Bioorganic & Medicinal Chemistry 18 (2010) 2067–2075

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry

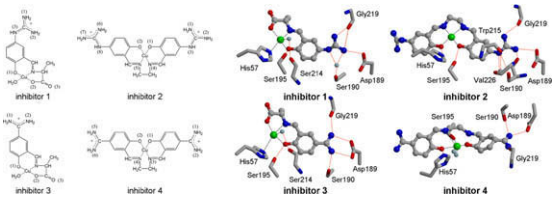
journal homepage: www.elsevier.com/locate/bmc

# Bioorganic & Medicinal Chemistry Volume 18, Issue 6, 2010

# Contents

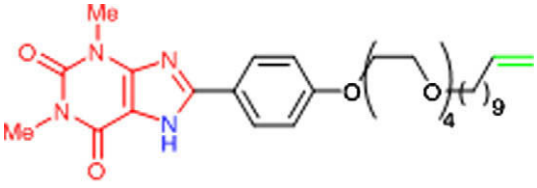
## ARTICLES






The crystal structures of the complexes of β-trypsin with *m*-guanidinosalicylidene-L-alaninato(aqua)copper(II) hydrochloride, [*N*,*N*′-bis(*m*-guanidinosalicylidene)ethylenediaminato]copper(II), and [*N*,*N*′-bis(*m*-amidinosalicylidene)ethylenediaminato]copper(II) have been determined. The structural and inhibitory activity data provide new avenues for designing novel inhibitors against physiologically important trypsin-like serine proteases.

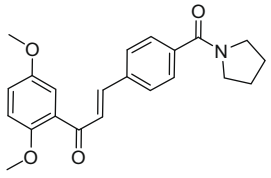





**2, *k*i= 4.16 nM**

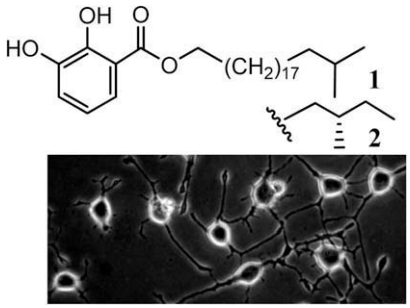
Synthesis of oligo(ethylene glycol)-alkene substituted the theophyllines (positions 7 and/or 8) is described. Compound **2** showed high affinity and selectivity for $A_{2B}$ receptor ($K_i$ = 4.16 nM, $K_{iA2A}/K_{iA2B}$ = 24.1). The alkenyl or azido substituents in some of the derivative allows for covalent attachment of them onto H-terminated silicon surfaces.





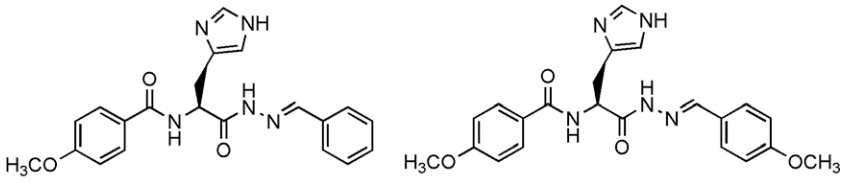

**17**

A series of novel 2′,5′-dimethoxylchalcone derivatives including 18 new compounds were synthesized and evaluated for cytotoxicities against two human cancer cell lines, NTUB1 (human bladder cancer cell line) and PC3 (human prostate cancer cell line) cell lines.




Two new alkyl 2,3-dihydroxybenzoates, gentisides A and B, were isolated from the traditional Chinese medicine *Gentiana rigescens* Franch. They showed a significant neuritogenic activity at 30 μM against PC12 cells that was comparable to that seen for the best nerve growth factor concentration of 40 ng/mL.

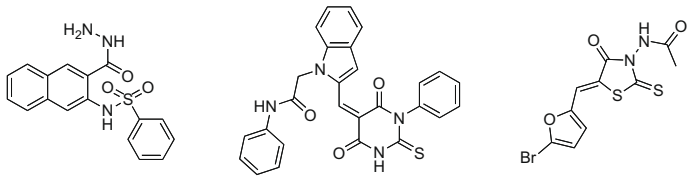





**8a** **8b**

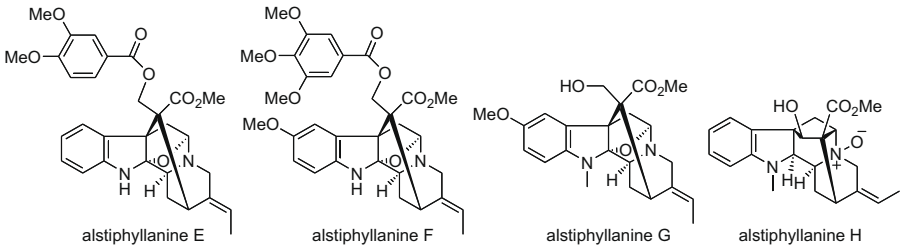
We studied SAR and molecular mechanism of novel acylhydrazone compounds targeting HIV-1 CA. Among synthesized compounds, **8a** and **8b** possessed the most promising antiviral activities.



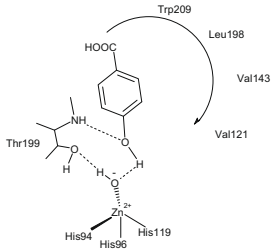


$IC_{50}$ = 5 μM $IC_{50}$ = 33 μM time dependent $IC_{50}$ = 41 μM



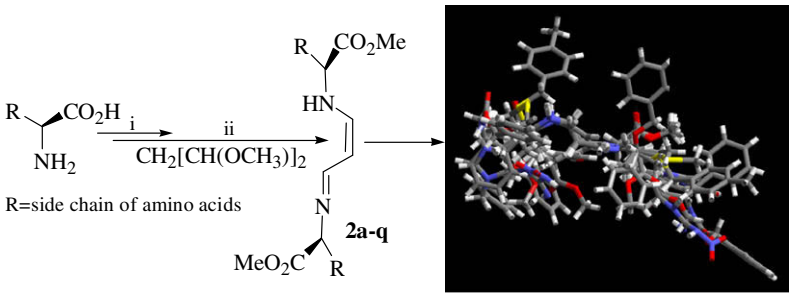


alstiphyllanine E alstiphyllanine F alstiphyllanine G alstiphyllanine H

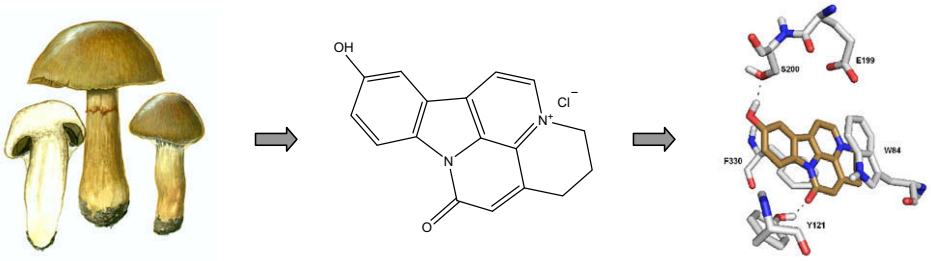



Ki = 0.92 μM (hCA I); Ki = 0.87 μM (hCA II); Ki = 3.73 μM (hCA IX)



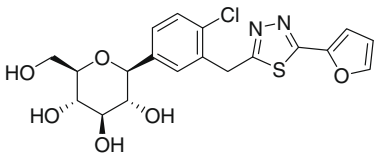




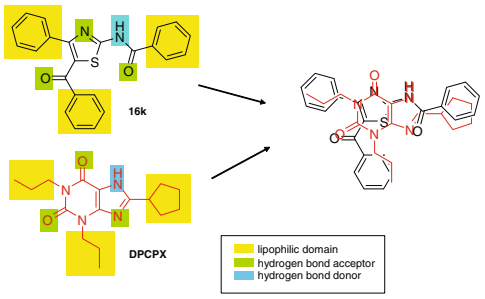

The isolation of acetylcholinesterase inhibitors ($IC_{50}$ = 9.7 μM) from fungal source is reported. The selective binding mode is resolved by docking studies. The pharmacological potential is further supported by Aβ-aggregation and cytotoxicity studies.



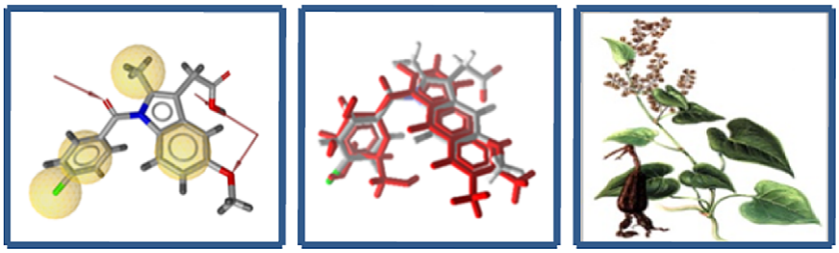



$IC_{50}$ (*h*SGLT2) = 7.03 nM

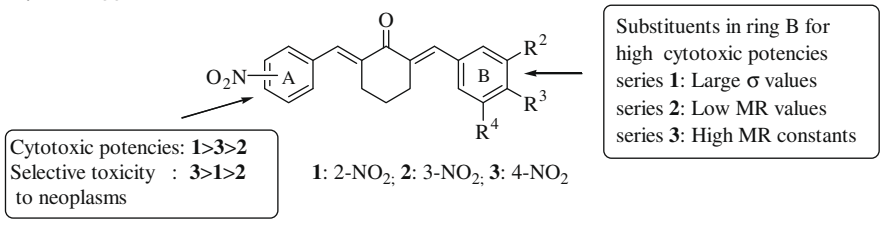
Novel C-aryl glucoside SGLT2 inhibitors containing 1,3,4-thiadiazole at the distal ring position were identified as potential antidiabetic agents. A selected compound demonstrated reasonable urinary glucose excretion and glucosuria in normal SD rats along with favorable blood glucose-lowering effects in db/db mice.





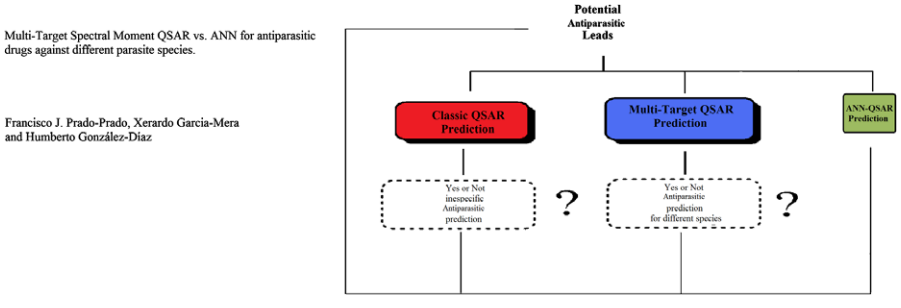



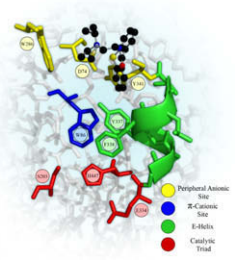




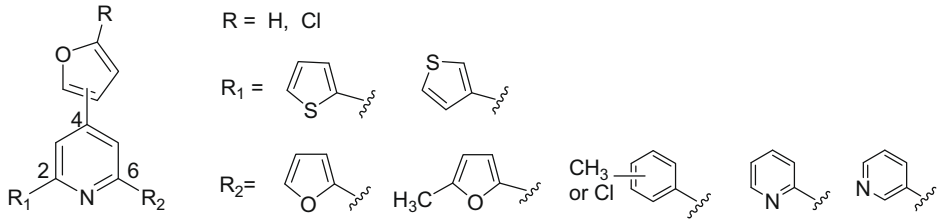

A number of 2-benzylidene-6-(nitrobenzylidene)cyclohexanones emerged as lead compounds which possess noteworthy cytotoxicity, selective toxicity towards neoplasms than non-malignant cells and well tolerated in mice in short-term toxicity studies.



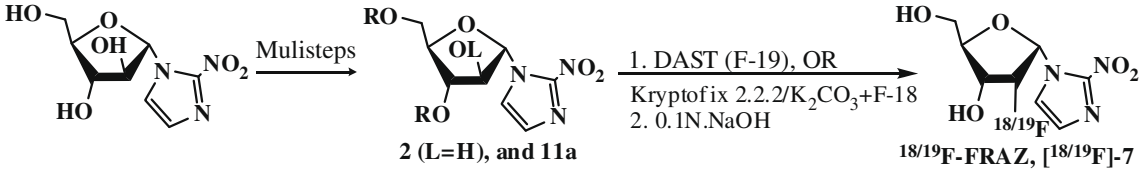




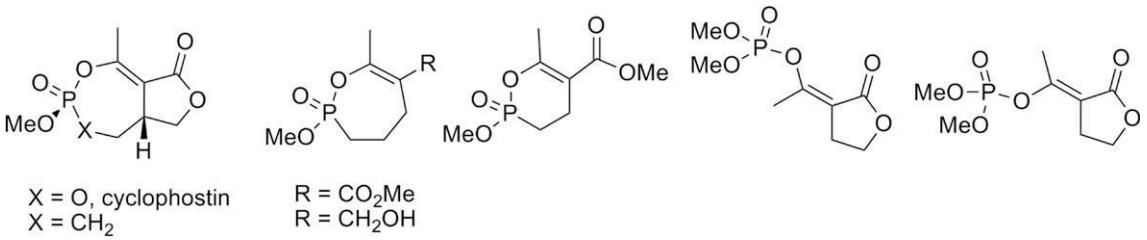


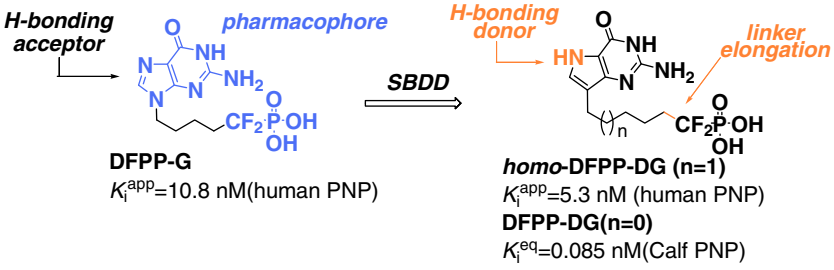




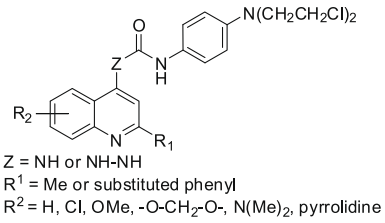







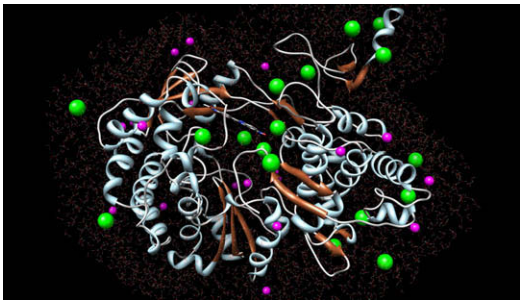


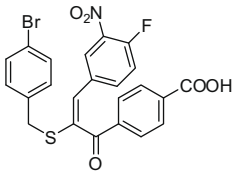






*Stylophora pystillata* (coral) CA is activated by amines and amino acids.

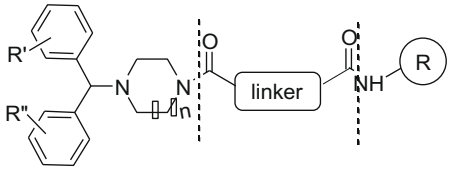




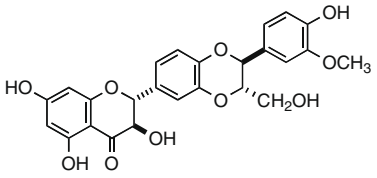



The design, synthesis and biological evaluation of novel (*E*)-α-benzylthio chalcones as BCR-ABL kinase inhibitors are described. The structure–activity relationship, in vitro cytotoxicity in K562, a human leukemic cell line and inhibition of BCR-ABL phosphorylation by these compounds is discussed.








The methanolic extract from the whole plants of *Anastatica hierochuntica* was found to inhibit melanogenesis in theophylline-stimulated murine B16 melanoma 4A5 cells. Among the constituents isolated, anastatin A, silybin A, isosilybins A and B, several flavonoids, etc. inhibited the melanogenesis with $IC_{50}$ values of 6.1–32 μM. With regard to the mechanism of action of silybins and isosilybins, the inhibition of tyrosinase activity suggested to be important. In addition, isosilybins A and B inhibited the mRNA expression of TRP-2, but silybins A and B oppositely enhanced the mRNA expression of tyrosinase, TRP-1 and -2 at 10 and/or 30 μM, and the inhibition of phosphorylation of extracellular signal-regulated kinases (ERK1/2) is involved in the enhanced expression of mRNA, at least in part.

## OTHER CONTENTS



*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].



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