SNS COLLEGE OF PHARMACY AND HEALTH SCIENCES

Coimbatore -641035

COURSE NAME : PHARMACOLOGY(ER20-21 T)

YEAR : DPHARM-II YEAR

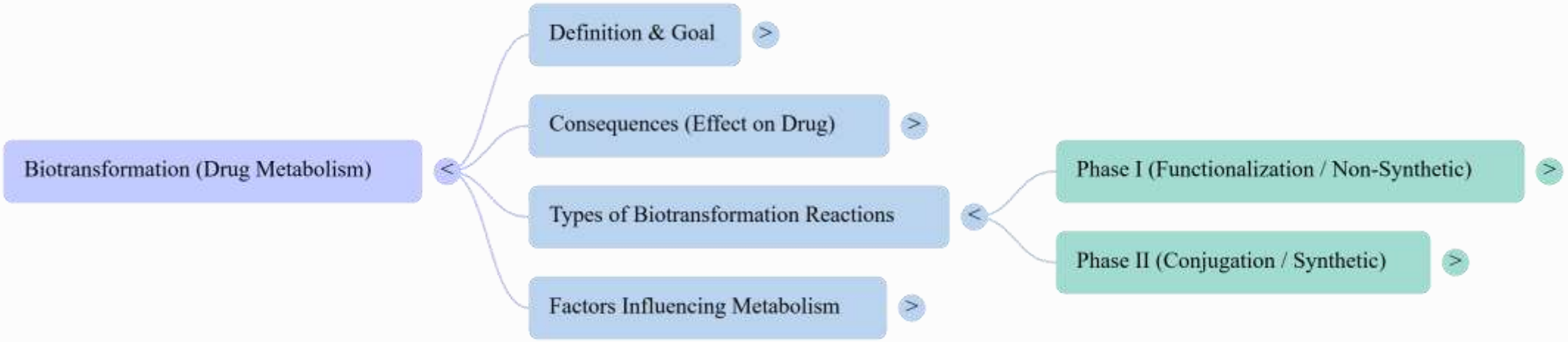
TOPIC 5 : PHARMACOKINETIC

(BIOTRANSFORMATION) METABOLISM

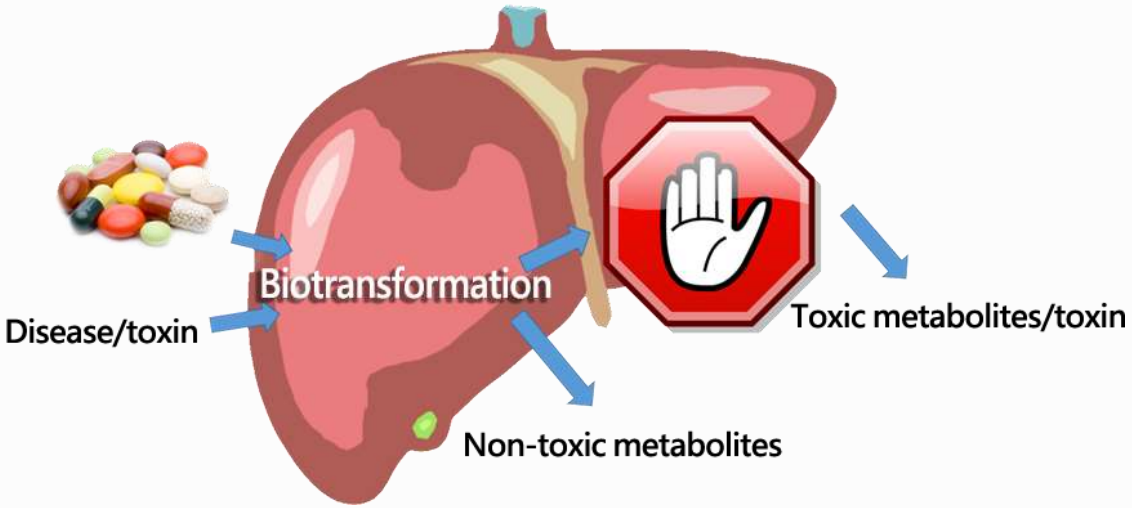
DESIGN THINKING IN BIOTRANSFORMATION

- **Empathize:** Deeply understand the patient's challenges with drug effects, metabolism issues, and experiences.
- **Define:** Reframe the problem based on insights from the empathize phase and establish clear context.
- **Ideate:** Brainstorm and explore a wide range of ideas and potential solutions, including innovative ways to enhance metabolic pathways or design prodrugs.
- **Prototype:** Simulate and build models of metabolic processes to test drug transformation and improve therapeutic outcomes.

MINDMAP

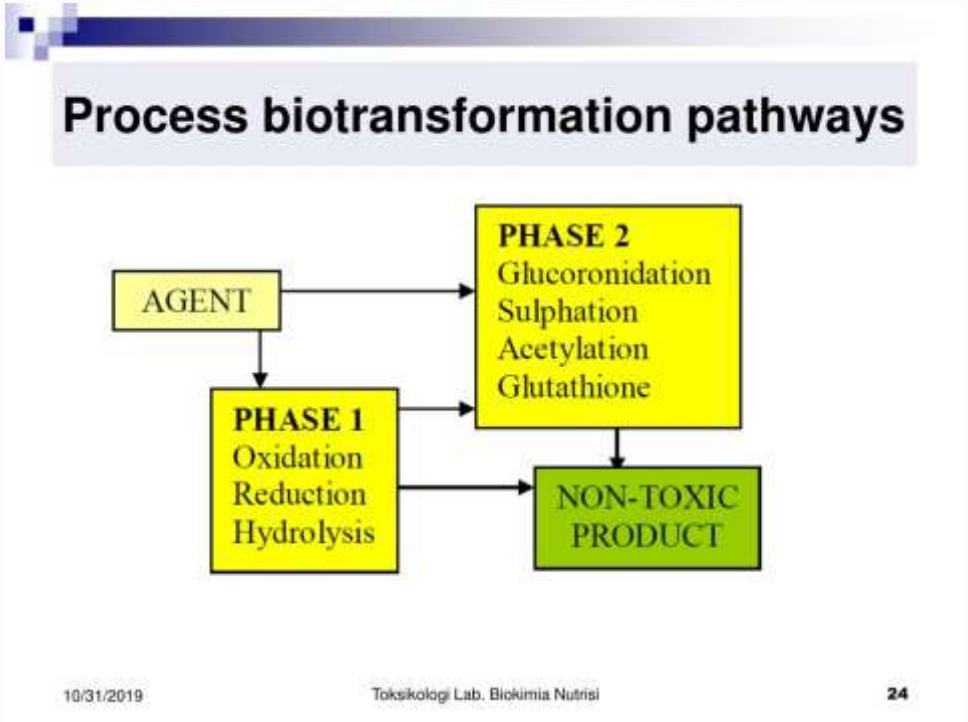

Biotransformation (Drug Metabolism)
Definition & Goal
Consequences (Effect on Drug)
Types of Biotransformation Reactions
Factors Influencing Metabolism
Phase I (Functionalization / Non-Synthetic)
Phase II (Conjugation / Synthetic)

INTRODUCTION

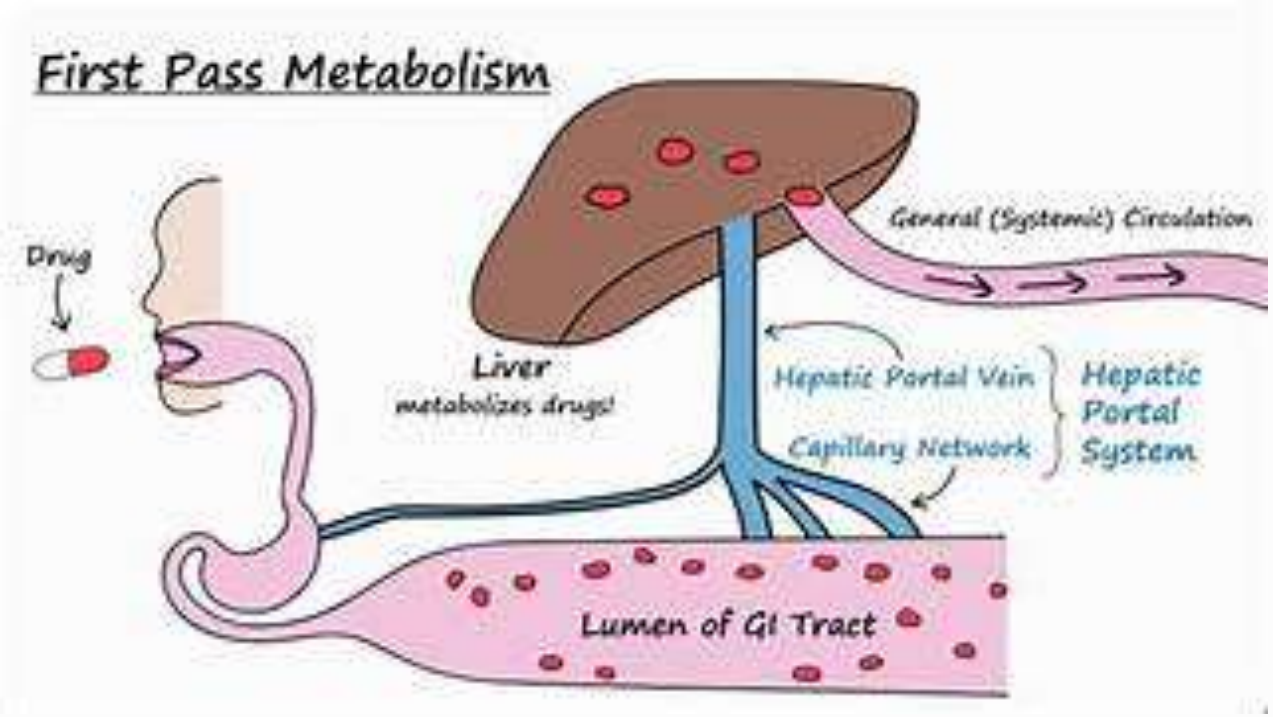


BIOTRANSFORMATION: classification	
Phase I reactions	**Phase II reactions (conjugations)**
1. Oxidation 2. Reduction 3. Hydrolysis	1. Glucuronidation 2. Sulfation 3. Conjugation with glycine (Gly) 4. Conjugation with glutathione (GSH) ********** 5. Acetylation 6. Methylation
The chemical role of Phase I and Phase II biotransformations:	
A *functional group* is added to the molecule or explored in the molecule at which conjugation can take place	An *organic acid (or acetyl or methyl group)* is conjugated to the molecule at a preexisting functional group or at a functional group acquired in Phase I biotransformation

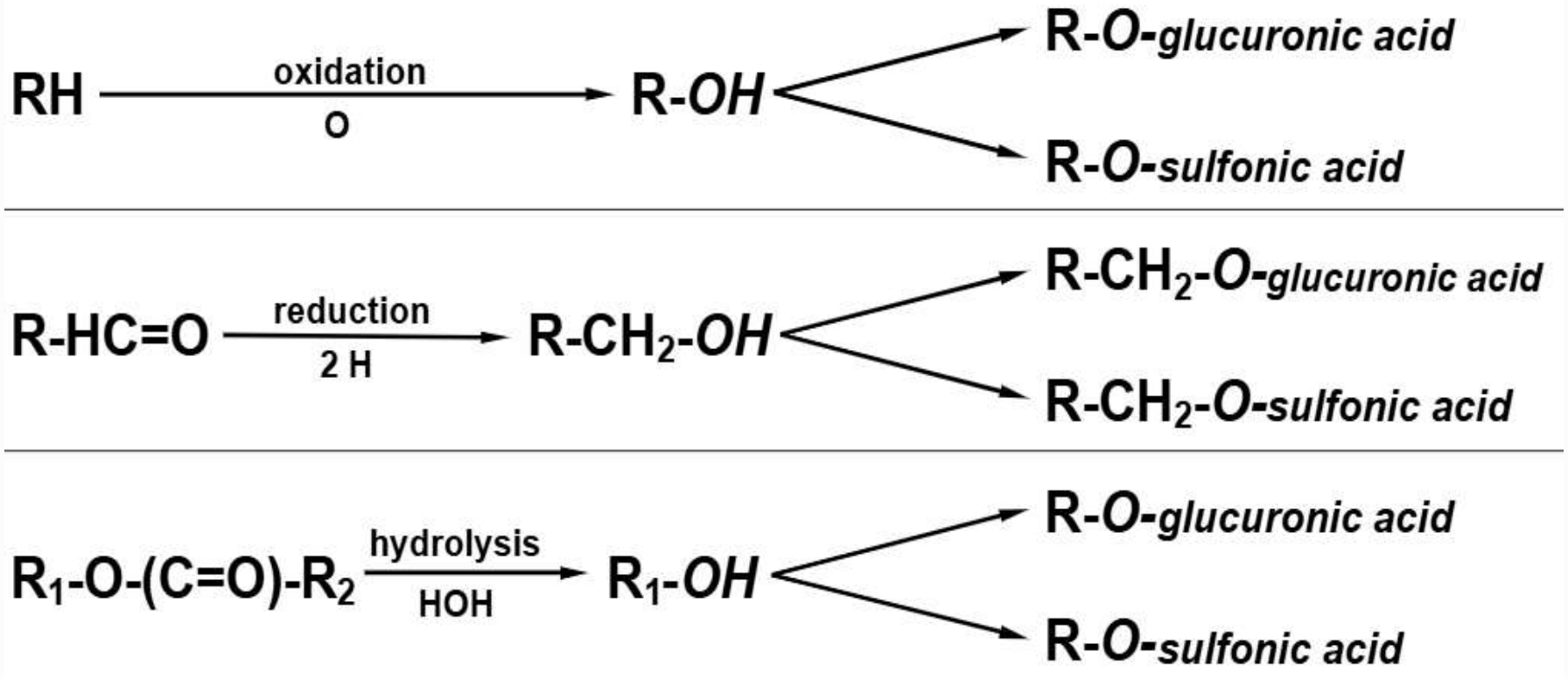
PATHWAYS OF BIOTRANSFORMATION



FIRST PASS METABOLISM

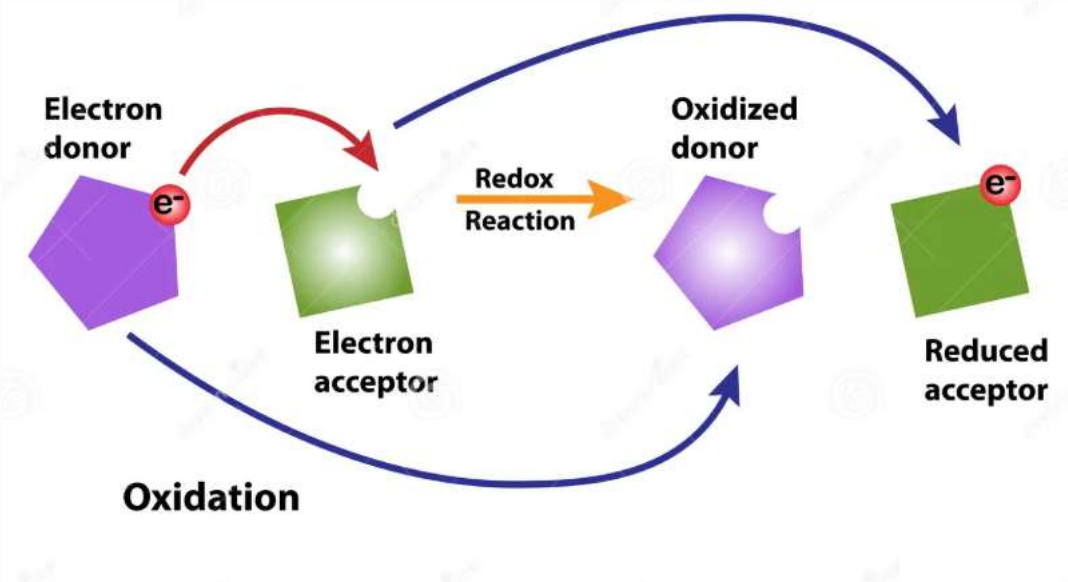


General examples



PHASE I REACTIONS

a) OXIDATION



1.OXIDATION AT NITROGEN ATOM

$RNH_2 \xrightarrow{O} RNHOH$

- Chlorpheniramine
- Dapsone
- Meperidine

2.OXIDATION AT SULPHUR ATOM

3.ALIPHATIC HYDROXYLATION

- Hydroxyl group added to drug

RCH_2CH_3 O $RCHOHCH_3$

4.AROMATIC HYDROXYLATION

5.DEALKYLATON AT OXYGEN ATOM

6. DEALKYLATON AT NITROGEN ATOM

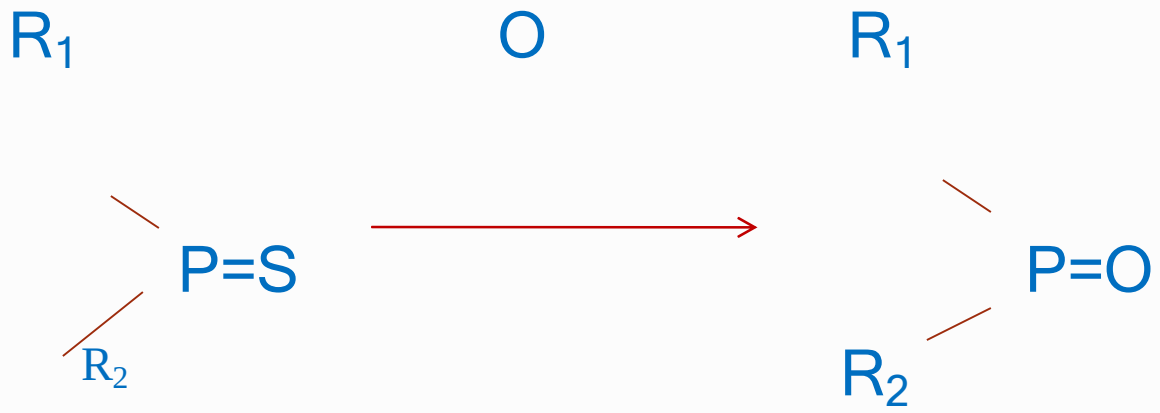
7.DEALKYLATON AT SULPHUR ATOM

$RSCH_3 \xrightarrow{O} RSH + CH_2O$

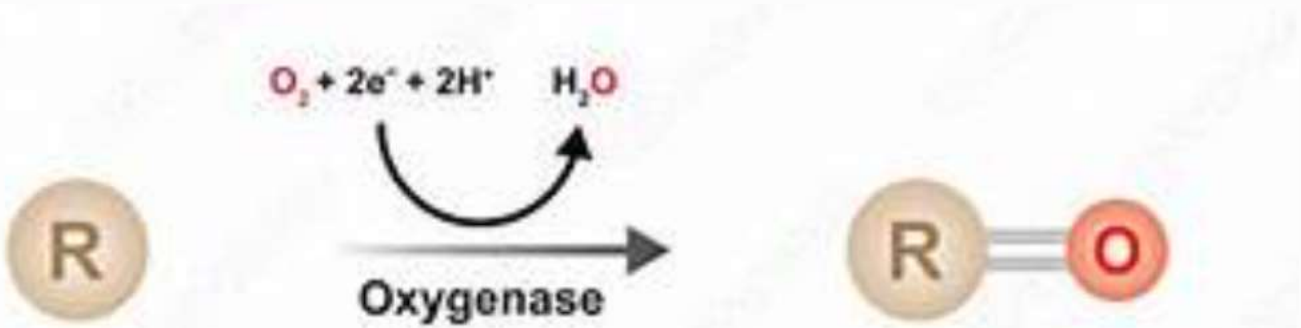
8.OXIDATIVE DEAMINATION

$RCHNH_2\,R \xrightarrow{O} RCOR + NH$

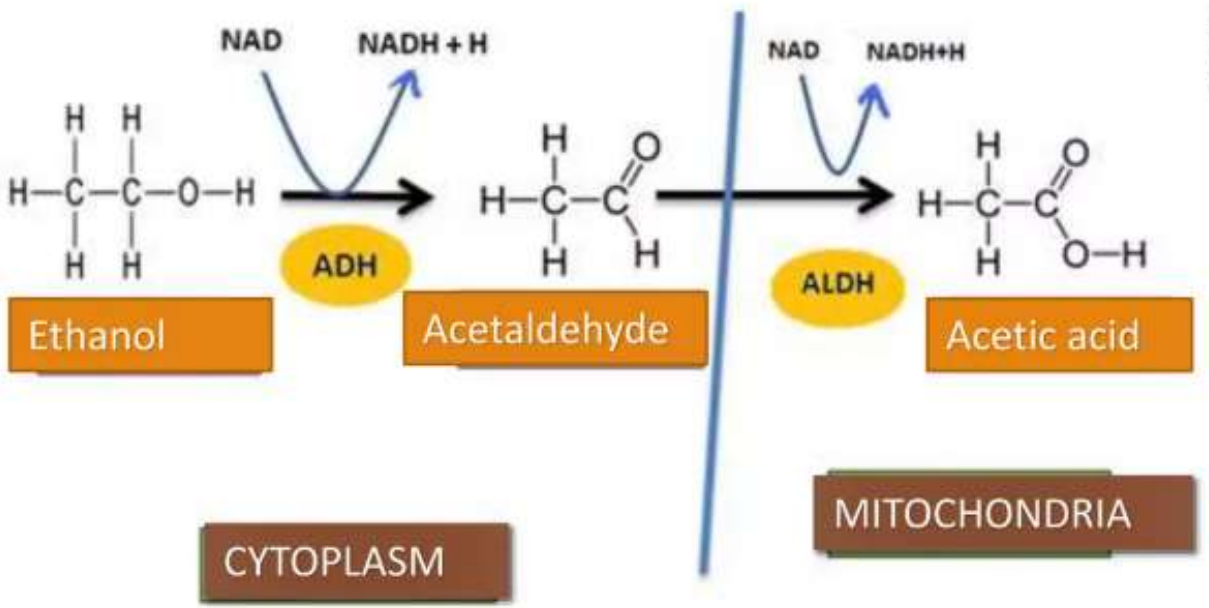
9.DESULFURATION



OXYGENASES

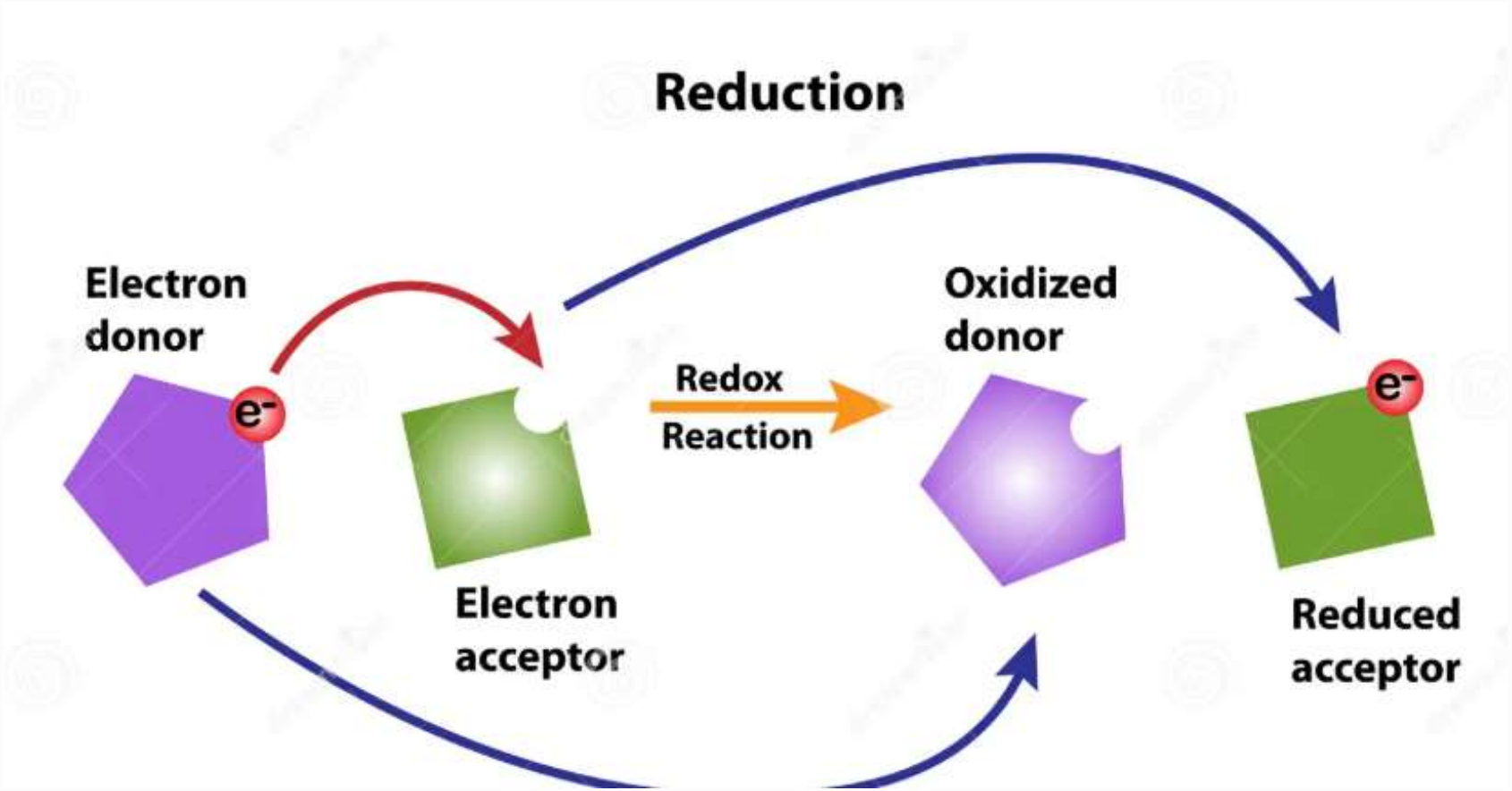


NON MICROSOMAL OXIDATION

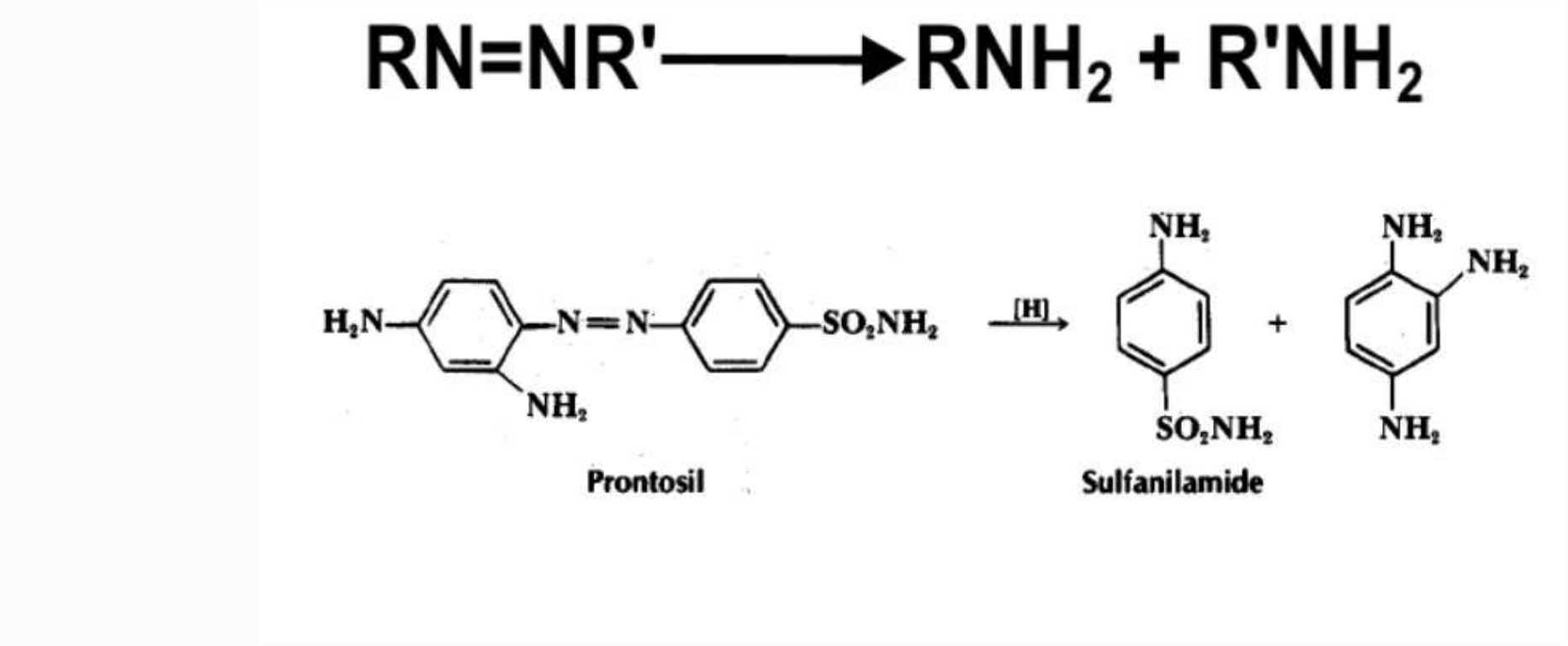


ADH- Alcohol dehydrogenase
ALDH- Aldehyde dehydrogenase

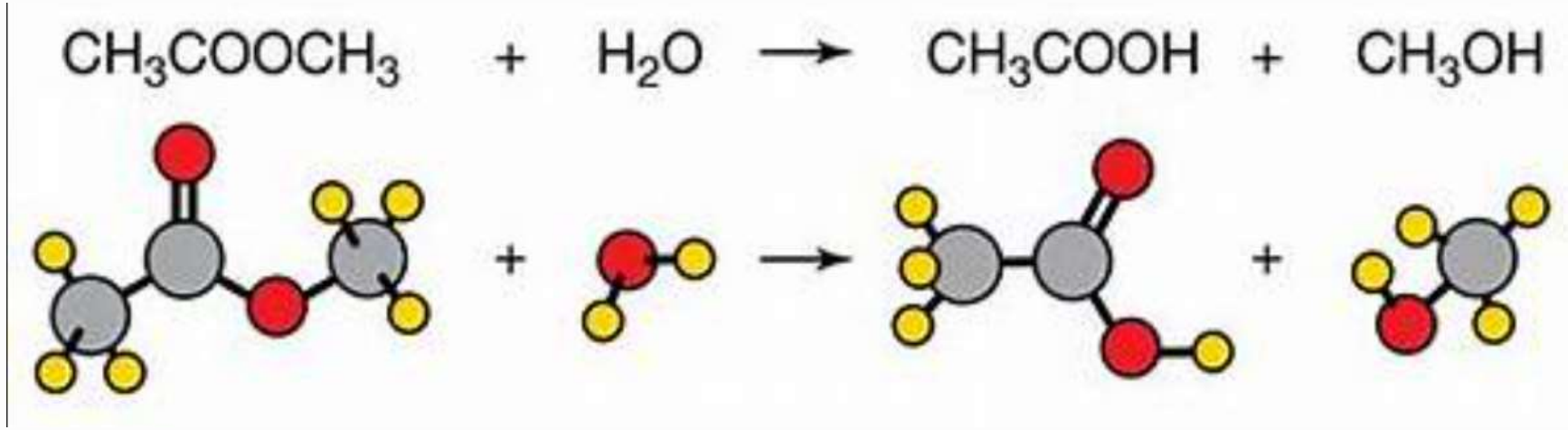
b) REDUCTION


Reduction
Electron donor
e-
Redox Reaction
Oxidized donor
e-
Electron acceptor
Reduced acceptor

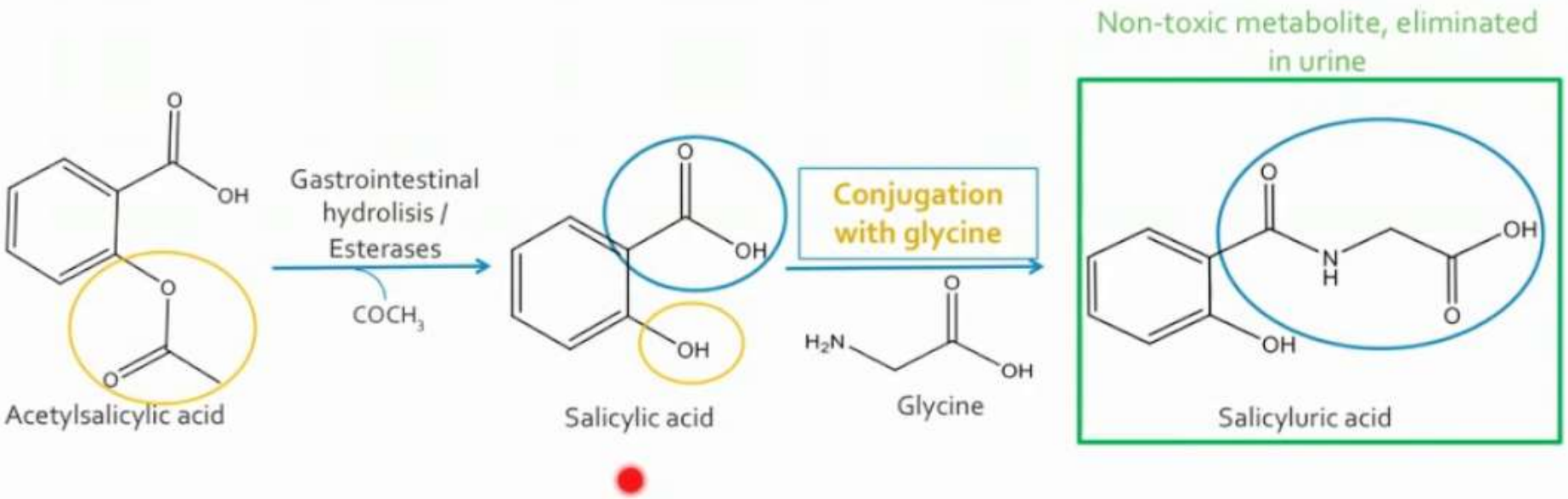
C. AZO REDUCTION



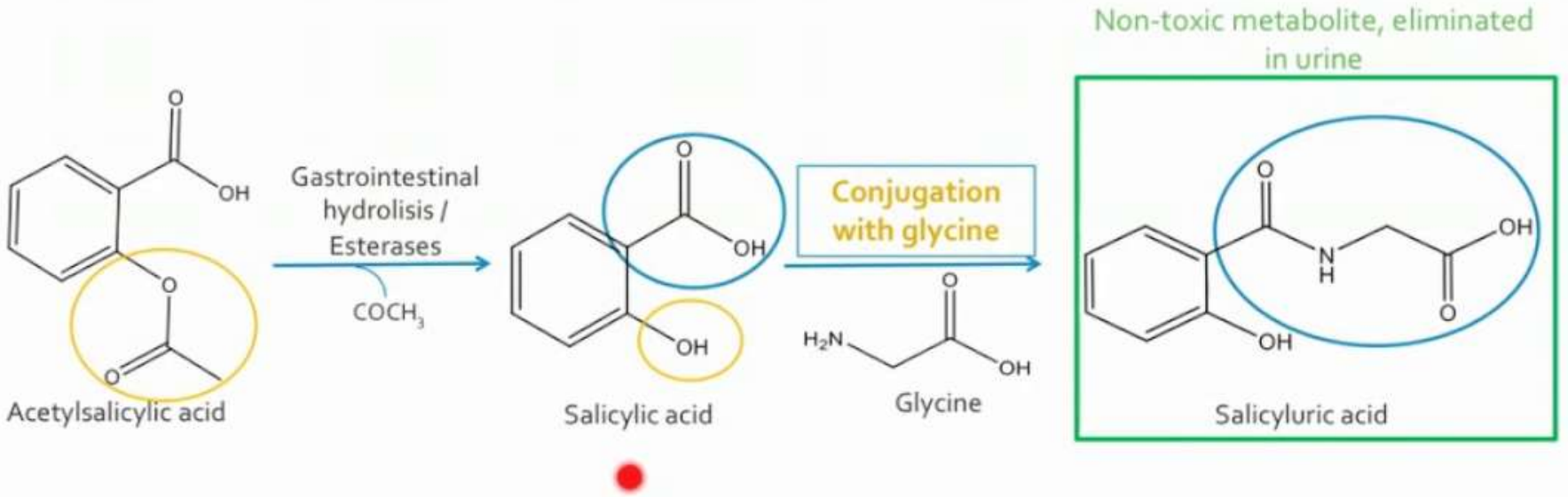
c) HYDROLYSIS



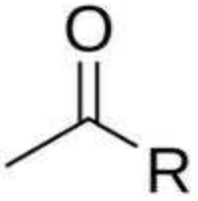
PHASE II REACTIONS CONJUGATION / TRANSFER



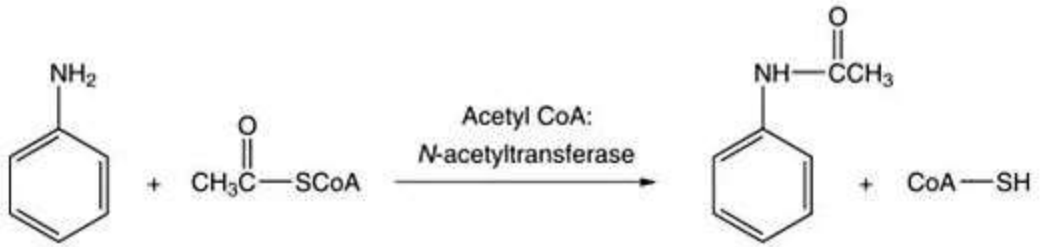
1.CONJUGATION WITH GLUCURONIC ACID



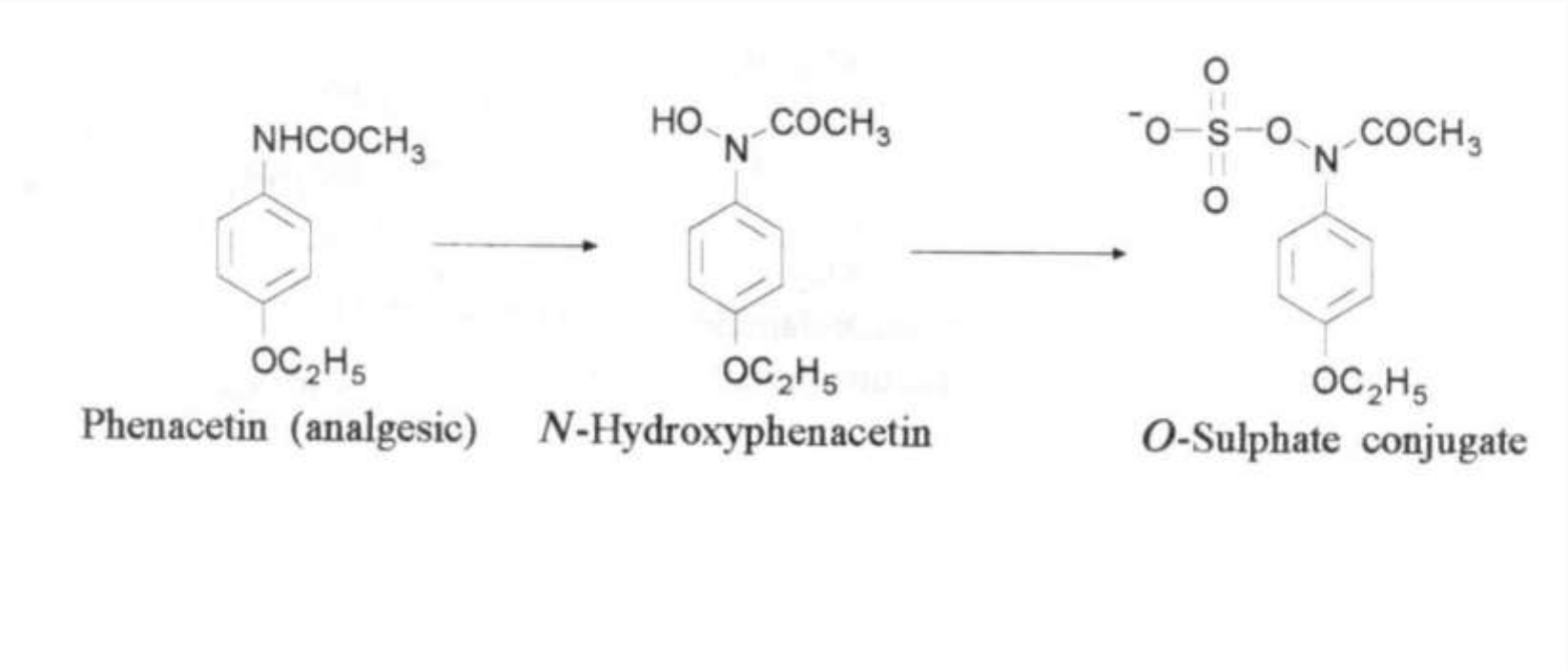
2. ACETYLATION



Acetylation chemical equation:

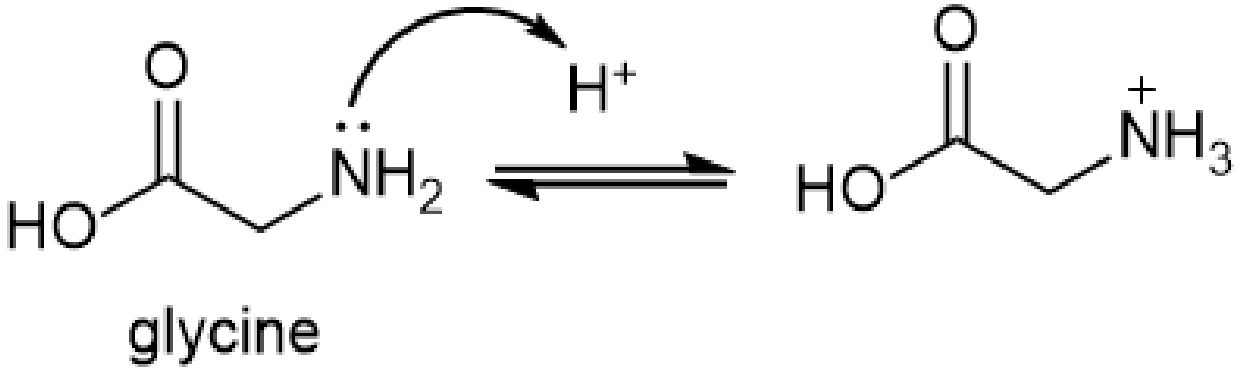


3. CONJUGATION WITH SULFATE



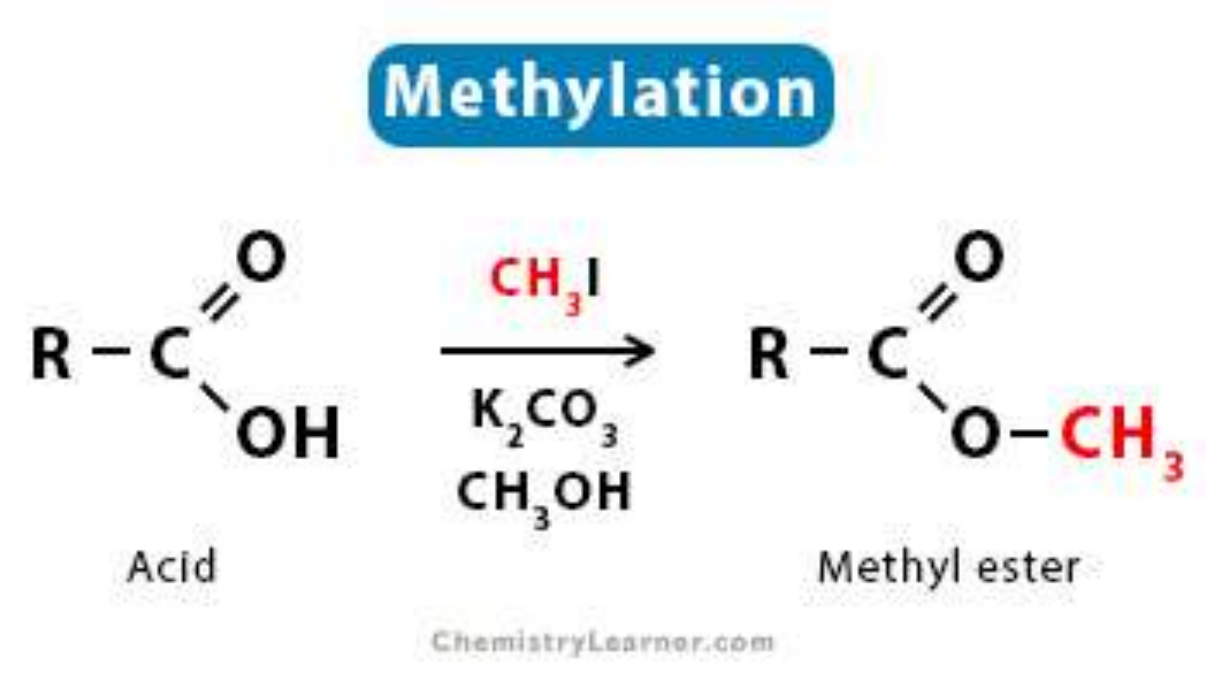
Phenacetin (analgesic) *N*-Hydroxyphenacetin *O*-Sulphate conjugate

4. CONJUGATION WITH GLYCINE

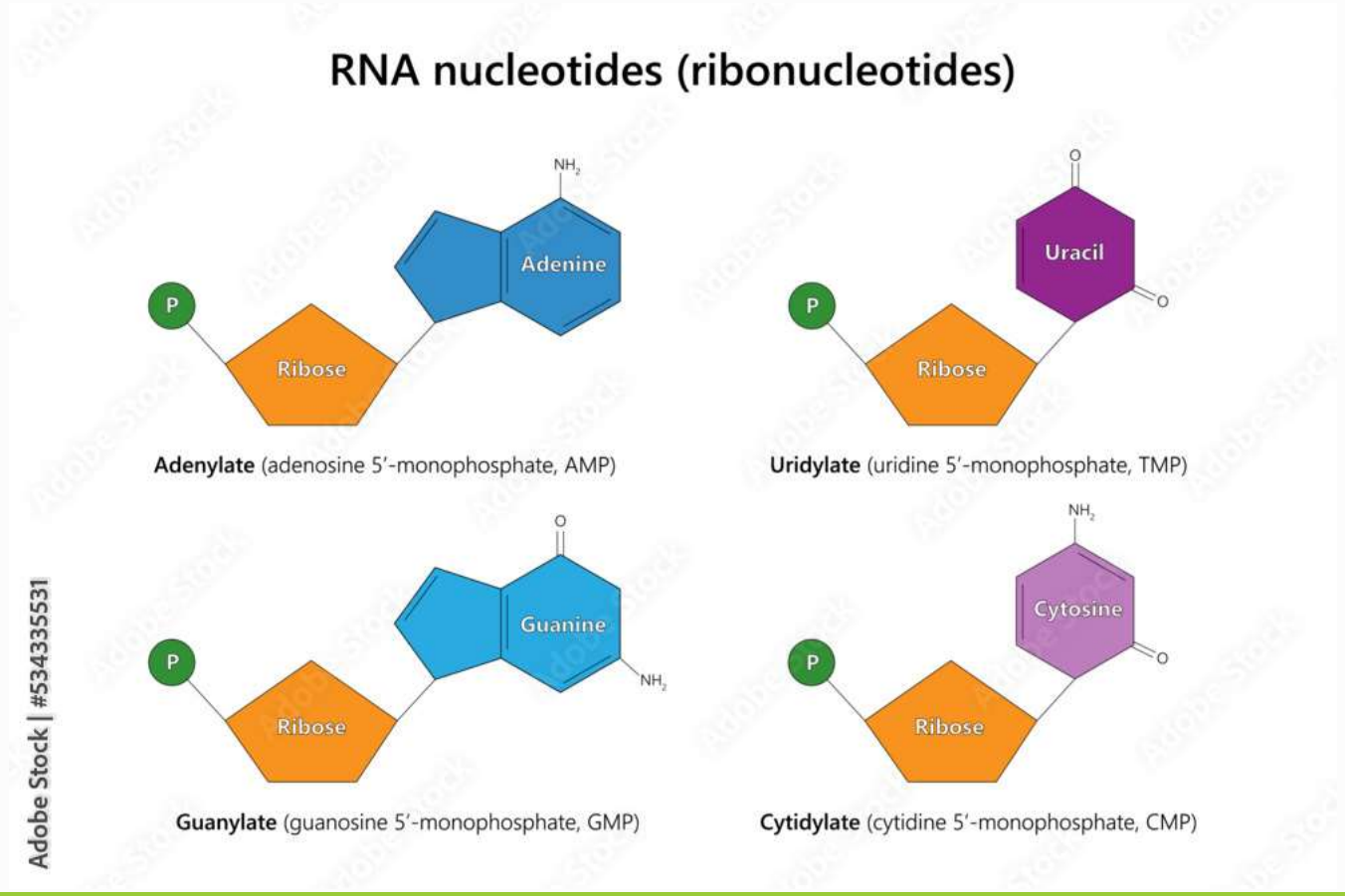


glycine

6. METHYLATION

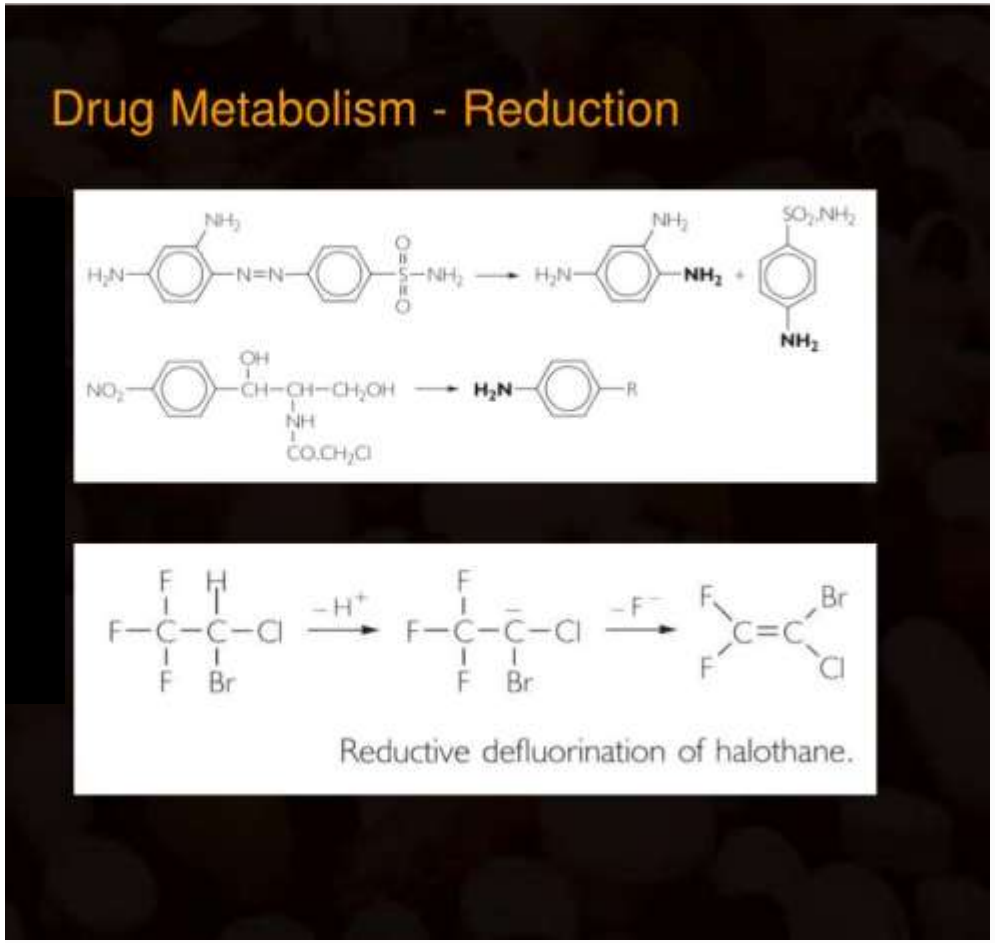


7. RIBONUCLEOTIDE /RIBONUCLEOSIDE SYNTHESIS



CLASS ASSESSMENTS

FIND THE REDUCTION REACTION?



SUMMARY

- Biotransformation is the enzymatic process that modifies drugs in the body, primarily in the liver, to enhance their excretion by converting lipid-soluble compounds into water-soluble metabolites.
- It occurs in two phases: Phase I (functionalization) involves reactions like oxidation, reduction, and hydrolysis, often catalyzed by cytochrome P450 enzymes, to introduce functional groups.
- Phase II (conjugation) attaches endogenous substances such as glucuronic acid or sulfate to form polar, excretable compounds, typically inactivating the drug.

REFERENCE

- Rang & Dale's Pharmacology, 9th Edition, Elsevier, 2019.
- Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 13th Edition, McGraw-Hill, 2018.
- Text book of Pharmacology by KD Tripathi


THANK YOU