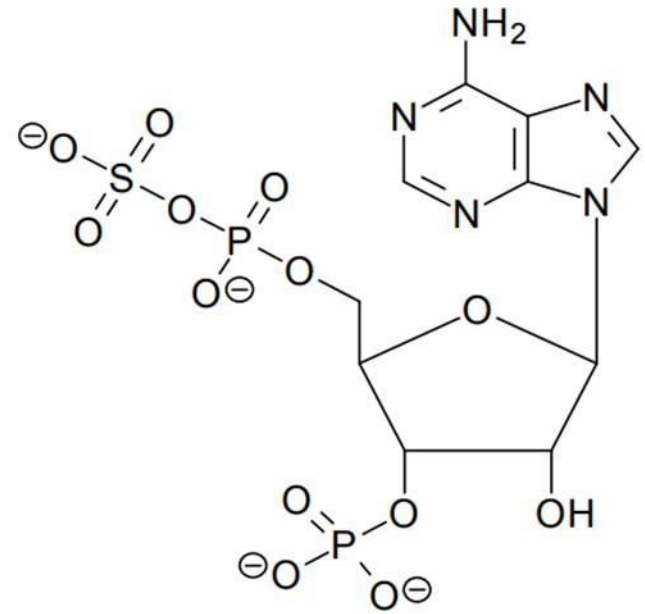
Conjugation reactions and reagents

Reaction	Reagent	Group in substrate
Glucuronidation	UDP-glucuronate	-OH, -COOH, $-NH_2$
Sulfation	PAPS	-OH, $-NH_2$, -SH
Methylation	SAM	-OH, $-NH_2$
Acetylation	acetyl-CoA	-OH, $-NH_2$
Sulfide formation	glutathione	Ar-halogen, Ar-epoxide
Amide formation	glycine, taurine	-COOH

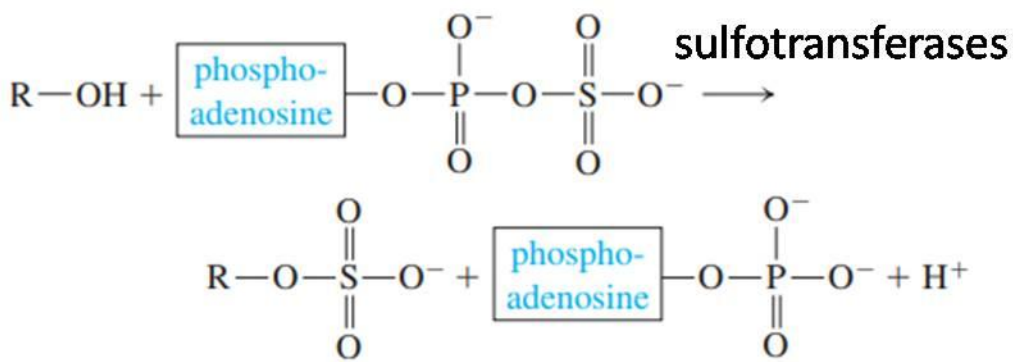
Sulfation

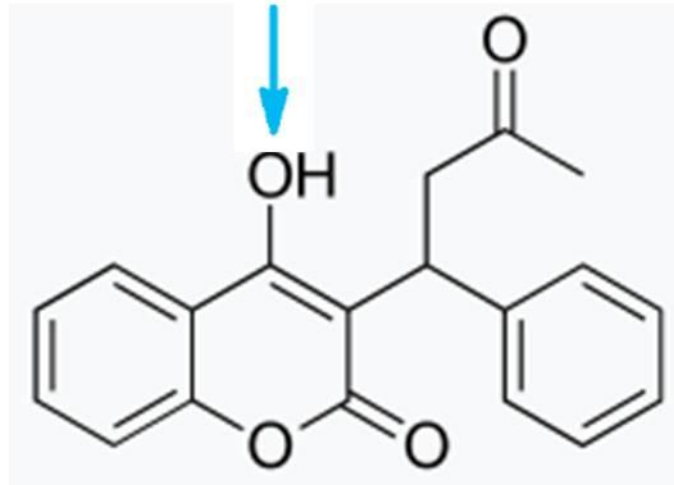
CONJUGATION WITH SULFATE

- Drug groups-Amino, Hydroxyl
- Cytoplasmic Enzymes - Sulfotransferases / Sulfokinases.
- Methyl dopa, Steroids,
  Chloramphenicol, Warfarin

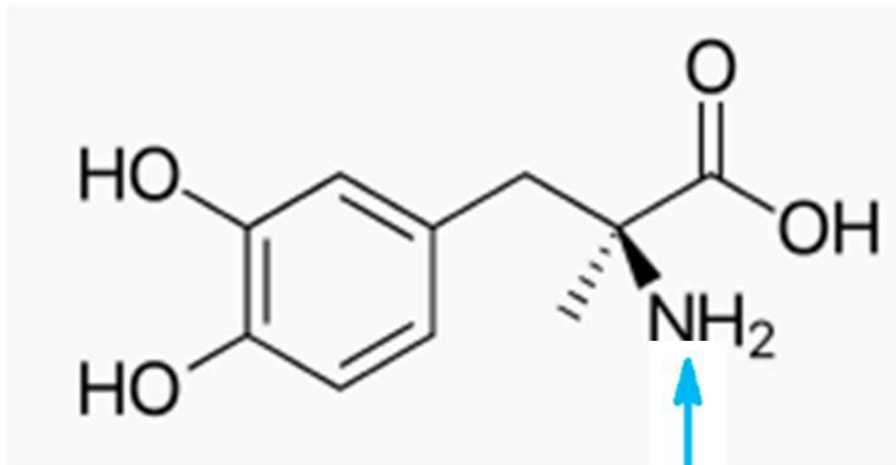


3'-phosphoadenosine 5'-phosphosulfate (PAPS)





Warfarin



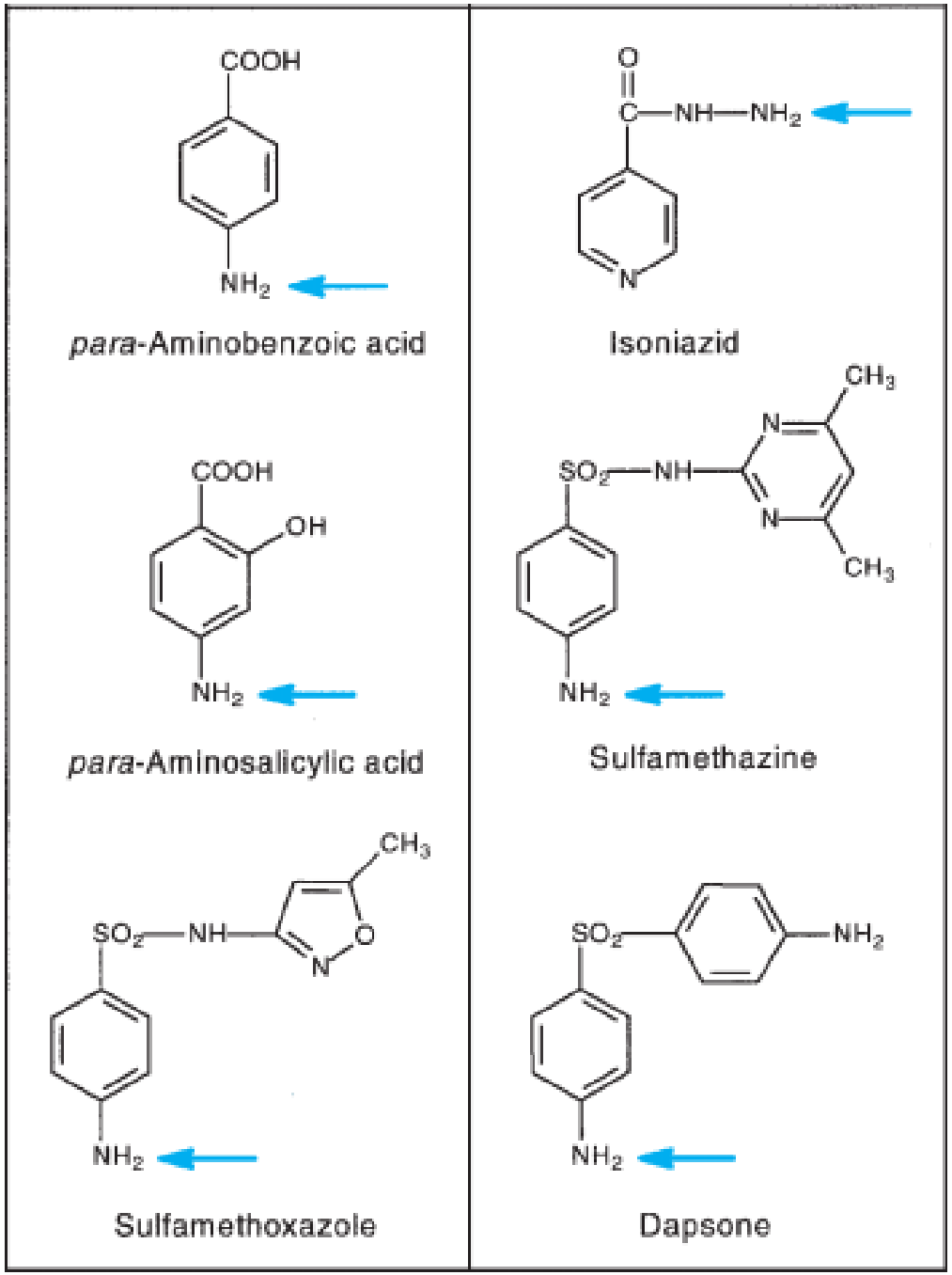
Methyl-DOPA

2. ACETYLATION

- Drugs with Amino or Hydrazine groups - INH,PAS,Hydralazine,Sulfonamides Procainamide,Dapsone. (Code - **SHIP**)

- $R\text{-}NH_2$ —(N Acetyl transferase; Acetyl CoA)→ $R\text{-}NHCOCH_3$

Acetylation



6. METHYLATION

- Drugs with Amino & Phenol groups
- Histamine, Adrenaline, Nicotinic acid, Dopamine, Methyl dopa, Captopril
- Enzyme- Methyl transferase
- Endogenous substance- Cysteine, Methionine

Methylation

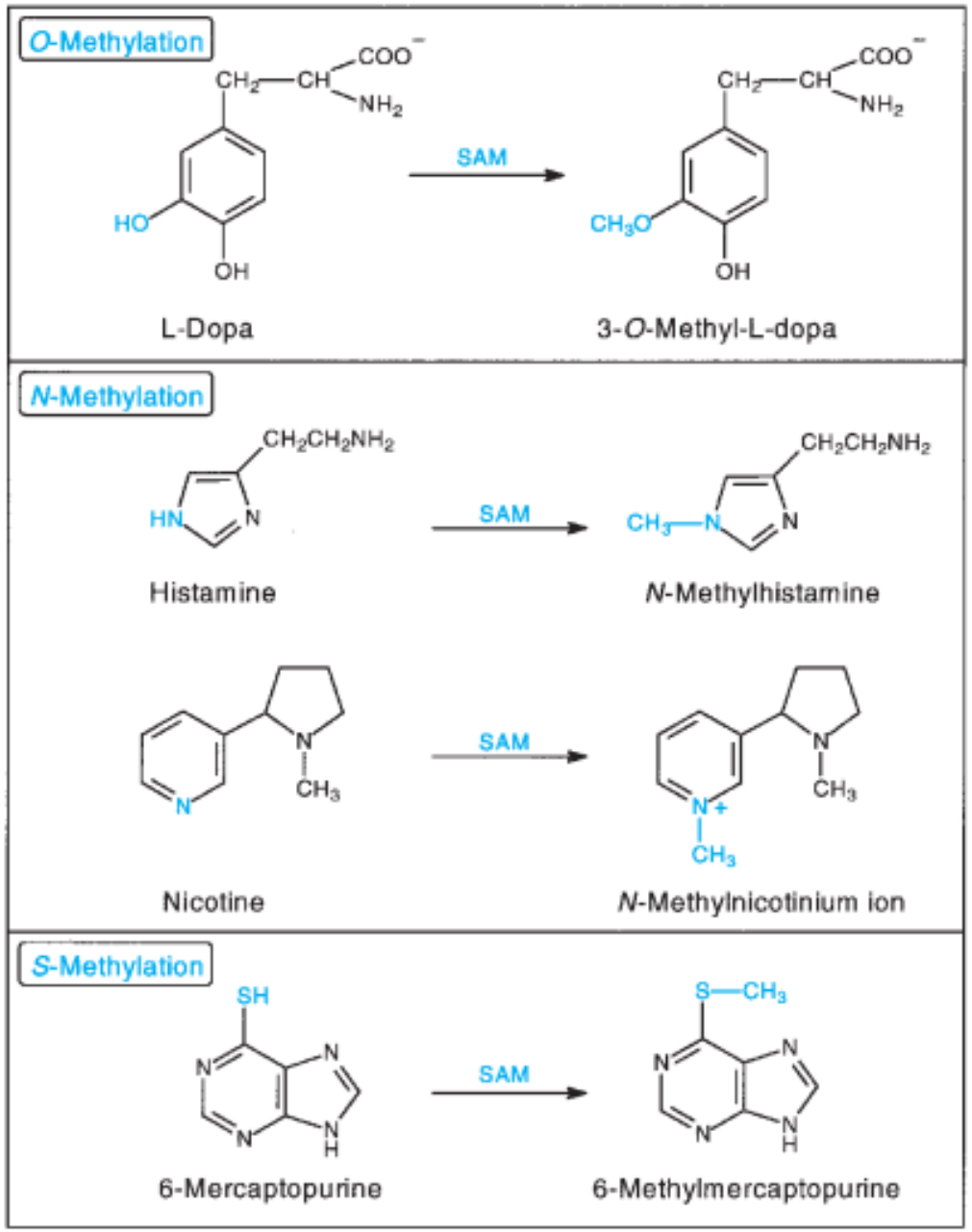
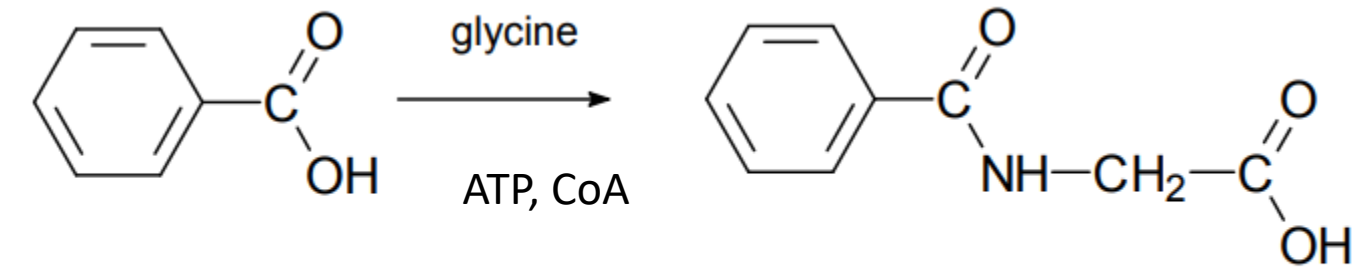


Figure 6-51. Examples of compounds that undergo **O-, N-,** *or* **S-methylation.**

CONJUGATION WITH GLYCINE

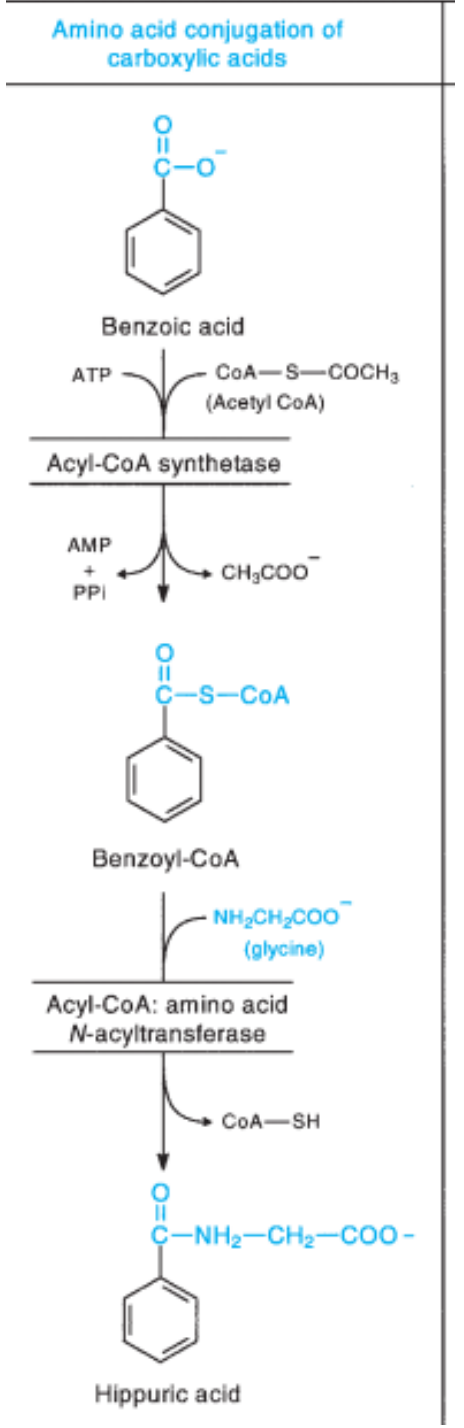
Drug group – Carboxylic acid

Salicylic acid , Benzoic acid



benzoic acid
(activated by CoA)

hippuric acid
(*N*-benzoylglycine)



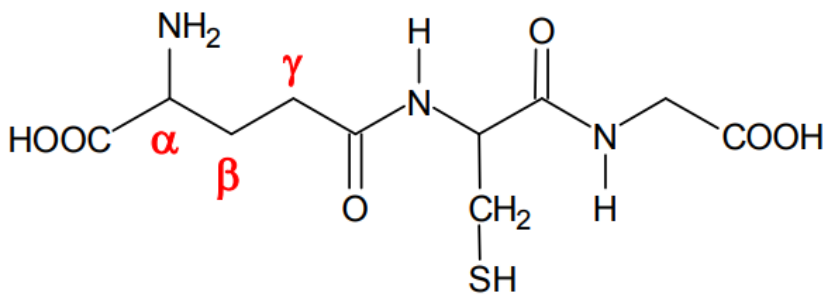
CONJUGATION WITH GLUTATHIONE

Drug groups-Epoxide, Quinone

Toxic metabolites of Paracetamol, Ethacrynic acid

Cytoplasmic Enzyme - Glutathione S- Transferase

Glutathione (GSH)

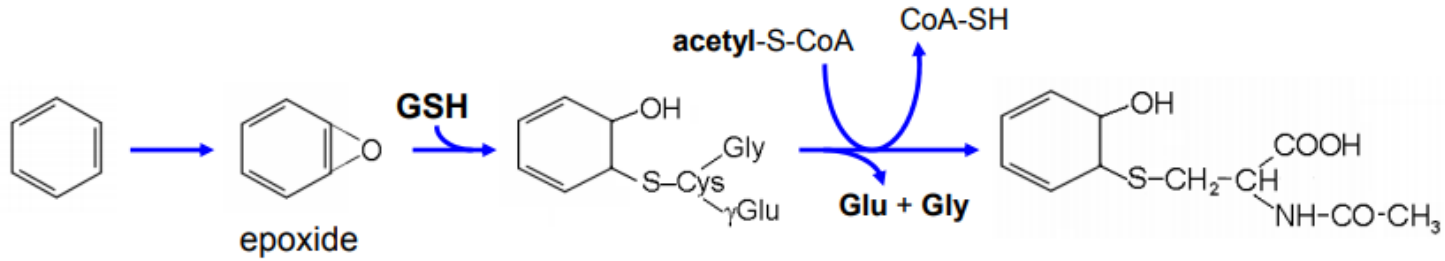


electrophilic site

R-X + GSH → R-SG + XH (R-X epoxides, halogenalkanes)

nucleophilic group

R-SG sulfide is converted to mercapturic acids and excreted



N-acetyl-*S*-substituted cysteine
(mercapturic acid)

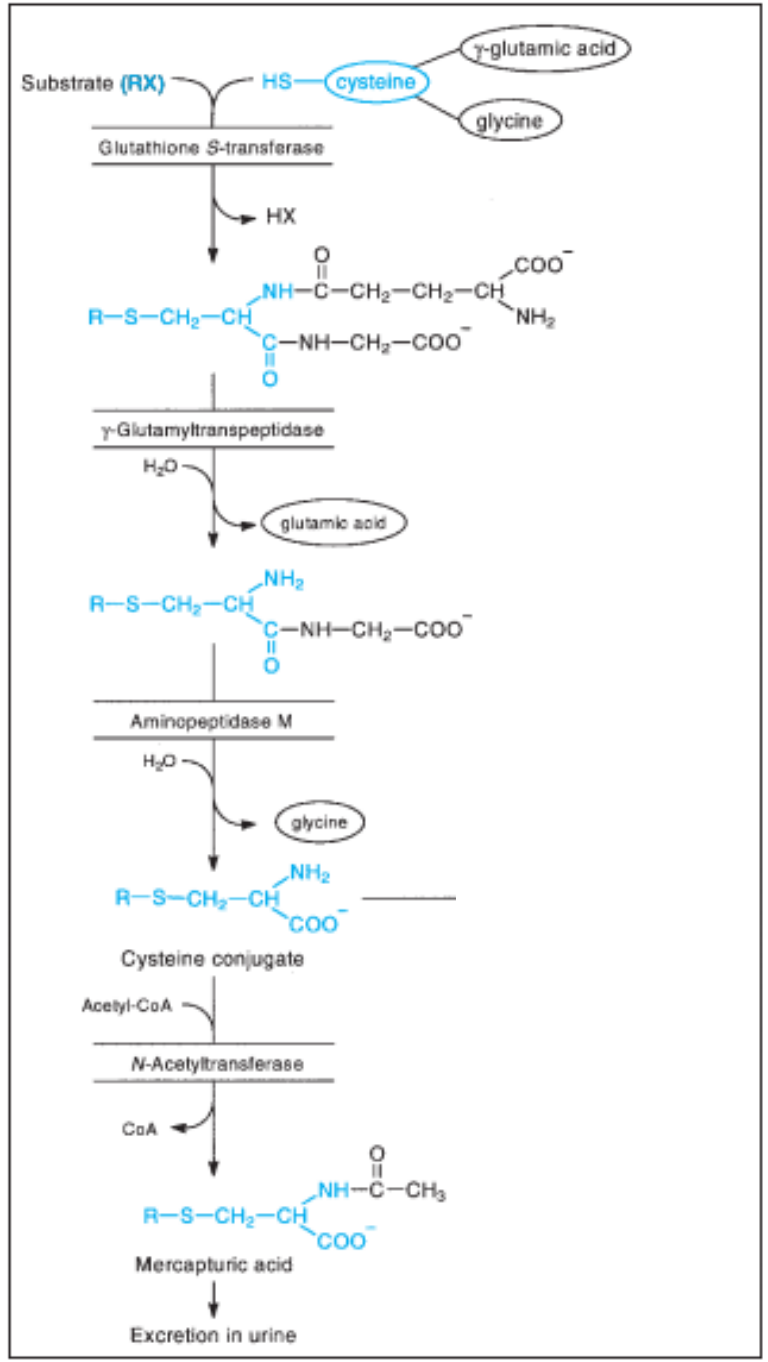


Figure 6-58. Glutathione conjugation and mercapturic acid biosynthesis.