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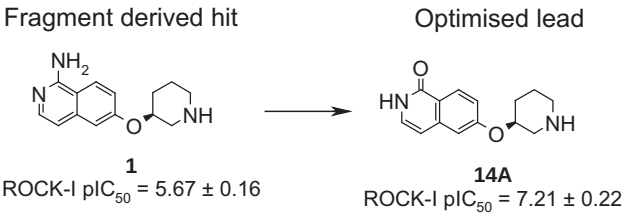
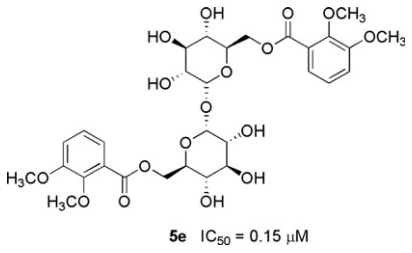
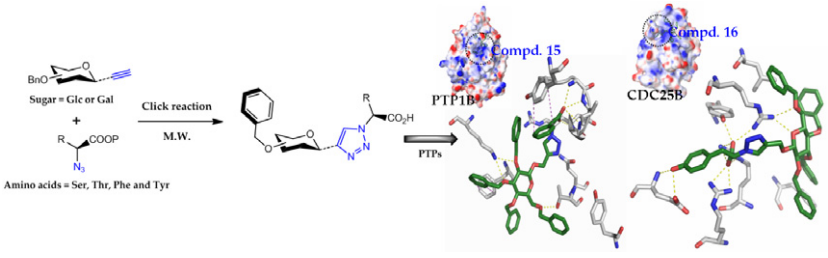
Contents

BMCL DIGEST

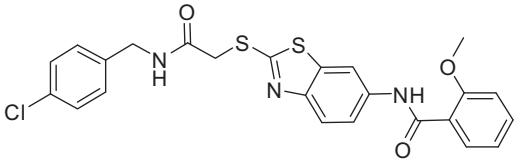


REGULAR ARTICLES



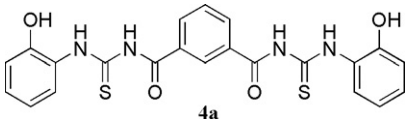


We report the 'click' fabrication of triazolyl glycopeptidomimetics as novel PTP1B and CDC25B inhibitors and their plausible binding modes with the targeted PTP via docking simulation.



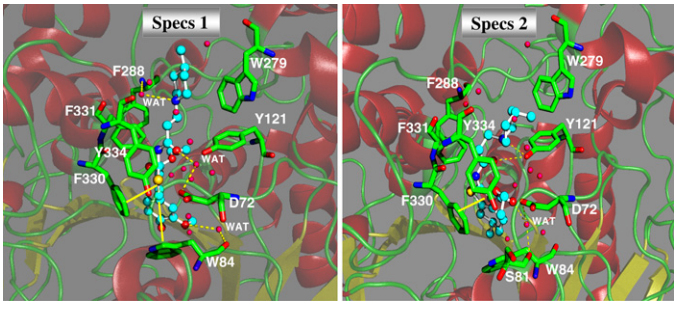
6m

A series of novel benzothiazole-2-thiol derivatives were synthesized and evaluated for antitumor. The most potent compound **6m** exhibited good inhibitory activities against a panel of different types of human cancer cell lines with IC_{50} values in the low micromolar range and induced apoptosis in HepG2 cancer cells.

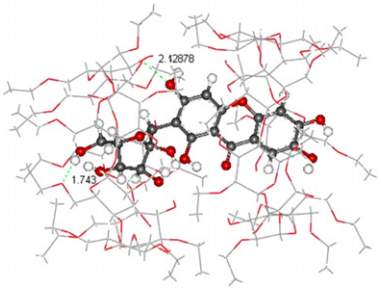


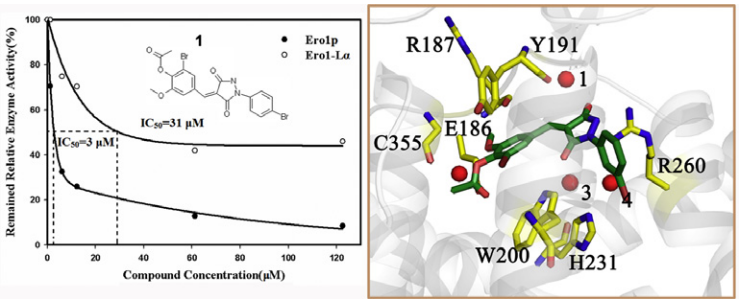
4a

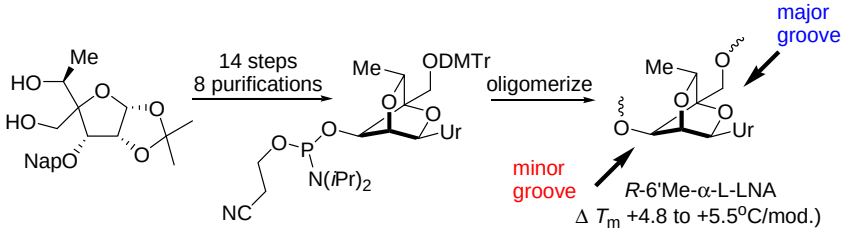
Dual binding site acetylcholinesterase (AChE) inhibitors are promising for the treatment of Alzheimer's disease (AD). Inhibitors showing both the anti-aggregating Aβ and anti-cholinesterase effect bind to these sub-sites, the so called dual binding site in AChE enzyme. We adopted a strategy, by systematically integrating the in vitro and in silico techniques throughout the present work, to discover new cholinesterase inhibitors **Specs1** and **Specs2,** having good ADMET properties for the treatment of AD.

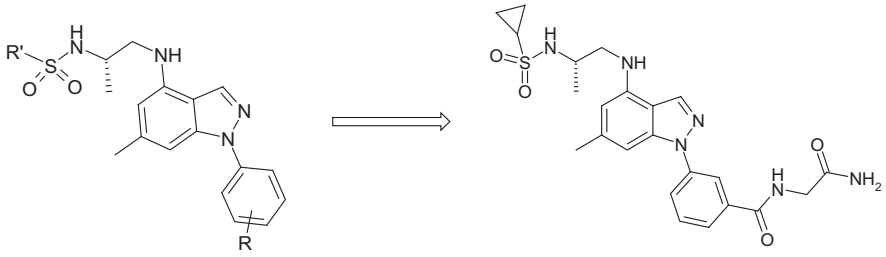


To elucidate a plausible complex structure for the supramolecular complex, we performed the molecular modelling study. The inclusion complex was emulated by entering the guest molecule from the large face of the CD cavity of the DE-β-CD molecule by steps. Subsequently, the energy minimization was carried out for each step without any constraint. Full-geometry optimization was performed, using the molecular mechanics MM+ method followed by the semiempirical AM1 method to obtain the minimum structure.

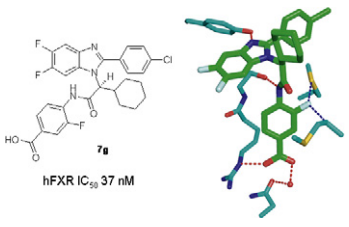


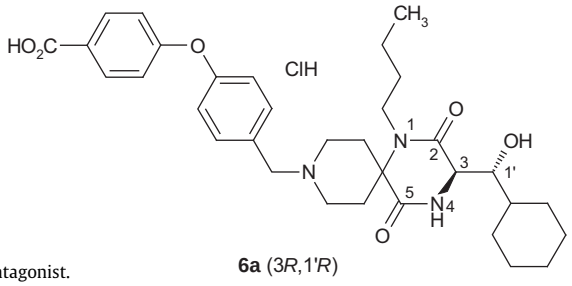






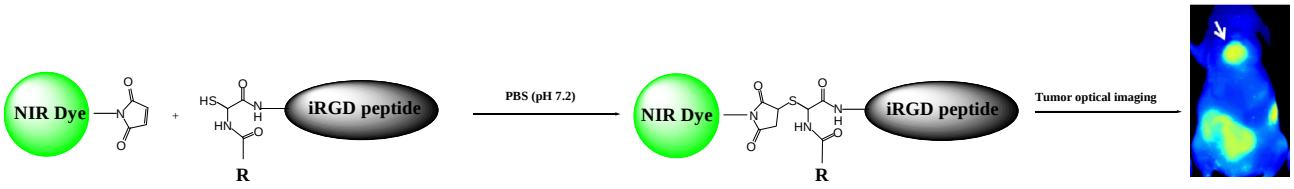
20a

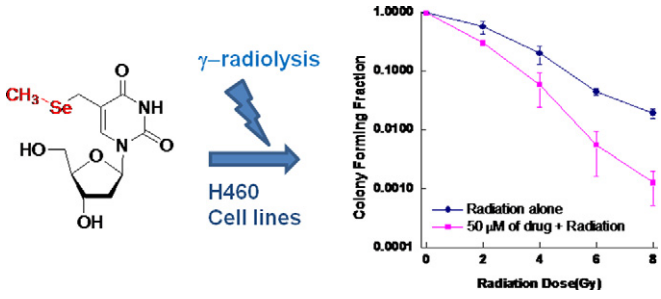


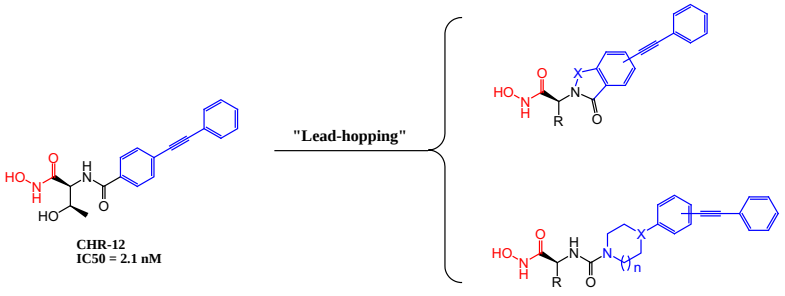


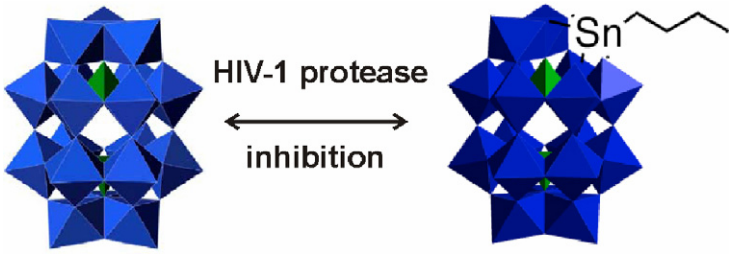
6a (3*R*,1'*R*)

Molecular design of a new orally-available CCR5 antagonist.

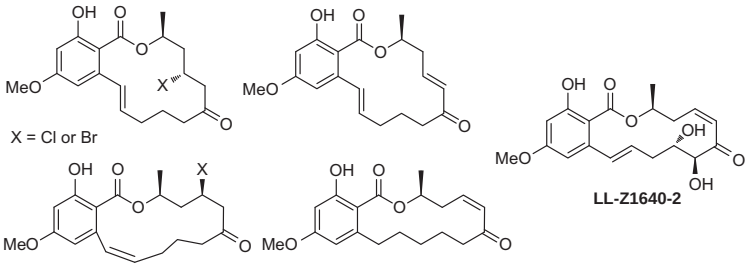


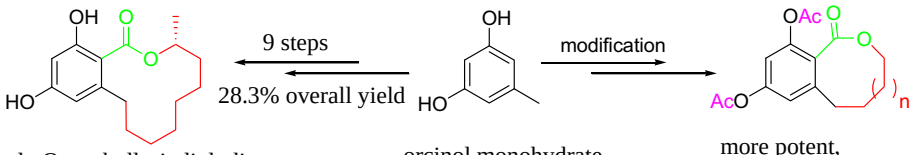






The inhibitory effect of functionalized polyoxotungstates with organic side chains on HIV-1 protease is investigated.

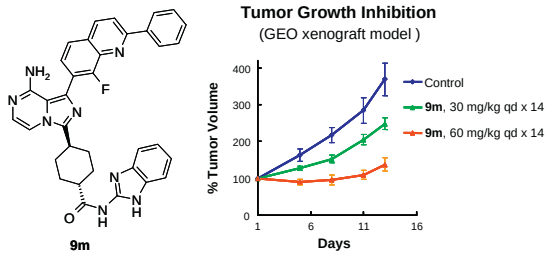


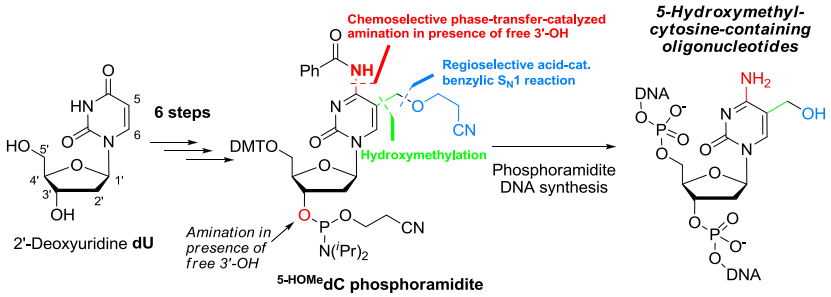


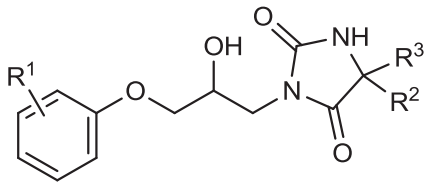
(*R*)-de-O-methyllasiodiplodin
Mineralocorticoid receptor(MR) antagonist
IC_{50} = 8.93 μM

orcinol monohydrate

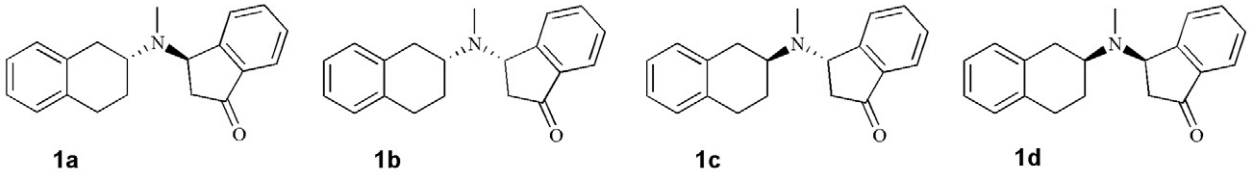
more potent,
18a n=4 IC_{50} = 0.58 μM
18b n=5 IC_{50} = 1.11 μM
18c n=6 IC_{50} = 0.825 μM
18d n=7 IC_{50} = 2.9 μM



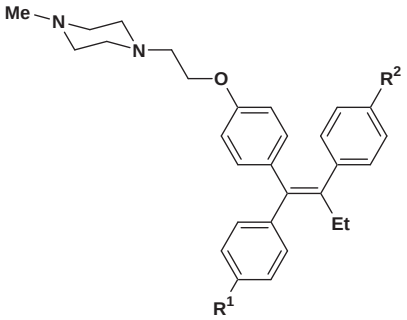




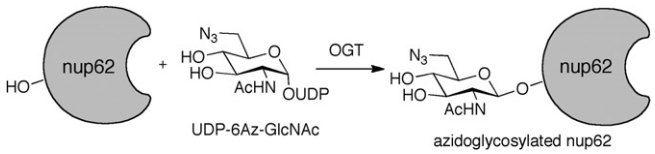
The synthesis and in vitro characterisation of a novel series of β-amino alcohol compounds based upon the hit compound identified from a screening program 3-[3′-(4″-cyclopent-2‴-en-1‴-ylphenoxy)-2′-hydroxypropyl]-5,5-dimethylimidazolidine-2,4-dione against prokaryotic arylamine *N*-acetyltransferase enzymes are reported.

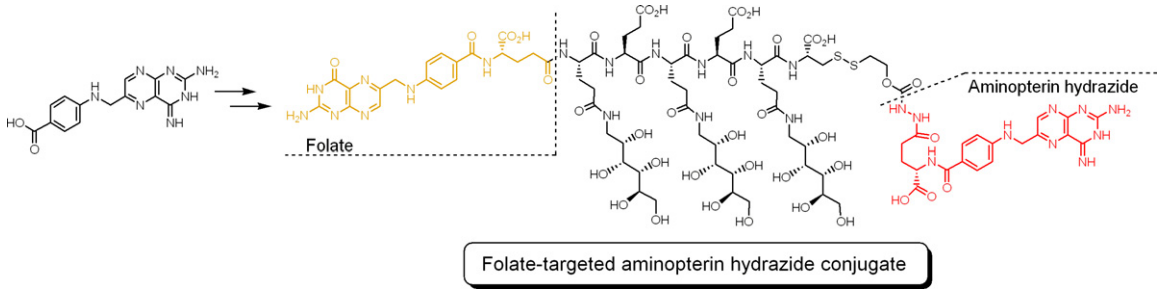


IC_{50} 1.51μM *vs.* 48/80 in RPMC
53% inhibition of anti IgE in PLMC
Most active isomer *in vivo* *vs.* PCA reaction

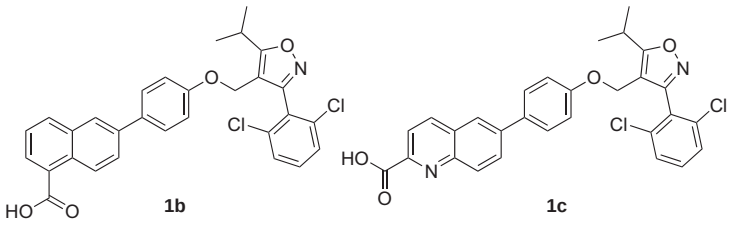


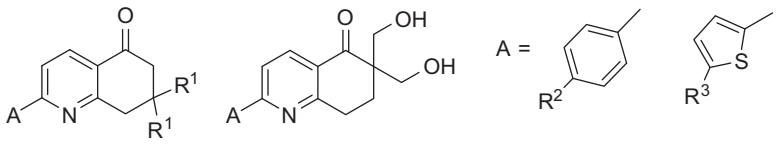
R^1 = *I, R^2 = H
R^1 = H, R^2 = *I
R^1 = H, R^2 = OCH_2CH_2*F
***Indicates position suitable for labelling with a [^{124}I] or [^{18}F] radionuclide**





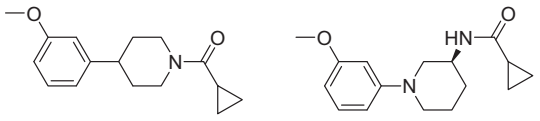
To improve on the drug properties of GSK8062 **1b**, a series of heteroaryl bicyclic naphthalene replacements were prepared. The quinoline **1c** was an equipotent FXR agonist with improved drug developability parameters relative to **1b**. In addition, GSK2324 **1c** lowered body weight gain and serum glucose in a DIO mouse model of diabetes.

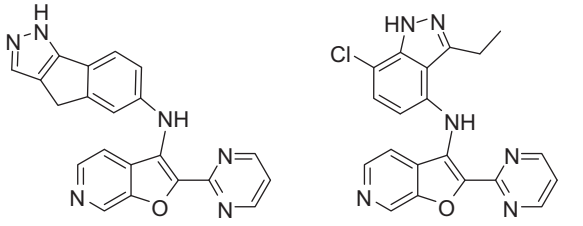


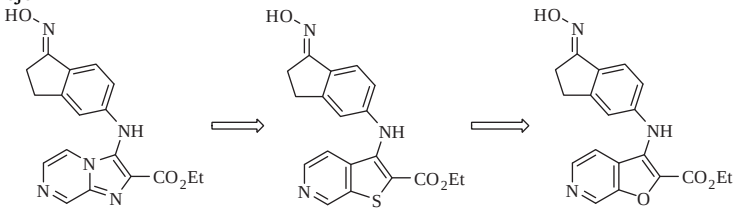


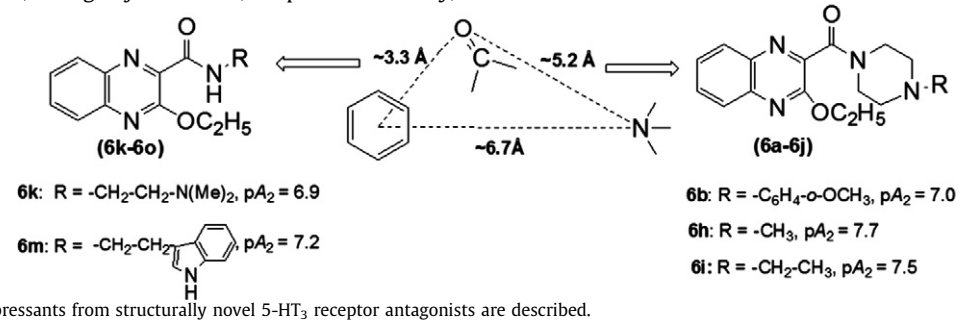
R^1= H, CH_3 R^2= H, CH_3, OCH_3 R^3= H, Cl, Br

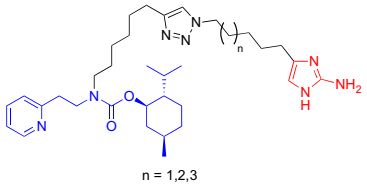
18 examples; **4e**: R^1= CH_3, R^3=Cl and **4f**: R^1= CH_3, R^3=Br (MIC= 3.13 μg/mL)

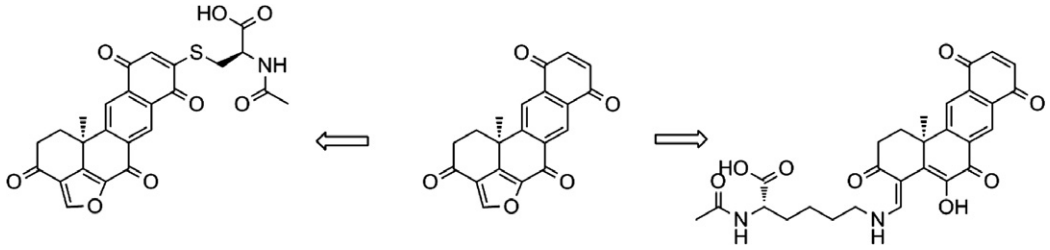


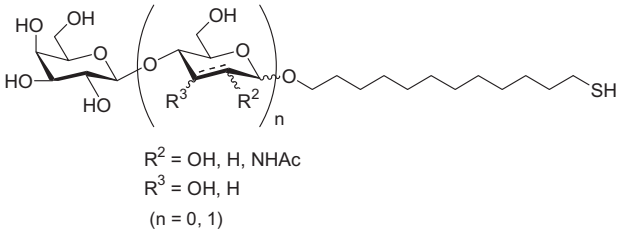




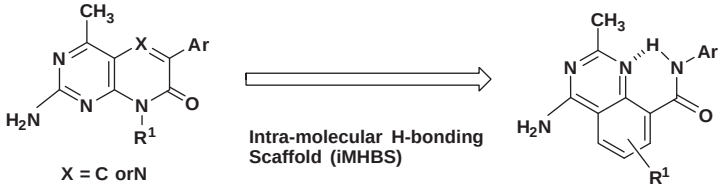




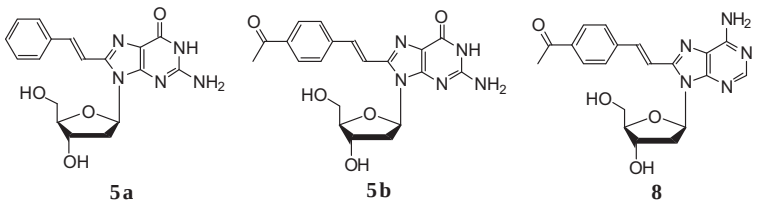




Synthesis of 12-mercaptododecyl β-galactoside-terminated glycosides and their galectin-binding activities evaluated by SPR measurements are described.

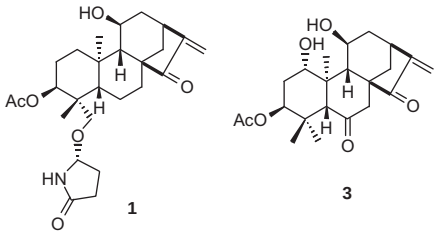


Intra-molecular hydrogen bonding was introduced to the quinazoline motif to form a pseudo ring (intra-molecular H-bond scaffold, iMHBS) to mimic our previous published core structures, pyrido[2.3-*D*]pyrimidin-7-one and pteridinone, as PI3K/mTOR dual inhibitors. This design results in potent PI3K/mTOR dual inhibitors and the purposed intra-molecular hydrogen bonding structure is well supported by co-crystal structure in PI3Kγ enzyme. In addition, a novel synthetic route was developed for these analogs.



Chemical structures of aromatic fluorophore substituted purine nucleosides.

A new pyrrolidinone diterpenoid, excisusin F (**1**), was isolated from the aerial parts of *Isodon excisus* (Lamiaceae), together with four known compounds, and their structures were determined mainly by NMR (1D and 2D) and mass spectrometry. Excisusin F (**1**) and inflexarabdonin E (**3**) showed potent inhibitory effects of LPS-induced nitric oxide production in RAW264.7 cells with the IC_{50} value of 10.4 and 3.8 μM, respectively.



OTHER CONTENT

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Botulinum neurotoxins are the most deadly toxins known to man, approximately 10 million times more deadly than cyanide. Botulinum neurotoxins are classified by the US Centers for Disease Control (CDC) as bioterrorism agents. The etiological agent responsible for botulinum intoxication is a metalloprotease; as such this is a key therapeutic target. Currently, there are no approved pharmacological treatments for botulinum intoxication. Discovering molecules that could be used as a path forward for therapeutic development as botulinum protease inhibitors is tantamount. A benzylidene cyclopentenedione-based inhibitor was found to be the first affinity reagent to covalently modify the active site of botulinum neurotoxin A light chain metalloprotease. Its kinetic parameters are reported and such an approach for inhibition of this deadly neurotoxin. [Capková, K.; Hixon, M. S.; Pellett, S.; Barbieri, J. T.; Johnson, E. A.; Janda, K. D. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 206.]

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