

SEACURRENT

INTELLIGENT ENERGY™

Ingredient Panel

Serving Size: 6g
Servings per container: 60

Alpha Keto Gluterate 150mg
Glycine..... 125mg
Magnesium 75mg
Niacinamide 20mg
*Cola nut extract 20mg



Proprietary blend of:

Calcium chelate, D-ribose, manganese, molybdenum, Tyrosine, Glutamate, Iron chelate, Pyruvate, Ionic sea minerals, Omega-3.....4.5g

Other ingredients..... Microcrystalline fructose, natural citrus flavor, natural kiwi flavor, stevia

**The Cola nut extract contains less than 2% unrefined caffeine (.4 grams) per serving meaning there is essentially NO refined or synthetic stimulant in the formula. Cola nut is used for flavor.*

Seabiotics SeaCurrent™

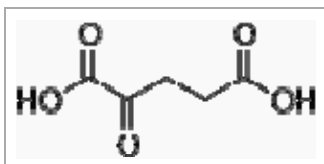
NEW PRODUCT IDENTIFICATION

FDA CFR 21 Part II

ALPHA KETO GLUTERATE

Alpha-ketoglutaric acid (CAS # 328-50-7) is one of two ketone derivatives of glutaric acid. (The term "ketoglutaric acid," when not further qualified, almost always refers to the alpha variant. Beta-ketoglutaric acid varies only by the position of the ketone functional group, and is much less common.)

Its anion, Alpha-ketoglutarate (also called oxo-glutarate) is an important biological compound. It is the keto acid produced by de-amination of glutamate, and is an intermediate in the Krebs cycle.



Another function is to combine with nitrogen released in the cell, therefore preventing nitrogen overload.

Alpha-ketoglutarate is one of the most important nitrogen transporter in metabolic pathways. The amino groups of amino acids are attached to it by transamination and carried to the liver where the urea cycle takes place.

Alpha-ketoglutarate is transaminated, along with glutamine, to form the excitatory neurotransmitter glutamate. Glutamate can then be decarboxylated (requiring vitamin B₆) into the inhibitory neurotransmitter GABA.

It is reported that high ammonia and/or high nitrogen levels may occur with high protein intake, excessive aluminum exposure, Reye's syndrome, cirrhosis, and urea cycle disorder.

Relationship to molecular oxygen

Acting as a co-substrate, it also plays important function in oxidation reactions involving molecular oxygen.

Molecular oxygen (O₂) directly oxidizes many compounds to produce useful products in an organism, such as antibiotics, etc., in reactions catalyzed by oxygenases. In many oxygenases, alpha-ketoglutarate helps the reaction by being oxidized together with the main substrate. In fact, one of the alpha-ketoglutarate-dependent oxygenases is an O₂ sensor, informing the organism the oxygen level in its environment.

Dietary supplement

Alpha-ketoglutaric acid is sold as a dietary supplement and to body builders as AKG or a-KG. Some believe it increases stamina.

Production

Alpha-ketoglutarate can be produced by:

- Oxidative decarboxylation of isocitrate by isocitrate dehydrogenase;
- Oxidative deamination of glutamate by glutamate dehydrogenase.

Alpha-ketoglutarate can be used to produce:

- Creatine-alpha ketoglutarate

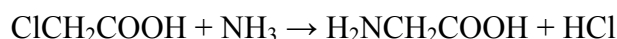
References

Merck Index, 13th Edition, 5320.

GLYCINE

Glycine (abbreviated as Gly or G) is the organic compound with the formula $\text{NH}_2\text{CH}_2\text{COOH}$. It is the smallest of the 20 amino acids commonly found in proteins, coded by codons GGU, GGC, GGA and GGG. Glycine is unique among the proteinogenic amino acids in that it is not chiral. Most proteins contain only small quantities of glycine. A notable exception is collagen, which contains about 35% glycine. In its solid, i.e., crystallized, form, glycine is a free-flowing, sweet-tasting crystalline material.

Glycine is manufactured industrially, either by treating chloroacetic acid with ammonia:

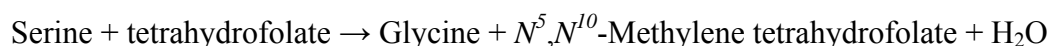


or via the Strecker amino acid synthesis.

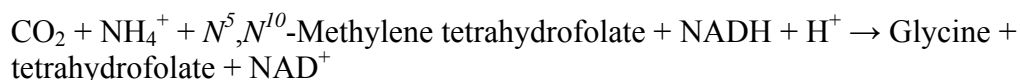
There are two producers of glycine in the United States. Chattem Chemicals, Inc., purchased by Sun Pharmaceutical, Mumbai, India and GEO Specialty Chemicals, Inc., who purchased the glycine and naphthalene sulfonate production facilities of Dow/Hampshire Chemical Corp.

Biosynthesis

Glycine is not essential to the human diet, since it is biosynthesized in the body from the amino acid serine, which is in turn derived from 3-phosphoglycerate. In most organisms, the enzyme Serine hydroxymethyltransferase catalyses this transformation by removing one carbon atom; pyridoxal phosphate is also necessary.

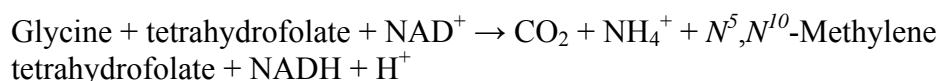


In the liver of vertebrates, glycine synthesis is catalyzed by glycine synthase (also called glycine cleavage enzyme). This conversion is readily reversible.



Degradation

Glycine is degraded via three pathways. The predominant pathway in animals involves the catalysis of glycine cleavage enzyme, the same enzyme also involved in the biosynthesis of glycine. The degradation pathway is the reverse of this synthetic pathway.



In the second pathway, glycine is degraded in two steps. The first step is the reverse of glycine biosynthesis from serine with serine hydroxymethyl transferase. Serine is then converted to pyruvate by serine dehydratase.

In the third pathway of glycine degradation, glycine is converted to glyoxylate by D-amino acid oxidase. Glyoxylate is then oxidized by hepatic lactate dehydrogenase to oxalate in an NAD⁺-dependent reaction.

Physiological function

As a biosynthetic intermediate

Glycine is a building block to numerous natural products. In higher eukaryotes, D-Aminolevulinic acid, the key precursor to porphyrins, is biosynthesized from glycine and succinyl-CoA. Glycine provides the central C₂N subunit of all purines.

As a neurotransmitter

Glycine is an inhibitory neurotransmitter in the central nervous system, especially in the spinal cord, brainstem, and retina. When glycine receptors are activated, chloride enters the neuron via ionotropic receptors, causing an Inhibitory postsynaptic potential (IPSP). Strychnine is a strong antagonist at ionotropic glycine receptors, whereas bicuculline is a weak one. Glycine is a required co-agonist along with glutamate for NMDA receptors. In contrast to the inhibitory role of glycine in the spinal cord, this behaviour is facilitated at the (NMDA) glutamergic receptors which are excitatory. The LD₅₀ of glycine is 7930 mg/kg in rats (oral), and it usually causes death by hyperexcitability.

As a potential antipsychotic

Dr. Daniel Javitt a clinical researcher had studied people who were addicted to PCP (angel dust) and Ketamine (special K) (Javitt, DC, Negative Schizophrenic Symptomatology and the Phencyclidine (PCP) Model of Schizophrenia, Hillside Journal of Psychiatry 1987 9:12-35. Their brains had been damaged by the use of this drug. In studies, it was found that their glutamate receptors had been damaged. Since use of PCP and ketamine creates psychosis similar to schizophrenia, it was hypothesized that giving glycine to people with schizophrenia would potentially reduce their psychotic symptoms. In a controlled study people with schizophrenia who were given glycine had their symptoms reduced in a measurable sense, primarily in the area of negative and cognitive symptoms when used as an adjunct to current antipsychotics. There have been some psychiatrists who have used it out of study as a primary antipsychotic with benefits on positive as well as negative and cognitive symptoms. Glycine's primary drawback is its required use in powdered format. However, as an NMDA receptor modulator, it is part of a class of antipsychotics in study that do not cause tardive dyskinesia or diabetes, the current long term side effects of dopaminergic antipsychotics as well as not creating extrapyramidal side effects (movement disorders), weight gain or sedation. These medications along with other new classes of medications in study may eventually replace

the current antipsychotics which, from Thorazine to Abilify, have all been based on the dopamine hypothesis and in depleting the levels of dopamine create tardive dyskinesia and other Parkinsonian movement disorders and potentially tardive psychosis which is still in study. Glycine, is part of a promising new class of treatment for schizophrenia that may promote a full recovery without debilitating physical side effects.

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1. ^ *Merck Index*, 11th Edition, 4386.
2. ^ IUPAC-IUBMB Joint Commission on Biochemical Nomenclature. "Nomenclature and Symbolism for Amino Acids and Peptides". *Recommendations on Organic & Biochemical Nomenclature, Symbols & Terminology etc.* Retrieved on 2007-05-17.
3. ^ Nelson, D. L. & Cox, M. M. (2005). *Lehninger Principles of Biochemistry*, 4th Edition. New York: W. H. Freeman and Company, p. 127. ISBN 0-7167-4339-6.
4. ^ <http://timesfreepress.com/news/2008/dec/03/chattanooga-mumbai-india-company-buys-chattem-chem/>
5. ^ U.S. International Trade Commission, "Glycine From China." Investigation No. 731-TA-718 (Second Review), Publication No. 3810, October 2005
6. ^ Nov. 1, 2005 Press Release [1]
7. ^ ^{a b} Nelson, D. L. & Cox, M. M. (2005). *Lehninger Principles of Biochemistry*, 4th Edition. New York: W. H. Freeman and Company, p. 844. ISBN 0-7167-4339-6.
8. ^ ^{a b c} Nelson, D. L. & Cox, M. M. (2005). *Lehninger Principles of Biochemistry*, 4th Edition. New York: W. H. Freeman and Company, pp. 675-677. ISBN 0-7167-4339-6.
9. ^ Nelson, D. L. & Cox, M. M. (2005). *Lehninger Principles of Biochemistry*, 4th Edition. New York: W. H. Freeman and Company, p. 854. ISBN 0-7167-4339-6.
10. ^ "Safety (MSDS) data for glycine". The Physical and Theoretical Chemistry Laboratory Oxford University (2005). Retrieved on 2006-11-01.
11. ^ "Notice of Preliminary Determination of Sales at Less Than Fair Value: Glycine From India" Federal Register 72 (7 November 2007): 62827.
12. ^ Glycine from the People's Republic of China, Inv. No. 731-TA-718 (Final),
13. USITC Pub. 2863 (Mar. 1995) ("Original Determination") at 1.

MAGNESIUM

Magnesium is a chemical element with the symbol Mg, atomic number 12, atomic weight 24.3050 and common oxidation number +2.

Magnesium, an alkaline earth metal, is the ninth most abundant element in the universe by mass. It constitutes about 2% of the Earth's crust by mass, which makes it the eighth most abundant element in the crust. It is the third most abundant element dissolved in seawater.

Magnesium is the 11th most abundant element by mass in the human body; its ions are essential to all living cells, but nearly 50% is found within the bones. The free element (metal) is not found on Earth. Once produced from magnesium salts, it is now mainly obtained by electrolysis of brine and is used as an alloying agent to make aluminium-magnesium alloys, sometimes called "magnalium" or "magnelium".

The magnesium ion is necessary for all life (see magnesium in biology), so magnesium salts are an additive for foods, fertilizers (Mg is a component of chlorophyll), and culture media.

Magnesium hydroxide is used in milk of magnesia, its chloride, oxide, gluconate, malate, orotate and citrate used as oral magnesium supplements, and its sulfate (Epsom salts) for various purposes in medicine, and elsewhere (see the article for more). Oral magnesium supplements have been claimed to be therapeutic for some individuals who suffer from Restless Leg Syndrome (RLS).

Magnesium borate, magnesium salicylate and magnesium sulfate are used as antiseptics.

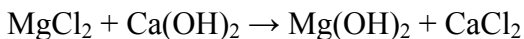
Magnesium bromide is used as a mild sedative (this action is due to the bromide, not the magnesium).

Dead-burned magnesite is used for refractory purposes such as brick and liners in furnaces and converters.

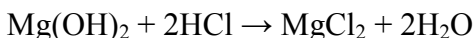
Magnesium carbonate (MgCO_3) powder is also used by athletes, such as gymnasts and weightlifters, to improve the grip on objects – the apparatus or lifting bar.

Magnesium from sea water

The Mg^{2+} cation is the second most abundant cation in seawater (occurring at about 12% of the mass of sodium there), which makes seawater and sea-salt an attractive commercial source of Mg. To extract the magnesium, calcium hydroxide is added to sea water to form magnesium hydroxide precipitate.



Magnesium hydroxide is insoluble in water so it can be filtered out, and reacted with hydrochloric acid to obtain concentrated magnesium chloride.



From magnesium chloride, electrolysis produces magnesium.

Biological role of magnesium

Magnesium ions are essential to the basic nucleic acid chemistry of life, and thus are essential to all cells of all known living organisms. Plants have an additional use for magnesium in that chlorophylls are magnesium-centered porphyrins. Many enzymes require the presence of magnesium ions for their catalytic action, especially enzymes utilizing ATP, or those which use other nucleotides to synthesize DNA and RNA. Magnesium deficiency in plants causes late-season yellowing between leaf veins, especially in older leaves, and can be corrected by applying epsom salts (which is rapidly leached), or else crushed dolomitic limestone to the soil.

Food sources of magnesium

Magnesium is a vital component of a healthy human diet, and plays a part in over 300 enzymes. Human magnesium deficiency is relatively common, with only 32% of the United States meeting the RDA-DRI, and has been implicated in the development of a number of human illnesses such as asthma, osteoporosis, and ADHD. Adult human bodies have about 24 grams of magnesium, with 60% in the skeleton, 39% intracellular (20% in skeletal muscle), and 1% extracellular. Serum levels are typically 0.7 – 1.0 mmol/L. Serum magnesium levels may appear normal even in cases of underlying intracellular deficiency, although no known mechanism maintains a homeostatic level in the blood. Intracellular magnesium is correlated with intracellular potassium. Magnesium is absorbed in the gastrointestinal tract, with more absorbed when status is lower. In humans, magnesium appears to facilitate calcium absorption. Low and high protein intake inhibit magnesium absorption, and other factors such as phosphate, phytate, and fat affect absorption. It is largely excreted through the feces. Magnesium status may be assessed roughly through serum and erythrocyte Mg concentrations and urinary and fecal excretion, but intravenous magnesium loading tests are likely the most accurate and practical in most people. In these tests, magnesium is injected intravenously; a retention of 20% or more indicates deficiency. Other nutrient deficiencies are identified through biomarkers, but none are established for magnesium.

Spices, nuts, cereals, coffee, cocoa, tea, and vegetables (especially green leafy ones) are rich sources of magnesium. Refining of food can reduce magnesium substantially, however, and fertilizers use less magnesium. This has led to observations of reduced dietary magnesium intake as compared to earlier generations.

There are a number of magnesium supplements available. Magnesium oxide, one of the most common, has been reported as the least bioavailable. Magnesium citrate has been reported as more bioavailable than oxide or amino-acid chelate (glycinate) forms.

Excess magnesium in the blood is freely filtered at the kidneys, and for this reason it is difficult to overdose on magnesium from dietary sources alone. With supplements overdose is possible, however, particularly in people with poor renal function, but severe hypermagnesemia can also occur without renal dysfunction. Alcoholism can produce a magnesium deficiency which is easily reversed by oral or parenteral administration, depending on the degree of deficiency.

CALCIUM CHELATED

One of the most abundant minerals in the human body, calcium accounts for approximately 1.5% of total body weight. Bones and teeth house 99% of the calcium in the body, while the remaining 1% is distributed in other areas.

Calcium also plays a role in many physiological activities not related to bones including blood clotting, nerve conduction, muscle contraction, regulation of enzyme activity, and cell membrane function. Because these physiological activities are essential to life, the body utilizes complex regulatory systems to tightly control the amount of calcium in the blood so that calcium is available for these activities. As a result, when dietary intake of calcium is too low to maintain normal blood levels of calcium, the body will draw on calcium stores in the bones to maintain normal blood concentrations, which, after many years, can lead to osteoporosis.

The following nutrients impact the absorption, utilization and/or excretion of calcium:

Vitamin D accelerates the absorption of calcium from the gastrointestinal tract.

High consumption of potassium reduces the urinary excretion of calcium.

High intakes of sodium, caffeine, or protein cause an increase in the urinary excretion of calcium.

Certain types of dietary fiber like the fiber found in wheat and oat bran, may interfere with calcium absorption by decreasing transit time (the amount of time it takes for digested foods to move through the intestines), limiting the amount of time during digestion for calcium to be absorbed. Dietary fiber also stimulates the proliferation of "friendly" bacteria in the gut, which bind calcium and make it less available for absorption.

Phytic acid, found in whole grains, nuts, and legumes, can bind to calcium to form an insoluble complex, thereby decreasing the absorption of calcium.

Oxalic acid, found in spinach, beets, celery, pecans, peanuts, tea and cocoa, can bind to calcium and form an insoluble complex that is excreted in the feces. While research studies confirm the ability of phytic acid and oxalic acid in foods to lower availability of calcium, the decrease in available calcium is relatively small.

Calcium impacts the absorption of the following nutrients:

Calcium in food and supplements decreases the absorption of heme and nonheme iron.

Magnesium and calcium compete with each other for intestinal absorption. Consequently, calcium supplements should not be taken at the same time as magnesium supplements.

Supplemental calcium is available in a variety of delivery forms including tablets, capsules, chewable tablets, antacids (for example, Tums(TM)) and fortified juices. Some dietary supplement manufacturers even sell chewy chocolate squares fortified with calcium. The different forms of calcium used in the manufacture of calcium supplements fall into three general categories: 1) naturally-derived calcium 2) refined calcium carbonate and 3) chelated calcium. Naturally-derived calcium, also known as unrefined calcium carbonate, appears in dietary supplements as bone meal, oyster shell, limestone, and dolomite (clay). Although these forms are typically less expensive than other forms of supplemental calcium, these supplements may also contain significant amounts of lead, a toxic metal that affects the brain, kidney, and red blood cells. Refined calcium carbonate is the most commonly used form of calcium in supplements. It is relatively inexpensive compared to chelated forms of calcium, but has been shown to be less well-absorbed than other forms. To improve absorption, calcium carbonate should be taken with meals, as the presence of food in the stomach causes the secretion of hydrochloric (stomach) acid, a compound that breaks down calcium carbonate. Chelated calcium is calcium bound to an organic acid, such as citrate, malate, lactate, or gluconate; or to an amino acid, such as aspartate. Research indicates that calcium chelates, especially calcium citrate, are more bioavailable than calcium carbonate. Calcium is also available as hydroxyapatite, the phosphorus-containing building block of the bone mineral matrix.

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D-RIBOSE

Ribose, primarily occurring as D-ribose (CAS 200-059-4), is an organic compound that occurs widely in nature. It is an aldopentose, that is a monosaccharide containing five carbon atoms that, in its acyclic form, has an aldehyde functional group at one end. Typically, this species exists in the cyclic form, as depicted in the upper right. It was first reported in 1905 by Phoebus Levene. It comprises the backbone of RNA, a biopolymer that is the basis of genetic transcription. It is related to deoxyribose, as found in DNA, by the removal of one hydroxy group. Ribose is also a subunit of ATP, NADH, and several other compounds that are critical to metabolism.

MANGANESE

Manganese (pronounced /ˈmæŋɡəni/) is a chemical element, designated by the symbol Mn. It has the atomic number 25. It is found as a free element in nature (often in combination with iron), and in many minerals. As a free element, manganese is a metal with important industrial metal alloy uses. Manganese ions are variously colored, and are used industrially as pigments and as oxidation chemicals. Manganese(II) ions function as cofactors for a number of enzymes; the element is thus a required trace mineral for all known living organisms.

Manganese is an essential trace nutrient in all forms of life.

The classes of enzymes that have manganese cofactors are very broad and include such classes as oxidoreductases, transferases, hydrolases, lyases, isomerases, ligases, lectins,

and integrins. The reverse transcriptases of many retroviruses (though not lentiviruses such as HIV) contain manganese. The best known manganese-containing polypeptides may be arginase, the diphtheria toxin, and Mn-containing superoxide dismutase (Mn-SOD).

Mn-SOD is the type of SOD present in eukaryotic mitochondria, and also in most bacteria (this fact is in keeping with the bacterial-origin theory of mitochondria). The Mn-SOD enzyme is probably one of the most ancient, for nearly all organisms living in the presence of oxygen use it to deal with the toxic effects of superoxide, formed from the 1-electron reduction of dioxygen. Exceptions include a few kinds of bacteria such as *Lactobacillus plantarum* and related lactobacilli, which use a different non-enzymatic mechanism, involving manganese (Mn^{2+}) ions complexed with polyphosphate directly for this task, indicating how this function possibly evolved in aerobic life.

The human body contains about 10 mg of manganese, which is stored mainly in the liver and kidneys.

Manganese is also important in photosynthetic oxygen evolution in chloroplasts in plants. The oxygen evolving complex (OEC), part of Photosystem II contained in the thylakoid membranes of chloroplasts, is responsible for the terminal photooxidation of water during the light reactions of photosynthesis, has a metalloenzyme core containing four atoms of manganese. For this reason, most broad-spectrum plant fertilizers contain manganese.

Manganese ore occurs principally as pyrolusite (MnO_2), braunite, ($Mn^{2+}Mn^{3+}6SiO_{12}$), psilomelane ($Ba(Mn^{2+})(Mn^{4+})_8O_{16}(OH)_4$), and to a lesser extent as rhodochrosite ($MnCO_3$). Land-based resources are large but irregularly distributed. Over 80% of the known world manganese resources are found in South Africa and Ukraine. Other important manganese deposits are in China, Australia, Brazil, Gabon, Ghana, India, and Mexico.

MOLYBDENUM

molybdenum (mə'līb`də'nəm) [Gr.,=leadlike], metallic chemical element; symbol Mo; at. no. 42; at. wt. 95.94; m.p. about 2,617°C;; b.p. about 4,612°C;; sp. gr. 10.22 at 20°C;; valence +2, +3, +4, +5, or +6. Molybdenum is a hard, malleable, ductile, high-melting, silver-white metal with a body-centered cubic crystalline structure. It is below chromium in Group 6 of the periodic table. Molybdenum resists corrosion at ordinary temperatures. In forming compounds, as in oxides, sulfides, and halides, it exhibits variable valence. In its most important compounds, however, it has an oxidation state of +6, as in the trioxide, which forms a series of compounds known as the molybdates. Molybdenum does not occur uncombined in nature (molybdenum disulfide, MoS_2). It also occurs in wulfenite (a lead molybdate) and powellite (a calcium molybdate-tungstate). It is widely but sparingly distributed throughout the world; it is found in the United States, Canada, Europe, Australia, Chile, Russia, and China. Large amounts of

molybdenite are mined at Climax, Colo. Molybdenum ore is also obtained as a byproduct of copper mining. The actual refining process depends on the ultimate use. The molybdenite may be purified for use in lubricants. Almost all molybdenum ore is converted by roasting to molybdic oxide, MoO_3 . The oxide may be added directly to steel or may be converted to ferromolybdenum by a thermal process; this alloy is used to add molybdenum to other iron and steel alloys. The oxide may be further purified by sublimation, or converting directly from the solid to vapor state, and then reduced to molybdenum powder by reaction with carbon, aluminum, or hydrogen. The oxide may be dissolved in ammonium hydroxide; the solution is filtered and evaporated to yield ammonium molybdate, $(\text{NH}_4)_2\text{Mo}_2\text{O}_7$. Molybdenum was recognized as a distinct element in 1778 by K. W. Scheele; its ore had earlier been confused with lead ore, hence its name. The element was isolated by P. J. Hjelm in 1782.

Tyrosine

Tyrosine (abbreviated as Tyr or Y) (CAS 60-18-4 or 4-hydroxyphenylalanine), is one of the 20 amino acids that are used by cells to synthesize proteins. This is a non-essential amino acid and it is found in casein. In fact, the word "tyrosine" is from the Greek *tyros*, meaning *cheese*, as it was first discovered in 1846 by German chemist Justus von Liebig in the protein casein from cheese.

Aside from being a proteogenic amino acid, tyrosine has a special role by virtue of the phenol functionality. It occurs in proteins that are part of signal transduction processes. It functions as a receiver of phosphate groups that are transferred by way of protein kinases (so-called receptor tyrosine kinases). Phosphorylation of the hydroxyl group changes the activity of the target protein.

A tyrosine residue also plays an important role in photosynthesis. In chloroplasts (photosystem II), it acts as an electron donor in the reduction of oxidized chlorophyll. In this process, it undergoes deprotonation of its phenolic OH-group. This radical is subsequently reduced in the photosystem II by the four core manganese cluster.

Biosynthesis

Plant biosynthesis of tyrosine from shikimic acid.

In plants and most microorganisms, tyr is produced via prephenate, an intermediate on the shikimate pathway. Prephenate is oxidatively decarboxylated with retention of the hydroxyl group to give *p*-hydroxyphenylpyruvate, which is transaminated using glutamate as the nitrogen source to give tyrosine and α -ketoglutarate.

Mammals synthesize tyrosine from the essential amino acid phenylalanine (phe), which is derived from food. The conversion of phe to tyr is catalyzed by the enzyme phenylalanine hydroxylase, a monooxygenase. This enzyme catalyzes the reaction

causing the addition of an hydroxyl group to the end of the 6-carbon aromatic ring of phenylalanine, such that it becomes tyrosine.

Metabolism

Catecholamine hormones produced from tyrosine metabolism.

Phosphorylation and sulfation

Some of the tyrosine residues can be *tagged* with a phosphate group (phosphorylated) by protein kinases. (In its phosphorylated state, it is referred to as phosphotyrosine). Tyrosine phosphorylation is considered to be one of the key steps in signal transduction and regulation of enzymatic activity. Phosphotyrosine can be detected through specific antibodies. Tyrosine residues may also be modified by the addition of a sulfate group, a process known as tyrosine sulfation.^[4] Tyrosine sulfation is catalyzed by tyrosylprotein sulfotransferase (TPST). Like the phosphotyrosine antibodies mentioned above, antibodies have recently been described that specifically detect sulfotyrosine.

Precursor to hormones

In the adrenal gland, tyrosine is converted to levodopa by the enzyme tyrosine hydroxylase (TH). TH is also the rate-limiting enzyme involved in the synthesis of the catecholamine hormones dopamine, norepinephrine (noradrenaline), and epinephrine.

The thyroid hormones triiodothyronine (T₃) and thyroxine (T₄) in the colloid of the thyroid also are derived from tyrosine.

Precursor to alkaloids

In *Papaver somniferum*, the opium poppy, tyrosine is used to produce the alkaloid morphine.

Precursor to pigments

Tyrosine is also the precursor to the pigment *melanin*.

Degradation

The decomposition of tyrosine to acetoacetate and fumarate. Two dioxygenases are necessary for the decomposition path. The end products can then enter into the citric acid cycle.

The decomposition of L-tyrosine (syn. *para*-hydroxyphenylalanine) begins with an α -ketoglutarate dependent transamination through the tyrosine transaminase to *para*-

hydroxyphenylpyruvate. The positional description *para*, abbreviated *p*, mean that the hydroxyl group and side chain on the phenyl ring are across from each other (see the illustration below).

The next oxidation step catalyzes by *p*-hydroxyphenylpyruvate-dioxygenase and splitting off CO₂ homogentisate (2,5-dihydroxyphenyl-1-acetate). In order to split the aromatic ring of homogentisate, a further dioxygenase, homogentisate-oxygenase is required. Thereby, through the incorporation of a further O₂ molecule, maleylacetoacetate is created.

Fumarylacetate is created maleylacetoacetate-*cis-trans*-isomerase through rotation of the carboxyl group created from the hydroxyl group via oxidation. This *cis-trans*-isomerase contains glutathione as a coenzyme. Fumarylacetoacetate is finally split via fumarylacetoacetate-hydrolase through the addition of a water molecule.

Thereby fumarate (also a metabolite of the citric acid cycle) and acetoacetate (3-ketobutyrate) are liberated. Acetoacetate is a ketone body, which is activated with succinyl-CoA, and thereafter it can be converted into acetyl-CoA which in turn can be oxidized by the citric acid cycle or be used for fatty acid synthesis.

Ortho- and meta-tyrosine

Enzymatic oxidation of tyrosine by phenylalanine hydroxylase (top) and non-enzymatic oxidation by hydroxyl free radicals (middle and bottom).

Three isomers of tyrosine are known. In addition to common amino acid L-tyrosine which is the *para* isomer (*para*-tyr, *p*-tyr or 4-hydroxyphenylalanine) there are two additional regioisomers, namely *meta*-tyrosine (*m*-tyr or 3-hydroxyphenylalanine or L-*m*-tyrosine) and *ortho*-tyrosine (*o*-tyr or 2-hydroxyphenylalanine) which occur in nature. The *m*-tyr and *o*-tyr isomers, which are rare, arise through non-enzymatic free-radical hydroxylation of phenylalanine under conditions of oxidative stress.

m-Tyrosine and analogues (rare in nature and therefore available synthetically) have shown application in Parkinson's Disease, Alzheimer's disease and arthritis.

Medical use

Tyrosine is a starting material for neurotransmitters and increases plasma neurotransmitter levels (particularly dopamine and norepinephrine) but has little if any effect on mood. The effect on mood is more noticeable in humans subjected to stressful conditions (see below).

A number of studies have found tyrosine to be useful during conditions of stress, cold, fatigue, prolonged work and sleep deprivation, with reductions in stress hormone levels, reductions in stress-induced weight loss seen in animal trials, improvements in cognitive

and physical performance seen in human trials. Because tyrosine hydroxylase is the rate limiting enzyme, however, effects are less significant than those of l-dopa.

Tyrosine does not seem to have any significant effect on mood, cognitive or physical performance in normal circumstances. A daily dosage supported in the literature is about 100 mg/kg for an adult. The usual dosage amounts to 500-1500 mg per day (dose suggested by most manufacturers; usually an equivalent to 1-3 capsules of pure tyrosine). It is not recommended to exceed 12000 mg (12 g) per day. In fact, too high doses result in reduced levels of dopamine. Tyrosine may decrease the absorption of other amino acids in high or chronic doses. It decreases absorption of l-dopa.

GLUTAMATE

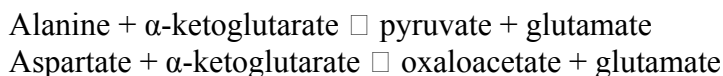
Glutamic acid (abbreviated as Glu or E) is one of the 20 proteinogenic amino acids and its codons are GAA and GAG. It is a non-essential amino acid. (CAS # 56-86-0) The carboxylate anions and salts of glutamic acid are known as glutamates. □

Metabolism

Glutamate is a key molecule in cellular metabolism. In humans, dietary proteins are broken down by digestion into amino acids, which serves as metabolic fuel for other functional roles in the body. A key process in amino acid degradation is transamination, in which the amino group of an amino acid is transferred to an α -ketoacid, typically catalysed by a transaminase. The reaction can be generalised as such:



A very common α -ketoacid is α -ketoglutarate, an intermediate in the citric acid cycle. Transamination of α -ketoglutarate gives glutamate. The resulting α -ketoacid product is often a useful one as well, which can contribute as fuel or as a substrate for further metabolism processes. Examples are as follows:



Both pyruvate and oxaloacetate are key components of cellular metabolism, contributing as substrates or intermediates in fundamental processes such as glycolysis, gluconeogenesis and also the citric acid cycle.

Glutamate also plays an important role in the body's disposal of excess or waste nitrogen. Glutamate undergoes deamination, an oxidative reaction catalysed by glutamate dehydrogenase, as follows:



Ammonia (as ammonium) is then excreted predominantly as urea, synthesised in the liver. Transamination can thus be linked to deamination, effectively allowing nitrogen from the amine groups of amino acids to be removed, via glutamate as an intermediate, and finally excreted from the body in the form of urea.

Neurotransmitter

Glutamate is the most abundant excitatory neurotransmitter in the mammalian nervous system. At chemical synapses, glutamate is stored in vesicles. Nerve impulses trigger release of glutamate from the pre-synaptic cell. In the opposing post-synaptic cell, glutamate receptors, such as the NMDA receptor, bind glutamate and are activated. Because of its role in synaptic plasticity, it is believed that glutamic acid is involved in cognitive functions like learning and memory in the brain.

Glutamate transporters are found in neuronal and glial membranes. They rapidly remove glutamate from the extracellular space. In brain injury or disease, they can work in reverse and excess glutamate can accumulate outside cells. This process causes calcium ions to enter cells via NMDA receptor channels, leading to neuronal damage and eventual cell death, and is called excitotoxicity. The mechanisms of cell death include

- Damage to mitochondria from excessively high intracellular Ca^{2+}
- $\text{Glu}/\text{Ca}^{2+}$ -mediated promotion of transcription factors for pro-apoptotic genes, or downregulation of transcription factors for anti-apoptotic genes.

Excitotoxicity due to glutamate occurs as part of the ischemic cascade and is associated with stroke and diseases like amyotrophic lateral sclerosis, lathyrism, autism, some forms of mental retardation and Alzheimer's disease.

Glutamic acid has been implicated in epileptic seizures. Microinjection of glutamic acid into neurons produces spontaneous depolarisations around one second apart, and this firing pattern is similar to what is known as paroxysmal depolarizing shift in epileptic attacks. This change in the resting membrane potential at seizure foci could cause spontaneous opening of voltage-activated calcium channels, leading to glutamic acid release and further depolarization.

Experimental techniques to detect glutamate in intact cells include using a genetically-engineered nanosensor. The sensor is a fusion of a glutamate-binding protein and two fluorescent proteins. When glutamate binds, the fluorescence of the sensor under ultraviolet light changes by resonance between the two fluorophores. Introduction of the nanosensor into cells enables optical detection of the glutamate concentration. Synthetic analogs of glutamic acid that can be activated by ultraviolet light have also been described. This method of rapidly uncaging by photostimulation is useful for mapping the connections between neurons, and understanding synapse function.

Brain nonsynaptic glutamatergic signaling circuits

Extracellular glutamate in *Drosophila* brains has been found to regulate postsynaptic glutamate receptor clustering, via a process involving receptor desensitization^[7]. A gene expressed in glial cells actively transports glutamate into the extracellular space^[7], while in the nucleus accumbens stimulating group II metabotropic glutamate receptors, this gene was found to reduce extracellular glutamate levels^[8]. This raises the possibility that this extracellular glutamate plays an "endocrine-like" role as part of a larger homeostatic system.

GABA precursor

Glutamic acid also serves as the precursor for the synthesis of the inhibitory GABA in GABA-ergic neurons. This reaction is catalyzed by glutamic acid decarboxylase (GAD), which is most abundant in the cerebellum and pancreas.

Stiff-man syndrome is a neurologic disorder caused by anti-GAD antibodies, leading to a decrease in GABA synthesis and therefore, impaired motor function such as muscle stiffness and spasm. Since the pancreas is also abundant for the enzyme GAD, a direct immunological destruction occurs in the pancreas and the patients will have diabetes mellitus.

Nutrient

All meats, poultry, fish, eggs, dairy products, as well kombu are excellent sources of glutamic acid. Some protein-rich plant foods also serve as sources. Ninety-five percent of the dietary glutamate is metabolized by intestinal cells in a first pass^[5]

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IRON

Iron, one of the most abundant metals on Earth, is essential to most life forms and to normal human physiology. Iron is an integral part of many proteins and enzymes that maintain good health. In humans, iron is an essential component of proteins involved in oxygen transport . It is also essential for the regulation of cell growth and differentiation . A deficiency of iron limits oxygen delivery to cells, resulting in fatigue, poor work performance, and decreased immunity [1,5-6]. On the other hand, excess amounts of iron can result in toxicity and even death .

Almost two-thirds of iron in the body is found in hemoglobin, the protein in red blood cells that carries oxygen to tissues. Smaller amounts of iron are found in myoglobin, a protein that helps supply oxygen to muscle, and in enzymes that assist biochemical reactions. Iron is also found in proteins that store iron for future needs and that transport iron in blood. Iron stores are regulated by intestinal iron absorption .

What foods provide iron?

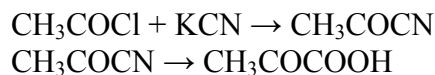
There are two forms of dietary iron: heme and nonheme. Heme iron is derived from hemoglobin, the protein in red blood cells that delivers oxygen to cells. Heme iron is found in animal foods that originally contained hemoglobin, such as red meats, fish, and poultry. Iron in plant foods such as lentils and beans is arranged in a chemical structure called nonheme iron. This is the form of iron added to iron-enriched and iron-fortified foods. Heme iron is absorbed better than nonheme iron, but most dietary iron is nonheme iron

Pyruvate

Pyruvic acid ($\text{CH}_3\text{COCO}_2\text{H}$) is the simplest alpha-keto acid. The carboxylate anion of pyruvic acid is known as pyruvate. (CAS # 127-17-3) Pyruvate plays an important role in biochemical processes.

Pyruvic acid is a colorless liquid with a smell similar to that of acetic acid. It is miscible with water, and soluble in ethanol and diethyl ether. In the laboratory, pyruvic acid may be prepared by heating a mixture of tartaric acid and potassium hydrogen sulfate, by the oxidation of propylene glycol by a strong oxidizer (eg. potassium permanganate or

bleach), or by the hydrolysis of acetyl cyanide, formed by reaction of acetyl chloride with potassium cyanide:



Biochemistry

Pyruvate is an important chemical compound in biochemistry. It is the output of the aerobic metabolism of glucose known as glycolysis. One molecule of glucose breaks down into two molecules of pyruvate, which are then used to provide further energy, in one of two ways. Pyruvate is converted into acetyl-coenzyme A, which is the main input for a series of reactions known as the Krebs cycle. Pyruvate is also converted to oxaloacetate by an anaplerotic reaction which replenishes Krebs cycle intermediates; alternatively, the oxaloacetate is used for gluconeogenesis. These reactions are named after Hans Adolf Krebs, the biochemist awarded the 1953 Nobel Prize for physiology, jointly with Fritz Lipmann, for research into metabolic processes. The cycle is also called the citric acid cycle, because citric acid is one of the intermediate compounds formed during the reactions.

If insufficient oxygen is available, the acid is broken down anaerobically, creating lactate in animals and ethanol in plants. Pyruvate from glycolysis is converted by anaerobic respiration to lactate using the enzyme lactate dehydrogenase and the coenzyme NADH in lactate fermentation, or to acetaldehyde and then to ethanol in alcoholic fermentation.

Pyruvate is a key intersection in the network of metabolic pathways. Pyruvate can be converted to carbohydrates via gluconeogenesis, to fatty acids or energy through acetyl-CoA, to the amino acid alanine and to ethanol. Therefore it unites several key metabolic processes.

The pyruvic acid derivative bromopyruvic acid is being studied for potential cancer treatment applications by researchers at Johns Hopkins University in ways that would support the Warburg hypothesis on the cause(s) of cancer.

Pyruvate production by glycolysis

In glycolysis, phosphoenolpyruvate (PEP) is converted to pyruvate by pyruvate kinase. This reaction is strongly exergonic and irreversible; in gluconeogenesis it takes two enzymes, pyruvate carboxylase and PEP carboxykinase to catalyze the reverse transformation of pyruvate to PEP.

OMEGA 3

Omega3 fatty acids are vital building blocks of our cell membranes, signaling pathways and neurological systems. They play a critical role in many functions in the body and are essential for good health.

These health effects were noted at first by studying the Inuit Indians, which ate a diet of marine and fish wildlife and had a significantly reduced risk of heart disease.

The benefits of omega3 fatty acids in cardiovascular disease are so well demonstrated that the American Heart Association has published statements since 1996 recommending increased fish intake and/or omega3 supplements. Scientists and physicians have also discovered many other benefits of omega-3 fatty acids and the research and benefits continue to grow.

Omega3 fatty acids are nutrients that are essential for good health. Omega3 fatty acids control blood clotting and building cell membranes in the brain, and since our bodies cannot make omega3 fats, we must get them through food or supplements.

Omega-3 fatty acids have many health benefits, including protection against heart disease and possibly even stroke. Additionally, omega3 fatty acids in high doses (e.g 6 to 10 capsules per day) are being used to treat depression. New studies are being published that show benefits for a wide range of conditions including cancer, lupus, psoriasis and rheumatoid arthritis.

NIACINAMIDE

Nicotinamide, also known as niacinamide and nicotinic acid amide,

Molecular formula	$C_6H_6N_2O$
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is the amide of nicotinic acid (vitamin B₃). Nicotinamide is a water-soluble vitamin and is part of the vitamin B group. Nicotinic acid, also known as niacin, is converted to niacinamide *in vivo*, and though the two are identical in their vitamin functions, niacinamide does not have the same pharmacologic and toxic effects of niacin, which occur incidental to niacin's conversion. Thus niacinamide does not reduce cholesterol or cause flushing, although nicotinamide may be toxic to the liver at doses exceeding 3 g/day for adults. In cells, niacin is incorporated into nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), although the pathways for nicotinamide and nicotinic acid are very similar. NAD⁺ and NADP⁺ are coenzymes in a wide variety of enzymatic oxidation-reduction reactions.

Nicotinamide has demonstrated anti-inflammatory actions which may be of benefit in patients with inflammatory skin conditions. These conditions include acne vulgaris, and the compound can suppress antigen induced-lymphocytic transformation and inhibit of 3'-5' cyclic AMP phosphodiesterase. Nicotinamide has demonstrated the ability to block

the inflammatory actions of iodides known to precipitate or exacerbate inflammatory acne.

Animal studies show that nicotinamide has anti-anxiety (anxiolytic) properties. It may work in a way similar to benzodiazepines.

Nicomide (take note the naming similarity), is an acne medication, and in its vitamin supplement form, the most predominant ingredient is 750 mg of nicotinamide, based on this area of research.

Nicotinamide lacks the vasodilator, gastrointestinal, hepatic, and hypolipemic actions of nicotinic acid. As such nicotinamide has not been shown to produce the flushing, itching and burning sensations of the skin as is commonly seen when large doses of nicotinic acid are administered orally. However, nicotinamide can produce liver toxicity at high doses. In overall, it rarely causes side effects, and is considered generally safe as a food additive, component in cosmetics and medication.

Nicotinamide is produced by the aqueous ammonolysis of 3-cyanopyridine (nicotinonitrile) and subsequent crystallisation.

Nicotinamide has been reported to restore cognition in Alzheimer's Disease transgenic mice.

Nicotinamide has been reported to increase the endurance of mice.

Nicotinamide, or Vitamin B3, prevents immunosuppression caused by UVA and UVB radiation, and could be added to sunscreen.

Nicotinamide has been reported to be an effective skin whitener in topical application.

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