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SCHOOL OF SCIENCE AND HUMANITIES

DEPARTMENT OF CHEMISTRY

UNIT – I–Alkaloids-SCY1615

Classification, isolation, purification, general methods of structure determination - functions of alkaloids. Structural elucidation of coniine, nicotine, piperine and papaverine.

Alkaloids

The alkaloids are now defined as ,physiologically active compounds of plant origin,in which atleast one nitrogen atom forms part of a cyclic system. Alkaloids are a group of naturally occurring chemical compounds that mostly contain basic nitrogen atoms. The term alkaloid was coined by Meissner, a German pharmacist, in 1819.

♣ Alkaloids are cyclic organic compounds containing nitrogen in a negative state of

♣ oxidation with limited distribution among living organisms.

Functions of alkaloids:

- They are of no importance and may be regarded as by-products of plant metabolism.
- They may act as reservoirs for protein synthesis.
- They may act as protective substances against the animal or insect attacks.
- Like hormones, they may function as plant stimulations or regulations in activities like growth metabolism and production.
- May functionating as detoxicating agents by methylating, condensing, and cyclising the compounds whose accumulation might otherwise cause damage to the plant.

Properties:

Most alkaloids contain oxygen in their molecular structure; those compounds are

- usually colorless crystals at ambient conditions. Some alkaloids are colored, like berberine (yellow) and sanguinarine (orange).
- Most alkaloids are weak bases, but some, such as theobromine and theophylline,
- are amphoteric. Many alkaloids dissolve poorly in water but readily dissolve in organic solvents.
- Most alkaloids have a bitter taste or are poisonous when ingested.

Classification:

- Pyridine-piperidine
- Tropane
- Quinoline
- Isoquinoline
- Indole
- Imidazole
- Steroids
- Purines
- Alkaloid amine

Isolation:

a) **Soxhlet Extraction Process**: The soxhlet assembly is a continuous extractor which is generally suitable for the extraction of alkaloids from powdered plant materials with the help of organic solvents. In this instance, the powdered drug is usually moistened with dilute ammonia solution and then packed loosely in the thimble of the Soxhlet apparatus; and the organic solvent affords a deep penetration of the moist drug thereby allowing the greatest possible extraction of the alkaloids from the exposed surfaces of the cells and tissues of the crude drug. Once, the extraction is ascertained to have completed, the solvent is filtered and evaporated in a Rotary Thin-Film Evaporator and the residue is treated further for the isolation of individual alkaloids.

b) **Stas-Otto Process**: The Stas-Otto process essentially consists of treating the powdered and sieved drug substance with 90–95% (v/v) ethanol, previously acidified with tartaric acid. The proportion of crude drug to solvent should be maintained as 1 Kg to 1 L. The alcohol is distilled off under vacuum and the resulting aqueous residue is treated with petroleumether (60-80°C) to remove the fatty components completely. If any alkaloid is removed by the petroleum ether, it must be recovered by treating it with dilute mineral acid. Thus, the resulting aqueous extract is mixed with the main bulk of aqueous extract. The combined aqueous extract is filtered and evaporated to dryness preferably in a Rotary Thin-Film Evaporator under vacuum. The residue is extracted with absolute ethanol thereby dissolving the total alkaloids.

Purification:

1. Direct crystallisation from solvent
2. Repeated acid base treatment
3. Chromatographic techniques Ex: Partition, ion-exchange and column chromatography
4. Precipitation method Ex: $AuCl_3$, $PtCl_4$, Mayer’s Reagent,

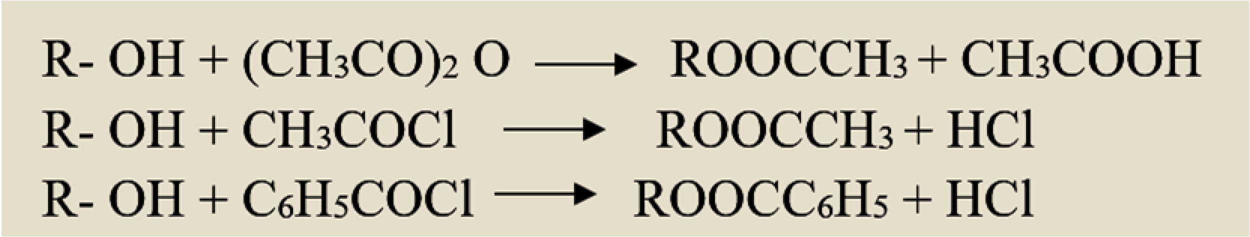
General methods of structural determination of alkaloids:

Molecular Formula : The first step in structural elucidation is the determination of molecular formula and optical rotatory power. Elemental composition and hence the empirical formula is found by combustion analysis.

Determination of Unsaturation: The unsaturation can be determined by adding bromine, halogen acids or by hydroxylation with $KMnO_4$ or by reduction (using either $LiAlH_4$ or $NaBH_4$). Number of Double bond: - Number of Rings present in an alkaloids can be determine by following formula- $C_a H_b N_c O_d$.

Functional Group Determination: By using the usual standard chemical tests or by infrared (IR) spectroscopy

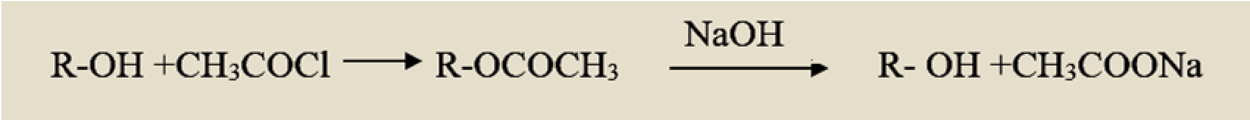
Hydroxyl group: - Formation of Acetate on treatment with Acetic anhydride /Acetyl chloride or benzoate on treatment with Benzyl chloride. By determining the amount of Acetic anhydride /Acetyl chloride or benzoate that reacted with alcohol to form an ester, the number of hydroxyl groups can be determined.



$$R\text{-}OH + (CH_3CO)_2O \longrightarrow ROOCCH_3 + CH_3COOH$$
$$R\text{-}OH + CH_3COCl \longrightarrow ROOCCH_3 + HCl$$
$$R\text{-}OH + C_6H_5COCl \longrightarrow ROOCC_6H_5 + HCl$$

Then check (alcoholic-OH or phenolic –OH) + $FeCl_3$ = color phenolic –OH Or if Soluble in NaOH = phenolic – If not Phenolic –OH: Alkaloid +H_2SO_4 -> unsaturated + $KMNO_4$ -> aldehyde or ketone or acid

If Primary amines are present in an alkaloids also give this test. Then Hydroxyl group is can be determined.



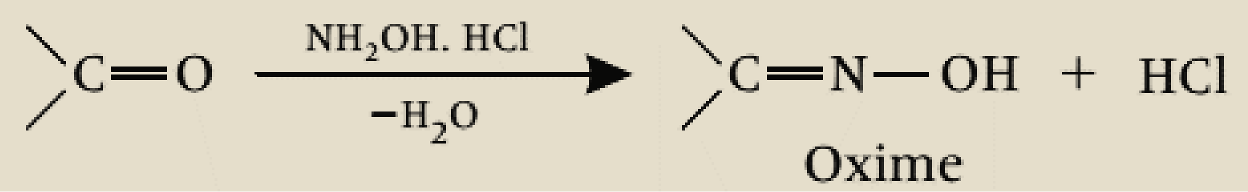
$$R\text{-}OH + CH_3COCl \longrightarrow R\text{-}OCOCH_3 \xrightarrow{NaOH} R\text{-}OH + CH_3COONa$$

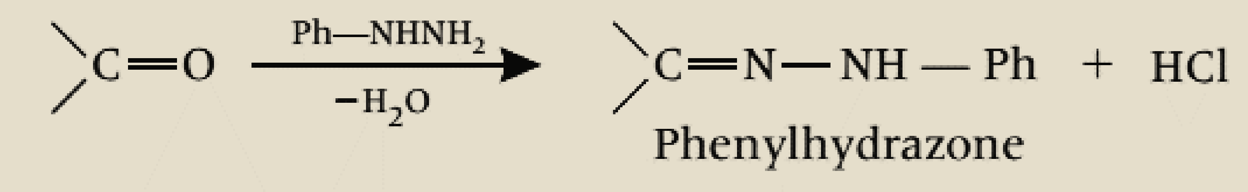
Excess of Alkali is estimated by titration with standard HCl. Number of -OH group can be calculated from the volume of Alkali used for Hydrolysis.

Carboxylic group: - soluble in aqueous solution sodium carbonate Na2CO3 or ammonia NH3 , on treat with alcohol form ester.

Specific IR and NMR signals. - Number of -COOH group can be determined byvolumetrically by titration against a standard Ba(OH)2 or NaOH solution using phenolphthalein as an indicator.

Carbonyl group: The presence of aldehydes and ketones can be detected by their reaction with hydroxylamine to form the corresponding oxime.

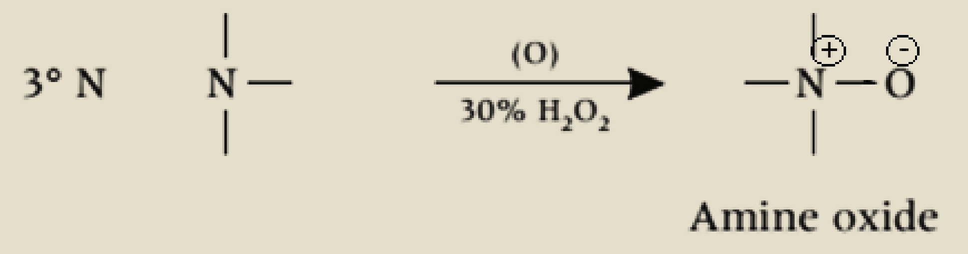




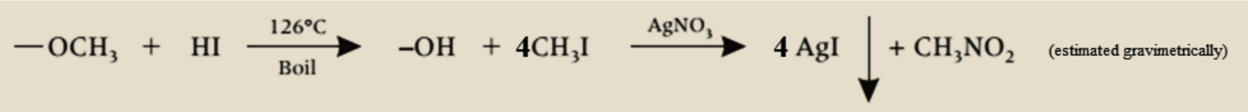
Nature of Nitrogen: General reactions of alkaloids with acetic acid, methyl iodide and nitrous acid indicates the nature of nitrogen.

If all reactions are negative – N2 probably tertiary Majority of nitrogen presence in alkaloids are secondary and tertiary: If tertiary when treated with H2O2 (30%) form amine oxide.

Nature and No. alkyl group attached to Nitrogen: Distillation with Aq. KOH, formation ofmethylamine, dimethylamine and trimethylamine (Vol. products)



Herzig- Mayer method: presence and number of N- methyl group



The aldehydes and ketones are distinguished by their oxidation or reduction products. The carbonyl groups of aldehyde, ketone and carboxyl groups are further confirmed by their spectral data such as IR, UV and NMR.

Methoxyle group: determination by Zeisel method: When methoxy group present in a alkaloids treated with HI at 1260C perform methyl iodide which can treated further with silver nitrite to perform silver iodide precipitate. Which estimated gravimetrically : e.g.. Papavarine.

Degradation of alkaloids: Study of degradation of alkaloids gives rise to some identifiable products of known structure. Knowing structure of the degraded products and the changes occurred during the degradation, it is convenient to know the structure of the original molecule.

Different degradation reactions

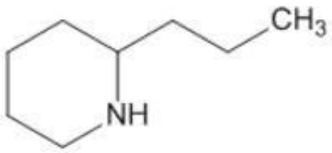
- Hoffman exhaustive methylation method

- Emde’s method
- Von Braun’s (VB) method for 3° cyclic amines
- Reductive degradation
- Oxidation
- Zinc distillation
- Alkali fusion Dehydrogenation

Structural elucidation of alkaloids:

CONNINE:

STRUCTURE:



Coniine

CONSTITUTION:

It is most important alkaloid of Hemlock group which is obtained from Conium]D +15.7Oαmaculatum .

Coniine is optically active [, colourless liquid b.p. 167OC with unpleasant odour and burning taste. It is historical alkaloid since this was used by Greek philosopher Socrate and was found dead in 399 B.C.

It was the first alkaloid, which was synthesized in laboratory in 1866. Structure

1. Molecular formula of coniine was found to be C8H17N on the basis of molecular weight determination ad elemental analysis.

2. When coniine was treated with benzoyl chloride it forms monobenzoyl derivatives which indicates the presence of secondary nitrogen atom (since there is no oxygen atom) (Van Braund’s method for secondary cyclic nitrogen)

3. Coniine on zinc dust distillation gives conyrine having molecular formula C8H11N which on further oxidation with potassium permanganate gives -picolinic acid).αpyridine-2-carboxylic acid

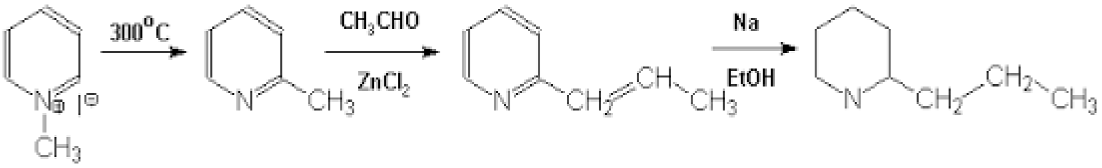
The formation of pyridine-2-carboxylic acid indicates that conyrine is 2-substituted pyridine and hence coniine must be 2-substituted piperidine.

Thus side chain must contain three carbon atoms, since two carbons are lost when conyrine is oxidized with KMnO4.

4. The difference in molecular formula of conyrine C8H11N and pyridine-2- carboxylic acid indicates that side chain may be either n-propyl or isopropyl and thus there may be two possible structure of coniine (I) and (II).

Coniine was found to have structure (I) on the basis of following facts: (i) Coniine when heated with hydriodic acid at 300 OC under pressure gives noctane whereas structure (II) would form isooctane.

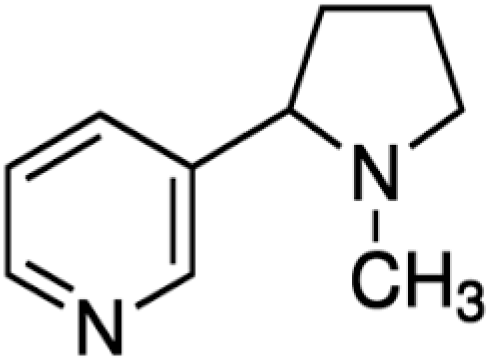
SYNTHESIS(Ladenbergs synthesis)



The original **synthesis** (shown below) of **Coniine** was performed by Ladenburg in 1886. Ladenburg heated N-methylpyridine iodide to 250 °C, to obtain 2-methylpyridine. He then performed a Knoevenagel condensation with acetaldehyde in anhydrous zinc chloride to yield 2-propenylpyridine.

NICOTINE:

STRUCTURE:



CONSTITUTION:

•Nicotine is the chief alkaloid of tobacco plant.

•IUPAC name 3-(1-methyl-2-pyrrolidinyl) pyridine.

•It is a bicyclic compound with a pyridine cycle and a pyrrolidine cycle.

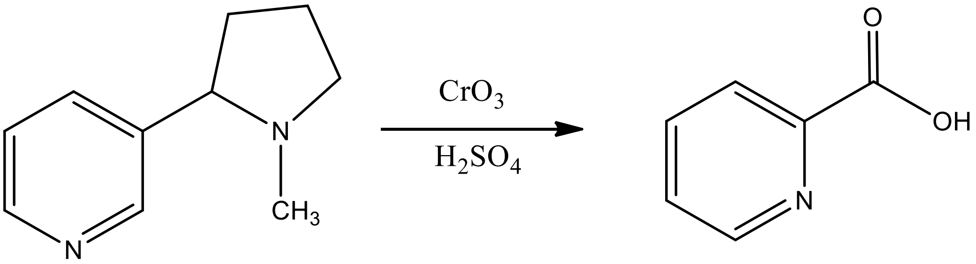
The molecule possess an asymmetric carbon and so exists in two enantiomeric compounds.

• It occurs in the plant leaves as salts of malic acid and citric acid to the extent of 4 to 5 percent. The alkaloid was named after the Frenchman NICOT who introduced tobacco in France in 1560.

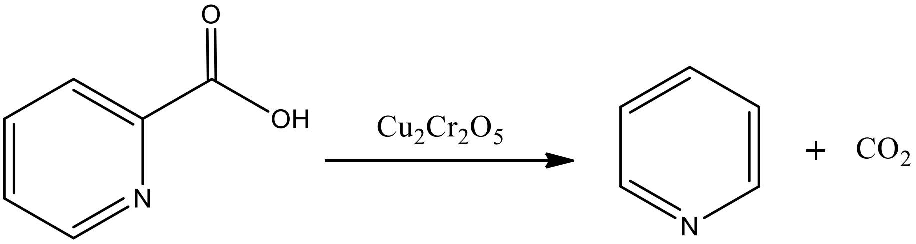
1. Elemental analysis and molecular weight determination leads to the molecular formula $C10H14N2$ for nicotine.

2.It absorbs two molecules of $CH3$ I, suggesting the tertiary nature of both the nitrogen atoms.

3.On oxidation with chromic acid, nicotine yields nicotinic acid (pyridine-3-carboxylic acid).



This shows that the alkaloid contains a pyridine nucleus with a side chain at the 3 position. That is the side chain has the composition($C10H14N2=C5H4N-C5H10N$). Therefore the formula for nicotine may be written as: NICOTINE TO NICOTINIC ACID



4. Nature and position of the side chain

a)The alkaloid forms an addition compound with zinc chloride, C10H14N2 .ZnCl2 ,which when heated with lime yields pyridine, pyrole, and methylamine.

b)When heated with concentrated hydriodic acid at 200-300oc, nicotine yields CH3 I, showing that methyl group is attached to N atom.Therefore,it appears that the side chain could be N- methylpyrrolidine.

c) Nicotine hydriodide when treated with CH3 I, forms nicotine isomethiodide which on oxidation with potassium ferricyanide yields nicotone. This on further oxidation with chromium trioxide produces hygrinic acid.

The above structure of nicotine is further confirmed as it explains the following reactions:

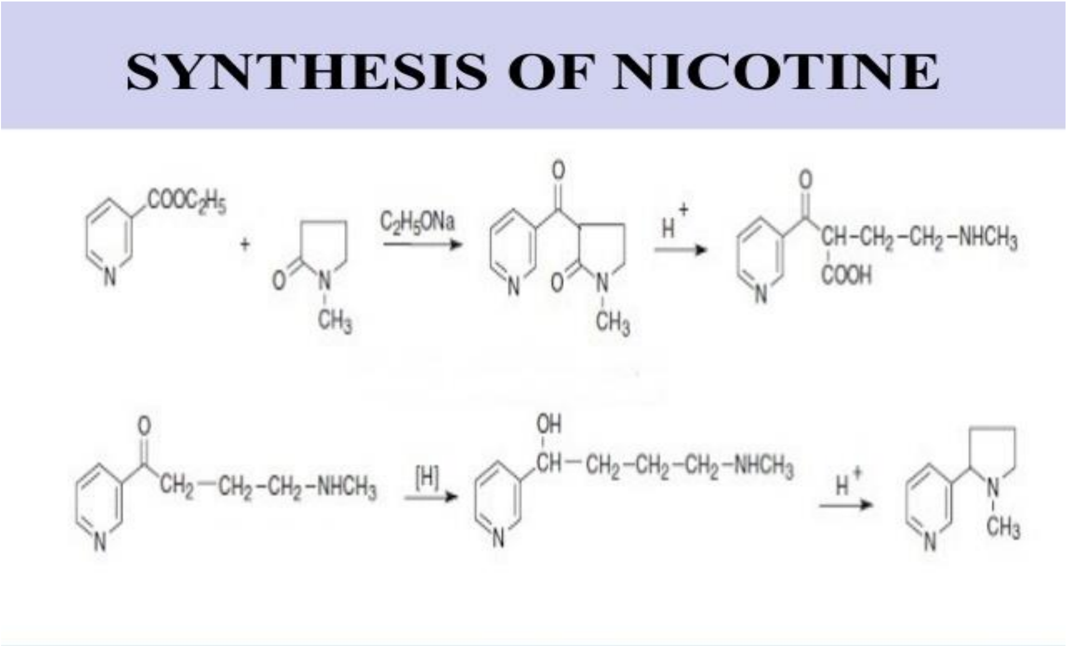
a) Nicotine when treated with bromine in acetic acid followed by aqueous sulphurous acid gives dibromocotinine,C10H10ON2Br2 .This upon oxidation with a mixture of sulphurous acid and sulphuric acid at 130-140 oc, yields 3-acetylpyridine,oxalic acid and methylamine.

b) Nicotine on reaction with bromine in hydrobromic acid gives dibromoticonine which when heated with barium hydroxide solution at 100oc,yields nicotinic acid,malonic acid and methylamine.

SYNTHESIS :

Finally the structure of nicotine was confirmed by the following synthesis accomplished by Spath(1928).This synthesis also confirms pinners formula for nicotine.

The racemic alkaloid obtained is resolved by means of (+)-tartaric acid to get (-)-nicotine which is found to be identical with the natural alkaloid.

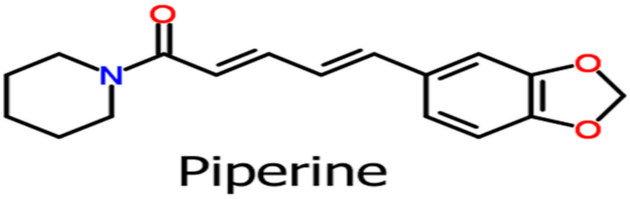


PIPERINE:

Piperine occurs in black pepper (*Piper nigrum*, Fam. Piparaceae).

The piperine content of black pepper is 6 to 11%. It is present in relatively smaller amounts in other piper species, e.g. *Piper longum* (~5%), *P nigrum* (~1.5%) Black pepper is employed commercially as a condiment. It has been used as a stimulant and a febrifuge. Piperine has insecticidal activity.

STRUCTURE:



CONSTITUTION: Piperine is the naturally occurring alkaloid that gives the spice black pepper its characteristic biting taste. The stereoselective synthesis of this natural product, in good yield from inexpensive and readily available starting materials, exemplifies the powerful synthetic utility afforded by the Wittig reaction and its variations such as the HornerWadsworth-Emmons reaction.

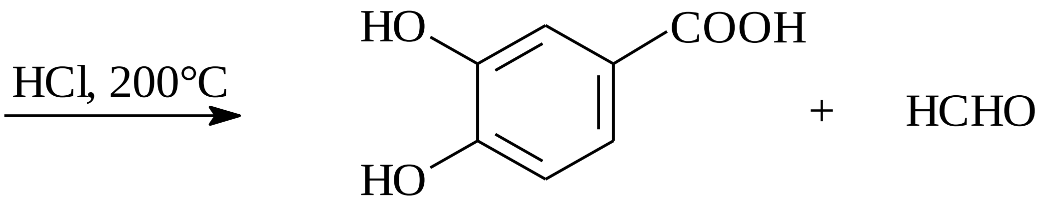
The important impact of the Wittig reaction on modern synthetic organic chemistry was recognized by the 1979 Nobel Prize that was awarded in part to Georg Wittig for his discovery and subsequent development of this reaction.

Piperine on hydrolysis yielded piperidine and piperic acid, indicating that the two fragments are linked with each other by means of an acid amide linkage.

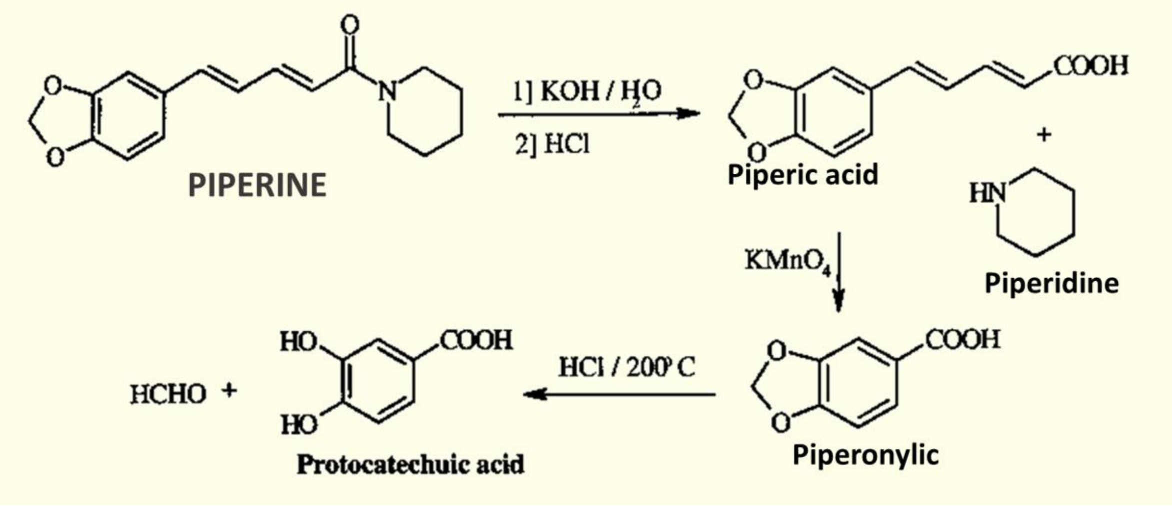
further oxidation of which gave piperonylic acid and tartaric acid.

Piperic acid has *trans*, *trans* geometry of the double bonds. ($2Br_2$!?)

$$\underset{C_{12}H_{10}O_4}{\text{Piperic acid}} \xrightarrow[\text{[O]}]{KMnO_4} \underset{C_8H_6O_3}{\text{Piperonal}} \xrightarrow{\text{[O]}} \underset{C_8H_6O_4}{\text{Piperonylic acid}}$$



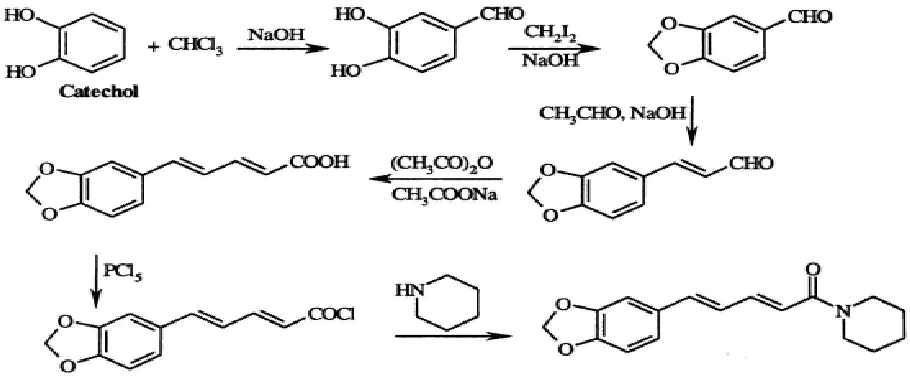
Protocatechuic acid



- Piperine was synthesized (Ladenburg, 1894) by the reaction of the piperic acid chloride with piperidine, which confirmed the structure of the molecule. The synthesis of piperic acid was achieved starting from piperonal, which was obtained from catechol using Reimer-Tiemann reaction followed by the condensation with diiodomethane in the presence of a base.

- Piperonal was condensed with acetaldehyde in the presence of sodium hydroxide and the product obtained was then heated with acetic anhydride and sodium acetate to yield piperic acid.

SYNTHESIS

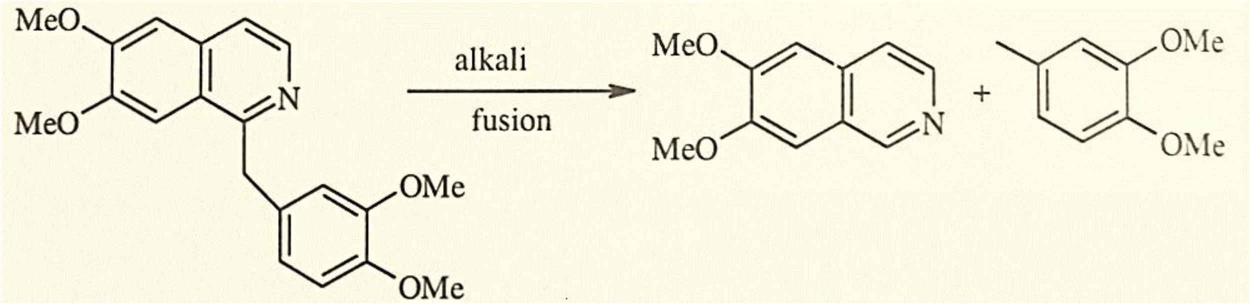


PAPAVARINE

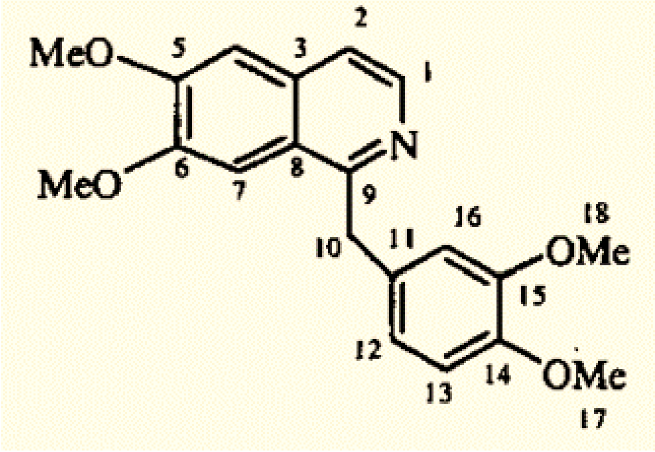
One of the opium constituents, papaverine has been studied particularly intensively because it has a clinical use as antispasmolytic agent. Papaverine is an optically inactive 1-benzyl-isoquinoline derivative.

1. Methoxyl determination: established that all four oxygen atoms are present as methoxyl groups proved by *Zeisel* determination method.

2. The structure was further elucidated from cleavage reactions leading to identifiable fragments. Thus, alkali fusion gives two fragments that account for all of the carbon atoms, a C-11-base identified as 6,7-dimethoxylisoquinoline and a C-9 ether identified as 4-methylcatechol dimethyl ether.



3. The point of linkage in the isoquinoline fragment was revealed by permanganate oxidation of papaverine, which results in attack at the methylene group to give ketone **papaveraldine** which on heating with potassium hydroxide degrades further into 1-4 four products.



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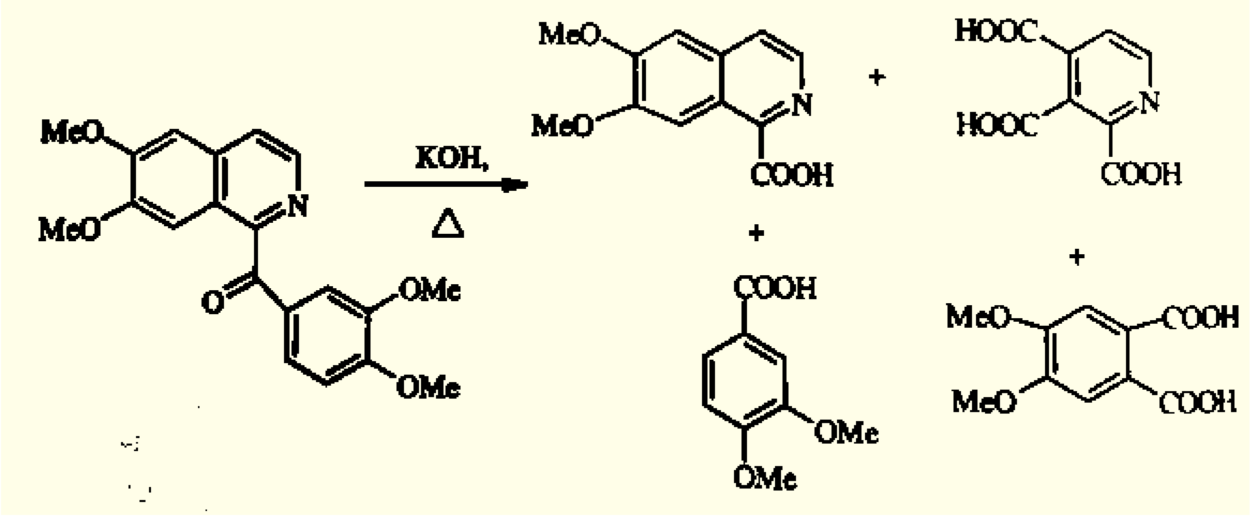


The position of carboxyl group in compounds **1** and **2** above, indicated that the isoquinoline unit is linked to dimethylcatechol unit at the position C1 through methylene bridge.

Reference:

Chemistry of Natural products,VOLUME-1.,O.P.AGARWAL

UNIT-2 –Terpenoids-SCY1615

Terpenoids: Introduction, classification, Isoprene rule - General methods of determining structure – Structural elucidation of citral, menthol, geraniol and camphor.

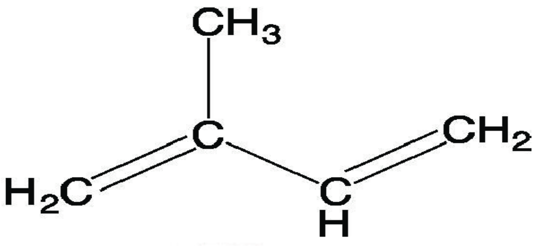
Carotenoids: Introduction, geometrical isomerism, structure determination and synthesis of β-carotene and vitamin A.

Terpenoids

The term ‘terpene’ was given to the compounds isolated from terpentine, a volatile liquid isolated from pine trees.The simpler mono and sesquiterpene is chief constituent of the essential oils obtained from sap and tissues of certain plant and trees.The di and tri terpenoids are not steam volatile. They are obtained from plant and tree gums and resins. The term ‘terpene’ was originally employed to describe a mixture of isomeric hydrocarbons of the molecular formula C10H16 occurring in the essential oils obtained from sap and tissue of plants, and trees. But there is a tendency to use more general term ‘terpenoids’ which include hydrocarbons and their oxygenated derivatives.

definition: “Terpenoids are the hydrocarbons of plant origin of the general formula (C5H8)n as well as their oxygenated, hydrogenated and dehydrogenated derivatives

ISOPRENE RULE: Isoprene rule Thermal decomposition of terpenoids give isoprene as one of the product.Otto Wallach pointed out that terpenoids can be built up of isoprene unit. Isoprene rule states that the terpenoid molecules are constructed from two or more isoprene unit. Special isoprene rule states that the terpenoid molecule is constructed of two or more isoprene units joined in a ‘head to tail’ fashion.



CLASSIFICATION OF TERPENOIDS:

Most natural terpenoids hydrocarbon have the general formula (C5H8)n.

They can be classified on the basis of value of n or number of carbon atoms present in the structure. Each class can be further subdivided into subclasses according to the number of rings present in the structure.

- Acyclic Terpenoids: They contain open structure.
- Monocyclic Terpenoids: They contain one ring in the structure.
- Bicyclic Terpenoids: They contain two rings in the structure.
- Tricyclic Terpenoids: They contain three rings in the structure.

Tetracyclic Terpenoids: They contain four rings in the structure.

General methods of determining structure:

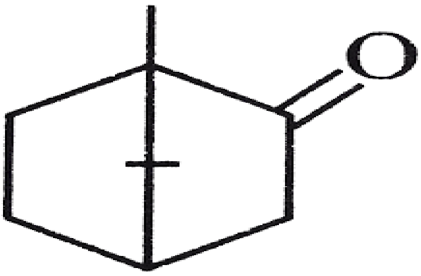
- i) Molecular formula: molecular formula is determined by usual quantitative analysis and mol.wt determination methods and by means of mass spectrometry. If terpenoid is optically active, its specific rotation can be measured.
- ii) Nature of oxygen atom present: If oxygen is present in terpenoids its functional nature is generally as alcohol aldehyde, ketone or carboxylic groups.
- a) Presence of oxygen atom present: presence of –OH group can be determined by the formation of acetates with acetic anhydride and benzoyate with 3.5-dinitirobenzoyl chloride.
- Primary alcoholic group undergo esterification more readily than secondary and tertiary alcohols.
- Presence of >C=O group: Terpenoids containing carbonyl function form crystalline addition products like oxime, phenyl hydrazone and bisulphite etc.
- If carbonyl function is in the form of aldehyde it gives carboxylic acid on oxidation without loss of any carbon atom whereas the ketone on oxidation yields a mixture of lesser number of carbon atoms.
- iii) Unsaturation: The presence of olefinic double bond is confirmed by means of bromine, and number of double bond determination by analysis of the bromide or by quantitative hydrogenation or by titration with monoperpthalic acid. Presence of double bond also confirmed by means of catalytic hydrogenation or addition of halogen acids. Number of moles of HX absorbed by one molecule is equal to number of double bonds present.
- Addition of nitrosyl chloride (NOCl) (Tilden’s reagent) and epoxide formation with peracid also gives idea about double bonds present in terpenoid molecule
- iv) Dehydrogenation: On dehydrogenation with sulphur, selenium, polonium or palladium terpenoids converted to aromatic compounds. Examination of these products the skelton structure and position of side chain in the original terpenoids can be determined.
- For example α-terpenol on Se-dehydrogenation yields pcymene.
- v) Oxidative degradation: Oxidative degradation has been the parallel tool for elucidating the structure of terpenoids. Reagents for degradative oxidation are ozone, acid, neutral or alkaline potassium permanganate, chromic acid, sodium hypobromide, osmium tetroxide, nitric acid, lead tetra acetate and peroxy acids. Since oxidizing agents are selective, depending on a particular group to be oxidized, the oxidizing agent is chosen with the help of structure of degradation products.
- vi) Number of the rings present: With the help of general formula of corresponding parent saturated hydrocarbon, number of rings present in that molecule can be determined.
- Vii) Relation between general formula of compound and type of compounds: Table 2 For example: limonene (mol. formula. C10H16) absorbs 2 moles of hydrogen to give tetrahydro limonene (mol. Formula C10H20) corresponding to the general formula. CnH2n. It means limonoene has monocyclic structure.
- viii) Spectroscopic studies: All the spectroscopic methods are very helpful for the confirmation of structure of natural terpenoids and also structure of degradation products.
- The various methods for elucidating the structure of terpenoids are;
- a) UV Spectroscopy: In terpenes containing conjugated dienes or α,β-unsaturated ketones, UV spectroscopy is very useful tool. The values of λmax for various types of terpenoids have been calculated by applying Woodward’s empirical rules. There is generally good agreement between

calculation and observed values. Isolated double bonds, α,β-unsaturated esters , acids, lactones also have characteristic maxima.

- b) IR Spectroscopy: IR spectroscopy is useful in detecting group such as hydroxyl group (~3400cm-1) or an oxo group (saturated 1750-1700cm-1). Isopropyl group, cis and trans also have characteristic absorption peaks in IR region.
- c) NMR Spectroscopy: This technique is useful to detect and identify double bonds, to determine the nature of end group and also the number of rings present, and also to reveal the orientation of methyl group in the relative position of double bonds.
- d) Mass Spectroscopy: It is now being widely used as a means of elucidating structure of terpenoids for determining mol. wt., mol. formula, and nature of functional groups present and relative positions of double bonds.
- . ix) X-ray analysis: This is very helpful technique for elucidating structure and stereochemistry of terpenoids.
- x) Synthesis: Proposed structure is finally confirmed by synthesis. In terpenoid chemistry, many of the synthesis are ambiguous and in such cases analytical evidences are used in conjunction with the synthesis.

Camphor:

Structure:



Important constituent of oil of camphor .colourless transparent mass of characterstic smell and burning taste, M.pt. 1790C and b.pt. 2040C .Optically active (+)and (-) forms occur naturally while the racemic form is usually a synthetic product .Main source is Cinnamomum camphora (camphor tree) which is extremely found In Formosa .Present in higher proportion in the trunk of the tree .industrially from α-pinene which in turn obtained from turpentine oil.

STRUCTURAL ELUCIDATION:

Molecular formula $C_{10}H_{16}O$.

oxime with NH2OH, semi carbazone and semi carbazide, and dicarboxylic acid having the same number of carbon atoms on oxidation

the presence of ketonic group in camphor ($C_{10}H_{18}O$) led $C_{10}H_{18}$ corresponds to C_nH_{2n-2} which confirms a bicyclic compounds .

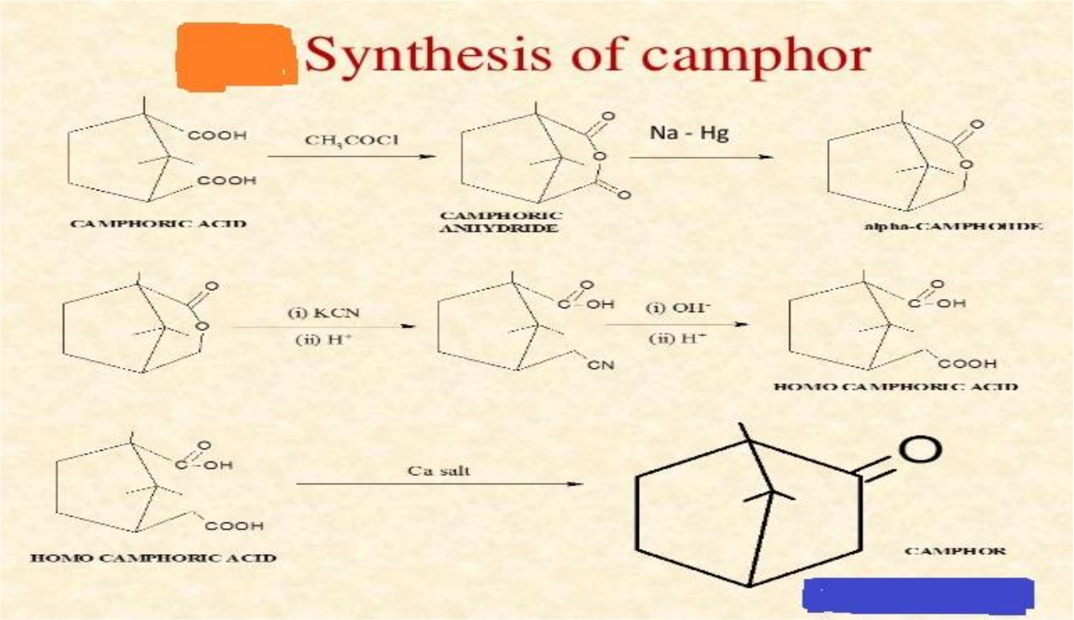
condensation with C6H5CHO forms monobenylidene derivative suggesting the presence of –CO-CH2 – group.

camphor on distillation with zinc chloride or phosphorous pentoxide gives p- cymene which suggests one six membered ring

distillation with iodine gives carvacrol suggest ketonic group in camphor

Oxidation with nitric acid gives camphoric acid followed by camphoric acid

SYNTHESIS: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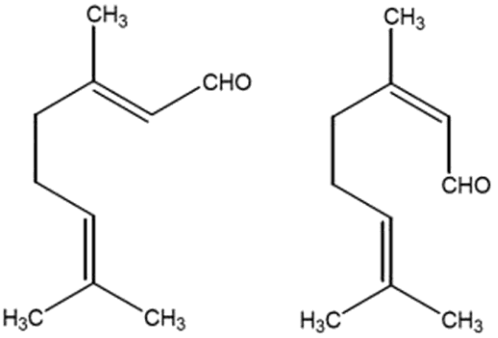
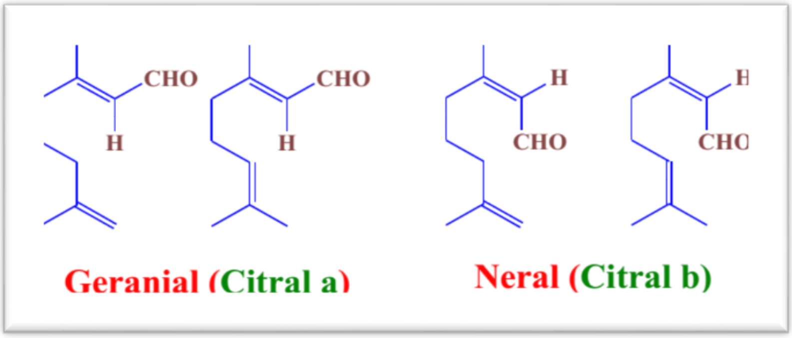
CITRAL:

STRUCTURE:



CONSTITUTION:

1) Molecular formula: $C_{10}H_{16}O$



2)

2) Presence of two double bond: Citral is treated with bromine or hydrogen, it forms citral tetrabromide. It indicate the presence of two double bond.

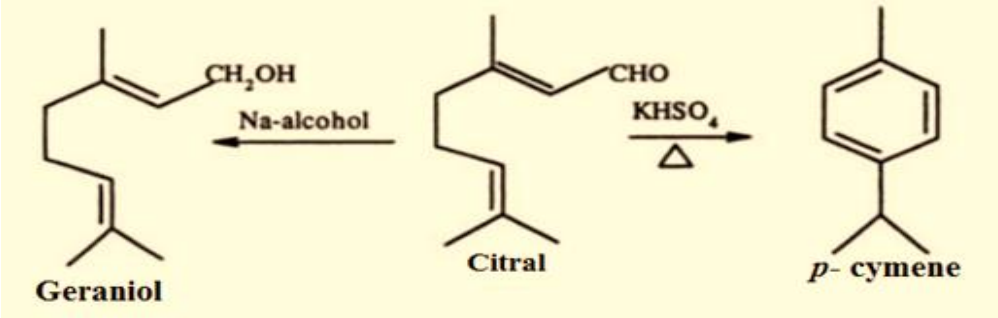
$C_{10}H_{16}O \rightarrow C_{10}H_{16}O.Br_4$

3) Citral as an acyclic compound

- Formation of above products shows that citral is an acyclic compound containing two double bonds.

- Corresponding saturated hydrocarbon of citral (molecular Formula C10H22) corresponds to the general formula CnH2n+2 for acyclic compounds, indicating that citral must be an acyclic compound.

3) Nature of Oxygen i) Presence of an aldehyde group Formation of an oxime with hydroxylamine indicates the presence of an oxo group in citral. ii) Citral on reduction with Na/Hg it gives an alcohol called geraniol. On oxidation with silver oxide to yield a Geranic acid same number of carbon atom as citral. iii) Indicate that oxo group in citral is an aldehyde group.

4) 

5) Position of Aldehyde group

- The UV spectrum of citral shows λmax at 230 nm which indicates conjugated aldehyde.

- On hydrolysis with aq. K2CO3 gives 6-methyl hept-5-ene-2- one and acetaldehyde by breaking α,β- double bond.

- Both reactions proved that citral is a conjugated aldehyde.

6) Carbon skeleton of citral

- Citral is heated with potassium hydrogen sulphate, it gives p-cymene (known compound).

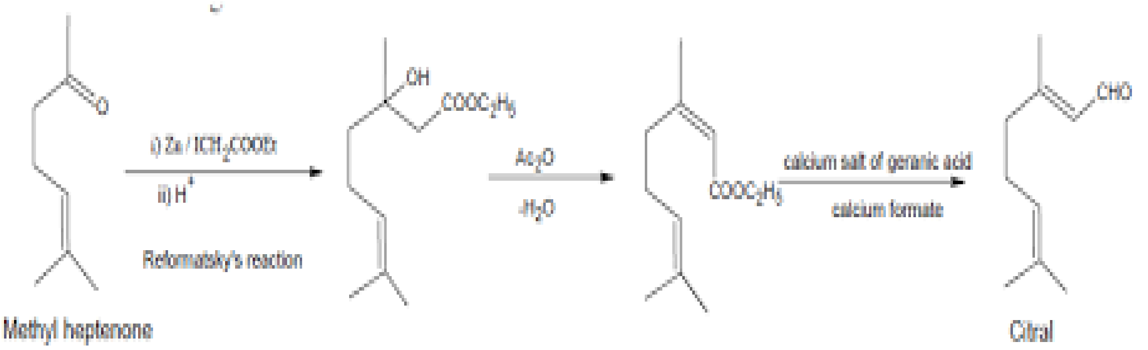
- Formation of p-cymene and product obtained from the ozonolysis reveals that C-skeleton (I) of citral is formed by the joining of two isoprene units in the head to tail fashion.

- Formation of p-cymene also reveals the position of methyl and isopropyl group in 1:4 position w.r.t. each other in citral.

7) Oxidation • Citral undergo oxidation with KMnO4 followed by CrO3 yield acetone, oxalic acid and laevulic acid.

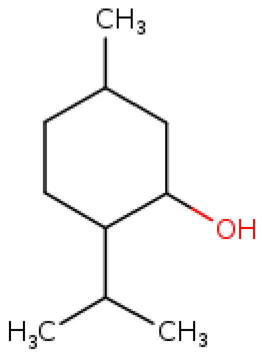
- Citral on ozonolysis yield acetone, laevulaldehyde and gyoxal. Formation of acetone in both reactions shows the presence of conjugated aldehyde.

SYNTHESIS:



MENTHOL:

STRUCTURE:



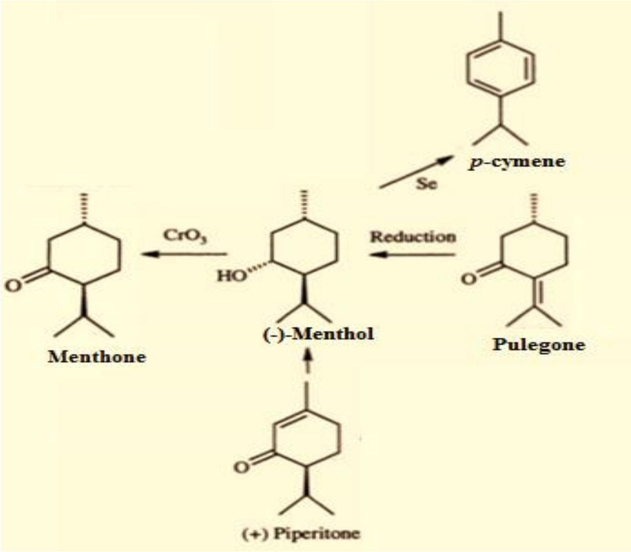
CONSTITUTION:

Chemical formula: $\mathbf{C_{10}H_{20}O}$, m.p. 34 °C, b.p. 213 °C, $[\alpha]_D$ -50°, η^{20}_{D} 1.4661.

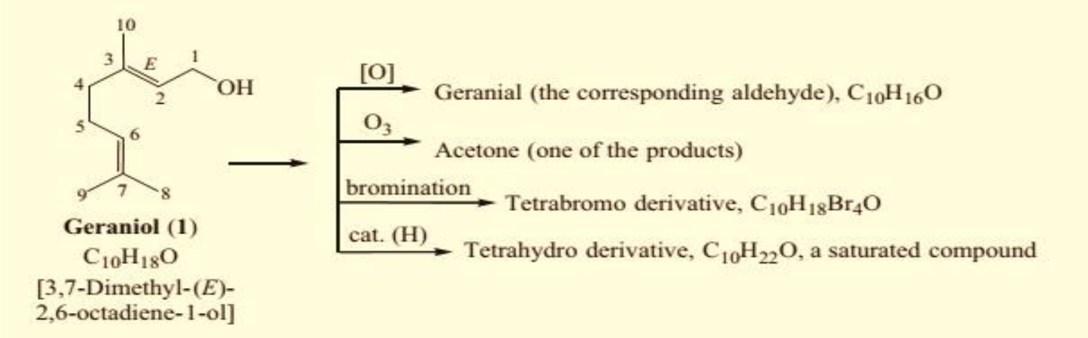
Menthol is the major constituent of *Mentha piperita* and has been known in India, China and Japan since ancient times. It is mainly used as flavouring agent and has a cooling effect. Medicinally it exhibits antiseptic and anaesthetic properties. It is the ingredient in cold balms.

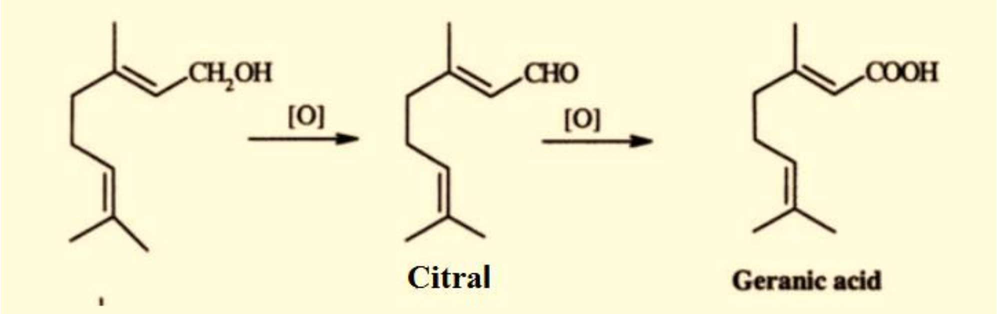
Molecular formula of menthol was determined as $\mathbf{C_{10}H_{20}O}$. On treatment with **phosphorus pentachloride** and **phosphorus pentoxide** menthol gave a chloride $\mathbf{C_{10}H_{19}Cl}$ and a **hydrocarbon** $\mathbf{C_{10}H_{18}}$ respectively, inferring that it is an alcohol.

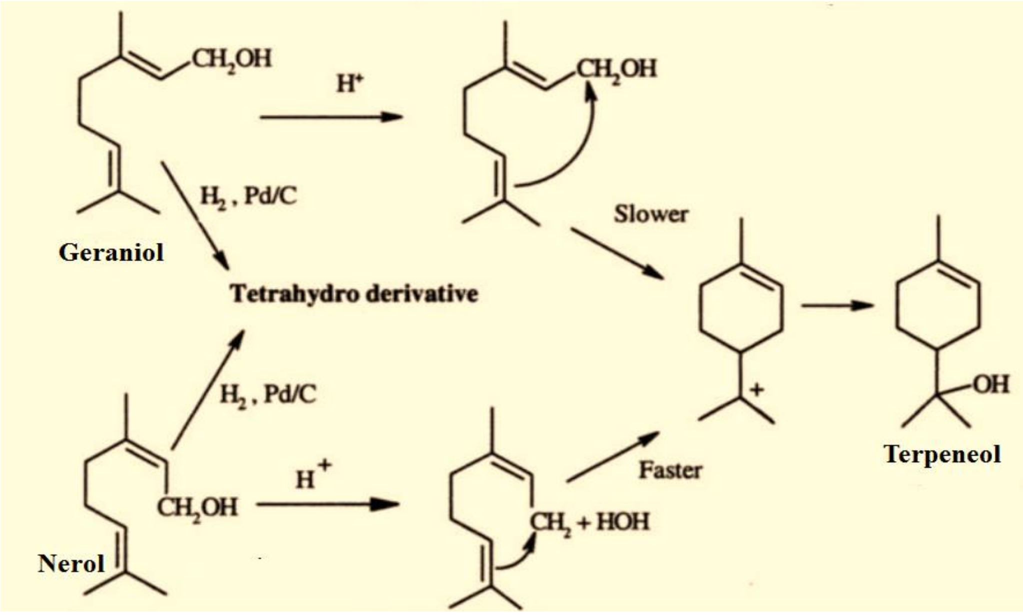
- Menthol was oxidized by chromic acid to a ketone, Menthone to prove that menthol contained a secondary hydroxyl group.
- Menthol was converted to *p*-cymene identified as 1-methyl-4-isopropylbenzene, which was also obtained by the dehydrogenation of pulegone whose structure was established as *p*-menth-4-(8)-en-3-one by chemical methods and confirmed by its synthesis.
- Therefore menthol must possess the same skeleton as pulegone. Pulegone on reduction yielded menthone, which on further reduction gave menthol.correlation of pulegone with menthol proved the structure of menthol.



Geraniol:

- Its molecular formula was established as $C_{10}H_{18}O$.
- Catalytic **hydrogenation** yielded a tetrahydro derivative $C_{10}H_{22}O$ indicating the presence of two double bonds.
- This was further supported by the formation of a tetrabromide when treated with bromine
- 

- On oxidation **geraniol** afforded **citral**. which on **reduction** gave two **alcohols.**
- 

- **Geraniol** and **nerol** are geometrical isomers.
- Both **geraniol** and **nerol** gave the same tetrahydro derivative on catalytic **hydrogenation**.
- Both of them underwent **cyclisation** to give **terpeneol** by the action of **sulphuric acid** and the rate of **cyclisation** in the case of **nero**l was 9 times faster compared to that of **geraniol.**
- Based on this Δ^2 -double bond in **nerol** was assigned as ***cis*** while the same double bond in **geraniol** as ***trans***.
- 

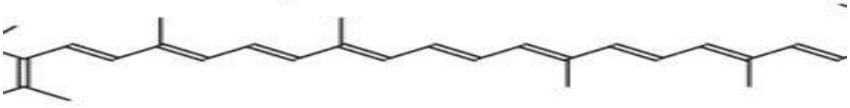
Carotenoids: Carotenoids are called as tetraterpenoids, an pigment that are produced by plant and algae.Carotenoids are contains eight isoprene units(C40).They are various colours usually in yellow to red pigments.

- There are two classes of caroteinoids
- A)carotenes: consists of carbon and hydrogen atoms. eg: beta-carotine.
- B)Xanthophylls : one or more oxygen atoms.
- Eg: lutein

Structure of common carotenoids:

Lycopene

β-Carotene



Lutein

- **Geometrical isomerism:** There are many factors influencing the formation and isomerization of carotenoids.
- Heat, light, and structural differences are the prominent factors that affect the isomerization of carotenoids in foods.
- Various processing methods, such as heating and drying also lead to the isomerization and even degradation of carotenoids.
- Oxidative degradation of carotenoids has also led to *cis*-*trans* isomerization and formation of carotenoid epoxides*cis*-isomer of carotenoids can be identified based on the absorption spectrum characteristics, *Q* ratios, and the relative intensity of the *cis* peak .
- The UV spectrum of *cis* carotenoids is characterized with their λ_{max} between 330–350 nm, which has greatest intensity when the double bond is located near or at the center of the chromophore .
- On the other hand, a hypsochromic shift in the λ_{max} and smaller extinction coefficient is observed. Thus, *cis-trans* isomerization of carotenoids leads to a decrease of color intensity . All-*trans*-β-carotene is very unstable and can be easily isomerized into *cis*-isomers, when exposed to heat and light.

Structural determination of carotenoids:

- Beta-carotene, with the molecular formula C40H58, belongs to the group of carotenoids consisting of isoprene units.
- The presence of long chains of conjugated double bonds donates beta-carotene with specific colors.
- It is the most abundant form of carotenoid and it is a precursor of the vitamin A.
- Beta-carotene is composed of two retinyl groups. It is an antioxidant that can be found in yellow, orange and green leafy vegetables and fruits.

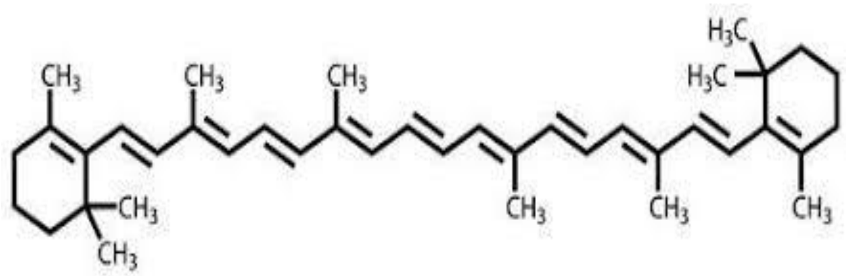
BETA-CAROTENE:

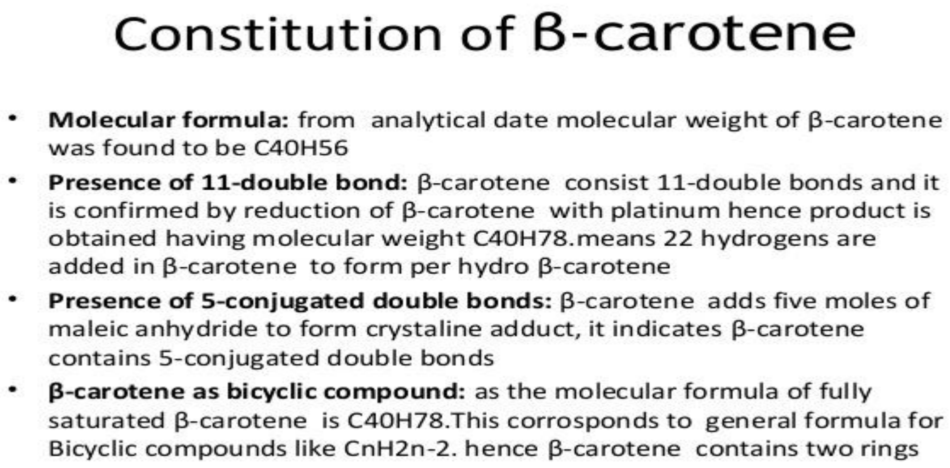
β-carotene is the molecule that gives carrots, sweet potatoes, squash, and other yellow or orange vegetables their orange color. It is part of a family of chemicals called the carotenoids, which are found in many fruit and vegetables, as well as some animal products such as egg yolks.

Carotenoids were first isolated in the early 19th century, and have been synthesized for use as food colorings since the 1950s.

Biologically, β-carotene is most important as the precursor of vitamin A in the human diet. It also has anti-oxidant properties and may help in preventing cancer and other diseases.

STRUCTURE:

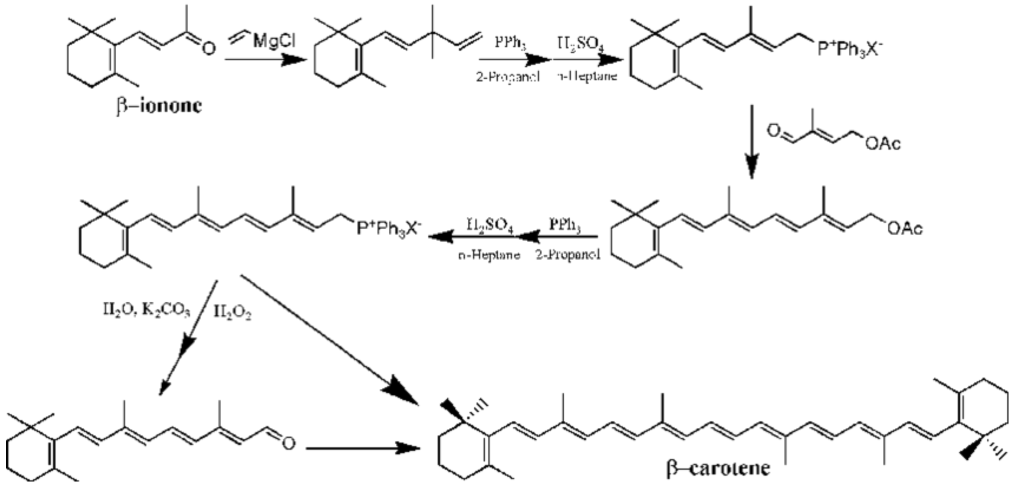




Constitution of β-carotene

- **Molecular formula:** from analytical date molecular weight of β-carotene was found to be C40H56
- **Presence of 11-double bond:** β-carotene consist 11-double bonds and it is confirmed by reduction of β-carotene with platinum hence product is obtained having molecular weight C40H78.means 22 hydrogens are added in β-carotene to form per hydro β-carotene
- **Presence of 5-conjugated double bonds:** β-carotene adds five moles of maleic anhydride to form crystaline adduct, it indicates β-carotene contains 5-conjugated double bonds
- **β-carotene as bicyclic compound:** as the molecular formula of fully saturated β-carotene is C40H78.This corrosponds to general formula for Bicyclic compounds like CnH2n-2. hence β-carotene contains two rings

SYNTHESIS



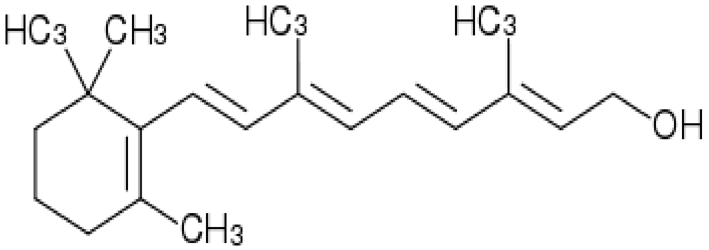
Vitamin-A:

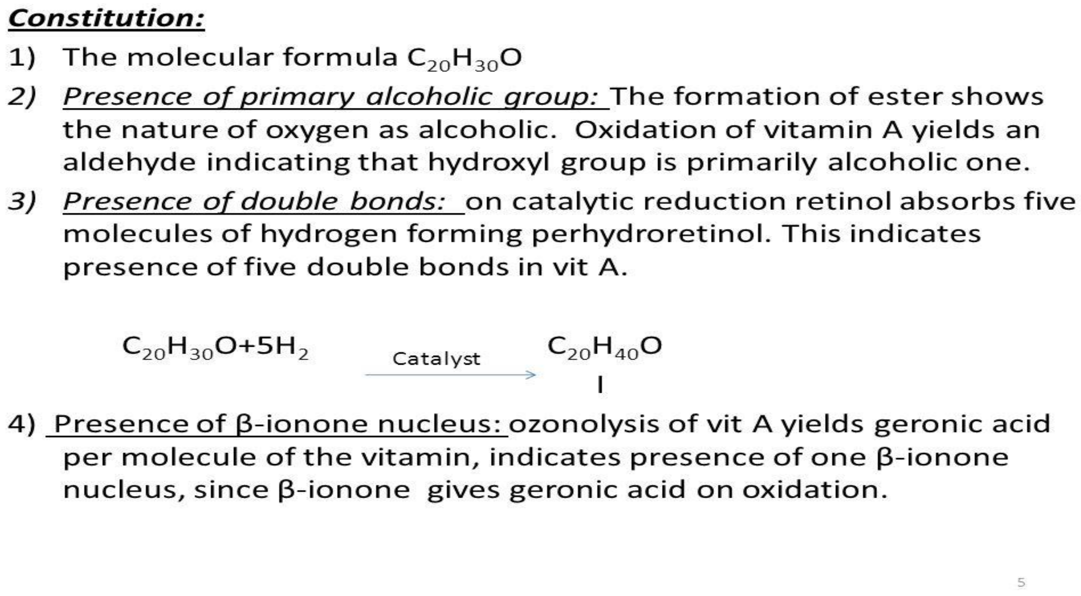
Vitamin A or retinol has a structure depicted to the right.

Retinol is the immediate precursor to two important active metabolites: retinal, which plays a critical role in vision, and retinoic acid, which serves as an intracellular messenger that affects transcription of a number of genes.

Vitamin A does not occur in plants, but many plants contain carotenoids such as beta-carotene that can be converted to vitamin A within the intestine and other tissues.

STRUCTURE:





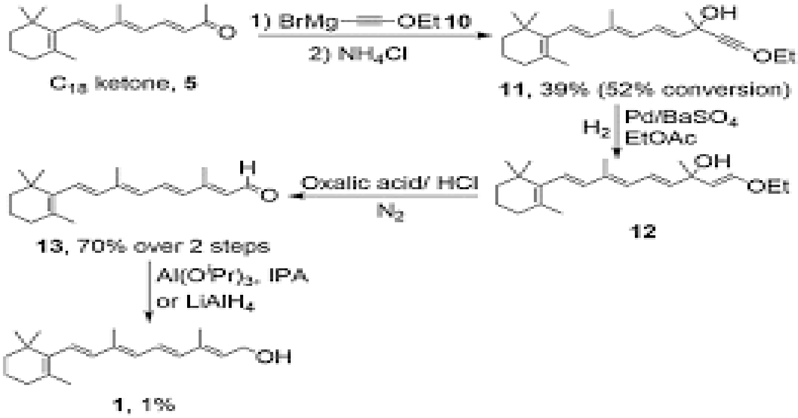
Constitution:

1) The molecular formula $C_{20}H_{30}O$
2) *Presence of primary alcoholic group:* The formation of ester shows the nature of oxygen as alcoholic. Oxidation of vitamin A yields an aldehyde indicating that hydroxyl group is primarily alcoholic one.
3) *Presence of double bonds:* on catalytic reduction retinol absorbs five molecules of hydrogen forming perhydroretinol. This indicates presence of five double bonds in vit A.

$$C_{20}H_{30}O+5H_2 \xrightarrow{\text{Catalyst}} \underset{\text{I}}{C_{20}H_{40}O}$$

4) Presence of β-ionone nucleus: ozonolysis of vit A yields geronic acid per molecule of the vitamin, indicates presence of one β-ionone nucleus, since β-ionone gives geronic acid on oxidation.

SYNTHESIS:



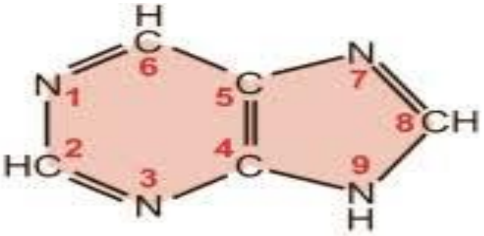
C18 ketone, 5
1) BrMg—≡—OEt 10
2) NH4Cl
OH
OEt
11, 39% (52% conversion)
H2
Pd/BaSO4
EtOAc
OH
OEt
12
Oxalic acid/ HCl
N2
H
O
13, 70% over 2 steps
Al(OiPr)3, IPA
or LiAlH4
OH
1, 1%

Purines: Introduction, biological importance - Structure and synthesis of Uric acid, Xanthine and Caffeine - Pyrimidines: Introduction, Structure and synthesis of Uracil and Thymine

Purines

Purines are the cyclic diureides(compounds having two urea residues-NH-CO.NH)with the skeleton of purine which consists of the pyrimidine ring fused with the an imidazole ringActually purine and hence its derivatives exist in two tautomeric forms and may be represented in either of the following two ways.

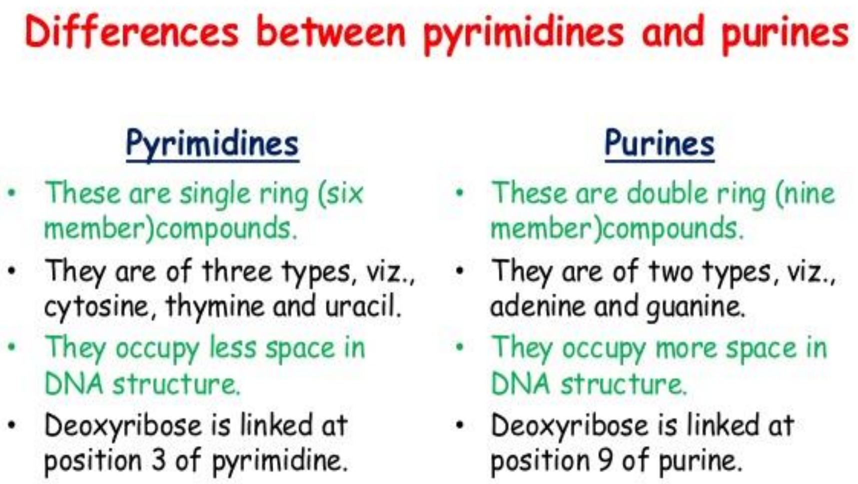
Pyrimidine



Purine

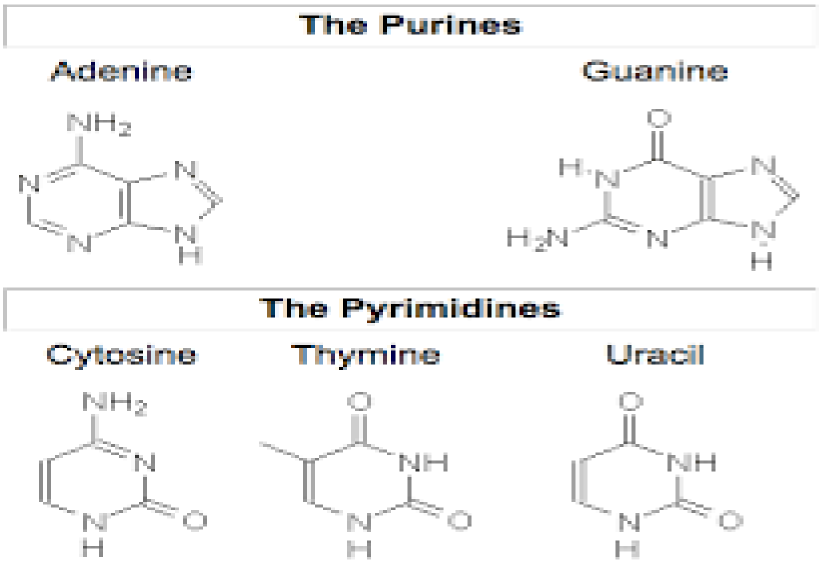
Classification of purines:

- Oxypurines or hydroxy purines(those having the hydroxyl group. Eg.,uric acid,xanthine and its bases.
- Aminopurines(those having the amino group eg.,adenine,guanine)

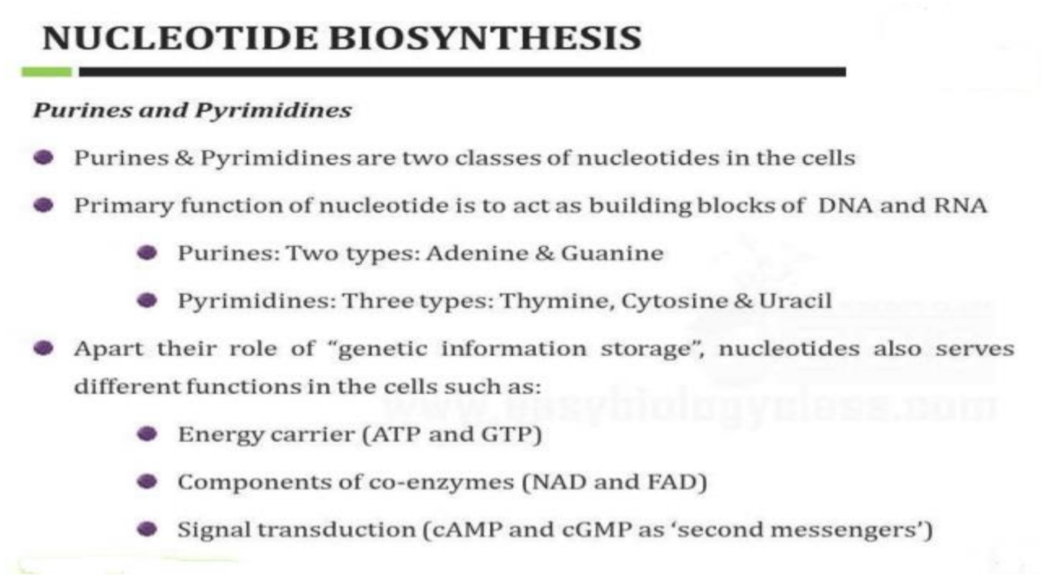


Differences between pyrimidines and purines

Pyrimidines	Purines
These are single ring (six member)compounds.	These are double ring (nine member)compounds.
They are of three types, viz., cytosine, thymine and uracil.	They are of two types, viz., adenine and guanine.
They occupy less space in DNA structure.	They occupy more space in DNA structure.
Deoxyribose is linked at position 3 of pyrimidine.	Deoxyribose is linked at position 9 of purine.



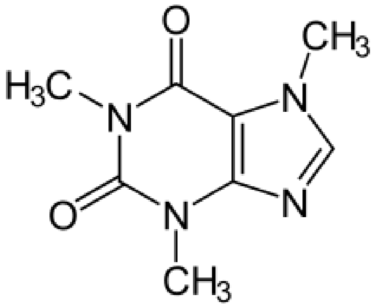
BIOLOGICAL IMPORTANCE:

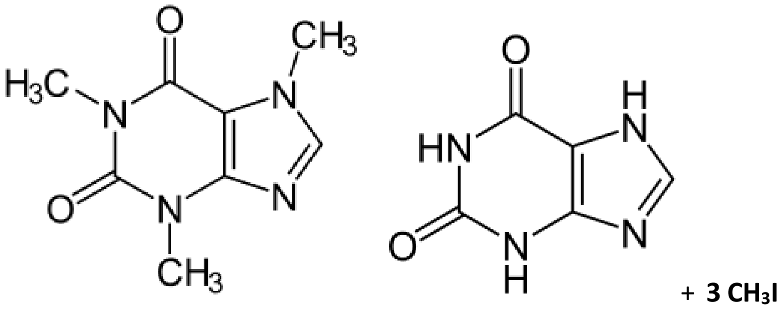


NUCLEOTIDE BIOSYNTHESIS

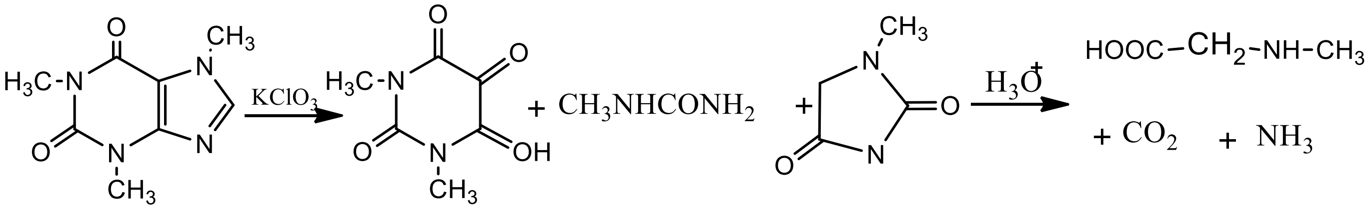
Purines and Pyrimidines

- Purines & Pyrimidines are two classes of nucleotides in the cells
- Primary function of nucleotide is to act as building blocks of DNA and RNA
  - Purines: Two types: Adenine & Guanine
  - Pyrimidines: Three types: Thymine, Cytosine & Uracil
- Apart their role of "genetic information storage", nucleotides also serves different functions in the cells such as:
  - Energy carrier (ATP and GTP)
  - Components of co-enzymes (NAD and FAD)
  - Signal transduction (cAMP and cGMP as 'second messengers')

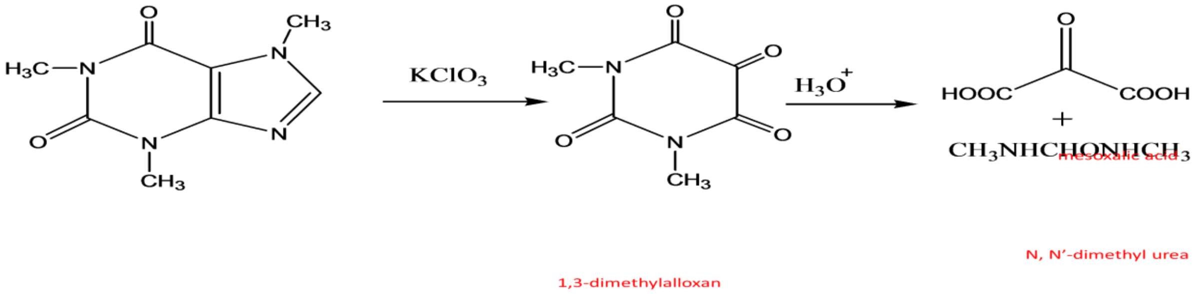
- **Caffeine**
- **STRUCTURE:**
- 
- **CONSTITUTION:**
- when subjected to *Herzig Meyer's* method of N-methyl determination gives 3 moles of methyl iodide and xanthine, indicating the presence of 3-N-methyl groups.

- 

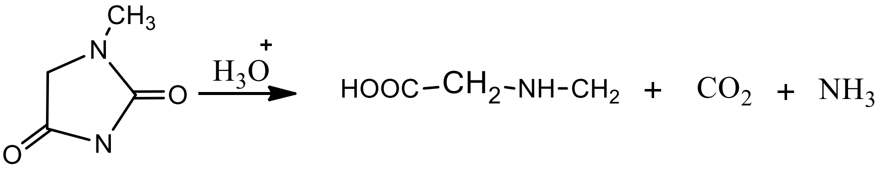
- Caffeine when oxidized with potassium chlorate in hydrochloric acid solution, yielded equimolar amounts of 1,3-dimethylalloxan**,** monomethyl urea, and N-methylhydantoin

- 

1,3-Dimethyl alloxan on further hydrolysis gave N, N'-dimethyl urea and mesoxalic acid.



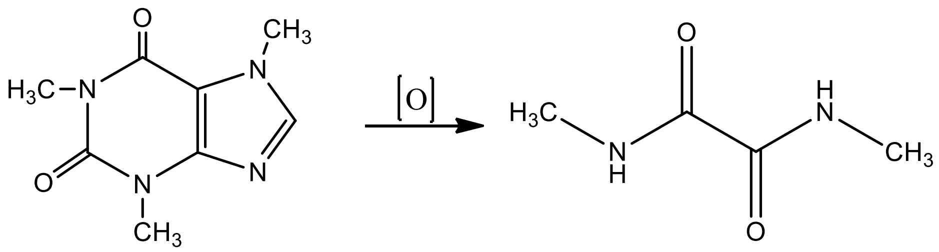
- N-methylhydantoin on hydrolysis afforded N-methyl glycine together with CO_2 and ammonia.



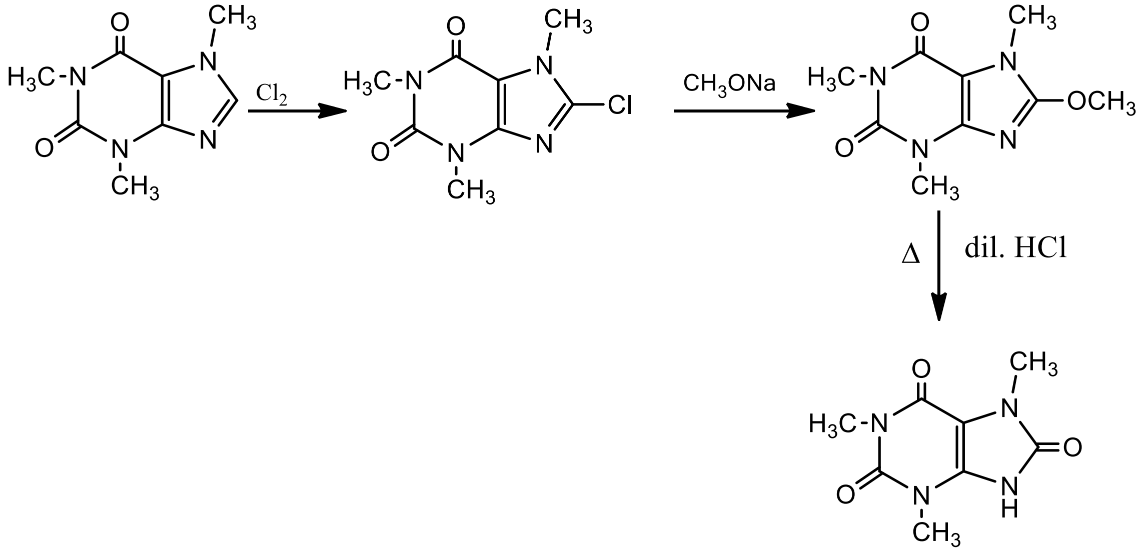
- The formation of 1,3-dimethyl-alloxan indicated the presence of pyrimidine ring containing two methyl groups. Similarly formation of N-methylhydantoin revealed the presence of imidazole ring with one N-methyl substituent.

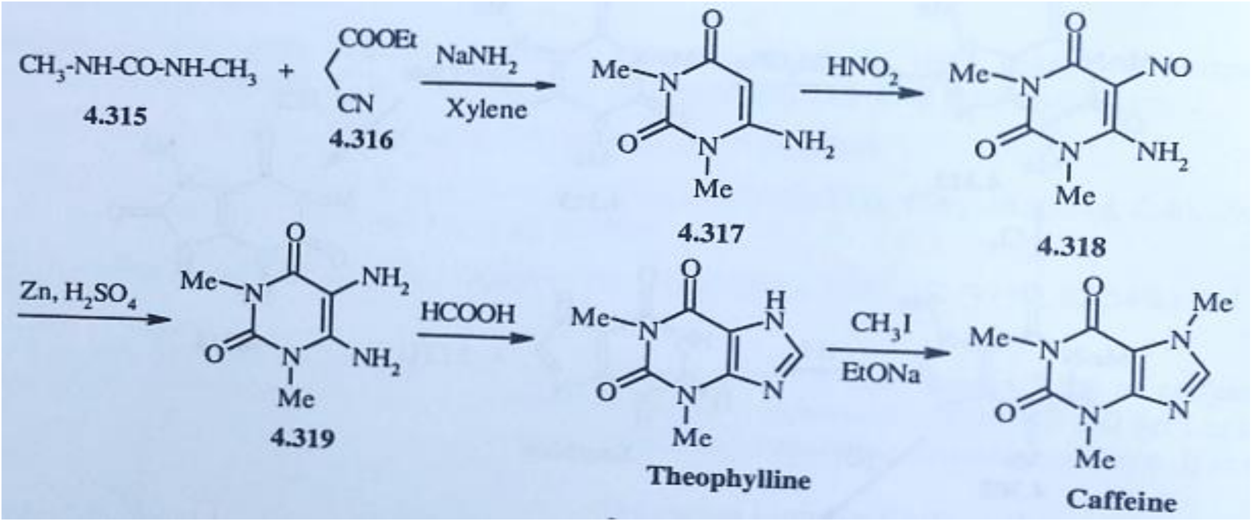
- Thus oxidation studies established the position of two methyl groups at 1 and 3 positions of xanthine skeleton of caffeine.

- The position of third methyl group, which may be at 7 or 9, was fixed from further oxidativedegradation.

- 

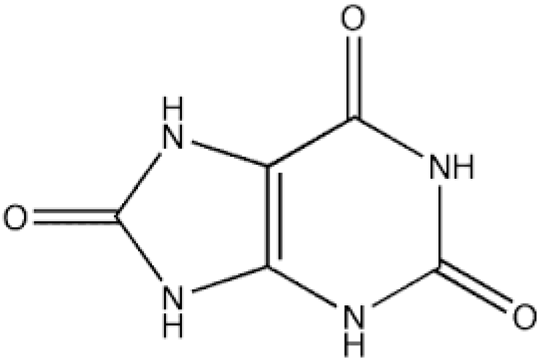
- Caffeine on chlorination gave chloro-caffeine, which on nucleophilic displacement with methoxide ion yielded methoxycaffine the hydrolysis of the latter compound yields oxycaffeine.

- 

- The structure of caffeine was further confirmed by total synthesis. Traube synthesized caffeine starting from N, N’-dimethyllurea and ethylcyanoacetate.
- 

- The condensation of N, N’-dimethylurea 4.315 with ethyl cyanoacetate 4.316 in the presence of sodamide yields 4-amino-1,3-dimethyl-uracil 4.317, which on treatment with nitrous acid followed by reduction of the resulting compound 4.318 in the presence of zinc/acid gave 1,3-dimethy -4.5-diaminouracil 4.319 The latter compound on treatment with formic acid underwent ring cyclization to yield theophylline. N-Methylation of theophylline yielded caffeine. (Book; Chemistry of Natural Products- Bhat.)
- **URIC ACID:**

STRUCTURE:

- 
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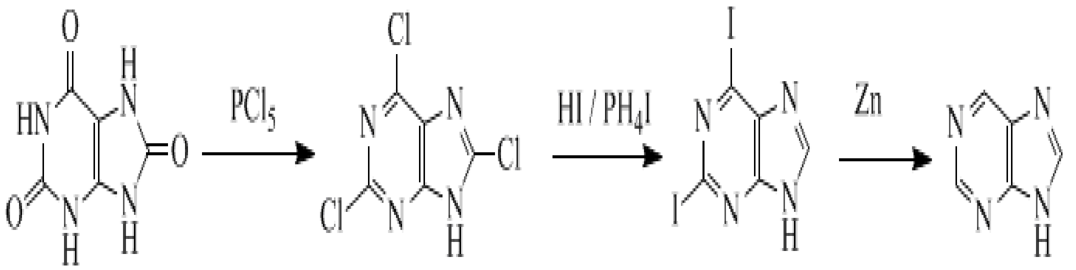


8 uric acid

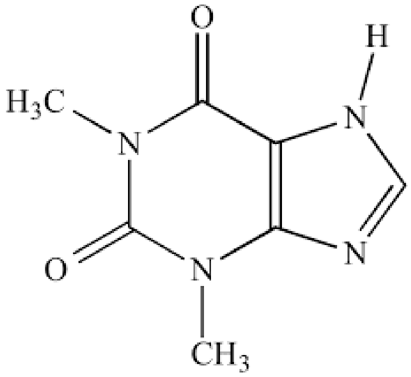
10

11

1 purine

XANTHINE

STRUCTURE:



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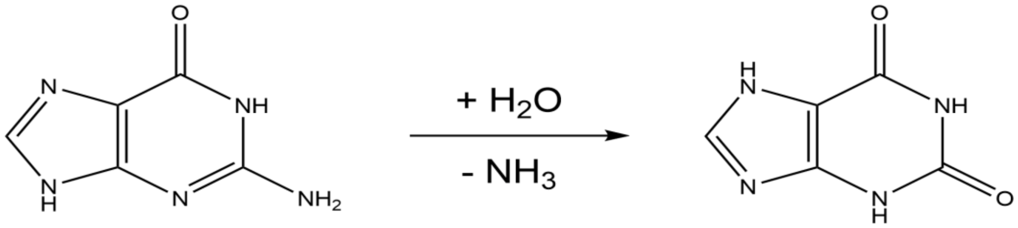


- PYRIMIDINES:

URACIL:

Uracil is one of the five main nucleobases found in the nucleic acids DNA and RNA. The others are adenine, cytosine, guanine, and thymine.

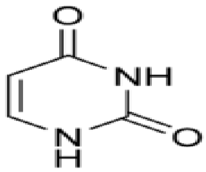
However, while the other four are found in DNA, Uracil is usually only found in RNA. Uracil (U), thymine (T), and cytosine (C) are pyrimidine derivatives, and guanine (G) and adenine (A) are purine derivatives.

In DNA, thymine and cytosine form hydrogen bonds with their complementary purine derivatives, adenine and cytosine, respectively.

In RNA, uracil replaces thymine as the usual complement of adenine. Thus, thymine is usually seen only in DNA and uracil only in RNA. Methylation of uracil produces thymine, providing a mechanism for repair and protection of DNA and improvement of DNA replication.

One of the common mutations of DNA involves two adjacent thymines.

STRUCTURE:



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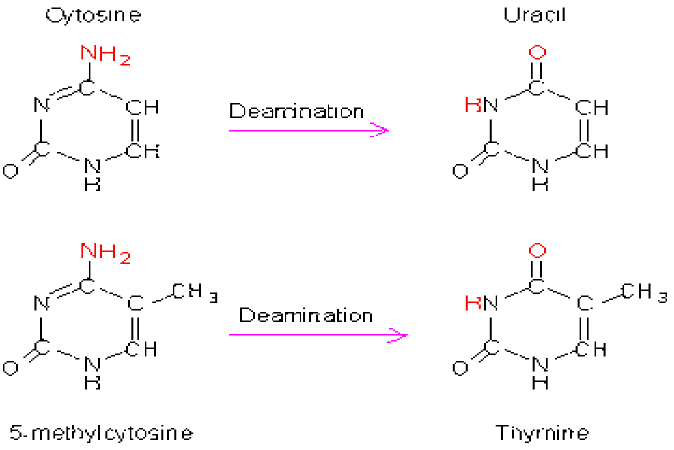
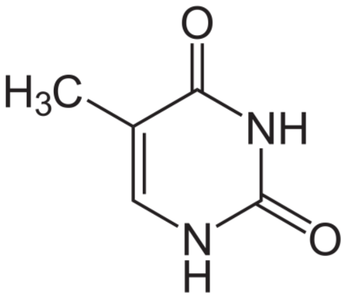


THYMINE:

STRUCTURE:



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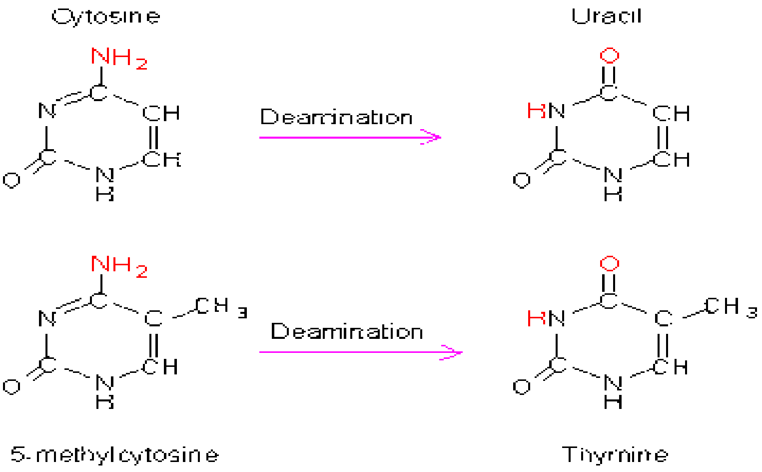


UNIT-4-Anthocyanins-SCY1615

Anthocyanins: Introduction to anthocyanins - Structure and general methods of synthesis of anthocyanins - Cyanidine chloride: structure and determination – Flavones and Isoflavones: Structure and determination of flavone and flavonoids - Quercetin: Structure determination and importance.

Anthocyanins:

Anthocyanins are members of the flavonoid group of phytochemicals, which is a group predominant in teas, honey, wines, fruits, vegetables, nuts, olive oil, cocoa and cereals.

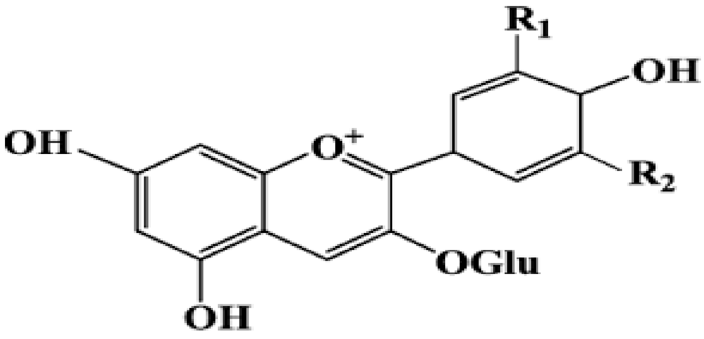
- The flavonoids are thought to be perhaps the most important single group of phenolics in food.
- The primary players in the flavonoid group include:
- Anthocyanins (cyaniding, pelargonidin, petunidin) Flavanols (quercetin, Kaempferol)
- Flavones (luteolin, apigenin)
- Flavanones (myricetin, naringin, hesperetin, naringenin)
- Flavan-3-ols (catechin, epicatechin, gallocatechin)
- Isoflavones (genistein, daidzein)

Phytochemicals in this group (flavonoids) are frequently referred to as bioflavonoids due to their multifaceted More on Anthocyanins roles in human health.

Where it will be found?

Anthocyanins can be found in berries (e.g. black currant, elderberries, blueberries, and strawberries), their juices, as well as red wine.

Structure of Anthocyanins:

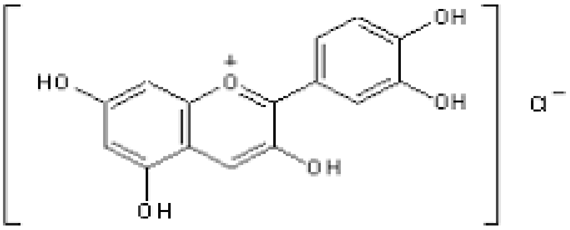


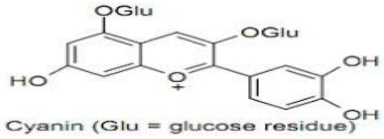
Cyanidine chloride:

Structure:

- Cyanidin is a natural organic compounds. It is a particular type of anthocyanidin (glycoside version called anthocyanins).
- It is a pigment found in many red berries including grapes, bilberry, blackberry, blueberry, cherry, cranberry, elderberry, hawthorn, loganberry, a çai berry and raspberry.
- It can also be found in other fruits such as apples and plums, and in red cabbage and red onion.
- It has a characteristic reddish-purple color, though this can change with pH; solutions of the compound are red at pH < 3, violet at pH 7-8, and blue at pH > 11.

In certain fruits, the highest concentrations of cyanidin are found in the seeds and skin.





Cyanin (Glu = glucose residue)

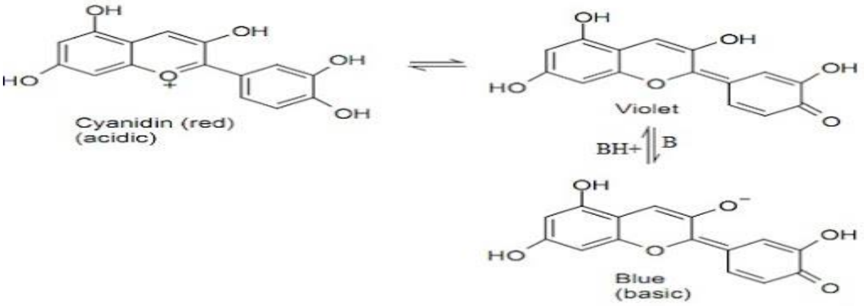
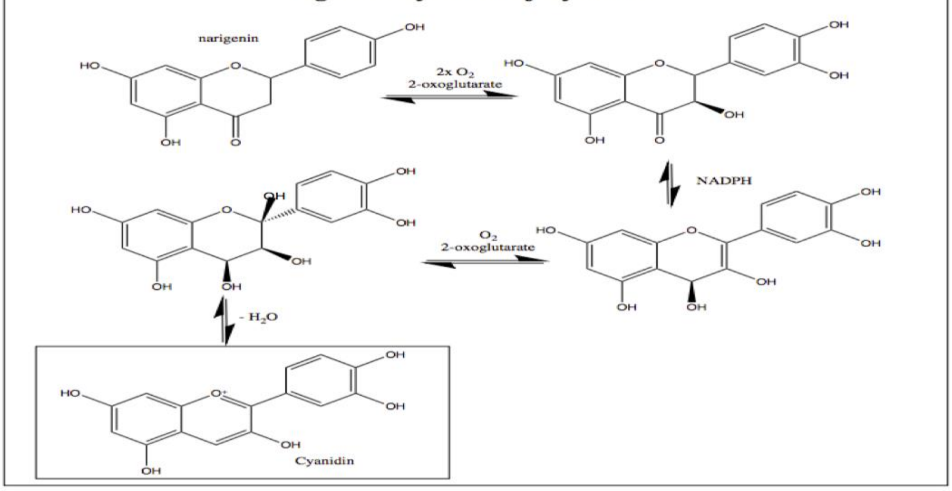


Figure 3: Synthesis of Cyanidin



Flavonoids:

Flavonoids in the broad sense of the term are virtually universal plant pigments. Almost always water-soluble, they are responsible for the color of flowers, fruits, and sometimes leaves. Examples are yellow flavonoids (chalcones, aurones, and yellow flovonols) and red, blue, or purple anthocyanins. When they are not directly visible, they contribute to the color by acting as copigments : for example, colorless flavone and flavonol copigments protect anthocyanins. All flavonoids – approximately 4000- have a common biosynthetic origin, and therefore possess the same basic structural element, namely the 2-phenylchromane skleton.

CHEMICAL STRUCTURE AND CLASSIFICATION All flavonids contain mostly a OH, OCH_3 , or O-gl at the 5,7 and 4’ positions. A flavonol always contains a substituent on the 3. position. Flavanones are characterized by the absence of 2,3 double bond. CGlycosylflavonoids are not rare. The bond is established between the asymmetric carbon on the sugar, and the C-6 or C-8 of the aglicone

Characterization

Although several color reactions allow the characterization of aglycones and glycosides in crude extracts, preliminary work on these extracts is conventionally dominated by TLC analysis.

- directly, since chalcones and aurones are usually visible, and turn orange and red respectively, in the presence of ammonia vapors;

- by examination under UV light before and after spraying with aluminium trichloride, or before and after exposure to ammonia vapors;

- after spraying with a 1% solution of the ester of 2-aminoethanol and diphenylboric acid, in other words the «Naturstoff Reagenz A (NA)»by examination under UV light;

- after spraying with ferric chloride, anisaldehyde, diazotized sulfanilic acid or other general reagents for phenols;

- by utilizing more or less specific reactions or properties, such as : - Reaction known as cyanidin (or Shibata) reaction, with magnesium powder, or with zinc (Shinoda) both in the presence of hydrochloric acid.

Flavones → Flavonols → ,

Flavanones → colors.

Structure elucidation : especially UV and NMR techniques are very useful..

Flavonols

Flavonols have a 3-hydroxyflavone structure, and are unstable to light as they undergo photooxidation resulting in fading or formation of darker colors.

This can explain why onions (Allium cepa) and marigolds (Tagetes spp.)

which are rich in flavonols, are highly colored.

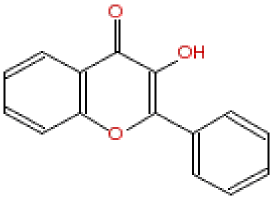
Flavonols are present in a wide variety of fruits and vegetables and find many applications in the dye and pharmaceutical industries.62 Flavonols benefit human health by displaying antioxidant and anti-carcinogenic properties, and protecting against coronary heart disease.

Quercetin, kaempferol, myricetin and isorhamnetin are commonly found flavonols.63 Dorsmanin C, isolated from the plant Dorstenia mannii (Moraceae), has antioxidant properties.

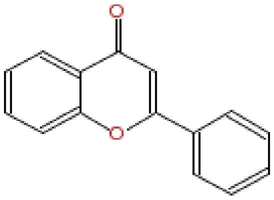
Isoflavones and isoflavonones

These are naturally occurring compounds generally acting as phytoestrogens in humans. These are produced almost exclusively by the Fabaceae family (Leguminosae). Isoflavones differ from flavones (2-phenyl-4H-1-benzopyr-4-one) in the location of the phenyl group.

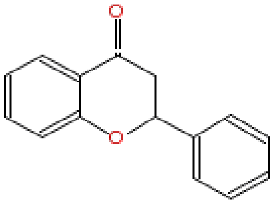
Isoflavones are major products in soy. Soy products contains diadzen, genistein and glycitein, their respective β-glycosides and their respective acetyl glycosides. Irigenin (glycitein , 8-hydroxyglycitein and licoisoflavone have been extracted from Nicotiana tabacum. Genistein has been isolated from the Bolusanthus speciosus (Fabaceae), Ficus chlamydocarpa (Moraceae), Erythrina latissima (Fabaceae), E. indica (Fabaceae), and exhibits antimicrobial activity. Griffonianone D from Millettia griffoniana exhibits cytotoxic activity, enzyme inhibition, estrogenic properties and anti-inflammatory activity.



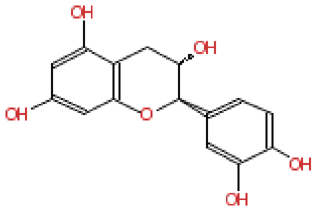
Flavonol



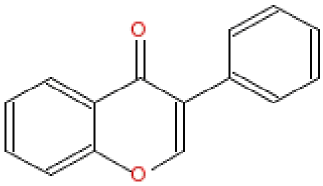
Flavone



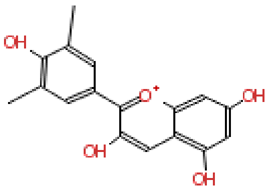
Flavanone



Flavanol (Catechins)



Isoflavone



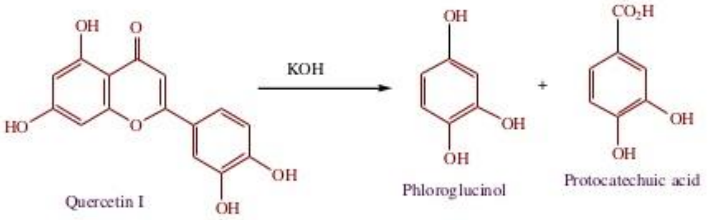
Anthocyanidine

Elucidation of Quercetin

- Widely distributed pigments occurs as rhamnosides (quercitine) in the bark of Quercus tinctoria.

$$\boxed{\text{Quercitine}} \xrightarrow{\text{HCl}} \boxed{\text{Rhamnose}} + \boxed{\text{Quercitin}}$$

- Mol formula is $C_{15}H_{10}O_7$
- It was found to contain **four hydroxyl** groups as it forms penta-acetyl and pentamethyl group.
- On fusion with KOH, it gives Phloroglucinol + protocatechuic acid- it indicates that quercetine is 5,7,3',4' – tetrahydroxy flavonol .

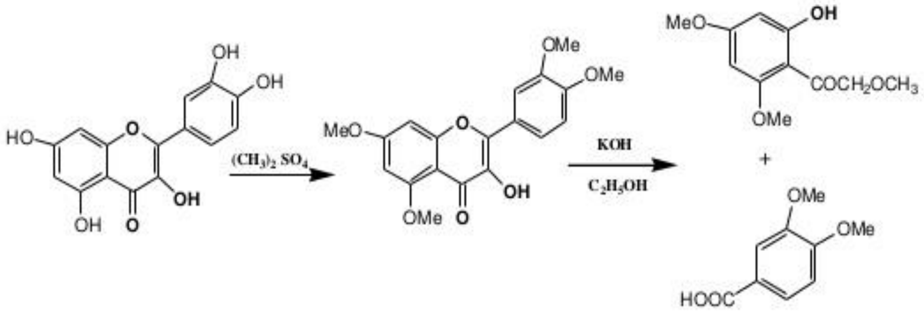


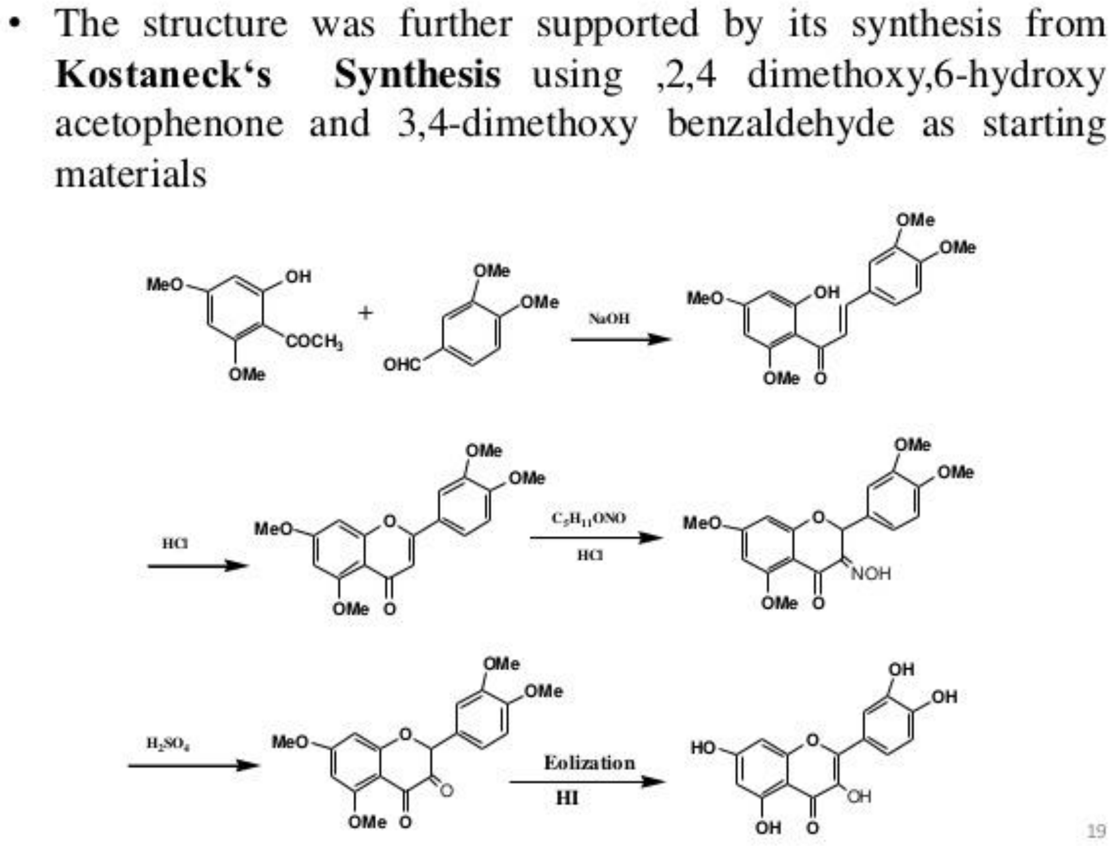
Quercetin I

Phloroglucinol

Protocatechuic acid

- The structure was further supported by the fact that on boiling with alcoholic potash pentamethyl quercetin gives 6-OH, ω,2,4-trimethyl acetophenone and veratric acid.





- The structure was further supported by its synthesis from **Kostaneck‘s Synthesis** using ,2,4 dimethoxy,6-hydroxy acetophenone and 3,4-dimethoxy benzaldehyde as starting materials

IMPORTANCE:

- Quercetin is a flavonoid with antioxidant properties.
- The ability of quercetin is claimed to exert many beneficial effects on health, including protection against various diseases such as osteoporosis, lung cancer, and cardiovascular disease.

UNIT-5-Harmones and Vitamins

Hormones: Introduction - Difference between hormones and vitamins. Classification - Structure and functions of steroid hormones: Androsterone - Progesterone - Testosterone – Estrone . Adrenocortical hormones: Cortisone. Vitamins: Structure and importance of Vitamin D - Folic acid – Nicotinamide .

Harmones

Hormones are chemical messengers that are secreted directly into the blood, which carries them to organs and tissues of the body to exert their functions.

There are many types of hormones that act on different aspects of bodily functions and processes. Some of these include:

- Development and growth
- Metabolism of food items
- Sexual function and reproductive growth and health
- Cognitive function and mood
- Maintenance of body temperature and thirst

Where are they secreted from?

- Hormones are secreted from the endocrine glands in the body.
- Pituitary gland
- Pineal gland
- Thymus
- Thyroid
- Adrenal glands
- Pancreas
- Testes
- Ovaries

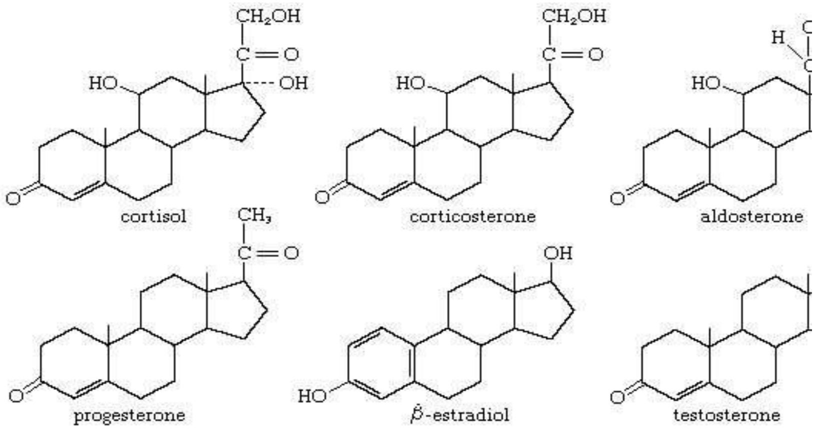
Vitamin:

- 1. Vitamins are synthesized in plants and taken by animals cheifle through diet.
- 2. Chemically these are various compounds like esters, organic acids, etc.
- 3. Mostly these are coenzymes or a constituents of coenzymes.
- 4. Vitamins have catalyc action.
- 5. Their deficiency causes specific deficiency disease(symptom).

Hormone:

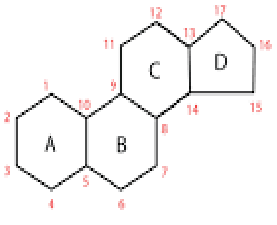
- 1. Hormones are secreted mostly by endrocrine glands and some by neurosecretory cells of animals.
- 2. These are water soluble amino acids and polypeptides or fat soluble steroids.
- 3. Mostly these are excitatory, sometimes inhibitory but never act as coenzyme.
- 4. Hormones directly influence gene expressions.
- 5. Deficiency causes metabolic disorder.

Classification of steroid hormones:

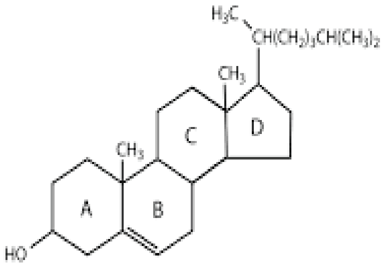


Steroid hormone,

- any of a group of hormones that belong to the class of chemical compounds known as steroids;
- they are secreted by three "steroid glands"—the adrenal cortex, testes, and ovaries—and during pregnancy by the placenta.
- All steroid hormones are derived from cholesterol.
- They are transported through the bloodstream to the cells of various target organs where they carry out the regulation of a wide range of physiological functions.



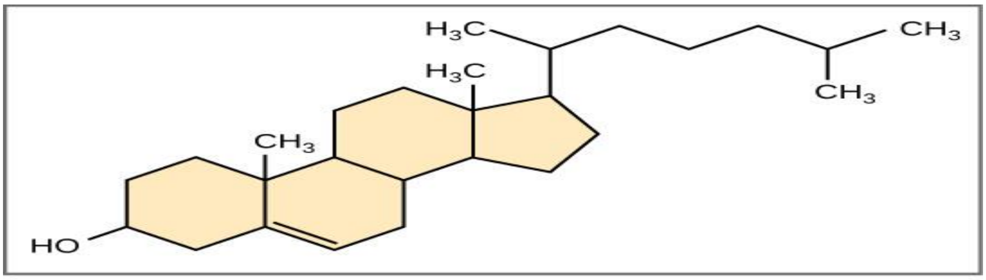
(a) Steroid skeleton



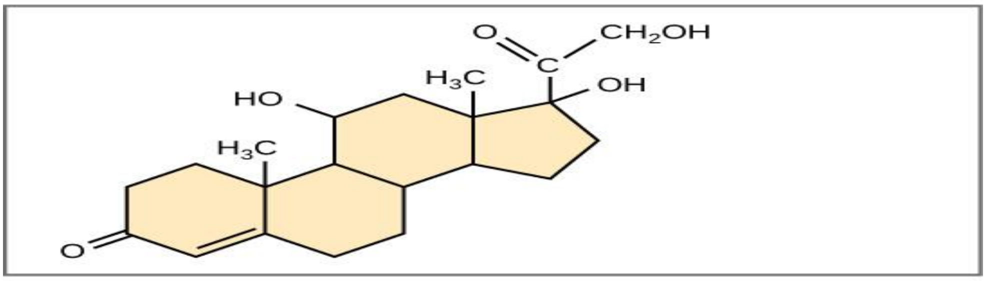
(b) Cholesterol

Structure of Steroid Molecules

- Unlike phospholipids and fats, steroids have a fused ring structure.
- Although they do not resemble the other lipids, they are grouped with them because they are also hydrophobic and insoluble in water.
- All steroids have four linked carbon rings, and many of them, like cholesterol, have a short tail.
- Many steroids also have the –OH functional group, and these steroids are classified as alcohols called sterols



Cholesterol



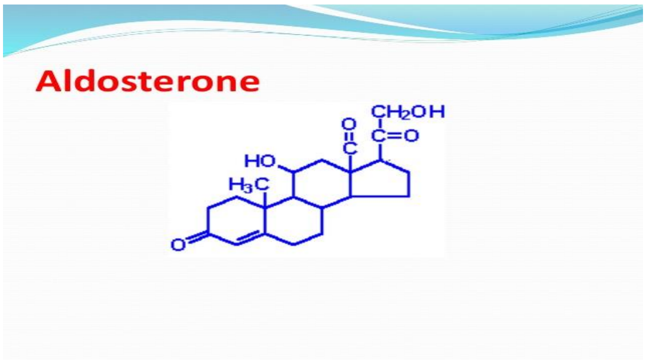
Cortisol

- Cholesterol is the most common steroid and is mainly synthesized in the liver; it is the precursor to vitamin D.
- Cholesterol is also a precursor to many important steroid hormones like estrogen, testosterone, and progesterone, which are secreted by the gonads and endocrine glands.
- Therefore, steroids play very important roles in the body's reproductive system.
- Cholesterol also plays a role in synthesizing the steroid hormones aldosterone, which is used for osmoregulation, and cortisol, which plays a role in metabolism.
- Cholesterol is also the precursor to bile salts, which help in the emulsification of fats and their absorption by cells.
- It is a component of the plasma membrane of animal cells and the phospholipid bilayer.
- Being the outermost structure in animal cells, the plasma membrane is responsible for the transport of materials and cellular recognition; and it is involved in cell-to-cell communication.

Thus, steroids also play an important role in the structure and function of membranes.

- It has also been discovered that steroids can be active in the brain where they affect the nervous system, These neurosteroids alter electrical activity in the brain.
- They can either activate or tone down receptors that communicate messages from neurotransmitters.
- Since these neurosteroids can tone down receptors and decrease brain activity, steroids are often used in anesthetic medicines.

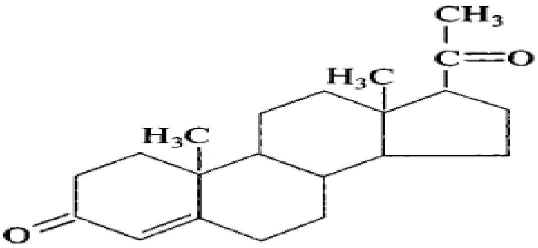
Aldosterone



Aldosterone

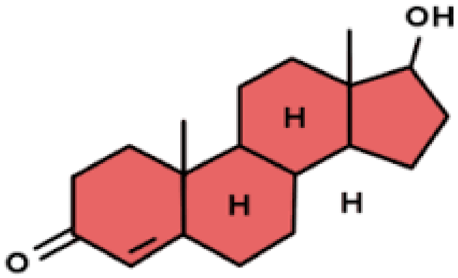
- a steroid hormone secreted by the adrenal glands.
- Aldosterone serves as the principal regulator of the salt and water balance of the body and thus is categorized as a mineralocorticoid.
- It also has a small effect on the metabolism of fats, carbohydrates, and proteins.
- Adrenal glands, also known as suprarenal glands.
- The primary mineralocorticoid is aldosterone.
- Mineralocorticoids are produced in the adrenal cortex and influence salt and water balances (electrolyte balance and fluid balance).
- Aldosterone is synthesized in the body from corticosterone, a steroid derived from cholesterol.
- Production of aldosterone (in adult humans, about 20–200 micrograms per day) in the zona glomerulosa of the adrenal cortex is regulated by the renin-angiotensin system.
- Renin is secreted from the kidneys in response to variations in blood pressure and volume and plasma sodium and potassium levels.
- **Renin** (etymology and pronunciation), also known as an angiotensinogenase.
- Renin acts on a protein circulating in the plasma called angiotensinogen, cleaving this substance into angiotensin I.
- Angiotensin I is subsequently converted to angiotensin II, which stimulates the release of aldosterone from the adrenal glands.

Progesterone



Testosterone

- Testosterone is the hormone responsible for the development of male sexual characteristics.
- Hormones are chemical messengers Source that trigger necessary changes in the body.
- Females also produce testosterone, usually in smaller amounts.



TESTOSTERONE

It is a type of androgen produced primarily by the testicles in cells called the Leydig cells.

In men, testosterone is thought to regulate a number of functions alongside sperm production. These include:

- sex drive
- bone mass
- fat distribution
- muscle size and strength
- red blood cell production
- Without adequate amounts of testosterone, men become infertile.
- This is because testosterone assists the development of mature sperm.
- Despite being a male sex hormone, testosterone also contributes to sex drive, bone density, and muscle strength in women.
- However, an excess of testosterone can also cause women to experience male pattern baldness and infertility.
- The brain and pituitary gland control testosterone levels.
- Once produced, the hormone moves through the blood to carry out its various important functions.

Testosterone imbalances

High or low levels of testosterone can lead to dysfunction in the parts of the body normally regulated by the hormone.

When a man has low testosterone, or hypogonadism, he may experience:

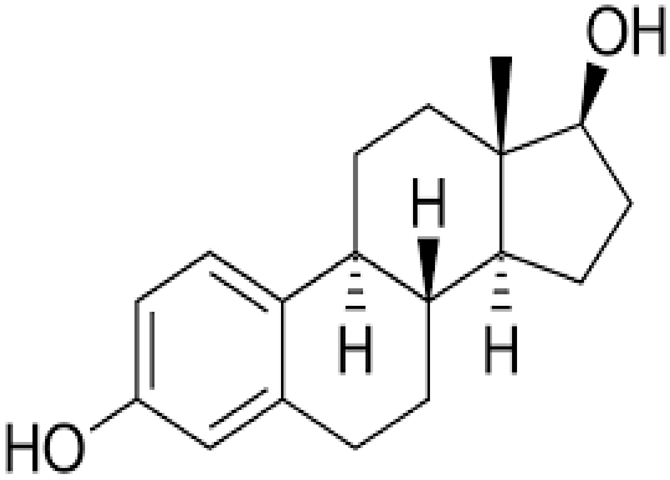
- reduced sex drive
- erectile dysfunction
- low sperm count

enlarged or swollen breast tissue

estrone

- ▶ Estrogen is a hormone that plays various roles in the body.

- In females, it helps develop and maintain both the reproductive system and female characteristics, such as breasts and pubic hair.
- Estrogen contributes to the , bone health, the function of the cardiovascular , and other essential bodily processes.
- The ovaries, adrenal glands, and fat tissues produce estrogen. Both female and male bodies have this hormone, but females create more of it.



Types of estrogen:

- There are different types of estrogen:

  Estrone

- This type of estrogen is present in the body after menopause. It is a weaker form of estrogen and one that the body can convert to other forms of estrogen, as necessary.

  Estradiol

- Both males and females produce estradiol, and it is the most common type of estrogen in females during their reproductive years.
- Too much estradiol may result in acne, loss of sex drive, osteoporosis, and depression. Very high levels can increase the risk of uterine and breast cancer. However, low levels can result in weight gain and cardiovascular disease.

Estriol

- Levels of estriol rise during pregnancy, as it helps the uterus grow and prepares the body for delivery. Estriol levels peak just before birth.

Function:

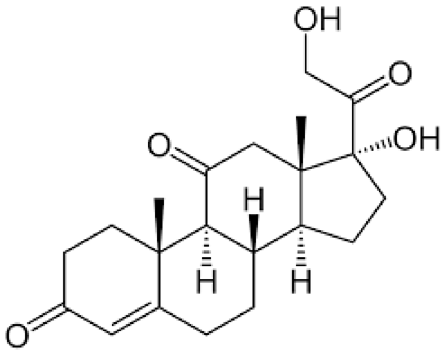
- Estrogen enables the following organs to function:
- **Ovaries:** Estrogen helps to stimulates the growth of the egg follicle.
- **Vagina:** In the vagina, estrogen maintain the thickness source of the vaginal wall and promotes lubrication.

- **Uterus:** Estrogen enhances and maintains the mucous membrane that lines the uterus. It also regulates the flow and thickness of uterine mucus secretions.
- **Breasts:** The body uses estrogen in the formation of breast tissue. This hormone also helps stop the flow of milk after weaning.

Adrenocortical harmones:

The **adrenocortical hormones** are steroid molecules produced and released by the **adrenal** cortex.
The **adrenal** cortex synthesizes two types of steroids: the corticosteroids, and the androgens.

Cortisone:



uses

- It is used as an anti-inflammatory medication. Hydrocortisone relieves inflammation in various parts of the body.
- Cortisone is used to treat or prevent allergic reactions.
- Cortisone is used as treatment of certain kinds of autoimmune diseases, skin conditions, asthma and other lung conditions.
- Cortisone is used as treatment for a variety of cancers, such as leukemia, lymphoma, and multiple myeloma.
- Cortisone is used to treat nausea and vomiting associated with some chemotherapy drugs.
- Cortisone is used to stimulate appetite in cancer patients with severe appetite problems.
- The lotion (topical) is used in treatment of allergic skin reactions, and relieves symptoms of itching, redness, and swelling.
- Cortisone is also used to replace steroids in conditions of adrenal insufficiency (low production of needed steroids produced by the adrenal glands).

- **How Cortisone Works**:
- Corticosteroids are naturally produced by the adrenal gland in the body. Corticosteroids influence the functioning of most of the body's systems (heart, immune, muscles and bones, endocrine and nervous system). They exert a wide array of effects including effects on the metabolism of carbohydrates, protein and fats. They help to maintain balance of fluids and electrolytes.
- Hydrocortisone is classified as a corticosteroid (more precisely a glucocorticosteroid), and has many uses in the treatment of cancer.
- One way that it works is to decrease inflammation (swelling). It does this by preventing infection-fighting white blood cells (polymorphonuclear leukocytes) from traveling to the area of swelling in your body. (This is why you are more prone to infection while taking steroids). Taking advantage of the anti-inflammatory properties of the medication, corticosteroids are used to decrease the swelling around tumors. For example, by decreasing swelling around tumors in the spine, brain, or bone, it can decrease

the pressure of the tumor on nerve endings and relieve pain or other symptoms caused by the pressing tumor.

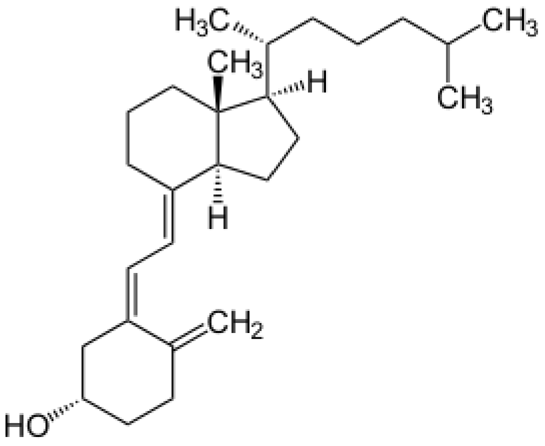
- Another way Cortisone works is by altering the body's normal immune system responses.
- In addition, it is thought that corticosteroids may help in the treatment of patients with blood disorders, such as multiple myeloma. Corticosteroids may work by causing programmed cell death (apoptosis) of certain cells, which may help to fight your disease.
- Corticosteroids are also used in the short-term treatment of nausea caused by chemotherapy. How it does this is not fully understood. They also have been used to stimulate appetite for patients with severe appetite problems.

Vitamins:

- Nutrients that our body does not make on its own. Thus we must obtain them from the foods we eat, or via vitamin supplements. They are essential for providing good health and are necessary for many life functions.

- Defn: synthetic or natural substances which can be purchased as pills, tablets, capsules, wafers, powders, or liquids.

Structure and importance of Vitamin D



Importance :

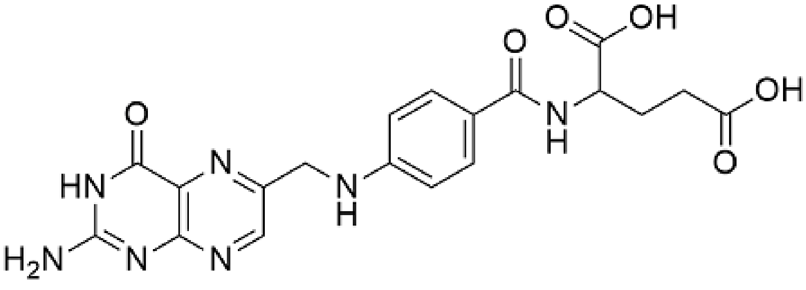
vitamin D has multiple roles in the body.

It assists in:

- promoting healthy bones and teeth
- supporting immune, brain, and nervous system health
- regulating insulin levels and supporting diabetes management
- supporting lung function and cardiovascular health
- influencing the expression of genes involved in cancer development

Folic acid:

structure:



Folic acid

Importance:

Folate is important for a range of functions in the body.

It helps the body make healthy new red blood cells, for example. Red blood cells carry oxygen throughout the body. If the body does not make enough of these, a person can develop anemia, leading to fatigue, weakness, and a pale complexion. Without enough folate, a person can also develop a type of anemia called folate deficiency anemia.

Folate is also important for the synthesis and repair of DNA and other genetic material, and it is necessary for cells to divide.

It is particularly important to get enough folate during pregnancy. Folate deficiency during pregnancy can lead to neural tube irregularities, such as spina bifida and anencephaly.

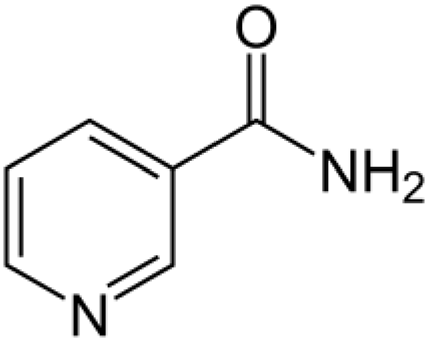
Because of its importance for health, the Food and Drug Administration (FDA) require manufacturers to add folic acid to enriched bread, pasta, rice, cereals, and other grain products in the United States. Since they introduced this, the number of babies born with neural tube irregularities has decreased.

Structure and importance of nicotinamide:

- The vitamin activity of niacin is provided by both nicotinic acid and nicotinamide.

Structurally, nicotinic acid is pyridine 3-carboxylic acid, whereas nicotinamide is nicotinic acid amide.

Structure :



Importance:

Niacin is one of the eight B vitamins, and it's also called vitamin B3.There are two main chemical forms and each has different effects on your body. Both forms are found in foods as well as supplements.

- Nicotinic acid: As a supplement, nicotinic acid is a form of niacin used to and lower your risk of heart disease.
- Niacinamide or nicotinamide: Unlike nicotinic acid, niacinamide doesn't lower cholesterol. However, it may help treat psoriasis and reduce your risk of non-melanoma skin cancer. Niacin iswater soluble, so your body doesn't store it. This also means that your body can excrete excess amounts of the vitamin if it's not needed.
- Niacin, also known as vitamin B3, is an important nutrient. In fact, every part of your body needs it to function properly.

As a supplement, niacin may help lower cholesterol, ease arthritis and boost brain function, among other benefits.However, it can also cause serious side effects if you take large doses. As with all B vitamins, niacin helps convert food into energy by aiding enzymes.

Reference:

o.p Agarwal.,organic chemistry chemistry of natural products

l.finar organic chemistry.,