architectures on the Indoline Scaffold: The discovery of a chemical probe of focal adhesion kinase signaling networks

pp 9596–9602

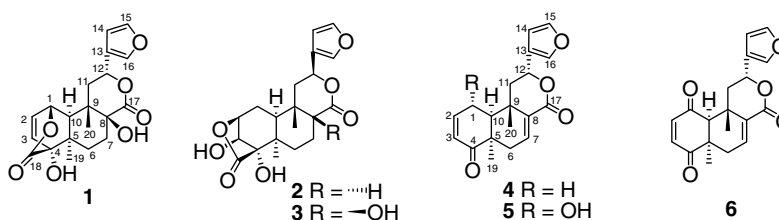
Michael Prakesch, Krikor Bijian, Valérie Campagna-Slater, Sophie Quevillon, Reni Joseph, Chang-Qing Wei, Esther Sesnilo, Ayub Reayi, Rajamohan R. Poondra, Michael L. Barnes, Donald M. Leek, Bin Xu, Caroline Loughheed, Matthieu Schapira, Moulay Alaoui-Jamali \*, Prabhat Arya \*



### Anti-inflammatory activities of furanoditerpenoids and other constituents from *Fibraurea tinctoria*

pp 9603–9609

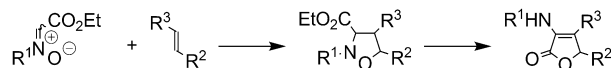
Chung-Ren Su, Yuh-Fung Chen, Meei-Jen Liou, Huei-Yann Tsai, Wen-Shin Chang, Tian-Shung Wu \*



### 3-Amino-2(5H)furanones as inhibitors of subgenomic hepatitis C virus RNA replication

pp 9610–9615

Daniela Iannazzo \*, Anna Piperno, Giovanni Romeo, Roberto Romeo, Ugo Chiacchio, Antonio Rescifina, Emanuela Balestrieri, Beatrice Macchi, Antonio Mastino, Riccardo Cortese



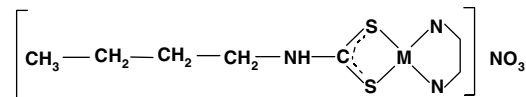
A new class of compounds able to block the replication of subgenomic HCV RNA in liver cells is described. 3-Amino-2(5H)furanones **4** may be regarded as diketoacid analogues and were obtained by basic rearrangement of the isoxazolidine nucleus.

**2,2'-Bipyridinebutyldithiocarbamatoplatinum(II) and palladium(II) complexes: Synthesis, characterization, cytotoxicity, and rich DNA-binding studies**

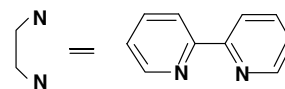
pp 9616–9625

Hassan Mansouri-Torshizi\*, Mahboube I-Moghaddam, Adeleh Divsalar, Ali-Akbar Saboury

Two platinum(II) and palladium(II) complexes have been synthesized and characterized by spectroscopic and nonspectroscopic methods. These water soluble complexes have been tested for their in vitro anti-tumor activity against chronic myelogenous leukemia cell line, K562. The interaction of these complexes with calf thymus DNA was extensively investigated by a variety of spectroscopic techniques. Electronic absorption titration and fluorescence studies showed that both the complexes exhibit cooperative binding and presumably intercalating in DNA.



M=Pd(II) or Pt(II)

**OTHER CONTENTS****Instructions to contributors**

p I

\*Corresponding author

+ Supplementary data available via ScienceDirect

**COVER**

An insight into biologically relevant chemical space showing the scaffolds of potential natural-product based inhibitors orbiting their target, the protein structure of protein 11-beta steroid dehydrogenase (PDB code 1xu7). Graphic produced using Pymol (<http://www.pymol.org>). [M. A. Koch, A. Schuffenhauer, M. Scheck, S. Wetzel, M. Casaulta, A. Odermatt, P. Ertl, H. Waldmann, Charting biologically relevant chemical space: A structural classification of natural products (SCONP), *PNAS* **2005**, 102, 17272–17277 and S. Wetzel, H. Waldmann, Cheminformatic analysis of natural products and their chemical space, *Chimia* **2007**, 61(6), 355–360].

Available online at

  
 ScienceDirect
   
[www.sciencedirect.com](http://www.sciencedirect.com)

Indexed/Abstracted in: Beilstein, Biochemistry & Biophysics Citation Index, CANCERLIT, Chemical Abstracts, Chemistry Citation Index, Current Awareness in Biological Sciences/BIOBASE, Current Contents: Life Sciences, EMBASE/Excerpta Medica, MEDLINE, PASCAL, Research Alert, Science Citation Index, SciSearch, TOXFILE



ELSEVIER

ISSN 0968-0896