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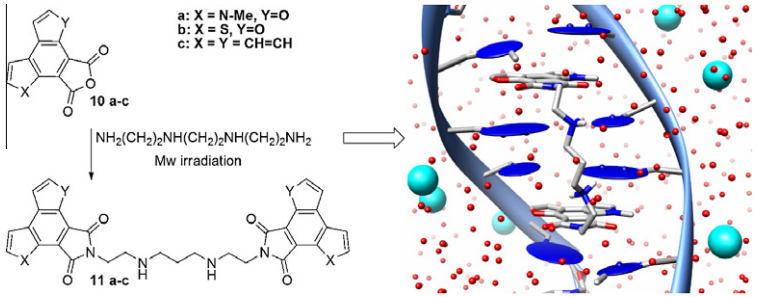
# Bioorganic & Medicinal Chemistry Volume 19, Issue 18, 2011

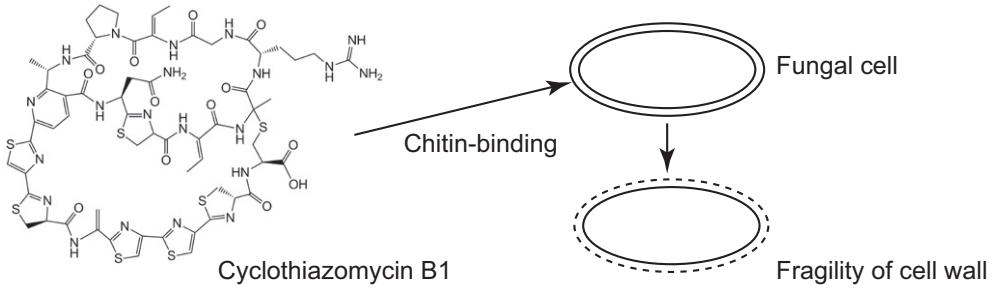
# Contents

## ARTICLES

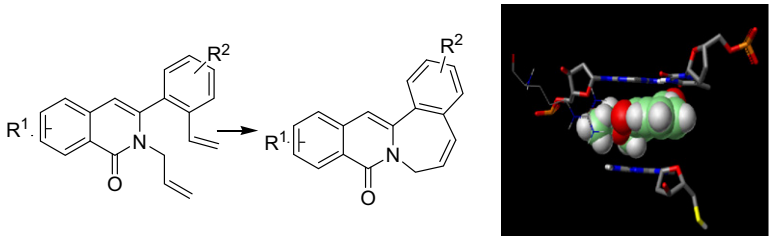


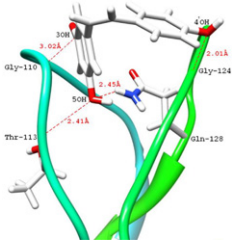




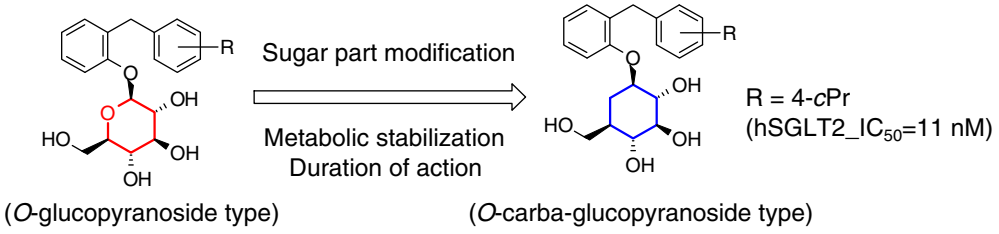


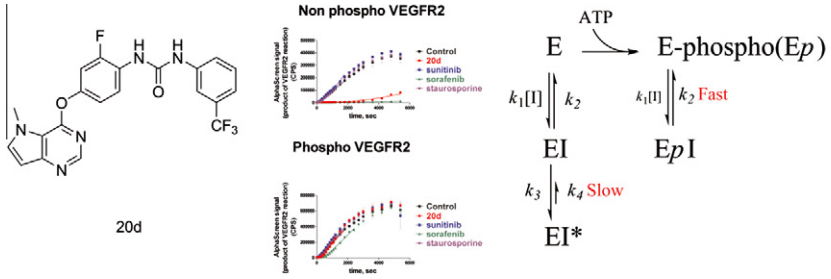



**Regulation of PKCα activity by resveratrol and its derivatives**

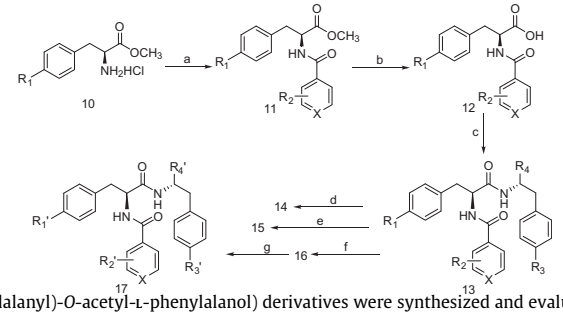




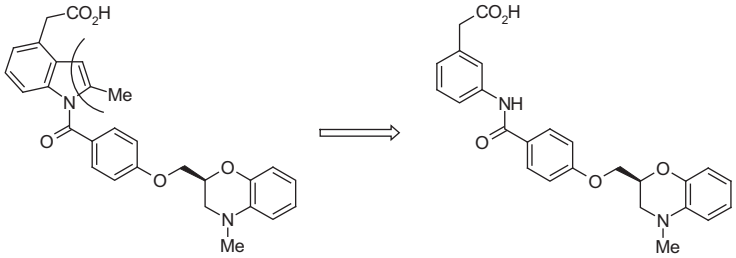




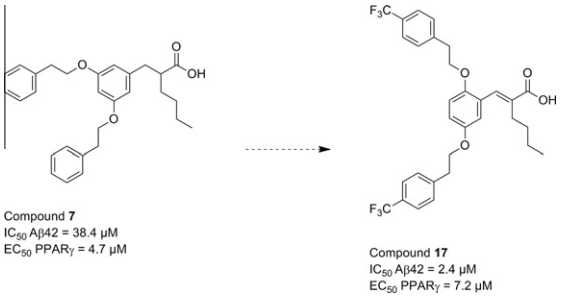




A series of Matijing-Su (MTS, *N*-(*N*-benzoyl-L-phenylalanyl)-*O*-acetyl-L-phenylalanol) derivatives were synthesized and evaluated for their anti-hepatitis B virus (HBV) activity in 2.2.15 cells.

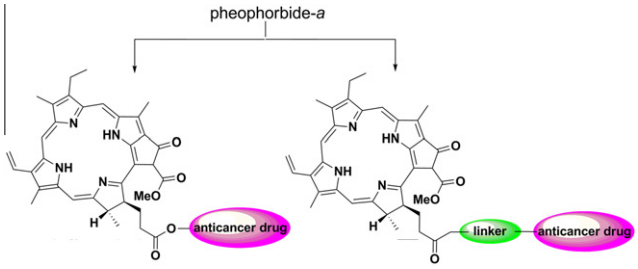



3-Benzoylaminophenylacetic acid **2a** was discovered as a new chemical lead for development of selective PGD2 receptor antagonists.

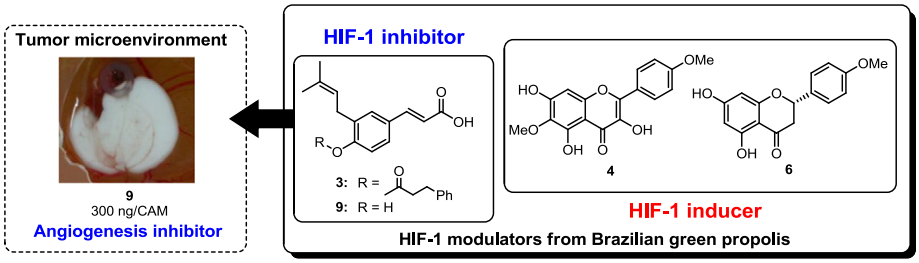


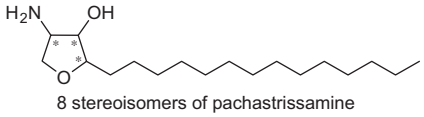




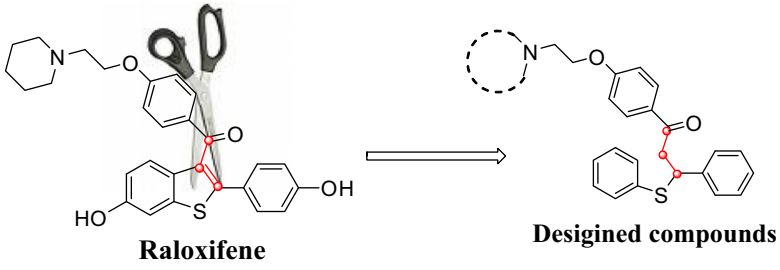





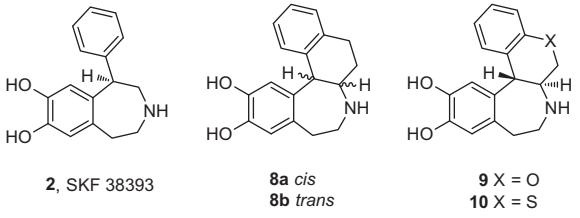





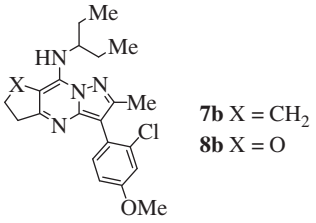


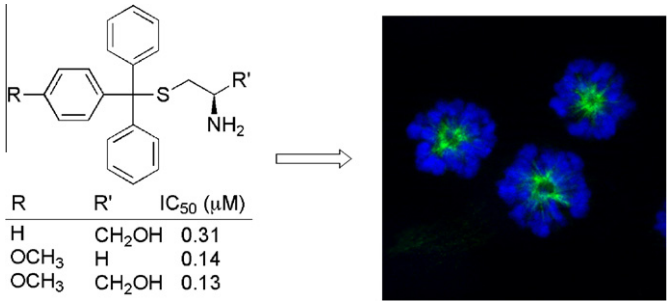





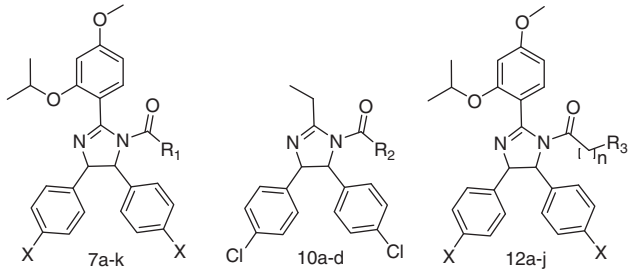




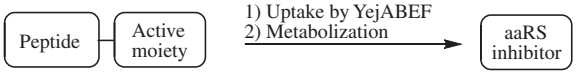

| R | R' | $IC_{50}$ (μM) |
|---|---|---|
| H | $CH_2OH$ | 0.31 |
| $OCH_3$ | H | 0.14 |
| $OCH_3$ | $CH_2OH$ | 0.13 |



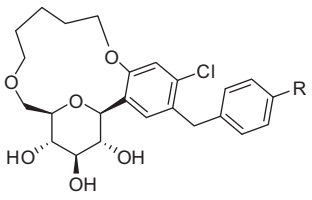



Three series of novel Nutlin analogs were designed, synthesized as p53–MDM2 binding inhibitors. Compound **7c** showed a promising inhibitory activity and induced cell cycle arrest in A549 cells.



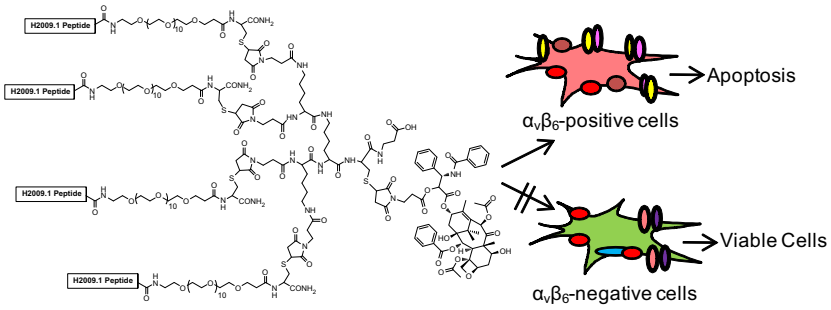




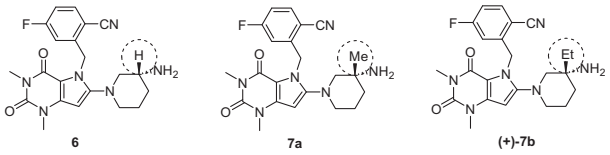




**33: R = OEt, $IC_{50}$ (hSGLT2) = 0.889 nM**
**42: R = Et, $IC_{50}$ (hSGLT2) = 0.778 nM**

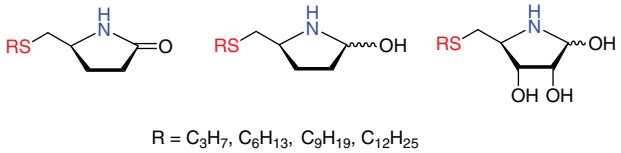
Novel macrocyclic *C*-aryl glucoside SGLT2 inhibitors were designed and synthesized. Two different synthetic routes of macrocyclization were adopted to prepare novel macrocyclic SGLT2 inhibitors. Among the compounds tested, [1,7]dioxacyclopentadecine macrocycles possessing ethylphenyl at the distal ring **42** or ethoxyphenyl at the distal ring **33** showed the best in vitro inhibitory activity in this series to date (**42**, $IC_{50}$ = 0.778 nM and **33**, $IC_{50}$ = 0.899 nM) against *h*SGLT2.





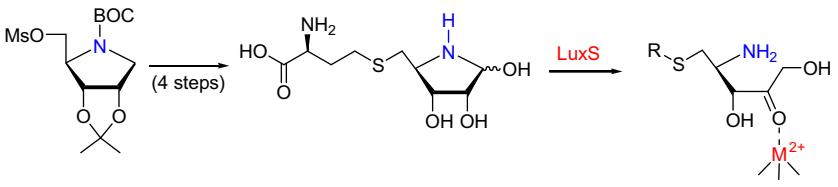


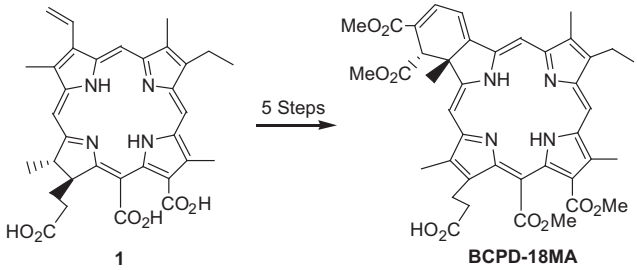

R = $C_3H_7$, $C_6H_{13}$, $C_9H_{19}$, $C_{12}H_{25}$

The cyclic azahemiacetals with propylthio or hexylthio substituent strongly inhibit both *las* and *rhl* signaling at higher concentrations while the propylthio analogue stimulates the *las* QS system at lower concentrations.



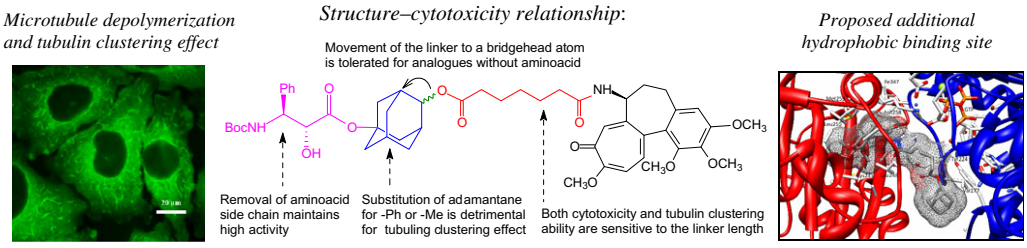



The [4-aza] *S*-ribosylhomocysteine analogue exhibited time-dependent inhibition of LuxS consistent with the enzyme-catalyzed ring opening and generation of 2- and/or 3-ketone intermediates.

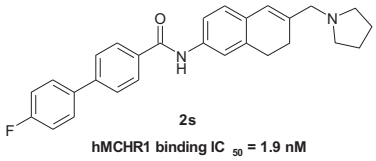



We describe the synthesis and biological properties of a novel chlorin photosensitizer benzochloroporphyrin monoacid derivative BCPD-18MA which is promising candidate for applications in PDT.

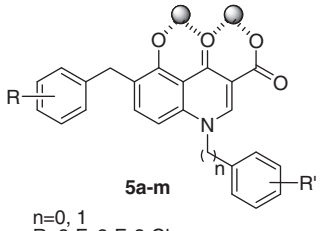




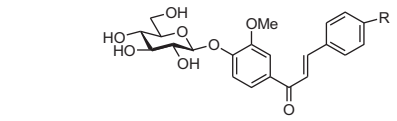




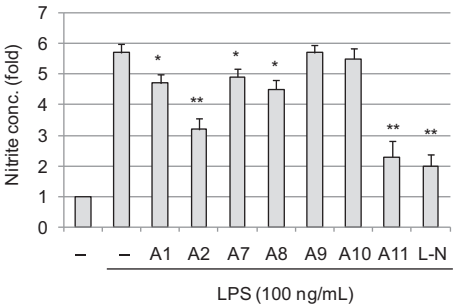




A series of new 5-hydroxylquinolone-3-carboxylic acids (HQCAs) with various aryl or benzyl substituents on N-1 position were synthesized with the aim of contributing to a better understanding of the structure–activity relationships of HQCAs.

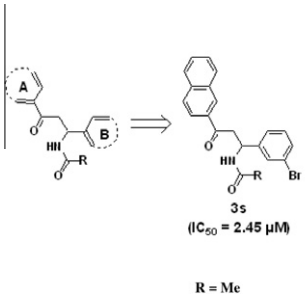


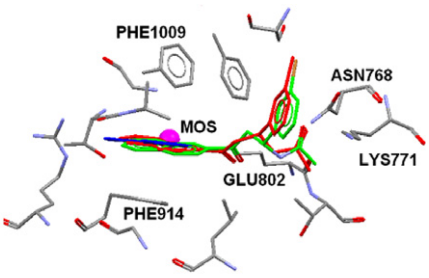

R=OMe; 4'-*O*-β-D-Glucopyranosyl-3',4-dimethoxychalcone **(A2)**

R=H; 4'-*O*-β-D-Glucopyranosyl-3'-methoxychalcone **(A11)**

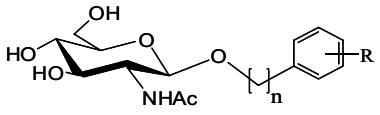




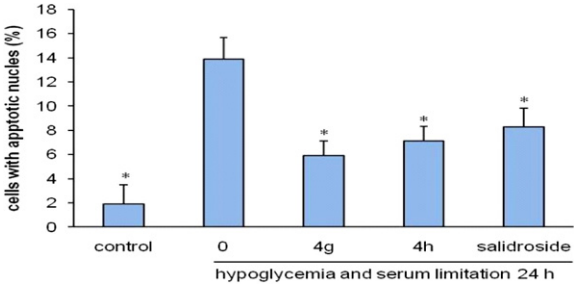





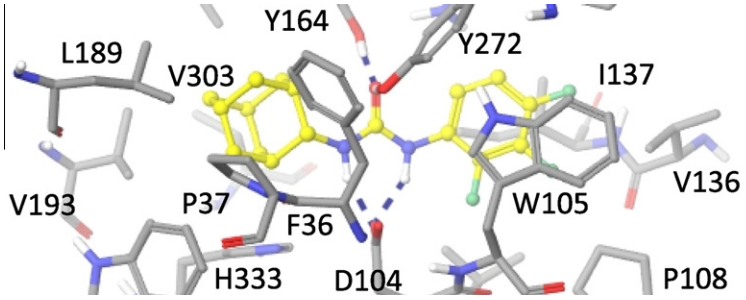



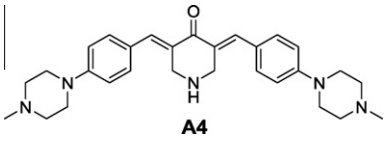

**4g**: R = 4-OMe, n = 2; **4h**: R = 4-OMe, n = 3




Most compounds showed strong neuroprotective effects, especially for **4g** and **4h**, which attenuated cell viability loss and apoptotic cell death in cultured PC12 cells.



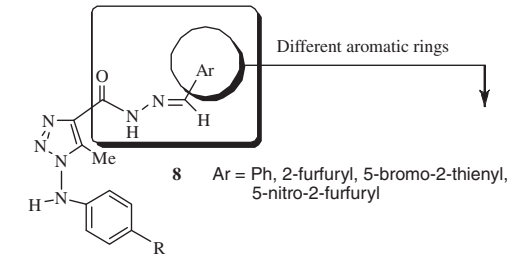




**A4**

A series of novel curcumin analogues were designed, synthesized, and biologically evaluated as multifunctional agents targeting β-amyloid, oxidative stress, and redox-active metal ions. Compound **A4** was found to have the most potent Aβ aggregation inhibitory activity (IC50 = 2.5 μM).

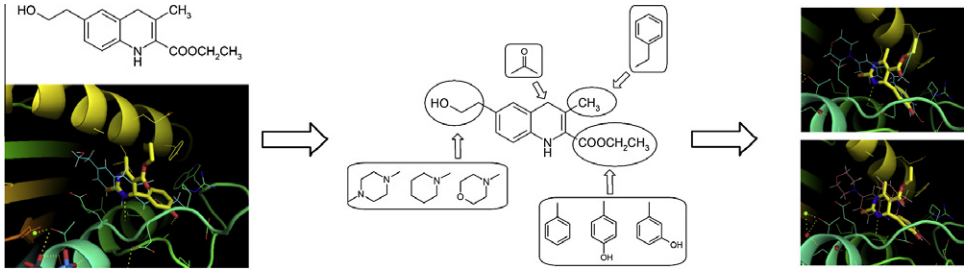




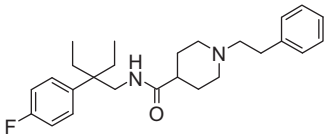

**8** Ar = Ph, 2-furfuryl, 5-bromo-2-thienyl, 5-nitro-2-furfuryl

R = H, Cl, Br and F



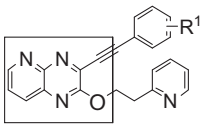




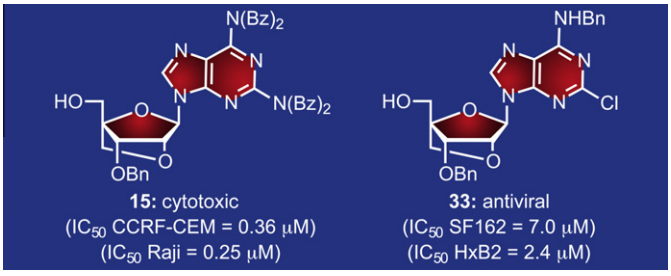
**20d**

1-Alkyl-*N*-[2-ethyl-2-(4-fluorophenyl)butyl]piperidine-4-carboxamide derivatives were synthesized and evaluated for their T-type $Ca^{2+}$ channel inhibitory activity.

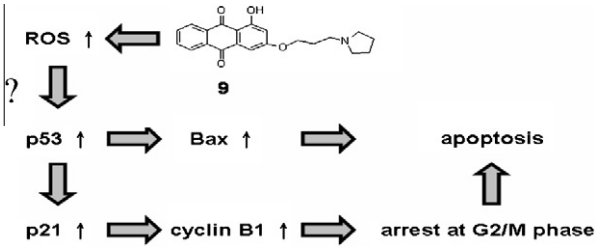



One hundred pyrido[2,3,-*b*]pyrazine derivatives were synthesized that were able to inhibit the Wnt/β-catenin signal pathway and a novel lead compound **954** (<0.2 μM) was identified by cell proliferation screening.



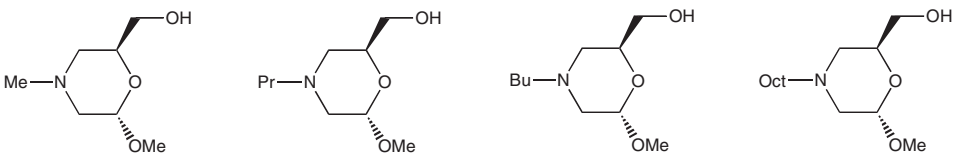




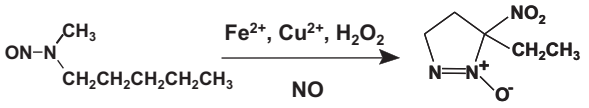

Thirteen anthraquinone derivatives **5**-**17** including two 3-(3-alkylaminopropoxy)-9,10-anthraquinone derivatives **5** and **6** and eleven 1-hydroxy-3-(3-alkylaminopropoxy)-9,10-anthraquinone derivatives **7**-**17** were synthesized. Compound **9** induced up-regulation of cyclin B1and p21 expressions. Biological results suggested that the induction of G2/M arrest, apoptosis, and cell death by **9** may associate with increased expression of p21 and cyclinB1, elevation of Bax and p53 levels, and generation of ROS in the cell.






$IC_{50}$ = 88.6 μM $IC_{50}$ =75.5 μM $IC_{50}$ = 70.3 μM $IC_{50}$ = 55.1 μM

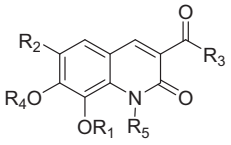
In this work libraries of morpholines and oxazepanes have been prepared via the reductive amination reaction between dialdehydes, derived from carbohydrates, and a range of amines. The inhibitory profiles of these targets against a range of glycosidase enzymes have been assessed. Good inhibition of the β-D-galactosidase enzyme derived from Bovine kidney was obtained for a range of the morpholine targets.




*N*-Nitroso-*N*-methylpentylamine

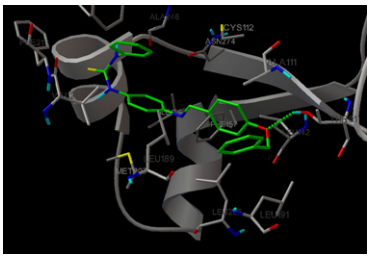
5-Ethyl-5-nitro-pyrazoline *N*-oxide





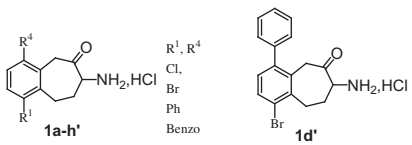

A series of fluorinated 2-oxo-quinoline derivatives were synthesized and their in vitro assay was performed against [$^3$H]CP-55,940, using the human cancer cell line U87, genetically engineered to express human CB2 or CB1 receptors. Of all the synthesized compounds, six compounds displayed inhibition constant ($K_i$) value at the level of nanomolar and sub-nanomolar concentrations. Preliminary in vitro results suggest that these six compounds may be useful for therapeutic application to neuropathic pain, neuroinflammatory diseases and immune disorders.



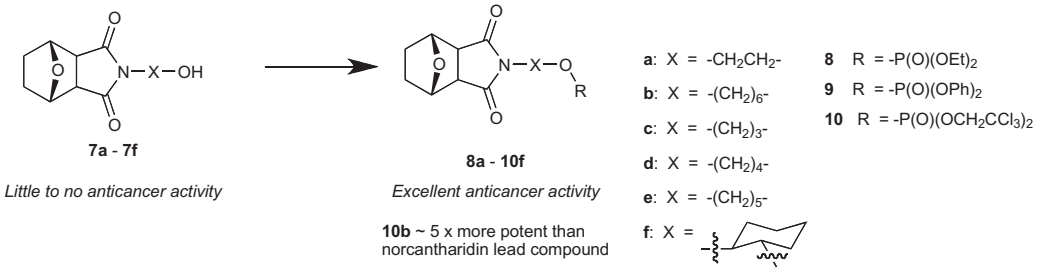


A series of novel Schiff base derivatives have been designed and synthesized, and their biological activities were also evaluated as potential inhibitors of FabH. These compounds were assayed for antibacterial activity against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Staphylococcus aureus*. Compounds with potent antibacterial activities were tested for their *E. coli* FabH inhibitory activity. Compound **3v** showed the most potent antibacterial activity with MIC of 1.56–6.25 μg/mL against the tested bacterial strains and exhibited the most potent *E. coli* FabH inhibitory activity with $IC_{50}$ of 4.3 μM. Docking simulation was performed to position compound **3v** into the *E. coli* FabH active site to determine the probable binding conformation.






Some racemic amino-benzosuberones **1a–h**′, were synthesised and evaluated as inhibitors of four representative members of zinc-dependent amino-peptidases. $K_i$ values in the nanomolar to picomolar range were obtained selectively against the 'one zinc' aminopeptidase AP-N/CD13. The bromo-phenyl derivative **1d**′ belongs to the most potent and selective non-peptidic known inhibitor ($K_i$ = 60 pM).






*Corresponding author
Supplementary data available via SciVerse 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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