**A Study on Biological Importance and Structural Elucidation of Vitamins- A Review**

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**ABSTRACT**

 Carbohydrates, fats and proteins are three major classes of food. To remain healthy, we must take in relatively large amounts of these substances. They are not, however, the nutrients we require, some of our needs are satisfied only by vitamins and minerals. Vitamin B1 may occur in the nature as free compound as in the form of its salts, Vitamin B1 – protein complex, pyrophosphate (co-carboxylase) and as vitamin B­1 – Phosphorus – protein complex. The relative amount of each form depends upon the source. Actually the word vitamin B6 refers to a group of three compounds, namely, pyridoxine (or) adermin, pyridoxal and pyridoxamine which are interconvertible in the form of their phosphates but as pyridoxine is the first member of this group it is alone also known as vitamin B6 as the vitamin is antidermatitic factor for rats, it is also known as adermin. Biotin is a heterocyclic sulfur containing monocarboxylic acid, the structure is formed by fusion of imidazole and thiophene rings. Biotin is covalently bound to €-amino groups of lysine to form biocytin in the enzymes. β - Biotin occurs mainly in combined forms bound to protein through the ∑-N-lysine moiety. To avoid deficiency and its causes there is a need of the study of its significance and structure.

**Keywords**: Vitamins, Classification, structural elucidation, Vit B1, B6, H

1. **GENERAL INTRODUCTION TO VITAMINS**

The term “vitamin” refers to an essential dietary factor that is required by an organism in small amounts and whose absence result in deficiency diseases,

1. Vitamins are the organic compounds which are required by animals, some bacteria and micro-organisms for the maintenance and normal growth of life, as they can’t be synthesized by them except vitamins D.
2. The role of vitamins in animal body is not definitely established, vitamins are not the building blocks of the animals body also they are not the source of energy. However certain vitamins become part of the enzyme systems which are actively involved in enzyme action.
3. However, vitamin D may be supplied in food or may be produced in the skin by irradiation (UV) of sterols. The metabolic functions of vitamins are the same for all the organisms, plants and most microbes can synthesize these compounds essential for normal cellular functioning. The bacterium E. coli can synthesize all them.
4. In general, the fresh and natural food contains all the necessary vitamins in appropriate amount, but as the human being and other animals take food which is prepared by some processes which result in the loss or deficiency of some vitamins in the food. The deficiency of a particular vitamins causes a specific disease (deficiency disease or avitaminosis) which can only be cured by the intake of that vitamin.[1]

**I.A. Discovery of vitamins**

In 1912, funk found that there are some compounds in the food which prevent beriberi, scurvy, pellagra, rickets etc, according to him all compounds contain nitrogen and thus due to their function and basic nature, he called such compounds as ‘vitamine’ (L, vita, life + amine) but later on it was found that all such other compounds do not contain nitrogen and therefore the term vitamine was modified to vitamin. [1]

**I.B Nomenclature of vitamins**

Vitamins are designated by alphabets like A, B, C, D, E in order of their discovery. furthermore, the subgroup of an individual vitamins is designated by the subscripts (e.g.: A1, A2, B1, B2, B3, B6, B12, D1, D2)

**I.C Classification of vitamins**

The vitamins are broadly divided into two categories depending on their solubility.

**I.C.1-Fat soluble vitamins:** this type includes vitamins A, D, E and K.

**1.C.2-Water soluble vitamins:** This type includes rest of vitamins like vitamins of B group, vitamins C etc.

However, vitamin H (biotin) is an exception as it is insoluble both in fat and in water.[2]

**Fat soluble vitamins**

**I.C.1.1 Vitamin A (A­1)**

Vitamin A or A1 also called as retinol or axerophthol, the IUPAC name of vitamin A or A1 is retinol; that of the corresponding aldehyde is retinol (retinene, retinene); and that of the corresponding acid is retinoic acid.

**Occurrence**

The most important source of vitamin A1 are fish like other source are butter, blood, milk, egg- yolk, sweet potatoes and sweet tomatoes.

**Structure**



**Significance**

 Vitamins A is required for the normal eye sight and for growth of mammals. the light sensitive pigments which function in photoreceptors in the retina of the eye are synthesized in the body form vitamin A. its deficiency causes retardation of growth, dryness of the skin and hair, less resistance to infection nigh blindness is also due to the deficiency of this vitamins and in severe deficiency it leads to xerophthalmia (hardening of cornea). the normal human being requires .0007gm (5000v sp units) of the vitamins A daily.

**1.C.1.2. Vitamin A2 (retinol2)**

**Occurrence**

Vitamin A2 is found mainly in the liver of fresh water fish, while the liver of salt water fish mainly contains vitamin A1

**Structure**



**1.C.1.3 Vitamin D**

Vitamin D represents a group of fat soluble vitamins which are structurally related to sterds, upto new fine vitamins of this group have been isolated viz D1, D2,D3,D4­ and D5. in fact vitamin D1 (or) D is found to be a molecular compound of D2 and lumisterol. the later is one of the intermediate products of irradiation of ergosted

All vitamins of this group are formed by irradiation of the specific sterols. the sterds are called pro-vitamins.[3]

**Structures of Vitamins D2,D3,D4 And D­5:**









**Significance**

 The deficiency of vitamin D leads to rickets, which is a disease results soft unqualified bone which is easily deformed when stressed.

Excessive doses of vitamins D are toxic and cause calcification of other tissues besides bones, for ex, walls of blood vessels may become calcified, producing a condition known as arteriosclerosis (or) hardening of arteries.

Vitamins D is marketed in the form of viosterol which is made by irradiating ergosterol and diluting the resulting product with maize oil.[6]

**1.C.1.4. Vitamins E**

Vitamin E is the antisterility factor which is necessary for fertility of the male and the birth process of the female and therefore it is also called tocopherols, because the word ‘tokos’ in gk means ‘childbirth’ and ‘phero’ means ‘to bear’

**Occurrence**

Tocopherols are generally found in the free form mostly in the seed oils, eg α and β tocopherols occur in wheat germ oil, ϒ- tocopherol in cotton seed oil and ς tocopherol in soyabean oil. Green leaves, cereal grains and nuts are rich source.

**Structure**



**Significance**

The major symptom of vitamin E deficiency in humans is an increase in red blood cell fragility. neurological disorders have been associated with vit E deficiencies associated with fat malabsorptive disorders.

**1.C.1.5. Vitamin K**

There are 2 important vitamin K, namely K1 and K2, which are isolated form the different sources. vitamins K1 was first obtained in a pure state by dametial., (1939). and doisty etal (1939) from alfalfa and in the same year vitamin K2 was isolated by Doisy etal., (1939) from purified fish, meat etc. subsequently vitamin K2 was detected in a number of bacteria.[4]

**Occurrence**

Vitamin K1 occurs in all green leaves and vegetables e.g. carrot tops, cabbage, cauliflower, spinach etc. It is found mainly in purified fish, meats and bacteria

**Structure**





**Significance**

The vitamin K are necessary for coagulation of blood; the deficiency of them lengthens the time of blood clotting and hence these are known as antihemorrhagic vitamins. vitamin K help in blood coagulation by activating the prothrombin, the precursor of thrombin, for the formation of blood clotting enzyme.

**1.C.2 Water Soluble Vitamins**

` Included in this classification are B2, B3, and B12. Details of vitamin B1, B6, and H are given chapters II, III and IV.

**1.C.2.1 Vitamin B2 (Riboflavin)**

Originally riboflavin was named as vitamin B2. since it was first isolated from milk, it is also known as lactoflavin it is known as riboflavin as it contains the ribose residue in its molecule. on the other hand, it being the first member of the B2 complex, is also known as vitamin B2.

**Occurrence**

Vitamin B2 may occur either as a free vitamin (or) as the phosphate or as a combination with specific protein to form enzymes. The best sources of vitamin B2 are yeast, green vegetables, liver, wheat germ, egg yolk, milk , meat, fish etc. very low content of riboflavin is also found in polished rice, retina of eye and potatoes.

**Structure**



**Significance**

Vitamin B2 is necessary for growth and health in man, a deficiency in riboflavin result in

1. Inflammation of the tongue
2. Cheilosis ( cracking of the lips and corners of the mouth).

It is a growth factor in most of the animals.[5]

**1.C.2.2 Vitamins B3**

This vitamin is widely distributed mainly in a combined form with protein.

**Occurrence**

 The richest source are yeast, egg-yolk, liver and kidney followed by heart, spleen, brain, pancreas, tongue, and lung. pantothenic acid is also produced by some moulds and green plants. the name pantothenic is derived from the greek meaning “from everywhere” because this vitamin is almost of universal occurrence.

**Structure**



**Significance**

 The symptoms of pantothenic acid deficiency in man are unknown. However, it is believed that its deficiency in man may cause burning sensation, muscle weakness, abdominal disorder and general depression.

**1.C.2.3 Vitamin B12**

 Vitamin B12 ­ is found in all animal tissues and was first of all isolated in 1948 and is also called cyanocobalamin

**Occurrence**

Milk, egg, cheese and meat contain 1-5 mg/100g of the material

**Structure**



**Significance**

 The deficiency causes pernicious anaemia which is accompanied by degradation of the spinal card, this disease is not simply due to the absence of vit B12 in dict because it has been seen that a secretien from the stomach ‘intrinsic factor’ is essential for the assimilation of vitamin B12.

Some of the vital vitamins structure elucidation is reviewed as follows,

**II. Vitamin B1**

**II.A. Biological importance of vitamin B1 (Thiamine)**

1. Vitamin B­1 deficiency in human being causes loss of appetite, gastrointestinal disturbances, muscular weakness, pain in arms and legs and decrease of the blood pressure.
2. In severe cases the entire nervous system is affected and birds. The deficiency of this vitamin lead to polyneuritis.
3. As it is the antineurotic facter is also known as aneurine; 1-3mg of the vitamin is generally required by man.
4. In adults two types of beri-beri, namely wet beri-beri and dry beri-beri occur. Infantile beri-beri that differs from adult beri-beri is also seen.
5. **Dry beri-beri:** This occurs due to lesser deficiency of thiamine. There occurs muscular weakness and loss of weight, neuritis, pain in the arms and legs and decrease in blood pressure. The person suffering from dry beri-beri responds rapidly to thiamine administration.
6. **Wet beri-beri-:** This occurs in case of severe deficiency of thiamine. In this ease, the entire nervous system is affected and results in a types of paralysis leading to edema and impaired cardiac function.
7. **Infantile beri-beri:** This is seen in infants born to mothers suffering from thiamine deficiency. The breast milk of these mothers contains low thiamine content and this is characterized by sleeplessness, restlessness, vomiting, conclusions, abdominal calico, death may occur due to the cardiac failure.

The biological activity of thiamine is mainly in the form of its pyrophosphate ester (cocarboxylase). The enzyme carboxylase, which requires the coenzyme. Co-carboxylase for the action, breaks town pyruvic acid into acetaldehyde in alcoholic fermentation and carbohydrate metabolism. [2]





**II.B. Structural elucidation of vitamin B1:**

1. The molecular formula of thiamine is feund to be C12H18ON4Cl2S.
2. Decomposition products: When thiamine is treated with a sedium sulphite solution saturated with sulphur dioxide at room temperature, thiamine undergoes decomposition quantitively into two compounds, say (A) & (B), containing thiazolering & pyrimidine ring respectively as follows:

 SO2

C12H18Cl2N4OS+Na2SO3 C6H9NOS+C6H9N3O3S + 2NaCl

 Thiamine (A) (B)

**II.C Structure of compound A**

1. The molecular formula has been found to be C6H9NOS.
2. Presence of tertiary nitrogen atom: As the compound (A) shows basic properties but foes not react with nitrous acid, this reveals that the nitrogen atom is in the tertiary state. Formation of quaternary ammonium salts with the compound (A) further confirms this fact.
3. Presence of primary alcoholic group: When the compound (A) is treated with hydrochloric acid, it forms hydrochloride, indicating that the hydroxyl group is a primary alcoholic group.
4. The UV spectrum of the chloroderivative is some as that of the parent compound (A). This shows that –OH group is present in side chain.
5. Presence of Sulphur in heterocyclic ring: the only Sulphur atom present in compound (A) fees neither give the usual reactions of a mercapto compound nor of a disulphide. This unreactivity or stability of Sulphur atom leads to a conclusion, that Sulphur atom leads to a conclusion, that sulphur atom is present in a heterocyclic ring.
6. Compound (A) has as absorption spectrum similar to that of triazole. Therefore, compound A is a derivative of triazole.
7. Oxidation: oxidation of compound (A) with nitric acid and isolated the product C5H5NO2S. The same product was also obtained by the direct oxidation of thiamine with nitric acid. The product C5H5No2­S was later identified as; 4-methylthiazole-5-carboxylic acid (I)



1. Compound (A) must have side chain at C-5 of compound (I) ∴Two possible structures can be written for compound ‘A’ are as follows:



Compound A is optically inactive and does not give iodoform test. Therefore, compound A must have structure II.

1. Synthesis of compound A:

This involves two steps:

1. In the first step, 3-chloro-5-ethoxy-2-pentanone is synthesized from ethylacetoacetate and β-bromotiethyl as follows.



In the second step, 3-chloro-5-ethoxy-2-pentanane obtained from step(a) is

made to condense with thioformamide followed by treatment first with HCL and then

boiling with water.



**II.D. Structure of compound B**

* 1. Molecular formula: this has been found to be C6H9N3O3S.
	2. Presence of sulphonic acid : When compound (B) is heated with water under pressure at 200oC it yields sulphuric acid. The compound (B), when heated with concentrated sodium hydroxide solution, also yields sodium sulphite both these reactions reveal that the compound (B) contains sulphonic acid group.
	3. The compound B was found to contain one –NH2 group as it formed monohydroxy derivative along with the evolution of nitrogen when treated with nitrous acid.
	4. The compound B on heating with HCl at 150oC under pressure yields ammonia and compound C. The formation of ammonia indicates the replacement of an – NH2 group by a – OH group. This type of reaction is the characteristic of 2 & 4 – aminopyrimidines; hence it was inferred that (B) is a pyrimidine derivative.



* 1. Further, the UV spectrum of compound C is very much similar to that of 4- hydroxy pyrimidine indicating that the compound (B) may be 4- aminopyrimidine derivative.
1. The compound B, when reduced with sodium in liquid ammonia, eliminates a sulphonic acid group and results in the formation of an aminodimethylpyrimidine. The UV spectrum of this compound, when compared with various synthetic compound, reveals that this compound (i.e. amino dimethyl pyrimidine) must be 4- amino-2,5-dimethylpyrimidine.



1. When thiamine is reduced with sodium in liquid NH3 a compound D is formed which was identified as 4-amino-5-aminomethyl pyrimidine by comparing the spectrum with synthetic compounds.

Therefore the structure of compound ‘B’ can be written as;



1. Synthesis of compound B:



Thus in compound (D), there is an amino group instead of the sulphonic acid group in B, hence the sulphonic acid in B can be represented as below:



**II.E. Combination of A & B**

1. It has already proved that (as above) that thiamine itself not possess sulphonic acid but it gets introduced into the compound B when thiamine is treated with sodium sulphite (Na2SO3­). Therefore, it means that the C-atom of (B) on which sulphonic acid is being introduced should be linked to the compound (A), i.e. the point of attachment of compound B is at the – CH2 group at position 5.
2. To account for all the reactions of vitamin B­1­, the compound B is connected to compound A via ‘N’-atom. ∴ Vitamin B1 must have the following structure



**II.F. Synthesis of vitamin B1**









**III.VITAMIN B6**

**III.A. Biological Importance of Vitamin B6**

1. In rats and many other animals, the initial vitamin B6 deficiency causes severs dermatitis. however, extreme deficiency in these animals causes convulsions similar to those of epilepsy and indicates a profound disturbance in central nervous system. the vitamin B6 also serves as growth factor for many bacteria.
2. In man, deficiency of vitamin B6 is associated with neurological symptoms such as depression, irritability, nervousness of mental confusion, convulsions and peripheral neuropathy are observed in sever deficiency.
3. Decrease in haemoglobin levels, associated with hypochromic microcytic anaemia, is seen in B6 deficiency, this is due to a reduction in heave production.
4. Directly deficiency of pyridoxine is rather rare and is mostly observed in women taking oral contraceptive, alcoholics and infants.[2]

**III.B. Structural Elucidation of Vitamin B6**

* 1. The molecular formula is C8H11NO3
	2. They behave as weak base therefore nitrogen may be present in the ring system. it may form heterocyclic ring.
	3. It does not contain any methoxy group (or) methylamine groups
	4. Zerewitnoff method showed the presence of three active hydrogen atoms.
	5. The formation of deep red color with Fecl3 and monomethylether with Fecl3; it forms diacetate with acetic anhydride and a hydrobromide of a dibromide with HBr., indicating thereby that the hydroxyl groups are alcoholic in nature.
	6. UV absorption spectrum of pyridoxine resembles that of 3-hydroxypyridine (or) β- hydroxypyridine , therefore vitamin B6 is a derivative of 3- hydroxypyridine,
	7. Position of – OH groups: when the monomethyl ether of pyridoxine is treated with. lead tetroacetate. its oxidatien does not take place, thereby confirming that the two alcoholic groups are not present on adjacent ‘C’ atoms in a side-chain of pyridoxine.
	8. Monomethyl ether of pyridoxine, when oxidised very carefully with alkaline potassium permanganate, gives a methoxypyridine tricarboxylic acid (C9H7NO7). this tricarboxylic acid gives a blood-red color with ferrous sulphate, a characteristic reaction of pyridine-2-carboxylic acid, thus one of the three acidic groups in the tricaboxylic acid must be in the 2-position.
	9. When monomethylether of pyridoxin is treated with KMnO4 under normal condition gives anhydride of dicarboxylic acid with liberation of CO2. Therefore carboxylic groups are on adjacent carbon atoms. (orthoposition with respect to each other)



Furthermore, the anhydride does not give blood red color with Feso4 therefore two possible structures can be written for monomethoxy-tricarboxylic acid.



Therefore, two carboxylic acid are obtained by oxidation of CH2OH one carboxylic acid is obtained by – CH3 groups.

 XI. The following structures are possible for the pyridoxine can be written as (A) or(B).

 

 A decision between the two structures was made on the basis of the following point.

1. Oxidation with Barium permanganate (mild), vitamin B6- monomethylether gives a dicarboxylic acid I. the dicarboxylic acid forms anhydride with acetic anhydride and gives a fluorescent dye with resorcinol indicating that the two-COOH groups are in O-positions to each other.
2. Moreover, the dicarboxylic acid I does not give color with Feso­4 solution showing that neither of the two-COOH groups is in α-position to the nitrogen, hence the structure of the dicarboxylic acid I , may be either A or B.



The position of the two-CooH groups in I corresponding to the two alcoholic groups in pyridoxine. However, Kuhn compared these two dicarboxylic acids with the synthetic compounds and found that the dicarboxylic acid obtained from pyridoxine is A as it resembles with synthetic dicarboxylic acid from 4-methyl is isoquinoline.



Therefore – OH groups and – CH3 groups must be adjacent to each other. therefore pyridoxine must have structure A.



III.C. Synthesis of Vitamin B6



 

**IV.VITAMIN H**

**IV.A. Biological Importance of Vitamin H**

* Vitamin H is a growth factor present in minute amounts in all living cells as the vitamin can be synthesized by the intestinal bacteria in man, a deficiency disease due to this vitamin is not known with certainly. however, its deficiency may cause dermatitis, loss of hair and progressive paralysis.
* It is also a growth factor for rats, yeast and some microorganisms.
* Biotin deficiency is uncommon, since it is well distributed in foods and also supplied by the intestinal bacteria. the deficiency may however, be associated
	1. Destruction of intestinal flora due to prolonged use of drugs such as sulfonamides.
	2. High consumption of raw egg, the raw egg white contains a glycoprotein- avidin, which tightly binds with the biotin and blocks its absorption from the intestine an intake of about 20 raw eggs per day is needed to produce biotin deficiency symptoms in humans, this is so called egg-white injury may be prevented by boiling the egg-white before feeding it or by feeding biotin.
	3. Consumption of occasional raw egg will not result in deficiency.[1]

**IV.B. Structural Elucidation of Biotin (or) β- Biotin or Vitamin H**

* 1. Molecular Formula: From analytical data, this has been found to be C10H16N2O3S.
	2. Saturated Compound: Biotin behaves as a saturated compound the usual tests show the absence of an ethylenic double bond in it.
	3. Effervescence with sodium bicarbonate indicated that it contains carboxylic group  it confirms the presence of one  by titration with standard alkali Therefore molecular formula can be modified as 
	4. Presence of Five Membered Cyclic Uride Structure: Biotin, when heated with barium hydroxide solution, under goes hydrolysis to yield a mixture of carbon dioxide and a diaminocarboxyolic acid C9H18N2O2S (designated as I)



& this carboxylic acid on reaction with COCl2 gives back β- biotin. Therefore, Partial structure of β- biotin can be written as;



* 1. Diaminocarboxylic acid on oxidation with alkaline KMnO4 gives adipic acid one of the two- COOH groups in adipic acid has shown to be the same as that of β- biotin as follows. the carbomethoxyl groups of the methylester of β- biotin is replaced by an aminogroup by curtius reaction the amine is hydrolysed with Ba(OH)2 to give triamine which does not give adipic acid an oxidation with alkaline permanganate . hence the β- biotin contains a –(CH2)4COOH side chain ( n- valeric acid side chain).
	2. Diaminocarboxylic acid forms quinoxaline derivative on reaction with phenanthraquinone which are given as structure I and II but UV spectral analysis favours I.



+



Hence It contains two amine ( - NH2) groups.

* 1. Stability of the sulphur atom: The stability (unreactivity) of the sulphur atom revealed that it is present as thioether (C-S-C) which can be proved as follows



i) Oxidation of β- Biotin Sulphone



ii) Methylester of β-BiotinSulphonium iodide

* 1. Presence of ς in five membered ring: Biotin heated with raney nickel loses its only Sulphur atom to form dethiobiotin the later compound on hydrolysis with HCl yields a diamino carboxylic acid, which on oxidation with periodic acid yields pimelic acid, these results can be interpreted by saying that sulphur atom is present in a five-membered ring and further n- valeric acid side-chain is present on the α-carbon atom to the ‘S’ atom. (a)

 



**IV.C. Synthesis of vitamin H**









1. **CONCLUSION**

 Nature has thoughtfully incorporated minute but adequate amount of vitamins into our various food stuffs. But some limits cause deficiency. A diet that includes plenty of [fruits, vegetables](https://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/vegetables-and-fruits/), [whole grains](https://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/whole-grains/), good [protein packages](https://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/protein/), and [healthful fats](https://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/fats-and-cholesterol/types-of-fat/) should provide most of the nutrients needed for good health. But not everyone manages to eat a healthful diet. Multivitamins can play an important role when nutritional requirements are not met through diet alone.

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