

Answers to end-of-chapter questions

1) In contrast to benzene, toluene has an accessible methyl group which can be manipulated easily by metabolic enzymes. Exposed methyl groups are susceptible to oxidation, and so the most likely metabolite is benzoic acid which could undergo further phase II conjugation reactions and be quickly excreted.



2) Fluphenazine contains an ester group which is susceptible to hydrolysis by esterases in the blood. If the drug is given by i.v. injection, the ester is quickly hydrolysed. If the ester is given by intramuscular injection, it takes longer for it to enter the blood supply and so its rate of hydrolysis is slower (see also section 14.6.2).



3) The quaternary salt of morphine contains a permanent positive charge. If the compound is administered *in vivo*, it has to cross the blood brain barrier in order to reach the analgesic receptors in the brain. However, the blood brain barrier is hydrophobic, and since the compound has a permanent positive charge, it cannot cross. Thus, the observed inactivity *in vivo* is due to the inability of the compound to reach the receptors in the brain.

In vitro tests are carried out on isolated receptors or cells and so there is no blood brain barrier to cross (see also section 24.5).

4) When codeine is administered, a certain proportion of it undergoes a metabolic reaction in the liver which results in the removal of the methyl ether and generation of morphine. This accounts for the analgesic activity observed (see also section 24.5).

Answers Chapter 4 Introduction To Medicinal Chemistry

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