Medicines and Drugs

Option D Summary

2010

SCH 3UE | Chemistry
Prashanth Srinivasan
Patrick Payne
William Lee

CONTENTS

- alters mood or emotions
- alters incoming sensory sensations
- alters a physiological state, including consciousness, activity level or co-ordination

D.1.1 ◊ PLACEBO EFFECT

- when a false drug (sugar pill) is administered, and **does not have any effect** on the problem
- may have some **perceived effect** (illusional)
- shows how important the mind and mental preparation is to recovery
- used in medicinal research to determine if the drug has any real effect
- blind tests, where patients don't know if they have a placebo
- double blind tests, where neither the patients or the doctors know if they are placebos

D.1.2 ◊ DEVELOPING A DRUG

- A disease is selected for treatment
- Targets identified that can be affected by drugs (e.g. enzyme or process involved in disease)
- Potential **"lead molecules"** selected:
    - molecules in other similar areas that have similar effects
    - computer designed molecules, using knowledge of biochemistry
    - stumbled upon by random robotized screenings of molecules
- Lead molecule selected. Choice made based one which are most effective, cheapest, advantages, and investment return
- **Preclinical trials:**
    - In vitro testing of the drug, to test potency of drug, and its selectivity
    - In vivo testing on animals, to see potency and side effects, as well as what changes the molecule goes under while in the body
- **Phase 1 trials:**
    - Done on small numbers of healthy volunteers
    - Done to assess toxicology of the drug
    - Occasionally done on terminally ill patients with their consent
- **Phase 2 trials:**
    - True clinical trial, including blind and double blind testing
    - Dosage and administration methods determined
- **Phase 3 trials:**
    - Largest testing phase: thousands of patients are given the drug and monitored
    - Massive amounts of data to satisfy regulations
- Data is all submitted to **regulatory agencies**. If all goes well, the drug is launched
- **Phase 4 trials:** post launch monitoring of the drug. May lead to new formulations, dosages, applications, product extension
- Whole process takes long time, between 10-15 years. Cost up to $500 million.
- No profits have been made until product has hit the market
- Glaxo-SmithKline: in 2007, had an R&D budget of 6.6 billion USD

D.1.3 ◊ THALIDOMIDE

- Drug prescribed from 1958 to 1963 for **morning sickness**
- Very little regulatory oversight at this time
- Caused many cases of **abnormal and dead births**
- Company sued into oblivion, regulations tightened
- Now used under different name for severe leprosy
- Some poor areas disregard warnings, abnormal births occur due to this

D.1.4 ◊ METHODS OF ADMINISTRATION

1. **Oral:**
   a. Capsule or syrup
   b. Subjected to digestive system, process may affect drug
   c. Easiest method of delivery
2. **Rectal:**
   a. Effective, but rejected due to cultural reasons
   b. Germany's favorite form of medicine
3. **Inhalation:**
   a. Rarely used unless the drug targets the lungs, or can be absorbed by them
4. **Injections:**
   a. Advantageous, can be put directly where it is needed
   b. Reduces dosage requirement and chance that it will be altered by the body
   c. Usually needs medical staff in order to administer
   d. Patients don't particularly like it
   e. **Intravenous:** into the bloodstream. Bypasses stomach acid, but spreads the drug throughout the body
   f. **Subcutaneous:** into the body fat. Good for drugs that are fat soluble
   g. **Intra muscular**: straight into muscle tissue
5. **Patches:** very good for molecules that can be absorbed over time
   a. Spreads dosage over an extended time
   b. Patients love it

D.2 ◊ ANTACIDS

D.2.1 ◊ PURPOSE OF ANTACIDS

- pH of normal stomach acid: 1.0-3.0. This is to suppress bacteria and help digestion
- Over-eating and stress cause ↑ in acidity
  - Causes discomfort, aka indigestion
  - Can eat away at protective mucus coating, causing stomach ulcers
- Antacids: a remedy for excess stomach acidity
  - Bases, metal oxides, hydroxides, carbonates, or hydrogen carbonates
  - Neutralize excess acid in the stomach, raise pH to desired level
  - Relieve indigestion and allow damage done by acid to repair itself

D.2.2 ◊ ACTIVE INGREDIENTS

- Active ingredients: include $Al(OH)_3$, $Mg(OH)_2$, $CaCO_3$, and $NaHCO_3$
  - Often have **alginates** → produce neutralizing layer over stomach acid → prevent acid reflux
  - Anti-foaming agents often added, which cause bubbles to coalesce
  - E.g. magnesium oxide: $MgO_{(s)} + 2HCl_{(aq)} = MgCl_{2(aq)} + H_2O_{(l)}$

D.2.3 ◊ SIDE EFFECTS

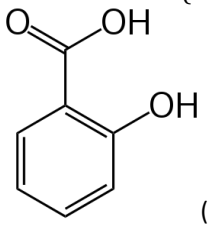
- **Aluminum Hydroxide:** constipation or irregularity
  - Aluminum ions can prevent the uptake of phosphate ions (they react)
- **Magnesium hydroxide:** laxative properties
- **Calcium carbonate:** kidney stones
- **Sodium** ions may lead to hypertension
- Dosage is hard to gauge, small ones do not significantly raise pH, high doses may lead to basic stomach

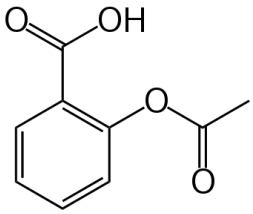
D.3 ◊ ANALGESICS

- **Analgesic:** drug which relieves pain without aid of sleep (i.e. narcotic effects)
  - **Mild analgesics:** more localized substances; far less potent and shorter-term effects
  - **Strong Analgesics:** target the nervous system to electrochemically inhibit sensory signal transfer

D.3.1 ◊ MILD ANALGESICS

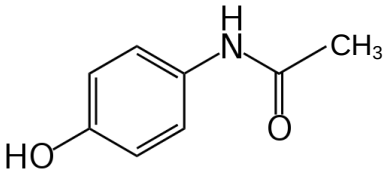
- **3 properties:**
  - ***Analgesic*:** pain relief
  - ***Antipyretic*:** fever reduction
  - ***Anti-inflammatory***: swelling reduction
- Work at site of pain to inhibit synthesis of ***prostaglandins*** - in most diagnoses, responsible for temperature ↑ (pyretic)
- Many commercial mild analgesic shapes allow binding to ***cyclooxygenase*** (hormone production) - no more pain-inducing hormones present at synapses)
- **Salicylic acid:** extract from Willow Bark (first 1860; used as analgesic since 1763) and from wildflower
  - Effective but unpleasant - high acidity (both **alkanoic** acid and **phenol**)
  - **1899:** Hoffman (German) working for Bayer Drugs, added acetyl group ($COCH_3$) - acetylsalicylic acid (





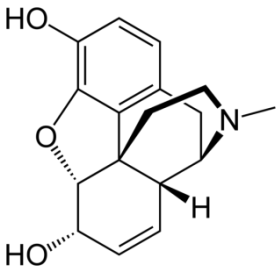
(left, salicylic acid; right, acetylsalicylic acid **aspirin**)

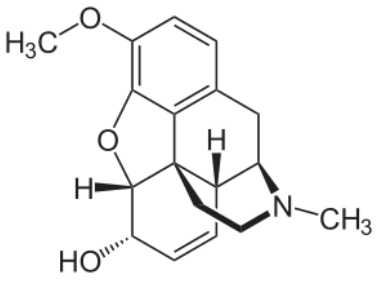
- **Aspirin:** 50 years, it was preferred analgesic, until adverse effects observed
  - **High acidity** → stomach ulcers and bleeding
  - **Anti-coagulant** → ↑s likelihood/severity of internal bleeding
  - **Allergenic**
  - Children → **Reye's Syndrome** (liver and brain disorder) - thus it is no longer preferred for <12
    - Still used for anti-coagulant properties - stroke / heart attack patient; supposed anti-carcinogenic
- **Paracetamol:** similar shape to aspirin (similar operation); today's preferred mild analgesic
  - In correct doses - none of adverse effects of aspirin
  - In overdoses - fatal liver damage (often used for suicide)
  - Syrup form - effective children's antipyretic



D.3.2 ◊ STRONG ANALGESICS

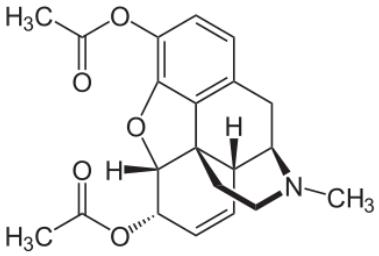
- Immediately target brain → bind with and block specific pain chemoreceptors - stop pain transmission





(left, morphine; right, codeine, a derivative)

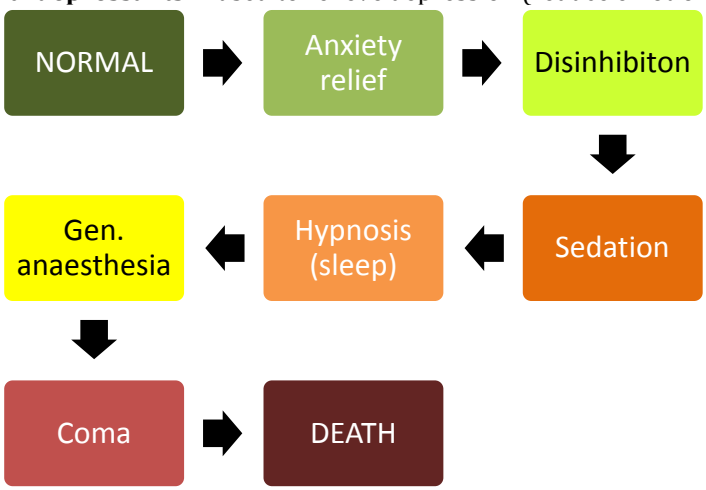
- Majority of strong analgesics related to **morphine**, extract from opium poppy (family **opium alkaloids** - similar molecular shape)
- **Codeine** → only change is replacement of one H^+ from alcohol w/ **methyl** ($-CH_3$)
- **Diacetylmorphine:** a.k.a. heroin - replace H of both alcohols for acetyl $COCH_3$
  - **Strongest analgesic** known
  - Removal of 2 hydroxyl -OH groups →reduces solubility in H_2O, ↑d in **fats** → must be injected into bloodstream, but passes **blood-brain barrier** easier than morphine
  - Thus, ↑ intensity, ↓ duration



- Main problem w/ opiates → **addiction** (physiological/psychological dependence)
- Brain produces own analgesics - **endorphins** (1979(
  - When released, same effect as opiates - block pain reception
  - E.g. under great trauma (war, car accident), victims often do not feel much pain
  - Morphine + opiates - inhibit endorphin production; even for normal operation small amount endorphins req'd
  - **Withdrawal:** result of endorphin levels decreased by opiate use; levels only ↑ with time
  - Analgesic power ↑ = addiction ↑

D.4 ◊ DEPRESSANTS

- ***Downers, tranquilizers, sedatives, hypnotics*** - calm and relax **central nervous system (CNS)** → interfere w/ nerve impulse transmission
- Slow activity of organs (e.g. brain and heart) - reduce breathing rate and emotional response
- Low doses - **little or no effect**
- Moderate doses - may induce **sedation** (soothing + anxiety reduction)
- High doses - induce sleep; if higher, coma and death
- Often called "**anti-depressants**" - used to relieve depression (reduce emotional response)



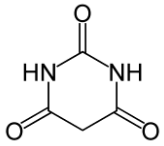
D.4.1 ◊ TRANQUILIZERS

- E.g. **alcohol, valium, librium**
- Reduce nervous tension + anxiety → do not produce sleep in normal doses
- Librium + valium (**diazepam**) → 2 common benzodiazepine tranqs for relieving anx. + tension
  - Safer than **barbiturates**

    Diazepam family of benzodiazepines - anxiety, insomnia, tension, seizures

D.4.2 ◊ SEDATIVES

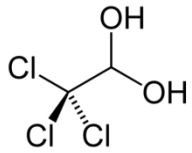
- **Barbiturates:** more powerful class of depressants, derived from barbituric acid; used most commonly in medicine for anesthesia



- Cause distress soothing w/o sleep (@ normal doses)
- Main difference from tranqs → much more potent in action
-

D.4.3 ◊ HYPNOTICS

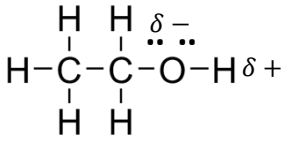
- Class of drug that **produces sleep** (soporific), e.g. chloral hydrate
- Some, e.g. Phenobarbital (also a barb) can act as sedative or hypnotic, or **both**



chloral hydrate, a common hypnotic or soporific compound

D.4.4 ◊ ETHANOLS

C_2H_5OH



- Presence of **dipolar hydroxyl** group (high EN of O) → H-bonds w/ water for high solubility (alcohol in beverages)
- Small molecules - fat-soluble → easily absorbed from GI tract
- Levels of intoxication:
  - **Mild** → 30-50mg/0.1L blood → sense of **euphoria; silly behaviour** in those unaccustomed
  - **Moderate** → ~100mg/0. 1L → neurological problems → slurred speech, staggering; aggression even in those accustomed
  - **High** → ~200mg/0.1L → vision and movement heavily impaired
  - **Very high** → ~400mg/0.1L → coma and death
- Alcoholism medically defined as disease → progressive and if untreated, fatal
- Has some **genetic background** - may be "passed down" → concentration of various **body enzymes**
- Now → few medical uses
  - Used as solvent for antiseptic tinctures (e.g. iodine, mouthwash)
  - NA and Europe → ~80% of population uses alcohol (adult)
- **Social effects of use and abuse:**
  - Sickness + death associated w/ alcohol → hospital treatment, productivity ↓, crime, motor traffic accidents, psychological pain of relatives, death
  - Developed nations → ~80% all alcohol-induced costs → society-induced

D.4.5 ◊ PHYSIOLOGICAL EFFECTS OF ALCOHOL (AB)USE

- **Alcoholism**: psychological addiction (inability to control intake, compulsion, inability to stop, physical addiction) → genetic factors involved
- Abuse → failure of major obligations (work, school, home), drinking while driving, machinery operation; physical or psychological harm to others
- **Physical dependence:** nausea, sweating, anxiety, ↑ BP (withdrawal)
- **Tolerance:** need for ↑d dose to feel same effects
- **Short-term:**
  - **CNS depressant →**reduces tension, anxiety, inhibitions → degree of CNS impairment ∝ conc. in blood
  - Moderation → euphoria, sociability, relaxation, self-confidence, decreased inhibition (dilation of blood vessels -- feeling of warmth)
  - As amount ↑, loss of judgment, perception, memory + comprehension - likelier driving accidents (↑ $reaction\ time$)
  - Then, aggression, slurred speech, vomiting, dizziness, double vision + loss of balance, nausea → then loss of consc. + death from breathing failure
- **Long-term:**
  - Cirrhosis (tissue scars), liver cancer, coronary heart disease, ↑ BP, stroke, gastritis (inflammation), peptic ulcers
  - Physical dependence and high tolerance → anxiety, depression + poor eating habits
  - W/ pregnancy → miscarriage, low birth mass, abnormality (Fetal Alcohol Syndrome) → mental/phys. Defects

D.4.6 ◊ SYNERGISTIC EFFECTS OF ALCOHOL

- When other drugs combined w/ alcohol -- much more harmful
  - E.g. alcohol + sedatives (sleeping pills, barbs) → heavy sedation + coma, death
  - Alcohol + aspirin causes/inc. stomach bleeding
  - Alcohol + cocaine → cocaethylene → extends "high"; far more toxic than cocaine → **vasoconstriction + arythmogenecity**
    - Narrowing of blood vessels = ↑ BP + irregular HB
  - Alcohol + 'pines (mogadon, valium) - complete suppression of CNS and death
- **Blood Alcohol Concentration (BAC)**: mass ethanol/0.1L blood; may be % mass, e.g. 0.08% limit for driving (80mg/0.1L)
- Ethanol passes stomach → bloodstream; sufficient volatility → lungs (equilibrium @ body temp.)
- Conc. Ethanol ↓ w/ time → removed by liver (metabolized)

D.4.7 ◊ METHODS OF ETHANOL ANALYSIS

- **Breathalyser:**
  - Redox rxn: acidified $K_2Cr_2O_7$ oxidizes alcohol in breath → CH_3COOH → orange Cr(IV) becomes green Cr(III) (+3 electrons /Cr):

$$\mathbf{2Cr_2O_7^{2-} + 3C_2H_5OH + 16H^+ \xrightarrow{yields} 4Cr^{3+} + 3CH_3COOH + 11H_2O}$$

  - Transfer of electrons generates EM field - converted to signal analyzed by device to indicate BAC → inaccurate + unreliable in legal cases
- **Gas Liquid Chromatography:**
  - Uses stationary phase (non-volatile liquid/solid) + mobile phase (inert carrier gas, N_2)
  - Breath components (CO_2, H_2O, alcohol) partitioned btwn. stat. and mob. (based on boiling points)
  - Components injected through column of solid phase → travel at difference speeds and exit at dif. Times - identified (changes in carrier gas speed) by recorder
  - **Retention time:** graph displays this, time taken for each component to pass thru → standard C_2H_5OH sample passed thru @ all **same conditions** (same carrier gas, flow rate, stat. phase and temp.) → **theoretical retention** time
  - Breath/urine sample then passed thru; compared → GLC identifies compound and amount (area under spike) - can also identify other drugs (e.g. btwn ethanol and antidiabetic propanone)

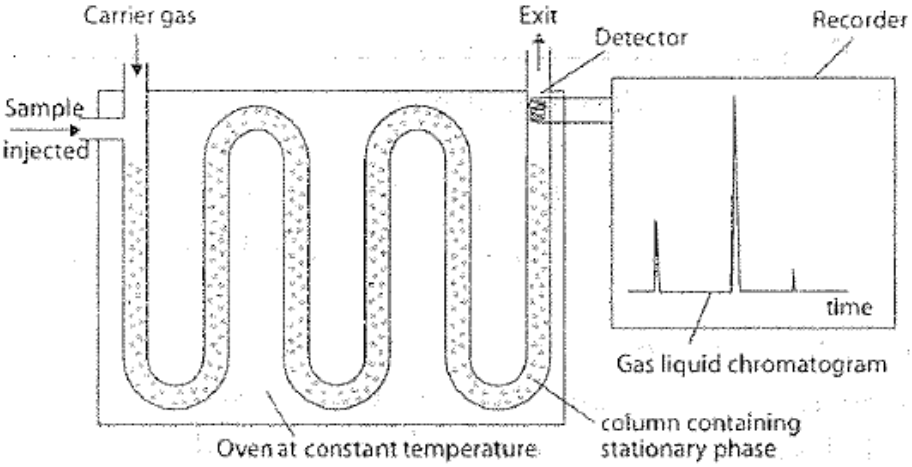


Figure 1512 A gas liquid chromatogram

- **Infrared Spectroscopy:**
  - IR energy not large enough for e^- shift to higher EL; instead vibrational movement (depends on mass and strength/length of molecular bonds w/I substance)
  - IR spectrum acts as fingerprint for bonds or functional groups in compound - "fingerprint"
  - IR wavenumber = $\frac{1}{\text{wavelength}}$ cm^{-1}, range 667-4000cm^{-1}
  - E.g. C-H bond in alcohol = 2950; O-H = 3340 (also in water vapour; thus 2950 used instead)
- **Intoximeter:**
  - IR spectrophotometer (radiation passed thru breath sample); for confirming breathalyser tests
  - If alcohol present, specific frequencies absorbed and rest transmitted - meter compares intensity of rad. thru air w/ thru breath
  - Then emits IR spectrum as %radiation transmittance (% through sample) - cannot distinguish between eth. and prop.
  - Size of peak @2950 = amount rad. absorbed = alcohol content

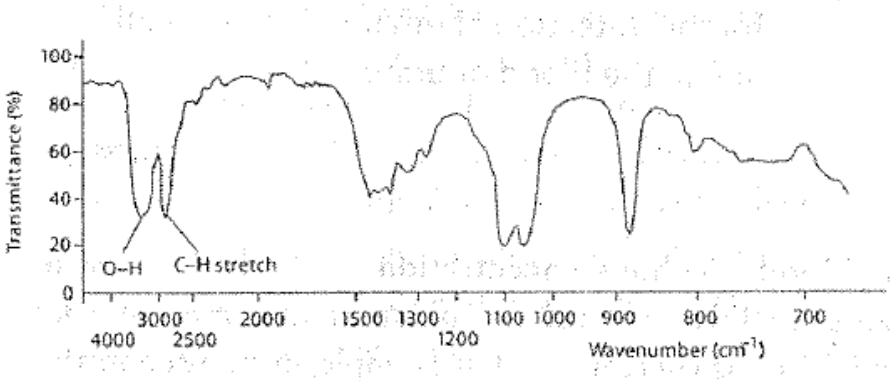
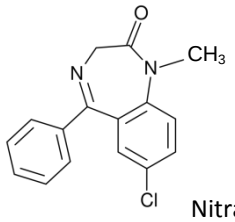


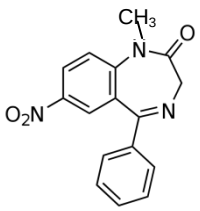
Figure 1513 The spectrum of ethanol showing the C–H stretch used for detection.

D.4.8 ◊ COMMERCIAL DEPRESSANTS

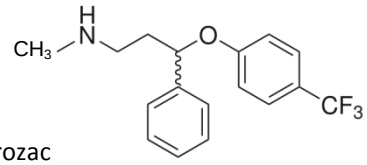
- **Valium:** diazepam, sedative; most prescribed in the world → anxiety + tension relief
- Interacts with neurotransmitters to block nerve transmission
- **Mogadon:** nitrazepam, sleeping pill (hypnotic); controls seizures and infant spasms
- Both known as **benzodiazepines** -- phenyl C_6H_5 + benzene ring + 7-part heterocyclic ring (2 N, one is amine -NH_2)
- On benzene, valium has Cl, Mogadon has NO_2
- **Prozac**: fluoxetine hydrochloride → anti-depressant for mental depression → ↑ serotonin (NT) activity
  - Structurally different → amine group + HCl → fluoxetine hydrochloride - hydrophilic



Diazepam



Nitrazepam



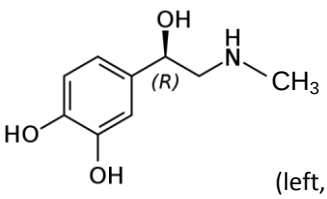
Prozac

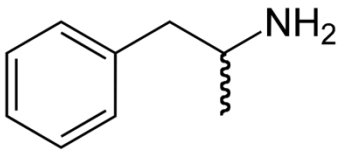
D.5 ◊ STIMULANTS

- ↑ alertness + greater sensitivity to external stimuli → mental processes speed up; feeling of elation or anxiety → **opposite of depressants**
- **Treatment** for mild depression, narcolepsy (chronic sleepfulness), asthma (drugs cause broncodilation)

D.5.1 ◊ AMPHETAMINE AND ADRENALINE

- Illustrate common tendency for synthetic to mimic natural (e.g. opiates and endorphins)
- **Adrenaline:** naturally occurring hormonal stimulant from adrenal gland (also called epinephrine)
  - Transported thru bloodstream to CNS areas for heart + breathing, pupil dilation, sweating
  - Released under stress "fight or flight" → ↑s heartbeat, pupil dilation, sweating, blood diversion to muscles, dec. blood clotting time
  - 3 hydroxyl -OH groups → hydrophilic but insoluble in fat → cannot pass through blood-brain barrier
  - Thus created in situ in brain, e.g. **norepinephrine**
- **Amphetamine:** primary amine - *sympathomimetic amine* → mimic chem. behaviour nervous system hormones (e.g. caffeine)
  - Can pass into brain - mimics norepinephrine - neurotransmitter which binds to neural protein to send signals to brain - specific proteins found under "stress" and "emotion" parts
  - So similar → it will replace nor. in storage sites - flood of displaced nor. Molecules - bind to all proteins → lots of signals → euphoria
- Both based on phenyl ethylamine → benzene ring + 2-carbon chain + amine @ end





(left, adrenaline; right, an amphetamine)

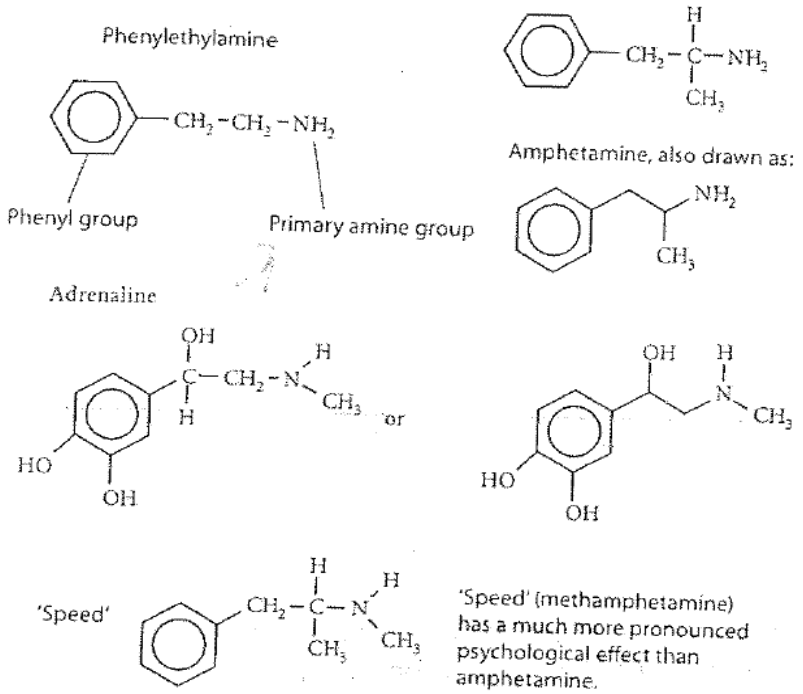


Figure 1516 Strucures of amphetamines and adrenaline

D.5.2 ◊ PHYSIOLOGICAL AND PSYCHOLOGICAL EFFECTS

- Decrease in **appetite** - sometimes used as diet pills
- ↑d state of **wakefulness**
- Heightened senses, **alertness**
- Sometimes, **state of agitation or anxiety**
- Contraction of arteries; ↑d **sweat production**
- Following usage, a psychological and phys. **low** - fatigue, irritability, depression - cause body to shift to **reserve energy** - blackout to collapse afterwards

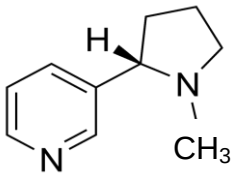
D.5.2 ◊ DESIGNER DRUGS

- **Ecstasy:** designer drug (illegal) - mod of amphetamine structure to avoid laws on brain-altering drugs
  - Structurally similar to methamphetamine (stim) and mescaline (hallu) - much more potent (pot. fatal after even one dose)

D.6.2 ◊ NICOTINE

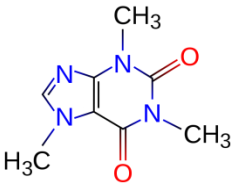
- Nitrogenous alkaloid in tobacco leaves - cigarette smoke → mild stimulant
- Stimulant effect very weak and short-lived - followed by depression, which encourages use
- Produces psychological dependence → tolerance → physiological dependence - more addictive than alcohol or barbs
- **Short-term effects:**
  - ↑d heart rate, BP, constriction of blood vessels - puts stress on heart - must pump harder than normal
  - Thus, greater long-term incidence of heart disease/failure for smoking
  - Reduced urine output

- **Long-term effects:**
  - Stress on heart ↑s risk of heart disease and coronary thrombosis (blood clotting) - may also cause rise in fatty acids in blood
  - Produces CO - inhibits hemoglobin ability to carry oxygen (CO binds instead; higher affinity than O_2) - even more coronary stress
  - Stimulant property → high acidity in stomach - peptic ulcers
  - Cig. Smoke also contains many other toxic chemicals
  - Lung, mouth, larynx cancer; jaundiced fingers + teeth
  - Blood vessel disease/damage
  - Emphysema - chronic lung condition w/ loss of elasticity of alveoli - breathing problems
  - Chronic bronchitis (inflammation of breathing tubes); air pollution and fires (50% in Canada caused)
- **Withdrawal:**
  - Weight gain
  - Nausea
  - Insomnia
  - Irritability
  - Fatigue
  - Inability to concentrate
  - Cigarette craving
  - Depression



D.6.2 ◊ CAFFEINE

- **Alkaloid** often found in tea and coffee, soft drinks - stimulant of CNS by working **inside** nerve cells to ↑ rate of **cellular metabolism** - rate of energy prod. from respiration ↑



- **Stimulates CNS**, heart, kidneys, lungs + arteries that supply blood to brain/heart
- Moderation - ↑ alertness well-being, energy, motivation, concentration - **sustained intellectual effort** possible
- Higher doses - affects physical coordination, timing; harmless in small amoutns
- Larger doses cause **insomnia**; ↑s **urine output** (stimulates kidneys)
- May result in tolerance but no true **physical addiction**; minor psychological dependence (morning grouchiness)
- Used in medicine to stimulate breathing, e.g. of newborn babies w/ resp. problems
- **Vasoconstrictor** (blood vessels) - may reduce headache (dilation in brain)
- Heterocyclic compound - ≥ 1 C-atoms in ring replaced by nitrogen (or any other) - like nicotine contains tertiary amine, R_3N (R represents any organic molecule)

D.6 ◊ ANTIBACTERIALS

D.6.1 ◊ BACTERIA

- Single-celled organisms → damage body tissue; not all are harmful though (e.g. GI tract bacteria)
- **Infectious disease** occurs when bacteria multiply faster than body's neutralization rate (i.e. antibody production)

D.6.2 ◊ ANTIBACTERIAL FUNCTION

- **Antibacterials (aka antibiotics):** drugs that inhibit growth of, or kill, microorganisms causing infectious disease
  - **Selective:** they act against infecting bacteria more than against human cells
  - Many diseases caused by microorganisms (germ theory of diseases)
  - **Microorganisms:** single-celled life forms capable of independent life given enough nutrients
  - Infectious diseases occur when the **body's defenses are inadequate**

D.6.3 ◊ BACTERIAL VS. VIRAL INFECTION

- Two main types of infectious agents: **bacteria** and **viruses**
  - Antibacterials **ineffective against viral infection**, as they do not target human cells
  - Antibiotics help stop bacterial infection by:
    - Inhibiting cell division (**bacteriostatic drugs**)
    - Directly killing bacteria (**bacteriocidal drugs**)
  - **Bacterial infections:** tetanus, tuberculosis, cholera, typhoid fever, syphilis, gonorrhea.
  - **Viral infections:** influenza, the common cold, hepatitis, measles, HIV/AIDS

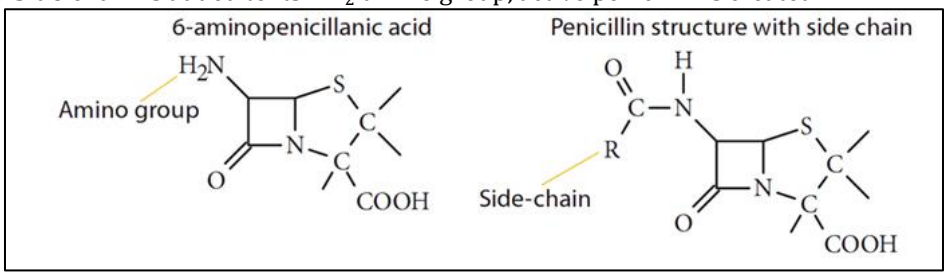
D.6.4 ◊ HISTORY OF PENICILLINS

1. **1890's:** scientists found that certain fungi killed bacteria
   - Mice exposed to just bacteria died
   - Mice exposed to bacteria and fungus lived
   - Results ignored
2. **1928:** Alexander Fleming found same thing with mold called ***penecillium notatum***
   - Found that no bacteria formed around the mold
   - Gave up after he found how difficult it was to extract active ingredient
3. **1940:** Florey and Chain renewed research effort
   - Injected mice with deadly bacteria
   - Those who also received penicillin did not die
   - First human use was on a police officer with blood poisoning
4. **1941:** program started to mass produce penicillin
   - **1943:** clinically available
   - **1945:** enough was available to meet demand (used in WW2)

D.6.5 ◊ PENICILLIN STRUCTURE

- 1st penicillin used → **Penicillin G**
- After the structure was determined by x-ray crystallography, others were made
  - Since penicillin G deactivated by stomach acids → **Penicillin V**
  - Created by keeping the basic structure, but **changing the side chains (R-group)**
- Some bacteria deactivate Penicillin G, ∴ other synthetic ones made that are **resistant**
- Structural feature common to all penicillins →**6-aminopenicillanic acid (6-APA)**

- If an **extra side chain** is added to its NH_2 amino group, active penicillin is created:



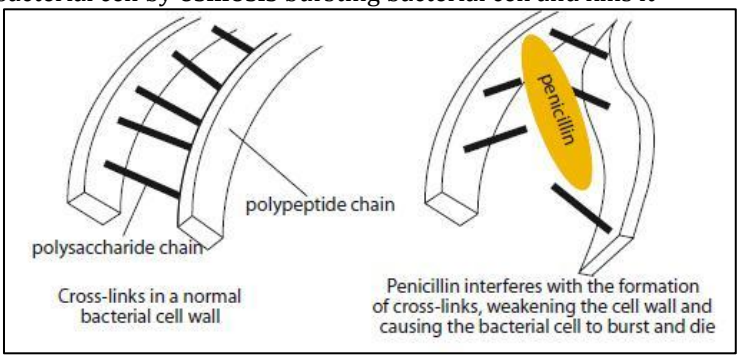
- **Note:** When R = C_6H_5-CH_2-: **Benzyl penicillin** or **penicillin G**; not acid resistant.
  When R = C_6H_5-CH_2- CH_2-: **Penicillin V**; acid resistant.
  When R = C_6H_5-C—C –**cloxaillin** ; acid and penicillinase resistant.

D.6.6 ◊ ANTIBIOTIC SPECTRUM

- **Broad spectrum** are effective against wide variety of bacteria (e.g. ampicillin and tetracyclines) as opposed to only certain types of bacteria (**narrow spectrum antibiotic**)
  - Most antibiotics are narrow spectrum
- **Repeated use** of broad-spectrum antibiotics may wipe out harmless/helpful bacteria in:
  - esophagus
  - stomach
  - large intestines
  - Destroyed bacteria may be replaced by harmful strains

D.6.7 ◊ PENICILLIN FUNCTION

- Interfere with **cross link formation** of chemicals connecting **bacteria cell walls** (dif. polysaccharides)
  - **Weakened cell walls** burst → kill bacteria
- **Cannot harm animals** as animal cells do not have cell walls (cell membranes → different structure)
- Bacteria **cannot assemble** molecular components of its cell wall when penicillin present
  - Prevents bacteria from keeping its size and shape
  - Water enters the bacterial cell by **osmosis** bursting bacterial cell and kills it



D.6.8 ◊ PENICILLIN SIDE EFFECTS

- ~10% of population experience allergic reactions + side effects from over-prescription:
  - Fever
  - Body rash
  - Shock
  - Death
- Repeated use → allergic reaction
- May wipe out helpful bacteria and be replaced with harmful ones

- **Genetic resistance** as a few bacterial cells **survive each time** antibiotics used
  - Survival of a few bacterial cells from penicillin wave → reproduce → **more resistant bacteria**
  - Genetic mutation producing enzymes that deactivate antibiotics
- Sometimes → must use combination of drugs to fix infection w/ patient - **multidrug treatment**
- Strict adherence to recommended treatment regime necessary for effective treatment
  - E.g. for tuberculosis

D.6.9 ◊ ANTIBIOTICS AND FEEDSTOCK

- Used to **control animal diseases** + **↑ growth rate** of livestock
- Meat production → kill dangerous bacteria, ↑ productivity
- Routine exposure to small doses → survival and reproduction of naturally **drug-resistant bacteria**
- Same antibiotics used to treat **infections** in livestock and humans
- Makes humans vulnerable to life-threatening diseases → ↑ cost of treatment

D.7 ◊ ANTIVIRALS

D.7.1 ◊ VIRUSES

- **Submicroscopic** non-cellular infectious particles - reproduce only w/I cell, w/ enzymatic machinery of that cell
- I.e. "cell hijacker" - attaches to host cell, assumes control by **injecting own DNA** and destroying original
- Viruses have central DNA core (nucleic acid) surrounded by **capsid** - no nucleus, cytoplasm, membrane (some do around outer coat)
- Do not require food - **do not grow**; instead reproduce using ribosomes of host

D.7.2 ◊ ANTIVIRAL ACTION

- Some antibiotics may be effective against viruses - depends on mechanism of drug - if able to **block genetic transfer**, then **yes**; if creating **unfavourable living environment**, **no**
- Most antibiotics do not target genetics - viruses can be controlled by inoculation - polio, smallpox, yellow fever, flu
- Viruses attach to host and stimulate cell to produce **viral nucleic acid** (DNA) instead of its own - once infected, viral particle, coated in protein, emerges and moves to next cell
- **Enzymes** responsible for each major process in viral infection (above) - many drugs target and block enzyme activity w/I host - virus now non-volatile
- Also, some drugs target **host ribosomes** and deactivate; damage them - cannot be used by virus

D.7.3 ◊ COMMERCIAL ANTIVIRALS

- **Acyclovir (Zovirax):** general topical use against herpes
  - Relieves pain and itching from genital herpes
  - Shortens outbreak duration - most effect @ point of initial infection
  - Does not prevent recurrences; does not work on all patients

D.7.4 ◊ LATENT VIRUSES

- Some cancers caused by viruses w/o immediate tumour formation → instead insert genetic material into **genome** of animal/plant host.
- Viral genetic mat. becomes part of host cell (adopted by host), and is passed on through cellular reproduction (i.e. mitosis) - known as **latent virus**
- E.g. ***herplex simplex*** virus - hides in nerve cells (latent) - when stimulated, leaves, reproduces, and causes cell damage -- **cold sore**

D.7.5 ◊ AIDS: A CASE STUDY

- Viruses can cross species - i.e. influenza originated in birds, they will then mutate - e.g. **Human Immunodeficiency Virus (HIV)** - **retrovirus** w/ RNA instead of DNA
- AIDS first reported in US 1981; caused by HIV, has become major global epidemic
- HIV targets and damages **white blood cells** - reduce immune defences - death from AIDS not actually from HIV, but **other disease**, e.g. cold/pneumonia - "**opportunistic infections**"
- "AIDS" - **advanced stages** of HIV infection
- Proteins on HIV surface bind to CD4 (receptor **glycoprotein**) on **T4 lymphocyte** membranes (certain white blood cell strain)
- T4 are like "guard" cells - circulate through bloodstream on "patrol" - **seek and destroy suspicious intrusions;** signal other cells in immune system to function "call to arms"
- When **disabled + killed by HIV** → no more guards; no more signalling to other immune agents
- HIV **similarity** (appearance, behaviour, metabolism) **to human cells** → antiviral treatment and vaccine development very difficult (**viral isolation** is hard)
- Control + treatment of AIDS - even harder due to **low availability** + **high price** of antiretrovirals; also **socio-economic factors**, i.e. corruption, genocide
- Prevalent in **sub-Saharan and southern Africa**, **Kenya, west Africa** - also other LEDCs

D.7.6 ◊ BATTLING RESISTANT STRAINS: A CASE STUDY

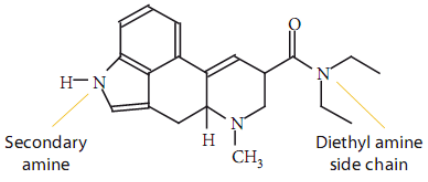
- HIV → remarkable elasticity and ability to mutate/adapt to environment
  - Becomes tolerant to newest drugs very quickly
  - New drug, **PA-457** → using adaptability to fight HIV
- **PA-457:**
  - Synthesised from **betulinic acid** - organic compound extract from plants, like **birch**
  - To find **mechanism of action** (how it goes about affecting HIV) →
    1. Encouraged HIV strain to develop resistance to PA-457
    2. Subjected HIV to small doses - more likely to survive and become tolerant
    3. Those that survived collected and examined (genetic sequences) - had mutation that controlled viral capsid formation
       - In normal HIV, formed protective coating around genetic material
    4. PA-457, unlike other antiviral, **does not attack genetic processes (reproduction enzymes)** - instead causes **capsid failure** and collapse (structural vs. genetic targeting)
    5. Structural failure causes automatic "shutoff" of RNA core - becomes defective
    6. Called a **"maturation inhibitor"** → prevents actual viral from maturing in late development
- Hoped that maturation inhibitors will produce **slower development of resistance** - likely prescribed **with** other AIDS drugs (attack at other stages of development too)
- **"Multidrug therapy":** harder to develop resistance, since they must now have **multiple mutations**, for each drug - less likely to occur together

D.10 ◊ MIND-ALTERING DRUGS

- aka **psychedelics**, **psychotomimetics** (simulating madness), **hallucinogens**
- **Hallucination:** mistaken notion, a perception or feeling with no external cause

D.10.1 ◊ LYSERGIC ACID DIETHYLAMIDE (LSD)

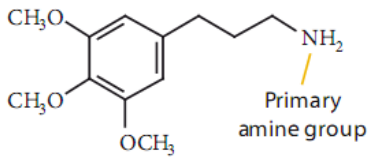
- Powerful **hallucinogen** → lysergic acid in fungus which grows on grains
- **Perception is magnified** manifold
- Impaired judgment (stupid things, jumping off buildings)
- Strong **opposing emotions** at once (e.g. relaxation + tension)
- Pupil dilation, ↑ heart rate, ↑ BP, ↑ temperature
- Sweating, sleeplessness, tremors
- Usually **no physical dependence**; tolerance appears/disappears rapidly



- **Psychological dependence** possible → not as strong as w/ other drugs
- Interacts w/ **serotonin** receptors on neurons → prevents neurotransmitters from facilitating connections between neurons in brain
- Backbone of **indole**: heterocyclic amine → N-atom part of ring →
  - indole is a fused ring heterocyclic structure = benzene ring + heterocyclic ring sharing common C=C bond.
  - The N atom bonded to 2 carbons and an a H atom is a secondary amine
- Fat soluble, thus easily enters **brain**
- Can easily cross **placental barrier** into a fetus
- Contains diethylamide side chain

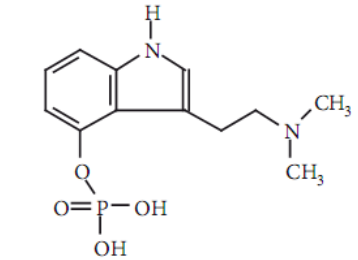
D.10.2 ◊ MESCALINE

- **Peyote cactus**, found in central and south America
- Similar effects to LSD, but far **less potent**
- Trip lasts around **12 hours**, and leads to decrease in appetite
- Worse effects w/ alcohol, **liver damage** from long term use
- Contains the **benzene ring**, but does **not** contain the **fused-ring heterocyclic structure**
- Instead, primary amine group $-NH_2$ → N bonded to only one C



D.10.3 ◊ PSILOCYBIN

- Hallucinogen in **magic mushrooms.**
- **Similar to LSD in terms of effects**, also less potent
- **Low doses:** feelings of relaxation similar to cannabis
- Trip lasts 4 hours; **not addictive** → develop some tolerance to it
- **Psilocybin** and **mescaline** are psycho-active like LSD because they closely resemble **serotonin**
- Besides **indole ring** in LSD, psilocybin → **dimethylamine** – $N(CH_3)_2$ side chain
- Also **dihydrogen phosphate** group on benzene ring
- Backbone structure psilocybin same as serotonin, but dif. side chain
- The difference in properties of different hallucinogens is caused by **different side functional groups** attached to the indole skeleton
- Affects fat-solubility - more soluble = get to brain easier = ↑ potency
- Effect increased by **non-polar groups**(**methyl** $[-CH_3]$); reduced by **polar groups**, (**phosphoric acid group** $(-OPO(OH)_2)$



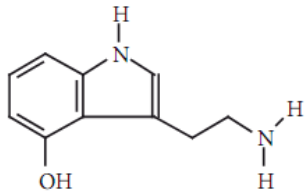


Figure 1535 The structure of serotonin

D.10.4 ◊ TETRAHYDROCANNABINOL (THC)

- Main medicinal in **Cannabis**
- Cannabis (marijuana) from ***Cannabis sativa***
- THC is a **mild hallucinogen**, and has similar effects to alcohol
- **Low doses** causes **excitement and silliness**
- **Higher doses** causes more **hallucinogenic effects**
- Initial joyous feelings can turn into anxiety, depression, uneasiness, panic attack and fearfulness
- Decisions become harder to make, more **open to suggestion** from others
- May result in user doing dumb things → **impaired judgment**
- **No tolerance** develops → regular use causes psychological dependence
- Marijuana smoke → similar effects to cigarette smoke

D.10.5 ◊ THE POLITICS OF MARIJUANA

For:

- Reduces crime and need for crime enforcement, allows police to focus on more important stuff
- Beneficial effects, and helps with some diseases →AIDS, cancer, glaucoma, usually due to appetite-inducing effects.
- Helps with glaucoma by reducing pressure in the eye
- Reduces stress and anxiety for terminally ill patients
- Allow government regulation and quality control, lots of tax money

Against:

- Regular use leads to respiratory issues, and suppresses the immune system
- Decreased fertility observed in some males
- Some evidence that brain damage occurs (to a lesser extent than alcohol)
- Some evidence that it cause chromosomal damage, may lead to birth defects
- Gateway drug effect: may lead to "harder" drugs