

← أسئلة كميّة في الامتحان

# PHARMACOKINETICS

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# Pharmacokinetics

what the body does to the drug?

■ Absorption

■ Distribution

■ Metabolism

■ Excretion.

لا يبدى إلى  
water soluble  
metabolism

from lipid soluble to  
water soluble →  
excretion

البدن يتلقى  
من الدواء

# Drug Biotransformation (METABOLISM)

1  
2  
3

➤ **The importance of biotransformation** is the conversion of

unionized drugs to ionized, water soluble metabolite which is easily excreted.

➤ **The liver** is the main organ of metabolism but can occur

not Heart

first pass metabolism  
Metabolism ← [ Systemic Circulation ]

in other organs like lung, kidney and intestine.

Skin

# Consequences of drug metabolism

Water soluble = polar drug

1. Convert ~~active drug~~ to ~~inactive metabolite~~ (most drugs)

→ lipid soluble, non-ionized

→ water soluble  
→ insoluble

2. Convert ~~inactive prodrug~~ into ~~active drug~~

“Prodrug”

e.g. enalapril <sup>for Hypertension</sup>  
<sub>lipid in April</sub> مفتاح ربط



enalaprilat (active) <sup>water soluble</sup>  
الزيادة في القوة

3. Convert ~~active drug~~ to ~~active metabolite~~

e.g. codeine <sup>كوداين</sup>



morphine. <sup>codeine active مرات 5 اكثر من كوداين</sup>  
5-time active more than codeine

4. Convert ~~drugs~~ to ~~toxic metabolites~~

سُمع رافع

e.g. Halothane & Paracetamol ---- hepatotoxic

epoxides.

# Biotransformation reaction

*Chemical reaction*

Phase I

- oxidation, reduction  
hydrolysis

=

Phase II

- Biosynthetic reactions  
"conjugation"

# Phase I

oxidation by **Cytochrome P450 (CYP)**.

= ER  
mitochondria

• كل احدى Phase I  
منى لا يفرغ من  
بشكل اذية phase II  
Phase I

active drug  
to inactive

prodrug to  
active drug

water  
soluble

not water soluble

Excreted by the kidney

Enters phase II

[ prodrug ]  
↑  
[ active ]  
الأنشطة  
النشطة

بصير اليا  
phase II

تصنيع جزئية جديدة  
**Phase II (biosynthetic)**  
water soluble  
منوم كان الدواء للنم يطبع  
"conjugation" reactions

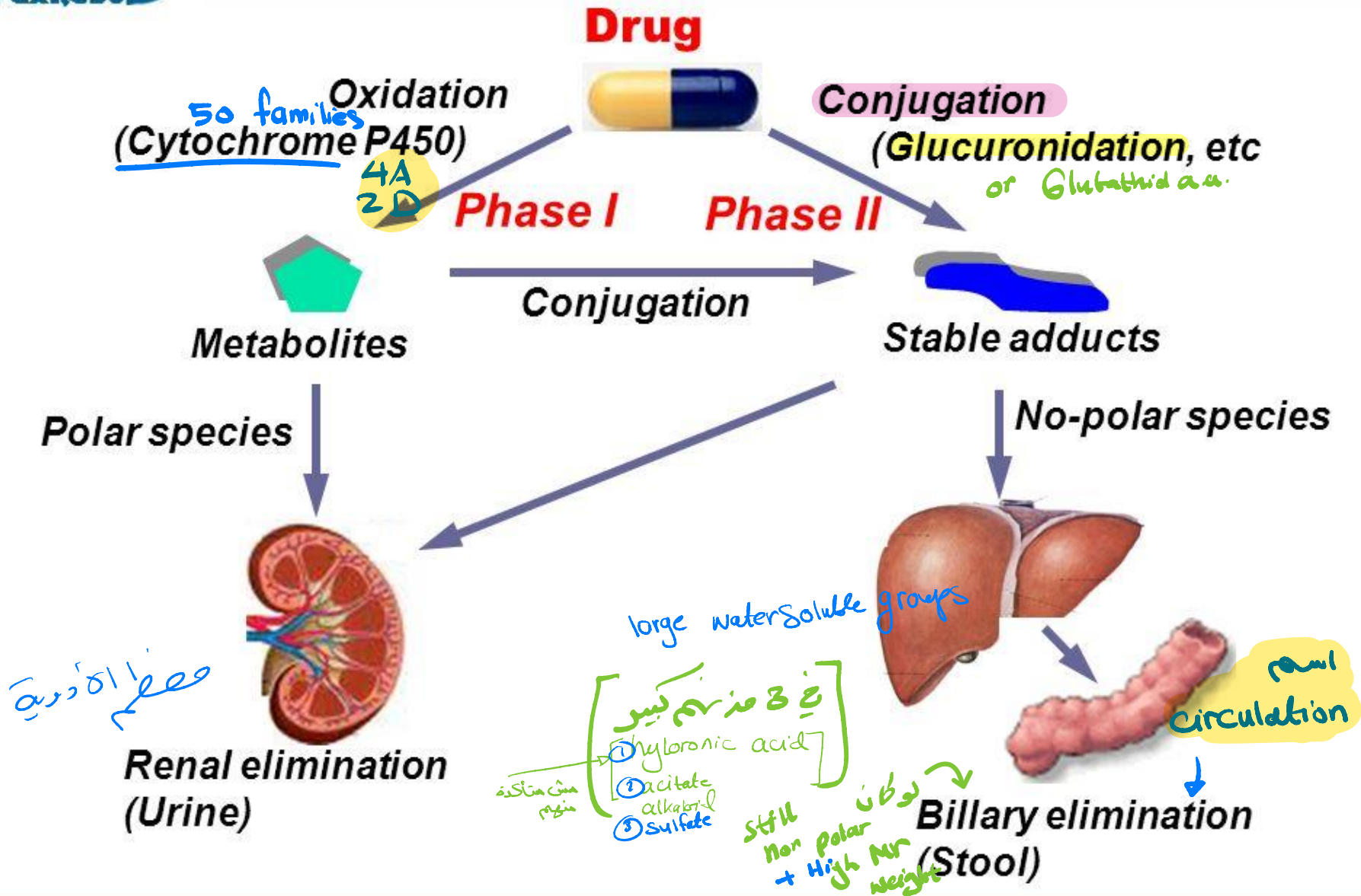
Water soluble  
محل مجموعة كبيرة

❖ An endogenous substrate e.g. glucuronic acid, sulfate,  
glutathione amino acids, or acetate is conjugated with the  
parent drug or its phase I metabolite.

انا بفوت المرحلة الأولى ما زبط ولسا ضل ليبد  
بروح مرحلة ٢ الي هي اجيب مادة water soluble كبيرة وبحطها  
عليه  
بدل ما احولها انا لزقتها بمركب water soluble فصارت زيه بالمعني  
يعني

❖ This result in formation of water soluble and rapidly  
eliminated conjugates..

# Phases of metabolism





# Factors affecting biotransformation

1. Physiological factors: age, Sex.

mature > liver adult full capacity  
immature < liver  
pathological linear

male أسرع

female أكثر من CYP450 male

2. Pathological factors: liver cell failure.

50 family

3. Pharmacogenetic variation in metabolizing

Genetic variation

enzymes e.g. slow and fast acetylators.

مثل Cytochrome 3A4

لأن لو ما كان موجود فكل الأدوية التي يتكسر من خلالها خارج يصير لها خطورة  
لأنه إذا ما تكسر صيغته مستوطني الدم من Toxicity

4. Enzyme induction & enzyme inhibition.

drug-drug interaction

# Enzyme induction

تغير activity و number من 450 P

❖ Many drugs are able to induce (increase activity and number) of microsomal enzymes resulting in increased rate of metabolism of the inducing drug as well as other drugs metabolized by the same microsomal enzymes.

Tolerance  
= reversible =

enzyme inducer drug

❖ Some inducing drugs : Phenobarbitone, phenytoin, anti epileptic drug, nicotine, rifampicin, carbamazepine.

ادوية  
الاصع

"Please Pass Nicotine Rapidly to Calm"\*\*\*

- Please: Phenobarbitone
- Pass: Phenytoin
- Nicotine: Nicotine
- Rapidly: Rifampicin
- Calm: Carbamazepine



# Consequences of enzyme induction:

1. Increase metabolism of the inducing drugs. This leads to **tolerance** e.g. phenobarbitone.
  2. Drug interactions:
    - ❑ Rifampicin enhances metabolism of warfarin *← بصير عديها طلبة مع دها بتوخذ دواد*
    - ❑ Antiepileptics increase the metabolism of each other. *أدوية الصرع*
  3. Prolonged use of **enzyme inducers** may produce **rickets** or **osteomalacia** due to **increased metabolism of vitamin D**.
- ❖ Enzyme induction is **reversible**. It occurs over few days and passes off over **2 - 3** weeks after withdrawal of inducer.

لو طفر كساع  
لو كبرو صانسة  
anti-coagulant

# Enzyme inhibition

➔ Many drugs inhibit activity of microsomal enzymes resulting in decreased rate of metabolism of other drugs i.e. potentiate their pharmacological actions.

po·ten·ti·ate | pə'ten(t)SHē.āt | verb

• increase the power, effect, or likelihood of (something), especially a drug or physiological reaction)

➔ Some enzyme **Inhibitor drugs**

❖ **Erythromycin, Clarithromycin, Cimetidine, Contraceptive pills**

“Eric and Clara traveled with Simon to look for contraceptive pills.”

“إيريك وكلارا سافروا مع سيمون للبحث عن حبوب منع الحمل”

- *Eric: Erythromycin*
- *Clara: Clarithromycin*
- *Simon: Cimetidine*
- *Contraceptive pills: Contraceptive pills*

# Consequences of enzyme inhibition on metabolized drugs

*exaggerate* | *ig'adzaret* | *transitive verb*  
(the importance, a claim) *بَالَعُ (في) ضَخَمَ، غَالَى (في)*

1) Exaggerated pharmacological actions.

2) Exaggerated adverse effects. ←

3) Drug interactions.

toxicity

adverse effect

A top-down view of a spiral-bound notebook with a white cover and lined pages. The notebook is open to a page with the words "TO BE CONTINUED" written in large, bold, black capital letters. The page is decorated with several crumpled balls of paper in various colors: pink, yellow, green, and orange. A yellow pencil lies diagonally across the bottom right corner of the notebook. The notebook is placed on a light brown, textured surface. Two dark grey horizontal bars are visible on the left and right sides of the image, partially overlapping the notebook's edges.

**TO BE  
CONTINUED**