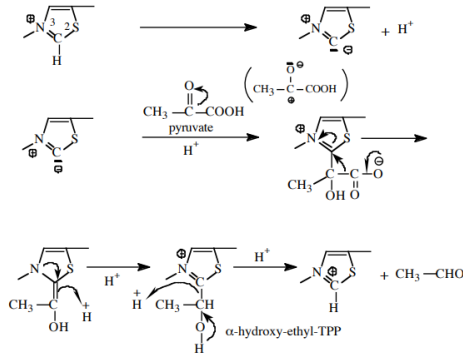


Water Soluble Vitamins Problem Set 2018 – Part 1 - Xu

1. What type of reactions use thiamin as a necessary cofactor? Does the pyrimidine ring or thiazole ring play a greater part in the reaction mechanism?

Thiamine (B1): is capable of acting as a nucleophile following the formation of a carbanion at the C-2 position of the thiazole ring (thiazolium ylide).



B1 is a necessary cofactor in the following reactions:

Oxidative decarboxylation of α-keto acids (ex. pyruvate dehydrogenase, α-ketoglutarate dehydrogenase)

Transfer of α-ketols (ex. pentose phosphate pathway)

2. Provide three reasons that alcoholics may be deficient in thiamine. What disease might result from chronic deficiency state?

- lower intake
- alcohol blocks thiamin to TPP conversion
- alcohol lowers absorption, active transport, and storage
- increased fluid intake and urine flow leads to thiamin washout

3. What test is done to check thiamin deficiency?

Thiamin deficiency is diagnosed by measuring transketolase activity in RBC.

(Also acceptable: Increased levels of pyruvate and lactate in plasma)

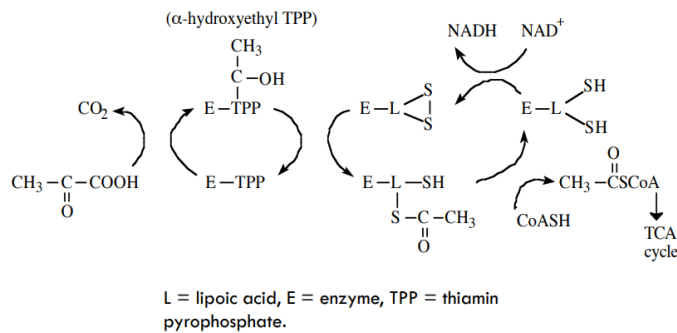
4. What test is done to check riboflavin deficiency?

Deficiency in Riboflavin (B2) can be diagnosed through the assessment of erythrocyte GSH reductase activity.

5. How does riboflavin play the role of antioxidant in human physiology?

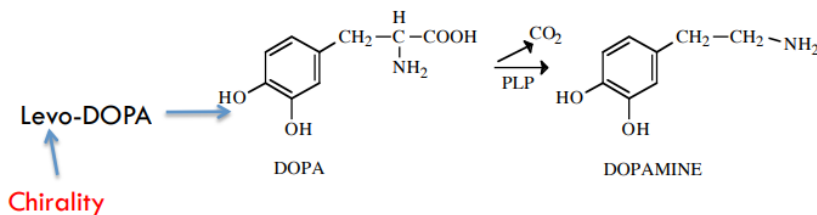
Riboflavin (B2) is a necessary cofactor for GSH reductase, which converts the oxidized form of glutathione (GSSG) into the reduced form (GSH). GSH is highly important in several pathways which protect against oxidative stress. For example, glutathione peroxidase uses GSH to reduce lipid hydroperoxides and free hydrogen peroxide which can cause oxidative damage in the organism.

6. What vitamins are involved in pyruvate dehydrogenase?



- Thiamin pyrophosphate (TPP) from thiamin (vitamin B1)
- Coenzyme A (CoA) from pantothenic acid (vitamin B5)
- NAD⁺/NADH from niacin (vitamin B3)

7. What is the coenzyme form of Vitamin B6 and why is it contraindicated with levo-DOPA therapy?



B6 is contraindicated in Levo-DOPA therapy because it enhances peripheral decarboxylation of Levo-DOPA to dopamine. Dopamine will not cross Blood Brain Barrier thus limiting the therapeutic effect of levo-DOPA.

8. How is low Vitamin B6 diagnosed?

Low Vitamin B6 is diagnosed by measuring erythrocyte transaminase activity.

9. What kind of drug can cause vitamin B6 deficiency? What is the mechanism?

Isoniazid (antituberculosis drug) can cause B6 deficiency by formation of a Schiff base that reduces the amount of free coenzyme available.

10. What can cause Wernicke-Korsakoff syndrome?

Wernicke (encephalopathy)-Korsakoff (dementia) (WKS) syndrome results from thiamin deficiency. Often WKS is caused by alcoholism. Although, other risk factors include increased carbohydrate intake or decreased thiamine absorption due to poor diet or gastrointestinal disease. WKS can also be caused by insufficient transketolase function stemming from mutations.

11. What is the role of vitamin B6 in homocysteine metabolism?

B6 (as pyridoxal-5-phosphate, PLP) participates in the conversion of homocysteine to cystathionine via cystathionine synthase. PLP is also required for further metabolism of Cystathionine into cysteine and α -ketoglutarate through cystathionine γ -lyase. (see slide 36 of 43, water soluble vitamins part 1)

12. What are the definitions of EAR, RDA, UL, and daily value (DV)?

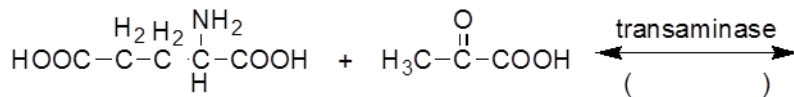
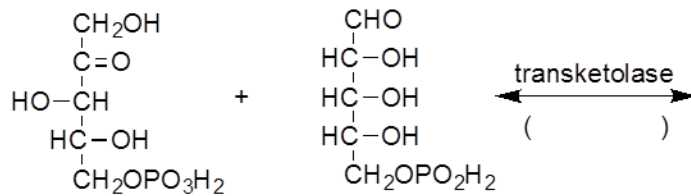
EAR (Estimated Average Requirement): The average daily nutrient intake level estimated to meet the requirements of half of the healthy individuals in a group

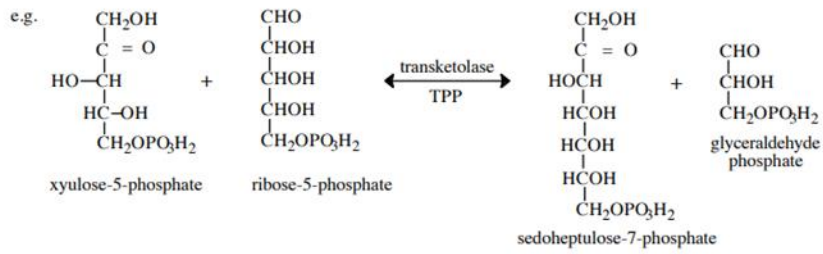
RDA (Recommended Daily Allowance): The average daily dietary intake level estimated to meet the nutrient requirements of nearly all (97-98%) healthy individuals in a group

UL (Tolerable Upper Limit): The maximum adult daily intake unlikely to cause harm

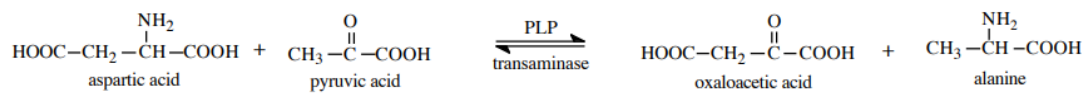
DV (Daily Value): DV primarily used for labeling purposes, %DV values on a label are for a 2000 calorie/day diet for adults and children over 4 years. It should be noted that DV is often used for energy producing macro-nutrients (carbohydrates, fats, protein) and occasionally Reference Daily Intake (RDI) is used to describe vitamins and minerals. The RDI value for a given nutrient is usually similar to the RDA value.

13. Please write the products for the following transformations and specify which vitamins participated as a cofactor.





Vitamin B1 (thiamin)



Vitamin B6 (pyridoxal-5-phosphate, PLP)