

# FORENSIC TOXICOLOGY: FROM CRIME SCENE TO VIRTUAL LAB

MODULE 1

CHAPTER 7: Over the Counter Pharmaceuticals



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# 01. INTRODUCTION



01.

# PHARMACY DRUG SCHEDULES



**Schedule I drugs:** require a **prescription** for sale and are provided by a pharmacist

**Schedule II drugs:** less strictly regulated, but still require **professional intervention** from the pharmacist at the point of sale and possibly referral to a practitioner.

**Schedule III drugs:** Although available **without a prescription**, these drugs are to be sold from the self-selection area of the pharmacy under the **direct supervision** of the pharmacist

**Unscheduled drugs:** can be sold **without professional supervision**. These drugs may be sold from **any retail outlet**



# LAW ENFORCEMENT DRUG SCHEDULING

Drug, substances, and certain chemicals used to make drugs are classified into five distinct categories or schedules depending on:

- the drug's acceptable medical use
- the drug's abuse or dependency potential

**Schedule I:** substances or chemicals with no current accepted medical use and a high potential for abuse  
E.g., heroin, LSD, ecstasy

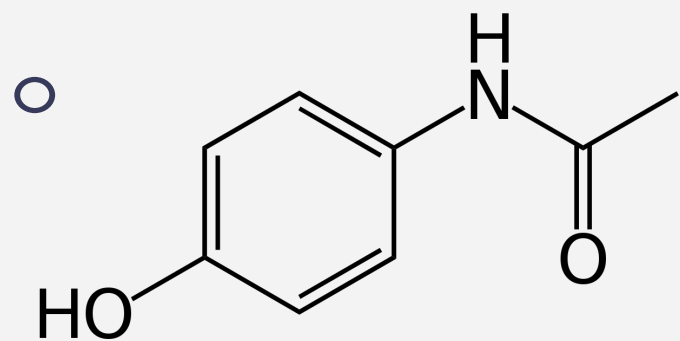
**Schedule II:** substances or chemicals with a high potential for abuse, with use potentially leading to severe psychological or physical dependence.  
E.g., cocaine, methamphetamine, hydromorphone, oxycodone, fentanyl, Adderall, Ritalin

**Schedule III:** substance or chemicals with a moderate to low potential for physical and psychological dependence.  
E.g., Tylenol with codeine, ketamine, anabolic steroids, testosterone

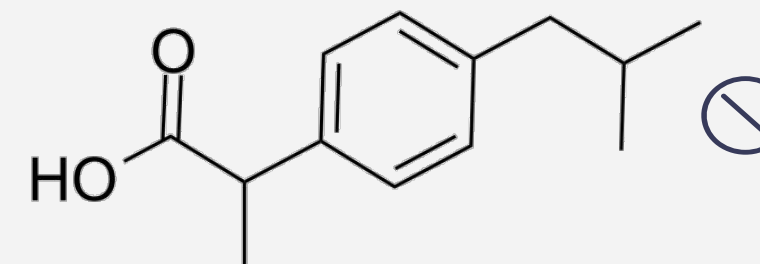
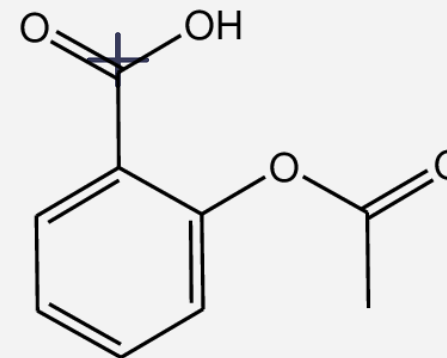
**Schedule IV:** substances or chemicals with low potential for abuse and low risk of dependence.  
E.g., Xanax, Valium, Ambien, Tramadol

**Schedule V:** substances or chemicals with lower potential for abuse than Schedule IV and consist of preparations containing limited quantities of certain narcotics. Usually used for antidiarrheal, antitussive, and analgesic purposes  
E.g., Lomotil, Motofen, Lyrica

01.



# DRUG SCHEDULES



Drug	Type	Schedule
<b>Acetylsalicylic acid and its salts</b>	80 mg or less per doses intended for pediatric use	II
	Adult use in strengths of 81 mg per dosage unit and 650 mg or greater per dosage unit	III
	325 mg and 500 mg per dosage unit	U
<b>Acetaminophen</b>	Administration by IV injection	I
	Fixed dose combinations containing more than 20,000 mg	II
	Sustained release formulations greater than 650 mg per unit or in package sizes of more than 50 units; Fixed-dose combinations, in package sizes containing 20,000 mg or less	III
	Sustained release formulations up to and including 650 mg per unit, in package sizes containing no more than 50 units; Immediate release tablets, capsules, suppositories or liquid	U
<b>Ibuprofen or its salts</b>	Except when sold in a dosage form that provides 400 mg or less per dosage unit or in a modified release oral dosage form that provides 600 mg or less per dosage unit	I
	Fixed dose combinations, containing more than 6,000 mg	II
	Immediate release containing 400 mg or less per dosage unit, in package sizes exceeding 18,000 mg; Modified-release that provides 600 mg or less per dosage; Fixed-dose combinations, in package sizes containing 6,000 mg or less	III
	Immediate release containing 400 mg or less per dosage unit in package sizes of up to 18,000 mg	U



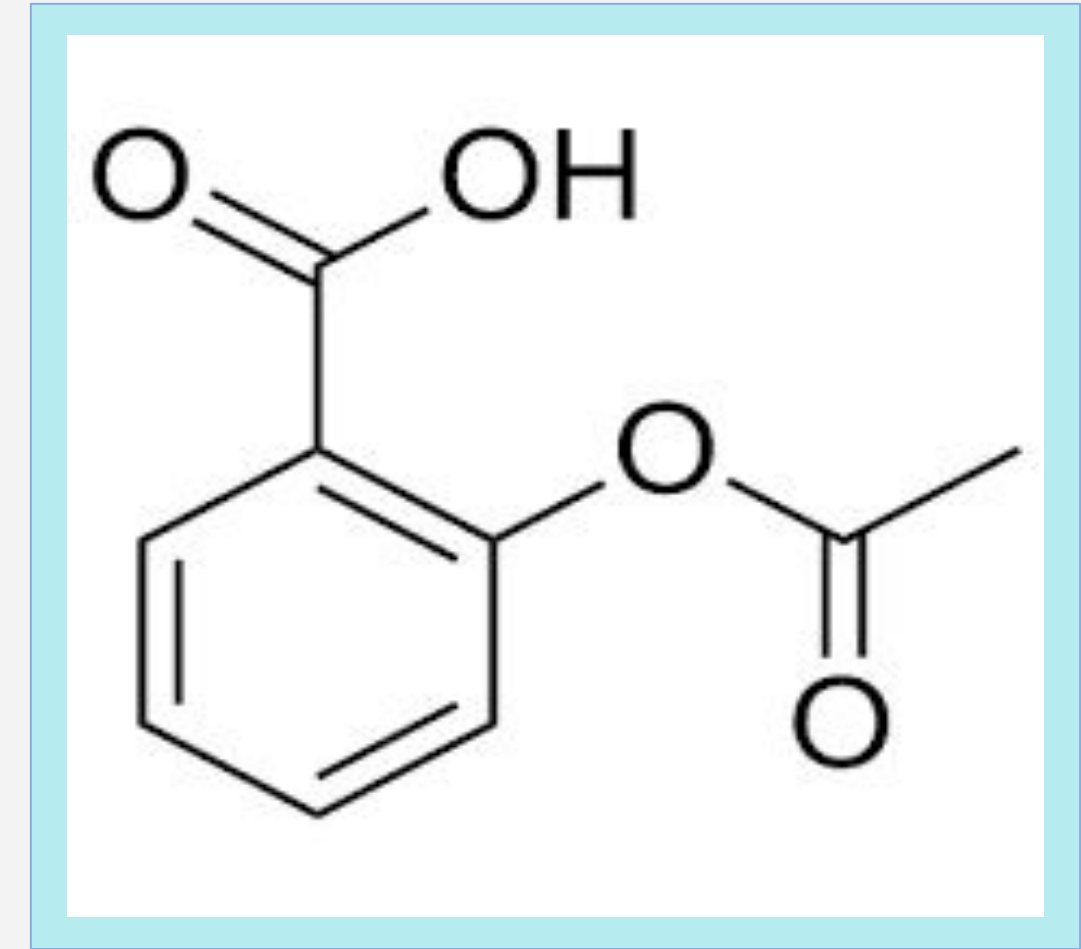


01.

# ASPIRIN

## WHAT is it?

Aspirin, or **acetylsalicylic acid** Is a drug in the family of **salicylates**



## General USES

- **analgesic** (against minor pains and aches),
- **antipyretic** (against fever)
- **anti-inflammatory**

It also has an **anticoagulant** effect and is used in low-term low-doses to **prevent heart attacks** and **cancer**

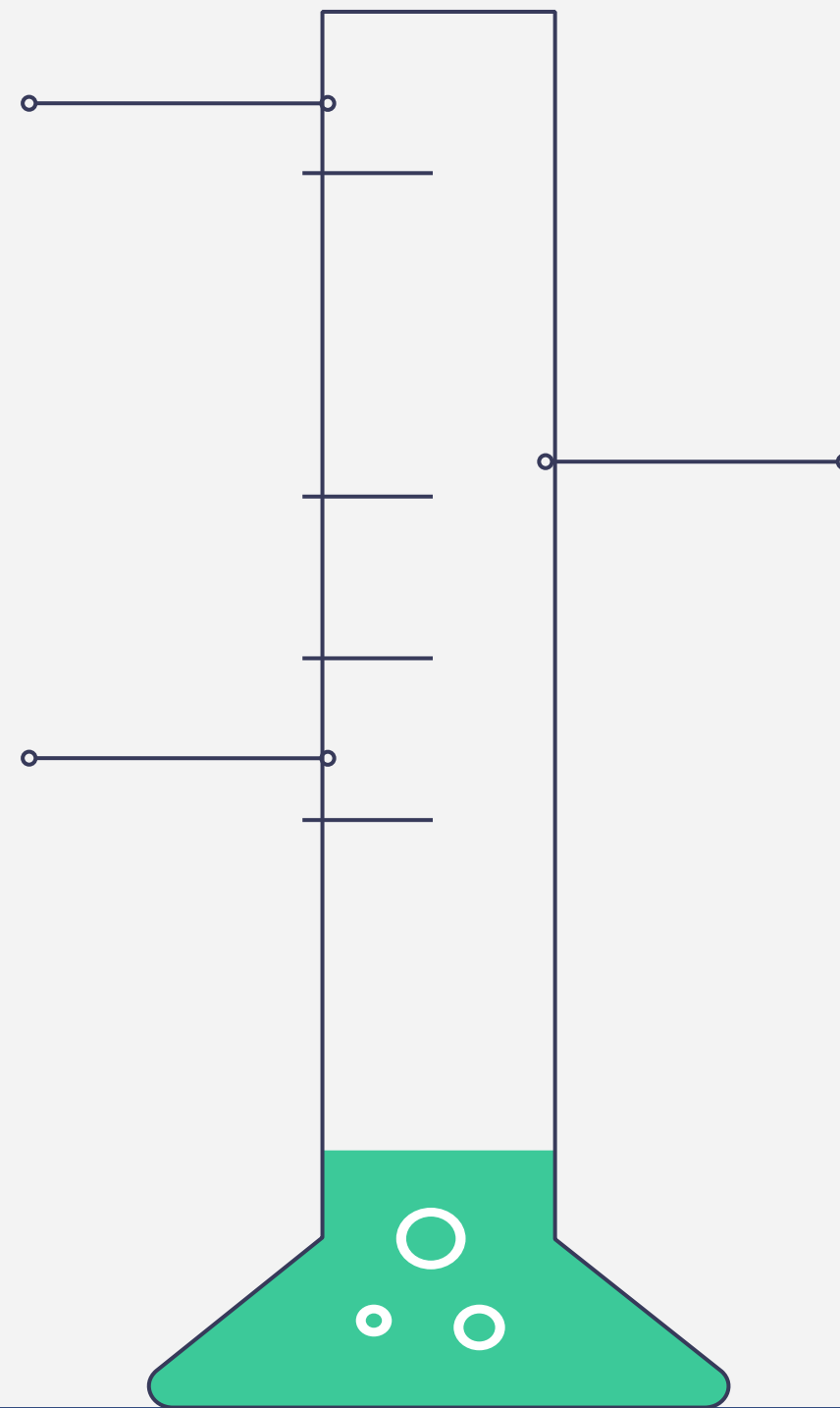
# HISTORY OF ASPIRIN

## 1839

Aspirin was first isolated from **meadowsweet** by German researchers. While the extract was **somewhat effective**, it also caused **digestive problems**, and even **death** when consumed in high doses

## 1897

German researchers Arthur Eichengrun and Felix Hoffman derivatized one of the **hydroxyl** functional groups in **salicylic acid** with an **acetyl** group, which greatly reduced the negative effects. This was the **first synthetic drug**, not a copy of something that existed in nature, and the start of the **pharmaceutical industry**.



## 1853

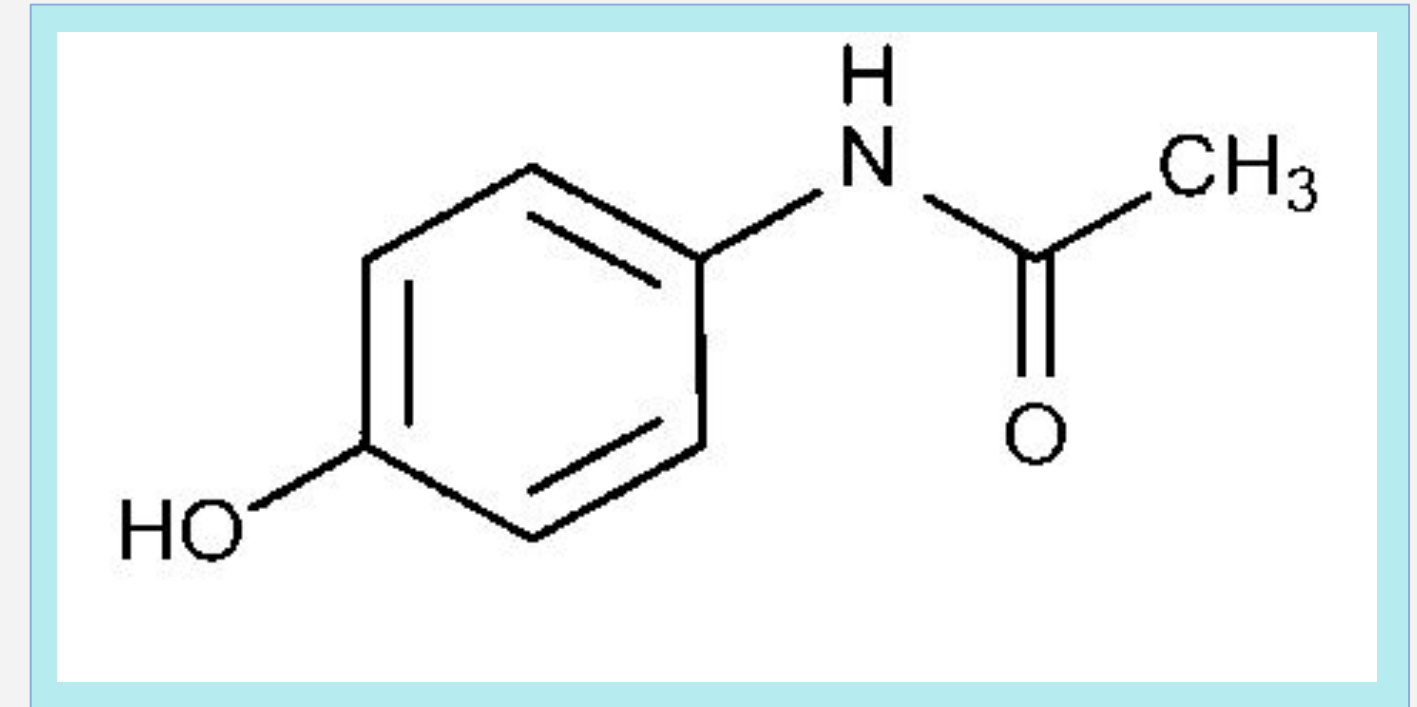
French chemist Charles Frederic Gerhardt **neutralized** salicylic acid by **buffering** it with **sodium** and **acetyl chloride**, creating **acetylsalicylic anhydride**. His product **worked**, but he had no desire to market it and abandoned his discovery



# ACETAMINOPHEN

## WHAT is it?

Acetaminophen, or paracetamol, is a **pain reliever** and a **fever reducer**



## General USES

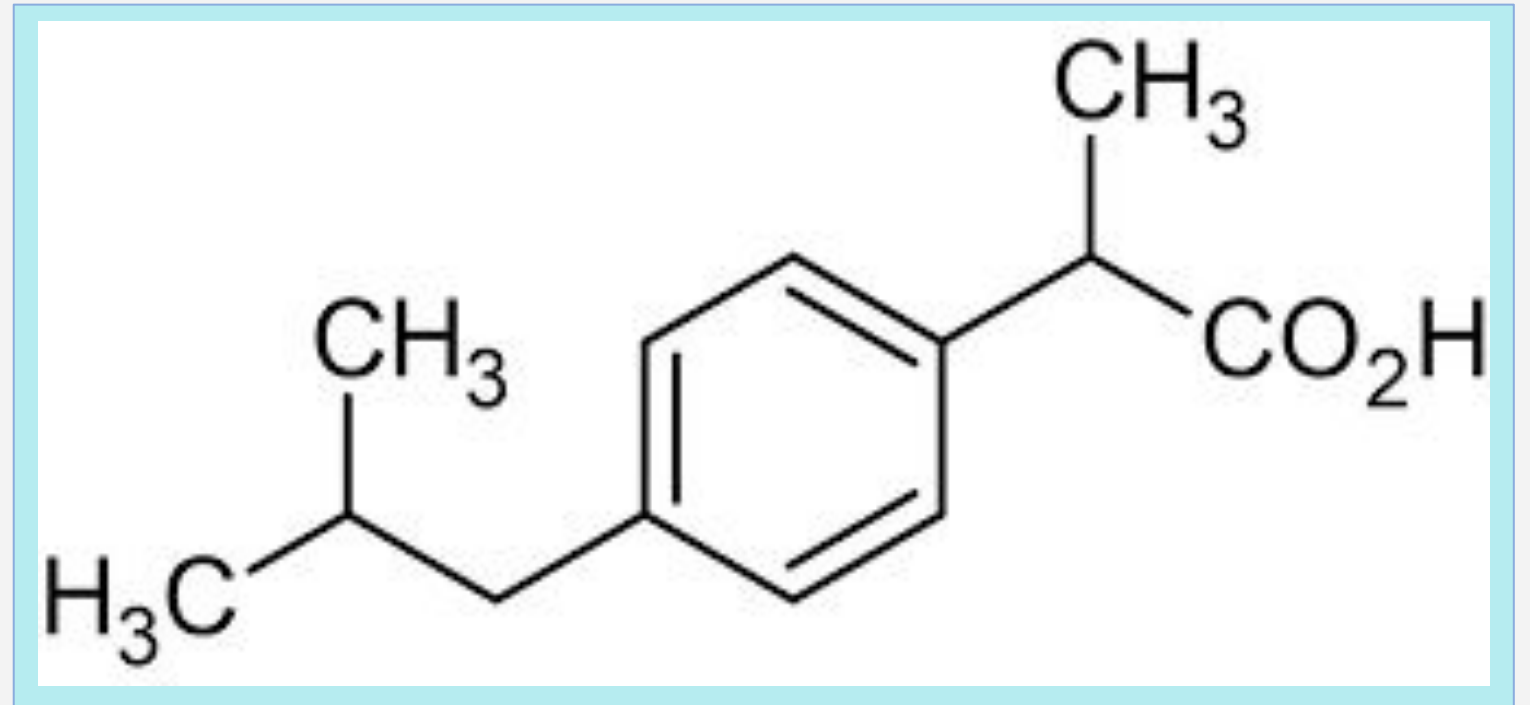
Acetaminophen is used to treat:

- mild to moderate pain
- Fever
- Headache
- Muscle aches
- Arthritis
- Backache
- Toothaches
- Sore throat
- Cold & flu

# IBUPROFEN

## WHAT is it?

Ibuprofen is a **nonsteroidal anti-inflammatory** drug (NSAID) widely marketed under **various trademarks** including Act-3, Advil, Brufen, Motrin, Nuprin, and Nurofen.

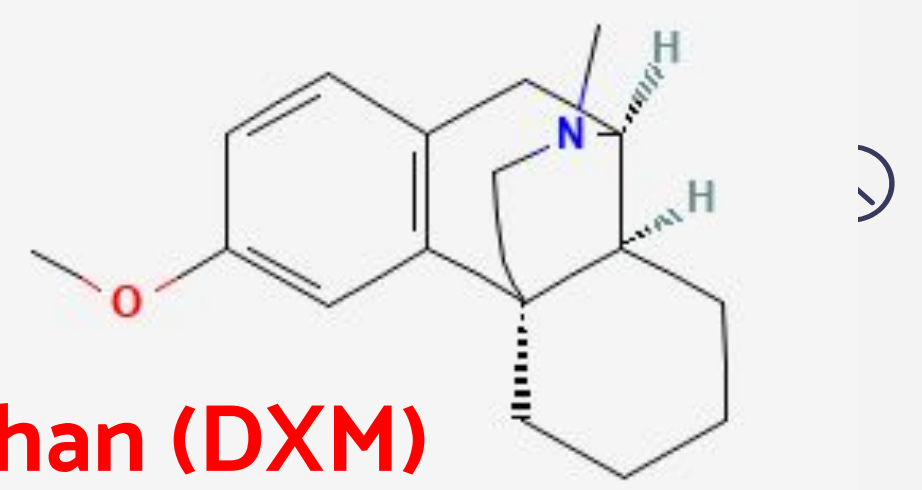


## General USES

- Treats **inflammation** such as **strain, sprains**, and **arthritis** pain
- Everyday painkiller for a **variety of aches** and pains including back pain and toothache
- Relieves **fever**

# O1. COMMONLY MISUSED Over the Counter (OTC) MEDICATIONS

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**Dextromethorphan (DXM)**

## WHAT

- Cough suppressant found in many OTC cold medicines
- Most common sources of abused DXM: “extra-strength” cough syrup, tablets and gel capsules
- May be swallowed in its original form, mixed with soda for flavour, called “robo-tripping” or “skittling”, or injected
- Often misused in combination with other drugs, such as alcohol and marijuana

## HOW

- An opioid without an effect on pain reduction
- Does not act on opioid receptors
- Causes a depressant effect in large doses, and sometimes a hallucinogenic effect, similar to PCP and ketamine
- Repeated use can lead to addiction

## EFFECTS

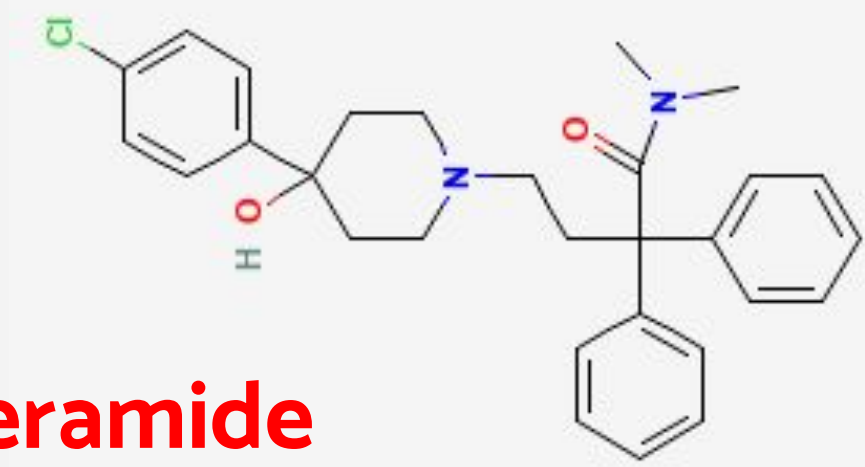
- Short-term effects: range from mild stimulation to alcohol- or marijuana-like intoxication
- At high doses, a person may have hallucinations or feelings of physical distortion, extreme panic, paranoia, anxiety, and aggression
- Misuse of DXM products containing acetaminophen can cause liver damage



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# COMMONLY MISUSED OTC MEDICATIONS

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**Loperamide**

## WHAT

- An anti-diarrheal available in tablet, capsule, or liquid form
- Misused by swallowing large quantities

## HOW

- Opioid designed not to enter the brain
- May act similar to other opioid when taken in large amounts or in combination with other substances

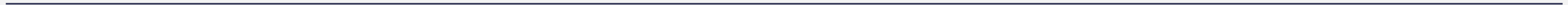
## EFFECTS

- Short term: misused to lessen cravings and withdrawal symptoms
- Can cause euphoria, lead to fainting, stomach pain, constipation, eye changes and loss of consciousness
- May also cause an erratic or rapid heartbeat, and kidney problems
- Effects may increase if combined with other substances



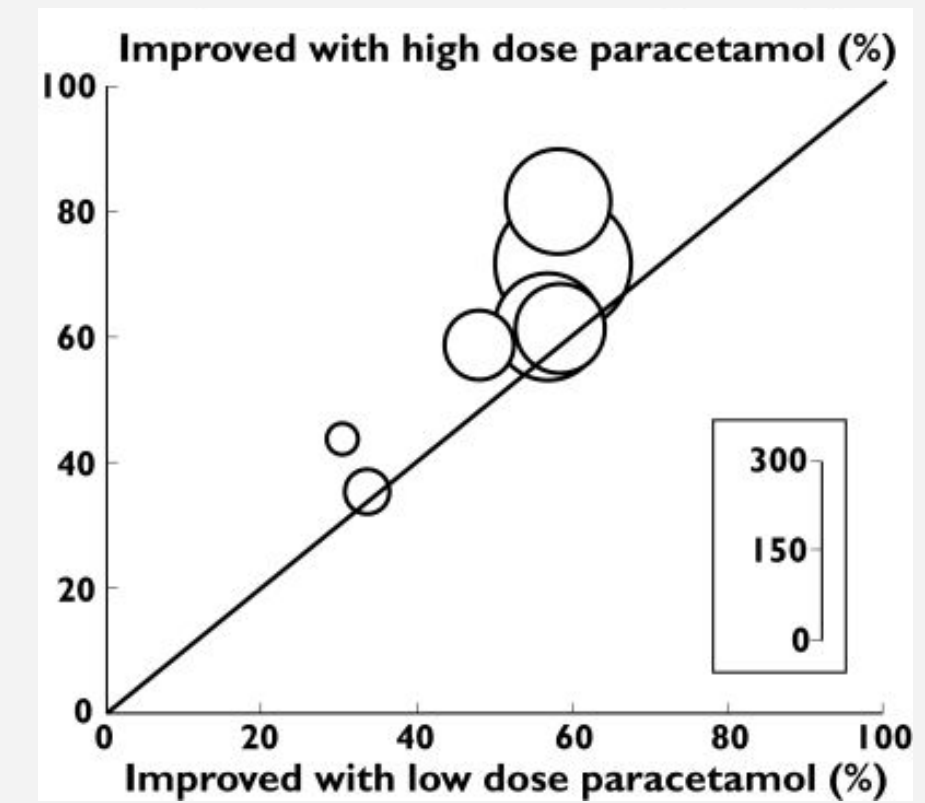
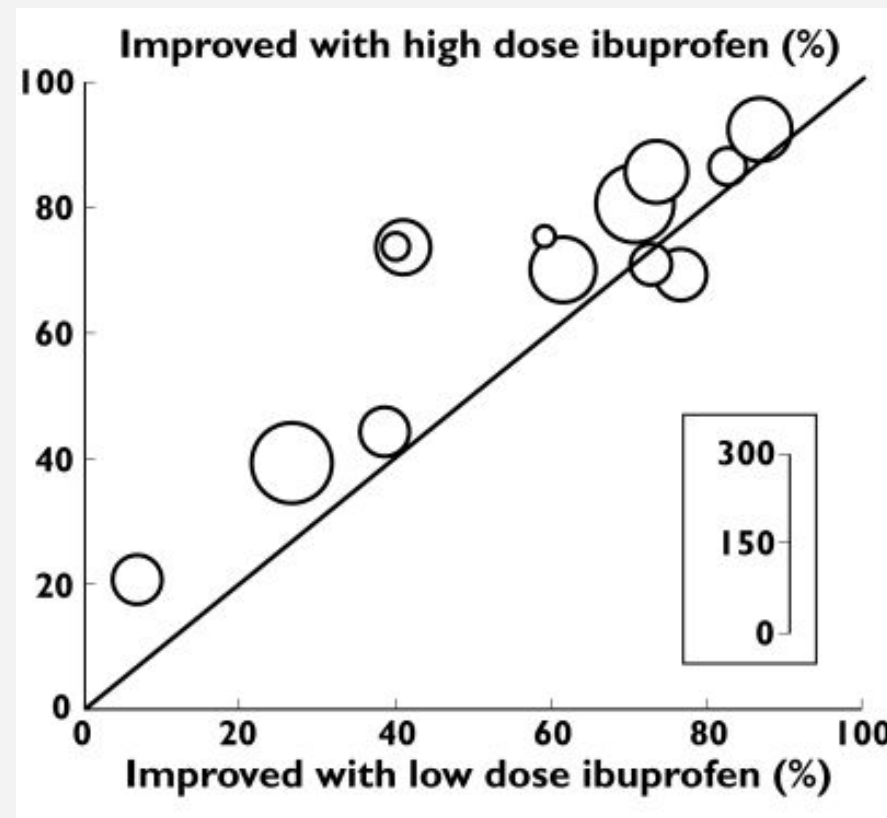
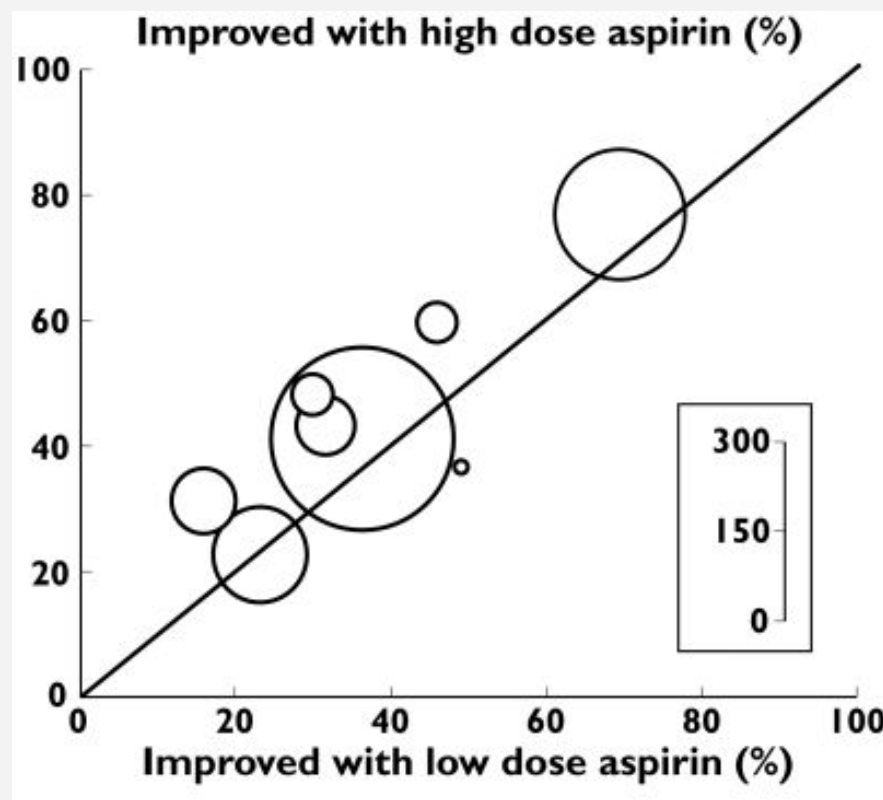


# 02. Toxicity





# DOSING AND EFFECTS

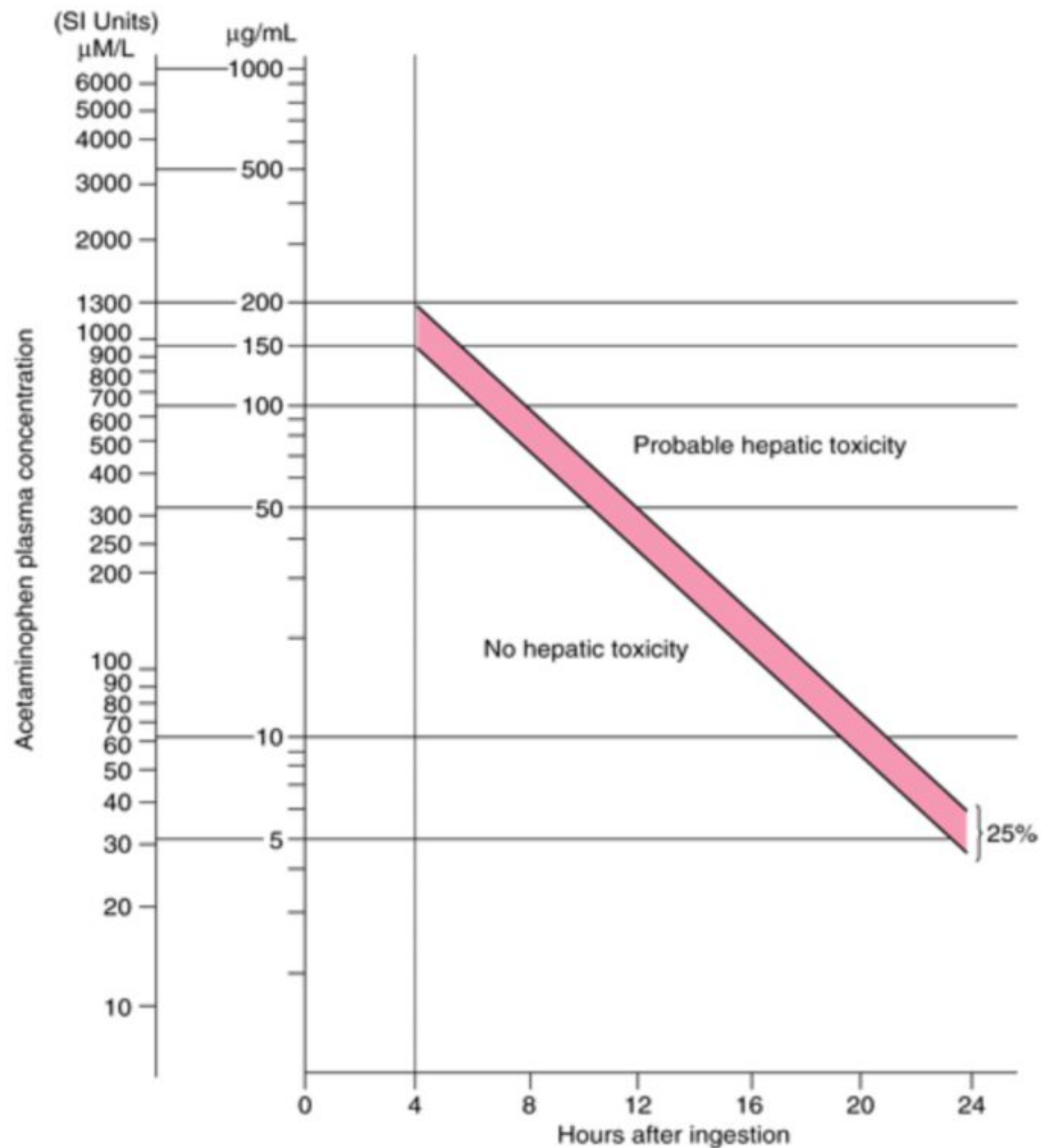


L'Abbé plots of the proportions of patients improved on high and low doses for the individual direct comparisons with aspirin, ibuprofen and acetaminophen. The size of the circle representing a trial is proportional to the number of patients studied in the trial

Analysis	Aspirin	Ibuprofen	Paracetamol
Number of trials with comparisons	18	20	12
Numerically better with higher dose	12	16	9
Statistical significance with higher dose	2	5	4



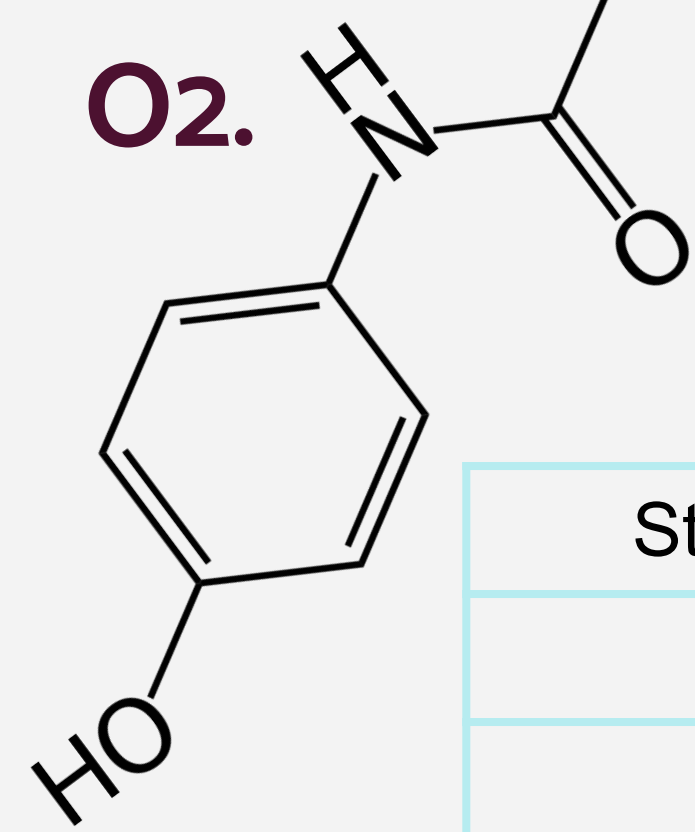
# ACUTE ACETAMINOPHEN INGESTION



Rumack-Matthew nomogram for single acute acetaminophen ingestions

- Semilogarithmic plot of **plasma acetaminophen levels vs time.**
- The time coordinates refer to **time after ingestion.**
- Serum levels drawn **before 4 hours** may not represent peak levels.
- The graph should be used only in relation to a **single acute ingestion.**
- The lower solid line 25% below the standard nomogram is included to allow for **possible errors** in acetaminophen plasma assays and estimated time from ingestion of an overdose.

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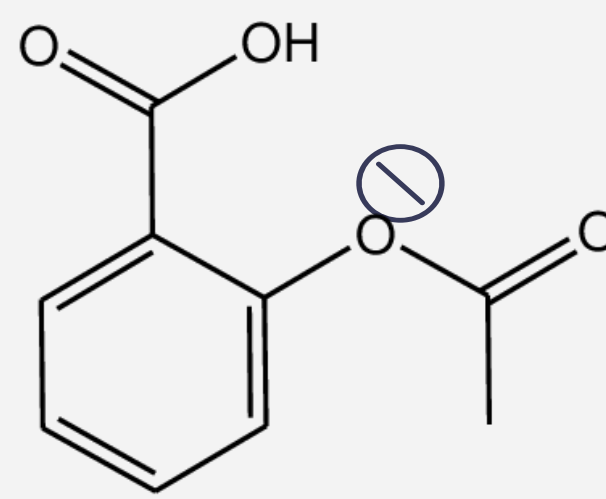


## STAGES OF ACUTE ACETAMINOPHEN POISONING

Stage	Time Post-Ingestion	Description
I	0-24 hours	Nausea, vomiting
II	24-72 hours	Right upper quadrant abdominal pain (common)
III	72-96 hours	Vomiting and symptoms of liver failure Sometimes renal failure and pancreatitis
IV	> 5 days	Resolution of hepatotoxicity or progression to multiple organ failure (sometimes fatal)

- Mild poisoning **may not** cause symptoms.
- When present, symptoms of acute acetaminophen poisoning are **usually minor** until **≥ 48 hours** after ingestion.
- Symptoms occur in **4 stages**, including **nausea, vomiting**, and **right upper quadrant abdominal pain**.
- **Renal failure** and **pancreatitis** may occur, occasionally without liver failure.
- After > 5 days, hepatotoxicity **resolves** or progresses to **multiple organ failure**, which can be **fatal**.

# SALICYLATE POISONING



## Signs of Aspirin and Other Salicylate Poisoning

- Vomiting
- Tinnitus
- Confusion
- Hyperthermia
- Respiratory alkalosis
- Metabolic acidosis
- Multiple organ failure



## Diagnosis of Aspirin and Other Salicylate Poisoning

If poisoning is suspected, the salicylate level in **blood serum** is measured, in addition to the **urine pH** and other medical tests

The serum must be analyzed at least **a few hours** after ingestion; **absorption** is usually almost complete **6 hours following ingestion**

**Significant salicylate toxicity** is suggested by serum levels much higher than the **therapeutic range** of 10-20 mg/dL (0.725 to 1.45 mmol/L).

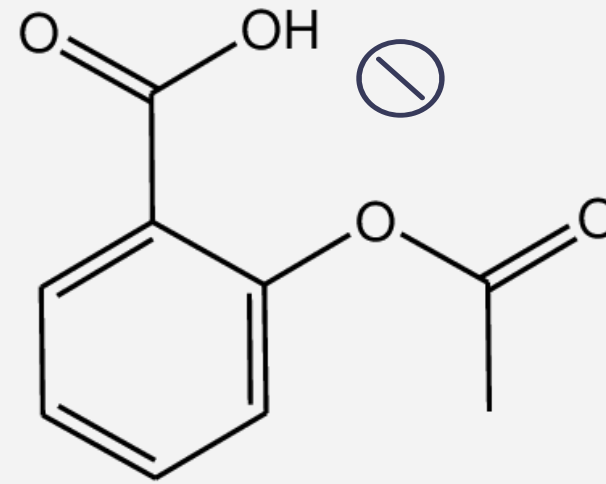


# SALICYLATE POISONING

## Adverse Effects of Salicylates

- Impair **cellular respiration** by uncoupling **oxidative phosphorylation**
- Stimulate **respiratory centers** in the **medulla**, causing **primary respiratory alkalosis**, which is often unrecognized in young children
- Eventually, as salicylates disappear from the **blood**, enter the **cells**, and **poison mitochondria**, **metabolic acidosis** becomes the primary acid-base abnormality
- Salicylate poisoning also causes **ketosis**, **fever**, and, even when systemic hypoglycemia is absent, **low brain glucose levels**

## Effects of pH

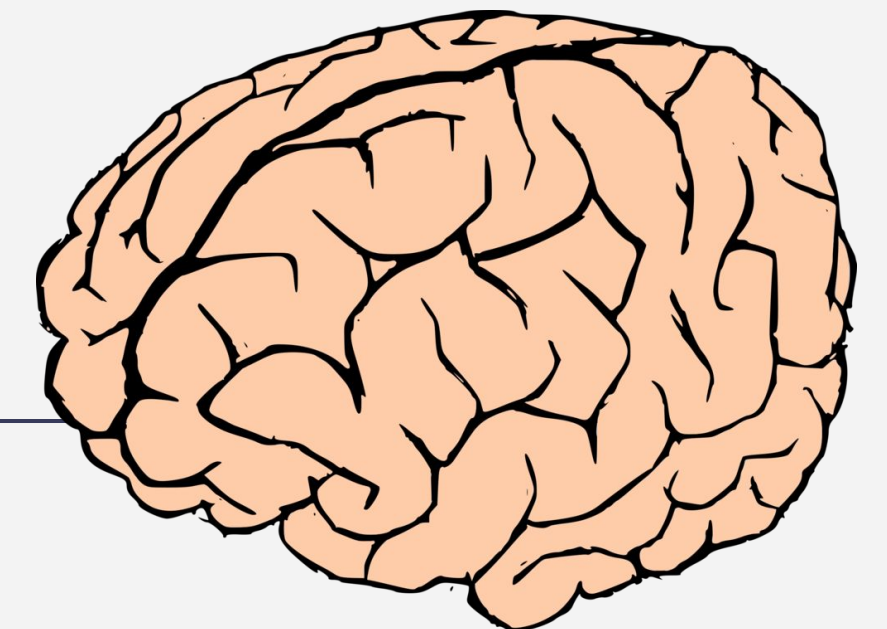


### Low pH

Salicylates are **weak acids** that cross cell membranes **relatively easily**; thus, they are **more toxic when blood pH is low**

### High pH

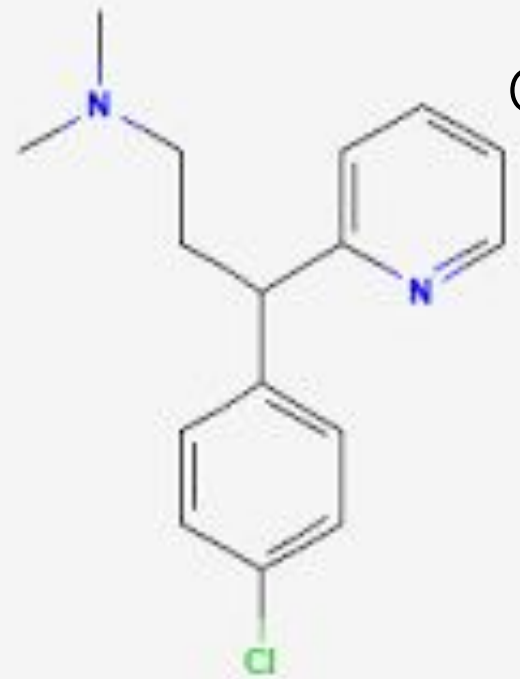
**Excretion** of salicylates **increases** when **urine pH increases**



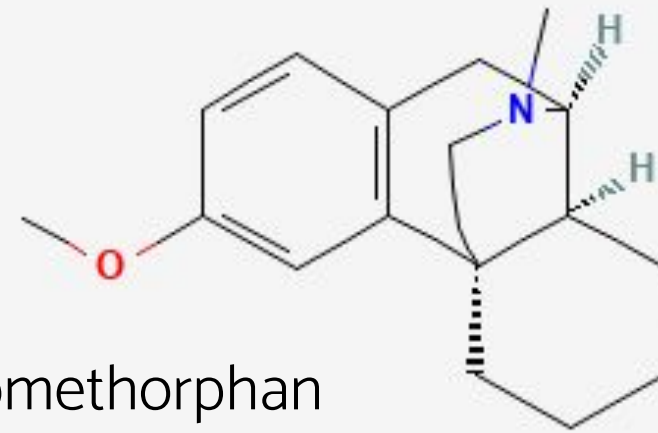




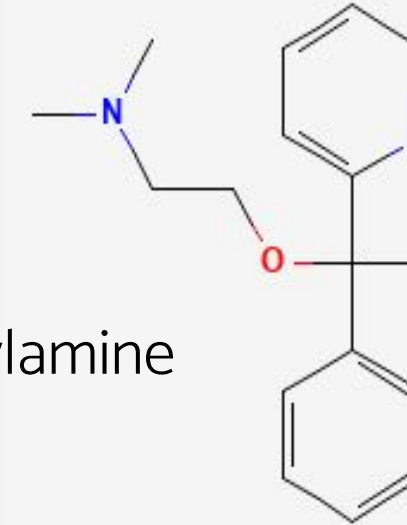
# PEDIATRIC FATALITIES ASSOCIATED WITH OTC MEDICATIONS



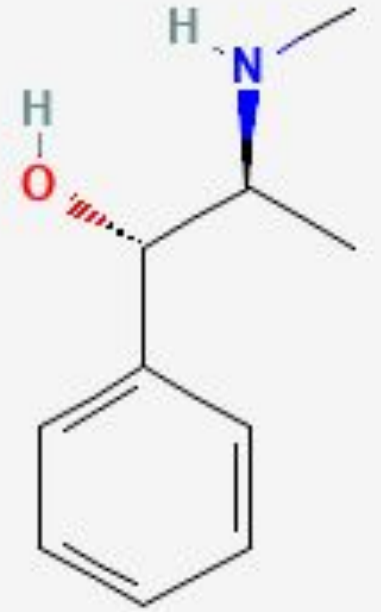
Chlorpheniramine



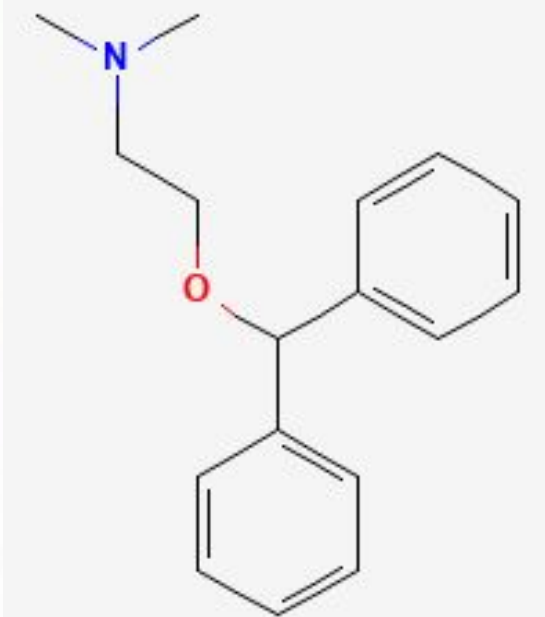
Dextromethorphan



Doxylamine

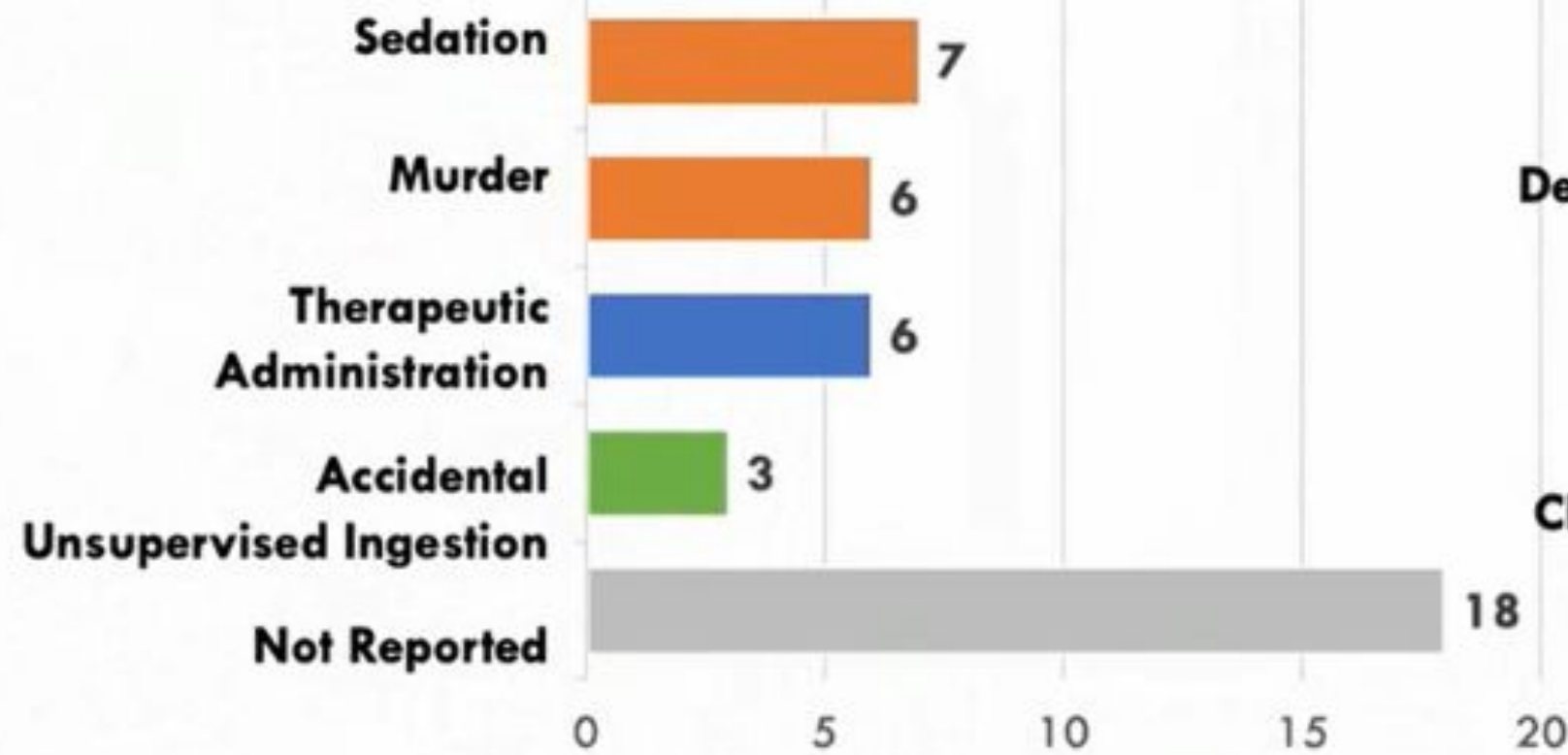


Pseudoephedrine

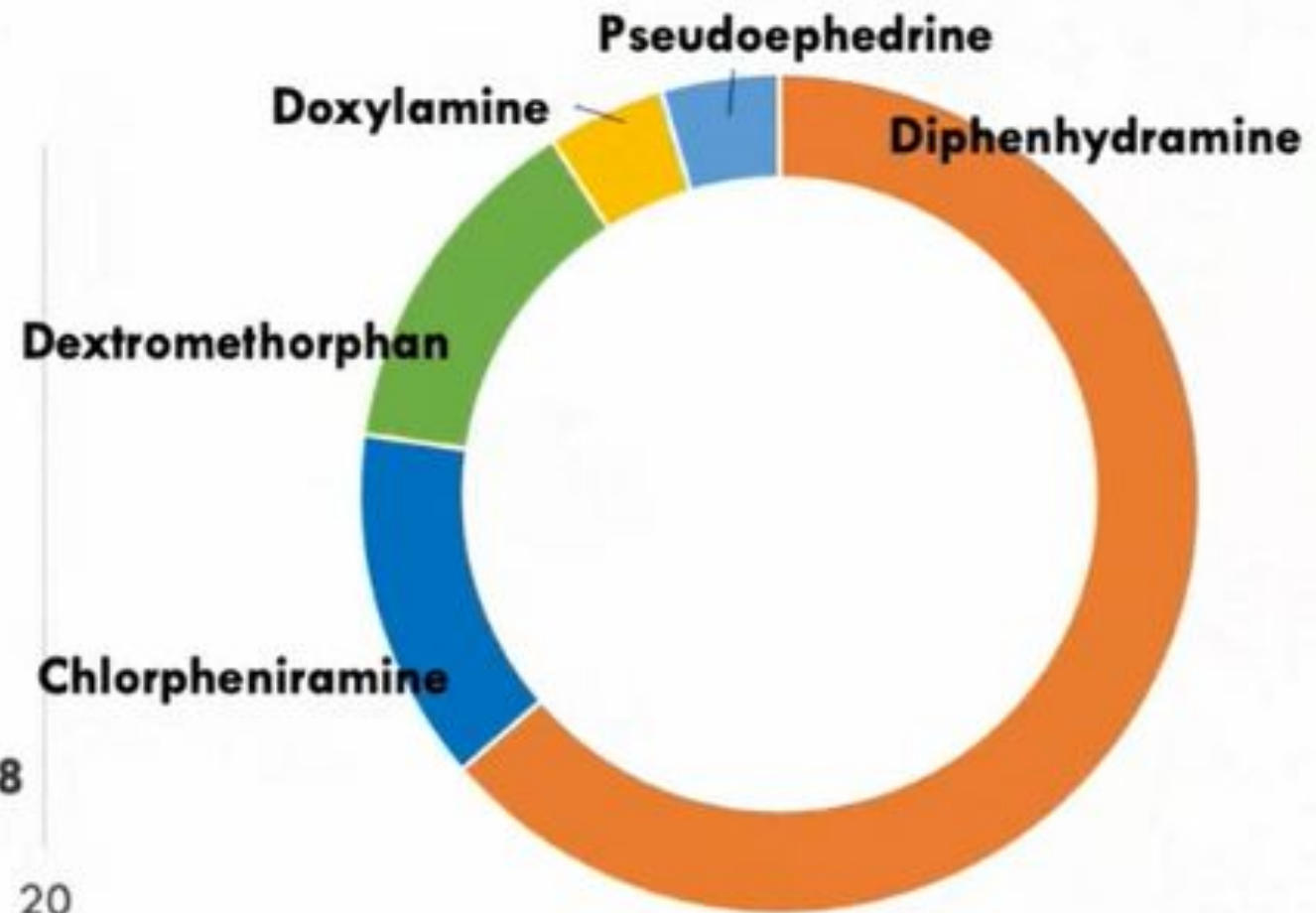


Diphenhydramine

### Contributing Factors to Fatalities

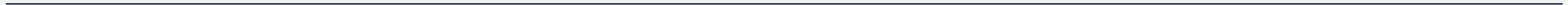


### Cough and Cold Medication Ingredients Involved





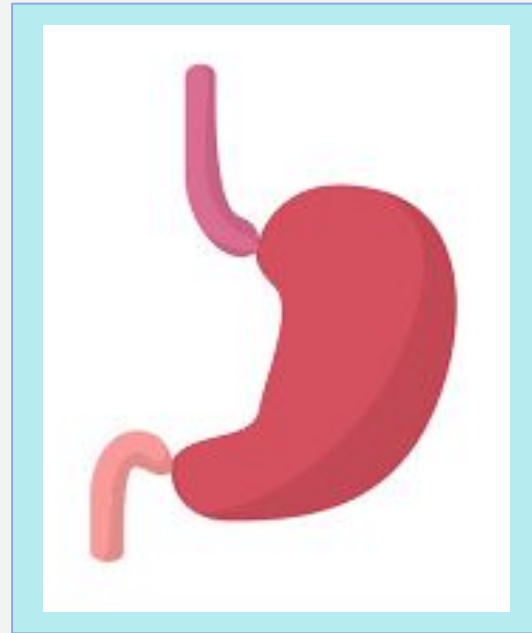
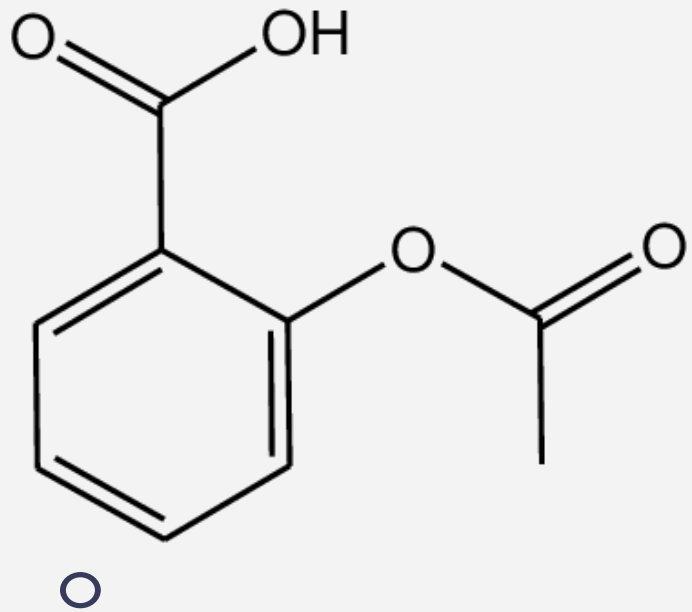
# 03. TOXICOKINETICS



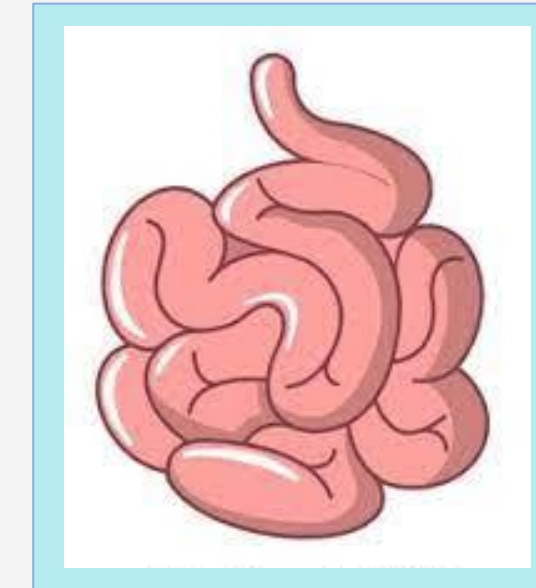




## ABSORPTION OF ASPIRIN



When ingested orally, acetylsalicylic acid is **rapidly absorbed** in both the **stomach** and **proximal small intestine**.



- The **non-ionized** acetylsalicylic acid passes through the stomach lining by **passive diffusion**
- Ideal absorption of salicylate in the stomach occurs in the pH range of **2.15 - 4.10**

**Peak plasma salicylate** concentrations occur between **1-2 hours** post-administration

- Intestinal absorption of acetylsalicylic acid occurs at a much **faster rate**
- At least **half** of the ingested dose is hydrolyzed to salicylic acid in the **first-hour post-ingestion** by **esterases** found in the gastrointestinal tract

Absorption may vary depending on several factors, including **route, dosage form**, rate of **tablet dissolution**, gastric **contents**, gastric **emptying time**, and gastric **pH**.



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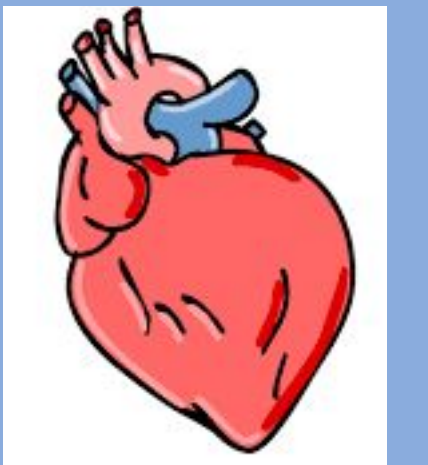
## DISTRIBUTION OF ASPIRIN



Aspirin is distributed to body tissues shortly after administration.



Aspirin is known to cross into the placenta.

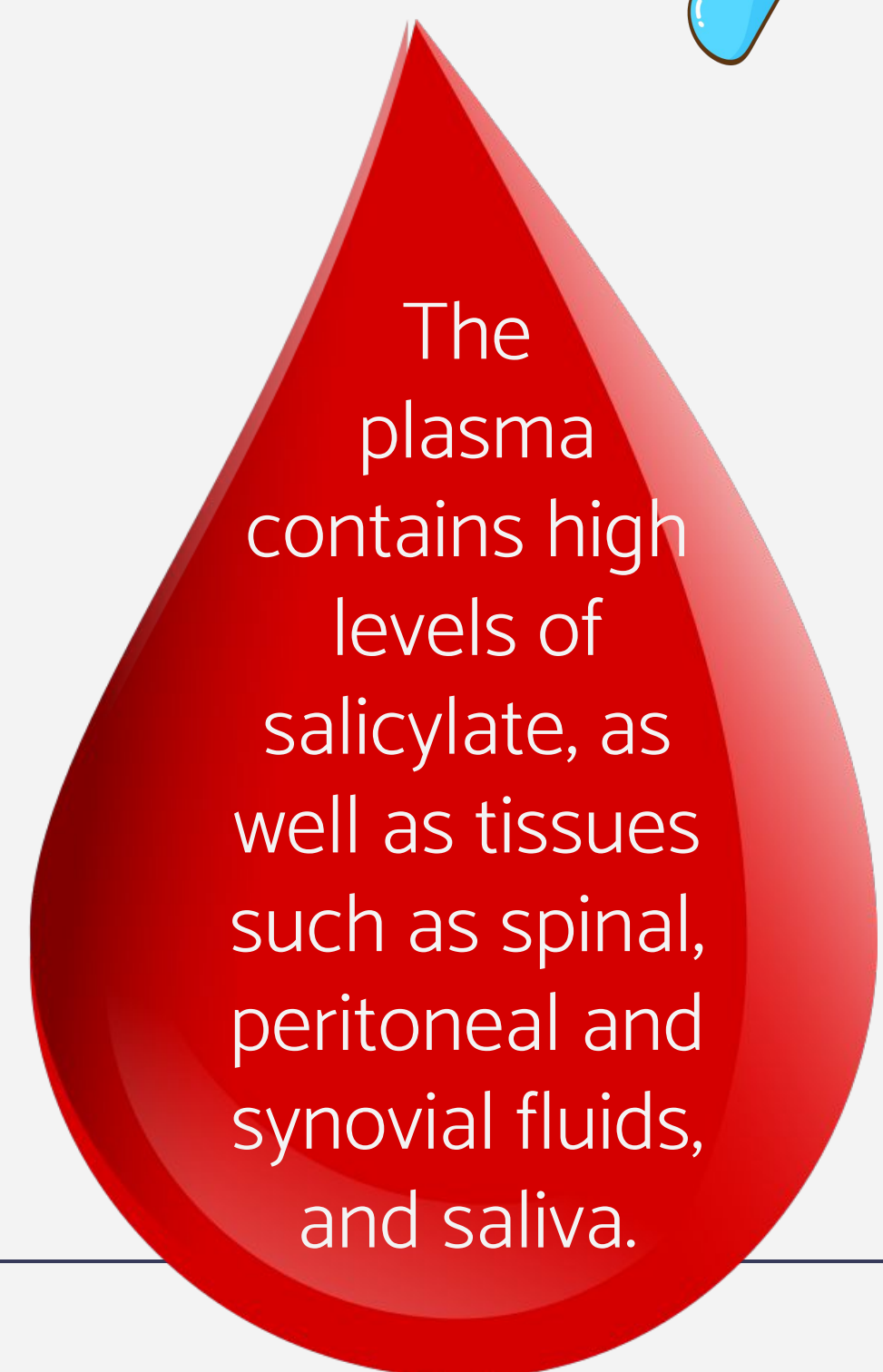


The kidney, liver, heart, and lungs are also found to be rich in salicylate concentration after dosing.

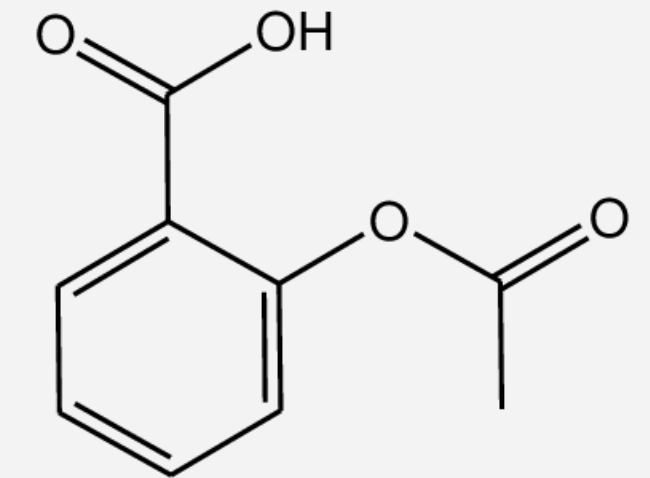
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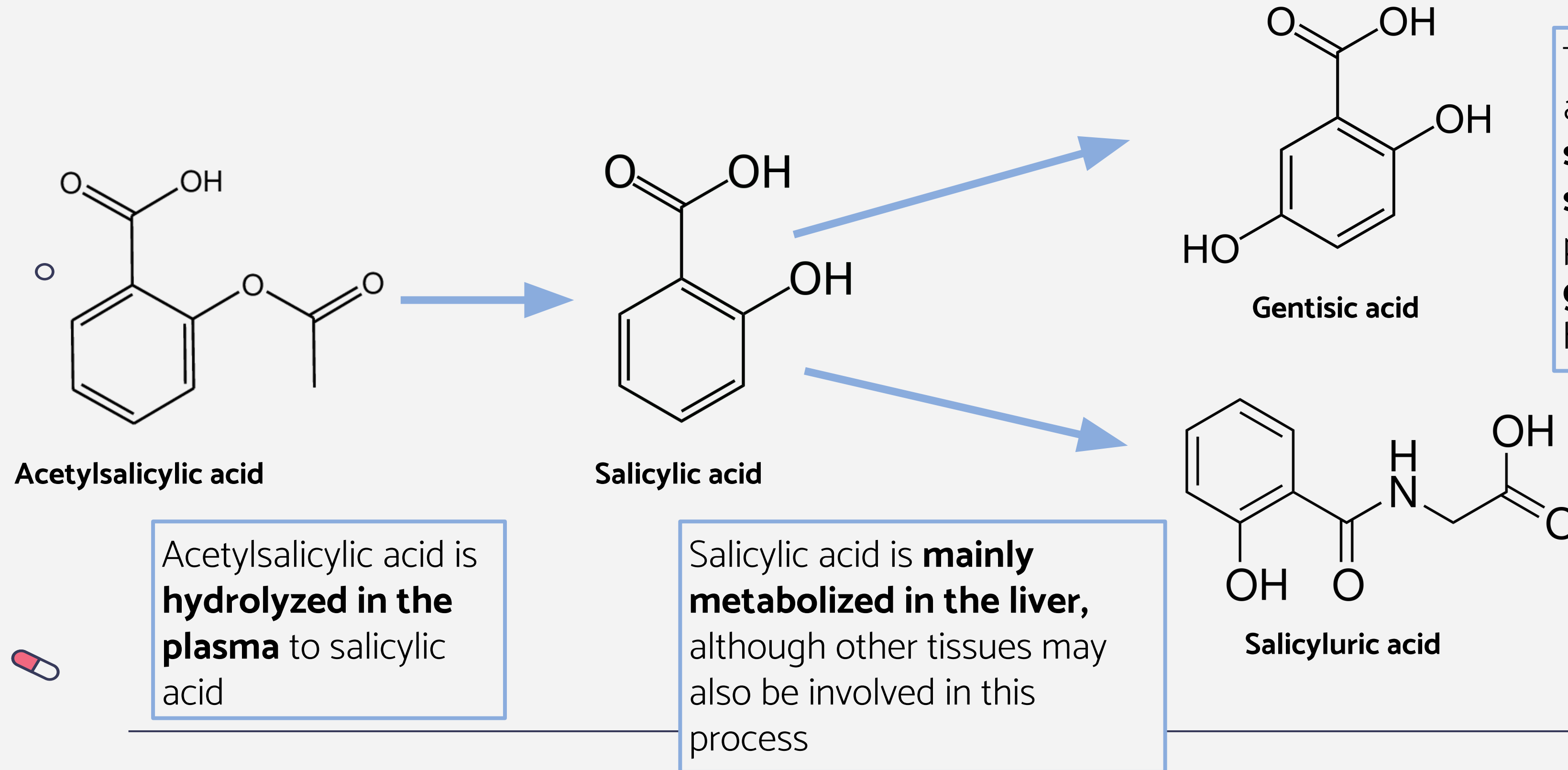
Minimal concentrations are found in feces, bile, and sweat



The plasma contains high levels of salicylate, as well as tissues such as spinal, peritoneal and synovial fluids, and saliva.



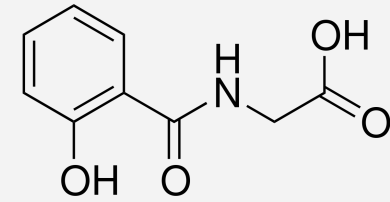
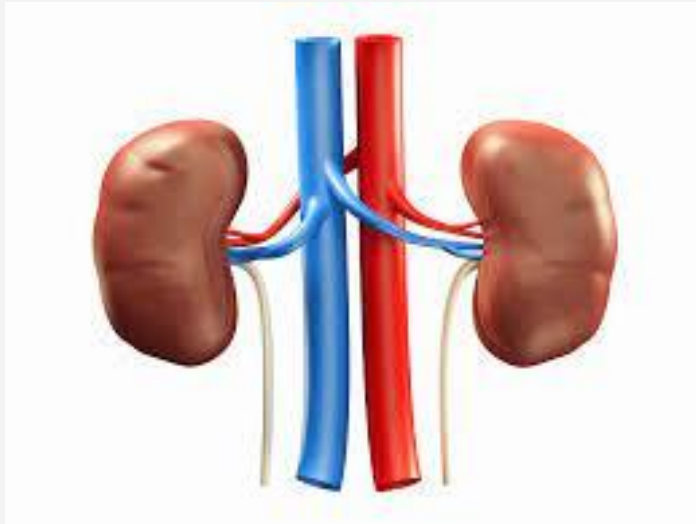
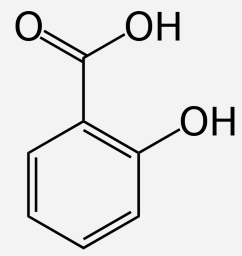
# METABOLISM OF ASPIRIN



The **major metabolites** of acetylsalicylic acid are **salicylic acid** and **salicyluric acid**. A small portion is converted to **gentisic acid** and other hydroxybenzoic acids

Acetylsalicylic acid is **hydrolyzed in the plasma** to salicylic acid

Salicylic acid is **mainly metabolized in the liver**, although other tissues may also be involved in this process



## ELIMINATION OF ASPIRIN



- Excretion of aspirin occurs mainly through the kidney in the form of free salicylic acid, salicyluric acid, and phenolic and acyl glucuronides

The rate of unmetabolized acetylsalicylic acid (ASA) is often **variable**, ranging from **10% to 85%** in the urine, and heavily depends on **urinary pH**. Acidic urine generally aids in reabsorption of ASA by the renal tubules, while alkaline urine increases excretion

### Half-life

- The half-life of ASA in the **circulation** ranges from **13 - 19 minutes**.
- Blood concentrations **drop rapidly** after **complete absorption**.
- The half-life of the ASA ranges between **3.5 and 4.5 hours**





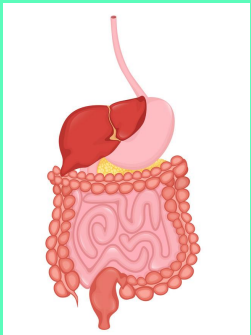
# ABSORPTION OF IBUPROFEN



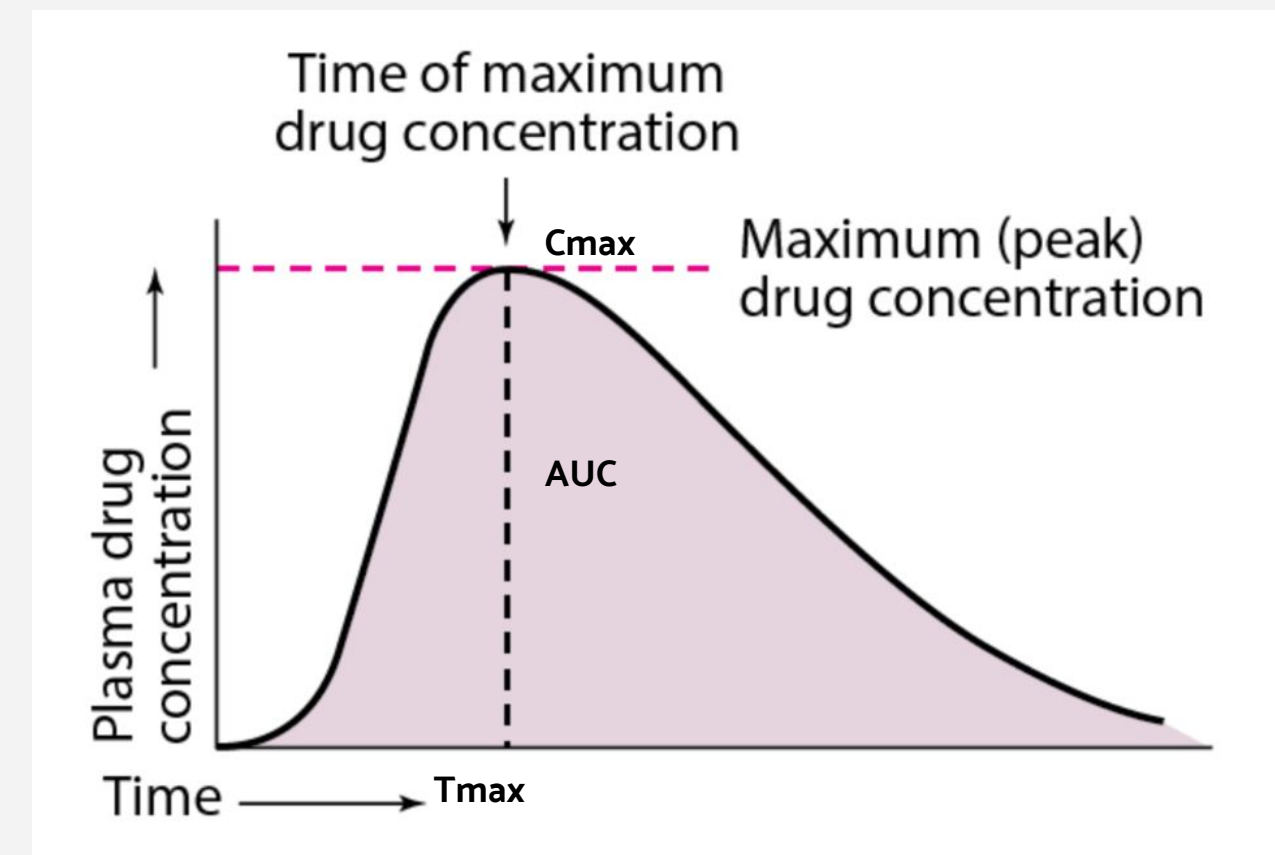
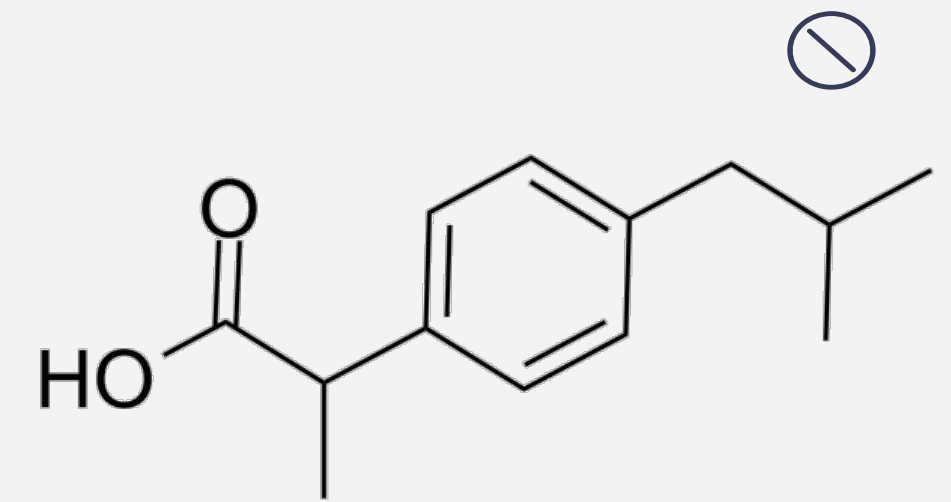
Absorbed well orally. The peak serum concentration can be attained in 1 to 2 hours



When ibuprofen is administered immediately after a meal there is a slight reduction in the absorption rate, but there is no change in the extent of the absorption



When orally administered, the absorption of ibuprofen in adults is very rapidly done in the upper GI tract



Average C<sub>max</sub>: 20 mcg/ml

Average T<sub>max</sub>: 2h

Average AUC: 70 mcg\*h/ml

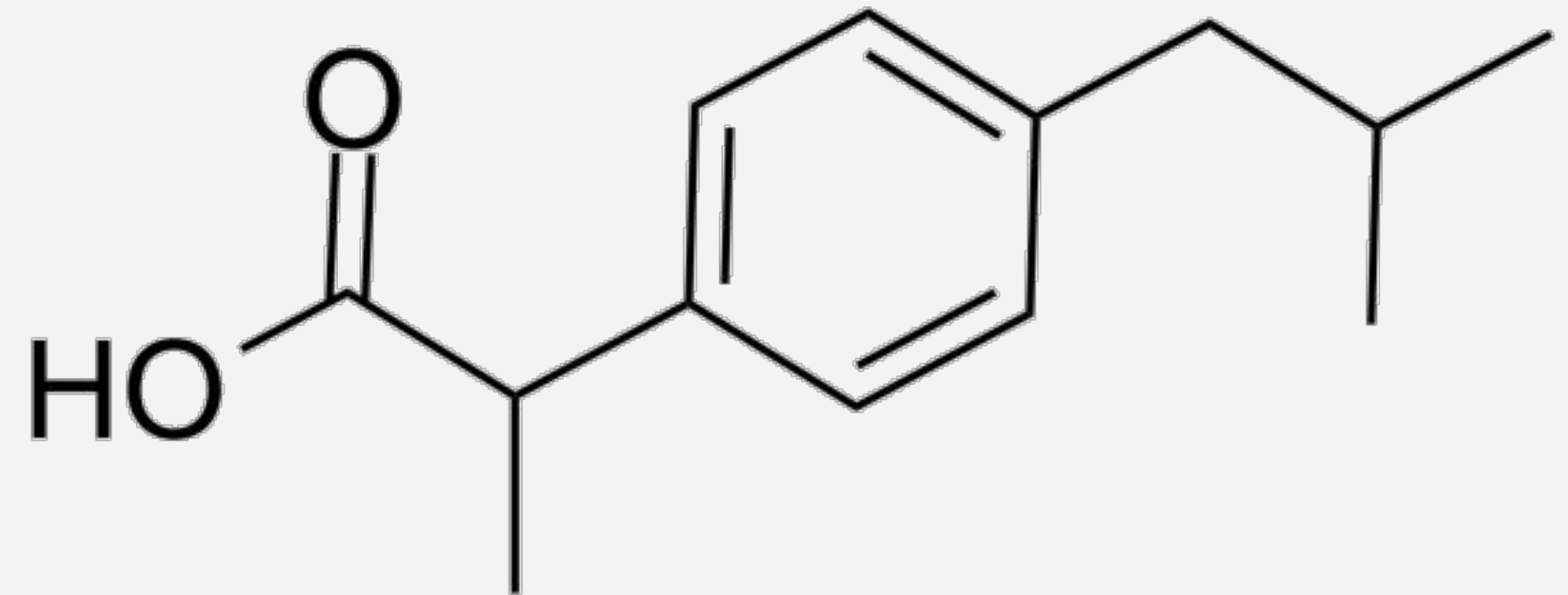
## DISTRIBUTION OF IBUPROFEN

### VOLUME OF DISTRIBUTION

The volume of distribution of ibuprofen is of 0.1L/kg

### PROTEIN BINDING

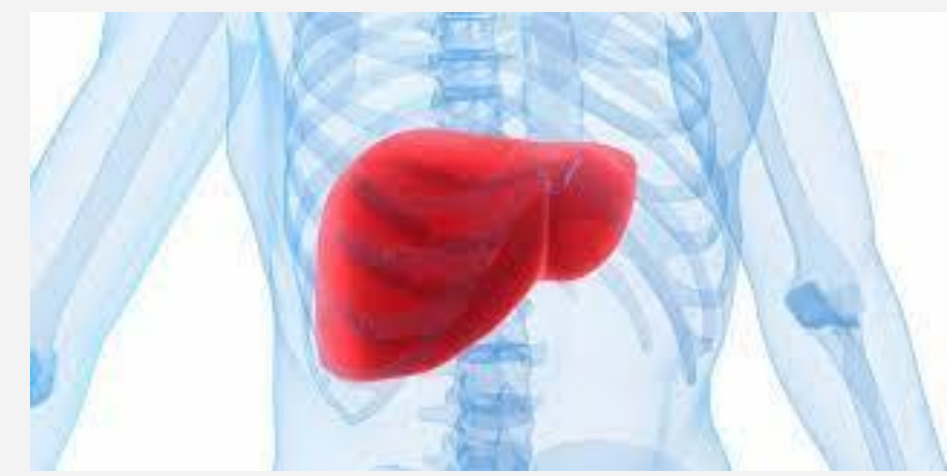
Ibuprofen dosage is **more than 99%** bound to **plasma proteins** and site II of purified albumin. Binding appears to be **saturable** and becomes non-linear at concentrations **exceeding 20 mcg/ml**.





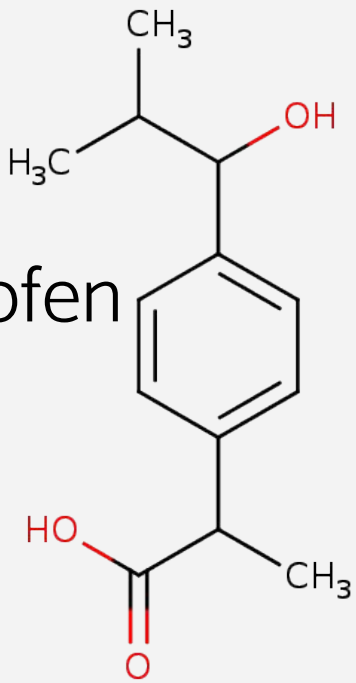
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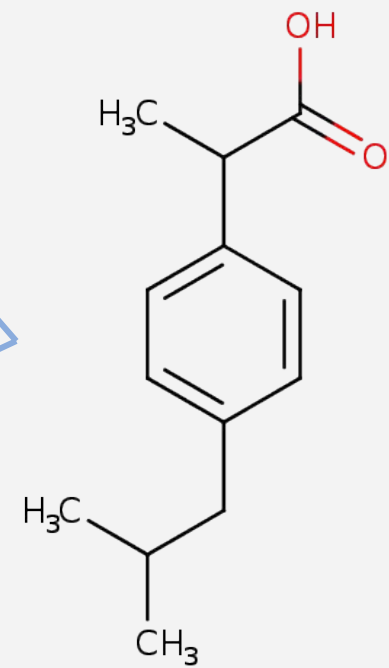


# METABOLISM OF IBUPROFEN

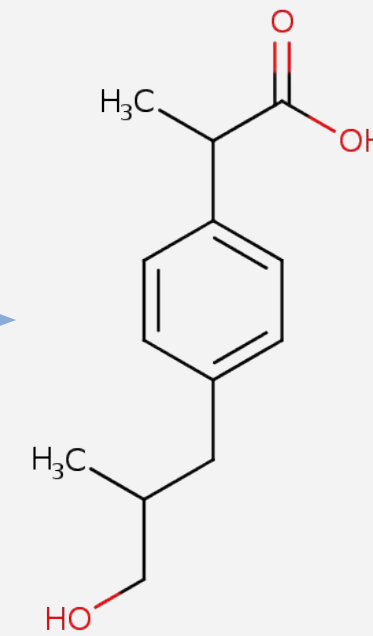
1-hydroxyibuprofen



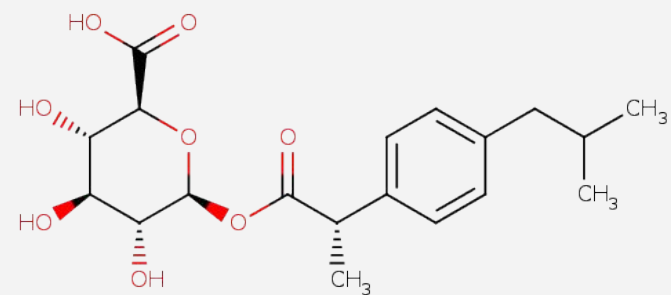
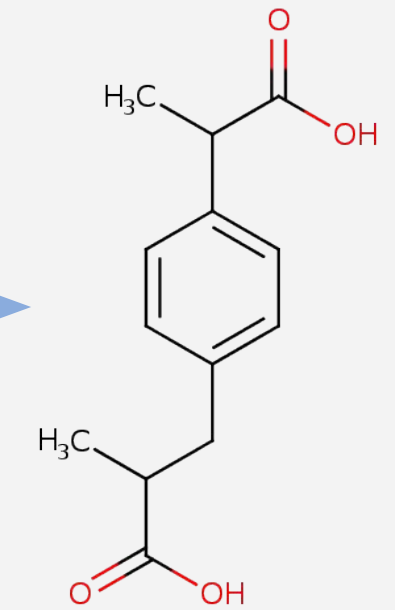
Ibuprofen



3-Hydroxyibuprofen



carboxy-ibuprofen

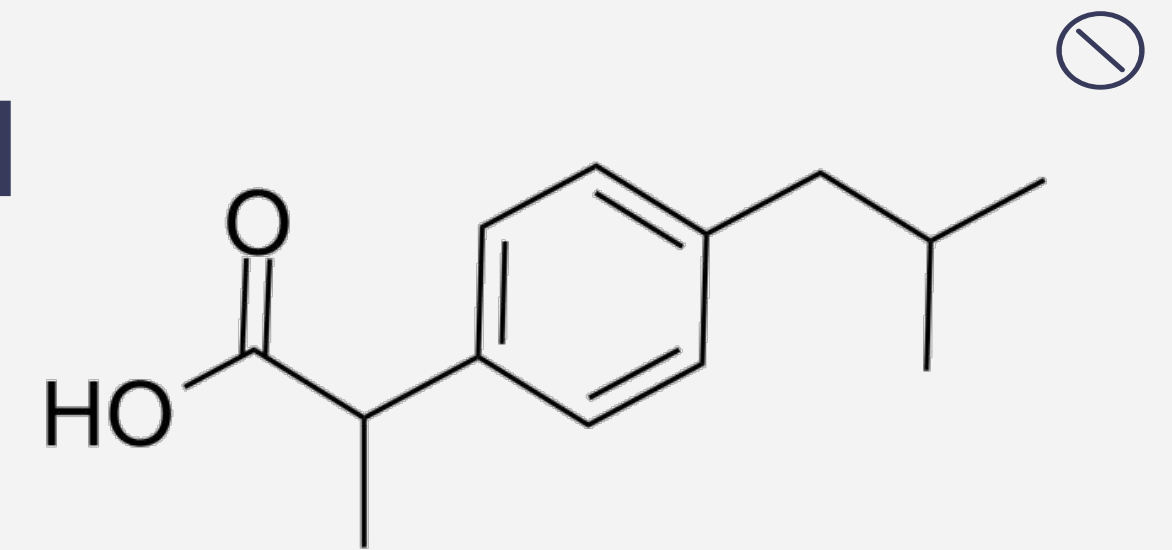


Ibuprofen glucuronide

Ibuprofen is rapidly metabolized and biotransformed in the liver to the formation of major metabolites which are the hydroxylated and carboxylated derivatives, and glucuronides

03.

## ELIMINATION OF IBUPROFEN



90% of the administered dose is eliminated in the urine

99% of the administered dose is excreted as metabolites. The other 1% is unchanged drug.



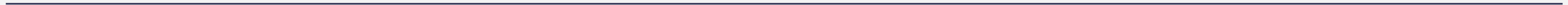
The **serum** half-life of ibuprofen is **1.2-2 hours**  
In patients with compromised liver function, the half-life can be **prolonged to 3.1-3.4 hours**

Ibuprofen is completely eliminated 24 hours after the last dose

The clearance rate ranges between **3-13 L/h** depending on the **route of administration** and **dosage**



# 04. BIOLOGICAL FLUID TESTING



# SALICYLATES IN BIOLOGICAL FLUIDS

**Therapeutic range** of salicylates: **150-300 mg/L**

Patients are often **symptomatic** at salicylate concentrations **higher than 400-500 mg/L**

Patients with salicylate concentrations approaching or **exceeding 1000 mg/L** usually have **serious or life threatening toxicity**

**Peak serum concentration** may not occur for **4-6 hours**, so concentrations obtained before that time may not reflect peak levels

Salicylate levels are typically monitored in the **blood** and the **urine**

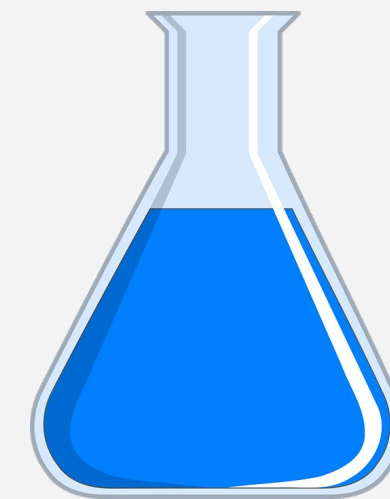
The **Trinder spot test** is a **presumptive test** to detect salicylates in the **urine**

The reagent is mixed with urine, and detects **salicylic acid** - a metabolite of salicylates

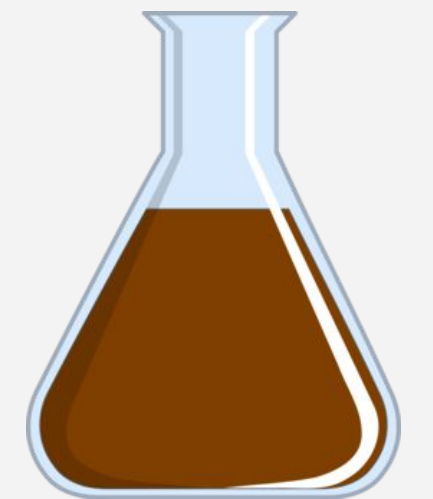
Solution is composed of mercuric chloride, water, hydrochloric acid, and ferric nitrate

- **Blue** or **purple** = **positive**
- No change = **negative**
- **Brown** = **false positive** caused by the presence of **phenothiazines**

**94% sensitivity** and **74% specificity** for identifying patients whose salicylate concentrations are **greater than 300 mg/L**



Positive Result



False Positive Result

**Confirmatory testing is done by HPLC**

# ACETAMINOPHEN IN BIOLOGICAL FLUIDS

Therapeutic concentration: 10-15 mg/L

Toxic concentration: 100-150 mg/L

Comatose-fatal concentration: 200-300 mg/L



Presumptive Colorimetric Test for Acetaminophen

- Performed on **urine** or protein-free filtrate of **blood**
- Hydrochloric acid is added and the solution is heated to 100°C
- A **blue colour** after the addition of 1% o-cresol in water and ammonium hydroxide constitutes a positive test for acetaminophen.

**Therapeutic** or **toxic** use of acetaminophen can be identified using this colour reaction

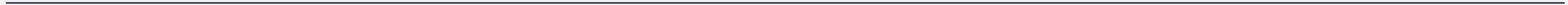
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Confirmatory testing is done using HPLC



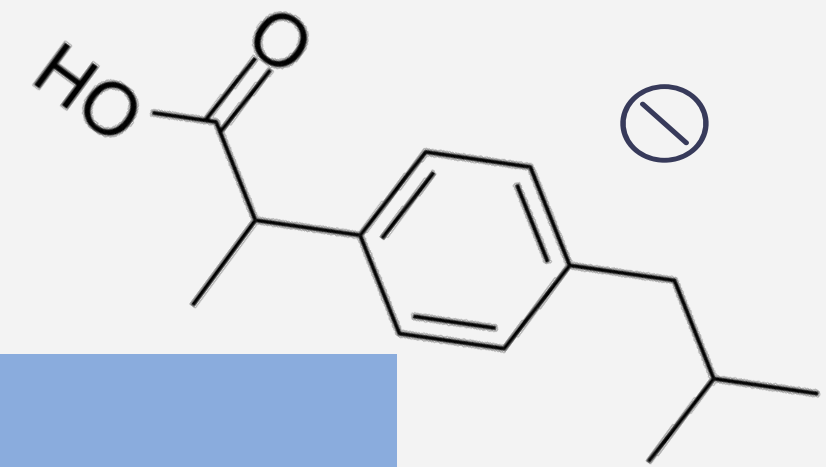
# 05. CASE REPORTS





05.

## CASE REPORT - IBUPROFEN OVERDOSE



### OVERVIEW

A 26-year-old female deliberately ingested up to **132 tablets** of **800 mg** sustained-release **ibuprofen**, equivalent to approximately **105 g**

Despite gut decontamination with multidose activated charcoal and correction of the metabolic acidosis with sodium bicarbonate and haemofiltration, the patient did not survive.

### TOXICOLOGY SCREENING

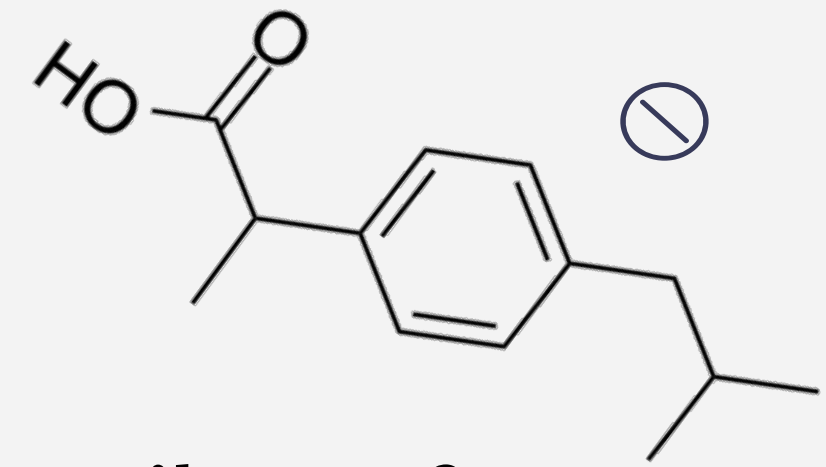
Post mortem samples of whole **blood**, **urine**, **gastric contents** and **liver** extract were analysed at the local toxicology laboratory for ibuprofen and other drugs.

Ibuprofen concentrations were measured by **high-pressure liquid chromatography** with **ultraviolet detection**.



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# CASE REPORT - IBUPROFEN OVERDOSE



## RESULTS

### In Blood...

Therapeutic dose: 15-30 mg/L

Toxic dose: >200 mg/L

Comatose-Fatal: >350 mg/L

Antemortem **serum** ibuprofen concentrations were **760 mg/L** on arrival, rising to a peak concentration of **1,050 mg/L** 90 minutes later.

### Postmortem ibuprofen concentrations:

- 518 mg/l whole blood
- 264 mg/l urine
- 116 mg/l gastric contents
- 74 mg/kg liver extract

No other drugs were detected in a broad toxicology screen; analysis of the antemortem and postmortem serum samples only detected atracurium and lignocaine given following admission to the hospital.



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## CHILD ACETAMINOPHEN OVERDOSE

1

**22-day-old** male admitted to the emergency room after realising that an **acute acetaminophen overdose** had occurred, following a routine procedure

4

The bottle of acetaminophen showed a concentration of **80 mg/mL**, which was **misinterpreted by the parents**, in that they believed that the bottle contained **80 mg of acetaminophen in total**

2

The parents had been instructed to give him **40 mg** of acetaminophen before the procedure. The infant's weight was **4.1 kg**, so this was a recommended dose of **10 mg/kg**.

5

The child was given **10 mL**, or about **half the bottle**, with the intent of giving him **40 mg**

3

However, the infant had mistakenly been given about **800 mg**, or **200 mg/kg**, of acetaminophen by his parents before the procedure.

6

After the procedure, the physician instructed the parents to give him another dose of acetaminophen if he seemed uncomfortable. At that point, the mother commented that “it **seemed like a lot of medicine**” and the error was discovered



## CHILD ACETAMINOPHEN OVERDOSE

7

The acetaminophen blood concentration drawn four hours after the overdose was substantially elevated at **1243 umol/L**. (upper end of **therapeutic range 66-199 umol/L**)

8

Given that the patient had received more than the **toxic dose of 150 mg/kg** and because the four-hour blood concentration level of acetaminophen was in the probable toxicity range on the Rumack-Matthew nomogram, treatment with **N-acetylcysteine** was recommended

9

N-acetylcysteine **reduces the hepatotoxic effects** of acetaminophen overdose by **replenishing glutathione stores**, thereby enhancing production of the **nontoxic metabolites**

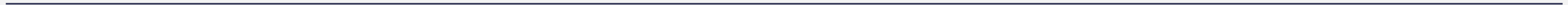
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The infant was **sent home after 48 hours**, remained clinically well, and **did not show evidence of long-term consequences** of the accidental overdose





# 06. CANLII CASE STUDY





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## E.D. v S.K., 2017

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**Issue:** The applicant, the patient's mother, expresses concern that the respondent, a physician, failed to provide appropriate medical care to her daughter

### BACKGROUND

1

On February 2, 2014, a 20 year old woman was brought to the hospital after she was found at her apartment **struggling to breathe** and with **decreased consciousness**

2

The patient had a medical history that included **idiopathic intracranial hypertension**, was on medications including acetazolamide, and had been prescribed **Tylenol 3** and **222s** (contain **ASA**, caffeine, & codeine)

3

The paramedics noted an almost **empty container of 222s** and thought the patient had overdosed. However the patient's mother advised health professionals that it was not an overdose and informed them of the **patient's medical history**

4

From the morning of February 3, 2014 and over the next few days, the diagnosis of cerebral death was confirmed. Life support was removed, and the patient passed away on February 7, 2014



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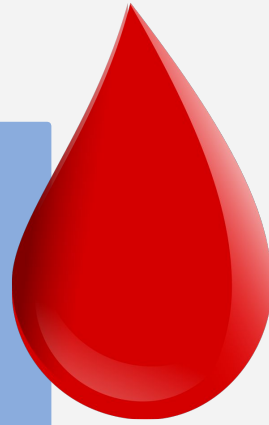
## E.D. v S.K., 2017



### TOXICOLOGICAL FINDINGS

#### Initial Results:

Arterial **blood** gas showed severe metabolic acidosis, salicylate at a **therapeutic level**, and opiates were found on **urine** toxicology, consistent with the patient's medication



### DECISION

The medical care provided was deemed **acceptable**, and the Board confirmed the committee's decision to **take no action** against the respondent

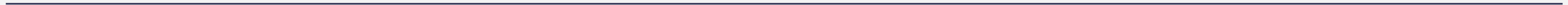
#### Opinion accidental poisoning by of Dr. M:

- **Low levels** of ASA/acetazolamide can be **toxic** if the use is **chronic** and **regular**
- ASA levels could be **low in the plasma** but **high in the tissues** and able to **cross the blood-brain barrier** when a patient is acidotic
- This effect is **amplified by acetazolamide** and explains why the ASA would be **undetectable** on the toxicology screen
- The patient's **brain was vulnerable** as she had idiopathic intracranial hypertension, causing high pressure in the brain and was on medications which had **unforeseen dangerous side effects**, even at **therapeutic doses**
- Concluded the patient suffered from **accidental poisoning** from chronic use of medication at **normal doses**.





# 07. LIST OF REFERENCES



# REFERENCES

1. [Outline of the Schedules](#)
2. [National Drug Schedules | NAPRA](#)
3. [Drug Scheduling](#)
4. [Human Metabolome Database: Showing metabocard for Aspirin \(HMDB0001879\)](#)
5. [Acetaminophen Uses, Dosage & Side Effects - Drugs.com](#)
6. [Showing metabocard for Ibuprofen \(HMDB0001925\)](#)
7. [Over-the-Counter Medicines DrugFacts | National Institute on Drug Abuse \(NIDA\)](#)
8. [Dose-response in direct comparisons of different doses of aspirin, ibuprofen and paracetamol \(acetaminophen\) in analgesic studies - McQuay - 2007 - British Journal of Clinical Pharmacology - Wiley Online Library](#)
9. <https://www.merckmanuals.com/en-ca/professional/injuries-poisoning/poisoning/acetaminophen-poisoning?query=acetaminophen%20poisoning>
10. [Aspirin and Other Salicylate Poisoning - Injuries; Poisoning - Merck Manuals Professional Edition](#)
11. [Pediatric Fatalities Associated With Over-the-Counter Cough and Cold Medications | Pediatrics | American Academy of Pediatrics](#)
12. [Aspirin: Uses, Interactions, Mechanism of Action | DrugBank Online](#)
13. [Drug Bioavailability - Clinical Pharmacology - Merck Manuals Professional Edition](#)
14. [Ibuprofen: Uses, Interactions, Mechanism of Action | DrugBank Online](#)
15. [Salicylates \(Color Test\)](#)
16. [Presumptive Chemical Tests](#)
17. [Fatality after deliberate ingestion of sustained-release ibuprofen: a case report | Critical Care | Full Text](#)
18. [Acetaminophen overdose in children](#)
19. [E.D. v S.K., 2017 CanLII 2643 \(ON HPARB\)](#)