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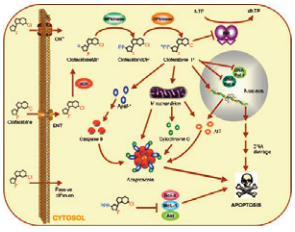
Contents

COMMENTARY

Mechanisms of anti-cancer action and pharmacology of clofarabine 1351–1359

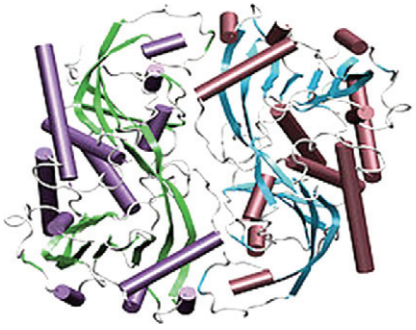
Anna Zhenchuk, Koroush Lotfi, Gunnar Juliusson, Freidoun Albertioni

Clofarabine's mechanism of action. Upon entering the cell, clofarabine is phosphorylated stepwise by deoxycytidine kinase (dCK), monophosphate kinase (MPkinase), and diphosphate kinase (DPkinase) to its triphosphate active form (clofarabineTP). ClofarabineTP acts as an inhibitor of DNA polymerase-α (DMA pol α) and -ε (DNA pol ε) by competing with the natural substrate dATP. When incorporated into DNA clofarabine leads to DNA damage, which signals activation or apoptotic pathways. It can further inhibit ribonucleotide reductase (RR), causing dNTP pool reduction and thus reinforcing its own incorporation into DNA. By directly affecting the mitochondrial transmembrane potential, clofarabine releases cytochrome c and apoptosis-inducing factor (AIF).



Commentary: Genome-based CNS drug discovery: D-Amino acid oxidase (DAAO) as a novel target for antipsychotic medications: Progress and challenges 1360–1365

Michael Williams



D-amino-acid oxidase

Image Courtesy of Wikipedia
http://en.wikipedia.org/w/index.php?title=D-amino_acid_oxidase&oldid=290629578

ANTIBIOTICS AND CHEMOTHERAPEUTICS

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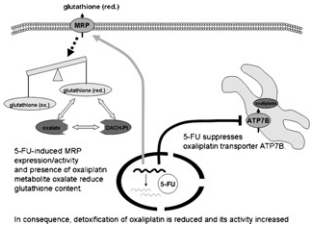
Dirk Theile, Sina Grebhardt, Walter Emil Haefeli, Johanna Weiss



doi:10.1016/S0006-2952(09)00834-X

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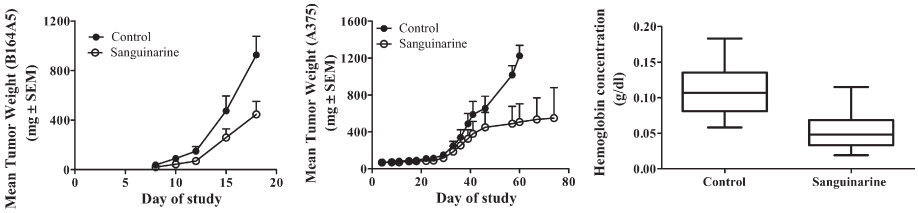

Inflammation and Immunopharmacology

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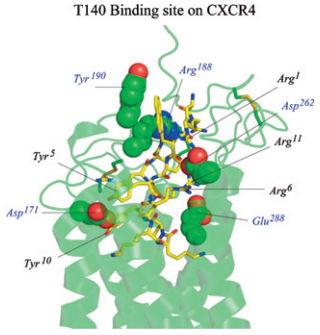
Philip E. Boulais, Dominic Dulude, Jérôme Cabana, Nikolaus Heveker, Emanuel Escher, Pierre Lavigne, Richard Leduc



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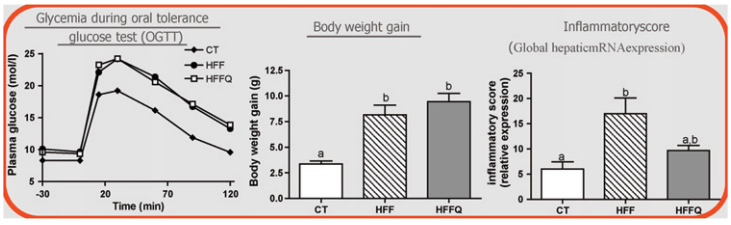
Florence M. Sohet, Audrey M. Neyrinck, Barbara D. Pachikian, Fabienne C. de Backer, Laure B. Bindels, Petra Niklowitz, Thomas Menke, Patrice D. Cani, Nathalie M. Delzenne



Neuropharmacology

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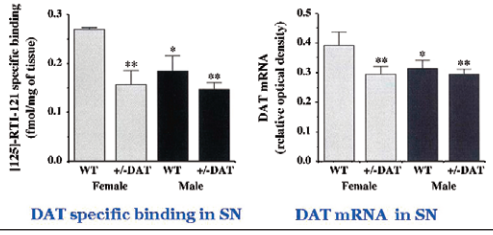
Jing Ji, Mélanie Bourque, Thérèse Di Paolo, Dean E. Dluzen

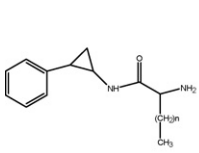


PHARMACOKINETICS AND DRUG METABOLISM

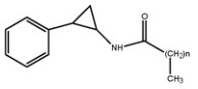
TCP-FA4: A derivative of tranylcypromine showing improved blood–brain permeability **1412–1417**

Kelly E. Desino, Rosario Pignatello, Salvatore Guccione, Livia Basile, Sabah Ansar, Mary Lou Michaelis, Rona R. Ramsay, Kenneth L. Audus

Derivatives of TCP containing FA or LAA moieties of varying side alkyl chain length were synthesized in an attempt to improve BBB permeability, by increasing the lipophilicity as well as amphiphatic character of the drug molecule. Results suggested that LAA promoieties containing medium to long side alkyl chains would be most useful in improving the permeability and membrane interaction of these compounds. TCP-FA4 may possess neuroprotective properties.



Compound	n
TCP-LAA6	3
TCP-LAA10	7
TCP-LAA12	9



Compound	n
TCP-FA4	2
TCP-FA12	10

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