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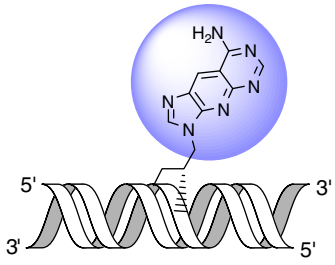
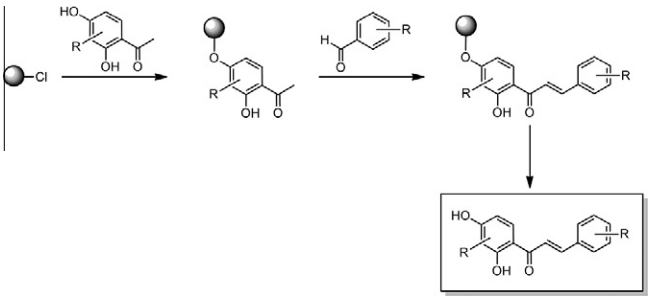
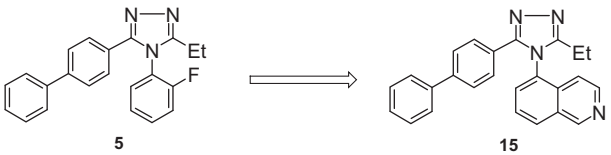
Contents

ARTICLES

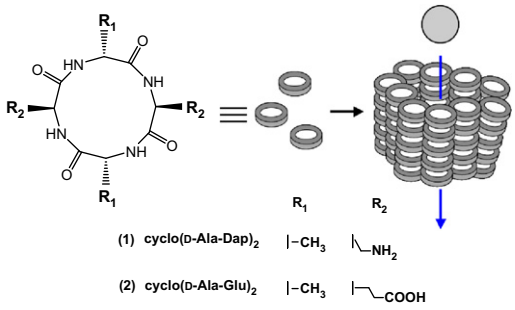


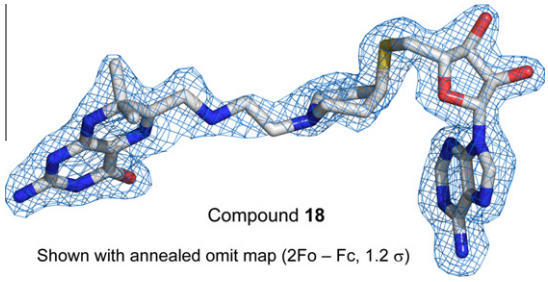


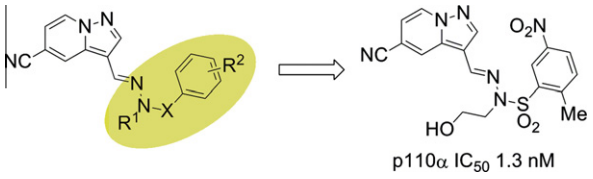
Thirty-one substituted 2′-hydroxychalcones were prepared via an aldol condensation via a solid-phase approach. Chalcones were tested for their growth inhibitory activity in three human tumor cell lines using a SRB assay. To gain further insight on the cellular mechanism of action of this class of compounds, studies of their effect on cell cycle profile as well as on induction of cellular apoptosis were also carried out.

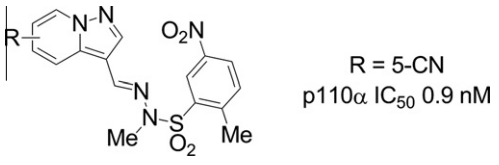


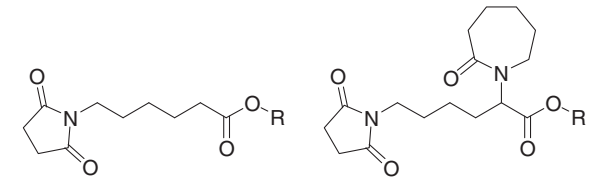
A series of 4*H*-1,2,4-triazole derivatives with heteroaromatic rings at the 4-position were synthesized as selective GlyT1 inhibitors. The modification of **5** led to identification of **15** with improved selectivity, solubility, and in vivo activity.



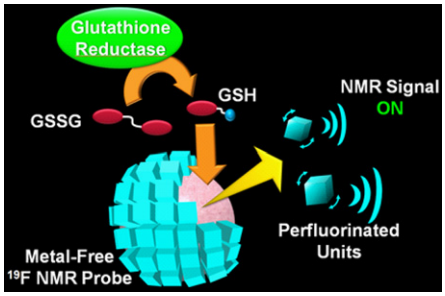


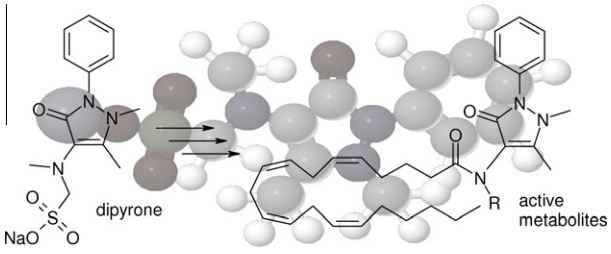




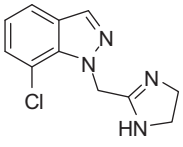


R = C_2H_5, C_6H_{13}, C_7H_{15}, C_8H_{17}, C_9H_{19}, $C_{10}H_{21}$, $C_{11}H_{23}$, $C_{12}H_{25}$

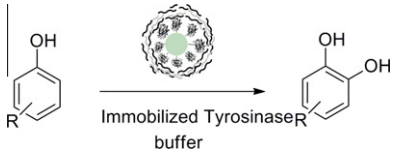


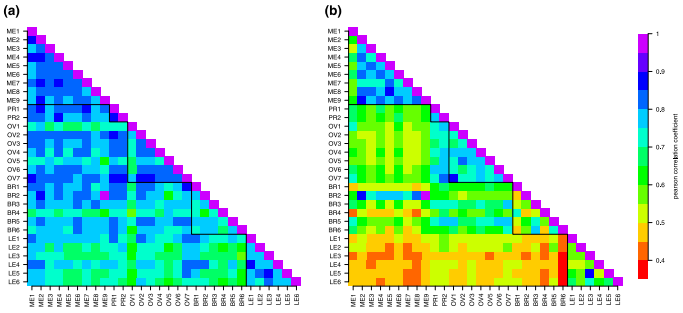


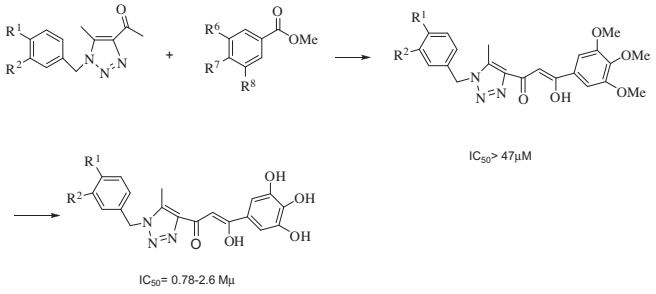
Biological activity *in vitro* :
α_1 K_i = 14.1 (nM)
α_2 K_i = 6.41 (nM)
negligible intrinsic activity
at human α_{2A} adrenoceptor



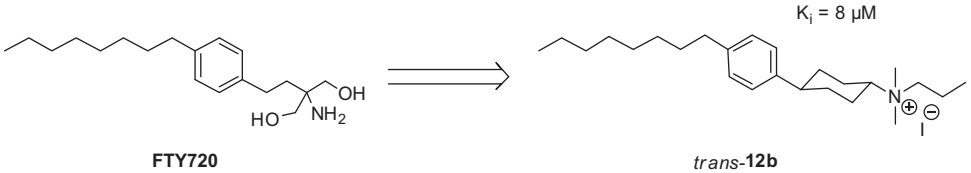
Circulatory effects in rats:
ΔMAP = -47.7 +/- 4.3 mmHg
ΔHR = -131.8 +/- 11.5 bpm
at dose 0.1 mg/kg i.v.



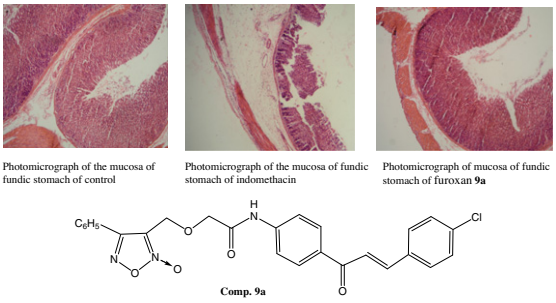


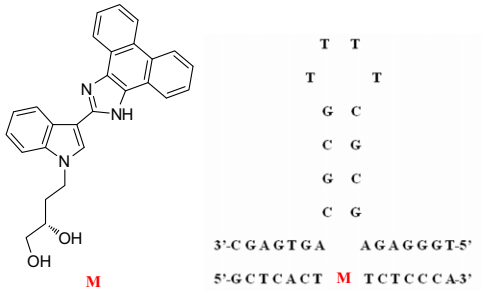


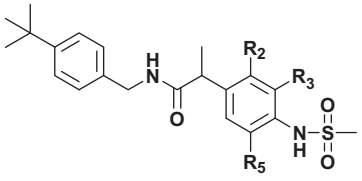
A series of novel β-diketo derivatives which combined the virtues of 1,3-diketo, 1,2,3-triazole and polyhydroxylated aromatics moieties were prepared and their HIV-1 IN inhibitory activities were evaluated. The polyhydroxylated aromatic moiety plays an important role in the inhibitory of HIV integrase.

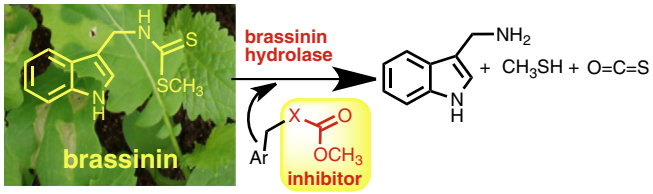


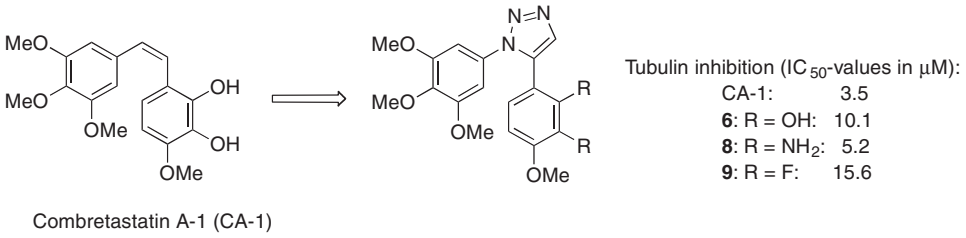
FTY720 *trans*-**12b**



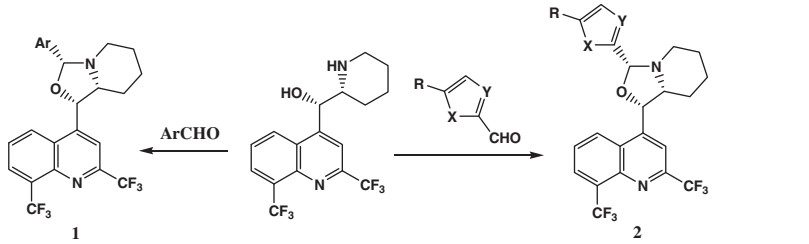






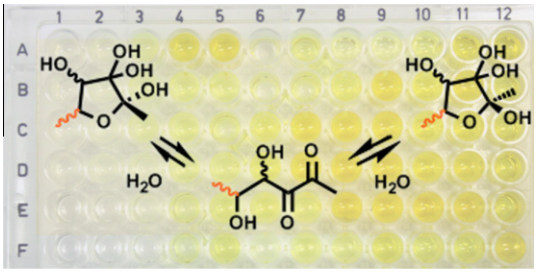


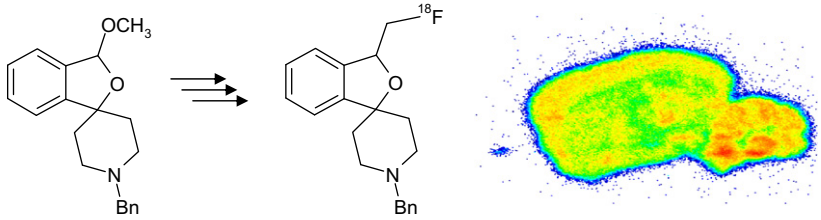
Combretastatin A-1 (CA-1)



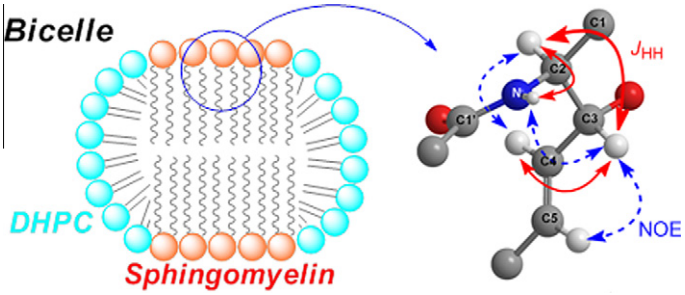
1 aryl = substituted phenyl

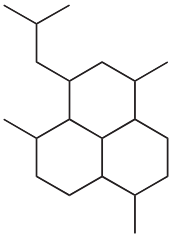
2 heteroaryl = 5-nitrothien-2-yl; 5-nitrofuran-2-yl and 4H-imidazol-2-yl

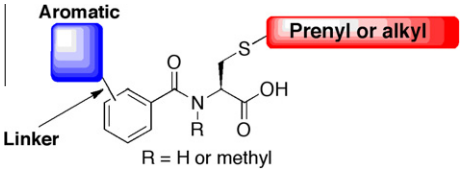


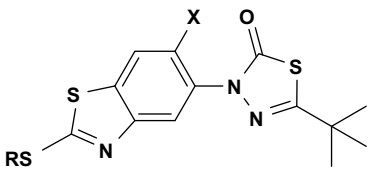


K_i (σ_1) = 0.74 nM

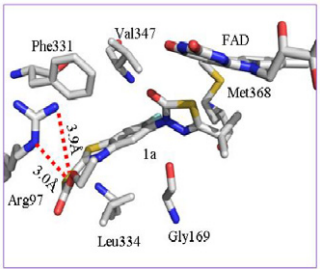


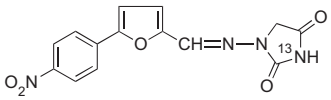




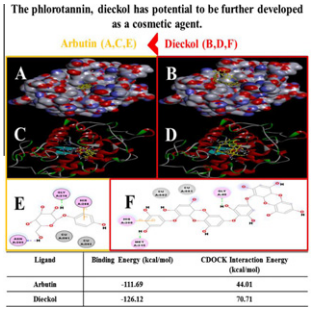


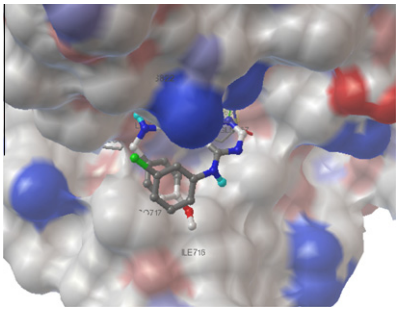
1a~w
1,3,4-Thiadiazol-2(*3H*)-ones



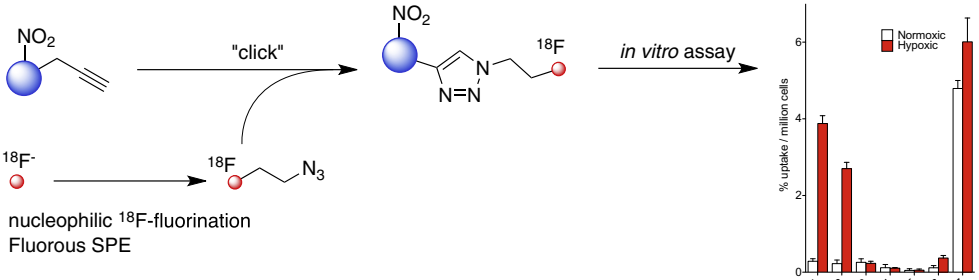


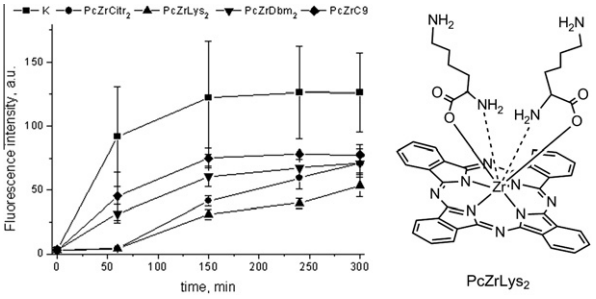
[^{13}N]dantrolene
([^{13}N]**1**)

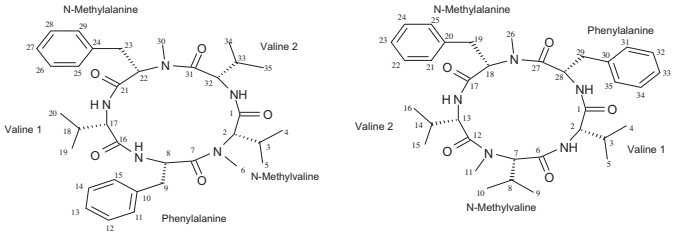




A type of novel 4,6-substituted-(diaphenylamino)quinazolines, which designed based on the 4-(phenylamino)quinazoline moiety, have been discovered as potential EGFR inhibitors. These compounds displayed good antiproliferative activity and EGFR-TK inhibitory activity. Especially, 4-((4-(3-bromophenylamino)quinazolin-6-ylamino)methyl)phenol (**5b**), showed the most potent inhibitory activity (IC_{50} = 0.28 μM for Hep G2, IC_{50} = 0.59 μM for A16-F10 and IC_{50} = 0.87 μM for EGFR) and effectively induces apoptosis in a dose-dependent manner in the Hep G2 cell line. Molecular docking of **5b** into EGFR TK active site was also performed. This inhibitor nicely fitting the active site might well explain its excellent inhibitory activity.

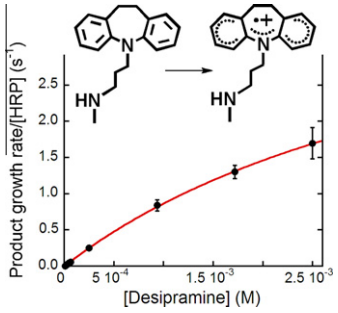


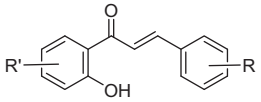




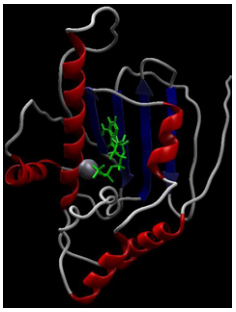
Persipeptide A (**1**) Persipeptide B (**2**)

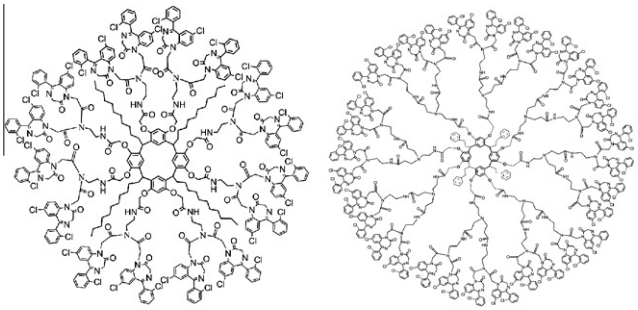
Two new N-methylated cyclopeptides, persipeptide A (**1**) and B (**2**), have been isolated from *Streptomyces* sp. UTMC1154. According to Marfey's method, all amino acids had the L-configuration. The two cyclic peptides had the same ring size and amino acid composition.

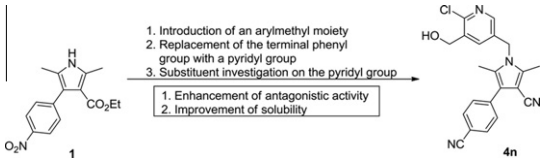




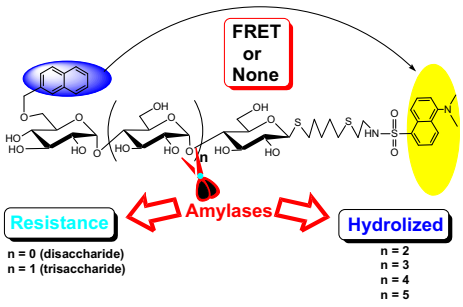
R'= OH, OCH_3, phenyl R = H, OCH_3, Cl

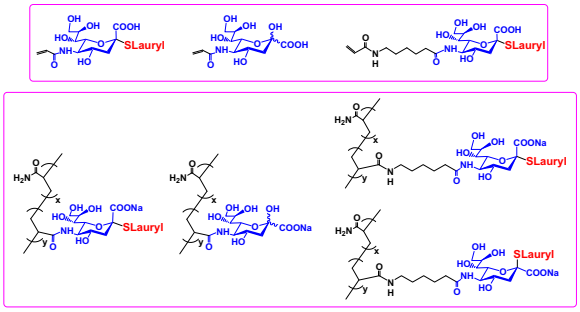


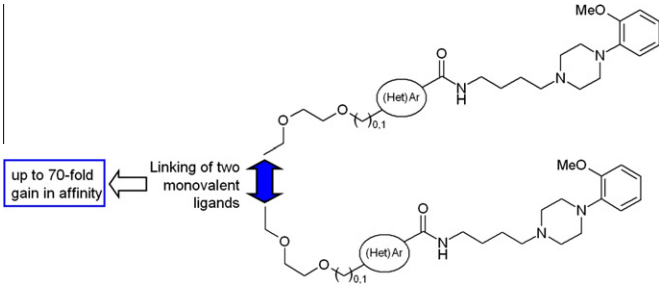


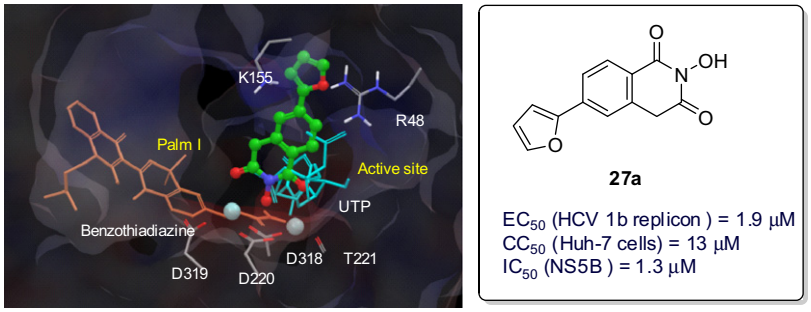


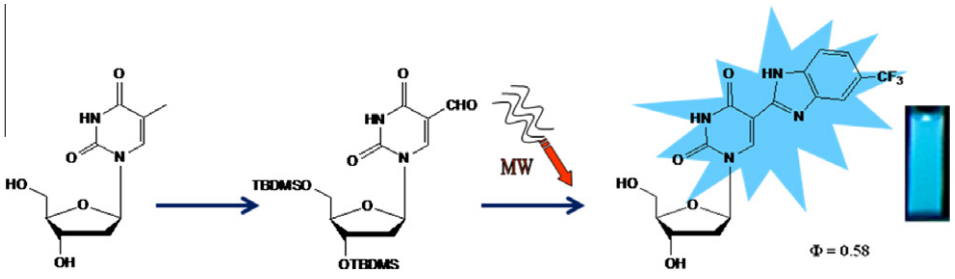
A series of 4-phenylpyrrole derivatives were designed, synthesized, and evaluated for their potential as novel orally available androgen receptor antagonists therapeutically effective against castration-resistant prostate cancers.

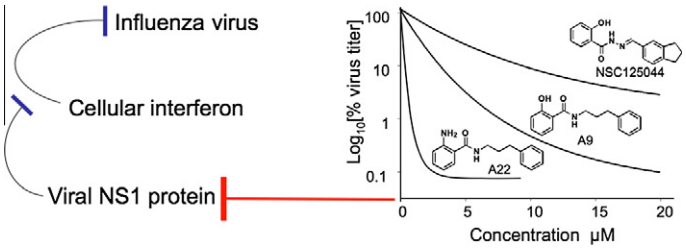


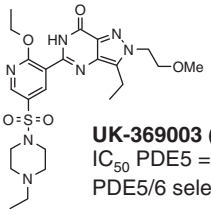






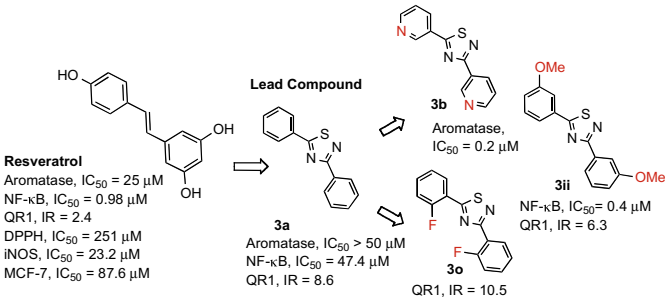


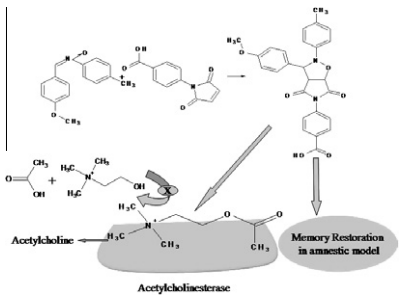




UK-369003 (19a)
IC_{50} PDE5 =1.23nM
PDE5/6 selectivity = 117

A potent series of PDE5 inhibitors has been synthesised which show PDE5 potency, selectivity over PDE6, metabolic stability and flux in the Caco-2 model of membrane permeability. The lead compound, UK-369003 (**19a**), has been progressed to man and shows efficacy in patients with lower urinary tract symptoms associated with benign prostate hyperplasia.





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*Corresponding author
ⓘ+ Supplementary data available via SciVerse ScienceDirect

COVER

Dipyrone (metamizol) is a common antipyretic drug and the most popular non-opioid analgesic in many countries. In spite of its long and widespread use, molecular details of its fate in the body are not fully known. Two unknown metabolites were now found, viz. arachidonoyl amides, and positively tested for cannabis receptor binding (CB1 and CB2) and cyclooxygenase inhibition. Two more puzzle pieces of the dipyrone story found! (Rogosch, T.; Sinning, C.; Podlewski, A.; Watzer, B.; Schlosburg, J.; Lichtman, A.H.; Cascio, M.G.; Bisogno, T.; Di Marzo, V.; Nüsing, R.; Imming, P. *Bioorg. Med. Chem.* **2012,** *20,* 103–109.]

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