Bioorganic & Medicinal Chemistry 19 (2011) 4679–4689

Contents lists available at ScienceDirect

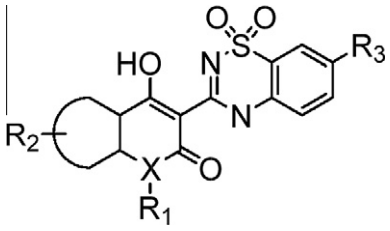
Bioorganic & Medicinal Chemistry

journal homepage: www.elsevier.com/locate/bmc

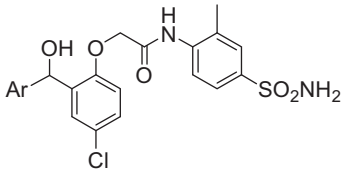
Bioorganic & Medicinal Chemistry Volume 19, Issue 16, 2011

Contents

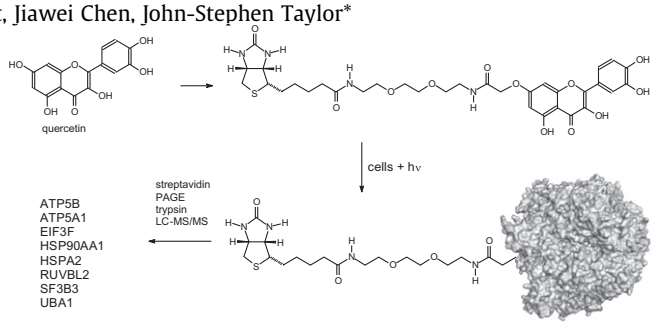
REVIEW

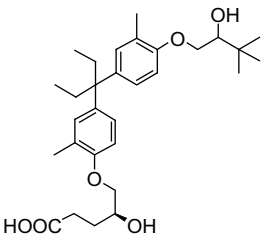


ARTICLES

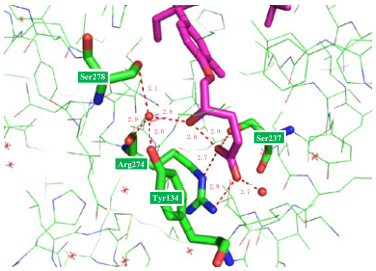


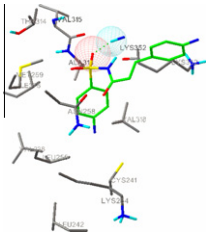
Ar = phenyl, substituted phenyl, naphthyl
(±)-benzhydrol derivatives



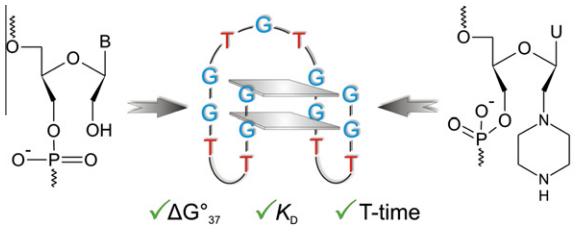


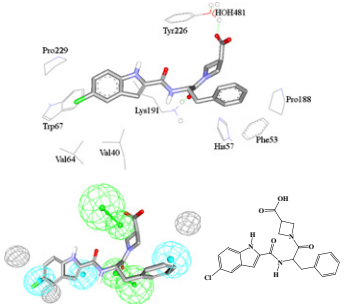
Compound 6a

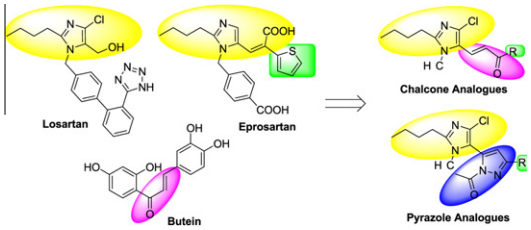




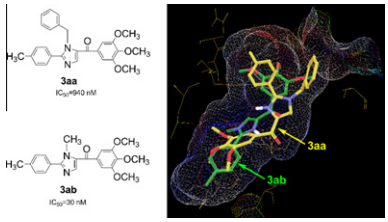
A series of cinnamic acyl sulfonamide derivatives have been designed and synthesized, and their biological activities were also evaluated for tubulin inhibitory activity. Compound **10c** possessed the most potent biological activity (IC_{50} = 0.8 μg/mL for B16-F10 and IC_{50} = 2.4 μg/mL for tubulin). Docking simulation was performed to explore the binding model of compound **10c** with tubulin.

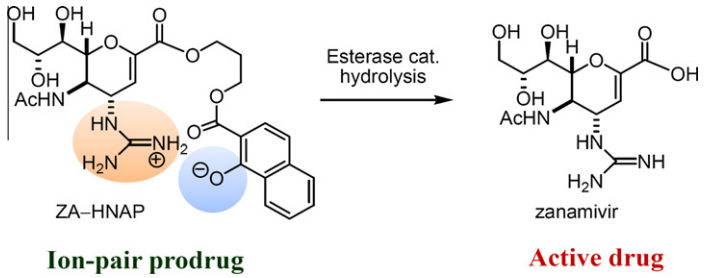




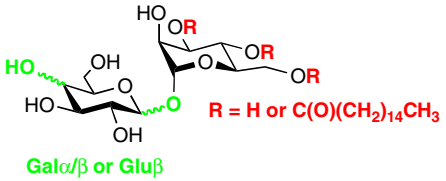


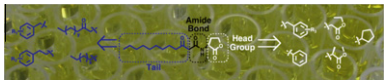
Screening all 36 new analogues of chalcones and pyrazoles using ACE inhibition assay, resulted three compounds as potent ACE inhibitors with IC_{50} of 2.24 μM, 2.68 μM, and 3.60 μM.

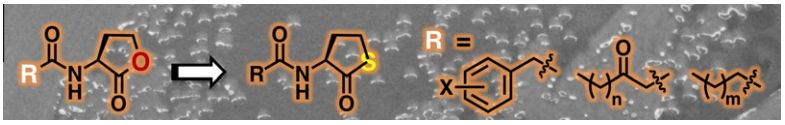




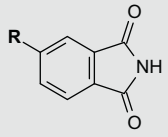
A new class of 1-hydroxy-2-napthoic acid modified prodrugs of zanamivir and guanidino-oseltamivir is designed as an intramolecular ion-pair with improved bioavailability.





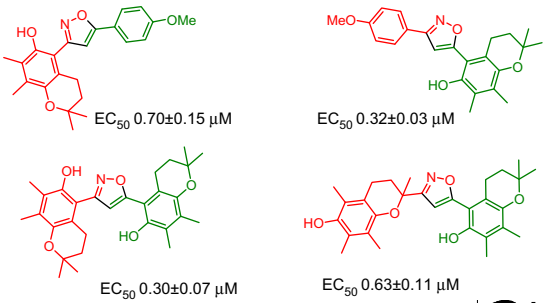


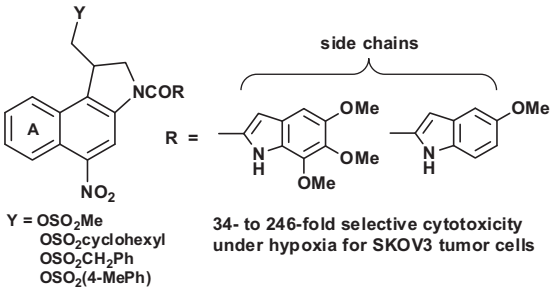
The synthesis of C5-substituted phthalimide analogues (**5**) with enhanced human MAO inhibition potencies compared to the lead compound phthalimide (**4**).

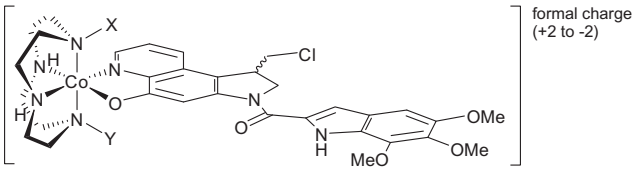


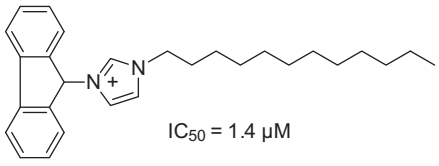
	R	IC_{50} MAO-A μM	IC_{50} MAO-B μM
4	H	165	134
5b	$C_6H_5CH_2O$	4.17	0.043
5c	$C_6H_5CH_2CH_2O$	3.58	0.017
5d	$C_6H_5(CH_2)_3O$	1.73	0.050

In an effort to optimize our previously identified neuroprotective chroman derivatives, 20 new 2 or 5-substituted chroman analogues bearing isoxazole moieties with aliphatic or aromatic substituents were synthesized and their activity against oxidative stress-induced damage in neuronal HT22 cells was evaluated. The differences in activity observed between regioisomers were attributed to specific structural characteristics.



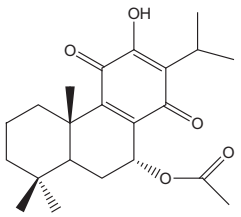




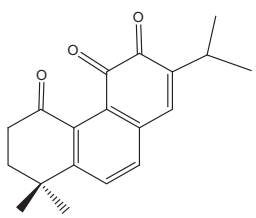


N,N′-Disubstituted imidazolium salts have been prepared and tested as LuxR dependent quorum sensing inhibitors. Some of them displayed IC_{50} in the micromolar range. These results suggest that a disubstituted imidazolium ring may be considered as a new pharmacophore for QS inhibition.

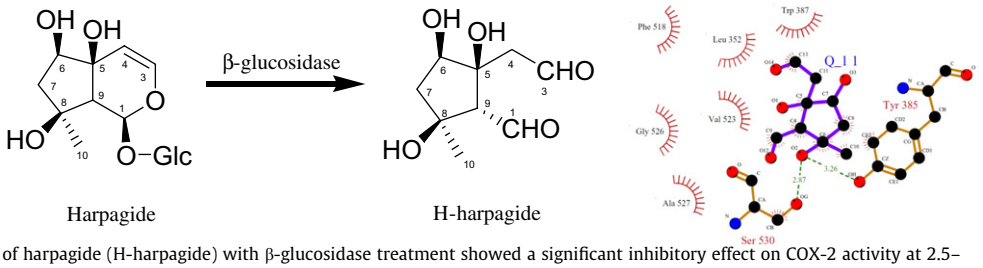
Phytochemical studies on *Peltodon longipes* afforded the isolation of twelve known abietane diterpenes being the active principle. The main diterpene, 7α-acetoxyroyleanone exhibited a similar strong cytotoxic activity against a pancreatic and a melanoma cancer cell line as tanshinone IIa the main compound from *Salvia miltiorrhiza*. Structure–activity relationship study was undertaken including 21 structurally different abietane diterpenes.



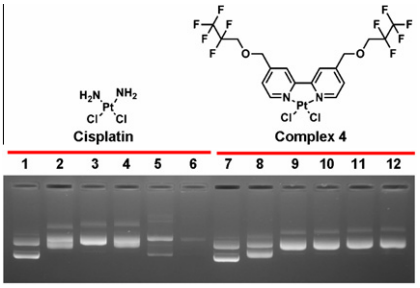
7α-acetoxyroyleanone



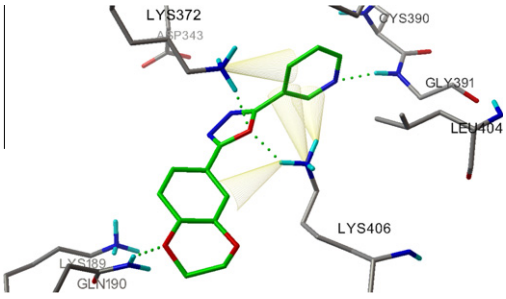
Tanshinone IIa



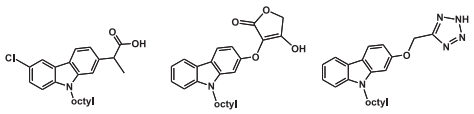
The hydrolyzed products of harpagide (H-harpagide) with β-glucosidase treatment showed a significant inhibitory effect on COX-2 activity at 2.5–100 μM in a concentration-dependent manner. H-harpagide could bind to the COX-2 active domain well through hydrophobic and hydrogen-bonding interactions, whereas harpagide and harpagoside could not.

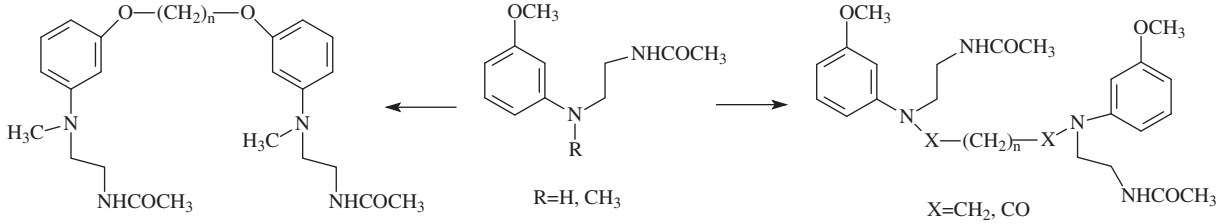


In the electrophoretogram the complex **4** (or cisplatin)-treated pSECTag 2/Hygro B plasmid DNA, significant comigration of open circular form and covalent closed circular form was observed and a coalescence of two main bands was found subsequently at low concentrations. A strong unwinding of negative supercoiled DNA to positive supercoiled DNA was detected at high concentrations of cisplatin, whereas the same binding mode with complex **4** was not observed.

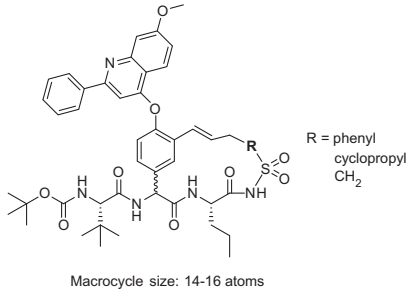


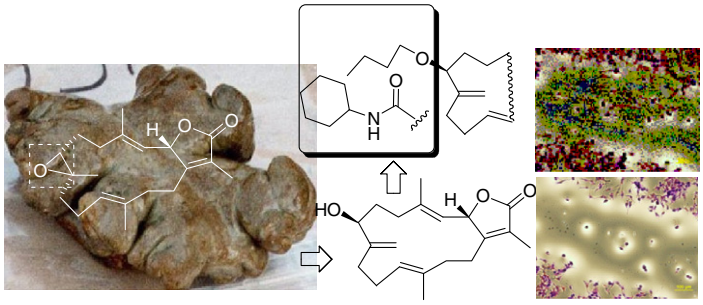
A series of oxadiazole derivatives containing 1,4-benzodioxan (**4a**–**4s**) have been designed, synthesized, structurally determined, and their biological activities were also evaluated as potential immunosuppressive agents. All the synthesized compounds were first synthesized. Among the compounds, compound **4i** showed the most potent biological activity against RAW264.7 cells (inhibition = 37.66 ± 2.34% for NO overproduction and IC_{50} = 0.05 μM for iNOS). Docking simulation was performed to position compound **4i** into the iNOS structure active site to determine the probable binding model. RT-PCR experiment results demonstrated that some of these compounds possessed good immunosuppressive activity against iNOS, especially for compound **4i**. Therefore, compound **4i** with potent inhibitory activity may be a potential agent.

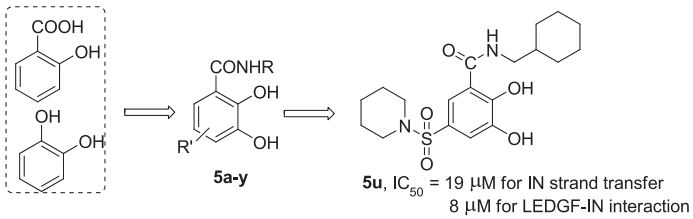


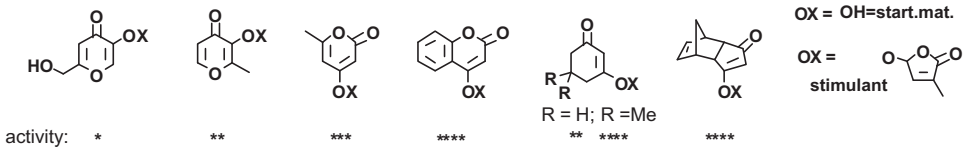


New dimeric melatonin receptor ligands with different bridging position and spacer length were synthesized and evaluated in vitro for their binding affinity and intrinsic activity at h-MT_1 and h-MT_2 receptors.

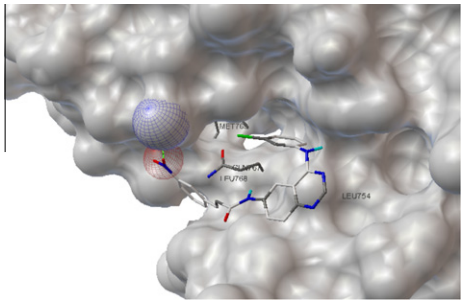


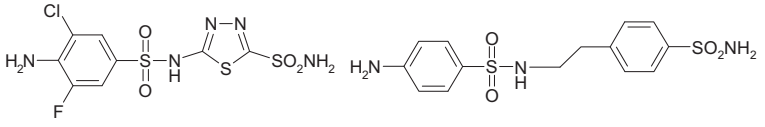






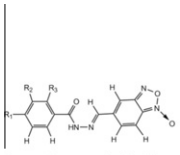
A novel type of cinnamic acid quinazoline amide derivatives (**20**–**42**), which designed the combination between quinazoline as the backbone and various substituted cinnamic acid as the side chain, have been synthesized and their biological activities were evaluated within cytotoxicity assay firstly and then potent EGFR inhibitory activity. Compound **42** demonstrated the most potent inhibitory activity (IC_{50} = 0.94 μM for EGFR), which could be optimized as a potential EGFR inhibitor in the further study. Docking simulation was performed to position compound **42** into the EGFR active site to determine the probable binding model. Analysis of the binding conformation of **42** in active site displayed compound **42** was stabilized by hydrogen bonding interactions with Lys822, which was different from other derivatives. In the further study, compounds **43** and **44** had been synthesized and their biological activities were also evaluated, which were the same as that we expected. Compound **43** has demonstrated significant EGFR (IC_{50} = 0.12 μM) and tumor growth inhibitory activity as a potential anticancer agent.

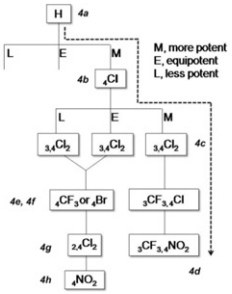


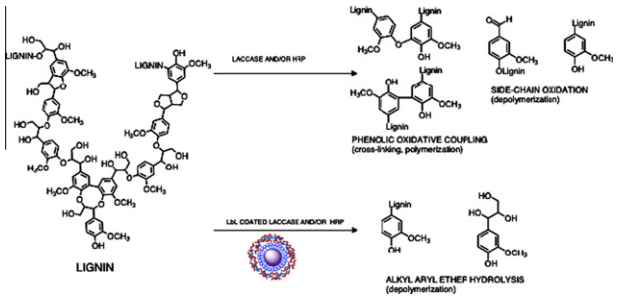


stCA 1:	Ki = 51 nM	Ki = 72 nM
stCA 2:	Ki =38 nM	Ki = 31 nM

A set of benzofuroxan derivatives, potential antimicrobial agents, was designed to exploring the physicochemical properties of the substituents. Topliss operational scheme orientated the select of substituent groups.







OTHER CONTENT

*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.]

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. Also covered in the abstract and citation database SCOPUS®. Full text available on ScienceDirect®

ELSEVIER

ISSN 0968-0896