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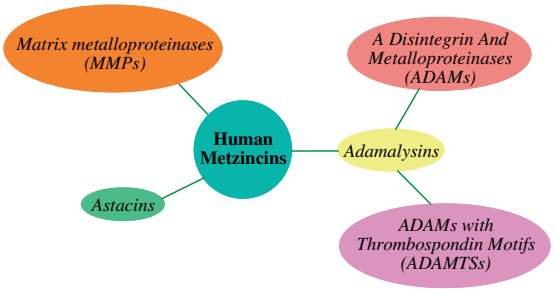
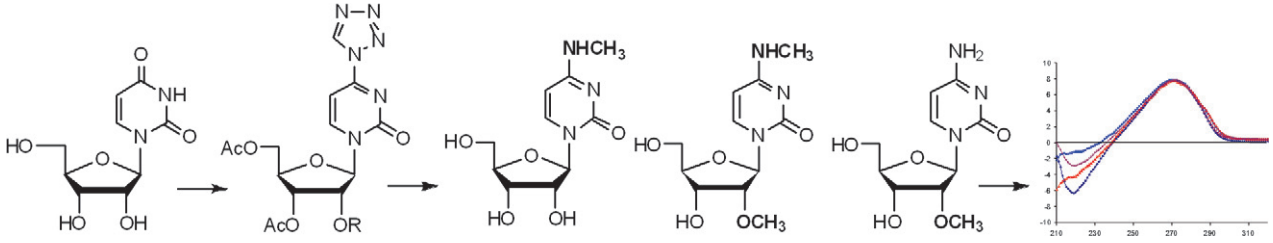
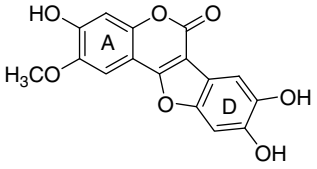
Contents

REVIEW



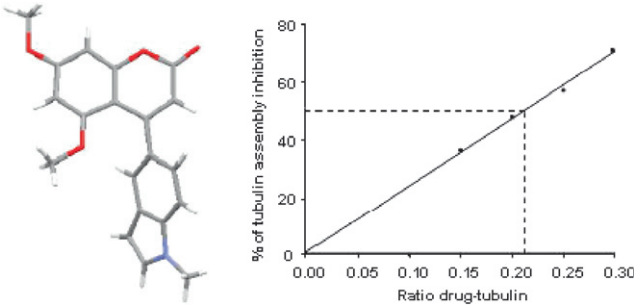
ARTICLES

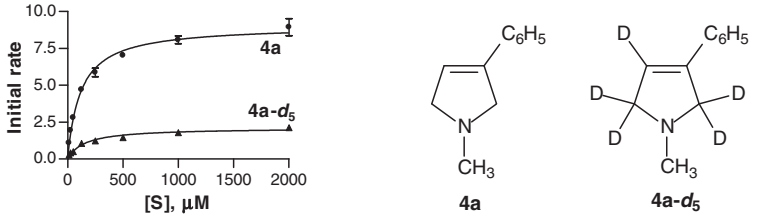


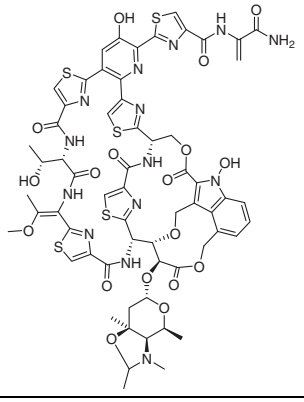


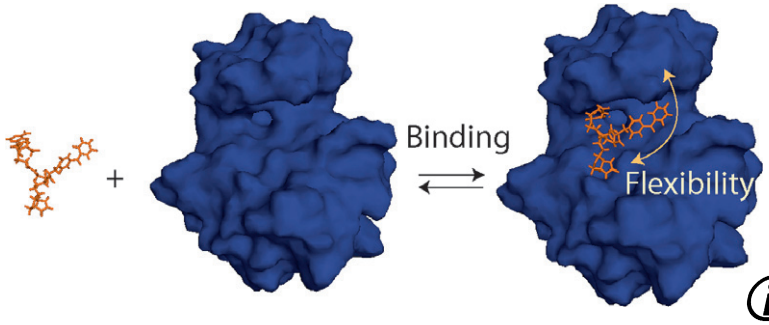
PCALC 36

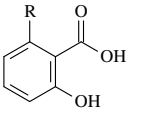
The molecular mechanism involved in Na^+,K^+-ATPase inhibition by 2-methoxy-3,8,9-trihydroxy coumestan (PCALC36) was investigated. The results suggest that this compound irreversibly oxidizes important sulfydryl groups of the enzyme, explaining its poor selectivity toward other P-type ATPases.





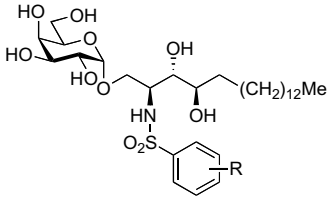




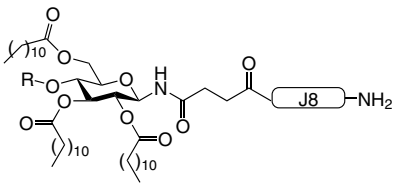


$R=C_{15}H_{31}, C_{12}H_{25}$

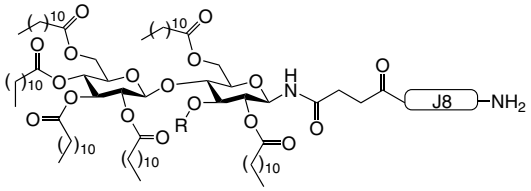
In this work, we describe the inhibitory effects of a small library of natural and synthetic anacardic acid derivatives against the enzyme glyceraldehyde-3-phosphate dehydrogenase from *Trypanosoma cruzi*. The most potent inhibitors, 6-*n*-pentadecyl- (**1**) and 6-*n*-dodecylsalicilic acids (**10e**), have IC_{50} values of 28 and 55 μM, respectively, and mechanistic studies showed noncompetitive inhibition with respect to both substrate and cofactor.



The sulfonamide analogues of KRN7000 induce NKT cells to produce Th2-biased cytokine production.

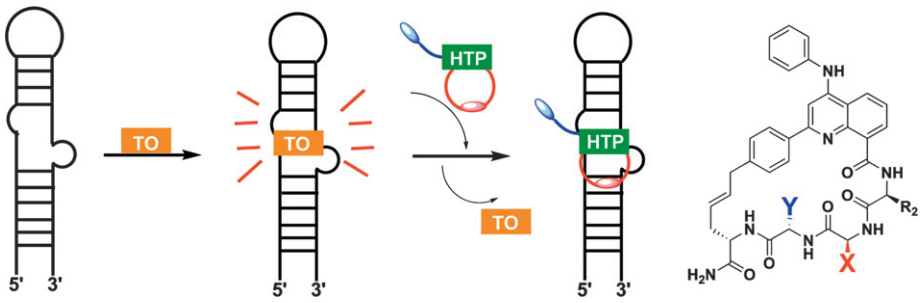


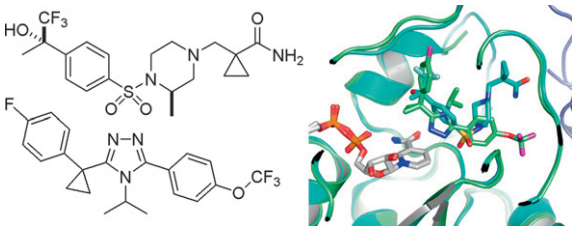
$Glc(Lau)_3$-J8 : R = H
$Glc(Lau)_4$-J8 : R = $CH_3(CH_2)_{10}CO$



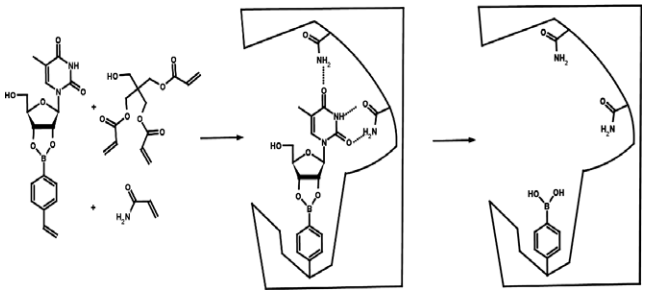
$Cel(Lau)_6$-J8 : R = H
$Cel(Lau)_7$-J8 : R = $CH_3(CH_2)_{10}CO$

J8: QAEDK VKQSR EAKKQ VEKAL KQLED KVQ

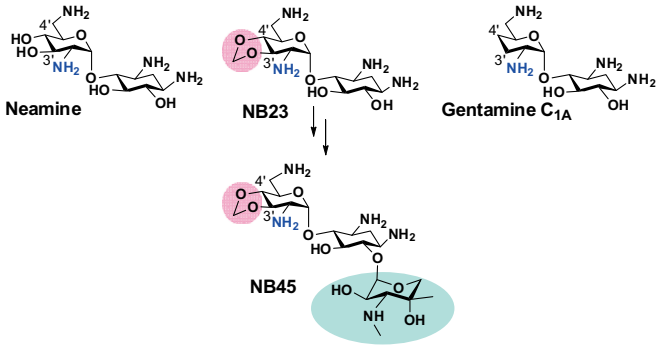


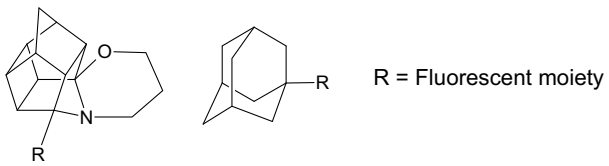


The synthesis, X-ray co-crystal structures and kinetic analysis of two novel and potent small molecule inhibitors of 11β-HSD1 are reported. Structural and kinetic analyses demonstrate two distinctive molecular inhibition mechanisms for the two classes of inhibitors.

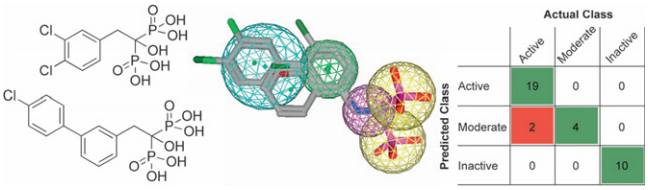


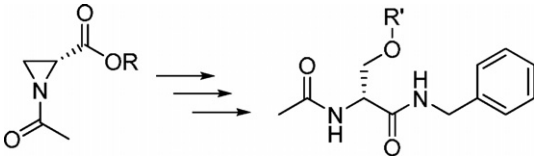
A new pseudo-disaccharide NB23 with a 3′,4′-methylidene protection was designed and its properties were evaluated in comparison to other two structurally related pseudo-disaccharides. The basicity of the 2′-amine was found to be well correlated to acute toxicity data in mice: the increase in the basicity is associated with the toxicity increase. Based on these data, a new pseudo-trisaccharide NB45 was constructed. NB45 exhibited significant antibacterial activity while at the same time retained low acute toxicity.



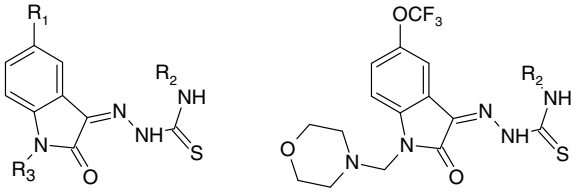


Indazole, isoindole and other fluorescent structures conjugated to polycyclic moieties inhibited NOS in low μM concentrations and Stokes shifts of 29–80 nm were observed.



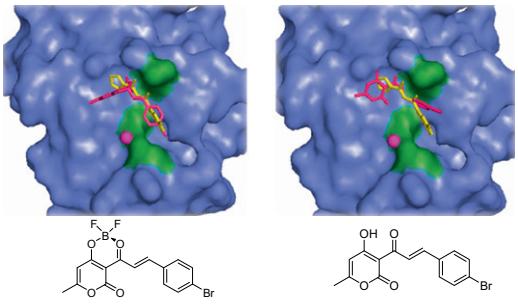


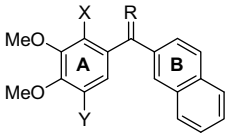
An expedient, stereospecific route to 3-oxysubstituted analogs of the neurological agent lacosamide has been developed.



3, **4** and **6** **5**

R_1= CH_3, OCF_3
R_2= alkyl, cycloalkyl, (non)substituted phenyl
R_3= H, CH_3



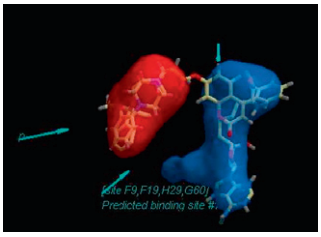


R = H/OH, H/OAc, O, NOH
NOAc, NNH_2, NNHMe,
NNHAc
X, Y = H, OMe

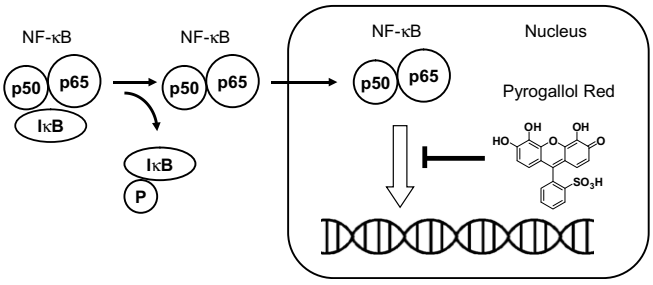
R	X	Y	IC_{50}(TPI)
O	H	OMe	1.1 μM
O	OMe	H	>20 μM

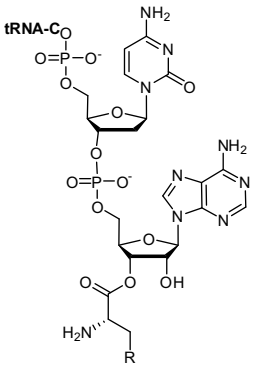
The synthesis and biological evaluation of naphthylphenstatins, modified on the bridge, are described.

Two new series of 2*H*-1-benzopyran-2-one derivatives substituted at C-6 and/or C-7 with propanolamines, and/or piperazine propanol derivatives have been synthesized and assayed for the H_1-histamine antagonist. Twelve of the 20 newly synthesized 4-substituted benzopyrones have shown potent antihistaminic H_1 activity. In addition, molecular modeling and docking of the tested compounds into high affinity histamine binding protein (HBP) and histamine *N*-methyltransferase (HNMT) active site in complex with its bound inhibitor (diphenhydramine) was performed in order to predict the affinity and orientation of these compounds at the active sites. The ICM score values show good agreement with predicted binding affinities obtained by molecular docking studies as verified by pharmacological screening. The results showed similar orientation of the target compounds at HBP, and HNMT active sites compared with reported histamine H_1 antagonist. Also, it was concluded that in order for the compounds to be active, they must bind with both active sites of HNMT enzyme (two pockets) to inhibit it. Compounds **8c**, **8i**, **11g**, **11i**, and **11k**; observe the maximum activities.

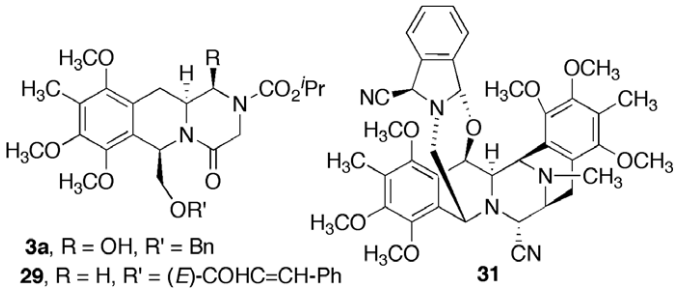


The interaction of pyrogallol red (PR) an inhibitor of NF-κB–DNA binding with zinc was studied by isolating the zinc–PR complex. The complex was characterized using IR, UV–visible, ^{1}H NMR, and thermal studies. Binding sites of PR were identified by molecular modeling using MM+ and PM3 methods and by generating molecular electrostatic map. These studies have confirmed the role of metal ion chelation in the inhibition of NF-κB–DNA binding.





R = $COOCH_3$
R = $CONH_2$
R = SO_2H
R = SO_3H
R = CH_2SO_3H
R = CH_2SH



*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].

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