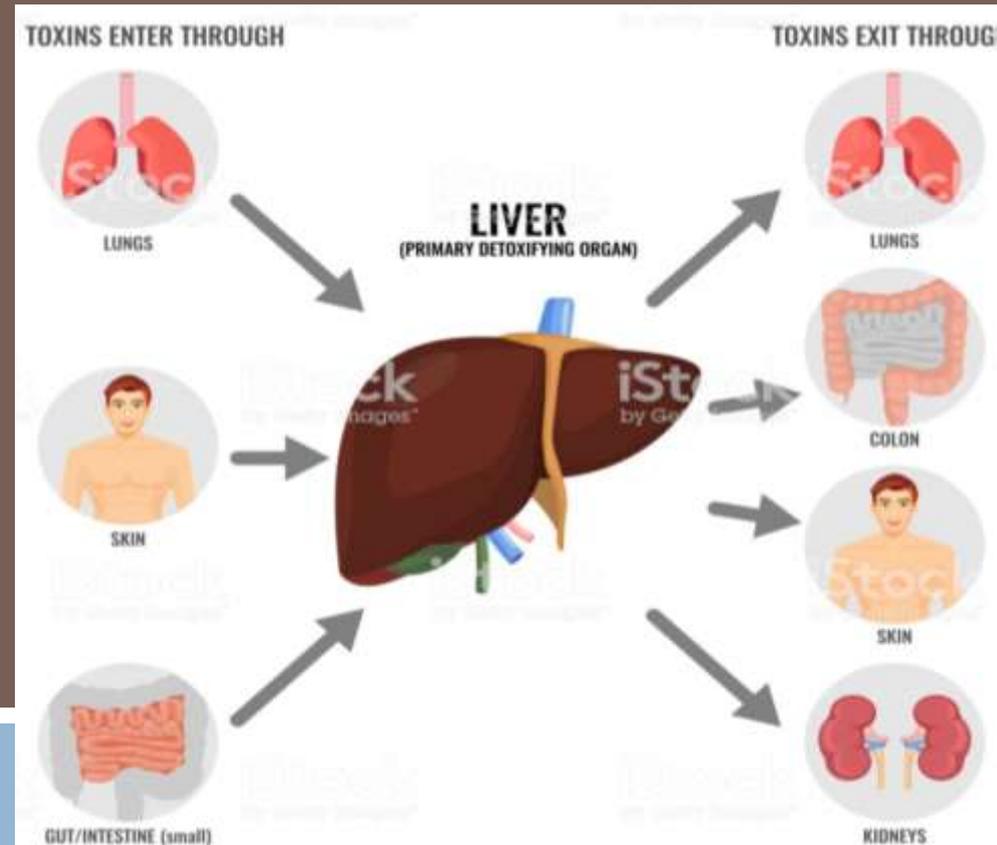


DETOXIFICATION

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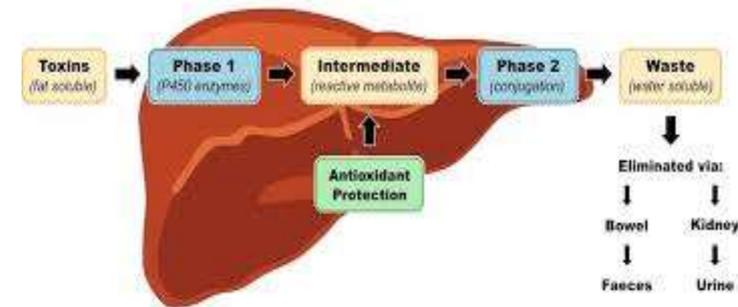
Detoxification:

- The term **detoxication** or **detoxification** refers to the series of biochemical reactions occurring in the body to convert the foreign (often toxic) compounds to non-toxic or less toxic, and more easily excretable forms.
- In recent years, the term detoxification is replaced by **biotransformation or metabolism** of xenobiotics (Greek : xenos—strange, foreign) or simply **metabolism of foreign compounds**.

Site of detoxification

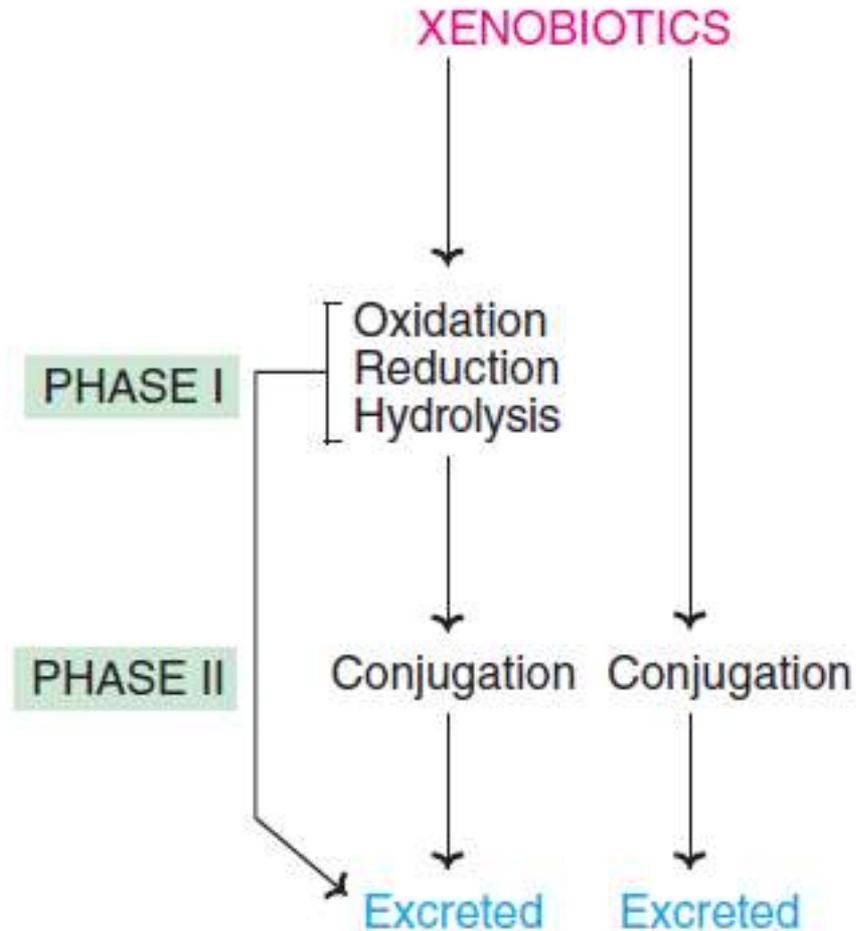
- The detoxification reactions are carried out mainly in the liver which is equipped with the enzyme machinery.

- Kidney and other organs may sometimes be involved.



- The products formed by detoxification are mostly excreted by the kidneys, less frequently excreted via feces or expired air.

MECHANISM OF DETOXIFICATION

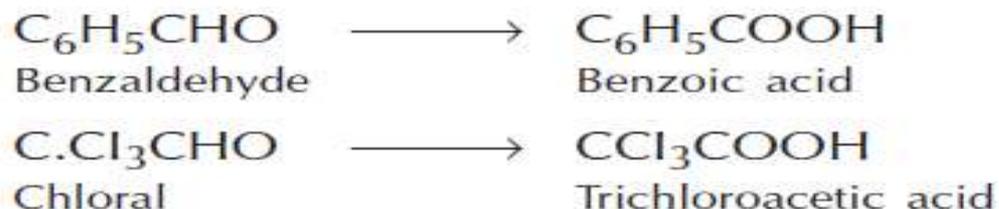


Oxidation reactions

- A large number of foreign substances are detoxified by oxidation.
- These include alcohols, aldehydes, amines, aromatic hydrocarbons and sulfur compounds.
- **Alcohols : Aliphatic and aromatic alcohols** undergo oxidation to form the corresponding acids.



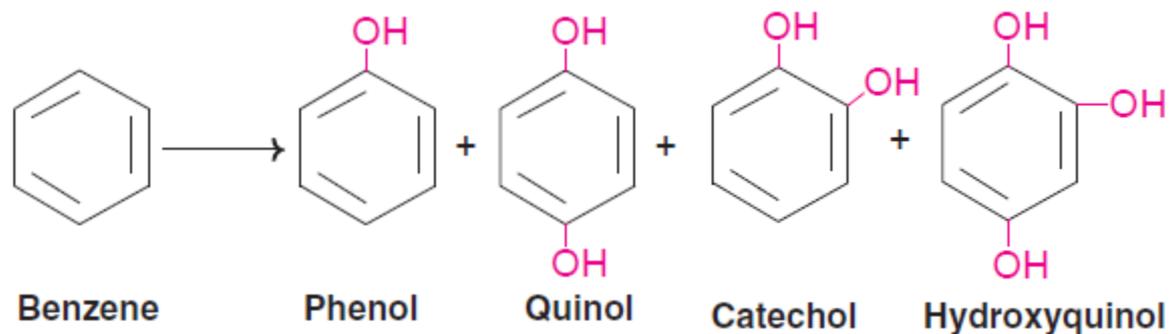
Aldehydes



Amines and their derivatives:



Aromatic hydrocarbons:



- **Sulfur compounds** : Organic sulfur is oxidized to sulfuric acid.
- **Drugs** : Meprobamate is a tranquilizer. It is oxidized to hydroxymeprobamate and excreted in urine.

Role of cytochrome P₄₅₀

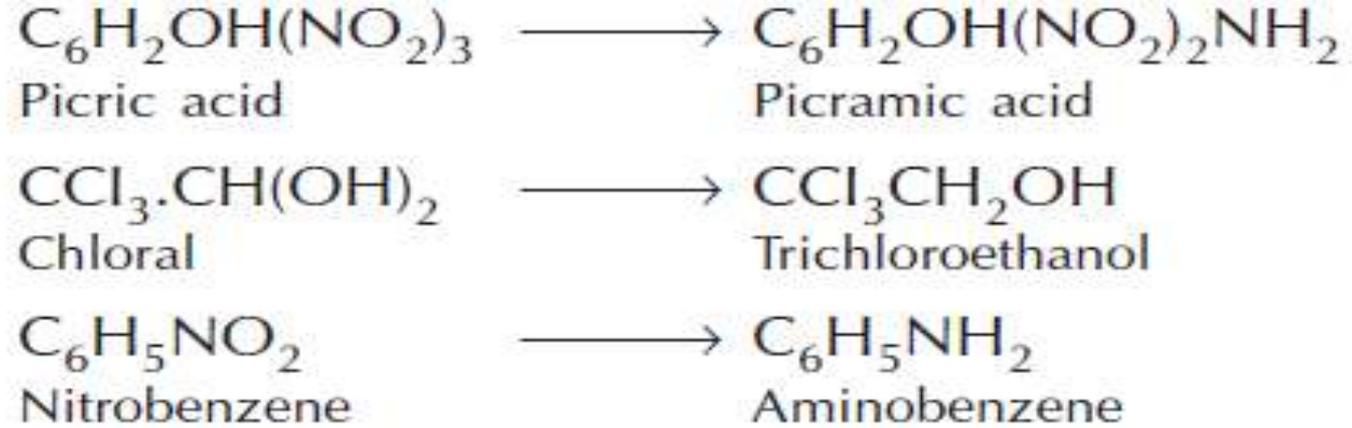
- Most of the oxidation reactions of detoxification are catalysed by monooxygenase or cytochrome P450.
- Most of the reactions of cytochrome P450 involve the addition of a hydroxyl group to aliphatic or aromatic compounds which may be represented as



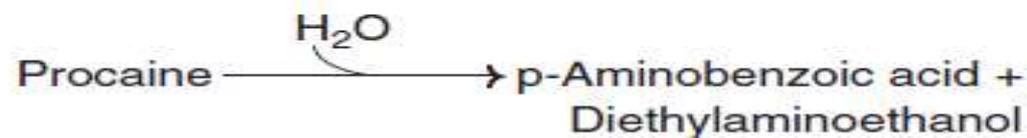
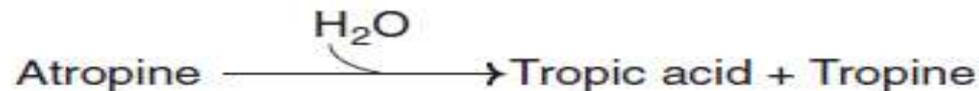
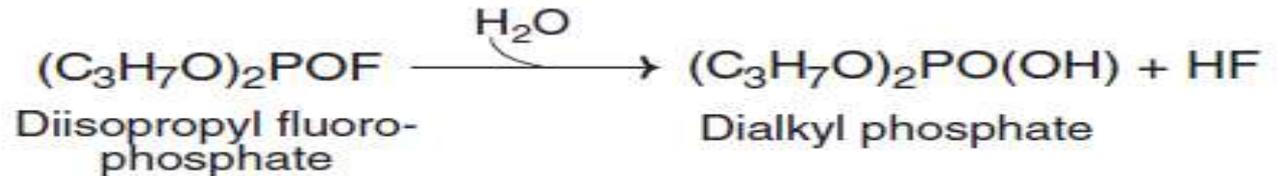
Salient features of cytochrome P₄₅₀

1. Multiple forms of cytochrome P450 are believed to exist, ranging from 20 to 200.
2. They are all **hemoproteins**, containing heme as the prosthetic group.
3. Cytochrome P450 species are found in the highest concentration in the microsomes of liver.
4. In the adrenal gland, they occur in mitochondria.
5. The mechanism of action of cytochrome P450 is complex and is dependent on NADPH.
6. Cytochrome P450 is an **inducible enzyme**. Its synthesis is increased by the administration of drugs such as phenobarbital.

Reduction

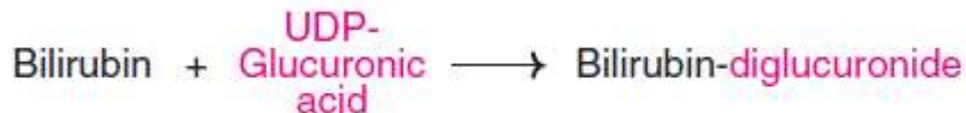
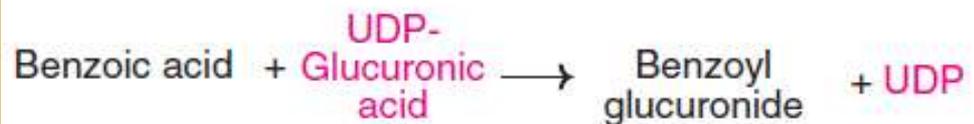
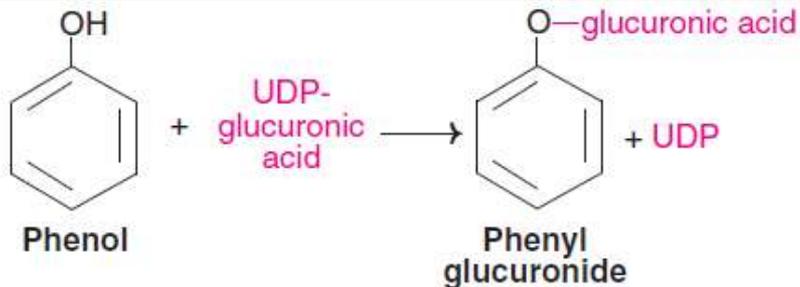
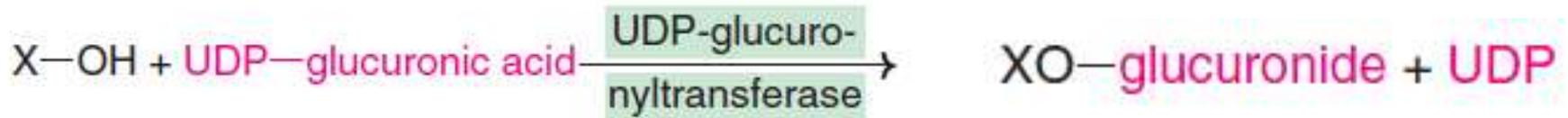


Hydrolysis:



Conjugation:

- Conjugation is the process in which a foreign compound combines with a substance produced in the body.



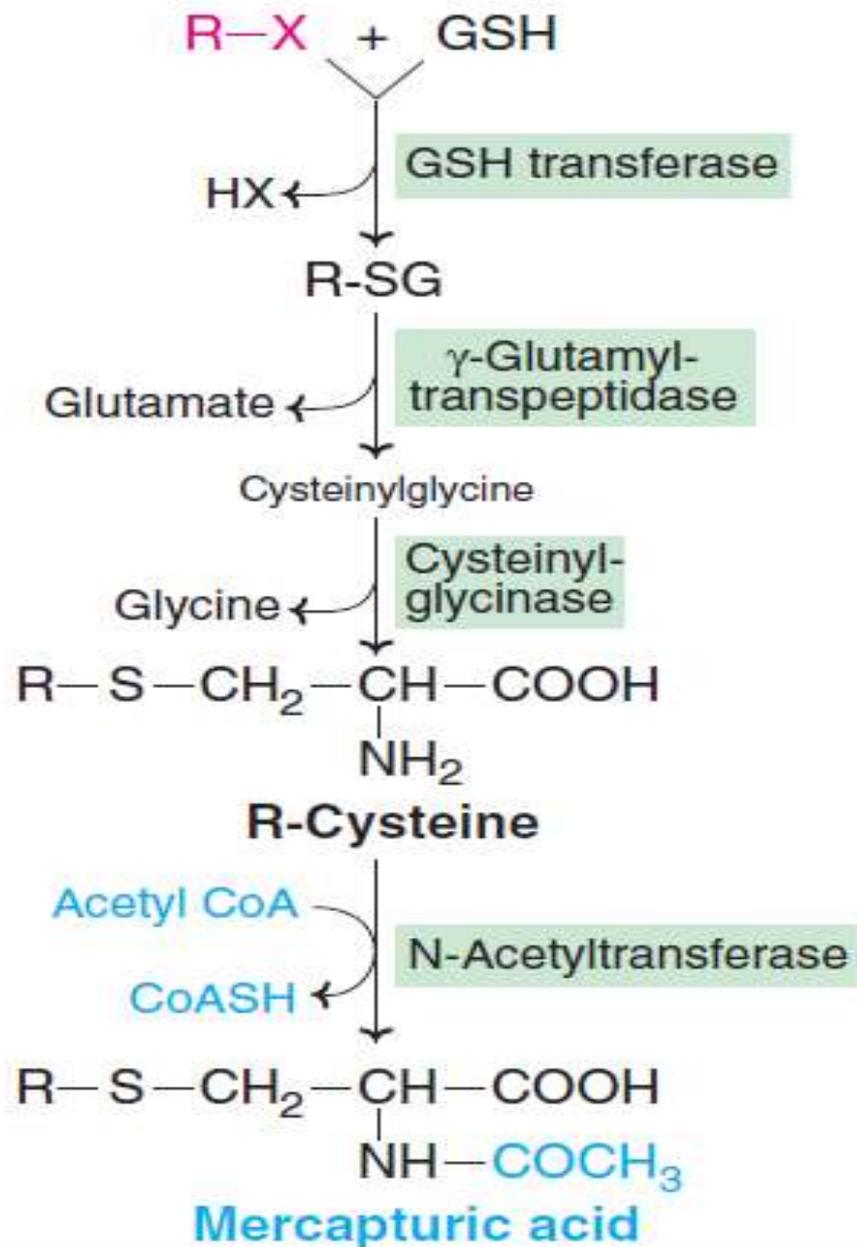


Fig. 31.2 : Role of glutathione in conjugation to form mercapturic acid (R-X–A xenobiotic; GSH–Glutathione).

Detoxification by drugs

- The toxic effects of certain metals such as arsenic, mercury and cadmium could be overcome by administering BAL (British antilewisite).
- It is believed that BAL readily combines with metals and gets easily excreted into urine.



thank you!