DRUG METABOLISM (BIOTRANSFORMATION)

PHARMACEUTICAL CHEMISTRY I

PHA385

2017-2018

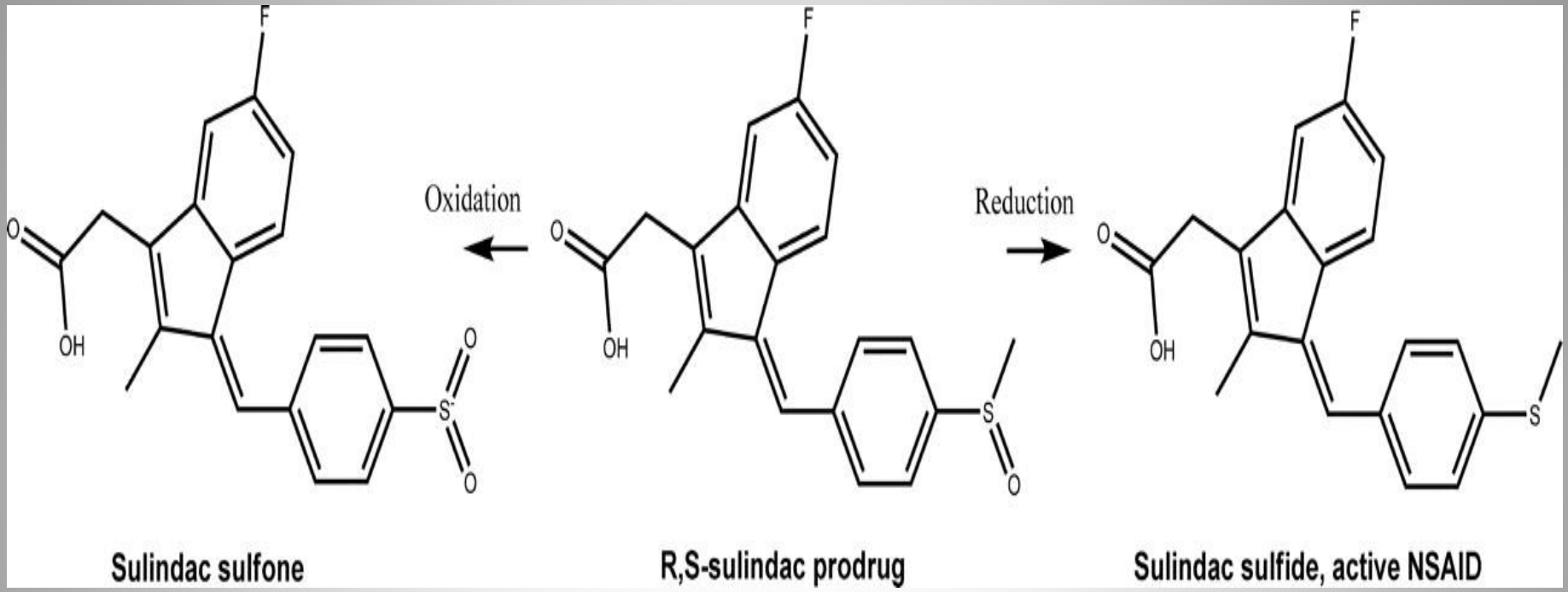
Drug metabolism is the metabolic breakdown / **chemical changes** of drugs by living organisms, usually through specialized enzymatic systems.

- **Metabolite** is the product of a drug after metabolic reactions.

- Metabolism is a very important mechanism for the elimination of drugs from the body.

PRO DRUG

- While not exhibiting any activity in vitro, they give the active compounds metabolically in vivo. These are called **pro drugs**.


F
O
OH
Oxidation
O
S
O
F
O
OH
S
O
Reduction
F
O
OH
S
Sulindac sulfone
R,S-sulindac prodrug
Sulindac sulfide, active NSAID

PHASES OF METABOLISM

Phase I Reactions

- Functionalization reactions

1. OXIDATION REACTIONS

- Aromatic oxidation (Aromatic hydroxylation)
- Alken epoxidation
- Oxidation of aliphatic and alicyclic carbon atoms
- Oxidation of carbons adjacent to an sp2 center

(Oxidation of carbon atoms in benzyl, allylic and carbonyl or imine α- position)

- Oxidation of carbon-nitrogen systems

(Oxidative N-dealkylation, oxidative deamination, N-oxide formation, N-hydroxylation)

- Oxidation of carbon-oxygen systems (Oxidative O-dealkylation)
- Oxidation of carbon-sulfur systems

(Oxidative S-dealkylation, S-oxidation, desulfurization)

- Alcohol and aldehyde oxidation

2. REDUCTION REACTIONS

- Carbonyl (aldehyde, ketone) reduction
- Nitro reduction
- Azo reduction

3. HYDROLYSIS REACTIONS

- Hydrolysis of esters and amides

Phase II Reactions

- Conjugation reactions

- **glucuronic acid**
- **sulfate**
- **acetate**
- **an amino acid**