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Chemistry

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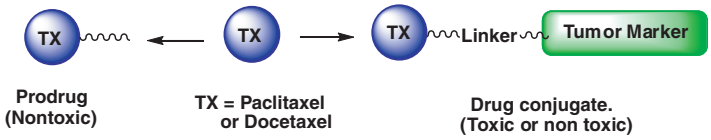
Contents

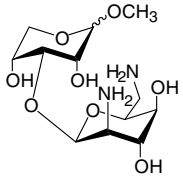
REVIEW



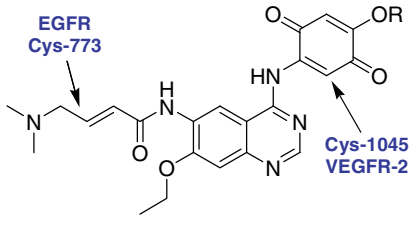
Paclitaxel (Taxol®) and docetaxel (Taxotere®) are very important anti-tumor drugs in clinical use for cancer. However, their clinical utility is limited due to systemic toxicity, low solubility, and inactivity against drug resistant tumors. To improve chemotherapeutic levels of these drugs, it would be highly desirable to design strategies which bypass the above limitations. In this respect various prodrug and drug targeting strategies have been envisioned either to improve oral bioavailability or tumor specific delivery of taxoids. Abnormal properties of cancer cells with respect to normal cells have guided in designing of these protocols. This review article records the designed biochemical strategies and their biological efficacies as potential taxoid chemotherapeutics.

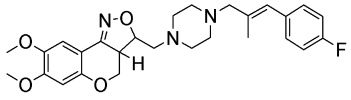
ARTICLES

Neomycin derivatives such as neamine, methyl neobiosaminide B, 2-deoxystreptamine, tetra-azidoneamine, tetra-*N*-acetylneamine, tetra-*N*-carboxy-benzylneamine, tetra-*N*-carboxy-methylneamine and tetra-*p*-methoxy-benzyliminoneamine were prepared and evaluated in cochlear and vestibular tissues and antibacterial screening. Methyl neobiosaminide B has shown the most selective vestibular activity suggesting its potential use in Ménière's disease.



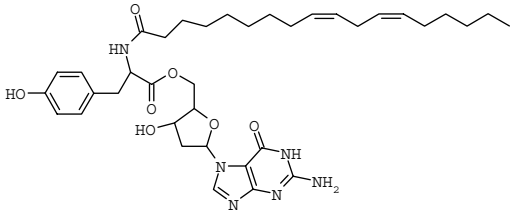
Compounds with two independent reactive centers were designed to function as dual irreversible inhibitors of the kinase domains of EGFR and VEGFR-2 where each reactive center targets a different, non-conserved, cysteine residue located in the ATP binding pocket of these enzymes.





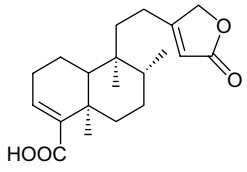
cis-(+)-5, R226161

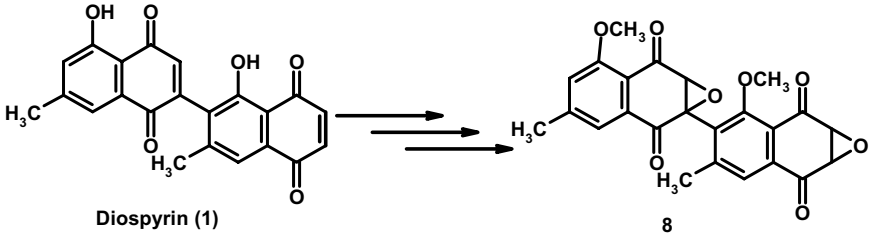
We report on the synthesis, in vitro binding and in vivo activity of R226161, identified within our series of tricyclic isoxazolines as a potential antidepressant combining 5-HT reuptake inhibition and α_2 antagonism.



(1) LTG

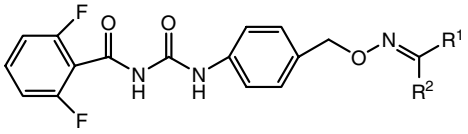
A novel marker was designed and synthesized for the characterization of oxidative stress in cells and organs. Analytical tools were developed to analyze products formed under its exposure to ROS.





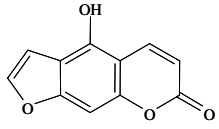
Diospyrin (1) 8

Novel quinonoids were produced through synthetic modification of diospyrin, a naturally occurring bioactive compound. The epoxide, **8**, proved to be the most potent derivative against three types of tumor cells, murine as well as human.

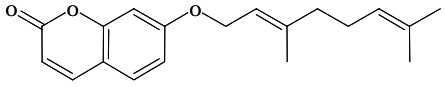


A variety of novel 1-(4-substitutedideneaminooxymethyl)-phenyl-3-(2,6-difluorobenzoyl)ureas were designed and synthesized by the reaction of 4-substitutedideneaminooxymethyl aniline with 2,6-difluorobenzoyl isocyanates in good yields. The title compounds were soluble in most organic solvents, which should make them easier to use. The preliminary bioassay showed that some of the title compounds show excellent insecticidal activity against *Mythimna separata* at the dosage of 25 mg kg^{-1} and moderate insecticidal activity against *Nephotettix cincticeps* at the dosage of 500 mg kg^{-1}. One title compound exhibited acaricidal activity against *Tetranychus urticae*.

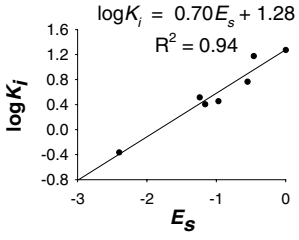
Bergaptol and geranylcoumarin were isolated from grapefruit and characterized using MS and NMR studies. Both the compounds were tested for their radical scavenging property using ABTS and DPPH methods. Bergaptol showed very good antioxidant potential and geranylcoumarin showed least activity. Further, these compounds were evaluated for cytochrome P450 CYP3A4 inhibition potential. Bergaptol and geranylcoumarin found to be potent inhibition of debenzylation activity of CYP3A4 enzyme with IC_{50} value of 24.92 and 42.93 μM, respectively.

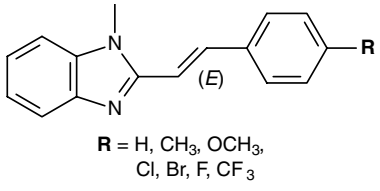


Bergaptol

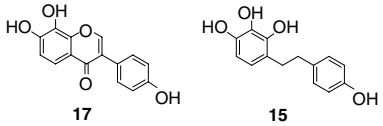


Geranylcoumarin



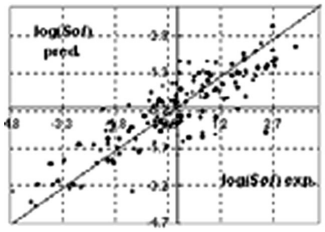


R = H, CH_3, OCH_3, Cl, Br, F, CF_3

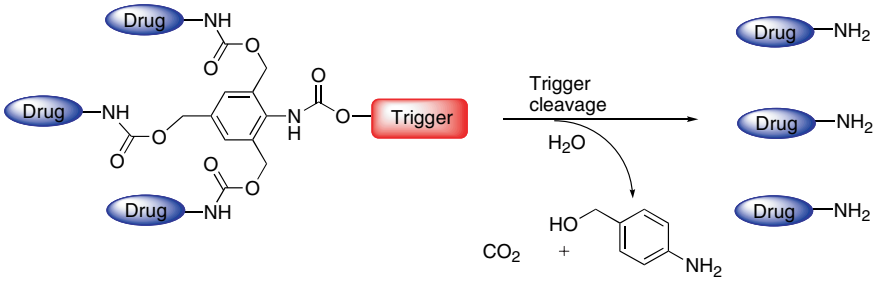


17 **15**

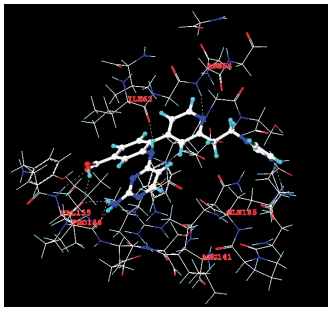
A series of polyphenols were synthesized and evaluated for inhibitory activity against *Helicobacter pylori* urease. Compounds **15** and **17** were the potent inhibitors with IC_{50} = 0.03 and 0.14 mM, respectively.

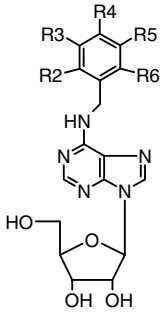


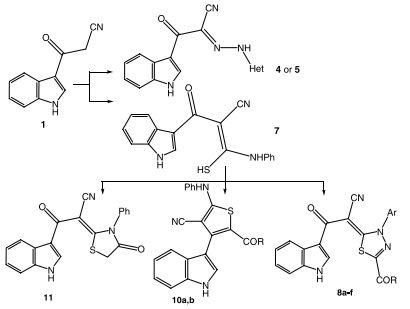
QSPR analysis for 148 drug-like compounds based on linear combinations of novel indices derived from Lipinski's 'rule of five' and Dragon-type of descriptor is described. Final solubility model is interpreted in structural terms.

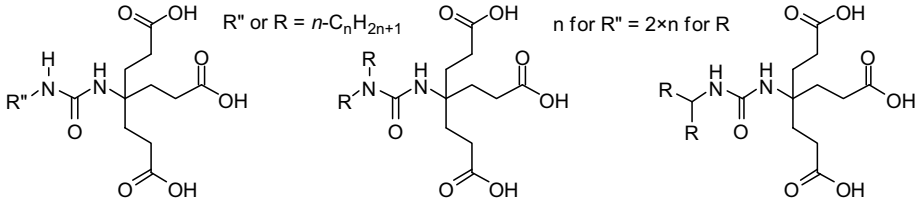


Structure based design has been successfully carried out to find a novel class of GSK-3 inhibitors using the Ludi de novo ligand design program. A total of 15 potential validated leads are suggested from the study.

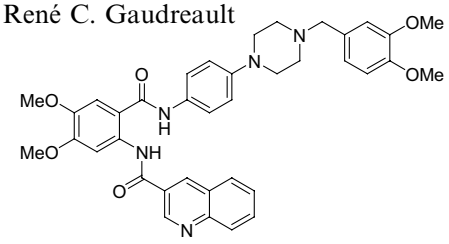




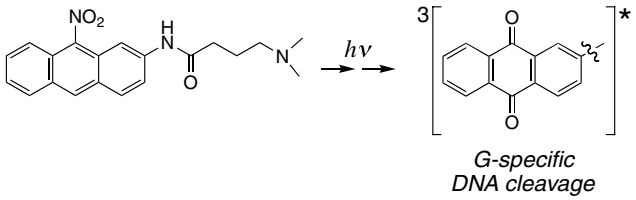


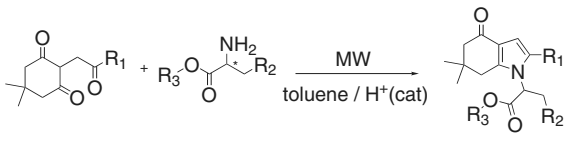


Antimicrobial activity of the water-soluble, dendritic tricarboxylato amphiphiles varies by microorganism as whether one or two tails or hydrophobicity or length predicts inhibition of growth.



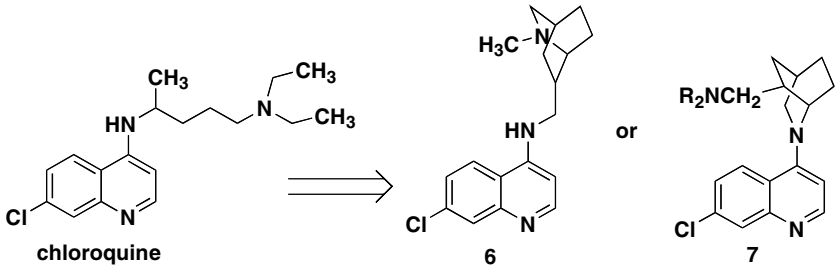
Synthesis and in vitro cytotoxicity assays of new anthranilamide MDR modulators have been performed to assess their potency of inhibition of P-glycoprotein (P-gp) and their effect on CYP450.



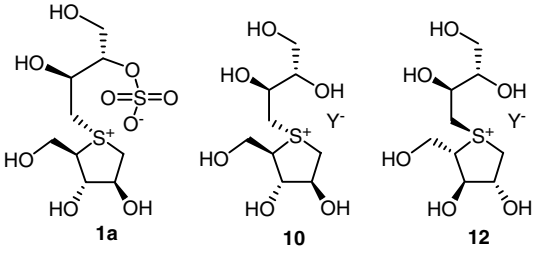


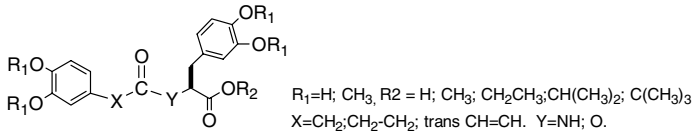
The new cytotoxic compounds with aminoacids residues incorporated were synthesized using the microwave technology. The *N*-(L)-cysteine ethyl ester derivatives inhibited the proliferation of all cancer cell lines tested.

The synthesis of new chloroquine analogs is reported. Some analogs showed good antimalarial activity against both chloroquine susceptible D6 and the resistant W2 strains of *Plasmodium falciparum*. All analogs also demonstrated significant antileishmanial activity.



Two de-O-sulfonated salacinols (**10a** and **10b**) and the diastereomer (**12a**) were synthesized and their inhibitory activity against intestinal α-glucosidase was examined. A potent inhibitory activity of **10a** and **10b** equal to that of **1a** against α-glucosidase indicated that the *O*-sulfonate anion moiety of **1a** is not essential for the inhibitory activity.





A series of non-peptide small antagonists for p56lck SH2 domain was synthesized and the binding affinity for the domain and in vitro T-cell inhibitory activity were measured.

OTHER CONTENTS

*Corresponding author
ⓘ+ Supplementary data available via ScienceDirect

COVER

Terfenadine (an antihistamine pulled from the market in 1997) bound to a model of an open form of the homo-tetrameric pore domain of hERG, produced using Schrödinger's ''Induced Fit Docking'' technology [Farid, R.; Day, T.; Friesner, R. A.; Pearlstein, R. A. *Bioorg. Med. Chem.* **2006,** *14*, 3160–3173].

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