

Detoxification

Biotransformatⁿ of Xenobiotics

→ detoxificatⁿ - series of biochemical reactions occurring in the body to convert foreign (toxic) compounds to non-toxic or less toxic & more easily excretable forms.

Biotransformatⁿ

→ it transforms absorbed nutrients (food, O₂, etc) into substances required for normal body fns.
→ eg:- phenoxyl benzamine

Xenobiotics

→ they're compounds which maybe
• accidentally ingested or
• taken as drugs or
• compounds produced in the body by bacterial metabolism.

→ human body has well developed capacity to biotransform most xenobiotics as well as body waste.

eg:- bilirubin

→ liver plays the most imp role in biotransformatⁿ.

→ the compounds that are detoxified

include:-

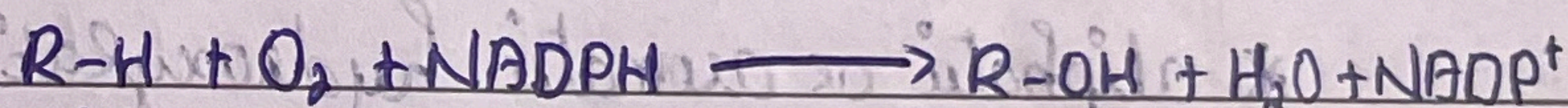
- compounds accidentally ingested like preservatives, food additives & adulterants
- drugs which are taken for therapeutic purposes
- compounds produced in the body which are to be eliminated, eg:- bilirubin, steroids
- compounds produced by bacterial metabolism, eg:- amines produced by decarboxylatⁿ of aa.

Enzyme Systems

→ Cyt. P450 enzyme family is involved in biotransformatⁿ.

→ these are heme containing membrane proteins, localised in SER of liver.

→ also called mixed fⁿ oxidases.



↳ xenobiotics

→ requires:- P450 flavoprotein - NADPH
P450 reductase

→ metabolise 50% of drugs, carcinogens & pollutants

Phases of Detoxificatⁿ Process

→ 3 phases, may occur together or separately.

→ phase 1 occurs - alternatⁿ of the toxic substance

→ phase 2 occurs - involves conjugatⁿ of the

altered toxic substances.
 → phase 3 rxns: pdts of phase 2 is further metabolised.
 → generally detoxificatⁿ of compound involves phase 1 & 2 rxns.

iii) hydrolysis:-
 → esters, amines, hydrazines, amides etc.
 aspirin → salicylic acid + acetic acid

Phase I:-

→ modify/alter foreign molecule by adding a functional group.
 → results in formatⁿ of compounds with less toxicity (detoxificatⁿ) & sometimes less toxicity (antitoxificatⁿ)
 → eg:- methanol → formic acid
 → phase I rxns include:- hydroxylatⁿ, oxidⁿ, redⁿ, hydrolysis, dealkylatⁿ etc.

Phase II:-

→ conjugatⁿ:-
 → a foreign compound combines with a conjugating agent & get converted into soluble, non-toxic derivatives which are easily excreted.
 → mainly occurs in liver
 → conjugatⁿ rxn occurs with a xenobiotic or its metabolite after phase I rxn.
 → the effect of conjugatⁿ is to make the compound more water soluble (polar) & therefore more easily excreted through urine or bile.

i) hydroxylatⁿ rxns:-

* aliphatic or aromatic hydroxylatⁿ:
 eg:- toluene → benzyl alcohol
 (mixed function oxidase)

* oxidⁿ & detoxificatⁿ of alcohol:-
 alcohol → aldehyde
 (alcohol DHase)
 aldehyde → acid
 (aldehyde DHase)

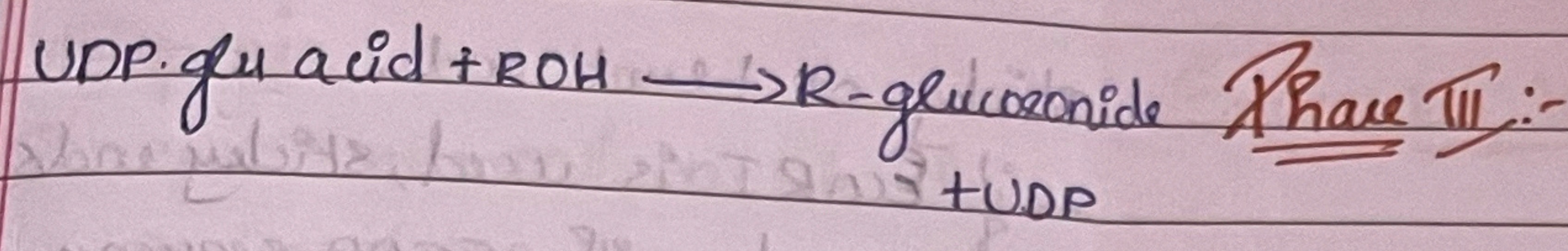
ii) reductive rxns:-

→ nitro compounds
 nitrobenzene → aniline

Conjugating agent	Active Form
Sulfate	PAPS
Acetic acid	acetyl coA
Methyl gp	SAM
Glucuronic acid	UDP glucuric acid
Cysteine	
Glycine	Glutathione

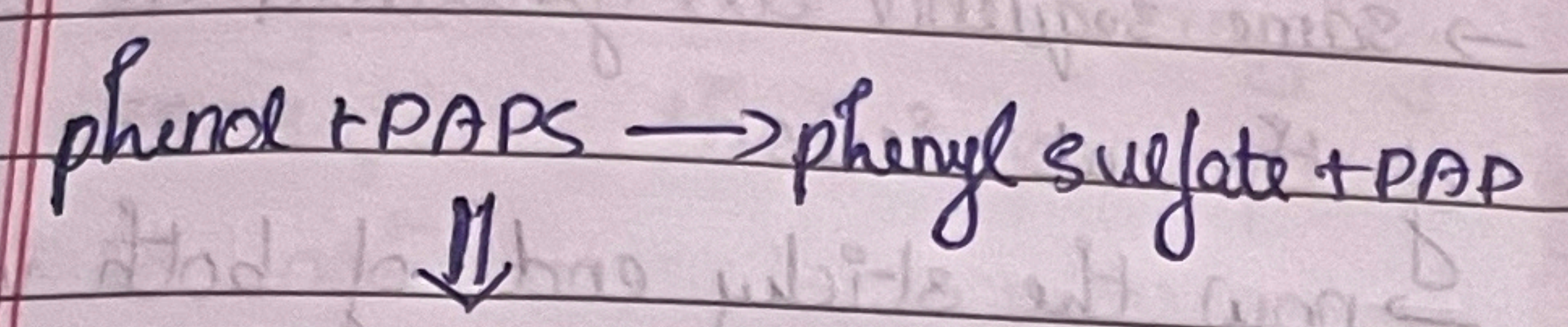
→ most common phase II rxns are:- sulfanilamide, isoniazide etc.

i) glucuronic acid:-
⇒ enzyme:- UDP glucosyl transferase * in some cases, phase II rxn may further be metabolised by phase III rxn.



Phase III:-

ii) Sulfate:-
⇒ enzyme:- sulfotransferases → not very common
→ further conjugatⁿ with glutathione in certain cases.



Environmental Toxins

3'-phospho adenosine-5-phospho-sulfate → these are cancer causing chemicals & endocrine disruptors

iii) Glycine:-
benzoic a + glycine → hippuric a → both naturally occurring & man-made

iv) methylatⁿ:-
⇒ SAM is the methyl donor
⇒ enzyme:- methyl transferase
epinephrine → metanephrine
Pb, Hg, Radon, Cd, BPA, phthalates, formaldehyde, benzene, pesticide.
→ in toxic doses, all these compounds can vely affect human health.

v) Glutamine:-
phenyl acetic a + glutamine → phenyl acetyl glutamine
→ Cancer:- radon, formaldehyde, benzene
→ endocrine disruptors:- BPA, pesticides, phthalates
→ organ failure / developmental pbms:- Pb, Hg, Cd.

vi) Acetyl atⁿ:-
→ conjugatⁿ with acetic acid
eg:- detoxificatⁿ of drugs like