

# رؤية الكلية

تتعهد كلية الصيدلة - جامعة الملك سعود  
بالعمل الدائم لضمان الريادة والتميز في  
العملية التعليمية وفي مجالات البحث العلمي  
وفي خدمة المجتمع وذلك بهدف الحفاظ على  
مكانتها ككلية صيدلة رائدة في منطقة الخليج  
و لتأكيد ريادتها على مستوى منطقة الشرق  
الأوسط.

# الرسالة

تلتزم كلية الصيدلة – جامعة الملك سعود بتقديم العلوم الصيدلانية وتطبيقاتها بأعلى مستويات الجودة إلى جميع طلابها، و ذلك لتحقيق غرس و تطوير المهارات اللازمة لممارسة مهنة الصيدلة ، وكذلك الوصول الى تطوير المعرفة الصيدلانية من خلال الأبحاث بما يؤدي الى خدمة المهنة وخدمة المجتمع.



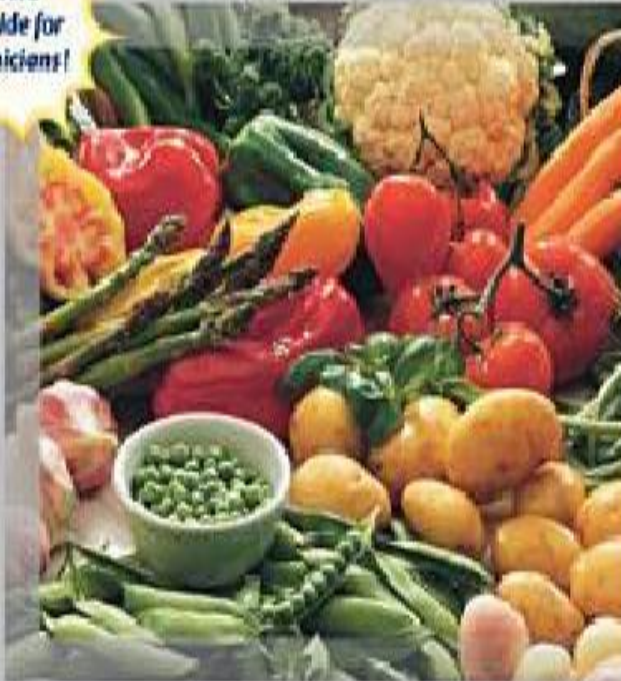
# An Evidence-Based Approach to Vitamins and Minerals

Complementary  
Medicine

Health Benefits and Intake Recommendations

Jane Higdon, Ph.D.

The  
guide for  
clinicians!



 Thieme

Department of Pharmacognosy – College of Pharmacy - KSU

# Dietary Supplements

المكملات الغذائية

PHG 311



**Dr. Hanan Aati**



*Creative Country Mom*  
VINTAGE HOME & GARDEN

First part of the course will be given by Dr. Hanan aati

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➤ **Topics to be covered (part I)**

**Vitamins (A, D, E, K, Vitamin B complex, C)**

**Minerals**

➤ **Reference Books**

Book	Authors	Year	Name of Publisher
An-Evidence-based Approach to vitamins and minerals, 2 <sup>nd</sup> Edition,	Jane Higdon & Victoria J. Drake	2012	Theime Medical publisher
PDR for herbal medicine, 4 <sup>th</sup> edition	Thomson Reuter	2007	

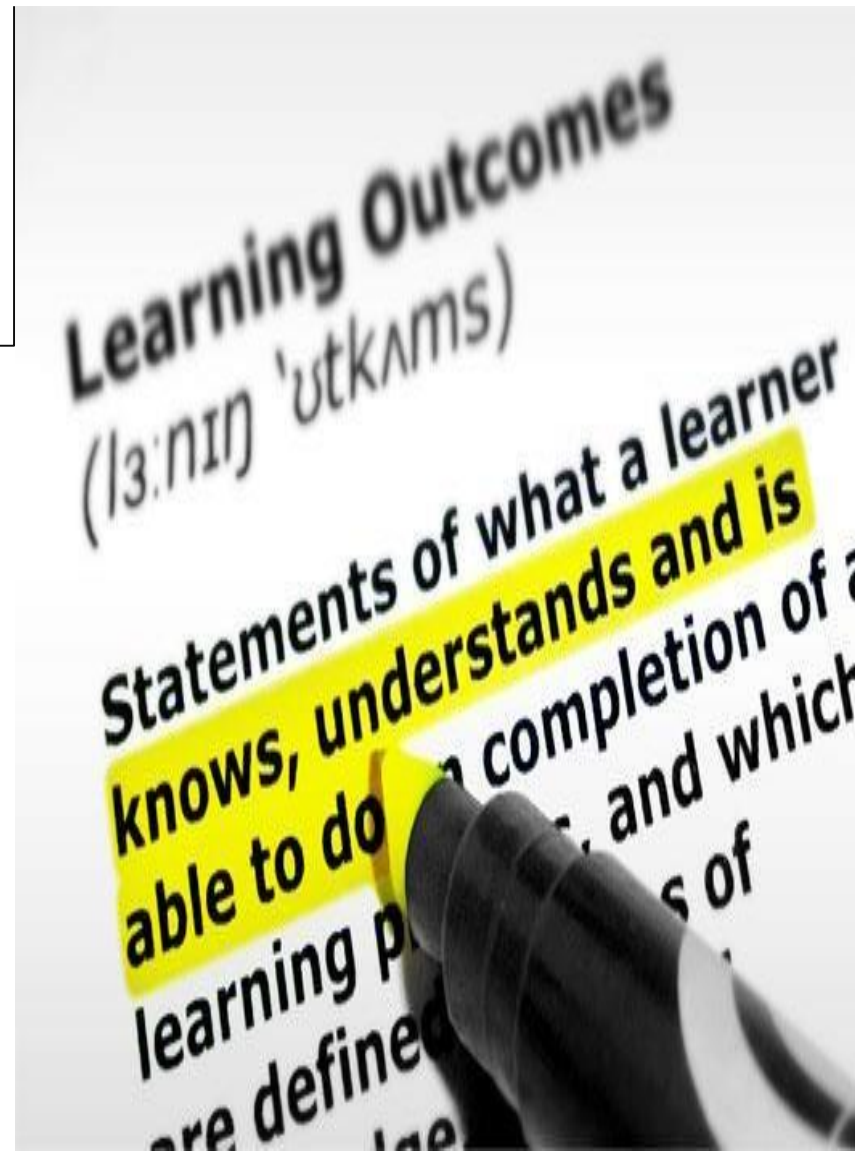
# Learning Outcomes



By completing this course, students should acquire a good knowledge on dietary supplements. This will help them to understand the physiological and therapeutic functions of these products to provide an effective clinical service by offering patients with safe drugs as well as useful consultation.

**You should be able to know:**

- **What are the fat & water soluble vitamins?**
- **Vitamins and minerals, types, sources, function, the recommended dose, deficiency and the toxicity of each.**



# Dietary supplements



# INTRODUCTION

## What is the meaning of Dietary Supplements?

- By definition, dietary supplements are products (other than tobacco)
- Is a product taken by **mouth** that contains a dietary ingredient intended to supplement the diet and meet at least one of the following criteria:
  - Contain a vitamins, minerals, herbs or other botanicals, or amino acids; or contain dietary substances to supplement the diet by increasing the total dietary intake; or contain concentrates, metabolites, constituents, extracts, or combination of any of the previously described ingredients
  - Intended for digestion in a tablet, capsule, powder, softgel, gelcap, or liquid form to increase dietary intake of essential nutrients and reduce disease risk
  - Labeled as a dietary supplement
  - Cannot be represented for use as a conventional food or as a sole item of a meal or diet

# Vitamins





## History

- Vitamins are among the nutrients required for the many physiological functions essential to life.
- They tend to have specific role.
- Usually required in small amounts.
- Vitamins from foods generally need activations.
- Only **13** compounds or groups of substances are considered vitamins (A, D, E, K, B1, B2, B3, B5, B6, B7, B9, B12 and C).

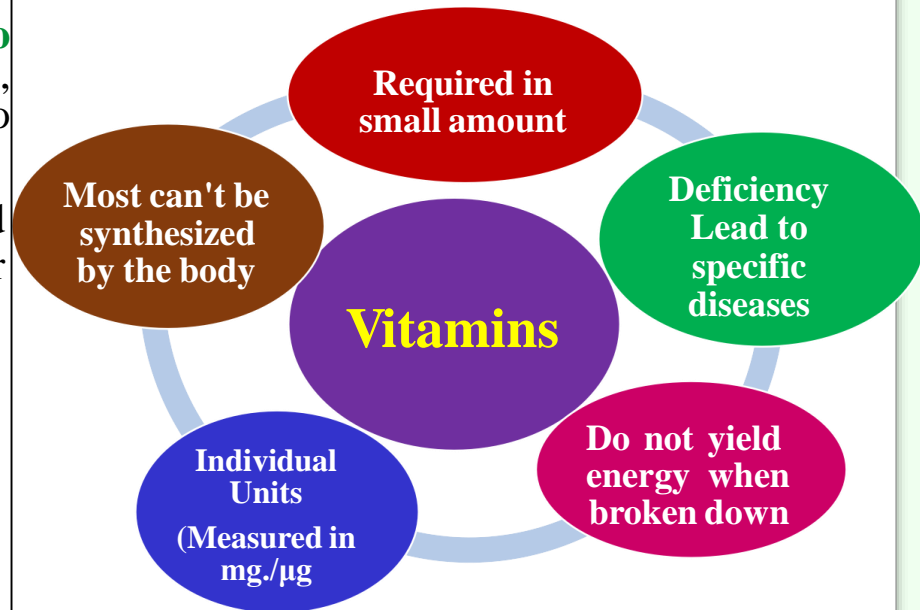
- The concept of vitamin emerge from the interrelationship between **diet** and **health**.
- 1- Diet are sources of many important nutrients.
  - 2- Low intakes of specific nutrients can cause certain disease.

# Vitamins

## Definition:

**Vitamins** are organic compounds distinct from fats, carbohydrates and proteins. They are needed in small amounts for **growth and maintenance of normal metabolic functions and good health.**

1. **Most vitamins cannot be synthesized by the body**, but are found naturally in food.
2. **The lack of specific vitamins leads to distinctive deficiency states** such as **beriberi**, **rickets**, **scurvy**, and **xerophthalmia**, or to conditions without definitive symptoms.
3. **Structure: Individual units**, NOT linked together – i.e. NOT building blocks like for glucose, fatty acids, amino acids.
4. **Function: Do not yield energy when broken down**, assist enzymes (coenzymes) and other **biological factors that release energy** from Carbohydrate, Protein, Fats.
5. **Amounts needed are measured in micrograms or milligrams**, not grams.



## Other terms in vitamin groups

- Vitamers: are members of the same vitamin family.
- Provitamin: the precursor of the actual active vitamin.

## Discovery of the vitamins

- Empirical phase
- Experimental phase

## Empirical phase

- Many societies had observed that human populations in markedly contrasting parts of the world tend to experience similar health standards despite the fact that they subsist on very different diets.

## **Germ theory**

- Perhaps the reason is that it seems easier for the human mind to believe that ill is caused by some positive evil agency, rather than by any mere absence of any beneficial property.

## Experiment phase

- In order for experimentation to yield informative results, it must be both **repeatable** and **relevant**.
  - Purified diet.
  - Animal models.
  - Story of Beriberi
- In 1888, Lunnin concluded his experiments:

A natural food such as milk must, therefore, contain besides these known principal ingredients small quantities of other and unknown substances essential to life.

- In 1906, Eijkman and Grijns published paper in which they wrote:

There is present in rice polishing a substance different from protein, and salts, which is indispensable to health and the lack of which causes nutritional polyneuritis.

- It is Casimir Funk, who isolated the amine, thiamine, and since it is vital for life, the term **vitamine** was proposed.
- These experiments lead to the emergence of two lines of inquiry leading to the discovery of the vitamins
  - 1- The study of substances that prevent deficiency diseases.
  - 2- The study of accessory factors required by animals fed purified diets.

## Classification of vitamins

- Few of the vitamins are single substances; almost all are families of chemically related substances.
- Vitamers sharing qualitatively (but not necessary quantitatively) biological activities.





# Types of Vitamins

There are 13 Vitamins for good health divided into 2 groups according to their solubility (water soluble and fat soluble )

## I- Fat soluble vitamins

- Vitamin A , Vitamin D, Vitamin E, Vitamin K (ADEK)

## II- Water soluble vitamins

- **Vitamin C** (ascorbic acid)
- **Vitamin B** : Thiamine (Vitamin B<sub>1</sub>), Riboflavin (Vitamin B<sub>2</sub>), Niacin (Vitamin B<sub>3</sub>),  
Pantothenic Acid (Vitamin B<sub>5</sub>), Pyridoxine (Vitamin B<sub>6</sub>), Biotin (Vitamin B<sub>7</sub>)  
(or vit H), Folic Acid (Vitamin B<sub>9</sub>), Cyanocobalamin (Vitamin B<sub>12</sub>)

	<b>Fat Soluble Vitamins</b>	<b>Water Soluble vitamins</b>
<b>Examples</b>	A, E, D, K	Vitamin C, B-complex
<b>Absorption</b>	Require bile acids to be dissolved and then absorbed into lymph then blood/protein carrier	Easily absorbed directly into blood
<b>Storage</b>	Can be stored in body: liver, and adipose tissue, long term stored.	Not stored in large quantities, short term stored.
<b>Excretion</b>	Less readily excreted - remain in fat storage sites	Kidneys detect and remove in urine
<b>Toxicity</b>	Toxicity is possible	Generally non-toxic
<b>Structure</b>	-To have predominantly aromatic and aliphatic characters -Fat soluble vitamins share some properties; each is composed either or entirely or primarily of five-carbon isoprenoid units.	-tend to have one or more polar or ionizable groups -Water soluble vitamins have diverse structures and biosynthetic pathways.

# I- Fat soluble vitamins

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## FAT SOLUBLE VITAMINS

Vitamin A

Vitamin D

Vitamin E

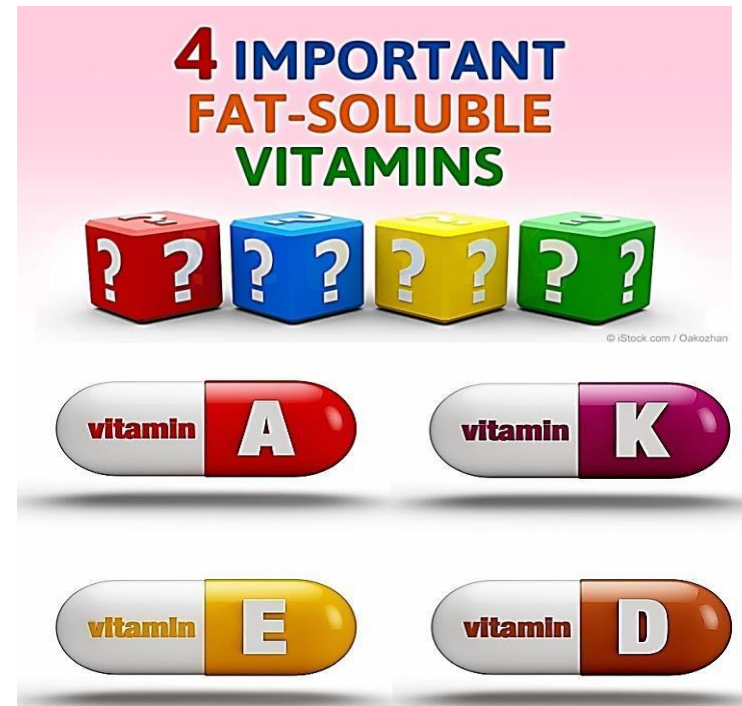
Vitamin K



# I- Fat soluble vitamins

**Fat-soluble vitamins (ADEK)** are a group of vitamins which are dissolved in fat and can be stored in liver and fat tissue until needed.

- **Fat-soluble vitamins** have a multitude of functions from keeping your **bones strong** to **helping your muscles move**.
- **Fat-soluble vitamins** are absorbed through the small intestine with dietary fat and are excreted slowly.
- **Toxicity:** Because fat-soluble vitamins are stored in your body longer they are more likely to cause toxicity,

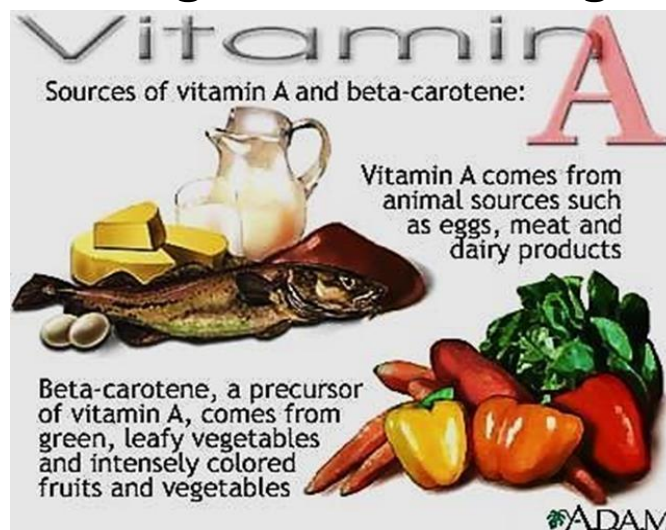


# 1- Vitamin A



## Sources of vitamin A

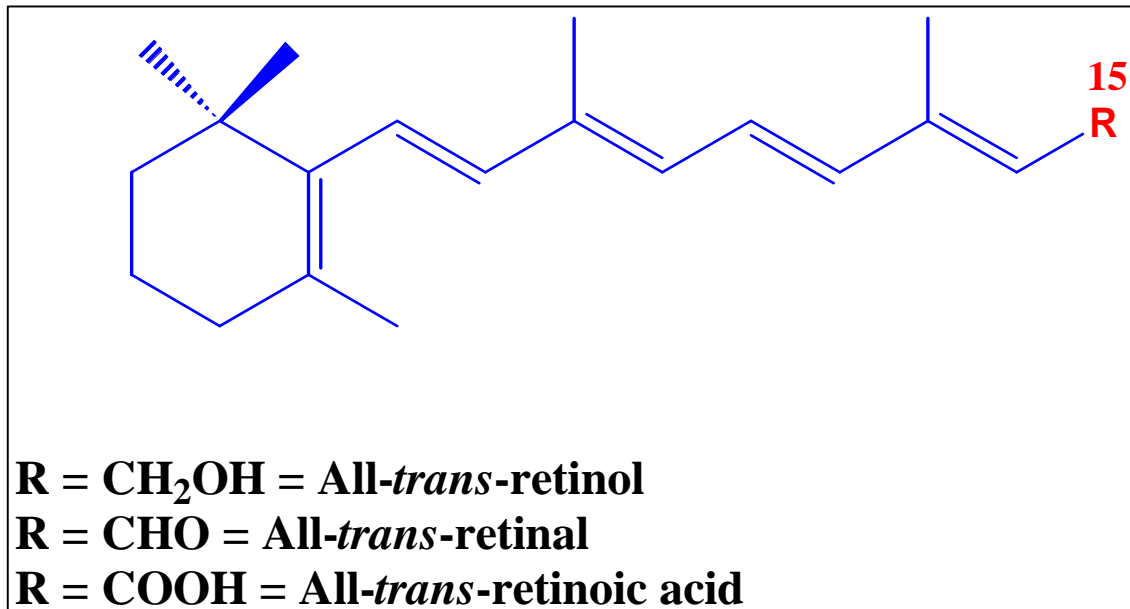
- Retinol is rarely found in foods.
- Retinyl palmitate, a precursor and storage form of retinol, is generally found in animal foods (egg yolks, liver, fish oil, milk, butter).
- Plant foods (beans, red peppers, carrots, peach). Provide only carotenoids (Poor people, vegetarian, developing countries).
- Plasma retinol level is within 40-50 ug/dl and well regulated.



- Vitamin A is a generic term for a large number of related compounds.
- **Retinol** and **retinal** are often referred to as preformed vitamin A.

# Chemical structures of vitamin A group

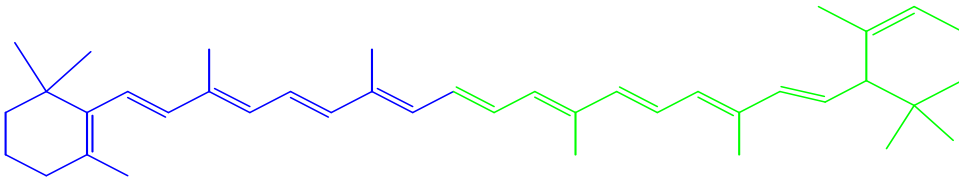
**1-Preformed vitamin A: Retinoids** (retinol, retinal, retinoic acid) [**Animal source**; heart, kidney, liver, eggs, dairy products, and fish]



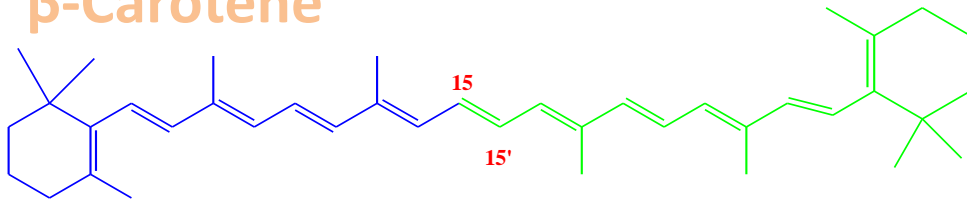


## 2-Provitamin A: Carotenoids ( $\alpha$ -carotene, $\beta$ -carotene and $\gamma$ -carotene) [Plant source; carrots and green leafy vegetable]

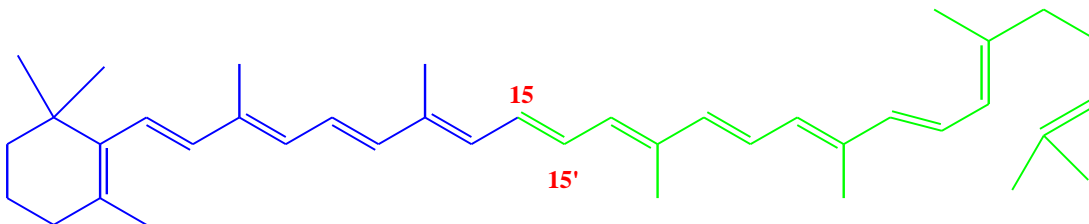
### $\alpha$ -Carotene



### $\beta$ -Carotene

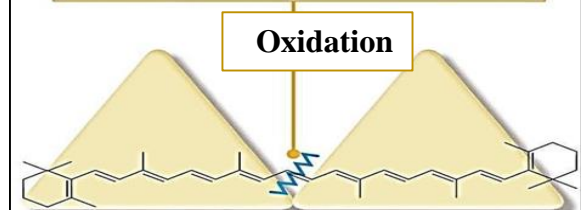


### $\gamma$ -Carotene



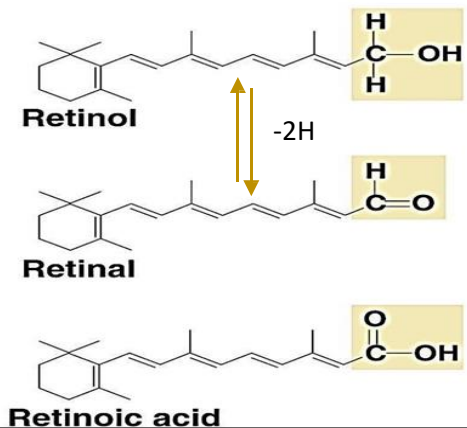
Once beta-carotene is absorbed, it can be cleaved in the middle to yield two molecules of vitamin A

Oxidation



Beta-carotene, a vitamin A precursor

A



**Retinoids** and **carotenoids** are precursors for the biosynthesis of 2 essential metabolites of vitamin A: **11-*cis*-retinal** and ***all-trans*-retinoic acid**.

## Chemistry of vitamin A

- Geometric isomers.
- Affected by oxygen, light, heat & aqueous solution.
- So, in diet supplements and as pharmaceuticals, it is usually presented in esterified forms.
- Group at position **15** determines specific chemical reactivity.

# How to measure vitamin A activity?

## 1- International unit (IU)

= 0.3  $\mu\text{g}$  all-*trans*-retinol

= 0.344  $\mu\text{g}$  retinyl acetate

= 0.6  $\mu\text{g}$   $\beta$ -carotene

= 1.2  $\mu\text{g}$  other provitamin A carotenoids

## 2- Retinol equivalent (RE)

= 1  $\mu\text{g}$  all-*trans*-retinol

= 6  $\mu\text{g}$   $\beta$ -carotene

= 12  $\mu\text{g}$  other provitamin A carotenoids

## Significance of vitamin A

- Vitamin A deficiency in children causes xerophthalmia (dry eyes).
- It is considered the single most important cause of childhood blindness in developing countries.

## Metabolism of vitamin A

- Vitamin A has three active forms (retinal, retinol and retinoic acid) and a storage form (retinyl ester).
  - Retinyl ester  $\leftarrow \rightarrow$  Retinol  $\leftarrow \rightarrow$  Retinal  $\rightarrow$  Retinoic acid.
- 1- Esterification to retinyl esters.
  - 2- Oxidation to retinal and then to retinoic acid.
  - 3- Isomerization to *cis* forms.
  - 4- Conjugation to retinyl glucuronide other sugars.

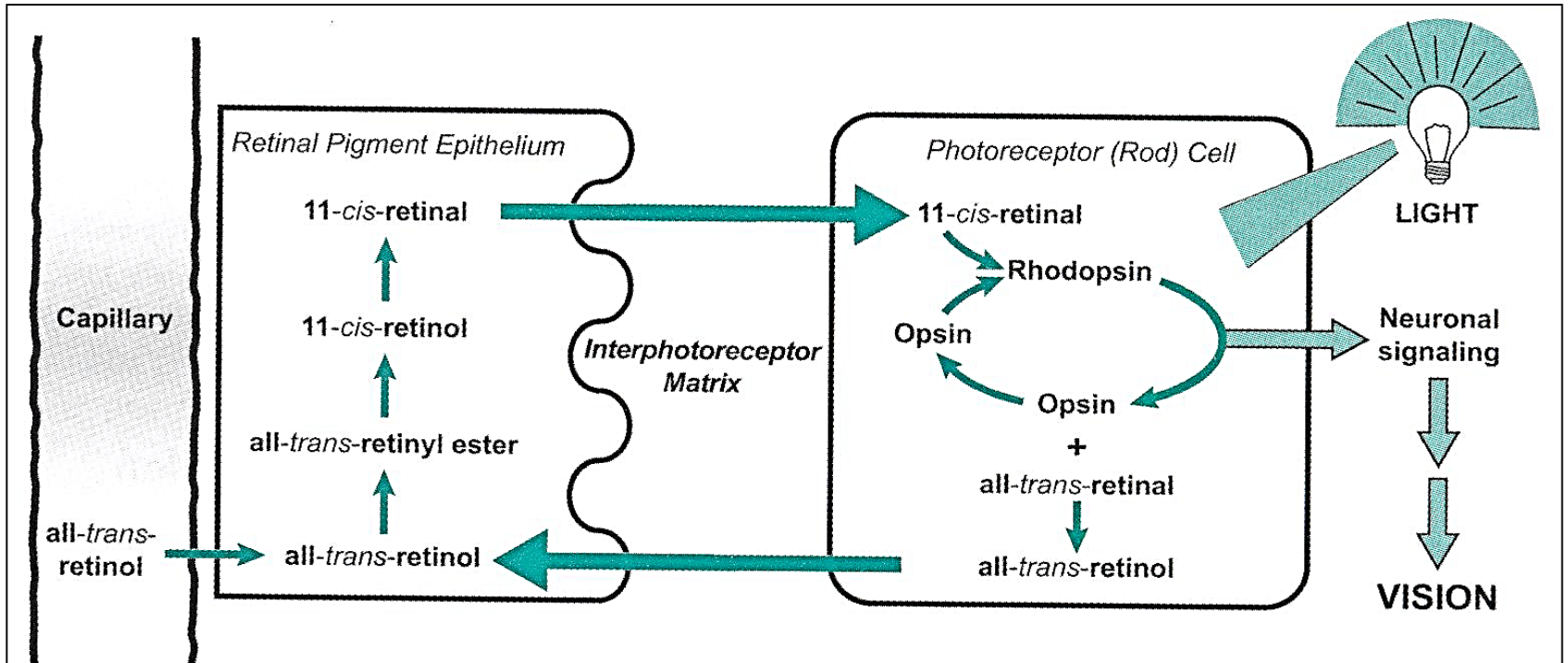
## **Metabolic functions of vitamin A**

- Retinol is involved in transportation and reproduction.
- Retinyl ester for storage.
- Retinal for vision.
- Retinoic acid involves in control cellular development and body processes.

## A- Vitamin A in vision

- The best elucidated function of the vitamin.
- 11-*cis*-retinal is the **photosensitive agent** and bound to rhodopsin in the retina of the eye.
- As light enters the eye, the 11-*cis*-retinal is isomerized to the all-*trans*-retinal.
- The all-*trans*-retinal dissociates from the opsin in a series of steps **called bleaching**.
- This isomerization induces a nervous signal along the optic nerve to the visual center of the brain.





B- Systemic functions of the vitamin A are much less well understood, but are more important.

1- **Epithelial cell "integrity"**: Many epithelial cells appear to require vitamin A for proper differentiation and maintenance. Lack of vitamin A leads to dysfunction of many epithelia - the skin becomes keratinized and scaly, and mucus secretion is suppressed (i.e. **Cell-keratinization**). It seems likely that many of these effects are due to impaired transcriptional regulation due to deficits in retinoic acid signaling.

2-**Bone remodeling**: Normal functioning of osteoblasts and osteoclasts is dependent upon vitamin A.

**3- Resistance to infectious disease:** In almost every infectious disease studied, **vitamin A deficiency** has been shown to **increase the frequency and severity of disease**. Several large trials with malnourished children have demonstrated dramatic reductions in mortality from diseases such as measles by the simple and inexpensive procedure of providing vitamin A supplementation. This "anti-infective" effect is undoubtedly complex, but is due, in part, to the **necessity for vitamin A in normal immune responses**. Additionally, many infections are associated with inflammatory reactions that lead to **reduced synthesis of retinol-binding protein** and thus, reduced circulating levels of retinol.

4- **Reproduction:** Normal levels of vitamin A are required for sperm production, reflecting a requirement for vitamin A by spermatogenic epithelial (Sertoli) cells. Similarly, normal reproductive cycles in females require adequate availability of vitamin A.

# Nutrient Interactions

## I- Zinc and Vitamin A

- a- Zinc deficiency results in decreased synthesis of retinol binding protein (RBP), which transports retinol through the circulation to tissues.
- b- Zinc deficiency results in decreased activity of the enzyme that releases retinol from its storage form in the liver.
- c- Zinc is required for the enzyme that converts retinol into retinal.

## II- Iron and Vitamin A

- Vitamin A deficiency may exacerbate iron deficiency anemia. Vitamin A supplementation has been shown to have beneficial effects on iron deficiency anemia and improve iron status among children and pregnant women. The combination of vitamin A and iron seems to reduce anemia more effectively than either iron or vitamin A alone.

## Recommended Daily Allowance (RDA)

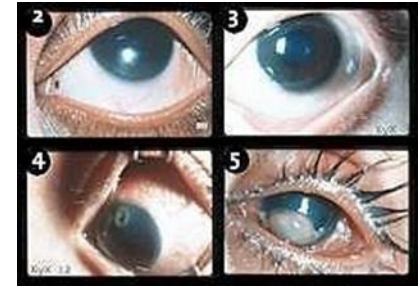
- 800 ug RE for adult women.
- 1000 ug RE for adult men.

The RDA value was based on:

- 1- The amount of vitamin needed to reverse night-blindness in vitamin A deficient subjects.
- 2- The amount needed to raise the plasma vitamin A levels to normal in depleted subjects.

## Vitamin A deficiency

- Primary vitamin A deficiency.
- Secondary vitamin A deficiency.
- usually results from **malnutrition**, but can also be due to **abnormalities in intestinal absorption of retinol or carotenoids**. Deficiency is prevalent in humans, especially children, in certain underdeveloped countries.
- Because the liver stores rather large amounts of retinol, deficiency states typically take several months to develop.
- Since vitamin A affects many organs in the body, its deficiency include many nonspecific signs.
- The only unequivocal signs are ocular lesions **nyctalopia (night blindness)**, and **xerophthalmia (dryness of cornea & conjunctiva)**.





## Uses of vitamin A

- 1- Treatment of vitamin A deficiency.
  - Aquasol A: oral or IM.
- 2- Treatment of acne and other skin diseases.
  - Tretinoin: topical.
  - Isotretinoin: oral and topical.
  - Tazarotene or Acitretin in the treatment of psoriasis.
- 3- Retinitis pigmentosa.
- 4- Treatment of Acute promyelocytic leukemia (APL).
  - Isotretinoin as a combination therapy with chemotherapy drugs.
  - Recently, in Japan, **Tamibarotene**, an orally active synthetic retinoid, was developed to overcome isotretinoin resistance.

## Vitamin A toxicity

- Acute toxicity occurs within a few hours or days after a very large intake as a result of accidental over-ingestion or inappropriate therapy. The estimated toxic dose is about 25,000 IU/kg.
- Chronic toxicity appears after ingestion of 25,000 IU or more daily for prolonged periods.
- **Hypervitaminosis A** in human is manifested mainly as changes in the skin and mucous membranes.
- Dry lips, dryness and fragility of the nasal mucosa and dry eyes.
- Skin lesions include dryness, pruritis, erythema, scaling, peeling of the palms and soles, hair loss and nail fragility.