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Editorial

# Biotransformation of Drugs and their Tissue Barriers

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## EDITORIAL NOTE

Most of these barriers are typically the same systems that animals use for defense against invasion by foreign agents. These barriers include the skin, the GIT membranes, blood-brain barrier and placenta.

**Skin:** The superficial layer of the skin, stratum corneum is particularly impermeable to most drugs. The skin permeability for the drugs is enhanced by using a co-solvent system such as ethanol/water which increases drug partition into the skin. The lipid domains of the buccal and nasal mucosa also restrict drug entry and the drugs which permeate are able to do so through passive diffusion using the hydrophilic trans-cellular spaces and direct permeation through the membrane.

**Tight junctions:** The gap junctions between cells in different cell types within a tissue can form channels for the passage of drugs between epithelial, endothelial, and mesothelial cells of the same tissue. These channels comprise of a group of proteins known as connexin. Cells in different tissues are however connected by tight junctions and these can impair transport between cells in different tissues. The tight therefore to use drug absorption enhancers such as bile salts and long chain acyl-carnitines which act as calcium chelatorsand disrupt the tight juncti junctions are dynamic structures, which normally regulate the trafficking of nutrients, medium sized compounds between cells, and form a regulated barrier in spaces between cells. There is need ons thereby improving transport across the junctions.

**Cerebrospinal Fluid Barrier (CSF):** Epithelial cells which are in contact with the brain ventricular spaces form a barrier to the movement of drugs. The zonulae severely restrict the passage of most molecules between the bloodstream and the parenchyma of the central nervous system. Drug entry across this barrier is through either passive diffusion or carrier mediated transport. Only the lipid soluble drugs cross into the CSF from blood.

**Placental barrier:** The placental membrane limits the amount of maternal blood following through the placenta to the foetus and passive diffusion is the main mechanism of drug entry from the maternal blood to the foetus. The shortest time required for equilibration of a drug between mother and foetus is about ten minutes and this delay is useful as it can allow a mother to be anaesthetized during final stages of labour.

## Drug biotransformation reactions

Drugs and other foreign substances (xenobiotics) undergo series of biotransformation reactions in the body. The biotransformation reactions act as first line defense strategy against these xenobiotics. It is armed with a battery of enzymes which convert the lipid-soluble xenobiotics into more water-soluble metabolites to allow more efficient excretion of the drugs in a limited volume of water in urine or bile. The enzymes involved in the biotransformation of endogenous chemicals are the same ones that are used in the biotransformation of xenobiotics. There is, therefore, a close relationship between drug biotransformation and fundamental homeostatic processes. In some clinical responses, the intensity of pharmacological action correlates better with the concentration of free drug in plasma, while in other responses there is no direct relationship between drug concentration and clinical response. The main variations of the drug response effects include: Drugs which combine with their receptors as quickly as they dissociate from them; for this category of drugs, the pharmacological effect increases or reduces in tandem with the plasma drug concentration. Drugs do not readily dissociate from their receptors. In this case the pharmacological effect persists despite the falling plasma concentration. Drugs which combine with receptors and irrespective of their rates of association/dissociation sets in motion a cascade of events which runs on despite falling plasma concentrations.

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