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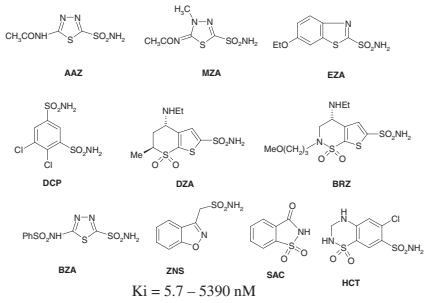
Contents

ARTICLES

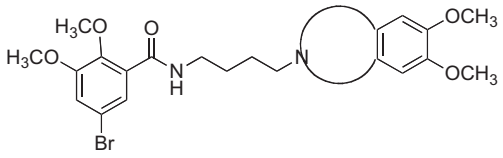
Purification and inhibition studies with anions and sulfonamides of an α-carbonic anhydrase from the Antarctic seal *Leptonychotes weddellii* **pp 1847–1851**

Alessandra Cincinelli, Tania Martellini, Alessio Innocenti*, Andrea Scozzafava, Claudiu T. Supuran*



Effect of structural modification in the amine portion of substituted aminobutyl-benzamides as ligands for binding σ_1 and σ_2 receptors **pp 1852–1859**

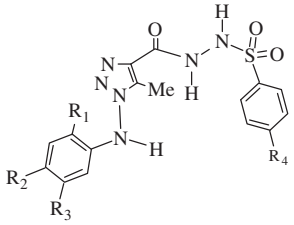
Kuo-Hsien Fan, John R. Lever, Susan Z. Lever*



A series of analogs, where the amine ring fused to the aromatic ring was varied in size (**5**–**7**) and the location of the nitrogen in this ring was modified, has been synthesized and assessed for their σ1/σ2 binding affinity and selectivity. Location of the nitrogen within a constrained ring is confirmed to be key to the exceptional σ2 receptor binding affinity and selectivity for this active series.

Synthesis and anti-HSV-1 activity of new 1,2,3-triazole derivatives **pp 1860–1865**

Alessandro K. Jordão, Vitor F. Ferreira, Thiago M. L. Souza, Gabrielle G. de Souza Faria, Viviane Machado, Juliana L. Abrantes, Maria C. B. V. de Souza, Anna C. Cunha*



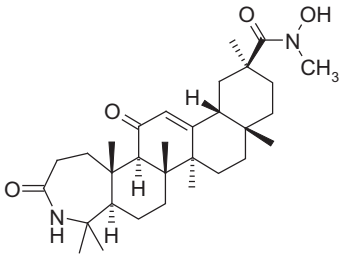
9a, $R_1 = R_2 = R_3 = R_4 = H$
9b, $R_1 = R_2 = R_3 = H$ and $R_4 = Me$
9c, $R_1 = R_2 = R_3 = H$ and $R_4 = OMe$
9d, $R_1 = R_3 = H$, $R_2 = F$ and $R_4 = Me$
9e, $R_1 = R_3 = R_4 = H$ and $R_2 = Cl$
9f, $R_1 = R_3 = R_4 = H$ and $R_2 = Br$
9g, $R_1 = R_3 = H$, $R_2 = Br$ and $R_4 = Me$
9h, $R_1 = R_3 = H$, $R_2 = Br$ and $R_4 = OMe$
9i, $R_1 = R_3 = Cl$ and $R_2 = R_4 = H$

In this work, a new series of arysulfonylhydrazide 1,2,3-triazole derivatives **9a–i** were synthesized, and their ability to inhibit the in vitro replication of HSV-1 was evaluated.

Synthesis of new glycyrrhetinic acid derived ring A azepanone, 29-urea and 29-hydroxamic acid derivatives as selective 11β-hydroxysteroid dehydrogenase 2 inhibitors pp 1866–1880

Rawindra Gaware, Rupesh Khunt, Laszlo Czollner, Christian Stanetty, Thierry Da Cunha, Denise V. Kratschmar, Alex Odermatt, Paul Kosma, Ulrich Jordis, Dirk Claßen-Houben*

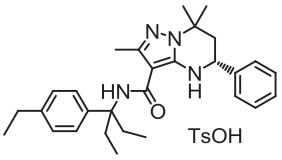
Starting from the natural compound glycyrrhetinic acid a set of 11β-HSD2 selective inhibitors was prepared. The most potent and most selective compound **28** is active against human 11β-HSD2 in the low nanomolar range with a more than 3600-fold selectivity over human 11β-HSD1.



28

Novel and potent calcium-sensing receptor antagonists: Discovery of (5*R*)-*N*-[1-ethyl-1-(4-ethylphenyl)propyl]-2,7,7-trimethyl-5-phenyl-4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyrimidine-3-carboxamide monotosylate (TAK-075) as an orally active bone anabolic agent pp 1881–1894

Masato Yoshida, Akira Mori, Shinji Morimoto, Etsuo Kotani, Masahiro Oka, Kohei Notoya, Haruhiko Makino, Midori Ono, Mikio Shirasaki, Norio Tada, Hisashi Fujita, Junko Ban, Yukihiro Ikeda, Tomohiro Kawamoto, Mika Goto, Hiroyuki Kimura, Atsuo Baba, Tsuneo Yasuma*

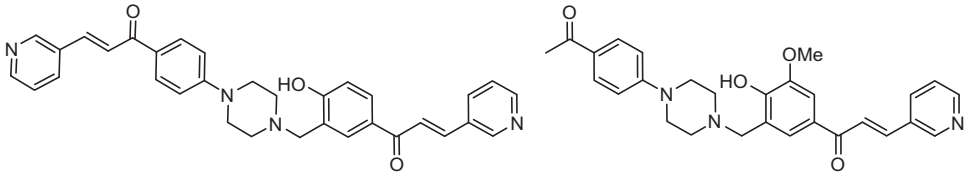


10m

Discovery of novel and potent tetrahydropyrazolopyrimidine derivatives as an orally active bone anabolic agent are reported.

New bichalcone analogs as NF-κB inhibitors and as cytotoxic agents inducing Fas/CD95-dependent apoptosis pp 1895–1906

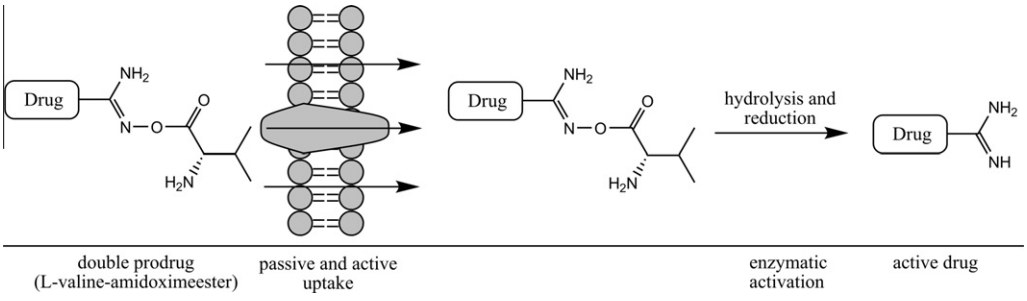
M. Vijaya Bhaskar Reddy, Yuh-Chiang Shen, Jai-Sing Yang, Tsong-Long Hwang, Kenneth F. Bastow, Keduo Qian, Kuo-Hsiung Lee*, Tian-Shung Wu*



4 **23**

Synthesis and biological evaluation of L-valine-amidoximeesters as double prodrugs of amidines pp 1907–1914

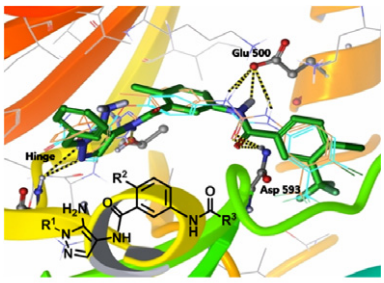
Joscha Kotthaus, Helen Hungeling, Christiane Reeh, Jürke Kotthaus, Dennis Schade, Silvia Wein, Siegfried Wolffram, Bernd Clement*

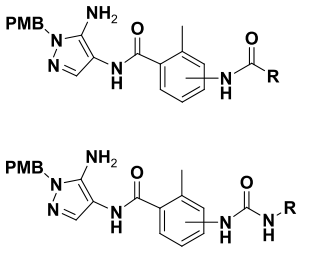


Structure based design and syntheses of amino-1*H*-pyrazole amide derivatives as selective Raf kinase inhibitors in melanoma cells **pp 1915–1923**

Mi-hyun Kim, Minjung Kim, Hana Yu, Hwan Kim, Kyung Ho Yoo, Taebo Sim, Jung-Mi Hah*

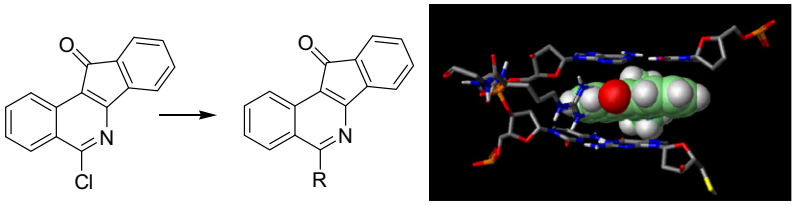
The synthesis of a novel series of 5-amiono-1*H*-pyrazol-4-yl phenyl amide derivatives **6a–n**, **7a–s** and their antiproliferative activities against A375P melanoma cell line were described.





Design, synthesis and docking study of 5-amino substituted indeno[1,2-*c*]isoquinolines as novel topoisomerase I inhibitors **pp 1924–1929**

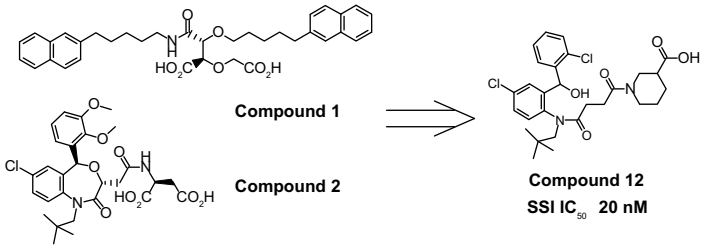
Daulat Bikram Khadka, Quynh Manh Le, Su Hui Yang, Hue Thi My Van, Thanh Nguyen Le, Suk Hee Cho, Youngjoo Kwon, Kyung-Tae Lee, Eung-Seok Lee, Won-Jea Cho*

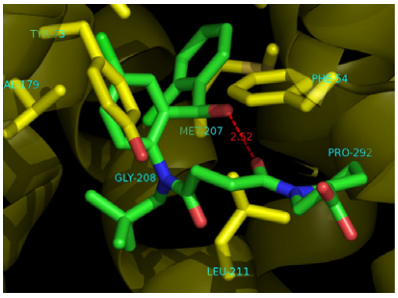


5-Amino group-substituted indeno[1,2-*c*]isoquinolines were designed and synthesized as topoisomerase I inhibitors and a docking model was proposed.

Discovery of a new 2-aminobenzhydrol template for highly potent squalene synthase inhibitors **pp 1930–1949**

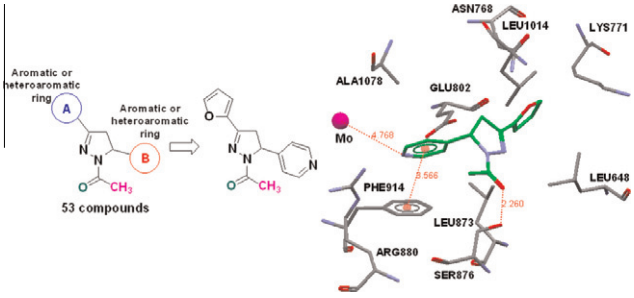
Masanori Ichikawa*, Aki Yokomizo, Masao Itoh, Kazuyuki Sugita, Hiroyuki Usui, Hironari Shimizu, Makoto Suzuki, Koji Terayama, Akira Kanda





A rational approach for the design and synthesis of 1-acetyl-3,5-diaryl-4,5-dihydro(1*H*)pyrazoles as a new class of potential non-purine xanthine oxidase inhibitors **pp 1950–1958**

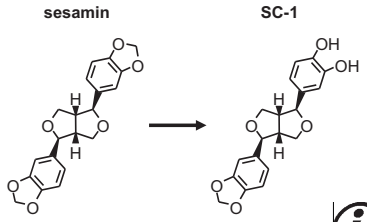
Kunal Nepali, Gurinderdeep Singh, Anil Turan, Amit Agarwal, Sameer Sapra, Raj Kumar*, Uttam C. Banerjee, Prabhakar K. Verma, Naresh K. Satti, Manish K. Gupta, Om P. Suri, K. L. Dhar



Involvement of heme oxygenase-1 induction via Nrf2/ARE activation in protection against H_2O_2-induced PC12 cell death by a metabolite of sesamin contained in sesame seeds pp 1959–1965

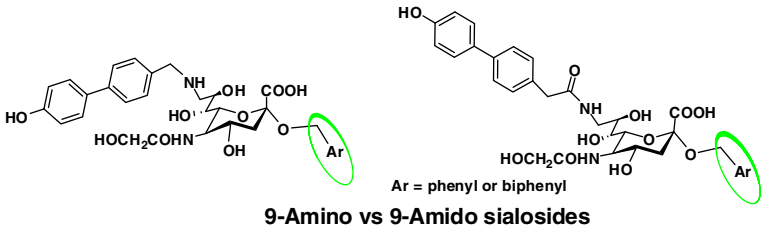
Nanako Hamada, Arisa Tanaka, Yasunori Fujita, Tomohiro Itoh, Yoshiko Ono, Yoshinori Kitagawa, Namino Tomimori, Yoshinobu Kiso, Yukihiro Akao, Yoshinori Nozawa, Masafumi Ito*

SC-1 {(1*R*,2*S*,5*R*,6*S*)-6-(3,4-dihydroxyphenyl)-2-(3,4-methylenedioxyphenyl)-3,7-dioxabicyclo-[3,3,0]octane}, a metabolite of sesamin contained in sesame seeds, is capable of protecting against H_2O_2-induced PC12 cell death by heme oxygenase-1 induction via Nrf2/ARE activation.



CD22-Antagonists with nanomolar potency: The synergistic effect of hydrophobic groups at C-2 and C-9 of sialic acid scaffold pp 1966–1971

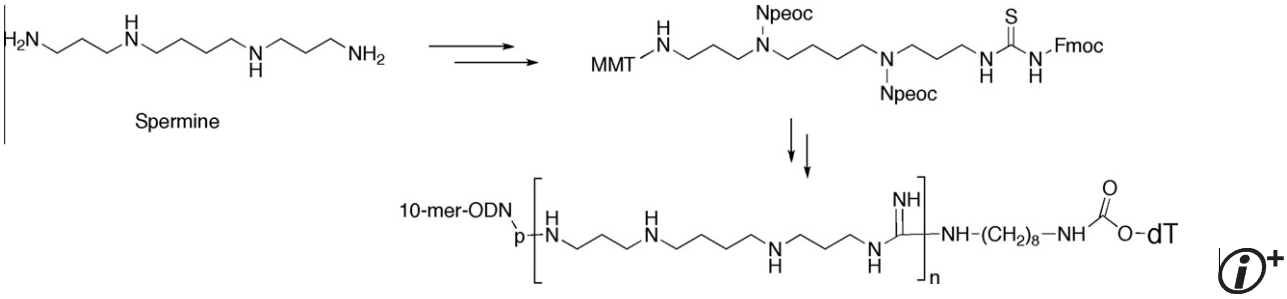
Hajjaj H. M. Abdu-Allah*, Kozo Watanabe, Gladys C. Completo, Magesh Sadagopan, Koji Hayashizaki, Chiaki Takaku, Taichi Tamanaka, Hiromu Takematsu, Yasunori Kozutsumi, James C. Paulson, Takeshi Tsubata, Hiromune Ando, Hideharu Ishida, Makoto Kiso*



Simple sialosides modified at C-2 and C-9 exhibited nanomolar potency and higher selectivity for CD22 than for MAG.

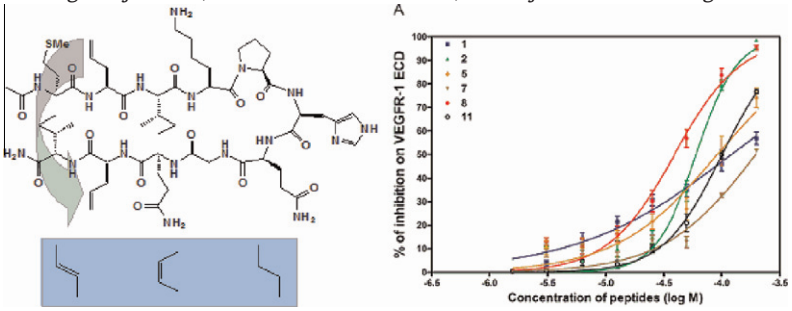
MMT, Npeoc-protected spermine, a valuable synthon for the solid phase synthesis of oligonucleotide oligospermine conjugates via guanidine linkers pp 1972–1977

Phanélie Perche, Mitsuharu Kotera*, Jean-Serge Remy

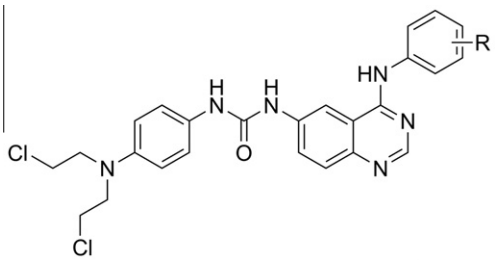


Parallel solid-phase synthesis of a small library of linear and hydrocarbon-bridged analogues of $VEGF_{81–91}$: Potential biological tools for studying the VEGF/VEGFR-1 interaction pp 1978–1986

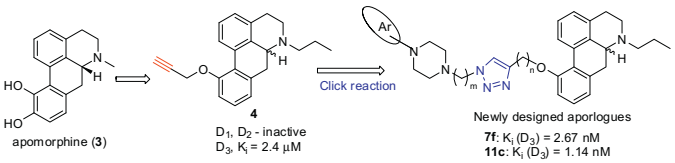
María Isabel García-Aranda, Patricia Marrero, Benoit Gautier, Mercedes Martín-Martínez, Nicolas Inguimbert, Michel Vidal, María Teresa García-López, María Angeles Jiménez, Rosario González-Muñiz, María Jesús Pérez de Vega*



Design, synthesis and antitumor evaluation of phenyl *N*-mustard-quinazoline conjugates **pp 1987–1998**
Bhavin Marvania, Pei-Chih Lee, Ravi Chaniyara, Huajin Dong, Sharda Suman, Rajesh Kakadiya, Ting-Chao Chou, Te-Chang Lee, Anamik Shah, Tsann-Long Su*

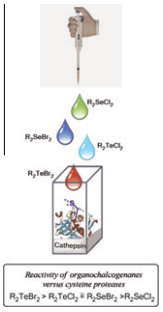


Further SAR study on 11-O-substituted aporphine analogues: Identification of highly potent dopamine D_3 receptor ligands **pp 1999–2008**
Na Ye, QianQian Wu, Liyuan Zhu, Longtai Zheng, Bo Gao, Xuechu Zhen*, Ao Zhang*

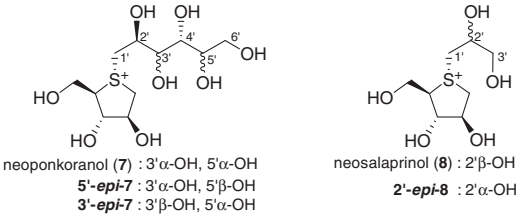


A series of new aporphine analogues (aporlogues) were prepared from appropriate aporphine precursors and arylpiperazines using the Click reaction protocol. Compounds **7f** and **11c** stood out as the most potent at the D_3 receptor among our newly synthesized aporlogues with K_i values of 2.67 and 1.14 nM, respectively. Further assay at the 5-HT_{1A} receptor revealed that aporlogues **7f** and **11c** also showed high affinity at this receptor.

Structure–activity relationships of hypervalent organochalcogenanes as inhibitors of cysteine cathepsins V and S **pp 2009–2014**
Leandro Piovan, Márcio F. M. Alves, Luiz Juliano, Dieter Brömme, Rodrigo L. O. R. Cunha*, Leandro H. Andrade*

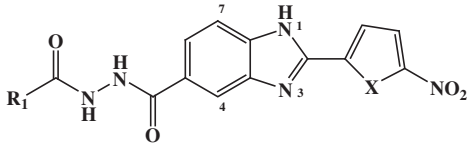


Isolation, structure identification and SAR studies on thiosugar sulfonium salts, neosalaprinol and neoponkoranol, as potent α-glucosidase inhibitors **pp 2015–2022**
Weijia Xie, Genzoh Tanabe, Junji Akaki, Toshio Morikawa, Kiyofumi Ninomiya, Toshie Minematsu, Masayuki Yoshikawa, Xiaoming Wu, Osamu Muraoka*



Synthesis and biological evaluation of benzimidazole-5-carbohydrazide derivatives as antimalarial, cytotoxic and antitubercular agents pp 2023–2029

José Camacho, Arthur Barazarte, Neira Gamboa, Juan Rodrigues, Rosario Rojas, Abraham Vaisberg, Robert Gilman, Jaime Charris*

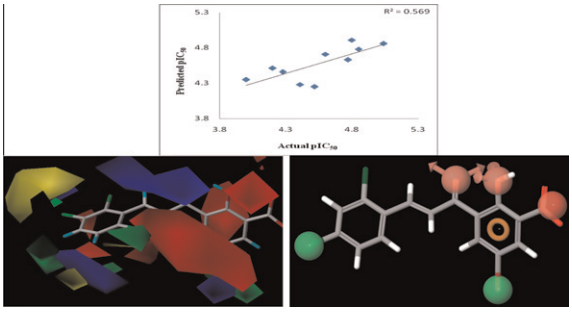


R_1: H, Ar. X: O, S

A series of N′-substituted-2-(5-nitrofuran or 5-nitrothiophe-2-yl)-3*H*-benzo[*d*]-imidazole-5-carbohydrazide derivatives were synthesized and investigated for their abilities to inhibit β-hematin formation, hemoglobin hydrolysis and in vivo for their antimalarial efficacy in rodent *Plasmodium berghei*. Selected analogues were screened for their antitubercular activity against sensitive MTB $H_{37}Rv$ and multidrug-resistant MDR-MTB strains, and cytotoxic activity against a panel of human tumor cell lines and two nontumorogenic cell lines.

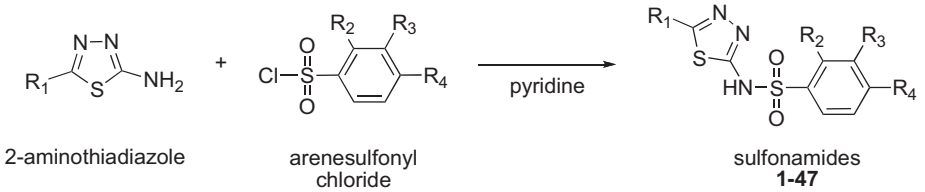
Synthesis, biological evaluation and 3D-QSAR studies of 3-keto salicylic acid chalcones and related amides as novel HIV-1 integrase inhibitors pp 2030–2045

Horrick Sharma, Shivaputra Patil, Tino W. Sanchez, Nouri Neamati, Raymond F. Schinazi, John K. Buolamwini*



Development of sulfonamide AKT PH domain inhibitors pp 2046–2054

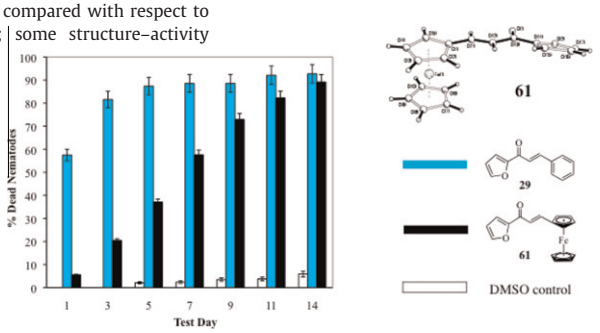
Ali Md. Ahad, Song Zuohe, Lei Du-Cuny, Sylvestor A. Moses, Li Li Zhou, Shuxing Zhang, Garth Powis, Emmanuelle J. Meuillet, Eugene A. Mash*



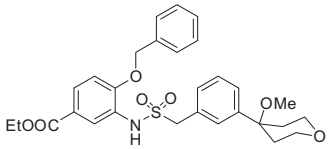
Ferrocenyl chalcones versus organic chalcones: A comparative study of their nematocidal activity pp 2055–2073

Saeed Attar*, Zachary O'Brien, Hasan Alhaddad, Melissa L. Golden, Alejandro Calderón-Urrea

A series of 30 organic chalcones and 33 ferrocenyl chalcones were prepared and compared with respect to their biological activity against the model nematode *Caenorhabditis elegans*; some structure–activity relationships (SARs) were determined.



Syntheses and characterization of nimesulide derivatives for dual enzyme inhibitors of both cyclooxygenase-1/2 and 5-lipoxygenase **pp 2074–2083**
Yue Li, Shu-Han Chen, Tian-Miao Ou, Jia-Heng Tan, Ding Li, Lian-Quan Gu, Zhi-Shu Huang*

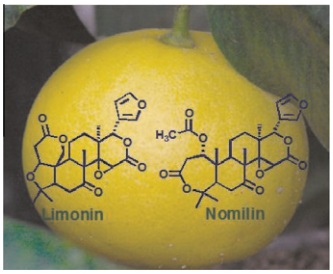


20f

IC_{50} for
COX-1: 11.6 μM
COX-2: 0.97 μM
5-LOX: 0.87 μM

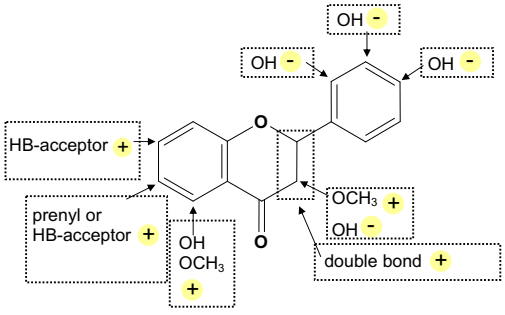
A variety of new nimesulide derivatives were synthesized through incorporation of a 5-LOX pharmacophore into nimesulide with some further modifications. Their structure–activity relationships were studied, and compound **20f** was found to be an excellent dual enzyme inhibitor.

Antiviral activity of seed extract from *Citrus bergamia* towards human retroviruses **pp 2084–2089**
Emanuela Balestrieri, Francesco Pizzimenti, Angelo Ferlazzo, Salvatore V. Giofrè, Daniela Iannazzo, Anna Piperno*, Roberto Romeo, Maria Assunta Chiacchio, Antonio Mastino, Beatrice Macchi*



Structure–activity relationships of flavonoids as inhibitors of breast cancer resistance protein (BCRP) **pp 2090–2102**
Anne Pick, Henrik Müller, Ralf Mayer, Britta Haenisch, Ilza K. Pajeva, Mathias Weigt, Heinz Bönisch, Christa E. Müller, Michael Wiese*

Summary of structural features influencing the inhibition of BCRP by flavonoids. Plus-circles indicate the positive contribution of structural elements to anti-BCRP activity. Minus-circles illustrate the negative impact on inhibitory potency. Results are based on data from the 3D QSAR approaches of the present study as well as the findings from 2D QSAR analyses of data taken from literature.



*Corresponding author
Supplementary data available via ScienceDirect

COVER

The known veterinary anthelmintic and proton ionophore, closantel, was recently discovered to also exhibit potent chitinase inhibition activity and inhibit molting in the parasitic nematode, *Onchocerca volvulus*, the causative agent of the neglected tropical disease onchocerciasis. [C. Gloeckner, A. L. Garner, F. Mersha, Y. Oksov, N. Tricoche, L. M. Eubanks, S. Lustigman, G. F. Kaufmann, K. D. Janda, Repositioning of an existing drug for the neglected tropical disease Onchocerciasis, *Proc. Natl. Acad. Sci., U.S.A.* **2010**, *107*, 3424.]

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