

**Homework 4**

**ENZYMES**

**Medicinal Chemistry 1**

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1. **(2)** The active site of AChE has 2 subsites Anionic site and Esteratic subsite.  
     
   The anionic subsite accommodates the positive quaternary amine of acetylcholine as well as other cationic substrates and inhibitors. The cationic substrates are not bound by a negatively-charged amino acid in the anionic site, but by interaction of 14 aromatic residues that line the gorge leading to the active site.  
     
   The esteratic subsite, where acetylcholine is hydrolyzed to acetate and choline, contains the catalytic triad of three amino acids: serine 200, histidine 440 and glutamate 327.The hydrolysis reaction of the carboxyl ester leads to the formation of an acyl-enzyme and free choline. Then, the acyl-enzyme undergoes nucleophilic attack by a water molecule, assisted by the histidine 440 group, liberating acetic acid and regenerating the free enzyme.
2. **(3)** Mechanism similar to that described for the hydrolysis of peptide bonds by chymotrypsin would be feasible involving a cataytic traid of serine, histidine and aspartate ( or glutamate). Serine would serve as nucleophile, histidine as an acid/base catalyst and asparate (or glutamate) as an activating and orientating group.