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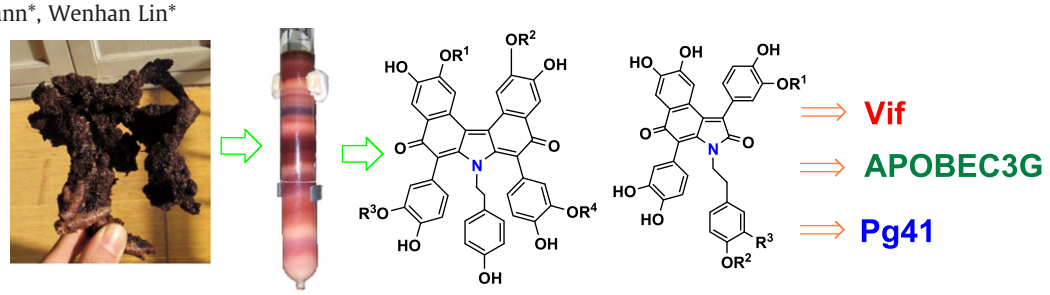
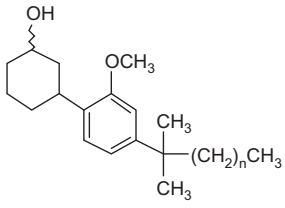
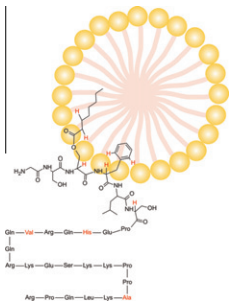
Contents

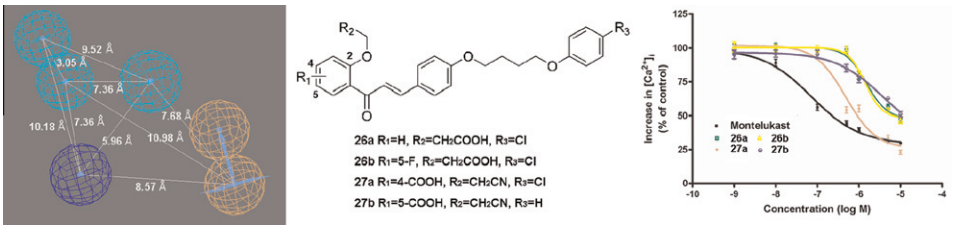
ARTICLES





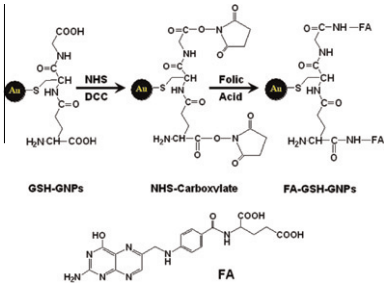
The synthesis and pharmacology of three 1-methoxy analogs of CP-47,497 (n = 4 and 5) are described. The CB_1 and CB_2 receptor affinities of these compounds are reported. Molecular modeling and receptor docking studies are presented.



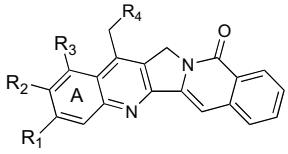


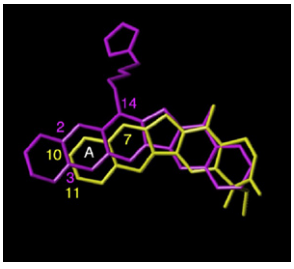
The pharmacophore model (Hypo1) for $CysLT_1$ antagonists was developed. Virtual screening against an in-house database using Hypo1 was performed. Retrieved hits **26a**,**b** and **27a**,**b** were synthesized and biological evaluated for their $CysLT_1$ antagonistic activities.

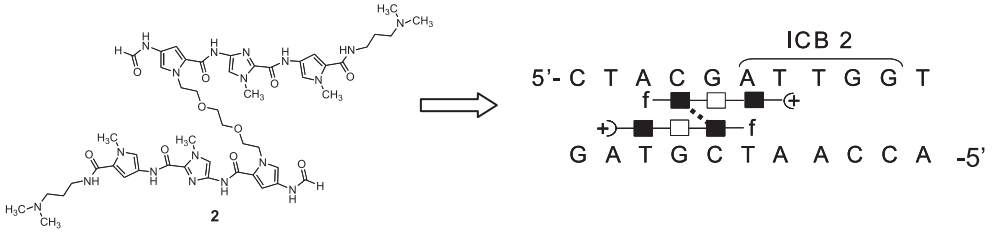
Folic acid-functionalized gold nanoparticles were prepared by a three-step approach. The thiol group of glutathione conjugates with gold nanoparticles through Au–S bond. DCC and NHS are used to activate the carboxyl groups of GSH, forming a highly reactive intermediate. The activated carboxyl groups react subsequently with the free amino group presented in folic acid, resulting in the formation of folic acid-conjugated nanoparticles.

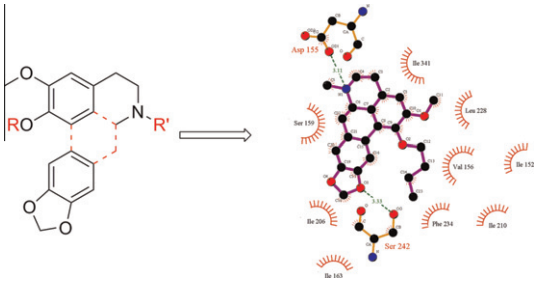


Novel aromathecins, substituted at four different positions, were prepared and evaluated against Top1 and human tumor cells. SAR trends mimic those of camptothecin and support our proposed camptothecin-like binding mode.



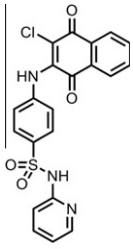




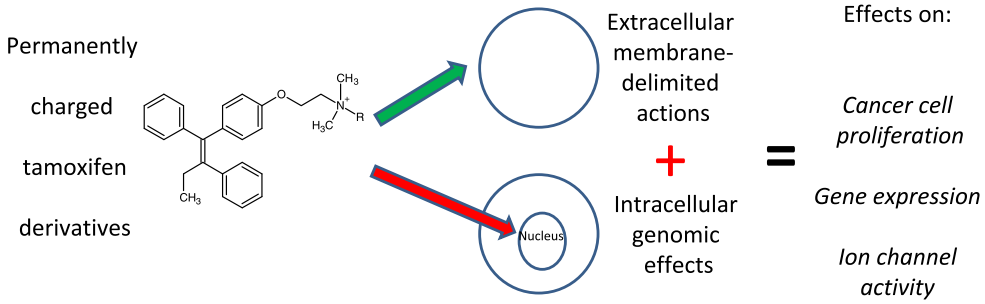


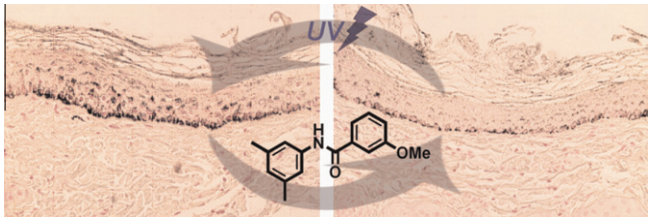
Homology modeling and docking. Thirteen examples.

PI-083 was identified as a chymotrypsin-like reversible proteasome inhibitor. A series of novel naphthoquinone derivatives were synthesized and evaluated for proteasome chymotrypsin-like activity. The SAR data showed pyridyl sulfonamide moiety in **PI-083** is crucial for activity. Other heterocyclic moieties such as thiazole, oxazole and thiadiazole moieties are tolerated.

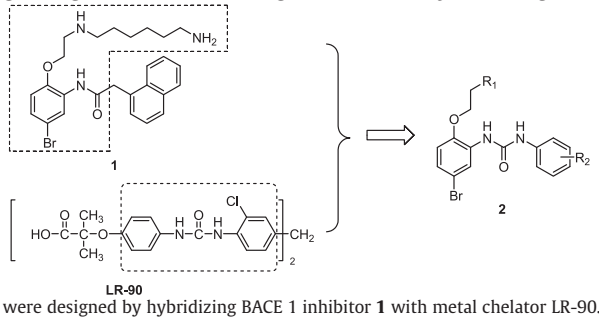


PI-083
(NSC-45382)

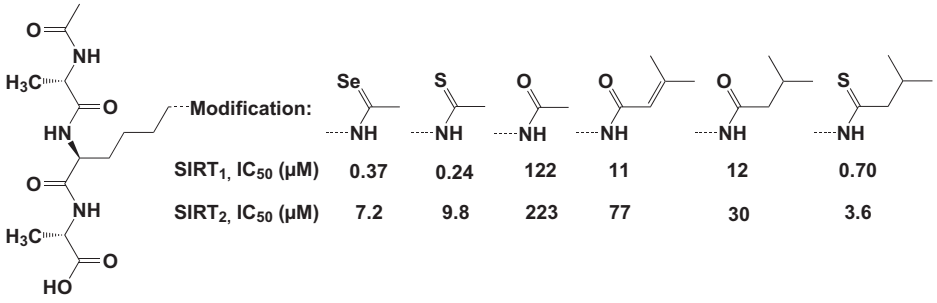


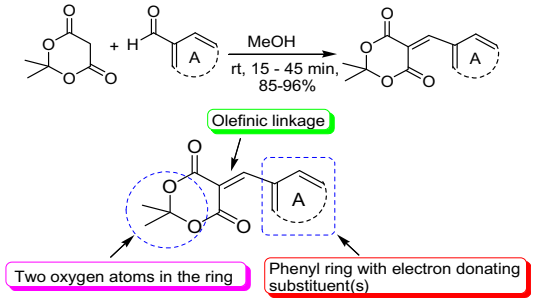


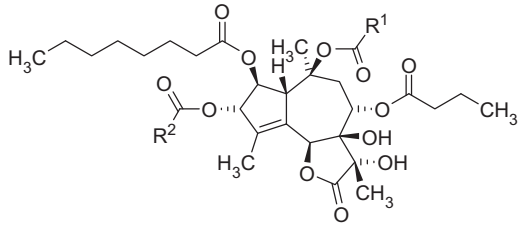
To discover safer and more effective compounds that reduce melanin production, the biaryl amide template was chosen. The use of parallel solution-phase synthesis techniques enabled the rapid preparation and identification of compounds with desired properties.

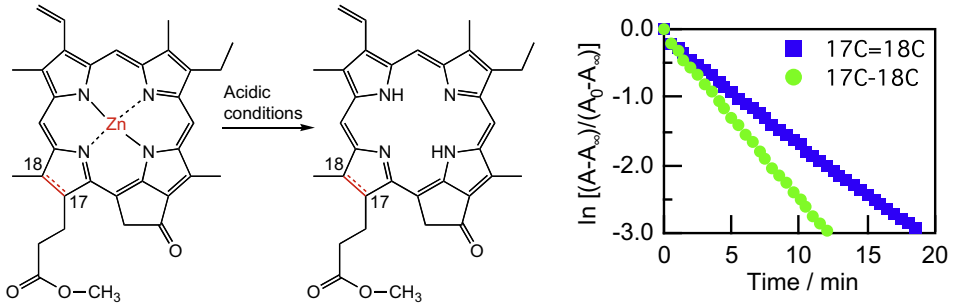


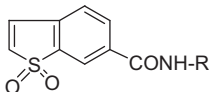
Dual-target-directed 1,3-diphenylurea derivatives were designed by hybridizing BACE 1 inhibitor **1** with metal chelator LR-90. Eleven compounds with favorable Fitvalues were selected, synthesized and evaluated for their BACE 1 inhibitory activities and the ability to function as metal chelators.







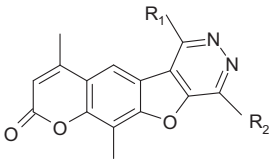




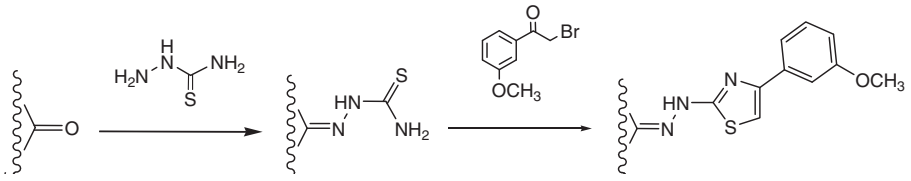
BTC

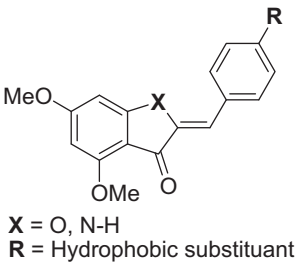
New BTC showed nM GI_{50} against HTB-54, CCRF-CEM and HeLa and sub-μM against K-562, MEL-AC and HT-29 tumour cell lines. BTC induced apoptosis in CCRF-CEM and a significant increase in the rate of intracellular ROS generation.

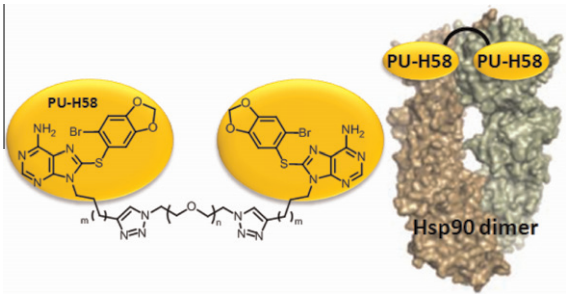
4: $R_1 = R_2 = H$
5: $R_1 = CONH(CH_2)_3N(CH_2CH_3)_2$; $R_2 = H$
6: $R_1 = R_2 = CONH(CH_2)_3N(CH_2CH_3)_2$
7: $R_1 = R_2 = CONH(CH_2)_3N(CH_3)_2$
8: $R_1 = R_2 = CONH(CH_2)_2N(CH_2CH_3)_2$
9: $R_1 = R_2 = CONH(CH_2)_2N(CH_3)_2$



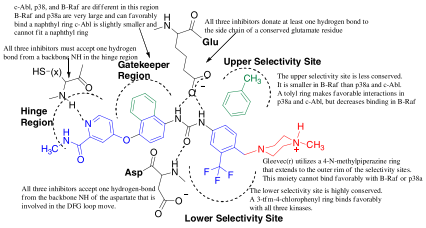
The synthesis of 6,10-dimethylpyridazino[4,5-*h*]psoralen derivatives is described. The new compounds demonstrate both a UVA-dependent and independent antiproliferative activity, intercalate into DNA and behave as topoisomerase II catalytic inhibitors.



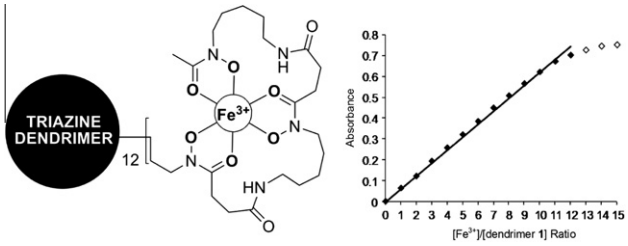




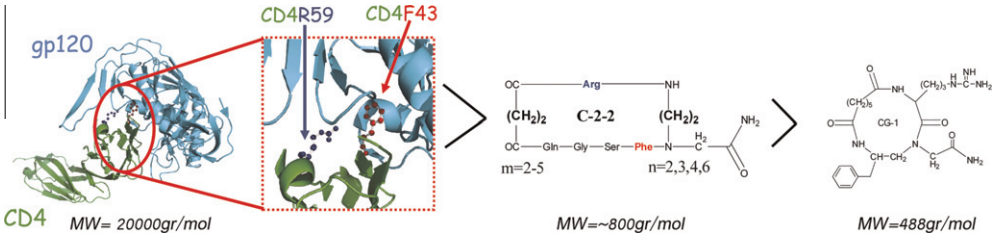
The PU-H58-dimers were designed as potential Hsp90 inhibitors and efficiently synthesized by the copper-catalyzed alkyne azide coupling (CuAAC) and their biological properties including binding affinity to the N-terminal domain of Hsp90, cytotoxicity, and client degradation activity were evaluated.



Here, we present a structural comparison of the important and similar interactions necessary for Gleevec®, Nexavar®, and BIRB-796 to bind to their respective DFG-out allosteric binding pockets and the selectivity of each with respect to c-Abl, B-Raf, and p38α. A structural analysis of their selectivity profiles has been generated from the synthesis and evaluation of eight additional DFG-out allosteric inhibitors that were developed directly from fragments of these successful scaffolds.



Spectrophotometry reveals noncooperative sequestration of Fe(III) by this multivalent, macromolecular compound.



Screening of backbone cyclic peptide library: an intermediate step in rational design of orally available macrocyclic HIV-1 infection inhibitor that mimics gp120 binding site in CD4.

*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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