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MATRIC NOS: 17/MHS01/056

DEPARTMENT: MBBS

Discuss in details the factors affecting drug metabolism.

The duration and intensity of pharmacological action of the most lipophilic drugs are determined by the rate they are metabolized to inactive products. The Cytochrome P450 monooxygenase is the most important pathway in this regard. In general, anything that increases the rate of metabolism(e.g enzyme induction) of a pharmacological active metabolite will decrease the duration and intensity of the drug action. The opposite is also true(e.g, enzyme inhibition). However,in cases where an enzyme is responsible for metabolizing a pro-drug into a dug, enzyme induction can speed up this conversion and increase drug levels, potentially causing toxicity. Various physiological and pathological factors can also affect drug metabolism. Physiological factors that can influence drug metabolism include age, individual variation( e.g pharmacogenetics), enterohepatic circulation, nutrition, intestinal flora or sex differences. In general, drugs are metabolized more slowly in fetal, neonatal and elderly humans and animals than in adults.

General variation(polymorphism) accounts for some of the variability in the effects of drugs. With N-acetyltransferases (involved in Phase II reactions), individual variation creates a group of people who acetylate slowly( slow acetylators) . This variation may have dramatic consequences, as the slow acetylators are more prone to dose-dependent toxicity. Cytochrome P450 monooxygenase system enzymes can also vary across individuals, with deficiencies occurring 1-30% of people, depending on their ethnic background. Dose, frequency, route of administration, tissue distribution and protein binding of the drug affect its metabolism. Pathological factors can also influence drug metabolism,including liver, kidney or heart diseases. In silico modelling and stimulation methods allow drug metabolism to be predicted to be predicted in virtual patient populations prior to performing clinical studies in human subjects. This can be used to identify individuals most at risk from adverse reaction.