

Choline

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Choline /ˈkoʊliːn/^{[1][2]} is a water-soluble [vitamin](#)-like essential nutrient.^{[3][4][5]} It is a basic constituent of [lecithin](#), which is present in many plants and animal organs.^[6] The term *cholines* refers to the class of [quaternary ammonium salts](#) containing the *N,N,N*-trimethylethanolammonium [cation](#) (X[−] on the right denotes an undefined [counteranion](#)).^[3]

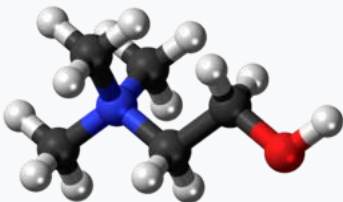
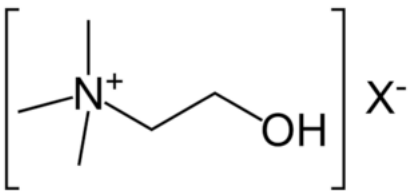
The cation appears in the head groups of [phosphatidylcholine](#) and [sphingomyelin](#), two classes of [phospholipid](#) that are abundant in [cell membranes](#). Choline is the precursor molecule for the neurotransmitter [acetylcholine](#), which is involved in many functions including memory and muscle control.

Some animals cannot produce choline, but must consume it through their diet to remain healthy. Humans make choline in the liver. Whether dietary or [supplemental](#) choline is beneficial or harmful to humans has not been determined.^[7] Possible benefits include reducing the risk of neural tube defects and fatty liver disease. It has also been found that intake of choline during pregnancy can have long-term beneficial effects on memory for the child.^[5]

According to the US [Institute of Medicine](#), there is not enough evidence to establish a [Recommended Daily Intake](#) for choline. The Australian and New Zealand national nutrition bodies note that while deficiency has been seen during experiments, there have been no reports of choline deficiency in the general population.^[8] All three have published an "Adequate Intake" value, discussed below. The European Union's food safety authority says there are no Recommended Daily Intakes in the EU and "no indications of inadequate choline intakes available in the EU".^[9]

[Methionine](#) and [folate](#) are known to interact with choline while [homocysteine](#) is undergoing methylation to produce methionine. Recent studies have shown that choline deficiency may have adverse effects, even when sufficient

Choline



Names

Preferred IUPAC name	2-Hydroxy- <i>N,N,N</i> -trimethylethan-1-aminium
Other names	2-Hydroxy- <i>N,N,N</i> -trimethylethanaminium Bilineurine (2-Hydroxyethyl)trimethylammonium

Identifiers

CAS Number	62-49-7
3D model (JSmol)	Interactive image
Beilstein Reference	1736748
ChEBI	CHEBI:15354
ChemSpider	299
DrugBank	DB00122
ECHA InfoCard	100.000.487
EC Number	200-655-4
Gmelin Reference	324597
IUPHAR/BPS	4551
KEGG	C00114
PubChem CID	6209

amounts of methionine and folate are present. [\[5\]](#)

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History [\[edit\]](#)






Choline was first isolated by [Adolph Strecker](#) from pig and ox [bile](#) (Greek: χολή, *chole*) in 1862.^[10] When it was first [chemically synthesized](#) by [Oscar Liebreich](#) in 1865,^[10] it was known as **neurine** until 1898 when it was shown to be chemically identical to choline.^[11] In 1998, choline was classified as an essential nutrient by the [Food and Nutrition Board](#) of the [Institute of Medicine](#) (USA).^[12]

Chemistry [\[edit\]](#)

Choline is a [quaternary ammonium salt](#) with the chemical formula $(\text{CH}_3)_3\text{N}^+(\text{CH}_2)_2\text{OHX}^-$, where X^- is a [counterion](#) such as [chloride](#) (see [choline chloride](#)), [hydroxide](#) or [tartrate](#). Choline chloride can form a low-melting [deep eutectic solvent](#) mixture with [urea](#) with unusual properties.^[13] The [salicylate](#) salt is used topically for pain relief of [aphthous ulcers](#).^{[14][15]}

Choline hydroxide [\[edit\]](#)

Choline hydroxide is one of the class of [phase transfer catalysts](#) that are used to carry the [hydroxide](#) ion into organic systems, and, therefore, is considered a strong [base](#). It is the least-costly phase transfer catalyst, and is used as an effective method of stripping [photoresists](#) in [circuit boards](#).^[16] Choline hydroxide is not completely stable, and it slowly breaks down into [trimethylamine](#).^[17]

UNII	N91BDP6H0X  
InChI	[show]
SMILES	[show]
Properties	
Chemical formula	C ₅ H ₁₄ NO ⁺
Molar mass	104.17080
Density	1.09 g/ml
Boiling point	305 °C (581 °F; 578 K)
Solubility in water	500 mg/ml
Except where otherwise noted, data are given for materials in their standard state (at 25 °C [77 °F], 100 kPa).	
 verify (what is   ?)	
Infobox references	

In humans [\[edit\]](#)

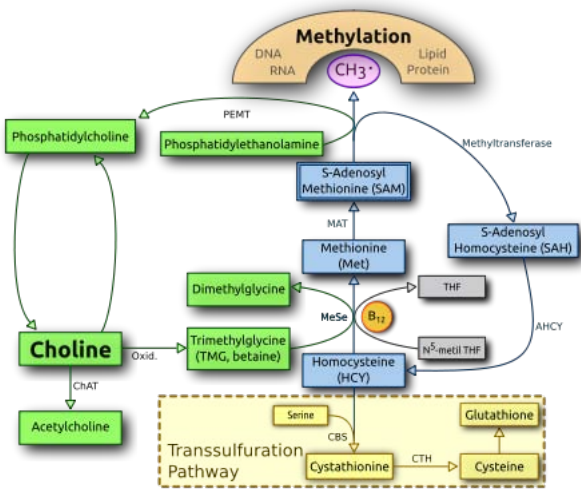
Physiology [\[edit\]](#)

Choline and its [metabolites](#) are needed for three main [physiological](#) purposes: structural integrity and [signaling](#) roles for cell membranes, cholinergic [neurotransmission](#) ([acetylcholine synthesis](#)), and a major source for [methyl groups](#) via its metabolite, [trimethylglycine](#) ([betaine](#)), which participates in the [S-adenosylmethionine](#) (S-AMe) synthesis [pathways](#).^{[18][19]}

Fish odor syndrome [\[edit\]](#)

Main article: [trimethylaminuria](#)

Choline is a [precursor](#) to [trimethylamine](#), which some persons are not able to break down due to a genetic disorder called [trimethylaminuria](#). Persons suffering from this disorder may suffer from a strong fishy or otherwise unpleasant [body odor](#), due to the body's release of odorous trimethylamine. A body odor will occur even on a normal diet – *i.e.*, one that is not particularly high in choline. Persons with trimethylaminuria are advised to restrict the intake of foods high in choline; this may help to reduce the sufferer's body odor.^[20]



Food sources of choline [\[edit\]](#)

The following are choline values for a selection of foods in quantities that people may consume in a day.

Animal and plant foods	Food amount (imperial)	Food amount (metric)	Choline (mg)	Choline (mg) in 100g food	Calories	% of diet to meet AI (smaller is better) ^[a 1]
Raw beef liver	5 ounces	142g	473	333	192 ^[nb 1]	9
Cauliflower	1 pound	454g	177	39	104 ^[nb 2]	13
Large egg	1	50g	147	294	78 ^[nb 3]	12
Broccoli	1 pound	454g	182	40	158 ^[nb 4]	19
Cod fish	0.5 pound	227g	190	84	238 ^[nb 5]	28
Spinach	1 pound	454g	113	25	154 ^[nb 6]	30
Wheat germ	1 cup	113g	202	179	432 ^[nb 7]	47
Soybeans , mature, raw	1 cup	186g	216	116	86 ^[nb 8]	51
Milk, 1% fat	1 quart	946mL (976g)	173	18	410 ^[nb 9]	52
					^[nb 10]	

Firm tofu	2 cups	504g	142	28	353	55
Sunflower seeds (kernels), raw	1 cup	140 g	77	55	584 ^[21]	
Chicken	0.5 pound	227g	150	66	543 ^[nb 11]	80
Cooked kidney beans	2 cups	354g	108	31	450 ^[nb 12]	92
Uncooked quinoa	1 cup	170g	119	70	626 ^[nb 13]	116
Peanuts	1 cup	146g	77	53	828 ^[nb 14]	237
Almonds	1 cup	143g	74	52	822 ^[nb 15]	244

Besides cauliflower, other [cruciferous vegetables](#) may also be good sources of choline.^[22]

The [USDA Nutrients Database](#)[🔗] has choline content for many foods.

Adequate Intake instead of Recommended Dietary Allowance ^[edit]

The Australian, New Zealand, and European Union national nutrition bodies note there have been no reports of choline deficiency in the general population.^{[23][9]} The USA joins these three in not publishing a Recommended Dietary Allowance (RDA), due to lack of consensus evidence. They have, however, published Adequate Intake (AI) values. The US Institute of Medicine (IOM) notes that these figures are based on just one study and that there was little data and the choline made by the body (assuming a dietary intake of zero) may be enough for some groups.^[24] Australia, New Zealand and Canada use the figures published by the US IOM. The [European Food Safety Authority](#) (EFSA) published its own Adequate Intake values, most recently in 2016.^{[9][25]} For U.S. dietary supplement labeling purposes the amount in a serving is expressed as a percent of Daily Value (%DV) based on the AI. For choline, as shown in [Reference Daily Intake](#), 100% of the Daily Value is 550 mg.

Group	EFSA Adequate Intake	US IOM Adequate Intake	US IOM Upper Limit
Infants	(mg/day)	(mg/day)	(mg/day)
0–6 months	-	125	ND
7–12 months	160	150	ND
Children			
1–3 yrs	140	200	1000
4–6 yrs	170	250	1000
7–8 yrs	250	250	1000
9–10 yrs	250	375	1000
11–13 yrs	340	375	2000
Males			
14 yrs	340	550	3000
15+ yrs	400	550	3500 (3000 for 15–18 yrs)
Females			
14 yrs	340	400	3000

15–18 yrs	400	400	3000
19+ yrs	400	425	3500
If pregnant	480	450	3500 (3000 if ≤ 18 yrs)
If lactating	520	550	3500 (3000 if ≤ 18 yrs)

Average or common intakes [\[edit\]](#)

Studies on a number of different populations have found that the average intake of choline was below the [Adequate Intake](#).^{[51][261][271]} In the United States, a recently published government survey on food consumption reported that for men and women ages 20 and older the average choline intakes were, respectively, 402 and 278 mg/day. For post-menopausal women, 280 mg/day^[281]

Health effects of dietary choline [\[edit\]](#)

Choline deficiency may play a role in [liver disease](#), [atherosclerosis](#), and possibly [neurological disorders](#).^[51] One sign of choline deficiency is an elevated level of the [liver enzyme ALT](#).^[41] If low choline intake causes an elevated [homocysteine](#) level, it raises the risk for [preeclampsia](#), [premature birth](#), and very low birth weight.^[51]

Involvement of choline in long-term health and development of [clinical disorders](#), such as [cardiovascular diseases](#), [cognitive decline](#) in aging and regulation of [blood lipid](#) levels, has not been well-defined.^[291]

As a dietary supplement [\[edit\]](#)

See also: [citicoline](#)

The US [Food and Drug Administration](#) requires that [infant formula](#) not made from cow's milk be supplemented with choline.^[301] Choline-providing dietary supplement ingredients include: choline chloride, choline bitartrate, citicoline (CDP-choline), L-alpha-glycerophosphocholine (Alpha-GPC), lecithin, phosphatidylcholine.

Medical imaging [\[edit\]](#)

Because of its involvement in biologic processes, several medical imaging techniques have been developed to monitor relative concentration and kinetics of choline in different diseases. Radiolabeling one of the nitrogen methyl groups on choline with [carbon-11](#) allows it to be used as a tracer in [PET imaging](#) studies. Carbon-11 is radioactive with a half-life of 20.38 minutes.^[311] By monitoring the gamma radiation resulting from the decay of carbon-11, the uptake and retention of carbon-11 choline in different parts of the body can be measured.

One of the first uses of carbon-11 choline in PET imaging was with [Alzheimer's disease](#) patients.^[321] Choline is the precursor to neurotransmitter [acetylcholine](#) whose cholinergic activity is impaired in many neurodegenerative diseases including Alzheimer's.^[331] While there was uptake of the tracer in the brain, no pharmacokinetic pattern was found.

Carbon-11 choline has found more success in cancer systems imaging.



Maximum intensity projection of a PET/CT with choline: Note the physiologic accumulation in the liver, pancreas, kidney, bladder, spleen, bone marrow

Choline is a precursor for the synthesis of [phospholipids](#) in our cells.^[34] When a cell is about to divide, it synthesizes these phospholipids to generate enough material to build the [cell membranes](#) of the two daughter cells. Thus it was hypothesized that highly proliferative tumors would uptake more choline than the surrounding healthy tissue. This was first tested in brain tumors after successful demonstration of choline uptake in the brain.^[35] It was found that these brain tumors had over 10x the uptake of carbon-11 choline than the surrounding brain tissue. Furthermore, because of the low choline uptake in healthy brain tissue, carbon-11 choline was found to be a superior PET tracer than fluorine-18 [Fludeoxyglucose](#) (FDG) when delineating brain tumors.^[36] Carbon-11 choline has also been used to detect tumors in the colon^[37] and esophagus^[38] and lung metastases.^[39] and salivary glands. A bone metastasis is in the left pubic bone.

Prostate cancer is another disease where carbon-11 choline PET imaging has found success. As with the brain, there is too much signal from the surrounding tissue, especially the bladder, to accurately measure tumor uptake with fluorine-18 FDG. While it was shown carbon-11 choline could be used to detect the initiation of prostate cancer,^[40] its value was found in detecting prostate cancer recurrence when it is the most deadly.^{[41][42][43][44]} In 2012, the U.S. Food and Drug Administration approved carbon-11 choline as an imaging agent to be used during a PET scan to detect recurrent prostate cancer.^{[45][46]}

Pregnancy and brain development ^[edit]



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The human body can produce choline by methylation of phosphatidylethanolamine by N-methyltransferase ([PEMT](#)) to form phosphatidylcholine in the liver, or it may be consumed from the diet. It has been demonstrated that both *de novo* production and dietary consumption are necessary, as humans eating diets lacking choline develop fatty liver, liver damage, and muscle damage. However, because of the close interplay between choline, folate, methionine, and vitamin B₁₂, (whose pathways overlap), the function of choline can be complex.

To begin with, methionine can be formed two ways, either from methyl groups derived from folate, or from methyl groups derived from betaine (which gets its methyl groups from choline). Changes in one of these pathways is compensated for by the other, and if these pathways do not adequately supply methyl groups to produce methionine, the precursor to methionine, homocysteine, rises.

Choline in food exists in either a free or esterified form (choline bound within another compound, such as phosphatidylcholine, through an [ester](#) linkage). Although all forms are most likely usable, some evidence indicates they are unequally bioavailable (able to be used by the body). Lipid-soluble forms (such as phosphatidylcholine) bypass the liver once absorbed, while water-soluble forms (such as free choline) enter the liver portal circulation and are generally absorbed by the liver.^[47] Both pregnancy and lactation increase demand for choline dramatically. This demand may be met by upregulation of [PEMT](#) via increasing estrogen levels to produce more choline *de novo*, but even with increased PEMT activity, the demand for choline is still so high that bodily stores are generally depleted. This is exemplified by the observation that *Pemt*^{-/-} mice (mice lacking functional PEMT) will abort at 9–10 days unless fed supplemental choline.^[48]

While maternal stores of choline are depleted during pregnancy and lactation, the placenta accumulates choline by pumping choline against the concentration gradient into the tissue, where it is then stored in various forms, most interestingly as acetylcholine, (an uncommon occurrence outside of neural tissue). The fetus itself is exposed to a very high choline environment as a result, and choline concentrations in

amniotic fluid can be ten times higher than in maternal blood. This high concentration is assumed to allow choline to be abundantly available to tissues and cross the blood-brain barrier effectively.^[48]

Functions in the fetus ^[edit]

Choline is in high demand during pregnancy as a substrate for building cellular membranes, (rapid fetal and mother tissue expansion), increased need for one-carbon moieties (a substrate for addition of methylation to DNA and other functions), raising choline stores in fetal and placental tissues, and for increased production of lipoproteins (proteins containing "fat" portions).^{[49][50][51]} In particular, there is interest in the impact of choline consumption on the brain. This stems from choline's use as a material for making cellular membranes, (particularly in making phosphatidylcholine). Human brain growth is most rapid during the third trimester of pregnancy and continues to be rapid to approximately five years of age.^[52] During this time, the demand is high for sphingomyelin, which is made from phosphatidyl choline (and thus from choline), because this material is used to myelinate (insulate) nerve fibers.^[53] Choline is also in demand for the production of the neurotransmitter acetylcholine, which can influence the structure and organization of brain regions, neurogenesis, myelination, and synapse formation. Acetylcholine is even present in the placenta and may help control cell proliferation/differentiation (increases in cell number and changes of multiuse cells into dedicated cellular functions) and parturition.^{[54][55]}

Choline uptake into the brain is controlled by a low-affinity transporter located at the blood-brain barrier.^[56] Transport occurs when arterial plasma choline concentrations increase above 14 μmol/l, which can occur during a spike in choline concentration after consuming choline-rich foods. Neurons, conversely, acquire choline by both high- and low-affinity transporters. Choline is stored as membrane-bound phosphatidylcholine, which can then be used for acetylcholine neurotransmitter synthesis later. Acetylcholine is formed as needed, travels across the synapse, and transmits the signal to the following neuron. Afterwards, acetylcholinesterase degrades it, and the free choline is taken up by a high-affinity transporter into the neuron again.^[57]

Neural tube closure ^[edit]

While folate is most well known for preventing neural tube nonclosure (the basis for its addition to prenatal vitamins), folate and choline metabolism are interrelated. Both choline and folate (with the help of vitamin B₁₂) can act as methyl donors to homocysteine to form methionine, which can then go on to form SAM ([S-Adenosyl methionine](#)) and act as a methyl donor for methylation of DNA. Dietary choline deficiency alone without concurrent folate deficiency can decrease SAM concentration, suggesting that both folate and choline are important sources of methyl groups for SAM production.^[48] Inhibition of choline absorption and use is associated with [neural-tube defects](#) in mice, and this may also occur in humans.^[47] A retrospective case control study (a study that collects data after the fact, from cases occurring without the investigator causing them to occur) of 400 cases and 400 controls indicated that women with the lowest daily choline intake had a four-fold greater risk of having a child with a [neural-tube defect](#) than women in the highest quartile of intake.^[27]

Choline and long-term memory ^[edit]

In humans, the brain continues to develop after birth, and does not become similar to its adult structure until around four years of age. By feeding infants formula instead of milk, and presumably through differences in choline amount in the breast milk of mothers consuming different choline levels, the still-developing brain of an infant may be impacted, which may, in part, contribute to the differences seen between individual adult humans in memory and recall.^[48]

Choline and lactation ^[edit]

The human mammary gland is composed of several cell types, including adipose (fat cells), muscle, ductal epithelium, and mammary epithelium (referred to sometimes as lactocytes). The mammary epithelium is the site for excretion of raw materials into the milk supply, including choline. This occurs, for the fat portion of the milk, by apocrine secretion, where vacuoles containing materials bud off the cell into the lumen (storage) of the alveolus (milk secretion gland). From here the milk will be released upon stimulation with oxytocin via suckling.^[58]

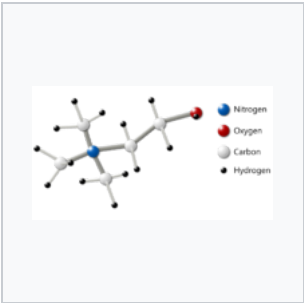
Choline in milk ^{[[edit](#)]}

Choline can be found in milk as free choline, phosphocholine, glycerophosphocholine, sphingomyelin, and phosphatidylcholine, and choline levels within breast milk are correlated with choline levels in maternal blood.^{[59][60]} Choline consumed via breast milk has been shown to impact blood levels of choline in breast-fed infants – indicating that choline consumed in breast milk is entering the neonatal system.^[60] Choline may enter the milk supply either directly from the maternal blood supply, or choline-containing nutrients may be produced within the mammary epithelium.^[61] Choline reaches the milk through a transporter specific for choline from the maternal blood supply (against a concentration gradient) into the mammary epithelial cells.^[62] At high concentrations (greater than that typically seen in humans), choline can diffuse across the cell membrane into the mammary epithelium cell. At more normal concentrations, it passes via what is believed to be a calcium/sodium-dependent, phosphorylation-related, active transporter into the cell.^[63]

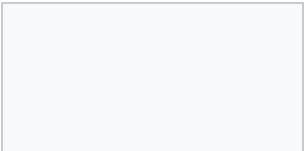
Differences between breast milk and formula ^{[[edit](#)]}

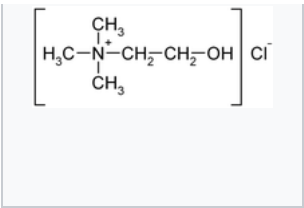
Human milk is rich in choline, but formulas derived from other sources, particularly soy, have lower total choline concentrations than human milk.^{[48][64][65]} Bovine milk and bovine-derived formulas had similar or higher glycerophosphocholine compared to human milk, and soy-derived formulas had lower glycerophosphocholine content. Phosphatidylcholine and sphingomyelin concentrations were similar between bovine formulas and human milk, but soy-derived infant formulas had more phosphatidylcholine than human or bovine sources. Soy-derived formulas had less sphingomyelin than human milk, which is a concern, since sphingomyelin is used for producing myelin, which insulates neurons. Free choline concentrations in mature human milk were 30–80% lower than those found in bovine milk or formulas. Mature human milk also has lower free choline than colostrum-transitional human milk. Phosphocholine is particularly abundant in human milk.^[66]

Additional images ^{[[edit](#)]}

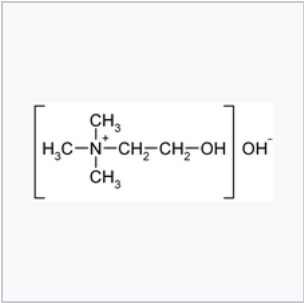


Choline (C5H14NO+)





Choline chloride



Choline hydroxide

See also [\[edit\]](#)

- [Acetylcholine](#)
- [Cytidine diphosphate choline](#)
- [Dimethylethanolamine](#)

Notes [\[edit\]](#)

1. [△] [Percentage of diet calculated using 2500 daily calories for an average adult male and 550mg for Adequate Intake \(AI\) using the figures from the table. As an example, even though peanuts contain some choline, they are a poor source given their 237% of diet to meet AI requirement, which means that a person who ate nothing but peanuts would have less than half of AI. Nearly identical figures are obtained for an average adult female when using 2000 calories and 425mg as assumptions; therefore, separate columns for male and female are not necessary.](#)

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1. [^] Entry for "Beef, variety meats and by-products, liver, raw" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

2. [^] Entry for "Cauliflower, cooked, boiled, drained, with salt" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

3. [^] Entry for one large "Egg, whole, cooked, hard-boiled" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

4. [^] Entry for "Broccoli, cooked, boiled, drained, with salt" in the [Nutritiondata database](#)

5. [^] Entry for "Fish, cod, Atlantic, cooked, dry heat" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

6. [^] Entry for "Spinach, frozen, chopped or leaf, cooked, boiled, drained, without salt" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

7. [^] Entry for "Cereals ready-to-eat, wheat germ, toasted, plain" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

8. [^] Entry for "Soybeans, mature seeds, sprouted, raw" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

9. [^] Entry for "Milk, lowfat, fluid, 1% milkfat, with added vitamin A and vitamin D" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

10. [^] Entry for "Tofu, firm, prepared with [calcium sulfate](#) and [magnesium chloride](#) (nigari) (1)" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

11. [^] Entry for "Chicken, broilers or fryers, meat and skin, cooked, roasted" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

12. [^] Entry for "Beans, kidney, all types, mature seeds, cooked, boiled, without salt" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

13. [^] Entry for "Quinoa, uncooked" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

14. [^] Entry for "Peanuts, all types, raw" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

15. [^] Entry for 1 cup whole "Nuts, almonds" in the [USDA Nutrients database](#) ^{Archived} 3 March 2015 at the [Wayback Machine](#).

<div>V • I • E •</div>	<div>Vitamins (A11)</div>	<div>[show]</div>
<div>V • I • E •</div>	<div>Dietary supplements</div>	<div>[show]</div>

Acetylcholine receptor modulators [show]	
 · · · Acetylcholine metabolism and transport modulators [show]	
Authority control	LCCN: sh85024656 ^{} · BNF: cb122695833 ^{} (data) ^{} · NDL: 00566629 ^{} ·

Categories: Alcohols | Cholinergics | Quaternary ammonium compounds | Dietary supplements | Vitamins