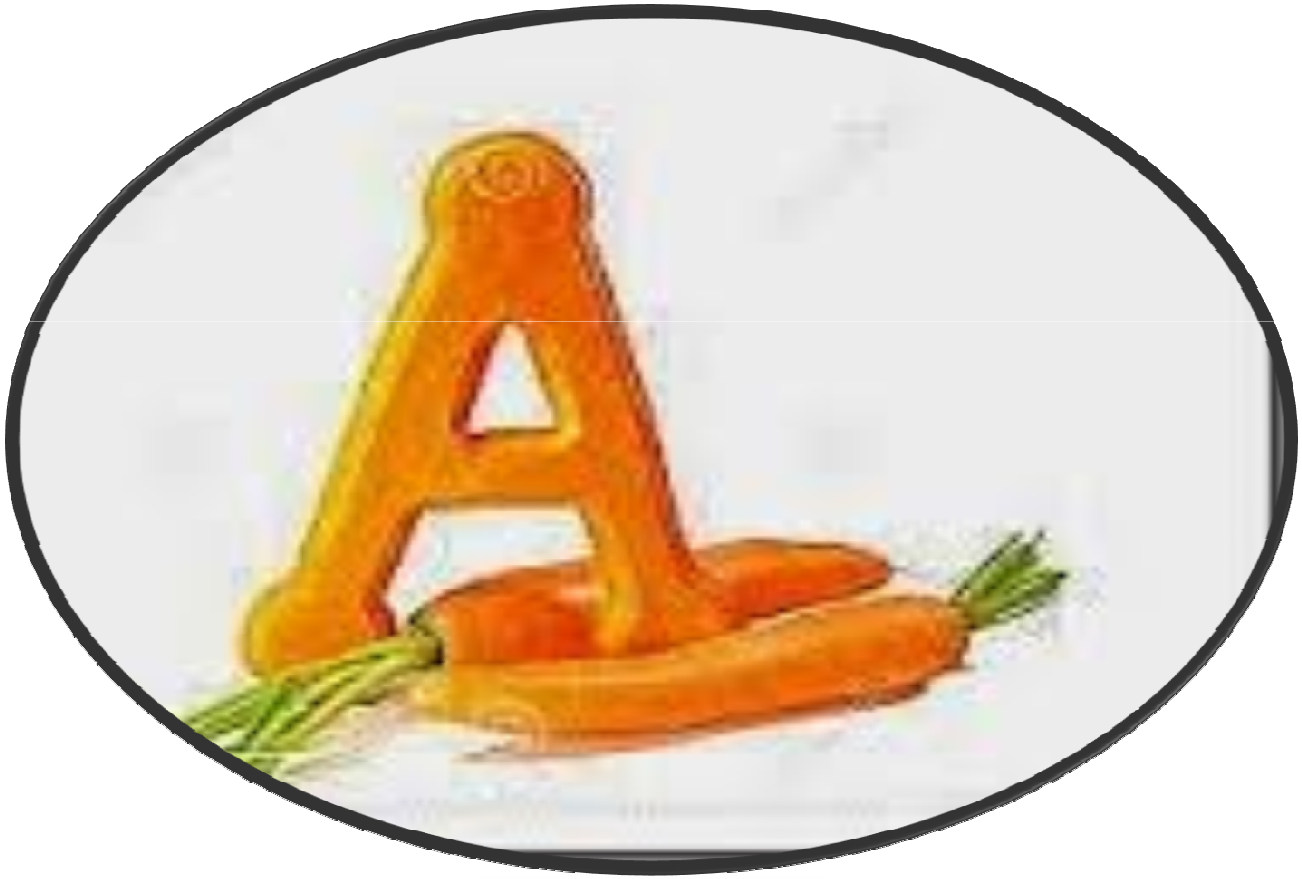
Fat Soluble Vitamins

Dr. Shivani Pandey, Department of Biochemistry

VITAMIN



Dr. Shivani Pandey, Department of Biochemistry

Vitamin A refers to **poly-isoprenoid** compounds.

Polyisoprenoid compounds consists of two distinct structures-

✓ a cyclohexenyl (β-ionone) ring

✓a side chain of isoprene units, which is attached to the cyclohexenyl ring.

✓B-ionone ring is required for biological activity of vit. A.

FORMS OF VITAMIN A

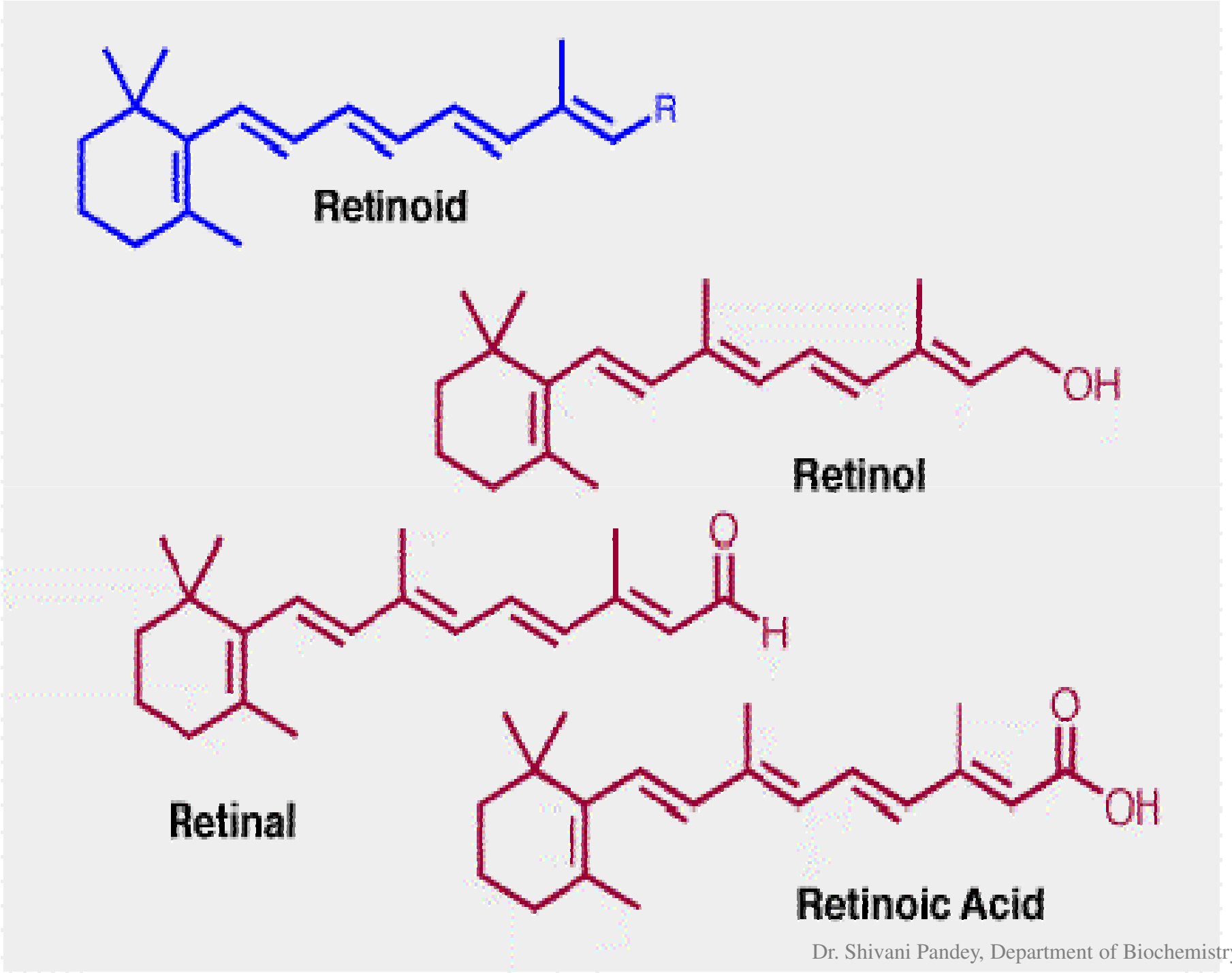
Vit .A occurs in 2 forms

1-RETINOIDS 2-CAROTENOIDS

- Foods from animal source provide various retinoids

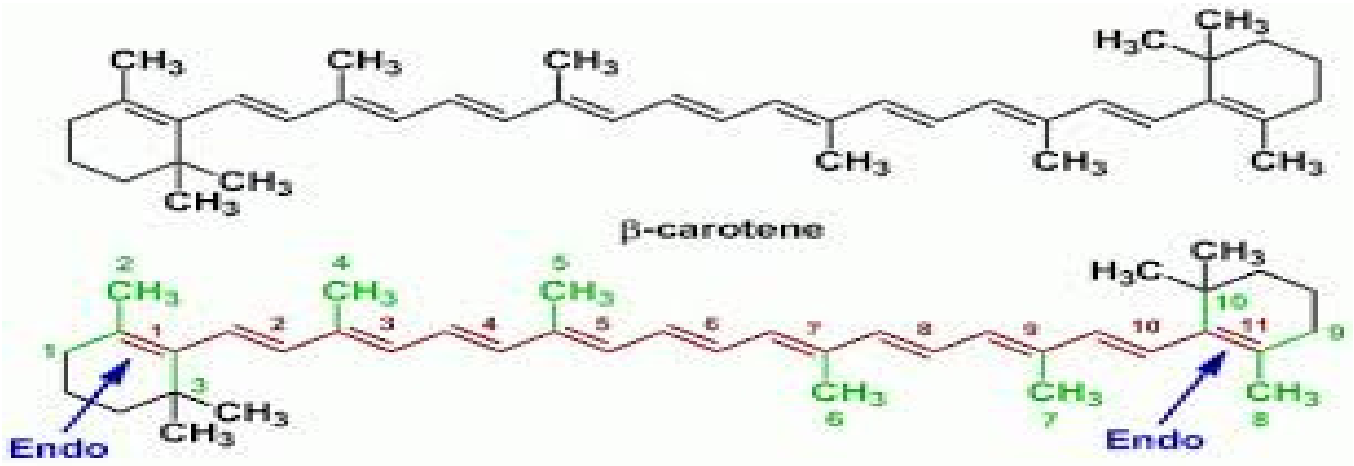
Retinoids occur in 3 different forms

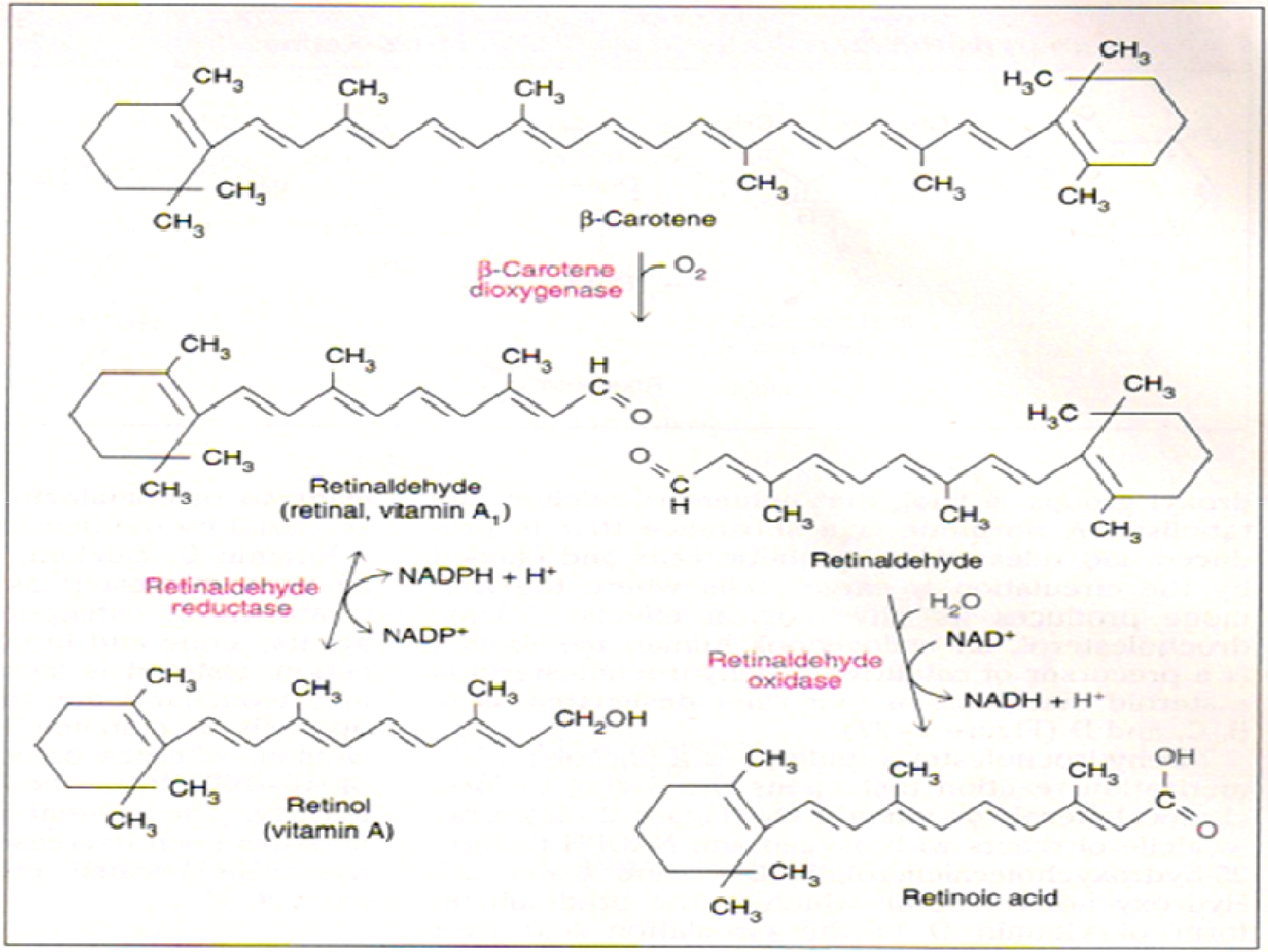
Retinol	an alcohol
Retinal	an aldehyde
Retinoic acid	an acid and most oxidized form


R
Retinoid
OH
Retinol
O
H
Retinal
O
OH
Retinoic Acid

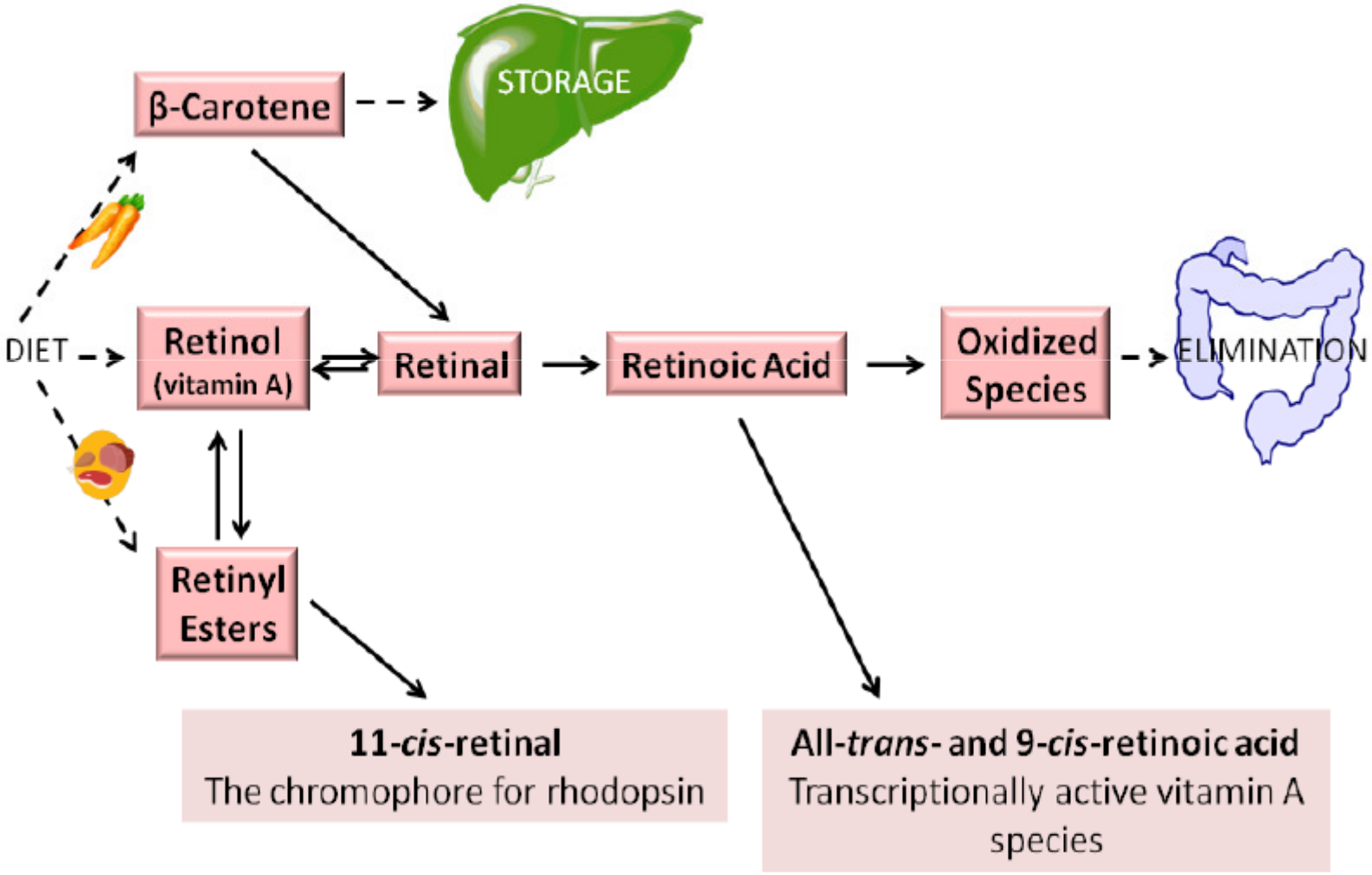
Foods from plant source provide **carotenoids**

- Over 500 carotenoids found in nature
- The most common form in food is β- carotene Inactive precursor(provitamins) forms of Vit A.
- β-carotene has two inoene rings and gives 2 molecules of Vit A(retinol)




β-Carotene
β-Carotene dioxygenase
O_2
Retinaldehyde (retinal, vitamin A_1)
Retinaldehyde
Retinaldehyde reductase
NADPH + H^+
$NADP^+$
Retinaldehyde oxidase
H_2O
NAD^+
NADH + H^+
Retinol (vitamin A)
Retinoic acid

Retinol is the immediate precursor to two important active metabolites: retinal and retinoic acid.



ABSORPTION

In food the vitamin exists as esters, which are hydrolyzed in the duodenum, a process that is assisted by bile salts

.

Absorption of the retinol and carotenes is facilitated by fat in diet being associated with micelles formed during fat digestion.

Dietary protein and zinc help utilization of both retinol and beta-carotene.

Absorption is aided by cellular retinal-binding protein type II situated on the epithelial cells of the small intestine

.

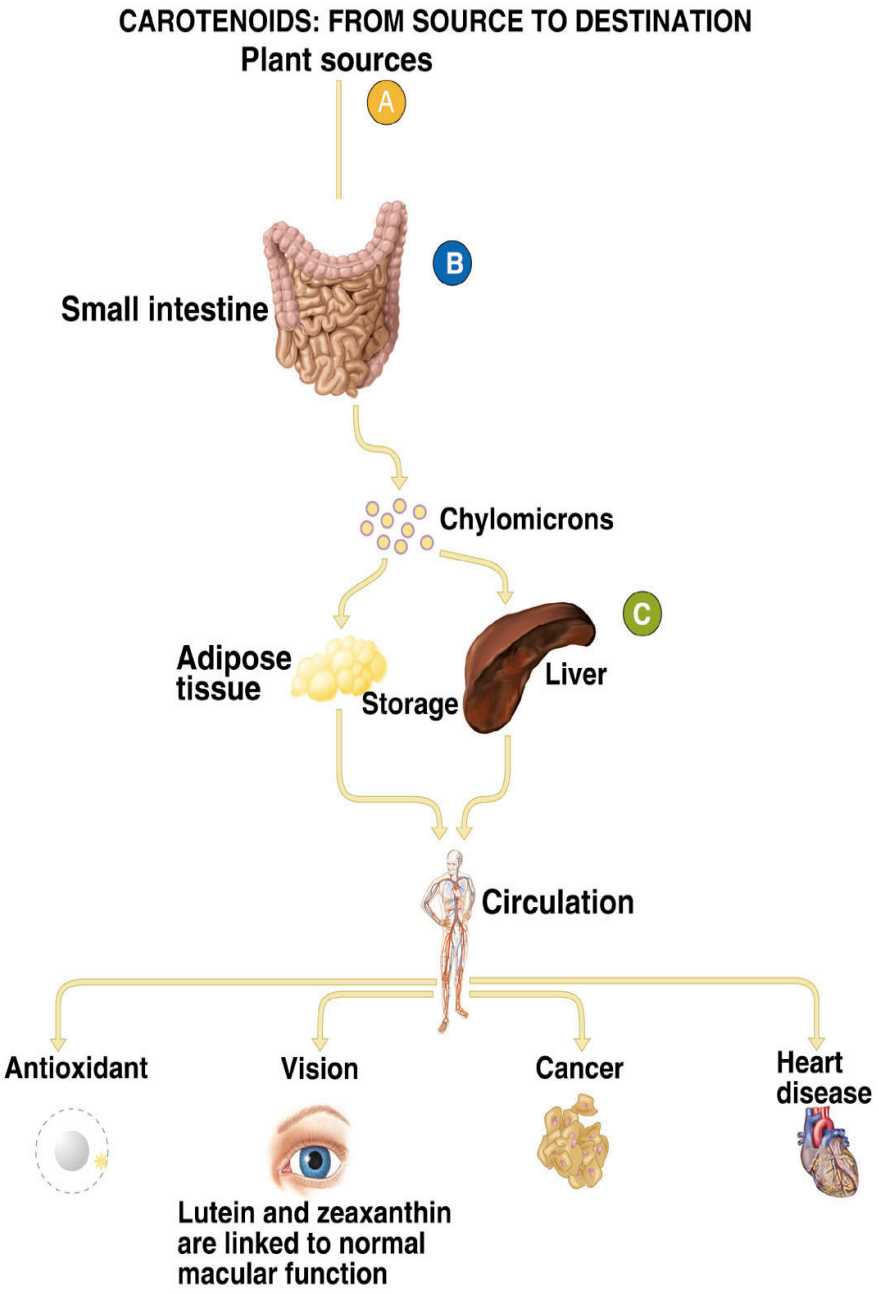
Carotene is converted into retinal, which is reduced to retinol as the next step.

Retinol is esterified with long chain saturated fatty acids and the esters are transported in to chylomicrones(molecule which transport fat from liver to peripheral tissues .

They are remained in chylomicrone remnants when triglycerides are removed by lipoprotein lipase(enzyme on endothelial surface to remove triglycerides) and they are taken up by liver and stored there.

Carotenoid Cleavage and Storage

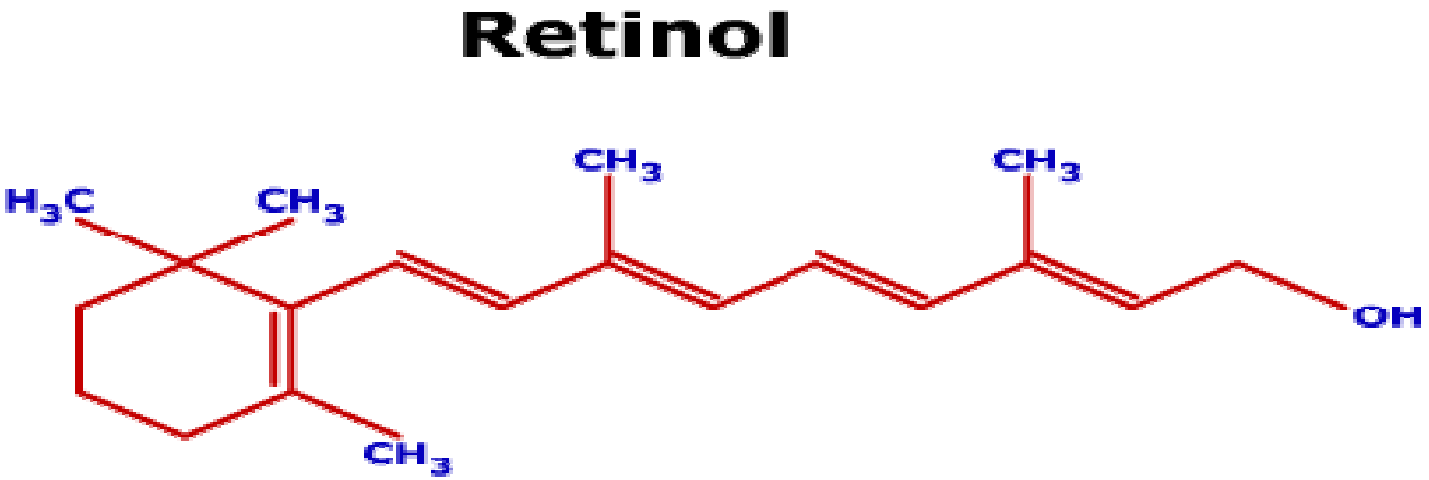
- β-carotene is converted to vitamin A in the intestinal mucosa
- 90% is stored in liver, mainly as the ester, retinyl palmitate (~ 6 months storage)
  - Small amounts in adipose and blood
- Transport
  - Retinol binding protein(RBP) acts to transport vitamin A from the liver and in the blood.
- Excretion
  - Small amount in urine



Transport & Storage

- ***Retinol*** Preformed vitamin A
  major transport and storage form

- retinol binding protein (RBP) picks up retinol from liver, carries it in blood



FUNCTIONS OF VIT A

RETINAL

Involved in VISION

RETINOL

Necessary for the reproductive system

RETINOIC ACID

Involved in growth and cellular differentiation

β Carotene

Plays antioxidant role.

METABOLIC FUNCTIONS OF VITAMIN A

- vital to good vision
- prevents night blindness
- antioxidant (β-carotene)
- necessary for healthy skin, hair growth
- keeps mucous membranes healthy
- promotes bone development
- support immunity (retinoic acid and carotenoids)

ROLE OF β-CAROTENE

- Antioxidant role of β-carotene
- Increased consumption of β-carotene is associated with decreased incidence of heart attacks skin and lung cancers
- High doses of carotene for long periods are not toxic.

Retinal's Role in Vision

Visual phototransduction light is converted into electrical signals in----------rod ,cone, ganglionic cells of the retina of the eyes.

11-*cis* retinal, (Vitamin A) acts as a visual pigment in our eyes, by absorbing photons.

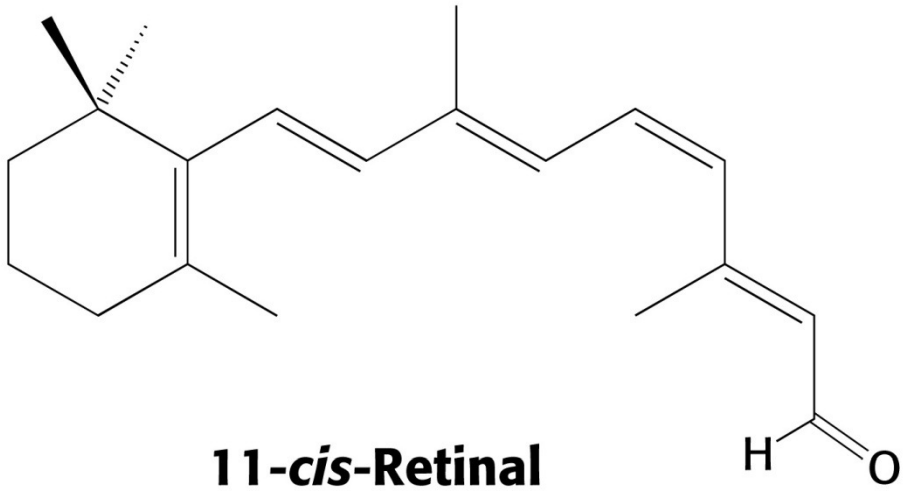
Visual Cycle, Rhodopsin Cycle , Wald's Cycle

- Active form of Vit A : ***11cis-retinal.***
- Adaptation to dark is function of photoreceptor cells in retina known as RODS.
- Rods contain photosensitive pigment called RHODOPSIN.

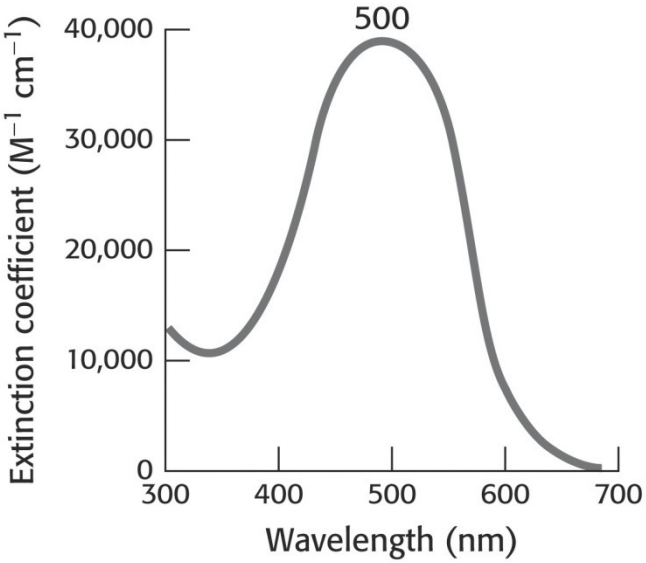
- To function, it is connected to the protein "opsin" via a Shiff's base. Together, the protein-pigment complex is called "rhodopsin."

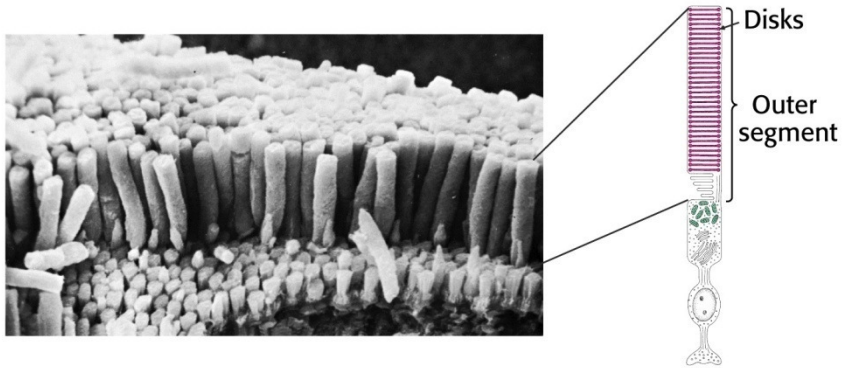
- The 11-*cis* double bond absorbs light, resulting in a conversion of the 11-*cis* to the 11-*trans* form. The light reaction takes only a few picoseconds and it starts a complex signal transduction pathway that leads to light being perceived in the brain.

Vitamin A as the Visual Pigment



11-*cis*-Retinal





- Rhodopsin Cycle comprises of 2 events

:Bleaching of Rhodopsin & Generation of nerve impulse

:Regeneration of Rhodopsin.

- When light falls on retina 11cis-retinal is isomerised to all trans retinal.

- Hence rhodopsin to active rhodopsin called Metarhodopsin11

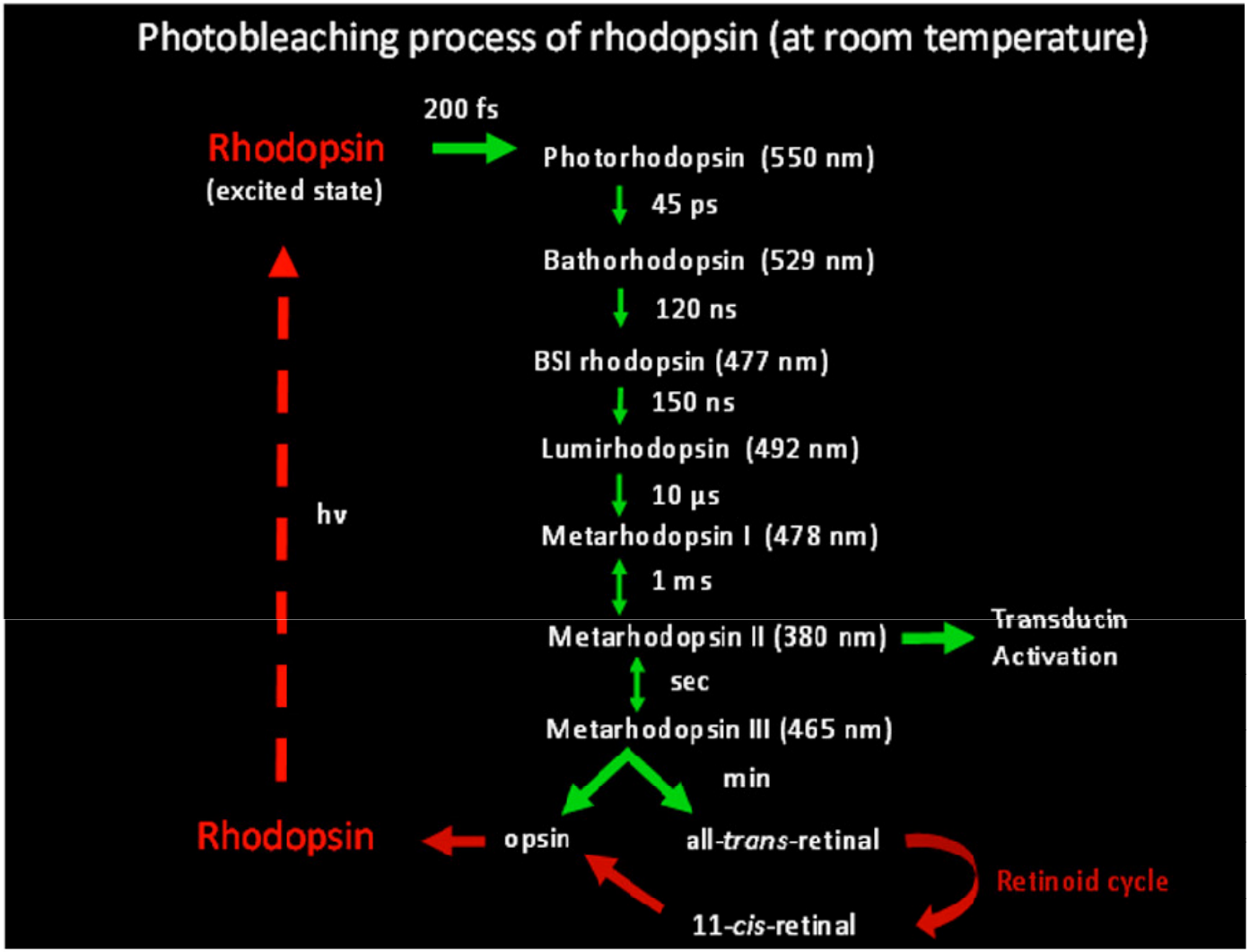
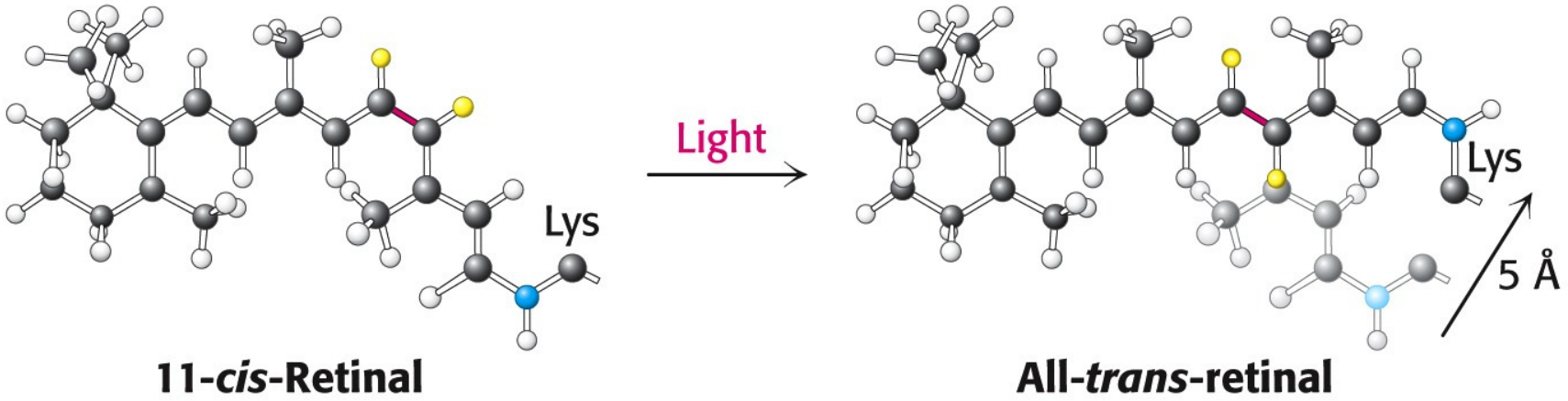
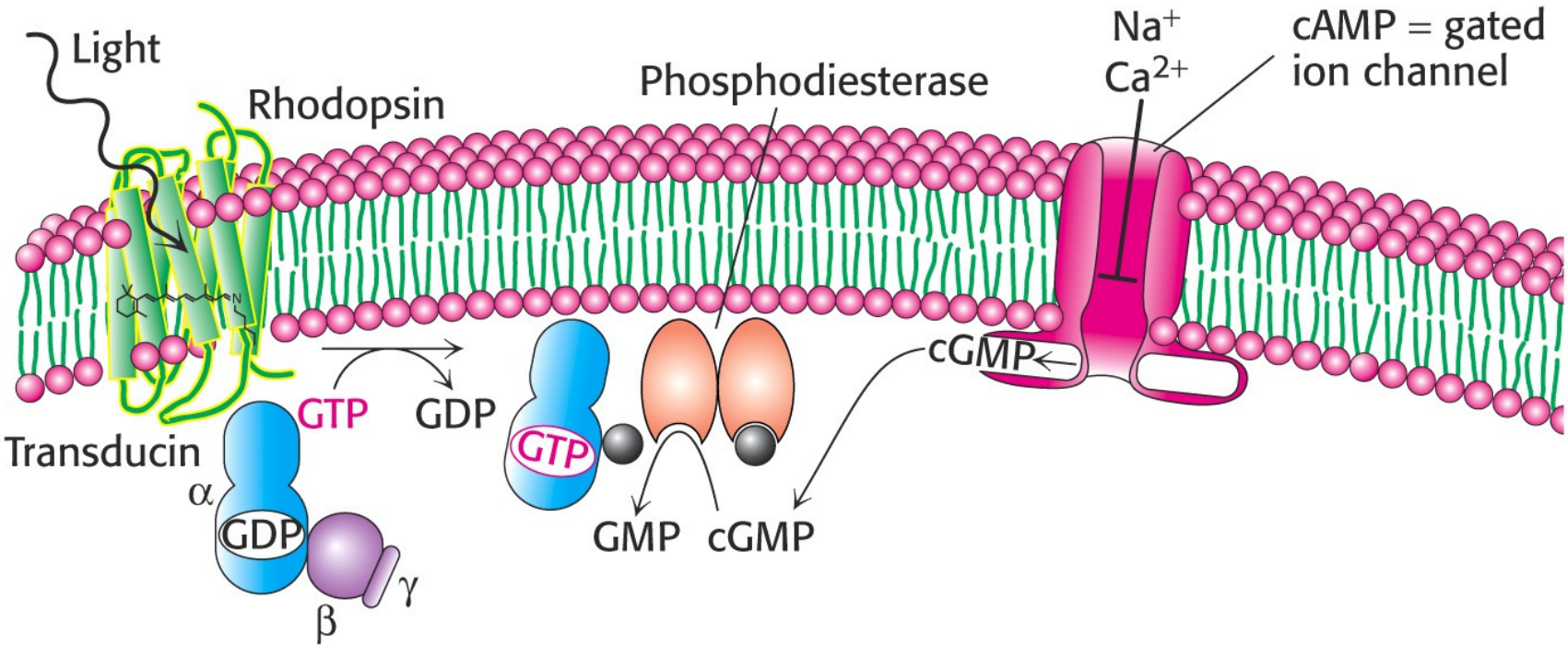


Figure 10. Photobleaching process of bovine rhodopsin. After photon absorption and electronic excitation, fast isomerization of the chromophore leads to the formation of a series of intermediate states of rhodopsin. This is called the "bleaching process" because rhodopsin loses its color. The intermediate states were identified by both low-temperature and time-resolved spectroscopy. The peak spectral sensitivity of each state was indicated. BSI, blue-shifted intermediate. Modified from Wolfgang Baehr.

- Conformational changes in metarhodopsin results in the activation of Transducin
- Transducin is a G protein.
- Activation of transducin results from binding of GTP to α subunit & release of beta and gamma subunit.
- Activated Transducin activate enzyme Phosphodiesterase(PDE).
- PDE. hydrolyses cyclic GMP to GMP thereby decreasing cGMP levels.

Vitamin A – Retinal's Role in Vision (Chapter 32)

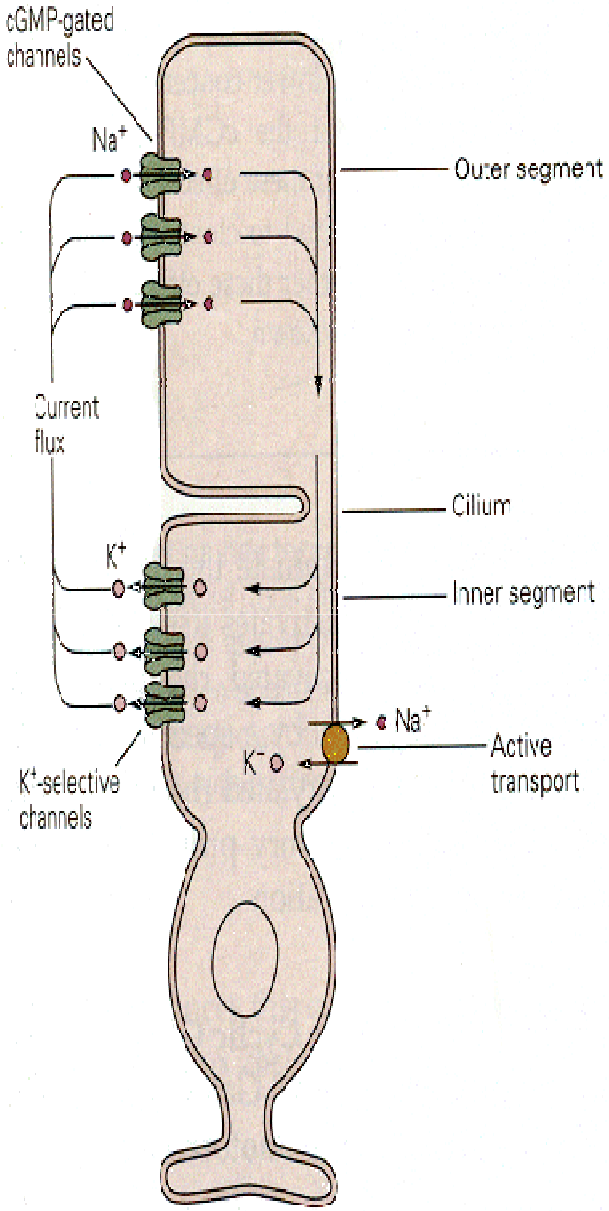




Low levels of cGMP results in closure of Na channels.

Closure of Na channels results in Hyperpolarisation.

Hyperpolarisation generates nerve impulse.



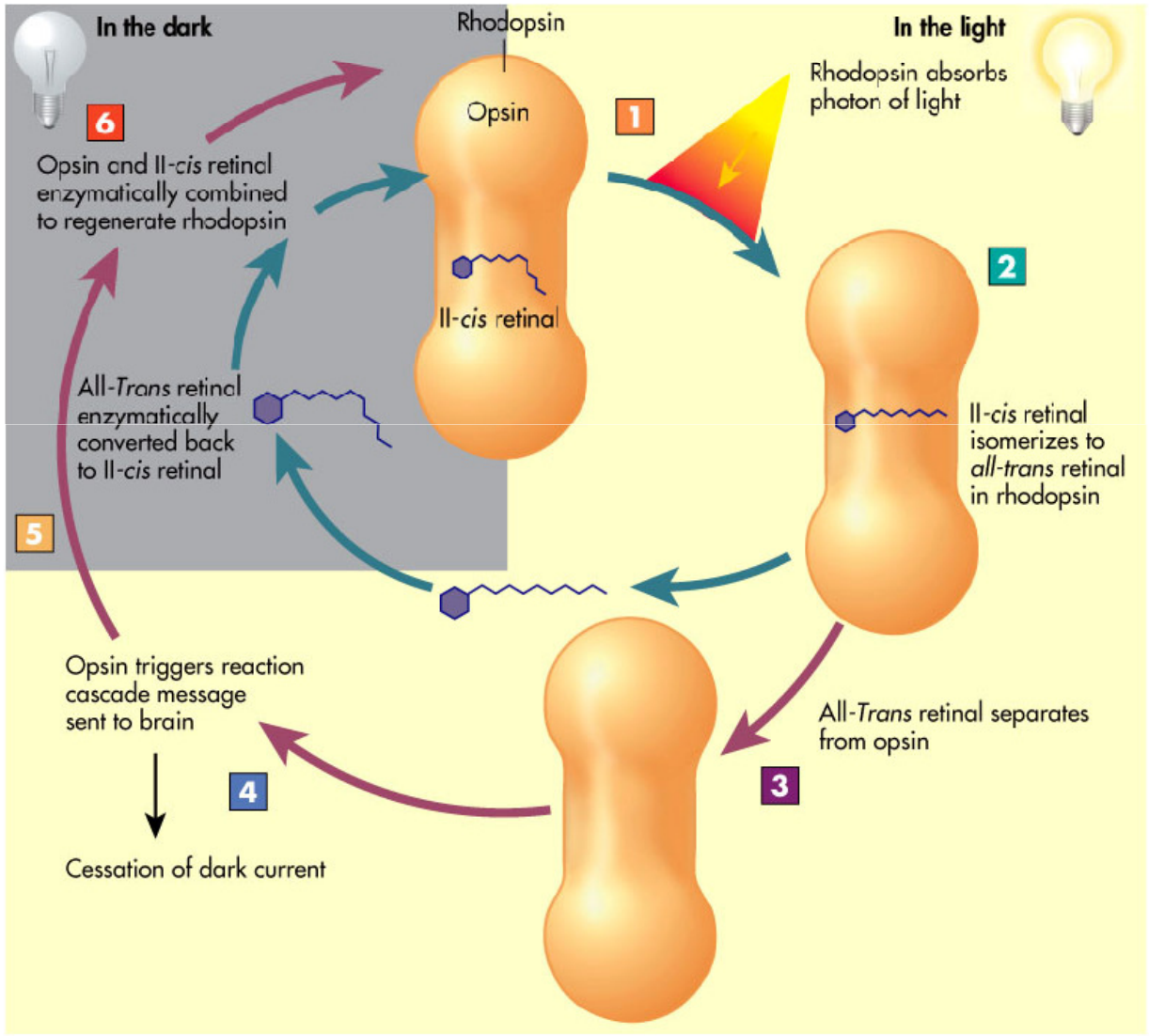
REGENERATION OF RHODOPSIN

PATHWAY 1:- All trans retinal is isomerised to 11 cis-retinal

Retinal by ISOMERASE enzyme in retina to form Rhodopsin.

- **PATHWAY 2:--**
- All trans retinal is reduced to all trans retinol in retina.
- This then reaches liver by blood circulation.
- Now all trans retinol is isomerised to all cis retinol.
- Now 11 cis retinol reaches retina and gets oxidized to 11 cis retinal.
- 11 cis retinal + opsin = rhodopsin.
- CYCLE REPEATS.

RHODOPSIN CYCLE OR WALD'S VISUAL CYCLE



- Rhodopsin: combination of a protein part (opsin) and 11-cis retinal (only cis form can bind with opsin).
- When light energy is absorbed by rhodopsin, the rhodopsin decompose: converts 11-cis retinal into all-trans retinal.
- In order to maintain the ability to detect light, the rods must reconvert the all-trans retinal into 11-cis retinal.
- This process only occurs under the dark environment.

- Dark adaptation time

RECOVERY

- To achieve a rapid response, the signal must be returned to its initial state.
- First step is to block activated Rhodopsin for continuous activating transducin.
- Rhodopsin kinase causes the phosphorylation of the carboxly terminus of activated rhodopsin R*

- Then **arrestin** an inhibitory protein binds to phosphorylated R* & prevents additional interaction with transducin.

- Secondly the α subunit of transducin must be returned to its inactive state to prevent further signaling.

- For this α subunit has built in GTPase activity that hydrolyzes GTP::::::::> GDP.

- The GDP form of transducin leaves phosphodiesterase & reassociates with βϒ subunits.

- Levels of c GMP must be raised to open the c GMP gated ion channels. The action of Guanylate Cyclase accomplishes this third step by synthesizing cGMP from GTP.

- Calcium ions play a essential role in controlling guanylate cyclase. How ?

- In the dark Na & Ca enter the rod cell through cGMP gated channels.

- Calcium ions are effluxed through an exchanger which uses 4 Na in & 1 K ion out to extrude one Ca ion.

- After illumination the entry of Ca through the cGMP gated channels stops but export through exchanger continues thus resulting in drop of cytoplasmic Ca.

- This drop stimulates gyuanylate cyclase rapidly restoring the concentration of cGMP to open the channels.

- **(cGMP)$\downarrow$ → Ion channels → (Ca^{2+})$\downarrow$ → Guanylate cyclase → cGMP$\uparrow$**

  closed **activated**

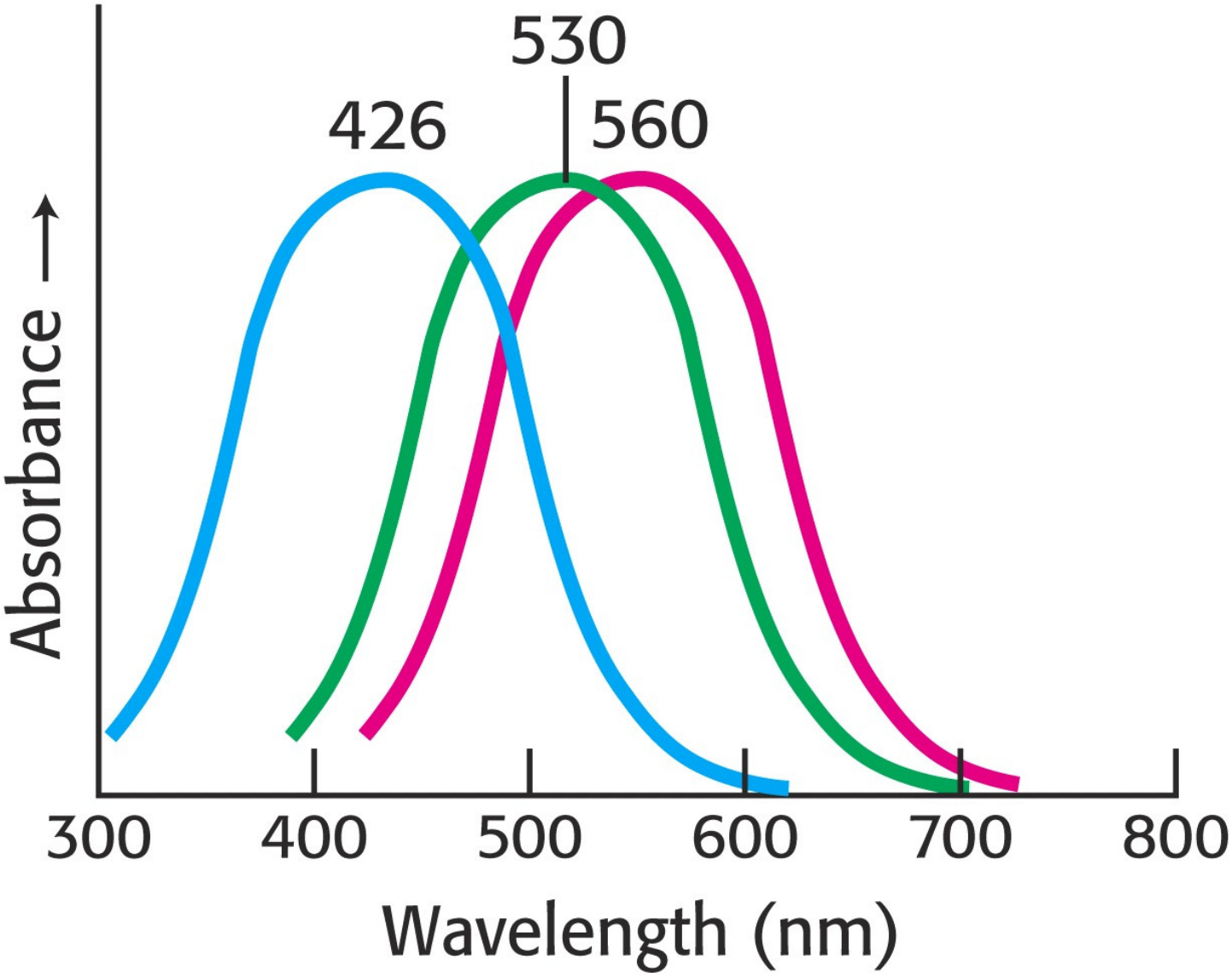
Activation **Recovery**

- Color Vision is possible because of three conopsin binding to three different opsin proteins in three different types of cone cells.

- Each protein has a slightly different amino acid composition, changing the environment of the 11-*cis*-retinal pigment

- This change shifts the absorption spectrum of these three proteins to the "blue," "green," and 'red" regions. Signals from each of these three different types of cells are the basis for our color perception.

Vitamin A – Retinal's Role in Vision (Chapter 32)



Retinal and Color Vision

- The genes for the color-shifted opsin proteins lie adjacent to each other on the human X chromosome and share a high degree of similarity.
- Slight changes in the base sequences of these genes result in spectral shifts for light absorption, leading to perceptual differences in the color of light we see.
- Human X chromosomes carry various numbers of color pigments genes. In the general population, the X-chromosome gene content varies significantly:

2% - 1 color pigment gene

20% - 2 color pigment genes

50% - 3 color pigment genes

20% - 4 color pigment genes

5% - 5 color pigment genes

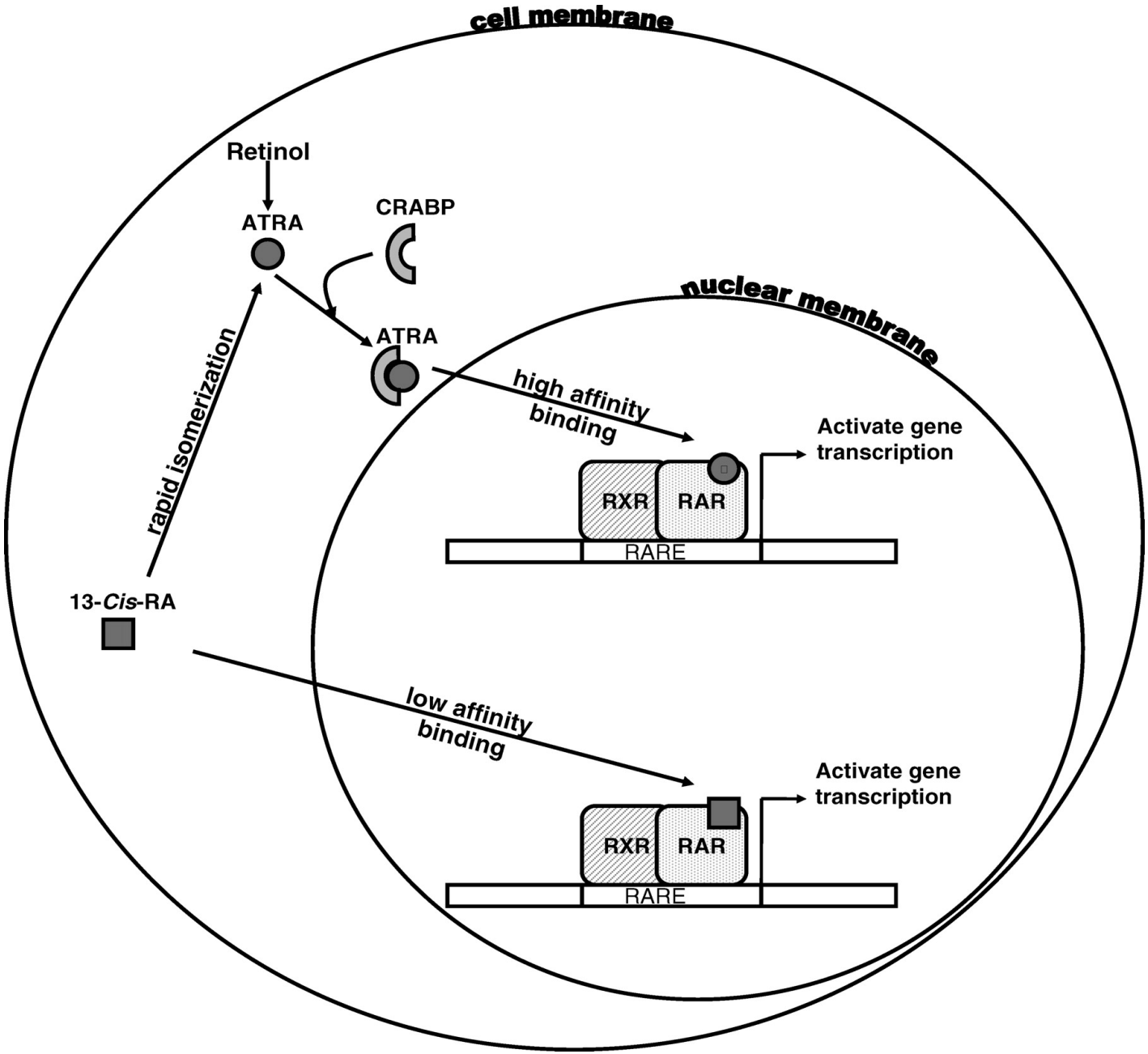
Color Blindness

- Due to the loci of these genes on the X chromosome, most colorblindness is sex-linked, with predominant expression in males.

- ~ 5% of males lack the green pigment gene. The resulting hybrid gene absorbs light between red and green, making differentiation of these two colors difficult.

VIT.A IN REPRODUCTION

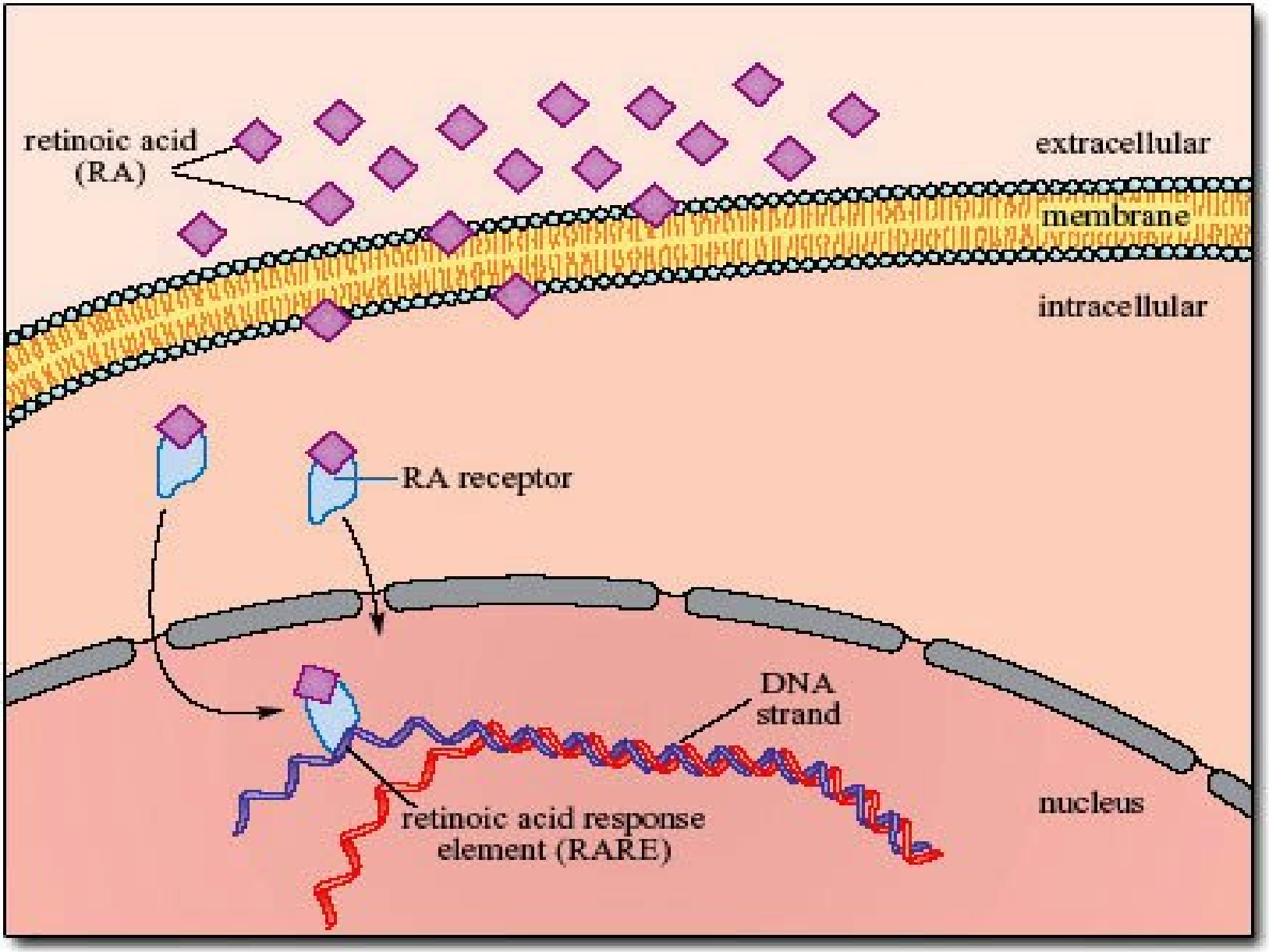
- ACTIVE FORM ***:- RETINOL***
- MECHANISM :- Retinol binds to CRBP.
- Retinol receptor complex binds to DNA & regulates the expression of genes required for reproductive function.
- Mechanism of action is similar to steroid hormone action.

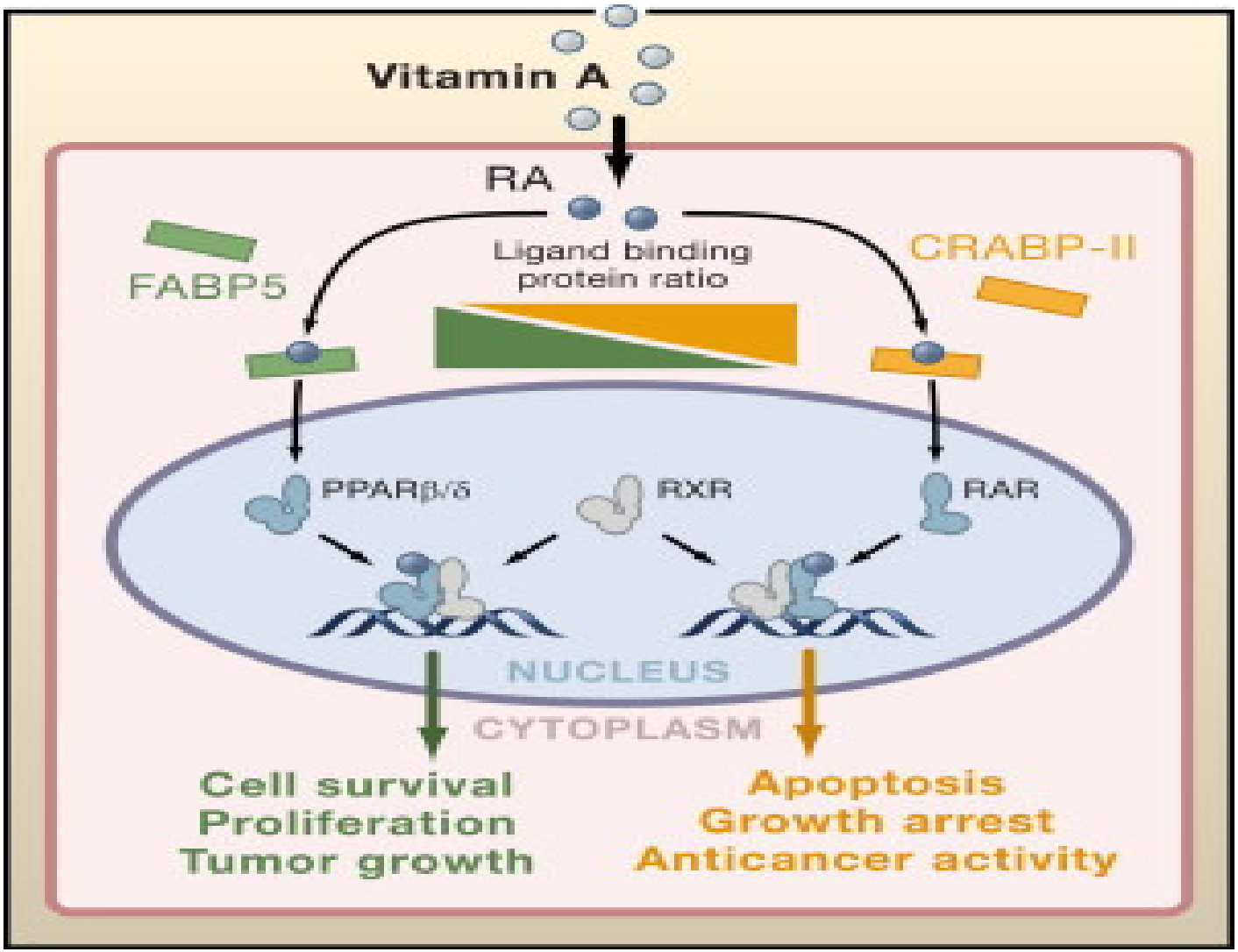

cell membrane
Retinol
ATRA
CRABP
ATRA
nuclear membrane
high affinity
binding
Activate gene
transcription
RXR
RAR
RARE
rapid isomerization
13-*Cis*-RA
low affinity
binding
Activate gene
transcription
RXR
RAR
RARE

VIT. A IN GROWTH & DIFFERENTIATION

Active form *:- Retionic acid*.

- Mechanism :- All trans retionic acid or 9 cis retionic acid binds to specific CRBP.
- This complex binds to DNA & regulates the gene reqd. for growth & differentiation.
- Used in cancer treatment : causes differentiation of tumors.
- Induces apoptosis (programmed cell death) of cancer cells.


retinoic acid
(RA)
extracellular
membrane
intracellular
RA receptor
DNA
strand
retinoic acid response
element (RARE)
nucleus


Vitamin A
RA
FABP5
Ligand binding protein ratio
CRABP-II
PPARβ/δ
RXR
RAR
NUCLEUS
CYTOPLASM
Cell survival
Proliferation
Tumor growth
Apoptosis
Growth arrest
Anticancer activity

VIT. A maintains: Epithelial Integrity &Glycoprotein Synthesis

Active form : ***- Retinol , Retinyl phosphate***

- Retinol is involved in both the above processes.
- Retinol prevents excess keratin synthesis.
- Retinyl phosphate is formed from retinol & is required for glycoprotein synthesis.
- Glycoproteins are important constituent of the mucous secreted by many epithelial cells.
- Retinyl phosphate forms glycosyl retinyl PO_4 & acts as donar of carbohydrates .

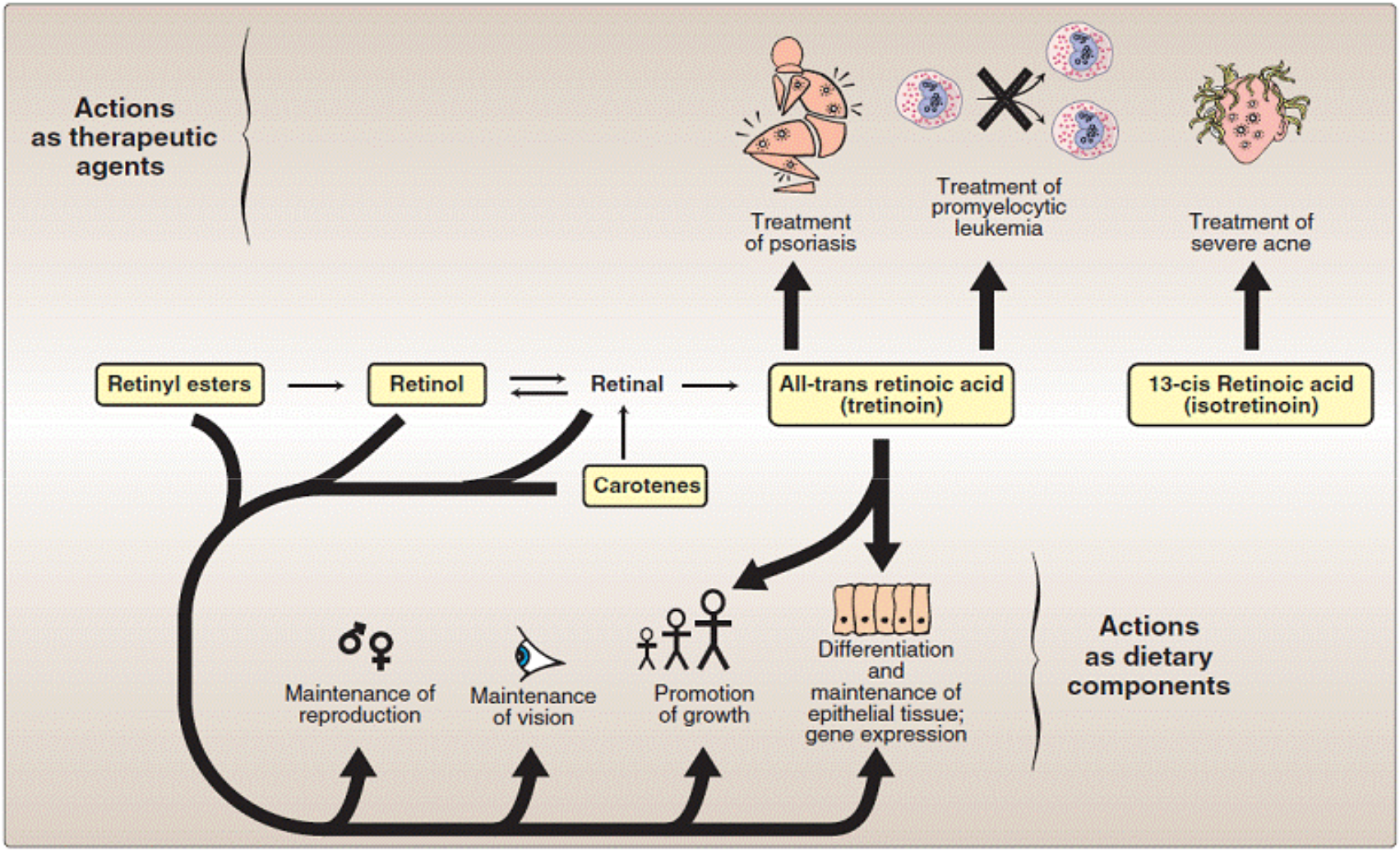
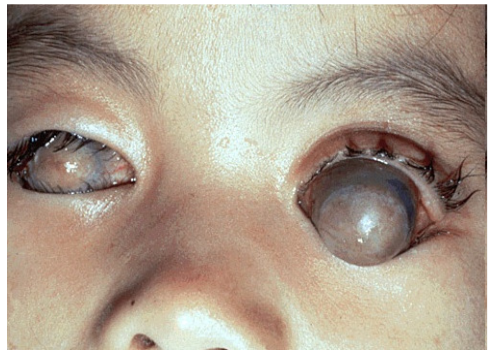


Figure 28.21
Summary of actions of retinoids. Compounds in boxes are available as dietary components or as pharmacologic agents.

VITAMIN A - DEFICIENCY



- More obvious deficiency symptoms than other vitamins
  - Night blindness
    - Leading cause of blindness in third world countries
  - Cell keratinization
    - Dry skin
    - Xerophthalmia (dryness of cornea & conjunctiva)
  - Reproductive failure
  - Abnormal skeletal development/maintenance

Immune dysfunction

Mucous linings harden

increased tendency for infection

vitamin A deficiency ***increases infection rate***

HOW ??

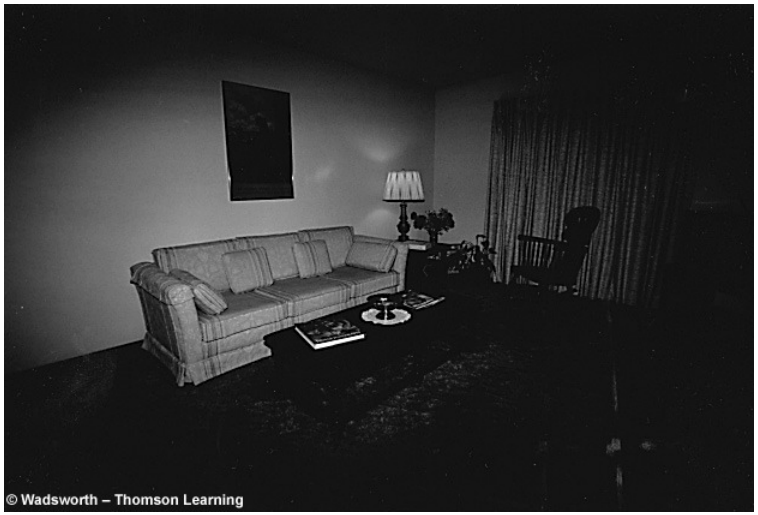
- Vitamin A deficiency reduces the activity of macrophages.

- It is postulated that mucus producing cells are replaced by keratin producing cells in respiratory, gastro-intestinal and genitor-urinary tracts and in the corneal-conjunctival epithelium which results in invasion of organisms causing infections

- Lysozyme which is an antiviral substance depends on vitamin A for its synthesis.

- Deficiency also reduces T lymphocyte activity to viral infections and levels of immunoglobulins in blood particularly immunoglobulin A..

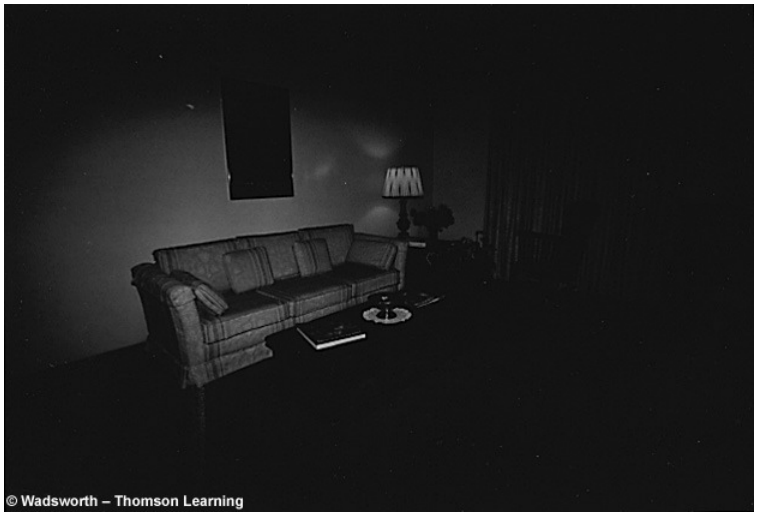
Vitamin A–Deficiency Symptom
Night Blindness



In dim light, you can make out the details in this room. You are using your rods for vision

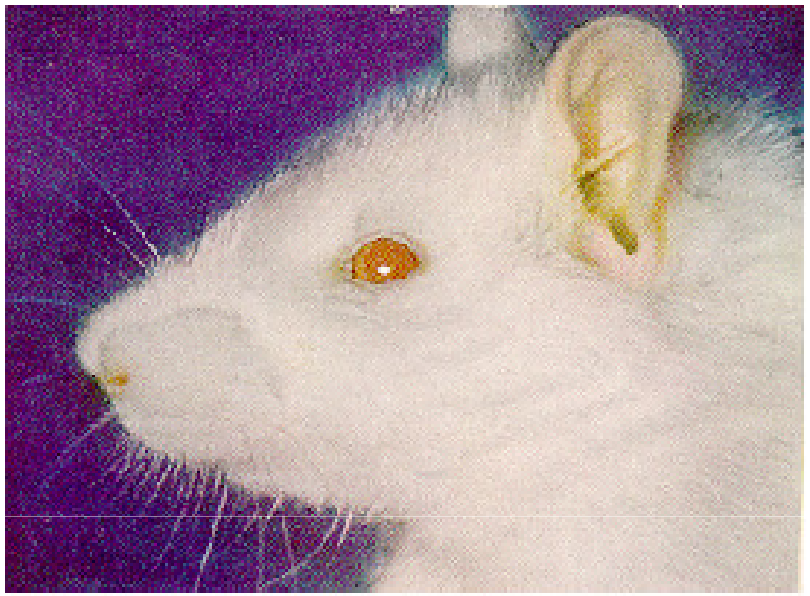
You quickly recover and can see the details again in a few seconds.

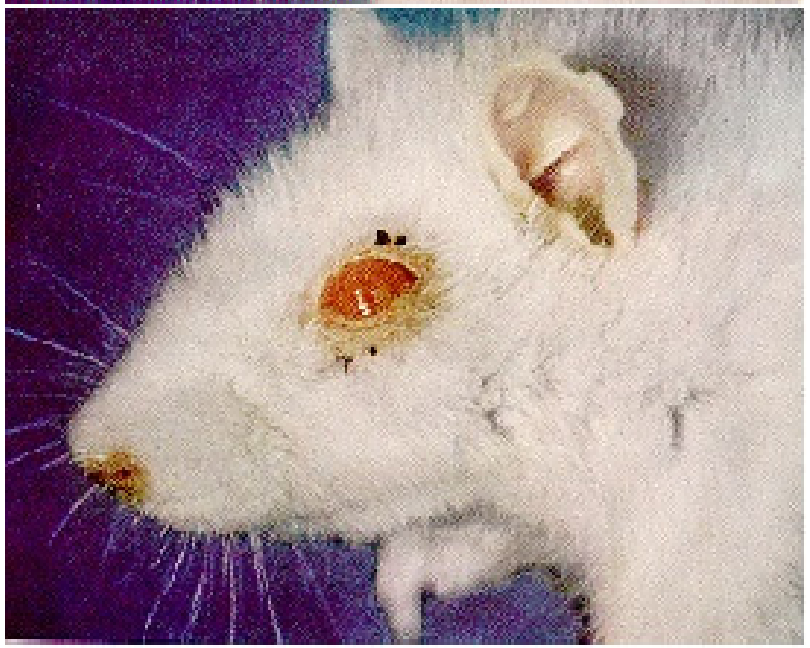
A flash of bright light momentarily blinds you as the pigment in the rods is bleached.



With inadequate vitamin A, you do not recover but remain blinded for many seconds.

Xerophthalmia



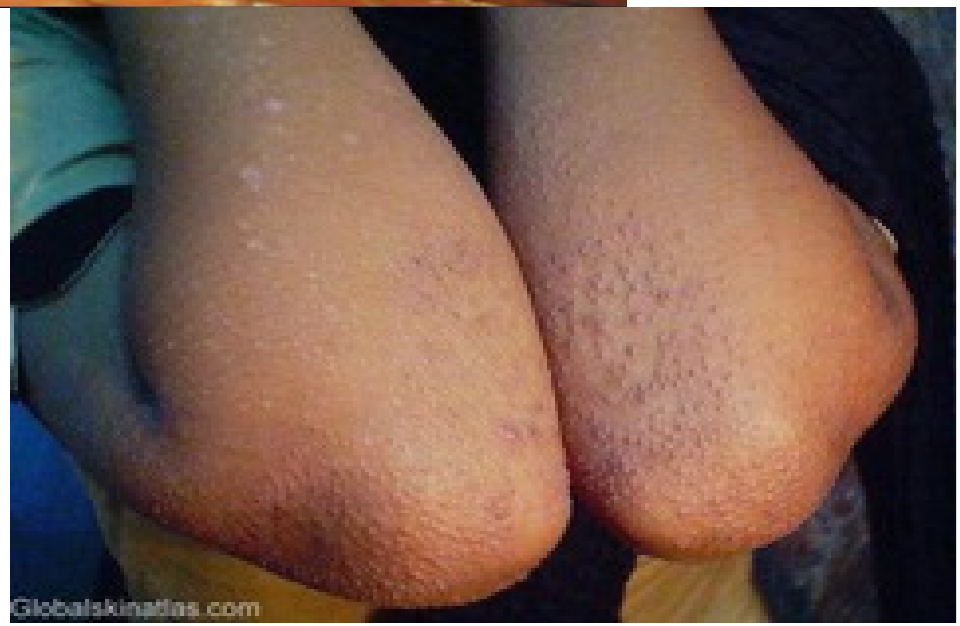


↑ curable early stage

after 8 days vitamin A ↗

incurable late stages →


What to Do ?
Bitot's Spots



Daily requirement

- Children

  2000 – 3500 I.U.

- Men

  5000 I.U.

- Women

  4000 I.U.

Bear in mind that too much of a good thing can have side effects and the same applies to vitamin A. Pregnant women should be wary that large doses of vitamin A can cause birth defects.

VITAMIN A TOXICITY

- **Acne medication** can cause birth defects

Overdosing

joint pains
loss of hair
Liver damage: jaundice
Blurred vision
Loss of appetite
Skin coloration
death

POLAR BEAR LIVER

One ounce of polar bear liver contains enough vitamin A (retinol) to kill a person!

Vit. A DEFICIENCY

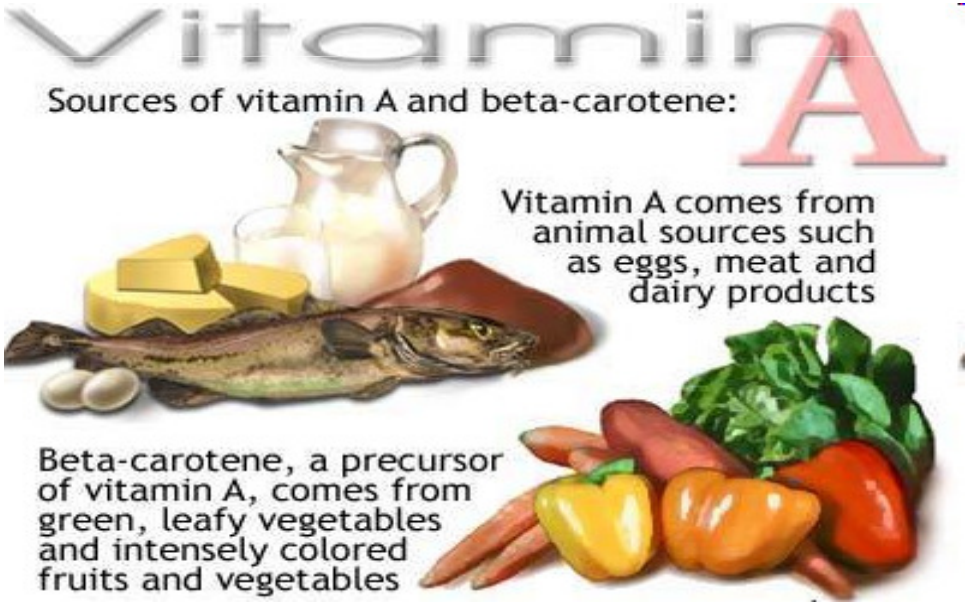
CAUSES

- Inadequate intake
- Impaired absorption due to Pancreatic diseases, Obstructive jaundice, small Intestinal diseases
- Impaired storage and transport due to LIVER cirrhosis
- Increased excretion due to Nephrotic syndrome
- Alcoholism

Vitamin A - Sources

- Animal sources
  - Liver
  - Milk
  - Egg yolk

- Plant sources
  - Carrots
  - Green leafy vegetables
  - Orange coloured fruits, e.g. mango and apricots
  - Dark green and yellow vegetables.

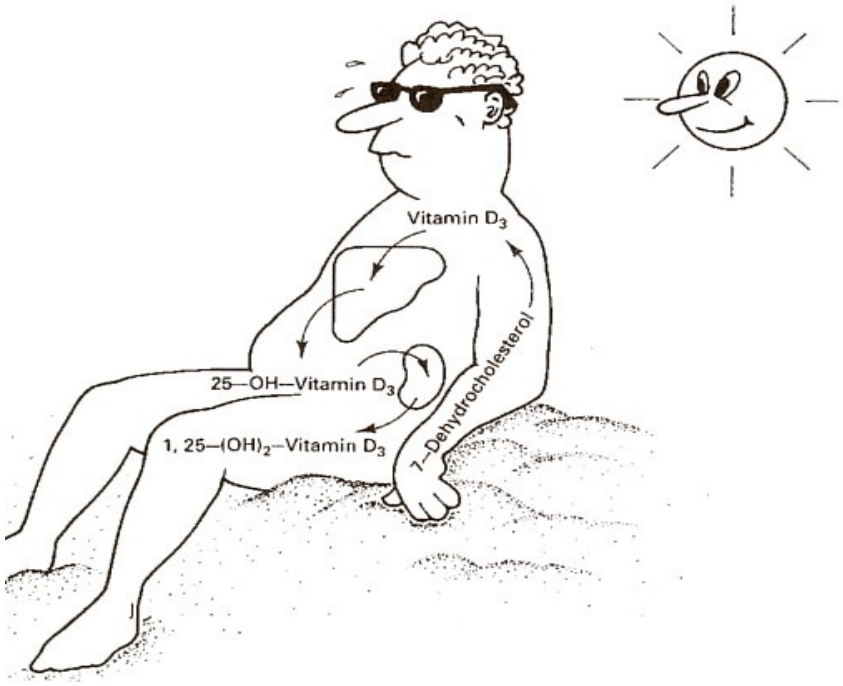


Vitamin D

Dr. Shivani Pandey, Department of Biochemistry

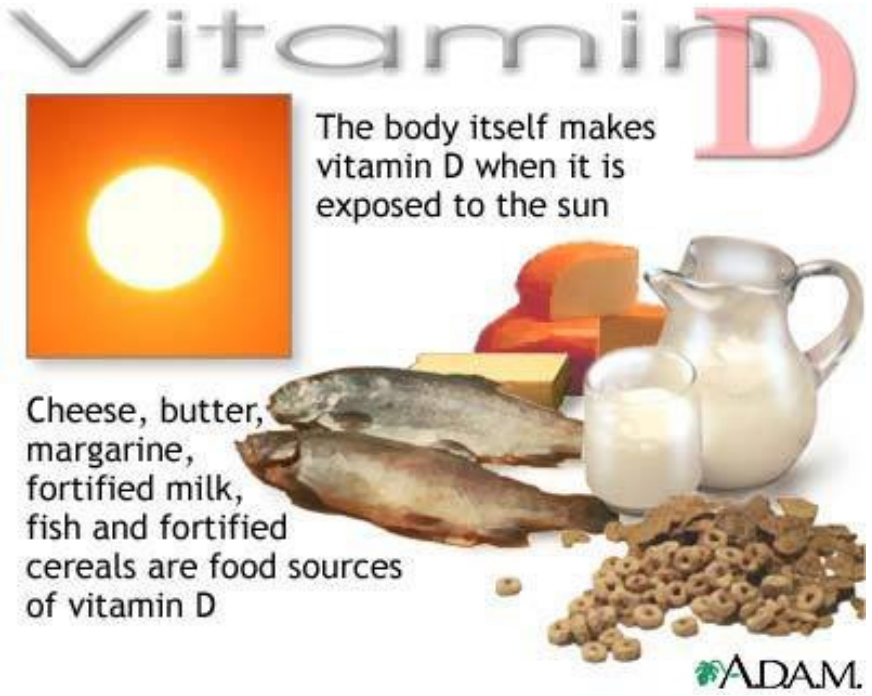
Vitamin D: Sunshine Vitamin

- Body can make it if exposed to enough sunlight
- Made from cholesterol in the skin



Vitamin D - Sources

- Synthesized in body
- Plants (ergosterol)
  - Sun-cured forages
- Fluid milk products are fortified with vitamin D
- Oily fish
- Egg yolk
- Butter
- Liver



- Daily Value
  - 10 micrograms

Vitamin D (calciferol)

- There are 2 major precursor forms:
  - 7-dehydrocholesterol
  - Ergosterol

- **Vitamin D_2** = *ergocalciferol*
  - Completely synthetic form produced by the irradiation of the plant steroid ergosterol

- **Vitamin D_3** = *cholecalciferol*
  - Produced photochemically by the action of sunlight or ultraviolet light from the precursor sterol 7-dehydrocholesterol

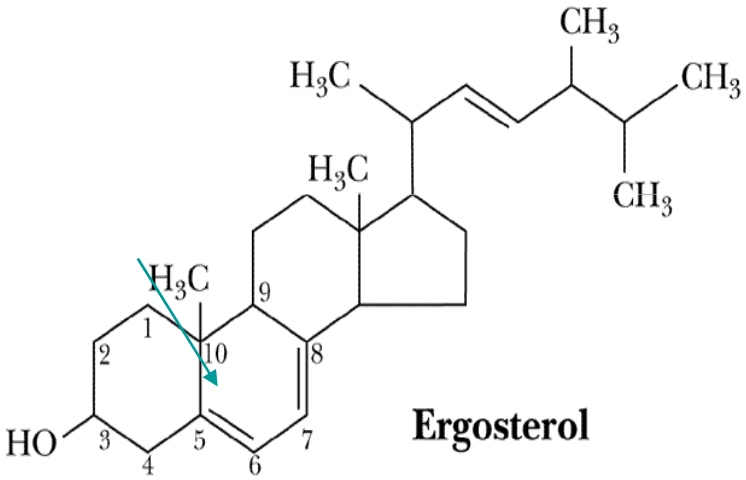
Formation of Vitamin D

- **Skin (UV light)**
  - **7-dehydro cholesterol → vitamin D_3**

- **Liver**
  - **OH-group added**
    - **25-hydroxy vitamin D_3**
    - **Storage form of vitamin (~3 months storage in liver)**

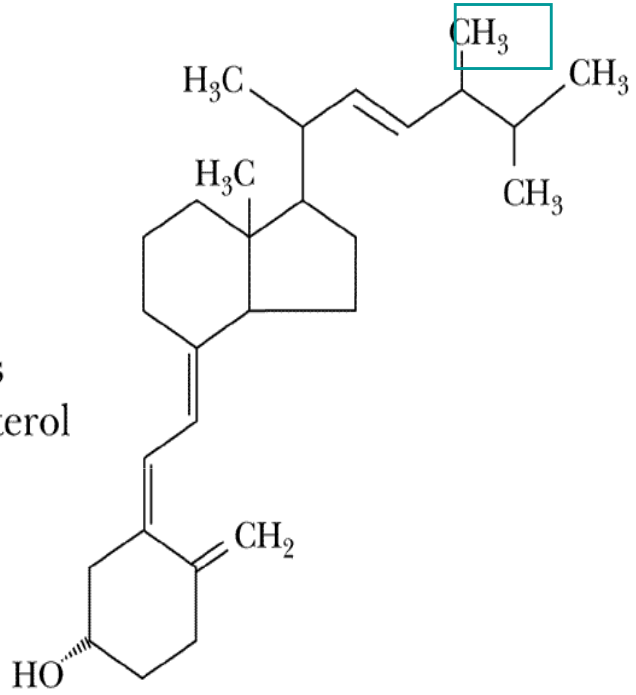
- **Kidney**
  - **OH-group added by 1-hydroxylase**
    - **1,25-dihydroxy vitamin D_3 (or 1,25-dihydroxy cholecalciferol, 1,25-DHCC)**
    - **Active form of vitamin D, a "steroid hormone"**
  - **OH-group added by 24-hydroxylase**
    - **24,25-dihydroxy vitamin D_3**
    - **Inactive form of vitamin D, ready for excretion**

(b)

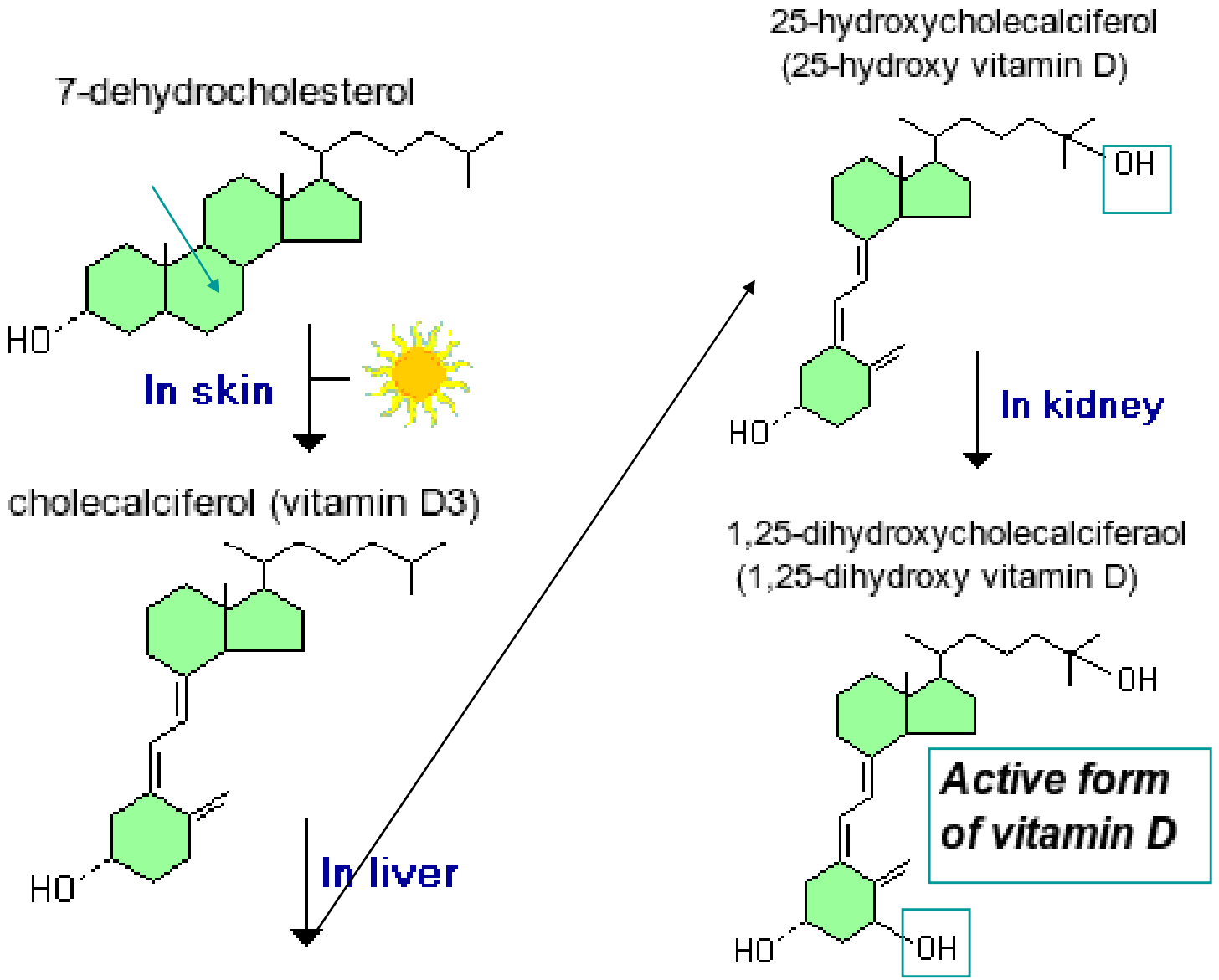


Ergosterol

Conversion to ergocalciferol via reactions analogous to 7-dehydrocholesterol pathway



Ergocalciferol (vitamin D_2)

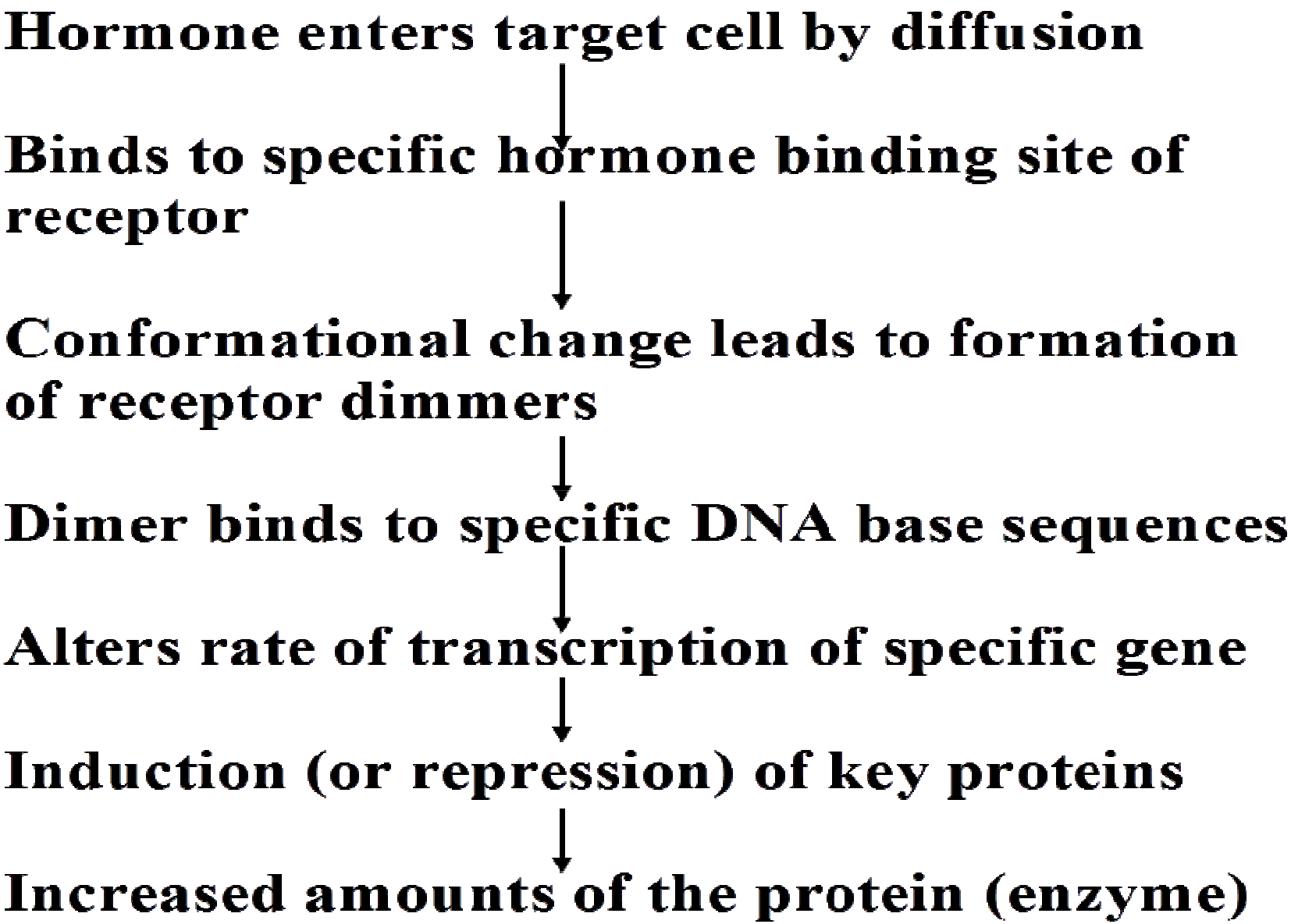


Calcitriol (1,25-dihydroxy-cholecalciferol, 1,25 DHCC)

Chemical name	Abbreviation	Generic name
Vitamin D_2	D_2	Ergocalciferol
Vitamin D_3	D_3	Cholecalciferol
25-hydroxy Vitamin D_3	$25(OH)D_3$	Calciferol
1,25-dihydroxy vitamin D_3	$1,25\text{-}(OH)_2D_3$	Calcitriol
24,25-dihydroxy vitamin D_3	$24,25\text{-}(OH)_2D_3$	Secalcifediol

Functions of Vitamin D

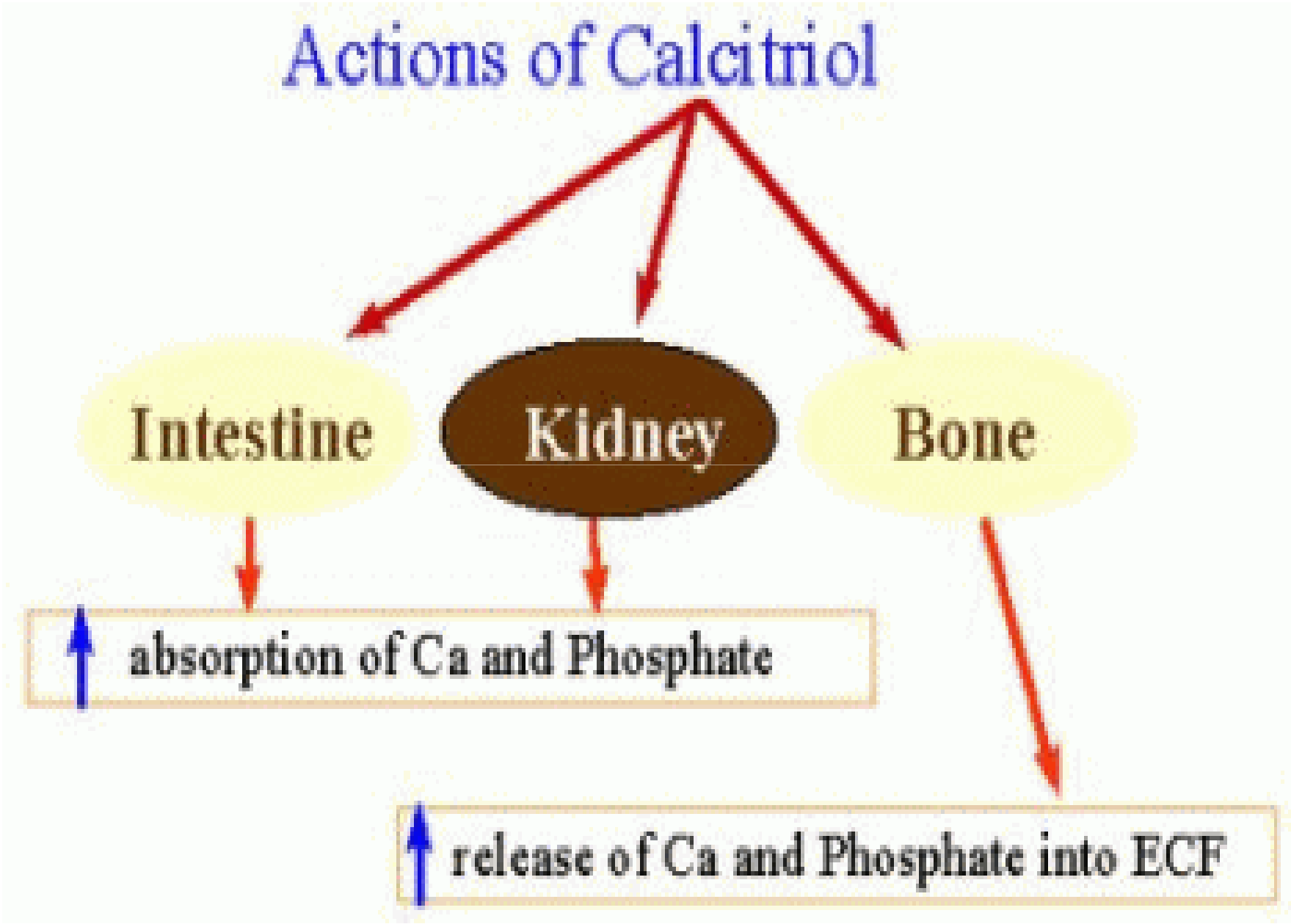
- Calcium and Phosphorus Homeostasis
  - Calcium and Phosphorus absorption (small intestine)
  - Calcium resorption (bone and kidney)
  - Maintain blood calcium levels
- Bone formation
  - Stimulate calcium uptake for deposition as calcium phosphate (Osteoblasts: bone-forming cells)
- Hormone
  - Regulation of gene expression
  - Cell growth


Hormone enters target cell by diffusion
Binds to specific hormone binding site of receptor
Conformational change leads to formation of receptor dimmers
Dimer binds to specific DNA base sequences
Alters rate of transcription of specific gene
Induction (or repression) of key proteins
Increased amounts of the protein (enzyme)

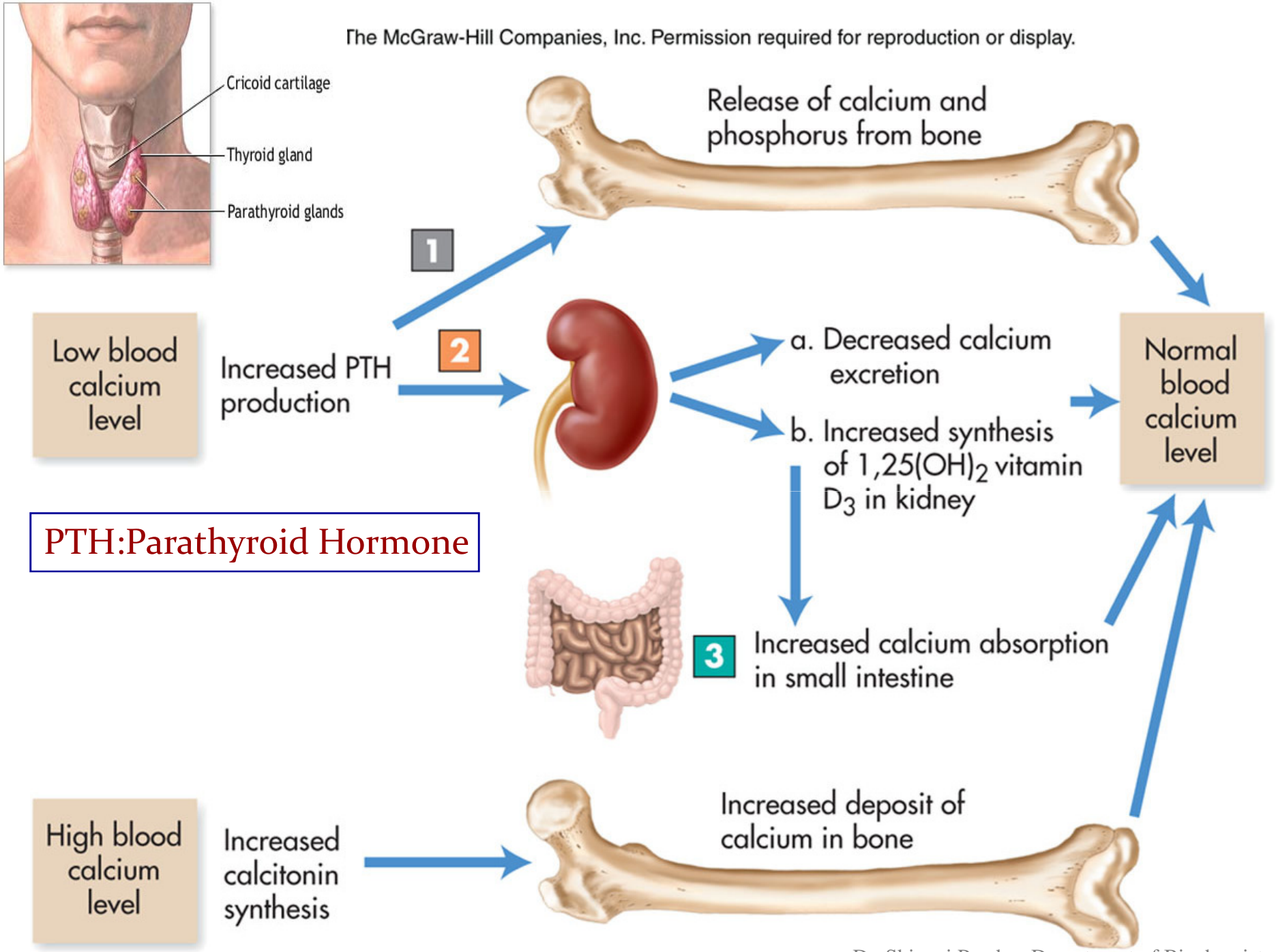
HORMONAL ACTION OF VIT. D

- It is important for regulation of differentiation & proliferation of various cells:

- Immunoregulatory cells
- Epidermal cells
- Malignant tumour cells
  - ✓ involved in immune modulation
  - ✓ depresses Ig production by
  - ✓ inhibiting function of helper T cells
  - ✓ thereby affecting B cell function


Actions of Calcitriol
Intestine
Kidney
Bone
absorption of Ca and Phosphate
release of Ca and Phosphate into ECF

- Stimulates synthesis of calcium binding proteins ***calbindins & osteocalcin*** thereby increasing absorption of Ca & P from intestine.
- Increases reabsorption of Ca & P from distal convulated tubule of kidney.
- Causes mobilization of Ca &P from bone.
- **Vit.D has both anabolic &catabolic role on bone.**
- Vit. D is also required for calcification of bone.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Cricoid cartilage
Thyroid gland
Parathyroid glands
Release of calcium and phosphorus from bone
1
Low blood calcium level
Increased PTH production
2
a. Decreased calcium excretion
b. Increased synthesis of 1,25(OH)2 vitamin D3 in kidney
Normal blood calcium level
PTH:Parathyroid Hormone
3
Increased calcium absorption in small intestine
High blood calcium level
Increased calcitonin synthesis
Increased deposit of calcium in bone

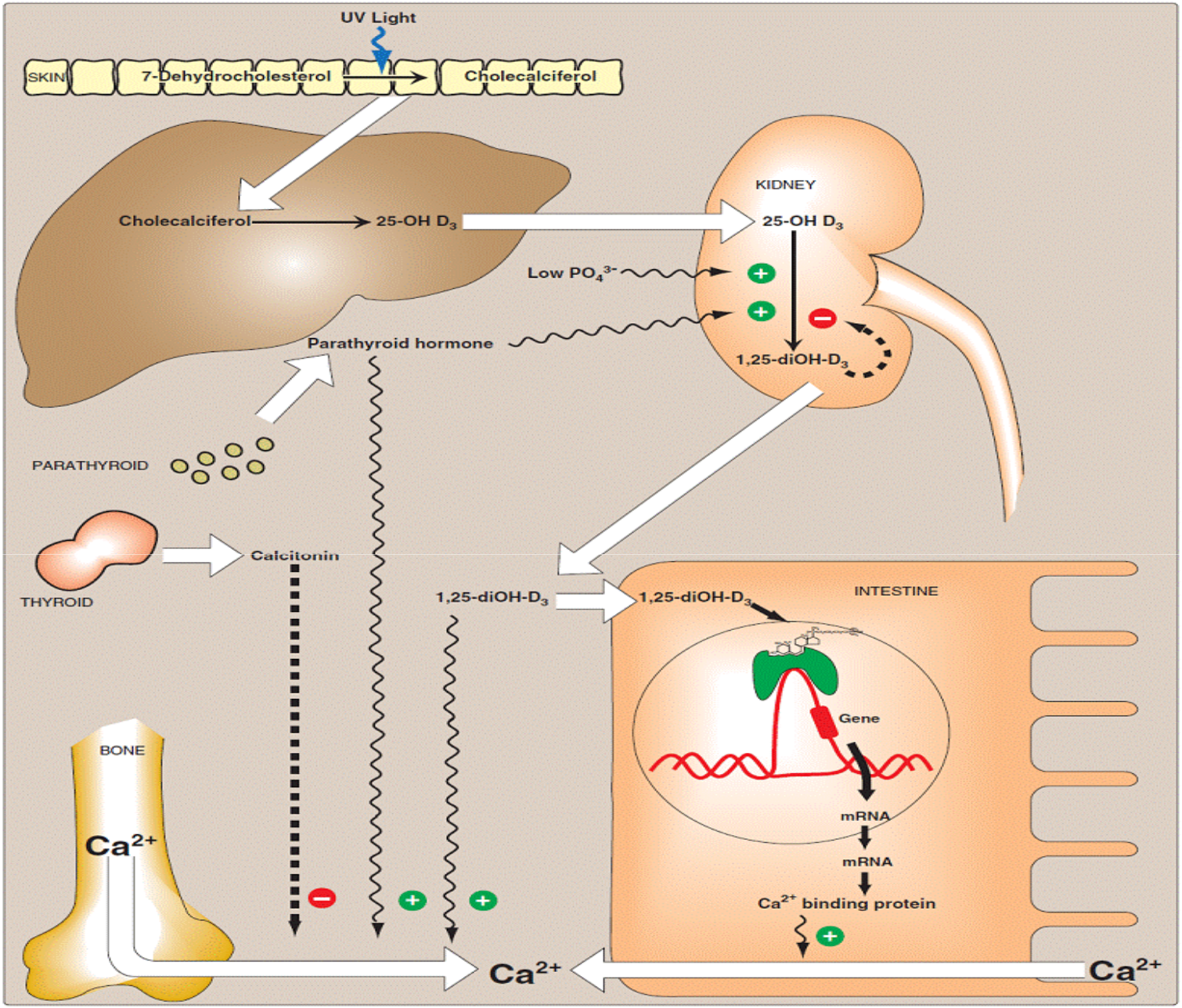


Figure 28.23
Metabolism and actions of vitamin D. [Note: Calcitonin, a thyroid hormone, decreases blood calcium by inhibiting mobilization from bone and reabsorption by the kidney.]

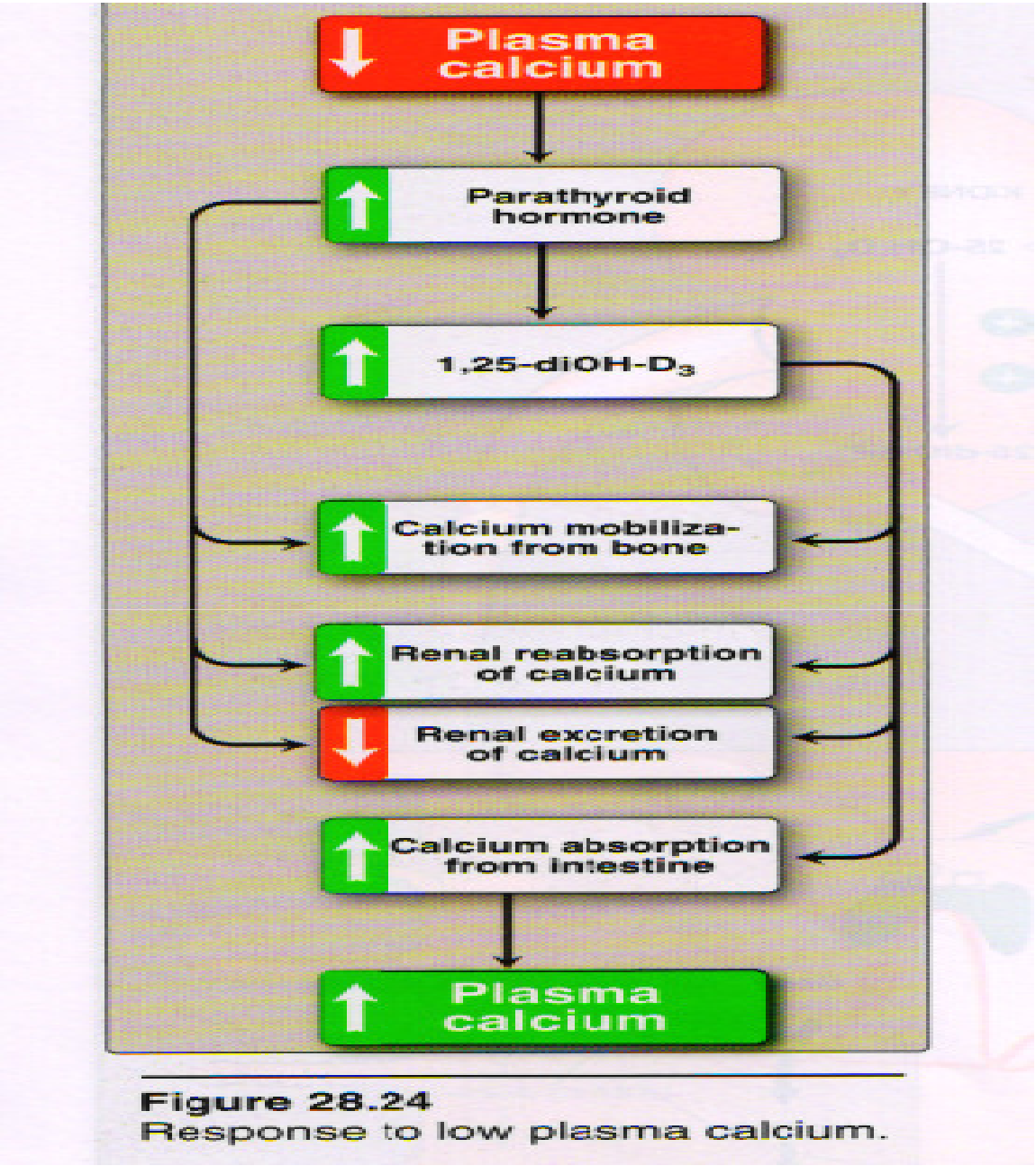
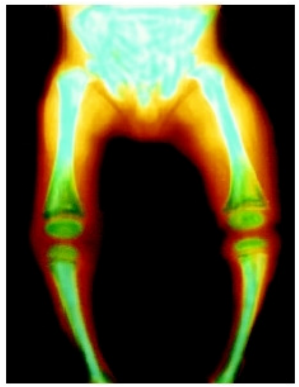
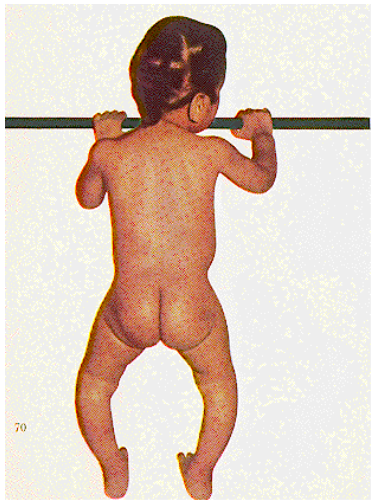


Figure 28.24
Response to low plasma calcium.

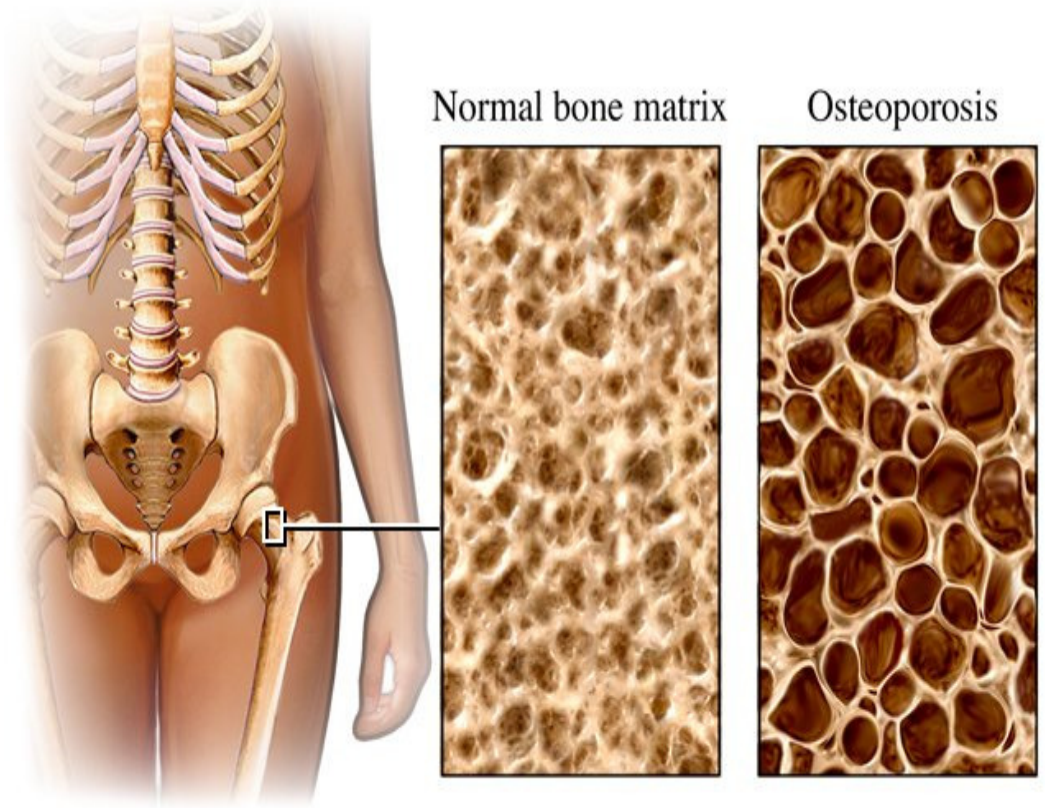
Vitamin D (antirachitic vitamin)- Deficiency





- Less common
- Young animals
  - Rickets (meaning: twist)
    - Failure of bones to grow properly
    - Results in "bowed" legs or knock-knees, outward bowed chest and knobs on ribs
- Older animals
  - Osteomalacia(Greek: osteon-bone, malakia-softness):
    - Adult form of rickets
  - Osteoporosis (porous bones):
    - Loss of vitamin D activity with advancing age
    - Associated with fractures → very serious for geriatrics

Osteoporosis



➢progressive loss of bone density, thinning of bone tissue and increased vulnerability to fractures in the elderly people of both sexes.

Vitamin D Toxicity

- Hypervitaminosis D
  - Among the vitamins, vitamin D is the most toxic in overdoses(10-100 times RDA)
  - Calcification of soft tissue
    - Lungs, heart, blood vessels
    - Hardening of arteries, stone formation in kidneys
- Does not occur from sunlight or dietary sources
- Does occur with supplementation
  - In general, vitamin D supplement are not recommended.
  - Upper limit: 50 micrograms a day

VITAMIN K

Dr. Shivani Pandey, Department of Biochemistry


Vitamin K
Food sources of vitamin K include cabbage, cauliflower, spinach and other green, leafy vegetables, as well as cereals
A.D.A.M.

This vit is also called an ***anti-hemorrhagic factor.***

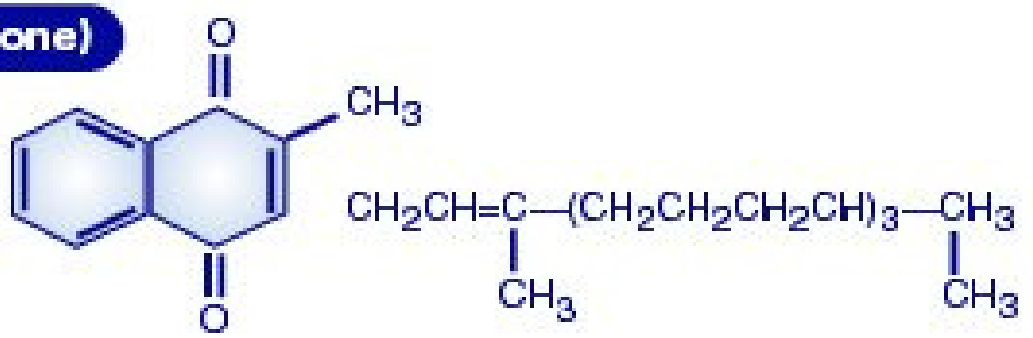
Deficiency produces uncontrolled hemorrhages due to defective blood coagulation.

STRUCTURE

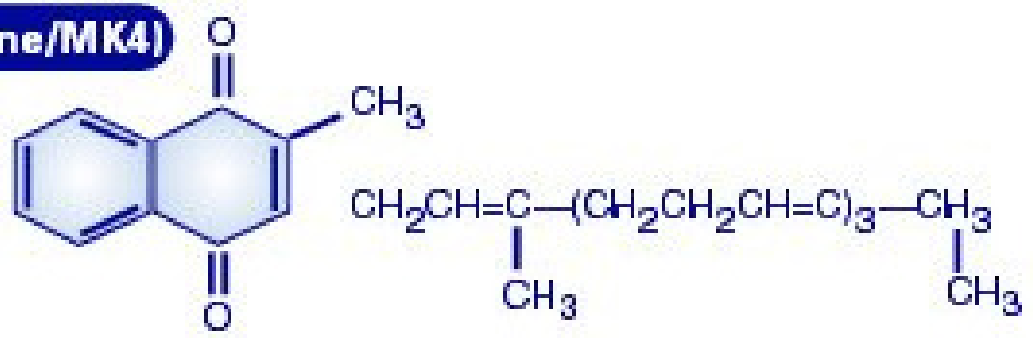
- Two naturally occurring forms:

- **Vitamin K1 or phylloquinone** derived from plants
- **Vitamin K2 or menaquinones** produced by microorganism
- Both have same activity : stable to heat and reducing agent.
- **Vitamin K3 or menadione** is a synthetic product, alkylated form of vit K2.

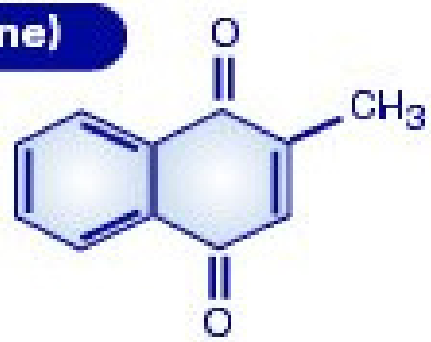
K_1 (Phylloquinone)



K_2 (Menatetrenone/MK4)



K_3 (Menadione)



ABSORPTION, TRANSPORT & STORAGE

- Naturally ocurring vit K are absored like other lipids in ***presence of bile salts***.
- Transported in the form of chylomicrons and stored in the liver.
- Menadione a water- soluble medicinal agent (synthetic vit K) is absorbed without bile salt directly into hepatic portal vein.

Functions of Vit. K

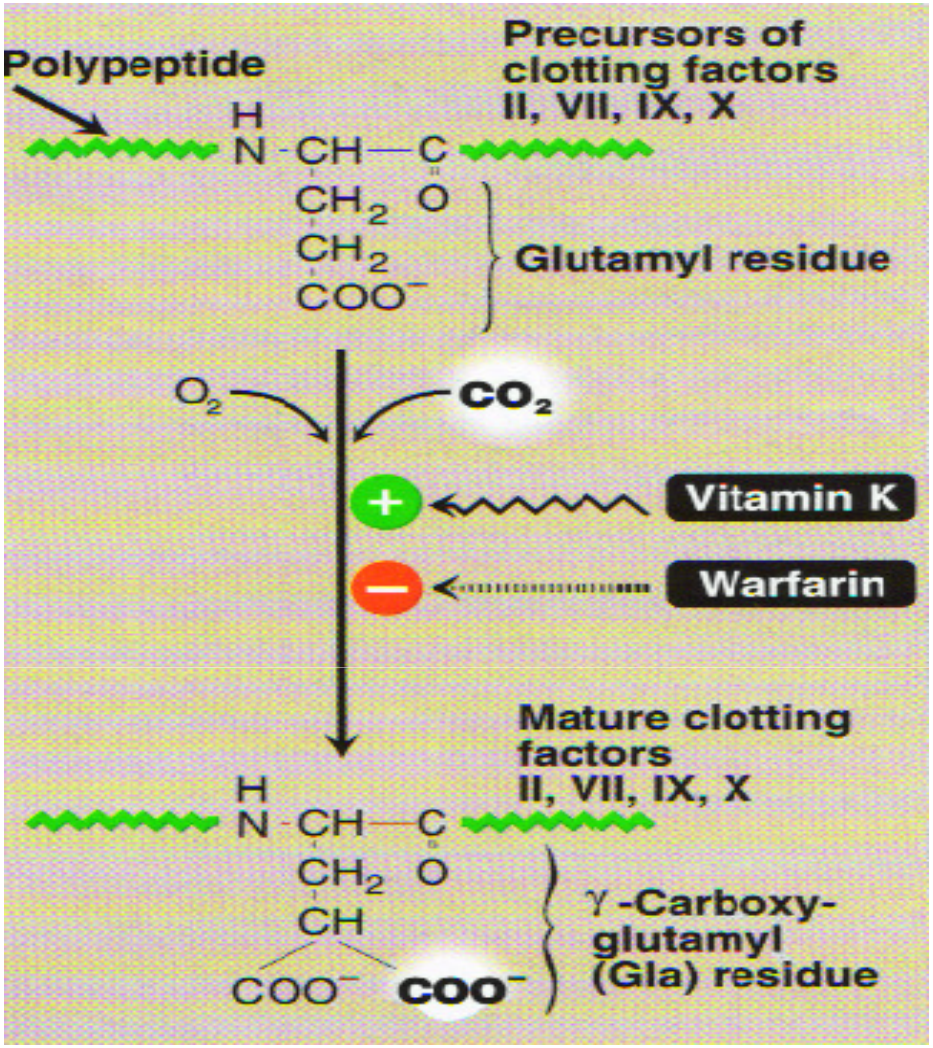
- Involved in maintenance of normal levels of blood clotting factors

Clotting factors II, VII, IX, X are synthesized as inactive precursor protein in liver

.

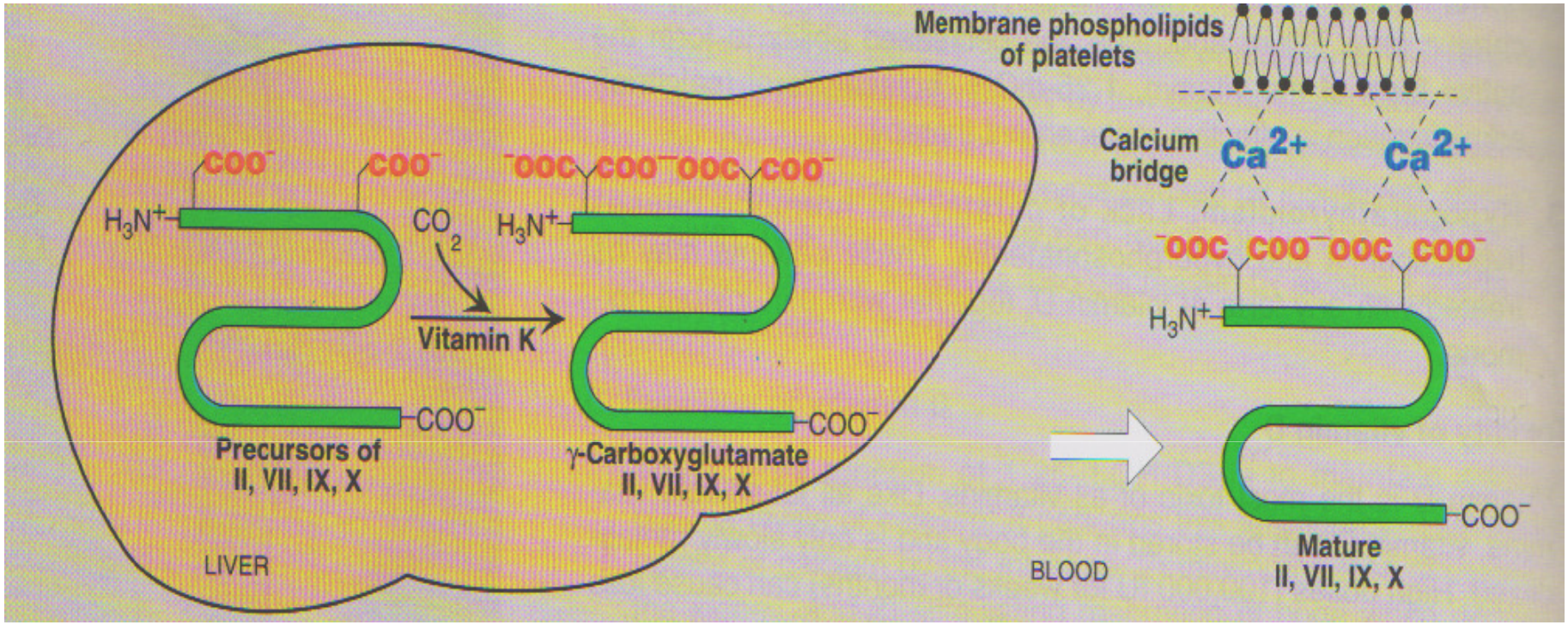
Conversion of inactive precursor requires post-transcriptional modification of specific ***glutamate residue.***

- This modification is carboxylation of glutamate residues by ***vitamin K dependent carboxlase enzyme & forms Ycarboxyglutamate (GLA)***



Carboxylation of glutamate to form ϒ-carboxy glutamate

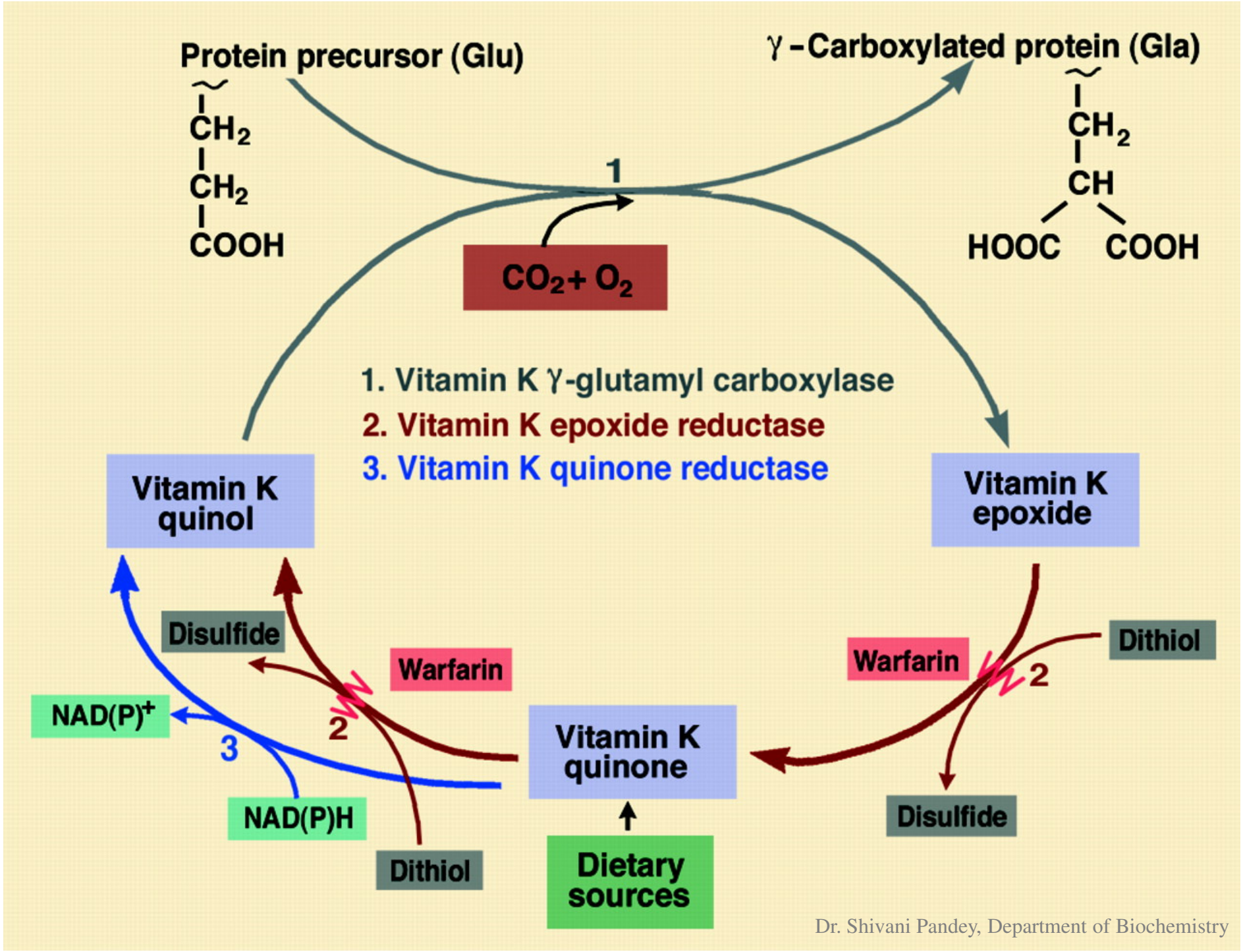
- γ-Gla have high affinity for Ca^{2+} and are effective Ca^{2+} chelators.
- Each GLA contains two negative charges which chelate the positive Ca^{2+} ion .
- The calcium then binds with negatively charged phospholipids on platelet cell membrane.
- This way bridging of phospholipids to the Gla residue of prothrombin occurs via Ca^{2+} ion.
- Protrombin is then proteolyzed to thrombin through the action of activated factor X.



Role of vit K in blood coagulation

VIT. K CYCLE

- Vit.K cycle exists in E.R. of liver.
- Here vit.K dependent carboxylase adds carboxy grp. of CO_2 to γ carbon of glutamate.
- Vit K acts as e^- donor & is converted to vit K epoxide.
- Epoxide form is converted to quinone form of vit K. by epoxide reductase & finally to hydroquinone by enzyme reductase &NADPH regenerating active form of vit. K


Protein precursor (Glu)
γ-Carboxylated protein (Gla)
CH2
CH2
COOH
CH2
CH
HOOC
COOH
1
CO2+ O2
1. Vitamin K γ-glutamyl carboxylase
2. Vitamin K epoxide reductase
3. Vitamin K quinone reductase
Vitamin K quinol
Vitamin K epoxide
Disulfide
Warfarin
Warfarin
Dithiol
2
2
NAD(P)+
3
Vitamin K quinone
NAD(P)H
Dithiol
Disulfide
Dietary sources

Vit K antagonists

- VIT K antagonists **dicoumarin or warfarin.**
- They:--

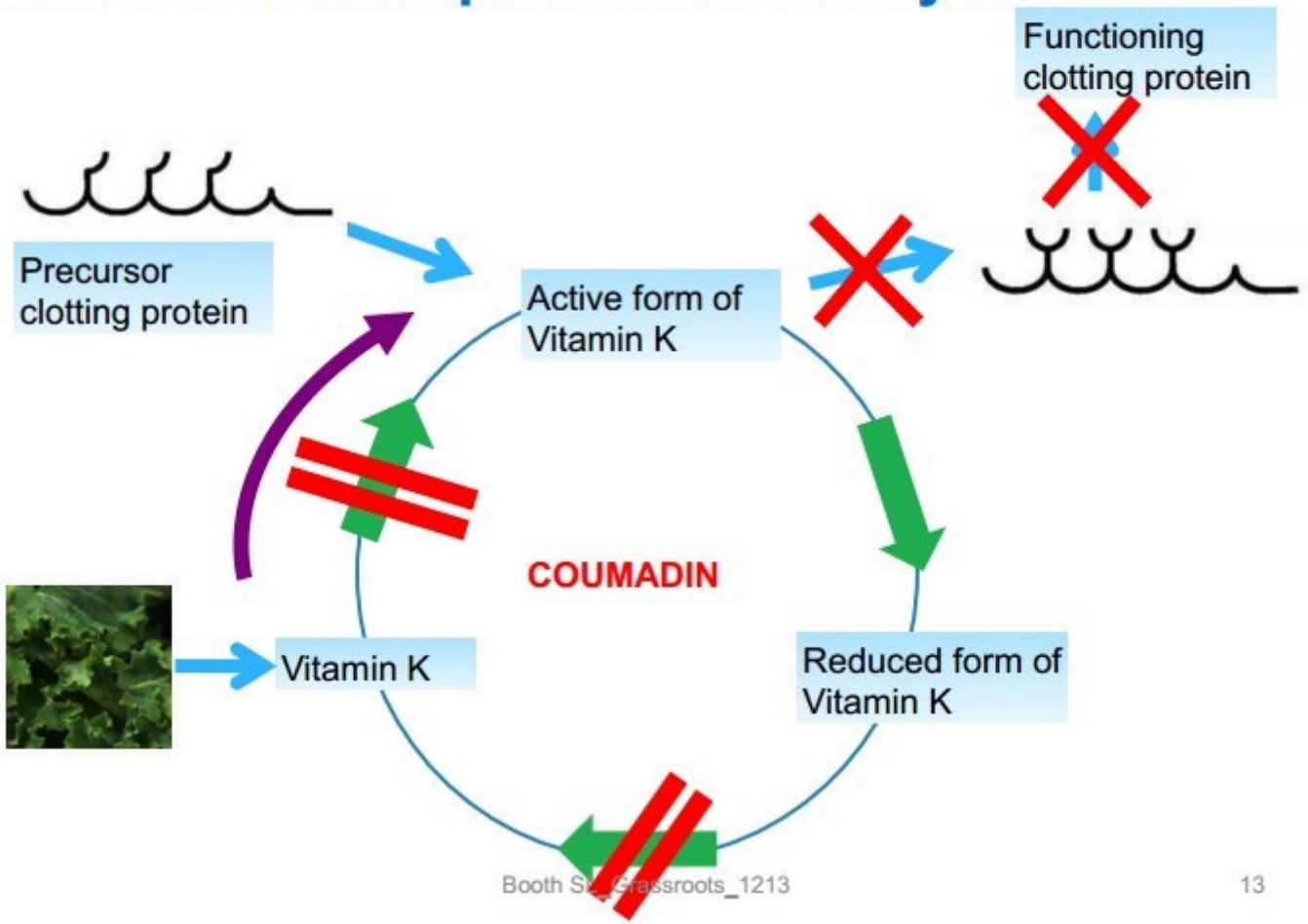
are competitive inhibitor of gamma carboxlation system

structurally similar to vit.K

inhibit enz. Epoxide reductase.

used in treatment of thrombosis

Warfarin Interrupts Vitamin K Cycle



- Vit. K is also required for carboxylation of glutamic acid of **osteocalcin** (synthesized by osteoblast) creating Ca binding sites ,which helps to retain calcium.

- Other proteins such as C-reactive protein and structural proteins of kidney, lungs & spleen also require vit K for carboxlation.

DEFICIENCY MANIFESTATION

- Widely distributed ,intestinal production by microflora ensures no deficiency.
- Deficiency occurs:
- **Patients with liver diseases & biliary obstruction**
- **In infants***
- **Following antibiotic therapy**
- **In fat malabsorption**

- Vit.K deficiency is associated with hemorrhagic diseases.
- Clotting time is increased
- Even minor cuts cause prolonged bleeding.
- Imp.deficiency sign is ***increase in prothrombin time & is*** used for evaluation of vit.K status.

THERAPEUTIC USE

- It is used as an antidote to poisoning by dicumarol type drug.

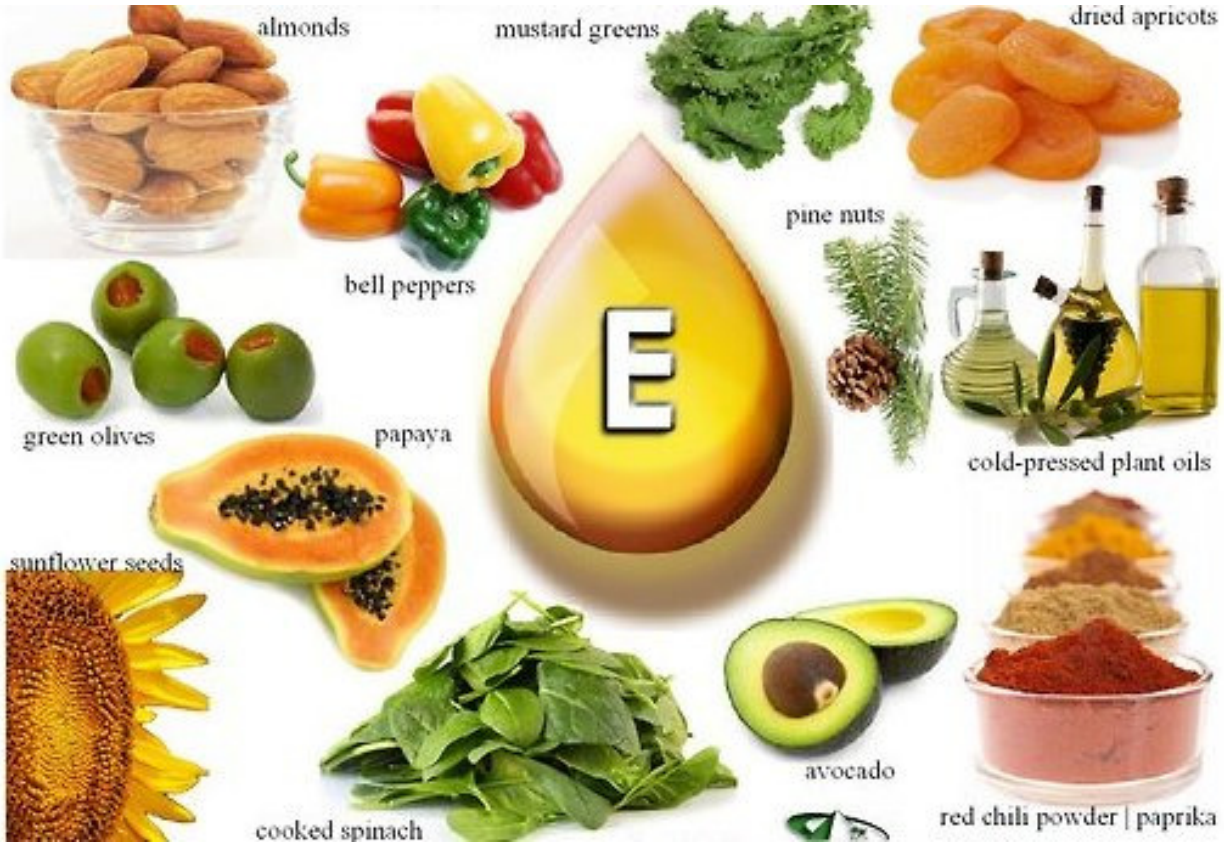
TOXICITY

Produces haemolytic anaemia in rats.

Krenicterus in infants with low birth weight.

Due to increased breakdown of RBC & undeveloped capacity for its conjugation.

VITAMIN E


almonds
mustard greens
dried apricots
bell peppers
pine nuts
E
green olives
papaya
cold-pressed plant oils
sunflower seeds
avocado
cooked spinach
red chili powder | paprika

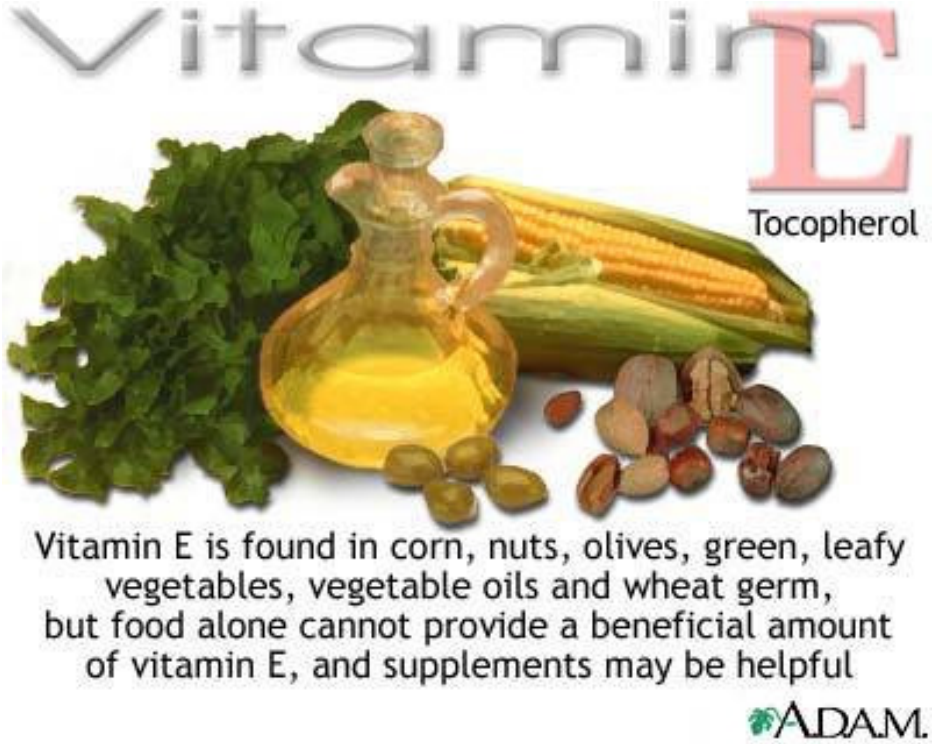
Vitamin E (tocopherol)

- A naturally occurring antioxidant.
- Essential for normal reproduction in many

animals.Tocopherol (Greek:tokos-child birth; pheros-bear; ol-alcohol), Anti-sterility vitamin.

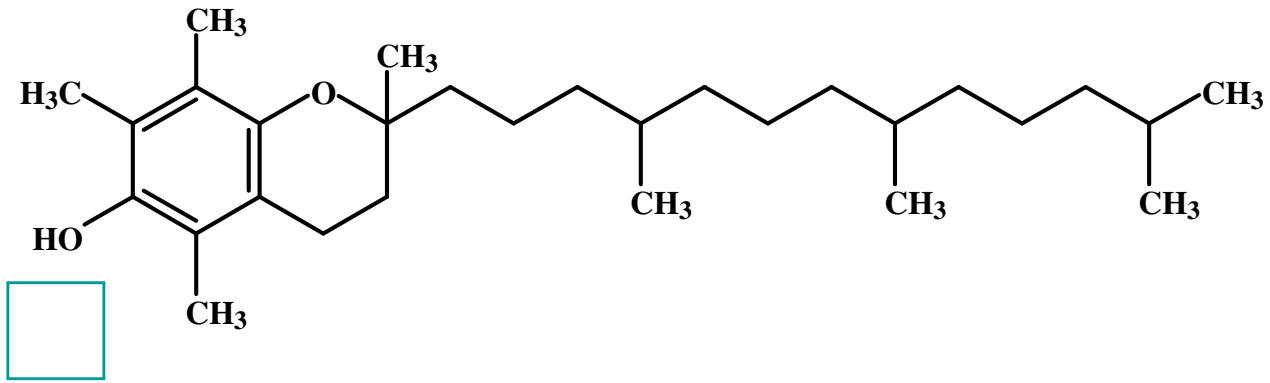
Vitamin E - Sources

- Plant sources
  - Cereal grains
    - Especially in germ
  - Vegetable and seed oils
- Animal sources
  - Meat,milk,butter,eggs
- RDA: 10 mg for men, and 8 mg for women



Vitamin E (tocopherol)

- The term vitamin E refers to a family of 8 related compounds, the tocopherols and the tocotrienols
- The four major forms of vitamin E are designated α, β, δ, γ, of which α -tocopherol is the most active.



ALPHA TOCOPHEROL

Absorption, Transport and Excretion of Vitamin E

Absorption and Transportation

- Micelles into chylomicrons
- Transported via lipoproteins
- Stored in adipose tissue

Excretion

- Bile, urine and skin

Major function in the body

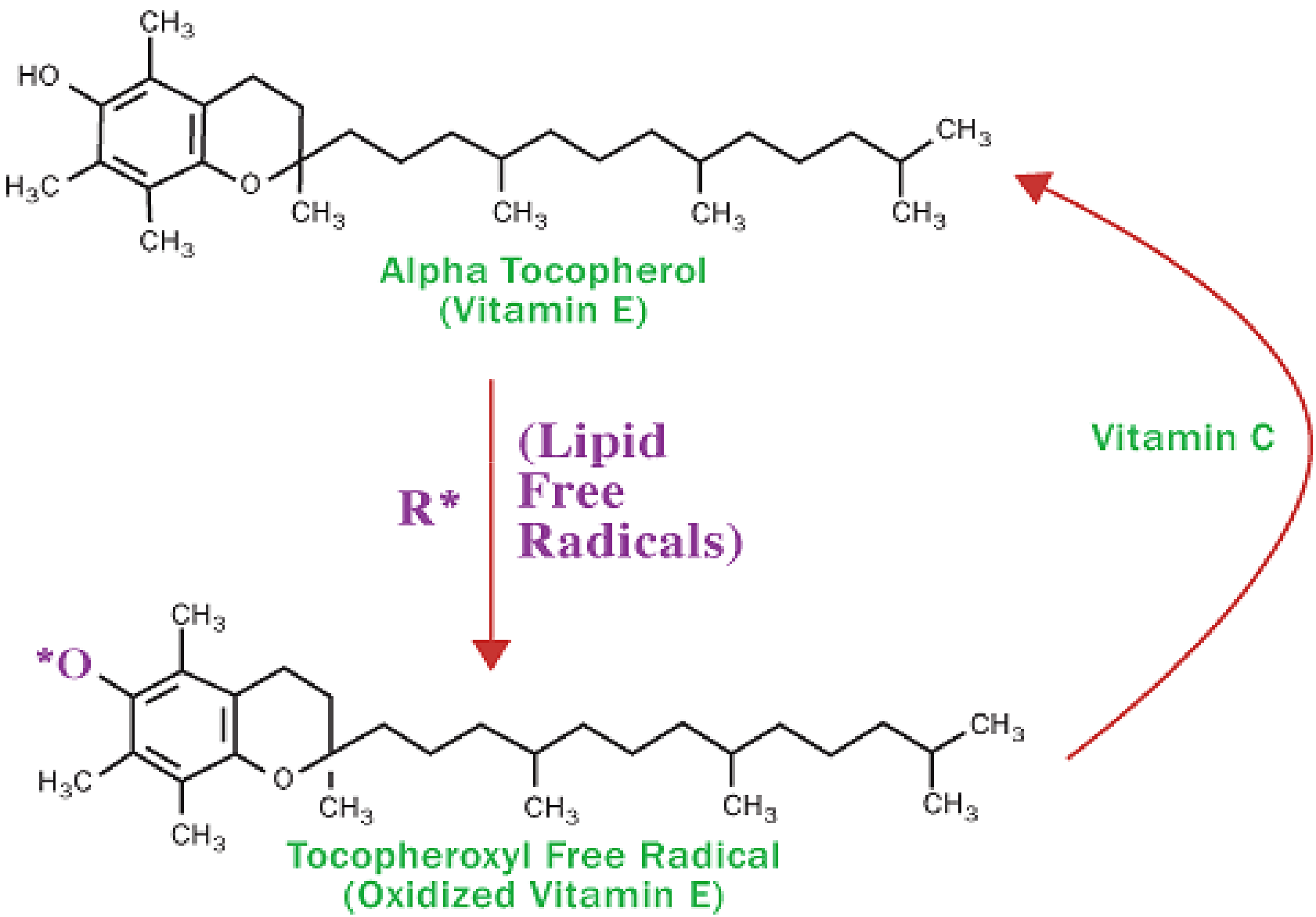
- ***Antioxidant***

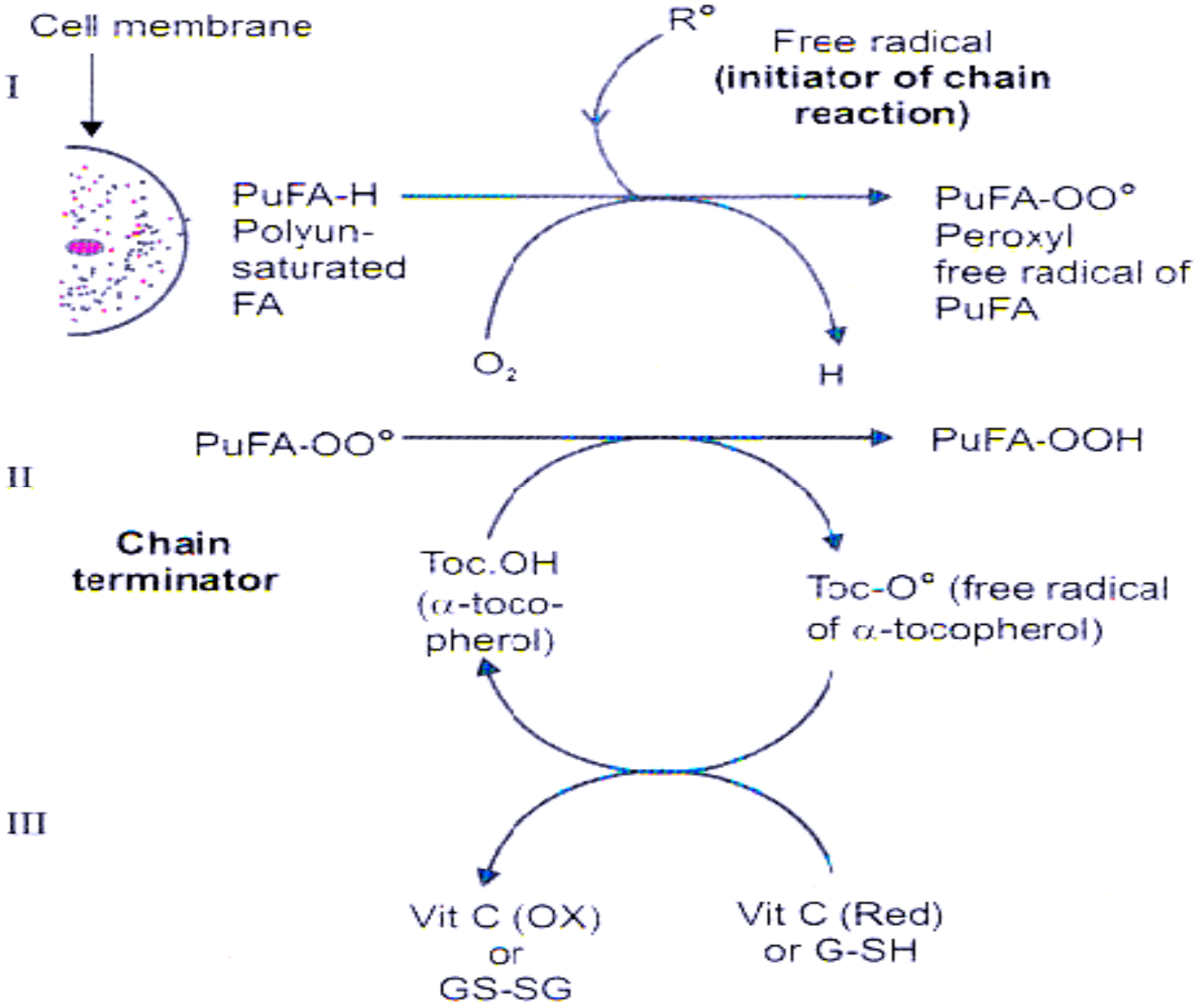
  Vitamin E is very unstable, easily oxidized

  protect cells against oxidative damage by free radicals, for example oxidation of the lipids in the cell membranes

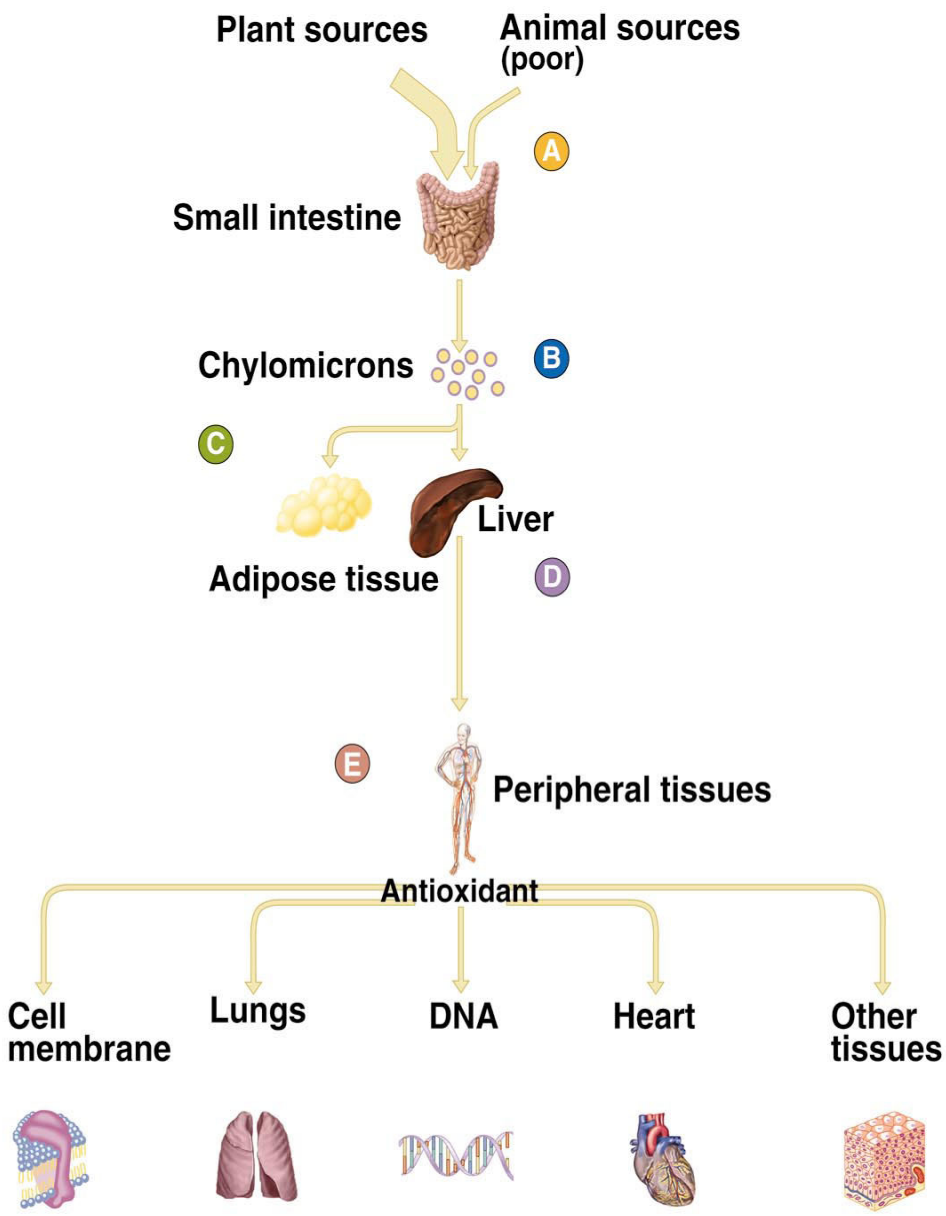
- plays a role in aging, sexual performance, or prevention of cancer and/or heart disease

IMPLICATED DISEASE STATES


HO
CH_3
H_3C
O
CH_3
CH_3
CH_3
CH_3
CH_3
Alpha Tocopherol
(Vitamin E)
R*
(Lipid
Free
Radicals)
Vitamin C
*O
CH_3
H_3C
O
CH_3
CH_3
CH_3
CH_3
CH_3
CH_3
Tocopheroxyl Free Radical
(Oxidized Vitamin E)


Cell membrane
I
R°
Free radical
(initiator of chain reaction)
PuFA-H
Polyun-
saturated
FA
PuFA-OO°
Peroxyl
free radical of
PuFA
O2
H
PuFA-OO°
PuFA-OOH
II
Chain
terminator
Toc.OH
(α-toco-
pherol)
Toc-O° (free radical
of α-tocopherol)
III
Vit C (OX)
or
GS-SG
Vit C (Red)
or G-SH

VITAMIN E: FROM SOURCE TO DESTINATION



Vitamin E - Deficiency

- **Rare**
  - Erythrocyte hemolysis and hemolytic anemia

    disruption of red blood cell membranes, perhaps due to polyunsaturated fatty acids (PUFAs) oxidation

  - Sterility: reproductive failure

Vitamin E Toxicity

- Toxicity rare: wide range of safe intake compared to other fat soluble vitamins

- Vitamin E is one of the most popular nutrient supplements. There are many health claims for supplementation – slowing of the aging process or an improvement in sexual potency.