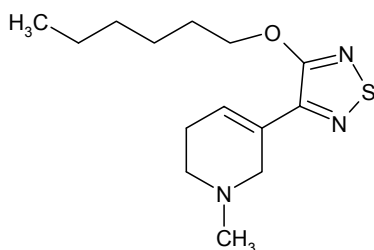


Enzymes and Receptors

1. One concept that has been mentioned few times in the course is the “purine salvage pathway”. Discuss the importance of this pathway in normal human metabolism and in the context of the life cycle of intracellular parasites. Use a chemical drawing program, such as IsisDraw, freely available from <http://www.mdli.com/> to make a reaction scheme showing how free guanine is salvaged.
2. Discuss the diverse roles of matrix metalloproteinases in humans. Identify three diseases in which involvement of matrix metalloproteinase has been suggested to play an important role. Provide one reference per disease to the original research literature (not to a review paper) where matrix metalloproteinase was shown to be linked to a disease.
3. The compound shown below was found to be effective agonist of the M1 subtype of muscarinic acetylcholine receptor and serves as a one of the leads to develop drugs to treat Alzheimer's disease.



- a) Name three roles of the muscarinic acetylcholine receptor in human body.
- b) What are the two main differences between the nicotinic acetylcholine receptor and the muscarinic acetylcholine receptor?
- c) The strength of hydrophobic interaction between a receptor and its ligand generally increases as the hydrophobic surface area of the ligand increases. For example, the analog with methyl ether side-chain binds about 10 times weaker than the hexyl ether analog shown above. Comment on the proposal that in order to further increase the efficacy of orally administered Alzheimer's drug, a significantly longer (e.g. decyl) alkyl ether side-chain analogs should be used. (*See the textbook for hints*)

Project development.

You will be submitting a drug design proposal at the end of this course. As a first part of this project, you are expected to identify a disease that you want to work on. As part of your second assignment, submit one-page outline where you discuss the nature of the disease, give statistics concerning its prevalence and mortality, and discuss current approaches that are used to tackle this disease.