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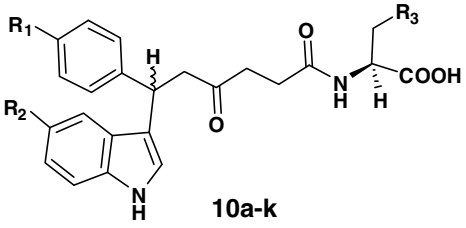
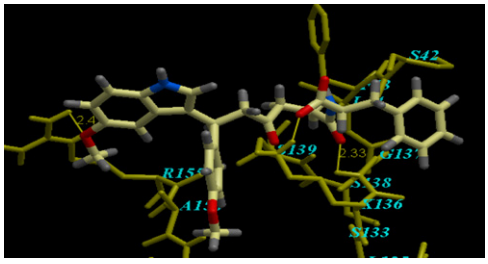
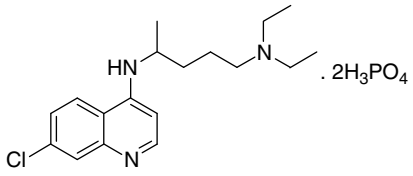
Contents

ARTICLES

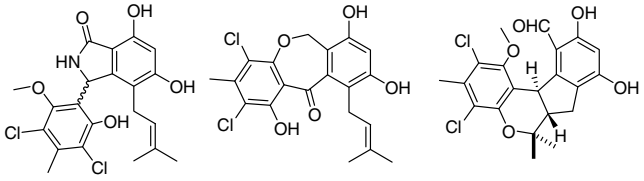






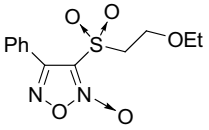
Chloroquine diphosphate (CQ)

In the present study, the combinational effects of CQ and Akt inhibitors were evaluated for their cell killing activity on cancer and non-cancer breast cells.



1 2 3

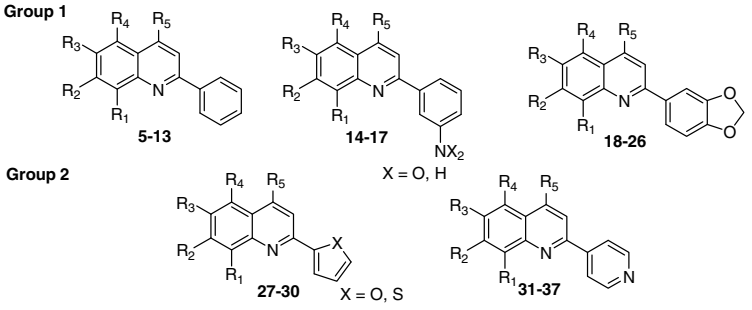
Pestalachlorides A–C (**1**–**3**), three new chlorinated benzophenones, have been isolated from the plant endophyte *Pestalotiopsis adusta* and evaluated for their antifungal activities.



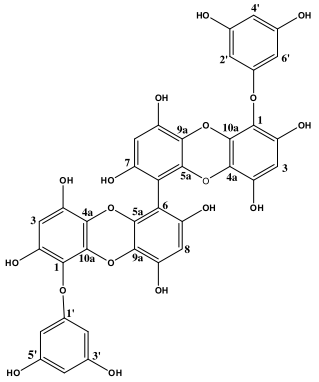
ID_{50} (μM)			
T. cruzi CL Brener	*T. cruzi* Y	*L. braziliensis* LTB300	*L. pifanoi* LV135
1.5	3.4	4.1	4.2

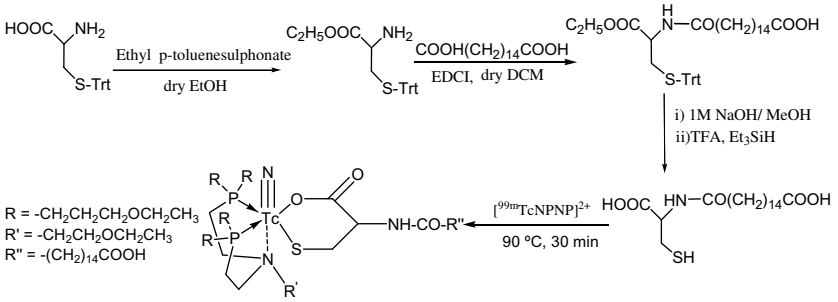
Over a hundred furoxans, alkylnitrates and related compounds were studied as growth inhibitors of *Trypanosoma cruzi* and *Leishmania* spp.

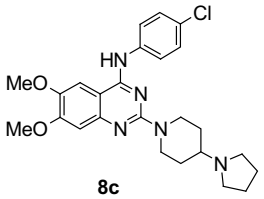
Thirty-three 2-aryl and 2-hetaryl derivatives of polyfunctionalized quinolines (groups 1 and 2) were tested for antifungal properties against standardized and isolates of clinically important fungi. The most active compounds belong to group 2 being playing the positions 4 and 8 of the quinoline ring an important role against dermatophytes.



The bioactive 6,6'-bieckol was isolated and characterized by NMR techniques. For the first time, human immunodeficiency virus type-1 (HIV-1) inhibitory activity of 6,6'-bieckol showed wild inhibition against HIV-1 induced syncytia formation (EC_{50} 1.72 μM), lytic effects (EC_{50} 1.23 μM), and viral p24 antigen production (EC_{50} 1.26 μM), respectively. This result was strongly and clearly supported by the further investigation also, which 6,6'-bieckol selectively inhibited the activity of HIV-1 reverse transcriptase (RT) enzyme with EC_{50} of 1.07 μM, as well as HIV-1 entry. Moreover, unlike most of other tannins, 6,6'-bieckol exhibited no cytotoxicity at concentrations which inhibited HIV-1 replication almost completely. Thus, it can be suggested that the potentially effective 6,6'-bieckol might be employed as a drug candidate for development of new generation therapeutic agents against HIV.

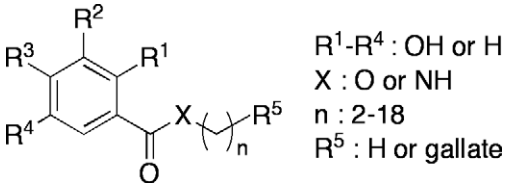




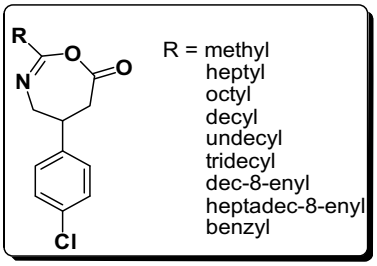


8c

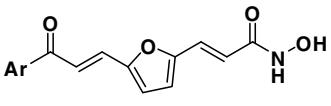
The novel *N*-(4-chlorophenyl)-6,7-dimethoxy-2-(4-pyrrolidin-1-ylpiperidin-1-yl)quinazolin-4-amine **8c** was found to be a potent competitive CCR4 antagonist and showed anti-inflammatory activity in a murine model of acute dermatitis.



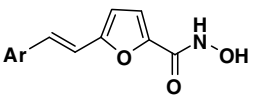
Various alkyl gallate and gallamide derivatives were synthesized and their antiproliferative/apoptosis-inducing activities were evaluated.



Nine new lipophilic cyclic analogues of baclofen were designed, synthesized and tested for their neuropharmacological activities.

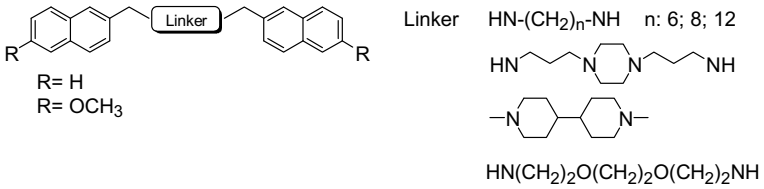


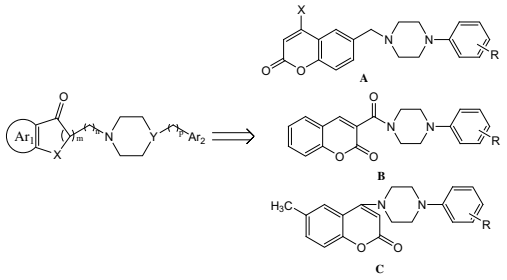
5a-j



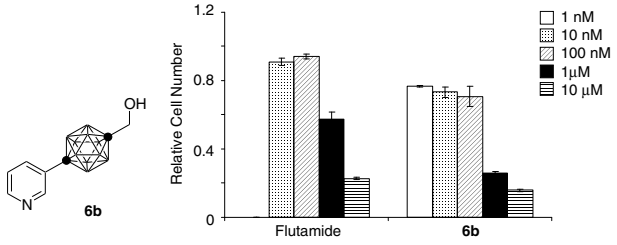
6a-h

A series of hydroxamic acids with conjugated stereodefined structure were designed as HDAC inhibitors.

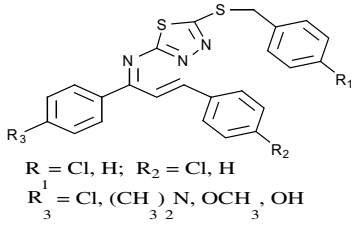




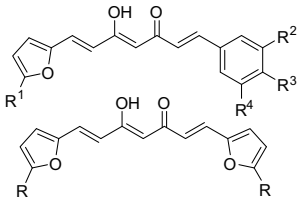
Three series of coumarin compounds were designed and synthesized. Their anti-AChE activities were also determined.



Compound **6b**, which was designed based on the structures of BA321 and BA341, exhibited more potent antiandrogenic activity than that of flutamide in SC-3 cell growth inhibition assay.



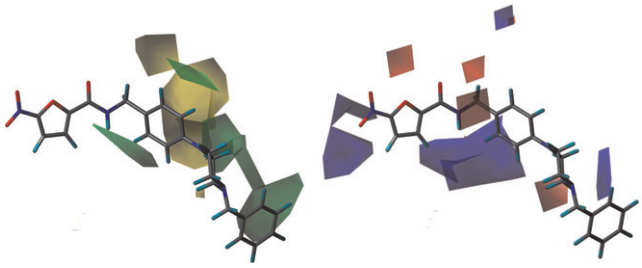
A series of imines of 1, 3, 4-thiadiazol-2-thiol and their thiobenzyl derivatives were synthesized from various chalcones in different reaction conditions and were evaluated for their anti-depressant and neurotoxic activity. Some of the compounds showed potent anti-depressant activity without any serious neurotoxicity as compared to standard drug imipramine.



Compd.	R^1	R^2	R^3	R^4	R	IC_{50} (μM)*
2a	CH3	H	OH	OMe	\	0.5
2c	CH2OH	OMe	OMe	OMe	\	2.0
2e	CH2OH	H	OH	OMe	\	1.0
2f	CH2OH	H	H	H	\	1.3
2g	CH2OH	H	OMe	H	\	0.8
4g	\	\	\	\	Me	0.3
4h	\	\	\	\	H	1.6
curcumin	\	\	\	\	\	38.3

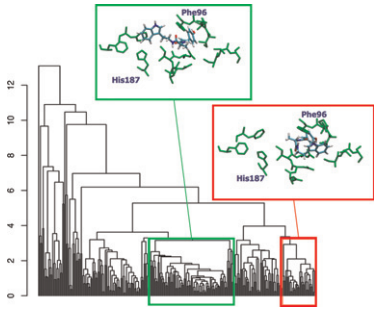
*, TrxR inhibition

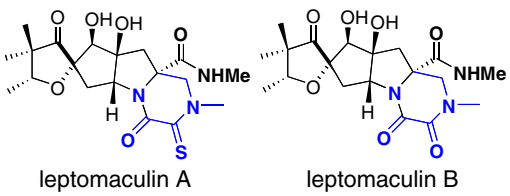
Series of curcumin derivatives were synthesized and evaluated for the inhibitory activities on TrxR by DTNB assay; it is found that most of the analogues can inhibit TrxR in vitro; SAR analysis reveals that analogues with furan moiety have excellent inhibitory effect on TrxR.



The development of a series of externally validated 3D-QSAR models with high predictive ability against nitrofuran agents with antimycobacterial activity is discussed.

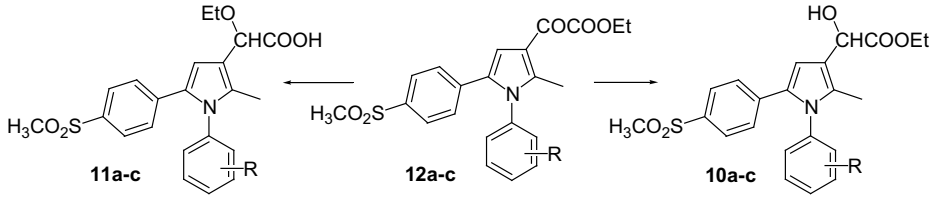
SIRT2 inhibitors with a *N*-(3-phenylpropenoyl)-glycine tryptamide backbone were studied, and their binding modes were analyzed with molecular modelling methods.





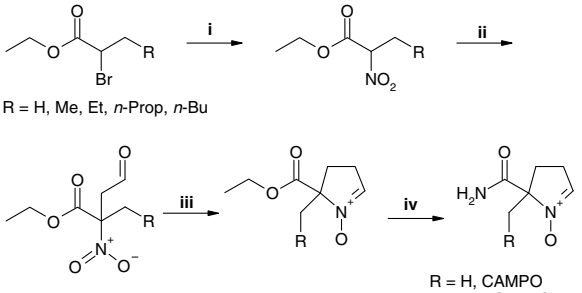
leptomaculin A leptomaculin B

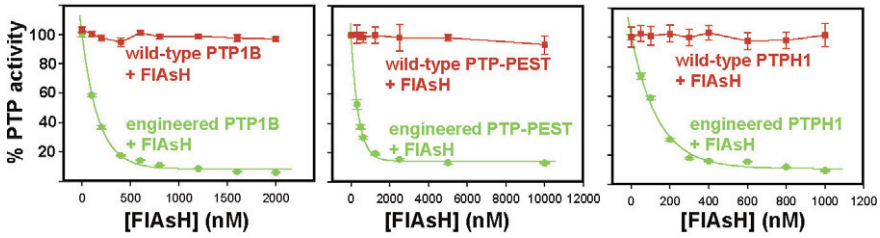
The chemical structures of the first natural 2,3-oxopiperazinethione and 2,3-dioxopiperazine, leptomaculins A and B, together with six new leptomaculins as well as biological activities and proposed biosynthetic pathways are reported.



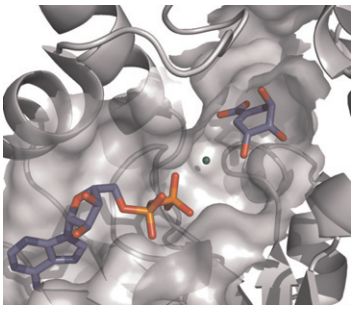
(−)-**10b**: R = 3-F, COX-2 affinity: 0.075 μM, COX-1/COX-2 selectivity >1300. (+)-**10c**: R = 4-OCH_3, COX-2 affinity: 0.079 μM, COX-1/COX-2 selectivity >1200. Celecoxib (**1b**): COX-2 affinity: 0.06 μM, COX-1/COX-2 selectivity: 61.7.

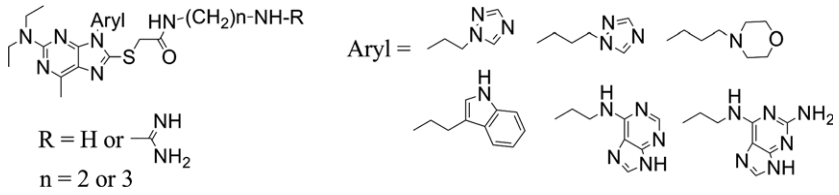
Synthesis and spin trapping properties of a series of EMPO-derived nitrones are reported.



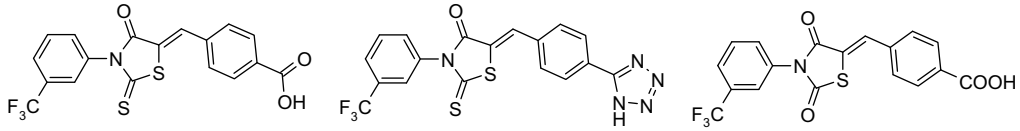


Complexes of *Ba*SK were modeled with natural substrates in different conformational states due ligand-binding. Molecular dynamics simulations have been performed to evaluate structural and dynamical properties of *Ba*SK.

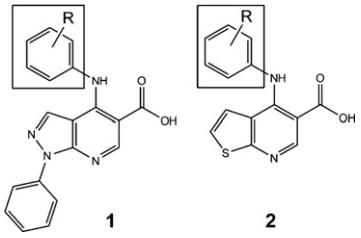


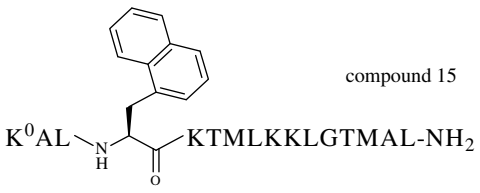


Twenty-four purine derivatives were designed and synthesized as HIV-1 Tat–TAR interaction inhibitors. The aryl groups at N9 position could affect the binding specificity between compounds and TAR.

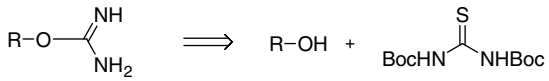


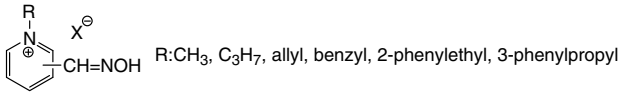
In this work, we report the antibacterial and theoretical evaluations of a pyrazolo[3,4-*b*]pyridine series (**1**, **1a**–**l**) and the comparison with a new isosteric thieno[2,3-*b*]pyridine derivatives series (**2**, **2a**–**l**). Several analyses that included molecular modeling studies and in silico ADMET evaluation revealed 1 series with four potential antibacterial lead compounds for treating infections caused by drug-resistant *Staphylococcus epidermidis* clinical strain.

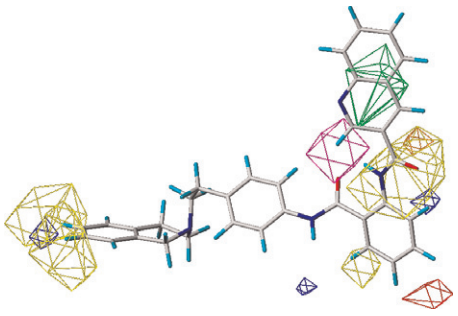


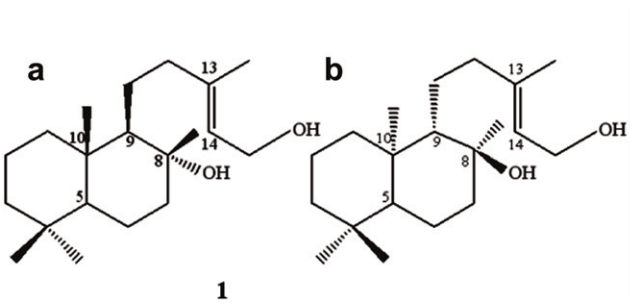


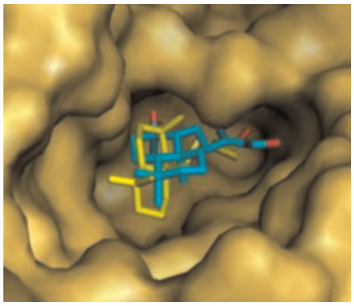
Novel dermaseptin S1 (DS1) analogues were synthesized and evaluated biologically. The replacement of Trp**3** with naphthyl-Ala and the insertion of a Lys**0** in the DS1(1–15) fragment generated a highly potent antimicrobial peptide.



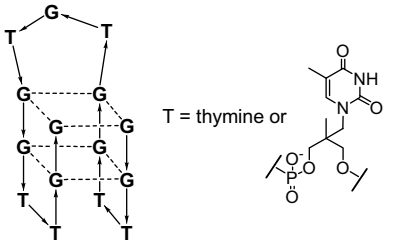




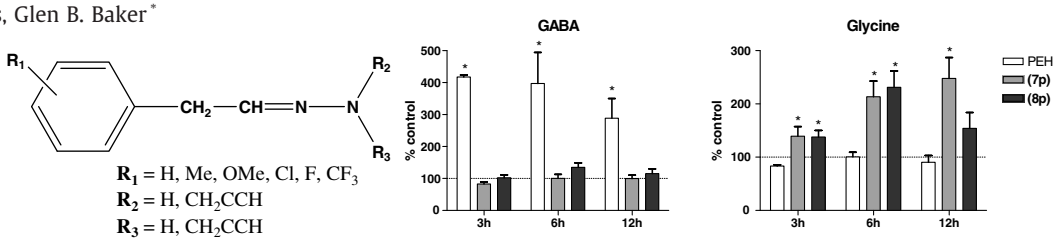




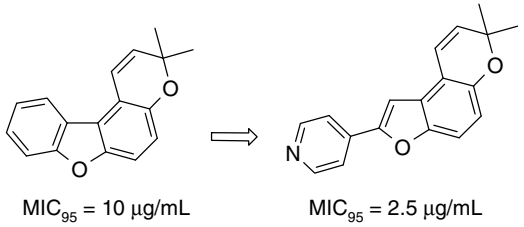
Best binding poses of the two enantiomers of labd-13(*E*)-ene-8a,15-diol (**1a**, colored yellow, and **1b**, colored blue) in the forskolin binding site of AC.

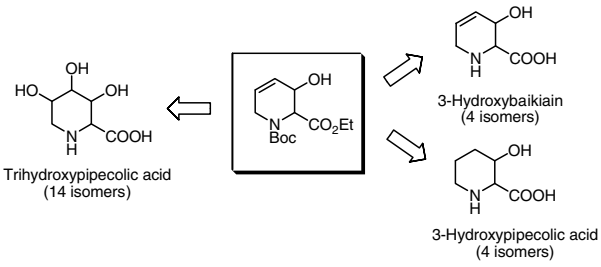


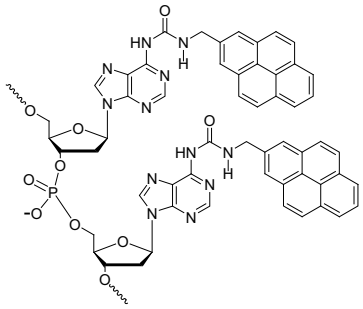
A series of new modified thrombin binding aptamers was synthesized by substitution, one at the time, of the T residues with a new acyclic nucleotide. The structural properties and the thrombin inhibitory activities of the new aptamers have been evaluated.

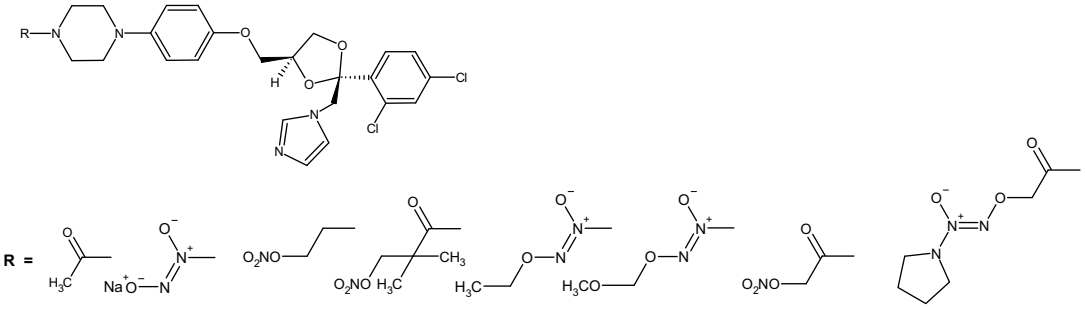


Analogs of β-phenylethylidenehydrazine (PEH) were synthesized and screened in vitro. **7p** (R_1=H, R_2=CH_2CCH, R_3=CH_2CCH) and **8p** (R_1=H, R_2=H, R_3=CH_2CCH) were tested ex vivo for effects on rat brain levels of amino acids (above) and enzyme activity.

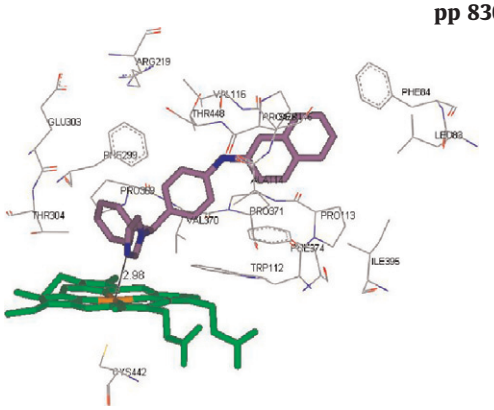








Antimicrobial activities of ketoconazole–NO-donor hybrids (MIC-values) against eight different fungal strains range from 0.6 to 1000 μM.



*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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