## 12.3: Biotransformation Sites

### Biotransformation Sites

Biotransforming enzymes are widely distributed throughout the body.

- The liver is the primary biotransforming organ due to its large size and high concentration of biotransforming enzymes.
- The kidneys and lungs are next with 10-30% of the liver's capacity.
- A low capacity exists in the skin, intestines, testes, and placenta.

# Primary Biotransformation Site: The Liver

Since the liver is the primary site for biotransformation, it is also potentially vulnerable to the toxic action of a xenobiotic that is activated to a more toxic compound.
Within the liver cell, the primary subcellular components containing the transforming enzymes are the **microsomes (small vesicles) of the endoplasmic reticulum** and the soluble fraction of the **cytoplasm (cytosol)**. The mitochondria, nuclei, and lysosomes contain a small level of transforming activity.

- Microsomal enzymes are associated with most Phase I reactions. Glucuronidation enzymes are also contained in microsomes.
- Cytosolic enzymes are non-membrane-bound and occur free within the cytoplasm. They are generally associated with Phase II reactions, although some oxidation and reduction enzymes are contained in the cytosol.
- The most important enzyme system involved in Phase I reactions are the **cytochromes P450**, also called the cytochrome P-450 system or the mixed function oxidase (MFO) system, but now mostly called CYP450 or CYPs by scientists and in research publications. It is found in microsomes and is responsible for oxidation reactions of a wide array of chemicals.

# Susceptibility of the Liver

The liver is particularly susceptible to damage by ingested toxicants because it biotransforms most xenobiotics and receives blood directly from the gastrointestinal tract. Blood leaving the gastrointestinal tract does not flow directly into the general circulatory system. Instead, it flows into the liver first via the portal vein. This process is known as the "first pass." Blood leaving the liver is eventually distributed to all other areas of the body; however, much of the absorbed xenobiotic has undergone detoxification or bioactivation. The liver may have removed most of the potentially toxic chemical. On the other hand, some toxic metabolites are highly concentrated in the liver.

Knowledge Check

### 1) The organ that has the greatest ability to biotransform xenobiotics is the:

a) Liver
b) Pancreas
c) Skin

**Answer**

Liver - **This is the correct answer.**
Biotransforming enzymes are widely distributed throughout the body. However, the liver has the largest concentration of all organs and thus has a very high capacity for biotransformation.

### 2) The "first pass" phenomenon pertains to:

a) The situation where xenobiotics that are absorbed from the GI tract first enter the circulating blood before going to the liver
b) A condition where the liver first biotransforms a xenobiotic by Phase II reaction before it is biotransformed by a Phase I reaction
c) An anatomical arrangement in which xenobiotics absorbed from the intestine go to the liver first rather than into the systemic circulation

**Answer**

An anatomical arrangement in which xenobiotics absorbed from the intestine go to the liver first rather than into the systemic circulation - **This is the correct answer.**

Blood leaving the gastrointestinal tract does not directly flow into the general circulatory system. Instead, it flows into the liver first via the portal vein. This is known as the "first pass" phenomena.

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