#### Option B – Medicine and Drugs IB Chemistry

## **Pharmaceutical Products**

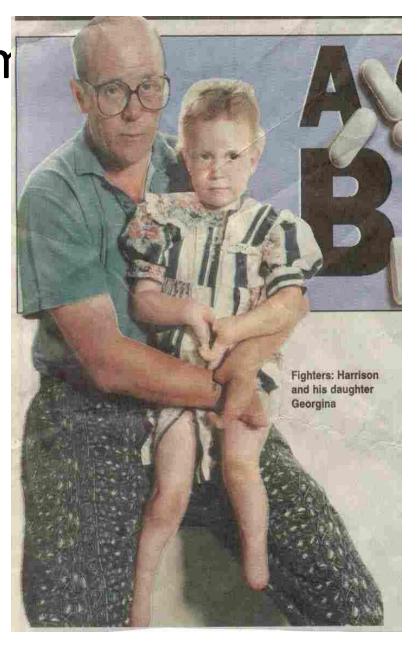
#### • A drug or medicine is any chemical which:

- Alters sensory sensations
- Alters mood or emotions
- Alters physiological state (consciousness, activity level, or coordination)

- Placebo effect:
  - A pharmacologically inert substance (often a sugar pill) produces a significant reaction because the patient expects, desires, or was told it would happen
  - Used as a control in clinical trials
  - Highlights the body's natural healing powers

- Research and Development:
  - Development of a new drug is a very costly, lengthy process controlled by the government:
    - In 1970, 3620 drugs were tested. 16 came on the market at an average cost of \$20 million
    - Only 1 in 2000 drugs eventually make it to the market
    - Phase I: Initial clinical trials on volunteers after the drug has proven safe when given to animals
    - Phase II: Thorough clinical investigation to eliminate investigator bias
    - Phase III: Extended clinical evaluation

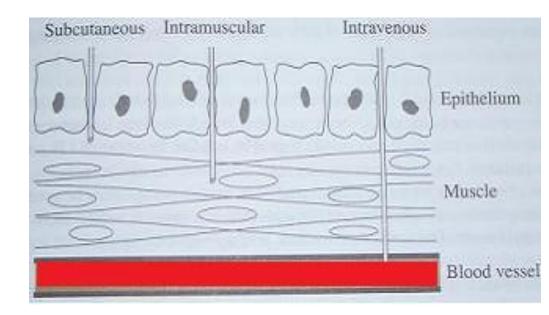
# Thalidon



#### • Methods of Administering Drugs:

- Orally
  - Effect varies because absorption is affected by stomach content and drug concentration
  - Primary site of absorption is the small intestine
- Rectally
  - Effective if a drug cannot be taken orally or if a drug is pH sensitive
- Inhalation
  - Rapid, systemic administration due to extensive network of blood vessels in lungs

- Parenteral (injection)
  - Subcutaneous
    - Beneath the skin
    - Slow absorption
  - Intra-muscular
    - Used when



immediate response is not required

- Used for large volumes of drug injection
- Intravenous
  - Near instantaneous effect
  - Concentration not affected by stomach content

• More about drugs

- Half-life is the time required for half of the drug to be eliminated

## • Toxicity

- LD<sub>50</sub> is the dose (in mg of substance per kg of body mass) that is lethal to to 50% of laboratory animals
- The lower the LD<sub>50</sub>, the more toxic the substance
  - Lowest LD<sub>50</sub> rating known as of yet: botulism toxin (BoTox) most toxic substance known LD50 of roughly 0.005-0.05 μg/kg

#### **Tolerance and Dependence**

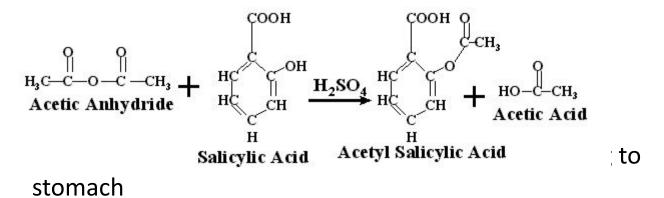


## Analgesics

#### - Prostaglandins:

- Constrict blood vessels
- Affect hypothalamus (region of brain controlling heat regulation
- Increase permeability of capillaries to allow for swelling
- Prevents transmission of pain impulses without depressing the central nervous system

- Mild analgesics
  - Aspirin (acetyl salicylic acid or ASA) produced from salicylic acid (relatively strong acid, difficult to take)



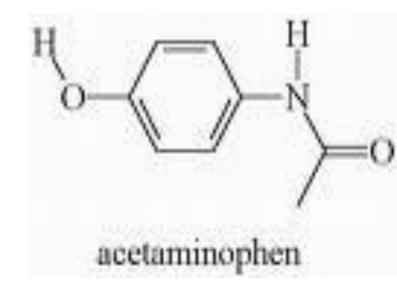
- ASA is called a prodrug: a less active form that is converted to the active form after administration
- ASA can also be used to produce alka-seltzer and other drugs by further modification

- Uses of salicylic acid and its derivatives:

- Relief from minor aches and pains
- Fever reduction (antipyretic)
- Anti-inflammatory agent
- Anti-clotting agent
- Disadvantages of aspirin:
  - Can cause upset stomach and ulceration
  - Risk of severe gastrointestinal bleeding following alcohol consumption
  - Small risk of allergy (.5% of population)
  - Accidental infant poisoning; small correlation to Reye's syndrome in children

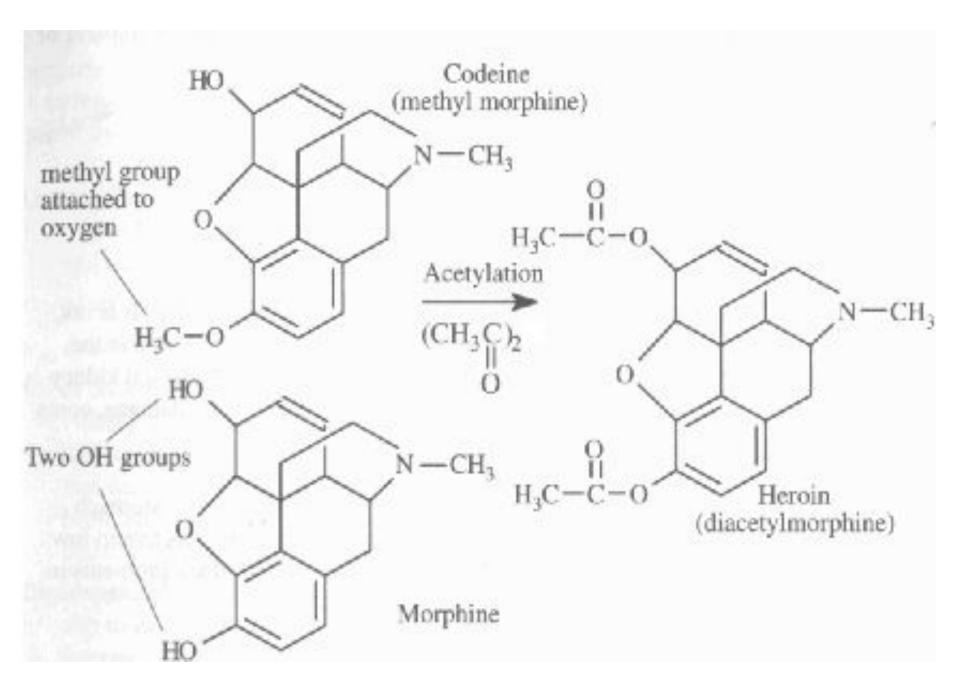
#### Aspirin substitutes

• Acetaminophen (paracetemol)



- Does not upset stomach or cause bleeding
- NOT an anti-inflammatory
- Safe in correct dose, but overdose ( >20 tablets) can cause serious liver damage, brain damage, and death)
- Ibuprofen
  - Many of the same effects as aspirin but fewer stomach problems

- Strong analgesics
  - Opium alkaloids (morphine, heroin, codeine)
    - Belong to "opiate" class (drug that exerts actions on the body similar to morphine) or "narcotics" (drug that produces a narcotic (sleep-inducing) effect as well as an analgesic (pain relieving) effect)
      - Morphine is principal alkaloid, making up about 10% by mass of raw opium
      - Codeine is about .5% of raw opium
      - Heroin is synthesized from morphine (semi-synthetic drug) via a simple acetylation



- Advantages of Opiates:
  - Pharmacological effects
    - Major effects on:
      - Nervous system
      - The eye
      - GI tract
    - Uses:
      - Strong analgesic for relieving severe pain
      - Treatment of diarrhea (produces constipation)
      - Cough suppressant

- Disadvantages:
  - Psychological effects
    - Drowsiness, mood change, mental fogginess, nausea and vomiting
    - Anxiety, fear, lethargy, sedation, lack of concern, inability to concentrate
  - Tolerance and Dependence
    - Cross-tolerance can occur (users tolerant to one opiate will be tolerant to other opiates)
    - Users may not function properly without the drug, experience withdrawal symptoms (addiction)

#### Depressants

- Drugs that calm and relax the central nervous system
  - Tranquilizers
    - Alcohol, valium, librium (Reduce distress but do not produce sleep)
  - Sedatives
    - Barbiturates (Reduce distress but do not produce sleep, stronger than tranquilizers)
  - Hypnotics
    - Chloral hydrate (produces sleep in larger doses)

- Alcohol
  - Small, fat-soluble organic molecule readily penetrates cell membrane and is easily absorbed from the GI tract
  - Social effects:
    - Costs
      - Sickness and death associated with abuse
      - Crime and traffic costs
  - Physiological effects
    - Short term:
      - Reduces anxiety and inhibitions
      - Impairs attention, judgment, and control
      - Violent or aggressive behavior
      - Loss of motor function
      - Effect depends on body mass and concentration of alcohol in the blood

- Long-term
  - Alcoholism is caused by an inability to reduce alcohol intake
    - » Withdrawal symptoms (nausea, sweating, anxiety, hypertension
    - » Tolerance
  - Cirrhosis (scarring) and cancer of the liver (the major detoxification organ)
  - Heart disease
  - Hypertension
  - Strokes
  - Gastritis
  - Ulcers
  - Depression
  - Birth defects

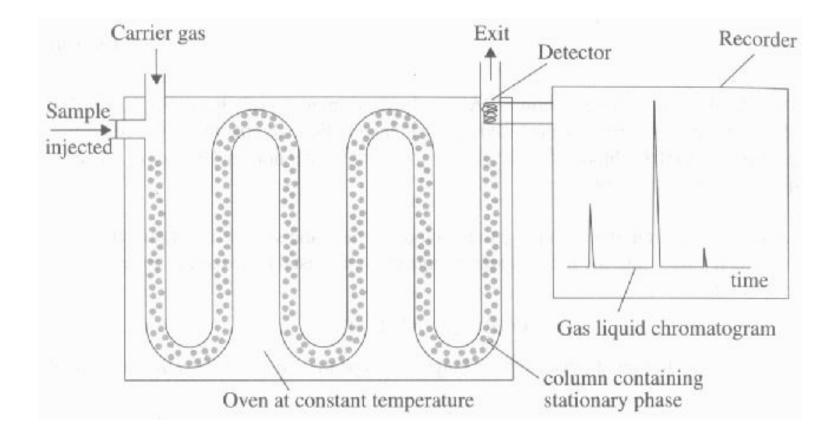
- Alcohol interacts with other drugs
  - Can produce coma or death when combined with sleeping pills or barbiturates
  - Can cause stomach bleeding with aspirin
  - Can inhibit breakdown of other drugs
- Measuring blood alcohol concentration (BAC)
  - Mass (g) of ethanol per 100 cm<sup>3</sup> of blood
    - .08% is legal limit in US (.080 g per 100  $\text{cm}^3$  of blood)
  - Ethanol is easily absorbed from the stomach to the blood, where it is exhaled by the lungs (ethanol is fairly volatile)

 $C_2H_5OH_{(I)} \square \square C_2H_5OH_{(g)}$ 

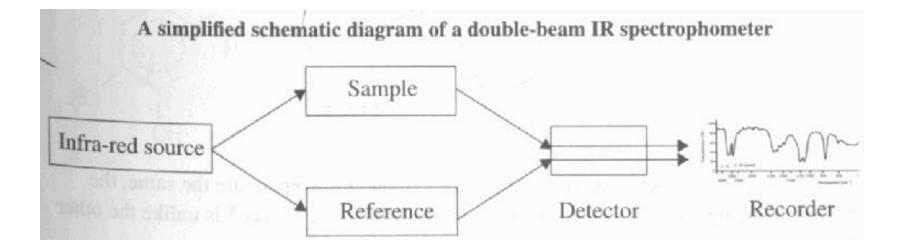
- The alcohol vapor can be detected by a number of methods

- Breathalyzer test
  - Subject breathes into an analyzer containing an oxidizing agent and a detector
  - Potassium dichromate  $(K_2 CrO_4)$  is the oxidizing agent
    - » Oxidizes ethanol to ethanoic acid
    - » This is an oxidation-reduction reaction that involves an electron transfer
    - » This electron transfer generates an electric current which can be detected by the machine
  - Unreliable in legal cases

- Gas Liquid Chromatography
  - More precise than breathalyzer
  - Uses a stationary phase (non-volatile liquid or solid support) and a mobile phase (inert gas, like N<sub>2</sub>)
  - Breath components (CO<sub>2</sub>, H<sub>2</sub>O, and alcohol vapor) are injected into the machine and partitioned (divided) between the stationary and mobile phases
  - Components exit at different intervals (each substance has a different affinity and bond strength for the two phases, and thus move through at different rates)
  - Components are detected
    - Retention time for each component is measured (time taken for each component to pass through the column)
    - » Blood alcohol's retention time is compared to the retention time for a standard ethanol sample



- Infra-Red Spectroscopy
  - IR light does not promote electrons to higher levels, but does provide enough energy to make molecules "vibrate"
    - » Vibrational motion depends on the mass of the molecule and the types of bonds present
  - IR spectrum therefore depends on types of molecules present ("molecular fingerprint")
  - Scale is based on wavenumber (1/wavelength)
  - Police use intoximeter (IR spectrometer) to confirm breathalyzer test
    - » IR radiation is passed through breath sample
    - » C-H group in alcohol absorbs a certain frequency of IR light
    - » % transmittance of the C-H frequency is determined, indicating amount of alcohol present

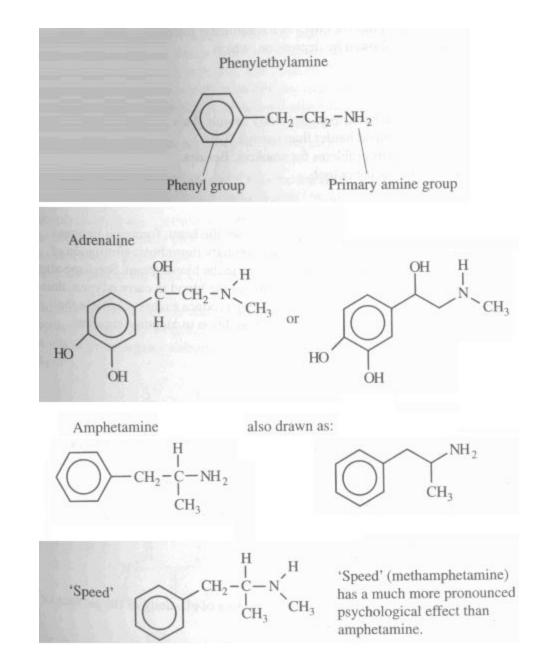


- Other Depressants
  - Diazepam (Valium) is a tranquilizer used to relieve anxiety and tension
  - Nitrazepam (Mogadon) is a hypnotic drug used to induce sleep
  - Fluoxetine hydrochloride (Prozac) is used to treat mental depression by increasing activity of serotonin (a neurotransmitter)

## Stimulants

- Stimulate brain and central nervous system
  - Cause increased alertness and awareness
  - Include amphetamines, nicotine, and caffeine

- Amphetamines
  - Have structures similar to adrenaline
    - Both are derived from Phenylethylamine
  - Mimic the actions of adrenaline (sympathomimetic)
  - Constrict arteries, increase sweat production, increase heart rate, blood pressure, respiration

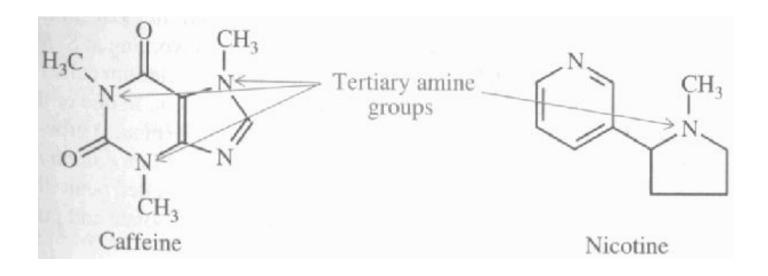


- Nicotine
  - Initial stimulant effect, followed by depression, which encourages frequent use
  - Short term effects:
    - Increased heart rate and blood pressure, putting stress on the heart
    - Reduces urine output
  - Long term effects
    - Increased risk of heart disease and blood clot (thrombosis)
    - Inhibits oxygen-carrying capacity of blood
    - Increased risk of peptic ulcers

- Smoking can also lead to
  - Lung cancer
  - Cancer of the larynx and mouth
  - Heart and blood vessel disease
  - Empyhsema
  - Chronic bronchitis
  - Air pollution
  - Fires!!
  - Stained fingers and teeth
  - Bad breath
- Very easy to develop dependence on nicotine compared to alcohol or barbiturates
  - Withdrawal symptoms: weight gain, nausea, insomnia, irritability, fatigue, depression, and inability to concentrate

- Caffeine
  - Increases rate of cellular metabolism and therefore respiration
  - In low doses, enhances wellbeing, alertness, energy, and motivation
  - In large amounts, physical coordination and timing are affected, and sleeplessness may also result.
  - Weak diuretic (increases urine flow)
  - Tolerance occurs, but no physical dependence
  - Vasoconstrictor (blood vessel constriction), so can help in treating migraines
  - Can help newborn babies to breathe as it increases respiration

 Caffeine, like nicotine, contains a tertiary amine group (nitrogen atom attached to three organic [i.e. carbon-containing] substituents):



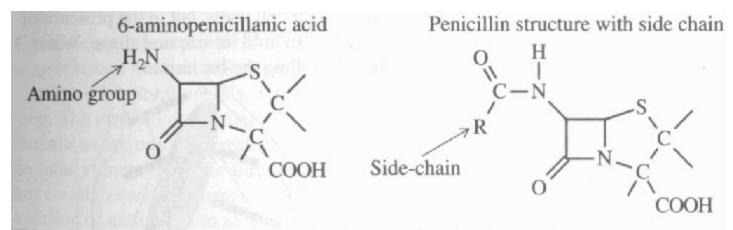
## Antibacterials

- Antibacterials are selective: they attack infectious bacteria rather than human cells
  - Can be
    - Bacteriostatic (inhibit bacterial cell division) or
    - Bacteriocidal (directly kill bacteria)
  - Normally ineffective against viruses because viruses live within host cell, which are unaffected by most antibiotics

- Penicillins:
  - Produced from fungi (*penicillium* genus)
  - Accidentally discovered by Alexander Fleming, who noticed that bacteria did not grow around a spot of *penicillium notatum* mold on a culture plate
    - Fleming could not isolate the "penicillin," and later gave up the research
    - Florey and Chain, at Oxford, renewed the research and started administering the drug to humans
      - Awarded the Nobel Prize
    - Thousands of lives were saved during WWII

- Structure
  - Penicillins all have a certain structural feature in common, the 6-APA group
    - (6-aminopenicillic acid)
      - Structure has no effect on bacterial growth, but when an extra side chain is added to the amino (NH<sub>2</sub>) group, it becomes "active"
        - Side chain varies between different types of penicillin:
          - » Penicillin G, the first type created, is not acid-resistant, and must be injected to bypass the stomach
          - » Penicillin V is acid-resistant
          - » Cloxacillin is acid and penicillinase (bacteria-produced enzyme that breaks down penicillin) resistant

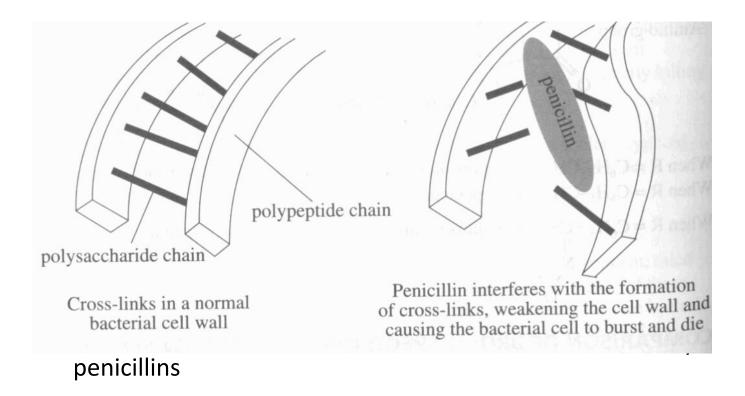
 Penicillins differ only in their type of side chain



When  $R = C_6H_5$ --CH<sub>2</sub>-: benzyl penicillin or penicillin G; not acid resistant. When  $R = C_6H_5$ --CH<sub>2</sub>--CH<sub>2</sub>-: penicillin V; acid resistant.

When  $R = C_6H_5 - C - C$  cloxacillin; acid and penicillinase resistant.

- Penicillins function by interfering with the cross-links that connect separate layers of the bacterial cell wall
  - Cell wall is weakened and the bacterial cell bursts, killing the bacteria



- Disadvantages of penicillins
  - About 10% of the population is allergic
    - Side effects include fever, body rash, shock, and death
  - Overprescription can result in destruction of harmless bacteria in the digestive tract, allowing harmful bacteria to colonize
  - Overprescription leads to genetics resistance over time, rendering the antibiotic eventually useless
    - Thus, antibiotics should only be prescribed when there is no other option that can reduce suffering or save a life

- Broad vs. Narrow Spectrum Antibiotics:
  - Broad spectrum
    - Effective against a wide variety of bacteria
      - Tetracyclines (Aureomycin, Terramycin)
      - Repeated use may wipe out harmless bacteria in the digestive tract, which may be replaced by harmful strains
  - Narrow spectrum
    - Effective against only certain types of bacteria
      - Penicillins
  - Typically, a broad spectrum is initially prescribed until the bacteria can be identified, at which point a narrow spectrum is prescribed

- Antibiotics in animal feed
  - Antibiotics are added to animal feed to prevent the spread of infection throughout livestock
  - However, this can encourage the development of drug-resistant bacteria that humans will eventually be exposed to

## Antivirals

- Viruses are submicroscopic, non-cellular infectious particles that can only reproduce inside a living host cell
- Unlike bacteria, which have a cellular structure, viruses have no nucleus, cytoplasm, or cell membrane
- This limits the effectiveness of antibacterial drugs on viruses

- Controlling viruses
  - Antibacterials may be effective if they block the transfer of genetic information, although few do
  - Vaccination is primary method of prevention
    - Patient is exposed to weakened or inert viral particles to stimulate immune system
      - Immune system produces antibodies, crucial in the immune response, specific to that virus
      - Future exposure to active viral particles is more easily controlled because antibodies have already been produced against it

- Many antiviral drugs work to inhibit the function of replication-specific enzymes
- Latent viruses are viruses that inject their genetic material into a host cell, but the material is not expressed until a later date
  - Herpes simplex virus, certain types of cancer
- AIDS virus
  - Attacks immune system by binding to a receptor glycoprotein (CD4) on T4 immune cells
  - Difficult to fight because of:
    - its ability to mutate (thus rendering a previous treatment ineffective)
    - Its metabolism is similar to human cells

### Stereochemistry in Drug Action and Design (HL only)

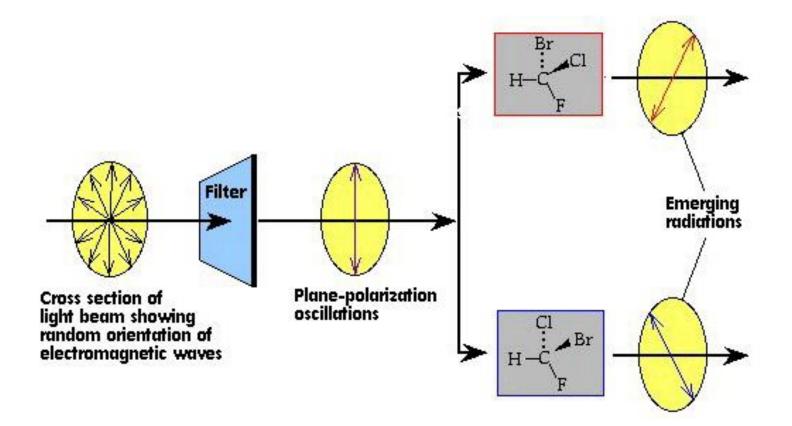
- Stereoisomers are isomers with the same molecular formula AND the same structural formula, but a different arrangement of atoms in space.
- Geometric isomers:
  - If a pair of stereoisomers contains a double bond, cis and trans arrangements can exist:
    - cis: substituents are on the same side of the double bond
    - trans: substituents are on opposite sides of the double bond

- Geometric isomers have:
  - different physical properties, including polarity, boiling point, melting point, and solubility
  - Different chemical properties, and thus different pharmacological effects
    - Ex. Cisplatin



• Square planar molecule, NH3 groups are either on same side of the square or opposite sides

- Optical isomers:
  - Different from geometric isomers:
    - The molecules are chiral (asymmetric, meaning that there are four different groups around a central atom)
    - The isomers are non-superimposable mirror images of one another
  - Each isomers differs in its optical activity (the ability to rotate the plane of polarized light)
    - One isomer (enantiomer) rotates the plane of polarized clockwise (+ form), the other rotates it counterclockwise (- form)



- An equimolar mixture of both enantiomers (<u>racemic mixture</u>) will not rotate the plane and is said to be optically inactive
- Drugs from natural sources are usually chiral and are generally found as a single enantiomer
  - Ex. Penicillin V
    - Opposite enantiomer can only be produced artificially and is pharmacologically inactive

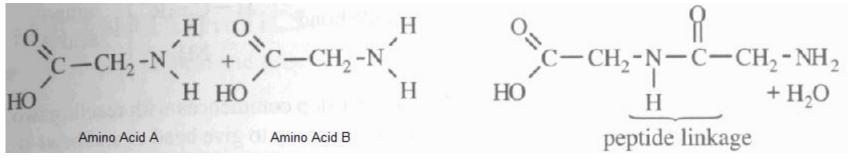
- Synthetic drugs, when chiral, are usually produced as racemic mixtures
  - Ex. : Ibuprofen
    - One enantiomer is pharmacologically inactive
    - Drug still produced as a racemic mixture to reduce costs
  - Thalidomide
    - One enantiomer alleviates morning sickness, the other can cause birth defects
    - Unknown before it was prescribed in the 1970's
    - Racemic mixture ("bad" and "good" enantiomers) can still be sold as a treatment for leprosy

- Synthesis of non-racemic mixtures is difficult, as both enantiomers are chemically identical in relation to non-chiral reagents
  - "chiral auxiliaries" (helping-hands) are used to produce a desired enantiomer from a non-chiral molecule
    - Attaches itself to non-chiral "building block" to create the stereochemical conditions necessary to force the reaction to follow a certain stereospecific path
    - Auxiliary can be removed and reused once the desired enantiomer has been formed
    - Eliminates the need to separate a racemic mixture

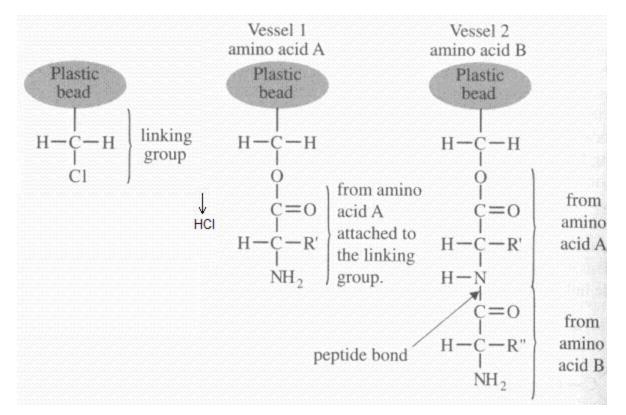
- Combinatorial chemistry
  - As drug R & D is very costly and time-consuming, most drug research begins with a "lead compound," (not lead as in metal, but "leed) whose main structure is left unaltered but other parts are changed to produce more effective drugs.
  - Combinatorial chemistry (combi-chem) involves creating a large number of molecules and quickly testing them for desirable biological activity
    - Sometimes compounds are "virtually tested" by computer simulation
  - Combi-chem involves reacting a set of starting materials in all possible combinations
    - Uses same methods as basic organic synthesis, but uses technology and computers to make very large libraries of related chemicals
      - Increases the chances of finding better drugs

- Libraries of a vast amount of related compounds are produced using robotics to perform repetitive work (ex. adding a fixed volume of a substance to a collection of chemicals) (parallel synthesis)
  - Products of these reactions are then tested, without animals, by studying their effects on enzymes

- Combi-chem began in the 1960's
  - Most importantly: Solid-phase synthesis:
    - Peptide bond is created between two amino acids through a condensation reaction:



 Solid-phase synthesis allows for the rapid creation of a large number of polypeptides by employing the use of plastic beads



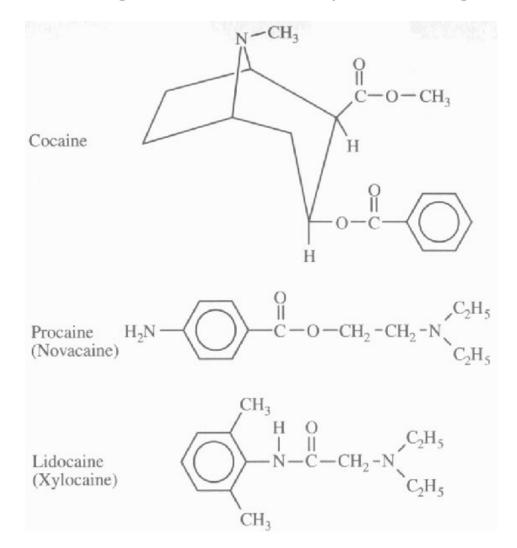
- "linking group" is attached to a plastic bead
- In vessel 1, amino acid A attaches to linking group, eliminating an HCl (Cl from linking group, H from OH group of acid portion of AA)
- Bead is placed in Vessel 2, where it attaches to amino acid B via a peptide linkage
- Process continues with any number of amino acids

- Procedure can be extended so that the first step reacts two amino acids, A and B, to produce bead A and bead B
  - These can be split into separate containers so that each now contains beads A and B, in a half and half mixture
  - In the second stage, one container is reacted with amino acid A to produce bead A-A and bead B-A
  - the other container is reacted with amino acid B to produce bead A-B and bead B-B
  - This two amino acid, two stage process produces 4 (2<sup>2</sup>) amino acids (A-A, B-A, A-B, and B-B)
    - Starting with 3 amino acids in a 2 stage process would produce 3<sup>2</sup> (9) peptides, 10 amino acids in a 4 stage process would produce 10<sup>4</sup> (10,000 polypeptides) etc.
    - A large polypeptide library can therefore be quickly produced
  - Process can also be extended to other molecules besides peptides to produce very extensive chemical libraries

## Anaesthetics

- Local vs. General
  - Local anaesthetics block pain in a specific area (injected under the skin or applied topically)
    - Cocaine, procaine, benzococaine, lidocaine
    - Block nerve conduction and decrease blood supply
    - Procaine and lidocaine do not affect the brain, but cocaine does

#### Cocaine, procaine, and lidocaine all contain a benzene ring and a tertiary amine group



- Cocaine, besides acting as a local anaesthetic, can also stimulate the central nervous system
  - Only used medically as a surface application in oral surgery, extremely dangerous when injected because it is a vasoconstrictor
  - Produces a strong psychological addiction, although no physical dependence or tolerance
- Procaine gives prolonged pain relief and immediate loss of feeling prior to dental surgery
  - Applied through injection and is short-lasting
- Lidocaine produces loss of feeling and is applied topically
  - More potent than procaine
  - Itching and swelling are side effects

- General anaesthetics act on the brain and produce unconsciousness, which can be readily reversed
  - Nitrous oxide (N2O), diethyl ether (C<sub>2</sub>H<sub>5</sub>-O-C<sub>2</sub>H<sub>5</sub>), chloroform (CHCl<sub>3</sub>), cyclopropane (C<sub>3</sub>H<sub>6</sub>), and halothane (CHClBrCF<sub>3</sub>)
  - Some disadvantages:
    - Nitrous oxide is not very potent
    - Trichloromethane (chloroform) can lead to liver damage
    - Ethoxyethane and cyclopropane are highly flammable
    - Halothane is harmful to the ozone layer

Name	Formula	Structure	Advantages	Disadvantages
Dinitrogen oxide (nitrous oxide, laughing gas)	N <sub>2</sub> O	N=N=Ö (linear)	Capable of inducing deep levels of anaesthesia (if adequate [O <sub>2</sub> ] is maintained)	Low potency anaesthetic (not very efficient), induces a state of disinhibition and euphoria and is thus an abused drug
Trichloro- methane (chloroform)	CHCly	H CI CI CI (tetrahedral)	Non- flammable	Leads to liver damage. Not a useful anaesthetic, its toxicity precludes widespread use. It has a narrow safety margin (i.e. a small difference between an anaesthetic and a lethal dose).

Name	Formula	Structure	Advantages	Disadvantages
Ethoxy- ethane (ethyl ether)	(CH <sub>1</sub> CH <sub>2</sub> ) <sub>2</sub> O	H <sub>3</sub> C <sub>2</sub> C <sub>2</sub> H <sub>5</sub> (bent at oxygen)	Alleviates the pain involved in surgical procedures	Highly flammable; (prome to ignite and explode violently), ether has been replaced by safer anaesthetics that result in fewer side effects and are more stable, safe and non- inflammable)
Cyclo- propane	$C_2H_8$	H H H H H (Trigonal planar ring)	A very potent general anaesthetic administered by inhalation; used for all types of surgical operations	Forms explosive mixtures with air; highly flammable can cause nausea vomiting and headaches
2-brome-2- chloro-1,1,1- trifluoro ethane (Halothane <sup>#</sup> trade name fluothane <sup>®</sup> )	CF <sub>3</sub> CBrCIH	F F=C=F H=C=F H=C=Br Cl *Chiral carbon, an optically active compound.	Widely used: a potent general anaesthetic for all types of surgical operations: bon- flammable; produces rapid recovery; non- irritating to the respiratory tract.	Induction to anaestheata is slow: prolonged recovery. Potentially harmful to the ozone layer - capable of producing CI and Br (chlorine and bromine free radicals) that can destroy the ozone layer; $O_3 + *CI \Rightarrow$ CIO* + O See Option D.9

- Dalton's Law of partial pressures can be used to calculate partial pressures of component gases in an anaesthetic mixture
  - Ideal gas law says:  $P_{total}V=n_{total}RT$
  - $P_{total} = P_{a} + P_{b} + P_{c}$
  - $N_{total} = n_a + n_b + n_c$
  - Example: Isoflourane, a halogenated volatile anaesthetic, is used with nitrous oxide to sustain anaesthesia during surgery. If the concentrations of isoflourane, N<sub>2</sub>O, and O<sub>2</sub> are 2.0%, 70%, and 28% respectively, calculate the partial pressure of each gas in the sample at 25°C and 1.0 atm.
    - P<sub>isoflourane</sub> = 2% x 1.0 atm = .02 x 1.0 atm = .02 atm
    - P<sub>N2</sub> = 70% x 1.0 atm = .70 x 1.0 atm = .70 atm
    - P<sub>02</sub> = 28% x 1.0 atm = .28 x 1.0 atm = .28 atm
  - See examples on pg. 452 of LGB

# Mind-altering drugs

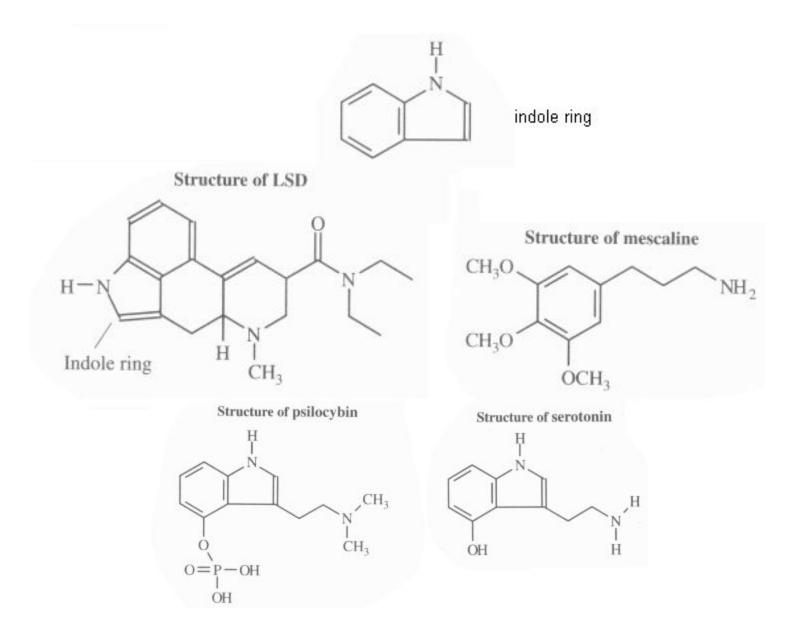
- Psychedelic drugs or psychotomimetics (simulate madness)
  - Cause hallucinations and distortion of senses
  - LSD (lysergic acid)
  - Mescaline
  - Psilocybin (peyote mushrooms)
  - THC (tetrahydrocannabinol in marijuana)

#### – LSD

- Powerful hallucinogen
- Effect depends on:
  - Dose
  - Physiological condition
  - Psychological condition
  - Expectations
- Magnifies perception
- Destroys sense of judgment
- Produces flashbacks without taking LSD
- Does not produce physical addition but can produce tolerance and psychological addition

- Mescaline
  - Produces color hallucinations
  - Lasts approximately 12 hours
- Psilocybin
  - Magnified perception
  - Low doses produce relaxation, high doses produce effects similar to LSD
- THC (marijuana)
  - Mild hallucinogen
  - Causes silliness and excitement at low doses
  - As dosage increases, perception changes and hallucinations result
  - Can cause extreme anxiety, depression, uneasiness, panic attack and fearfulness in high doses
  - Driving and other tasks requiring thinking are difficult
  - Psychological dependence is possible

- LSD, mescaline, and psilocybin all contain a benzene ring (6 carbon); LSD and psilocybin contain an indole ring (6 carbon benzene ring fused to a 5-membered ring containing a secondary nitrogen)
- LSD is fat-soluble and easily diffuses into the brain
- Psilocybin mimics the structure of the brain hormone serotonin



- Cannabis
  - *cannabis sativa*, contains pharmacologically active compounds (cannabinoids)
  - Legalization is a hotly contested issue
    - Arguments for:
      - Relieves symptoms from AIDS, cancer (allows for weight gain by suppressing nausea), and glaucoma (alleviates harmful pressure in the eye)
    - Arguments against:
      - Leads to respiratory ailments
      - Suppresses immune system
      - Decreases fertility
      - Causes brain damage and chromosomal damage leading to birth defects
      - "Gateway drug"
      - Users of marijuana and other drugs obtain them by illegal sources, leading to a host of crimes (prostitution, theft, murder, etc.)