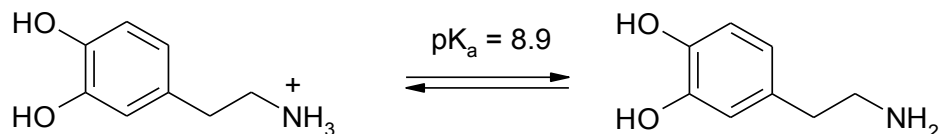


Drug Metabolism, Prodrugs, Drug Delivery

- 1) Parkinson's disease is characterized by a progressive loss of neurotransmitter dopamine. The equilibrium between the protonated and the neutral form is shown below.



- Why the oral administration of dopamine is not an effective treatment of Parkinson's disease?
 - Propose a prodrug approach to overcome the limited efficacy of oral dopamine?
 - How could you ensure that the formation of dopamine from your prodrug occurs mainly in the nervous tissue?
 - Propose a major metabolic reaction that leads to the inactivation of dopamine in the brain
 - Propose a major metabolic reaction that leads to inactivation of the prodrug outside the brain
 - Propose approaches to protect the prodrug or dopamine from degradation, thus prolonging their action.
- 2) In his presentation about cell-penetrating peptides (<http://www.chtm.unm.edu/incbnigert/Presentations/Ruoslahti.pdf>) Dr. Erkki Ruoslahti mentions a 9-aa cyclic peptide called the CAR peptide (sequence CARSKNKDC). Perform literature search to identify one promising application of this peptide.