

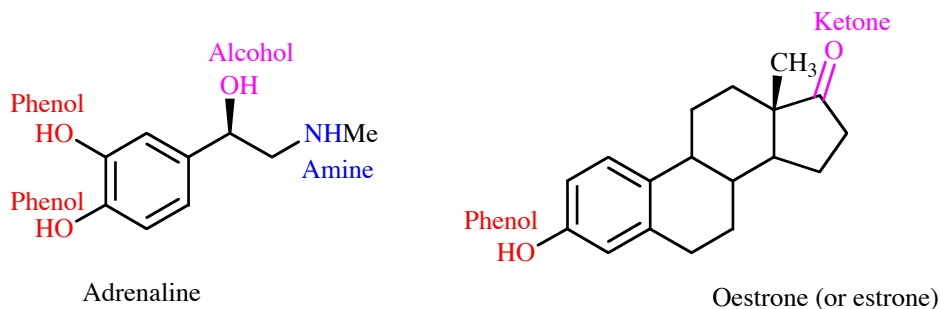
Answers to end-of-chapter questions

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.

Oestrone 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.

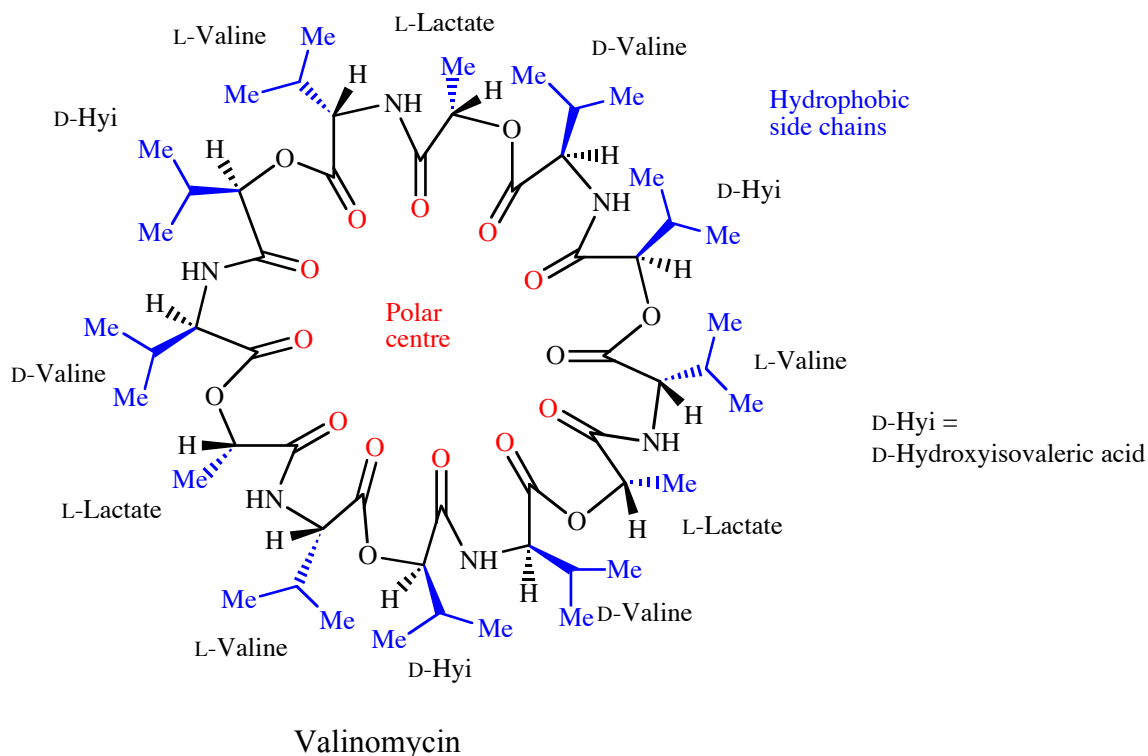
Adrenaline has four polar functional groups and a much smaller carbon skeleton.

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.

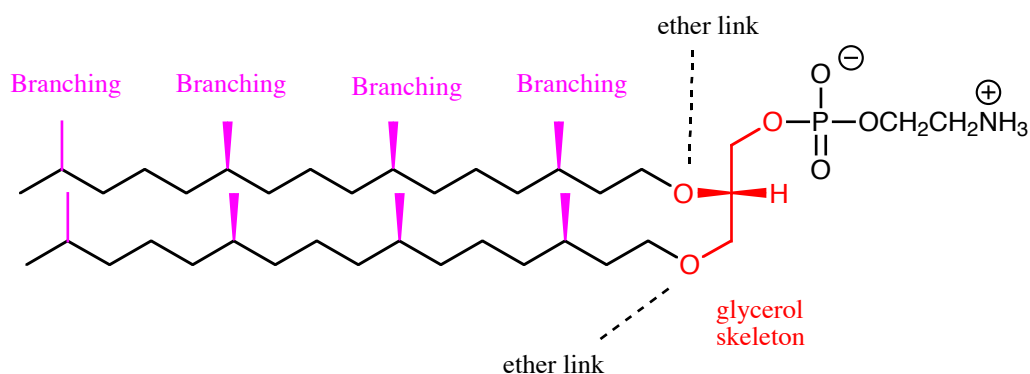


There is another factor which makes it difficult for adrenaline to cross the cell membrane. In aqueous solution, the four polar groups will be highly solvated with water molecules. In order to cross the cell membrane, these water molecules have to be 'stripped away' and this involves an energy penalty.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

2) Valinomycin has a macrocyclic structure where carbonyl oxygens are pointed towards the centre, making this area polar and capable of accommodating a polar ion. The outside of the ring is dominated by alkyl side chains which are hydrophobic in nature. As a result, the molecule can dissolve easily in fatty cell membranes and encapsulate polar ions, allowing these ions to be transported across cell membranes. Further details are provided in section 10.6.2.

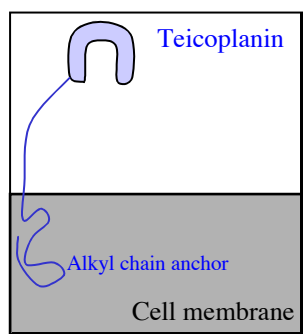
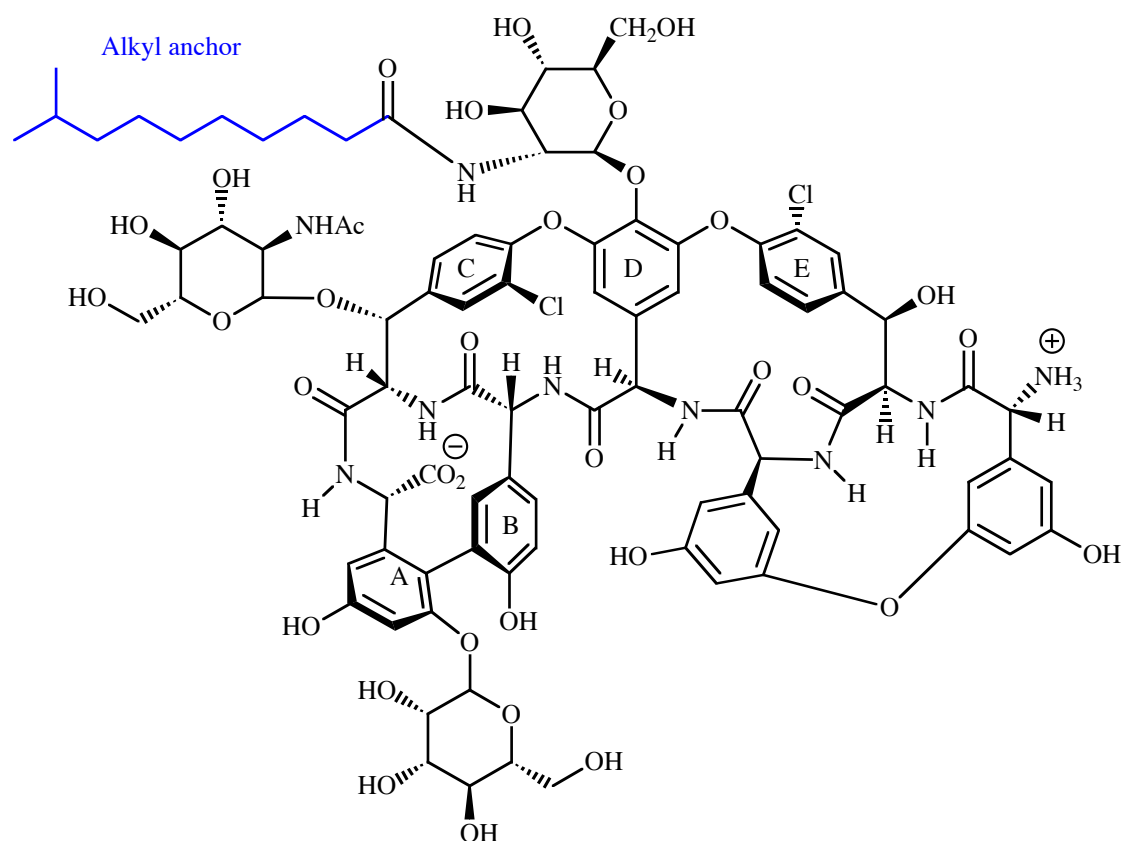


3) The alkyl chains are linked to the glycerol skeleton by ether linkages rather than by ester linkages. Ethers are chemically more stable than esters to extreme conditions.

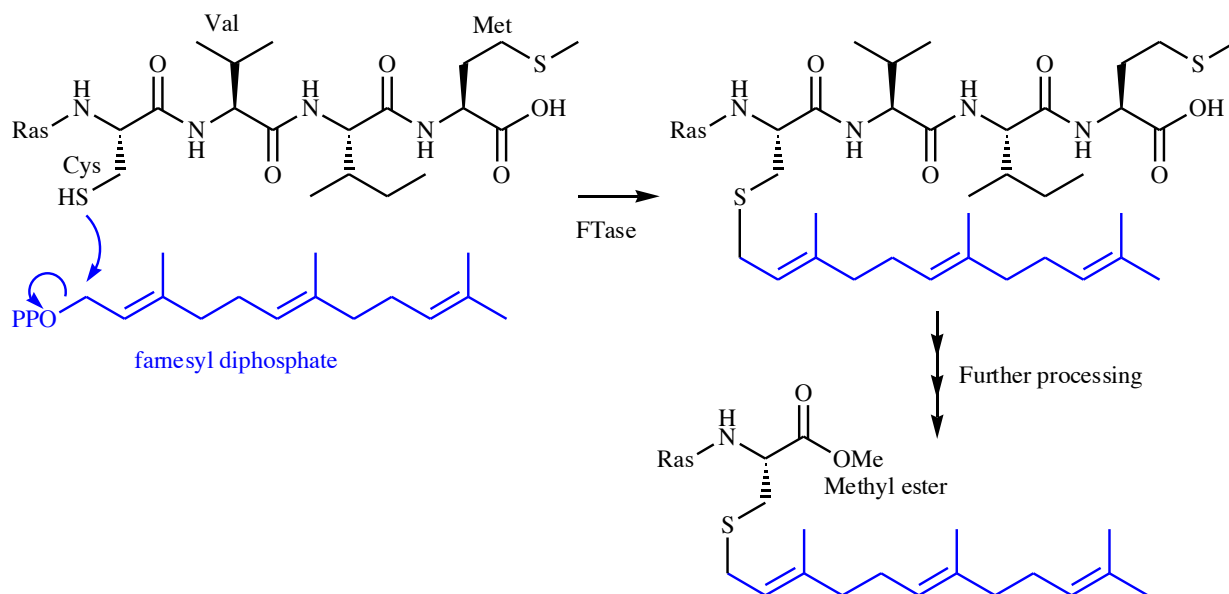


The long alkyl chains are also branched, unlike those in eukaryotic cell membranes. Branching makes the chains more resistant to oxidation.

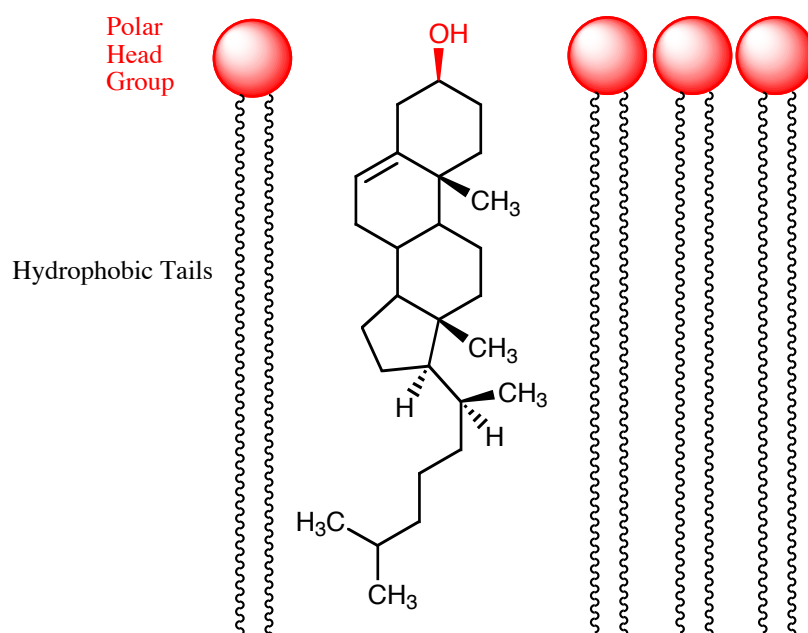
4) The alkyl group is hydrophobic and is embedded into the cell membrane. As a result, the drug is anchored to the cell membrane and is located on its outer surface such that it is ideally located to interfere with cell wall synthesis. Further details can be found in section 19.5.5.2.



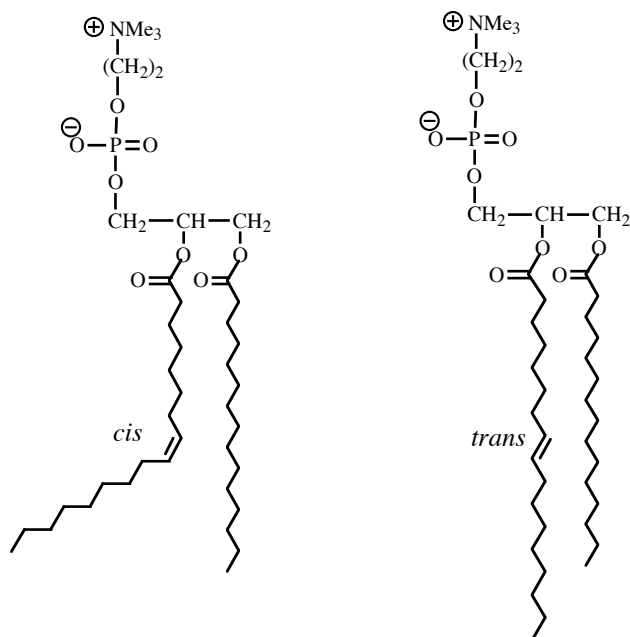
5) A hydrophobic chain could be attached to the Ras protein which would serve to anchor it to the inner surface of the cell membrane, in the same way in which teicoplanin is anchored to the outer surface of cell membranes (compare answer 4 above). The actual process by which a hydrophobic chain is attached to the Ras protein is shown below where the chain is attached to a cysteine residue. More details can be found in section 21.6.1.



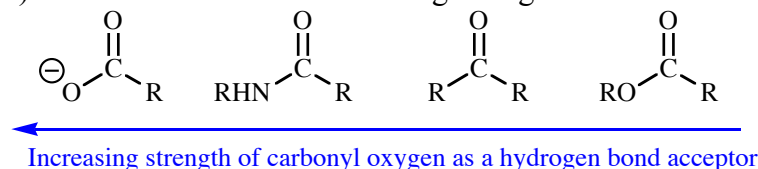
6) Cholesterol has one polar group - the alcohol group. This can form a H-bond to the polar head group of phospholipids. The rest of the molecule is hydrophobic and will sink into the cell membrane to form hydrophobic interactions with the alkyl side chains of the phospholipids.



7) *cis*-Double bonds introduce a kink into the chain which will hinder the regular packing of the hydrophobic chains. This increases the fluidity of the cell membrane.



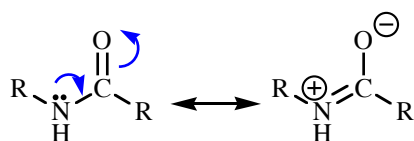
8) The relative order of H-bonding strength is shown below



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.

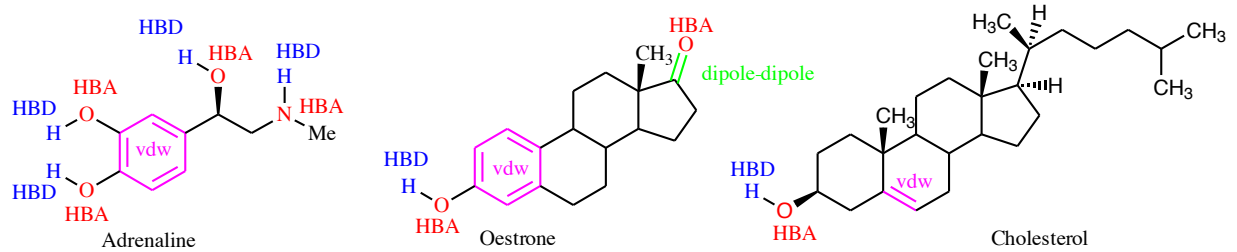
The carbonyl oxygen of the amide will also act as a good hydrogen bond acceptor since the lone pair of electrons on nitrogen can interact with the carbonyl group to increase electron density on the carbonyl oxygen as shown below.



Amide - N acts as poor HBA
O acts as a good HBA

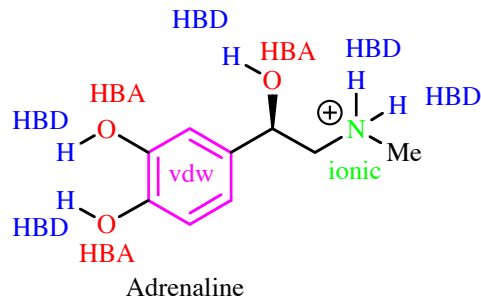
No such interaction occurs for the ketone or ester carbonyl groups, but the carbonyl groups are still polarised resulting in the oxygen having a slightly negative charge. Consequently the carbonyl oxygen in these functional groups can still act as a hydrogen bond acceptor, but less strongly.

9) The diagram below shows the possible intermolecular bonding interactions for the various functional groups present in each molecule (HBA = hydrogen bond acceptor; HBD = hydrogen bond donor; vdw = van der Waals interactions)



Notes

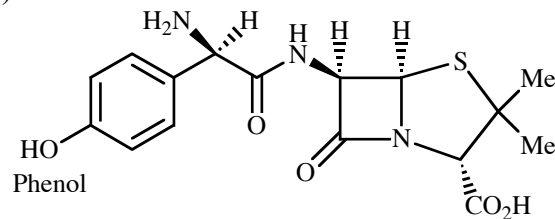
- * It cannot be assumed that all the interactions shown actually occur.
- * Adrenaline can also exist in the ionised form below, resulting in the potential interactions shown



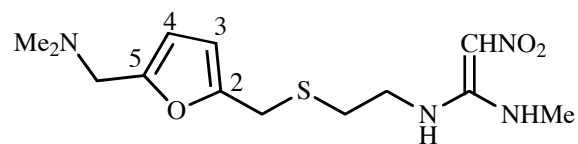
- * The remainder of the carbon skeleton in each molecule has the potential to interact with other hydrophobic molecules through van der Waals interactions. This is particularly the case for the steroid structures.

10) Trade names are in brackets

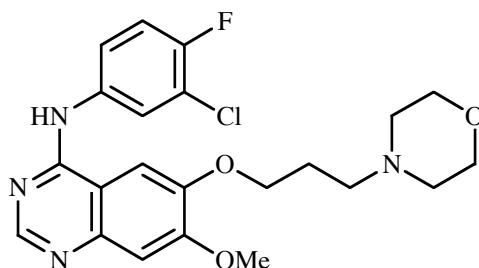
Amoxicillin (Amoxil)



Ranitidine (Zantac)



Gefitinib (Iressa)



Atracurium (Tacrrium)

