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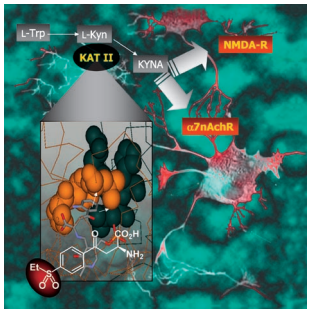
COVER PICTURE

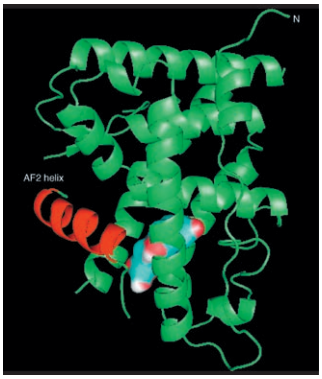


The cover picture shows one branch of the kynurenine pathway of tryptophan metabolism, which is mainly localized in astrocytes. One key metabolite, kynurenic acid (KYNA), is transported in the extracellular space, where it modulates synaptically localized $\alpha 7$ nicotinic acetylcholine receptors and NMDA receptors. The inset shows the active site of kynurenine aminotransferase II (KAT II), the enzyme that synthesizes KYNA in the CNS, and the structure of (*S*)-4-(ethylsulfonyl)benzoylalanine, a potent and selective KAT II inhibitor. Selective inhibition of KAT II may have a fundamental role in the understanding of CNS processes related to cognitive function. For more details, see the Communication by R. Pellicciari et al. on p. 528 ff. (Daniele Bellocchi is acknowledged for the cover image.)

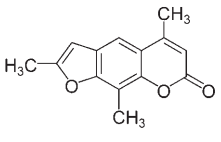
NEWS

REVIEWS

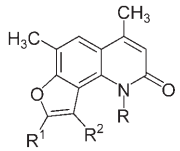
Targeting the nuclear receptors: The ligand-binding domain of the glucocorticoid receptor (ribbon) bound with the ligand, dexamethasone (space-filling) is just one of the many pictures that are becoming clearer in the field of nuclear receptor (NR) research. Recent developments in drug discovery show great promise for the treatment of many NR-related diseases.



COMMUNICATIONS

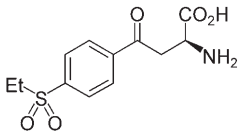


TMP



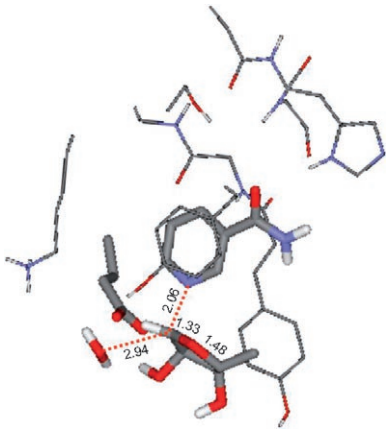
FQ: R = R^1 = CH_3; R^2 = H
HFQ: R = H; R^1 = R^2 = CH_3

TMP, FQ, and HFQ kill T4 phage under mild experimental conditions in its virion form, but not in its vegetative form. The process occurs through a two-step irradiation procedure, characteristic of DNA bifunctional lesions. We hypothesize the induction of DNA–protein cross-links in mature phages that can inhibit the infection process.

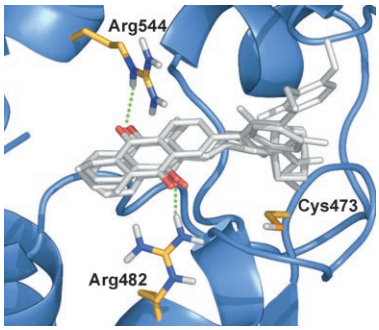


(*S*)-4-(Ethylsulfonyl)benzoylalanine is a potent and selective inhibitor of kynurenine aminotransferase II (KAT II) with no significant effect on KAT I or other enzymes of the kynurenine pathway. This compound is able to pronouncedly inhibit the formation of kynurenic acid (KYNA) in rat brain.

FULL PAPERS



Poly(ADP-ribose) polymerase, a nuclear enzyme activated by DNA single-strand breaks, is an attractive target for a variety of diseases. A combined quantum mechanics/molecular mechanics study was performed with the aim of gaining insight into the catalytic mechanism of PARP-mediated hydrolysis. The results obtained are useful for the design of transition-state analogues as inhibitors.



Using the crystal structure of Cdc25B, we performed docking simulations to produce structural models for the interaction of different Cdc25B inhibitors with this enzyme. The coherent picture of possible interactions of the inhibitors with the active site provides an improved basis for structure-based ligand design and suggests a possible explanation for the inhibition mechanism.

CONTENTS

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

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BOOKS

SERVICE

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