

CARDIOVASCULAR DISEASE PROBLEM # 2

CHEMISTRY 161

Spring, 2009

Due Date: March 9th

- High cholesterol is one of the strongest predictors for coronary artery disease. Statins are a class of drugs used to treat high cholesterol. Statins work by inhibiting the enzyme HMG-CoA reductase.
 - Show the complete reaction (structures of reactants and products) catalyzed by this enzyme.
 - Why does inhibiting this enzyme result in lower blood cholesterol? Cite your source.
 - One of the most widely prescribed statins has the tradename Lovastatin. Shown below are some data collected for HMG-CoA reductase in the presence and absence of this drug. Plot the data in both Michaelis-Menten and Lineweaver-Burk formats and determine the K_m and V_{max} in the presence and absence of Lovastatin. *In your answer, provide the K_m and V_{max} determined using both types of plots (M-M and L-B).* Use this data to determine what type of inhibition Lovastatin confers on the enzyme. Use Excel and attach your plots to your problem set. V_o is in $\mu\text{mol}/\text{min}$.

S (mM)	V_o (-)	V_o (+)
0	0	0
0.05	11.1	6.8
0.1	16.39	10.2
0.125	18.5	11.76
0.25	21.2	14.9
0.5	23.6	19.5
0.75	24.4	21.6
1	25	23.3

- Provide a detailed mechanism for the reaction of DIFP with acetylcholinesterase, using a serine side from the AChase active site as one of the reactants. Assume an S_N2 reaction with formation of a tetrahedral intermediate.