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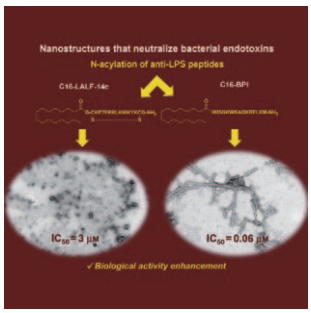
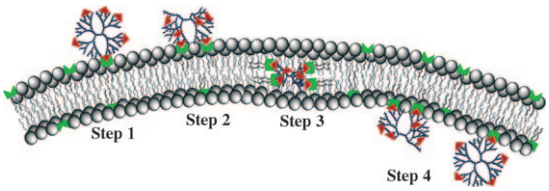
COVER PICTURE



The cover picture shows how the N-acylation (i.e. palmitoylation) of LPS-neutralizing peptides, LALF-14c and BPI, promotes the formation of well-defined nanostructures, such as micelles or fibrils. These peptides show greater biological activities than their nonacylated counterparts. For details, see the Full Paper by F. Albericio et al. on p. 1748 ff.

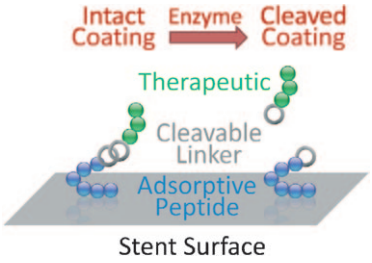
NEWS

MINIREVIEWS

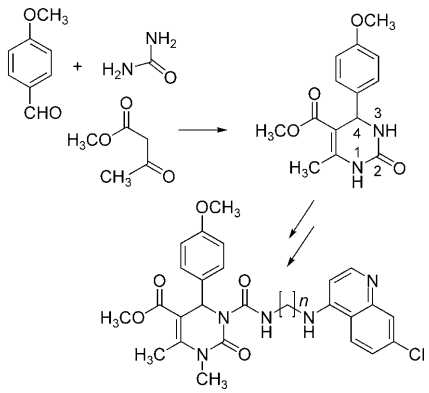


Intracellular delivery of therapeutic molecules is an issue of significant scientific and practical interest, especially in drug and gene delivery. Molecular transporters encompass a diversity of structures and aggregates that enable or enhance transport across biological membranes. In the present review the transport of guanidinylated dendritic polymers through model liposomal and cell membranes is addressed and the elucidation of their transport mechanism is also discussed.

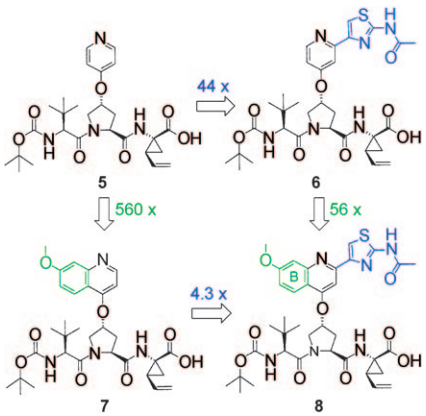
COMMUNICATIONS



Implanted medical devices inevitably promote inflammation of the surrounding tissue. A method for enzymatically triggered localized drug delivery would have marked benefits in dealing with this response. Herein we present a rationally designed peptide coating for use with medical devices such as stents, that contains three distinct domains: 1) an implant-adsorptive sequence, 2) an enzymatically cleavable release mechanism, and 3) a therapeutic to be delivered.

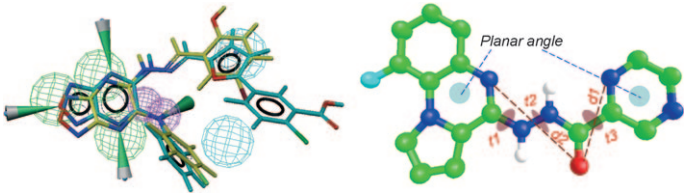


The synthesis, cytotoxicity, and antimalarial activity of resistance-reversing bifunctional dihydropyrimidone–chloroquinoline conjugates are reported herein. In vitro assay results indicate this class of compounds is highly active against both chloroquine-resistant and chloroquine-sensitive strains of *P. falciparum*.

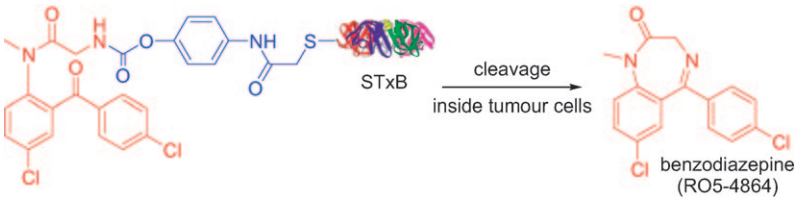


Things don't always add up: Our understanding of biomolecular recognition processes is often complicated by the fact that the binding contributions of individual ligand–protein subcontacts do not add up in a linear fashion. Chemical double-mutant cycles are useful analyses to quantify the degree of nonadditivity in such binding phenomena, and peptidyl inhibitors of hepatitis C virus NS3 protease are used to exemplify this.

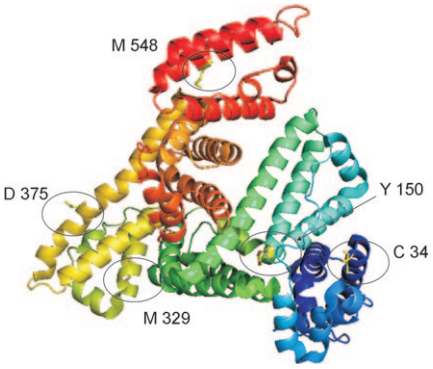
FULL PAPERS



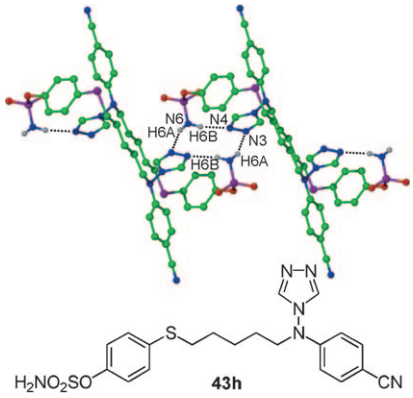
Predictive pharmacophores: Conformational sampling of a small lead molecule followed by representative pharmacophore model development is shown to be an efficient approach to the rational design of novel antitumor agents with similar or better potency over the original lead compound, but with different physicochemical properties.



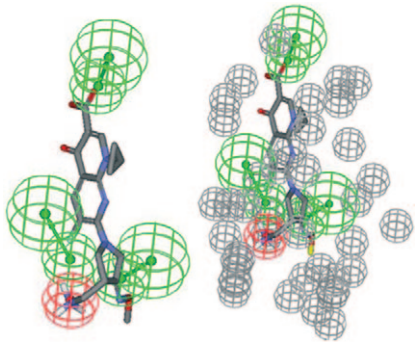
A water-soluble benzodiazepine: RO5-4864, a pro-apoptotic benzodiazepine, was solubilised by conjugation with STxB (B-subunit of Shiga toxin). After receptor recognition and internalisation of the prodrug, the active principle is released and kills tumour cells.



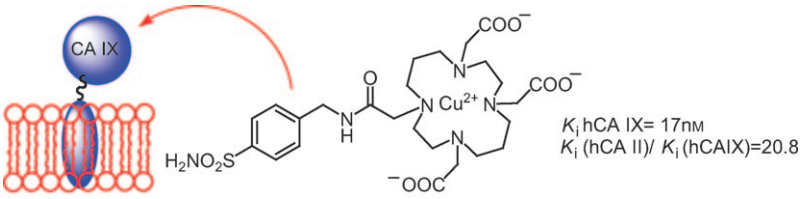
First oxygen, then sulfur: Combined biphasic liquid chromatography and ESI tandem mass spectrometry have been employed to identify specific cisplatin binding sites in blood serum proteins. Five coordinating residues were characterised for both human serum albumin (HSA) and serotransferrin (Trfe), including C34, M329 and M548 for the former, and M256 for the latter protein. The remaining residues all contain O-donor sites (D, E, T, Y), which also dominate for other abundant serum proteins.



Linking an aryl alcohol and aryl sulfamate motif to 4-(4*H*-1,2,4-triazol-4-ylamino)benzonitrile generates novel aromatase and dual aromatase–sulfatase inhibitors, respectively, some of which are amenable to X-ray crystallography. SAR using in vitro evaluation in JEG-3 cells shows that some aromatase inhibitors are remarkably potent, with IC_{50} values as low as 0.26 nM. A dual inhibitor shows potent in vivo oral activity and >90% inhibition of both enzymes.



Designing drugs for diabetes: Dipeptidyl peptidase deactivates the natural hypoglycemic incretin hormones. Inhibition of this enzyme should restore glucose homeostasis in diabetic patients making it an attractive target for the development of new antidiabetic drugs. Herein, the pharmacophoric space of DPP IV was explored using a set of 358 known inhibitors with the aiming of identifying possible lead compounds.



Copper carbonic anhydrase inhibitors: The synthesis of carbonic anhydrase inhibitors incorporating metal-complexing moieties was carried out. Complexation with copper gave impermeable inhibitors, which can target the transmembrane tumor associated CA IX. Incorporation of radioactive copper isotopes may lead to interesting diagnostic/therapeutic applications.

Supporting information on the WWW (see article for access details).

A video clip is available as Supporting Information on the WWW (see article for access details).

* Author to whom correspondence should be addressed.

BOOKS

SERVICE

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Issue 10, 2008, was published online on October 10, 2008.

