

# ***Xenobiotics ( Part 5)***



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# Xenobiotics



## Phase 1 reactions:

Phase I reactions include:

- Oxidation
- Reduction
- Hydrolysis reactions

They are also called Hydroxylation reactions since they introduce or expose a functional group (e.g., -OH) that serves as the active center for sequential conjugation in a phase II reaction.

# Xenobiotics



## Oxidation:

A large number of foreign substances are destroyed by oxidation in the body.

Examples- Oxidation of methyl group containing compounds  
Methyl group- is oxidized to acid through formation of alcohol and aldehyde  
 $\text{CH}_3 \text{ CH}_2\text{OH CHO COOH}$

# Xenobiotics



## Phase 2 –

### **Conjugation:**

- Conjugation is a process by which the foreign molecules and their metabolites are coupled with a conjugating agent and are converted to soluble, non toxic derivatives which are easily excreted in urine
- Conjugation reactions can occur independently or can follow phase 1(hydroxylation) reactions



# Xenobiotics



## Phase 2 –

### **Conjugation ( Contd..)**

- Conjugation takes place primarily in liver but can occur in kidney also
- After conjugation the products are generally rendered nontoxic but in certain conditions they are left unchanged or become more toxic.

# Xenobiotics



- In biotransformation the parent xenobiotic compound is converted into metabolites and then conjugates are formed.
- Example– benzene undergoes oxidation a phase 1 reaction, to form phenol ,which conjugates with sulphate,a phase 2 reaction.
- The metabolites and conjugates are usually more water soluble and polar ,hence more readily excretable.

# Biotransformation Reactions



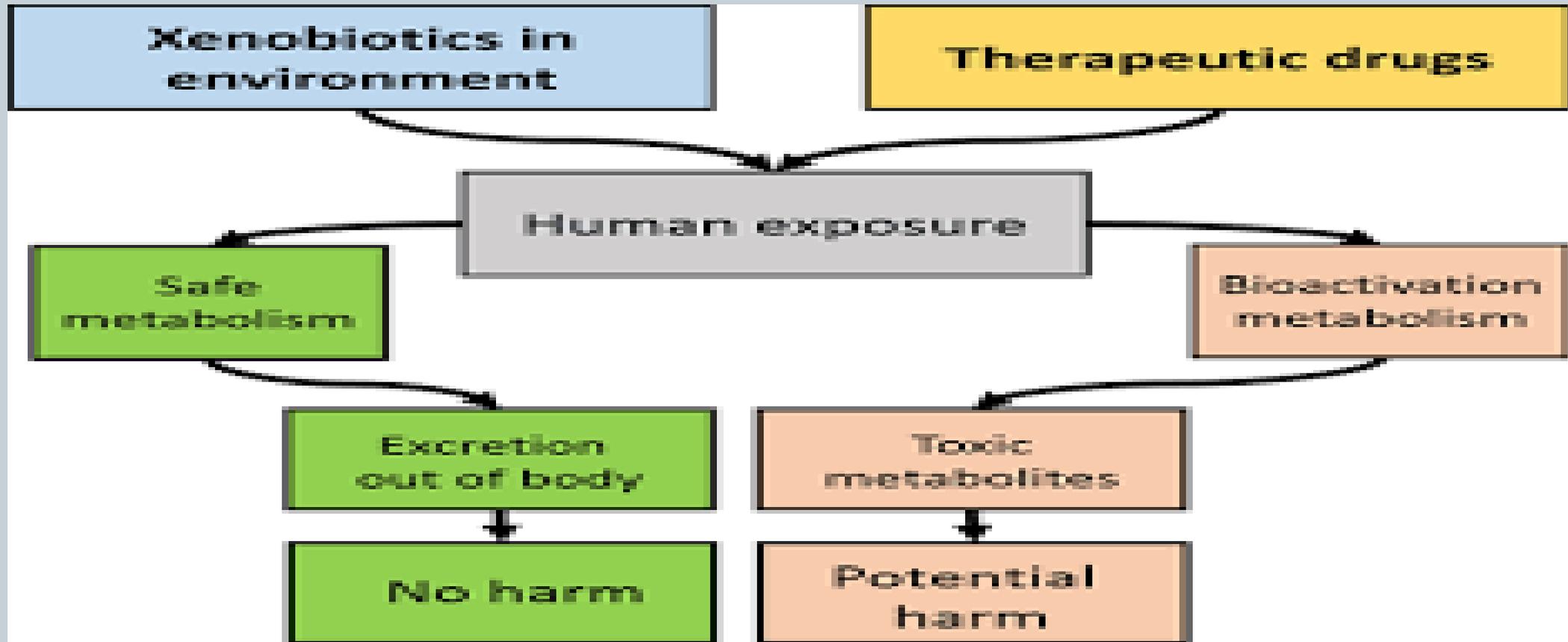
## I. phase of biotransformation: examples of reactions

Reaction	Xenobiotic (example)
<b>Hydroxylation (P-450)</b>	(hetero)aromatic compounds ( $\text{Ar-H} \rightarrow \text{Ar-OH}$ )
Sulfoxidation	dialkylsulfide ( $\text{R-S-R}$ ) $\rightarrow$ sulfoxide ( $\text{R-SO-R}$ )
Dehydrogenation	alcohol / aldehyde hydrate $\rightarrow$ aldehyde / acid
Reduction	nitrocompounds ( $\text{R-NO}_2$ ) $\rightarrow$ amines ( $\text{R-NH}_2$ )
Hydrolysis	ester $\rightarrow$ acid + alcohol

Reactions occur mainly in ER, some in cytosol

Enzymes of I. phase are rather non-specific – **advantage !!**

# Xenobiotics Elimination



*Thank You*

