COURSE CODE: *CHM 326*

COURSE TITLE: *Natural Products*

NUMBER OF UNITS: *2 Units*

COURSE DURATION: *Two hours per week*

COURSE DETAILS:

Course Coordinator: **Dr. Lasisi, A. A. (B Sc., M. Sc., Ph D)**
E-mail: **lasialiyu@yahoo.com**
Office Location: **ROOM B108, COLNAS**

COURSE CONTENT:

1 **NATURAL PRODUCTS: General Introduction of Natural Products**
2 **TERPENOIDS**
3 **STEROIDS**
4 **ALKALOIDS**
5 **FLAVONOIDS**
6 **PERICYCLIC REACTIONS AND MOLECULAR ORBITAL SYMMETRY**

COURSE REQUIREMENTS:

This is a compulsory course for 300 level students in the Departments of Chemistr. In this respect, students are expected to participate in all the course activities and have minimum of 75% attendance to be able to write the final examination.

READING LIST:

1. George, H., Schmid. Organic Chemistry, New York, Mosby, 1995.
2. Geissmann, T. A. and Cront, D. H. G. Organic Chemistry of secondary plant metabolism, Freeman, San Francisco, 1969
3. Lock Bu J. D., The Biosynthesis of Natural Products, Mc Graw Hill, London, 1965.
4. Hendricleson, J. B. The Molecules of Nature, Benjamin, New York, 1965.

LECTURE NOTES

COURSE CODE: CHM 326
COURSE TITTLE: NATURAL PRODUCTS

Chemistry of Natural Products deals with the chemistry of metabolites. Metabolites are naturally-occurring organic compounds synthesised by plants, through metabolic actitivities in plants, aided by enzymes.There are two types of metabolites, viz:

(a) Primary metabolites such as carbohydrates, proteins, fatty acids and glycerol, mevalonic acids, etc.

(b) Secondary metabolites such as steroids, Alkaloids, Triterpenes, tannins, saponnins, flavonoids, etc.

Chemistry of Natural Products is dated far back to early century. An aspect of Natural Products that deals with plants is known as **Phytochemistry**.

Natural Products is define as organic compounds and other chemicals synthesised by plants through metabolic processes aided by sunlight, involving CO_2, H_2O vapour and chlorophyll. Generally, natural products are characterised by specific functions they perform in plants and animals. Categories of natural Products are called metabolites.

Primary metabolites are usually found in all living organisms such as plants and animals. They form the fundamental building block of living material e.g. mevalonic acids and nucleotides. Primary metabolites have wide distribution in living systems and are usually involved in essential life processes.

However, secondary metabolites are chemicals synthesised by plants but are not directly used by them, but are used indirectly by man as a source of pharmaceutical preparations. Secondary metabolites are generally built from primary metabolites. Secondary metabolites have restricted distribution and are characteristics of individual genera or species. Secondary metabolites are essential to the existence of the organism but play an important role to the survival of the plant. Reports have shown presence of secondary metabolites in yeast and microbes.

All living organisms from the simplest protozoan to the most developed animals contain a wide range of organic compounds. Millions of secondary metabolites have been isolated from plants and animals, some of which are known to have medicinal features. Examples are: the popular Quinine-an antimalarial drug and Chloroquuine isolated from medicinal plants.

It is good to note that Natural Products is restricted specifically to major organic compounds obtained from natural origin, especially from marine plants and plants growing on land.

Plants are generally classified on the basis of the family they belong. Each family of plant contains a GENUS and SPECIES.

Leguminoseae is a family of a pant of the genus *Berlinia* and several species of *Berlinia* exists; such as *B. confusa*, B. *grandiflora*, *B. auriculata*, etc.

In the present days, millions of secondary metabolites are in existence; and majorities are isolated from natural sources such as plants. Examples are steroids, terpenoids, alkaloids,

glycosides, flavonoids, etc. However, some secondary metabolites have varying structures within a group or a specific specie e.g. monoterpenoids, diterpenoids, triterpenoids, sesquiterpenoids, etc. Some are acyclic while others are cyclic in their structures.

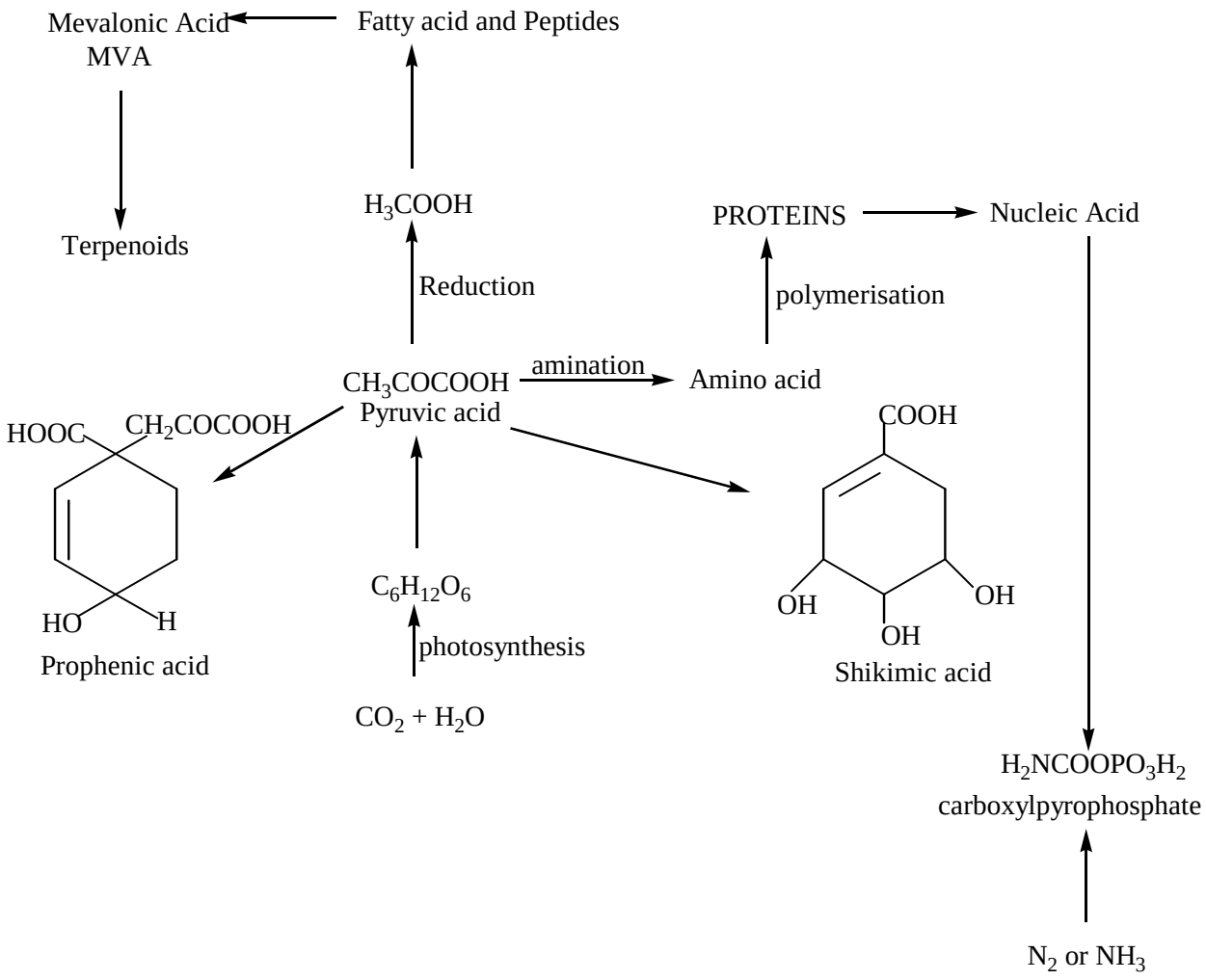
Some secondary metabolites are synthesised via biosynthesis and or biogenesis.

Higher plants synthesised chemical compounds *in vivo* and degrade them by means of series of chemical reactions, each aided by enzymes, by a process known as **metabolism**. The products of metabolic pathways are called **metabolites**.

Acetyl-coenzyme A (AScOA), Nucleotides and Mevalonic acids (MVA) constitutes primary metabolites from which secondary metabolites are derivable. A complex web of enzyme-catalyzed reactions may involve the use of inorganic compounds such as H_2O, CO_2, solar energy through the process known as **Photosynthesis**. The reaction scheme is shown below.

$$6\,CO_2 + 6\,H_2O \xrightarrow[\text{chlorophyll}]{\text{sunlight}} \underset{\text{glucose}}{C_6H_{12}O_6} + 6\,O_2 + \text{Energy}$$

Series of chemical interconversion takes place with glucose to give various chemical compounds illustrated below:

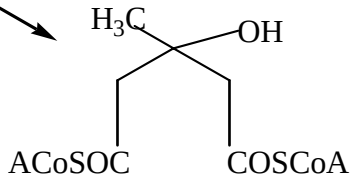


In biogenetic synthesis, several reactions occur involving a kind of arrangement and in most cases they are not synthetic, but are of generic origin. Mevalonic acid (MVA) can be synthesised biogenetically following the procedure below:

(1) $CH_3COOH + ATP + HSCOA \longrightarrow CH_3COSCoA$
Acetylcoenzyme A

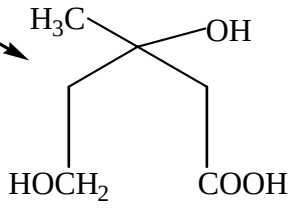
(2) $CH_3COSCoA \xrightarrow[\text{Claisen condensation}]{\text{condensation reaction}} CH_3COCH_2COSCoA$
Acetoacetyl coenzyme A

(3) $CH_3COCH_2COSCoA + CH_3COSCoA \xrightarrow{Mg^{2+}}$



Hydroxylmethylglutonic coenzyme A
HMGCOA

(4) HMGCOA →



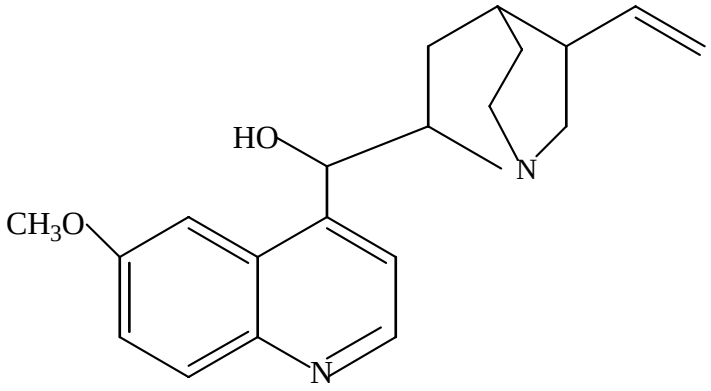
Mevalonic Acid

ALKALOIDS

Alkaloids are naturally-occurring organic compounds containing nitrogen moiety, and are usually heterocyclic in nature. They are nitrogen based organic compounds, with nitrogen enclosed in an heterocyclic ring.
The alkyl amines are referred to as proalkaloids.

Characteristics of alkaloids

(1)They are basic in nature due to the presence of nitrogen in their ring.
(2) They have complex structures.
(3) They have bitter principles.
(4) They are mostly obtained from plant materials.
(5) They have high pharmacological and physiological activities.
Examples of alkaloids are:
(1) Quinine — an antimalarial drug isolated from a plant called *Cinchonia officialis*

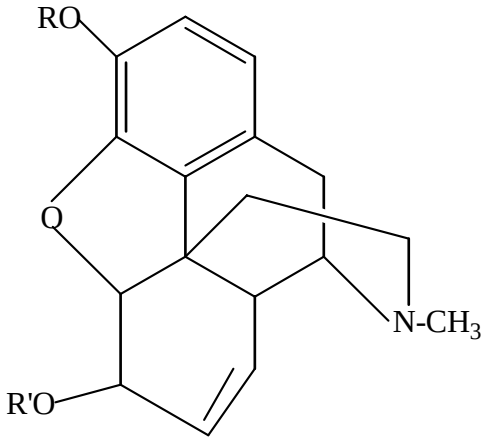


Quinine

Quinine is an antipyretic alkaloid. Its molecular formular is $C_{20}H_{24}N_2O_2$.

Functional groups present in quinine are: methoxyl $–OCH_3$, hydroxyl –OH, tertiary amine group, etc.

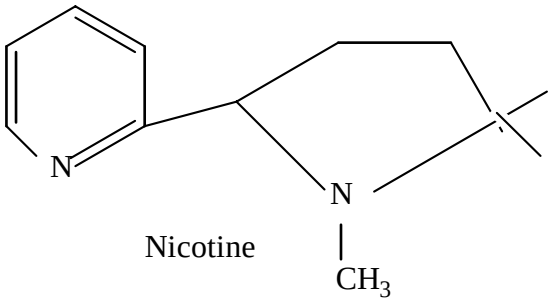
Other examples of alkaloids are: morphine, cocaine, heroine, etc. Most are highly narcotic in nature.



R = R' = H Morphine alkaloid
R =H, R' = CH_3 Codeine
R = R' = $COCH_3$ Heroine

- Morphine is highly narcotic
- Morphine is analgesic
- Morphine is isolated from the plant *Papavera omniferous*
- Morphine is an opium alkaloid.

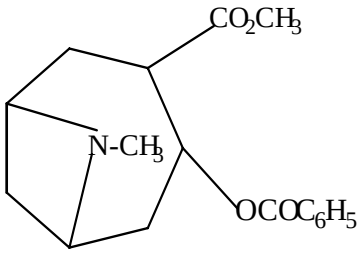
Nicotine is another example of alkaloid



Nicotine

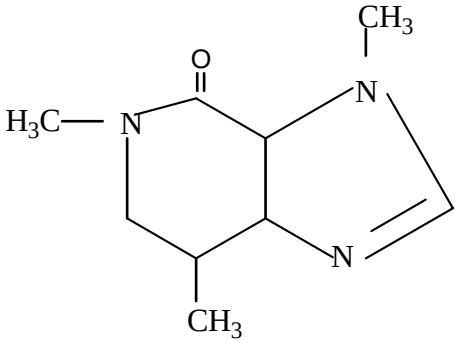
Cocaine is an alkaloid.

- Cocaine is obtained from coca leaves,
- Cocaine is the first local unaesthetic ever discovered by man,
- Cocaine is highly narcotic,
- Cocaine stimulates the central nervous system i.e. CNS depressant,
- Cocaine can lead to psychiatric problem when taken in high dose or when addicted to it.



Cocaine

Caffeine is an alkaloid obtained from coffee tea. It is also a strong stimulant which can increase alertness, thereby causing insomnia when the body gets addicted. It is found in Nescafe drink. Structure of caffeine is shown below:



Caffeine

Occurrence of Alkaloids

Like other natural products, alkaloids are found in tissues of plants at point of intense cell activities, found majorly in stems, leaves and roots, seeds and barks of plants. Alkaloids are common in some higher plants such as Rubiaceae, Rotaceae, Papaveraceae,

etc. They perform certain functions in plants and animals as a result of their pharmacological activities. Pharmacologically, they acts as chelating agents, in which case they select one metal in preference to another from the soil while rejecting others. They are usually solid, though some exists in liquid form.

Nomenclature of Alkaloids

There is no systemic nomenclature for alkaloids due to the complexity in their structures; hence trivial names are often employed in the nomenclature of alkaloids. However, the names often end with **-ine** and this indicates the basic nature of the compound. Sometimes, names of alkaloid depict the source of the alkaloid in question. An example is **Nicotine** isolated from the plant *Nicotina tobaccullum*. At times, names of alkaloids indicates the discoverer of such alkaloid or even the society or tradition where such plants originated; e.g. morphine alkaloid came from the name **Morphens** (the ancient god of Greek).

Classification of alkaloids

Alkaloids are classified into two broad classes:

(a) Classification based on the nature of the ring systems;

(b) Classification on the basis of plant sources.

Classification based on plant source

The classifications based on plant's source: in this case alkaloids are classified on the basis of the plant source such as the family and the genus. However, structurl overlap may occur, using this classification. For instance, morphine alkaloid is from Apocynaceae family. Opium alkaloids such as morphine, codeine, nicotine and papaverine are derived from opium plant.

Rauwolfia alkaloids is reserpine, derived from Rauwolfia family.

Reserpine is an antihypertensive alkaloid. It equally act as tranquilizer.

Chintonia Alkaloids: Quinine, from Cinchonine, etc.

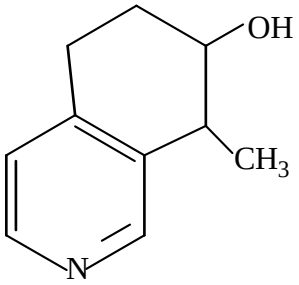
Coca Alkaloods: from Erythroxyllum species

Solonaceae alkaloids: from Solanaceae family, etc.

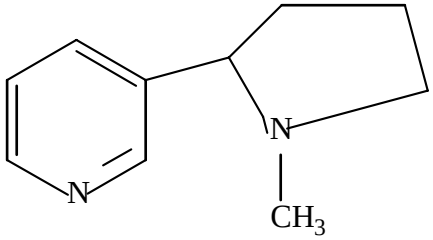
Classification based on the Chemical structure of Alkaloids

(a) **Heterocyclic** Alkaloids: pyrollidine nucleus
Pyridine nucleus,
Piperidine nucleus
Pyridine- Piperidine nucleus, etc

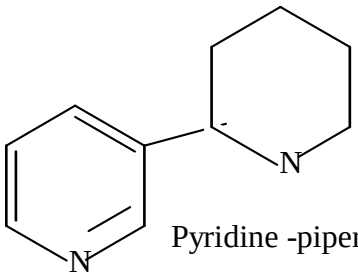
Structures of the various classification based on chemical structures are illustrated below



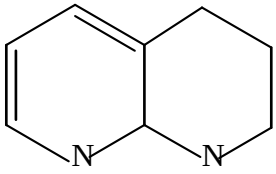
Pyridine nucleus



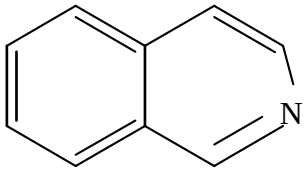
Pyridine -pyrrolidine nucleus



Pyridine -piperidine nucleus



Quinoline nucleus



IsoquinOline nucleus

Structural Elucidation of Alkaloids

Isolation of Alkaloids

In order to isolate pure alkaloid from plant source, the procedures to be followed are as follows:

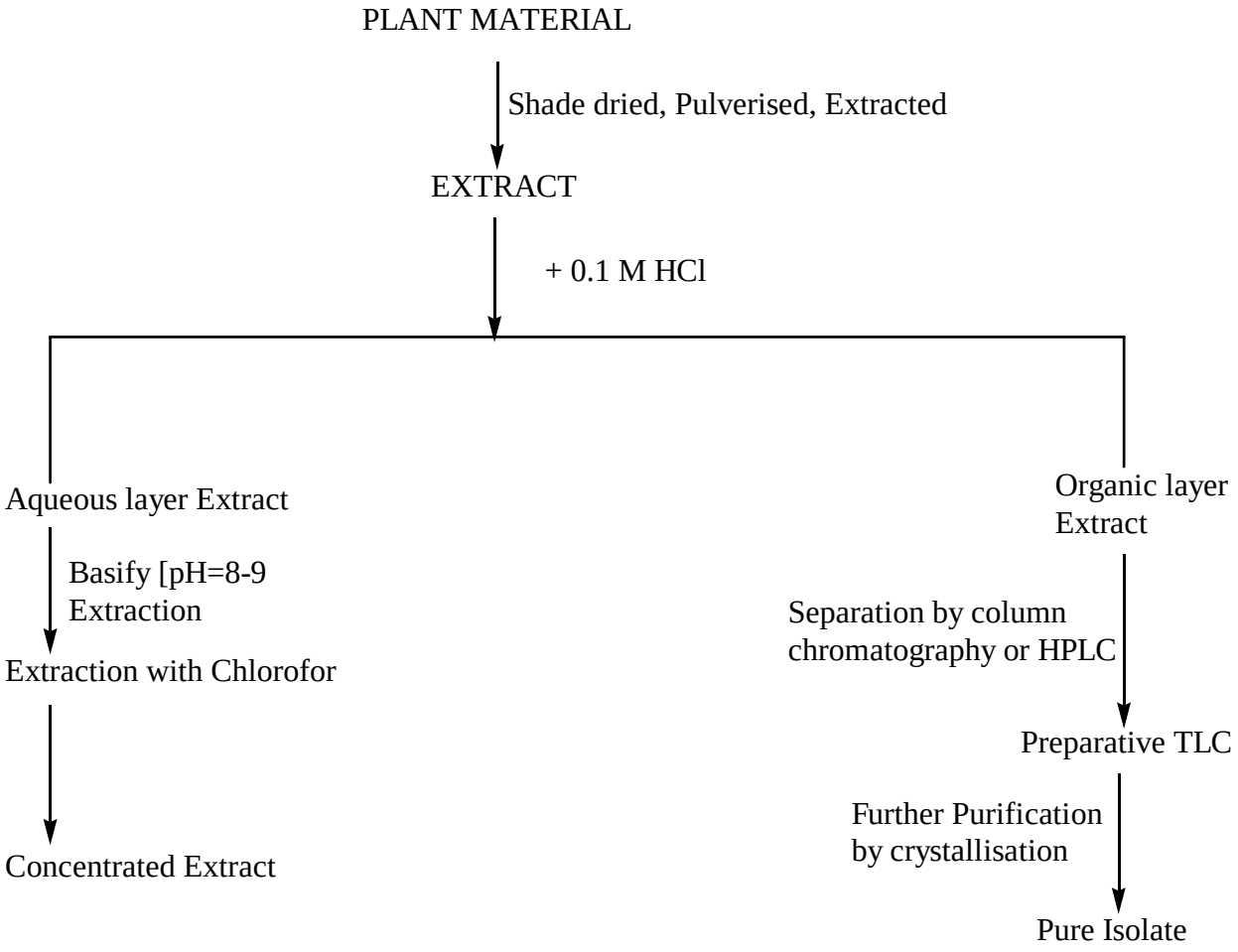
Step 1: Collection of plant material, air-drying the plant material to remove water, pulverization of the air-dried plant material and solvent extraction protocol of the powdered plant materials.

Step 2: Purification of the alkaloid-This is done to separate alkaloid from the solution. This is done by running chromatography on the syrupy form of the extract.

Step 3: involves the crystallization and further purification of the isolates.

Extraction method for Alkaloids

The extraction procedure often used in the isolation of alkaloid is summarized in the table below.



Physical Methods of Structural elucidation

Determination of melting point: this is to ascertain the purity of the isolate.

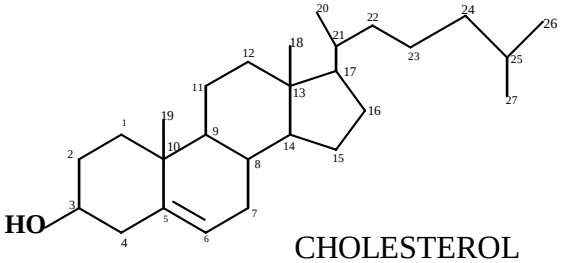
Elucidation of the structures: This is done by using spectroscopic technique such as Infra-Red, Ultra-violet, Nuclear Magnetic Resonance and Mass spectroscopic techniques.

Chemical Methods of Identification of Alkaloids

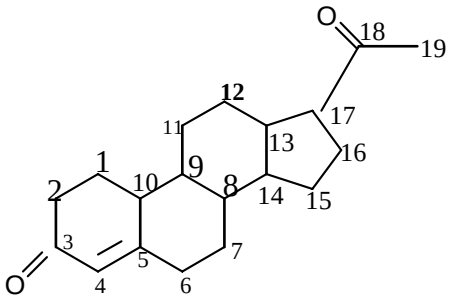
Several methods are involved. \
(1) Test for functional group and Chemical transformation involving chemical tests for functional groups. Other method such as functional group interconversion is equally used for structural proof. Example is the conversion of phenol to an acetate derivative of phenol via acetylating step.
Detection of –OH group – this is done by acetylation or benzoylation or even methylation steps. Acetylation involves treatment with acetic anhydride in the presence of pyridine. Detection of phenolic compound is by treatment with Ferric chloride solution, in which a yellow precipitate confirms a phenolic compound.

STEROIDS

Steroids are groups of secondary metabolite found in all plants and animal tissues. They occur mostly in the brain and spinal cords in mammals. Examples of sterols are the zoosterol, cholesterols, bile acids, sex hormones such as estrogen and testosterone. Example of phytosterols are ergosterol, stigmasterol. The most common sterol in animal is cholesterol. Cholic acid found in bile acid. Other common sterols are the sex hormones such as oestrones and progesterone, responsible for secondary sexual characteristic.



CHOLESTEROL

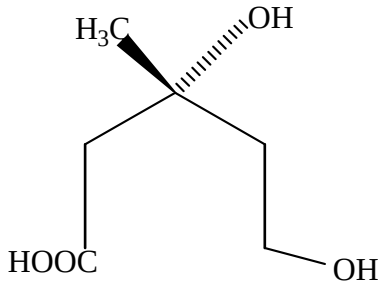


Progesterone

Cholesterol is the most common among the sterols. It has a molecular formular $C_{27}H_{46}O$. An adult human being has 200-300 g of cholesterol in their body. It comprises 15% of the brain of human. Several circulatory and heart diseases are closely associated to level of cholesterol in the body. This is because cholesterol precipitates in the arteries thereby causing arteriosclerosis and other heart diseases. It is important because it forms the synthetic routes or starting material for other sterols.
There are eight chiral canters in cholesterol and 2^8 stereo isomers.

Synthesis of cholesterol

Cholesterol and other sterols are synthesised from primary metabolite such as Mevalonic acid (MVA). This is a biogenetic synthesis.



3-methyl-3,5-dihydroxylpentanoic acid [MVA]

The steps involved in the synthesis are illustrated below: