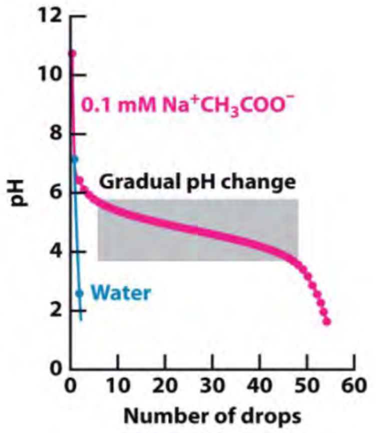
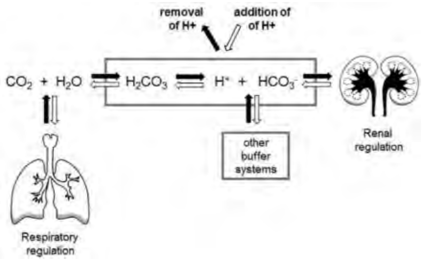
Proteins: Unit 2 – Buffers

- pH: $-\log_{10}[H^+]$; describes the acidity/basicity of a solution
- pKa: $-\log_{10} K_a$; dissociation constant that describes the property of weak acid side chain to lose a proton
- Buffer: solution that resist pH changes; can maintain a nearly constant pH if it is diluted, or if relatively small amounts of strong acids or bases are added



- pH range in human blood: very tight range between 7.35 and 7.45
  - Blood in lung: tends towards a higher pH (less acidic)
  - Blood in tissues: tends towards a lower pH (more acidic; promotes the release of oxygen at the tissue)

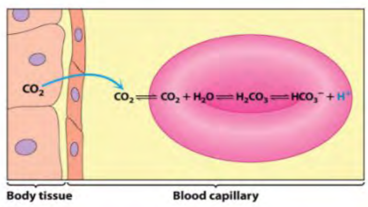
Systems that maintain human blood pH		
System	Timeframe	Description
Respiratory system	Short term	At higher pH, respiratory rate decreases, while at lower pH, respiratory rate increases to remove CO_2 from the system
Renal system	Long term	Regulate reabsorption of carbonic acid in the tubule instead of secretion through urine
Chemical buffering systems	Immediate	Small amount of acid/base does not dramatically change pH like water
Bicarbonate		Dissolution of carbon dioxide in water catalysed by carbonic anhydrase to carbonic acid to dissociate into bicarbonate and H^+ and vice versa
Proteins		Contributes to buffering capacity via their electrically-charged side chains or other ionisable protein groups
Phosphates		Dissolution of phosphates into its conjugate base form and H^+ and vice versa



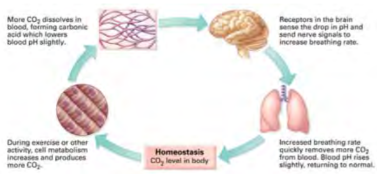
- All these systems interplay to keep the blood pH tightly regulated (see diagram on right)

- Bicarbonate system in the blood: equilibrium among CO_2, H_2CO_3, HCO_3^-
  - Carbon dioxide transfer: carbon dioxide is transferred from body tissue to blood, to RBC
  - Carbonic acid formation: carbon dioxide and water is converted to carbonic acid by carbonic anhydrase
  - Buffer system: carbonic acid can dissociate into bicarbonate ion; act as a buffer

  - Note that the bicarbonate system is the most dominant buffer system



- pH regulation by respiratory system:
  - More CO_2: more CO_2 is produced due to active cell metabolism
  - Lower PH: more CO_2 dissolved in blood lowers blood pH slightly
  - Brain signalling: receptors in the brain sense the drop in pH and send nerve signals to increase breathing rates
  - Removable of CO_2: increased breathing rate quickly removes more CO_2 to maintain homeostasis



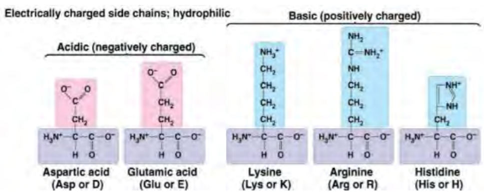
- Reason for multiple mechanisms:
  - Redundancy: act as a 'backup' to ensure maintenance of constant pH
  - Timing: systems act on different timing for different purposes

- Forms of amino acids for proteins: each side chain will have a distinct pKa value, which, when compared to the pH, can help to identify which form the amino acid is most likely found in
  - pH < pK_a: equilibrium to the left; protonated (acidic) form
  - pH = pKa: both form exists in 50:50 mixture
  - pH > pKa: equilibrium to the right, deprotonated (basic) form

$$HA \rightleftharpoons H^{\oplus} + A^{\ominus}$$

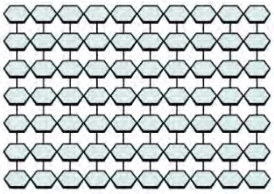
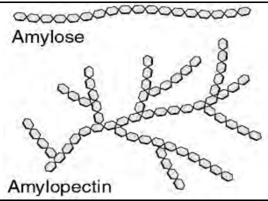
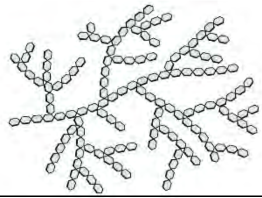
Acid — Proton — Conjugate Base

  - **Aspartic and glutamic acid**: low pK_a; at standard physiological pH, we expect these to be deprotonated
  - **Lysine and arginine**: high pK_a; at standard physiological pH, we expect these to be protonated
  - **Histidine**: this protein typically displays a wide pKa range and may be protonated or deprotonated at neutral pH depending on the environment the amino acid is exposed to



Polysaccharides

- Polysaccharide: consists of long chain of multiple monosaccharides (e.g. starch)
  - Variety: differ from each other in the types of monosaccharide unit, length of their chains, type of bond, branching
  - Common in nature: most carbohydrate found in nature occurs and polysaccharides (cellulose/starch most common)

	Cellulose	Starch	Glycogen
Source	Plants	Plants	Animals (e.g. humans)
Diagram			
Composition	β-glucose	α-glucose	α-glucose
Bonding	1-4 linkage	1-4 linkage, 1-6 linkage	1-4 linkage, 1-6 linkage
	Each β-glucose is added to the chain at 180° to the previous	Each α-glucose is added to the previous chain; additional branching occurs every 12-20 unit (amylopectin)	Each α-glucose is added to the previous chain with frequent branching occurring every 8-12 unit
Structure	Linear	Helical (natural curvature); globular	Helical (natural curvature); globular
Characteristics	Straight chains that can form bundles by hydrogen bonds	Amylose – unbranched helix Amylopectin – globular	Branched, irregular and compact globular structure
Solubility	Less soluble	More soluble	More soluble
Function	Structural component - forms cell walls in plant cells	Energy storage – readily mobilized storage; storage of glucose in plants	Energy storage – readily mobilized storage; storage of glucose in animals
Location	Cell walls	Chloroplasts and storage organ	Liver

- Starch composition: starch is comprised of linear and branched glucose polymers (amylose and amylopectin)

	Amylose	Amylopectin
Percentage in starch	20%	80%
Type of polysaccharide	Linear polysaccharide	Branched polysaccharide
Bonding	1 to 4 glycosidic linkage	1 to 4 glycosidic linkage 1 to 6 glycosidic linkage every 12-20 units
Solubility	Insoluble	Soluble
Structure	Cylinder-like helix, compact	Random

- Glycosidic bond orientation underlies the structural differences between different glucose polymers

- Solubility of polysaccharides: amylose of starch is more soluble than cellulose
  - Explanation:
    - α 1-4 linkage: α 1-4 linkage gives a curvature to the chain that creates a helical structure
    - OH group orientation: in the helical structure, OH groups are facing outwards
    - Hydrogen bonding: OH can form hydrogen bonds with surrounding water molecules

  - Significance: solubility is important for storage; molecules must be hydrolysed by enzyme to yield glucose, while for cellulose, insolubility is important to maintain structural integrity

- Unique cellulose features: β 1-4 linkage gives cellulose distinct features from other glucose polysaccharides
  - Indigestible: cellulose glucose linkage is beta, and thus cannot be digested for energy by humans
  - Very strong: β chains can be held together in parallel bundles with hydrogen bonding for up to 2000 chains
  - Insoluble: such strong hydrogen bonding between each other makes cellulose very insoluble to water

- Branching in glycogen: glycogen has shorter branches than starch to allow for faster hydrolysis; energy yield is faster
  - Advantage: animals require faster cellular respiration for movement such as predator avoidance

- Chitin: structural polysaccharide found in exoskeleton of arthropods (such as insects, spiders, crustaceans)
  - Structure: similar to cellulose (1-4 β linkage), except it contains a nitrogen-containing appendage on each glucose
  - Other natural location: structural support for the cell walls of many fungi
  - Industrial use: renewable resource isolated from crab and shrimp waste; can be used as biomedical material coating

Industrial processing of carbohydrates

- Fructose: processing of fructose for use in sweetener in soft drinks and processed food
- Cellulose: current research in transforming cellulose in to starch for a potential food source derived from non-food plants
- Chitin: use as coating of normal biomedical materials such as surgical thread; or use as binder in dye, fabrics, adhesives et cetera

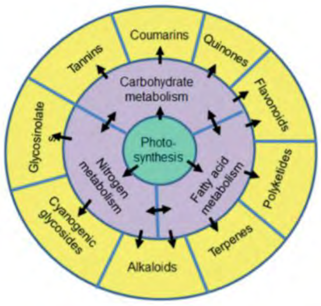
Plant Biochemistry: Unit 3 – Plant Medicinal

Plants in pharmaceutical/nutraceutical sector

- Pre-historical usage of plants: people have used plants as medicines since pre-history
  - Medicinal plants: chemicals preserved in 50000 year old Neanderthal teeth suggest chamomile as medicinal use
  - Bedding: 77000 year old South African *Cryptocarya woodii* leaves used for bedding; toxic to mosquitoes

- Primary metabolites: organic compounds found in most organisms that include those required for basic metabolism

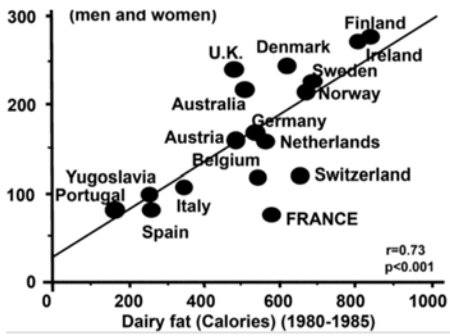
- Secondary metabolites: organic compounds produced by plants that are not directly involved in the normal growth, development, or reproduction of the plant
  - Specific: only produced by specific plant species
  - Significance: current pharmaceutical/nutraceutical sector is dominated by plant productions
  - Example: salicylic acid from willow (first industrial pharmaceutical)
  -
  - Classification: simple classification including three main groups
    - Terpenes: from mevalonic acid; composed of C and H
    - Phenolics: made from simple sugars; containing ring and CHO
    - Nitrogen-containing compounds: compounds with N but occasionally with S – extremely diverse



  - Roles of secondary metabolites in plants:
    - Defence: evolved to defend against harmful organisms such as herbivores, bacteria, fungi, insects etc.
    - Attractants: attractants to promote fertility

  - Roles of secondary metabolites (plant) in humans:
    - Phytonutrients: not essential but good for your health; have long term health benefits
    - Medicinal: healing properties for recovery; treat and cure diseases; relieve pain

- French paradox: observation of low coronary heart disease (CHD) death rates despite high intake of cholesterol and saturated fat in France
  - Explanation by tannin: French consume a lot of red wine, which contains tannin, which may reduce incidence of CHD
  - Explanation by type of fat: French diet contains more short chain saturated fatty acid, which is less harmful



Nitrogen containing compounds (secondary metabolites)

Alkaloids

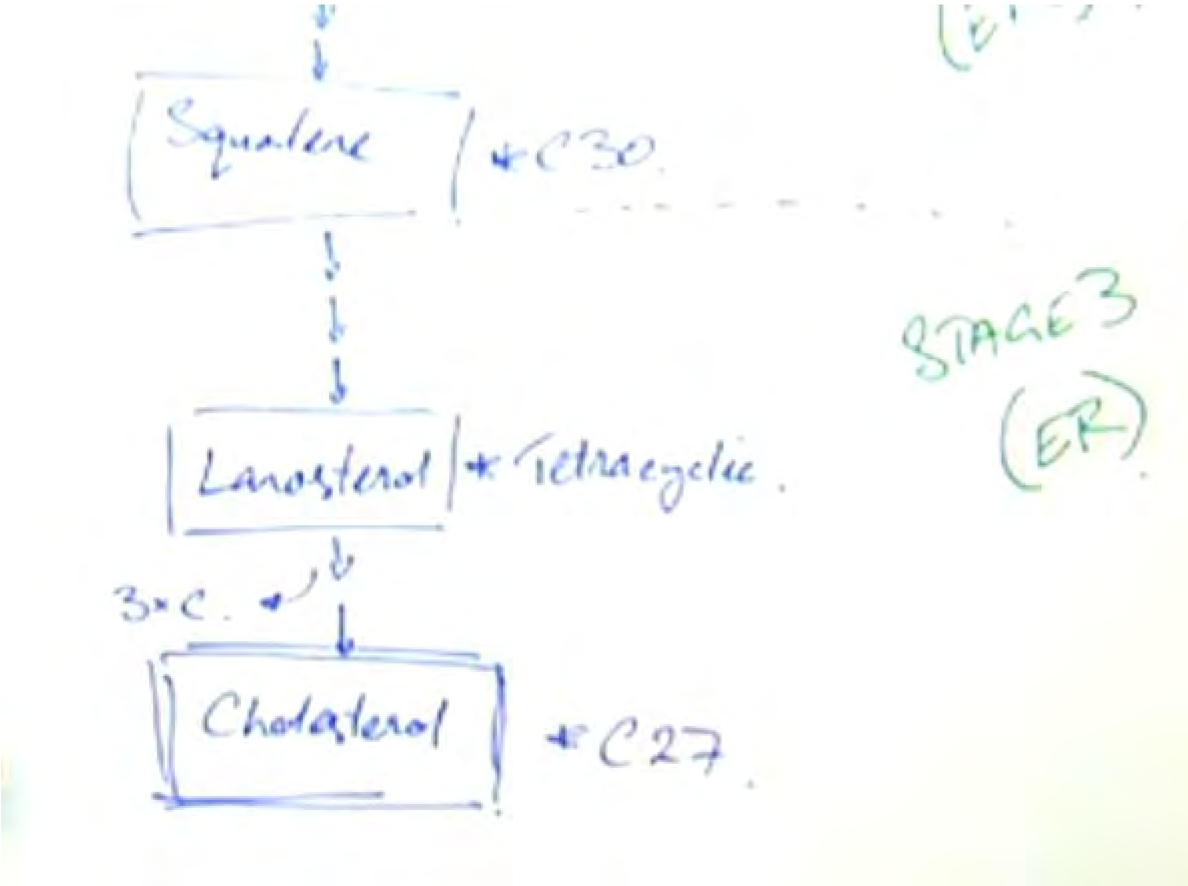
- Alkaloids: water soluble organic nitrogenous basic compounds found mainly in plants
  - Features of alkaloids:
    - Contains nitrogen: contains at least one N, which is usually (not always) in an heterocyclic ring
    - Basic: nitrogen often cause compound to be basic (pH>7)
    - Diverse structure: not an homogenous group of chemical
    - Often toxic: many are toxic to humans and animals

  - Derivatives for alkaloids:
    - Purine derivatives: caffeine, theobromine, theophylline
    - Amino acid derivatives: alkaloids derived from proteinogenic and non-proteinogenic amino acids
      - Ornithine (non-proteinogenic) → nicotine
      - Histidine → pilocarpine
      - Tyrosine → opiates (morphine, codeine, thebaine, oripavine)

  - Functions of alkaloids:
    - Plants: provide plant defence (e.g. nicotine – potent insecticides)
    - Humans: can act as poisons, narcotics stimulants and medicine
    - Common pharmaceutical: source for approximately 25% of pharmaceuticals

  - Economic significance: are economically importance
  - Easy isolation: as they are water soluble, they are easily isolated and purified from plant sources
  - Difficult to synthesize: artificial synthesis of some alkaloids are difficult/expensive in lab (so extract from plants)

- Theobromine and theophylline: methyl derivatives of xanthine (purine base) found in cocoa plants
  - Function in humans: Targets CNS; inhibits phosphodiesterase causing increase in cAMP and release of adrenaline
  - Strength: effects generally weaker than caffeine


Squalene
* C30.
STAGE 3
(ER)
Lanosterol
* Tetracyclic.
3×C.
Cholesterol
* C27.