



# Metabolism of cyclophosphamide

تقدير اسم oxidase

- the products of cyclophosphamide activation can be converted to the inactive metabolites by the action of alcohol and aldehyde dehydrogenase
- additionally, cyclophosphamide can undergo N-dealkylation on either chain
- the product of this reaction is chloroacetaldehyde, which is highly nephrotoxic and neurotoxic
- it can be further oxidized by the action of aldehyde dehydrogenase to chloroacetic acid





CYCLOPHOSPHAMIDE



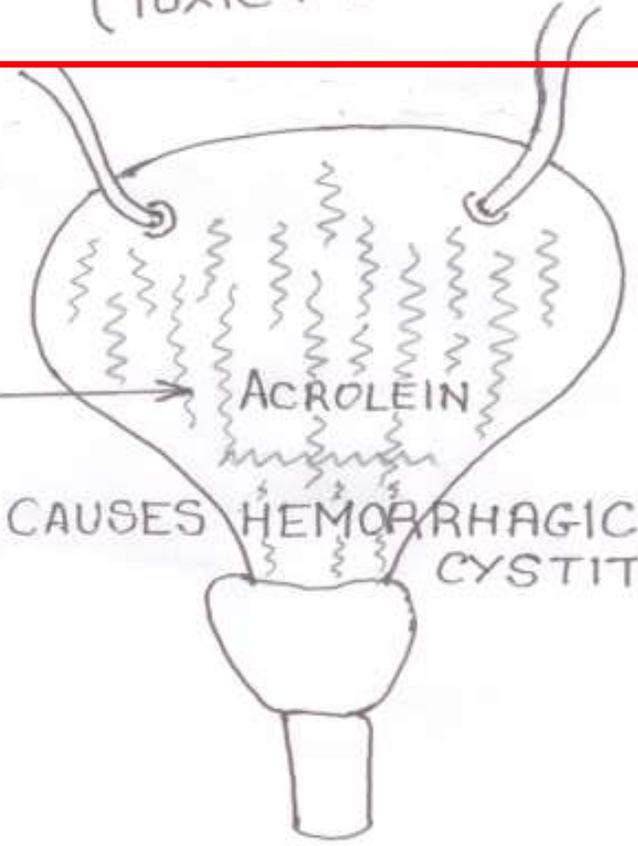
ALDOPHOSPHAMIDE

Covelant bond with bladder and kidney

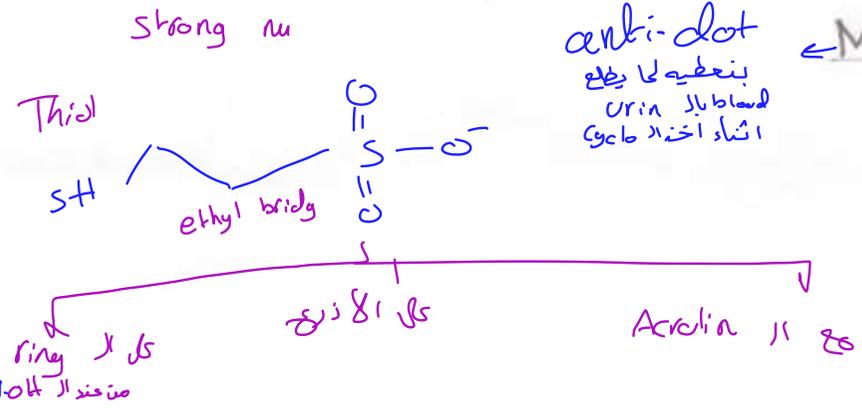


ACROLEIN (TOXIC METABOLITE)

PHOSPHORAMIDE MUSTARD (CYTOTOXIC EFFECT)



Mesna (SH-Compound)



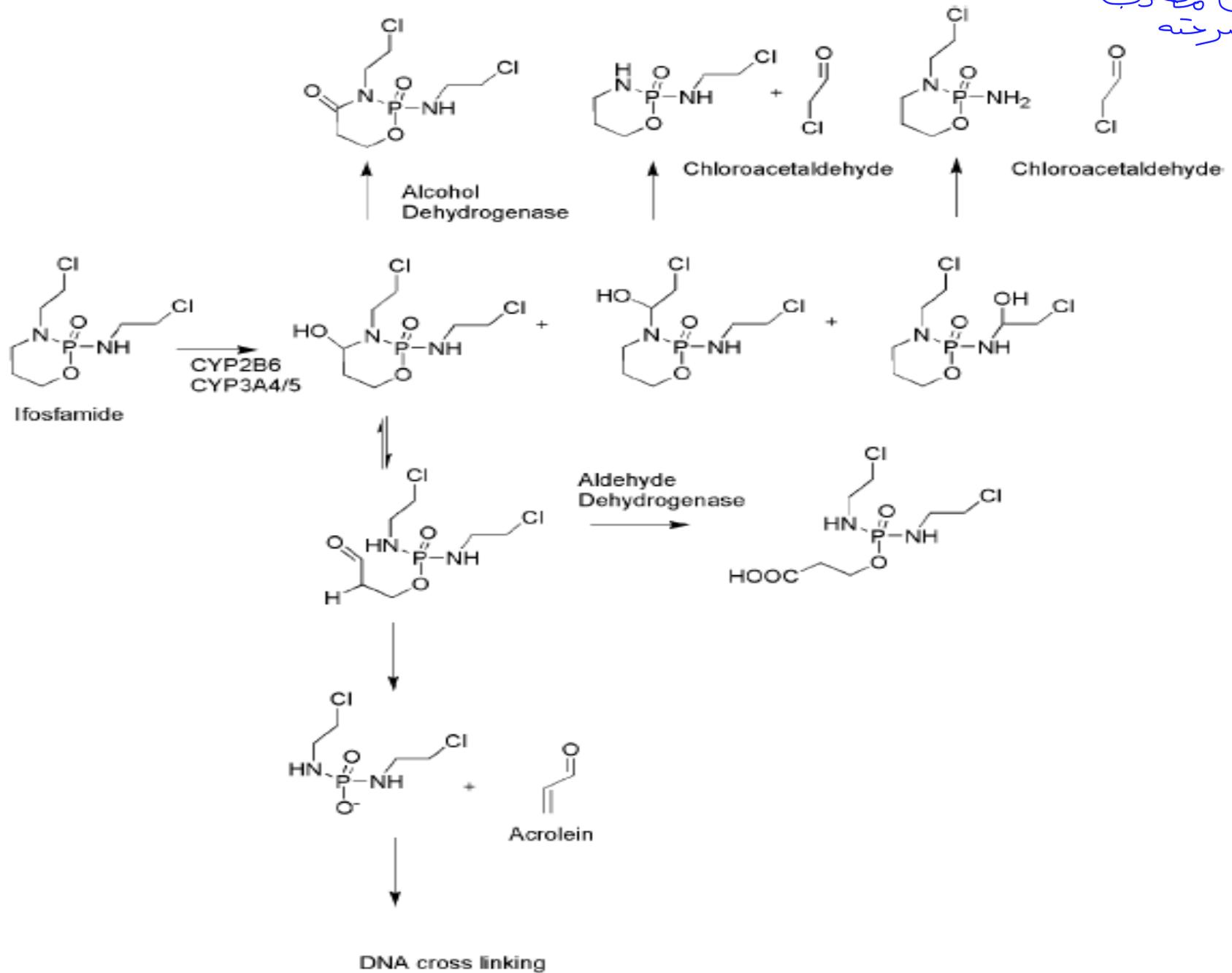
CAUSES HEMORRHAGIC CYSTITIS







حکمت میں مطلوب  
منا لایہ شرحہ  
بالہ Cyclo



Scheme 10.7 • Metabolic and chemical activation of Ifosfamide.





# Alkylating Agents—Nitrosoureas

- Carmustine, Lomustine, Semustine: Also activated in vivo بجسم
- Alkylate DNA BUT alk'n proteins → toxicity Protein alkylation لا حيز ازا صار toxicity في
- Pharmacokinetics:
- Nitrosoureas are highly lipophilic and reach cerebrospinal fluid concentrations that are about 30% of plasma concentrations.
- Indications: تغير نسبة حيز
- Because of their excellent CNS penetration, carmustine and lomustine have been used to treat brain tumors.





# Fate of decomposition products of nitrosoureas

- THE AZOHYDROXIDE that is generated by thermal decomposition of a nitrosourea can decompose to nitrogen and a chloroethyl cation *يعرف من جهته*
- this cation can serve as a biological alkylating agent (bis-alkylating agent) or ~~undergo reaction with water (to form an alcohol) or Cl<sup>-</sup> (to form dichloroethane)~~
- it can also rearrange to react with water to produce acetaldehyde *مش صميت*

## ISOCYANATE:

- isocyanates that are generated by decomposition of nitrosoureas can react with amino groups on Lys side chains of proteins
- the amino groups are said to be carbamoylated which alters protein structure may lead to inhibition of several types of DNA repair enzymes
- the isocyanate that is generated by decomposition of nitrosoureas, is probably responsible for adverse effects by carbamoylating amino acid side chains that are contained in proteins

هذا ال enzyme عبارة عن protein  
من ذل ال enzyme تقصوا النطقة  
التي صار عليها الalkylation و  
يرجعو يعلو قطعه DNA جديده  
بده: الisocyanate وال  
رج يرتبط معم ويعد Inhibition  
نحسب وينه رج يرتبط رج يكون  
↓  
goad @B toxic  
↓  
Concer cell human cell











