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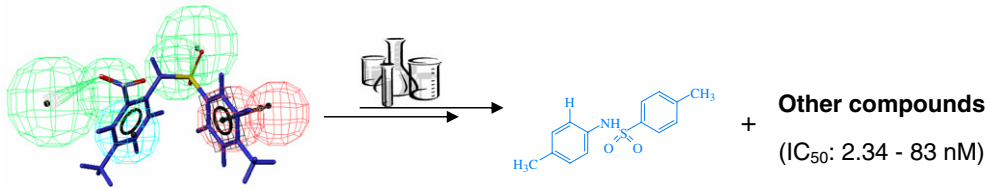
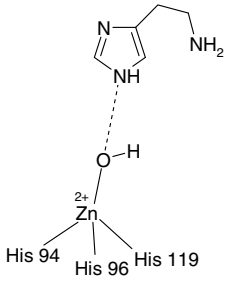
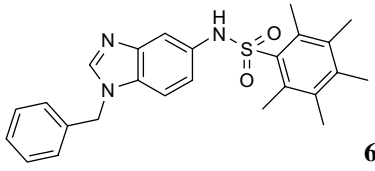
Contents

ARTICLES



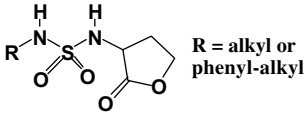


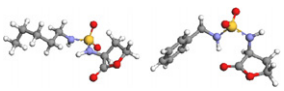


6n

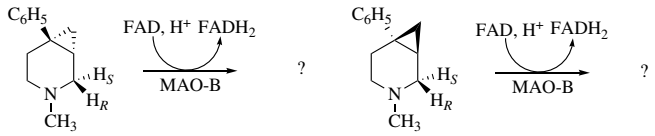
In this study, we identified compound **6n** as a potent agonist of hPXR with active concentration in the subnanomolar range.

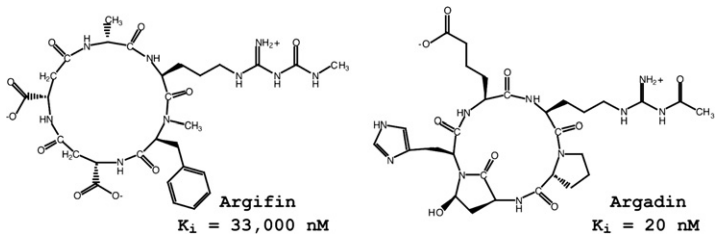
A series of 9 homoserine lactone-derived sulfonylureas, were prepared and found to inhibit the acyl-homoserine lactones-dependent *Vibrio fischeri* quorum sensing regulator. Molecular modelling suggested that the inhibitory activity could be related to the perturbation of the hydrogen-bond network in the ligand–protein complexes.



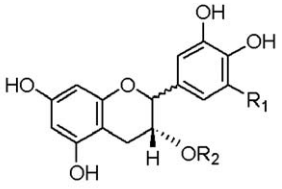


The most potent compounds





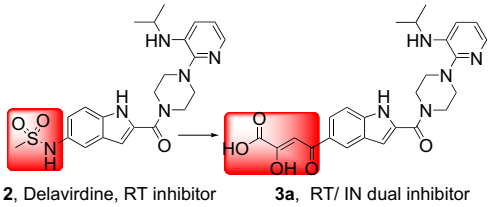
A possible cause of the different binding affinities of argifin and argadin with Chitinase B was investigated using the MM-PBSA free-energy analysis.

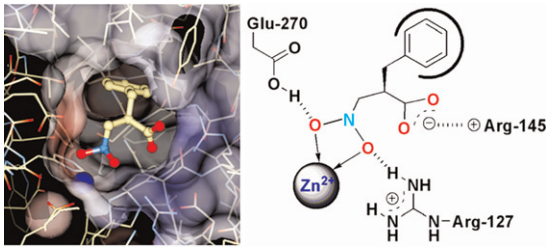


R_1 : H or OH

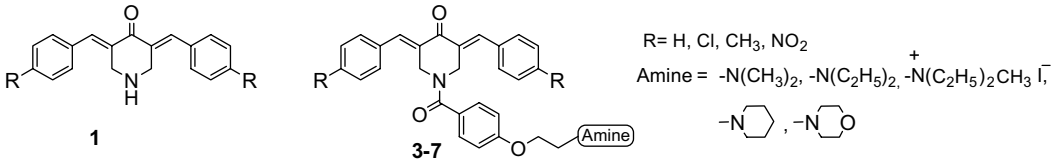
R_2 : H IC_{50}>>1000

R_2 : 3,4,5-trihydroxybenzoyl IC_{50}=0.18 μM~0.25 μM

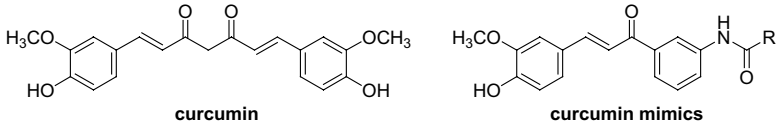




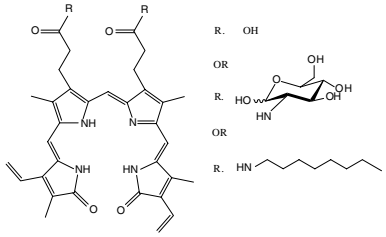
X-ray crystallography of carboxypeptidase A-(*R*)-2-benzyl-3-nitropropanoic acid complex disclosed that the nitro group chelate the zinc ion in the active site of CPA in an *O*,*O*′-bidentate fashion.



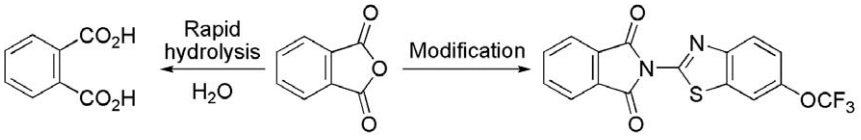
A number of 3,5-bis(benzylidene)-4-piperidones **1** and related *N*-4-(2-aminoethoxy)phenylcarbonyl analogs **3**–**7** were screened against *Mycobacterium tuberculosis* $H_{37}Rv$ and for neurotoxicity in mice. A number of lead molecules were identified as potent antitubercular agents which are well tolerated in mice.

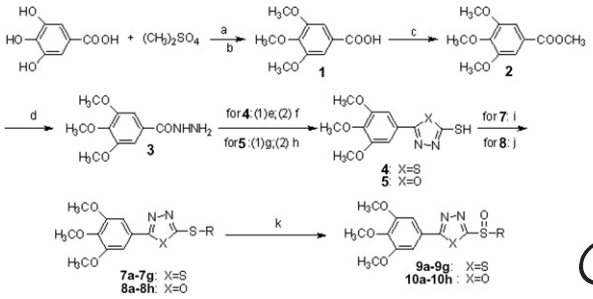


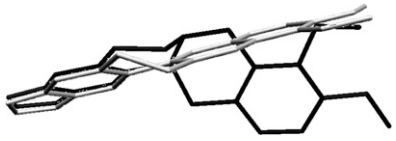
The unsymmetrical curcumin mimics with various amide moieties were synthesized and evaluated their multidrug resistance (MDR) reversal activities in MDR cell line KBV20C.



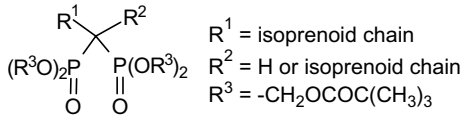
Hydrophilic and lipophilic conjugates of biliverdin were prepared. Native and conjugated bile pigments were then tested in Caco-2 cell permeability and stability assays.

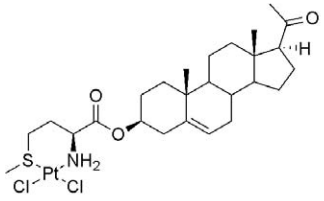




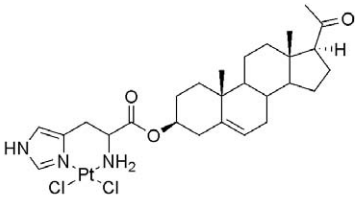


The cytotoxic effects of four alkaloids, berberine, canadine, anonaine, and antioquine were evaluated. The antioxidant activity of canadine, combined with its low-toxic effect, indicated that this alkaloid is a promising candidate for a novel antioxidant agent. The figure shows the stereoview of overlapping of berberine (light gray) and canadine (black).

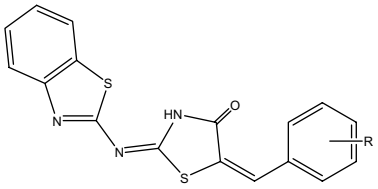




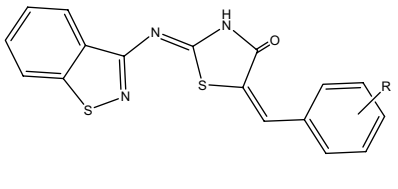
4c



4f

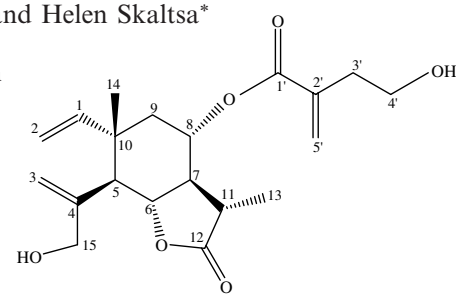


2a – 2j

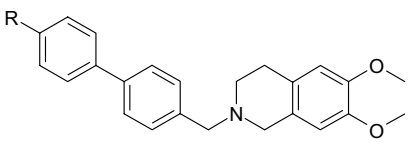


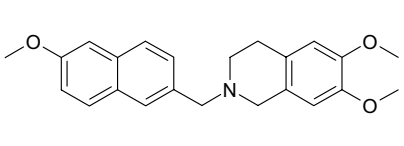
3a – 3j

8α-*O*-(4-Hydroxy-2-methylenebutanoyloxy)melitensine. A novel elemanolide with an α-methyl-γ-lactone moiety isolated from *Centaurea pullata*.

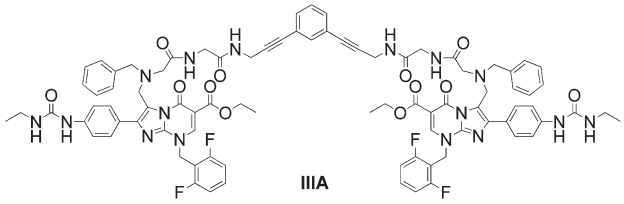


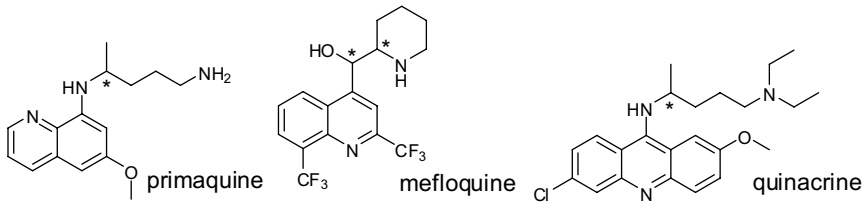
8*α*-*O*-(4-hydroxy-2-methylenebutanoyloxy) melitensine.



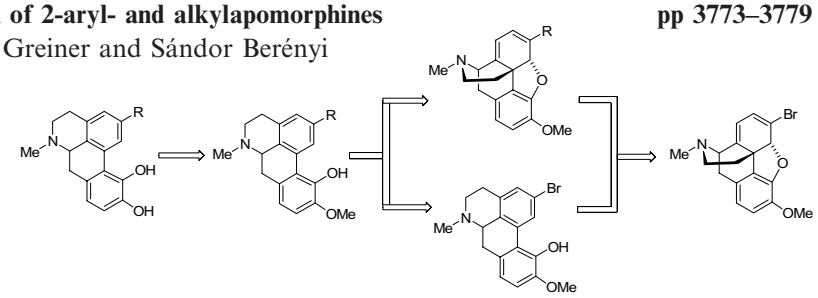


Biphenyl **4c** (R = H, EC_{50} = 0.10 μM) and **4d** (R = OH, EC_{50} = 0.05 μM) derivatives and 2-naphthyl **7g** (EC_{50} = 0.45 μM) derivative as potent P-gp modulating agents.

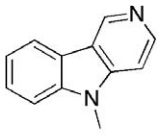




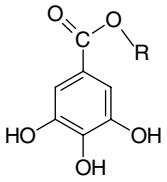
The acute-phase component serum α_1-acid glycoprotein is an important contributor in plasma protein binding of antimalarial agents of quinoline and acridine type.



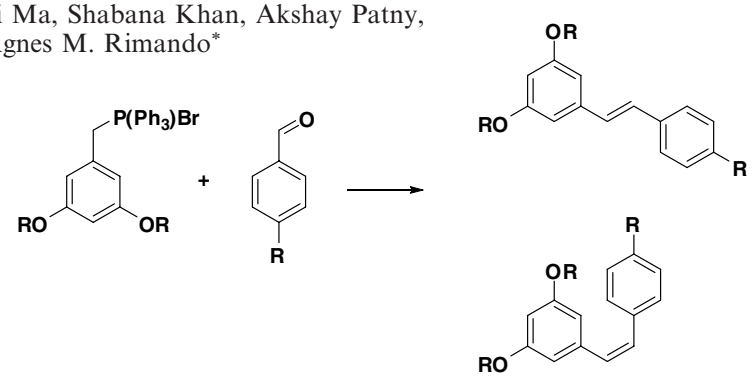
A novel synthesis has been elaborated for the pharmacologically remarkable 2-arylapomorphines described and characterized in the last few years. This new procedure contains two alternative synthetic routes and has allowed the preparation of several hitherto-unknown compounds as well. The pharmacological profile of the previously published and the novel 2-alkyl- and arylapomorphines has been determined with the application of in vitro and in vivo techniques. For 2-phenyl- (**2**) and 2-(4-hydroxyphenyl)apomorphines (**3**) the superior dopamine agonist profile has been confirmed and for the novel compounds some remarkable results have been observed.

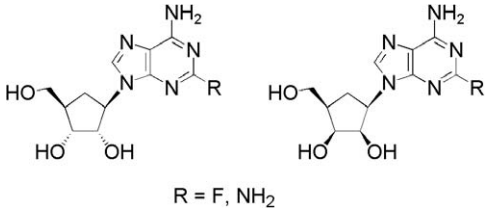


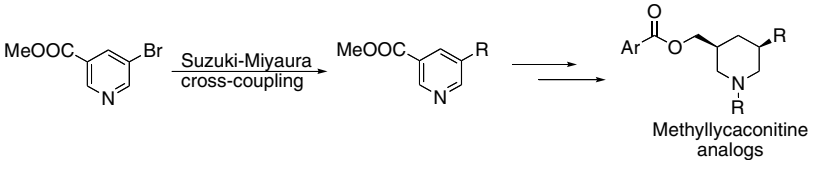
Based on anti-viral screening of our heteroaromatics derived from thalidomide, the γ-carboline skeleton has been identified as a superior scaffold structure for compounds with potent anti-bovine viral diarrhea virus (BVDV) activity. Structural development studies led to a potent anti-viral agent, SK5M (5-methyl-γ-carboline), with the EC_{50} of 0.26 μM.

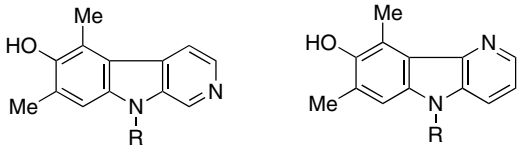


Gallic acid ester derivatives, with the same number of hydroxyl groups, varying the carbon side chain length, induced cell death through apoptosis in a leukemia cell line.



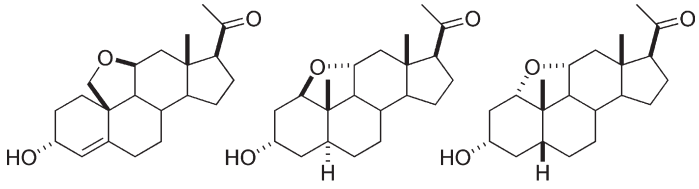






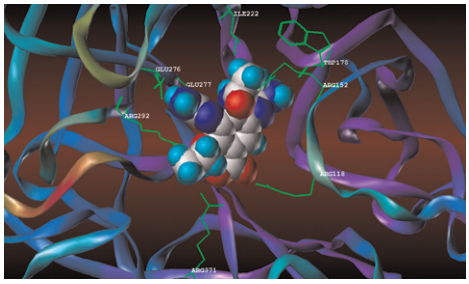
1: R = H
2: R = Me

3: R = H
4: R = Me

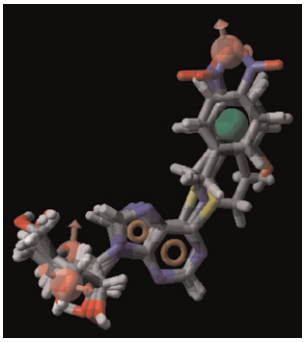


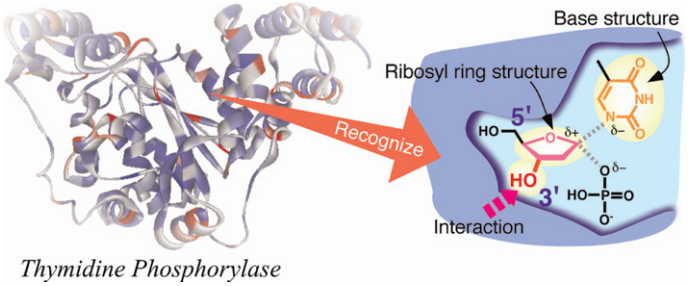
4 **5** **6**

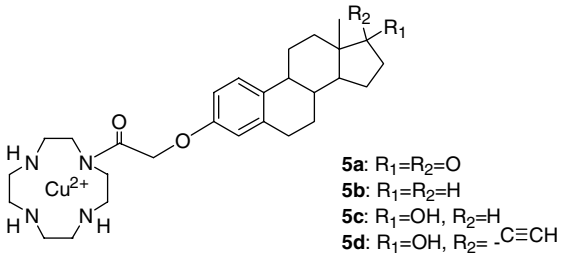
Superposition of compound **12** bound to influenza A (H3N2) neuraminidase. Structure-based design has led to the synthesis of a series of influenza neuraminidase (NA) inhibitors containing benzoic acid. Several compounds exhibit some specific activity against influenza A (H3N2).

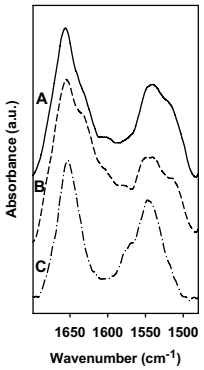


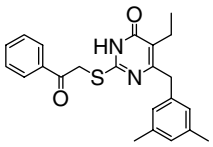
3D Pharmacophore model and suggested bioactive conformation of NBMPR and analogues at their ENT1 transporter-binding site.

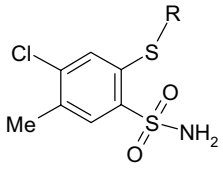


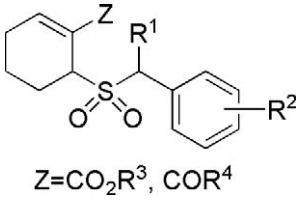




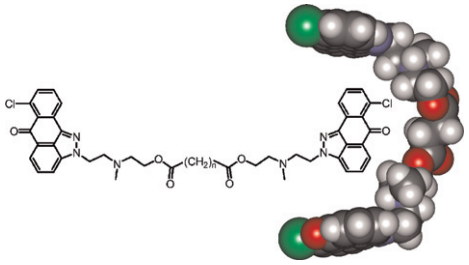


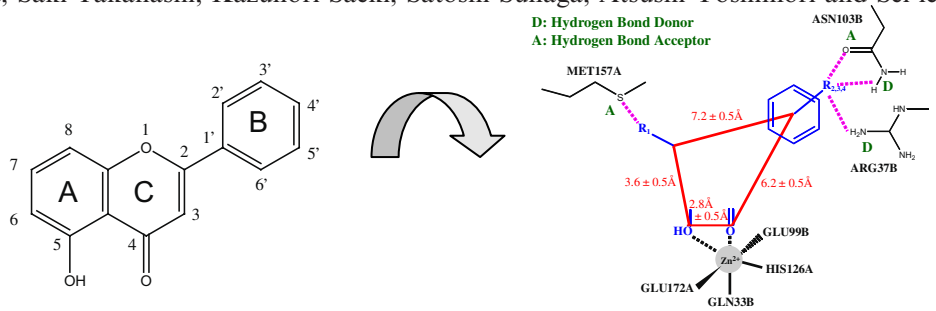




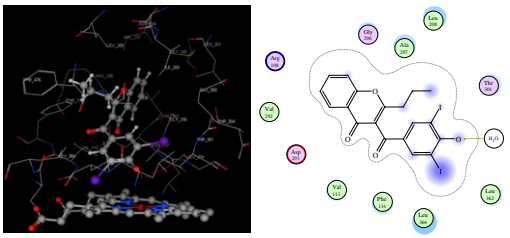


A series of cyclohexane derivatives were synthesized and evaluated for inhibitory activities of NO and cytokine production.



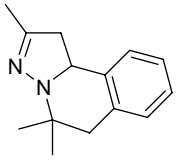


A basic structure of natural flavonoids and their deduced pharmacophore on the human GLO I

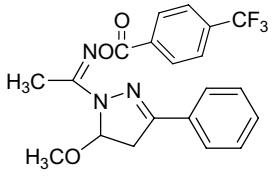


Proposed binding modes of inhibitory analogs would lead to an interaction of the phenolate anion with a water molecule stabilized by Ala 297.

A series of novel 1-(5-substituted-3-substituted-4,5-dihydropyrazol-1-yl)ethanone oxime ester derivatives and the unusual heterocyclic compound 2,5,5-trimethyl-1,5,6,10b-tetrahydropyrazolo[5,1-*a*]isoquinoline are synthesized. The title compounds **14** and **26c** showed potent antibacterial activities against *Staphylococcus aureus* and *Escherichia coli* which was superior to the positive control penicillin.

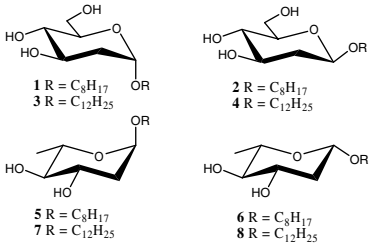


14

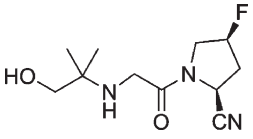


26c

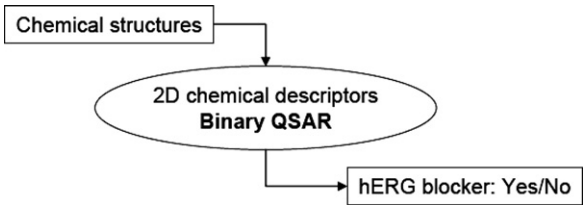
Synthesis, surface properties, antimicrobial activity, and toxicity.



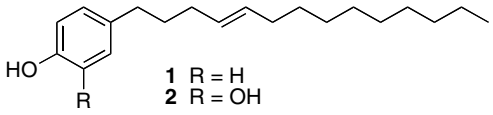
1 R = C_8H_{17} **2** R = C_8H_{17}
3 R = $C_{12}H_{25}$ **4** R = $C_{12}H_{25}$
5 R = C_8H_{17} **6** R = C_8H_{17}
7 R = $C_{12}H_{25}$ **8** R = $C_{12}H_{25}$



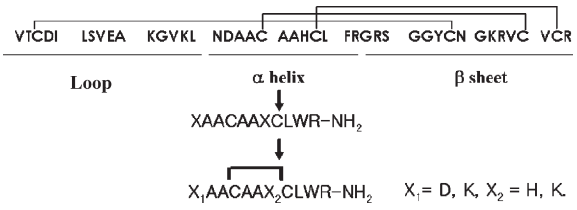
We report the identification of a potent and stable DPP-IV inhibitor (TS-021) with a long-term persistent plasma drug concentration and a potent antihyperglycemic activity.

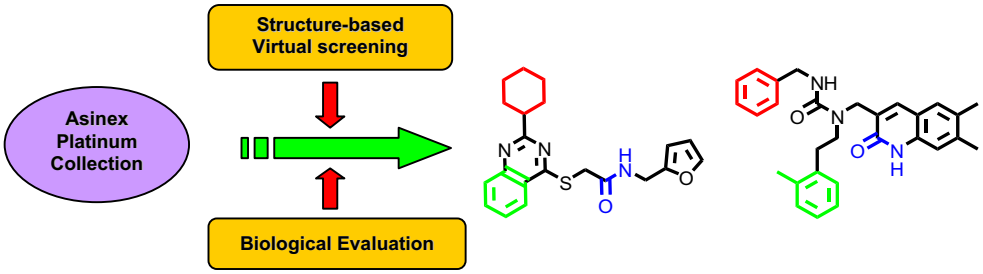


We describe the development and validation of binary QSAR models for rapid classification of hERG potassium channel blockers.

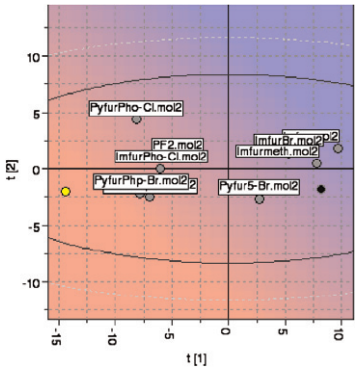


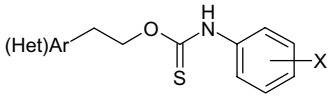
Two new alkenylphenols, obliquol A (**1**) and obliquol B (**2**), possessing anti-NF-κB activity by targeting early events in the TNFα-induced NF-κB inflammatory pathway, were isolated from *Piper obliquum*.





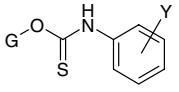
Novel inhibitors of the SARS-3CL^{pro} were identified using a combination of structure-based virtual screening and biological evaluation.

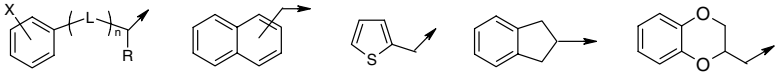




(Het)Ar = 2- and 4-pyridyl; 2-thienyl; phenyl

X = H; 2-, 3-, 4-CH_3; 4-C_2H_5; 4-$CH(CH_3)_2$; 4-CF_3; 4-CN; 4-$COCH_3$; 3-, 4-F; 2-, 3-, 4-Cl; 4-Br; 4-I; 4-$N(CH_3)_2$; 3-, 4-NO_2; 4-OCH_3; 2,5-F_2; 2,6-F_2; 3,5-F_2; 2,4-Cl_2; 3,4-Cl_2; 3-Cl-4-CH_3; 4-Cl-3-CF_3; 4-Cl-3-NO_2



G = 

X = H; 2-, 3-, 4-CH_3; 4-Ph; 2-, 3-, 4-Cl; 4-Br; 4-NO_2; 2-, 3-, 4-OH; 2-, 3-, 4-OCH_3; 3-OPh; 2,6-Cl_2
n = 0, 1 L = CH_2; $CH(CH_3)$; $C(CH_2CH_2)$; CHPh; CH_2CH_2; CH=CH; OCH_2; SCH_2
R = H, CH_3, C_2H_5 Y= H; 4-CH_3; 4-F; 4-Cl; 4-NO_2; 4-OCH_3; 3,4-Cl_2; 3-Cl-4-CH_3;4-Cl-3-NO_2

OTHER CONTENTS

*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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