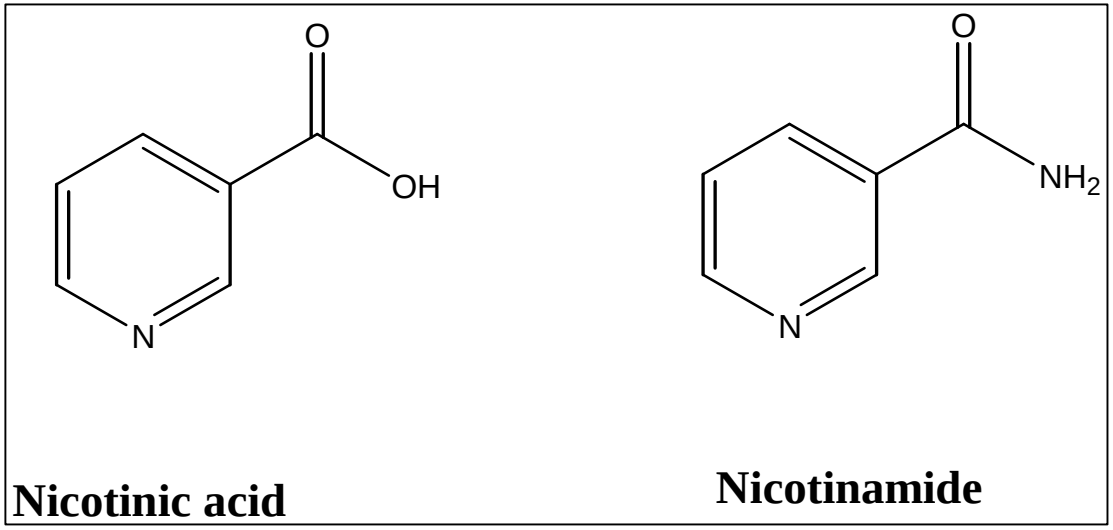
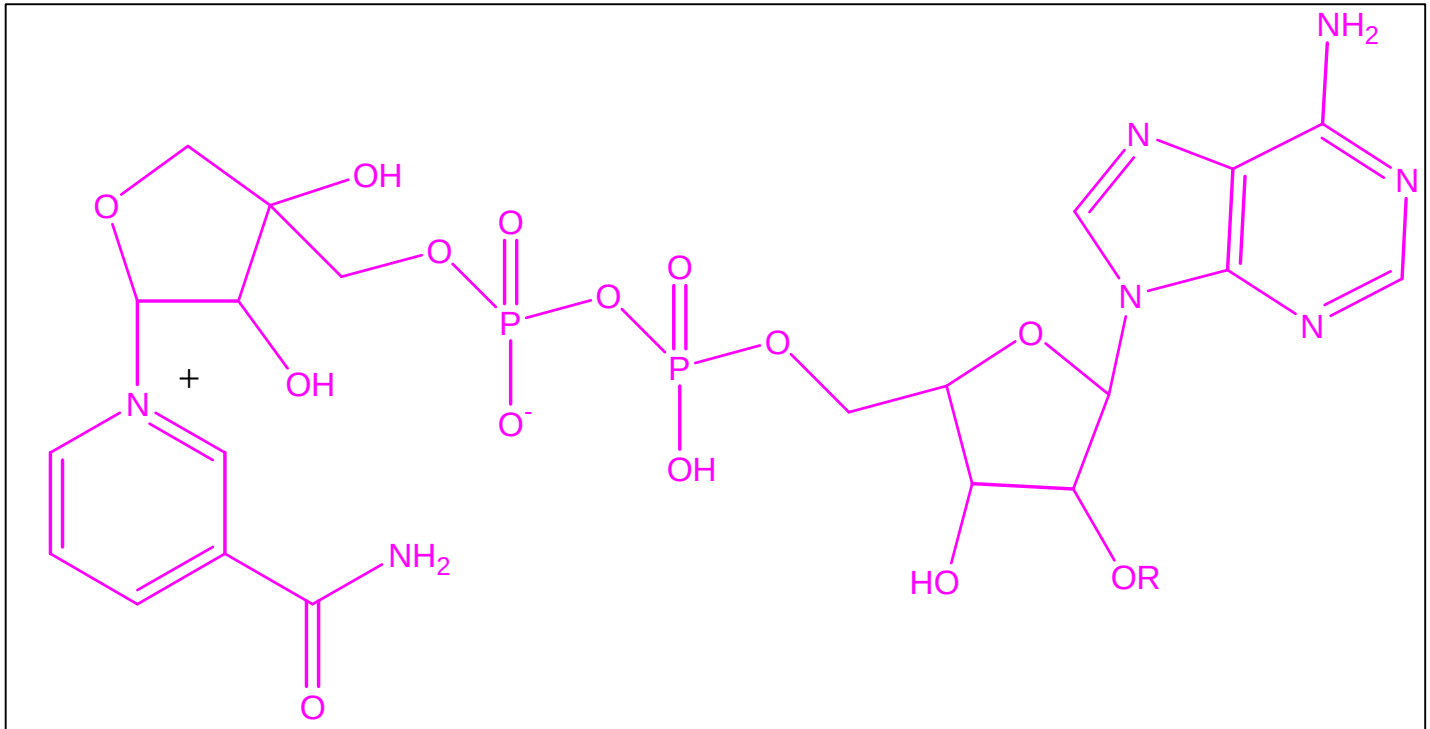
c- Vitamin B_3

(Niacin)

Vitamin B_3

- It is called Niacin.
- It is the generic descriptor for pyridine-3-carboxylic acid and derivatives exhibiting qualitatively the biological activity of nicotinamide.





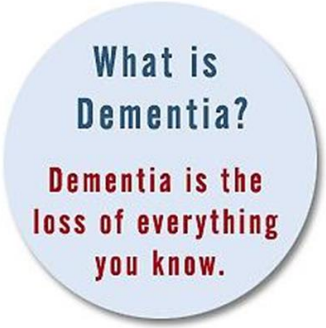
Nicotinamide adenine dinucleotide (NAD^+), R = H

Nicotinamide adenine dinucleotide phosphate ($NADP^+$), R = PO_3H_2

- Nicotinic acid and nicotinamide are colorless crystalline compounds.
- They are very stable in dry form.
- The coenzyme forms of niacin are the pyridine nucleotides; NAD(H) and NADP(H).
- It is the reaction of hydride ions (H^-) that is the basis of the enzymatic hydrogen transfer by these nucleotides.
- The reaction involves transfer of two electrons in a single step.

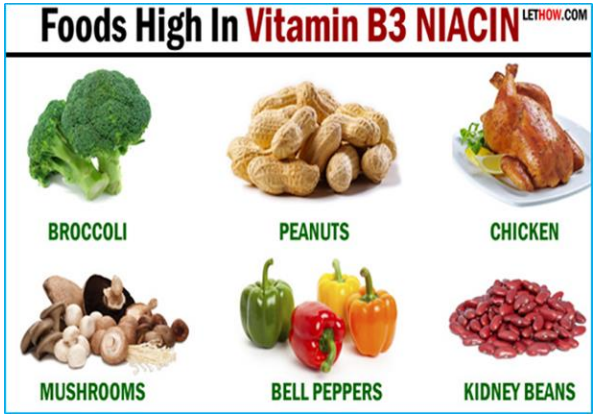
Significance of niacin

- Historically, niacin deficiency, was prevalent among people who relied on maize (corn) as their major food.
- In addition, niacin insufficiency more frequently results from poor bioavailability rather than scarcity.
- Its deficiency produces a disease called pellagra (is classically described by "the 4 D's": **D**iarrhea, **D**ermatitis, **D**ementia, **D**eath.



Sources of niacin

- Niacin occurs in good quantities in brewer's yeasts and meats and peanuts.
- In plant products, niacin found as protein-bound nicotinic acid (NA).
- In animal products, niacin found as protein-bound nicotinamide (NAm) in NAD and NADP forms.
- Niacin is very stable to storage and normal means of food preparations.

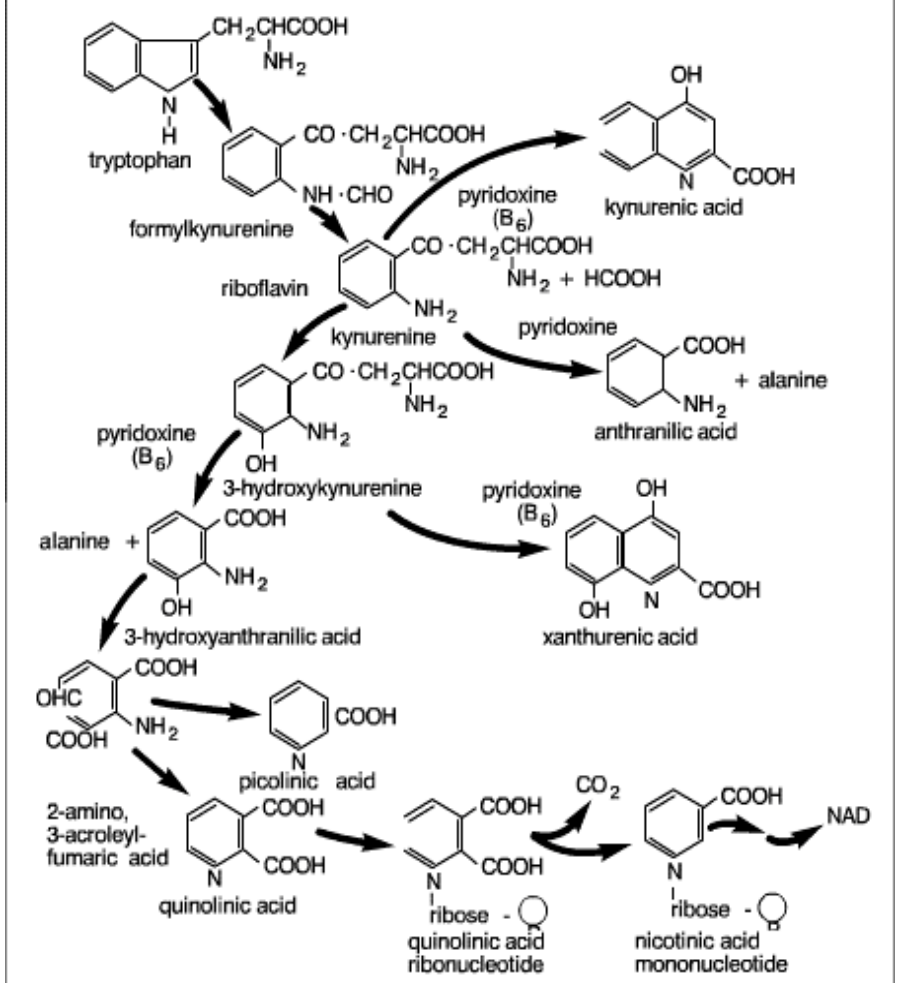


- Niacin is found in many food covalently bound to peptides and carbohydrates and is not easily digestible.
- Therefore, its bioavailability is poor.
- Human can also get niacin from tryptophan.
- About 60 mg of tryptophan is required to produce 1 mg of niacin.

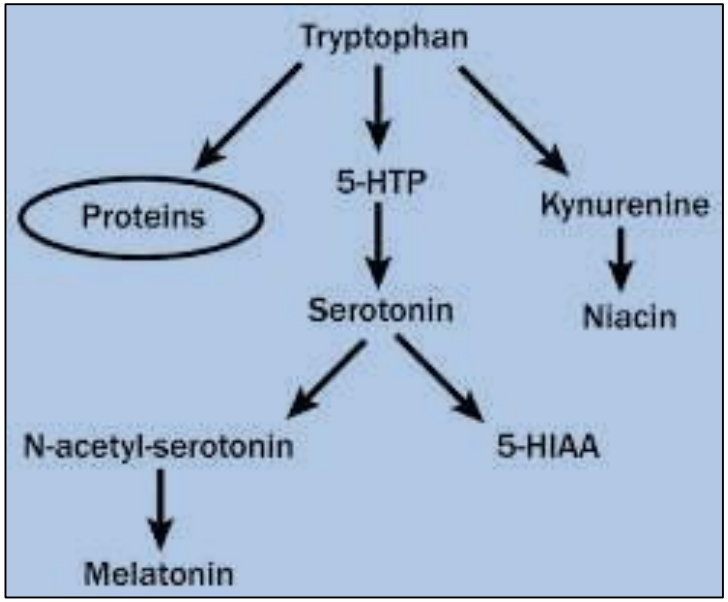
Metabolism of niacin

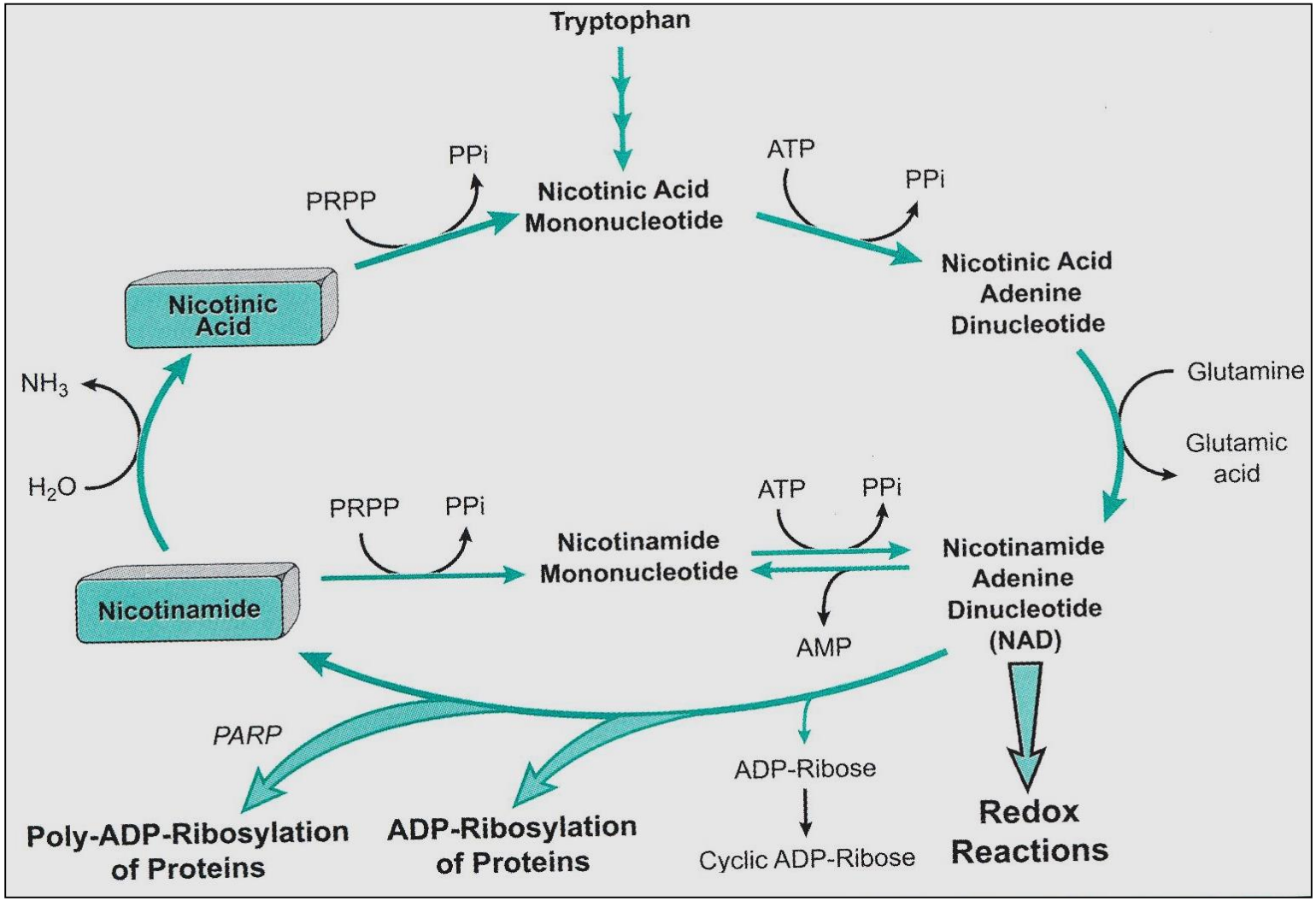
- All animals including human are capable of biosynthesizing the metabolically active forms of niacin from tryptophan.
- Therefore, there are three sources of niacin; NA, NAm and tryptophan.
- During niacin deficiency, tryptophan brings only 2/3 of the requirement of the vitamin.
- Vitamin B_6 is needed in the biosynthesis cascade of niacin from tryptophan.

Figure 1: Conversion of Tryptophan to Nicotinic Acid Mononucleotide Plus Some Side Reactions



Adapted from McDowell (2000)



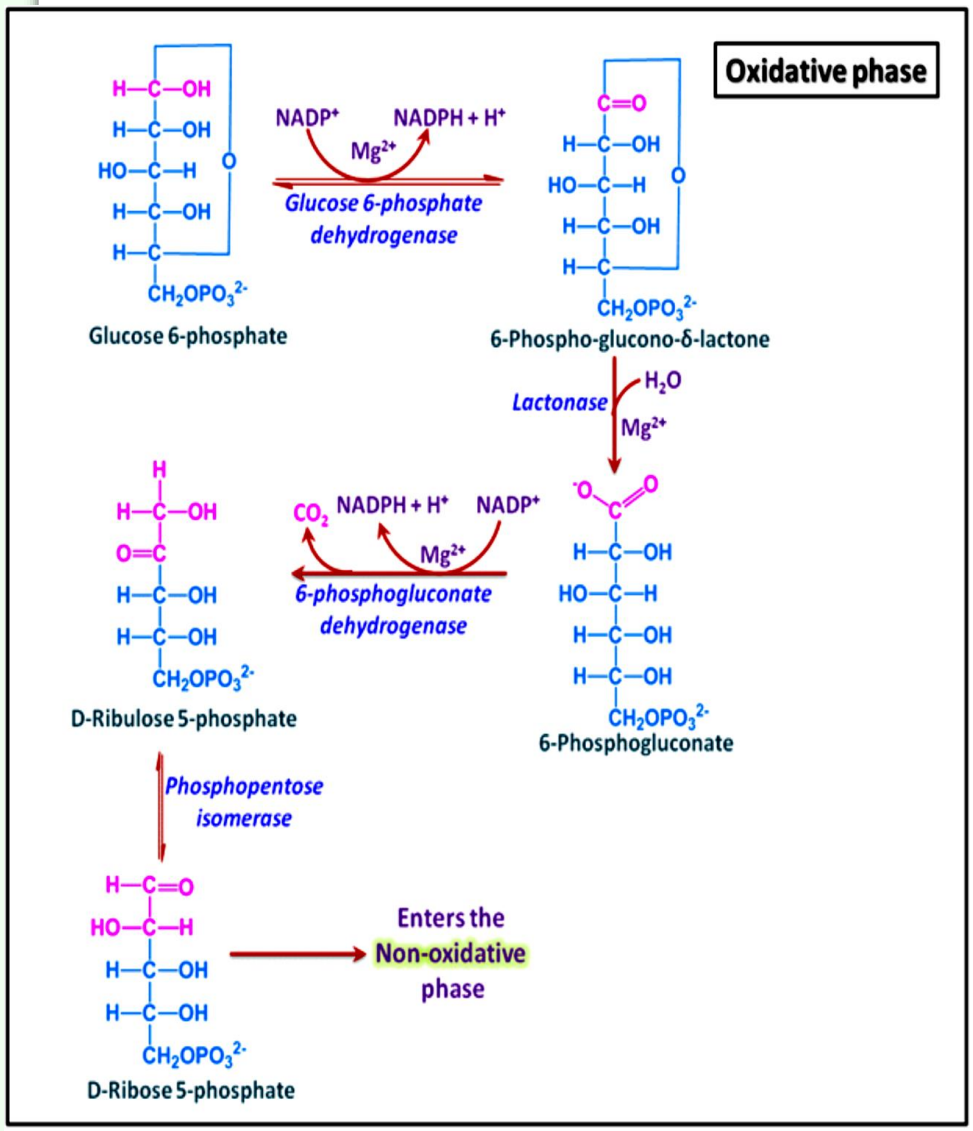

Tryptophan
PPi
PRPP
Nicotinic Acid Mononucleotide
ATP
PPi
Nicotinic Acid Adenine Dinucleotide
Nicotinic Acid
NH3
H2O
Glutamine
Glutamic acid
PRPP
PPi
ATP
PPi
Nicotinamide Mononucleotide
Nicotinamide Adenine Dinucleotide (NAD)
Nicotinamide
AMP
PARP
ADP-Ribose
Poly-ADP-Ribosylation of Proteins
ADP-Ribosylation of Proteins
Cyclic ADP-Ribose
Redox Reactions

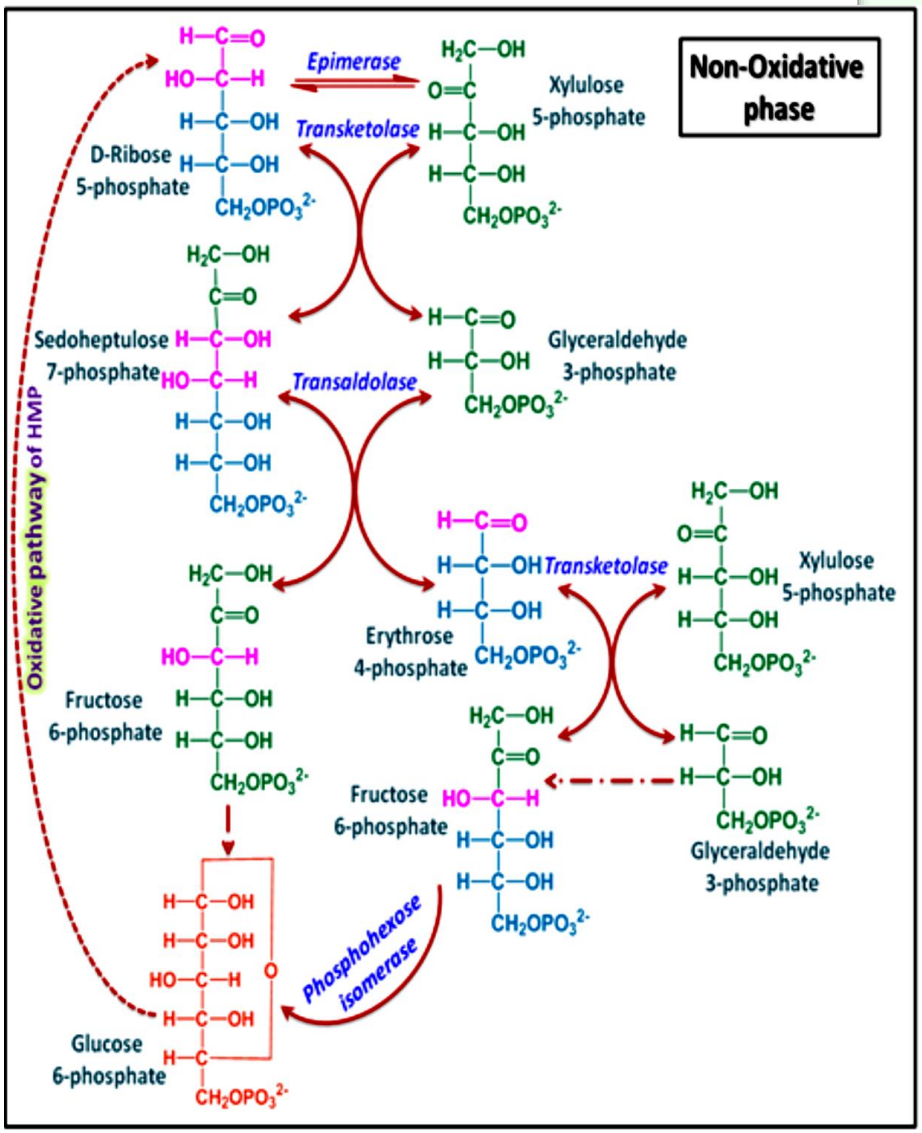
Metabolic functions of niacin

- Through its metabolically active forms, they are working as intermediate in most of the hydrogen transfers in metabolism of carbohydrates, fatty acids and amino acids.
- The hydrogen transport by the pyridine nucleotides is accomplished by two-electron transfers in which the hydride ion serves as a carrier for both electrons.

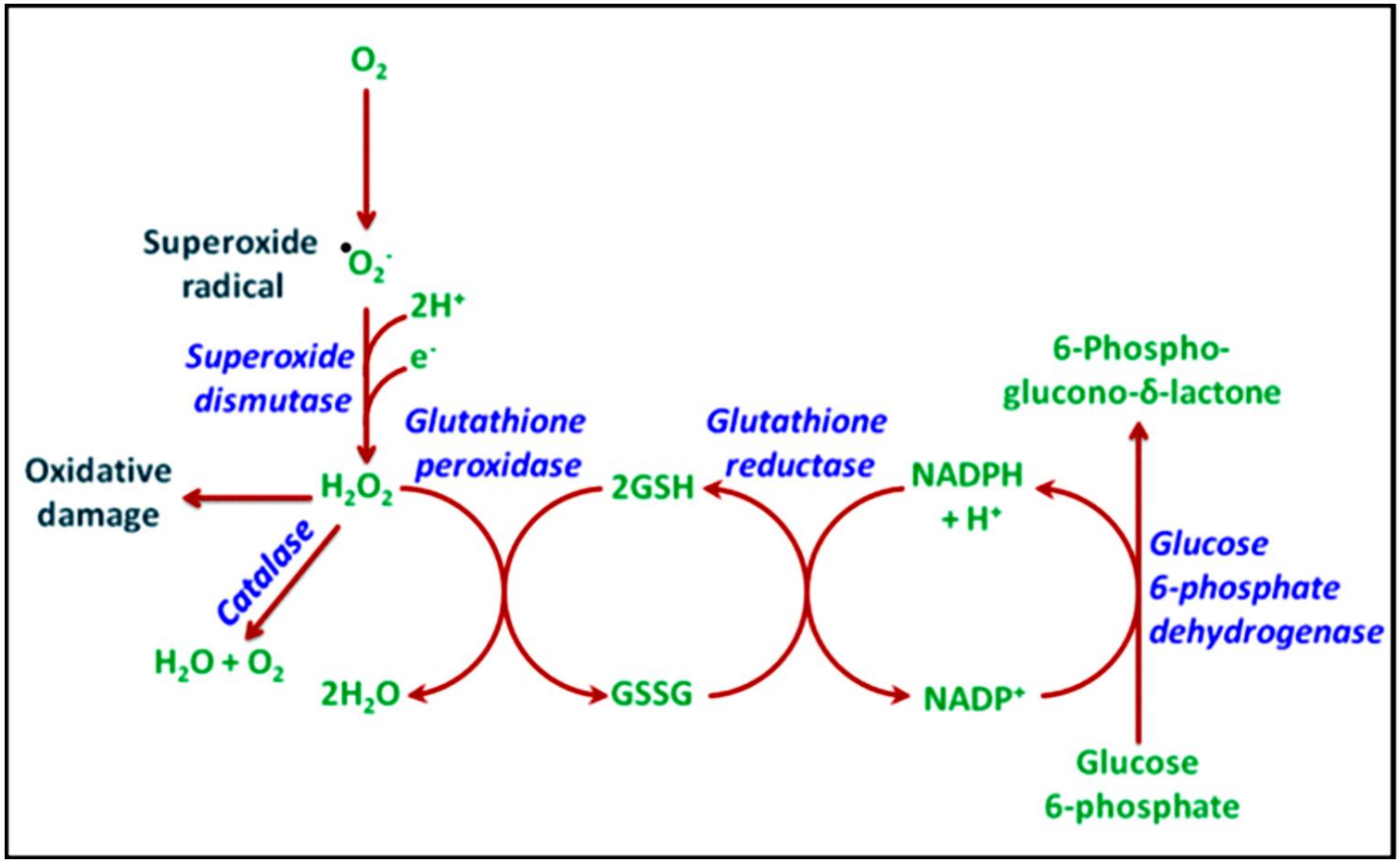
- NAD(H) and NADP(H) have quite different metabolic roles and most dehydrogenases have specificity for one or the other.
- In the reactions involving NAD(H), its oxidized form NAD^+ usually serves as a hydrogen acceptor forming NAD(H), which in turn functions as a hydrogen donor to the respiratory chain for ATP production.
- In the reactions involving NADP(H), the reduced form NADPH usually serves as a source of reducing equivalents for biosynthetic reactions.

HMP (hexose monophosphate pathway)





Role of NADPH and glutathione in preventing oxidative damage in cells



Recommended Daily Allowance (RDA)

- 14 mg/day to men from 14 years of age.
- 11 mg/day for women from 14 years of age.
- 16 mg/day for Pregnant women and breastfeeding.

Niacin deficiency

- Since its intake involves tryptophan and vitamin B_6, therefore, the clinical manifestation of niacin deficiency will include evidence of unbalanced diet and multifactorial.
- The deficiency resulted in changes in the skin, gastrointestinal tract and nervous system.
- The dermatological changes, which are the most prominent (called pellagra), are most pronounced in the parts of the skin that exposed to sunlight.
- Neurological symptoms include anxiety, depression and fatigue.
- Pellagra is characterized by the **4Ds**: **D**ermatitis, **D**iarrhea, **D**ementia and **D**eath.

Uses of niacin

- Nicotinic acid and nicotinamide are used for treatment of niacin deficiency.
- Nicotinic acid is used for hyperlipidemia at very high dose (500 mg) due to:

1- Inhibition of lipolysis in adipose tissue.

2- Inhibition of hepatic synthesis and secretion of VLDL.

3- Lowering the plasma concentration of LDL & VLDL.

4- Increasing plasma HDL.

Niacin toxicity

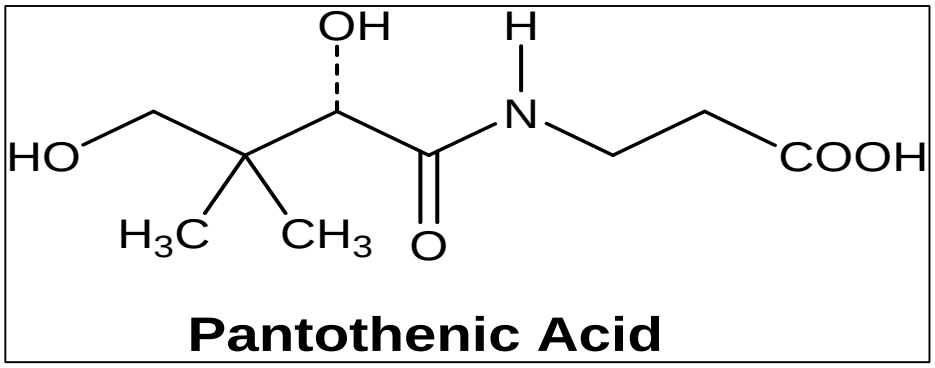
- It is low.
- High doses of the vitamin showed flushing, itching and urticaria and GIT discomfort like heartburn, nausea, vomiting.
- Nicotinamide appears to be more toxic than nicotinic acid.

d- Vitamin B_5

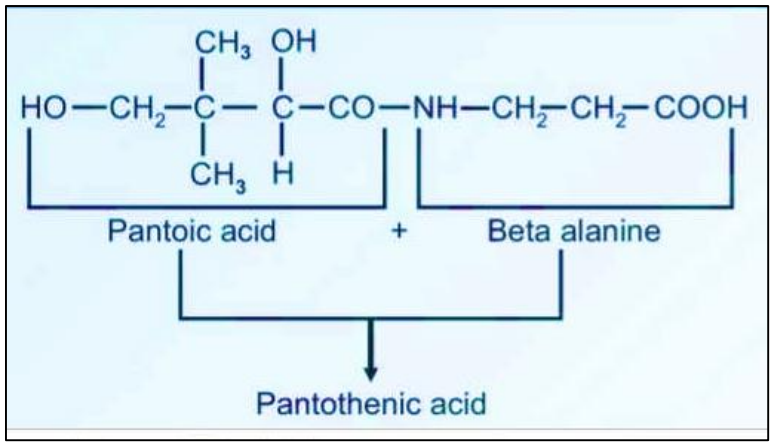
(Pantothenic Acid)

Vitamin B_5

- It is called Pantothenic acid.
- It is the trivial name of the compound dihydroxy-β,β-dimethylbutyryl-β-alanine.



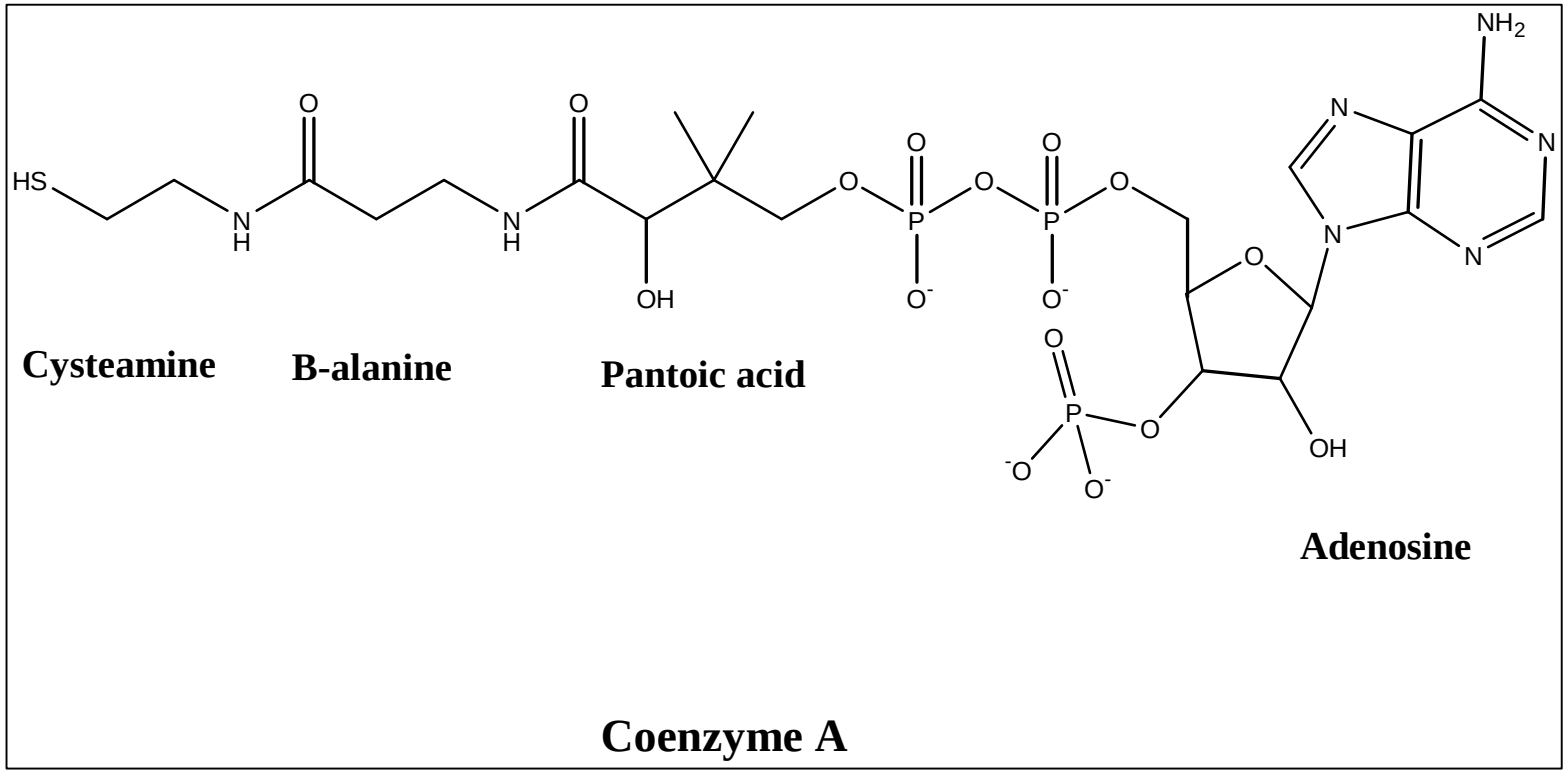
Pantothenic Acid



The vitamin has two metabolically active forms:

1- Coenzyme A, in which the vitamin is linked via a phosphodiester group with adenosine-3',5'-diphosphate.

2- Acyl-carrier protein, in which it is linked via a phosphodiester to a serinyl residue of the protein.


HS
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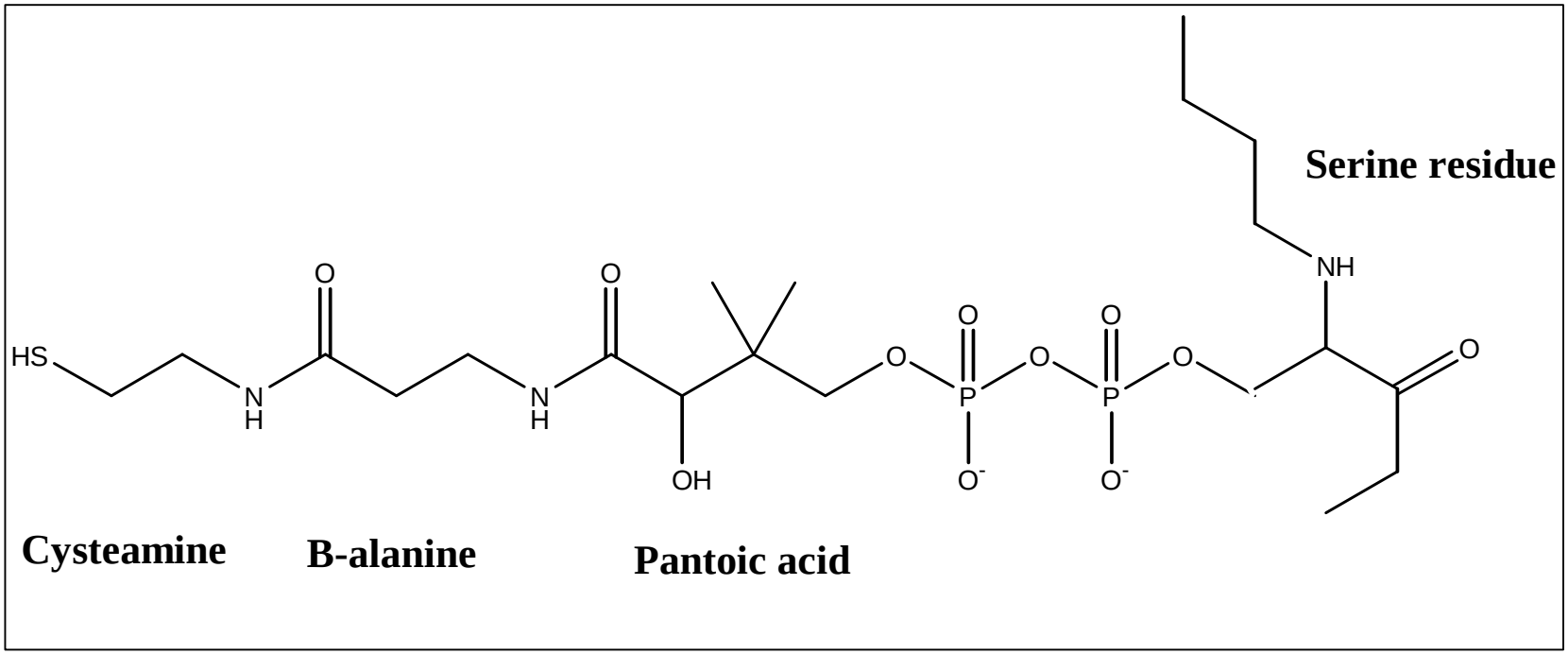
NH2
Cysteamine
B-alanine
Pantoic acid
Adenosine

Coenzyme A



Acyl-carrier protein

- The *R*-enantiomer, usually called D-(+)-pantothenic acid, is biologically active and occurs naturally.
- Pantothenic acid is yellow viscous oil.
- Salts of pantothenic acid are colorless crystalline and calcium pantothenate is the main product of commerce.
- It is unstable to heat.
- The salts are stable to air and light; but they are hygroscopic.

Significance of vitamin B_5

- It has a critical role in the metabolism of amino acids, fatty acids and carbohydrates through its active forms (CoA and ACP).
- It is observed that rates of tissue CoA synthesis are not affected by deprivation of the vitamin suggested recycling of the vitamin with unclear regulatory mechanism.

Sources of the vitamin B_5

- It is widely distributed in foods.
- It occurs mainly in bound forms.
- Royal jelly is the richest source of the vitamin.
- Liver, heart, mushrooms, avocados and broccoli are among the rich sources of the vitamin.
- It is affected by storage.

Metabolic functions of the vitamin B_5

- Both CoA and ACP function as carriers of acyl groups.
- CoA forms high energy thioester bonds with carboxylic acids.
- The most important is acetic acid, which can come from the metabolism of fatty acids, amino acids or carbohydrates.
- As acetyl-CoA, it can enter Krebs cycle to produce energy, can be used for the synthesis of fatty acids or can be used in acetylations of alcohols, amines and amino acids.

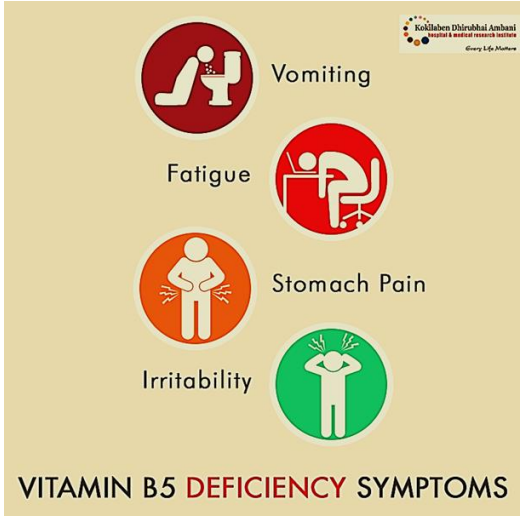
- CoA is also serve as acyl donor for proteins.
- Acylated proteins have been shown to have a wide variety of essential roles, including signal transduction in cells.
- ACP is a component of the multienzyme complex fatty acid synthase.
- It works as a cofactor in this synthesis of fatty acids.

Recommended Daily Allowance (RDA)

- 5 mg/day for men and women above 14 years of age.
- 6 mg/day for pregnant women.

Deficiency of pantothenic acid

- Deficiency of the vitamin is rare.
- It is appeared only in severely malnourished patients.
- The patient will show nonspecific signs like depression, fatigue, insomnia and weakness.



- The most distinctive of the deficiency symptoms are paresthesias of the extremities or "burning foot" syndrome

Pantothenic acid toxicity

- The vitamin is nontoxic.
- Ingestion of large doses (10 g/day) have not produced reactions more severe than mild intestinal distress and diarrhea.