



Alcohols : محاضرة

Jeneen Alhasan : الصيدلانية



لجان التفتعات





# Alcohols

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Pharmacology II

الانسان يتعرض للكحول بطريقتين ، اما عن طريق شرب الكحول او اثناء التعامل مع التصنيع في المختبرات و ممكن يستنشقها او تنكب عليه

# Alcohols

- *most common* **Ethanol** is the most important alcohol of pharmacologic interest.
- It has *تقليل التوتر* anxiolytic and sedative effects, but its toxic potential outweighs its benefits.
- Its abuse causes major medical and socioeconomic problems.
- *يستخدمها كثير في الصناعة* Other alcohols of toxicologic importance are **methanol** and **ethylene glycol**.

الmetabolism بصير بالliver بخطوتين اول اشي بتحول الايثانول ل acetaldehyde و هاي بتكون عن طريق انزيم alcohol dehydrogenase او microsomal ethanol Oxidizing system

# Ethanol in liver

و هاي بتكون بالblood و بيشتغل لما توصل نسبة الايثانول في الدم لكميات كبيرة يعني اكثر من ١٠٠مغ/ديسيليتير و هدول الانزيمين بحولوا الكحول ل acetaldehyde بعد هيك ال acetaldehyde نفسه toxic للجسم لذلك لازم يصير عنا خطوة تانية منحول ال acetaldehyde لمركب اقل خطورة و اسهل انه يطلع من جسم الاتسان و هاد الحكي بصير عن طريق انزيم تاني اسمه aldehyde dehydrogenase

• Two enzyme systems metabolize ethanol to acetaldehyde. بحول ال Acetaldehyde

1. Alcohol dehydrogenase (ADH) ل acetate و هي عبارة عن volatile compound و بطلع من الجسم عن طريق ال breathing

• NAD<sup>+</sup>-dependent enzymes, found mainly in the liver. ف اذا بدهم يفحصوا واحد انه شارب كحول او لا عن طريق النفس

• It accounts for the metabolism of low to moderate doses of ethanol.

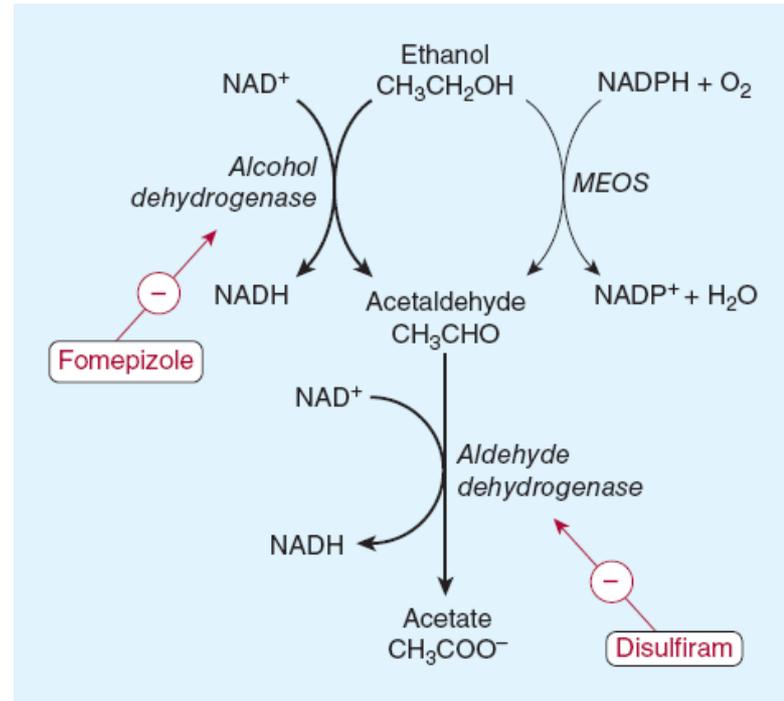
• Has zero-order kinetics, resulting in a fixed capacity for ethanol metabolism. عنده حد معين للمetabolism

2. Microsomal ethanol-oxidizing system (MEOS)

• Contributes significantly to ethanol metabolism at blood ethanol levels higher than 100 mg/dL.

# Ethanol

- **Acetaldehyde Metabolism**
- Acetaldehyde formed from the oxidation of ethanol by either ADH or MEOS is rapidly metabolized to acetate by aldehyde dehydrogenase, a mitochondrial enzyme found in the liver and many other tissues.
- Aldehyde dehydrogenase is inhibited by **disulfiram**.



الكحول و الإيثانول بالأخص بتأثر كثير على ال **metabolism** للأدوية بطريقتين حسب استهلاك الكحول ف اذا كان الاستهلاك **chronic** يعني بشكل يومي بشرب مرتين ل اربع مرات و التأثير رح يختلف عن تأثير ال **acute** اللي كل اسبوع او اسبوعين

# Alcohol-Drug Interactions

الباراسيتامول بصيرله

ميثابوليزم بال **liver** عن

طريق **cytochrome P450 enzymes** و بالخطوة الاولى بتحول ل **hepatotoxic metabolite** اسمهم **reactive oxygen species** او **free radicals** و بالخطوة الثانية ال **free radicals** بترتبط مع مادة ثانية اسمها **glutathione** و يتخلص منها الجسم و بتكون موجودة بال **liver** و هاي الخطوة بتصير لأنه ال **free radical** بتكون **unstable** و بدها ترتبط مع اشي بس لما تكون عملية الميثابوليزم سريعة

- Interactions between ethanol and other drugs can have important clinical effects resulting from alterations in the pharmacokinetics or pharmacodynamics of the second drug.

بصير عملية تحويل الباراسيتامول

ل **free radical** بكميات اكبر فكمية

ال **glutathione** الموجودة ما رح تقدر تكفي انها تعمل **elimination**

لل **free**

- **Prolonged** intake of alcohol without damage to the liver can **enhance** the metabolic biotransformation of other drugs.

**Radicals**

فاللي ضلوا

بترتبطوا مع

خلايا الكبد

و بعملوا

**Hepato**

**Toxic**

**Metabolites**

- Ethanol-mediated induction of hepatic cytochrome P450 enzymes is particularly important with regard to **acetaminophen**. Chronic consumption of three or more drinks per day increases the risk of hepatotoxicity due to toxic or even high therapeutic levels of acetaminophen as a result of **increased P450-mediated conversion of acetaminophen to reactive hepatotoxic metabolites.**

- Current FDA regulations require that over-the-counter products containing acetaminophen carry a warning about the relation between ethanol consumption and **acetaminophen-induced hepatotoxicity.**

اكثر عنده تباين  
باستهلاك الكحول همد  
ال liver ر الطبع اسوأ  
لما بتحولك باراحتياصك

بارا سيتامول



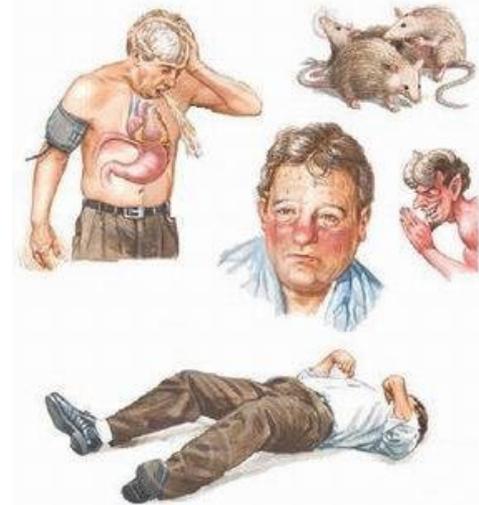
# Alcohol-Drug Interactions

- In contrast, acute alcohol use can inhibit metabolism of other drugs because of decreased enzyme activity or decreased liver blood flow.
- Phenothiazines, tricyclic antidepressants, and sedative-hypnotic drugs are the most important drugs that interact with alcohol by this pharmacokinetic mechanism.
- Pharmacodynamic interactions are also of great clinical significance.
- The additive CNS depression that occurs when alcohol is combined with other CNS depressants, particularly sedative-hypnotics, is most important.

سيداتيف هايپ و  
كحول  
بنظيرين مع بعض

# Alcohol Withdrawal Symptoms

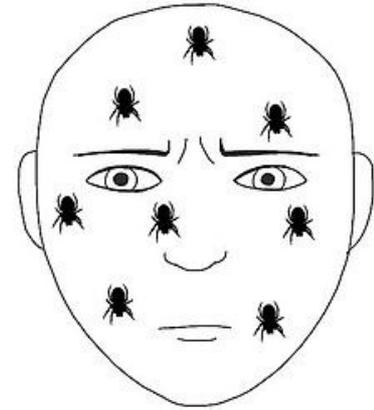
- In individuals physically dependent on ethanol, discontinuance can lead to a withdrawal syndrome characterized by **insomnia, tremor, anxiety**, and, in severe cases, life-threatening **seizures** and **delirium tremens** (which is characterized by delirium, agitation, autonomic nervous system instability, low-grade fever).
- Peripheral effects include nausea, vomiting, diarrhea, and arrhythmias.



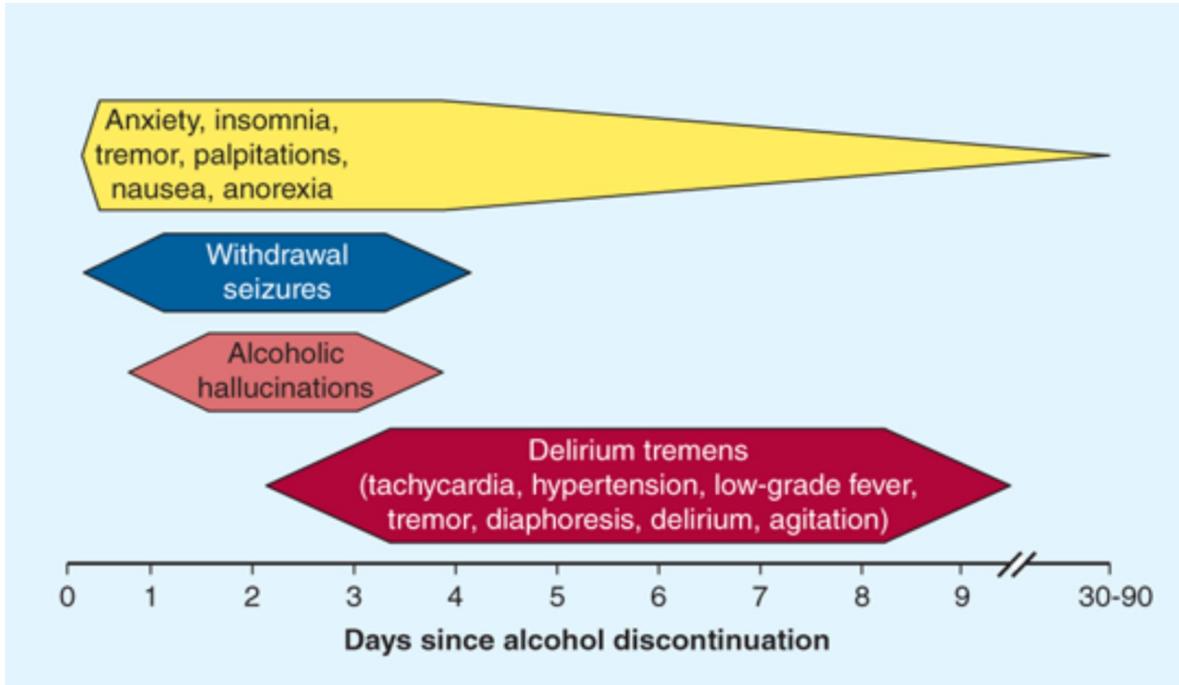
هنا الأعراض بتكون مرتنة وتبطل متجدد

إذا شخص مدمن كحول و فجأة قرر يوقف لحاله رح يواجه اعراض withdrawal ممكن تكون خفيفة و ممكن تكون life threatening زي ال seizures او delirium tremens يعني هذيان يبطل مركز

ال ANS instability يعني لحظات يكون عنده activation لل sympathetic nervous system و لحظات لا و التغيرات هاي بتصير بنفس اليوم



# Alcohol Withdrawal Symptoms



Source: Bertram G. Katzung, Anthony J. Trevor: Basic & Clinical Pharmacology, 13th Ed.  
[www.accesspharmacy.com](http://www.accesspharmacy.com)

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# Management of Alcohol Withdrawal Symptoms

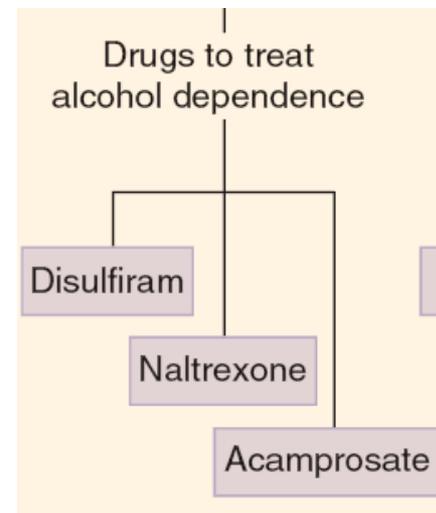
حالات ال tremors و ال seizures هي بتكون نتيجة خرابطة بال electrolytes (زيادة بالصوديوم و الكالسيوم و نقص بالبوتاسيوم...)

- The withdrawal syndrome is managed by:
  1. correction of electrolyte imbalance
  2. administration of <sup>vit. B1</sup> thiamine *vitamen B complex including thiamine*
  3. a sedative-hypnotic.
    - A long-acting benzodiazepine (eg, diazepam, chlordiazepoxide) is preferred unless the patient has compromised liver function, in which case a short-acting benzodiazepine with less complex metabolism (eg, lorazepam) is preferred.

انا صعبا نعالج ال withdrawal symp حتى الادمان

# Treatment of alcoholism (alcohol dependence)

- Alcoholism is a complex socio-medical problem, characterized by a high relapse rate.
- Three drugs—**disulfiram**, **naltrexone**, and **acamprosate**—have FDA approval for adjunctive treatment of alcohol dependence.



# Treatment of alcoholism (alcohol

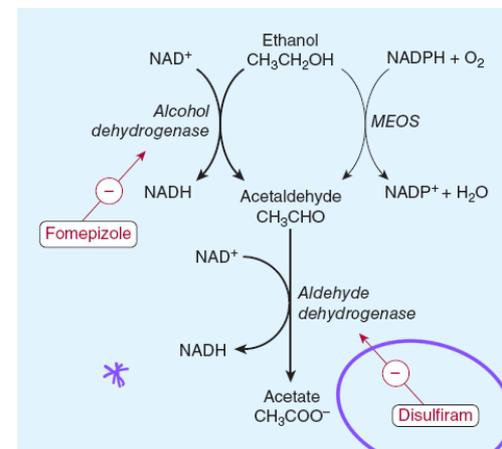
هاي الادوية تباعه عال ليطلعهم من قادمات  
بين التأخر تبعها مش سريع

# dependence)

فكرة هاد الدوا انه المريض بكون ماشي عليه و لما  
يجي عباله يشرب كحول بتظهر عليه هاي الاعراض ف  
هو بصير يبعد عن الكحول عشان بخاف تظهر عليه  
هاي الاعراض

## 1. Disulfiram:

- Disulfiram blocks the oxidation of acetaldehyde to acetic acid by inhibiting aldehyde dehydrogenase. This results in the accumulation of acetaldehyde in the blood, causing **flushing, throbbing headache, nausea, vomiting, sweating, hypotension, and confusion** which occur within a few minutes after an individual taking disulfiram drinks alcohol.
- Disulfiram has found some use in the patient seriously desiring to stop alcohol ingestion. A conditioned avoidance response is induced so that the patient gives up alcohol to prevent the unpleasant effects of disulfiram-induced acetaldehyde accumulation.



# Treatment of alcoholism (alcohol dependence)

مع استخدام Morphine عبر النخاع ليجب شربه كحول ← ادمان

## 2. Naltrexone:

- Naltrexone is a long-acting **opiate antagonist** that should be used in conjunction with supportive psychotherapy.
- Studies in experimental animals first suggested a link between alcohol consumption and opioids. Injection of small amounts of opioids was followed by an increase in alcohol drinking, whereas administration of opioid antagonists **inhibited self-administration of alcohol**.
- Naltrexone is better tolerated than disulfiram and does not produce the aversive reaction that disulfiram does.
- The combination of naltrexone plus disulfiram should be avoided, since both drugs are potential hepatotoxins.

سليخه تاثير المورفين المدمم

النخاع نفسه يبتلع ليجب عليه شرب كحول

# Treatment of alcoholism (alcohol dependence)

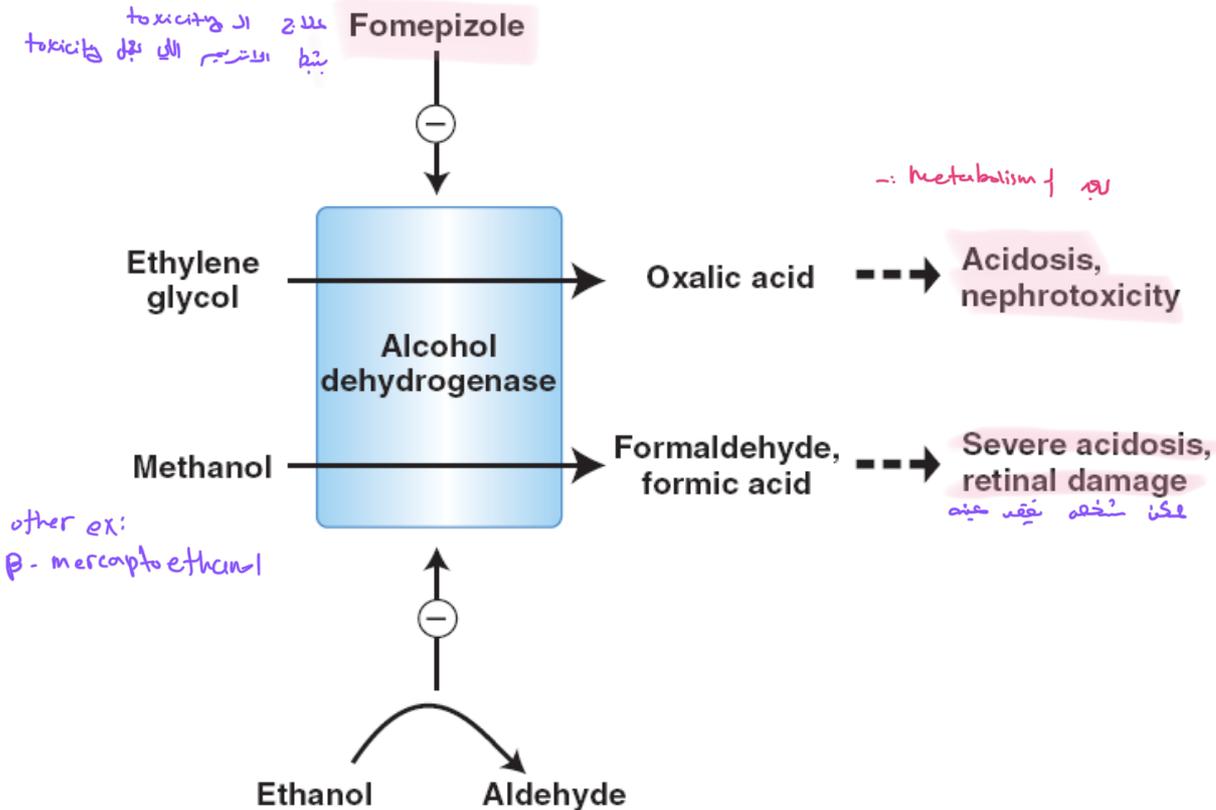
لحد ال ٤٨٦ ال MoA صني مرفوعة

## 3. Acamprosate:

- Acamprosate is an agent used in alcohol dependence treatment programs with an as yet poorly understood mechanism of action.
  - Acamprosate has many molecular effects including actions on GABA, glutamate, serotonergic, noradrenergic, and dopaminergic receptors.
- Acamprosate reduced short-term and long-term (more than 6 months) relapse rates when combined with psychotherapy.

انه يرفع السكر

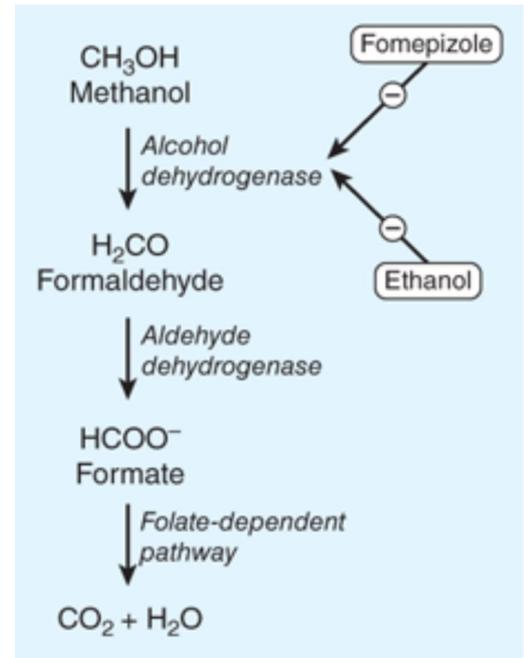
# Other Alcohols



# Other Alcohols

## A. Methanol

- Intoxication causes visual dysfunction, gastrointestinal distress, shortness of breath, loss of consciousness, and coma.
- Since the conversion of methanol to its toxic metabolites is relatively slow, there is often a delay of 6–30 hours before the appearance of severe toxicity.
- The formation of formaldehyde is reduced by prompt intravenous administration of **fomepizole**, an inhibitor of alcohol dehydrogenase, or **ethanol**, which competitively inhibits alcohol dehydrogenase oxidation of methanol.

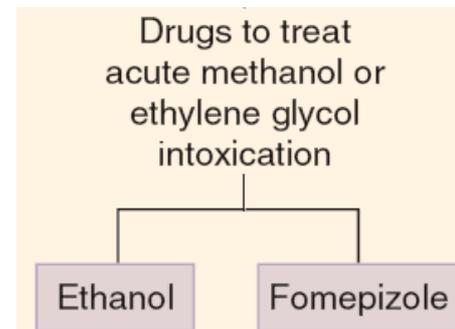


Source: Bertram G. Katzung, Anthony J. Trevisan, et al. [www.accesspharmacy.com](http://www.accesspharmacy.com)  
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# Other Alcohols

## B. Ethylene Glycol

- Industrial exposure to ethylene glycol (by inhalation or skin absorption) or self-administration (eg, by drinking antifreeze products) leads to severe acidosis and renal damage from the metabolism of ethylene glycol to oxalic acid.
- Prompt treatment with intravenous **fomepizole** or **ethanol** may slow or prevent formation of this toxic metabolite.
- Hemodialysis effectively removes ethylene glycol and its toxic metabolites and is recommended for patients with a serum ethylene glycol concentration above 50 mg/dL, significant metabolic acidosis, and significant renal impairment.



# QUESTIONS??



Say  
NO  
to  
Alcohol.....