Suicide Substrates

A very clever, if workable, idea for neutralizing an enzyme which is causing some unwanted effect in an organism (either on its own, or by catalyzing some unwanted reaction) was realized in the early 1980s. The basic idea is the following: suppose you introduce a dummy substrate which can also interact with the enzyme. In the enzyme-dummy complex, suppose there is a possibility that the enzyme configures into an inactive state which cannot be undone, so that we can assume the following series of chemical reactions:



You should assume the law of mass action holds for each reaction with the specific rates. Here S stands for the dummy substrate, P for the dummy product, E for the enzyme, and E^* for the inactive enzyme. Let S, P, E and Z denote respectively the concentrations for these species, and X be the concentration of E:S.

- (a) Write down the rate equations.
- (b) Show that the total enzyme concentration $E_{\rm T}$ is preserved, and use this to remove the dynamics of X.
- (c) Suppose that $S(0) = S_0$ and that $E(0) = E_T$ are the only nonzero initial conditions. Show that with these variables introduced, the dynamics can be reduced to a pair of second order differential equations for E and S.
- (d) What is the smallest value of S_0 such that $\lim_{t\to\infty} E(t) = 0$?

You should find that there are certain choices of parameters where we can entirely neutralize the harmful enzyme using these "suicide substrates". Penicillin is without a doubt the most famous example of a clinical suicide substrate, but they have been used to treat everything from breast cancer to HIV/AIDS.