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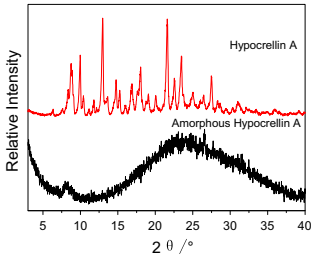
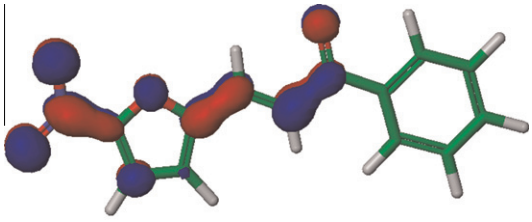
Contents

ARTICLES

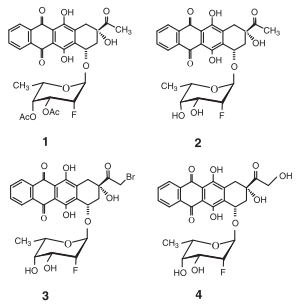


We have synthesized and characterized a water-soluble hypocrellin A (HA) by making its amorphous formulation (AM-HA) with excellent water-solubility and photosensitizing properties. In vitro, AM-HA retains high light-toxicity and reduces dark-toxicity simultaneously compared to traditional delivery vehicles [Tween-80 micelle embedded hypocrellin A (TW-HA)]. These properties of AM-HA could make it a promising candidate to be used in photodynamic therapy.

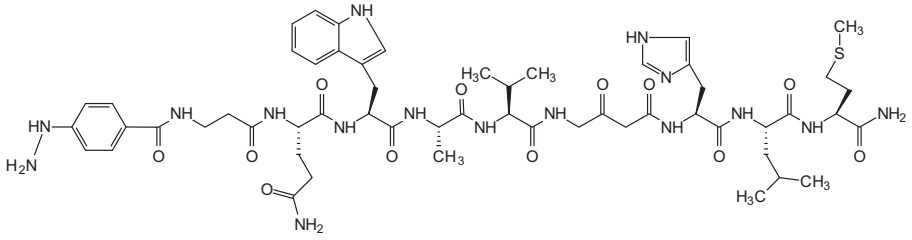


LUMO map for one of the synthesized compound

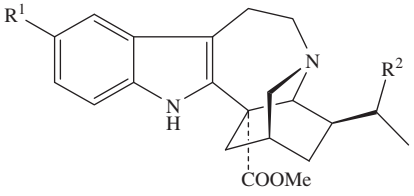
Based on stereoelectronic feature analysis using density functional theory (DFT) at B3LYP/3-21*G level, a series 4-(5-nitrofuran-2-yl)prop-2-en-1-one derivatives were envisaged as potential antitubercular agents. As expected, synthesis and biological evaluation showed that target compounds were potent inhibitors of *Mycobacterium tuberculosis*. Thus, this study shows the potential of stereoelectronic property analysis in developing improved nitroaromatics as antitubercular agents.



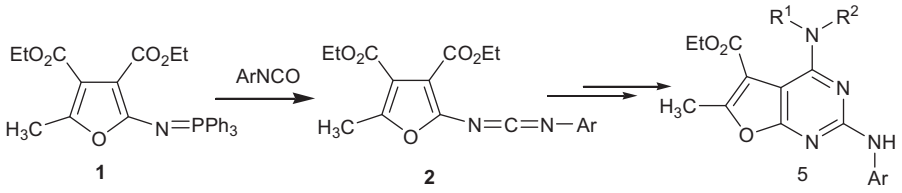
Four 4-demethoxy-3′-deamino-2′-fluoro-3′-hydroxy anthracycline analogs (**1**–**4**) were compared with adriamycin (doxorubicin) for their growth-inhibitory effects against five human-tumor cell lines.



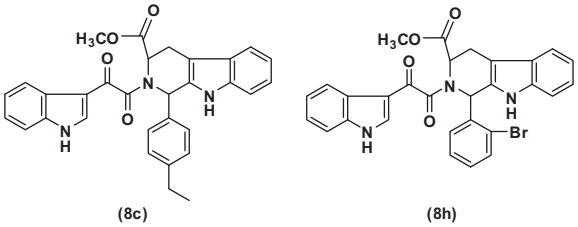
Preparation of technetium-labeled bombesin derivative for tumor identification.



Eight indole alkaloids were isolated from the stems of *Ervatamia hainanensis*, in which compounds **1** and **3** exhibited the same level of activities as galantamine, a marketed cholinesterase inhibitor for the treatment of Alzheimer's disease.



Synthesis and biological evaluation of indolyl glyoxylamides as a new class of antileishmanial agents **pp 6191–6194**
Shikha S. Chauhan, Leena Gupta, Monika Mittal, Preeti Vishwakarma, Suman Gupta, Prem M. S. Chauhan*



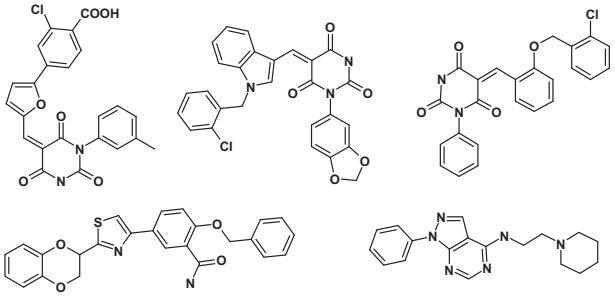
(8c)

Antiamastigote activity:
IC_{50} = 5.17 μM,
Selectivity index = 31.48.

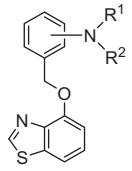
(8h)

Antiamastigote activity:
IC_{50} =3.79 μM,
Selectivity index = 7.94.

A series of indolylglyoxylamide derivatives have been synthesized and screened for their in vitro antileishmanial activity against *Leishmania donovani*.

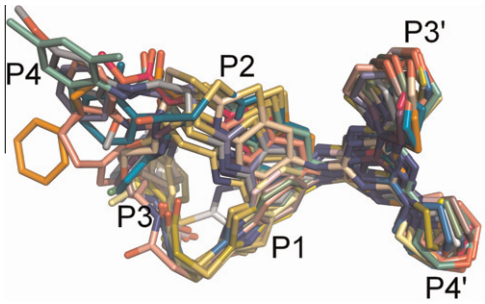


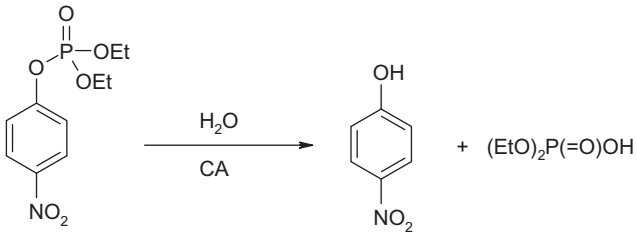
We have discovered five novel inhibitors of TNF-α based on the structure-based virtual screening and in vitro cell-based immunoassay.

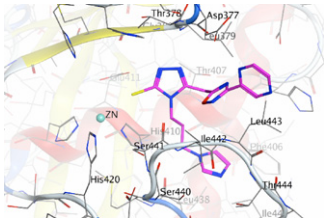


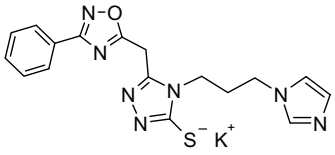
Synthesis of series of benzothiazole derivatives and their inhibitory activities on the NO production in lipopolysaccharide-activated macrophages are reported.

Twenty-two compounds derived from compound **1** were studied via in silico and in vitro approaches against BACE-1. Compound **5** bearing pyrrolidinyls at 4- and 6-positions on triazine and a P4 phenyl acetamide group showed IC_{50} of 0.12 μM.

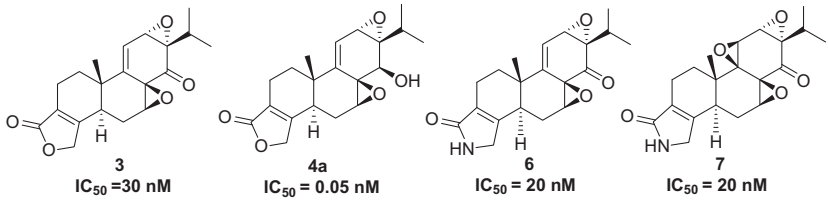




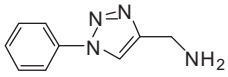




IC_{50} ADAMTS-5 = 6 μM



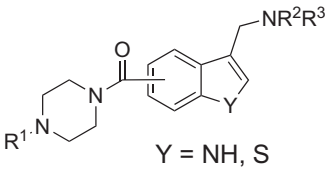
3 IC_{50} =30 nM
4a IC_{50} = 0.05 nM
6 IC_{50} = 20 nM
7 IC_{50} = 20 nM



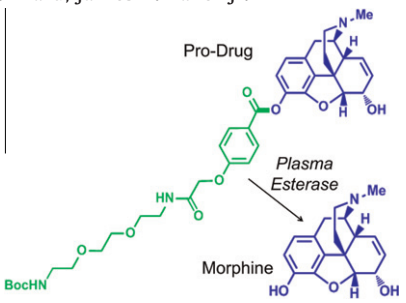
a9

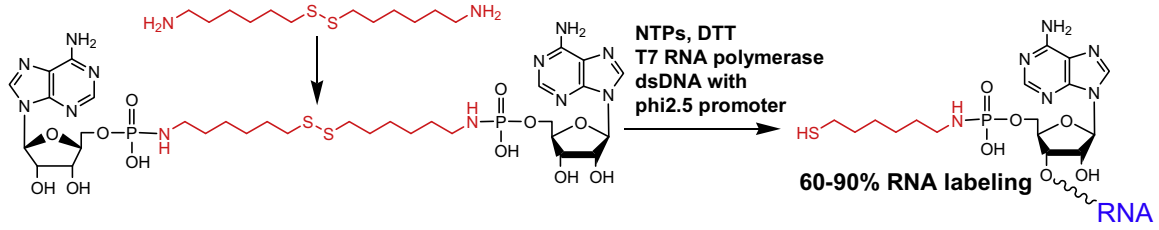
MAO-A: IC_{50} = 0.97 uM
SI = 526.33

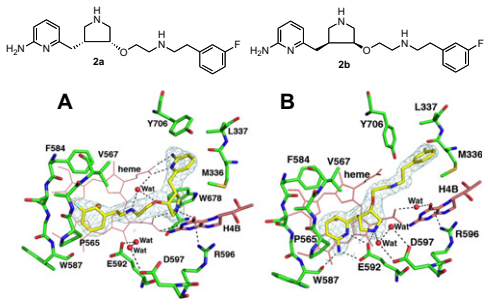
An efficient strategy for the fast construction of 108 compounds library was developed using click chemistry. The fingerprint of inhibitory activity toward MAO-A/B against this library was obtained, and four hit compounds were identified as selective inhibitors toward MAO-A. Docking study was carried out to demonstrate the binding mode between **a9** and MAO-A/B, and the result reveals that **a9** localized in the 'aromatic cage' and oriented to establish π–π stacking interactions with Tyr407, Tyr444 and FAD in MAO-A rather than in MAO-B.

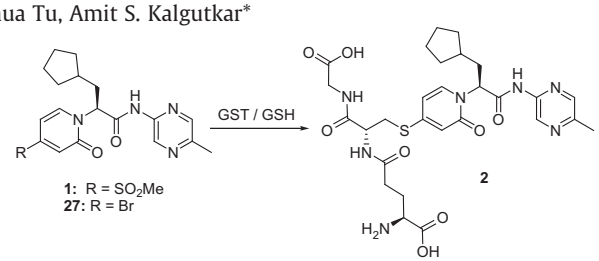


Y = NH, S

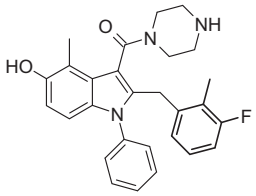




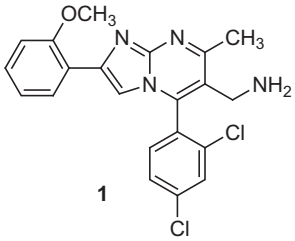




The role of glutathione-*S*-transferase in the nucleophilic displacement reaction on 4-substituted-2-pyridone derivatives by glutathione (GSH) was examined. The principal in vivo clearance mechanism of **1** in rats involved GSH conjugation leading to the formation of **2**.

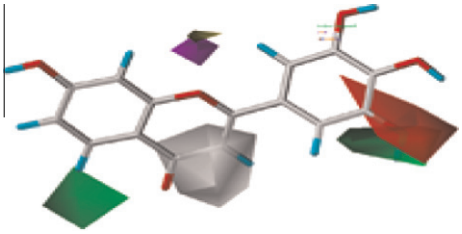


Renin-Inhibitor (IC_{50} = 0.002 μM)

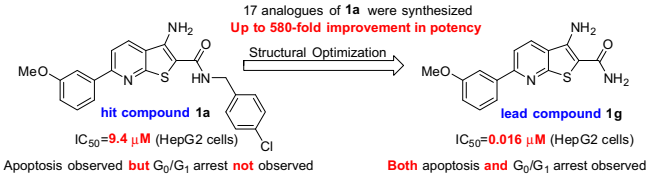


1

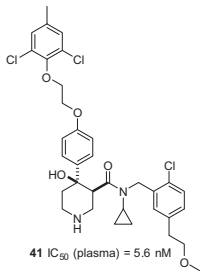
The synthesis and SAR of aminomethyl-substituted imidazolopyrimidine DPP4 inhibitors bearing varied pendant aryl groups is described. Compound **1**, which exists as a separable mixture of non-interconvertible atropisomers was used as the starting point for investigation. The effects of substituent pattern and type as well as stereochemical effects on inhibitor potency are discussed.



Isoflavones are known to have anti-inflammatory and anti-tumor activities, due, in part, to inhibition of NF-κB activity. However, the structural moiety of isoflavones responsible for the inhibition of NF-κB is not clearly understood. In this work, structure–activity relationships of isoflavone derivatives were examined with regard to NF-κB inhibition, using CoMFA and CoMSIA.



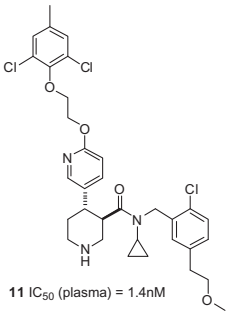
Among 17 analogs of **1a**, the most potent analog **1g** possesses hepatocellular carcinoma (HCC)-specific anticancer activity. It was inactive toward a panel of five different types of human cancer cell lines.



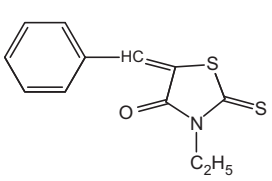
41 IC_{50} (plasma) = 5.6 nM

A novel series of piperidine-based renin inhibitors with improved efficacy in a double transgenic rat model is reported. Piperidines such as **41** (IC_{50} in plasma = 5.6 nM) showed high efficacy on blood pressure reduction (−36 mmHg) at low dose (3 mg/kg).

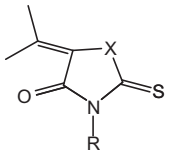
The optimization of the 4-position of 3,4-disubstituted piperidine-based renin inhibitors is reported herein. This work culminated in the discovery of **11**, a renin inhibitor with a suitable profile for development.



11 IC_{50} (plasma) = 1.4nM

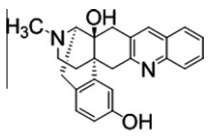


BTR-1



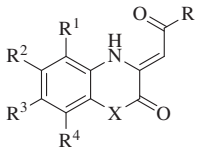
ITO-1; R = C_2H_5, X = O
ITR-1; R = C_2H_5, X = S
ITH-1; R = CH_3, X = CH_3

We have designed and synthesized three novel compounds, 5-isopropylidiene derivatives of 3-dimethyl-2-thiohydantoin (ITH-1), 3-ethyl-2-thio-2,4-oxazolidinedione (ITO-1), and 5-benzilidene-3-ethyl rhodanine (BTR-1), and have tested their chemotherapeutic properties using different assays. We find that among the three compounds, BTR-1 is most potent.

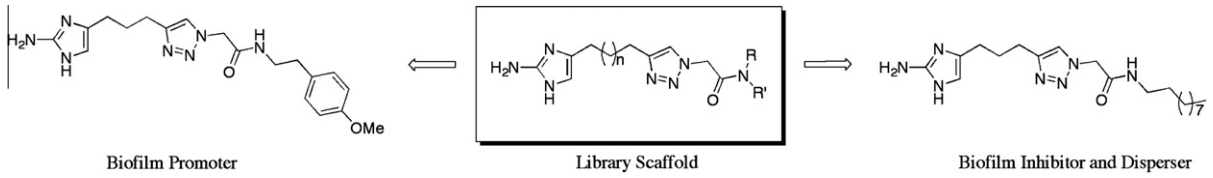


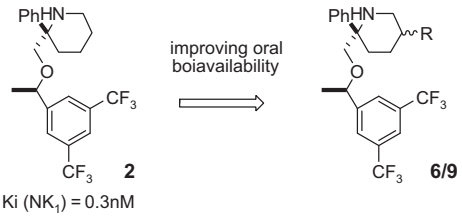
KNT-127

We designed novel δ-agonists, effective in systemic administration. One of the agonists, KNT-127, is expected to be a useful tool to clarify the real pharmacological effects mediated via the δ-receptor including analgesia and addiction.

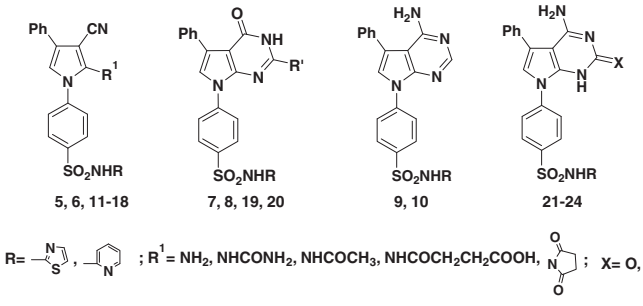


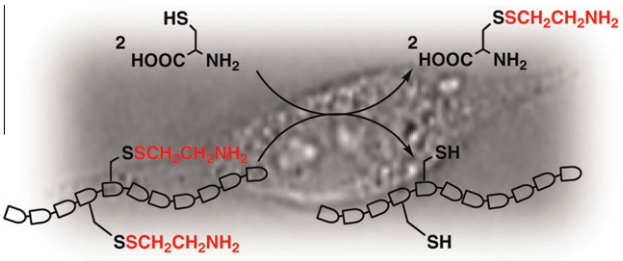
Several 1,4-benzoxazines were identified in a HTS directed at MenB, the 1,4-dihydroxy-2-naphthoyl-CoA synthase in the *Mycobacterium tuberculosis* menaquinone biosynthesis pathway. Subsequent SAR studies resulted in the discovery of compounds with MIC values as low as 0.6 μg/ml against H37Rv.

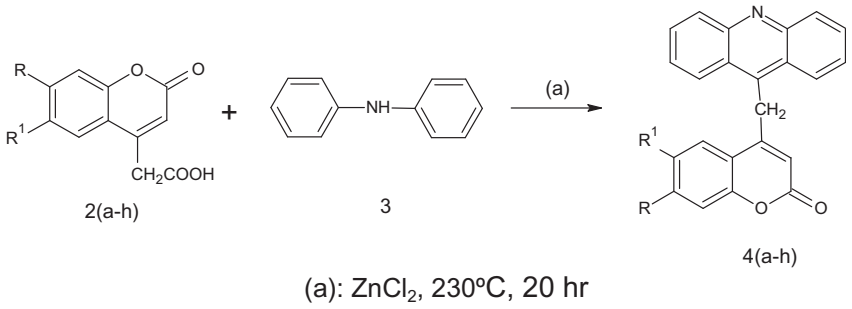


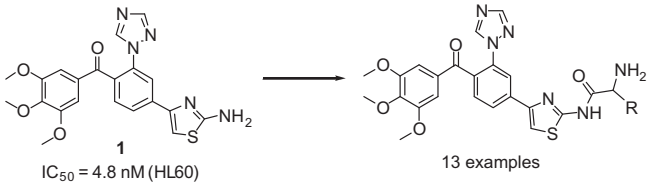


Modification of prototype NK_1 antagonist **2** resulted in the synthesis of a series of simple amides **6** and retroamides **9**. These compounds were shown to be potent and orally active NK_1 antagonists.









Synthesis and evaluation of various amino acid prodrugs of **1** led to the discovery of **3·HCl** (R = (*S*)-isopropyl) which was shown to have potent antitumor efficacy in mouse xenografts. Pharmacokinetic study in rats was also described.

*Corresponding author
Supplementary data available via ScienceDirect

COVER

Overlay of high resolution co-crystal structures of *R*-**22**-ADP (cyan) and **1**-ADP (green) bound in an allosteric binding site of the mitotic kinesin KSP. [Roecker, A. J.; Coleman, P. J.; Mercer, S. P.; Schreier, J. D.; Buser, C. A.; Walsh, E. S.; Hamilton, K.; Lobell, R. B.; Tao, W.; Diehl, R. E.; South, V. J.; Davide, J. P.; Kohl, N. E.; Yan, Y.; Kuo, L. C.; Li, C.; Fernandez-Metzler, C.; Mahan, E. A.; Prueksaritanont, T.; Hartman, G. D. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5677.]

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