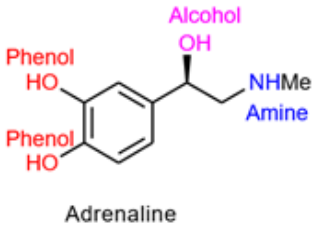
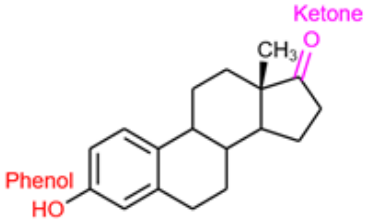
Chapter 1: Drugs and drug targets

1: The ability of a molecule to cross the fatty cell membrane has little to do with its size, but more with its hydrophobic character.
Estrone is more hydrophobic than adrenaline since it has a larger carbon skeleton and only two polar functional groups. Thus, the molecule is hydrophobic in character and can dissolve through the fatty cell membrane.
Adrenaline has four polar functional groups and a much smaller carbon skeleton. Thus, the polar functional groups dominate in determining the character of the molecule making it very polar and unlikely to pass through the cell membrane.



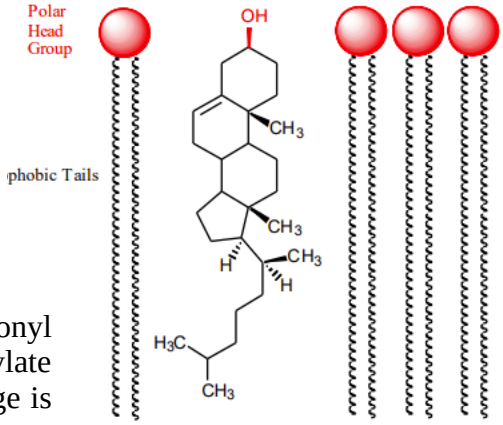
Adrenaline

There is another factor which hinders adrenaline's ability to cross the cell membrane. In aqueous solution, the four polar groups will be highly solvated with water molecules. In order to cross the cell membrane, these water molecules have to be 'stripped away' and this involves an energy penalty. The energy of desolvation for estrone is less since it has only two polar functional groups solvated.



Estrone

6: Cholesterol has one polar group - the alcohol group. This can form a H-bond to the polar head group of phospholipids. The rest of the molecule is hydrophobic and will sink into the cell membrane to form hydrophobic interactions with the alkyl side chains of the phospholipids.



phobic Tails

8: This reflects the fact that the greater the electron density on the carbonyl oxygen, the stronger it will act as a hydrogen bond acceptor. The carboxylate group is the strongest hydrogen bond acceptor since a full negative charge is shared between both oxygens.
The carbonyl oxygen of the amide will also act as a good hydrogen bond acceptor because the lone pair of electrons on nitrogen interacts with the carbonyl group as shown below. This increases electron density on the carbonyl oxygen.
No such interaction occurs for the ketone or ester carbonyl groups, but the carbonyl groups are still polarised resulting in the oxygen having a slightly negative charge. Consequently the carbonyl oxygen in these functional groups can still act as a hydrogen bond acceptor, but less strongly.