Sphingolipids are major membrane components. They are found in neuronal tissue.

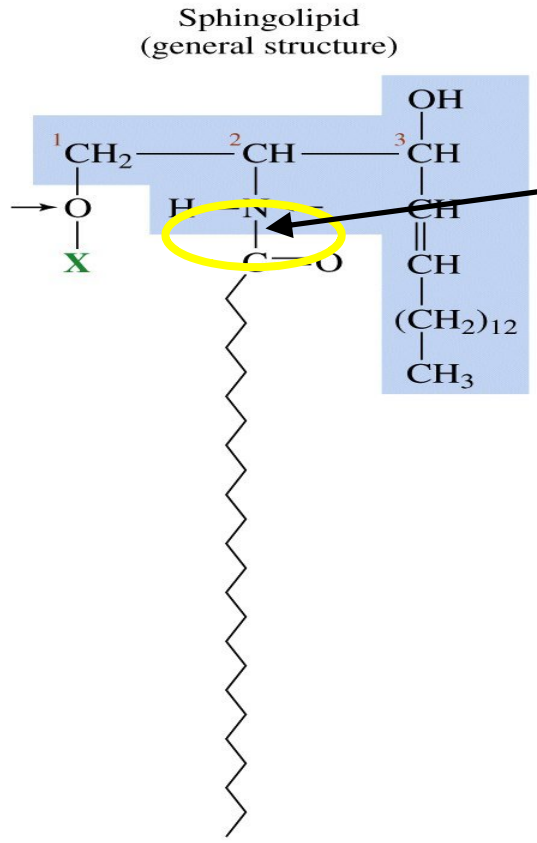
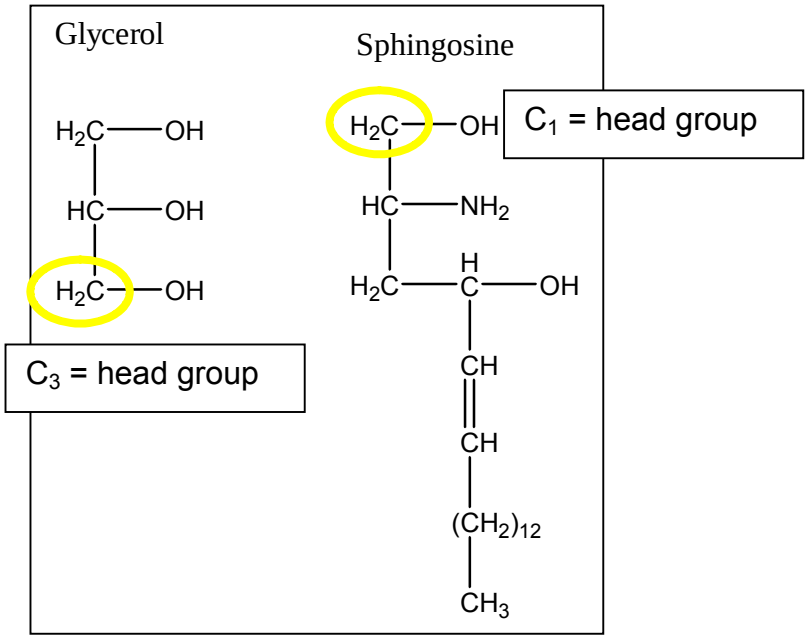


Figure 8-8 part 1 Concepts in Biochemistry, 3/e
© 2006 John Wiley & Sons

Amide linkage

Note the sphingosine backbone which is not glycerol (like fatty acids).



The head group on a spingolipid is at C_1.
The head group on a phospholipid (which has a glycerol backbone) is at C_3.

The head groups include:

- Hydrogen = **ceramide**
- Phosphocholine = **sphingomyelin**, the most common ceramide, also called **sphingophospholipids**
- Monosaccharides = **cerebrosides**
  - Galactose ➔ found in neuronal tissue
  - Glucose ➔ found in non-neuronal tissue
- Complex oligosaccharides = **gangliocides**

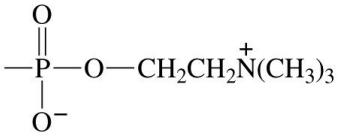
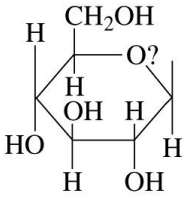
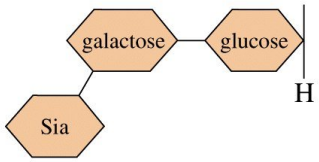
Name of X	Structure of X	Name of Sphingolipid
(b) Hydrogen	—H	Ceramide
(c) Phosphocholine		Sphingomyelin
(d) Glucose		Glucosylcerebroside
(e) Complex oligosaccharide		Ganglioside

Figure 8-8 part 2 Concepts in Biochemistry, 3/e
© 2006 John Wiley & Sons

Gangliocides are the most complex glycospingolipids. They are considered glycosides.

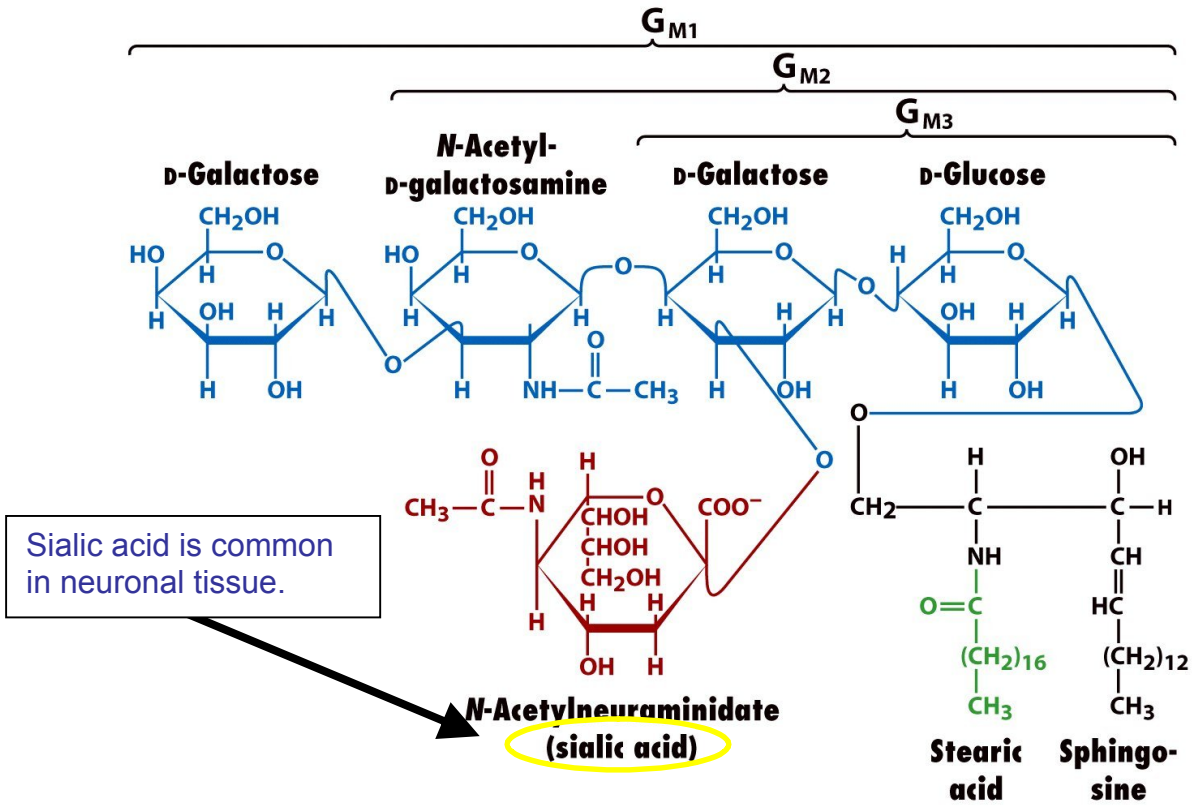
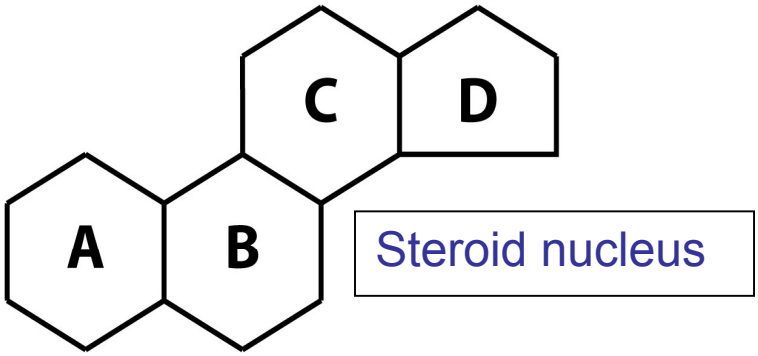


Figure 9-9a Fundamentals of Biochemistry, 2/e
© 2006 John Wiley & Sons



Cyclopentanoperhydrophenanthrene

Unnumbered figure pg 242a Fundamentals of Biochemistry, 2/e

Cholesterol is the most abundant **steroid**. It's a major component of animal plasma membranes.

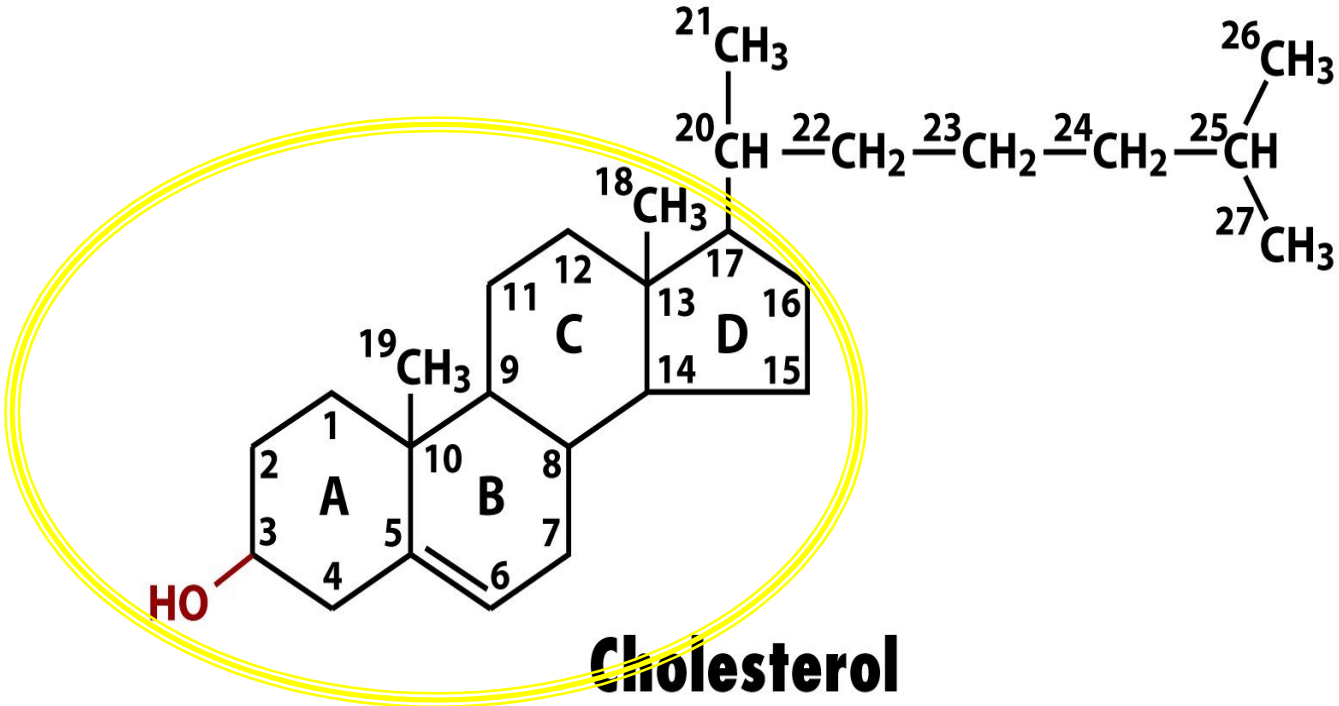


Figure 9-10a Fundamentals of Biochemistry, 2/e

**Note the presence of the steroid head.

Cholesterol is

- Polar
- Mostly hydrophobic
- Can act amphipathic in a membrane
  - But usually if cholesterol exists by itself in solution, the molecules will aggregate and precipitate out of solution.

Examples of steroid hormones (note the head)

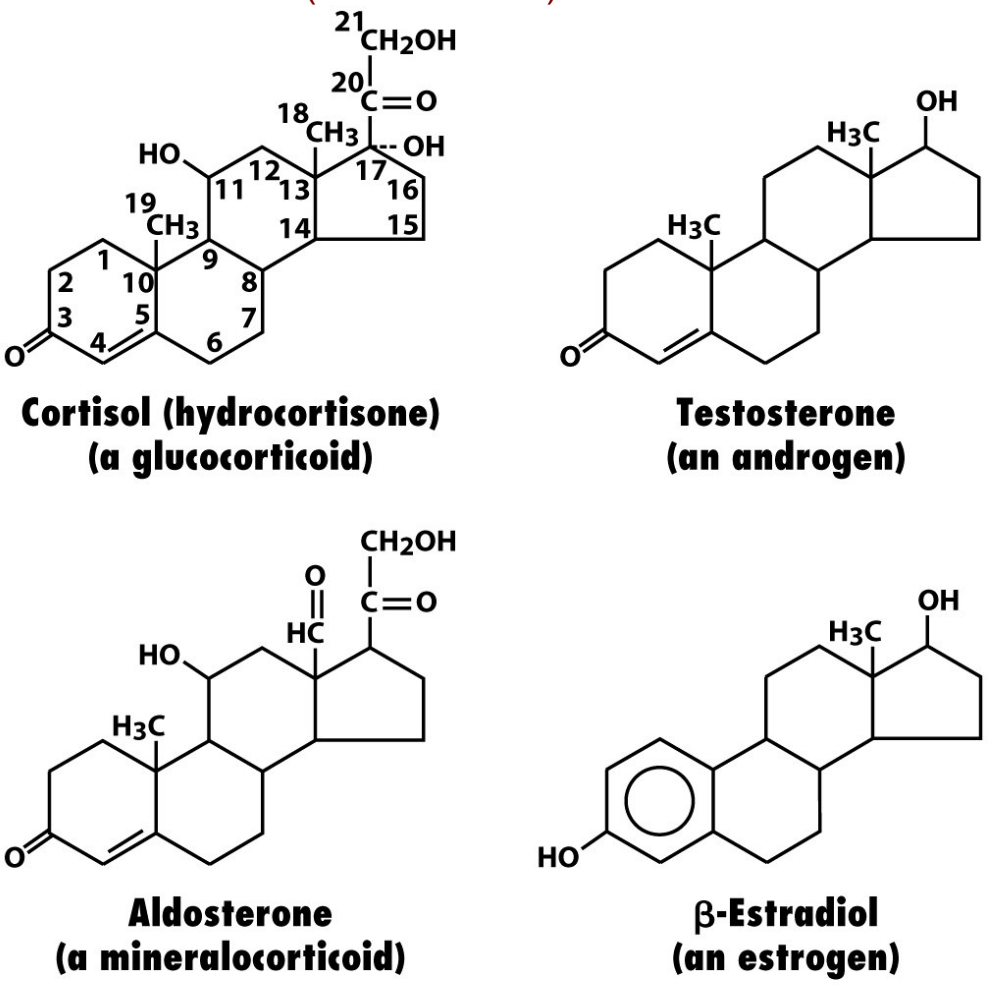
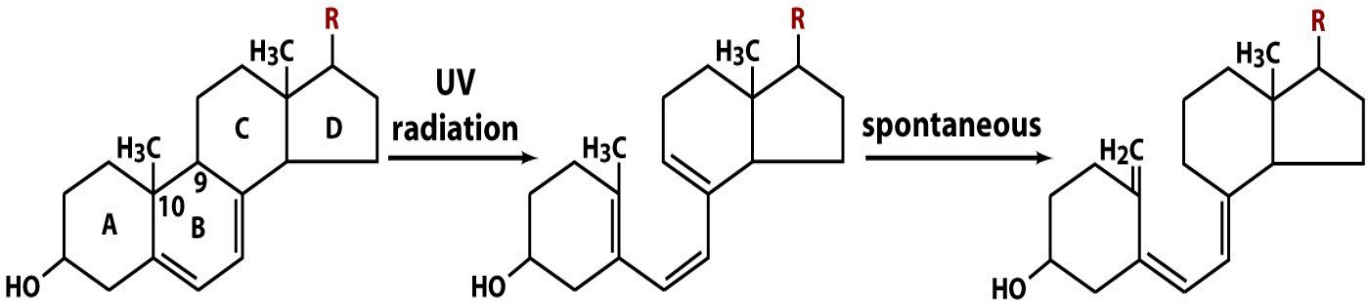


Figure 9-11 Fundamentals of Biochemistry, 2/e

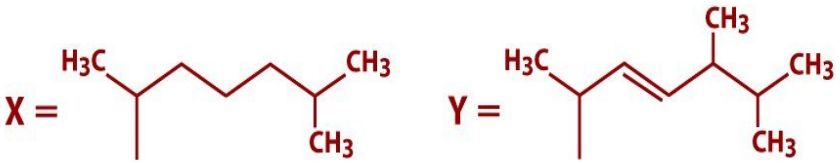
Steroid hormones:

- Glucocorticoid ➔ involved in inflammatory responses and stress
  - Ex. Cortisol
- Mineralocorticoid ➔ regulate the excretion of salt and water by kidneys
  - Ex. Aldosterone
- Sex hormones➔ regulate sexual development & function
  - Ex. Androgen, estrogen, testosterone



R = X 7-Dehydrocholesterol
R = Y Ergosterol

R = X Vitamin D_3 (cholecalciferol)
R = Y Vitamin D_2 (ergocalciferol)

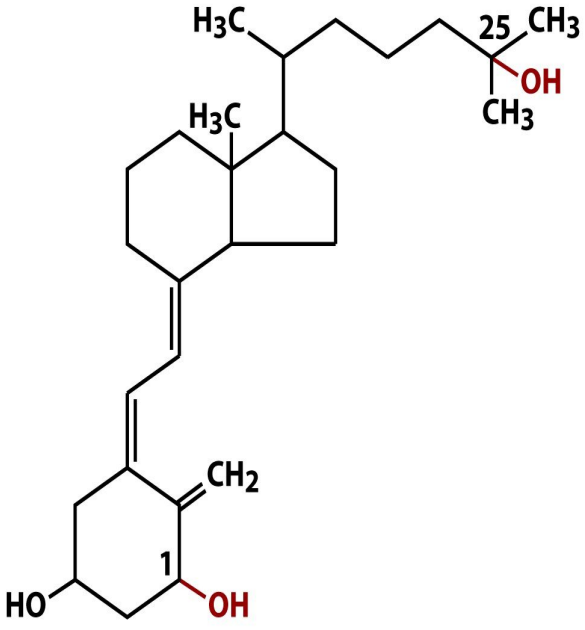


Unnumbered figure pg 244a Fundamentals of Biochemistry, 2/e

Prefix:
**ERGO = plant
**CHOLE = animal

Vitamin D's various forms are sterol derivatives and are really hormones.

- The steroid precursor is found in the cell membrane in the skin.
- Light (UV radiation) hits the molecule and begins the reaction to form vitamin D.



Hydroxyl groups are enzymatically added in the liver and kidney to give the active form of Vitamin D.

← (active form of Vitamin D)

1α,25-Dihydroxycholecalciferol

Unnumbered figure pg 244b Fundamentals of Biochemistry, 2/e

Vitamin D regulates the calcium levels in the blood by promoting their absorption from food in the intestines (specifically by acting as a **transcription factor** stimulating second messengers which are responsible for calcium absorption in the intestines) , and by promoting re-absorption of calcium in the kidneys.

The ***thyroid*** and ***parathyroid*** also play an important role by responding to the increased or decreased Ca^{+2} in blood.

The ***thyroid*** produces **calcitonin. ($\downarrow$ Ca^{+2})**

Calcitonin reduces blood Ca^{2+} levels by:

- Decreasing Ca^{2+} absorption by the intestines
- Decreasing Ca^{2+} re-absorption by the kidneys
- Discouraging the re-absorption of Ca^{+2} from bones

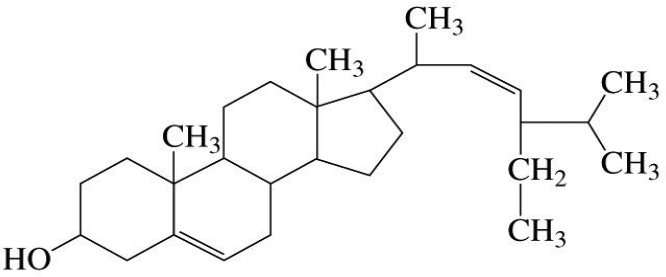
The ***parathyroid*** produces **PTH (parathyroid hormone). ($\uparrow$ Ca^{+2})**

PTH increases blood Ca^{+2} levels by:

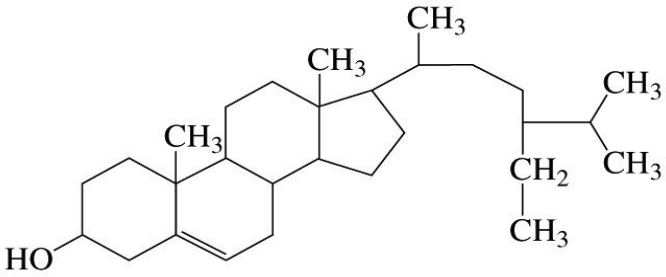
- Increasing Ca^{2+} absorption by the intestines
- Increasing Ca^{2+} re-absorption by the kidneys
- Encouraging the re-absorption of Ca^{+2} from bones

So, overall, to synthesize vitamin D, we need:

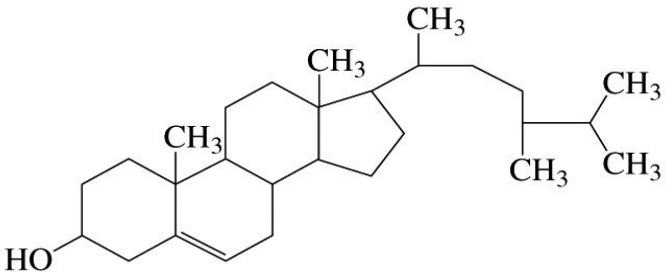
- Cholesterol
- Sunlight
- A function thyroid & parathyroid



Stigmasterol



β-Sitosterol

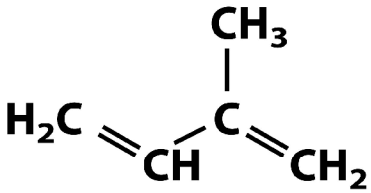


Campesterol

Figure 8-12 Concepts in Biochemistry, 3/e

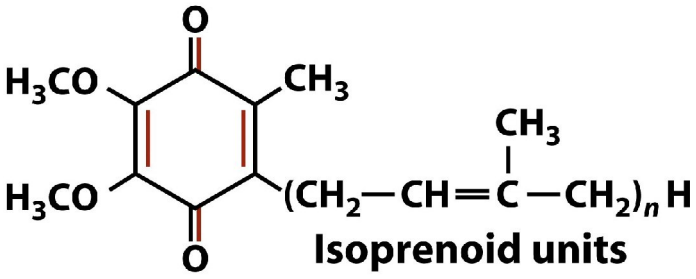
- Also called nutraceuticals or functional foods.
- All three compounds reduce serum cholesterol levels by 10-15%.
- β-Sitosterol has also been shown to reduce symptoms of enlarged prostrate and may inhibit prostrate cancer growth (*due to its biological action being similar to estrogen*).

Isoprenoids are polymers of isoprene units. Isoprene consists of a five carbon unit:



Isoprene

Cholesterol is synthesized from isoprene units, but is not labeled an isoprene due to the presence of the characteristic steroid head.



Coenzyme Q (CoQ) or ubiquinone

Unnumbered figure pg 245b Fundamentals of Biochemistry, 2/e

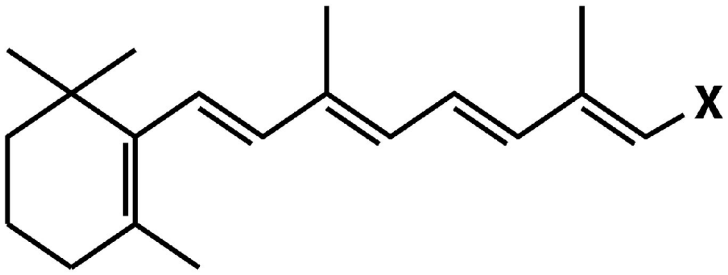
An example of an isoprenoid is **ubiquinone**, which is a *hydrophobic* byproduct of cholesterol synthesis.

It is involved in electron transport in the mitochondria and so is responsible for the synthesis of ATP.

Ubiquinone's synthesis is blocked by anti-cholesterol drugs (e.g. Lipitor, Zocor) and patients on such drugs often report feeling fatigued. Patients' drug regimens are often supplemented with CoQ.

It is often sold in health food stores, marketed as an antioxidant to promote heart health.

Many isoprenoids are found in plants, like Retinol (vitamin A), derived from β-carotene.

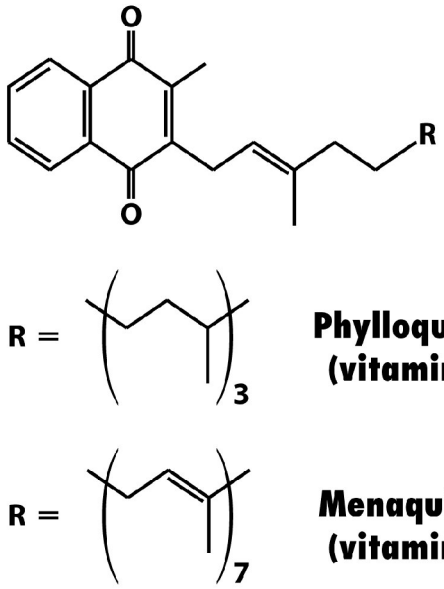


X = CH_2OH Retinol (vitamin A)
X = CHO Retinal

Unnumbered figure pg 246a Fundamentals of Biochemistry, 2/e

Retinol (alcohol) is oxidized to Retinal (aldehyde) when hit with UV light. Retinal is the eye's photoreceptor.

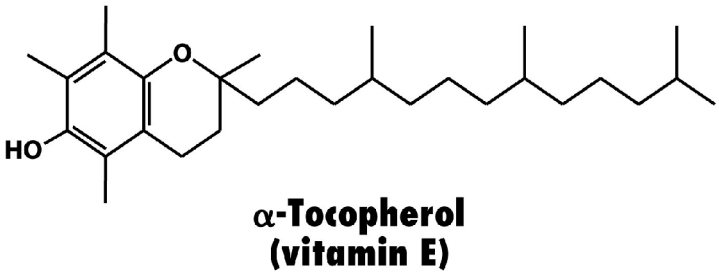
Large doses of retinol can lead to muscle weakness, cancer, and turning orange.



Unnumbered figure pg 246b Fundamentals of Biochemistry, 2/e

Vitamin K is a lipid synthesized by plant and is important for blood clotting.

When dosing for blood thinner (e.g. coumadin) the vitamin K level must be kept constant.



Unnumbered figure pg 246c Fundamentals of Biochemistry, 2/e

Vitamin E in a highly hydrophobic molecule found in cell membranes, where is protects the membrane proteins and lipids from oxidative damage.

SUMMARY:

Sphingolipids	
Molecule	**Function**
• ceremide • spingomyelin • cerebrosides • gangliocide	components of neuronal tissue

Steroids	
Molecule	**Function**
Cholesterol	animal plasma membrane
Glucocorticoid	inflammatory responses and stress (ex. cortisol)
Mineralocorticoid	regulates the excretion of salt and water from kidneys (ex. aldosterone)
Sex hormones	regulate sexual development & function (ex. androgen, estrogen)
Vitamin D	calcium regulation
β-Sitosterol	reduce symptoms of enlarged prostate
• Stigmasterol • β-Sitosterol • Campesterol	• reduce serum cholesterol • neutraceuticals

Isoprenoids	
Molecule	**Function**
Ubiquinone (CoQ)	electron transportin mitochondria
Retinol (Vitamin A)	sight
Vitamin K	blood clotting
Vitamin E	protects lipids and proteins in cell membrane