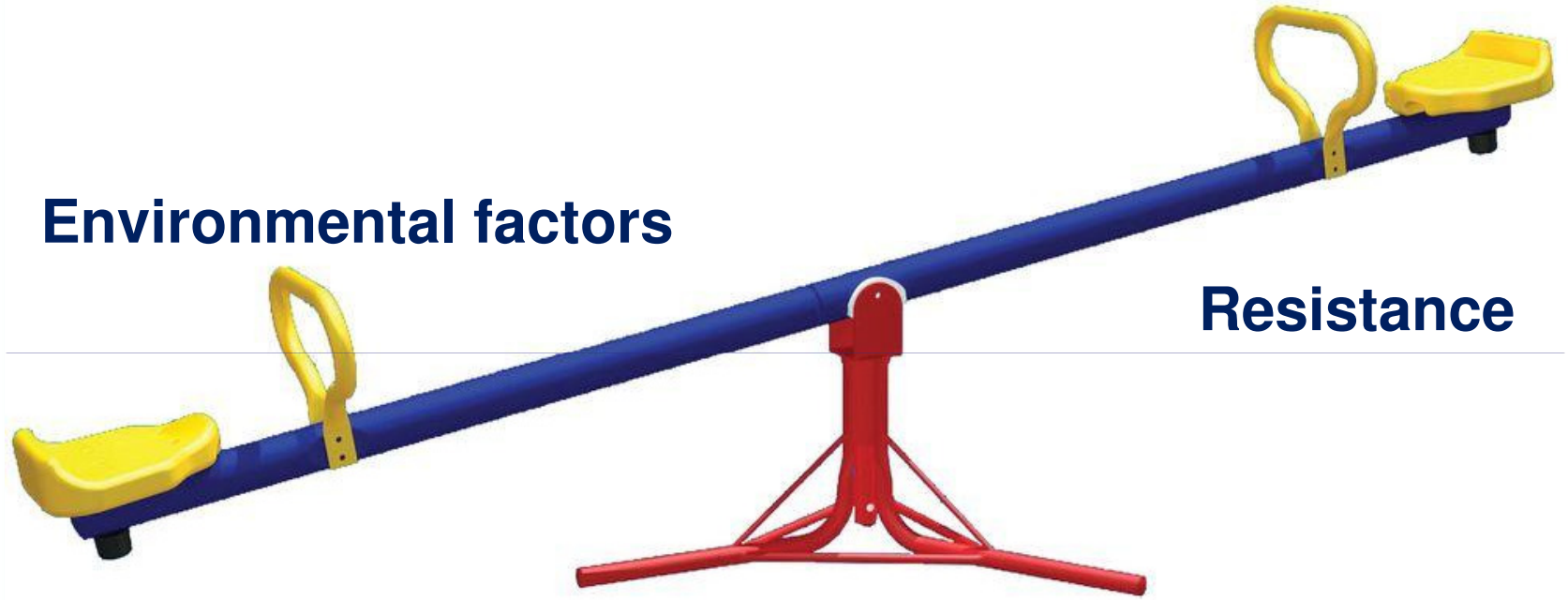
Phospholipids and Mitochondria

ParkinsonsTryptamine binds to human trace amine-associated receptor 1 (TAAR1) as an agonist. Chromosome 6q

Alzheimers -Theobromine

Health

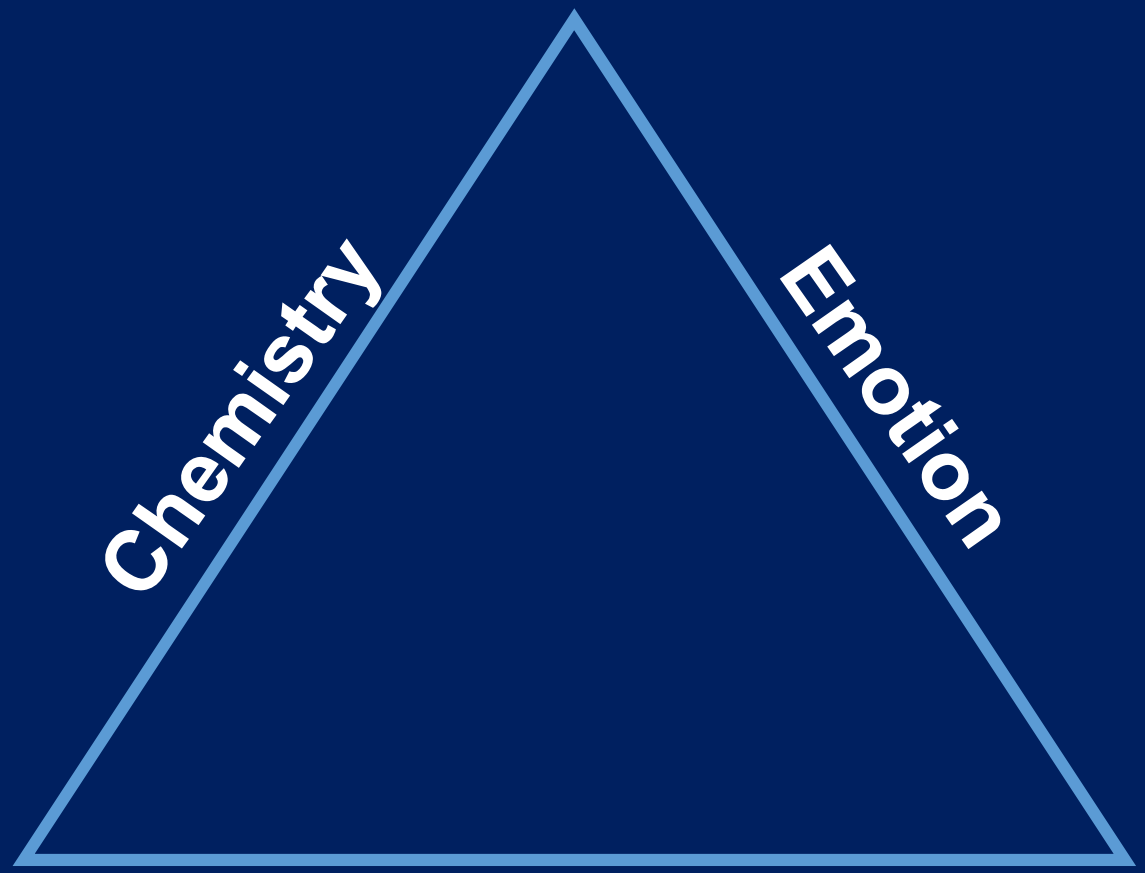


Dr W. D. Harper DC

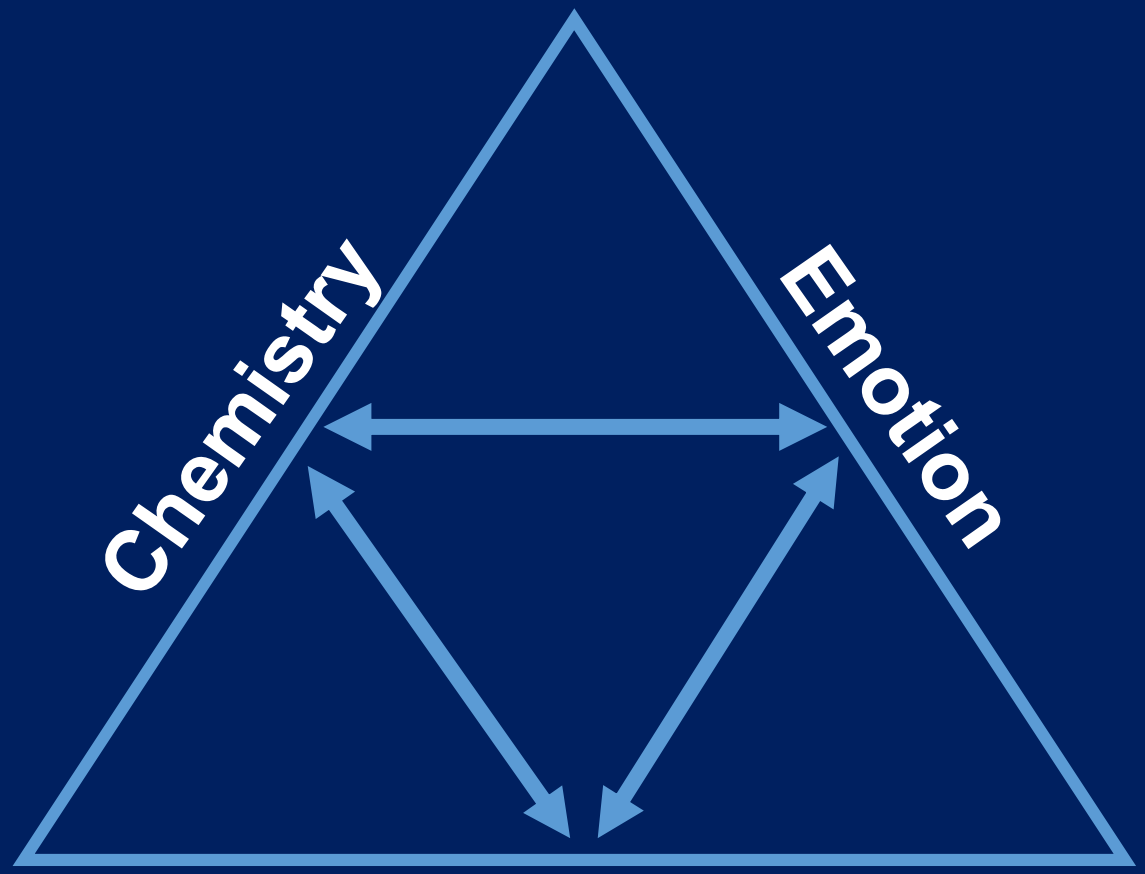
Disease

Dr W, D. Harper DC

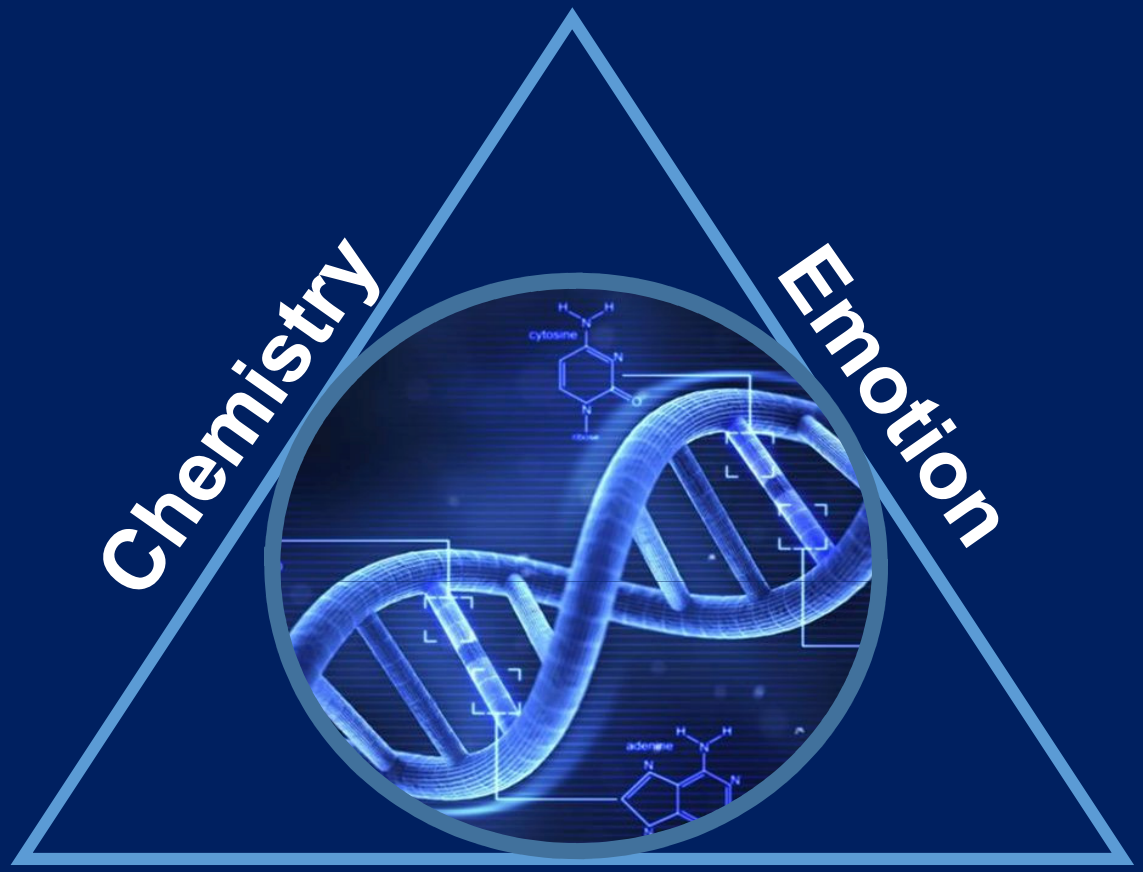
Triad of Health

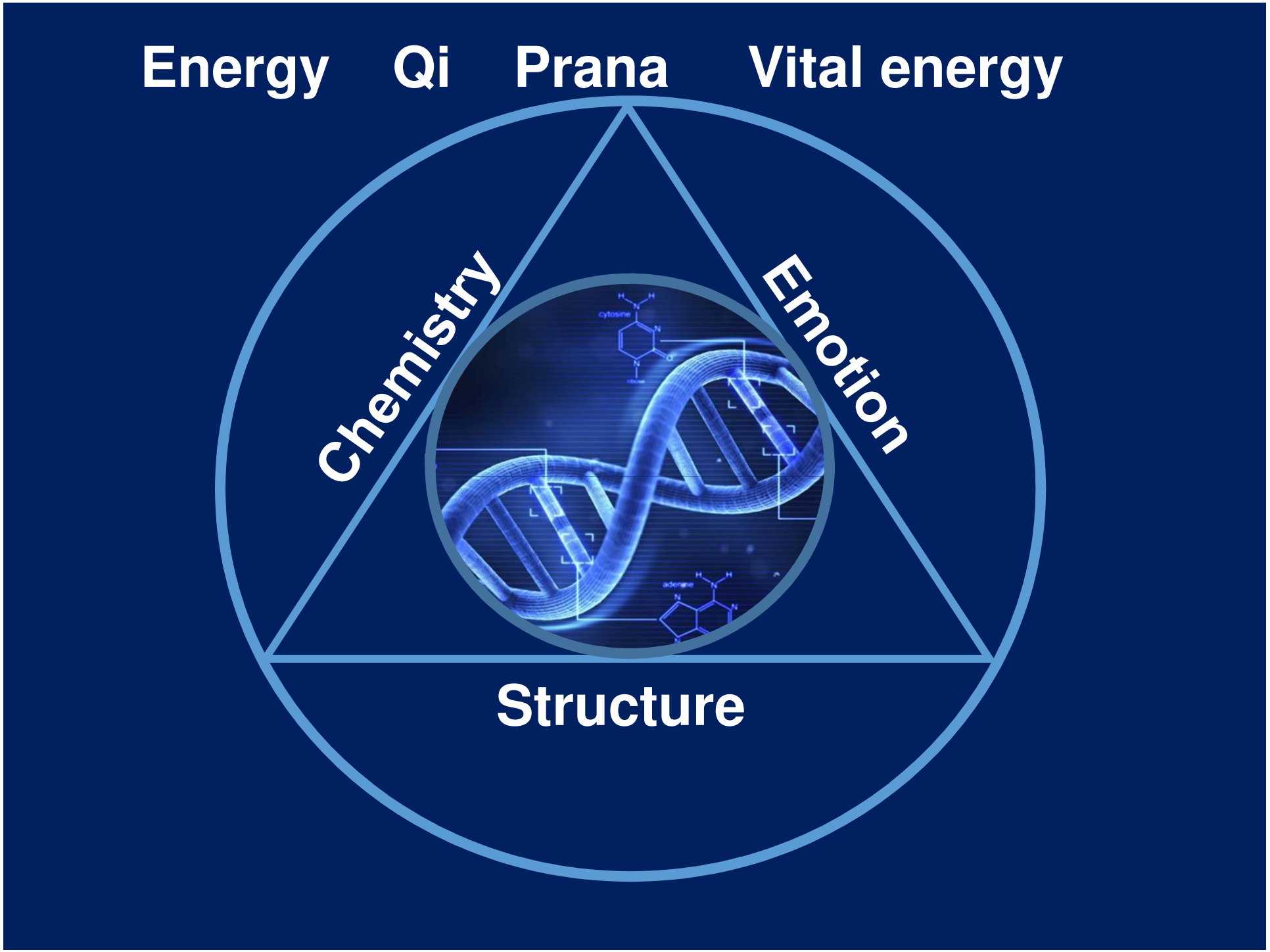


Triad of Health



Triad of Health




Energy
Qi
Prana
Vital energy
Chemistry
Emotion
Structure

Disease

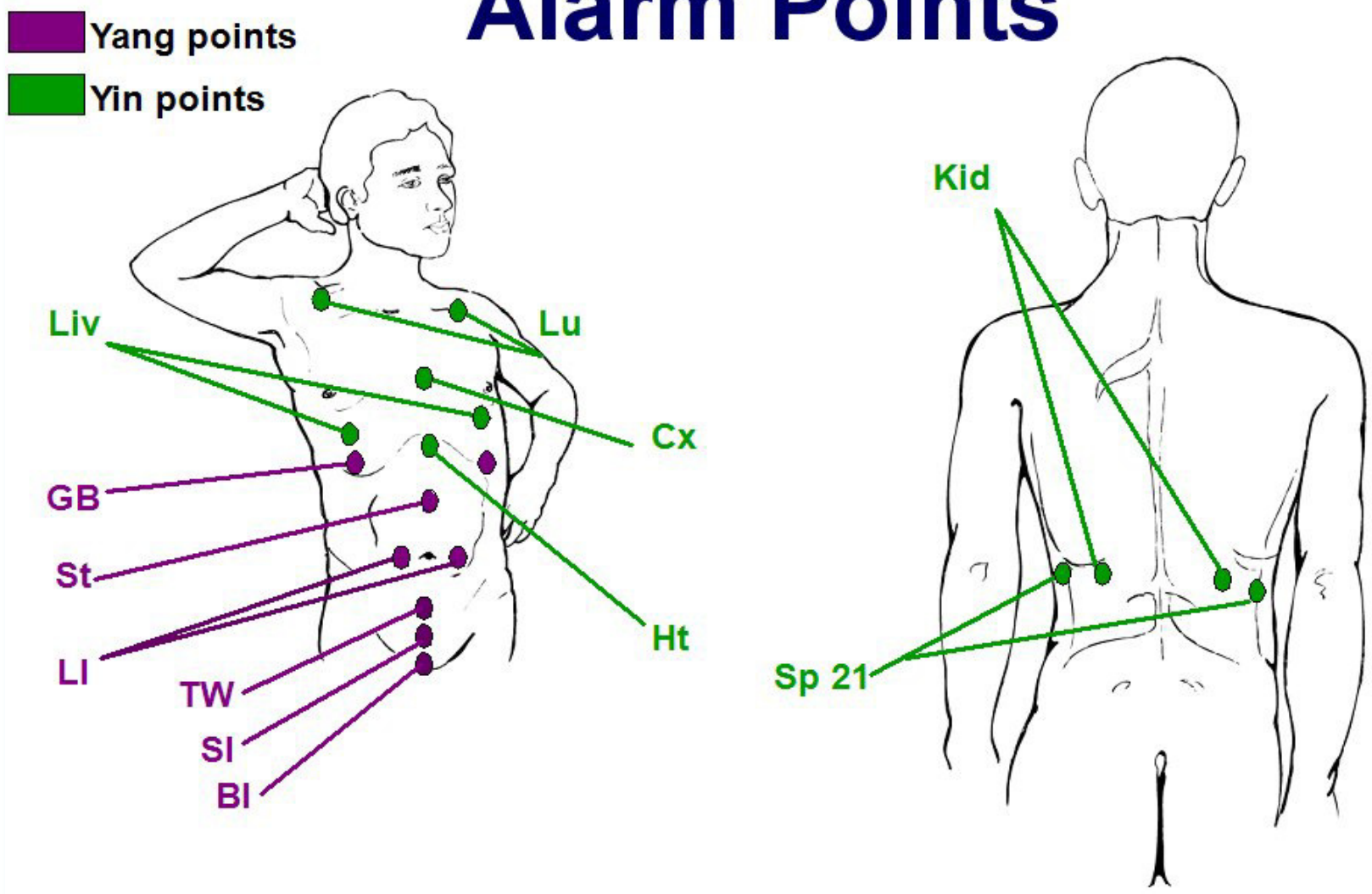
Which is the Cause and which is the Effect?

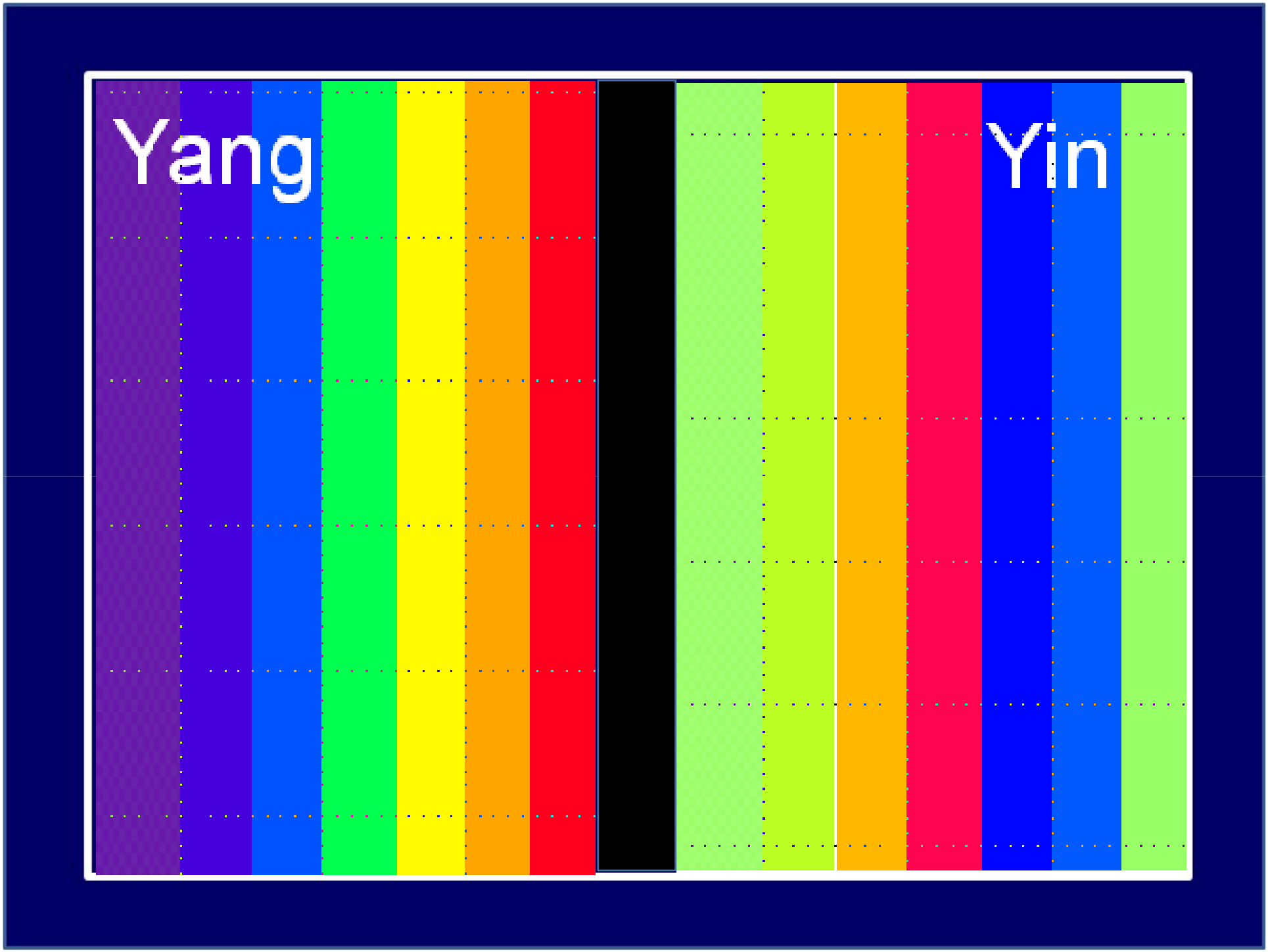
Finding the Causal Meridian

Using the composite acetates test Yang / Yin with eyes closed.
Then test each separate meridian to identify **Causal meridian.**

Effect meridian is the one that negates this meridian.

Alarm Points




Yang
Yin

Maintain causal meridian acetate and tap SCN point 60x at 2Hz. This will lock the patient into the causal body clock.

The Effect meridian will negate the Causal meridian and now will weaken in the clear.

There will be weak associated muscles on both meridians found and tapped in.

These can be used to establish optimal remedies.

How much of a supplement do we absorb?

Liposomes

v

Capsules

v

Aqueous solutions

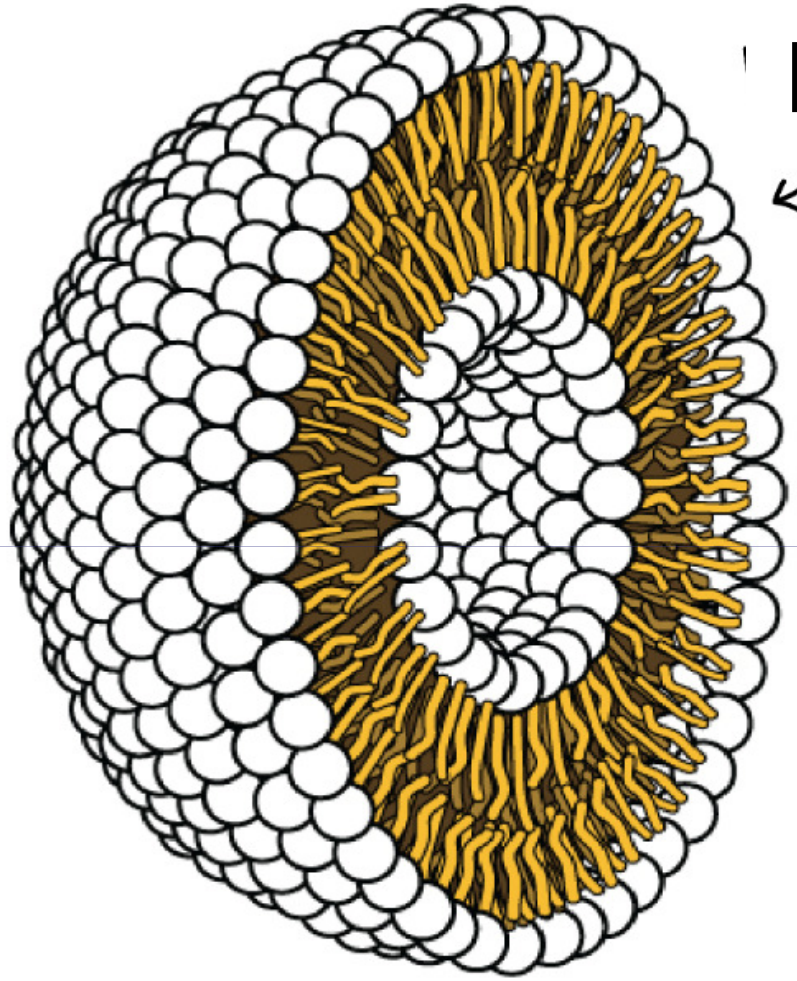
Only 30% of dietary magnesium is absorbed.

Some minerals only get absorbed in an acid medium, some in an alkali medium.

All fat soluble vitamins only get absorbed when accompanied by oil in the diet.

Co-enzymes are better absorbed in glycerine.

Putting nutrients into liposomes has been shown to maximise absorption and delivery inside thre cells.



Liposome

Micelle (emulsion)

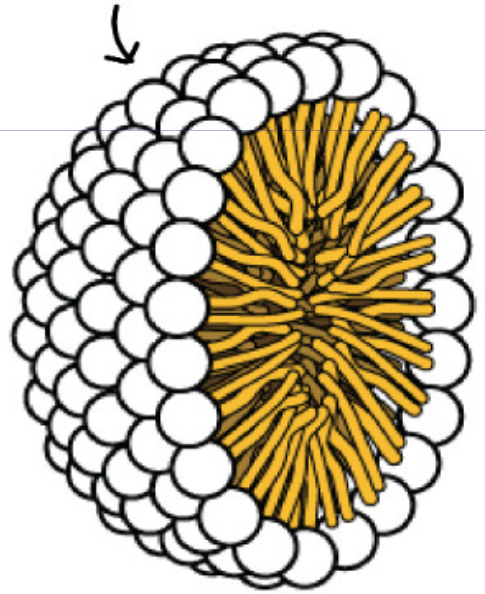


Image credit: modification of work by OpenStax Biology, originally by Mariana Ruiz Villareal.

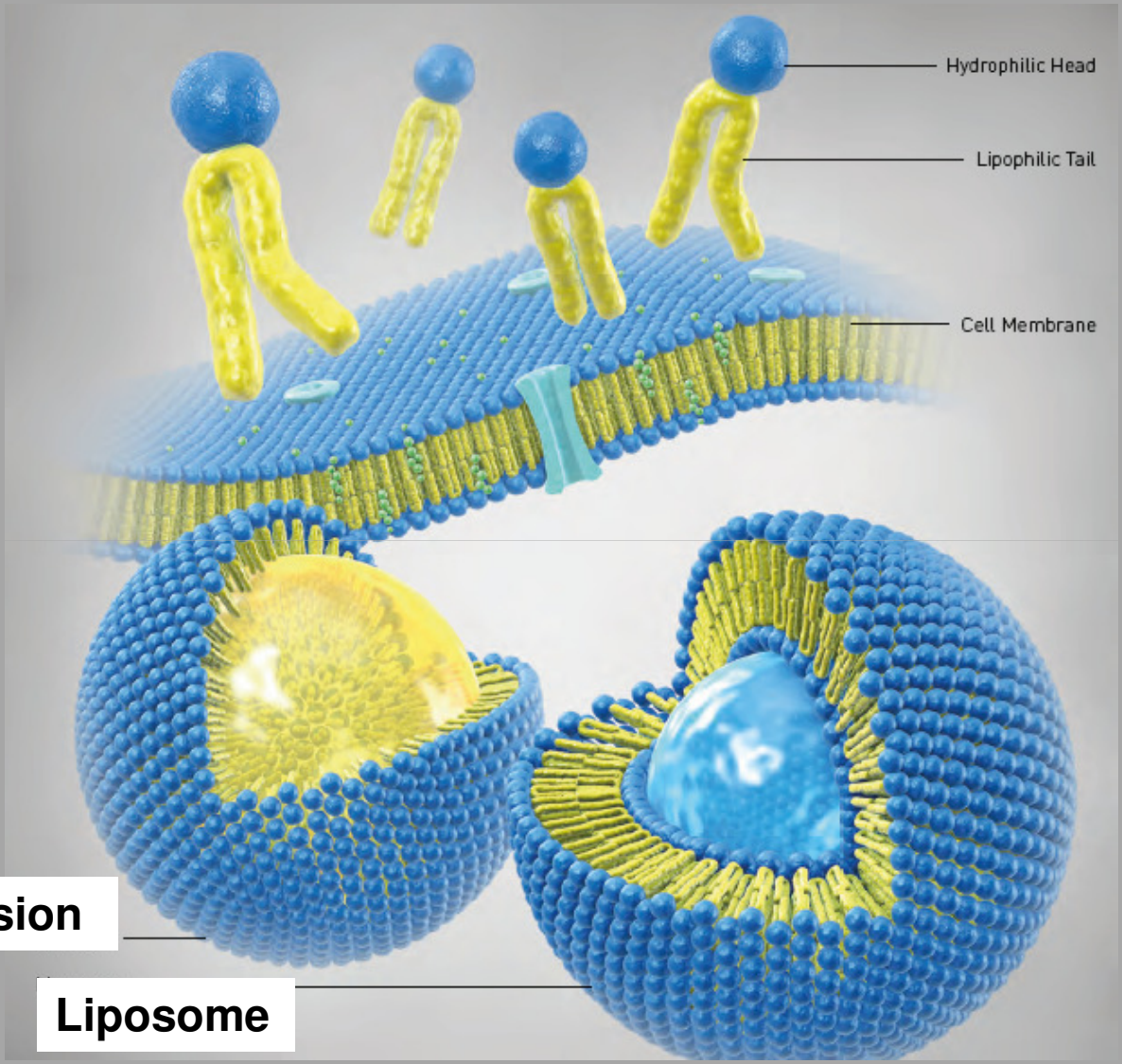
If the phospholipids have small tails, they may form a micelle (a small, single-layered sphere), while if they have bulkier tails, they may form a liposome (a hollow droplet of bilayer membrane).

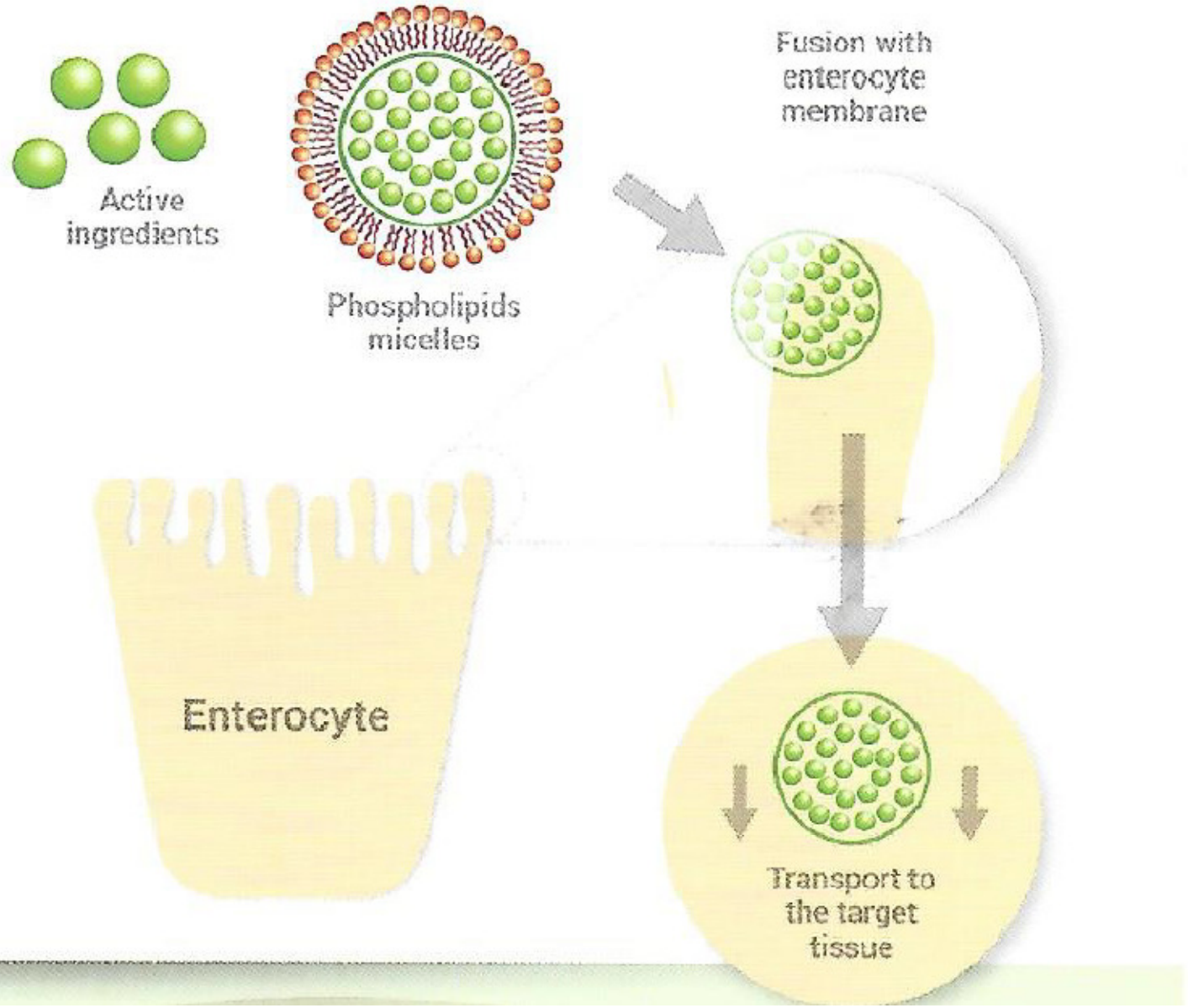
Phospholipids are amphiphilic molecules and consist of a hydrophilic and a lipophilic moiety.

In water they can form a “shell” which encloses a fat droplet (lipophilic ingredient) to form a micelle which allows phospholipids – the dispersion in aqueous media.

This is called an **emulsion.** In absence of non-polar lipids and the presence of water, phospholipids organize as bilayer structures which are called **liposomes.**

The aqueous core of a liposome can be loaded with hydrophilic nutrients like minerals and vitamins.


Hydrophilic Head
Lipophilic Tail
Cell Membrane
Emulsion
Liposome


Active ingredients
Phospholipids micelles
Fusion with enterocyte membrane
Enterocyte
Transport to the target tissue

For the preparation of liposomes, phospholipids are mixed with water and the desired active ingredients.

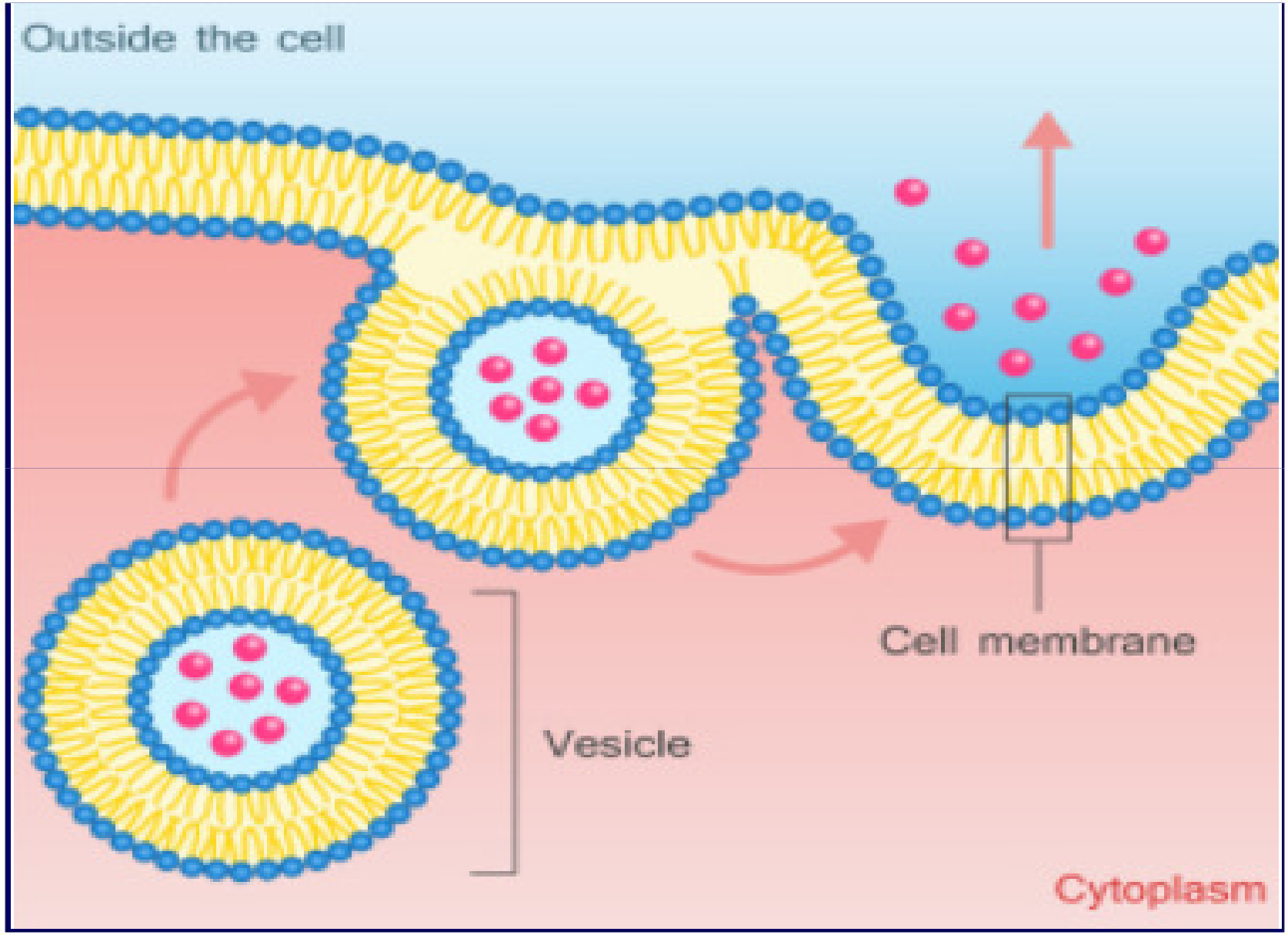
Ethanol or glycerol may be added to improve the stability of the product or to enhance the solubility of the ingredients.

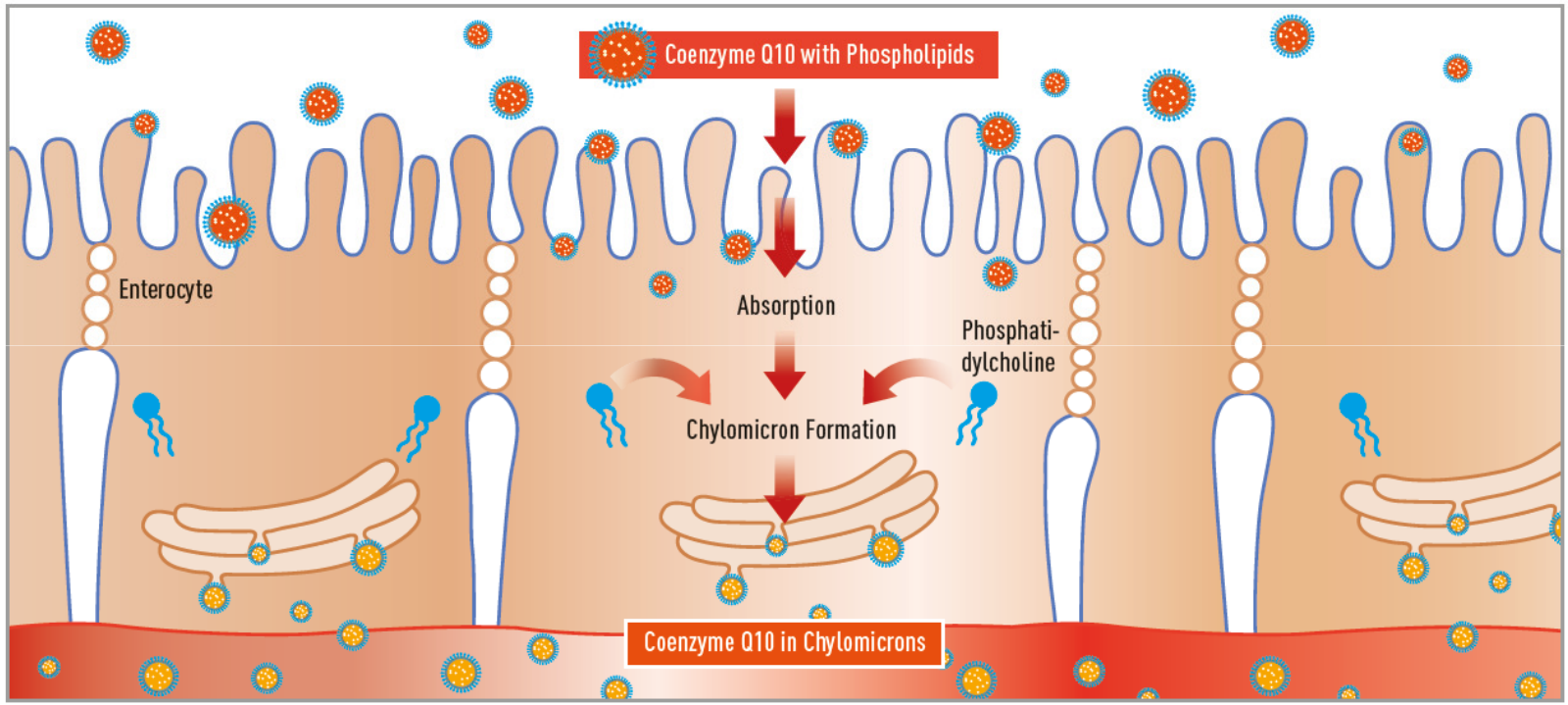
High-shear mixing is usually applied for the preparation of liposomes.

In a second step, high-pressure homogenization is used to obtain smaller and homogenously distributed liposomes.

With the help of phospholipids fat-soluble nutrients such as coenzyme Q10 can be solubilized into liposomes.

With this technology the uptake into the enterocytes of the small intestine is significantly improved.


Outside the cell
Cell membrane
Vesicle
Cytoplasm

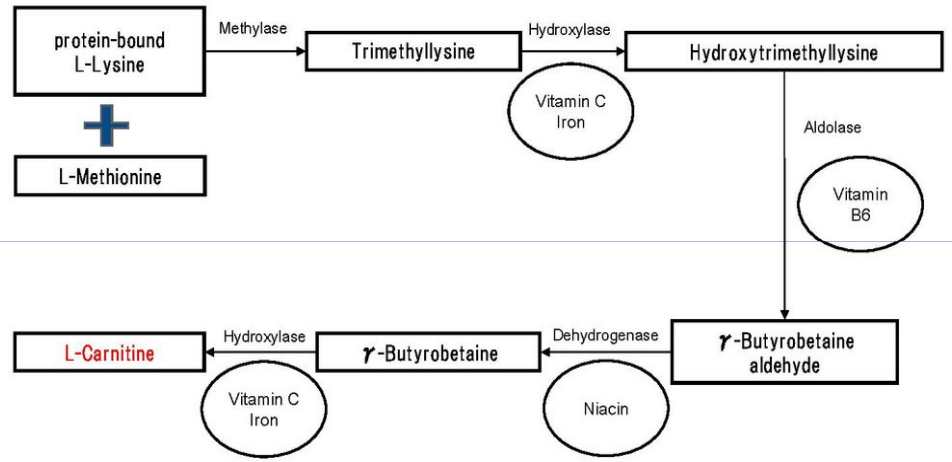

Coenzyme Q10 with Phospholipids
Enterocyte
Absorption
Phosphati-
dylcholine
Chylomicron Formation
Coenzyme Q10 in Chylomicrons

Common diseases associated with chronic intracellular deficiencies.

Alzheimer's – Zinc, CoQ10
Multiple sclerosis – Sulphur*, Vit D, Vit B12
Parkinson's – Magnesium, Indole-3- carbinol, CoQ10
Type 1 Diabetes - Manganese
.

Carnitine as a source of Sulfur*

Used in the Carnitine Shuffle.



Leon Chaitow "Thorsons Guide to Amino acids" page 72
"*Acetyl-L-carnitine. Monograph"(PDF). *Alternative Medicine Review*. 15 (1): 76–83. April 2010.

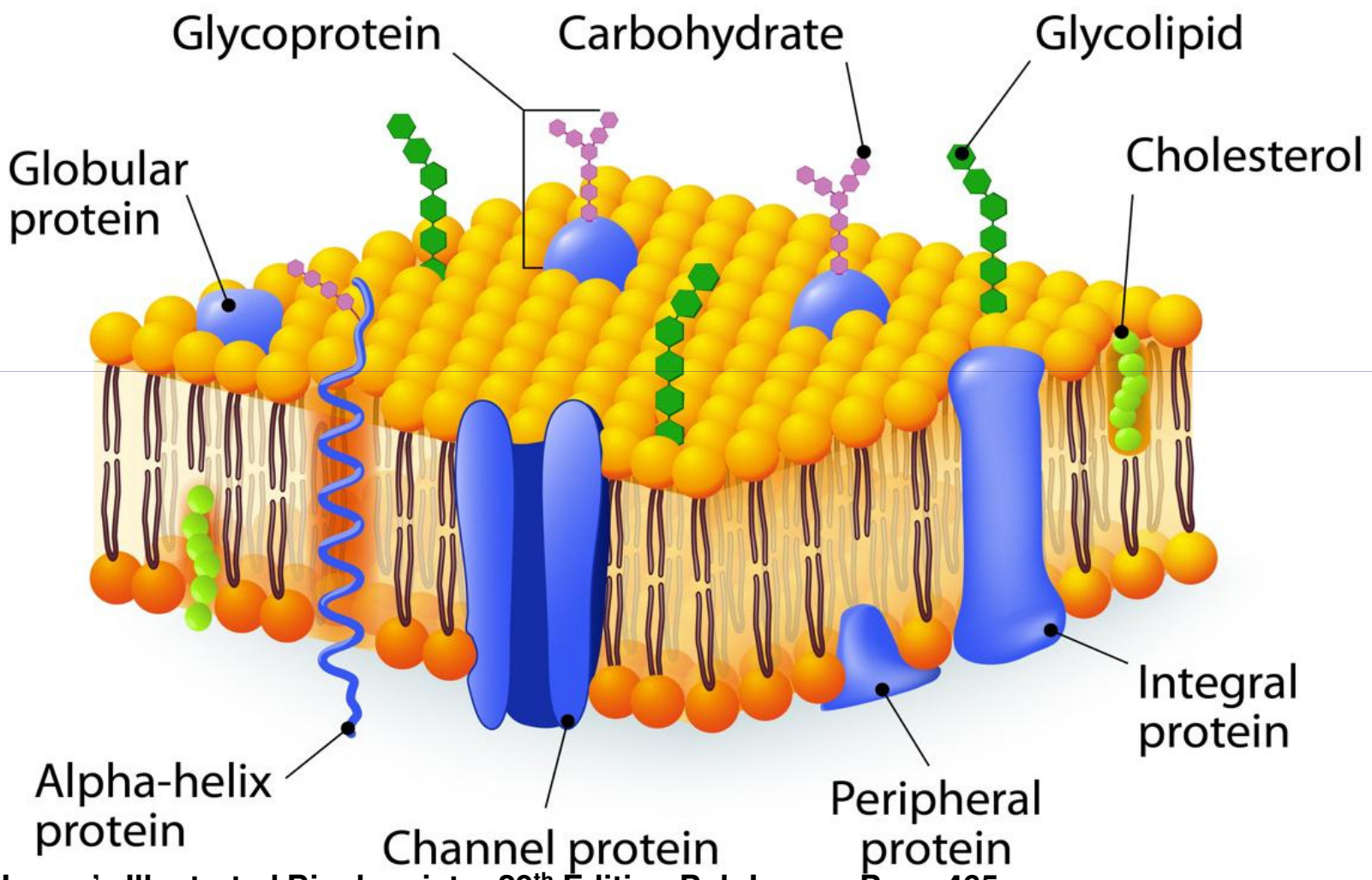
Cancer – Selenium or Selenium methionine
Gout – Taurine, Vit C
Osteoarthritis – Vitamin B5, Vit C,
MND - Molybdenum
Rheumatoid arthritis – Iron
Diabetes type 2 – Carnitine, Zinc
Angina / Atherosclerosis- Vit B6, Vitamin C

Myocardial infarct – Vitamin C, Magnesium

CVA – Ischemic - B. Complex, Vit E, EPA, DHA.

- Hemorragic - Vitamin B6, Folate, Hydroxycobalamin, Zinc, Vitamin C

Cell Membranes

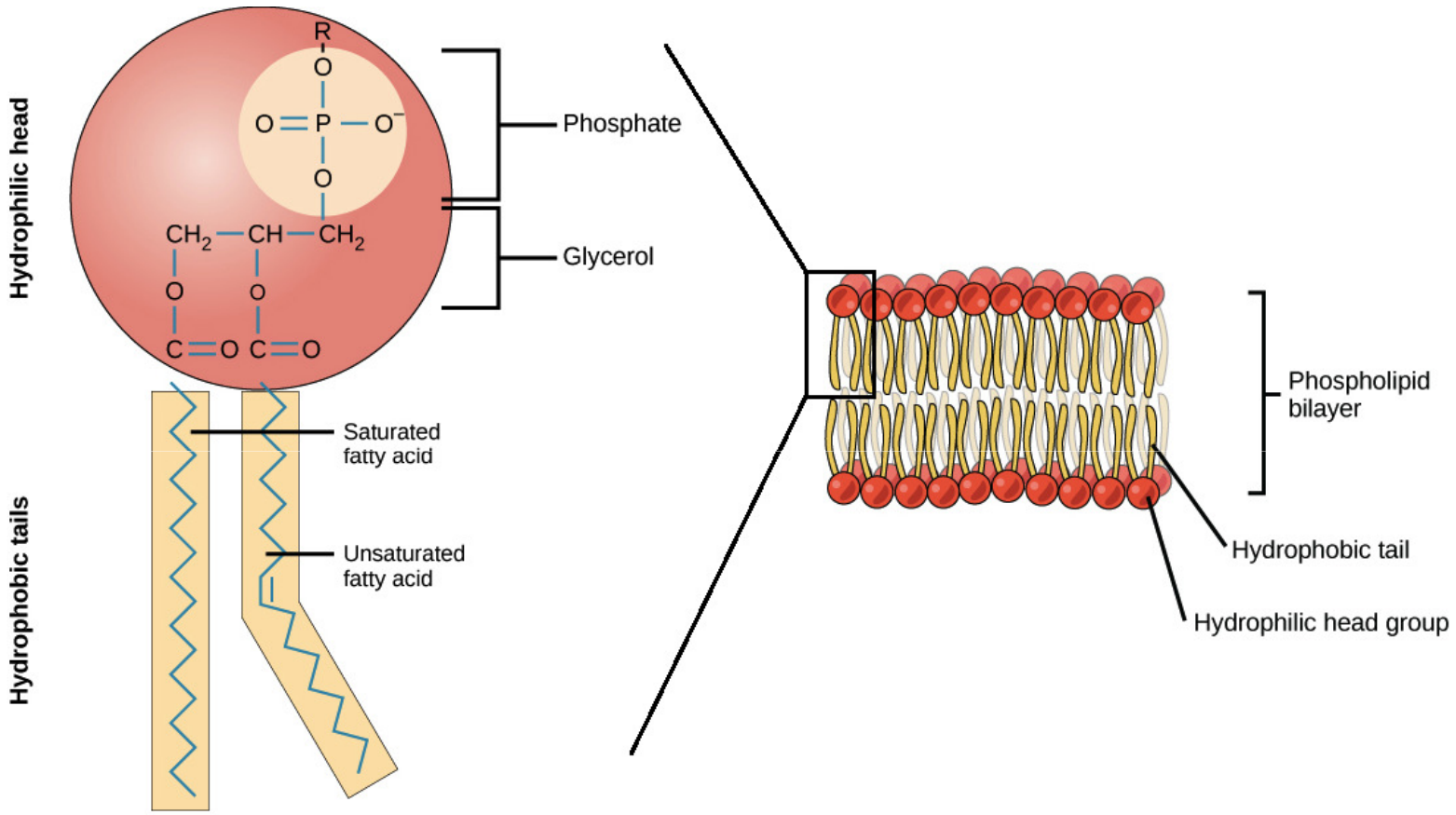


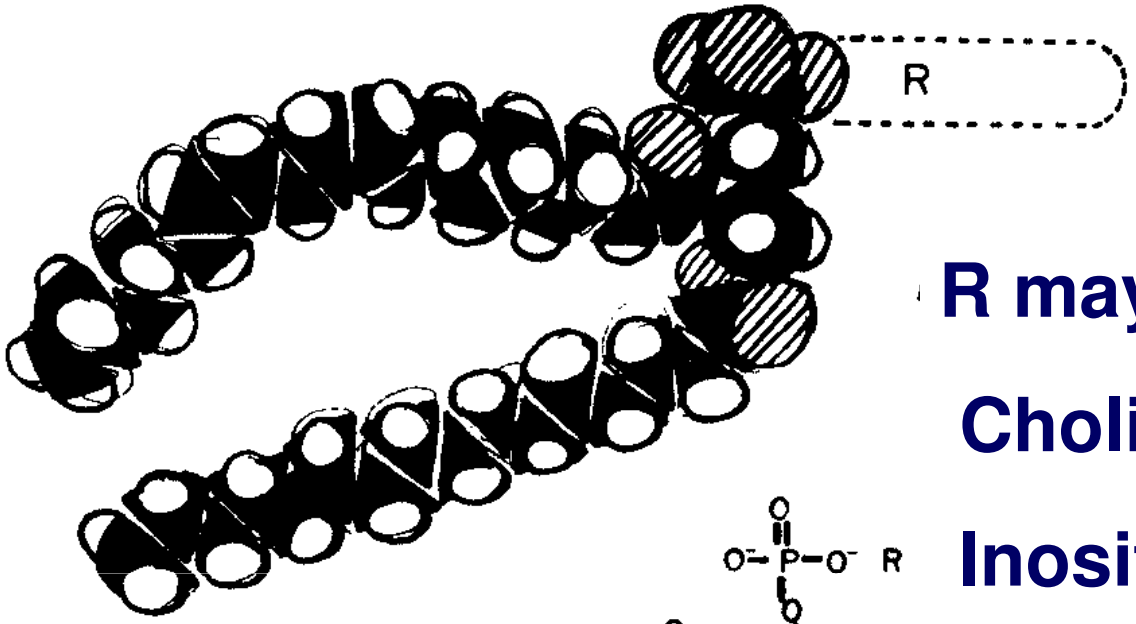
Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 465

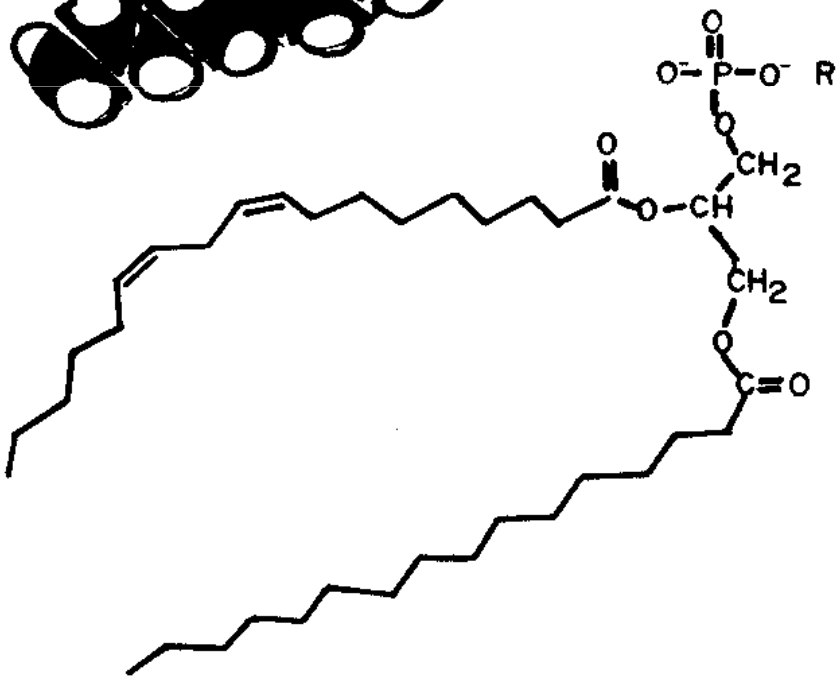
The components of the plasma membrane

Component	Location
Phospholipids	Main fabric of the membrane **40%**
Cholesterol	Tucked between the hydrophobic tails of the membrane phospholipids
Integral proteins	Embedded in the phospholipid bilayer; may or may not extend through both layers **50%**
Peripheral proteins	On the inner or outer surface of the phospholipid bilayer, but not embedded in its hydrophobic core
Carbohydrates	Attached to proteins or lipids on the extracellular side of the membrane (forming glycoproteins and glycolipids) **10%**

Table modified from OpenStax Biology.


Hydrophilic head
Hydrophobic tails
R
O
O = P — O⁻
O
CH2 — CH — CH2
O O
C = O C = O
Phosphate
Glycerol
Saturated fatty acid
Unsaturated fatty acid
Phospholipid bilayer
Hydrophobic tail
Hydrophilic head group





R maybe

Choline

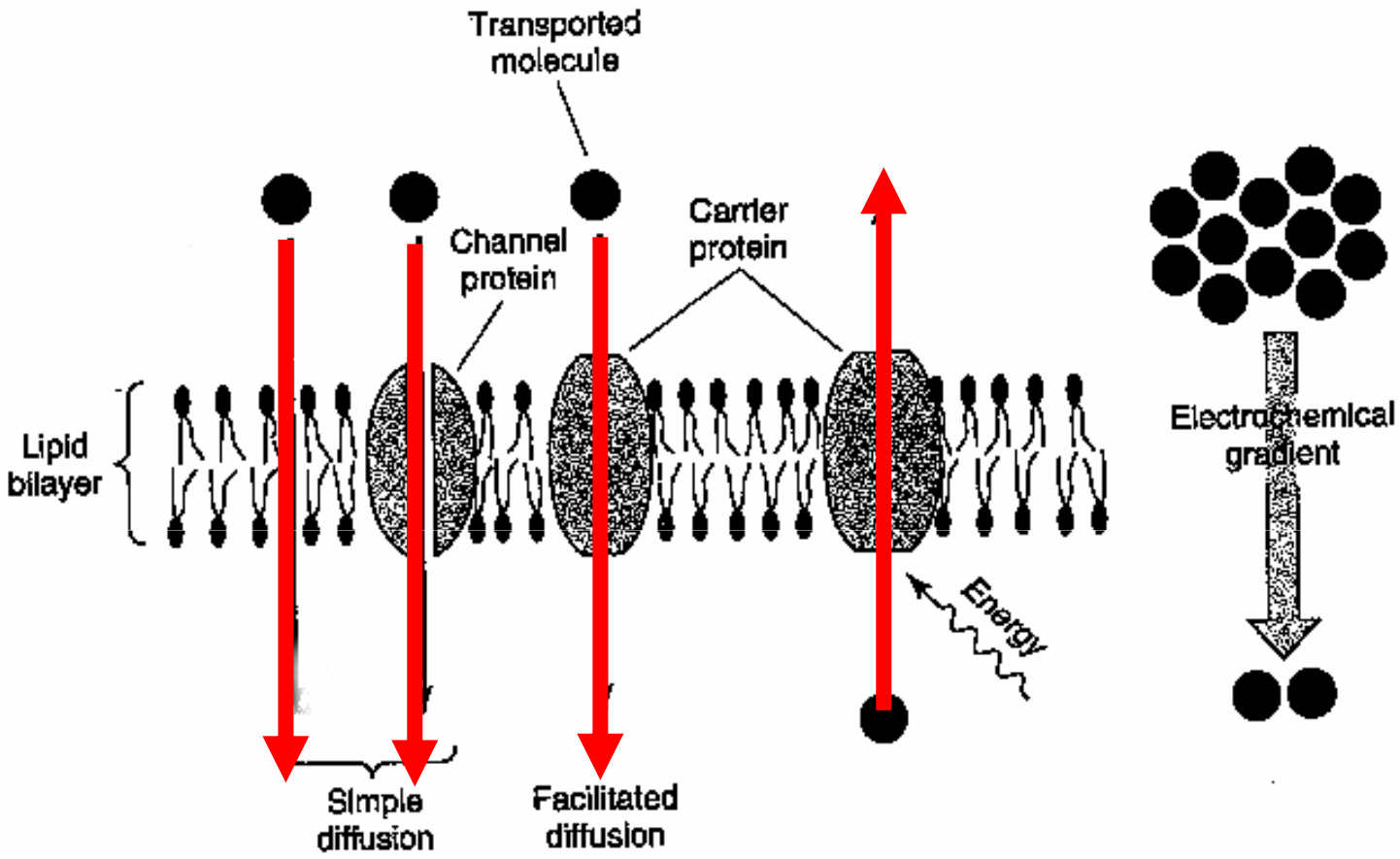
Inositol

Ethanolamine

Serine

The integral cell membrane proteins act as a conduit to allow nutrients to get into the cell from outside and waste products to be eliminated.

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 463



Passive transport Active transport

Harper's Illustrated Biochemistry 29th Edition Pub Lange. Page 468

Plasma membranes consist of both lipids and proteins. The fundamental structure of the membrane is the phospholipid bilayer, which forms a stable barrier between two aqueous compartments. In the case of the plasma membrane, these compartments are the inside and the outside of the cell.

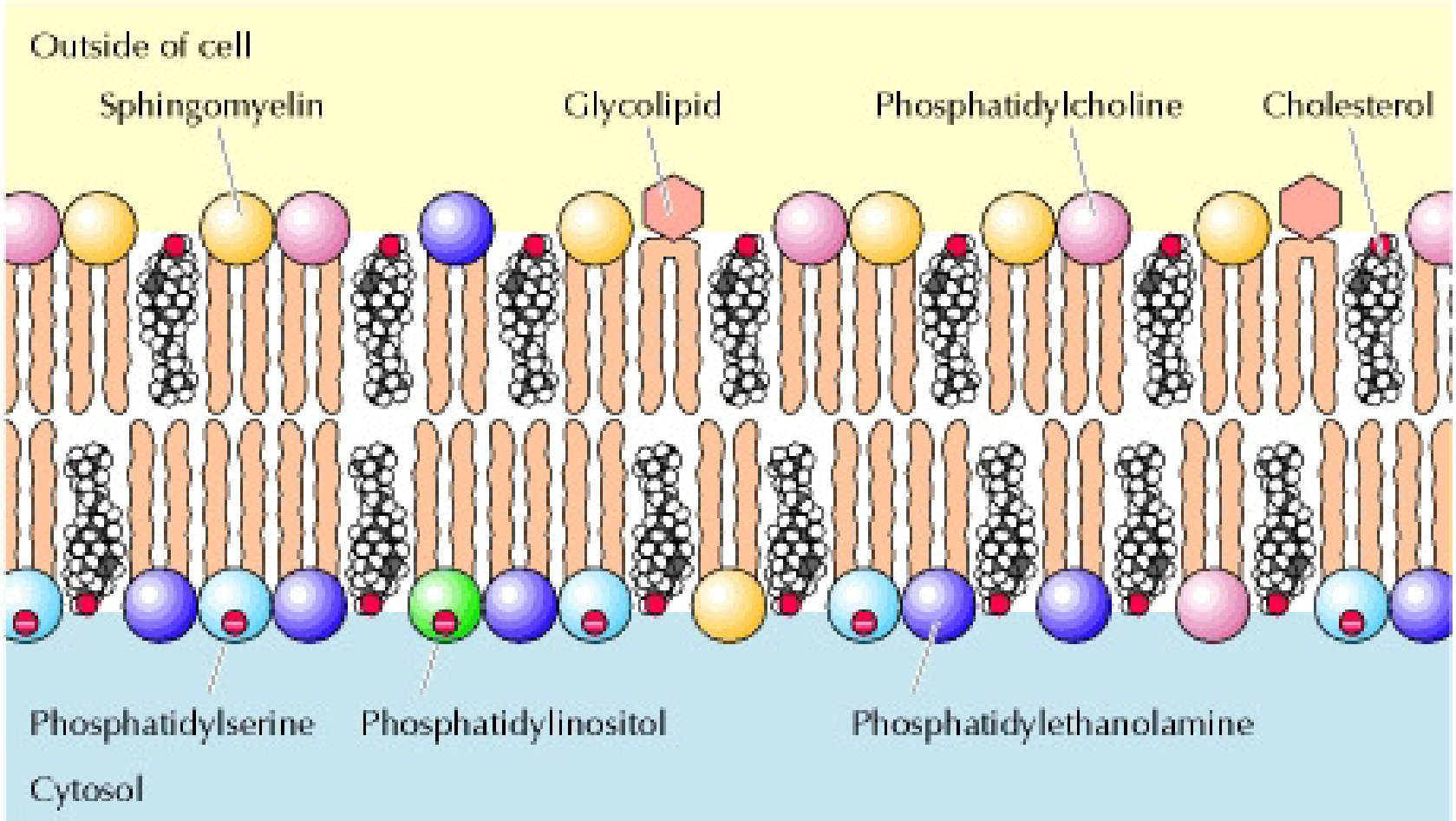
Plasma membranes of human cells contain four major phospholipids

1. Phosphatidylcholine,
2. Phosphatidylethanolamine
3. Phosphatidylserine,
4. Sphingomyelin

which together account for more than half of the lipid in most membranes.

The outer leaflet consists mainly of phosphatidylcholine, sphingomyelin and glycolipids

Where as phosphatidylethanolamine, phosphatidylserine and phosphatidylinositol are the predominant phospholipids of the inner leaflet.



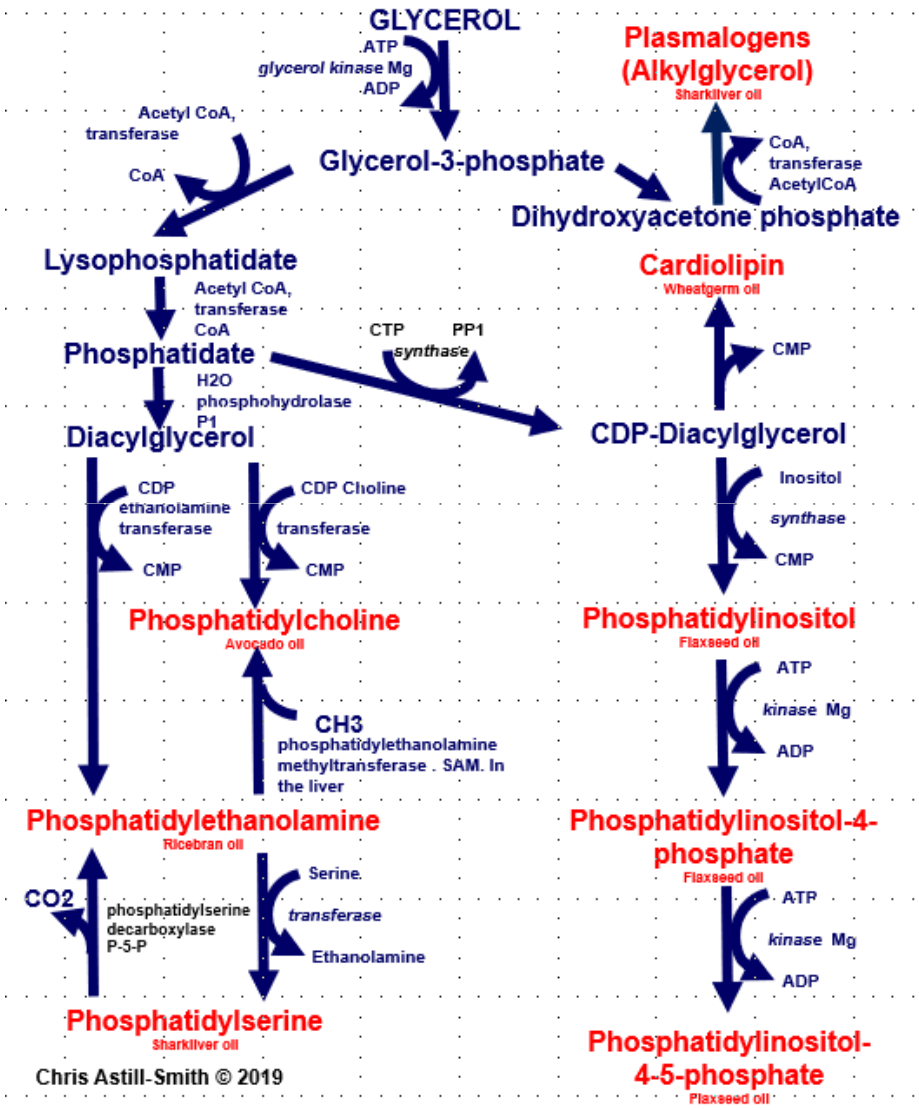
The outer leaflet consists predominantly of phosphatidylcholine, sphingomyelin, and glycolipids, whereas the inner leaflet contains phosphatidylethanolamine, phosphatidylserine, and phosphatidylinositol. Cholesterol is distributed in both leaflets.

In addition to the phospholipids, the plasma membranes of animal cellscontain glycolipids and cholesterol. The glycolipids are found exclusively in the outer leaflet of the plasma membrane, with their carbohydrate portions exposed on the cell surface.

They are relatively minor membrane components, constituting only about 2% of the lipids of most plasma membranes.

Cholesterol is a major membrane constituent of human cells, being present in about the same molar amounts as the phospholipids.

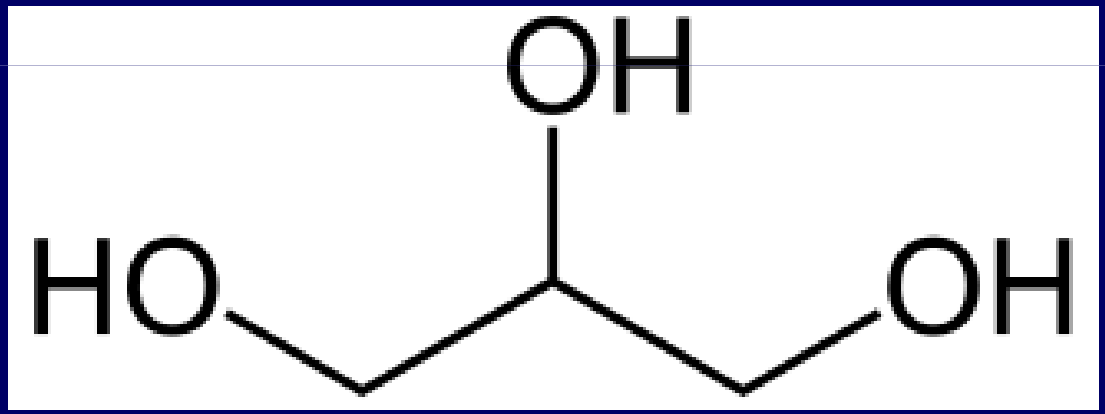
Phospholipid synthesis



Glycerol

Glycerol also called glycerine is a simple polyol compound. It is a colourless,odourless, viscous liquid that is sweet-tasting and non-toxic. The glycerol backbone is found in many lipids which are known as glycerides.

Glycerol has three hydroxyl groups that are responsible for its solubility in water and its hydroscopic nature.*



*Christoph, Ralf; Schmidt, Bernd; Steinberner, Udo; Dilla, Wolfgang; Karinen, Reetta (2006). "Glycerol". Ullmann's Encyclopedia of Industrial Chemistry. Ullmann's Encyclopedia of Industrial Chemistry.

Glycerol is a precursor for synthesis of triacylglycerols and of phospholipids in the liver and adipose tissue.

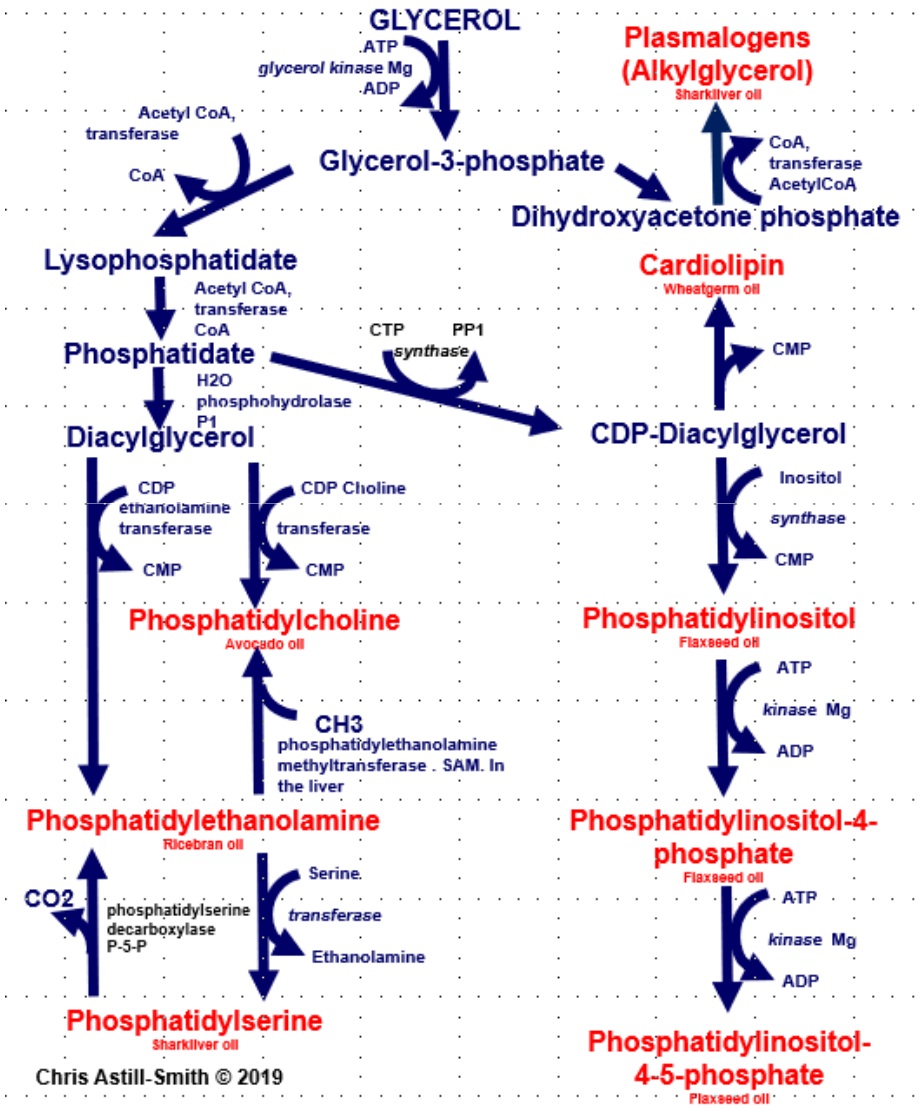
When the body uses stored fat as a source of energy, glycerol and fatty acids are released into the bloodstream.

Before glycerol can enter the pathwayof glycolysis or gluconeogenesis (depending on physiological conditions), it must be converted to the intermediate glyceraldehyde 3-phosphate.*

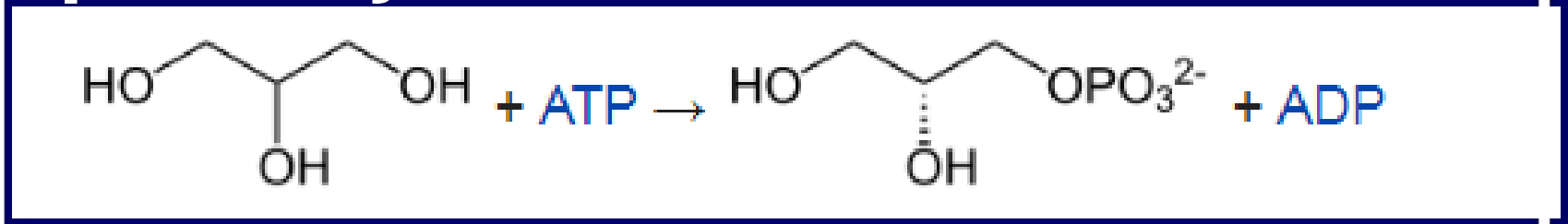
*Tildon, J. T.; Stevenson Jr, J. H.; Ozand, P. T. (1976). "Mitochondrial glycerol kinase activity in rat brain". *The Biochemical Journal*. 157 (2): 513–6.

Glycerol 3-phosphate

Phospholipid synthesis



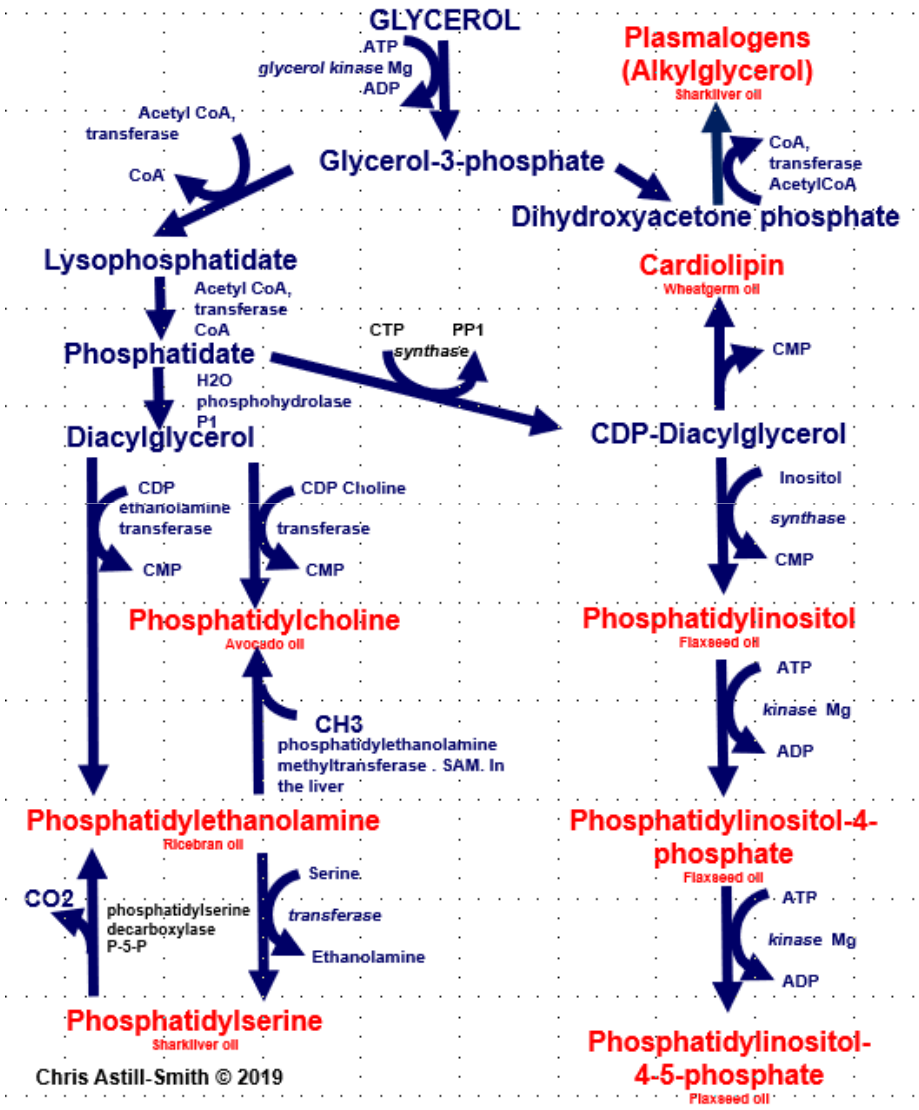
It is synthesized by **phosphorylating** glycerol generated upon hydrolyzing fats with glycerol kinase, and can feed into glycolysis or gluconeogenesis pathways.*



*G. P. Moss (ed.). "Nomenclature of Phosphorus-Containing Compounds of Biochemical Importance". Retrieved 2015-05-20.

Phosphatidic acid
(Phosphatidate)

Phospholipid synthesis



Phosphatidic acid consists of a glycerol backbone, with, in general, a saturated fatty acid bonded to carbon-1, an unsaturated fatty acid bonded to carbon-2, and a phosphate group bonded to carbon-3.*

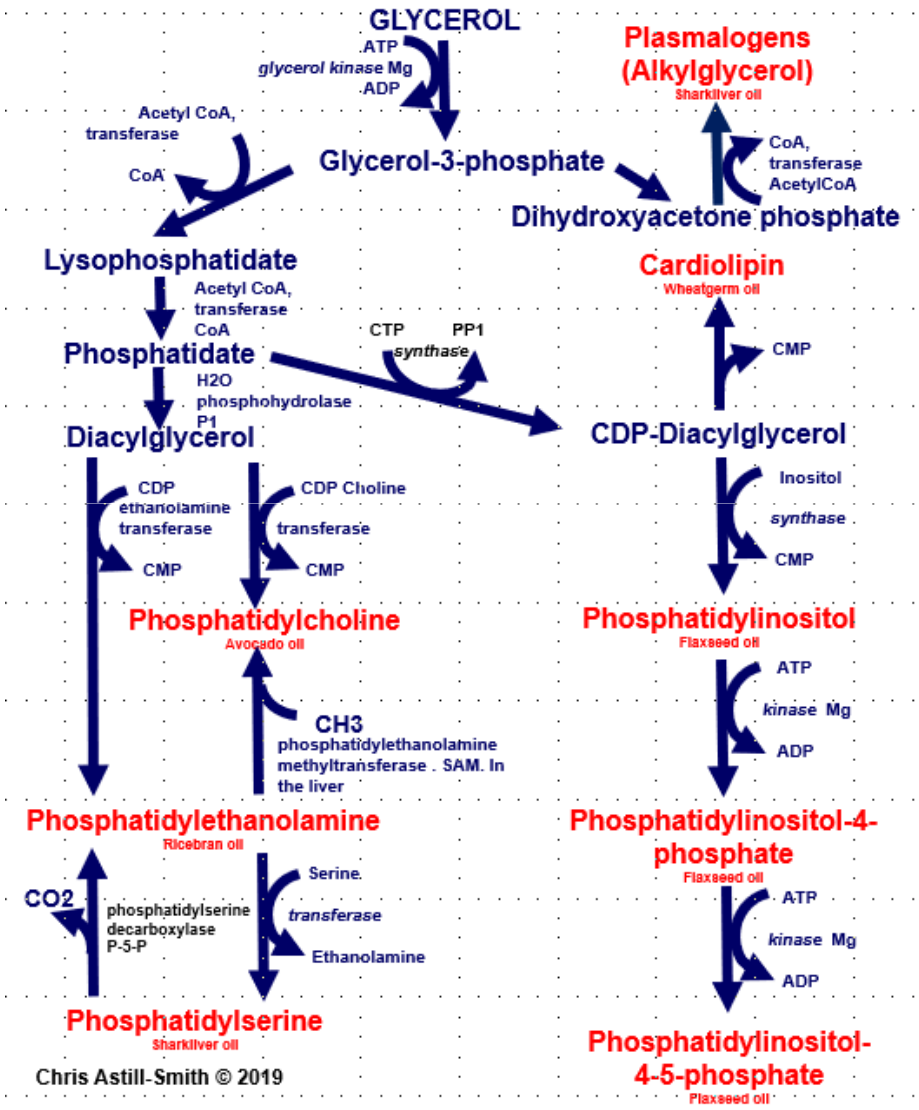
*William W. Christie (4/10/2009). "Phosphatidic Acid, Lysophosphatidic Acid and Related Lipids". Archived from the original on 23 October 2004.

They constitute about 0.25% of phospholipids in the bilayer.*

*William W. Christie (4/10/2009). "Phosphatidic Acid, Lysophosphatidic Acid and Related Lipids". Archived from the original on 23 October 2004.

Diacylglycerol

Phospholipid synthesis

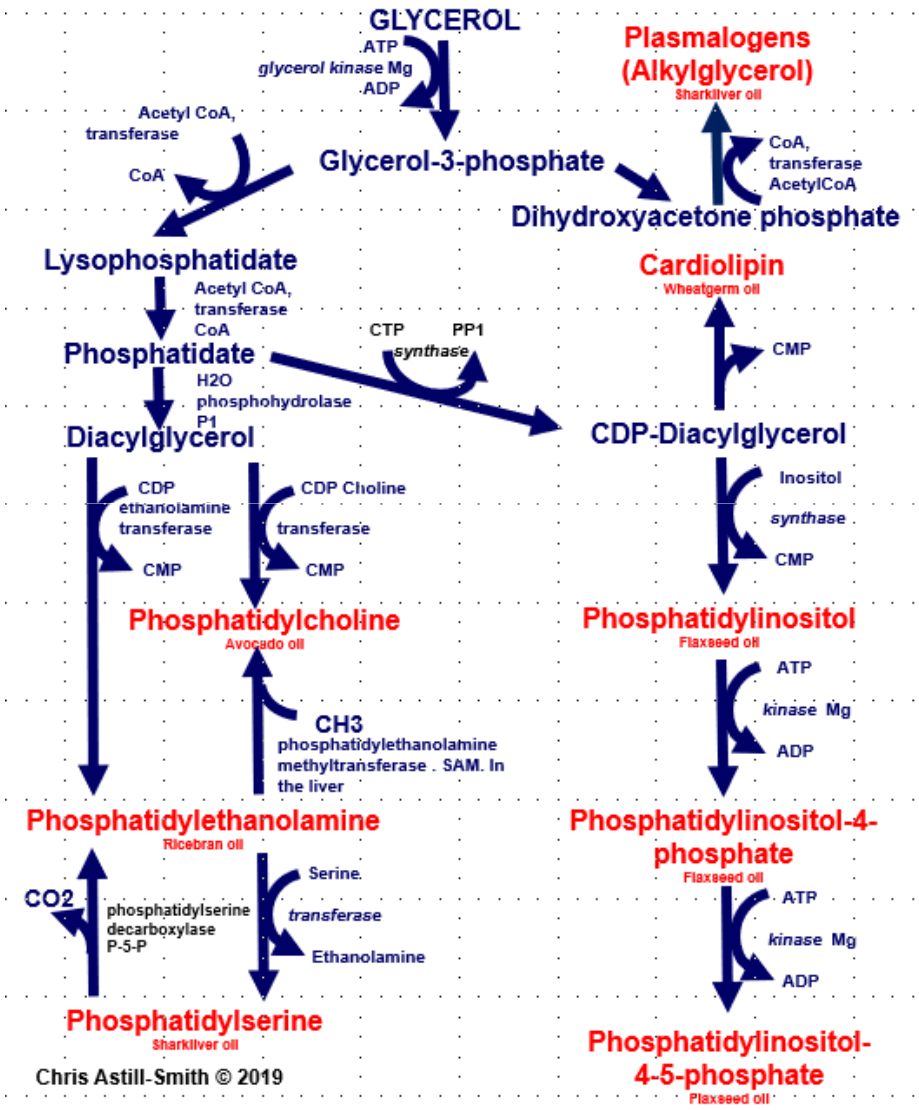


Diacylglycerol (DAG), is
a glyceride consisting of two fatty acid chains covalently bonded to a glycerol molecule
through ester linkages.*
It can act as surfactants and are commonly used as emulsifiers in processed foods.

*IUPAC, *Compendium of Chemical Terminology*, 2nd ed. (the "Gold Book") (1997). Online corrected version: (2006–) "glycerides"

Phosphatidylethanolamine

Phospholipid synthesis



Phosphatidylethanolamines are a class of phospholipids found in biological membranes.*
They are synthesized by the addition of cytidine diphosphate-ethanolamine to diglycerides, releasing cytidine monophosphate.

*Wellner, Niels; Diep, Thi Ai; Janfelt, Christian; Hansen, Harald Severin (2012). "N-acylation of phosphatidylethanolamine and its biological functions in mammals". *Biochimica et Biophysica Acta*. 1831 (3): 652–62.

***S*-Adenosyl Methionine (SAM)** can subsequently methylate the amine of phosphatidylethanolamines to yield phosphatidylcholines.
It can mainly be found in the inner (cytoplasmic) leaflet of the lipid bilayer.*

* Mishkind, Michael (2000). "Phosphatidylethanolamine – in a pinch". Trends in Cell Biology. 10 (9): 368.

Phosphatidylethanolamines are found in all living cells, composing 25% of all phospholipids. *

*Vance, Jean E.; Tasseva, Guergana (2012). "Formation and function of phosphatidylserine and phosphatidylethanolamine in mammalian cells". *Biochimica et Biophysica Acta*. 1831 (3): 543–54.

In human physiology, they are found particularly in nervous tissue such as the white matter of brain, nerves, neural tissue, and in spinal cord, where they make up 45% of all phospholipids.*

*Vance, Jean E.; Tasseva, Guergana (2012). "Formation and function of phosphatidylserine and phosphatidylethanolamine in mammalian cells". *Biochimica et Biophysica Acta*. 1831 (3): 543–54.

Functions

In membrane fusion.

Regulates membrane curvature.

Blood clotting.

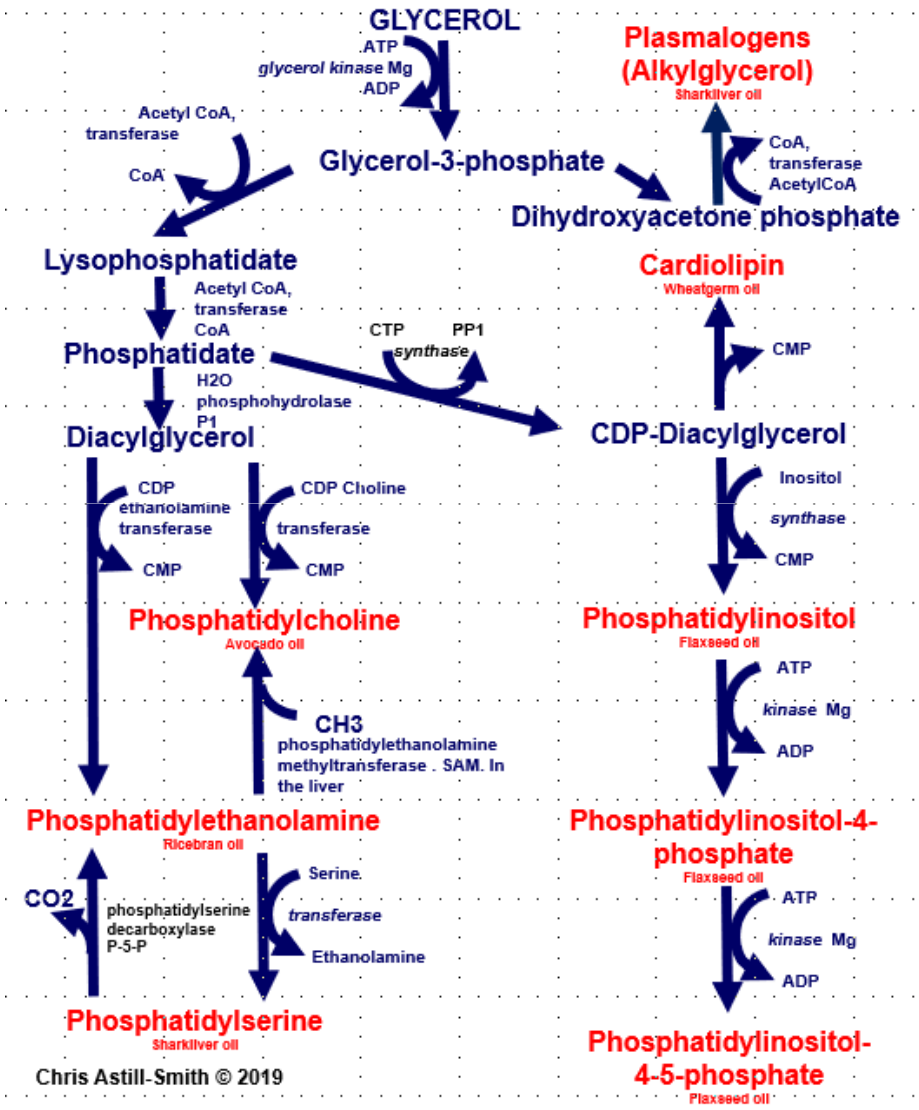
Secretion of lipoproteins in the liver.

Synthesis of
Phosphatidylethanolamine
through
the phosphatidylserine
decarboxylation pathway occurs
rapidly in the inner
mitochondrial membrane.

A lesser-known compound in fish, dimethylaminoethanol (DMAE), is increasingly favoured for its role in boosting brain power. DMAE has shown positive results in the treatment of a variety of cognitive and disruptive disorders, including attention-deficit hyperactivity disorder (ADHD) and memory lapses. DMAE is even being used in skin care products designed to treat sagging skin and age spots.

Phosphatidylserine

Phospholipid synthesis



Phosphatidylserine is a phospholipid and is a component of the cell membrane.
It plays a key role in cell cycle signalling, specifically in relation to apoptosis. *

*Meertens L, Carnec X, Lecoin MP, Ramdasi R, Guivel-Benhassine F, Lew E, Lemke G, Schwartz O, Amara A (October 2012). "The TIM and TAM families of phosphatidylserine receptors mediate dengue virus entry". *Cell Host & Microbe*. 12 (4): 544–57.

Phosphatidylserine coming from plants and phosphatidylserine coming from animals differ in fatty acid composition.*

*EFSA Panel on Dietetic Products, Nutrition and Allergies (2010-10-01). "Scientific Opinion on the substantiation of health claims related to phosphatidyl serine

Functions

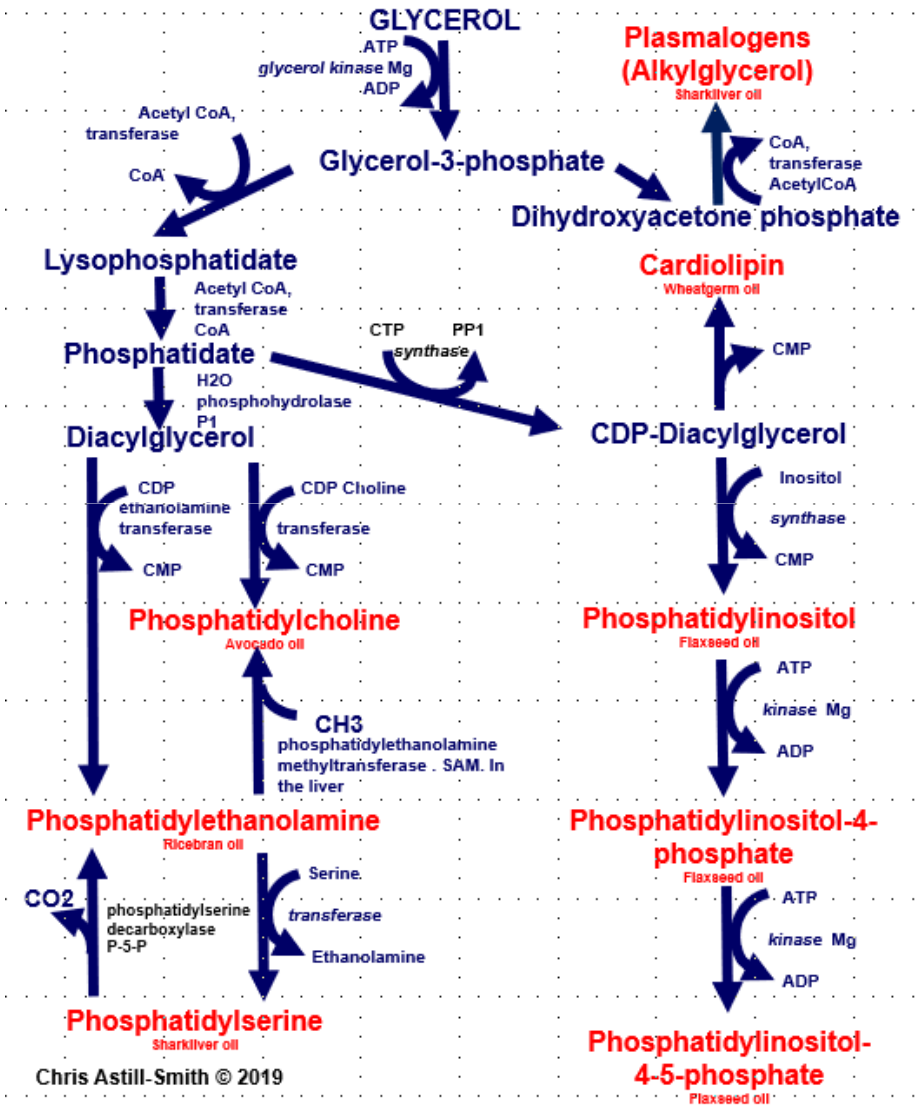
Cell signaling.

Coagulation.

Food	PS Content in mg/100 g
Bovine brain	713
Atlantic mackerel	480
Chicken heart	414
Atlantic herring	360
Eel	335
Offal (average value)	305
Pig's spleen	239
Pig's kidney	218
Tuna	194
Chicken leg, with skin, without bone	134

Phosphatidylcholine

Phospholipid synthesis



Phosphatidylcholines (PC) are a class of phospholipids that incorporate choline as a headgroup. They are a major component of biological membranes and can be easily obtained from a variety of readily available sources, such as egg yolk, sunflower seeds or soybeans.

Phosphatidylcholine is a major constituent of cell membranes and pulmonary surfactant, and is more commonly found in the outer leaflet of a cell membrane. It plays a role in membrane-mediated cell signaling.*

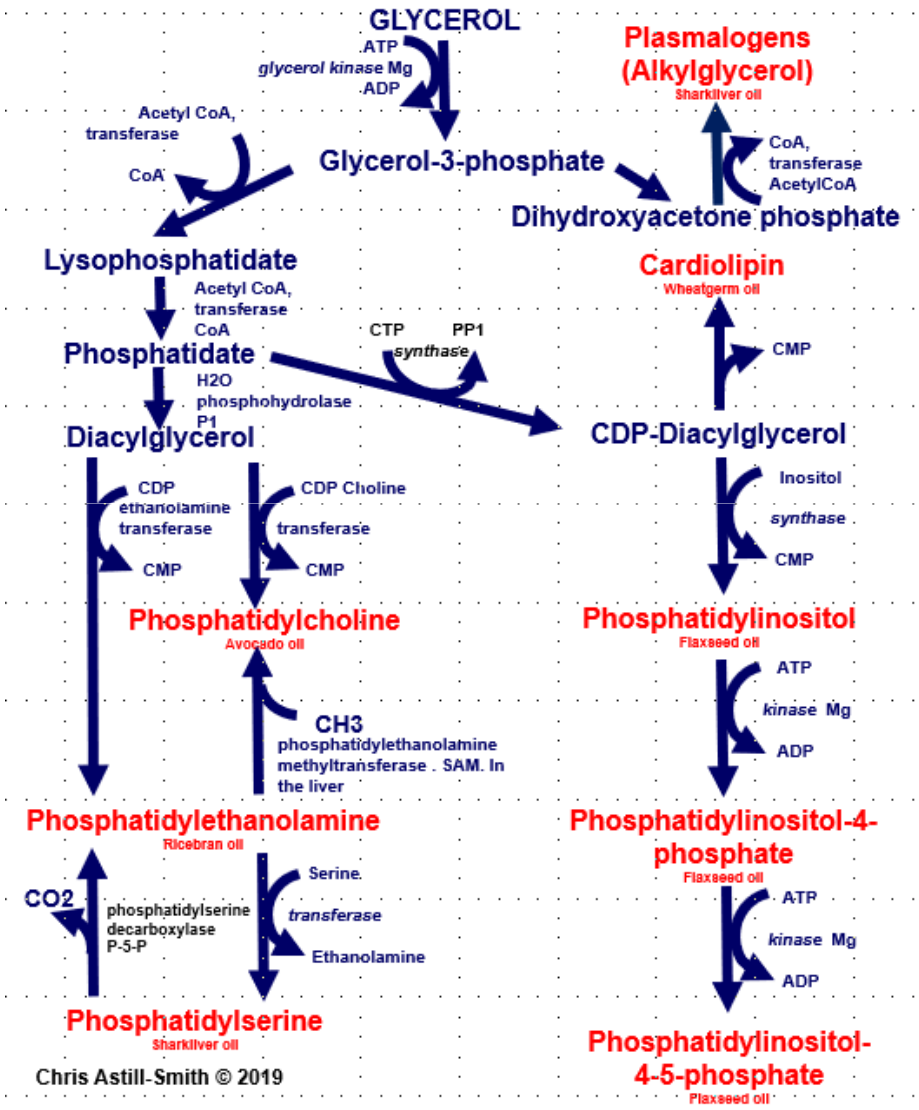
*Kanno K, Wu MK, Agate DS, Fanelli BJ, Wagle N, Scapa EF, Ukomadu C, Cohen DE (October 2007). "Interacting proteins dictate function of the minimal START domain phosphatidylcholine transfer protein/StarD2". *The Journal of Biological Chemistry*. 282

Treatment of ulcerative colitis with oral intake of phosphatidylcholine has been shown to result in decreased disease activity.*

*Kokkinidis DG, Bosdelekidou EE, Iliopoulou SM, Tassos AG, Texakalidis PT, Economopoulos KP, Kousoulis AA (September 2017). "Emerging treatments for ulcerative colitis: a systematic review". *Scandinavian Journal of Gastroenterology*. 52 (9): 923–931.

Phosphatidylinositol

Phospholipid synthesis



Phosphatidylinositol consists of a class of
the phosphatidylglycerides.

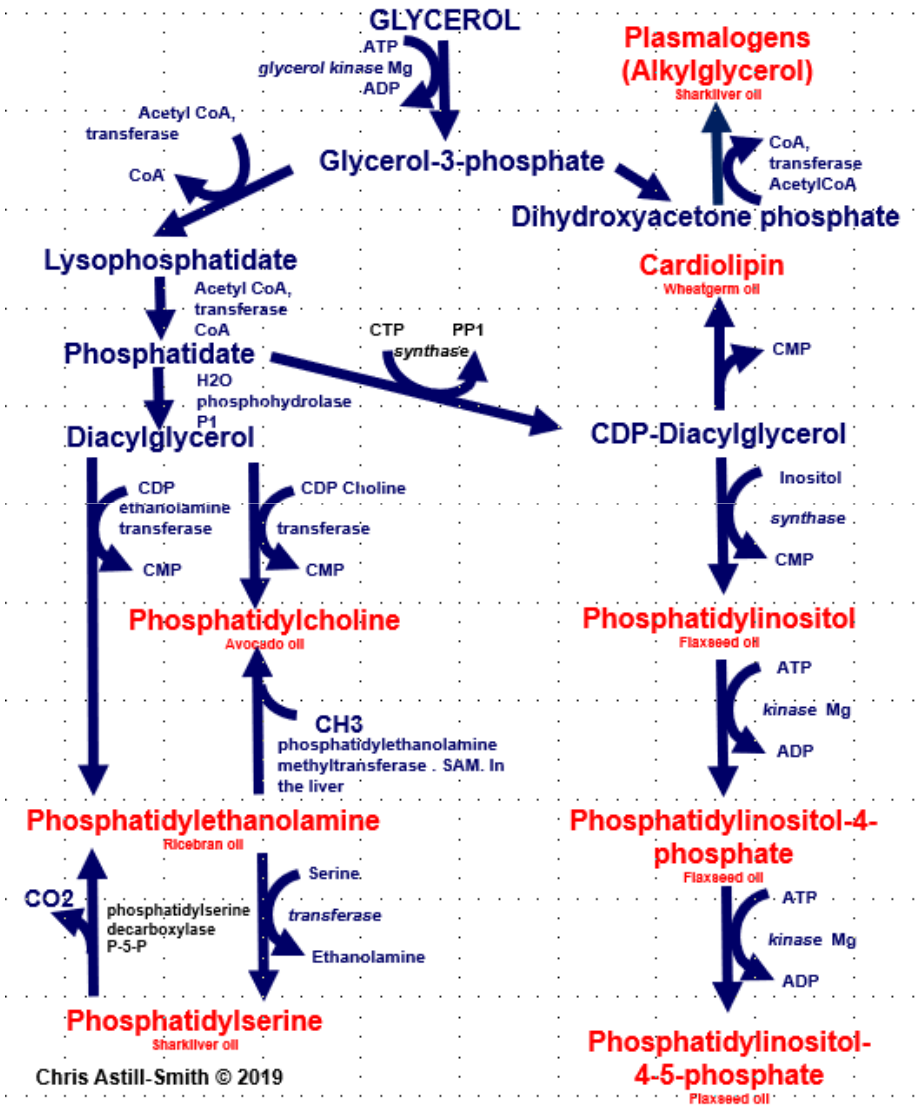
Typically phosphatidylinositols form a minor component on the cytosolic side of cell membranes.

The phosphatidylinositol can be phosphorylated to form phosphatidylinositol 4-phosphate, phosphatidylinositol 4,5-phosphate and phosphatidylinositol 3,4,5-phosphate.
All are involved with cell signaling.*

*Whitman M, Downes CP, Keeler M, Keller T, Cantley L (April 1988). "Type I phosphatidylinositol kinase makes a novel inositol phospholipid, phosphatidylinositol-3-phosphate". *Nature*. 332

Alkylglycerol (Plasmalogens)

Phospholipid synthesis



The C-1 position is typically derived from C16:0, C18:0, or C18:1 fatty alcohols while the C-2 position is most commonly occupied by polyunsaturated fatty acids. The most common head groups present in plasmalogens are ethanolamine or choline.

Found particularly in the nervous, immune, and cardiovascular system.*

In human heart tissue, nearly 30–40% of choline glycerophospholipids are plasmalogens.

*Nagan, N.; Zoeller, R. A. (2001). "Plasmalogens: Biosynthesis and functions". *Progress in Lipid Research*. 40 (3): 199–229.

Even more striking is the fact that 32% of the glycerophospholipids in the adult human heart and 20% in brain and up to 70% of myelin sheath ethanolamine glycerophospholipids are plasmalogens.*

*Farooqui, A. A.; Horrocks, L. A. (2001). "Plasmalogens: Workhorse lipids of membranes in normal and injured neurons and glia". The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry. 7 (3): 232–245.

They can protect mammalian cells against the damaging effects of reactive oxygen species.*

In addition, they have been implicated as being signaling molecules and modulators of membrane dynamics.

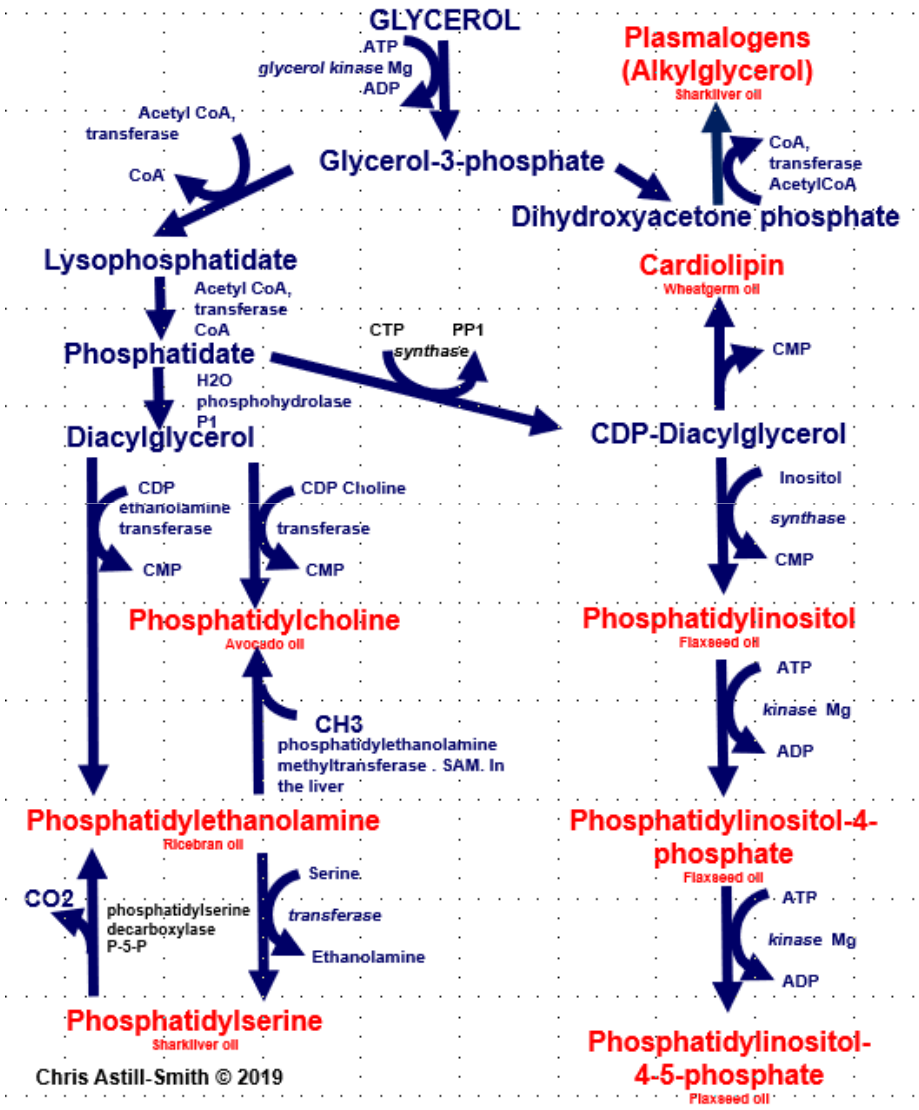
*Gorgas, K.; Teigler, A.; Komljenovic, D.; Just, W. W. (2006). "The ether lipid-deficient mouse: Tracking down plasmalogen functions". *Biochimica et Biophysica Acta (BBA) - Molecular Cell Research*. 1763 (12): 1511–1526.

There is some evidence that there are reduced levels of plasmalogens in the brain in neurodegenerative disorders including Alzheimer disease, Parkinson's disease, Down syndrome, and multiple sclerosis.*

*Braverman, NE; Moser, AB (September 2012). "Functions of plasmalogen lipids in health and disease". *Biochimica et Biophysica Acta*. 1822 (9): 1442–52.

Cardiolipin

Phospholipid synthesis



Cardiolipin is an important component of the inner mitochondrial membrane, where it constitutes about 20% of the total lipid composition. The name 'cardiolipin' is derived from the fact that it was first found in animal hearts.*

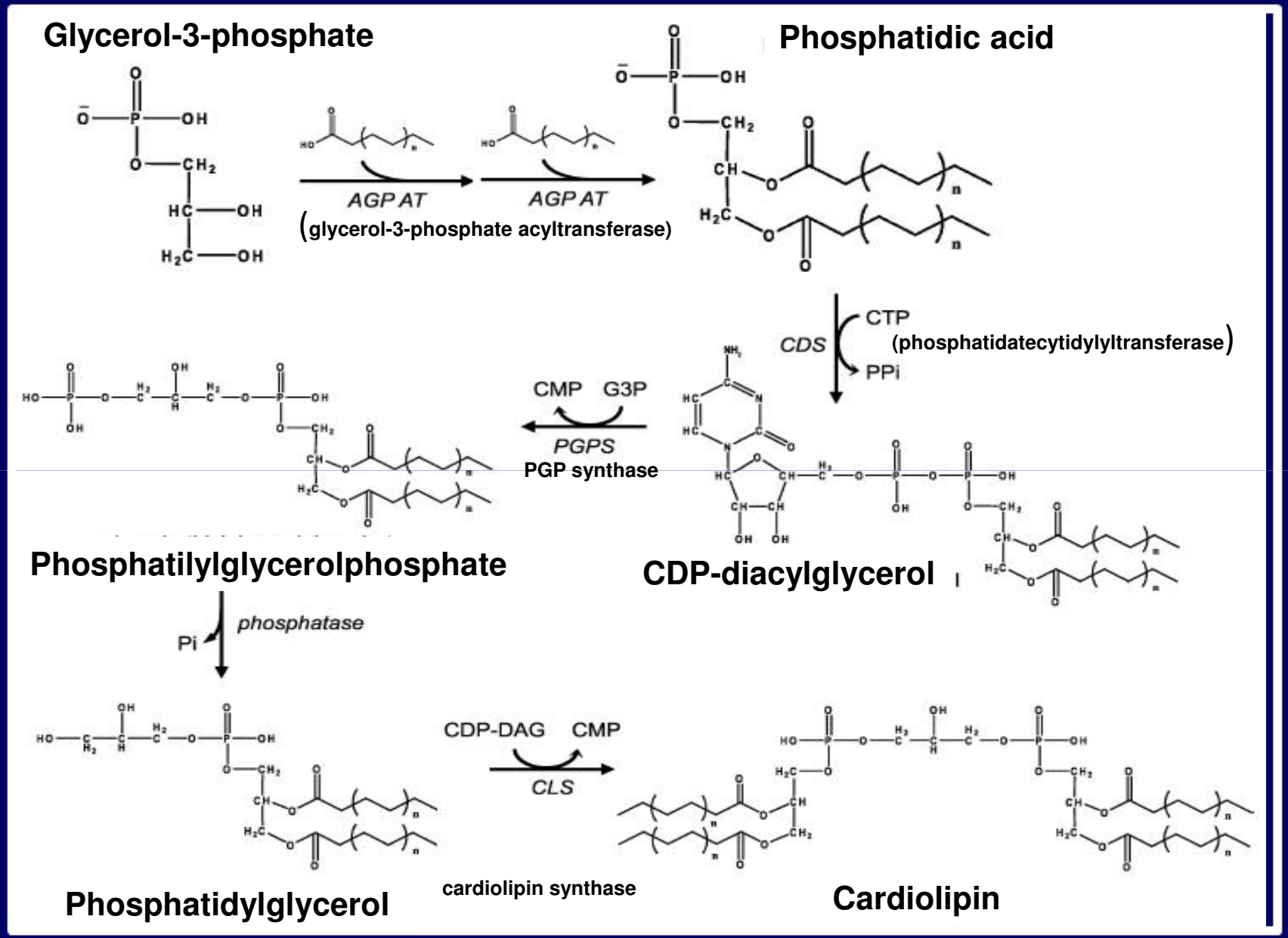
*Pangborn M. (1942). "Isolation and purification of a serologically active phospholipid from beef heart". J. Biol. Chem. 143: 247–256

In mammalian cells cardiolipin (CL) is found almost exclusively in the inner mitochondrial membrane where it is essential for the optimal function of numerous enzymes that are involved in mitochondrial energy metabolism.

*Pangborn M. (1942). "Isolation and purification of a serologically active phospholipid from beef heart". J. Biol. Chem. 143: 247–256

Cardiolipin (CL) is a kind of diphosphatidylglycerol lipid. Two phosphatidic acid moieties connect with a glycerol backbone in the centre to form a dimeric structure.

*Pangborn M. (1942). "Isolation and purification of a serologically active phospholipid from beef heart". J. Biol. Chem. 143: 247–256


Glycerol-3-phosphate
Phosphatidic acid
AGPAT
AGPAT
(glycerol-3-phosphate acyltransferase)
CTP
CDS
(phosphatidatecytidylyltransferase)
PPi
CMP
G3P
PGPS
PGP synthase
Phosphatilylglycerolphosphate
CDP-diacylglycerol
Pi
phosphatase
CDP-DAG
CMP
CLS
cardiolipin synthase
Phosphatidylglycerol
Cardiolipin

Source	Molecular species				
	Fatty acid R1	Fatty acid R2	Fatty acid R3	Fatty acid R4	Amount (Mol%)
Linoleic 18:2 **a-Linolenic 18:3** Bovine heart	18:2	18:2	18:2	18:2	48
	18:3	18:2	18:2	18:2	21
	18:2	18:3	18:2	18:2	
	18:2	18:2	18:2	18:3	
	18:2	18:2	18:3	18:2	
	18:2	18:1	18:2	18:2	15
	18:2	18:2	18:2	18:1	
Rat liver	18:2	18:2	18:2	18:2	57
	18:2	18:1	18:2	18:2	35
	18:2	18:2	18:2	18:1	

Functions

1. Regulates aggregate structures and membrane fusion.*

* Antonio Ortiz; J. Antoinette Killian; Arie J. Verkleij; Jan Wilschut (1999). "Membrane fusion and the lamellar-to-inverted-hexagonal phase transition in cardiolipin vesicle systems induced by divalent cations". *Biophysical Journal*. 77 (4): 2003–2014.

2. Complex IV has been shown to require two associated cardiolipin molecules in order to maintain its full enzymatic function. Complex III also needs cardiolipin to maintain its quaternary structure and functional role.*

*Baltazar Gomez Jr.; Neal C. Robinson (1999). "Phospholipase Digestion of Bound Cardiolipin Reversibly Inactivates Bovine Cytochrome bc1". *Biochemistry*. 38 (28): 9031–9038.

3. Triggers apoptosis. Cardiolipin distribution to the outer mitochondrial membrane would lead to apoptosis of the cells, as evidenced by cytochrome c release.*

*Paradies, G; Petrosillo, G; Paradies, V; Ruggiero, FM (2009). "Role of cardiolipin peroxidation and Ca2+ in mitochondrial dysfunction and disease". *Cell Calcium*. 45 (6): 643–650.

4. Cardiolipin is suggested to function as a proton trap within the mitochondrial membranes.*

*Thomas H. Haines; Norbert A. Dencher (2002). "Cardiolipin: a proton trap for oxidative phosphorylation". FEBS Lett. 528 (1–3): 35–39.

Other functions

Cholesterol translocation from outer to the inner membrane of mitochondrial.

Activates mitochondrial cholesterol side-chain cleavage.

Import protein into mitochondrial matrix.

Anticoagulant function.

Other functions

Anticoagulant function.

Modulates α-synuclein - malfunction of this process is thought to be a cause of Parkinson's disease.*

*Ryan, Tammy; Bamm, Vladimir V.; Stykel, Morgan G.; Coackley, Carla L.; Humphries, Kayla M.; Jamieson-Williams, Rhiannon; Ambasudhan, Rajesh; Mosser, Dick D.; Lipton, Stuart A. (2018-02-26). "Cardiolipin exposure on the outer mitochondrial membrane modulates α-synuclein". *Nature Communications*. 9 (1): 817.

Parkinson's disease and Alzheimer's disease.

Oxidative stress and lipid peroxidation are believed to be contributing factors leading to neuronal loss and mitochondrial dysfunction in the substantia nigra in Parkinson's disease, and may play an early role in the pathogenesis of Alzheimer's.

It is reported that cardiolipin content in the brain decreases with aging, and a recent study on rat brain shows it results from lipid peroxidation in mitochondria exposed to free radical stress.*

Note WGO a high source of cardiolipin and Vit E.

*Ruggiero FM, Cafagna F, Petruzzella V, Gadaleta MN, Quagliariello E (1991). "Lipid composition in synaptic and nonsynaptic mitochondria from rat brains and effect of aging". *J Neurochem*. 59 (2): 487–491.

Another study shows that the cardiolipin biosynthesis pathway may be selectively impaired, causing 20% reduction and composition change of the cardiolipin content. *

*Ellis CE, Murphy EJ, Mitchell DC, Golovko MY, Scaglia F, Barcelo-Coblijn GC, Nussbaum RL (2005). "Mitochondrial Lipid Abnormality and Electron Transport Chain Impairment in Mice Lacking α-Synuclein". *Mol Cell Biol*. 25 (22): 10190–10201.

It's also associated with a 15% reduction in linked complex I-III activity of the electron transport chain, which is thought to be a critical factor in the development of Parkinson's disease.* Importance of supplementing with CoQ10.

*Dawson TM, Dawson VL (2003). "Molecular pathways of neurodegeneration in Parkinson's disease". *Science*. 302 (5646): 819–822

Sphingosine

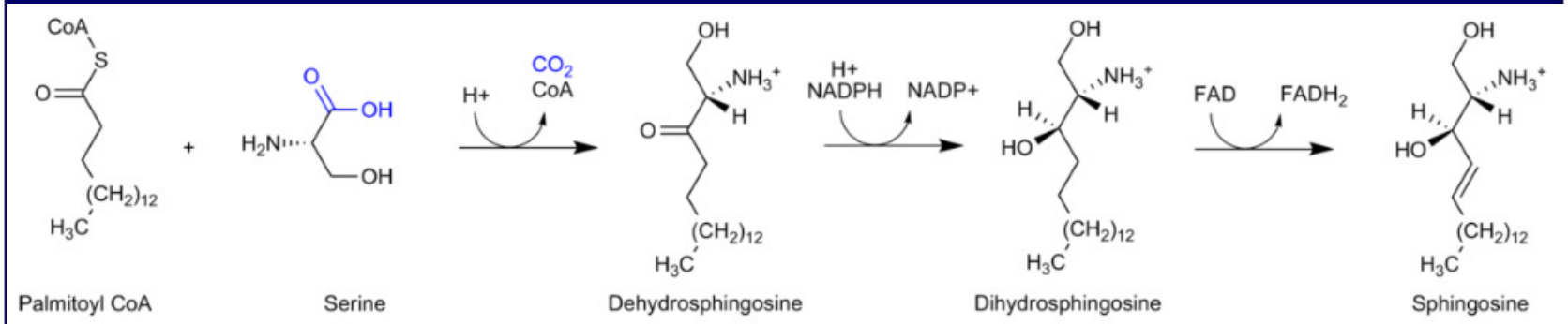
Sphingosine is an 18-carbon amino alcohol with an unsaturated hydrocarbon chain, which forms a primary part of sphingolipids, a class of cell membrane lipids that include sphingomyelin, an important phospholipid..

Sphingosine can be phosphorylated in vivo via two kinases, sphingosine kinase type 1 (392nm 17q) and sphingosine kinase type 2 (395nm 19q). This leads to the formation of sphingosine-1-phosphate, a potent signaling lipid.

Sphingolipid metabolites, such as ceramides, sphingosine and sphingosine-1-phosphate, are lipid signaling molecules involved in diverse cellular processes.

Sphingosine is synthesized from palmitoyl CoA and serine in a condensation required to yield dehydrosphingosine.

Dehydrosphingosine is then reduced by NADPH to dihydrosphingosine (sphinganine), and finally oxidized by FAD to sphingosine.*

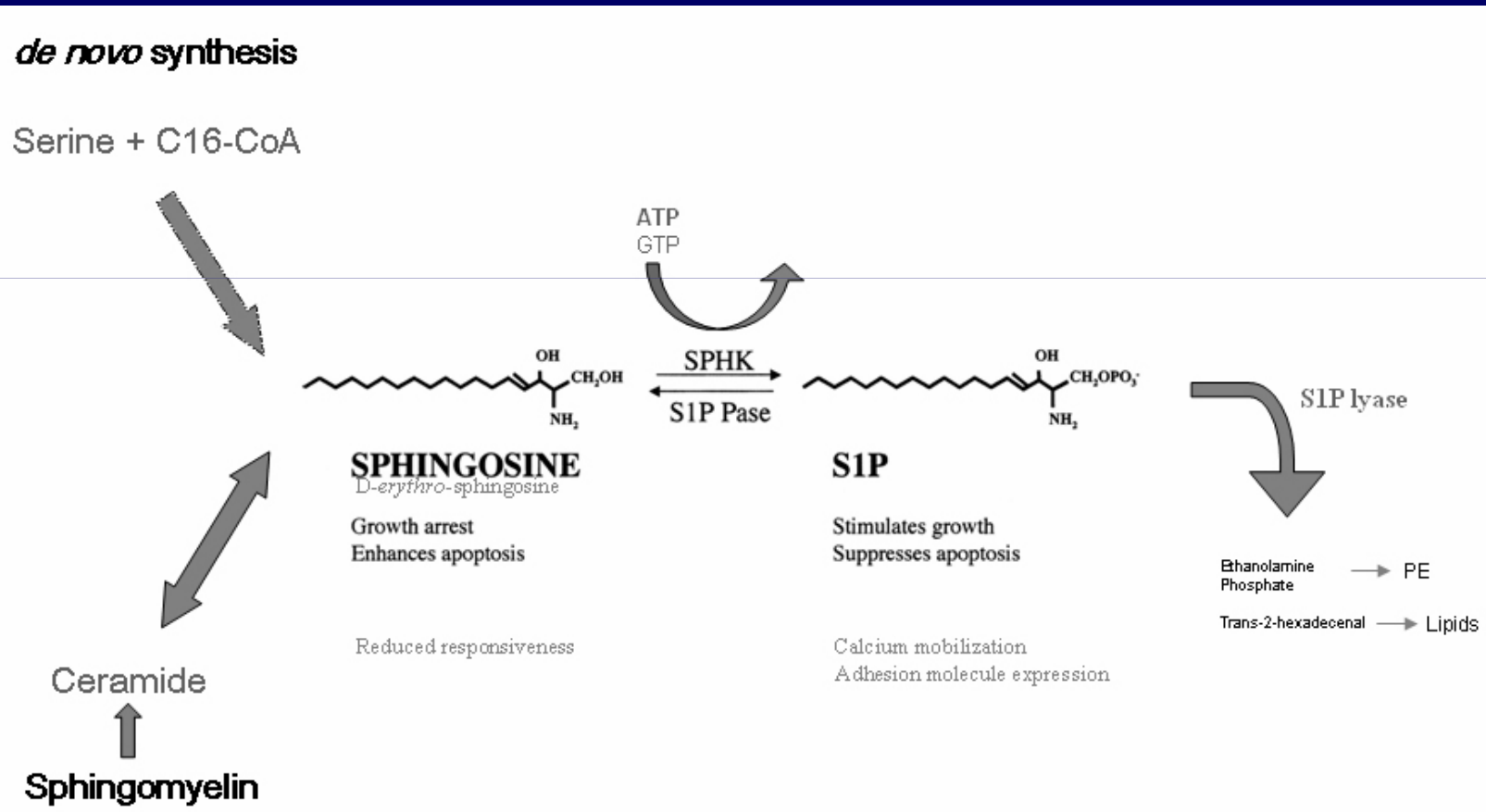


*Carter, H. E., F. J. Glick, W. P. Norris, and G. E. Phillips. 1947. Biochemistry of the sphingolipides. III. Structure of sphingosine. J. Biol. Chem. 170: 285–295

Sphingosine-1-phosphate (S1P) is a signaling sphingolipid, also known as lysosphingolipid. It is also referred to as a bioactive lipid mediator.

Sphingosine can be released from ceramides, a process catalyzed by the enzyme ceramidase.

Phosphorylation of sphingosine is catalyzed by sphingosine kinase.



S1P can be dephosphorylated to sphingosine by sphingosine phosphatases and can be irreversibly degraded by an enzyme, sphingosine phosphate lyase.

Ceramides

Ceramides are a family of waxy lipid molecules. A ceramide is composed of sphingosine and a fatty acid. Ceramides are found in high concentrations within the cell membranes, since they are component lipids that make up sphingomyelin, one of the major lipids in the lipid bilayer.

Ceramide has been implicated in a variety of physiological functions including apoptosis, cell growth arrest, differentiation, cell senescence, cell migration and adhesion.*

*Hannun, Y.A.; Obeid, L.M. (2008). "Principles of bioactive lipid signalling: lessons from sphingolipids". Nature Reviews Molecular Cell Biology. 9 (2): 139–150

Roles for ceramide and its downstream metabolites have also been suggested in a number of pathological states including cancer, neuro-degeneration, diabetes, microbial pathogenesis, obesity, and inflammation.*

*Zeidan, Y.H.; Hannun, Y.A. (2007). "Translational aspects of sphingolipid metabolism". *Trends Mol. Med.* 13 (8): 327–336.

Ceramides induce skeletal muscle insulin resistance when synthesized as a result of saturated fat activation. In mitochondria, ceramide suppresses the electron transport chain and induces production of reactive oxygen species.*

*Kogot-Levin A, Saada A (2014). "Ceramide and the mitochondrial respiratory chain". *Biochimie*. 100: 88–94.

Increased ceramide synthesis leads to both leptin resistance and insulin resistance.*

Ceramide generation is induced by

Heat, Homocysteine, ROS, Ionizing radiation, Cannabinoids, 1, 25 OH Vit D3

*Febbraio, Mark (2014). "Role of interleukins in obesity:implications for metabolic disease". *Trends in Endocrinology and Metabolism*. 25(6): 312–319.

Gangliosides

GLYCOSPHINGOLIPIDS

Ceramide

UDPGlucose

UDP

Glucosyl cerebroside

Different saccharides

Gangliosides

Ceramide

UDPGalactose

UDP

Galactosyl cerebroside

¼ of all myelin

PAPs

Sulfatides

rich in myelin

Gangliosides

The fatty acid maybe Palmitic, Stearic, Behenic or Lignoceric acids or a monounsaturated fatty acid such as Nervonic acid

Ganglioside GM3	Ganglioside GM2	Ganglioside GM1
Sphingosine +	Sphingosine +	Sphingosine +
Fatty acid +	Fatty acid +	Fatty acid +
Glucose +	Glucose +	Glucose +
Galactose+	Galactose+	Galactose+
N.A.Neuraminic	N.A.Neuraminic +	N.A.Neuraminic +
	N.A.Galactosamine	N.A.Galactosamine +Galactose

Saccharides are attached by UDP and CMP carriers

The level of gangliosides in myelin is low but Ganglioside GM1 prevails. Specific binding has been proven for many kinds of gangliosides. When administered parenterally, gangliosides:

1. Circulate in the bloodstream continuously.
2. Do not express toxicity.
3. Pass through blood-brain barrier.
4. Incorporate themselves into neuronal membranes.

Ganglioside GM1

1. Restores dopaminergic neurons after damage to nigro-striatal system, enhances uptake of dopamine and activity of tyrosine hydroxylase.

2. Restores cholinergic neurons after damage to the hippocampus, enhances activity of choline acetyl transferase and acetylcholinesterase.

3. Restores high-affinity uptake of choline in the cortex after injuries of the forebrain.
4. Protects serotonin and noradrenergic neurons from neurotoxin-induced degeneration.
5. Diminishes cerebral oedema and restores ionic balance after cerebral traumas.

6. Stimulates regeneration of the optic nerve.
7. Possibly restores melatonin uptake.

Sphingomyelin

Sphingomyelin is a type of sphingolipid found in cell membranes, especially in the membranous myelin sheath that surrounds some nerve cell axons. Role in signal transduction, cell apoptosis and formation of lipid rafts in the membranes.*

* Li, Z; Zhang, H; Liu, J; Liang, CP; Li, Y; Li, Y; Teitelman, G; Beyer, T; Bui, HH; Peake, DA; Zhang, Y; Sanders, PE; Kuo, MS; Park, TS; Cao, G; Jiang, XC (October 2011). "Reducing plasma membrane sphingomyelin increases insulin sensitivity". Molecular and Cellular Biology. 31 (20): 4205–18.

It usually consists of phosphocholine and ceramide, or a phosphoethanolamine head group; therefore, sphingomyelins can also be classified as sphingophospholipids.*

*Donald J. Voet; Judith G. Voet; Charlotte W. Pratt (2008). "Lipids, Bilayers and Membranes". *Principles of Biochemistry, Third edition*. Wiley. p. 252.

The composition allows sphingomyelin to play significant roles in signaling pathways: the degradation and synthesis of sphingomyelin produce important second messengers for signal transduction.

As a result of the autoimmune disease multiple sclerosis (MS), the myelin sheath of neuronal cells in the brain and spinal cord is degraded, resulting in loss of signal transduction capability. MS patients exhibit upregulation of certain cytokines in the cerebrospinal fluid, particularly TNFa.

This activates sphingomyelinase, an enzyme that catalyzes the hydrolysis of sphingomyelin to ceramide; sphingomyelinase activity has been observed in conjunction with cellular apoptosis.*

Hednce need for MS patients to take anti inflammatory nutrients.

*Jana, A; Pahan, K (December 2010). "Sphingolipids in multiple sclerosis". *Neuromolecular Medicine*. 12 (4): 351–61.

Sulfatides

Sulfatide, also known as sulfated galactocerebroside, is a class of sulfolipids, specifically a class of sulfoglycolipids, which are glycolipids that contain a sulfate group.* Of all of the galactolipids that are found in the myelin sheath, one fifth of them are sulfatide.

*Eckhardt, Matthias (June 2008). "The Role and Metabolism of Sulfatide in the Nervous System". *Molecular Neurobiology*. 37 (2–3): 93–103.

Sulfatide is primarily found on the extracellular leaflet of the myelin plasma membrane produced by the oligodendrocytes in the central nervous system and in the Schwann cells in the peripheral nervous system.

Aside from being a membrane component, sulfatide functions in protein trafficking, cell aggregation and adhesion, neural plasticity, memory, and glial-axon interactions.*

*Xiao, S; Finkielstein, CV; Capelluto, DG (2013). The enigmatic role of sulfatides: new insights into cellular functions and mechanisms of protein recognition. Advances in Experimental Medicine and Biology. 991. pp. 27–40.

Sulfatide also plays a role in several physiological processes and systems, including the nervous system, the immune system, insulin secretion, blood clotting, viral infection, and bacterial infection.

As a result, sulfatide is associated with, able to bind to, and/or is present
in kidney tissues, cancer cells tissues, the surface of red blood cells and platelets, CD1 a-d cells in the immune system,
many bacteria cells,
several viruses, myelin, neurons, and astrocytes.

In Alzheimer's disease, sulfatide in the brain tissue decreases tremendously, starting in the early stages of the disease. In the mild stages of Alzheimer's disease, the loss of sulfatide can be up to 50% in the white matter and up to 90% in the grey matter in the brain.*

*Han, x. (2010). "The Pathogenic Implication of Abnormal Interaction Between Apolipoprotein E Isoforms, Amyloid-beta Peptides, and Sulfatides in Alzheimer's Disease". Molecular Neurobiology. 41 (2–3): 97–106.

Vitamin K has been found to be associated with sulfatide. Not only in animals, but also in bacteria, vitamin K has been observed to influence sulfatide concentrations in the brain.*

*Tsaioun, k. (1999). "Vitamin K-dependent Proteins in the Developing and Aging Nervous System". Nutrition Reviews. 57 (8): 231–240

Vitamin K in the nervous system is responsible for the activation of enzymes that are essential for the biosynthesis of brain phospholipids, such as sulfatide.*

*Tsaioun, k. (1999). "Vitamin K-dependent Proteins in the Developing and Aging Nervous System". Nutrition Reviews. 57 (8): 231–240

Neuronal cell membranes

Glial cells – the C1 position is taken by a saturated fatty acid and C2 by an unsaturated fatty acid

Neurones – in many neurones the C1 position is taken by Arachidonic acid and C2 by DHA.

Retina – both C1 and C2 positions are taken by DHA.

Neuronal cell membranes

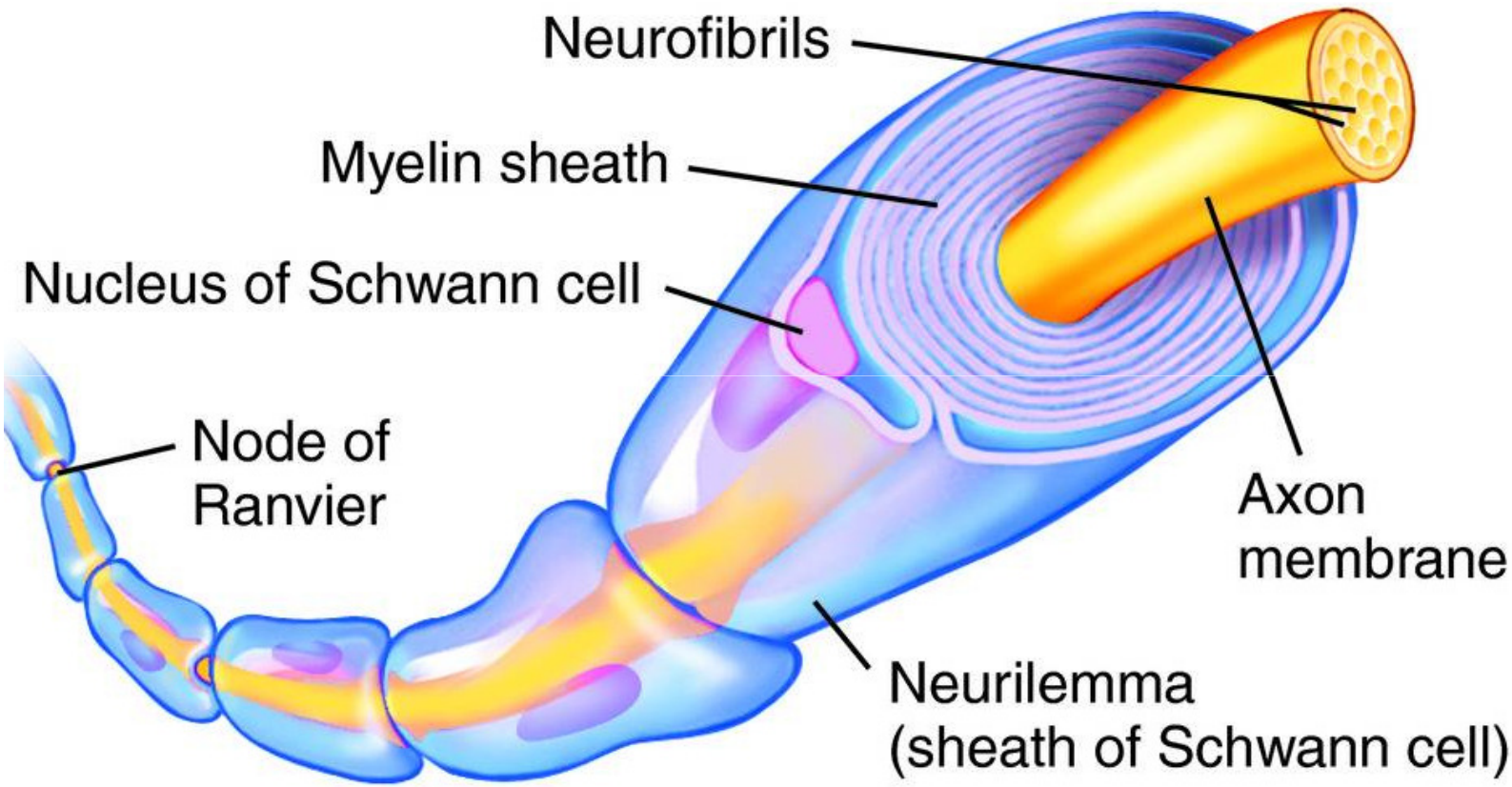
Phospholipids
- Phosphatidyl Choline
- Phosphatidyl Ethanolamine
- Phosphatidyl Serine
- Phosphatidyl Inositol
- Phosphatidyl Inositol 4.5 Diphosphate
- Plasmalogen

Sphinglomyelin

Cerebrosides

Ganglioside GM1

Cholesterol 25% of total brain lipid


Neurofibrils
Myelin sheath
Nucleus of Schwann cell
Node of
Ranvier
Axon
membrane
Neurilemma
(sheath of Schwann cell)

Structure of Myelin

A kind of glial cell, the **oligodendrocyte**, has extensions from its cell body, which wrap around the axons (outgoing cell processes) of the neurons to protect and insulate the electric currents that travel through them.

The wrapping is called the "myelin sheath". Myelin is produced by these cells and is structured like rolls of concentric layering of cell membrane tissues around the myelinated nerves. There are some glial cell bodies visible between the layers.

Myelin is composed of 30% protein and 70% lipid

Basic protein and proteolipid

Phospholipids and Plasmalogens

Sphinglomyelins

Glycospinglolipids

i.e. Cerebrosides and Gangliosides

Cholesterol

High molecular weight proteins

} included in myelin on maturation

GLIAL PROTEINS

1. Myelin Basic Protein
2. α_2-Glycoprotein
3. Glial fibrillar acid protein
4. Other proteins of microglial cells: NAD(P)H oxidase, peroxidase, lysosomal cationic proteins, lysozyme, lactoferrin etc.

GLIAL LIPIDS

Lipid content of the brain is as high as 50% dry weight, while myelin contains approximately 70% lipids. CNS is characterised by the most structural diversity of membrane lipids compared to other organs. In myelin, 18:1 (Oleic acid) and 18:0 (Stearic acid) are prevalent.

Myelin contains

1. **Phospholipids (especially Phosphatidylinositol 4,5-Diphosphate, Phosphatidic acid, Phosphatidyl choline, Phosphatidyl ethanolamine, Phosphatidyl serine, Phosphatidyl glycerol and Phosphatidyl inositol), Plasmalogens and Sphingomyelins (45%),**
2. **Glycosphingolipids and Ganglioside GM1 (27-30%)**
3. **Cholesterol (25-28%).**

CU CHOLINE

for optimising the development of cell membranes i.e.
Phosphatidylcholine
Cardiolipin
Phosphatidylinositol
Plasmalogen

for optimising the development of receptor sites which are rich in
Cerebrosides
Sulfatides
Gangliosides GM3, GM2 and GM1

Memory recall

Restricted cerebral blood flow.

Stress - high cortisol.

Toxins.

Low ACh neurotransmitter. (Low ACh people don't dream).

Nutritional deficiency

- Low Magnesium,
- Phosphatidyl- serine,
- Choline,
- Dimethylethanolamine (DMAE)

A lesser-known compound in fish, dimethylaminoethanol (DMAE), is increasingly favoured for its role in boosting brain power. DMAE has shown positive results in the treatment of a variety of cognitive and disruptive disorders, including attention-deficit hyperactivity disorder (ADHD) and memory lapses. DMAE is even being used in skin care products designed to treat sagging skin and age spots.

Liposomal Brain Formula

Liposomal mix of Phosphatidylcholine and Phosphatidylserine (250mg),

DMAE 25mg.

5ml to delivers

- beta Alanine 50mg
- Pantothenic acid 50mg
- NADH 1mg
- Riboflavin-5-phosphate 5mg
- Thiamine 5mg
- ATP 5mg

Additional memory supplements

Vitamin E

Polyphenolics - Sulfurophane

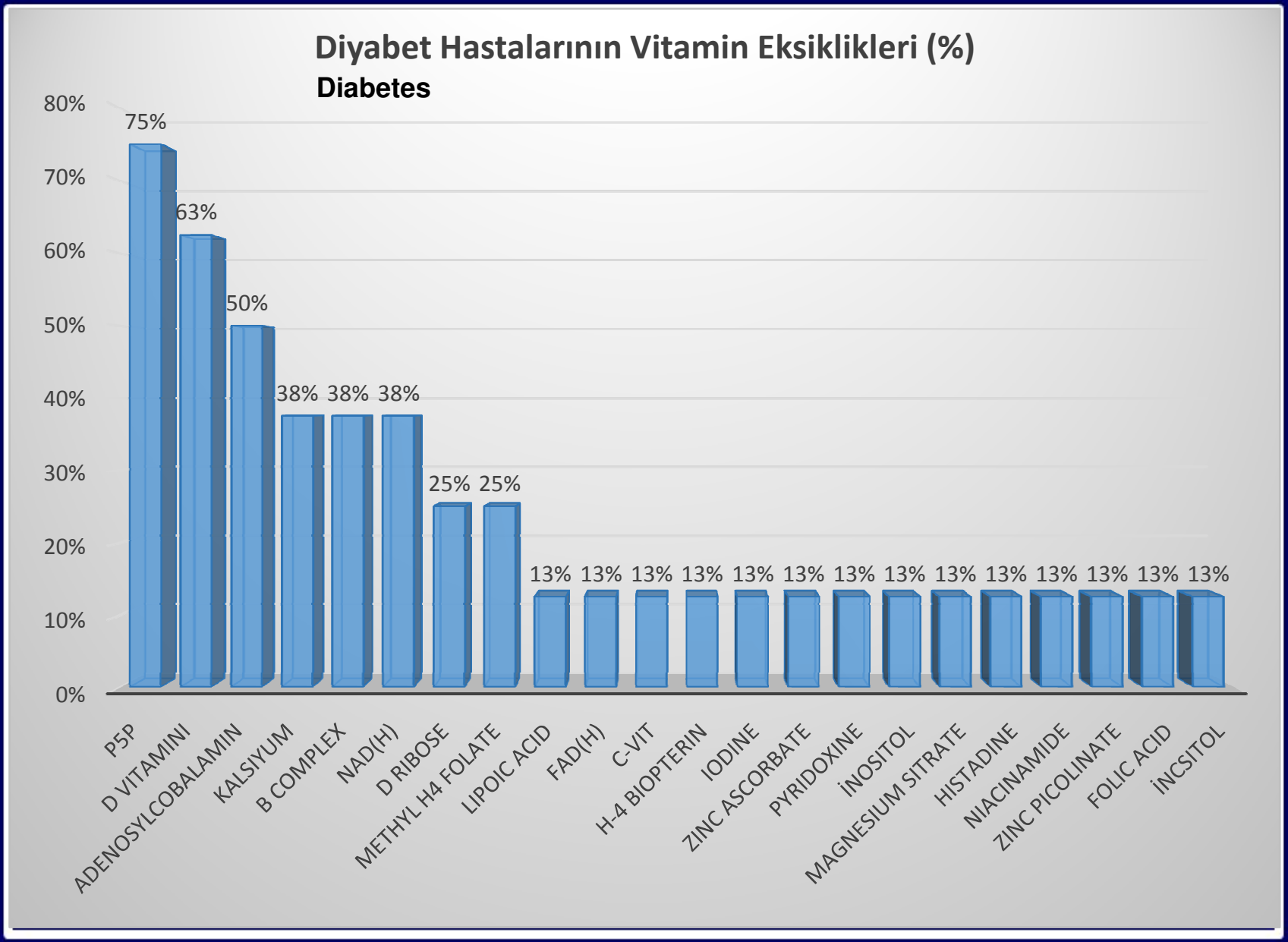
Astaxanthin

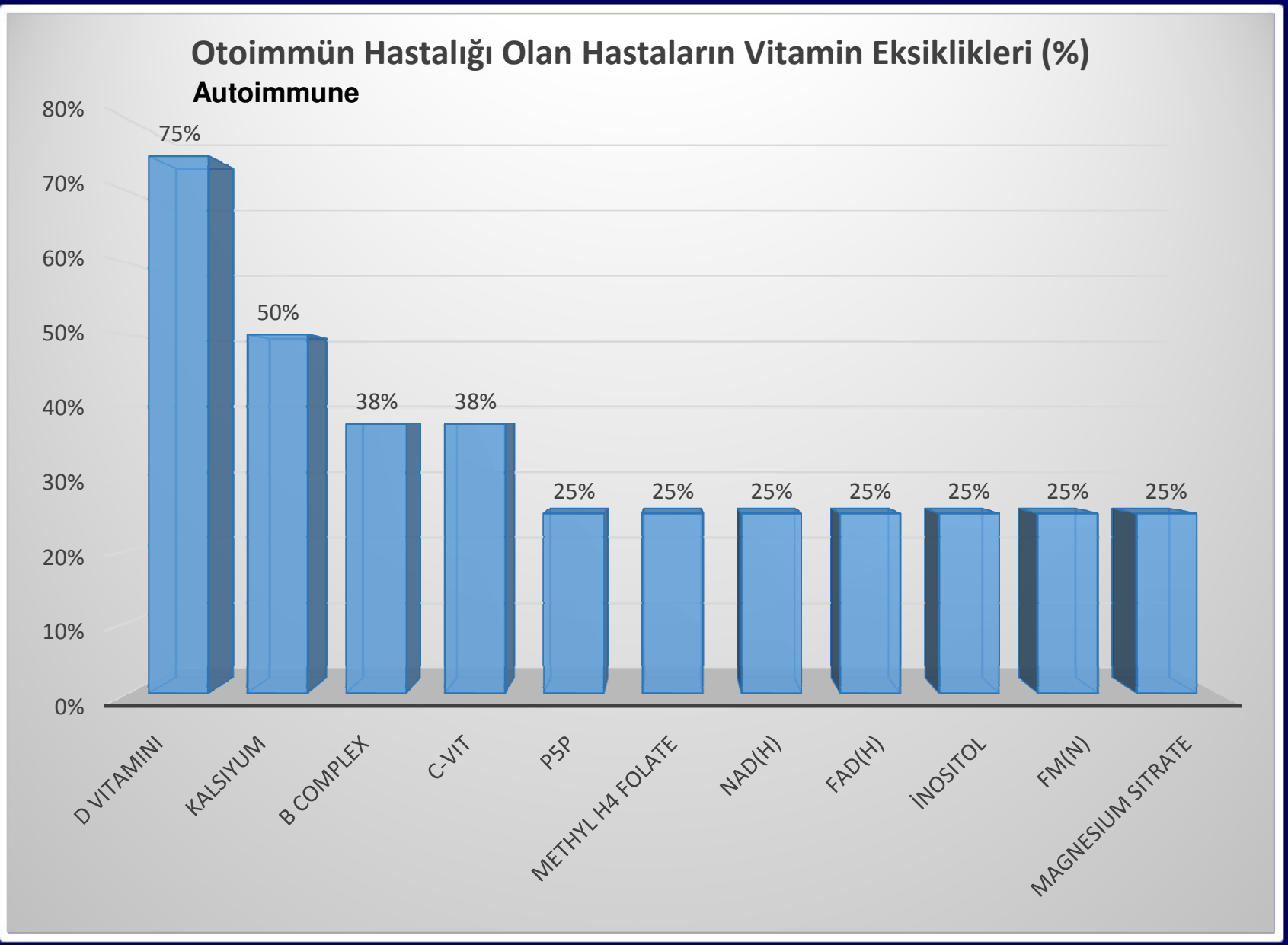
Selenium

Omega 3

Glutathione

Rosemary


Diyabet Hastalarının Vitamin Eksiklikleri (%)
Diabetes
80%
70%
60%
50%
40%
30%
20%
10%
0%
75%
63%
50%
38%
38%
38%
25%
25%
13%
13%
13%
13%
13%
13%
13%
13%
13%
13%
13%
13%
13%
13%
P5P
D VITAMINI
ADENOSYLCOBALAMIN
KALSIYUM
B COMPLEX
NAD(H)
D RIBOSE
METHYL H4 FOLATE
LIPOIC ACID
FAD(H)
C-VIT
H-4 BIOPTERIN
IODINE
ZINC ASCORBATE
PYRIDOXINE
İNOSITOL
MAGNESIUM SITRATE
HISTADINE
NIACINAMIDE
ZINC PICOLINATE
FOLIC ACID
İNCSITOL


Otoimmün Hastalığı Olan Hastaların Vitamin Eksiklikleri (%)
Autoimmune
80%
70%
60%
50%
40%
30%
20%
10%
0%
75%
50%
38%
38%
25%
25%
25%
25%
25%
25%
25%
D VITAMINI
KALSIYUM
B COMPLEX
C-VIT
P5P
METHYL H4 FOLATE
NAD(H)
FAD(H)
İNOSITOL
FM(N)
MAGNESIUM SITRATE