Nutrition, Diet, and Supplements for Peak Physical & Mental Performance

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Nutrition Overview:

In order to sustain life, we consume food, which contains nutrients, which supply energy or building materials to our cells, or which improve the living conditions of the cells. Carbohydrates, lipids, and proteins are called macronutrients. Smaller quantities of micronutrients are also required. Micronutrients include vitamins and minerals. In addition to nutrients, a healthy diet contains water, fiber, anti-oxidants, anti-inflammatories, and signaling molecules. A diet composed of a combination of natural vegetarian foods can supply all of the necessary macronutrients and fiber, as well as many of the micronutrients and anti-oxidants. Dietary supplements can be purchased which provide additional vitamins, minerals, herbal extracts, and anti-oxidants. Especially important are vitamins D, C, E, N-acetyl-cysteine (NAC), and alpha-Lipoic acid.

Research into aging and longevity is indicating that lifespan might be increased and aging might be slowed by following a diet that is very low in calories, but contains enough micronutrients and extra antioxidants. This is referred to as "calorie restriction", "CR", "dietary restriction", or "DR". At least CR, exercise, and adequate sleep can reduce excess accumulations of harmful fat. Links to this research can be found on the web at:

https://LegendaryPharma.com/jdf/aging.html

It is worth remembering that individual people may differ somewhat in their needs and in their ability to assimilate various foods and supplements. Optimal dose probably varies with age, weight, gender, and genetic background. It is important to pay attention to your own body as you experiment with your diet and lifestyle.

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You can support John Furber's ongoing expenses of connecting researchers and students in fields related to Biogerontology, producing meeting notes, and updating the "Systems Biology of Human Aging" wall chart.

If you would like to send a check, please mail it to: John D. Furber, PO Box 14200, Gainesville FL 32604-2200 USA

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Thank you for your encouragement and support.

Good Foods:

Foods in the following list are especially beneficial to eat frequently, because they are very high in anti-oxidants, nutrients, or cancer-preventing components:

- Cruciferous vegetables (broccoli, cauliflower, cabbage, Brussels sprouts) contain fiber and glucoraphanin, believed to aid in preventing some types of cancer. Broccoli is also a good source of lysine, an essential amino acid. Furthermore, broccoli contains sulforaphane, which increases levels of phase 2 enzymes in liver cells. Broccoli and tomatoes together significantly shrink prostate tumors. [Erdman] They probably deliver the most nutrition when lightly cooked for 2-3 minutes, neither raw nor overcooked. If you sprout broccoli seeds, the sprouts contain much more sulforaphane per gram than the mature vegetable.
- **Tomatoes** and **tomato sauce** contain fiber and carotenoids including *lycopene* and *beta carotene*. They are also high in vitamins C and B-complex. Carotenoids are oil-soluble anti-oxidants. Cooking tomatoes with olive oil makes the lycopene much more available to your body.
- Colored berries, such as **Blueberries**, **Strawberries**, **purple grapes**, **cranberries**, **elderberries**, **wolfberries** (**goji**), and other **fresh or frozen fruits** contain antioxidants, anti-inflammatories, signaling molecules, fiber and vitamins. Berries which have been cooked must be eaten right away or they lose their potency.
 - [The Color Code. James A. Joseph, Daniel A. Nadeau, Anne Underwood. Hyperion. 2002]
- Oranges and tangerines contain flavonoids that inhibit proliferation of cancer cell lines.
- **Green tea, white tea**, and **black tea** (Freshly prepared; not bottled or canned) are very high in antioxidant polyphenols that can cross the blood-brain barrier. These polyphenols also chelate excess iron, which provides further protection from oxidative stress. Tea is also a source of manganese.
- White Tea inhibits elastase and collagenase enzymes, and thus might protect human extracellular matrix fibers from deterioration with age.
- Carrots, cooked or raw, contain fiber and antioxidant carotenes.
- **Raw nuts** and pumpkin seeds contain protein, fiber, omega-3 oils, and antioxidants. Raw walnuts help to prevent endothelial inflammation, protecting arteries from the effects of saturated fats in the diet. http://www.medscape.com/viewarti-cle/545790?sssdmh=dm1.218121&src=nldne
- Whole grains: brown rice, oatmeal, and other whole grains contain fiber, protein, and complex carbohydrates.
- Allium vegetables: (garlic, onions, scallions) (raw or barely cooked) are reportedly beneficial to the cardiovascular system and may prevent some cancers. Garlic diallyl sulfide protects against H. pylori bacteria, which can cause stomach ulcers and other problems. Red onions are the best food source of quercetin, which is a polyphenol antioxidant, and can kill off harmful senescent cells.
- **Spinach** (cooked or raw) is high in anti-oxidants, folic acid, and lutein. It may be the highest food source of lipoyllysine (13 μg/g dry weight), which is a natural variation of alpha-Lipoicacid.
- **Tofu** and **tempeh** are high protein foods made from soybeans. Tofu is a good source of lysine, an essential amino acid. Soy activates cancer-fighting genes.
- Flax oil or freshly ground flax seed (raw, never heated) is very high in essential omega-3 fatty acids. Flax oil must be kept refrigerated and in the dark, because it is easily oxidized.
- **Salmon** or salmon oil. Salmon oil is very high in long-chain, essential omega-3 fatty acids (EFA and DHA), because the salmon live in cold water. They are not top predator fish, so they do not have so much mercury in them. Vegetarians can avoid salmon and obtain the benefits of essential omega-3 fatty acids by eating plenty of **flax** oil and freshly-ground flax seed.
- **Nutritional yeast** (such as Red Star or Milwaukee Food Yeast) is a good source of B-vitamins and chromium.

• **Turmeric** is an Indian spice comprising the root of the turmeric plant. It contains about 3% **curcumin**, which has antioxidant and anti-inflammatory activities. It seems to be helpful for inflamed joints and tendons, such as arthritis and carpal tunnel syndrome. Turmeric also appears to help fight off colon cancer and prevent Alzheimer's dementia. However, some imported turmeric (*Pran* brand from Bangaladesh) has been adulterated with lead, a toxic heavy metal. It would be wise to avoid *Pran* brand and buy from reputable USA suppliers, or test each batch for lead contamination.

Kaul, Gitika. <u>"FDA Cracks Down on Imported Spices After Turmeric Tests Positive for Lead"</u>. *Yahoo! News*. ABC News, 28 Oct 2013.

"Lead Poisoning From Imported Asian Spices" (PDF). Arizona Department of Health Services. Arizona Department of Health Services. May 2012.

- http://epicureandigest.com/2014/12/19/turmeric-does-your-supply-pass-the-test/
- **Vinegar** with a meal helps to slow the conversion of starches into simple sugars. This can reduce the spike in blood sugar and insulin after eating starches. **Cinnamon** with a meal is also helpful in regulating blood sugar levels.
- Extra virgin olive oil, balsamic vinegar, grape seed oil, and red wine all contain a substance (DMB) that interferes with the production of TMAO by gut microbes. TMAO is a chemical that is harmful to the heart. It is produced by gut microbes from carnitine and lecithin, especially when we eat red meat. [Stanley Hazen. Cleveland Clinic. Cell]
- Parsley and celery: Eating 2 oz (70 g) per day of parsley improves insulin signaling in the brain. Apigenin improves spatial memory in mice. It acts as a cytokine-suppressive anti-inflammatory agent. [Andre Kleinridders, German Institute of Human Nutrition Potsdam-Rehbrücke, 2017]. Apigenin is found in many fruits and vegetables, but parsley, celery, celeriac, and chamomile tea are the most common sources [Wikipedia].

<u>Muscle Building:</u> Some trainers suggest a diet containing 1.2 grams of protein per kg of body weight *in combination with* **Resistance Exercise** 2-3 times per week and frequent sauna use. This combination improves protein synthesis inside the muscle cells. But so much dietary protein is not helpful nor recommended for obese or sedentary people. [Dr. Rhonda Patrick, FoundMyFitness, 2022]

Recipes on the Web:

- I have written a few easy vegetarian recipes, which emphasize the foods listed above. [https://legendarypharma.com/jdf/recipes.html]
- <u>FATFREE</u> The Low Fat Vegetarian Recipe Archive. [www.fatfree.com]

Foods and Drugs to Avoid:

- MSG or Monosodium glutamate might be neurotoxic for a few people, especially infants. However, for most adults, it is probably as harmless as any other protein.
- Aspartame or NutraSweet might be neurotoxic for some people, especially infants.
- Hydrogenated vegetable oils are even worse for your heart and cardiovascular system than saturated fats in meat and dairy because hydrogenation produces trans-fatty acids, which cause atherosclerosis.
- **Iron** supplementation should generally be avoided unless prescribed for iron-deficiency anemia. Iron promotes oxidation and free-radical damage to cells and membranes. Iron may interfere with the absorption of other vitamins. Most people get plenty of iron in their food. If you take

supplementary iron, do NOT mix it with your vitamins. Children are especially vulnerable to brain damage from excess iron.

- Acetaminophen (also called paracetamol or Tylenol) is a liver toxin, which is even more toxic when taken on the same day as alcohol. Regular, frequent use of acetaminophen (Tylenol) can cause lactic acidosis, even when taken in the correct dosage. This is because it can cause an accumulation of pyroglutamic acid in the blood. (https://www.healthline.com/health/lactic-acidosis#causes)
- Empty calories: Avoid eating most white flour products, white rice, corn chips, soft drinks, sweet snacks, and sweet cereals. Those which lack vitamins, minerals, and fiber are called "empty calorie foods." They contribute to rapid aging, fat gain, glycation, and possibly the development of diabetes
- Large predator fish, such as **tuna**, **swordfish**, **king mackerel**, **shark**, and **tilefish**, contain dangerously high levels of mercury because they concentrate the mercury from the smaller fish that they eat. Furthermore, these large species are endangered by overfishing.
- The herb, Aristolochia, contains aristolochic acid, which binds to DNA, causing kidney failure.
- The herb, **comfrey**, contains toxic chemicals which harm the liver and may be carcinogenic. [http://www.cfsan.fda.gov/~dms/dspltr06.html]
- **Tobacco smoke** generates free radicals in the blood and in the lungs, promoting the development of several diseases, including:
 - Cardiovascular diseases, hardened arteries, and heart attacks;
 - Lung cancer, mouth cancer, throat cancer;
 - Emphysema;
 - Blindness from macular degeneration.
- **Teflon** levels in human blood are correlated with incidence of thyroid disease. Teflon is the non-stick lining of non-stick cooking pans.

Nutrition Information Sources:

For further information, you can educate yourself by visiting your local public library and medical school library. You can learn about medical research results and current scientific thinking in the field by searching the online databases for relevant biomedical journal articles. Links to useful resources on the worldwide web can be found at:

https://LegendaryPharma.com/jdf/nutrition.html.

The report that follows lists dosages of more than 30 vitamins, minerals, antioxidants, and herbs that appear to be beneficial supplements to a healthy diet. It also lists some inexpensive sources of quality ingredients, suggests how to mix them, and the best times of day to take them. Detailed descriptions are provided for each ingredient, with references to a bibliography of more than 25 books and journal articles. Additional information is provided on proteins, amino acids, fats, carbohydrates, and hormones. To contribute to the costs of research and production, please see the box on the previous page.

Dietary Supplements:

A good diet of healthy foods can by augmented by purchasing dietary supplements, which provide additional vitamins, minerals, herbal extracts, and antioxidants. I have been taking large doses of dietary supplements since 1982, and modifying the doses as I learn more, in my ongoing self-experimentation program.

Note: Optimal supplement dose probably varies with age, weight, gender, and genetic background, as well as the foods eaten. I am a male, 140 lb, in my mid-60's.

Table 1, below, lists the supplements I currently take every day, in addition to a well-designed vegetarian diet.

Table 2, below, lists additional supplements I take when fighting off illness. These tables are kept updated on the web at:

https://LegendaryPharma.com/jdf/supplements.html Table 1: John Furber's Daily Total Experimental Doses of Supplements

Description	Active Dose		Notes
Vitamins			
Vitamin B1, Thiamin	100	mg	
Vitamin B2, Riboflavin	100	mg	
Vitamin B3, Niacin (nicotinic acid)	500	mg	
Vitamin B5, Pantothenate	900	mg	
Vitamin B6, Pyridoxine	100	mg	
Vitamin B12, Cyanocobalamin	100	micrograms	
Vitamin C, ascorbate	1000	mg	I
Ascorbyl Palmitate	1000	mg	FF
Vitamin D3	5000	IU	FF
Vitamin E, alpha-tocopherol	400	IU	FF
Vitamin E, gamma-tocopherol	200	mg	FF
Vitamin E, delta-tocopherol	67	mg	FF
Vitamin E, beta-tocopherol	5	mg	FF
Vitamin K2, (as MK-4)	50	micrograms	
Minerals			
Calcium in CaCO₃	954	mg	F
Chromium picolinate	100	micrograms	X, F
Lithium (as Li orotate)	4.3	mg Li	
Magnesium in MgO	230	mg	F
Selenium	100	micrograms	X, F
Zinc gluconate	50	mg	X, F
Amino Acids & Peptides			
Acetyl-L-Carnitine Cl	1000	mg	
N-Acetyl-Cysteine (NAC)	1000	mg	1
L-Lysine HCI	1000	mg	I
Nattokinase	0	mg	
Serrapeptase	0	mg	
Taurine	3000	mg	F
Antioxidants & Misc.			
BHT	500	mg	
Biotin	150.0	micrograms	
AGE-crosslink Breaker (LegendaryPharma.com)	100 - 200	mg	Α
Choline	1200	mg	
Coenzyme Q ₁₀	130	mg	A, FF
DMAE Bitartrate	200	mg	
Folic Acid	800	micrograms	
Alpha-Lipoic Acid (Racemic)	400	mg	4 x 100 mg caps
AAKG (Arginine Alpha Keto Glutarate)	1,689	mg	enteric caps
Potassium orotate	500	mg	F

"Quinn" (quinoline derivative) (LegendaryPharma.com)	100-200	mg	F
Plant Products			
Ashwagandha	250	mg	F
Astragalus extract, 0.5%	500-1000	mg	Swanson, VC
Bacopa extract	300	mg	PureBulk 50%
Berberine	400	mg	Swanson
Blueberries (fresh or frozen)	half	cup	
Strawberries (fresh or frozen)	half	cup	
Fisetin	100	mg	Р
Flax oil or freshly ground flax seed	1-2	tablespoons	
Genistein	125	mg	
Ginkgo biloba extract	120	mg	
Pterostilbene	50	mg	F
Saw Palmetto extract	640	mg	FF
Grape seed extract	100	mg	F
Coffee (med roast, fresh ground)	1	Liter (dilute)	
Green Tea, freshly brewed	1	cup	Т
Black Tea, freshly brewed	1	cup	Т
White Tea, freshly brewed	1	cup	Т
Reishi Tea (Ling Zhi, Ganoderma Lucidum)	1	cup	Boil 2 hours
Cinnamon bark powder	100	mg	Т
Spirulina	500	mg	F
Turmeric root powder	1	teaspoon	with coffee or food

DOSAGE TIMING NOTES:

I divide most of these daily doses into several parts. Spreading the dosage throughout the day helps to maintain a consistently high level of antioxidants in the bloodstream. The notes below refer to the tables above.

- A Age-related dose. Younger people take less.
- **B** Bedtime. Take when going to sleep.
- **D** Divide this amount into smaller portions to take several times during the day.
- **M** For men. Not for women.
- E Should be taken on an empty stomach, once per day. (e.g. Bedtime or upon awakening.)
- **F** Absorption is best when consumed with food.
- FF Absorption is best when consumed with food containing fats or oils.
- **P** As an alternative for Fisetin dosage: Dr. Bernd Friedlander (4 Apr 2022) suggests taking a large dose (1500 mg) 3 days in a row; then none for a month. Repeat every month.
- I I increase this dose when fighting off infectious illness.
- **S** Smaller amounts spaced every hour or two.
- T Brewed in hot water with tea
- X Caution: Do not exceed this dose.

Table 2: Special Extra Doses of Supplemental Nutrients taken to Enhance Immunity when Fighting off Illnesses (Daily <u>Totals</u>)

Description	Active Dose		Notes
Vitamins			
Vitamin C, ascorbate	3000	mg	S
Amino Acids & Peptides			
N-Acetyl-Cysteine (NAC)	3000	mg	S
L-Lysine HCI	3000	mg	S
Antioxidants & Misc.			
Pycnogenol	25	mg	F
Alpha-Lipoic Acid (Racemic)	1000	mg	D
Source Naturals Wellness Formula Herbal Defense	See package		caps easier to swallow than tablets.
Plant Products			
Shitake mushrooms, cooked with food	several		F
Elderberries, cooked with oatmeal	0.5	teaspoon	F
Wolfberries (goji, <i>Lycium</i> chenense, <i>Lycii fructus</i>), cooked with oatmeal	1	tablespoon	F
Spirulina	500	mg	F

Also good for enhancing immunity and fighting off illnesses is soaking in a <u>very warm bathtub</u>, and getting plenty of <u>sleep</u> in a warm bed.

Ingredients of Experimental Daily Doses of Nutrients and Antioxidants

In my quest to attain nutritional supplements at low cost, I have been purchasing different items from different suppliers. Some are in the form of bulk powders, which can be combined and taken at the same time. Others are in the form of tablets, capsules, or liquids. The bulk powders can be mixed more easily and accurately in large batches every few months. Table 3 shows how much of each powder is used to mix up a batch of mealtime supplements. Table 5 lists the other pills and capsules taken each day. This document is kept updated on the web at:

https://LegendaryPharma.com/jdf/supplements.html

Table 3: Powder Mix taken with Meals

(Caution: Not for children or pregnant women.)

Item	Active			Weight/	Suppliers
	Dose	unit	units/mg	day (mg)	
Ascorbyl palmitate (Vitamin C)	1000	mg	1.000	1000	BaC, PB
Ascorbic acid (Vitamin C)	1000	mg	1.000	1000	LEF, PB
Astragalus	500	mg	0.5	1000 mg	BS
Calcium carbonate	880	mg Ca	0.390	2256	LEF
Carnitine (Acetyl-L-carnitine)	1000	mg	1.0	1000 mg	
Bacopa extract	150	mg	0.5	300 mg	PB
Berberine	400	mg	1	400 mg	PB
BHT	500	mg	1		Making Cosmetics
Calcium pantothenate (Vit B5)	800	mg B5	0.915	874	LEF
	73	mg Ca	0.083		
CoEnzyme Q10	130	mg	1.0	130	WN
N-Acetyl-Cysteine (NAC)	1000	mg	1.000	1000	
L-Lysine HCI	800	mg	0.800	1000	
Grape seed extract	100	mg	1.000	100	
Choline bitartrate	1200	mg	0.410	2927	LEF
DMAE bitartrate	200	mg	0.370	541	PureBulk
Fisetin	100	mg	.5	200	PB
Quercetin dihydrate	100	mg	1	100	
"Quinn" (quinoline derivative)	200	mg	1	200	LegendaryPharma.com
Pterostilbene pTeroPure	99	mg	99	100	
Saw palmetto extract (25% ?)	640	mg	1	640	
Sodium bicarbonate	1,200	mg		1,200	Neutralizes acidity
Taurine	3,000	mg	1	3000	
Zinc gluconate	50	mg	0.136	368	LEF
Magnesium oxide	350	mg	0.600	583	LEF

Swallowing Powders:

- The Mealtime powder mix (Table 3 above) is dissolved in warm juice and drunk, or stirred into warm soup. Warm liquid dissolves MUCH better than cold.
- Weighing is more accurate than measuring spoons.



Mixing a large batch of powders:

The powders are sifted and mixed together ahead of time in the proper proportions, and then measured out into the daily dose. The most suitable way to measure and mix the powders is with a laboratory scale in a large batch (for example, a 120 day supply). Very accurate scales are available on

LegendaryPharma.com/amazonSome of the powders are very acidic; others are very alkaline. Mixing them will allow them to neutralize each other for palatability and will protect

the teeth from being dissolved by the acidity.

Stir powders together, and then tumble the batch for several hours to mix the dry powders completely. Then the daily dose can be measured out for each day into a small container. Tumbling requires that a large container (with a tight lid) be big enough to be no more than half full, to allow room for mixing. After you put the powder in and tighten the lid, tape the lid securely. Then put the container into a big plastic bag, and tie it shut, in case the lid comes off. Set your clothes dryer on "Air/Fluff, No Heat". Pack pillows, sleeping bags, etc loosely around the container in the dryer so it won't rattle around. Orient the container so that it will tumble end-over-end. Start the dryer. Every few minutes, tap the container to keep powder from sticking in the corners and failing to mix. I usually tumble for a couple of hours.

Supplement storage: For long-term storage, freshness is best preserved by freezing. However, opening a cold jar of powder or pills will cause immediate moisture condensation from the air, quickly ruining the contents. So, any jar which

has been frozen must be allowed about an hour to come to room temperature before opening it. I keep a two-week supply of mealtime powder mix at room temperature. For traveling, it can be handy to preweigh each day's supply into small, one-ounce, wide-mouth Nalgene containers, with a daily dose in each. Everything else goes in the freezer. It's a good idea to put a few **silica gel packets** into the supplement bottles to help keep the contents dry. When necessary to re-dry them, bake the packets in an oven for one hour at 210-220 F, so that you can reuse them. You can find sources by Googling <u>silica desiccant</u>, or you can reuse silica packets from the vitamins you buy.

Table 5: Separate Tablets and Capsules

Item	Active Dose Dose		Daily	Suppliers	
	per day	Timing	Dose		
AAKG (Arg-alpha-keto-glutarate)	456 mg AKG	4 per day	4x430 AAKG	4 enteric capsules	
Ashwagandha, 5% extract			2x250 mg		
Astaxanthin (BioAstin)	24 mg	F	2 cap	PB, VC, Swanson	
Vitamin B-complex 50	50-150 mg	F	1 cap		
Vitamin B3 - Nicotinic acid	500 mg	E	1 cap	NOT niacinamide	
Vitamin D3	5000 IU	FF	1 gelcap	TJ, VC, CL	
Vitamin E mixed tocopherols	400 IU	FF	1 cap	VC. CL	
Vitamin K-2	50 microgram	F		NOW	
Chromium picolinate	100 microgram	F	½ tab	WN,S	
alpha-Lipoic Acid	200-300 mg	F	3 caps	VC,Jv,TJ,WN, PB	
AGE-crosslink Breaker	100-200 mg	Α	100-200 mg	LegendaryPharma.com	
Ginkgo biloba extract	120 mg	4	3 tabs	S. or powder	
	204 mg Ca				
Lithium Orotate	5 mg		1 cap	Swanson, VC	
Metformin	1000 mg	2/d	2 tabs	Rx	
Piracetam	800-2400 mg	D		LL,PB,VC	
"Quinn"	100-200 mg	A, FF	100-200 mg	LegendaryPharma.com	
Potassium orotate	500 mg	F	1 cap	LEF	
Rhodiola		F	1 cap		
Selenium	100 microgram	F, X	½ tab	TJ,WN,S	

Table 6: Extra-cost Items

Extra Cost Item	Active	Timing	Daily	\$/tab	\$/day	Supplier
Ergoloid mesylates	12 mg	sublingual	12	0.16	1.92	Rx
			tabs			

GENERAL COMMENTS:

- These quantities should not be taken by children, nor by pregnant or lactating women. When in doubt, reduce the dose and consult a knowledgeable professional.
- Start gradually. When starting on supplements, start out with much smaller doses (about 1/4 of the amounts listed here) and gradually work up over a period of weeks to give your body time to adjust.
- Where convenient, these daily doses are divided into several parts. Spreading the dosage throughout the day helps to maintain a consistently high level of supplements in the bloodstream.

ABBREVIATIONS:

g = gram 1 mg = milligram = 0.001 gram 1 μ g = 1 mcg = 1 microgram = 0.001 mg

Vit = vitamin 1 tsp = level, packed teaspoon = 5 mL = 5 cc

cap = capsule d = day p = powder tab = tablet

Ca = calcium Mg = magnesium Zn = zinc

SOURCES and SUPPLIERS:

- Az Amazon. Please use my link to get to your account. www.LegendaryPharma.com/amazon
- BS **BulkSupplements** https://www.bulksupplements.com/

has bulk powders of amino acids and various other nutritional supplements.

CL Country Life

Jv **Juvenon** has their "Juvenon Energy Formula", which contains acetyl-L-carnitine and alpha-Lipoic acid. https://www.juvenon.com/

LEF Life Extension [https://lifeextension.com]

Legendary Pharmaceuticals [https://legendarypharma.com]

- Lx **Longevinex** [www.longevinex.com] sells red wine extract containing resveratrol in airtight capsules. (866) 405-4000
- MC Making Cosmetics has BHT crystals.
- PB PureBulk [https://purebulk.com/]
- PH Planetary Herbals
- Rx Prescription drug available at any pharmacy.
- S Store. Wherever supplements are sold.
- SN Source Naturals
- Sw Swanson [https://www.swansonvitamins.com]
- TJ **Trader Joe's** is a chain of food stores in several states. Not mail order. http://www.traderjoes.com Trader Joe's has good quality supplements at good prices, including:
 - CoEnzyme Q₁₀ capsules
 - Ginkgo biloba tablets
 - Vitamin C (ascorbic acid) in tablets and bulk powder
 - Vitamin D gel caps
 - Vitamin E alphaTocopherol softgels
 - Calcium/Magnesium/Zinc tablets
 - Saw palmetto softgels
 - Pycnogenol tablets
 - Spirulina tablets
- VC VitaCost [http://www.vitacost.com]
- VRP Vitamin Research Products, Inc., 3579 Highway 50 East, Carson City NV 89701, USA. Phone: 800-877-2447; Fax: 800-877-3292; https://www.vrp.com; vrp@delphi.com (Free catalog) Products include Lithium orotate capsules.
- WN **Wholesale Nutrition**, PO Box 1848, Palatine IL 60078, USA. https://www.nutri.com; wn@nutri.com Phone: U.S. and Canada 800-325-2664;

Wholesale Nutrition has:

- CoEnzyme Q10 as bulk powder, softgel capsules, or chewable wafers
- Alpha-Lipoic acid tablets

Commentary on Nutrients and Anti-oxidant Dietary Supplements

In the following notes, information sources in [brackets] refer the reference list at the end of this section. Doses listed are those suggested by each listed author, and may NOT be the amount which I take. Refer to the preceding section or my website for which supplements I take, and the amounts.

Substances are arranged alphabetically within the following categories:

- Vitamins:
- Proteins and Amino Acids;
- Minerals;
- Hormones:
- Carbohydrates;
- Herbs;
- Oils and Fats (Lipids);
- Fiber;
- Non-Steroidal Anti-Inflammatory Drugs (NSAIDs);
- Other Supplements and Antioxidants

VITAMINS:

Vitamin A (retinoic acid)

WARNING: NOT FOR PREGNANT WOMEN. (Pearson)

WARNING: Excessive retinoic acid may induce birth defects and may be harmful to bone health. Antioxidant. However, the body can make Vitamin A from Beta Carotene (see below), so you may safely take Beta Carotene instead of Vitamin A. It is harmful to take more than 2,500 IU of Vitamin A every day for extended periods. Although vitamin A can prevent decrease of thymus weight with age, and prevents cancer, it is safer to take the provitamin form (beta carotene). (Linus Pauling Institute)

Vitamin B-1 (thiamin HCL) 250-500 mg (4)

Antioxidant. It is a thiol compound, and possibly acts as an immune system stimulant. [Pearson 1982, p.87]

<u>Benfotiamine</u> is a lipid-soluble form of vitamin B1. It might be helpful for diabetes, but it is probably not beneficial for non-diabetics.

<u>Vitamin B-2</u> (riboflavin) 100-200 mg (4)

Vitamin B-3 (niacin or nicotinic acid, not niacinamide)

250 mg-3 g [Pearson 1984, p.28]; 3 g [Pearson 1982, p.469] (4)

Niacin may induce temporary skin redness and itching, especially if taken on empty stomach. This is harmless and lasts about 5-20 minutes. Avoid "sustained-release" niacin. Large doses of sustained-release niacin can cause serious problems, while the same doses of ordinary (immediate release) niacin do not [Edell 1 Mar 94].

Niacinamide or nicotinamide 250 mg-3 g [Pearson 1984, p.38] (4)

Said to reduce anxiety. Our cells can make it from excess tryptophan [Lehninger p.770]

Vitamin B-5 (Calcium pantothenate) 1 g [Walford p.47]; 1-2 g [Pearson 1982, p.469] (4)

Antioxidant. Principal constituent of royal jelly. Helps brain cells to convert choline into the neurotransmitter, acetylcholine.

<u>Vitamin B-6</u> (pyridoxine HCL) 250-500 mg (4) Antioxidant.

I.Gangsaas. "Dispelling the Myths of Vitamin B-6," Nutrition Bytes. Vol 1, No 1 (1995).

https://digital.library.ucla.edu/nutritionbytes/librarian?ITEMID=NUTBB950103

Wikipedia says that different forms of B-6, pyridoxine and pyridoxamine can interconvert.

Vitamin B-12 (cobalamin, coenzyme B₁₂) 500 μg (f)

"Vitamin B12 is the largest and most complex of all the vitamins. It is unique among vitamins in that it contains a metal ion, cobalt. For this reason cobalamin is the term used to refer to compounds having B12 activity. Methylcobalamin and 5-deoxyadenosyl cobalamin are the forms of vitamin B12 used in the human body. The form of cobalamin used in most supplements, cyanocobalamin, is readily converted to

 $5-deoxy adenosyl\ and\ methyl cobalamin."\ [http://lpi.oregon state.edu/infocenter/vitamins/vitaminB12/b12.html]$

Cobalamin increases manufacture of RNA by brain cells and improves learning [Pearson 1982, p.170, 477].

Cobalamin contains the metal cobalt. The human requirement is about 10 µg/day, but it is not well absorbed. Persons lacking *intrinsic factor* are unable to absorb sufficient cobalamin from normal diets, and they develop *pernicious anemia*. [Stryer pp. 642-645]

"Cyanocobalamin is the principal form of vitamin B12 used in supplements but methylcobalamin is also available. Cyanocobalalmin is available by prescription in an injectable form and as a nasal gel for the treatment of pernicious anemia. Over the counter preparations containing cyanocobalamin include multivitamin, vitamin B-complex, and vitamin B12 supplements. No toxic or adverse effects have been associated with large intakes of vitamin B12 from food or supplements in healthy people. Doses as high as 1 mg (1000 mcg) daily by mouth or 1 mg monthly by intramuscular (IM) injection have been used to treat pernicious anemia, without significant side effects. When high doses of vitamin B12 are given orally only a small percentage can be absorbed, which may explain its low toxicity. Because of the low toxicity of vitamin B12, no tolerable upper intake level (UL) was set by the Food and Nutrition Board in 1998 when the RDA was revised."...
"A varied diet should provide enough vitamin B12 to prevent deficiency in most individuals 50 years of age and younger. Individuals over the age of 50, strict vegetarians, and women planning to become pregnant should take a multivitamin tablet daily or eat a fortified breakfast cereal, which would ensure a daily intake of 6 to 30 mcg of vitamin B12 in a form that is easily absorbed."

"Older adults (65 years and over): Because vitamin B12 malabsorption and vitamin B12 deficiency are more common in older adults, some respected nutritionists recommend 100 to 400 mcg/day of supplemental vitamin B12, an amount provided by a number of vitamin B-complex supplements." Vitamin B12 injections are considered not necessary unless an individual has *pernicious anemia*.

[https://lpi.oregonstate.edu/infocenter/vitamins/vitaminB12/b12.html]

Vitamin C (Ascorbic Acid or Calcium ascorbate) 3-18 g (4) [Pauling p.xi]

Vitamin C is an antioxidant which helps to regenerate the antioxidant activity of vitamin E. It inhibits viruses including herpes and some flues. It also protects against cancer [Rubin p709]. Pure ascorbic acid is very acidic and can dissolve teeth or irritate stomach in large doses. The chemical formula is C₆H₈O₆. Molecular weight 176.13 g/mol. Powdered ascorbic acid can be mixed with basic powders, such as MgO and CaCO₃ to create a neutral mix. "Time-release" forms of ascorbic acid may irritate stomach and intestines. Calcium ascorbate and sodium ascorbate are buffered, so they are not acidic. Calcium ascorbate also supplies the important mineral, calcium.

https://en.wikipedia.org/wiki/Ascorbic acid

https://micro.magnet.fsu.edu/vitamins/pages/vitaminc.html

Vitamin C (Ascorbyl palmitate) 600 mg [Walford p.141] (FF)

Vitamin C is an antioxidant. Ascorbyl palmitate is a fat soluble form of Vitamin C, so it may be able to help prevent unwanted oxidation and rancidity of cell membranes and stored lipids.

Vitamin D₃ (cholecalciferol) or Vitamin D₂ (ergocalciferol) (FF)

Vitamin D is a fat soluble vitamin which is necessary for effective absorption of dietary calcium. It also helps deposit calcium in bone and teeth. The skin cells make vitamin D₃ naturally when exposed to sunlight. If blood testing is done, the optimal target range is 20-36 ng/mL. Older references underestimated the importance of vitamin D supplementation. "Half an hour of direct sunlight on the cheeks of a baby each day is sufficient." [Lehninger (1982) p.776] However, because sun exposure also causes photoaging, wrinkling, and skin cancers, sun exposure should be limited. The 1998 AI dietary recommendations depend on age:

- 200 International Units (5 micrograms) infants, children, teenagers and adults to age 50.
- 400 International Units (10 micrograms) adults age 51 to 69.
- 600 International Units (15 micrograms) adults age 70 and older.

However, more recent studies suggest that optimal blood concentrations are achieved with

- 400 IU/day infants, children, and adolescents.
 - 2000 IU/day healthy adults and seniors.

https://lpi.oregonstate.edu/infocenter/vitamins/vitaminD/index.html

One cup of fortified cow's milk contains 100 IU of vitamin D. However, other milk products, such as yogurt, ice cream, and cheese, are generally not fortified, and contain very little vitamin D. Some brands of soymilk are also fortified with vitamin D. (Read the label.)

Vegetarians who don't get much direct sunlight SHOULD take vitamin D supplements.

CAUTION: Vitamin D is toxic in high doses. For safety, do NOT exceed 10,000 IU (250 micrograms/day).

Vitamin E (tocopherol) 30-200 IU [Linus Pauling Institute, 2008] (FF)

http://lpi.oregonstate.edu/mic/vitamins/vitamin-E

The term vitamin E describes a family of eight antioxidants: four tocopherols (alpha-, beta-, gamma-, and delta-) and four tocotrienols (alpha-, beta-, gamma-, and delta-). Alpha-tocopherol is the only form of vitamin E that is actively maintained in the human body; therefore, it is the form of vitamin E found in the largest quantities in blood and tissues. t is also the only form that meets the latest Recommended Dietary Allowance (RDA) for vitamin E. For years, alpha-tocopherol was the only form of Vitamin E available in supplements. Now mixed tocopherols can be found in some supplements. Some research suggests that mixed tocopherols found in whole foods are even healthier than alpha-tocopherol alone. But other research suggests that d-alpha-tocopherol alone is healthier than mixed tocopherols.

Vitamin E is a cellular membrane stabilizer [Pearson 1984, p.326] and one of the most important antioxidant dietary supplements. It has been found to slow the progression of Alzheimer's Dementia, and may possibly help to prevent it as well. [Sano] Vitamin E protects against cancer [Rubin p709] and also protects against heart disease and heart attacks. The **succinate** ester of vitamin E, alpha-tocopherol succinate, is reportedly more effective than alpha-tocopherol, alpha-tocopherol **acetate**, or alpha-tocopherol **nicotinate** in inducing differentiation and inhibiting cancer cells [Prasad] [Lee] Alpha-tocopherol supplements made from entirely natural sources contain only RRR-alpha-tocopherol (also labeled d-al-

Alpha-tocopherol supplements made from entirely natural sources contain only RRR-alpha-tocopherol (also labeled d-alpha-tocopherol). RRR-alpha-tocopherol is the isomer preferred for use by the body, making it the most bioavailable form of alpha-tocopherol. Synthetic alpha-tocopherol, which is often found in food additives and nutritional supplements, is usually labeled all-*rac*-alpha-tocopherol or dl-alpha-tocopherol, meaning that all eight isomers of alpha-tocopherol are present in the mixture. Because half of the isomers of alpha-tocopherol present in all-rac-alpha-tocopherol are not usable by the body, synthetic alpha-tocopherol is only half as bioavailable and only half as potent by weight.

In a large placebo-controlled intervention trial, supplementation of individuals who had moderate neurological impairment with 2,000 IU of synthetic alpha-tocopherol daily for two years (equivalent to 900 mg/day of RRR-alpha-tocopherol) resulted in a significant slowing of the progression of Alzheimer's dementia.

Vitamin K (K-2)

The U.S. Dietary Reference Intake (DRI) for an Adequate Intake (AI) of vitamin K for a 25-year-old male is $120 \text{ micrograms} (\mu g)$ per day. The AI for adult women is $90 \mu g/\text{day}$.

These amounts are easily surpassed by eating cooked green vegetables, so no additional supplementation is required. For example, 100 grams of broccoli contains about 100 µg of vitamin K [Wikipedia: broccoli]. The absorption is greater when accompanied by fats such as butter or oils; some <u>fruits</u>, such as <u>avocado</u>, <u>kiwifruit</u> and <u>grapes</u>, are also high in vitamin K. https://en.wikipedia.org/wiki/Vitamin K#Recommended amounts

Vitamin K2 is a group of compounds largely obtained from meats, cheeses, and eggs, and synthesized by bacteria. Vitamin K2, (menaquinone) found in dairy, fermented foods, and animal products. Recently, some people have looked to vitamin K2 to treat osteoporosis and steroid-induced bone loss, but the research is conflicting. Scientists studying vitamin K2's effects suggest its benefits come with a daily intake of between 10 and 45 micrograms. Vitamin K breaks down calcium in our bodies, and this effect helps **prevent hard deposits (calcium and fatty material) from forming in artery walls.**Our bodies need calcium to build and maintain bones. When it breaks down calcium in our bodies, vitamin K2 activates a protein that helps the mineral bind to our bones to do its job.

While research is ongoing, studies show a higher K2 intake **improves bone** density and reduces the risk of bone fractures. Researchers have found that vitamin K2 may slow or stop **cancer** cell activity.

Natto is high in many nutrients that promote good gut health and is the richest source of vitamin K2 available.

An **egg yolk** can contain between 67 and 192 micrograms of vitamin K2, depending on what the hen eats https://www.webmd.com/diet/foods-high-in-vitamin-k2

Protein and Amino Acids:

Proteins (f) perform many essential functions in our bodies. Our cells make the proteins they need from 20 different kinds of smaller molecules called **amino acids**. Our cells can manufacture 11 kinds of amino acids, but it is easier to get them from the food we eat. The remaining 9 kinds *must* be obtained from food because our cells are unable to manufacture them, so they are called **"essential amino acids."** When we eat protein, digestion breaks it down into individual amino acids, which enter the bloodstream and are taken to cells which use them to make the proteins they need. [Stryer] A balanced diet supplies sufficient quantities of proteins including all of the essential amino acids. The adult requirement for protein is 0.2 g per pound of body weight. This equals 30 g/day for a 150 lb person. Growing children need more, [Pauling p.35] and so do older adults, because they assimilate it less well. The U.S. RDA of protein is set at about 54 grams per day for adults. Tofu (soybean curd) contains well balanced protein (375 grams of tofu supplies 30 grams of protein), and is lower in fat and calories than meat or whole milk sources of protein. It is important for humans to take in sufficient dietary protein to maintain healthy bodies and minds, but consumption of excess protein over a long period of time may be harmful. Vegetarian sources of protein include Red Star nutritional yeast (50%) [lesaffrehumancare], tempeh (19%), tofu (10%) [calculated from package labels], and broccoli (3%). [USDA]

Agmatine Sulfate: 1 gram/day

https://en.wikipedia.org/wiki/Agmatine

Agmatine has been shown to enhance glomerular filtration rate (GFR) and to exert nephroprotective effects. Agmatine sulfate is a bioactive metabolite of arginine. Agmatine is produced through decarboxylation of arginine. Agmatine is transformed into N-carbamoylputrescine by agmatine imino hydroxylase (AIH). Next, N-carbamoylputrescine is converted into putrescine. Finally, putrescine is converted to **spermidine**.

https://en.wikipedia.org/wiki/Spermidine

The molecular weight of agmatine sulfate (CAS Number <u>2482-00-0</u>) is 228 Daltons. The molecular weight of agmatine is 130 Daltons. Therefore, agmatine sulfate is 57% agmatine by weight.

Box 4: The polyamine stress response system. From The molecular bases of the suicidal brain Gustavo Turecki. Nature Reviews Neuroscience 15, pp. 802–816 (2014) doi:10.1038/nrn3839 http://www.nature.com/nrn/journal/v15/n12/box/nrn3839 BX4.html

Spermidine is a polyamine small molecule found in all cells. Spermidine is a longevity agent in mammals due to various mechanisms of action, which are just beginning to be understood. I am considering including spermidine in my daily supplement mix in future, but I have not yet found a good supply. So it may be more expedient to just add agmatine sulfate to my supplement mix. Spermidine has been tested and discovered to encourage hair shaft elongation and lengthen hair growth. Spermidine has also been found to reduce the amount of aging in yeast, flies, worms, and human immune cells by inducing autophagy. [Wikipedia] Spermidine is found in peas, soybeans, lentils, and Natto, which is a fermented soybean product.

<u>alpha-keto-glutarate</u> (AKG or Ca-AKG or AAKG) 1 gram/day of Ca-AKG or 1.7 g/day of AAKG.

AKG requires "enteric-release" capsules to carry it safely past the acidic stomach and into the intestines for proper absorption. It might be best to take several divided doses per day, rather than all in 1 dose.

AKG is being tested in clinical trials at the National University of Singapore as a supplement to help older people to maintain or build muscle mass. It works in conjunction with resistance exercise.

Cysteine, N-acetylcysteine, and glutathione: Glutathione is extremely important in quenching intracellular peroxides and free radicals [Stryer][Staal], but glutathione levels decline with age. "Glutathione deficiency contributes to overall depression of immune functions." Intracellular glutathione levels are increased and immune functions are improved by taking Nacetylcysteine (NAC) orally. [Staal] Glutathione is made in the cells from three amino acids: glutamate, cysteine, and glycine. Glutathione exists in either reduced or oxidized forms, but only the reduced form functions as an anti-oxidant. The site of the oxidation is the sulfur on the cysteine. Dietary supplementation with glutathione or cysteine can improve intracellular levels of glutathione. However, oral glutathione is more expensive and no more effective than oral cysteine because oral glutathione is broken down by digestion into glutamate, cysteine, and glycine. It thus only serves as an expensive source for oral cysteine. Cysteine is a sulfur-containing amino acid, and is also an important antioxidant when in its reduced form. The cysteine is carried by the blood to the cells, where it serves as an antioxidant and is assembled into glutathione. However, cysteine in water is rapidly oxidized to cystine, which is not an antioxidant. Furthermore, oxidized cystine can be harmful. Older references suggested taking cysteine in combination with 3 times as much Vitamin C to inhibit the oxidation. [300 mg Walford] [1000 - 2000 mg Pearson] Recent references suggest taking N-acetylcysteine, (sometimes called NAC) a modified form of cysteine which is more stable, and which is an excellent antioxidant in its own right, as well as being a precursor of glutathione. Furthermore, N-acetylcysteine exhibits antiretroviral activity. [Staal] Among its many beneficial effects, glutathione protects the eye lens from the destructive effects of UV light, such as cataracts. [Cole] Hair is 8% cysteine.

L-Carnosine: (\$.84/gram + S&T from JoMar)

Carnosine is the name given to the dipeptide β-alanyl-L-histidine. (Molar mass=226.23 g·mol⁻¹)

It is often found in the tissues of long-lived mammals at relatively high concentrations (up to 20 mM). *In vitro*, carnosine reacts with carbonyl groups on oxidized proteins. Carnosine appears to inhibit the glycation of proteins or the subsequent formation of glycation-mediated crosslinks. Carnosine also chelates copper, protecting extracellular proteins from copper-mediated oxidation [Decker]. *In vivo*, carnosine may prevent oxidized proteins from crosslinking, or it may mark oxidized proteins for degradation [Brownson]. Hipkiss hypothesizes that a carnosine reaction with protein carbonyl groups can occur inside of cells, but so far we do not have any evidence for intracellular carnosinylation [Hipkiss]. Carnosine supplementation (100 mg/kg) improves the health of mice under conditions of severe redox stress, but does not extend the life of normal mice [Gallant].

Other than possibly inhibiting damage to extracellular proteins, it is unlikely that dietary supplementation with carnosine improves human health beyond the benefits already achieved from naturally occurring levels of carnosine. The increase observed in cell culture proliferative lifespan was probably due to carnosine's intracellular effects, and not due to inhibiting extracellular glycation. Note that human muscle already contains 20 mM carnosine, whereas mouse muscle contains only 1 mM [Holliday]. Furthermore, skeletal muscle does not take up carnosine from the blood, so that dietary carnosine would not be expected to contribute to the muscle tissue pool. Stuerenburg and other scientists are quoted out of context by LEF and VRP to support their selling of dietary supplements. Stuerenburg actually says that although "A decline in free carnosine concentration of 63% takes place between age 10 and age 70 in [skeletal muscle of] human subjects... It has been shown that under normal conditions for muscle function, carnosine from blood is not accumulated by muscle cells. In consequence, the phenomenon reported here is probably not related to altered or reduced nutrient supply in aging, but appears to be a muscle-specific phenomenon... Experimental denervation of muscle results in a marked decrease in the level of histidine-containing dipeptides [i.e. carnosine], so that this mechanism could be involved in the age-induced reduction in tissue carnosine." [Stuerenburg]

A small group of Russian entrepreneurs have been touting carnosine eyedrops as a cure for cataracts. However, this is not well substantiated. Carnosine eyedrops (20 mM) reportedly reverse senile cataracts [Wang], said to be a result of its antiglycation effects. Subjects used 1-2 drops in each eye, 3-4 times per day for 3-6 months.

Creatine Monohydrate: (4 grams has been suggested)

"Creatine supplementation for sporting performance enhancement is considered safe for short-term use but there is a lack of safety data for long term use, or for use in children and adolescents. Creatine is reported to have a beneficial effect on brain function and cognitive processing, although the evidence is difficult to interpret systematically and the appropriate dosing is unknown. Creatine-monohydrate is suitable for vegetarians and vegans, as the raw materials used for the production of the supplement have no animal origin." https://en.wikipedia.org/wiki/Creatine

"The degenerative loss of skeletal muscle mass, bone density, and strength are commonly associated with aging. While resistance training improves musculoskeletal health during aging, the combination of creatine supplementation and exercise leads to greater physiological benefits, specifically in older adults. A meta-analysis – a type of statistical analysis combining the results of multiple scientific studies – found that resistance training and creatine supplementation can improve lower and upper body strength, increase fat-free mass, increase muscular endurance, and increase bone mineral density. These studies suggest that creatine supplementation in combination with resistance training can slow age-related muscular decline compared to resistance training alone. Creatine supplementation has also been tested as a potential agent to lower blood lipids and enhance glycemic control." [research summary by Rhonda Patrick, https://www.foundmyfitness.com]

L-Dopa: 250 mg for middle-age, 500 mg for older people (1b)

Dopa is an abbreviation for **3,4-dihydroxyphenylalanine**. Dopa is made from **tyrosine**, and dopa is converted into the neurotransmitters dopamine, norepinephrine, and epinephrine.

Lysine: 1.5 g [RDA]; 2-3 g [Rand]; 5 g [Linus Pauling interview]

Lysine (molecular wt = 146.19 g/mol) is an essential amino acid. The U.S. RDA is 1.5 grams per day, which is easily supplied by a balanced diet. A recent review suggests that 30mg/kg/day would be beneficial [Rand]. This is about 2 grams for a 150 lb person. Tofu is 0.532% lysine by weight, so that 188g tofu supplies 1g lysine. [USDA] Besides building proteins, lysine is a precursor for biosynthesis of L-carnitine (see Acetyl-L-Carnitine), which is required for burning fat to power muscle contraction [Pauling p.96, 187]. When first digested, lysine increases the insulin released in response to digested sugar [Guyton 861]. Some people report that taking lysine supplements seems to prevent or speed the healing of cold sores. Vegetarian sources of lysine include tofu (0.532%) and broccoli (0.141%) [USDA]. Supplement powders of L-Lysine HCl (molecular wt = 182.65 g/mol) are 80% Lysine by weight.

https://www.chemie.fu-berlin.de/chemistry/bio/aminoacid/lysin_en.html

<u>Methionine:</u> Recent research suggests that excess dietary methionine causes harmful effects, at least in small animals, such as mice [Kalani A, 2015]. Previous recommendation of methionine supplementation, such as [Walford p140-144, 120 mg] no longer appear to be appropriate. Methionine is a sulfur-containing, anti-oxidant amino acid. It is also a precursor for biosynthesis of L-carnitine (see Acetyl-L-Carnitine).

L-Phenylalanine 300-400 mg [Pearson 1984, p.6, 28] [Pearson 1982, p.127] (1e)

Previously, L-Phenylalanine had been recommended by Pearson. However, newer research suggests NOT to supplement with it. [Higher Phenylalanine Concentration Is Associated With More Rapid Telomere Shortening in Men. Johan Eriksson, et.al. *American J of Clin Nutr.* 2016]

Following is from an older book [Pearson 1982]: See CAUTION if you have high blood pressure, irregular heart rhythms, malignant melanoma, or are taking MAO inhibitor drugs. Phenylalanine is an essential amino acid. The U.S. RDA is 2.02 grams per day. We probably get about 2.4 grams of phenylalanine in the protein of the foods we eat. The brain converts L-phenylalanine into L-tyrosine (see below) which is converted into the neurotransmitter, norepinephrine (NE), in conjunction with vitamins B-6 and C. Therefore, if you take phenylalanine, there is probably no need to take tyrosine. Phenylalanine acts as mood elevator and helps to bring some people out of depression. It can help the brain to recover from depletion of NE caused by abuse of amphetamines or cocaine. Cells can decarboxylate phenylalanine to form phenylethylamine (PEA), a neurotransmitter found in chocolate, and associated with feeling in love. Amino acids compete with each other to cross the blood-brain barrier, so the brain will benefit more from this amino acid if you avoid ingesting other protein for 90 minutes before and after.

Taurine 3000 mg

Taurine (2-aminoethane-sulfonic acid) is a sulfur-containing amino acid which is not used for protein synthesis. In several studies Taurine is shown to protect against sarcopenia and neurodegenerative disorders. [Nutrition Investigator, 13 June 2021]

Studying various animals, Singh *et al.* found that the amount of the semi-essential amino acid taurine in circulation decreased with age (see the Perspective by McGaunn and Baur). Supplementation with taurine slowed key markers of aging such as increased DNA damage, telomerase deficiency, impaired mitochondrial function, and cellular senescence. Loss of taurine in humans was associated with aging-related diseases, and concentrations of taurine and its metabolites increased in response to exercise. Taurine supplementation improved life span in mice and health span in monkeys. Rhesus monkeys were fed 250 mg/kg body weight, once per day, starting in middle age.

["Taurine deficiency as a driver of aging", Science. 9 June 2023] Full article at

https://doi.org/10.1126/science.abn9257

Good sources of taurine include brewer's yeast, eggs and other dairy products and fish and red meat. [https://purebulk.com/products/taurine?variant=14294881697841]

Sarcopenia prevention research:

https://pubmed.ncbi.nlm.nih.gov/27875962/

https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-015-0610-1

Neurodegenerative Disorder research:

https://www.nature.com/articles/s41419-018-0468-2

https://link.springer.com/chapter/10.1

L-Tyrosine 300-400 mg [Pearson 1984, p.6, 28] (1e)

See CAUTION if you have high blood pressure, irregular heart rhythms, malignant melanoma, or are taking MAO inhibitor drugs. The brain uses this amino acid to make the neurotransmitter, NE, in conjunction with vitamins B-6 and C. If you take phenylalanine (see above), there is no need to take tyrosine, because your cells make tyrosine from phenylalanine. It acts as mood elevator and helps to bring some people out of depression. It can help the brain to recover from depletion of NE caused by abuse of amphetamines or cocaine. Amino acids compete with each other to cross the blood-brain barrier, so the brain will benefit more from this amino acid if you avoid ingesting other protein for 90 minutes before and after. We probably get about 2.4 grams of tyrosine in the protein of the foods we eat.

Minerals:

Calcium 1000-1500 mg [Berger 143, Walford Appendix A, Pauling p199] (6)

Calcium protects against ischemic heart disease and cerebrovascular disease. [Pauling p.199] Calcium is important for maintaining healthy bones. Calcium supplementation of 700 mg/day reduces the risk of colon cancer in men by 40%. [Wu]

Calcium citrate is more water soluble than calcium carbonate, but it costs more and probably doesn't provide any better calcium supply to the tissues than does calcium carbonate. Avoid "coral calcium". Distributors make false claims about it. Consumer Reports [Jan 2005] found high levels of lead in coral calcium. Calcium carbonate powder also neutralizes the acidity of powdered choline chloride, PABA, ascorbic acid, and DMAE. [Pearson 1982, p.487]

Some food sources of calcium (mg per half cup): Tofu = 260; spinach = 115; bok choy = 80; kale = 60.

To minimize bone loss, older men and postmenopausal women should consume a total (diet plus supplements) of 1,200 mg/day of calcium.

https://lpi.oregonstate.edu/infocenter/minerals/calcium/index.html

Calcium is found in calcium ascorbate (vitamin C), calcium pantothenate (vitamin B-5), and some ginkgo biloba extract formulations, as well as in mineral supplements and food.

Chromium picolinate 0.050 - 0.200 mg chromium [Pearson] 0.200 - 1.0 mg chromium [Anderson] (f)

Required for insulin to work properly in regulating blood sugar levels. It is especially helpful for people with adult-onset diabetes. It reduces blood levels of glycated hemoglobin, fasting blood sugar, fasting insulin, and serum cholesterol. [Anderson] Weinsier claims that brewer's yeast (such as Red Star or Milwaukee Food Yeast) is a good source of chromium. [Weinsier] However, the analysis of nutritional yeast finds only trace amounts. http://www.lesaffreyeastcorp.com/nutritional/consumer/yeg.html

Broccoli provides 11 micrograms/half cup. The Linus Pauling Institute suggests supplementation of about 100 micrograms/day is adequate.

https://lpi.oregonstate.edu/infocenter/minerals/chromium/index.html

<u>Copper:</u> The adult US RDA is 1.5 - 3.0 mg. Cytosolic **superoxide dismutase (SOD)**, an important antioxidant enzyme, is copper dependent, as is the enzyme **thiol oxidase**, which cross links proteins at their SH groups. Food sources of copper include chocolate (2.13 mg/150 g), lentils (0.5 mg/150 g), oatmeal (0.5 mg/100 g), beer (0.4 mg/500 g), and walnuts (0.34 mg/25 g). [Bender p.431 - 433]

Germanium: "There is no evidence that germanium is essential, nor that its consumption confers any benefits." [Bender p.416]

<u>Iron</u> supplementation should generally be avoided unless prescribed for iron-deficiency anemia. Iron promotes oxidation and free-radical damage to cells and membranes. Iron may interfere with the absorption of other vitamins. For most people, a balanced diet provides plenty of iron without supplementation. If you take supplementary iron, do NOT mix it with your vitamins.

<u>Lithium</u> in very small doses 1-5 mg/day) is probably beneficial. [Schrauzer; Fukumoto; Ward Dean, www.vrp.com] It is used in moderate doses to treat bipolar disorder. Overdoses can cause tremors, renal impairment, neurotoxicity, convulsions, and death. [Werbach, Bender p.420]

Schrauzer reports, "Lithium is found in variable amounts in foods; primary food sources are grains and vegetables; in some areas, the drinking water also provides significant amounts of the element. Human dietary lithium intakes depend on location and the type of foods consumed and vary over a wide range. Traces of lithium were detected in human organs and fetal tissues already in the late 19th century, leading to early suggestions as to possible specific functions in the organism. However, it took another century until evidence for the essentiality of lithium became available. In studies conducted from the 1970s to the 1990s, rats and goats maintained on low-lithium rations were shown to exhibit higher mortalities as well as reproductive and behavioral abnormalities. In humans defined lithium deficiency diseases have not been characterized, but low lithium intakes from water supplies were associated with increased rates of suicides, homicides and the arrest rates for drug use and other crimes. Lithium appears to play an especially important role during the early fetal development as evidenced by the high lithium contents of the embryo during the early gestational period. The biochemical mechanisms of action of lithium appear to be multifactorial and are intercorrelated with the functions of several enzymes, hormones and vitamins, as well as with growth and transforming factors. The available experimental evidence now appears to be sufficient to accept lithium as essential; a provisional RDA for a 70 kg adult of 1 mg/day is suggested." [Schrauzer] (1 mg = 1 milligram = 1,000 micrograms).

Lithium orotate has CAS number 5266-20-6.

Magnesium oxide 400 mg [Walford Appendix A]; 350 mg [Lehninger 779] (6)

The 1999 US RDA is 310-410 mg, depending on age and gender. Magnesium protects bones. [Berger 143] Powdered magnesium oxide neutralizes the acidity of powdered choline chloride, PABA, ascorbic acid, and DMAE. [Pearson 1982, p.487] Mg is involved in second messenger signaling for insulin. Intracellular Mg levels tend to drop with aging. Daily doses of 240-480 mg can help diabetes mellitus [Paolisso] An important function in cells is to transport energy in the magnesium - ATP complex. Mg is also required for potassium transport and calcium channel activity in neuromuscular transmission. [Bender pp.420-421, 435] Mg is included in some Vitamin D supplements and Mg Orotate. Dietary sources of Mg include spinach, green, leafy vegetables, nuts, and seeds. [Lehninger 779] Magnesium deficiency in healthy individuals

who are consuming a balanced diet is quite rare because magnesium is abundant in both plant and animal foods and because the kidneys are able to limit urinary excretion of magnesium when intake is low. The Linus Pauling Institute supports the latest RDA for magnesium intake (420 mg/day for men over 30 years of age and 320 mg/day for women over 30 years of age). Following the Linus Pauling Institute recommendation to take a daily multivitamin/multimineral supplement will ensure an intake of at least 100 mg of magnesium/day. Few multivitamin/multimineral supplements contain more than 100 mg of magnesium due to its bulk. Because magnesium is plentiful in foods, eating a varied diet that provides green vegetables and whole grains daily should provide the rest of an individual's magnesium requirement. Older adults are less likely than younger adults to consume enough magnesium to meet their needs, and should therefore, take care to eat magnesium-rich foods in addition to taking a multivitamin/mineral supplement daily. Because older adults are more likely to have impaired kidney function, they should avoid taking more than 350 mg/day of supplemental magnesium without medical consultation

https://lpi.oregonstate.edu/infocenter/minerals/magnesium/index.html

NIH fact sheet at https://www.cc.nih.gov/ccc/supplements/magn.html

CAUTION: Persons with chronic kidney disease may have difficulty excreting Mg, so they should consult a doctor regarding Mg supplementation.

CAUTION: Do not take Mg if you are taking the antibiotic, tetracycline, as Mg reduces the absorption of tetracycline into the bloodstream.

CAUTION: In large doses, Mg oxide may act as a laxative for some people. [New pp.51,55,62]

Magnesium orotate: See "Orotate" in the section "Other Supplements".

Selenium: $100 \mu g + food$ [Walford 1994, pp. 75-76] $200 \mu g$ [Pearson 1984, p.54], $250 \mu g$ [Pearson 1982, p], $160 \mu g + food$ [Walford 1983, p140] (f)

Antioxidant and immune stimulant [Pearson 82:162]. Selenium is a component of the antioxidant enzymes, **glutathione peroxidase** and **thioredoxin reductase**. [Stryer, Sen] The inorganic form is better converted by the body into the enzyme than is the yeast form of Se [Walford 1983, p142]. Walford personally took 80 mg of each form. Inorganic selenite or yeast forms are preferable to methionine or cysteine forms because these amino acids may be improperly incorporated into proteins [Pearson 1982, p.471]. Selenium helps to prevent cancer [Rubin p.709] and cataracts [Pearson 1984, p.54]. CAUTION: Too much selenium can also be toxic [Walford 1983, p142]. "The most frequently reported symptoms of selenosis are hair and nail brittleness and loss" [LPI web site].

The current U.S. RDA for selenium is 55 mcg/day for adults. A typical American meat diet provides about 100 mcg/day of selenium, an amount that appears sufficient to maximize plasma and cellular glutathione peroxidase activity. The selenium content of grains, nuts, fruits, and vegetables depends upon the selenium content of the soil in which they are grown. Brazil nuts can provide between 10 and 100 mcg *per nut*, depending upon where they are grown [LPI web site] Red Star nutritional yeast provides 22.4 mcg per 16 gram serving [lesaffrehumancare web site] (about 50 mL or 10 teaspoons of dry flakes).

https://www.lesaffrehumancare.com/index.asp

"Men taking supplemental selenium in order to reduce the risk of prostate cancer should not exceed 200 mcg/day and should take precautions to reduce the risk of squamous cell carcinoma, such as using sunscreen and avoiding prolonged sun exposure."

https://lpi.oregonstate.edu/infocenter/minerals/selenium/index.html

Zinc gluconate 50 mg [Pearson 1984, p.54] (f)

Zinc acts as an antioxidant and helps to prevent cancer. Sucking on a zinc gluconate tablet at the first sign of a sore throat and getting some rest can sometimes ward off an impending cold or flu. "There is evidence that wound healing is impaired in moderate zinc deficiency...Zinc also has a role in protection against oxygen radical damage. It is an essential (structural) component of cytoplasmic **superoxide dismutase (SOD)**. Zinc ions will bind to sulphydryl groups in proteins, thus protecting them against oxidation, and, at least *in vitro*, it reduces the non-enzymatic formation of hydroxyl and superoxide radicals by iron in the presence of oxygen." [Bender p 425]

Hormones:

<u>Dehydroepiandrosterone</u> (<u>DHEA</u>): DHEA is a steroid hormone, similar to testosterone, which is naturally produced in the body. DHEA levels in blood normally decrease with age after maturity. [Finch] Early experiments feeding DHEA to rodents showed increased lifespan and vitality, similar to the results of dietary restriction experiments. However, more recent long-term studies showed some deleterious effects, and failed to show much benefit.

Estrogen: Estrogen supplementation for post-menopausal women has been controversial. While it seems to be helpful for maintaining some aspects of health and preventing osteoporosis, the oral form is associated with increased cancer risks. Creams and patches applied to the skin do not appear to increase cancer risk. The reason for the difference is that oral

estrogen is absorbed in the intestine, and goes directly from there to the liver (the "first pass effect"). Benefits from estrogen supplementation might also depend upon when it is begun. It might turn out that it is beneficial if begun at the beginning of menopause, but harmful if begun a few years after the end of menopause. There is some evidence that restoring estrogen after a few years of low estrogen may be harmful.

<u>Growth hormone</u>: Growth hormone is naturally produced in the body. It is released into the bloodstream during sleep (especially sleeping on an empty stomach) and during exercise. GH supplementation requires a prescription. Because GH would be digested and destroyed in the stomach, GH supplementation must be injected. Oral and sublingual preparations sold without a prescription do not contain real GH and are not effective. Experimental supplementation of GH improves muscle tone in middle-aged and elderly men. However, animal studies of long-term GH supplementation show deleterious effects, so perhaps GH supplementation would best be avoided except perhaps in the frail elderly. The safest, most proven method of improving strength, balance, and muscle mass is by a progressive program of resistance exercise, even in the frail elderly.

Melatonin: Melatonin levels decline with age. There is some evidence for anti-aging effects. "We conclude that the daily use of 3 mg melatonin seems to protect the retina and to delay macular degeneration. No significant side effects were observed." [Yi, et.al.] Many people report that it helps them with sleeping. Melatonin appears to have antioxidant activity, but I don't know whether this is important for someone who already takes other antioxidants. I take 3 - 6 mg at bedtime.

Vasopressin (Anti-diuretic hormone, ADH) nasal spray (Sandoz Diapid Lypressin)

Improves memory. Use one snort in each nostril immediately before memory exercises, such as debates and tests. [Pearson 1982, Dean] Prescription required.

Carbohydrates:

Carbohydrates include sugars and starch. They are used by the body to provide energy, which is often measured in **Calories**. Complex carbohydrates are broken down more slowly than simple sugars, and release their sugar into the bloodstream more slowly and evenly, over a period of time. The body attempts to regulate the levels of sugar in the blood because excessively high or low levels can be harmful. Sugar in the bloodstream stimulates the release of insulin into the bloodstream. Insulin signals cells to take sugar from the blood, bringing blood sugar levels back down to normal. Chromium picolinate helps in the regulation of blood sugar and insulin levels.

Research into aging and longevity is indicating that reducing dietary calories (caloric restriction), while maintaining levels of micronutrients and increasing anti-oxidants, may increase lifespan and slow the aging process. Links to this research can be found at

[https://www.legendarypharma.com/jdf/aging.html] and

[https://www.legendarypharma.com/senescence.html]

<u>Sugar:</u> Excess dietary sugar appears to contribute to the development of Type 2 diabetes mellitus. Preliminary evidence suggests that excess dietary sugar may cause cataracts. [Kinoshita] Sugar in the blood attaches to proteins in a process called "glycation" or "browning." This interferes with the operation of the proteins, and contributes to hardening of the arteries and other effects of aging.

Herbs:

Ashwagandha: 250 mg

https://ods.od.nih.gov/factsheets/Ashwagandha-HealthProfessional/?utm_medium=email&utm_source=govdelivery

Astragalus root extract: 250-1,000 mg of standardized (0.4% 4'-hydroxy-3'-methoxyisoflavone).

Or standardized (0.5% calycosin 7-O-beta d-glucopyranoside).

It was tested by Geron Corporation and found to stimulate the telomerase enzyme to extend the telomeres on chromosomes in cells. The extract is available in pill form from Swanson, VitaCost, and other companies.

Astragalus propinquus (A. membranaceus): The **dried root**, not the extract, is used in traditional Chinese medicine. It can be boiled with tea or rice.

Bacopa monneiri: 250-600 mg of 45-50% extract.

Bacognize bacopa extract is standardized to 45% bacosides.

Bacopin brand is standardized for a minimum 1.5% of Bacosides.

PureBulk has extract standardized to ≥50% Bacosides.

Improvement of cognition [Kongkeaw].

According to Wikipedia:

Bacopa monnieri displays <u>in vitro</u> <u>antioxidant</u> and cell-protective effects. [20] It also inhibits <u>acetylcholinesterase</u>, activates <u>choline acetyltransferase</u>, and increases cerebral blood flow. [21] In rats, bacoside A enhances antioxidation, increasing <u>superoxide dismutase</u>, <u>catalase</u>, and <u>glutathione peroxidase</u> activities. [22] *Bacopa monnieri* augments Th1 and Th2 <u>cytokine</u> production. [23]

Several studies have suggested that *Bacopa monnieri* extracts may have protective effects in animal models of <u>neurodegeneration</u>. [24][25][26][27][28][29][30] There have also been preliminary clinical studies suggesting improvement of cognitive function in humans.

Roodenrys reports a significant effect of 300 mg of Bacopa monneiri extract (equivalent to 6g and 9g dried rhizome) on a test for the retention of new information. Follow-up tests showed that the rate of learning was unaffected, suggesting that Brahmi decreases the rate of forgetting of newly acquired information

Neuropsychopharmacology (2002) 27, 279–281. doi:10.1016/S0893-133X(01)00419-5

Chronic Effects of Brahmi (Bacopa monnieri) on Human Memory.

Steven Roodenrys Ph.D1, Dianne Booth MSc1, Sonia Bulzomi G.Dip.App.Psyc1, Andrew Phipps G.Dip.App.Psyc1, Caroline Micallef G.Dip.App.Psyc1 and Jaclyn Smoker G.Dip.App.Psyc1

Curcumin: 100 mg - 8 grams/day

Curcumin may protect against a variety of inflammatory diseases, as well as diabetes and cancers. 80 mg/day seems to enhance cognitive function. 200 mg/day during the menstrual cycle seems to reduce the severity of PMS. Curcumin is extracted from turmeric root. It is not very soluble in water and not well absorbed through the gut. It has poor bioavailability. It is unclear whether doses less than 3.6 g/day are biologically active in humans. Bioavailability is enhanced be combining it with 2% piperine (extracted from black pepper), and probably by consuming it during a meal with oily foods. Some curcumin supplements also contain piperine to increase the bioavailability of curcumin. It is safe up to 12 g/day. https://lpi.oregonstate.edu/mic/dietary-factors/phytochemicals/curcumin

Fisetin: 100 mg/day (or see note below)

3,7,3',4'-Tetrahydroxyflavone. C15H1@O6 MW: 286,24 g/mol. Light yellow powder.

CAS Number: 528-48-3. This is a structure related to quercetin. It is found in strawberries, onions, and other fruits and vegetables. Beneficial effects on neurons and memory have been reported by Pam Maher, Dave Schubert, and Antonio Currais of the Salk Institute.

160 μg/g in strawberries (Scalbert & Williamson, 2000) = 72mg/Lb ~30 mg/cup strawberries.

Pamela Maher, Richard Dargusch, Jennifer L. Ehren, Shinichi Okada, Kumar Sharma, David Schubert. **Fisetin Lowers Methylglyoxal Dependent Protein Glycation and Limits the Complications of Diabetes**. *PLoS ONE*, 2011; 6 (6): e21226 DOI: 10.1371/journal.pone.0021226

Ongoing experiments at Mayo Clinic and elsewhere are testing fisetin as a senolytic compound. Effective dose is 20 mg/kg on 2 consecutive days. One of their studies is looking at reducing frailty in adults age 70 and older. (*ClinicalTrials.gov identifier (NCT number):* **NCT03675724**) Participants will be encouraged to reduce caffeine use by 50% prior to and during the 2-day drug dosing period. Due to drug-drug interaction, subjects may not clear the caffeine from their system properly/as usual.

(2022 Review article on senolytics, including Fisetin, Quercetin, Dasatinib: https://doi.org/10.1111/febs.16350)

Dr. Bernd Friedlander (4 Apr 2022) suggests taking Fisetin 20 mg/kg for 3 days in a row; then none for a month. Repeat every month.

Mouse experiments used daily oral Fisetin (5-25 mg/kg) for improved memory and brain function with aging. Rat experiments used daily oral 15 mg/kg. (Maher. Brain Plasticity. 2020; 6(2): 155-166.)

Genistein 125 mg

Clears amyloidβ from cells and lowers plaque number in brain of rodent Alzheimer's model. It probably also enhances the activity of Vitamin D. A study looking at Italians older than 50 found that those with the highest genistein intake had the lowest odds of cognitive impairment. Isoflavones such as genistein and daidzein are found in a number of plants including lupin, fava beans, soybeans, kudzu, and psoralea being the primary food source, also in the medicinal plants, Flemingia vestita and F. macrophylla, Illian and coffee. [Wikipedia]

It occurs naturally in many vegetables (soy, potatoes, beans) and plants (psoralea, shells or coffee beans). It has confirmed anti-cancer activity, mainly as a cancer metastatic inhibitor with high efficiency in the treatment of prostate cancer and breast cancer. In addition, it has an antioxidant, cardioprotective and anti-osteoporotic effect. It also regulates hormonal balance and alleviates menopause symptoms. [Science & Sports Volume 36, Issue 5, October 2021, Pages 359-367] Dr. Ordman takes 125 mg every night to restore and preserve muscles.

Ginkgo biloba: 100-300 mg of extract

Gingko biloba (Gb) is a tree whose leaves contain active pharmacological agents which have been studied in rats, cell cultures, and in controlled clinical trials. Extracts of the fresh green leaves of the ginkgo biloba tree improve circulation, including circulation in the brain. It improves learning, memory, neuroplasticity, and improves peripheral nerve regeneration. It protects against heart disease and atherosclerosis. Gb acts as a free-radical scavenger and protects against free radical damage. Gb promotes hair regrowth in shaved mice. Gb reduces PMS symptoms of congestion and psychological changes. Gb inhibits the harmful enzymes of gingivitis bacteria. Finally, Bilobalide inhibits the growth of *Pneumocystis carinii*. Experimental human doses are generally 50 up to 600 mg per day. Experimental rat and mouse doses are generally 80 up to 150 mg per kg of body weight, which would be equivalent to a human dose of about 6000 mg per day. Positive results are most commonly reported after daily dosage for several weeks. Most capsules sold in stores have 50-60 mg of extract with a minimum of 24% heterosides and 6% terpenoids (including 0.8% ginkgolide B). Trader Joe's has a good, inexpensive formulation.

<u>Gotu Kola (Centella asiatica)</u>: (60 mg extract TID, or make tea with 600 mg dried leaves in a cup of hot water.) [Medscape.com] [WebMD.com]

Triterpene compounds stimulate connective tissue repair, keratinization. Asiaticoside derivatives protect neurons from beta-amyloid toxicity. [Medscape.com]

Neuroceutical, cogniceutical, reduces oxidative stress, A levels, and apoptosis, promotes dendritic growth and mitochondrial health, improves mood and memory. [Julie Gregory, Dale Bredesen, et. al., Biomolecules. 2021]

It is used as a culinary vegetable and as a medicinal herb [2]. The berb may have adverse effects on liver function when

It is used as a culinary vegetable and as a medicinal herb.[2] The herb may have adverse effects on liver function when used over many months.[10][11] [Wikipedia]

Theoretically, gotu kola might increase the effects of metformin by pharmacological synergy [Medscape.com]

According to Mt Sinai Hospital, "Gotu kola has been used in some studies that lasted up to one year. However, gotu kola has the potential to be harmful to the liver. It is best not to use gotu kola for more than 6 weeks without talking to your doctor. You may need to take a 2-week break before taking the herb again.

Asiaticoside, a major part of gotu kola, has also been link with tumor growth in mice. Anyone with a history of precancerous or cancerous skin lesions, such as squamous cell, basal cell skin cancer, or melanoma, should not use gotu kola. People with liver disease, or who take medications that affect the liver, should not take gotu kola. [https://www.mountsinai.org/health-library/herb/gotu-kola]

Green tea, White tea, and Black tea: All three forms of tea come from the same species of plant, *Camellia Sinensis*, but processing is different. As a result, each contains a different profile of antioxidants. Each contains antioxidants and some caffeine, and each helps to prevent cancer. It is beneficial to drink some of each kind of tea. Black tea may also be effective at reducing the quantity of ROS produced by iron in brain cells. Studies show that green tea consumption is associated with improved (greater) bone density in older adults.

<u>Huperizia serata:</u> is an herb grown in the mountains of China for tea, said to improve the memory of the elderly. Huperizine-A, a synthetic derivative, may be beneficial for Alzheimer's patients and be more effective than tacrine. Huperizine-A increases acetylcholine levels in the brain.

<u>Nattokinase</u>: Nattokinase is a bacterial serine protease enzyme found in the fermented soybean food product, "*natto*". Preliminary experiments have shown that this enzyme can degrade several kinds of amyloid molecules *in vitro* (Hsu et al 2009). It is interesting that it remains active in the bloodstream after oral assimilation, and that it is part of a traditional human food. Further research is needed to determine whether it can clear up TTR-amyloid or other deposits in older people.

Black Pepper: A common spice from fruit of PIPER NIGRUM. Black pepper is picked unripe and heaped for a few days to ferment. **White Pepper** is the ripe fruit dehulled by maceration in water. **Piperine** is an extract from black pepper, and is a key component used medicinally to increase gastrointestinal assimilation of other supplements and drugs, such as turmeric, curcumin, and Quinn. http://www.ncbi.nlm.nih.gov/mesh?term=black%20pepper

<u>Piperine</u>: 20 mg/day. Synonyms:(E,E)-1-[5-(1,3-Benzodioxol-5-yl)-1-oxo-2,4-pentadienyl]-piperidine. Appearance:White crystalline powder. CAS Registry Number: 94-62-2. Molecular Formula: C17H19NO3. Molecular Weight: 285.34 Piperine is a kind of alkaloid extracted from pepper fruit. High-purity piperine is needle-shaped or short rod-shaped light yellow or white crystal powder. Recent medical studies have shown piperine to be very helpful in increasing the absorption of certain vitamins such as Selenium, Vitamin B, and Beta-Carotene. Piperine apparently has the ability to increase the body's natural thermogenic activities. http://www.bikudo.com/buy/details/196729/piperine.html

Bioperine is a brand of piperine extracted from black pepper by Sabinsa Corp. It is 95% piperine.

http://sabinsa.com/products/standardized-phytoextracts/bioperine/

http://www.bioperine.com/

<u>Piperlongumine</u> is an extract from the root of *piper longum L*. Early research is suggesting that it has anti-cancer properties. *piper longum L*. is an herb used in Ayurvedic medicine.

Pterostilbene 50 mg/day. is a doubly methylated relative of resveratrol, which is better absorbed than resveratrol. It is found in blueberries and grapes.

Elysium Basis contains 50 mg pTerostilbene per capsule, which is their recommended daily dose.

Chromadex was a supplier of pTerostilbene for many major supplement companies. They marketed with the trade name "pTeroPure".

Bulk Supplements now supplies pterostilbene in bulk powder form.

"Pterostilbene (trans-3,5-dimethoxy-4-hydroxystilbene) is a naturally derived compound found primarily in blueberries and Pterocarpus marsupium (PM) heartwood [1, 2]. The amount of daily pterostilbene consumption varies according to dietary fruit intake, and it has been estimated that pterostilbene content per blueberry varies from 99ng to 520ng/gram depending on the type of berry ingested [3, 4]. Substantial evidence suggests that pterostilbene may have numerous preventive and therapeutic properties in a vast range of human diseases that include neurological, cardiovascular, metabolic, and hematologic disorders. Further benefits of pterostilbene have been reported in preclinical trials, in which pterostilbene was shown to be a potent anticancer agent in several malignancies [5]. Pterostilbene is structurally similar to resveratrol, a compound found in red wine that has comparable antioxidant, anti-inflammatory, and anticarcinogenic properties; however, pterostilbene exhibits increased bioavailability due to the presence of two methoxy groups which cause it to exhibit increased lipophilic and oral absorption (Figure 1) [6–10]. In animal studies, pterostilbene was shown to have 80% bioavailability compared to 20% for resveratrol making it potentially advantageous as a therapeutic agent [6]."

[McCormack and McFadden http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3649683/]

http://www.pteropure.com/ptero/resv.html

Pterostilbene activates a very specific nuclear receptor known as PPAR-alpha. Nuclear receptors are proteins that activate gene expression. PPAR-alpha is activated during fasting states or the prolonged periods without food. Once activated, PPAR-alpha controls lipid metabolism among other essential functions.

pTeroPure is a 99% pure synthesized trans-pTerostilbene sold by Chromadex.

https://www.chromadex.com/pteropure/

Neurobiol Aging. 2012 Sep;33(9):2062-71. doi: 10.1016/j.neurobiolaging.2011.08.015. Epub 2011 Oct 7.

Low-dose pterostilbene, but not resveratrol, is a potent neuromodulator in aging and Alzheimer's disease.

Chang J¹, Rimando A, Pallas M, Camins A, Porquet D, Reeves J, Shukitt-Hale B, Smith MA, Joseph JA, Casadesus G. PMID: 21982274

11/112 (11/012 / 1

Pycnogenol: Antioxidant polyphenol extract from French maritime pine tree bark.

Reishi mushroom tea (Ling Zhi) This dried mushroom is very difficult to cut. So it is easier to buy the slices from www.lifegourmetshop.com. You may optionally shred the slices in a coffee grinder. Boil a few slices of mushroom in about 300 mL of water for an hour or two. Allow to cool; strain and drink the tea. You may reboil a second time. Discard the slices. A small clinical trial showed that reishi can enhance immune response in advanced-stage cancer patients. More studies are needed. See the book, *Mycelium Running*, by Paul Stamets.

Laboratory studies suggest that reishi mushroom may have antihistamine effects, but that has not been tested in humans.

Apr 12, 2019 Memorial Sloan Kettering Cancer Center

https://www.mskcc.org/cancer-care/integrative-medicine/herbs/reishi-mushroom

Resveratrol in cell culture suppresses the growth of human ovarian cancer cells {Surh]. Bioavailability is very low when swallowed. It might be better dissolved in alcohol and absorbed through the lining of the mouth. See also pTerostilbene, which is better absorbed.

Quercetin: Quercetin is a polyphenol antioxidant, and is one of the *senolytic* agents, which kill some harmful senescent cells in mice. [Zhu, Kirkland, et.al. 2015]. The authors suggest that senolytics need not be taken every day, only at long intervals, such as yearly, to kill senescent cells. Mice were given 50 mg/kg weekly. Quercetin is found in red onions, and smaller amounts in other fruits and vegetables. Absorption when taken orally is low. Quercetin also acts as an antihistamine and anti-inflammatory. As a dietary supplement, the safe dosage for quercetin is 1 g/day, and the absorption is up to 60%. [Health Benefits of Quercetin in Age-Related Diseases. Deepika and Pawan Kumar Maurya. *Molecules*. 2022.]

https://en.wikipedia.org/wiki/Quercetin

See "Fisetin", above for more references.

<u>Saw Palmetto Extract:</u> 160 - 640 mg/day. The berry of the saw palmetto is said to reduce benign prostate enlargement and to improve male sexual performance.

<u>Serrapeptase:</u> is an enzyme from silkworms. It is said to inhibit blood clotting. It is measured in SU (serrapeptidase units).

Oils and fats (Lipids):

Our cells require for their healthy functioning that we include a small amount of **essential fatty acids** in our diets. We get fatty acids when we digest fats and oils. The most important to include in the diet are the **omega-3 polyunsaturated fatty** acids (The Greek letter "omega" is ω , so they are written as ω 3 or **n-3 PUFAs**). Members of this family include:

- ALA, or alpha-linolenic acid (18:3 cis-Δ9, Δ12, Δ15 ω3), also called alpha-linolenate,
- EPA eicosapentaenoic acid (20:5 ω3),
- **DPA** docosapentaenoic acid (22:5 ω3),
- DHA docosahexaenoic acid (22:6 ω3).

Our cells cannot make omega-3 fatty acids, but we can convert ALA into EPA and DPA.

Although we also require small amounts of omega-6 and omega-9 PUFAs, they are so common in foods, that we do not need to make any special efforts to seek them out:

- linoleic acid (18:2 cis-Δ9, Δ12 ω6) (omega-6 polyunsaturated fatty acids or linoleate) and
- oleic acid (18:1 $\Delta 9 \omega 9$) (omega-9 monounsaturated fatty acids or oleate).

On the other hand, eating too much **omega-6** polyunsaturated fatty acids can hinder absorption of the essential omega-3 PUFAs. Dietary omega-3 PUFAs inhibit inflammation, while dietary omega-6 PUFAs promote inflammation. Generally, inflammation contributes to neurodegeneration and cell loss associated with diseases of aging.

Saturated fats are solid at room temperature. They are also called **grease** or **shortening**, and they do not contain essential fatty acids. Saturated fats are common in meat and dairy products, as well as in *hydrogenated* vegetable oil. Frequent consumption of saturated fats contributes to clogged arteries, heart disease, and strokes. Saturated fats are preferred by the processed food industry because they resist oxidation and therefore have a longer shelf-life.

Unsaturated fats are liquid at room temperature. They are also called oils. Most are derived from plant seeds and nuts. Some oils are extracted from the meat of cold-water fish. Most oils have only a small amount of $\omega 3$ fatty acids. For example, corn oil is mostly $\omega 6$, and lacks any $\omega 3$ fats. Several older studies link dietary unsaturated fats with increased incidence of cancers [Pearson 1982, p.338]. However, these studies did not distinguish oils containing high levels of essential omega-3 unsaturated fats from oils containing mostly omega-6 ($\omega 6$) polyunsaturated fats. Unsaturated oils must be kept tightly capped in a lightproof container and refrigerated to minimize peroxidation or rancidity. Peroxidized oils are harmful and should be discarded. Further protection from peroxidation can be gained by mixing 1 teaspoon of BHT and 1/4 teaspoon of ascorbyl palmitate per quart of oil when it is first opened after purchase.

Trans-fatty acids are by-products of manufacturing saturated fats from unsaturated oils. This manufacturing process is called "hydrogenation." Trans-fatty acids are found in "hydrogenated oils" and "partially hydrogenated oils." Small amounts of trans-fatty acids are naturally present in meat and milk. Recent evidence indicates that trans-fatty acids may by more harmful to the cardiovascular system than either natural saturated fats or unsaturated fats.

Many people are developing health problems because they eat far too much saturated fats and trans-fats. (On the other hand, the healthful essential fatty acids are rather scarce in the most common oils and fats.) Many processed foods and snack foods contain large amounts of hidden unhealthy fats, but very little of the essential omega-3 polyunsaturated fats.

Olive oil (f)

Mono-unsaturated oleic acid (18:1 ω 9) from **olive oil** is probably quite beneficial in moderation, as part of a diet which also contains omega-3 oils, such as flax oil. Olive oil hardens in the refrigerator. This is not harmful, but it doesn't pour until it warms up again. You may keep it at room temperature for more convenient pouring. For more protection from oxidation, you can refrigerate the olive oil. Try this... pour it into a glass, wide-mouth jar to store it in the refrigerator. Then you can scoop it out with a spoon, as needed.

Canola oil (Canadian Rapeseed oil) (f)

Canola oil is high in essential fatty acids, although not as high in beneficial omega-3 ALA as flax oil. It can be used for cooking and salad dressings. As with all oils, peroxidation is minimized by keeping cooking temperatures and times as low as practical, and storing the oil in the refrigerator.

Flax oil (f)

Flax oil is higher in beneficial omega-3 ALA than Canola oil, but it oxidizes very easily. Do not heat it. It must be kept refrigerated in a lightproof container, such as brown glass. It can be used in dressings, or as a substitute for butter on potatoes, oatmeal, popcorn, etc. One or two tablespoons provides the daily requirement of essential fatty acids.

Fiber:

After reviewing the available evidence, experts at the American Gastroenterological Association are recommending that American adults consume 30 g to 35 g of dietary fiber per day to reduce the risk of colorectal cancer. A diet composed of a combination of natural vegetarian foods can supply all of the necessary fiber. Meat and dairy products contain no fiber. (The chewy texture of meat is due to collagen protein, which is not fiber.)

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs):

"Anti-Inflammatory Agents, Non-Steroidal" [MESH]

NSAIDs are anti-inflammatory agents that are not steroids. There is evidence that they may inhibit the formation of cancers. [Marx] Evidence is accumulating that inflammation is involved in neurodegenerative processes of aging, Alzheimer's dementia, and Parkinson's disease. [Chen] It is possible that regular low doses of anti-inflammatory drugs may provide some protection against the development of Alzheimer's Dementia and excitatory neurotoxicity. In addition to anti-inflammatory actions, some NSAIDs have analgesic, antipyretic, and platelet-inhibitory actions. They are used primarily in the treatment of chronic arthritic conditions and certain soft tissue disorders associated with pain and inflammation. They act by blocking the synthesis of prostaglandins by inhibiting cyclooxygenase (COX), which converts arachidonic acid to cyclic endoperoxides, precursors of prostaglandins. Inhibition of prostaglandin synthesis accounts for their analgesic, antipyretic, and platelet-inhibitory actions; other mechanisms may contribute to their anti-inflammatory effects. Inhibition of prostaglandin synthesis may be responsible for protection against developing some forms of cancer, including colon, esophagus, ovary, and breast. [Mayo] Certain NSAIDs also may inhibit lipoxygenase enzymes or phospholipase C or may modulate T-cell function. (AMA Drug Evaluations Annual, 1994, p 1814-1815)

Differences among specific NSAIDs are described below.

Acetaminophen (Tylenol, paracetamol)

WARNING: Acetaminophen is a liver poison. Do not take it.

Unlike aspirin and ibuprofen, acetaminophen does not inhibit COX-1 or COX-2. Acetaminophen appears to inhibit COX-3. [Nature]

Aspirin (acetylsalicylate) 81 mg (1/4 standard tablet = 1 baby aspirin) (f)

Aspirin is a nonsteroidal anti-inflammatory drug (NSAID) which provides neuroprotective effects. It inhibits inflammation by inhibiting the COX-1 and COX-2 enzymes, blocking prostaglandin synthesis. The optimal dosage has not been determined (maybe a quarter tablet or 81 mg/day?). In addition to anti-inflammatory and neuroprotective activities, aspirin also inhibits blood clotting, which can help to prevent myocardial infarction and blockage strokes. However, this effect of aspirin may increase bruising or the chance of serious bleeding and bleeding strokes in some people. In contrast, ibuprofen does not inhibit blood clotting as aspirin does. Ibuprofen is much more effective at preventing both Alzheimer's and Parkinson's diseases than is aspirin. [Chen] Thus the choice between aspirin or ibuprofen, or both, will be different for different people. Aspirin seems to inhibit the formation of pathological Advanced Glycation Endproduct crosslinks between proteins. Supporting this is evidence that chronic users of aspirin have fewer cataracts. [Bucala] However, there are other, more effective drugs to inhibit or reverse these crosslinks, such as Breaker 45C.

CAUTION: If you notice excessive bleeding or bruising, discontinue aspirin use.

CAUTION: Aspirin may cause Reye's Syndrome if taken by children or teenagers with viral fever.

Ibuprofen 50 mg (1/4 tablet) (f)

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) which may provide some neuroprotective effects. It inhibits inflammation by inhibiting the COX-1 and COX-2 enzymes, blocking prostaglandin synthesis. The optimal dosage has not been determined (maybe a quarter tablet or 50 mg/day?). Unlike aspirin, ibuprofen does not inhibit blood clotting. Ibuprofen may be much more effective at preventing both Alzheimer's and Parkinson's diseases than is aspirin. [Chen] Taking it with food will reduce the chance of stomach injury.

Other Supplements and Anti-Oxidants:

Aminoguanidine 300 mg

Aminoguanidine inhibits crosslinking of proteins due to glycation with sugar. Such crosslinking contributes to many pathologies of diabetes and aging in humans, including high blood pressure, heart disease, kidney damage, cataracts, peripheral nerve degeneration, skin wrinkles, and Alzheimer's Dementia. [Bucala] Healthy people usually take 300 mg while diabetics may take 600 mg daily. Aminoguanidine has been tested for safety and effectiveness in human clinical trials. It has undesirable side effects, and the clinical trials were abandoned. It has not been approved for sale as a drug by the FDA. Further information is at

[www.LegendaryPharma.com/glycation.html]

Astaxanthin 2-24 mg

See Wikipedia article on astaxanthin. "Some research supports the assumption that it may protect body tissues from oxidative and ultraviolet damage through its suppression of NF-κB activation. [31][32] In addition to the compound's anti-inflammatory and anti-oxidative capabilities, animal evidence suggests that astaxanthin has the potential to modulate aging... Astaxanthin is found in microalgae, yeast, salmon, trout, krill, shrimp, crayfish, crustaceans, and the feathers of some birds. It provides the red-orange color of salmon meat and the red color of cooked shellfish... The microalgae <u>Haematococcus pluvialis</u> seems to accumulate the highest levels of astaxanthin in nature and is currently, the primary industrial source for natural astaxanthin production where more than 40 g of astaxanthin can be obtained from one kg of dry biomass."

WebMD says, "Astaxanthin is a reddish pigment that belongs to a group of chemicals called carotenoids. It occurs naturally in certain algae and causes the pink or red color in salmon, trout, lobster, shrimp, and other seafood. Astaxanthin is taken by mouth for treating Alzheimer's disease, Parkinson's disease, stroke, high cholesterol, age-related macular degeneration (age-related vision loss), and preventing cancer. It is also used for metabolic syndrome, which is a group of conditions that increase the risk of heart disease, stroke and diabetes. It is also used for improving exercise performance, decreasing muscle damage after exercise, and decreasing muscle soreness after exercise. Also, astaxanthin is taken by mouth for carpal tunnel syndrome, dyspepsia, male infertility, symptoms of menopause, and rheumatoid arthritis. Astaxanthin is applied directly to the skin to protect against sunburn, to reduce wrinkles, and for other cosmetic benefits."

https://www.webmd.com/vitamins-supplements/ingredientmono-1063-ASTAXANTHIN.aspx

https://www.lifeextension.com/magazine/2013/4/astaxanthin-provides-broad-spectrum-protection/page-01

Unlike many other antioxidant molecules, astaxanthin crosses the blood-brain barrier, allowing it to saturate and protect brain tissue. ¹⁴ **12 mg/day** astaxanthin improved cognitive health scores and learning scores in a study of healthy middle-aged and elderly subjects with age-related forgetfulness. ⁶⁸

Berberine 400 mg

Wikipedia states, "Berberine is under investigation to determine whether it may have applications for treating arrhythmia, diabetes, hyperlipidemia, and cancer."

"There is some evidence that berberine may have anti-aging (gero-suppressive) properties... Its mitochondrial localization is consistent with inhibition of complex I of respiratory chain, decrease of ATP production, and subsequent activation of AMPK, which leads to suppression of mTOR signaling."

https://en.wikipedia.org/wiki/Berberine

WebMD reports that "Berberine might decrease how fast the body breaks down cyclosporine... and sildenafil (Viagra)."

"Some early research suggests that taking 500 mg of berberine 2-3 times daily for up to 3 months might control blood sugar as effectively as metformin or rosiglitazone... Taking 500 mg of berberine twice daily for 3 months seems to reduce total cholesterol, low-density lipoprotein (LDL or "bad") cholesterol, and triglyceride levels in people with high cholesterol... Berberine might lower blood pressure. Use with caution in people with low blood pressure...

"The appropriate dose of berberine depends on several factors such as the user's age, health, and several other conditions. At this time there is not enough scientific information to determine an appropriate range of doses for berberine."

http://www.webmd.com/vitamins-supplements/ingredientmono-1126-berberine.aspx? active ingredientid = 1126 & active ingredientname = berberine

BHT (butylated hydroxytoluene) 500 mg (1b)

BHT is a lipid-soluble antioxidant. BHT inhibits viruses including herpes and some flues, as well as some virus-induced cancers [Pearson 1982, p.478-479]. BHT has been extensively tested as a food preservative and is generally regarded as safe by the FDA. It suppresses the development of cancer tumors in lab animals [Rubin p709] and suppresses DNA

damage in cell cultures [Walford p. 143]. BHT can be added to oils after opening to inhibit oxidation (1 tsp per quart) [Pearson 1982, p.368].

Acetyl-L-Carnitine: 1000 mg/day [Ames, Juvenon]

Carnitine has a central role in transporting fatty acids across the inner mitochondrial membrane into the matrix for β -oxidation. Carnitine is synthesized from **lysine**, an essential amino acid [Stryer pp 607-608]. In his nutrition reference handbook, Bender stated that carnitine supplementation is unnecessary: "Claims were made for effects in human beings, ranging from growth stimulation to the treatment of obesity, ...but there is no evidence of its efficacy." Carnitine is synthesized in muscle and liver tissue. [Bender p.381] However, Bruce Ames' more recent research shows that acetyl-L-carnitine (ALC) supplementation restores the cardiolipin content of mitochondrial membranes in older rats to more youthful levels. Cardiolipin is essential for proper functioning of the mitochondrial electron transport chain. [Scheffler p. 238] Ames believes that ALC supplementation helps the cells of older people to compensate for the reduced efficiency of mitochondrial enzymes which use it as a substrate. [Liu] It appears that ALC supplementation has no significant effect on the cells of young people or young animals. Supplements providing more than 3,000 mg/day may cause a "fishy" body odor [Linus Pauling Inst]. **CAUTION:** Ames has stated that ALC supplementation should only be done in combination with α -Lipoic Acid, which quenches the additional ROS generated.

CAUTION: Research in 2013 suggests that gut bacteria produce TMA from carnitine in the diet. TMA is converted to TMAO in the liver. TMAO might contribute to atherosclerosis [Koeth]. I have not seen similar research with acetyl-L-carnitine. However, according to Steven Zeisel, TMAO is cleared by the kidney, unless there is kidney problem. With kidney problems, TMAO can contribute to atherosclerosis [Zeisel].

Beta Carotene 100 mg [Pearson 1982, p.]; 45 mg [Pearson 1984, p.58] (f)

Beta Carotene is one of several carotenes found in fruits, carrots, yams, and yellow vegetables. They are all beneficial anti-oxidants, but beta carotene is the easiest to buy as a food supplement. Some studies have indicated that it prevents cancer. The body converts it to vitamin A, as needed. 15 mg of beta carotene can be converted to 25,000 IU of vitamin A. Beta carotene does not cause vitamin A overdose toxicity. However, recent studies have found that beta carotene supplementation was correlated with increased cancer risk among tobacco smokers. This suggests that eating fruits and vegetables for their mixed carotenes is healthier than taking beta carotene capsules.

Alagebrium Chloride (4,5-dimethyl-3-(2-oxo-2-phenylethyl)-thiazolium chloride) 100 - 400 mg

Also called PTC, ALT-711, or "AGE-Breaker". Alagebrium breaks crosslinks between extracellular proteins that have formed due to glycation with sugar. Such crosslinking contributes to many pathologies of diabetes and aging in humans, including high blood pressure, heart disease, kidney damage, cataracts, peripheral nerve degeneration, skin wrinkles, and Alzheimer's Dementia. [Bucala] Clinical trials have established the safety and effectiveness of Alagebrium in humans, but it has not yet been approved for sale as a drug by the FDA. Self-experimenters may be able to obtain it as an experimental compound. Further information is at www.LegendaryPharma.com/glycation.html

<u>Choline</u>: 1-3 g [Pearson 1982, p.613], 3 g [Pearson 1984, p.39], 3 g [Morgenthaler p.91] (f) (Choline is supplied by some B-complex tablet formulations, but not in others.)

HO-CH₂-CH₂-N-(CH₃)₃. Choline is a molecule which forms part of phosphatidylcholine diacylglyceride (**lecithin**, a membrane lipid) and **acetylcholine** (a neurotransmitter, ACh). ACh is synthesized in axon terminals from acetyl-CoA and choline. Each neural impulse releases about 300 vesicles, each containing 10,000 ACh molecules. Choline is reabsorbed by the axon terminal and reused to make more ACh. [Guyton 485] Mammals require choline supplied from diet to make phosphatidyl choline. [Stryer 550, 688] In bacteria, SAM methylates phosphatidyl **ethanolamine** to phosphatidyl choline [Stryer 549], and humans may be able to do this when there is plenty of **methionine** in the diet [Lehninger]. Dietary lecithin can increase neurotransmitter levels in brain. [Hirsch] Dietary lecithin can supply choline to the body, although it is also high in fatty acids, and may become rancid on the shelf. Lecithin consumption may be helpful in slowing the progression of Alzheimer's Disease, [Dysken] and this effect is probably due to the choline content of the lecithin. Dietary choline supplementation increases verbal fluency.

It is important to take Vitamin B-5 at the same time as choline. The nervous system requires vitamin B-5 to convert choline to acetylcholine. Start taking choline at a low dosage and increase gradually to prevent headache or muscle tension. Choline supplements are usually **choline bitartrate** powder, **choline citrate** powder, **choline chloride** liquid, or **lecithin** granules. Because choline bitartrate is very acidic, mixing it with CaCO3 or MgO will neutralize its acidity to protect your teeth and stomach lining. Choline bitartrate has a laxative effect upon some people, while choline chloride does not. Choline chloride is only available as a liquid, so it can not be premixed with other powdered nutrients.

CAUTION: Research in 2013 suggests that gut bacteria produce TMA from choline in the diet. TMA is converted to TMAO in the liver. TMAO might contribute to atherosclerosis [Tang]. However, according to Steven Zeisel, TMAO is cleared by the kidney, unless there is a kidney problem. With kidney problems, TMAO can contribute to atherosclerosis [Zeisel].

DEAE (diethylaminoethanol) is probably similar to DMAE.

DMAE (dimethylaminoethanol) 120 mg [Walford p.147] 200-300 mg [Pearson 1982, p.737, 749] (f)

DMAE crosses the blood-brain barrier, and is converted to acetylcholine in the brain. DMAE acts as a cellular membrane stabilizer. It reportedly inhibits the buildup of age pigment in brain cells and removes age spots from skin. It is approved by the FDA for human anti-aging experiments. [Walford p.149] There are some reports of increased sex drive. [Pearson 1982, p.751] Because DMAE bitartrate is very acidic, mix it with CaCO3 or MgO to neutralize it. "Deaner" is a brand name for DMAE by Riker.

EDTA: Ethylenediaminetetraacetic acid is a chelation agent which can remove heavy metals from solution. Clinical EDTA chelation of the blood is used to treat acute lead or mercury poisoning. Do NOT try this at home. Excessive chelation can cause severe deficiencies in essential minerals.

Ethanolamine: May be required in the diet to make the membrane lipid, phosphatidyl ethanolamine, which possibly can be methylated to make phosphatidyl choline [Stryer 550]

Ergoloid Mesylates 12 mg [Pearson 1982, p.] [Dean p.117] sublingual or oral tablets

This is a prescription antioxidant drug. It was developed by Dr. Albert Hofmann at Sandoz Pharmaceuticals, under the brand name "Hydergine." The generic form is less expensive than Sandoz Hydergine. It can be obtained in either sublingual tablets or oral tablets. Sublingual tablet are dissolved slowly under the tongue; oral tablets are simply swallowed with meals. This antioxidant helps to protect brain from shock and lack of oxygen. Controlled studies have shown that it improves memory and intelligence in humans and other animals.

Glucosamine and Chondroitin sulfate

A common dose is glucosamine 1500 mg, chondroitin 1200 mg.

- G&C consumption reduces lung cancer risk by 25%.
- G&C consumption reduces NFκB, Lowers CRP.

(Johanna W. Lampe, Oxygen Club of California, 2016)

Produced commercially by the https://en.wikipedia.org/wiki/Glucosamine] of https://en.wikipedia.org/wiki/Glucosamine] of https://en.wikipedia.org/wiki/Glucosamine]

Inositol 1-3 g [Pearson 1982, p.] 1-5 g [Pearson 1984, p.28, 38] (4) [Alberts 702]

It is also called "muscle sugar." It acts as a membrane stabilizer in cells. [Pearson 1984, p.326] It is said to reduce hair loss and sometimes darken gray hair (although this has not been my experience). It may help arthritis and help to heal crushing injuries. [Pearson 1982, p.477] Inositol plays an important role in cell second-messenger systems. Inositol is found in many plant and animal tissues [Lehninger 251], so it is common in natural foods. Furthermore, it appears that our cells can synthesize inositol, so dietary supplementation is probably not needed.

[https://micro.magnet.fsu.edu/vitamins/pages/inositol.html]

Alpha-Lipoic Acid (α-Lipoic Acid) 400 mg [Ames, Juvenon]

Lipoic acid has several functions:

- 1) As a co-enzyme, it forms part of some important enzyme complexes.
- 2) It is a very special antioxidant because it can be regenerated by cellular enzymes, and it in turn can regenerate other antioxidants like glutathione and Vitamins C and E. It is a very effective antioxidant which is a powerful inhibitor of iron-dependent lipid peroxidation.
- 3) It chelates free iron inside the cells so that the iron is less able to generate free radicals.

Lipoic acid crosses the blood-brain barrier and enters mitochondrial membranes to protect them. It has been shown to enhance the performance of lab rats in tests of strength, balance, and memory. [Liu] Spinach may be the highest source in food, where it is present as lipoyllysine (13 μ g/g dry weight).

[https://lpi.oregonstate.edu/infocenter/othernuts/la/la.html]

[https://www.vrp.com]

[https://www.juvenon.com]

N-propyl gallate

N-propyl gallate is an antioxidant.

Orotate (Magnesium Orotate or Potassium Orotate or Calcium Orotate or Lithium Orotate) 400 mg

The Orotate ion is a key intermediate in the biosynthetic pathway of pyrimidines and is shown to improve the energy status of injured myocardium by stimulating the synthesis of glycogen and ATP. Orotate is a precursor to the pyrimidine nucleotide, uricil. Pyrimidine nucleotides are critical for DNA and RNA synthesis, so they are important for regeneration and wound healing. The ionic formula of orotate is C₅H₃N₂O₄ with a charge of -1 and a weight of 156 g/mol. As a dietary supplement, orotate is sold as magnesium, potassium, calcium or lithium salt. Magnesium orotate from KAL is mixed with magnesium stearate, so it is impossible to calculate the amount of orotate it contains. Potassium orotate 500 mg capsules from Atrium contain 400 mg of orotate and 100 mg of potassium. This is also sold by Life Extension Foundation. Lithium orotate from VRP contains 125 mg of orotate per capsule.

However, a recent mouse metabolomic study collaboration of Jackson Labs with Calico found that orotate levels are **negatively** correlated with lifespan. [Luanne Peters, American Aging Association meeting 2018]

A different recent study indicates that orotate supplementation is **beneficial** for prevention and treatment of ventricular hypertrophy and heart failure [*Int. J. Mol. Sci.* **2021**, *22*(7), 3321; https://doi.org/10.3390/ijms22073321]

PABA (para-aminobenzoic acid) 1-3 g [Pearson 1982, p.] (4) [Pearson 55, 77]

Cellular membrane stabilizer. [Pearson 1984, p.326] Antioxidant. Reportedly protects against ozone in polluted air. Said to sometimes help prevent male hair loss or darken white hair. (I have not seen evidence to support this.) PABA is found in folic acid; it is made in our cells [Lehninger 262], so dietary supplementation is not needed. Because it is very acidic, mix it with CaCO3 and MgO to neutralize the acidity.

CAUTION: PABA nullifies sulfa drugs, so discontinue PABA for the duration of sulfa drug treatments.

Phosphatidylserine

Phosphatidylserine is readily synthesized in human cells from phosphatidate, cytidine triphosphate, and serine. These are all commonly available in cells. Serine is an amino acid which human cells readily synthesize from food. [Stryer p 686-687] There appears to be **no need to supplement** the diet with phosphatidylserine.

Quinn 25 - 200 mg/day

Quinn appears to enhance the health of neurons and facilitate clearing of harmful amyloid beta from the brain. Clinical trials have established the safety and effectiveness of Quinn in humans, but it has not yet been approved for sale as a drug by the FDA. Self-experimenters may be able to obtain it as an experimental compound.

RNA 2 g (f) [Pearson 1982, p.169]

This antioxidant is reported to increase rat lifespan by 20%. RNA is found in almost all living cells, so it is common in natural foods. This is a very old reference, and **may not be currently recommended**.

CAUTION: RNA supplementation should NOT be used by people with elevated serum uric acid or urates or gout. HAVE A BLOOD TEST for serum uric acid BEFORE starting to take RNA. Have another blood test six months after starting to take RNA.

<u>SS-31</u>: Small polypeptide that enhances mitochondria energy production. Currently in clinical trials by Stealth Pharmaceuticals.

Thiodipropionic acid and Dilauryl thiodipropionate

Food anti-oxidants on the U.S. FDA "Generally Regarded as Safe" (GRAS) list. [Pearson 1982, p.476]

Ubiquinone or Ubiquinol (Coenzyme Q 10 or CoQ or Q10) 50-200 mg

CoQ is a lipophilic (fat-soluble) molecule which carries electrons in the mitochondrial electron transport chain. CoQ is found in all of the lipid membranes within human cells. It also circulates in the blood with LDL and may help to protect them from peroxidation. CoQ is used clinically to treat heart disease and mitochondrial disease. CoQ is produced by our cells, but production seems to decline with age. Statin drugs inhibit production of CoQ. Linnane and others have demonstrated that oral supplementation does increase CoQ concentration in skeletal muscle of older humans. Several scientists who research aging are taking CoQ daily. CoQ10 is fat-soluble and absorption is significantly improved when it is chewed with a fat-containing food.

http://cancernet.nci.nih.gov/cam/Q10.htm

http://wwwcsi.unian.it/coenzymeQ/index.html

http://www.vrp.com

http://lpi.oregonstate.edu/infocenter/othernuts/cog10/index.html

The following is quoted from Clinical Pearls Online Research Updates for the Week of December 14, 2004 (03E05). COENZYME Q10 - Angina, Atherosclerosis, Cardiac Surgery, Congestive Heart Failure, Hypertension - Statins may reduce blood levels of coenzyme Q10, which has doctors increasingly recommending this substance to patients. In the June 2000 issue of Archives of Neurology, Rundek, et al, from Columbia University, measured coenzyme Q10 levels in 34 individuals before and after taking 80 mg of atorvastatin per day. The mean blood level of

coenzyme Q10 in the subjects was 1.2 mcg/ml at baseline and decreased to 0.62 mcg/ml after 30 days of atorvastatin. The authors suggest that the widespread inhibition of coenzyme Q10 synthesis may explain the commonly reported adverse side effects of statins, which include exercise intolerance, myalgia and myoglobinuria. These side effects may be reversed with supplementation... Coenzyme Q10 is involved in energy production pathways in the cell and is a powerful antioxidant on its own and in combination with vitamin E. Humans can synthesize coenzyme Q10, but coenzyme Q10 production declines with aging. It may be a nutrient needed by elderly individuals. The heart contains high concentrations of coenzyme Q10 due to its large energy requirements. It has also been observed in congestive heart failure patients that coenzyme Q10 myocardial levels are lower in those with severe failure versus milder cases. Higher doses of bioavailable coenzyme O10 may be warranted for better results, such as 300 mg vs 100 mg. In animal models of atherosclerosis, coenzyme Q10 has prevented atherosclerotic lesions, and it has been shown to reduce the expression of cell adhesion molecules that recruit monocytes to blood vessel walls. In cardiac surgery in 3 or 4 placebo-controlled trials, pre-treating patients with coenzyme Q10 before bypass surgery provided short-term outcome benefits. In 5 small placebo-controlled trials evaluating the effects of coenzyme Q10 in addition to conventional medical therapy for patients with chronic stable angina, there was improved exercise tolerance and a reduction in electrocardiographic changes. In small uncontrolled trials, coenzyme Q10 was shown to possibly benefit hypertension. "Heart of the Matter: A Naturally Occurring Enzyme Is the Subject of Increasing Interest in Heart Disease." Fricker J, Nursing Standard, November 3, 2004;19(8):18. 42298

<u>Vinpocetine</u> is sold with claims of increasing blood flow in the brain, and acting as a blood thinner. However, Albert Szent-Györgyi University Medical School reports that it causes degenerative atropy of neurons in the brain, and inhibits retrograde transport of nerve growth factor (NGF). (Knyihar-Csillik 2007) Wikipedia noted, "Some people have anecdotally noted that their continued use of vinpocetine reduces immune function. <u>Commission E</u> warned that vinpocetine reduced immune function and could cause <u>apoptosis</u> in the long term" (Commission E). **This appears to be bad** for long-term usage.

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