



Medical Committee
The University of Jordan



SLIDE



SHEET

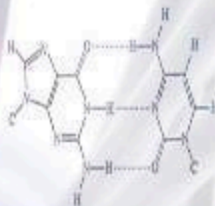


SLIDE : 10



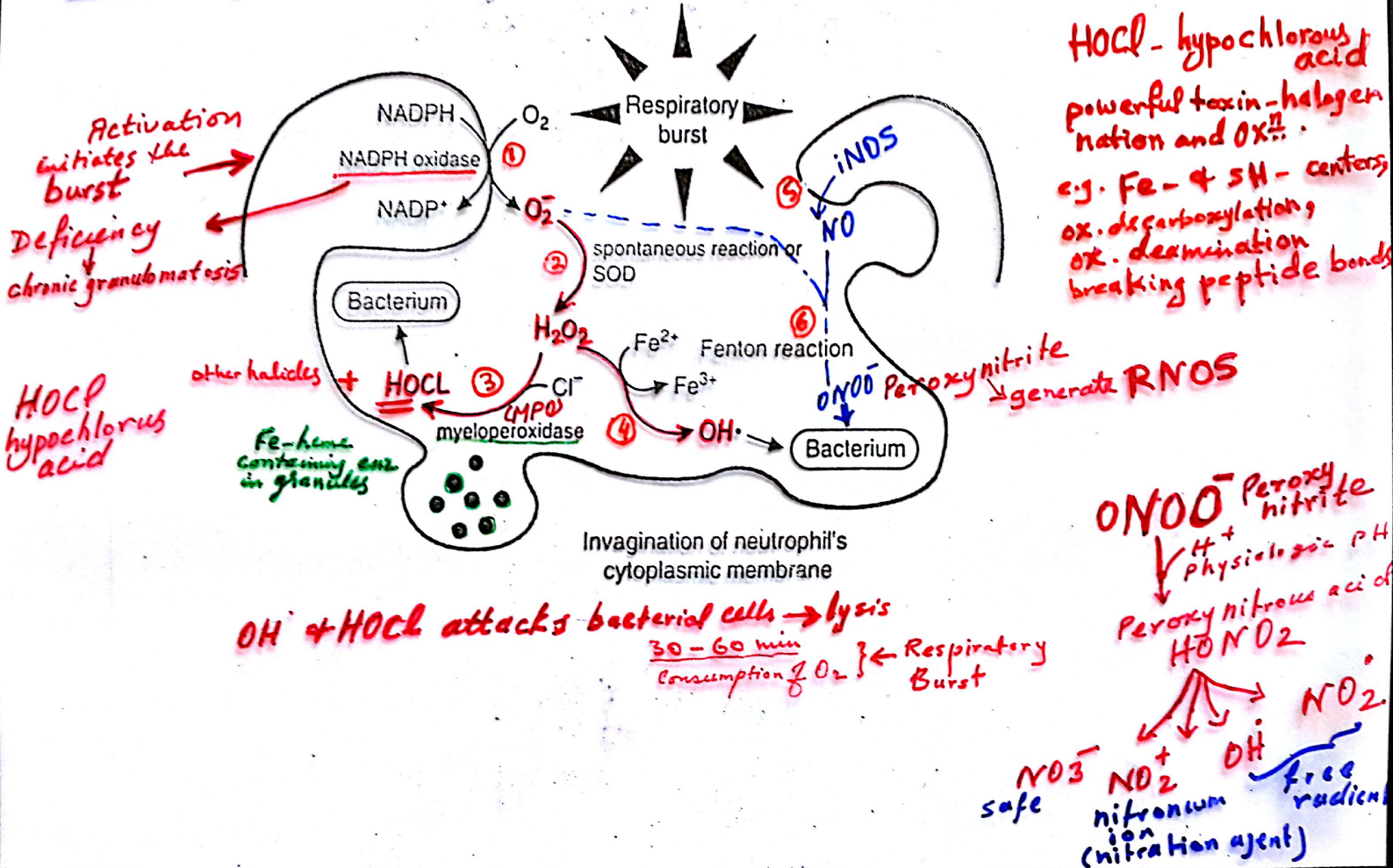
DR.NAME: Nayef Kradshah

Biochemistry



Majida Al-Foqaraa'

Production of reactive Oxygen species during the phagocytic Respiratory burst by activated macrophages, neutrophils & eosinophils.



NO and RNOS

8

- NO is a free radical, diffuses readily.
- Essential to life and toxic
- Neurotransmitter, vasodilator
Prevents platelet aggregation | ^{at low} concentration
- At high concentration combines with O_2 or O_2 to form RNOS
RNOS are involved in neurodegenerative diseases and inflammatory diseases

NO Synthase

- nNOS - Isoform I (neural)
- eNOS - Isoform III (endothelium)

Both are constitutive enz. produce small amount of NO as neurotransmitter + hormone

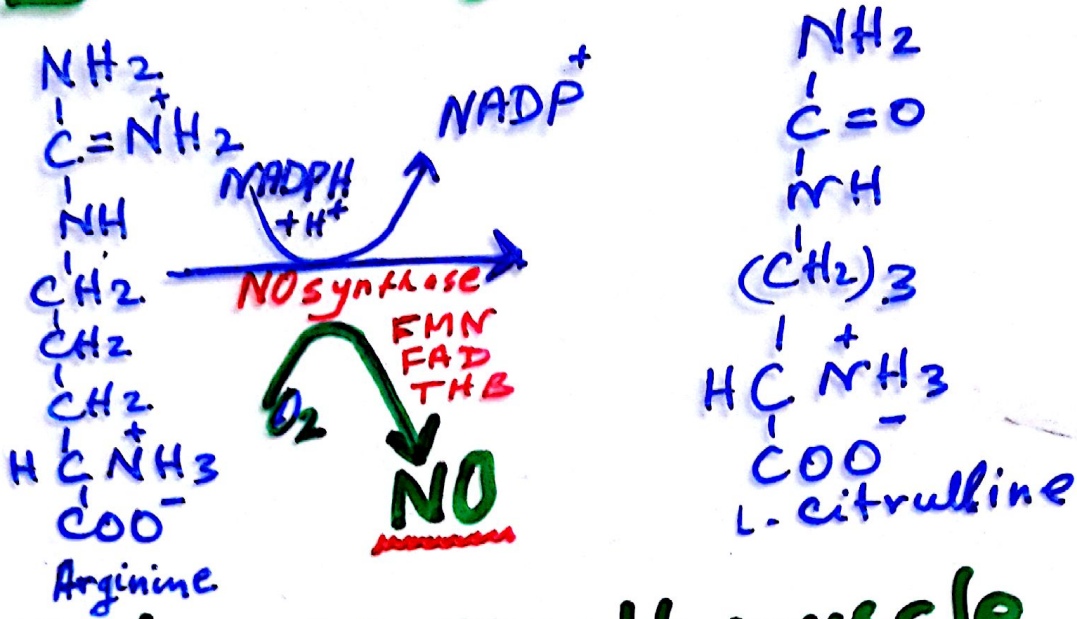
- iNOS - Isoform II (inducible)

Induction of transcription in many cells of immune system → large amount of NO

↑ NO → RNOS to kill invading bacteria.

Synthesis of Nitric Oxide (NO)

9



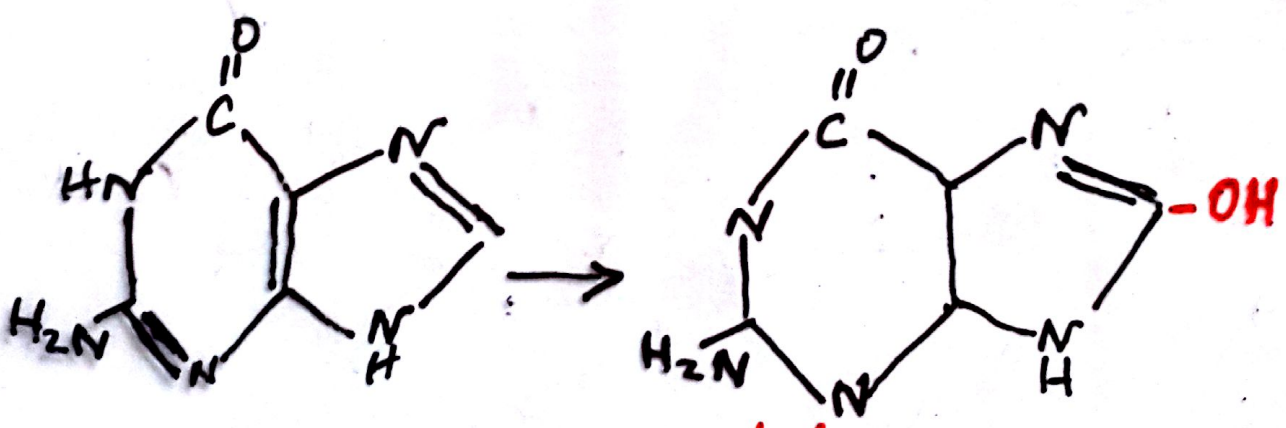
- Relaxes smooth muscle

- $\text{GTP} \xrightarrow[\text{NO}(+)]{\text{cyclase}} \text{cGMP}$
- cGMP activates PKG
- PKG phosphorylates Ca^{2+} protein channels which decrease Ca^{2+} entry to muscle cells which decrease Ca^{2+} entry to muscle cells myosin light chain kinase therefore decreasing muscle contraction and favoring relaxation of vascular smooth muscle

- Prevents platelet aggregation
- Neurotransmitter in brain
- Mediates tumoricidal and bactericidal actions of macrophages

Net oxidative and free radical damage of RNOS :-

- Inhibition of large number of enzymes :- attacking met & -SH gr
- mitochondrial lipid peroxidation
- Inhibition of electron transport chain and energy depletion.
- Single- and double-stranded breaks in DNA
- Modification of bases in DNA



8-hydroxyguanine

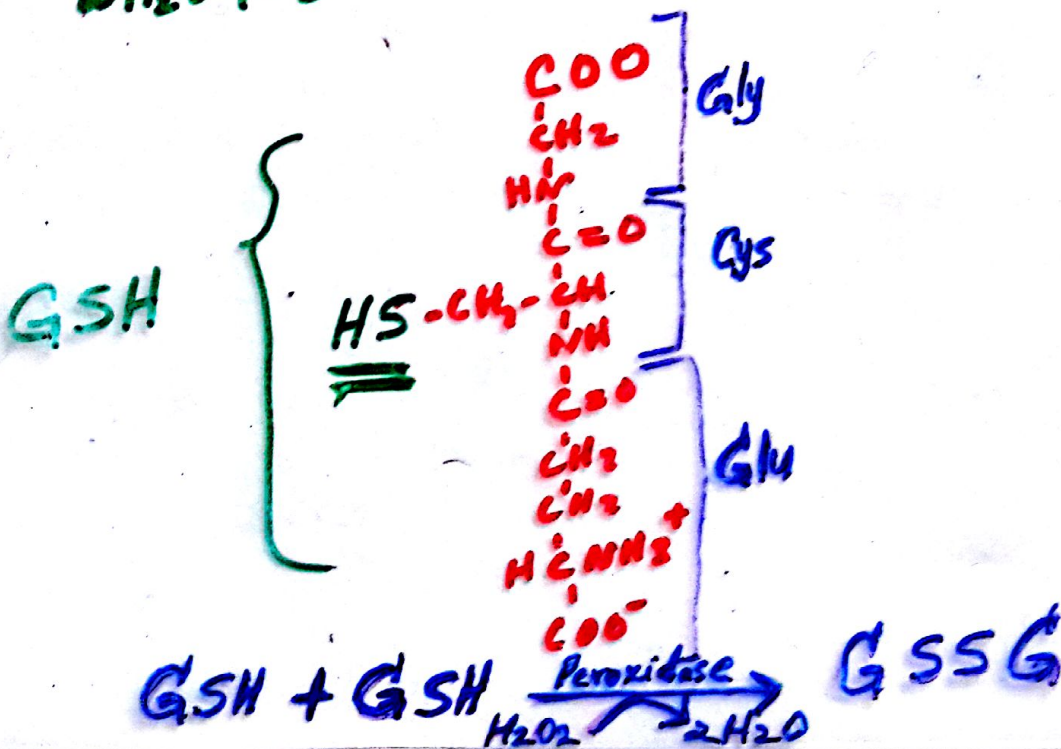
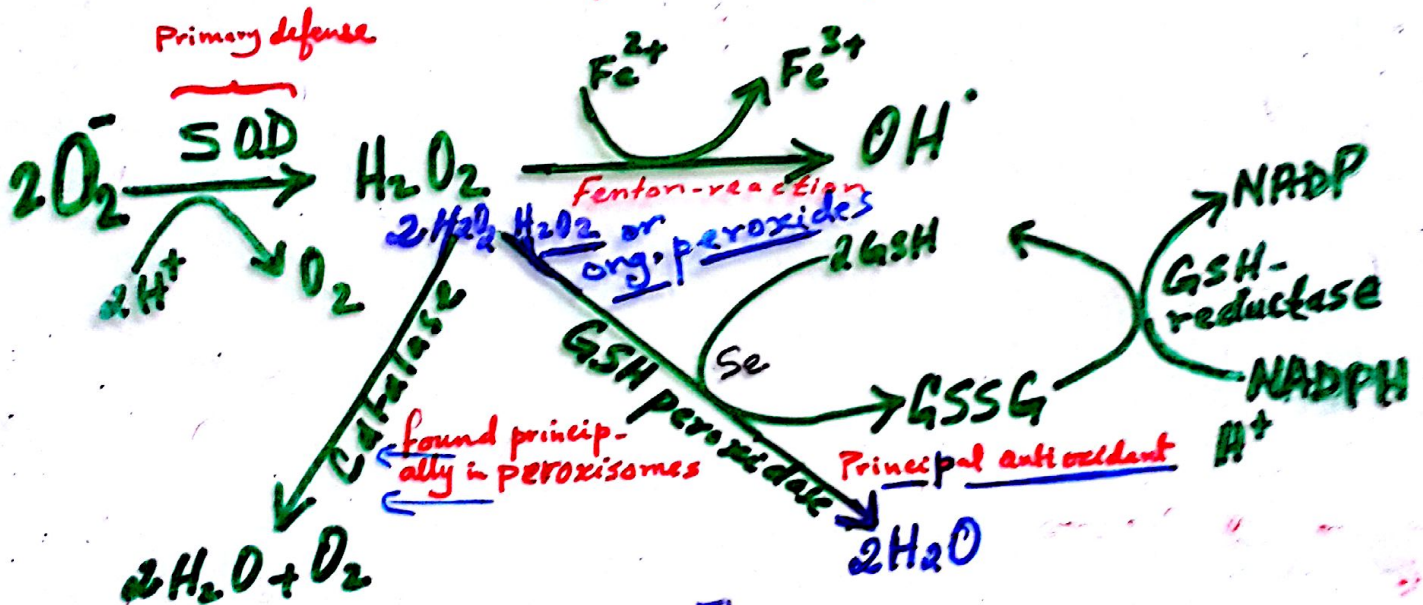
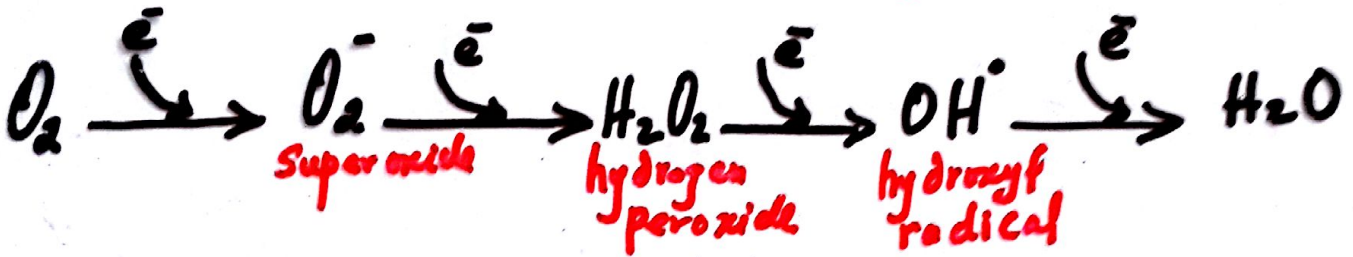
base pairs with T

Creating A-T in daughter cells

Cellular Defence Against O₂ toxicity:- 10

Primary Antioxidants - Antioxidant Enzymes

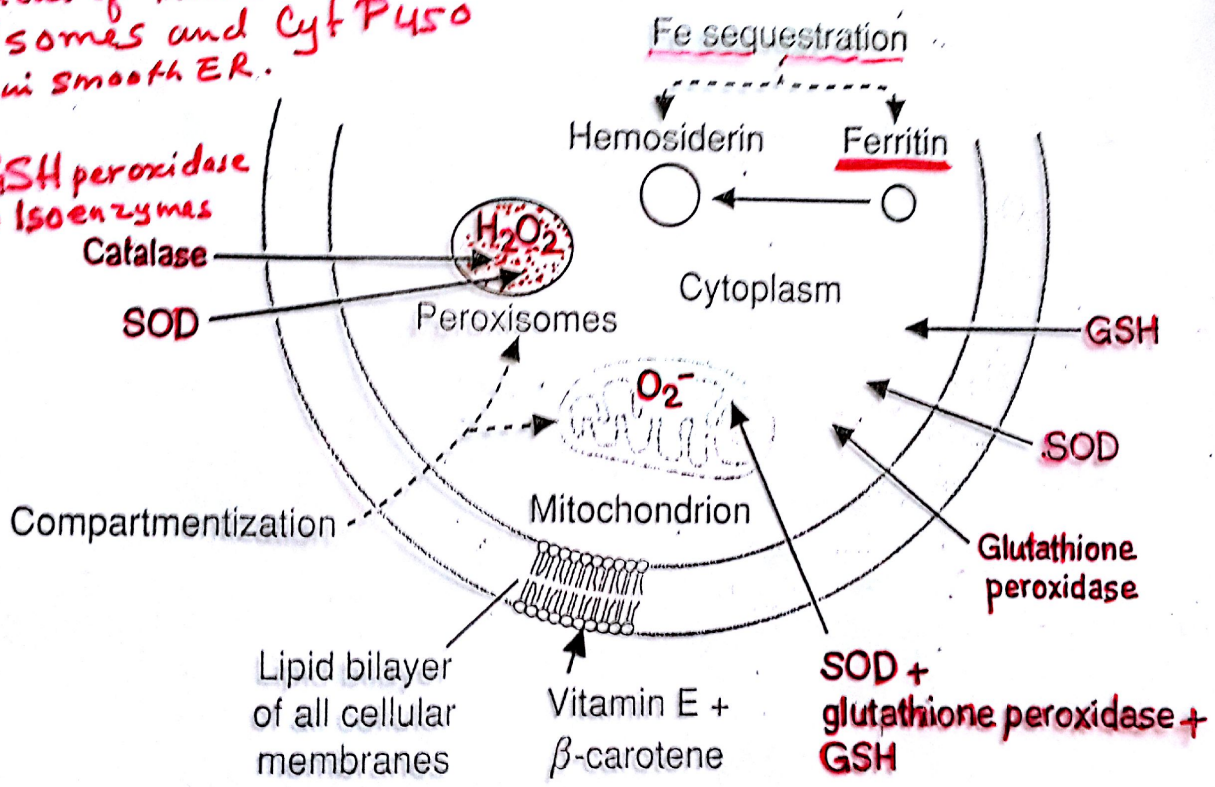
SOD; Catalase, GSH peroxidase, GSH reductase. Highest conc. in liver, adrenal & kidney (high content of peroxisomes & mt)



Compartmentalization of free-radical defenses

- Highest activities are in liver, adrenal gland + kidney
- ↑ high content of mitochondria, peroxisomes and Cyt P450 enzymes in smooth ER.

- SOD and GSH peroxidase are present as isoenzymes



- Secondary Antioxidants

A. Dietary :-

(1) Vitamins

Vitamin E (tocopherol)

Vitamin C

β -carotenes

(2) other dietary antioxidants

B. Endogenous antioxidants

C. Repair Mechanism of
DNA, oxidized fatty acids &
membrane lipids and oxidized amino
acids

D. Compartmentation

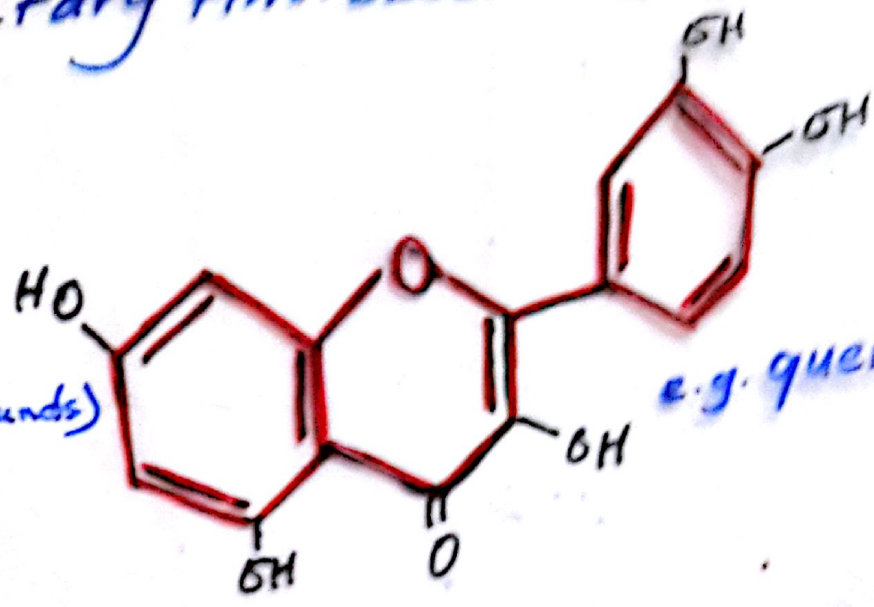
e.g. peroxisomes, ferritin for Fe^{2+}
... etc.

Other Dietary Antioxidants

Flavonoids

(polyphenolic compounds)

- green-tea
- chocolate
- red wine
- fruits skin, veg. (e.g. onion)



e.g. quercetin

- Possible functions {
- inhibition of O_2^- production eg. $X.O. \downarrow$ (xanthine oxidase)
 - free radical scavenger
 - chelate Fe + Cu
 - maintenance of Vit E

Endogenous Antioxidants

- Uric acid
- GSH
- melatonin
- Bilirubin
- lipoic acid
- Ubiquinone (Co Q10)

Some Flavonoids:

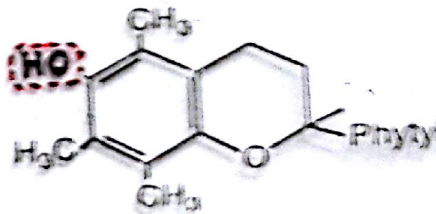
- Catechins :- strawberries, green & black tea
- Kaempferol :- brussel sprouts & apple
- quercetin :- beans, onions, apples and fruits skin
- Epicatechin :- Cocoa, red wine

Vitamin Antioxidants:-

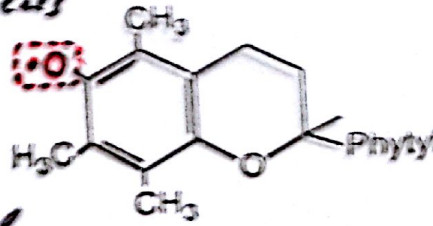
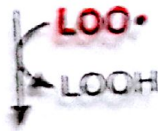
- Chain-breaking antioxidants

Terminate free radical lipid peroxidation by:

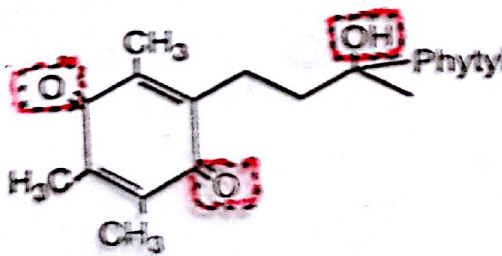
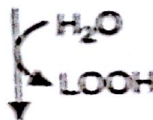
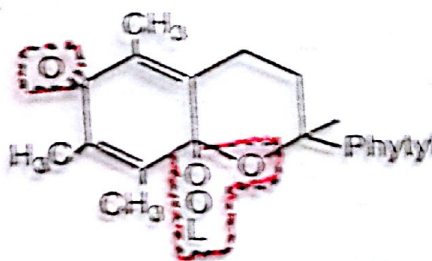
- Vit. E donate single e
- Carotenoids accept e from lipid peroxy radicals
- Vit C accepts single e from O_2^- , H_2O_2 , OH^+ , $HOCl$ & peroxy radicals
- Vit C regenerates the reduced form of Vit. E



α -Tocopherol



Tocopheryl radical



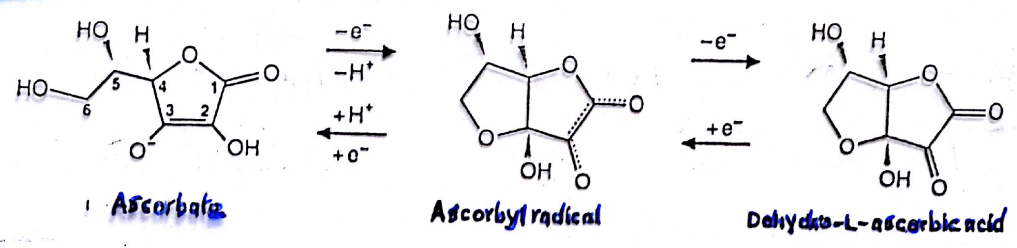
Tocopheryl quinone

Vit. E: most widely distributed antioxidant

- sole physiological role is to quench free radical reactions

Fig. 21.15. Vitamin E. Vitamin E terminates free radical lipid peroxidation by donating single electrons to form the stable, fully oxidized tocopheryl quinone. Of the eight or more different tocopherols that comprise vitamin E, α -tocopherol, shown here, is the most common in the diet.

Vit. C



B-carotenes — precursor of Vit. A

Carotenoids :-

