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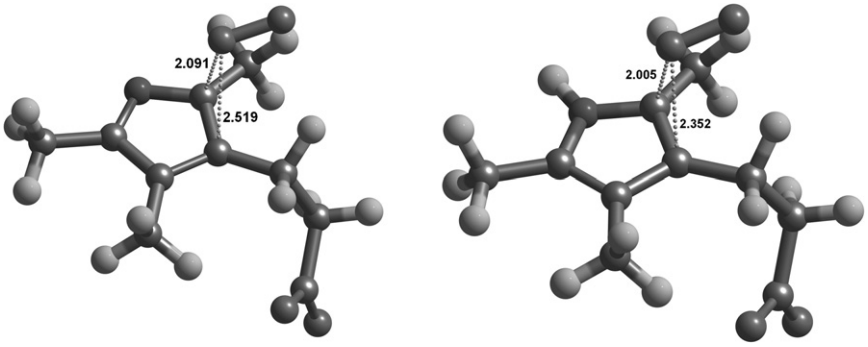
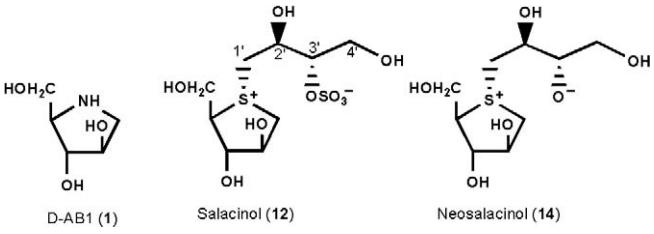
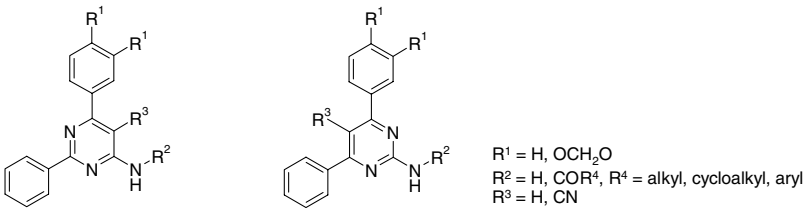
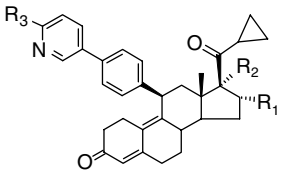
Contents

ARTICLES



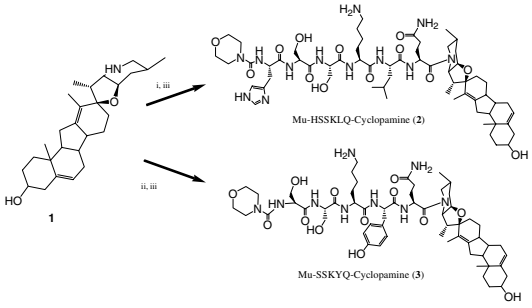


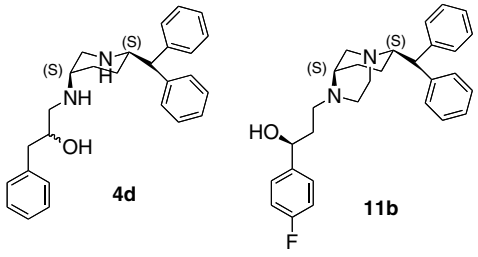


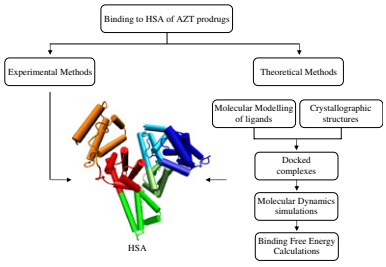


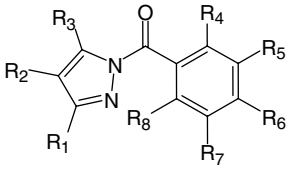
11-(Pyridinylphenyl)steroids and a series of heteroaryl analogs were prepared which show a remarkable mixed progesterone agonist/antagonist profile, wherein the efficacies for both activities range from 40% to 60%.

Novel peptide-cyclopamine conjugates as prostate-specific antigen (PSA)-activated prodrugs for use against prostate cancer.



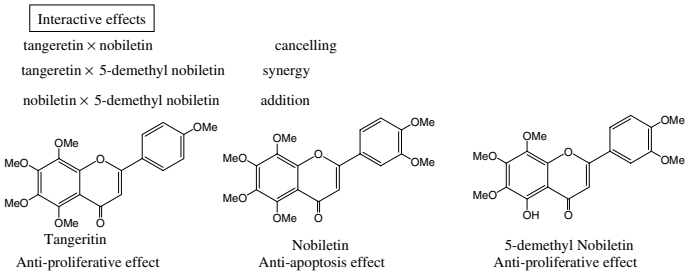


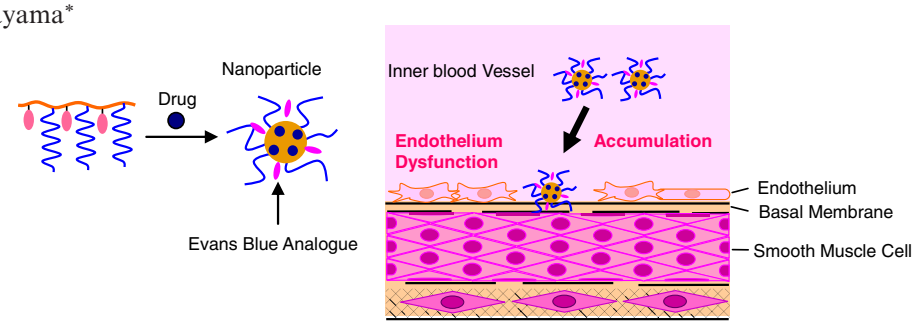


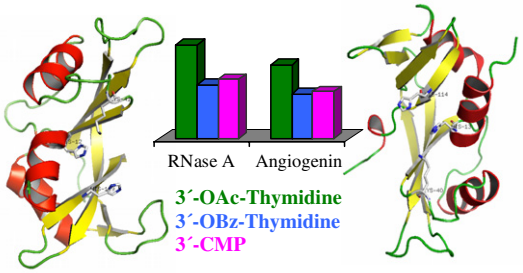


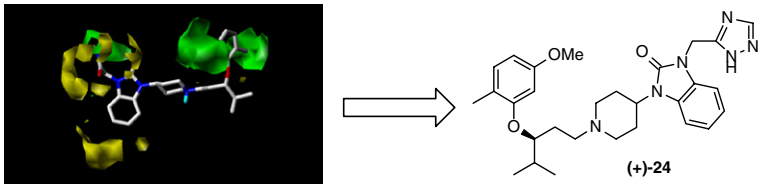
SAR analysis of 53 *N*-benzoylpyrazoles using atom pair descriptors and 2-dimensional molecular descriptors represents a simplified approach to predict inhibitors of human neutrophil elastase.

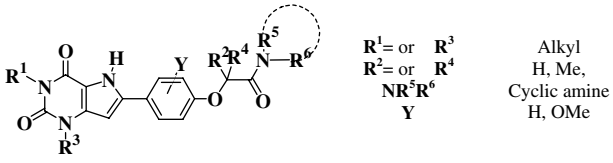
Nobiletin, a typical polymethoxy flavone from *Citrus*, had a preventive effect on H_2O_2-induced apoptosis at 20–30 mM in human neuroblastoma SH-SY5Y cells. Nobiletin acted as a signal modulator to attenuate the activation of intrinsic pathway in the apoptosis induced by H_2O_2 exposure. Tangeretin and 5-demethyl nobiletin, which are also polymethoxy flavones from *Citrus*, were shown to have a growth inhibitory effect. We found that tangeretin, nobiletin, and 5-demethyl nobiletin exhibited a cancelling, synergistic, or addition effect in various combinations of two compounds.

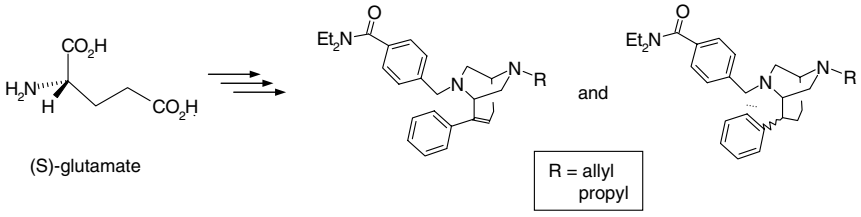


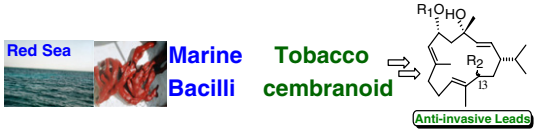


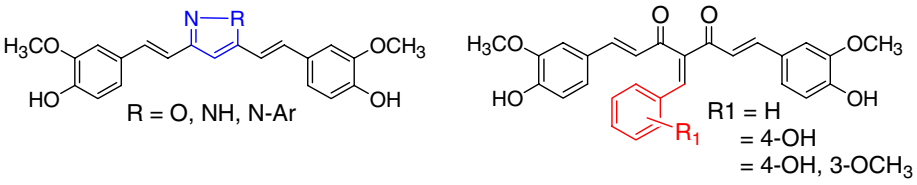




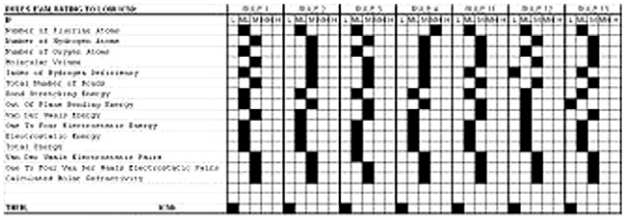




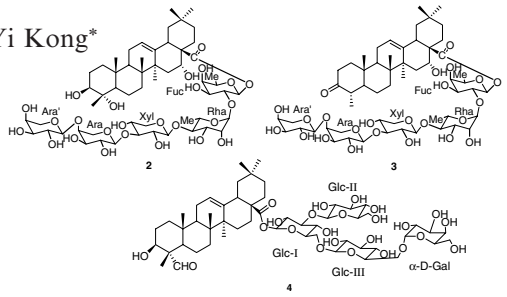




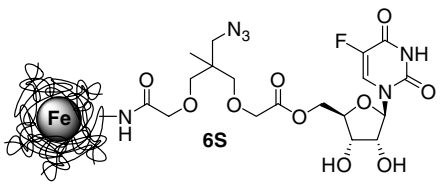
Novel curcumin analogues were prepared and evaluated for its anti-malarial activity against CQ-S and CQ-R *Plasmodium falciparum* culture. Compound **3**, **6** and **11** were found to be the most potent analogue with IC_{50} values 0.48, 0.87, and 0.92 μM against CQ-S and 0.45, 0.89, and 0.75 μM against CQ-R.



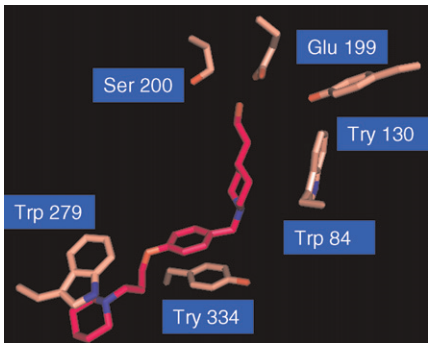
IF/THEN rules for IC_{50} predictions

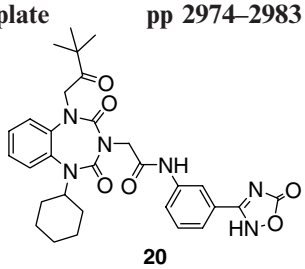


Seven new triterpenoid saponins have been isolated from the roots of *Gypsophila oldhamiana*, in which of them **2**–**4** showed significant inhibitory activities.



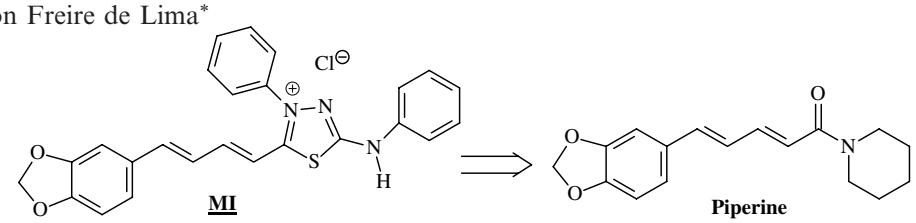
5-Fluorouridine-SPIONs were characterized and evaluated as anti-cancer agents using human melanoma cells. The 5-fluorouridine-SPION **6S** with an optimized ester linker was taken up by cells and proved to be efficient anti-tumor agent.





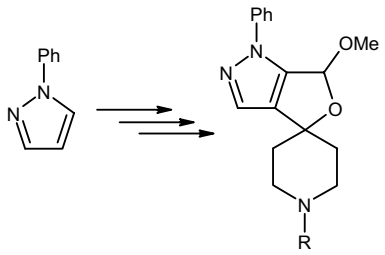
20

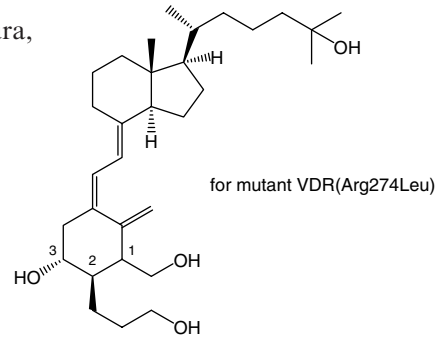
$pK_I = 8.92$ ($hCCK_2$)
$pK_I = 6.50$ ($hCCK_1$)

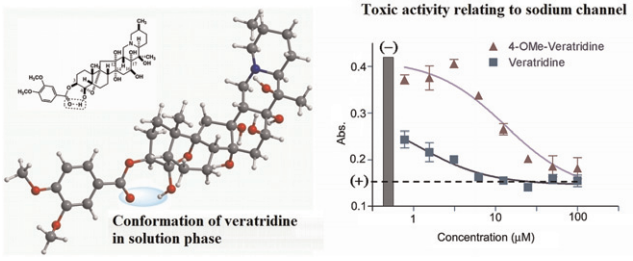


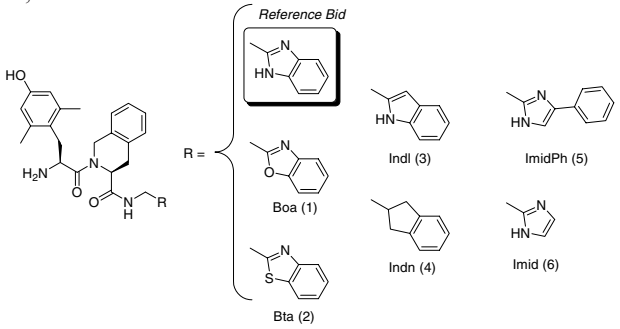
MI **Piperine**

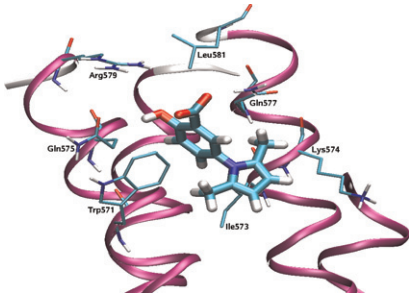
Synthesis and evaluation of trypanocidal activity of nine new 1,3,4-thiadiazolium-2-phenylamine chlorides derived from natural amide piperine are reported. Among them **MI** showed potent trypanocidal activity with reduced toxicity to macrophages.

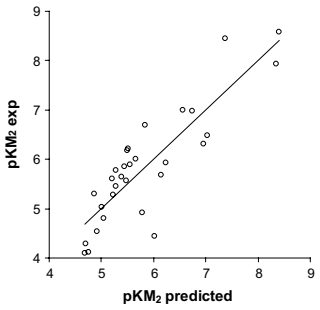


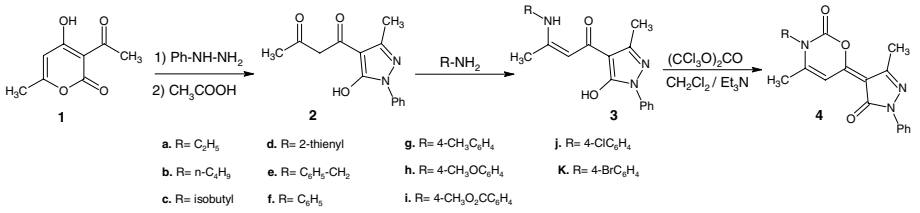




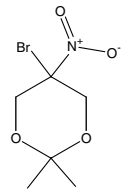




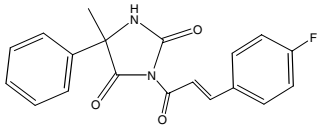




Eleven N-substituted pyrazolo-1,3-oxazin-2-ones were synthesised and their biological activity spectra were predicted by computer program PASS. COX-1 inhibitory activity of the compounds was confirmed by experimental data.



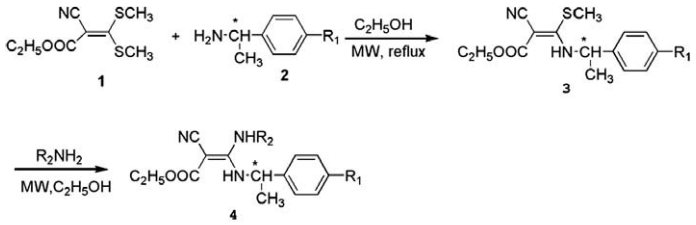
5-bromo-2,2-dimethyl-5-nitro-1,3-dioxane



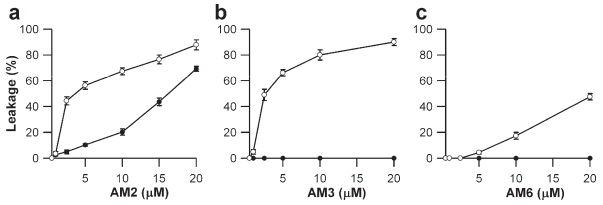
(E)-3-(3-(4-fluorophenyl)acryloyl)-5-methyl-5-phenylimidazolidine-2,4-dione

Representatives of two series that directly disrupt inactivation of the Kv1.1/β1 complex.

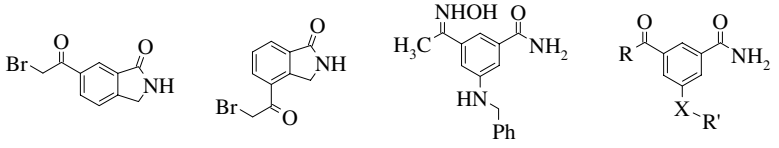
Nucleophilic attack of the appropriate amine under microwave irradiation on 3 generates the chiral (E) isomers of title compound **4** exhibiting weak to good anti-TMV bioactivity, (*R*)-4p showing significant enhancement of disease resistance in tobacco leaves.



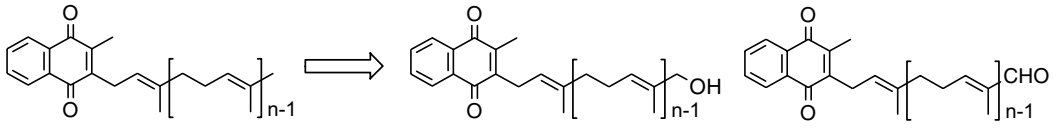
R1 : F, Br, H; R2 = benzylamino; 2-nitrophenylamino; 3-nitrophenylamino; 2, 4-dinitrophenylamino; 4-trifluoromethylphenylamino; 6-nitrobenzothiazol-2-amino; 4-methylbenzothiazole-2-amino.



Among amphidinols tested, only AM2 revealed membrane-permeabilizing activity to unsaturated lipid membrane.



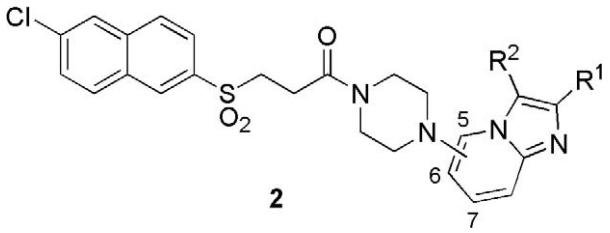
4 **5** **6**



menaquinone-n ω-hydroxyl menaquinones ω-aldehyde menaquinones

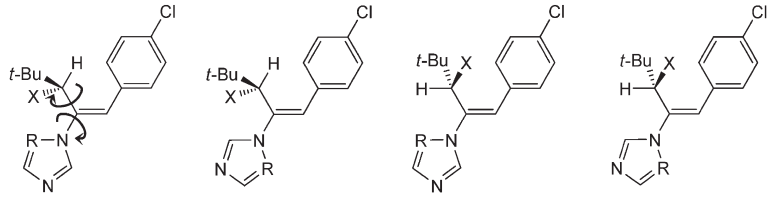
Novel ω-oxygenated vitamin K_2 analogues were efficiently synthesized and their biological activities were evaluated.

IC_{50} = 0.19 μM (U937 human lymphoma cells)

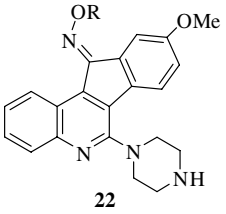


2

A new series of piperazinylimidazo[1,2-*a*]pyridines **2** as orally active FXa inhibitors are reported.

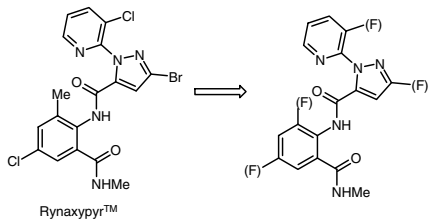


X = OH, OMe, F, H
R = N, CH



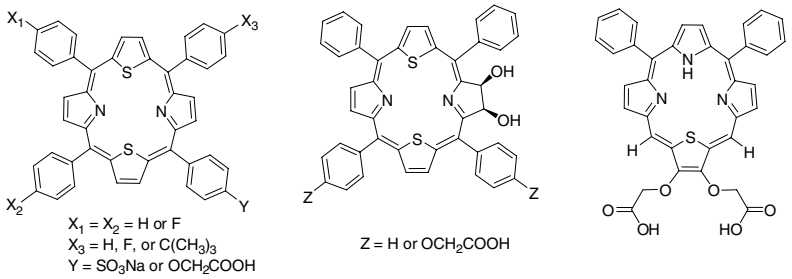
22

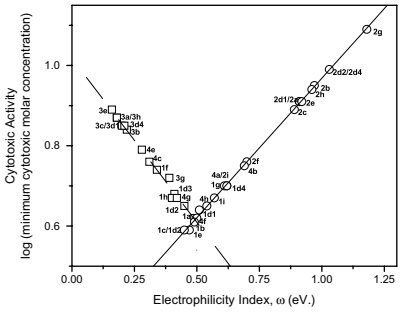
a: R = —$(CH_2)_2NMe_2$
b: R = —$(CH_2)_3NH_2$
c: R = —$(CH_2)_3NMe_2$
d: R = —$(CH_2)_2$—N
e: R = —CH_2

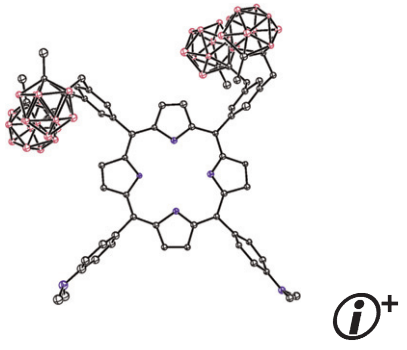


Rynaxypyr™

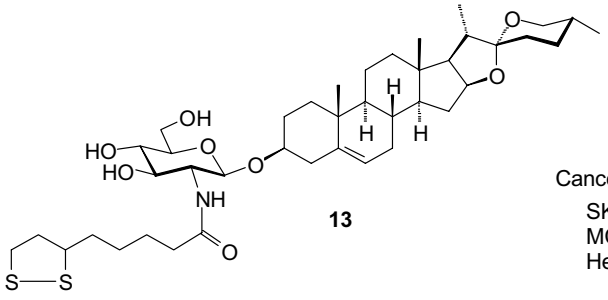
Fluorinated analogs of Rynaxypyr™ have been prepared in a search for plant-systemic insecticides for the control of Hemiptera.







The synthesis of *closo*-carboranylporphyrins containing either amine or phosphonic acid functionalities is described. These compounds show no dark cytotoxicity up to 100 μM, are readily taken up by human glioma T98G cells, deliver therapeutic amounts of boron to these cells, and localize preferentially within the lysosomes.



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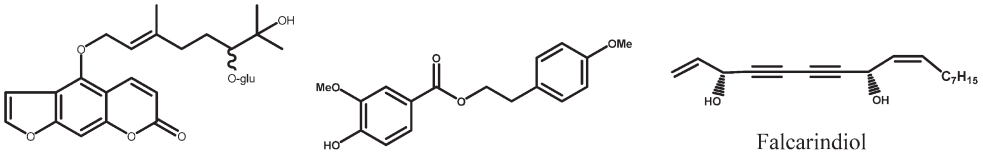
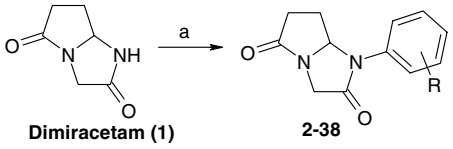
Cancer cell line	IC_{50} (μM)
SK-N-SH	4.8
MCF-7	6.9
HeLa	7.3

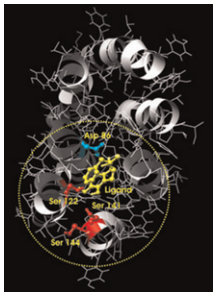


Falcarindiol

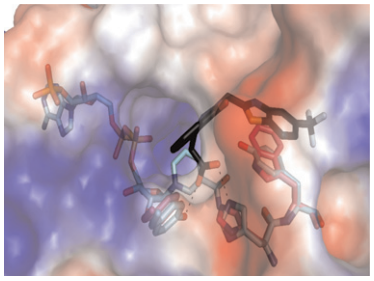
New coumarin glycoside and phenethyl vanillate, along with 17 known compounds, were isolated from *Notopterygium forbesii*. Falcarindiol showed the highest binding affinities to the opioid and dopamine receptors.



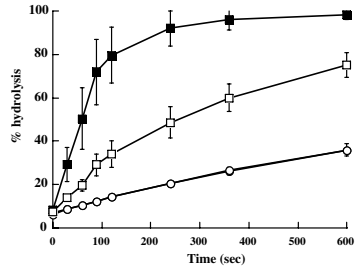
Dimiracetam (1) **2-38**

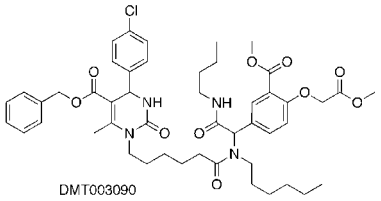


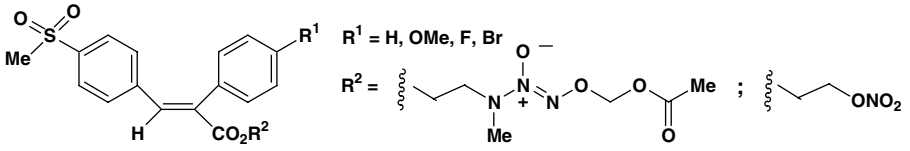
N-[2-(4,5-Dihydroxyphenyl)-methyl-ethyl]-4,5-dihydroxy-2-aminoindan hydrobromide (**3**) demonstrated an inhibitory effect on dopaminergic-induced behavior and renal action. In contrast *N*-[2-(-methyl-ethyl)]-4,5-dihydroxy-2-aminoindan hydrobromide (**4**) produces an agonistic response. To better understand the experimental results we performed molecular dynamics simulations of two complexes: compound **3**/D_2DAR (dopamine receptor) and compound **4**/D_2DAR.

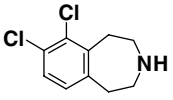


Aldose reductase (AR) inhibitors were evaluated against (3)17α-hydroxysteroid dehydrogenase (AKR1C21). Compounds that showed competitive inhibition patterns were modelled into the active site of AKR1C21 and the inhibitor-binding sites of the two enzymes were compared.



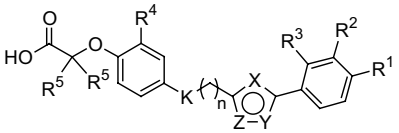




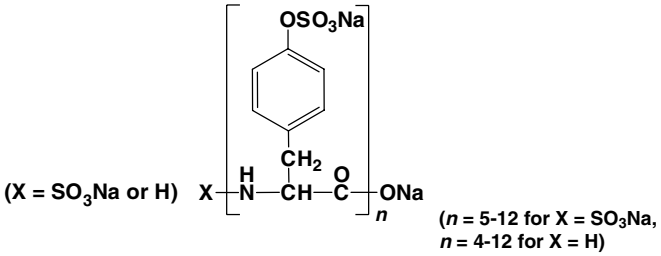


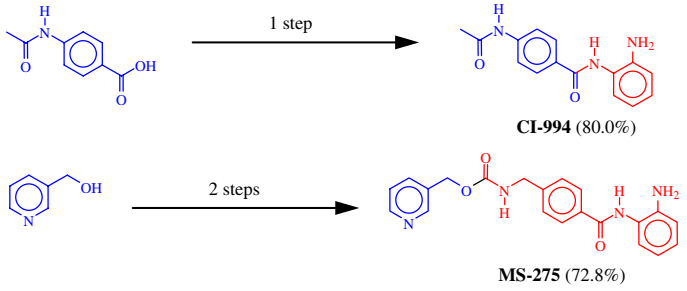
6

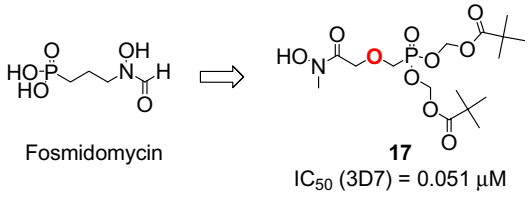
A novel series of benzazepine derivatives was prepared, and their binding affinities for 5-HT$_{2C}$, 5-HT$_{2A}$, and 5-HT$_{2B}$ receptors were evaluated. Synthesis and structure–activity relationships, including in vivo evaluation, are discussed.

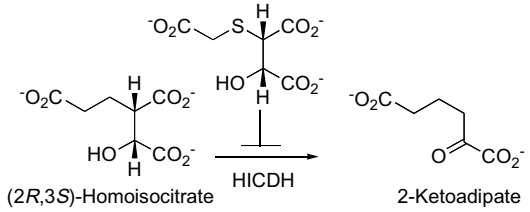


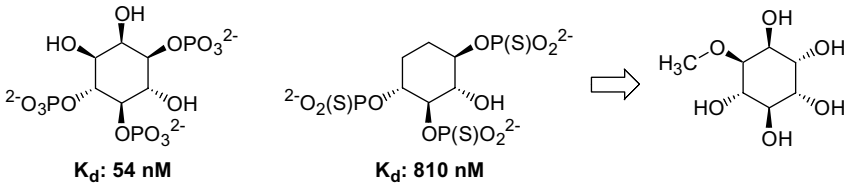
Using PPARδ selective agonist (GW501516) as the lead, we conducted the structure–activity relationship study and identified the [1,2,4]thiadiazole-derivatives as potent and orally active peroxisome proliferators-activated receptors α/δ dual agonists.

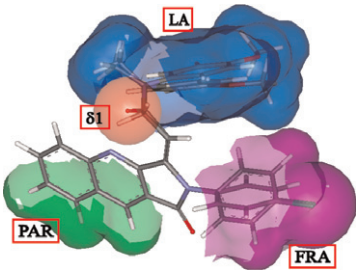


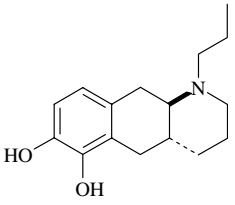




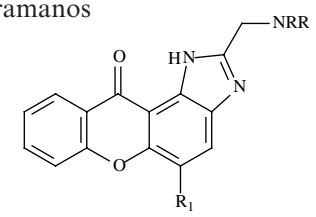




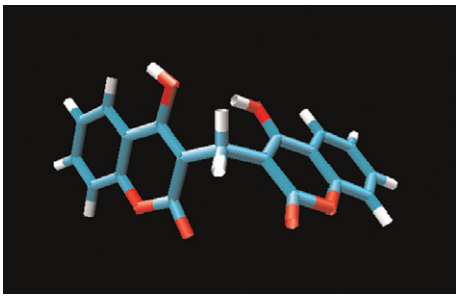




1-Propyl-1,2,3,4,4a,5,10,10a-octahydrobenzo[*g*]quinoline-6,7-diol is an extremely potent dopamine receptor agonist. As a catecholamine, this compound is comparable to apomorphine for the treatment of Parkinson's disease.



R_1= H, NO_2, $NHCOCH_2NRR$
NRR= $N(CH_3)_2$, $N(C_2H_5)_2$, $N(CH_2)_4$, $N(CH_2)_5$



OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

A deoxygenated phosphorothioate inositol phosphate analog binds to the inositol 1,4,5-trisphosphate [Ins(1,4,5)P_3] receptor and is resistant to metabolism. Figure was created using X-ray data downloaded from the protein data bank from the following publication: Bosanac, I., Alattia, J. R., Mal, T. K., Chan, J., Talarico, S., Tong, F. K., Tong, K. I., Yoshikawa, F., Furuichi, T., Iwai, M., Michikawa, T., Mikoshiba, K., Ikura, M. (2002) Structure of the inositol 1,4,5-trisphosphate receptor binding core in complex with its ligand. *Nature* 420: 696–700 [Liu, X.; Moody, E. C.; Hecht, S. S.; Sturla, S. J. *Bioorg. Med. Chem.* **2008,** *16,* 3429–3429].

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