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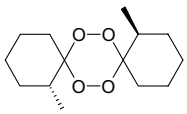
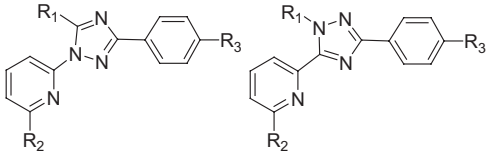
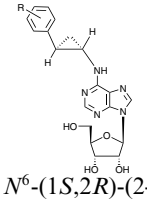
Contents

ARTICLES

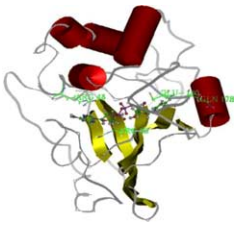


Quantum chemical calculations and automated molecular docking simulations of 13 dispiro-1,2,4,5-tetraoxane compounds were carried out to elucidate the most probable isomer(s) responsible for their antimalarial activity and to investigate an influence of stereoisomer on their binding mode with heme and on antimalarial activity.

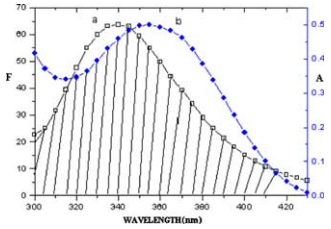




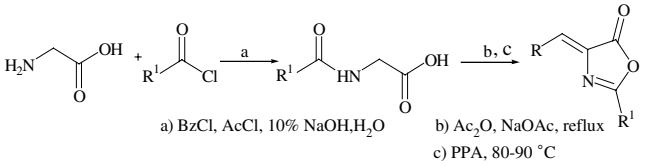
We have synthesized phenyl ring-substituted analogues of N^6-(1*S*,2*R*)-(2-phenyl-1-cyclopropyl)adenosine, which is highly potent in binding to the human A_3AR with a K_i value of 0.63 nM. The effects of these structural changes on affinity at human and rat adenosine receptors and on intrinsic efficacy at the human A_3AR were measured. A QSAR study of the N^6-region provided a model that was complementary to the putative A_3AR binding site in a rhodopsin-based homology model.



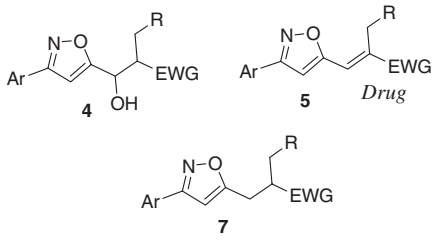
The NAD^+–enzyme complex is developed by molecular dynamics simulation, which indicates the key binding-site residues are Arg48, Glu180, Ser138, Asn134, Arg85, and Gln179.

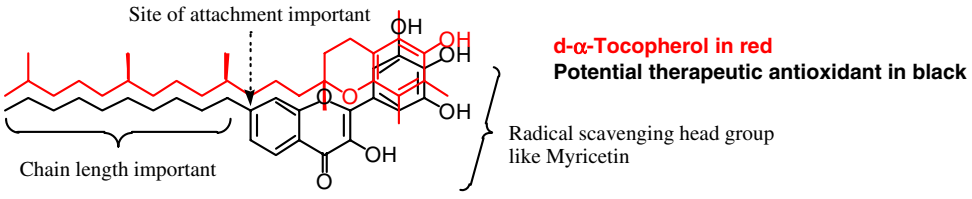


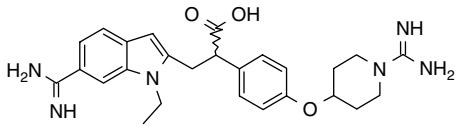
According to Förster dipole–dipole nonradiative energy transfer theory, we determined the energy transfer effect E, the critical distance R_0, and the distance between drugs and amino acid residue in LYSO r. This work shows that the energy transfer between the drugs and LYSO is nonradiative energy transfer. The main acting force between the drugs and LYSO is noncovalent bond action.



Eleven oxazolone derivatives were synthesized, characterized and screened for phagocyte chemiluminescence, neutrophil chemotaxis, T-cell proliferation, cytokine production from mononuclear cells and cytotoxicity.

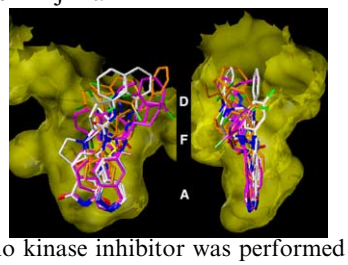




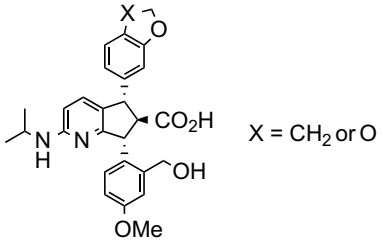


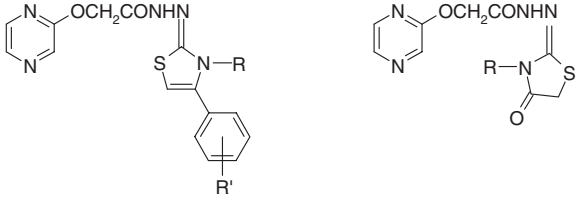
38

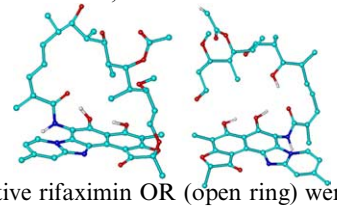
Compound **38** exhibited a high activity toward factor Xa and also showed prolongation of APTT after oral administration in rat.

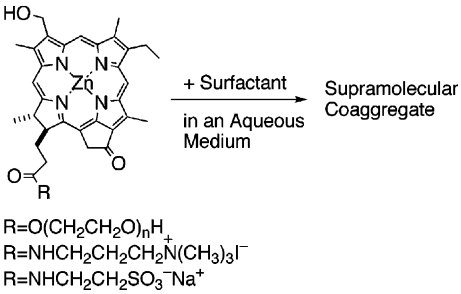


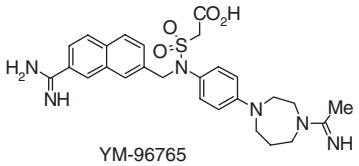
Structure-based design of several scaffolds of Rho kinase inhibitor was performed by using pharmacophore information obtained from a high-throughput screening and the enzyme homology model.











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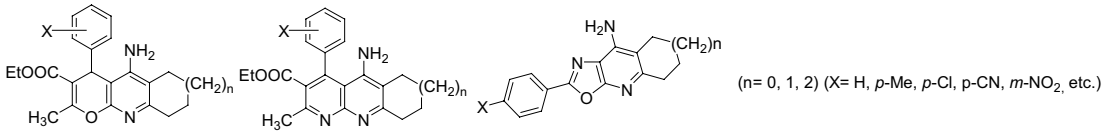
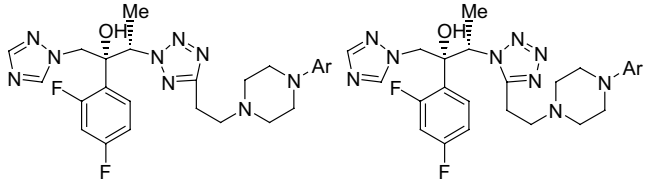
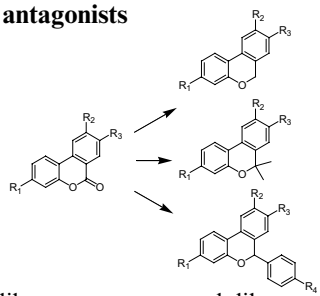


The structural similarities of SARS-CoV main proteinase with HAV 3c protease and HCV Ns3 protease suggest that the available inhibitors in these proteases could be useful for anti-SARS drug design.

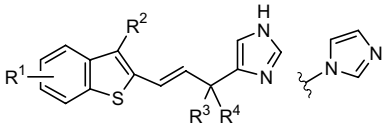


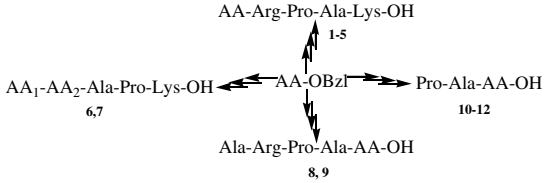
11 **12**

A series of (2*R*,3*S*)-2-(2,4-difluorophenyl)-3-(5-{2-[4-aryl-piperazin-1-yl]-ethyl}-tetrazol-2-yl/1-yl)-1-[1,2,4]-triazol-1-yl-butan-2-ol **11** and **12** has been synthesized and screened for their antifungal activity.

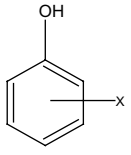


Some new tricyclic molecules namely substituted dibenzopyranones and dibenzopyrans bridged between the active molecules of 3,4-diaryl chroman and 2,3-diaryl benzopyrans have been synthesised and screened for their oestrogen receptor agonist and antagonist activities.

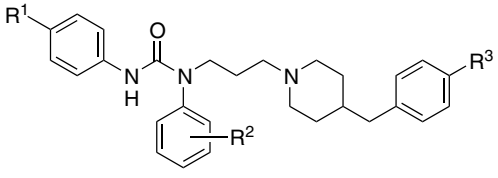


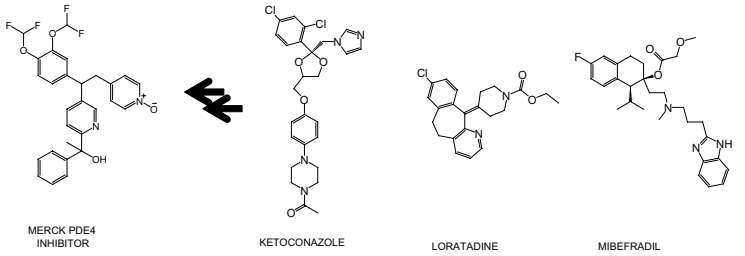


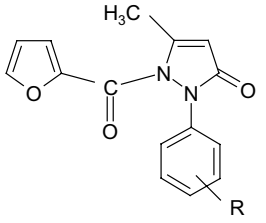
In **1**–**5** AA=Ala (**1**), Gln (**2**), Gly (**3**), Lys (**4**), Arg (**5**), respectively; in **6** AA_1=Ala, AA_2=Arg; in **7** AA_1, AA_2, and Ala together=Ala; in **8** AA=*n*Leu; in **9** AA=Arg; in **10** AA=*n*Leu; in **11** AA=Arg; in **12** AA=Lys. Comparing with Ala-Arg-Pro-Ala-Lys-OH in the in vivo and in vivo thrombolytic assays the Pro-Ala-Lys-OH sequence containing peptides exhibited comparable or enhanced activity, and the non-Pro-Ala-Lys-OH peptides exhibited no activity.



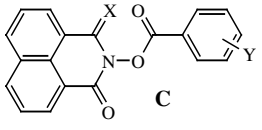
The phenolic activity ($\log 1/C$) of a large series of phenols against L1210 leukaemia cells was modelled using physicochemical parameters, other than conventional electronic and steric parameters. Attempts have also been made to examine need or otherwise of the hydrophobic parameter ($\log P$), in such studies. The results have shown that contribution of $\log P$ in modelling $\log 1/C$ is favourable.





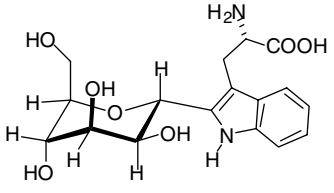


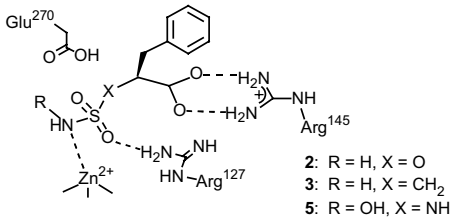
Novel HIV-1 integrase inhibitors were designed using a de novo design method LeapFrog, synthesized, and tested for in vitro inhibition of HIV-1 integrase.

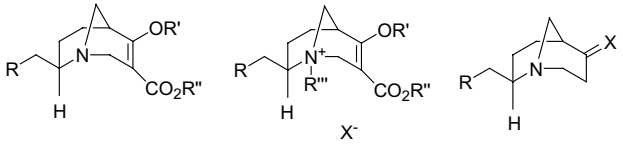


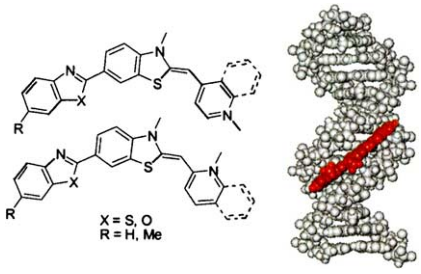
C

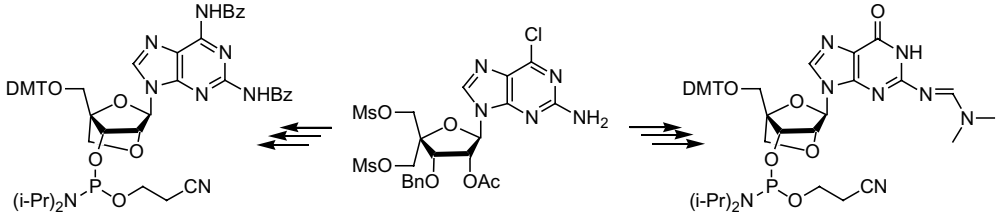
C0 X=O,Y=H
C1 X=S, Y=H
C2 X=S, Y=F
C3 X=S, Y=Cl
C4 X=S, Y=CH_3
C5 X=S, Y=OCH_3
C6 X=S, Y=*m*-Cl_2
C7 X=S, Y=*m*-Me_2
C8 X=S, Y=*o*-F, *p*-Cl
C9 X=S, Y=*m*, *p*-OMe_2
C10 X=S, Y=*o*-Cl, *m*-Pyridine
C11 X=S, Y=*o*-furanyl

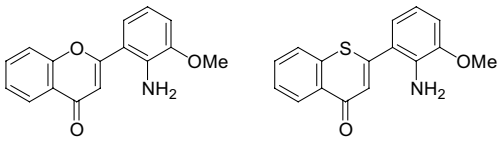




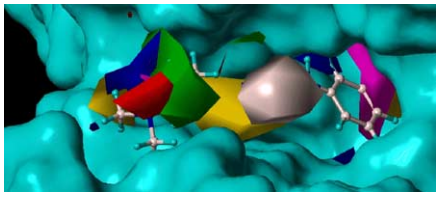




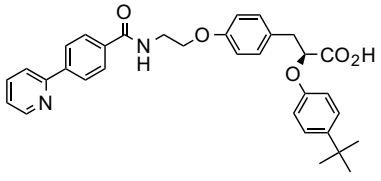


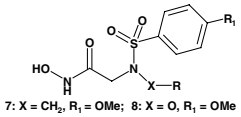


In a cell-based assay, 2-(2′-amino-3′-methoxyphenyl)-4*H*-1-benzothiopyran-4-one (**8b**) showed a more potent inhibitory effect than the corresponding oxygen compound (PD98059, **1**) on the Raf-induced activation of the ERK-MAP kinase pathway as well as cell proliferation.



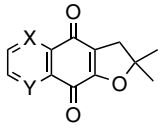
One hundred and twenty four EGFR PTK's inhibitors with different scaffolds were used in CoMFA and CoMSIA studies. Highly reliable and predictive 3D-QSAR models were derived, which reveal how steric, electrostatic, and hydrophobic interactions contribute to inhibitors' bioactivities.





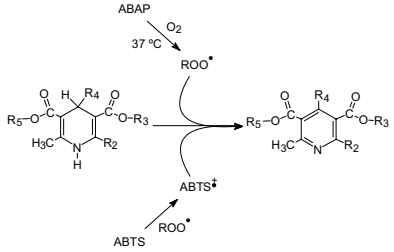
7: X = CH_2, R_1 = OMe; 8: X = O, R_1 = OMe
9: X = CH_2, R_1 = Ph; 10: X = O, R_1 = Ph

New *N*-arylsulfonyl-substituted alkoxyaminoaceto hydroxamic acid derivatives of types **8** and **10** were synthesized and tested for their inhibitory activities on some matrix metalloproteinases. The combination of a biphenylsulfonamide group with oxyamino oxygen in the pharmacophoric central skeleton of sulfonamide-based MMPi obtained in the new sulfonamides **10** seems to be able to give selectivity for MMP-2 over MMP-1. The most potent derivative of this type shows anti-invasive properties in an in vitro model of invasion on matrigel, carried out on cellular lines of fibrosarcoma HT1080.

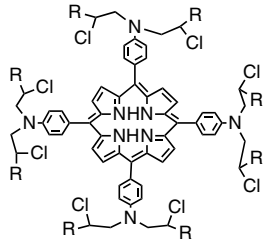


10 X = C, Y = N
11 X = N, Y = C

The synthesis and trypanocidal activity of some dihydronaphthofurandiones and dihydrofuroquinolinediones is described. Compounds **10** and **11** have shown potent trypanocidal activity. Relationships between the stereoelectronic properties and the trypanocidal activity of these heterocyclic quinones are discussed.

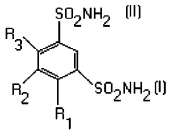


A series of eight commercial C-4 substituted 1,4-dihydropyridines and other synthesized related compounds were tested for direct potential scavenger effect towards alkylperoxyl radicals and ABTS radical cation in aqueous Britton–Robinson buffer pH 7.4. The pyridine derivative was confirmed by GC/MS technique as the final product of reaction.

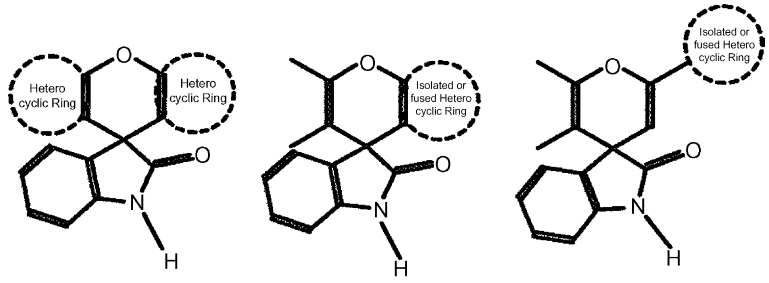


R = H, CH_3, CH_2Cl

Fifteen new chloroalkyl piperazine and nitrogen mustard porphyrins have been synthesized. Most of the synthetic porphyrins had good anticancer activity toward bel-7404 liver cancer cell in the absence of light. They might have potential applications in medicine.



The paper deals with quantitative structure–activity relationship (QSAR) study on CA inhibitory activity ($\log IC_{50}$) of disulfonamides using a large series of distance-based topological indices. The study discusses effect due to halogen-substitution nearer (*o*-position) to $-SO_2NH_2$ groups. The results have shown that halogen substitution at R_3 has pronounced effect on the inhibitory activity. Predictive power of the proposed models is discussed on the basis of regression data and cross-validation parameters.



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*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

2004: Overlaps of the eight known aldolase alpha-beta barrels in 2-deoxyribose-5-phosphate aldolase (DERA). Ribbon model for DERA is shown in green, with key Lys residues capable of Schiff base formation highlighted in stick figure. Reactive Lys167 is shown in yellow. DeSantis, G.; Liu, J.; Clark, D. P.; Heine, A.; Wilson, I. A.; and Wong, C.-H. *Bioorganic & Medicinal Chemistry* **2003**, *11*, 43–52.

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