Underactive Thyroid

Information collated from Wikipedia
By
Your Online Consultant

This booklet accompanies the article: "Thyroid health supplements: do they work?"
http://health-matters.yolasite.com/thyroidsupplements.php

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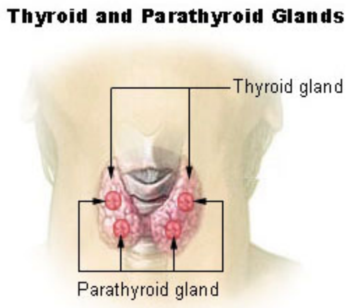
	
Thyroid and parathyroid.	
Latin	*glandula thyroidea*
Gray's	*subject #272 1269* [1]
System	Endocrine system
Precursor	Thyroid diverticulum (an extension of endoderm into 2nd Branchial arch)
MeSH	*Thyroid+Gland* [2]
Dorlands/Elsevier	*Thyroid gland* [3]

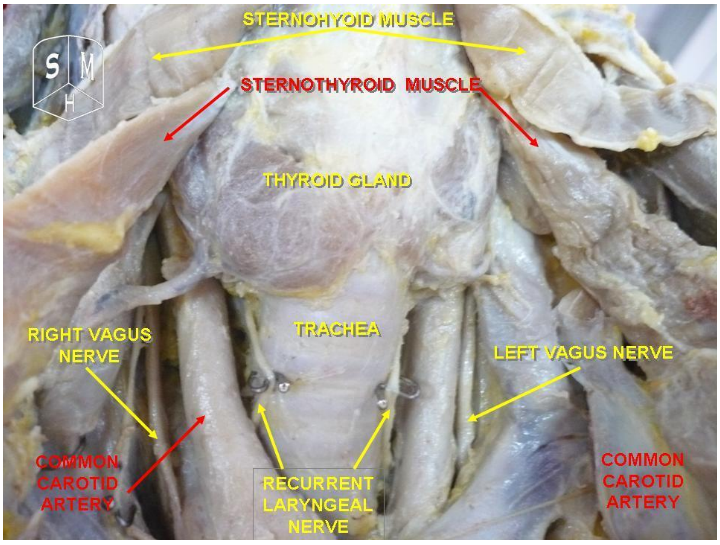
The **thyroid gland** or simply, the **thyroid** /ˈθaɪrɔɪd/, in vertebrate anatomy, is one of the largest endocrine glands. The thyroid gland is found in the neck, below the thyroid cartilage (which forms the laryngeal prominence, or "Adam's apple"). The isthmus (the bridge between the two lobes of the thyroid) is located inferior to the cricoid cartilage.

The thyroid gland controls how quickly the body uses energy, makes proteins, and controls how sensitive the body is to other hormones. It participates in these processes by producing thyroid hormones, the principal ones being triiodothyronine (T_3) and thyroxine which can sometimes be referred to as tetraiodothyronine (T_4). These hormones regulate the rate of metabolism and affect the growth and rate of function of many other systems in the body. T_3 and T_4 are synthesized from both iodine and tyrosine. The thyroid also produces calcitonin, which plays a role in calcium homeostasis.

Hormonal output from the thyroid is regulated by thyroid-stimulating hormone (TSH) produced by the anterior pituitary, which itself is regulated by thyrotropin-releasing hormone (TRH) produced by the hypothalamus.

The thyroid gets its name from the Greek word for "shield", due to the shape of the related thyroid cartilage. The most common problems of the thyroid gland consist of an overactive thyroid gland, referred to as hyperthyroidism, and an underactive thyroid gland, referred to as hypothyroidism.

Anatomy



Thyroid gland

The thyroid gland is a butterfly-shaped organ and is composed of two cone-like lobes or wings, *lobus dexter* (right lobe) and *lobus sinister* (left lobe), connected via the isthmus. The organ is situated on the anterior side of the neck, lying against and around the larynx and trachea, reaching posteriorly the oesophagus and carotid sheath. It starts cranially at the oblique line on the thyroid cartilage (just below the laryngeal prominence, or 'Adam's Apple'), and extends inferiorly to approximately the fifth or sixth tracheal ring.[4] It is difficult to demarcate the gland's upper and lower border with vertebral levels because it moves position in relation to these during swallowing.

The thyroid gland is covered by a fibrous sheath, the *capsula glandulae thyroidea*, composed of an internal and external layer. The external layer is anteriorly continuous with the *lamina pretrachealis fasciae cervicalis* and posteriorolaterally continuous with the carotid sheath. The gland is covered anteriorly with infrahyoid muscles and laterally with the sternocleidomastoid muscle also known as sternomastoid muscle. On the posterior side, the gland is fixed to the cricoid and tracheal cartilage and cricopharyngeus muscle by a thickening of the fascia to form the posterior suspensory ligament of Berry.[5][6] The thyroid gland's firm attachment to the underlying trachea is the reason behind its movement with swallowing.[7] In variable extent, Lalouette's Pyramid, a pyramidal extension of the thyroid lobe, is present at the most anterior side of the lobe. In this region, the recurrent laryngeal nerve and the inferior thyroid artery pass next to or in the ligament and tubercle.

Between the two layers of the capsule and on the posterior side of the lobes, there are on each side two parathyroid glands.

The thyroid isthmus is variable in presence and size, can change shape and size, and can encompass a cranially extending pyramid lobe (*lobus pyramidalis* or *processus pyramidalis*), remnant of the thyroglossal duct. The thyroid is one of the larger endocrine glands, weighing 2-3 grams in neonates and 18-60 grams in adults, and is increased in pregnancy.

The thyroid is supplied with arterial blood from the superior thyroid artery, a branch of the external carotid artery, and the inferior thyroid artery, a branch of the thyrocervical trunk, and sometimes by the thyroid ima artery, branching directly from the brachiocephalic trunk. The venous blood is drained via superior thyroid veins, draining in the internal jugular vein, and via inferior thyroid veins, draining via the *plexus thyroideus impar* in the left brachiocephalic vein.

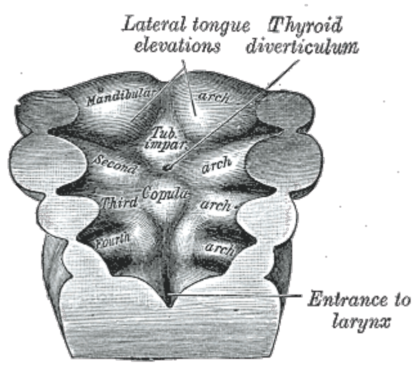
Lymphatic drainage passes frequently the lateral deep cervical lymph nodes and the pre- and parathracheal lymph nodes. The gland is supplied by parasympathetic nerve input from the superior laryngeal nerve and the recurrent laryngeal nerve.

Evolution

Phylogenetically, thyroid cells are derived from primitive iodide-concentrating gastroenteric cells. Given the essential nature of iodine compounds in living organisms, organisms moving from iodine-rich seas to iodine-deficient land needed stronger systems for uptake and storage of that element. The thyroid appears to have evolved to serve that need. Venturi et al.[8] suggested that iodide has an ancestral antioxidant function in all iodide-concentrating cells from primitive algae to more recent vertebrates. In 2008, this ancestral antioxidant action of iodides has been experimentally confirmed by Küpper et al.[9] Thyroxine has a 700 million year history. It is present, while showing no hormonal action, in the fibrous exoskeletal scleroproteins of the lowest invertebrates, Porifera and Anthozoa. The active hormone, triiodothyronine (T_3), became active in metamorphosis and thermogenesis, allowing for better adaptation of organisms to terrestrial environment (fresh water, atmosphere, gravity, temperature and diet).

Embryological development

In the fetus, at 3–4 weeks of gestation, the thyroid gland appears as an epithelial proliferation in the floor of the pharynx at the base of the tongue between the tuberculum impar and the copula linguae at a point later indicated by the foramen cecum. The thyroid then descends in front of the pharyngeal gut as a bilobed diverticulum through the thyroglossal duct. Over the next few weeks, it migrates to the base of the neck, passing anterior to the hyoid bone. During migration, the thyroid remains connected to the tongue by a narrow canal, the thyroglossal duct.



Floor of pharynx of embryo between 18 and 21 days.

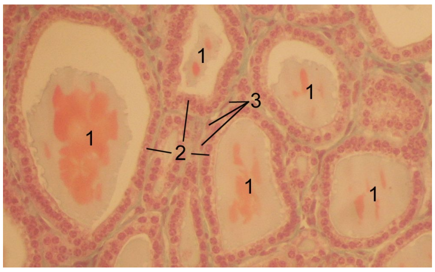
Thyrotropin-releasing hormone (TRH) and thyroid-stimulating hormone (TSH) start being secreted from the fetal hypothalamus and pituitary at 18-20 weeks of gestation, and fetal production of thyroxine (T_4) reach a clinically significant level at 18–20 weeks.[10] Fetal triiodothyronine (T_3) remains low (less than 15 ng/dL) until 30 weeks of gestation, and increases to 50 ng/dL at term.[10] Fetal self-sufficiency of thyroid hormones protects the fetus against e.g. brain development abnormalities caused by maternal hypothyroidism.[11] However, preterm births can suffer neurodevelopmental disorders due to lack of maternal thyroid hormones due their own thyroid being insufficiently developed to meet their postnatal needs.[12]

The portion of the thyroid containing the parafollicular C cells, those responsible for the production of calcitonin, are derived from the neural crest. This is first seen as the ultimobranchial body, which joins the primordial thyroid gland during its descent to its final location in the anterior neck.

Aberrations in embryological development can cause various forms of thyroid dysgenesis.

Histology

At the microscopic level, there are three primary features of the thyroid:[13]



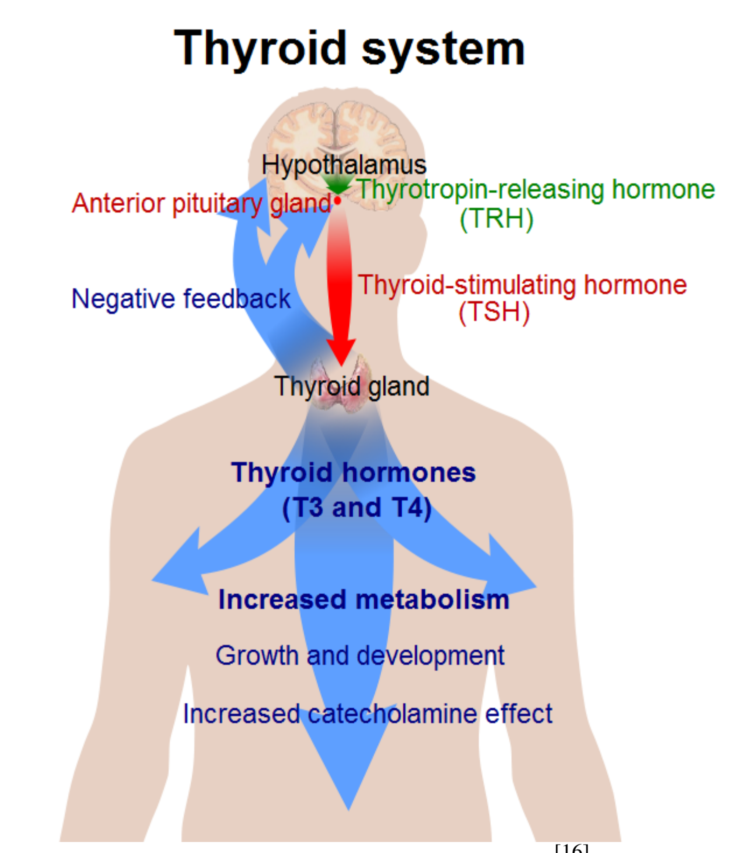
Histological section through the thyroid of a horse. 1 follicles, 2 follicular epithelial cells, 3 endothelial cells

Feature	Description
Follicles	The thyroid is composed of spherical follicles that selectively absorb iodine (as iodide ions, I^-) from the blood for production of thyroid hormones, but also for storage of iodine in thyroglobulin, in fact iodine is necessary for other important iodine-concentrating organs as breast, stomach, salivary glands, thymus etc. (see iodine in biology). Twenty-five percent of all the body's iodide ions are in the thyroid gland. Inside the follicles, colloid serves as a reservoir of materials for thyroid hormone production and, to a lesser extent, acts as a reservoir for the hormones themselves. Colloid is rich in a protein called thyroglobulin.
Thyroid epithelial cells (or "follicular cells")	The follicles are surrounded by a single layer of thyroid epithelial cells, which secrete T_3 and T_4. When the gland is not secreting T_3/T_4 (inactive), the epithelial cells range from low columnar to cuboidal cells. When active, the epithelial cells become tall columnar cells.
Parafollicular cells (or "C cells")	Scattered among follicular cells and in spaces between the spherical follicles are another type of thyroid cell, parafollicular cells, which secrete calcitonin.

Physiology

The primary function of the thyroid is production of the hormones triiodothyronine (T_3), thyroxine (T_4), and calcitonin. Up to 80% of the T_4 is converted to T_3 by peripheral organs such as the liver, kidney and spleen. T_3 is several times more powerful than T_4, which is largely a prohormone, perhaps four[14] or even ten times more active.[15]

T_3 and T_4 production and action

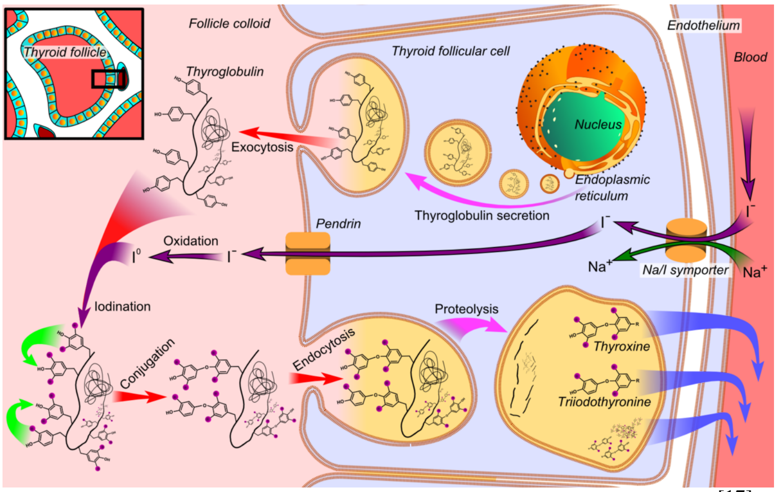


The system of the thyroid hormones T_3 and T_4.[16]

Thyroxine (T_4) is synthesised by the follicular cells from free tyrosine and on the tyrosine residues of the protein called thyroglobulin (Tg). Iodine is captured with the "iodine trap" by the hydrogen peroxide generated by the enzyme thyroid peroxidase (TPO)[19] and linked to the 3' and 5' sites of the benzene ring of the tyrosine residues on Tg, and on free tyrosine. Upon stimulation by the thyroid-stimulating hormone (TSH), the follicular cells reabsorb Tg and cleave the iodinated tyrosines from Tg in lysosomes, forming T_4 and T_3 (in T_3, one iodine atom is absent compared to T_4), and releasing them into the blood. Deiodinase enzymes convert T_4 to T_3.[20] Thyroid hormone secreted from the gland is about 80-90% T_4 and about 10-20% T_3.[14][15]

Cells of the developing brain are a major target for the thyroid hormones T_3 and T_4. Thyroid hormones play a particularly crucial role in brain maturation during fetal development.[21] A transport protein that seems to be important for T_4 transport across the blood–brain barrier (OATP1C1 [22]) has been identified.[23] A second transport protein (MCT8 [24]) is important for T_3 transport across brain cell membranes.[23]

Non-genomic actions of T_4 are those that are not initiated by liganding of the hormone to intranuclear thyroid receptor. These may begin at the plasma membrane or within cytoplasm. Plasma membrane-initiated actions begin at a receptor on the integrin alphaV beta3 that activates ERK1/2. This binding culminates in local membrane actions on ion transport systems such as the Na(+)/H(+) exchanger or complex cellular events including cell proliferation. These integrins are concentrated on cells of the vasculature and on some types of tumor cells, which in part explains the proangiogenic effects of iodothyronines and proliferative actions of thyroid hormone on some cancers including gliomas. T_4 also acts on the mitochondrial genome via imported isoforms of nuclear thyroid receptors to affect several mitochondrial transcription factors. Regulation of actin polymerization by T_4 is critical to cell migration in neurons and glial cells and is important to brain development.



Synthesis of the thyroid hormones, as seen on an individual thyroid follicular cell:[17]- Thyroglobulin is synthesized in the rough endoplasmic reticulum and follows the secretory pathway to enter the colloid in the lumen of the thyroid follicle by exocytosis. - Meanwhile, a sodium-iodide (Na/I) symporter pumps iodide (I^-) actively into the cell, which previously has crossed the endothelium by largely unknown mechanisms. - This iodide enters the follicular lumen from the cytoplasm by the transporter pendrin, in a purportedly passive manner.[18]- In the colloid, iodide (I^-) is oxidized to iodine (I^0) by an enzyme called thyroid peroxidase. - Iodine (I^0) is very reactive and iodinates the thyroglobulin at tyrosyl residues in its protein chain (in total containing approximately 120 tyrosyl residues). - In *conjugation*, adjacent tyrosyl residues are paired together.- The entire complex re-enters the follicular cell by endocytosis. - Proteolysis by various proteases liberates thyroxine and triiodothyronine molecules, which enters the blood by largely unknown mechanisms.

T_3 can activate phosphatidylinositol 3-kinase by a mechanism that may be cytoplasmic in origin or may begin at integrin alpha V beta3.

In the blood, T_4 and T_3 are partially bound to thyroxine-binding globulin (TBG), transthyretin, and albumin. Only a very small fraction of the circulating hormone is free (unbound) - T_4 0.03% and T_3 0.3%. Only the free fraction has hormonal activity. As with the steroid hormones and retinoic acid, thyroid hormones cross the cell membrane and bind to intracellular receptors (α_1, α_2, β_1 and β_2), which act alone, in pairs or together with the retinoid X-receptor as transcription factors to modulate DNA transcription[25].

T_3 and T_4 regulation

The production of thyroxine and triiodothyronine is regulated by thyroid-stimulating hormone (TSH), released by the anterior pituitary. The thyroid and thyrotropes form a negative feedback loop: TSH production is suppressed when the T_4 levels are high.[26] The TSH production itself is modulated by thyrotropin-releasing hormone (TRH), which is produced by the hypothalamus and secreted at an increased rate in situations such as cold exposure (to stimulate thermogenesis). TSH production is blunted by somatostatin (SRIH), rising levels of glucocorticoids and sex hormones (estrogen and testosterone), and excessively high blood iodide concentration.

An additional hormone produced by the thyroid contributes to the regulation of blood calcium levels. Parafollicular cells produce calcitonin in response to hypercalcemia. Calcitonin stimulates movement of calcium into bone, in opposition to the effects of parathyroid hormone (PTH). However, calcitonin seems far less essential than PTH, as calcium metabolism remains clinically normal after removal of the thyroid (thyroidectomy), but not the parathyroids.

Disorders

Thyroid disorders include hyperthyroidism (abnormally increased activity), hypothyroidism (abnormally decreased activity) and thyroid nodules, which are generally benign thyroid neoplasms, but may be thyroid cancers. All these disorders may give rise to goiter, that is, an enlarged thyroid.

Hyperthyroidism

Hyperthyroidism, or overactive thyroid, is the overproduction of the thyroid hormones T_3 and T_4, and is most commonly caused by the development of Graves' disease, an autoimmune disease in which antibodies are produced which stimulate the thyroid to secrete excessive quantities of thyroid hormones. The disease can result in the formation of a toxic goiter as a result of thyroid growth in response to a lack of negative feedback mechanisms. It presents with symptoms such as a thyroid goiter, protruding eyes (exopthalmos), palpitations, excess sweating, diarrhea, weight loss, muscle weakness and unusual sensitivity to heat. The appetite is often increased.

Beta blockers are used to decrease symptoms of hyperthyroidism such as increased heart rate, tremors, anxiety and heart palpitations, and anti-thyroid drugs are used to decrease the production of thyroid hormones, in particular, in the case of Graves' disease. These medications take several months to take full effect and have side-effects such as skin rash or a drop in white blood cell count, which decreases the ability of the body to fight off infections. These drugs involve frequent dosing (often one pill every 8 hours) and often require frequent doctor visits and blood tests to monitor the treatment, and may sometimes lose effectiveness over time. Due to the side-effects and inconvenience of such drug regimens, some patients choose to undergo radioactive iodine-131 treatment. Radioactive iodine is administered in order to destroy a proportion of or the entire thyroid gland, since the radioactive iodine is selectively taken up by the gland and gradually destroys the cells of the gland. Alternatively, the gland may be partially or entirely removed surgically, though iodine treatment is usually preferred since the surgery is invasive and carries a risk of damage to the parathyroid glands or the nerves controlling the vocal cords. If the entire thyroid gland is removed, hypothyroidism results.[27]

Hypothyroidism

Hypothyroidism is the underproduction of the thyroid hormones T_3 and T_4. Hypothyroid disorders may occur as a result of congenital thyroid abnormalities (see congenital hypothyroidism), autoimmune disorders such as Hashimoto's thyroiditis, iodine deficiency (more likely in poorer countries) or the removal of the thyroid following surgery to treat severe hyperthyroidism and/or thyroid cancer. Typical symptoms are abnormal weight gain, tiredness, baldness, cold intolerance, and bradycardia. Hypothyroidism is treated with hormone replacement therapy, such as levothyroxine, which is typically required for the rest of the patient's life. Thyroid hormone treatment is given under the care of a physician and may take a few weeks to become effective.[28]

Negative feedback mechanisms result in growth of the thyroid gland when thyroid hormones are being produced in sufficiently low quantities as a means of increasing the thyroid output; however, where the hypothyroidism is caused by iodine insufficiency, the thyroid is unable to produce T_3 and T_4 and as a result, the thyroid may continue to grow to form a non-toxic goiter. It is termed non-toxic as it does not produce toxic quantities of thyroid hormones, despite its size.

Initial hyperthyroidism followed by hypothyroidism

This is the overproduction of T_3 and T_4 followed by the underproduction of T_3 and T_4. There are two types: Hashimoto's thyroiditis and postpartum thyroiditis.

Hashimoto's thyroiditis or Hashimoto's Disease is an autoimmune disorder whereby the body's own immune system reacts with the thyroid tissues in an attempt to destroy it. At the beginning, the gland may be overactive, and then becomes underactive as the gland is damaged resulting in too little thyroid hormone production or hypothyroidism. Some patients may experience "swings" in hormone levels that can progress rapidly from hyper-to-hypothyroid (sometimes mistaken as severe moodswings, or even being bipolar, before the proper clinical diagnosis is made). Some patients may experience these "swings" over a longer period of time, over days or weeks or even months. Hashimoto's is more common in females than males, usually appearing after the age of 30, and tends to run in families meaning it can be seen as a genetic disease. Also more common in individuals with Hashimoto's Thyroiditis are type 1 diabetes and celiac disease.[29]

Postpartum thyroiditis occurs in some females following the birth of a child. After delivery, the gland becomes inflamed and the condition initially presents with overactivity of the gland followed by underactivity. In some cases, the gland may recover with time and resume its functions. In others it may not. The etiology is not always known, but can sometimes be attributed to autoimmunity, such as Hashimoto's Thyroiditis or Graves' Disease.

Cancers

In most cases, the thyroid cancer presents as a painless mass in the neck. It is very unusual for the thyroid cancers to present with symptoms, unless it has been neglected. One may be able to feel a hard nodule in the neck. Diagnosis is made using a needle biopsy and various radiological studies.[30]

Non-cancerous nodules

Further information: Thyroid nodule

Many individuals may find the presence of thyroid nodules in the neck. The majority of these thyroid nodules are benign (non cancerous). The presence of a thyroid nodule does not mean that one has thyroid disease. Most thyroid nodules do not cause any symptoms, and most are discovered on an incidental examination. Doctors usually perform a needle aspiration biopsy of the thyroid to determine the status of the nodules. If the nodule is found to be non-cancerous, no other treatment is required. If the nodule is suspicious then surgery is recommended.

Congenital anomalies

A persistent thyroglossal duct or cyst is the most common clinically significant congenital anomaly of the thyroid gland. A persistent sinus tract may remain as a vestigial remnant of the tubular development of the thyroid gland. Parts of this tube may be obliterated, leaving small segments to form cysts. These occur at any age and might not become evident until adult life. Mucinous, clear secretions may collect within these cysts to form either spherical masses or fusiform swellings, rarely larger than 2 to 3 cm in diameter. These are present in the midline of the neck anterior to the trachea. Segments of the duct and cysts that occur high in the neck are lined by stratified squamous epithelium, which is essentially identical to that covering the posterior portion of the tongue in the region of the foreamen cecum. The anomalies that occur in the lower neck more proximal to the thyroid gland are lined by epithelium resembling the thyroidal acinar epithelium. Characteristically, next to the lining epithelium, there is an intense lymphocytic inflitrate. Superimposed infection may convert these lesions into abscess cavities, and rarely, give rise to cancers.

Other disorders

- Limited research shows that seasonal allergies may trigger episodes of hypo- or hyperthyroidism.[31][32]
- A ectopic thyroid is an entire or parts of the thyroid located in another part of the body than what is the usual case.

Thyroid function tests

Test	Abbreviation	Normal ranges[33]
Serum thyrotropin/thyroid-stimulating hormone	**TSH**	**0.3–3.0 μU/ml**
Free thyroxine	**FT_4**	**7–18 ng/l = 0.7–1.8 ng/dl**
Serum triiodothyronine	**T_3**	**0.8–1.8 μg/l = 80–180 ng/dl**
Radioactive iodine-123 uptake	**RAIU**	**10–30%**
Radioiodine scan (gamma camera)	N/A	N/A - thyroid contrasted images
Free thyroxine fraction	FT4F	0.03–0.005%
Serum thyroxine	T_4	46–120 μg/l = 4.6–12.0 μg/dl
Thyroid hormone binding ratio	THBR	0.9–1.1
Free thyroxine index	FT4I	4–11
Free triiodothyronine l	FT_3	230–619 pg/d
Free T3 Index	FT3I	80–180
Thyroxine-binding globulin	TBG	12–20 ug/dl T4 +1.8 μg
TRH stimulation test	Peak TSH	9–30 μIU/ml at 20–30 min.
Serum thyroglobulin l	Tg	0-30 ng/m
Thyroid microsomal antibody titer	TMAb	Varies with method
Thyroglobulin antibody titer	TgAb	Varies with method

- μU/ml = mU/l, microunit per milliliter
- ng/dl, nanograms per deciliter
- μg, micrograms
- pg/d, picograms per day
- μIU/ml = mIU/l, micro-international unit per milliliter
- See [34] for more information on medical units of measure

Significance of iodine

In areas of the world where iodine is lacking in the diet, the thyroid gland can become considerably enlarged, a condition called endemic goiter. Pregnant women on a diet that is severely deficient of iodine can give birth to infants who can present with thyroid hormone deficiency (congenital hypothyroidism), manifesting in problems of physical growth and development as well as brain development (a condition referred to as endemic cretinism). In many developed countries, newborns are routinely tested for congenital hypothyroidism as part of newborn screening. Children with congenital hypothyroidism are treated supplementally with levothyroxine, which facilitates normal growth and development.

Thyroxine is critical to the regulation of metabolism and growth throughout the animal kingdom. Among amphibians, for example, administering a thyroid-blocking agent such as propylthiouracil (PTU) can prevent tadpoles from metamorphosing into frogs; in contrast, administering thyroxine will trigger metamorphosis.

Because the thyroid concentrates this element, it also concentrates the various radioactive isotopes of iodine produced by nuclear fission. In the event of large accidental releases of such material into the environment, the uptake of radioactive iodine isotopes by the thyroid can, in theory, be blocked by saturating the uptake mechanism with a large surplus of non-radioactive iodine, taken in the form of potassium iodide tablets. One consequence of the Chernobyl disaster was an increase in thyroid cancers in children in the years following the accident.[35]

The use of iodised salt is an efficient way to add iodine to the diet. It has eliminated endemic cretinism in most developed countries, and some governments have made the iodination of flour, cooking oil, and salt mandatory. Potassium iodide and sodium iodide are typically used forms of supplemental iodine.

As with most substances, either too much or too little can cause problems. Recent studies on some populations are showing that excess iodine intake could cause an increased prevalence of autoimmune thyroid disease, resulting in permanent hypothyroidism.[36]

History

There are several findings that evidence a great interest for thyroid disorders just in the Medieval Medical School of Salerno (12th century). Rogerius Salernitanus, the Salernitan surgeon and author of "Post mundi fabricam" (around 1180) was considered at that time the surgical text par excellence all over Europe. In the chapter "De bocio" of his magnum opus, he describes several pharmacological and surgical cures, some of which nowadays are reappraised quite scientifically effective.[37]

In modern times, the thyroid was first identified by the anatomist Thomas Wharton (whose name is also eponymised in Wharton's duct of the submandibular gland) in 1656.[38]

Thyroxine was identified only in the 19th century.

In 1909, Theodor Kocher from Switzerland won the Nobel Prize in Medicine "for his work on the physiology, pathology and surgery of the thyroid gland".[39]

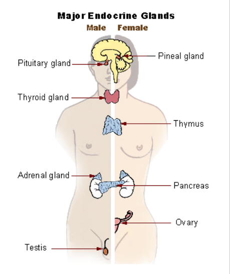
In other animals

The thyroid gland is found in all vertebrates. In fish, it is usually located below the gills and is not always divided into distinct lobes. However, in some teleosts, patches of thyroid tissue are found elsewhere in the body, associated with the kidneys, spleen, heart, or eyes.[40]

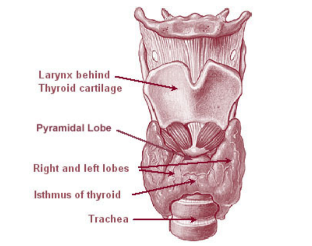
In tetrapods, the thyroid is always found somewhere in the neck region. In most tetrapod species, there are two paired thyroid glands - that is, the right and left lobes are not joined together. However, there is only ever a single thyroid gland in most mammals, and the shape found in humans is common to many other species.[40]

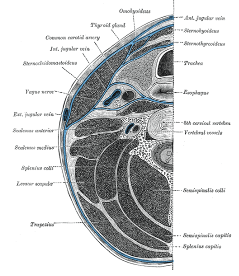
In larval lampreys, the thyroid originates as an exocrine gland, secreting its hormones into the gut, and associated with the larva's filter-feeding apparatus. In the adult lamprey, the gland separates from the gut, and becomes endocrine, but this path of development may reflect the evolutionary origin of the thyroid. For instance, the closest living relatives of vertebrates, the tunicates and *Amphioxus*, have a structure very similar to that of larval lampreys, and this also secretes iodine-containing compounds (albeit not thyroxine).[40]

Additional images



Position of the Thyroid in Males and Females




Section of the neck at about the level of the sixth cervical vertebra.

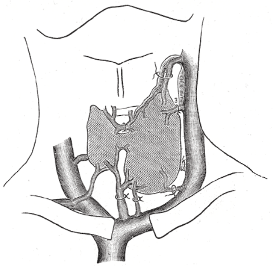
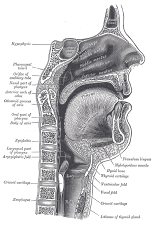
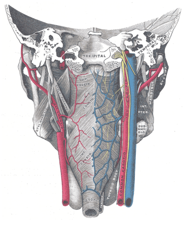
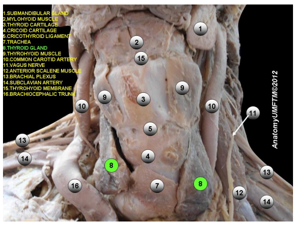
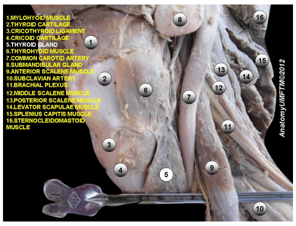


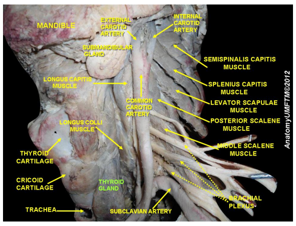
Diagram showing common arrangement of thyroid veins.


Sagittal section of nose mouth, pharynx, and larynx.

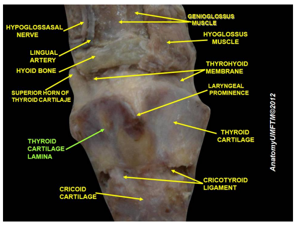

Muscles of the pharynx, viewed from behind, together with the associated vessels and nerves.


Thyroid


Thyroid gland



Thyroid gland



Thyroid cartilage lamina

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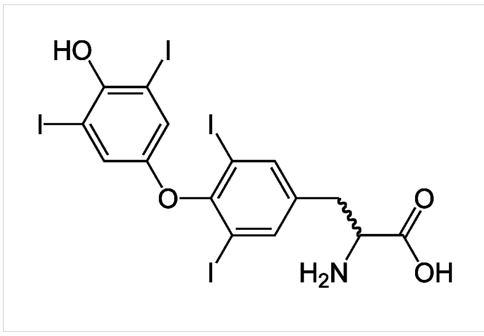
External links

- EndocrineWeb.com for more information on thyroid disease, hormones, and surgery (http://www.EndocrineWeb.com)
- American Thyroid Association (http://www.thyroid.org) (Thyroid Information and professional organization)
- Histology at KUMC *epithel-epith03* (http://www.kumc.edu/instruction/medicine/anatomy/histoweb/epithel/epith03.htm) "Thyroid Gland"

Hypothyroidism

Hypothyroidism

Classification and external resources



Thyroxine (T4) normally produced in 20:1 ratio to triiodothyronine (T3)

ICD-10	E03.9 [1]
ICD-9	244.9 [2]
DiseasesDB	6558 [3]
eMedicine	med/1145 [4]
MeSH	D007037 [5]

Hypothyroidism /ˌhaɪpəˈθaɪrɔɪdɪzəm/ is a condition in which the thyroid gland does not make enough thyroid hormone.

Iodine deficiency is often cited as the most common cause of hypothyroidism worldwide but it can be caused by many other factors. It can result from a lack of a thyroid gland or from iodine-131 treatment, and can also be associated with increased stress. Severe hypothyroidism in infants can result in cretinism.

A 2011 study concluded that about 8% of women over 50 and men over 65 in the UK suffer from an under-active thyroid and that as many as 100,000 of these people could benefit from treatment they are currently not receiving.[6]

Classification

Hypothyroidism is often classified by association with the indicated organ dysfunction (see below):[7][8]

Type	Origin	
Primary	Thyroid gland	The most common forms include Hashimoto's thyroiditis (an autoimmune disease) and radioiodine therapy for hyperthyroidism.
Secondary	Pituitary gland	Occurs if the pituitary gland does not create enough thyroid-stimulating hormone (TSH) to induce the thyroid gland to produce enough thyroxine and triiodothyronine. Although not every case of secondary hypothyroidism has a clear-cut cause, it is usually caused by damage to the pituitary gland, as by a tumor, radiation, or surgery.[9] Secondary hypothyroidism accounts for less than 5%[10] or 10%[11] of hypothyroidism cases.
Tertiary	Hypothalamus	Results when the hypothalamus fails to produce sufficient thyrotropin-releasing hormone (TRH). TRH prompts the pituitary gland to produce thyroid-stimulating hormone (TSH). Hence may also be termed *hypothalamic-pituitary-axis hypothyroidism.* It accounts for less than 5% of hypothyroidism cases.[10]

Signs and symptoms

Early hypothyroidism is often asymptomatic and can have very mild symptoms. *Subclinical hypothyroidism* is a state of normal thyroid hormone levels, thyroxine (T4) and triiodothyronine (T3), with mild elevation of thyrotropin, thyroid-stimulating hormone (TSH). With higher TSH levels and low free T4 levels, symptoms become more readily apparent in *clinical* (or overt) *hypothyroidism*.

Hypothyroidism can be associated with the following symptoms:[12][13][14]

Early

- Cold intolerance, increased sensitivity to cold
- Constipation
- Weight gain and water retention[15][16][17]
- Bradycardia (low heart rate – fewer than sixty beats per minute)
- Fatigue
- Decreased sweating
- Muscle cramps and joint pain
- Dry, itchy skin
- Thin, brittle fingernails
- Rapid thoughts
- Depression
- Poor muscle tone (muscle hypotonia)
- Female infertility, any kind of problems with menstrual cycles
- Hyperprolactinemia and galactorrhea
- Elevated serum cholesterol

Late

- Goiter
- Slow speech and a hoarse, breaking voice – deepening of the voice can also be noticed, caused by Reinke's Edema.
- Dry puffy skin, especially on the face
- Thinning of the outer third of the eyebrows (sign of Hertoghe)
- Abnormal menstrual cycles
- Low basal body temperature
- Thyroid-Related Depression

Uncommon

- Impaired memory[18]
- Impaired cognitive function (brain fog) and inattentiveness.[19]
- A slow heart rate with ECG changes including low voltage signals. Diminished cardiac output and decreased contractility
- Reactive (or post-prandial) hypoglycemia[20]
- Sluggish reflexes
- Hair loss
- Anemia caused by impaired haemoglobin synthesis (decreased EPO levels), impaired intestinal iron and folate absorption or B_{12} deficiency[21] from pernicious anemia
- Difficulty swallowing
- Shortness of breath with a shallow and slow respiratory pattern

- Increased need for sleep
- Irritability and mood instability
- Yellowing of the skin due to impaired conversion of beta-carotene[22] to vitamin A (carotoderma)
- Impaired renal function with decreased glomerular filtration rate
- Acute psychosis (myxedema madness) (a rare presentation of hypothyroidism)
- Decreased libido in men[23] due to impairment of testicular testosterone synthesis
- Decreased sense of taste and smell (anosmia)
- Puffy face, hands and feet (late, less common symptoms)
- Gynecomastia
- Deafness[24]
- Enlarged tongue [25]

Subclinical hypothyroidism

Subclinical hypothyroidism occurs when thyrotropin (TSH) levels are elevated but thyroxine (T_4) and triiodothyronine (T_3) levels are normal.[26] In primary hypothyroidism, TSH levels are high and T_4 and T_3 levels are low. TSH usually increases when T_4 and T_3 levels drop. TSH prompts the thyroid gland to make more hormone. In subclinical hypothyroidism, TSH is elevated but below the limit representing overt hypothyroidism. The levels of the active hormones will be within the laboratory reference ranges.

Pregnancy and fertility

During pregnancy there is a substantially increased need of thyroid hormones and substantial risk that a previously unnoticed, subclinical or latent hypothyroidism will turn into overt hypothyroidism. See thyroid disease in pregnancy for more details.

Subclinical hypothyroidism in early pregnancy, compared with normal thyroid function, has been estimated to increase the risk of pre-eclampsia with an odds ratio (OR) of 1.7 and the risk of perinatal mortality with an OR of 2.7.[27]

Even mild or subclinical hypothyroidism are known to adversely affect fertility.

Epidemiology

0.3% of the general American population have overt hypothyroidism, and 4.3 % have subclinical hypothyroidism.[28] A 1995 survey in the UK found the mean incidence (with 95% confidence intervals) of spontaneous hypothyroidism in women was 3.5/1000 survivors/year (2.8-4.5) rising to 4.1/1000 survivors/year (3.3-5.0) for all causes of hypothyroidism and in men was 0.6/1000 survivors/year (0.3-1.2).[29]

Estimates of subclinical hypothyroidism range between 3–8%, increasing with age; incidence is more common in women than in men.[30]

Causes

Iodine deficiency is the most common cause of hypothyroidism worldwide.[31] In iodine-replete individuals hypothyroidism is frequently caused by Hashimoto's thyroiditis, or otherwise as a result of either an absent thyroid gland or a deficiency in stimulating hormones from the hypothalamus or pituitary.

Factors such as iodine deficiency or exposure to iodine-131 from nuclear fallout, which is absorbed by the thyroid gland like regular iodide and destroys its cells, can increase the risk.

Congenital hypothyroidism is very rare accounting for approximately 0.2% and can have several causes such as thyroid aplasia or defects in the hormone metabolism. Thyroid hormone insensitivity (most often T3 receptor defect) also falls into this category although in this condition the levels of thyroid hormones may be normal or even markedly elevated.

Hypothyroidism can result from postpartum thyroiditis, a condition that affects about 5% of all women within a year of giving birth. The first phase is typically hyperthyroidism; the thyroid then either returns to normal, or a woman develops hypothyroidism. Of those women who experience hypothyroidism associated with postpartum thyroiditis, one in five will develop permanent hypothyroidism requiring life-long treatment.

Hypothyroidism can result from de Quervain's thyroiditis, which, in turn, is often caused by having a bad flu that enters and destroys part, or all, the thyroid.[32]

Hypothyroidism can also result from sporadic inheritance, sometimes autosomal recessive.

Temporary hypothyroidism can be due to the Wolff-Chaikoff effect. A very high intake of iodine can be used to temporarily treat hyperthyroidism, especially in an emergency situation. Although iodide is a substrate for thyroid hormones, high levels reduce iodide organification in the thyroid gland, decreasing hormone production. The antiarrhythmic agent amiodarone can cause hyper- or hypothyroidism due to its high iodine content.

Hypothyroidism can be caused by lithium-based mood stabilizers, usually used to treat bipolar disorder (previously known as manic depression).[31] In fact, lithium has occasionally been used to treat hyperthyroidism.[33] Other drugs that may produce hypothyroidism include interferon alpha, interleukin-2, and thalidomide.[31]

Stress and hypothyroidism

Stress is known to be a significant contributor to thyroid dysfunction: this can be environmental stress as well as lesser-considered homeostatic stress such as fluctuating blood sugar levels and immune problems. Moreover, adrenal stress's effect on thyroid function can be indirect, through its effects on blood sugar levels (dysglycemia),[34][35] but can also have more direct effects. Stress can cause hypothyroidism or reduced thyroid functioning through disrupting the HPA axis which down-regulates thyroid function,[36] reducing the conversion of T4 to T3,[37] weakening the immune system thus promoting autoimmunity,[38] causing thyroid hormone resistance,[39] and resulting in hormonal imbalances:[40] indeed, excess estrogen in the blood caused by chronic cortisol elevations (which reduce the liver's ability to clear excess estrogen[41]), can result in hypothyroid symptoms by decreasing levels of active T3.[42] Stress also affects thyroid functioning through the sympathetic nervous system.[43] Refugees from East Germany in a 1994 study who experienced chronic stress were found to have a very high rate of hypothyroidism or subclinical hypothyroidism, although not all refugees displayed clinical or behavioral symptoms associated with this reduced thyroid functioning.[44] TSH levels correlate positively with physiological stress.[45][46]

Symptoms of adrenal stress include

- Fatigue
- Headaches
- Decreased immunity
- Difficulty falling asleep, staying asleep and waking up
- Mood swings
- Sugar and caffeine cravings
- Irritability or lightheadedness between meals
- Eating to relieve fatigue
- Dizziness when moving from sitting or lying to standing
- Gastric ulcers[40]

Weak adrenal glands can also result in hypothyroid symptoms without affecting the thyroid itself.[47]

Diagnosis

The only validated test to diagnose primary hypothyroidism, is to measure thyroid-stimulating hormone (TSH) and free thyroxine (T4).[48] However, these levels can be affected by non-thyroidal illnesses.

High levels of TSH indicate that the thyroid is not producing sufficient levels of thyroid hormone (mainly as thyroxine (T_4) and smaller amounts of triiodothyronine (T_3)). However, measuring just TSH fails to diagnose secondary and tertiary hypothyroidism, thus leading to the following suggested blood testing if the TSH is normal and hypothyroidism is still suspected:

- Free triiodothyronine (fT_3)
- Free thyroxine (fT_4)
- Total T_3
- Total T_4

Additionally, the following measurements may be needed:

- Free T_3 from 24-hour urine catch[49]
- Antithyroid antibodies — for evidence of autoimmune diseases that may be damaging the thyroid gland
- Serum cholesterol — which may be elevated in hypothyroidism
- Prolactin — as a widely available test of pituitary function
- Testing for anemia, including ferritin
- Basal body temperature

Treatment

Hypothyroidism is treated with the levorotatory forms of thyroxine (levothyroxine) (L-T_4) and triiodothyronine (liothyronine) (L-T_3). Synthroid is, in the US, the most common name form of the pill Levothyroxine. Synthroid is also the most common pill prescribed by doctors that has the synthetic thyroid hormone in it. This medicine can improve symptoms of thyroid deficiency such as slow speech, lack of energy, weight gain, hair loss, dry skin, and feeling cold. It also helps to treat goiter. It is also used to treat some kinds of thyroid cancer along with surgery and other medicines. Both synthetic and animal-derived thyroid tablets are available and can be prescribed for patients in need of additional thyroid hormone. Thyroid hormone is taken daily, and doctors can monitor blood levels to help assure proper dosing. Levothyroxine is best taken 30–60 minutes before breakfast, as some food can diminish absorption. Calcium can inhibit the absorption of levothryoxine. [50] Compared to water, coffee reduces absorption of levothyroxine by about 30 percent.[51] Some patients might appear to be resistant to levothyroxine, when in fact they do not properly absorb the tablets - a problem which is solved by pulverizing the medication.[52] There are several different treatment protocols in thyroid-replacement therapy:

T_4 only

> This treatment involves supplementation of levothyroxine alone, in a synthetic form. It is currently the standard treatment in mainstream medicine.[53]

T_4 and T_3 in combination

> This treatment protocol involves administering both synthetic L-T_4 and L-T_3 simultaneously in combination.[54]

Desiccated thyroid extract

> Desiccated thyroid extract is an animal-based thyroid extract, most commonly from a porcine source. It is also a combination therapy, containing natural forms of L-T_4 and L-T_3.[55]

Treatment controversy

The potential benefit from substituting some T3 for T4 has been investigated, but no conclusive benefit for combination therapy has been shown.[56][57]

The 2002 Laboratory Medicine Practice Guidelines of the National Academy of Clinical Biochemistry state that during pregnancy: "The L-T4 dose should be increased (usually by 50 mcg/day) to maintain a serum TSH between 0.5 and 2.0 mIU/L and a serum FT4 in the upper third of the normal reference interval." Doctors however often assume that if your TSH is in the "normal range", sometimes defined as high as 5.5 mIu/L, it has no effect on fertility. Healthy pregnant women however have a TSH level of around 1.0 mIU/L.

Subclinical hypothyroidism

There is a range of opinion on the biochemical and symptomatic point at which to treat with levothyroxine, the typical treatment for overt hypothyroidism. Reference ranges have been debated as well. As of 2003, the American Association of Clinical Endocrinologists (ACEE) considers 0.3–3.0 mIU/L within normal range.[58]

There is always the risk of overtreatment and hyperthyroidism. Some studies have suggested that subclinical hypothyroidism does not need to be treated. A 2007 meta-analysis by the Cochrane Collaboration found no benefit of thyroid-hormone replacement except "some parameters of lipid profiles and left-ventricular function."[59] A 2002 meta-analysis looking into whether subclinical hypothyroidism may increase the risk of cardiovascular disease, as has been previously suggested,[60] found a possible modest increase and suggested further studies be undertaken with coronary-heart disease as an end point "before current recommendations are updated."[61]

Alternative treatments

Compounded slow-release T3 has been suggested for use in combination with T4, which proponents argue will mitigate many of the symptoms of functional hypothyroidism and improve quality of life. This is still controversial and is rejected by the conventional medical establishment.[62]

Non-human presentation

Hypothyroidism is also a relatively common disease in domestic dogs, with some specific breeds having a definite predisposition.[63]

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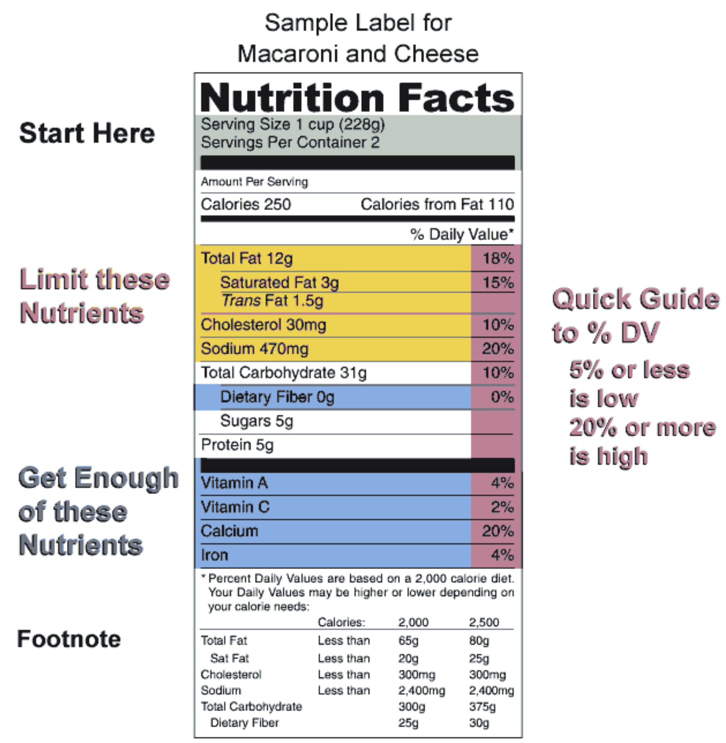
External links

- Hypothyroidism Booklet - American Thyroid Association (http://www.thyroid.org/patients/brochures/Hypothyroidism _web_booklet.pdf)

Nutrition

Nutrition (also called **nourishment** or **aliment**) is the provision, to cells and organisms, of the materials necessary (in the form of food) to support life. Many common health problems can be prevented or alleviated with a healthy diet.



The "Nutrition Facts" table indicates the amounts of nutrients which experts recommend to limit or consume in adequate amounts.

The diet of an organism is what it eats, which is largely determined by the perceived palatability of foods. Dietitians are health professionals who specialize in human nutrition, meal planning, economics, and preparation. They are trained to provide safe, evidence-based dietary advice and management to individuals (in health and disease), as well as to institutions. Clinical nutritionists are health professionals who focus more specifically on the role of nutrition in chronic disease, including possible prevention or remediation by addressing nutritional deficiencies before resorting to drugs. While government regulation of the use of this professional title is less universal than for "dietician", the field is supported by many high-level academic programs, up to and including the Doctoral level, and has its own voluntary certification board,[1] professional associations, and peer-reviewed journals, e.g. the American Society for Nutrition and the *American Journal of Clinical Nutrition*.

A poor diet can have an injurious impact on health, causing deficiency diseases such as scurvy[2] and kwashiorkor;[3] health-threatening conditions like obesity[4][5] and metabolic syndrome;[6] and such common chronic systemic diseases as cardiovascular disease,[7][8] diabetes,[9][10] and osteoporosis.[11][12][13]

Animal nutrition

Overview

Nutritional science investigates the metabolic and physiological responses of the body to diet. With advances in the fields of molecular biology, biochemistry, nutritional immunology, molecular medicine and genetics, the study of nutrition is increasingly concerned with metabolism and metabolic pathways: the sequences of biochemical steps through which substances in living things change from one form to another.

Carnivore and herbivore diets are contrasting, with basic nitrogen and carbon proportions being at varying levels in particular foods. Carnivores consume more nitrogen than carbon while herbivores consume less nitrogen than carbon, when an equal quantity is measured.

The human body contains chemical compounds, such as water, carbohydrates (sugar, starch, and fiber), amino acids (in proteins), fatty acids (in lipids), and nucleic acids (DNA and RNA). These compounds in turn consist of elements such as carbon, hydrogen, oxygen, nitrogen, phosphorus, calcium, iron, zinc, magnesium, manganese, and so on. All of these chemical compounds and elements occur in various forms and combinations (e.g. hormones, vitamins, phospholipids, hydroxyapatite), both in the human body and in the plant and animal organisms that humans eat.

The human body consists of elements and compounds ingested, digested, absorbed, and circulated through the bloodstream to feed the cells of the body. Except in the unborn fetus, the digestive system is the first system involved . In a typical adult, about seven liters of digestive juices enter the lumen of the digestive tract. These digestive juices break chemical bonds in ingested molecules, and modify their conformations and energy states. Though some molecules are absorbed into the bloodstream unchanged, digestive processes release them from the matrix of foods. Unabsorbed matter, along with some waste products of metabolism, is eliminated from the body in the feces.

Studies of nutritional status must take into account the state of the body before and after experiments, as well as the chemical composition of the whole diet and of all material excreted and eliminated from the body (in urine and feces). Comparing the food to the waste can help determine the specific compounds and elements absorbed and metabolized in the body. The effects of nutrients may only be discernible over an extended period, during which all food and waste must be analyzed. The number of variables involved in such experiments is high, making nutritional studies time-consuming and expensive, which explains why the science of human nutrition is still slowly evolving.

In general, eating a wide variety of fresh, whole (unprocessed), foods has proven favorable for one's health compared to monotonous diets based on processed foods.[14] In particular, the consumption of whole-plant foods slows digestion and allows better absorption, and a more favorable balance of essential nutrients per Calorie, resulting in better management of cell growth, maintenance, and mitosis (cell division), as well as better regulation of appetite and blood sugar . Regularly scheduled meals (every few hours) have also proven more wholesome than infrequent or haphazard ones,[15] although a recent study has also linked more frequent meals with a higher risk of colon cancer in men.[16]

Nutrients

There are six major classes of nutrients: carbohydrates, fats, minerals, protein, vitamins, and water.

These nutrient classes can be categorized as either macronutrients (needed in relatively large amounts) or micronutrients (needed in smaller quantities). The macronutrients include carbohydrates (including fiber), fats, protein, and water. The micronutrients are minerals and vitamins.

The macronutrients (excluding fiber and water) provide structural material (amino acids from which proteins are built, and lipids from which cell membranes and some signaling molecules are built) and energy. Some of the structural material can be used to generate energy internally, and in either case it is measured in Joules or kilocalories (often called "Calories" and written with a capital *C* to distinguish them from little 'c' calories). Carbohydrates and proteins provide 17 kJ approximately (4 kcal) of energy per gram, while fats provide 37 kJ (9 kcal) per gram.,[17] though the net energy from either depends on such factors as absorption and digestive effort, which vary substantially from instance to instance. Vitamins, minerals, fiber, and water do not provide energy, but are required for other reasons. A third class of dietary material, fiber (i.e., non-digestible material such as cellulose), is also required, for both mechanical and biochemical reasons, although the exact reasons remain unclear.

Molecules of carbohydrates and fats consist of carbon, hydrogen, and oxygen atoms. Carbohydrates range from simple monosaccharides (glucose, fructose, galactose) to complex polysaccharides (starch). Fats are triglycerides, made of assorted fatty acid monomers bound to glycerol backbone. Some fatty acids, but not all, are essential in the diet: they cannot be synthesized in the body. Protein molecules contain nitrogen atoms in addition to carbon, oxygen, and hydrogen. The fundamental components of protein are nitrogen-containing amino acids, some of which are essential in the sense that humans cannot make them internally. Some of the amino acids are convertible (with the expenditure of energy) to glucose and can be used for energy production just as ordinary glucose in a process known as gluconeogenesis. By breaking down existing protein, some glucose can be produced internally; the remaining amino acids are discarded, primarily as urea in urine. This occurs normally only during prolonged starvation.

Other micronutrients include antioxidants and phytochemicals, which are said to influence (or protect) some body systems. Their necessity is not as well established as in the case of, for instance, vitamins.

Most foods contain a mix of some or all of the nutrient classes, together with other substances, such as toxins of various sorts. Some nutrients can be stored internally (e.g., the fat soluble vitamins), while others are required more or less continuously. Poor health can be caused by a lack of required nutrients or, in extreme cases, too much of a required nutrient. For example, both salt and water (both absolutely required) will cause illness or even death in excessive amounts.

Carbohydrates

Carbohydrates may be classified as monosaccharides, disaccharides, or polysaccharides depending on the number of monomer (sugar) units they contain. They constitute a large part of foods such as rice, noodles, bread, and other grain-based products. Monosaccharides, disaccharides, and polysaccharides contain one, two, and three or more sugar units, respectively. Polysaccharides are often referred to as *complex* carbohydrates because they are typically long, multiple branched chains of sugar units.

Traditionally, simple carbohydrates were believed to be absorbed quickly, and therefore raise blood-glucose levels more rapidly than complex carbohydrates. This, however, is not accurate.[18][19][20][21] Some simple carbohydrates (e.g. fructose) follow different metabolic pathways (e.g. fructolysis) which result in only a partial catabolism to glucose, while many complex carbohydrates may be digested at essentially the same rate as simple carbohydrates.[22]

Fiber

Dietary fiber is a carbohydrate (or a polysaccharide) that is incompletely absorbed in humans and in some animals. Like all carbohydrates, when it is metabolized it can produce four Calories (kilocalories) of energy per gram. However, in most circumstances it accounts for less than that because of its limited absorption and digestibility. Dietary fiber consists mainly of cellulose, a large carbohydrate polymer that is indigestible because humans do not have the required enzymes to disassemble it. There are two subcategories: soluble and insoluble fiber. Whole grains, fruits (especially plums, prunes, and figs), and vegetables are good sources of dietary fiber. There are many health benefits of a high-fiber diet. Dietary fiber helps reduce the chance of gastrointestinal problems such as constipation and diarrhea by increasing the weight and size of stool and softening it. Insoluble fiber, found in whole wheat flour, nuts and vegetables, especially stimulates peristalsis – the rhythmic muscular contractions of the intestines which move digesta along the digestive tract. Soluble fiber, found in oats, peas, beans, and many fruits, dissolves in water in the intestinal tract to produce a gel which slows the movement of food through the intestines. This may help lower blood glucose levels because it can slow the absorption of sugar. Additionally, fiber, perhaps especially that from whole grains, is thought to possibly help lessen insulin spikes, and therefore reduce the risk of type 2 diabetes. The link between increased fiber consumption and a decreased risk of colorectal cancer is still uncertain. [23]

Fat

A molecule of dietary fat typically consists of several fatty acids (containing long chains of carbon and hydrogen atoms), bonded to a glycerol. They are typically found as triglycerides (three fatty acids attached to one glycerol backbone). Fats may be classified as saturated or unsaturated depending on the detailed structure of the fatty acids involved. Saturated fats have all of the carbon atoms in their fatty acid chains bonded to hydrogen atoms, whereas unsaturated fats have some of these carbon atoms double-bonded, so their molecules have relatively fewer hydrogen atoms than a saturated fatty acid of the same length. Unsaturated fats may be further classified as monounsaturated (one double-bond) or polyunsaturated (many double-bonds). Furthermore, depending on the location of the double-bond in the fatty acid chain, unsaturated fatty acids are classified as omega-3 or omega-6 fatty acids. Trans fats are a type of unsaturated fat with *trans*-isomer bonds; these are rare in nature and in foods from natural sources; they are typically created in an industrial process called (partial) hydrogenation. There are nine kilocalories in each gram of fat. Fatty acids such as conjugated linoleic acid, catalpic acid, eleostearic acid and punicic acid, in addition to providing energy, represent potent immune modulatory molecules.

Saturated fats (typically from animal sources) have been a staple in many world cultures for millennia. Unsaturated fats (e. g., vegetable oil) are considered healthier, while trans fats are to be avoided. Saturated and some trans fats are typically solid at room temperature (such as butter or lard), while unsaturated fats are typically liquids (such as olive oil or flaxseed oil). Trans fats are very rare in nature, and have been shown to be highly detrimental to human health, but have properties useful in the food processing industry, such as rancidity resistance.

Essential fatty acids

Most fatty acids are non-essential, meaning the body can produce them as needed, generally from other fatty acids and always by expending energy to do so. However, in humans, at least two fatty acids are essential and must be included in the diet. An appropriate balance of essential fatty acids—omega-3 and omega-6 fatty acids—seems also important for health, although definitive experimental demonstration has been elusive. Both of these "omega" long-chain polyunsaturated fatty acids are substrates for a class of eicosanoids known as prostaglandins, which have roles throughout the human body. They are hormones, in some respects. The omega-3 eicosapentaenoic acid (EPA), which can be made in the human body from the omega-3 essential fatty acid alpha-linolenic acid (ALA), or taken in through marine food sources, serves as a building block for series 3 prostaglandins (e.g. weakly inflammatory PGE3). The omega-6 dihomo-gamma-linolenic acid (DGLA) serves as a building block for series 1 prostaglandins (e.g. anti-inflammatory PGE1), whereas arachidonic acid (AA) serves as a building block for series 2 prostaglandins (e.g. pro-inflammatory PGE 2). Both DGLA and AA can be made from the omega-6 linoleic acid (LA) in the human body, or can be taken in directly through food. An appropriately balanced intake of omega-3 and omega-6 partly determines the relative production of different prostaglandins, which is one reason why a balance between omega-3 and omega-6 is believed important for cardiovascular health. In industrialized societies, people typically consume large amounts of processed vegetable oils, which have reduced amounts of the essential fatty acids along with too much of omega-6 fatty acids relative to omega-3 fatty acids.

The conversion rate of omega-6 DGLA to AA largely determines the production of the prostaglandins PGE1 and PGE2. Omega-3 EPA prevents AA from being released from membranes, thereby skewing prostaglandin balance away from pro-inflammatory PGE2 (made from AA) toward anti-inflammatory PGE1 (made from DGLA). Moreover, the conversion (desaturation) of DGLA to AA is controlled by the enzyme delta-5-desaturase, which in turn is controlled by hormones such as insulin (up-regulation) and glucagon (down-regulation). The amount and type of carbohydrates consumed, along with some types of amino acid, can influence processes involving insulin, glucagon, and other hormones; therefore the ratio of omega-3 versus omega-6 has wide effects on general health, and specific effects on immune function and inflammation, and mitosis (i.e. cell division).

Protein


Most meats such as chicken contain all the essential amino acids needed for humans.

Proteins are the basis of many animal body structures (e.g. muscles, skin, and hair). They also form the enzymes that control chemical reactions throughout the body. Each molecule is composed of amino acids, which are characterized by inclusion of nitrogen and sometimes sulphur (these components are responsible for the distinctive smell of burning protein, such as the keratin in hair). The body requires amino acids to produce new proteins (protein retention) and to replace damaged proteins (maintenance). As there is no protein or amino acid storage provision, amino acids must be present in the diet. Excess amino acids are discarded, typically in the urine. For all animals, some amino acids are *essential* (an animal cannot produce them internally) and some are *non-essential* (the animal can produce them from other nitrogen-containing compounds). About twenty amino acids are found in the human body, and about ten of these are essential and, therefore, must be included in the diet. A diet that contains adequate amounts of amino acids (especially those that are essential) is particularly important in some situations: during early development and maturation, pregnancy, lactation, or injury (a burn, for instance). A *complete* protein source contains all the essential amino acids; an *incomplete* protein source lacks one or more of the essential amino acids.

It is possible to combine two incomplete protein sources (e.g. rice and beans) to make a complete protein source, and characteristic combinations are the basis of distinct cultural cooking traditions. Sources of dietary protein include meats, tofu and other soy-products, eggs, legumes, and dairy products such as milk and cheese. Excess amino acids from protein can be converted into glucose and used for fuel through a process called gluconeogenesis. The amino acids remaining after such conversion are discarded.

Minerals

Dietary minerals are the chemical elements required by living organisms, other than the four elements carbon, hydrogen, nitrogen, and oxygen that are present in nearly all organic molecules. The term "mineral" is archaic, since the intent is to describe simply the less common elements in the diet. Some are heavier than the four just mentioned, including several metals, which often occur as ions in the body. Some dietitians recommend that these be supplied from foods in which they occur naturally, or at least as complex compounds, or sometimes even from natural inorganic sources (such as calcium carbonate from ground oyster shells). Some minerals are absorbed much more readily in the ionic forms found in such sources. On the other hand, minerals are often artificially added to the diet as supplements; the most famous is likely iodine in iodized salt which prevents goiter.

Macrominerals

Many elements are essential in relative quantity; they are usually called "bulk minerals". Some are structural, but many play a role as electrolytes.[24] Elements with recommended dietary allowance (RDA) greater than 200 mg/day are, in alphabetical order (with informal or folk-medicine perspectives in parentheses):

- Calcium, a common electrolyte, but also needed structurally (for muscle and digestive system health, bone strength, some forms neutralize acidity, may help clear toxins, provides signaling ions for nerve and membrane functions)
- Chlorine as chloride ions; very common electrolyte; see sodium, below
- Magnesium, required for processing ATP and related reactions (builds bone, causes strong peristalsis, increases flexibility, increases alkalinity)
- Phosphorus, required component of bones; essential for energy processing[25]
- Potassium, a very common electrolyte (heart and nerve health)
- Sodium, a very common electrolyte; not generally found in dietary supplements, despite being needed in large quantities, because the ion is very common in food: typically as sodium chloride, or common salt. Excessive sodium consumption can deplete calcium and magnesium, leading to high blood pressure and osteoporosis.
- Sulfur, for three essential amino acids and therefore many proteins (skin, hair, nails, liver, and pancreas). Sulfur is not consumed alone, but in the form of sulfur-containing amino acids

Trace minerals

Many elements are required in trace amounts, usually because they play a catalytic role in enzymes.[26] Some trace mineral elements (RDA < 200 mg/day) are, in alphabetical order:

- Cobalt required for biosynthesis of vitamin B12 family of coenzymes. Animals cannot biosynthesize B12, and must obtain this cobalt-containing vitamin in the diet
- Copper required component of many redox enzymes, including cytochrome c oxidase
- Chromium required for sugar metabolism
- Iodine required not only for the biosynthesis of thyroxine, but probably, for other important organs as breast, stomach, salivary glands, thymus etc. (see Extrathyroidal iodine); for this reason iodine is needed in larger quantities than others in this list, and sometimes classified with the macrominerals
- Iron required for many enzymes, and for hemoglobin and some other proteins
- Manganese (processing of oxygen)
- Molybdenum required for xanthine oxidase and related oxidases
- Nickel present in urease
- Selenium required for peroxidase (antioxidant proteins)
- Vanadium (Speculative: there is no established RDA for vanadium. No specific biochemical function has been identified for it in humans, although vanadium is required for some lower organisms.)
- Zinc required for several enzymes such as carboxypeptidase, liver alcohol dehydrogenase, and carbonic anhydrase

Vitamins

As with the minerals discussed above, some vitamins are recognized as essential nutrients, necessary in the diet for good health. (Vitamin D is the exception: it can be synthesized in the skin, in the presence of UVB radiation.) Certain vitamin-like compounds that are recommended in the diet, such as carnitine, are thought useful for survival and health, but these are not "essential" dietary nutrients because the human body has some capacity to produce them from other compounds. Moreover, thousands of different phytochemicals have recently been discovered in food (particularly in fresh vegetables), which may have desirable properties including antioxidant activity (see below); however, experimental demonstration has been suggestive but inconclusive. Other essential nutrients that are not classified as vitamins include essential amino acids (see above), choline, essential fatty acids (see above), and the minerals discussed in the preceding section.

Vitamin deficiencies may result in disease conditions, including goitre, scurvy, osteoporosis, impaired immune system, disorders of cell metabolism, certain forms of cancer, symptoms of premature aging, and poor psychological health (including eating disorders), among many others.[27] Excess levels of some vitamins are also dangerous to health (notably vitamin A), and for at least one vitamin, B6, toxicity begins at levels not far above the required amount. Deficient or excess levels of minerals can also have serious health consequences.

Water

A manual water pump in China

Water is excreted from the body in multiple forms; including urine and feces, sweating, and by water vapour in the exhaled breath. Therefore it is necessary to adequately rehydrate to replace lost fluids.

Early recommendations for the quantity of water required for maintenance of good health suggested that 6–8 glasses of water daily is the minimum to maintain proper hydration.[28] However the notion that a person should consume eight glasses of water per day cannot be traced to a credible scientific source.[29] The original water intake recommendation in 1945 by the Food and Nutrition Board of the National Research Council read: "An ordinary standard for diverse persons is 1 milliliter for each calorie of food. Most of this quantity is contained in prepared foods."[30] More recent comparisons of well-known recommendations on fluid intake have revealed large discrepancies in the volumes of water we need to consume for good health.[31] Therefore, to help standardize guidelines, recommendations for water consumption are included in two recent European Food Safety Authority (EFSA) documents (2010): (i) Food-based dietary guidelines and (ii) Dietary reference values for water or adequate daily intakes (ADI).[32] These specifications were provided by calculating adequate intakes from measured intakes in populations of individuals with "desirable osmolarity values of urine and desirable water volumes per energy unit consumed."[32] For healthful hydration, the current EFSA guidelines recommend total water intakes of 2.0 L/day for adult females and 2.5 L/day for adult males. These reference values include water from drinking water, other beverages, and from food. About 80% of our daily water requirement comes from the beverages we drink, with the remaining 20% coming from food.[33] Water content varies depending on the type of food consumed, with fruit and vegetables containing more than cereals, for example.[34] These values are estimated using country-specific food balance sheets published by the Food and Agriculture Organisation of the United Nations.[34] Other guidelines for nutrition also have implications for the beverages we consume for healthy hydration- for example, the World Health Organization (WHO) recommend that added sugars should represent no more than 10% of total energy intake.[35]

The EFSA panel also determined intakes for different populations. Recommended intake volumes in the elderly are the same as for adults as despite lower energy consumption, the water requirement of this group is increased due to a reduction in renal concentrating capacity.[32] Pregnant and breastfeeding women require additional fluids to stay hydrated. The EFSA panel proposes that pregnant women should consume the same volume of water as non-pregnant women, plus an increase in proportion to the higher energy requirement, equal to 300 mL/day.[32] To compensate for additional fluid output, breastfeeding women require an additional 700 mL/day above the recommended intake values for non-lactating women.[32]

For those who have healthy kidneys, it is somewhat difficult to drink too much water,[32] but (especially in warm humid weather and while exercising) it is dangerous to drink too little. While overhydration is much less common than dehydration, it is also possible to drink far more water than necessary which can result in water intoxication, a serious and potentially fatal condition.[36] In particular, large amounts of de-ionized water are dangerous.[32]

Other nutrients

Other micronutrients include antioxidants and phytochemicals. These substances are generally more recent discoveries that have not yet been recognized as vitamins or as required. Phytochemicals may act as antioxidants, but not all phytochemicals are antioxidants.

Antioxidants

As cellular metabolism/energy production requires oxygen, potentially damaging (e.g. mutation causing) compounds known as free radicals can form. Most of these are oxidizers (i.e. acceptors of electrons) and some react very strongly. For the continued normal cellular maintenance, growth, and division, these free radicals must be sufficiently neutralized by antioxidant compounds. Recently, some researchers suggested an interesting theory of evolution of dietary antioxidants. Some are produced by the human body with adequate precursors (glutathione, Vitamin C), and those the body cannot produce may only be obtained in the diet via direct sources (Vitamin C in humans, Vitamin A, Vitamin K) or produced by the body from other compounds (Beta-carotene converted to Vitamin A by the body, Vitamin D synthesized from cholesterol by sunlight). Phytochemicals (*Section Below*) and their subgroup, polyphenols, make up the majority of antioxidants; about 4,000 are known. Different antioxidants are now known to function in a cooperative network. For example, Vitamin C can reactivate free radical-containing glutathione or Vitamin E by accepting the free radical itself. Some antioxidants are more effective than others at neutralizing different free radicals. Some cannot neutralize certain free radicals. Some cannot be present in certain areas of free radical development (Vitamin A is fat-soluble and protects fat areas, Vitamin C is water soluble and protects those areas). When interacting with a free radical, some antioxidants produce a different free radical compound that is less dangerous or more dangerous than the previous compound. Having a variety of antioxidants allows any byproducts to be safely dealt with by more efficient antioxidants in neutralizing a free radical's butterfly effect.

Although initial studies suggested that antioxidant supplements might promote health, later large clinical trials did not detect any benefit and suggested instead that excess supplementation may be harmful.[37][38]

Phytochemicals


Blackberries are a source of polyphenol antioxidants

A growing area of interest is the effect upon human health of trace chemicals, collectively called phytochemicals. These nutrients are typically found in edible plants, especially colorful fruits and vegetables, but also other organisms including seafood, algae, and fungi. The effects of phytochemicals increasingly survive rigorous testing by prominent health organizations. One of the principal classes of phytochemicals are polyphenol antioxidants, chemicals that are known to provide certain health benefits to the cardiovascular system and immune system. These chemicals are known to down-regulate the formation of reactive oxygen species, key chemicals in cardiovascular disease.

Perhaps the most rigorously tested phytochemical is zeaxanthin, a yellow-pigmented carotenoid present in many yellow and orange fruits and vegetables. Repeated studies have shown a strong correlation between ingestion of zeaxanthin and the prevention and treatment of age-related macular degeneration (AMD).[39] Less rigorous studies have proposed a correlation between zeaxanthin intake and cataracts.[40] A second carotenoid, lutein, has also been shown to lower the risk of contracting AMD. Both compounds have been observed to collect in the retina when ingested orally, and they serve to protect the rods and cones against the destructive effects of light.

Another carotenoid, beta-cryptoxanthin, appears to protect against chronic joint inflammatory diseases, such as arthritis. While the association between serum blood levels of beta-cryptoxanthin and substantially decreased joint disease has been established,[41] neither a convincing mechanism for such protection nor a cause-and-effect have been rigorously studied. Similarly, a red phytochemical, lycopene, has substantial credible evidence of negative association with development of prostate cancer.

As indicated above, some of the correlations between the ingestion of certain phytochemicals and the prevention of disease are, in some cases, enormous in magnitude. Yet, even when the evidence is obtained, translating it to practical dietary advice can be difficult and counter-intuitive. Lutein, for example, occurs in many yellow and orange fruits and vegetables and protects the eyes against various diseases. However, it does not protect the eye nearly as well as zeaxanthin, and the presence of lutein in the retina will prevent zeaxanthin uptake. Additionally, evidence has shown that the lutein present in egg yolk is more readily absorbed than the lutein from vegetable sources, possibly because of fat solubility.[42] At the most basic level, the question "should you eat eggs?" is complex to the point of dismay, including misperceptions about the health effects of cholesterol in egg yolk, and its saturated fat content.

As another example, lycopene is prevalent in tomatoes (and actually is the chemical that gives tomatoes their red color). It is more highly concentrated, however, in processed tomato products such as commercial pasta sauce, or tomato soup, than in fresh "healthy" tomatoes. Yet, such sauces tend to have high amounts of salt, sugar, other substances a person may wish or even need to avoid.

The following table presents phytochemical groups and common sources, arranged by family:

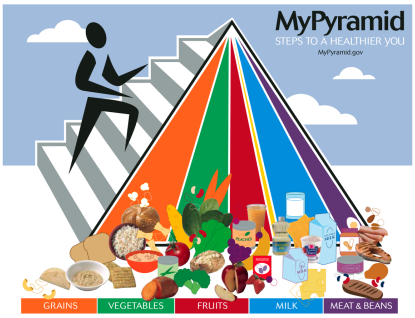
Family	Sources	Possible benefits
Flavonoids	Berries, herbs, vegetables, wine, grapes, tea	General antioxidant, oxidation of LDLs, prevention of arteriosclerosis and heart disease
Isoflavones (phytoestrogens)	Soy, red clover, kudzu root	General antioxidant, prevention of arteriosclerosis and heart disease, easing symptoms of menopause, cancer prevention [43]
Isothiocyanates	Cruciferous vegetables	cancer prevention
Monoterpenes	Citrus peels, essential oils, herbs, spices, green plants, atmosphere[44]	Cancer prevention, treating gallstones
Organosulfur compounds	Chives, garlic, onions	cancer prevention, lowered LDLs, assistance to the immune system
Saponins	Beans, cereals, herbs	Hypercholesterolemia, Hyperglycemia, Antioxidant, cancer prevention, Anti-inflammatory
Capsaicinoids	Chili peppers	Topical pain relief, cancer prevention, cancer cell apoptosis

Intestinal bacterial flora

It is now also known that animal intestines contain a large population of gut flora. In humans, these include species such as *Bacteroides*, *L. acidophilus* and *E. coli*, among many others. They are essential to digestion, and are also affected by the food we eat. Bacteria in the gut perform many important functions for humans, including breaking down and aiding in the absorption of otherwise indigestible food; stimulating cell growth; repressing the growth of harmful bacteria, training the immune system to respond only to pathogens; producing vitamin B12, and defending against some infectious diseases.

Advice and guidance

Government policies



The updated USDA food pyramid, published in 2005, is a general nutrition guide for recommended food consumption for humans.

In the US, dietitians are registered (RD) or licensed (LD) with the Commission for Dietetic Registration and the American Dietetic Association, and are only able to use the title "dietitian," as described by the business and professions codes of each respective state, when they have met specific educational and experiential prerequisites and passed a national registration or licensure examination, respectively. In California, registered dietitians must abide by the "Business and Professions Code of Section 2585-2586.8" [45].Anyone may call themselves a nutritionist, including unqualified dietitians, as this term is unregulated. Some states, such as the State of Florida, have begun to include the title "nutritionist" in state licensure requirements. Most governments provide guidance on nutrition, and some also impose mandatory disclosure/labeling requirements for processed food manufacturers and restaurants to assist consumers in complying with such guidance.

In the US, nutritional standards and recommendations are established jointly by the US Department of Agriculture and US Department of Health and Human Services. Dietary and physical activity guidelines from the USDA are presented in the concept of a food pyramid, which superseded the Four Food Groups. The Senate committee currently responsible for oversight of the USDA is the *Agriculture, Nutrition and Forestry Committee*. Committee hearings are often televised on C-SPAN as seen here.

The U.S. Department of Health and Human Services provides a sample week-long menu which fulfills the nutritional recommendations of the government.[46] Canada's Food Guide is another governmental recommendation.

Government programs

Federal and state governmental organizations have been working on nutrition literacy interventions in non-primary health care settings to address the nutrition information problem in the U.S. Some programs include:

The Family Nutrition Program (FNP) is a free nutrition education program serving low-income adults around the U.S. This program is funded by the Food Nutrition Service's (FNS) branch of the United States Department of Agriculture (USDA) usually through a local state academic institution which runs the program. The FNP has developed a series of tools to help families participating in the Food Stamp Program stretch their food dollar and form healthful eating habits including nutrition education.

Expanded Food and Nutrition Education Program [47] (ENFEP) is a unique program that currently operates in all 50 states and in American Samoa, Guam, Micronesia, Northern Marianas, Puerto Rico, and the Virgin Islands. It is designed to assist limited-resource audiences in acquiring the knowledge, skills, attitudes, and changed behavior necessary for nutritionally sound diets, and to contribute to their personal development and the improvement of the total family diet and nutritional well-being.

An example of a state initiative to promote nutrition literacy is Smart Bodies [48], a public-private partnership between the state's largest university system and largest health insurer, Louisiana State Agricultural Center and Blue Cross and Blue Shield of Louisiana Foundation. Launched in 2005, this program promotes lifelong healthful eating patterns and physically active lifestyles for children and their families. It is an interactive educational program designed to help prevent childhood obesity through classroom activities that teach children healthful eating habits and physical exercise.

Teaching

Nutrition is taught in schools in many countries. In England and Wales the Personal and Social Education and Food Technology curricula include nutrition, stressing the importance of a balanced diet and teaching how to read nutrition labels on packaging. In many schools a Nutrition class will fall within the Family and Consumer Science or Health departments. In some American schools, students are required to take a certain number of FCS or Health related classes. Nutrition is offered at many schools, and if it is not a class of its own, nutrition is included in other FCS or Health classes such as: Life Skills, Independent Living, Single Survival, Freshmen Connection, Health etc. In many Nutrition classes, students learn about the food groups, the food pyramid, Daily Recommended Allowances, calories, vitamins, minerals, malnutrition, physical activity, healthful food choices and how to live a healthy life.

A 1985 US National Research Council report entitled *Nutrition Education in US Medical Schools* concluded that nutrition education in medical schools was inadequate.[49] Only 20% of the schools surveyed taught nutrition as a separate, required course. A 2006 survey found that this number had risen to 30%.[50]

Healthy diets

Whole plant food diet

Heart disease, cancer, obesity, and diabetes are commonly called "Western" diseases because these maladies were once rarely seen in developing countries. An international study in China found some regions had essentially no cancer or heart disease, while in other areas they reflected "up to a 100-fold increase" coincident with shifts from diets that were found to be entirely plant-based to heavily animal-based, respectively.[51] In contrast, diseases of affluence like cancer and heart disease are common throughout the developed world, including the United States. Adjusted for age and exercise, large regional clusters of people in China rarely suffered from these "Western" diseases possibly because their diets are rich in vegetables, fruits and whole grains, and have little dairy and meat products.[51] Some studies show these to be, in high quantities, possible causes of some cancers. There are arguments for and against this controversial issue.

The United Healthcare/Pacificare nutrition guideline recommends a whole plant food diet, and recommends using protein only as a condiment with meals. A *National Geographic* cover article from November 2005, entitled *The Secrets of Living Longer*, also recommends a whole plant food diet. The article is a lifestyle survey of three populations, Sardinians, Okinawans, and Adventists, who generally display longevity and "suffer a fraction of the diseases that commonly kill people in other parts of the developed world, and enjoy more healthy years of life." In sum, they offer three sets of 'best practices' to emulate. The rest is up to you. In common with all three groups is to "Eat fruits, vegetables, and whole grains."

The *National Geographic* article noted that an NIH funded study of 34,000 Seventh-day Adventists between 1976 and 1988 "...found that the Adventists' habit of consuming beans, soy milk, tomatoes, and other fruits lowered their risk of developing certain cancers. It also suggested that eating whole grain bread, drinking five glasses of water a day, and, most surprisingly, consuming four servings of nuts a week reduced their risk of heart disease."

The French "paradox"

The French paradox is the observation that the French suffer a relatively low incidence of coronary heart disease, despite having a diet relatively rich in saturated fats. A number of explanations have been suggested:

- Saturated fat consumption does not cause heart disease[52]
- Reduced consumption of processed carbohydrate and other junk foods.
- Regular consumption of red wine.
- More active lifestyles involving plenty of daily exercise, especially walking; the French are much less dependent on cars than Americans are.
- Higher consumption of artificially produced trans-fats by Americans, which has been shown to have greater lipoprotein effects per gram than saturated fat.[53]

However, statistics collected by the World Health Organization from 1990–2000 show that the incidence of heart disease in France may have been underestimated and, in fact, may be similar to that of neighboring countries.[54]

Sports nutrition

Protein

Protein is an important component of every cell in the body. Hair and nails are mostly made of protein. The body uses protein to build and repair tissues. In addition, protein is used to make hormones and other chemicals in the body. Protein is also an important building block of bones, muscles, cartilage, skin, and blood.

Protein milkshakes, made from protein powder (center) and milk (left), are a common bodybuilding supplement.

The protein requirement for each individual differs, as do opinions about whether and to what extent physically active people require more protein. The 2005 Recommended Dietary Allowances (RDA), aimed at the general healthy adult population, provide for an intake of 0.8 – 1 grams of protein per kilogram of body weight (according to the BMI formula), with the review panel stating that "no additional dietary protein is suggested for healthy adults undertaking resistance or endurance exercise".[55] Conversely, Di Pasquale (2008), citing recent studies, recommends a minimum protein intake of 2.2 g/kg "for anyone involved in competitive or intense recreational sports who wants to maximize lean body mass but does not wish to gain weight".[56]

Water and salts

Water is one of the most important nutrients in the sports diet. It helps eliminate food waste products in the body, regulates body temperature during activity and helps with digestion. Maintaining hydration during periods of physical exertion is key to peak performance. While drinking too much water during activities can lead to physical discomfort, dehydration in excess of 2% of body mass (by weight) markedly hinders athletic performance.[57] Additional carbohydrates and protein before, during, and after exercise increase time to exhaustion as well as speed recovery. The amount of water needed is based on work performed, lean body mass, and environmental factors, especially ambient temperature and humidity. Maintaining the right amount is key.

Carbohydrates

The main fuel used by the body during exercise is carbohydrates, which are stored in muscle as glycogen—a form of sugar. During exercise, muscle glycogen reserves can be used up, especially when activities last longer than 90 min. Because the amount of glycogen stored in the body is limited, it is important for athletes to replace glycogen by consuming a diet high in carbohydrates. Meeting energy needs can help improve performance during the sport, as well as improve overall strength and endurance.

There are different kinds of carbohydrates—simple or refined, and unrefined. A typical American consumes about 50% of their carbohydrates as simple sugars, which are added to foods as opposed to sugars that come naturally in fruits and vegetables. These simple sugars come in large amounts in sodas and fast food. Over the course of a year, the average American consumes 54 gallons of soft drinks, which contain the highest amount of added sugars.[58] Even though carbohydrates are necessary for humans to function, they are not all equally healthful. When machinery has been used to remove bits of high fiber, the carbohydrates are refined. These are the carbohydrates found in white bread and fast food.[59]

Nutrition literacy

At the time of this entry, we were not able to identify any specific nutrition literacy studies in the U.S. at a national level. However, the findings of the 2003 National Assessment of Adult Literacy (NAAL) provide a basis upon which to frame the nutrition literacy problem in the U.S. NAAL introduced the first ever measure of "the degree to which individuals have the capacity to obtain, process and understand basic health information and services needed to make appropriate health decisions," - an objective of Healthy People 2010 [60] and of which nutrition literacy might be considered an important subset. On a scale of below basic, basic, intermediate and proficient, NAAL found 13 percent of adult Americans have proficient health literacy, 44% have intermediate literacy, 29 percent have basic literacy and 14 percent have below basic health literacy. The study found that health literacy increases with education and people living below the level of poverty have lower health literacy then those above it.

Another study examining the health and nutrition literacy status of residents of the lower Mississippi Delta found that 52 percent of participants had a high likelihood of limited literacy skills.[61] While a precise comparison between the NAAL and Delta studies is difficult, primarily because of methodological differences, Zoellner et al. suggest that health literacy rates in the Mississippi Delta region are different from the U.S. general population and that they help establish the scope of the problem of health literacy among adults in the Delta region. For example, only 12 percent of study participants identified the My Pyramid graphic two years after it had been launched by the USDA. The study also found significant relationships between nutrition literacy and income level and nutrition literacy and educational attainment[61] further delineating priorities for the region.

These statistics point to the complexities surrounding the lack of health/nutrition literacy and reveal the degree to which they are embedded in the social structure and interconnected with other problems. Among these problems are the lack of information about food choices, the lack of understanding nutritional information and its application to individual circumstances, limited or difficult access to healthful foods, and a range of cultural influences and socioeconomic constraints such as low levels of education and high levels of poverty that decrease opportunities for healthful eating and living.

The links between low health literacy and poor health outcomes has been widely documented[62] and there is evidence that some interventions to improve health literacy have produced successful results in the primary care setting. More must be done to further our understanding of nutrition literacy specific interventions in non-primary care settings[61] in order to achieve better health outcomes.

Malnutrition

Malnutrition refers to insufficient, excessive, or imbalanced consumption of nutrients by an organism. In developed countries, the diseases of malnutrition are most often associated with nutritional imbalances or excessive consumption.

Although there are more organisms in the world who are malnourished due to insufficient consumption, increasingly more organisms suffer from excessive over-nutrition; a problem caused by an over abundance of sustenance coupled with the instinctual desire (by animals in particular) to consume all that it can.

Nutritionism is the view that excessive reliance on food science and the study of nutrition can, paradoxically, lead to poor nutrition and to ill health. It was originally credited to Gyorgy Scrinis,[63] and was popularized by Michael Pollan. Since nutrients are invisible, policy makers rely on nutrition experts to advise on food choices. Because science has an incomplete understanding of how food affects the human body, Pollan argues, nutritionism can be blamed for many of the health problems relating to diet in the Western World today.[64][65]

Insufficient

Under consumption generally refers to the long-term consumption of insufficient sustenance in relation to the energy that an organism expends or expels, leading to poor health.

Excessive

Over consumption generally refers to the long-term consumption of excess sustenance in relation to the energy that an organism expends or expels, leading to poor health and, in animals, obesity. It can cause excessive hair loss, brittle nails, and irregular premenstrual cycles for females

Unbalanced

When too much of one or more nutrients is present in the diet to the exclusion of the proper amount of other nutrients, the diet is said to be unbalanced.

Illnesses caused by improper nutrient consumption

Nutrients	Deficiency	Excess
Macronutrients		
Calories	Starvation, marasmus	Obesity, diabetes mellitus, cardiovascular disease
Simple carbohydrates	None	Obesity, diabetes mellitus, cardiovascular disease
Complex carbohydrates	Micronutrient deficiency	Obesity, cardiovascular disease (high glycemic index foods)
Protein	Kwashiorkor	Rabbit starvation, ketoacidosis (in diabetics)
Saturated fat	None	Obesity, cardiovascular disease
Trans fat	None	Obesity, cardiovascular disease
Unsaturated fat	Fat-soluble vitamin deficiency	Obesity, cardiovascular disease
Micronutrients		
Vitamin A	Xerophthalmia and night blindness	Hypervitaminosis A (cirrhosis, hair loss)
Vitamin B_1	Beri-Beri	?
Vitamin B_2	Skin and corneal lesions	?
Niacin	Pellagra	Dyspepsia, cardiac arrhythmias, birth defects

Vitamin B_{12}	Pernicious anemia	?
Vitamin C	Scurvy	Diarrhea causing dehydration
Vitamin D	Rickets	Hypervitaminosis D (dehydration, vomiting, constipation)
Vitamin E	Neurological disease	Hypervitaminosis E (anticoagulant: excessive bleeding)
Vitamin K	Hemorrhage	?
Omega-3 fats	Cardiovascular Disease	Bleeding, Hemorrhages, Hemorrhagic stroke, reduced glycemic control among diabetics
Omega-6 fats	None	Cardiovascular Disease, Cancer
Cholesterol	None	Cardiovascular Disease
Macrominerals		
Calcium	Osteoporosis, tetany, carpopedal spasm, laryngospasm, cardiac arrhythmias	Fatigue, depression, confusion, nausea, vomiting, constipation, pancreatitis, increased urination, kidney stones
Magnesium	Hypertension	Weakness, nausea, vomiting, impaired breathing, and hypotension
Potassium	Hypokalemia, cardiac arrhythmias	Hyperkalemia, palpitations
Sodium	Hyponatremia	Hypernatremia, hypertension
Trace minerals		
Iron	Anemia	Cirrhosis, hepatitis C, heart disease
Iodine	Goiter, hypothyroidism	Iodine toxicity (goiter, hypothyroidism)

Mental agility

Research indicates that improving the awareness of nutritious meal choices and establishing long-term habits of healthful eating have a positive effect on cognitive and spatial memory capacity, potentially increasing a student's potential to process and retain academic information.

Some organizations have begun working with teachers, policymakers, and managed foodservice contractors to mandate improved nutritional content and increased nutritional resources in school cafeterias from primary to university level institutions. Health and nutrition have been proven to have close links with overall educational success.[66] Currently, less than 10% of American college students report that they eat the recommended five servings of fruit and vegetables daily.[67] Better nutrition has been shown to have an impact on both cognitive and spatial memory performance; a study showed those with higher blood sugar levels performed better on certain memory tests.[68] In another study, those who consumed yogurt performed better on thinking tasks when compared to those who consumed caffeine free diet soda or confections.[69] Nutritional deficiencies have been shown to have a negative effect on learning behavior in mice as far back as 1951.[70]

> "Better learning performance is associated with diet induced effects on learning and memory ability".[71]
>
> The "nutrition-learning nexus" demonstrates the correlation between diet and learning and has application in a higher education setting.
>
> "We find that better nourished children perform significantly better in school, partly because they enter school earlier and thus have more time to learn but mostly because of greater learning productivity per year of schooling."[72]
>
> 91% of college students feel that they are in good health while only 7% eat their recommended daily allowance of fruits and vegetables.[67]
>
> Nutritional education is an effective and workable model in a higher education setting.[73][74]
>
> More "engaged" learning models that encompass nutrition is an idea that is picking up steam at all levels of the learning cycle.[75]

There is limited research available that directly links a student's Grade Point Average (G.P.A.) to their overall nutritional health. Additional substantive data is needed to prove that overall intellectual health is closely linked to a person's diet, rather than just another correlation fallacy.

Mental disorders

Nutritional supplement treatment may be appropriate for major depression, bipolar disorder, schizophrenia, and obsessive compulsive disorder, the four most common mental disorders in developed countries.[76] Supplements that have been studied most for mood elevation and stabilization include eicosapentaenoic acid and docosahexaenoic acid (each of which are an omega-3 fatty acid contained in fish oil, but not in flaxseed oil), vitamin B12, folic acid, and inositol.

Cancer

Cancer is now common in developing countries. According to a study by the International Agency for Research on Cancer, "In the developing world, cancers of the liver, stomach and esophagus were more common, often linked to consumption of carcinogenic preserved foods, such as smoked or salted food, and parasitic infections that attack organs." Lung cancer rates are rising rapidly in poorer nations because of increased use of tobacco. Developed countries "tended to have cancers linked to affluence or a 'Western lifestyle' — cancers of the colon, rectum, breast and prostate — that can be caused by obesity, lack of exercise, diet and age."[77]

Metabolic syndrome

Several lines of evidence indicate lifestyle-induced hyperinsulinemia and reduced insulin function (i.e. insulin resistance) as a decisive factor in many disease states. For example, hyperinsulinemia and insulin resistance are strongly linked to chronic inflammation, which in turn is strongly linked to a variety of adverse developments such as arterial microinjuries and clot formation (i.e. heart disease) and exaggerated cell division (i.e. cancer). Hyperinsulinemia and insulin resistance (the so-called metabolic syndrome) are characterized by a combination of abdominal obesity, elevated blood sugar, elevated blood pressure, elevated blood triglycerides, and reduced HDL cholesterol. The negative impact of hyperinsulinemia on prostaglandin PGE1/PGE2 balance may be significant.

The state of obesity clearly contributes to insulin resistance, which in turn can cause type 2 diabetes. Virtually all obese and most type 2 diabetic individuals have marked insulin resistance. Although the association between overweight and insulin resistance is clear, the exact (likely multifarious) causes of insulin resistance remain less clear. Importantly, it has been demonstrated that appropriate exercise, more regular food intake and reducing glycemic load (see below) all can reverse insulin resistance in overweight individuals (and thereby lower blood sugar levels in those who have type 2 diabetes).

Obesity can unfavourably alter hormonal and metabolic status via resistance to the hormone leptin, and a vicious cycle may occur in which insulin/leptin resistance and obesity aggravate one another. The vicious cycle is putatively fuelled by continuously high insulin/leptin stimulation and fat storage, as a result of high intake of strongly insulin/leptin stimulating foods and energy. Both insulin and leptin normally function as satiety signals to the hypothalamus in the brain; however, insulin/leptin resistance may reduce this signal and therefore allow continued overfeeding despite large body fat stores. In addition, reduced leptin signalling to the brain may reduce leptin's normal effect to maintain an appropriately high metabolic rate.

There is a debate about how and to what extent different dietary factors— such as intake of processed carbohydrates, total protein, fat, and carbohydrate intake, intake of saturated and trans fatty acids, and low intake of vitamins/minerals—contribute to the development of insulin and leptin resistance. In any case, analogous to the way modern man-made pollution may potentially overwhelm the environment's ability to maintain homeostasis, the recent explosive introduction of high glycemic index and processed foods into the human diet may potentially overwhelm the body's ability to maintain homeostasis and health (as evidenced by the metabolic syndrome epidemic).

Hyponatremia

Excess water intake, without replenishment of sodium and potassium salts, leads to hyponatremia, which can further lead to water intoxication at more dangerous levels. A well-publicized case occurred in 2007, when Jennifer Strange died while participating in a water-drinking contest.[78] More usually, the condition occurs in long-distance endurance events (such as marathon or triathlon competition and training) and causes gradual mental dulling, headache, drowsiness, weakness, and confusion; extreme cases may result in coma, convulsions, and death. The primary damage comes from swelling of the brain, caused by increased osmosis as blood salinity decreases. Effective fluid replacement techniques include water aid stations during running/cycling races, trainers providing water during team games, such as soccer, and devices such as Camel Baks, which can provide water for a person without making it too hard to drink the water.

Antinutrient

Antinutrients are natural or synthetic compounds that interfere with the absorption of nutrients. Nutrition studies focus on antinutrients commonly found in food sources and beverages.

Processed foods

Since the Industrial Revolution some two hundred years ago, the food processing industry has invented many technologies that both help keep foods fresh longer and alter the fresh state of food as they appear in nature. Cooling is the primary technology used to maintain freshness, whereas many more technologies have been invented to allow foods to last longer without becoming spoiled. These latter technologies include pasteurisation, autoclavation, drying, salting, and separation of various components, all of which appear to alter the original nutritional contents of food. Pasteurisation and autoclavation (heating techniques) have no doubt improved the safety of many common foods, preventing epidemics of bacterial infection. But some of the (new) food processing technologies undoubtedly have downfalls as well.

Modern separation techniques such as milling, centrifugation, and pressing have enabled concentration of particular components of food, yielding flour, oils, juices and so on, and even separate fatty acids, amino acids, vitamins, and minerals. Inevitably, such large scale concentration changes the nutritional content of food, saving certain nutrients while removing others. Heating techniques may also reduce food's content of many heat-labile nutrients such as certain vitamins and phytochemicals, and possibly other yet to be discovered substances.[79] Because of reduced nutritional value, processed foods are often 'enriched' or 'fortified' with some of the most critical nutrients (usually certain vitamins) that were lost during processing. Nonetheless, processed foods tend to have an inferior nutritional profile compared to whole, fresh foods, regarding content of both sugar and high GI starches, potassium/sodium, vitamins, fiber, and of intact, unoxidized (essential) fatty acids. In addition, processed foods often contain potentially harmful substances such as oxidized fats and trans fatty acids.

A dramatic example of the effect of food processing on a population's health is the history of epidemics of beri-beri in people subsisting on polished rice. Removing the outer layer of rice by polishing it removes with it the essential vitamin thiamine, causing beri-beri. Another example is the development of scurvy among infants in the late 19th century in the United States. It turned out that the vast majority of sufferers were being fed milk that had been heat-treated (as suggested by Pasteur) to control bacterial disease. Pasteurisation was effective against bacteria, but it destroyed the vitamin C.

As mentioned, lifestyle- and obesity-related diseases are becoming increasingly prevalent all around the world. There is little doubt that the increasingly widespread application of some modern food processing technologies has contributed to this development. The food processing industry is a major part of modern economy, and as such it is influential in political decisions (e.g. nutritional recommendations, agricultural subsidising). In any known profit-driven economy, health considerations are hardly a priority; effective production of cheap foods with a long shelf-life is more the trend. In general, whole, fresh foods have a relatively short shelf-life and are less profitable to produce and sell than are more processed foods. Thus, the consumer is left with the choice between more expensive, but nutritionally superior, whole, fresh foods, and cheap, usually nutritionally inferior, processed foods. Because processed foods are often cheaper, more convenient (in both purchasing, storage, and preparation), and more available, the consumption of nutritionally inferior foods has been increasing throughout the world along with many nutrition-related health complications.

History

Humans have evolved as omnivorous hunter-gatherers over the past 250,000 years. The diet of early modern humans varied significantly depending on location and climate. The diet in the tropics tended to be based more heavily on plant foods, while the diet at higher latitudes tended more towards animal products. Analysis of postcranial and cranial remains of humans and animals from the Neolithic, along with detailed bone modification studies have shown that cannibalism was also prevalent among prehistoric humans.[80]

Agriculture developed about 10,000 years ago in multiple locations throughout the world, providing grains such as wheat, rice, potatoes, and maize, with staples such as bread, pasta, and tortillas. Farming also provided milk and dairy products, and sharply increased the availability of meats and the diversity of vegetables. The importance of food purity was recognized when bulk storage led to infestation and contamination risks. Cooking developed as an often ritualistic activity, due to efficiency and reliability concerns requiring adherence to strict recipes and procedures, and in response to demands for food purity and consistency.[81]

From antiquity to 1900

The first recorded nutritional experiment is found in the Bible's Book of Daniel. Daniel and his friends were captured by the king of Babylon during an invasion of Israel. Selected as court servants, they were to share in the king's fine foods and wine. But they objected, preferring vegetables (pulses) and water in accordance with their Jewish dietary restrictions. The king's chief steward reluctantly agreed to a trial. Daniel and his friends received their diet for 10 days and were then compared to the king's men. Appearing healthier, they were allowed to continue with their diet.[82]

Anaxagoras

Around 475 BC, Anaxagoras stated that food is absorbed by the human body and therefore contained "homeomerics" (generative components), suggesting the existence of nutrients.[81] Around 400 BC, Hippocrates said, "Let food be your medicine and medicine be your food."[83]

In the 16th century, scientist and artist Leonardo da Vinci compared metabolism to a burning candle. In 1747, Dr. James Lind, a physician in the British navy, performed the first scientific nutrition experiment, discovering that lime juice saved sailors who had been at sea for years from scurvy, a deadly and painful bleeding disorder. The discovery was ignored for forty years, after which British sailors became known as "limeys." The essential vitamin C within lime juice would not be identified by scientists until the 1930s.

Around 1770, Antoine Lavoisier, the "Father of Nutrition and Chemistry" discovered the details of metabolism, demonstrating that the oxidation of food is the source of body heat. In 1790, George Fordyce recognized calcium as necessary for fowl survival. In the early 19th century, the elements carbon, nitrogen, hydrogen and oxygen were recognized as the primary components of food, and methods to measure their proportions were developed.

In 1816, François Magendie discovered that dogs fed only carbohydrates and fat lost their body protein and died in a few weeks, but dogs also fed protein survived, identifying protein as an essential dietary component. In 1840, Justus Liebig discovered the chemical makeup of carbohydrates (sugars), fats (fatty acids) and proteins (amino acids.) In the 1860s, Claude Bernard discovered that body fat can be synthesized from carbohydrate and protein, showing that the energy in blood glucose can be stored as fat or as glycogen.

In the early 1880s, Kanehiro Takaki observed that Japanese sailors (whose diets consisted almost entirely of white rice) developed beriberi (or endemic neuritis, a disease causing heart problems and paralysis), but British sailors and Japanese naval officers did not. Adding various types of vegetables and meats to the diets of Japanese sailors prevented the disease.

In 1896, Eugen Baumann observed iodine in thyroid glands. In 1897, Christiaan Eijkman worked with natives of Java, who also suffered from beriberi. Eijkman observed that chickens fed the native diet of white rice developed the symptoms of beriberi, but remained healthy when fed unprocessed brown rice with the outer bran intact. Eijkman cured the natives by feeding them brown rice, discovering that food can cure disease. Over two decades later, nutritionists learned that the outer rice bran contains vitamin B1, also known as thiamine.

From 1900 to the present

In the early 20th century, Carl Von Voit and Max Rubner independently measured caloric energy expenditure in different species of animals, applying principles of physics in nutrition. In 1906, Wilcock and Hopkins showed that the amino acid tryptophan was necessary for the survival of rats. He fed them a special mixture of food containing all the nutrients he believed were essential for survival, but the rats died. A second group of rats were fed an amount of milk containing vitamins.[84] Sir Frederick Hopkins recognized "accessory food factors" other than calories, protein and minerals, as organic materials essential to health, but which the body cannot synthesize. In 1907, Stephen M. Babcock and Edwin B. Hart conducted the single-grain experiment, which took nearly four years to complete.

In 1912, Casimir Funk coined the term vitamin, a vital factor in the diet, from the words "vital" and "amine," because these unknown substances preventing scurvy, beriberi, and pellagra, were thought then to be derived from ammonia. The vitamins were studied in the first half of the 20th century.

In 1913, Elmer McCollum discovered the first vitamins, fat soluble vitamin A, and water soluble vitamin B (in 1915; now known to be a complex of several water-soluble vitamins) and named vitamin C as the then-unknown substance preventing scurvy. Lafayette Mendel and Thomas Osborne also performed pioneering work on vitamins A and B. In 1919, Sir Edward Mellanby incorrectly identified rickets as a vitamin A deficiency because he could cure it in dogs with cod liver oil.[85] In 1922, Elmer McCollum destroyed the vitamin A in cod liver oil, but found that it still cured rickets. Also in 1922, H.M. Evans and L.S. Bishop discover vitamin E as essential for rat pregnancy, originally calling it "food factor X" until 1925.

In 1925, Hart discovered that trace amounts of copper are necessary for iron absorption. In 1927, Adolf Otto Reinhold Windaus synthesized vitamin D, for which he won the Nobel Prize in Chemistry in 1928. In 1928, Albert Szent-Györgyi isolated ascorbic acid, and in 1932 proved that it is vitamin C by preventing scurvy. In 1935 he synthesized it, and in 1937, he won a Nobel Prize for his efforts. Szent-Györgyi concurrently elucidated much of the citric acid cycle.

In the 1930s, William Cumming Rose identified essential amino acids, necessary protein components which the body cannot synthesize. In 1935, Underwood and Marston independently discovered the necessity of cobalt. In 1936, Eugene Floyd Dubois showed that work and school performance are related to caloric intake. In 1938, Erhard Fernholz discovered the chemical structure of vitamin E. It was synthesised by Paul Karrer.

In 1940, rationing in the United Kingdom during and after World War II took place according to nutritional principles drawn up by Elsie Widdowson and others. In 1941, the first Recommended Dietary Allowances (RDAs) were established by the National Research Council.

In 1992, The U.S. Department of Agriculture introduced the Food Guide Pyramid. In 2002, a Natural Justice study showed a relation between nutrition and violent behavior. In 2005, a study found that obesity may be caused by adenovirus in addition to bad nutrition.[86]

Plant nutrition

Plant nutrition is the study of the chemical elements that are necessary for plant growth. There are several principles that apply to plant nutrition. Some elements are directly involved in plant metabolism. However, this principle does not account for the so-called beneficial elements, whose presence, while not required, has clear positive effects on plant growth.

A nutrient that is able to limit plant growth according to Liebig's law of the minimum, is considered an essential plant nutrient if the plant cannot complete its full life cycle without it. There are 17 essential plant nutrients.

Macronutrients:

- N = Nitrogen
- P = Phosphorus
- K = Potassium
- Ca = Calcium
- Mg = Magnesium
- S = Sulfur
- Si = Silicon

Micronutrients (trace levels) include:

- Cl = Chlorine
- Fe = Iron
- B = Boron
- Mn = Manganese
- Na = Sodium
- Zn = Zinc
- Cu = Copper
- Ni= Nickel
- Mo = Molybdenum

Macronutrients

Calcium

Calcium regulates transport of other nutrients into the plant and is also involved in the activation of certain plant enzymes. Calcium deficiency results in stunting.

Nitrogen

Nitrogen is an essential component of all proteins. Nitrogen deficiency most often results in stunted growth.

Phosphorus

Phosphorus is important in plant bioenergetics. As a component of ATP, phosphorus is needed for the conversion of light energy to chemical energy (ATP) during photosynthesis. Phosphorus can also be used to modify the activity of various enzymes by phosphorylation, and can be used for cell signaling. Since ATP can be used for the biosynthesis of many plant biomolecules, phosphorus is important for plant growth and flower/seed formation.

Potassium

Potassium regulates the opening and closing of the stoma by a potassium ion pump. Since stomata are important in water regulation, potassium reduces water loss from the leaves and increases drought tolerance. Potassium deficiency may cause necrosis or interveinal chlorosis.

Silicon

Silicon is deposited in cell walls and contributes to its mechanical properties including rigidity and elasticity

Micronutrients

Boron

Boron is important in sugar transport, cell division, and synthesizing certain enzymes. Boron deficiency causes necrosis in young leaves and stunting.

Copper

Copper is important for photosynthesis. Symptoms for copper deficiency include chlorosis. Involved in many enzyme processes. Necessary for proper photosythesis. Involved in the manufacture of lignin (cell walls). Involved in grain production.

Chlorine

Chlorine is necessary for osmosis and ionic balance; it also plays a role in photosynthesis.

Iron

Iron is necessary for photosynthesis and is present as an enzyme cofactor in plants. Iron deficiency can result in interveinal chlorosis and necrosis.

Manganese

Manganese is necessary for building the chloroplasts. Manganese deficiency may result in coloration abnormalities, such as discolored spots on the foliage.

Molybdenum

Molybdenum is a cofactor to enzymes important in building amino acids.

Nickel

In higher plants, Nickel is essential for activation of urease, an enzyme involved with nitrogen metabolism that is required to process urea. Without Nickel, toxic levels of urea accumulate, leading to the formation of necrotic lesions. In lower plants, Nickel activates several enzymes involved in a variety of processes, and can substitute for Zinc and Iron as a cofactor in some enzymes.

Sodium

Sodium is involved in the regeneration of phosphoenolpyruvate in CAM and C4 plants. It can also substitute for potassium in some circumstances.

Zinc

Zinc is required in a large number of enzymes and plays an essential role in DNA transcription. A typical symptom of zinc deficiency is the stunted growth of leaves, commonly known as "little leaf" and is caused by the oxidative degradation of the growth hormone auxin.

Processes

Plants uptake essential elements from the soil through their roots and from the air (mainly consisting of nitrogen and oxygen) through their leaves. Green plants obtain their carbohydrate supply from the carbon dioxide in the air by the process of photosynthesis.Carbon and oxygen are absorbed from the air, while other nutrients are absorbed from the soil. .Nutrient uptake in the soil is achieved by cation exchange, wherein root hairs pump hydrogen ions (H^+) into the soil through proton pumps. These hydrogen ions displace cations attached to negatively charged soil particles so that the cations are available for uptake by the root. In the leaves, stomata open to take in carbon dioxide and expel oxygen. The carbon dioxide molecules are used as the carbon source in photosynthesis.

Although nitrogen is plentiful in the Earth's atmosphere, very few plants can use this directly. Most plants therefore require nitrogen compounds to be present in the soil in which they grow. This is made possible by largely inert atmospheric nitrogen being changed in a nitrogen fixation process to biologically usable forms in the soil by bacteria.[87]

Plant nutrition is a difficult subject to understand completely, partially because of the variation between different plants and even between different species or individuals of a given clone. Elements present at low levels may cause deficiency symptoms, and toxicity is possible at levels that are too high. Furthermore, deficiency of one element may present as symptoms of toxicity from another element, and vice-versa.

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External links

- Diet, Nutrition and the prevention of chronic diseases (http://www.who.int/nutrition/topics/dietnutrition_and_chronicdiseases/en/) by a Joint WHO/FAO Expert consultation (2003)
- United States Department of Agriculture (USDA) Frequently asked questions (http://www.ars.usda.gov/Services/docs.htm?docid=7886)
- Nutritional Status Assessment and Analysis – e-learning from FAO (http://www.foodsec.org/dl/elcpages/food-security-courses.asp?pgLanguage=en&leftItemSelected=food-security-courses)
- International Organization of Nutritional Consultants (http://www.ionc.org/)
- UN Standing Committee on Nutrition (http://www.unscn.org/) – In English, French and Portuguese
- Health-EU Portal (http://ec.europa.eu/health-eu/my_lifestyle/nutrition/index_en.htm) Nutrition
- Small meals or big ones? (http://womensportsfitness.com/?id=4e24f66c)
- How much water your body needs? (http://www.europeanhydrationinstitute.org/hydration_and_beverages.html)

Databases and search engines

- Nutrition Data (http://www.nutritiondata.com/)
- Restaurant Nutrition Database (http://www.nutritionix.com/restaurants)
- Recipe Nutrition – extends USDA database with friendly names for common ingredients, recipe nutrition calculator and additional specialized ingredients (http://www.recipenutrition.com/)
- German Nutrition Data with fast search on www.lexolino.de (http://www.lexolino.de/c,kultur_alltagskultur_gesundheit_ernährung_nährwerttabellen)
- USDA National Nutrient Database for Standard Reference (http://www.nal.usda.gov/fnic/foodcomp/search/) Search By Food
- USDA National Nutrient Database for Standard Reference Nutrient Lists (http://www.ars.usda.gov/Services/docs.htm?docid=22114) Search By Nutrient
- Nutri Explorer - smartphone application using USDA National Nutrient Database with searching and sorting by nutrient information (http://www.nutriexplorer.com/)

B vitamins

B vitamins are a group of water-soluble vitamins that play important roles in cell metabolism. The B vitamins were once thought to be a single vitamin, referred to as **vitamin B** (much as people refer to vitamin C or vitamin D). Later research showed that they are chemically distinct vitamins that often coexist in the same foods. In general, supplements containing all eight are referred to as a **vitamin B complex**. Individual B vitamin supplements are referred to by the specific name of each vitamin (e.g., B_1, B_2, B_3 etc.).

B vitamin supplement tablets

List of B vitamins

- **Vitamin B_1** (thiamine)
- **Vitamin B_2** (riboflavin)
- **Vitamin B_3** (niacin or niacinamide)
- **Vitamin B_5** (pantothenic acid)
- **Vitamin B_6** (pyridoxine, pyridoxal, or pyridoxamine, or pyridoxine hydrochloride)
- **Vitamin B_7** (biotin)
- **Vitamin B_9** (folic acid)
- **Vitamin B_{12}** (various cobalamins; commonly cyanocobalamin in vitamin supplements)

Health benefits

The B vitamins are necessary to:

- Support and increase the rate of metabolism
- Maintain healthy skin, hair and muscle tone
- Enhance immune and nervous system function
- Promote cell growth and division, including that of the red blood cells that help prevent anemia
- Reduce the risk of pancreatic cancer - one of the most lethal forms of cancer[1] - when consumed in food, but not when ingested in vitamin tablet form.[2][3]

All B vitamins are water-soluble, and are dispersed throughout the body. Most of the B vitamins must be replenished regularly, since any excess is excreted in the urine.[4] This can result in the urine produced being a bright green-yellow colour.

B vitamins have also been hypothesized to reduce the symptoms of attention deficit hyperactivity disorder.[5]

B vitamin deficiency

Several named vitamin deficiency diseases may result from the lack of sufficient B-vitamins. Deficiencies of other B vitamins result in symptoms that are not part of a named deficiency disease.

Vitamin	Name	Deficiency effects'
Vitamin B_1	thiamine	Deficiency causes beriberi. Symptoms of this disease of the nervous system include weight loss, emotional disturbances, Wernicke's encephalopathy (impaired sensory perception), weakness and pain in the limbs, periods of irregular heartbeat, and edema (swelling of bodily tissues). Heart failure and death may occur in advanced cases. Chronic thiamine deficiency can also cause Korsakoff's syndrome, an irreversible psychosis characterized by amnesia and confabulation.
Vitamin B_2	riboflavin	Deficiency causes ariboflavinosis. Symptoms may include cheilosis (cracks in the lips), high sensitivity to sunlight, angular cheilitis, glossitis (inflammation of the tongue), seborrheic dermatitis or pseudo-syphilis (particularly affecting the scrotum or labia majora and the mouth), pharyngitis (sore throat), hyperemia, and edema of the pharyngeal and oral mucosa.
Vitamin B_3	niacin	Deficiency, along with a deficiency of tryptophan causes pellagra. Symptoms include aggression, dermatitis, insomnia, weakness, mental confusion, and diarrhea. In advanced cases, pellagra may lead to dementia and death (the 3(+1) Ds: dermatitis, diarrhea, dementia, and death).
Vitamin B_5	pantothenic acid	Deficiency can result in acne and paresthesia, although it is uncommon.
Vitamin B_6	pyridoxine	Deficiency may lead to microcytic anemia (because pyridoxyl phosphate is the cofactor for heme synthesis), depression, dermatitis, high blood pressure (hypertension), water retention, and elevated levels of homocysteine.
Vitamin B_7	biotin	Deficiency does not typically cause symptoms in adults but may lead to impaired growth and neurological disorders in infants. Multiple carboxylase deficiency, an inborn error of metabolism, can lead to biotin deficiency even when dietary biotin intake is normal.
Vitamin B_9	folic acid	Deficiency results in a macrocytic anemia, and elevated levels of homocysteine. Deficiency in pregnant women can lead to birth defects. Supplementation is often recommended during pregnancy. Researchers have shown that folic acid might also slow the insidious effects of age on the brain.
Vitamin B_{12}	cobalamin	Deficiency results in a macrocytic anemia, elevated homocysteine, peripheral neuropathy, memory loss and other cognitive deficits. It is most likely to occur among elderly people, as absorption through the gut declines with age; the autoimmune disease pernicious anemia is another common cause. It can also cause symptoms of mania and psychosis. In rare extreme cases, paralysis can result.

B vitamin toxicity

Although most B vitamins are eliminated regularly in the urine, taking large doses of certain B vitamins may produce harmful effects.

Vitamin	Name	Tolerable Upper Intake Level	Harmful effects
Vitamin B_1	thiamine	None[6]	No known toxicity from oral intake. There are some reports of anaphylaxis caused by high-dose thiamin injections into the vein or muscle. However, the doses were greater than the quantity humans can physically absorb from oral intake.[6]
Vitamin B_2	riboflavin	None.[7]	No evidence of toxicity based on limited human and animal studies. The only evidence of adverse effects associated with riboflavin comes from *in vitro* studies showing the production of reactive oxygen species (free radicals) when riboflavin was exposed to intense visible and UV light.[7]
Vitamin B_3	niacin	35 mg/day from supplements, drugs or fortified food[8]	Intake of 3000 mg/day of nicotinamide and 1500 mg/day of nicotinic acid are associated with nausea, vomiting, and signs and symptoms of liver toxicity. Other effects may include glucose intolerance, and (reversible) ocular effects. Additionally, the nicotinic acid form may cause vasodilatory effects, also known as flushing, including redness of the skin, often accompanied by an itching, tingling, or mild burning sensation, which is also often accompanied by pruritus, headaches, and increased intracranial blood flow, and occasionally accompanied by pain.[8] Medical practitioners prescribe recommended doses up to 2000 mg. per day of niacin, usually in time release format, to combat arterial plaque development in cases of high lipid levels.[9]

Vitamin B_5	pantothenic acid	None	No known toxicity
Vitamin B_6	pyridoxine	100 mg/day from supplements, drugs or fortified food[10]	Intake of more than 1000 mg/day is associated with peripheral sensory neuropathy; other effects are unconfirmed: dermatological lesions [causal association is unlikely]; B_6 dependency in newborns [causal association is also unlikely].[10]
Vitamin B_7	biotin	None	No known toxicity
Vitamin B_9	folic acid	1 mg/day [11]	Masks B_{12} deficiency, which can lead to permanent neurological damage[11]
Vitamin B_{12}	cyanocobalamin	None established.[12]	Acne-like rash [causality is not conclusively established].[12][13]

B vitamin sources

B vitamins are found in whole unprocessed foods. Processed carbohydrates such as sugar and white flour tend to have lower B vitamin than their unprocessed counterparts. B vitamins are particularly concentrated in meat such as turkey and tuna, in liver and meat products.[14] Good sources for B vitamins include kombucha, whole grains, potatoes, bananas, lentils, chili peppers, tempeh, beans, nutritional yeast, brewer's yeast, and molasses. Although the yeast used to make beer results in beers being a source of B vitamins,[15] their bioavailability ranges from poor to negative as drinking ethanol inhibits absorption of thiamine (B_1),[16][17] riboflavin (B_2),[18] niacin (B_3),[19] biotin (B_7),[20] and folic acid (B_9).[21][22] In addition, each of the preceding studies further emphasizes that elevated consumption of beer and other ethanol-based drinks results in a net deficit of those B vitamins and the health risks associated with such deficiencies.

The B_{12} vitamin is of note because it is not available from plant products, making B_{12} deficiency a concern for vegans. Manufacturers of plant-based foods will sometimes report B_{12} content, leading to confusion about what sources yield B_{12}. The confusion arises because the standard US Pharmacopeia (USP) method for measuring the B_{12} content does not measure the B_{12} directly. Instead, it measures a bacterial response to the food. Chemical variants of the B_{12} vitamin found in plant sources are active for bacteria, but cannot be used by the human body. This same phenomenon can cause significant over-reporting of B_{12} content in other types of foods as well.[23]

Vitamin B may also be delivered by injection to reverse deficiencies.[24]

Another popular means of increasing one's vitamin B intake is through the use of dietary supplements. B vitamins are also commonly added to energy drinks, many of which have been marketed with large amounts of B vitamins[25] with claims that this will cause the consumer to "sail through your day without feeling jittery or tense."[25] Nutritionists, such as Case Western University Professor Hope Barkoukis, dismiss these claims: "It's brilliant marketing, but it doesn't have any basis [in fact]." While B vitamins do "help unlock the energy in foods," just about everyone in America already gets all of the B vitamins they could possibly need in their diets.[25]

In general, extra B vitamins are just flushed out of the system, although everyone's limit of absorption is different in regards to B complex vitamins, and no one knows how much is needed on an individual basis of these vitamins…"[25] The elderly and athletes may need to supplement their intake of B_{12} and other B vitamins due to problems in absorption and increased needs for energy production. Both type 1 and type 2 diabetics may also be advised to supplement thiamine based on high prevalence of low plasma thiamine concentration and increased thiamine clearance associated with diabetes.[26] Also, Vitamin B_9 (folic acid) deficiency in early embryo development has been linked to neural tube defects. Thus, women planning to become pregnant are usually encouraged to increase daily dietary folic acid intake and/or take a supplement.[27] However, for "most typical consumers of energy supplements or drinks, B vitamins are nothing more than a 'gimmick'."[25]

Related nutrients

Many of the following substances have been referred to as vitamins because they were believed to be vitamins at one time. They are not considered vitamins anymore and the numbers that were assigned to them now form the "gaps" in the true series of B-complex vitamins described above (e.g. there is no vitamin B_4). Some of them, though not essential to humans, are essential in the diets of other organisms; others have no known nutritional value and may even be toxic under certain conditions.

- **Vitamin B_4**: adenine, a nucleobase, is synthesized by the human body.[28]
- **Vitamin B_7**: is also known as "vitamin I" of Centanni E. (1935)—also called "Enteral factor"—is a water and alcohol-soluble rice-bran factor that prevents digestive disturbance in pigeons. It governs the anatomical and functional integrity of the intestinal tract. Later found in yeast. Possible candidates for this substance are inositol, niacin (nicotinic acid), and biotin. Carnitine was also claimed to be a candidate but is not soluble in alcohol. Ref: Biochim, e terap. sper. 22:137 (April 30)1935 E. Centenni. Presse med. 51 No6 66-7 1943 R. Jacquot (on enteral B7 in Yeast) *et al.*
- **Vitamin B_8**: adenosine monophosphate, or alternately myo-inositol, is synthesized by the human body.
- **Vitamin B_{10}**: *para*-aminobenzoic acid (PABA)
- **Vitamin B_{11}**: pteryl-hepta-glutamic acid—chick growth factor, which is a form of folic acid. Later found to be one of five folates necessary for humans; also known as vitamin S or factor S.
- **Vitamin B_{13}**: orotic acid, now known not to be a vitamin.
- **Vitamin B_{14}**: cell proliferant, anti-anemia, rat growth factor, and antitumor pterin phosphate named by Earl R. Norris. Isolated from human urine at 0.33ppm (later in blood), but later abandoned by him as further evidence did not confirm this. He also claimed this was not xanthopterin.
- **Vitamin B_{15}**: pangamic acid
- **Vitamin B_{16}**: dimethylglycine (DMG)
- **Vitamin B_{17}**: nitrilosides, amygdalin or Laetrile. These substances are found in a number of seeds, sprouts, beans, tubers, and grains. While toxic in large quantities, proponents claim that it is effective in cancer treatment and prevention despite a lack of scientific evidence.[29]
- **Vitamin B_{18}**:
- **Vitamin B_{19}**:
- **Vitamin B_{20}**: carnitine
- **Vitamin B_{21}**:
- **Vitamin B_{22}**: often claimed as an ingredient of Aloe vera extracts but also in many other foods. Claimed by one source to be vitamin B_{12}b-δ.
- **Vitamin B_h**: biotin
- **Vitamin B_m**: "mouse factor": also used to designate inositol
- **Vitamin B_p**: choline Choline is only required for survival of some mutants. Most commonly it is synthesized in vivo de novo.[30] May be added as supplement especially when methionine supply is limited
- **Vitamin B_t**: L-carnitine
- **Vitamin B_v**: a type of B_6 but not pyridoxine
- **Vitamin B_w**: a type of biotin but not d-biotin
- **Vitamin B_x**: *para*-aminobenzoic acid

Note: **B_{16}**, **B_{17}**, **B_{18}**, **B_{19}**, **B_{20}**, **B_{21}** & **B_{22}** do not appear to be animal factors but are claimed by some naturopaths as human therapeutic factors.

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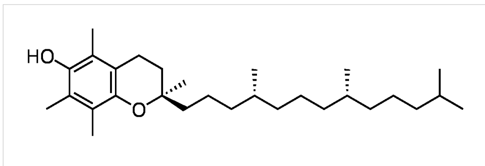
Vitamin E

Vitamin E	
Drug class	
 The α-tocopherol form of vitamin E	
Use	Vitamin E deficiency, antioxidant
Biological target	Reactive oxygen species
ATC code	A11H
External links	
MeSH	D014810 [1]
AHFS/Drugs.com	MedFacts Natural Products [2]

Vitamin E refers to a group of eight fat-soluble compounds that include both tocopherols and tocotrienols.[3] There are many different forms of vitamin E, of which γ-tocopherol is the most common in the North American diet.[4] γ-Tocopherol can be found in corn oil, soybean oil, margarine and dressings.[5][6] α-Tocopherol, the most biologically active form of vitamin E, is the second most common form of vitamin E in the North American diet. This variant of vitamin E can be found most abundantly in wheat germ oil, sunflower, and safflower oils.[6][7] It is a fat-soluble antioxidant that stops the production of reactive oxygen species formed when fat undergoes oxidation.[8][9][10]

Health effects

While it was initially hoped that vitamin E supplementation would have a positive effect on health, research has not supported these conclusions.[11] Vitamin E does not decrease mortality in adults, even at large doses,[12] and may slightly increase it.[13] It does not improve blood sugar control in an unselected group of people with diabetes mellitus[12] or decrease the risk of stroke.[14] Daily supplementation of vitamin E does not decrease the risk of prostate cancer and may increase it.[15] Studies on its role in age related macular degeneration are ongoing as, even though it is of a combination of dietary antioxidants used to treat the condition, it may increase the risk.[16] A Japanese study in 2012 found that vitamin E may contribute to osteoporosis.[17]

Deficiency

Vitamin E deficiency can cause:

- spinocerebellar ataxia[18]
- myopathies[6]
- peripheral neuropathy[8][19][20]
- ataxia[8][19][20]
- skeletal myopathy[8][19][20]
- retinopathy[8][19][20]
- impairment of the immune response[8][19][20]
- erythrocyte hemolysis[21]

Functions

Vitamin E has many biological functions; the antioxidant function being the most important and/or best known.[22] Other functions include enzymatic activities, gene expression and neurological function(s). It's also been suggested that the most important function of vitamin E is in cell signaling (and, that it may not have a significant role in antioxidant metabolism).[23][24]

- As an antioxidant, vitamin E acts as a peroxyl radical scavenger, preventing the propagation of free radicals in tissues, by reacting with them to form a tocopheryl radical which will then be oxidized by a hydrogen donor (such as Vitamin C) and thus return to its reduced state.[25] As it is fat-soluble, it is incorporated into cell membranes, which protects them from oxidative damage.
- As an enzymatic activity regulator, for instance, protein kinase C (PKC), which plays a role in smooth muscle growth, can be inhibited by α-tocopherol. α-Tocopherol has a stimulatory effect on the dephosphorylation enzyme, protein phosphatase 2A, which in turn, cleaves phosphate groups from PKC leading to its deactivation, bringing the smooth muscle growth to a halt.[26]
- Vitamin E also has an effect on gene expression. Macrophages rich in cholesterol are found in the atherogenetic tissue. Scavenger receptor CD36 is a class B scavenger receptor found to be up-regulated by oxidized low density lipoprotein (LDL) and binds it.[27] Treatment with alpha tocopherol was found to downregulate the expression of the CD36 scavenger receptor gene and the scavenger receptor class A (SR-A)[27] and modulates expression of the connective tissue growth factor (CTGF).[28][29] CTGF gene, when expressed, is responsible for the repair of wounds and regeneration of the extracellular tissue that is lost or damaged during atherosclerosis.[29]
- Vitamin E also plays a role in neurological functions,[30] and inhibition of platelet aggregation.[31][32][33]
- Vitamin E also protects lipids and prevents the oxidation of polyunsaturated fatty acids (PUFAs.)[21]

So far, most human supplementation studies about vitamin E have used only alpha-tocopherol. This can affect levels of other forms of vitamin E, e.g. reducing serum gamma- and delta-tocopherol concentrations. Moreover, a 2007 clinical study involving alpha-tocopherol concluded that supplementation did not reduce the risk of major cardiovascular events in middle aged and older men.[34]

Dietary sources

mg/(100 g)[35]		Some foods with vitamin E content[8]
low	high	
150		Wheat germ oil
41		Sunflower oil
34		Safflower oil
15	26	Nuts and nut oils, like almonds and hazelnuts[36]
15		Palm oil[37]
1.5	3.4	High-value green, leafy vegetables: spinach, turnip, beet, collard, and dandelion greens[38]
2.1		Avocados
1.1	1.5	Asparagus[39]
1.5		Kiwifruit (green)
0.78	1.5	Broccoli[40]
0.8	1	Pumpkin[41]
0.26	0.94	Sweet potato[42][43]
0.9		Mangoes
0.54	0.56	Tomatoes[44]
0.36	0.44	Rockfish[45]
0.3		Papayas
0.13	0.22	Low-value green, leafy vegetables: lettuce[46]

Recommended daily intake

The Food and Nutrition Board at the Institute of Medicine (IOM) of the U.S. National Academy of Sciences report the following dietary reference intakes for vitamin E:[8][47]

mg/day	Age
Infants	
4	0 to 6 months
5	7 to 12 months
Children	
6	1 to 3 years
7	4 to 8 years
11	9 to 13 years
Adolescents and Adults	
15	14 and older

One IU of vitamin E is defined as equivalent to either: 0.67 mg of the natural form, RRR-alpha-tocopherol, also known as d-alpha-tocopherol; or 0.45 mg of the synthetic form, all-rac-alpha-tocopherol, also known as dl-alpha-tocopherol.[8]

History

The first use for vitamin E as a therapeutic agent was conducted in 1938 by Widenbauer. Widenbauer used wheat germ oil supplement on 17 premature newborn infants suffering from growth failure. 11 out of the original 17 patients recovered and were able to resume normal growth rates.[22] Later on, in 1948, while conducting experiments on alloxan effects on rats, Gyorge and Rose noted that the rats receiving tocopherol supplements suffered from less hemolysis than those that did not receive tocopherol.[48] In 1949, Gerloczy administered all-rac-α-tocopheryl acetate to prevent and cure edema.[49][50] Methods of administration used were both oral, that showed positive response, and intramuscular, which did not show a response.[22] This early investigative work on the benefits of vitamin E supplementation was the gateway to curing the vitamin E deficiency caused hemolytic anemia described during the 1960s. Since then, supplementation of infant formulas with vitamin E has eradicated this vitamin's deficiency as a cause for hemolytic anemia.[22]

Forms

The eight forms of vitamin E are divided into two groups; four are tocopherols and four are tocotrienols. They are identified by prefixes alpha-, beta-, gamma-, and delta-. Natural tocopherols occur in the RRR-configuration only. The synthetic form contains eight different stereoisomers and is called *all-rac*-α-tocopherol.[51]

α-Tocopherol

α-Tocopherol is an important lipid-soluble antioxidant. It performs its functions as antioxidant in what is known by the glutathione peroxidase pathway[52] and it protects cell membranes from oxidation by reacting with lipid radicals produced in the lipid peroxidation chain reaction.[18][9] This would remove the free radical intermediates and prevent the oxidation reaction from continuing. The oxidized α-tocopheroxyl radicals produced in this process may be recycled back to the active reduced form through reduction by other antioxidants, such as ascorbate, retinol or ubiquinol.[53] However, the importance of the antioxidant properties of this molecule at the concentrations present in the body are not clear and it is possible that the reason why vitamin E is required in the diet is unrelated to its ability to act as an antioxidant.[54] Other forms of vitamin E have their own unique properties; for example, gamma-tocopherol is a nucleophile that can react with electrophilic mutagens.[55]

Tocotrienols

Compared with tocopherols, tocotrienols are sparsely studied.[56][57][58] Less than 1% of PubMed papers on vitamin E relate to tocotrienols.[59] The current research direction is starting to give more prominence to the tocotrienols, the lesser known but more potent antioxidants in the vitamin E family. Some studies have suggested that tocotrienols have specialized roles in protecting neurons from damage[59] and cholesterol reduction[60] by inhibiting the activity of HMG-CoA reductase; delta-tocotrienol blocks processing of sterol regulatory element-binding proteins (SREBPs).

Oral consumption of tocotrienols is also thought to protect against stroke-associated brain damage in vivo.[61] Until further research has been carried out on the other forms of vitamin E, conclusions relating to the other forms of vitamin E, based on trials studying only the efficacy of alpha-tocopherol, may be premature.[62]

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[35] "USDA Nutrient Data Laboratory" (http://www.nal.usda.gov/fnic/foodcomp/search/). . In notes 2–11, USDA NDL Release 24 numbers are given as mg/(100 g). Low and high values vary some by raw versus cooked and by variety.

[36] 26 almonds, 15 hazelnuts.

[37] "Wolfram Alpha" (http://www.wolframalpha.com/input/?i=palm+oil+100ml). http://www.wolframalpha.com. .

[38] Spinach (2.0 raw, 2.1 cooked), turnip (2.9 raw, 1.9 cooked), beet (1.5 raw, 1.8 cooked), collard (2.3 raw, 0.88 cooked), and dandelion greens (3.4 raw, 2.4 cooked)

[39] 1.1 raw, 1.5 cooked.

[40] 0.78 raw, 1.5 cooked.

[41] 1. raw, 0.8 cooked.

[42] 0.26 raw, 0.94 boiled.

[43] 0.94 mg/(100 g) corresponds to 1.6 kg of boiled sweet potatoes per day of the recommended intake for adults. The desired amount of vitamin E ÷ food's E value = amount of food. Thus, (15 (mg/day))÷((0.94 mg)/(100 g)) = (15 (~~mg~~/day))*((100 g)/(0.94 ~~mg~~)) = (15*100 g)/(0.94 day) ≈ 1596 g/day ≈ 1.6 kg/day.

[44] 0.54 raw, 0.56 cooked.

[45] 0.36 raw, 0.44 cooked.

[46] Lettuce (0.18 iceburg, 0.22 green leaf, 0.13 romaine, 0.15 red leaf, 0.18 butterhead).

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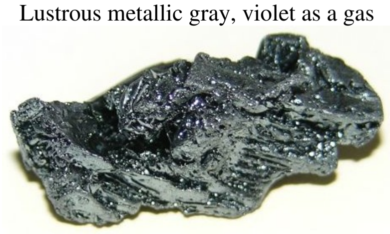
External links

- Vitamin E bound to proteins (http://www.ebi.ac.uk/pdbe-srv/PDBeXplore/ligand/?ligand=VIT) in the PDB
- Vitamin E (http://www.nlm.nih.gov/medlineplus/ency/article/002406.htm) Medline Plus, Medical Encyclopedia, U.S. National Library of Medicine
- Vitamin E (http://dietary-supplements.info.nih.gov/factsheets/vitamine.asp) Office of Dietary Supplements, National Institutes of Health
- Jane Higdon, " Vitamin E (http://lpi.oregonstate.edu/infocenter/vitamins/vitaminE//)", Micronutrient Information Center, *Linus Pauling Institute, Oregon State University*
- Vitamin E Food Charts (http://healthyeatingclub.com/info/books-phds/books/foodfacts/html/data/data3d.html)

Iodine

Iodine	
Appearance	
Lustrous metallic gray, violet as a gas 	
General properties	
Name, symbol, number	iodine, I, 53
Pronunciation	/ˈaɪ.ɵdaɪn/ ***EYE**-o-dyne*, /ˈaɪ.ɵdɪn/ ***EYE**-o-dən*, or /ˈaɪ.ɵdiːn/ ***EYE**-o-deen*
Element category	halogen
Group, period, block	17, 5, p
Standard atomic weight	126.90447 $g{\cdot}mol^{-1}$
Electron configuration	[Kr] $4d^{10}\ 5s^2\ 5p^5$
Electrons per shell	2, 8, 18, 18, 7 (Image)
Physical properties	
Phase	solid
Density (near r.t.)	4.933 $g{\cdot}cm^{-3}$
Melting point	386.85 K,113.7 °C,236.66 °F
Boiling point	457.4 K,184.3 °C,363.7 °F
Triple point	386.65 K (113°C), 12.1 kPa
Critical point	819 K, 11.7 MPa
Heat of fusion	(I_2) 15.52 $kJ{\cdot}mol^{-1}$
Heat of vaporization	(I_2) 41.57 $kJ{\cdot}mol^{-1}$
Specific heat capacity	(25 °C) (I_2) 54.44 $J{\cdot}mol^{-1}{\cdot}K^{-1}$
Vapor pressure (rhombic)	

P/Pa	1	10	100	1 k	10 k	100 k
at *T*/K	260	282	309	342	381	457

Atomic properties	
Oxidation states	**7**, 5, 3, 1, -1 (strongly acidic oxide)
Electronegativity	2.66 (Pauling scale)

Ionization energies	1st: 1008.4 kJ·mol^{-1}
	2nd: 1845.9 kJ·mol^{-1}
	3rd: 3180 kJ·mol^{-1}
Atomic radius	140 pm
Covalent radius	139±3 pm
Van der Waals radius	198 pm
Miscellanea	
Crystal structure	orthorhombic
Magnetic ordering	diamagnetic[1]
Electrical resistivity	(0 °C) 1.3×10^{7}Ω·m
Thermal conductivity	(300 K) 0.449 W·m^{-1}·K^{-1}
Bulk modulus	7.7 GPa
CAS registry number	7553-56-2
Most stable isotopes	

iso	NA	half-life	DM	DE (MeV)	DP
^{123}I	syn	13 h	ε, γ	0.16	^{123}Te
^{127}I	100%	^{127}I is stable with 74 neutron			
^{129}I	trace	15.7×10^{6} y	β^{-}	0.194	^{129}Xe
^{131}I	syn	8.02070 d	β^{-}, γ	0.971	^{131}Xe

Iodine is a chemical element with the symbol **I** and atomic number 53. The name is pronounced /ˈaɪ.ɵdaɪn/ ***EYE**-o-dyne*, /ˈaɪ.ɵdɪn/ ***EYE**-o-dən*, or /ˈaɪ.ɵdiːn/ ***EYE**-o-deen* in both American[2] and British[3] English.[4] The name is from Greek ἰοειδής *ioeidēs*, meaning violet or purple, due to the color of elemental iodine vapor.[5]

Iodine and its compounds are primarily used in nutrition, and industrially in the production of acetic acid and certain polymers. Iodine's relatively high atomic number, low toxicity, and ease of attachment to organic compounds have made it a part of many X-ray contrast materials in modern medicine. Iodine has only one stable isotope. A number of iodine radioisotopes are also used in medical applications.

Iodine is found on Earth mainly as the highly water-soluble iodide I^-, which concentrates it in oceans and brine pools. Like the other halogens, free iodine occurs mainly as a diatomic molecule I_2, and then only momentarily after being oxidized from iodide by an oxidant like free oxygen. In the universe and on Earth, iodine's high atomic number makes it a relatively rare element. However, its presence in ocean water has given it a role in biology. It is the heaviest essential element utilized widely by life in biological functions (only tungsten, employed in enzymes by a few species of bacteria, is heavier). Iodine's rarity in many soils, due to initial low abundance as a crust-element, and also leaching of soluble iodide by rainwater, has led to many deficiency problems in land animals and inland human populations. Iodine deficiency affects about two billion people and is the leading preventable cause of intellectual disabilities.[6]

Iodine is required by higher animals, which use it to synthesize thyroid hormones, which contain the element. Because of this function, radioisotopes of iodine are concentrated in the thyroid gland along with nonradioactive iodine. The radioisotope iodine-131, which has a high fission product yield, concentrates in the thyroid, and is one of the most carcinogenic of nuclear fission products.

Characteristics

Iodine under standard conditions is a bluish-black solid. It can be seen apparently sublimating at standard temperatures into a violet-pink gas that has an irritating odor. This halogen forms compounds with many elements, but is less reactive than the other members of its Group VII (halogens) and has some metallic light reflectance.

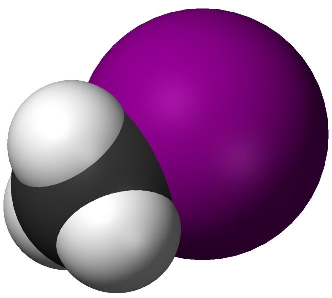
In the gas phase, iodine shows its violet color.

Elemental iodine dissolves easily in most organic solvents such as hexane or chloroform owing to its lack of polarity, but is only slightly soluble in water. However, the solubility of elemental iodine in water can be increased by the addition of potassium iodide. The molecular iodine reacts reversibly with the negative ion, generating the triiodide anion I_3^- in equilibrium, which is soluble in water. This is also the formulation of some types of medicinal (antiseptic) iodine, although tincture of iodine classically dissolves the element in aqueous ethanol.

The colour of solutions of elemental iodine changes depending on the polarity of the solvent. In non-polar solvents like hexane, solutions are violet; in moderately polar dichloromethane, the solution is dark crimson, and, in strongly polar solvents such as acetone or ethanol, it appears orange or brown. This effect is due to the formation of adducts.

Iodine melts at the relatively low temperature of 113.7 °C, although the liquid is often obscured by a dense violet vapor of gaseous iodine.

Occurrence

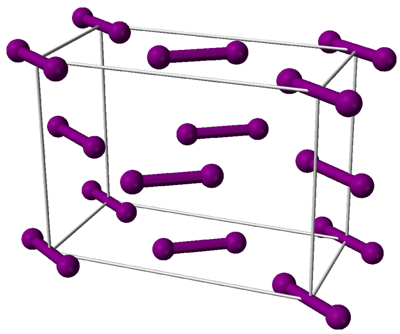


Iodomethane

Iodine is rare in the solar system and Earth's crust (47–60th in abundance); however, iodide salts are often very soluble in water. Iodine occurs in slightly greater concentrations in seawater than in rocks, 0.05 vs. 0.04 ppm. Minerals containing iodine include caliche, found in Chile. The brown algae *Laminaria* and *Fucus* found in temperate zones of the Northern Hemisphere contain 0.028–0.454 dry weight percent of iodine. Aside from tungsten, iodine is the heaviest element to be essential in living organisms. About 19,000 tonnes are produced annually from natural sources.[7]

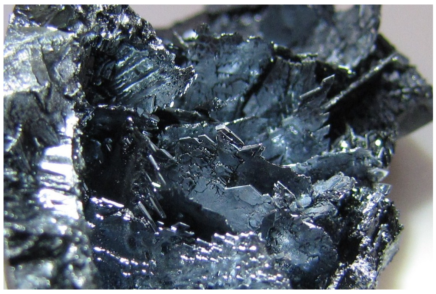
Organoiodine compounds are produced by marine life forms, the most notable being iodomethane (commonly called methyl iodide). About 214 kilotonnes/year of iodomethane is produced by the marine environment, by microbial activity in rice paddies and by the burning of biological material.[8] The volatile iodomethane is broken up in the atmosphere as part of a global iodine cycle.[8][9]

Structure and bonding


Structure of solid iodine

Iodine normally exists as a diatomic molecule with an I-I bond length of 270 pm,[10] one of the longest single bonds known. The I_2 molecules tend to interact via the weak van der Waals force called the London Forces, and this interaction is responsible for the higher melting point compared to more compact halogens, which are also diatomic. Since the atomic size of Iodine is larger, its melting point is higher. The solid crystallizes as orthorhombic crystals. The crystal motif in the Hermann–Mauguin notation is Cmca (No 64), Pearson symbol oS8. The I-I bond is relatively weak, with a bond dissociation energy of 36 kcal/mol, and most bonds to iodine are weaker than for the lighter halides. One consequence of this weak bonding is the relatively high tendency of I_2 molecules to dissociate into atomic iodine.

Production


Crystalline iodine

Of the several places in which iodine occurs in nature, only two sources are useful commercially: the caliche, found in Chile, and the iodine-containing brines of gas and oil fields, especially in Japan and the United States. The caliche contains sodium nitrate, which is the main product of the mining activities, and small amounts of sodium iodate and sodium iodide. In the extraction of sodium nitrate, the sodium iodate and sodium iodide are extracted.[11] The high concentration of iodine in the caliche and the extensive mining made Chile the largest producer of iodine in 2007.

Most other producers use natural occurring brine for the production of iodine. The Japanese Minami Kanto gas field east of Tokyo and the American Anadarko Basin gas field in northwest Oklahoma are the two largest sources for iodine from brine. The brine has a temperature of over 60°C owing to the depth of the source. The brine is first purified and acidified using sulfuric acid, then the iodide present is oxidized to iodine with chlorine. An iodine solution is produced, but is dilute and must be concentrated. Air is blown into the solution, causing the iodine to evaporate, then it is passed into an absorbing tower containing acid where sulfur dioxide is added to reduce the iodine. The hydrogen iodide (HI) is reacted with chlorine to precipitate the iodine. After filtering and purification the iodine is packed.[11][12]

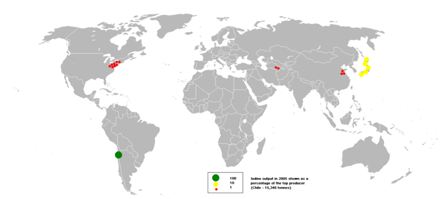
$$2\ HI + Cl_2 \rightarrow I_2\uparrow + 2\ HCl$$

$$I_2 + 2\ H_2O + SO_2 \rightarrow 2\ HI + H_2SO_4$$

$$2\ HI + Cl_2 \rightarrow I_2\downarrow + 2\ HCl$$

The production of iodine from seawater via electrolysis is not used owing to the sufficient abundance of iodine-rich brine. Another source of iodine is kelp, used in the 18th and 19th centuries, but it is no longer economically viable.[13]

Commercial samples often contain high concentrations of impurities, which can be removed by sublimation. The element may also be prepared in an ultra-pure form through the reaction of potassium iodide with copper(II) sulfate, which gives copper(II) iodide initially. That decomposes spontaneously to copper(I) iodide and iodine:



Iodine output in 2005

$$Cu^{2+} + 2\ I^{-} \rightarrow CuI_2$$

$$2\ CuI_2 \rightarrow 2\ CuI + I_2$$

There are also other methods of isolating this element in the laboratory, for example, the method used to isolate other halogens: oxidation of the iodide in hydrogen iodide (often made *in situ* with an iodide and sulfuric acid) by manganese dioxide (see below in *Descriptive chemistry*).

Isotopes and their applications

Of the 37 known (characterized) isotopes of iodine, only one, ^{127}I, is stable.

The longest-lived radioisotope, ^{129}I, has a half-life of 15.7 million years. This is long enough to make it a permanent fixture of the environment on human time scales, but far too short for it to exist as a primordial isotope today. Instead, iodine-129 is an extinct radionuclide, and its presence in the early solar system is inferred from the observation of an excess of its daughter xenon-129. This nuclide is also newly-made by cosmic rays and as a byproduct of human nuclear fission, which it is used to monitor as a very long-lived environmental contaminant.

The next-longest-lived radioisotope, iodine-125, has a half-life of 59 days. It is used as a convenient gamma-emitting tag for proteins in biological assays, and a few nuclear medicine imaging tests where a longer half-life is required. It is also commonly used in brachytherapy implanted capsules, which kill tumors by local short-range gamma radiation (but where the isotope is never released into the body).

Iodine-123 (half-life 13 hours) is the isotope of choice for nuclear medicine imaging of the thyroid gland, which naturally accumulates all iodine isotopes.

Iodine-131 (half-life 8 days) is a beta-emitting isotope, which is a common nuclear fission product. It is preferably administered to humans only in very high doses which destroy all tissues that accumulate it (usually the thyroid), which in turn prevents these tissues from developing cancer from a lower dose (paradoxically, a high dose of this isotope appears safer for the thyroid than a low dose). Like other radioiodines, I-131 accumulates in the thyroid gland, but unlike the others, in small amounts it is highly carcinogenic there, it seems, owing to the high local cell mutation due to damage from beta decay. Because of this tendency of ^{131}I to cause high damage to cells that accumulate it and other cells near them (0.6 to 2 mm away, the range of the beta rays), it is the only iodine radioisotope used as direct therapy, to kill tissues such as cancers that take up artificially iodinated molecules (example, the compound iobenguane, also known as MIBG). For the same reason, only the iodine isotope I-131 is used to treat Grave's disease and those types of thyroid cancers (sometimes in metastatic form) where the tissue that requires destruction, still functions to naturally accumulate iodide.

Nonradioactive ordinary potassium iodide (iodine-127), in a number of convenient forms (tablets or solution) may be used to saturate the thyroid gland's ability to take up further iodine, and thus protect against accidental contamination from iodine-131 generated by nuclear fission accidents, such as the Chernobyl disaster and more recently the Fukushima I nuclear accidents, as well as from contamination from this isotope in nuclear fallout from nuclear weapons.

History

Iodine was discovered by Bernard Courtois in 1811.[14][15] He was born to a manufacturer of saltpeter (a vital part of gunpowder). At the time of the Napoleonic Wars, France was at war and saltpeter was in great demand. Saltpeter produced from French niter beds required sodium carbonate, which could be isolated from seaweed collected on the coasts of Normandy and Brittany. To isolate the sodium carbonate, seaweed was burned and the ash washed with water. The remaining waste was destroyed by adding sulfuric acid. Courtois once added excessive sulfuric acid and a cloud of purple vapor rose. He noted that the vapor crystallized on cold surfaces, making dark crystals. Courtois suspected that this was a new element but lacked funding to pursue it further.

Courtois gave samples to his friends, Charles Bernard Desormes (1777–1862) and Nicolas Clément (1779–1841), to continue research. He also gave some of the substance to chemist Joseph Louis Gay-Lussac (1778–1850), and to physicist André-Marie Ampère (1775–1836). On 29 November 1813, Dersormes and Clément made public Courtois's discovery. They described the substance to a meeting of the Imperial Institute of France. On December 6, Gay-Lussac announced that the new substance was either an element or a compound of oxygen.[16][17][18] It was Gay-Lussac who suggested the name *"iode"*, from the Greek word ιώδες (iodes) for violet (because of the color of iodine vapor).[14][16] Ampère had given some of his sample to Humphry Davy (1778–1829). Davy did some experiments on the substance and noted its similarity to chlorine.[19] Davy sent a letter dated December 10 to the Royal Society of London stating that he had identified a new element.[20] Arguments erupted between Davy and Gay-Lussac over who identified iodine first, but both scientists acknowledged Courtois as the first to isolate the element.

Applications

Catalysis

The major application of iodine is as a co-catalyst for the production of acetic acid by the Monsanto and Cativa processes. In these technologies, which support the world's demand for acetic acid, hydroiodic acid converts the methanol feedstock into methyl iodide, which undergoes carbonylation. Hydrolysis of the resulting acetyl iodide regenerates hydroiodic acid and gives acetic acid.[7]

Animal feed

The production of ethylenediammonium diiodide (EDDI) consumes a large fraction of available iodine. EDDI is provided to livestock as a nutritional supplement.[7]

Disinfectant and water treatment

Elemental iodine is used as a disinfectant in various forms. The iodine exists as the element, or as the water-soluble triiodide anion I_3^- generated *in situ* by adding iodide to poorly water-soluble elemental iodine (the reverse chemical reaction makes some free elemental iodine available for antisepsis). In alternative fashion, iodine may come from iodophors, which contain iodine complexed with a solubilizing agent (iodide ion may be thought of loosely as the iodophor in triiodide water solutions). Examples of such preparations include:[21]

- Tincture of iodine: iodine in ethanol, or iodine and sodium iodide in a mixture of ethanol and water.
- Lugol's iodine: iodine and iodide in water alone, forming mostly triiodide. Unlike tincture of iodine, Lugol's has a minimized amount of the free iodine (I_2) component.
- Povidone iodine (an iodophor)

Health, medical, and radiological use

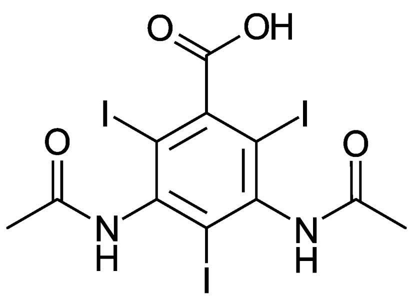
In most countries, table salt is iodized. Iodine is required for the essential thyroxin hormones produced by and concentrated in the thyroid gland.

Potassium iodide has been used as an expectorant, although this use is increasingly uncommon. In medicine, potassium iodide is used to treat acute thyrotoxicosis, usually as a saturated solution of potassium iodide (SSKI). It is also used to block uptake of iodine-131 in the thyroid gland (see isotopes section above), when this isotope is used as part of radiopharmaceuticals (such as iobenguane) that are not targeted to the thyroid or thyroid type tissues.

Iodine-131 (in the chemical form of iodide) is a component of nuclear fallout and a particularly dangerous one owing to the thyroid gland's propensity to concentrate ingested iodine, where it is kept for periods longer than this isotope's radiological half-life of eight days. For this reason, if people are expected to be exposed to a significant amount of environmental radioactive iodine (iodine-131 in fallout), they may be instructed to take non-radioactive potassium iodide tablets. The typical adult dose is one 130 mg tablet per 24 hours, supplying 100 mg (100,000 micrograms) iodine, as iodide ion. (Note: typical daily dose of iodine to maintain normal health is of order 100 micrograms; see "Dietary Intake" below.) By ingesting this large amount of non-radioactive iodine, radioactive iodine uptake by the thyroid gland is minimized. See the main article above for more on this topic.[22]

Radiocontrast agent

Iodine, as a physically dense element with high electron density and high atomic number, is quite radio-opaque (i.e., it absorbs X-rays well). This property can be fully exploited by filtering imaging X-rays so that they are more energetic than iodine's "K-edge" at 33.3 keV, or the energy where the iodine begins to absorb X-rays strongly due to the photoelectric effect from electrons in its K shell. [23] Organic compounds of a certain type (typically iodine-substituted benzene derivatives) are thus used in medicine as X-ray radiocontrast agents for intravenous injection. This is often in conjunction with advanced X-ray techniques such as angiography and CT scanning. At present, all water-soluble radiocontrast agents rely on iodine.



Diatrizoic acid, a radiocontrast agent

Other uses

Inorganic iodides find specialized uses. Hafnium, zirconium, titanium are purified by the van Arkel Process, which involves the reversible formation of the tetraiodides of these elements. Silver iodide is a major ingredient to traditional photographic film. Thousands of kilograms of silver iodide are consumed annually for cloud seeding.[7]

The organoiodine compound erythrosine is an important food coloring agent. Perfluoroalkyl iodides are precursors to important surfactants, such as perfluorooctanesulfonic acid.[7]

Iodine chemistry

Iodine adopts a variety of oxidation states, commonly ranging from (formally) I^{7+} to I^-, and including the intermediate states of I^{5+}, I^{3+} and I^+. Practically, only the 1- oxidation state is of significance, being the form found in iodide salts and organoiodine compounds. Iodine is a Lewis acid. With electron donors such as triphenylphosphine and pyridine it forms a charge-transfer complex. With the iodide anion it forms the triiodide ion.[24] Iodine and the iodide ion form a redox couple. I_2 is easily reduced and I^- is easily oxidized.

Solubility

Being a nonpolar molecule, iodine is highly soluble in nonpolar organic solvents, including ethanol (20.5 g/100 ml at 15 °C, 21.43 g/100 ml at 25 °C), diethyl ether (20.6 g/100 ml at 17 °C, 25.20 g/100 ml at 25 °C), chloroform, acetic acid, glycerol, benzene (14.09 g/100 ml at 25 °C), carbon tetrachloride (2.603 g/100 ml at 35 °C), and carbon disulfide (16.47 g/100 ml at 25 °C).[25] Elemental iodine is poorly soluble in water, with one gram dissolving in 3450 ml at 20 °C and 1280 ml at 50 °C. Aqueous and ethanol solutions are brown reflecting the role of these solvents as Lewis bases. Solutions in chloroform, carbon tetrachloride, and carbon disulfide are violet, the color of iodine vapor.

One of the most distinctive properties of iodine is the way that its solubility in water is enhanced by the presence of iodide ions. The dissolution of iodine in aqueous solutions containing iodide (e.g., from hydroiodic acid, potassium iodide, etc.) results from the formation of the I_3^- ion. Dissolved bromides also improve water solubility of iodine.

Redox reactions

In everyday life, iodides are slowly oxidized by atmospheric oxygen in the atmosphere to give free iodine. Evidence for this conversion is the yellow tint of certain aged samples of iodide salts and some organoiodine compounds.[7] The oxidation of iodide to iodine in air is also responsible for the slow loss of iodide content in iodized salt if exposed to air.[26] Some salts use iodate to prevent the loss of iodine.

Iodine is easily reduced. Most common is the interconversion of I^- and I_2. Molecular iodine can be prepared by oxidizing iodides with chlorine:

$$2\ I^- + Cl_2 \rightarrow I_2 + 2\ Cl^-$$

or with manganese dioxide in acid solution:[27]

$$2\ I^- + 4\ H^+ + MnO_2 \rightarrow I_2 + 2\ H_2O + Mn^{2+}$$

Iodine is reduced to hydroiodic acid by hydrogen sulfide and hydrazine:[28]

$$8\ I_2 + 8\ H_2S \rightarrow 16\ HI + S_8$$

$$2\ I_2 + N_2H_4 \rightarrow 4\ HI + N_2$$

When dissolved in fuming sulfuric acid (65% oleum), iodine forms an intense blue solution. The blue color is due to I_2^+ cation, the result of iodine being oxidized by SO_3:[29]

$$2\ I_2 + 2\ SO_3 + H_2SO_4 \rightarrow 2\ I_2^+ + SO_2 + 2\ HSO$$

The I_2^+ cation is also formed in the oxidation of iodine by SbF_5 or TaF_5. The resulting $I_2^+Sb_2F$ or $I_2^+Ta_2F$ can be isolated as deep blue crystals. The solutions of these salts turn red when cooled below −60°C, owing to the formation of the I_4^{2+} cation:[29]

$$2\ I_2^+ \rightleftharpoons I_4^{2+}$$

Under slightly more alkaline conditions, I_4^{2+} disproportionates into I_3^+ and an iodine(III) compound. Excess iodine can then react with I_3^+ to form I_5^+ (green) and I_{15}^{3+} (black).[29]

Oxides of iodine

The best-known oxides are the anions, IO_3^- and IO_4^-, but several other oxides are known, such as the strong oxidant iodine pentoxide.

By contrast with chlorine, the formation of the hypohalite ion (IO^-) in neutral aqueous solutions of iodine is negligible.

$I_2 + H_2O \rightleftharpoons H^+ + I^- + HIO \quad (K = 2.0\times10^{-13})$[27] In basic solutions (such as aqueous sodium hydroxide), iodine converts in a two stage reaction to iodide and iodate:[27]

$$I_2 + 2\,OH^- \rightarrow I^- + IO^- + H_2O \quad (K = 30)$$

$$3\,IO^- \rightarrow 2\,I^- + IO_3^- \quad (K = 10^{20})$$

Organic derivatives of hypoiodate (2-Iodoxybenzoic acid, and Dess-Martin periodinane) are used in organic chemistry.

Iodic acid (HIO_3), periodic acid (HIO_4) and their salts are strong oxidizers and are of some use in organic synthesis. Iodine is oxidized to iodate by nitric acid as well as by chlorates:[30]

$$I_2 + 10\,HNO_3 \rightarrow 2\,HIO_3 + 10\,NO_2 + 4\,H_2O$$

$$I_2 + 2\,ClO_3^- \rightarrow 2\,IO_3^- + Cl_2$$

Inorganic iodine compounds

Iodine forms compounds with all the elements except for the noble gases. From the perspective of commercial applications, an important compound is hydroiodic acid, used as a co-catalyst in the Cativa process for the production of acetic acid. Titanium and aluminium iodides are used in the production of butadiene, a precursor to rubber tires.[7]

Alkali metal salts are common colourless solids that are highly soluble in water. Potassium iodide is a convenient source of the iodide anion; it is easier to handle than sodium iodide because it is not hygroscopic. Both salts are mainly used in the production of iodized salt. Sodium iodide is especially useful in the Finkelstein reaction, because it is soluble in acetone, whereas potassium iodide is less so. In this reaction, an alkyl chloride is converted to an alkyl iodide. This relies on the insolubility of sodium chloride in acetone to drive the reaction:

R-Cl (acetone) + NaI (acetone) → R-I (acetone) + NaCl (s)

Despite having the lowest electronegativity of the common halogens, iodine reacts violently with some metals, such as aluminium:

$$3\,I_2 + 2\,Al \rightarrow 2\,AlI_3$$

This reaction produces 314 kJ per mole of aluminium, comparable to thermite's 425 kJ. Yet the reaction initiates spontaneously, and if unconfined, causes a cloud of gaseous iodine due to the high temperature.

Interhalogen compounds

Interhalogen compounds are well known; examples include iodine monochloride and trichloride; iodine pentafluoride and heptafluoride.

Organic compounds

Many organoiodine compounds exist; the simplest is iodomethane, approved as a soil fumigant. Iodinated organic compounds are used as synthetic reagents.

Organic synthesis

Organoiodine compounds can be made in many ways. For example, methyl iodide can be prepared from methanol, red phosphorus, and iodine.[31] The iodinating reagent is phosphorus triiodide that is formed *in situ*:

$$3\ CH_3OH + PI_3 \rightarrow 3\ CH_3I + H_3PO_3$$

The iodoform test uses an alkaline solution of iodine to react with methyl ketones to give the labile triiodomethide leaving group, forming iodoform, which precipitates.

Aryl and alkyl iodides both form Grignard reagents. Iodine is sometimes used to activate magnesium when preparing Grignard reagents. Alkyl iodides such as iodomethane are good alkylating agents. Some drawbacks to use of organoiodine compounds in chemical synthesis are:

- iodine compounds are more expensive than the corresponding bromides and chlorides, in that order
- iodides are much stronger alkylating agents, and so are more toxic (e.g., methyl iodide is very toxic (T+).[32]
- low-molecular-weight iodides tend to have a much higher equivalent weight, compared to other alkylating agents (e.g., methyl iodide versus dimethyl carbonate), owing to the atomic mass of iodine.

Analytical chemistry and bioanalysis

Iodine is a common general stain used in thin-layer chromatography. In particular, iodine forms an intense blue complex with the glucose polymers starch and glycogen. Several analytical methods rely on this property:


Testing a seed for starch with a solution of iodine

- Iodometry. The concentration of an oxidant can be determined by adding it to an excess of iodide, to destroy elemental iodine/triiodide as a result of oxidation by the oxidant. A starch indicator is then used as the indicator close to the end-point, in order to increase the visual contrast (dark blue becomes colorless, instead of the yellow of dilute triiodide becoming colorless).
- An Iodine test may be used to test a sample substance for the presence of starch. The Iodine clock reaction is an extension of the techniques in iodometry.
- Iodine solutions are used in counterfeit banknote detection pens; the premise being that counterfeit banknotes made using commercially available paper contain starch.
- Starch-iodide paper are used to test for the presence of oxidants such as peroxides. The oxidants convert iodide to iodine, which shows up as blue. A solution of starch and iodide can perform the same function.[33]
- During colposcopy, Lugol's iodine is applied to the vagina and cervix. Normal vaginal tissue stains brown owing to its high glycogen content (a color-reaction similar to that with starch), while abnormal tissue suspicious for cancer does not stain, and thus appears pale compared to the surrounding tissue. Biopsy of suspicious tissue can then be performed. This is called a Schiller's Test.

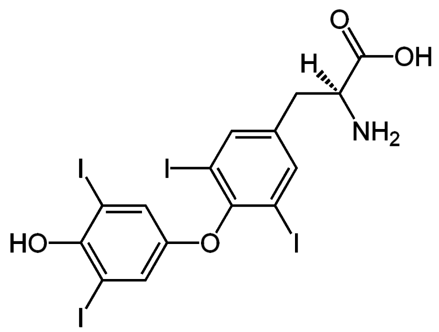
Clandestine synthetic chemical use

In the United States, the Drug Enforcement Administration (DEA) regards iodine and compounds containing iodine (ionic iodides, iodoform, ethyl iodide, and so on) as reagents useful for the clandestine manufacture of methamphetamine.[34][35]

Biological role

Iodine is an essential trace element for life, the heaviest element commonly needed by living organisms. Only tungsten, a component of a few bacterial enzymes, has a higher atomic number and atomic weight.

Iodine's main role in animal biology is as a constituent of the thyroid hormones *thyroxine* (T4) and *triiodothyronine* (T3). These are made from addition condensation products of the amino acid tyrosine, and are stored prior to release in an iodine-containing protein called thyroglobulin. T4 and T3 contain four and three atoms of iodine per molecule, respectively. The thyroid gland actively absorbs iodide from the blood to make and release these hormones into the blood, actions that are regulated by a second hormone TSH from the pituitary. Thyroid hormones are phylogenetically very old molecules that are synthesized by most multicellular organisms, and that even have some effect on unicellular organisms.



Thyroxines are iodine-containing hormones that justify the widespread use of iodised salt.

Thyroid hormones play a basic role in biology, acting on gene transcription to regulate the basal metabolic rate. The total deficiency of thyroid hormones can reduce basal metabolic rate up to 50%, while in excessive production of thyroid hormones the basal metabolic rate can be increased by 100%. T4 acts largely as a precursor to T3, which is (with minor exceptions) the biologically active hormone.

Iodine has a nutritional relationship with selenium. A family of selenium-dependent enzymes called deiodinases converts T4 to T3 (the active hormone) by removing an iodine atom from the outer tyrosine ring. These enzymes also convert T4 to reverse T3 (rT3) by removing an inner ring iodine atom, and convert T3 to 3,3'-diiodothyronine (T2) also by removing an inner ring atom. Both of the latter are inactivated hormones that are ready for disposal and have, in essence, no biological effects. A family of non-selenium-dependent enzymes then further deiodinates the products of these reactions.

Iodine accounts for 65% of the molecular weight of T4 and 59% of the T3. Fifteen to 20 mg of iodine is concentrated in thyroid tissue and hormones, but 70% of the body's iodine is distributed in other tissues, including mammary glands, eyes, gastric mucosa, the cervix, and salivary glands. In the cells of these tissues, iodide enters directly by sodium-iodide symporter (NIS). Its role in mammary tissue is related to fetal and neonatal development, but its role in the other tissues is unknown.[36]

Dietary intake

The daily Dietary Reference Intake recommended by the United States Institute of Medicine is between 110 and 130 µg for infants up to 12 months, 90 µg for children up to eight years, 130 µg for children up to 13 years, 150 µg for adults, 220 µg for pregnant women and 290 µg for lactating mothers.[37] The Tolerable Upper Intake Level (UL) for adults is 1,100 µg/day (1.1 mg/day).[38] The tolerable upper limit was assessed by analyzing the effect of supplementation on thyroid-stimulating hormone.[36]

The thyroid gland needs no more than 70 micrograms/day to synthesize the requisite daily amounts of T4 and T3. The higher recommended daily allowance levels of iodine seem necessary for optimal function of a number of body systems, including lactating breast, gastric mucosa, salivary glands, oral mucosa, thymus, epidermis, choroid plexus, etc.[39][40][41] The high iodide-concentration of thymus tissue in particular suggests an anatomical rationale for this role of iodine in the immune system.[42] The trophic, antioxidant and apoptosis-inductor actions and the presumed anti-tumour activity of iodides has been suggested to also be important for prevention of oral and salivary glands diseases.[43]

Natural sources of iodine include sea life, such as kelp and certain seafood, as well as plants grown on iodine-rich soil.[44][45] Iodized salt is fortified with iodine.[45]

As of 2000, the median intake of iodine from food in the United States was 240 to 300 μg/day for men and 190 to 210 μg/day for women.[38] In Japan, consumption is much higher, owing to the frequent consumption of seaweed or kombu kelp.[36]

After iodine fortification programs (e.g., iodized salt) have been implemented, some cases of iodine-induced hyperthyroidism have been observed (so called Jod-Basedow phenomenon). The condition seems to occur mainly in people over forty, and the risk appears higher when iodine deficiency is severe and the initial rise in iodine intake is high.[46]

It should also be noted that information processing, fine motor skills, and visual problem solving are improved by iodine repletion in moderately iodine-deficient children.[47]

Deficiency

In areas where there is little iodine in the diet,[9] typically remote inland areas and semi-arid equatorial climates where no marine foods are eaten, iodine deficiency gives rise to hypothyroidism, symptoms of which are extreme fatigue, goitre, mental slowing, depression, weight gain, and low basal body temperatures.[48] Iodine deficiency is the leading cause of preventable mental retardation, a result that occurs primarily when babies or small children are rendered hypothyroidic by a lack of the element. The addition of iodine to table salt has largely eliminated this problem in the wealthier nations, but, as of March 2006, iodine deficiency remained a serious public health problem in the developing world.[49] Iodine deficiency is also a problem in certain areas of Europe.

Other possible health effects being investigated as being related to deficiency include:

- **Breast cancer.** The breast strongly and actively concentrates iodine into breast-milk for the benefit of the developing infant, and may develop a goiter-like hyperplasia, sometimes manifesting as fibrocystic breast disease, when iodine level are low.
- **Stomach cancer**. Some researchers have found an epidemiologic correlation between iodine deficiency, iodine-deficient goitre and gastric cancer.[50][51][52] A decrease of the incidence of death rate from stomach cancer after implementation of the effective iodine-prophylaxis has been reported also.[53]

Precautions and toxicity of elemental iodine

Elemental iodine (I_2) is mildly toxic if taken orally. The lethal dose for an adult human is 30 mg/kg, which is about 2,1-2,4 grams (even if experiments on rats demostrated that this animals could survive after eating a 14000 mg/kg dose). Excess iodine can be more cytotoxic in the presence of selenium deficiency.[54] Iodine supplementation in selenium-deficient populations is, in theory, problematic, partly for this reason.[36] Its toxicity derives from its oxidizing properties, which make it able to denaturate proteins (and so also enzymes).

Elemental iodine is an oxidizing irritant and direct contact with skin can cause lesions, so iodine crystals should be handled with care. Solutions with high elemental iodine concentration such as tincture of iodine and Lugol's solution are capable of causing tissue damage if their use for cleaning and antiseptics is prolonged.

Iodine sensitivity

Some people develop a sensitivity to iodine. Application of tincture of iodine can cause a rash. Some cases of reaction to Povidone-iodine (Betadine) resulted in chemical burns.[55] Eating iodine-containing foods can cause hives . Medical use of iodine (i.e. as a contrast agent, see above) can cause anaphylactic shock in highly iodine-sensitive patients. Some cases of sensitivity to iodine can be formally classified as iodine allergies. Iodine sensitivity is rare but has a considerable effect given the extremely widespread use of iodine-based contrast media.[56]

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External links

- "Micronutrient Research for Optimum Health", Linus Pauling Institute, OSU Oregon State University (http://lpi.oregonstate.edu/infocenter/minerals/iodine/)
- ATSDR – CSEM: Radiation Exposure from Iodine 131 (http://www.atsdr.cdc.gov/csem/iodine/) U.S. Department of Health and Human Services (public domain)
- ChemicalElements.com – Iodine (http://chemicalelements.com/elements/i.html)
- who.int, WHO Global Database on Iodine Deficiency (http://whqlibdoc.who.int/publications/2004/9241592001.pdf)
- Oxidizing Agents > Iodine (http://www.organic-chemistry.org/chemicals/oxidations/iodine.shtm)

Selenium

Selenium	
Appearance	
Black and red allotropes 	
General properties	
Name, symbol, number	selenium, Se, 34
Pronunciation	/sɪˈliːniəm/ *si-**LEE**-nee-əm*
Element category	nonmetal
Group, period, block	16, 4, p
Standard atomic weight	78.96 g·mol^{-1}
Electron configuration	[Ar] 3d^{10} 4s^{2} 4p^{4}
Electrons per shell	2, 8, 18, 6 (Image)
Physical properties	
Phase	solid
Density (near r.t.)	(gray) 4.81 g·cm^{-3}
Density (near r.t.)	(alpha) 4.39 g·cm^{-3}
Density (near r.t.)	(vitreous) 4.28 g·cm^{-3}
Liquid density at m.p.	3.99 g·cm^{-3}
Melting point	494 K,221 °C,430 °F
Boiling point	958 K,685 °C,1265 °F
Critical point	1766 K, 27.2 MPa
Heat of fusion	(gray) 6.69 kJ·mol^{-1}
Heat of vaporization	95.48 kJ·mol^{-1}
Specific heat capacity	(25 °C) 25.363 J·mol^{-1}·K^{-1}
Vapor pressure	

P/Pa	1	10	100	1 k	10 k	100 k
at *T*/K	500	552	617	704	813	958

Atomic properties

Oxidation states	**6**, **4**, **2**, 1,[1] -2 (strongly acidic oxide)
Electronegativity	2.55 (Pauling scale)
Ionization energies	1st: 941.0 $kJ\cdot mol^{-1}$
	2nd: 2045 $kJ\cdot mol^{-1}$
	3rd: 2973.7 $kJ\cdot mol^{-1}$
Atomic radius	120 pm
Covalent radius	120±4 pm
Van der Waals radius	190 pm
Miscellanea	
Crystal structure	hexagonal
Magnetic ordering	diamagnetic[2]
Thermal conductivity	(300 K) (amorphous) 0.519 $W\cdot m^{-1}\cdot K^{-1}$
Thermal expansion	(25 °C) (amorphous) 37 $\mu m\cdot m^{-1}\cdot K^{-1}$
Speed of sound (thin rod)	(20 °C) 3350 m/s
Young's modulus	10 GPa
Shear modulus	3.7 GPa
Bulk modulus	8.3 GPa
Poisson ratio	0.33
Mohs hardness	2.0
Brinell hardness	736 MPa
CAS registry number	7782-49-2
Most stable isotopes	

iso	NA	half-life	DM	DE (MeV)	DP
^{72}Se	syn	8.4 d	ε	-	^{72}As
			γ	0.046	-
^{74}Se	0.87%	^{74}Se is stable with 40 neutron			
^{75}Se	syn	119.779 d	ε	-	^{75}As
			γ	0.264, 0.136, 0.279	-
^{76}Se	9.36%	^{76}Se is stable with 42 neutron			
^{77}Se	7.63%	^{77}Se is stable with 43 neutron			
^{78}Se	23.78%	^{78}Se is stable with 44 neutron			
^{79}Se	trace	3.27×10^5 y	β^-	0.151	^{79}Br
^{80}Se	49.61%	^{80}Se is stable with 46 neutron			
^{82}Se	8.73%	1.08×10^{20} y	$\beta^-\beta^-$	2.995	^{82}Kr

Selenium (/sɪˈliːniəm/ *sə-**LEE**-nee-əm*) is a chemical element with atomic number 34, chemical symbol **Se**, and an atomic mass of 78.96. It is a nonmetal with properties that are intermediate between those of its periodic table column-adjacent chalcogen elements sulfur and tellurium. It rarely occurs in its elemental state in nature, or as pure ore compounds. Selenium (Greek σελήνη *selene* meaning "Moon") was discovered in 1817 by Jöns Jakob Berzelius, who noted the similarity of the new element to the previously-known tellurium (named for the Earth).

Selenium is found impurely in metal sulfide ores, where it partially replaces the sulfur. Commercially, selenium is produced as a byproduct in the refining of these ores, most often during copper production. Minerals that are pure selenide or selenate compounds are known, but are rare. The chief commercial uses for selenium today are in glassmaking and in pigments. Selenium is a semiconductor and is used in photocells. Uses in electronics, once important, have been supplanted by silicon semiconductor devices. It has recently seen a resurgence in use in the synthesis of one type of fluorescent quantum dot.

Selenium salts are toxic in large amounts, but trace amounts are necessary for cellular function in many organisms, including all animals. Selenium is a component of the antioxidant enzymes glutathione peroxidase and thioredoxin reductase (which indirectly reduce certain oxidized molecules in animals and some plants). It is also found in three deiodinase enzymes, which convert one thyroid hormone to another. Selenium requirements in plants differ by species, with some plants requiring relatively large amounts, and others apparently requiring none.[3]

Characteristics

Physical properties

Black selenium

The most stable allotrope of selenium is a dense reddish-gray solid. In terms of structure, it adopts a helical polymeric chain.[4] The Se-Se distance is 2.37 Å and the Se-Se-Se angle is 103°. It is a semiconductor and is used in photocells. Gray selenium resists oxidation by air and is not attacked by non-oxidizing acids. With strong reducing agents, it forms polyselenides.

Molecular allotropes

The second major allotrope of Se is red selenium. The solid consists of individual molecules of eight-membered ring molecules, like its lighter cousin sulfur. The Se-Se distance is 2.34 Å and the Se-Se-Se angle is 106°. Unlike sulfur, however, the red form converts to the gray polymeric allotrope with heat. Other rings with the formula Se_n are also known.[5]

Elemental selenium produced in chemical reactions invariably appears as the amorphous red form: an insoluble, brick-red powder. When this form is rapidly melted, it forms the black, vitreous form, which is usually sold industrially as beads. The red allotrope crystallizes in three habits.[6][7] Selenium does not exhibit the unusual changes in viscosity that sulfur undergoes when gradually heated.[7][8]

Isotopes

Selenium has six naturally occurring isotopes, five of which are stable: ^{74}Se, ^{76}Se, ^{77}Se, ^{78}Se, and ^{80}Se. The last three also occur as fission products, along with ^{79}Se, which has a half-life of 327,000 years.[9][10] The final naturally occurring isotope, ^{82}Se, has a very long half-life (~10^{20} yr, decaying via double beta decay to ^{82}Kr), which, for practical purposes, can be considered to be stable. Twenty-three other unstable isotopes have been characterized.[11]

See also Selenium-79 for more information on recent changes in the measured half-life of this long-lived fission product, important for the dose calculations performed in the frame of the geological disposal of long-lived radioactive waste.[11]

Occurrence


Native selenium

Native (i.e., elemental) selenium is a rare mineral, which does not usually form good crystals, but, when it does, they are steep rhombohedra or tiny acicular (hair-like) crystals.[12] Isolation of selenium is often complicated by the presence of other compounds and elements.

Selenium occurs naturally in a number of inorganic forms, including selenide-, selenate-, and selenite-containing minerals, but these minerals are rare. The common mineral selenite is *not* a selenium mineral, and contains no selenite ion, but is rather a type of gypsum (calcium sulfate hydrate) named like selenium for the moon well before the discovery of selenium. Selenium is most commonly found quite impurely, replacing a small part of the sulfur in sulfide ores of many metals.[13][14]

In living systems, selenium is found in the amino acids selenomethionine, selenocysteine, and methylselenocysteine. In these compounds, selenium plays a role analogous to that of sulfur. Another naturally occurring organoselenium compound is dimethyl selenide.[15][15]

Certain solids are selenium-rich, and selenium can be bioconcentrated by certain plants. In soils, selenium most often occurs in soluble forms such as selenate (analogous to sulfate), which are leached into rivers very easily by runoff.[13][14] Ocean water contains significant amounts of selenium.[16][17]

Anthropogenic sources of selenium include coal burning and the mining and smelting of sulfide ores.[18]

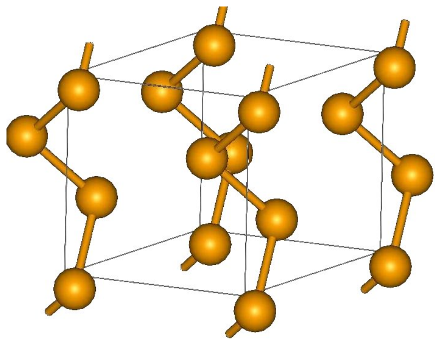
History

Selenium (Greek σελήνη *selene* meaning "Moon") was discovered in 1817 by Jöns Jakob Berzelius and Johan Gottlieb Gahn.[19] Both chemists owned a chemistry plant near Gripsholm, Sweden producing sulfuric acid by the lead chamber process. The pyrite from the Falun mine created a red precipitate in the lead chambers which was presumed to be an arsenic compound, and so the pyrite's use to make acid was discontinued. Berzelius and Gahn wanted to use the pyrite and they also observed that the red precipitate gave off a smell like horseradish when burned. This smell was not typical of arsenic, but a similar odor was known from tellurium compounds. Hence, Berzelius's first letter to Alexander Marcet stated that this was a tellurium compound. However, the lack of tellurium compounds in the Falun mine minerals eventually led Berzelius to reanalyze the red precipitate, and in 1818 he wrote a second letter to Marcet describing a newly found element similar to sulfur and tellurium. Because of its similarity to tellurium, named for the Earth, Berzelius named the new element after the Moon.[20][21]

In 1873, Willoughby Smith found that the electrical resistance of grey selenium was dependent on the ambient light. This led to its use as a cell for sensing light. The first of commercial products using selenium were developed by Werner Siemens in the mid-1870s. The selenium cell was used in the photophone developed by Alexander Graham Bell in 1879. Selenium transmits an electric current proportional to the amount of light falling on its surface. This phenomenon was used in the design of light meters and similar devices. Selenium's semiconductor properties found numerous other applications in electronics.[22][23][24] The development of selenium rectifiers began during the early 1930s, and these replaced copper oxide rectifiers because of their superior efficiencies.[25][26][27]

Selenium came to medical notice later because of its toxicity to human beings working in industries. Selenium was also recognized as an important veterinary toxin, which is seen in animals that have eaten high-selenium plants. In 1954, the first hints of specific biological functions of selenium were discovered in microorganisms.[28][29] Its essentiality for mammalian life was discovered in 1957.[30][31] In the 1970s, it was shown to be present in two independent sets of enzymes. This was followed by the discovery of selenocysteine in proteins. During the 1980s, it was shown that selenocysteine is encoded by the codon UGA. The recoding mechanism was worked out first in bacteria and then in mammals (see SECIS element).[32]

Production



Structure of trigonal selenium

Selenium is most commonly produced from selenide in many sulfide ores, such as those of copper, silver, or lead. Electrolytic metal refining is particularly conducive to producing selenium as a byproduct, and it is obtained from the anode mud of copper refineries. Another source was the mud from the lead chambers of sulfuric acid plants but this method to produce sulfuric acid is no longer used. These muds can be processed by a number of means to obtain selenium. However, most elemental selenium comes as a byproduct of refining copper or producing sulfuric acid.[33][34] Since the invention of Solvent extraction and electrowinning (SX/EW) for the production of copper this method takes an increasing share of the world wide copper production.[35] This changes the availability of selenium because only a comparably small part of the selenium in the ore is leached together with the copper.[36]

Industrial production of selenium usually involves the extraction of selenium dioxide from residues obtained during the purification of copper. Common production from the residue then begins by oxidation with sodium carbonate to produce selenium dioxide. The selenium dioxide is then mixed with water and the solution is acidified to form selenous acid (oxidation step). Selenous acid is bubbled with sulfur dioxide (reduction step) to give elemental selenium.[37][38]

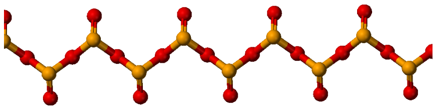
Chemical compounds

Selenium compounds commonly exist in the oxidation states −2, +2, +4, and +6.

Chalcogen compounds

Selenium forms two oxides: selenium dioxide (SeO_2) and selenium trioxide (SeO_3). Selenium dioxide is formed by the reaction of elemental selenium with oxygen:[7]

$$Se_8 + 8\ O_2 \rightarrow 8\ SeO_2$$



Structure of the polymer SeO_2. The (pyramidal) Se atoms are yellow.

It is a polymeric solid that forms monomeric SeO_2 molecules in the gas phase. It dissolves in water to form selenous acid, H_2SeO_3. Selenous acid can also be made directly by oxidizing elemental selenium with nitric acid:[39]

$$3\ Se + 4\ HNO_3 + H_2O \rightarrow 3\ H_2SeO_3 + 4\ NO$$

Unlike sulfur, which forms a stable trioxide, selenium trioxide is thermodynamically unstable and decomposes to the dioxide above 185 °C:[7][39]

$$2\ SeO_3 \rightarrow 2\ SeO_2 + O_2\ (\Delta H = -54\ \text{kJ/mol})$$

Selenium trioxide is produced in the laboratory by the reaction of anhydrous potassium selenate (K_2SeO_4) and sulfur trioxide (SO_3).[40]

Salts of selenous acid are called *selenites*. These include silver selenite (Ag_2SeO_3) and sodium selenite (Na_2SeO_3).

Hydrogen sulfide reacts with aqueous selenous acid to produce selenium disulfide:

$$H_2SeO_3 + 2\ H_2S \rightarrow SeS_2 + 3\ H_2O$$

Selenium disulfide consists of 8-membered rings of a nearly statistical distribution of sulfur and selenium atoms. It has an approximate composition of SeS_2, with individual rings varying in composition, such as Se_4S_4 and Se_2S_6. Selenium disulfide has been use in shampoo as an anti-dandruff agent, an inhibitor in polymer chemistry, a glass dye, and a reducing agent in fireworks.[39]

Selenium trioxide may be synthesized by dehydrating selenic acid, H_2SeO_4, which is itself produced by the oxidation of selenium dioxide with hydrogen peroxide:[41]

$$SeO_2 + H_2O_2 \rightarrow H_2SeO_4$$

Hot, concentrated selenic acid is capable of dissolving gold, forming gold(III) selenate.[42]

Halogen compounds

Iodides of selenium are not well known. The only stable chloride is selenium monochloride (Se_2Cl_2), which might be better; the corresponding bromide is also known. These species are structurally analogous to the corresponding disulfur dichloride. Selenium dichloride is an important reagent in the preparation of selenium compounds (e.g. the preparation of Se_7). It is prepared by treating selenium with sulfuryl chloride (SO_2Cl_2).[43] Selenium reacts with fluorine to form selenium hexafluoride:

$$Se_8 + 24\ F_2 \rightarrow 8\ SeF_6$$

In comparison with its sulfur counterpart (sulfur hexafluoride), selenium hexafluoride (SeF_6) is more reactive and is a toxic pulmonary irritant.[44] Some of the selenium oxyhalides, such as selenium oxyfluoride ($SeOF_2$) and selenium oxychloride ($SeOCl_2$) have been used as specialty solvents.[7]

Selenides

Analogous to the behavior of other chalcogens, selenium forms a dihydride H_2Se. It is a strongly odiferous, toxic, and colorless gas. It is more acidic than H_2S. In solution it ionizes to HSe^-. The selenide dianion Se^{2-} forms a variety of compounds, including the minerals from which selenium is obtained commercially. Illustrative selenides include mercury selenide (HgSe), lead selenide (PbSe), zinc selenide (ZnSe), and copper indium gallium diselenide ($Cu(Ga,In)Se_2$). These materials are semiconductors. With highly electropositive metals, such as aluminium, these selenides are prone to hydrolysis:[7]

$$Al_2Se_3 + 6\ H_2O \rightarrow Al_2O_3 + 6\ H_2Se$$

Alkali metal selenides react with selenium to form polyselenides, Se, which exist as chains.

Other compounds

Tetraselenium tetranitride, Se_4N_4, is an explosive orange compound analogous to tetrasulfur tetranitride (S_4N_4).[7][45][46] It can be synthesized by the reaction of selenium tetrachloride ($SeCl_4$) with $[((CH_3)_3Si)_2N]_2Se$.[47]

Selenium reacts with cyanides to yield selenocyanates:[7]

$$8\ KCN + Se_8 \rightarrow 8\ KSeCN$$

Organoselenium compounds

Selenium, especially in the II oxidation state, forms stable bonds to carbon, which are structurally analogous to the corresponding organosulfur compounds. Especially common are selenides (R_2Se, analogues of thioethers), diselenides (R_2Se_2, analogues of disulfides), and selenols (RSeH, analogues of thiols). Representatives of selenides, diselenides, and selenols include respectively selenomethionine, diphenyldiselenide, and benzeneselenol. The sulfoxide in sulfur chemistry is represented in selenium chemistry by the selenoxides (formula RSe(O)R), which are intermediates in organic synthesis, as illustrated by the selenoxide elimination reaction. Consistent with trends indicated by the double bond rule, selenoketones, R(C=Se)R, and selenaldehydes, R(C=Se)H, are rarely observed.[48]

Applications

The demand for Se was around 2300 tonnes/y in the years 1989–1991.[49]

Manganese electrolysis

During the electro winning of manganese an addition of selenium dioxide decreases the power necessary to operate the electrolysis cells. China is the largest consumer of selenium dioxide for this purpose. For every ton of manganese an average of 2 kg selenium oxide is used.[50][51]

Glass production

The largest commercial use of Se, accounting for about 50% of consumption, is for the production of glass. Se compounds confer a red color to glass. This color cancels out the green or yellow tints that arise from iron impurities that are typical for most glass. For this purpose various selenite and selenate salts are added. For other applications, the red color may be desirable, in which case mixtures of CdSe and CdS are added.[49]

Alloys

Selenium is used with bismuth in brasses to replace more toxic lead. The regulation of lead in drinking water applications with the Safe Drinking Water Act of 1974 made a reduction of lead in brass necessary. The new brass is marketed under the name EnviroBrass.[52] Like lead and sulfur, selenium improves the machinability of steel at concentrations of 0,15 %.[53][54] The same improvement is also observed in copper alloys and therefore selenium is also used in machinable copper alloys.[55]

Solar cells

Copper indium gallium selenide is a material used in the production of solar cells.[56]

Other uses

Small amounts of organoselenium compounds are used to modify the vulcanization catalysts used in the production of rubber.[36]

The demand for selenium by the electronics industry is declining, despite a number of continuing applications.[57] Because of its photovoltaic and photoconductive properties, selenium is used in photocopying[58][59][60][61], photocells, light meters and solar cells. Its use as a photoconductor in plain-paper copiers once was a leading application but in the 1980s, the photoconductor application declined (although it was still a large end-use) as more and more copiers switched to the use of organic photoconductors. It was once widely used in selenium rectifiers. These uses have mostly been replaced by silicon-based devices or are in the process of being replaced. The most notable exception is in power DC surge protection, where the superior energy capabilities of selenium suppressors make them more desirable than metal oxide varistors.

Zinc selenide was the first material for blue LEDs but gallium nitride is dominating the market now.[62] Cadmium selenide has recently played an important part in the fabrication of quantum dots. Sheets of amorphous selenium convert x-ray images to patterns of charge in xeroradiography and in solid-state, flat-panel x-ray cameras.[63]

Selenium is a catalyst in some chemical reactions but it is not widely used because of issues with toxicity. In X-ray crystallography, incorporation of one or more selenium atoms in place of sulfur helps with Multi-wavelength anomalous dispersion and Single wavelength anomalous dispersion phasing.[64]

Selenium is used in the toning of photographic prints, and it is sold as a toner by numerous photographic manufacturers. Its use intensifies and extends the tonal range of black-and-white photographic images and improves the permanence of prints.[65][66][67]

Biological role

NFPA 704
Fire diamond for elemental selenium

Although it is toxic in large doses, selenium is an essential micronutrient for animals. In plants, it occurs as a bystander mineral, sometimes in toxic proportions in forage (some plants may accumulate selenium as a defense against being eaten by animals, but other plants such as locoweed require selenium, and their growth indicates the presence of selenium in soil).[3] See more on plant nutrition below.

Selenium is a component of the unusual amino acids selenocysteine and selenomethionine. In humans, selenium is a trace element nutrient that functions as cofactor for reduction of antioxidant enzymes, such as glutathione peroxidases[68] and certain forms of thioredoxin reductase found in animals and some plants (this enzyme occurs in all living organisms, but not all forms of it in plants require selenium).

The glutathione peroxidase family of enzymes (GSH-Px) catalyze certain reactions that remove reactive oxygen species such as hydrogen peroxide and organic hydroperoxides:

$$2\ GSH + H_2O_2\text{----}GSH\text{-}Px \rightarrow GSSG + 2\ H_2O$$

Selenium also plays a role in the functioning of the thyroid gland and in every cell that uses thyroid hormone, by participating as a cofactor for the three of the four known types of thyroid hormone deiodinases, which activate and then deactivate various thyroid hormones and their metabolites: the iodothyronine deiodinases are the subfamily of deiodinase enzymes that use selenium as the otherwise rare amino acid selenocysteine. (Only the deiodinase iodotyrosine deiodinase, which works on the last break-down products of thyroid hormone, does not use selenium).[69]

Selenium may inhibit Hashimoto's disease, in which the body's own thyroid cells are attacked as alien. A reduction of 21% on TPO antibodies was reported with the dietary intake of 0.2 mg of selenium.[70]

Evolution in biology

From about three billion years ago, prokaryotic selenoprotein families drive the evolution of selenocysteine. Selenium is incorporated into several prokaryotic selenoprotein families in bacteria, archaea and eukaryotes as selenocysteine,[71] where selenoprotein peroxiredoxins protect bacterial and eukaryotic cells against oxidative damage. Selenoprotein families of GSH-Px and the deiodinases of eukaryotic cells seem to have a bacterial phylogenetic origin. The selenocysteine-containing form occurs in species as diverse as green algae, diatoms, sea urchin, fish and chicken. Selenium enzymes are involved in utilization of the small reducing molecules glutathione and thioredoxin. One family of selenium-containing molecules (the glutathione peroxidases) destroy peroxide and repair damaged peroxidized cell membranes, using glutathione. Another selenium-containing enzyme in some plants and in animals (thioredoxin reductase) generates reduced thioredoxin, a dithiol that serves as an electron source for peroxidases and also the important reducing enzyme ribonucleotide reductase that makes DNA precursors from RNA precursors.[72]

At about 500 Mya, plants and animals began to transfer from the sea to rivers and land, the environmental deficiency of marine mineral antioxidants (as selenium, iodine, etc.) was a challenge to the evolution of terrestrial life.[73] Trace elements involved in GSH-Px and superoxide dismutase enzymes activities, i.e. selenium, vanadium, magnesium, copper, and zinc, may have been lacking in some terrestrial mineral-deficient areas.[71] Marine organisms retained and sometimes expanded their seleno-proteomes, whereas the seleno-proteomes of some terrestrial organisms were reduced or completely lost. These findings suggest that, with the exception of vertebrates, aquatic life supports selenium utilization, whereas terrestrial habitats lead to reduced use of this trace element.[74] Marine fishes and vertebrate thyroid glands have the highest concentration of selenium and iodine. From about 500 Mya, freshwater and terrestrial plants slowly optimized the production of "new" endogenous antioxidants such as ascorbic acid (Vitamin C), polyphenols (including flavonoids), tocopherols, etc. A few of these appeared more recently, in the last 50–200 million years, in fruits and flowers of angiosperm plants. In fact, the angiosperms (the dominant type of plant today) and most of their antioxidant pigments evolved during the late Jurassic period.

The deiodinase isoenzymes constitute another family of eukaryotic selenoproteins with identified enzyme function. Deiodinases are able to extract electrons from iodides, and iodides from iodothyronines. They are, thus, involved in thyroid-hormone regulation, participating in the protection of thyrocytes from damage by H_2O_2 produced for thyroid-hormone biosynthesis.[75] About 200 Mya, new selenoproteins were developed as mammalian GSH-Px enzymes.[76][77][78][79]

Nutritional sources of selenium

Dietary selenium comes from nuts, cereals, meat, mushrooms, fish, and eggs. Brazil nuts are the richest ordinary dietary source (though this is soil-dependent, since the Brazil nut does not require high levels of the element for its own needs). In descending order of concentration, high levels are also found in kidney, tuna, crab, and lobster.[80][81] The human body's content of selenium is believed to be in the 13–20 milligram range.[82]

Indicator plant species

Certain species of plants are considered indicators of high selenium content of the soil, since they require high levels of selenium to thrive. The main selenium indicator plants are *Astragalus* species (including some locoweeds), prince's plume (*Stanleya* sp.), woody asters (*Xylorhiza* sp.), and false goldenweed (*Oonopsis* sp.)[83]

Medical use

The substance loosely called selenium sulfide (approximate formula SeS_2) is the active ingredient in some anti-dandruff shampoos.[84] The selenium compound kills the scalp fungus *Malassezia*, which causes shedding of dry skin fragments. The ingredient is also used in body lotions to treat Tinea versicolor due to infection by a different species of *Malassezia* fungus.[85]

Detection in biological fluids

Selenium may be measured in blood, plasma, serum or urine to monitor excessive environmental or occupational exposure, confirm a diagnosis of poisoning in hospitalized victims or to assist in a forensic investigation in a case of fatal overdosage. Some analytical techniques are capable of distinguishing organic from inorganic forms of the element. Both organic and inorganic forms of selenium are largely converted to monosaccharide conjugates (selenosugars) in the body prior to being eliminated in the urine. Cancer patients receiving daily oral doses of selenothionine may achieve very high plasma and urine selenium concentrations.[86]

Toxicity

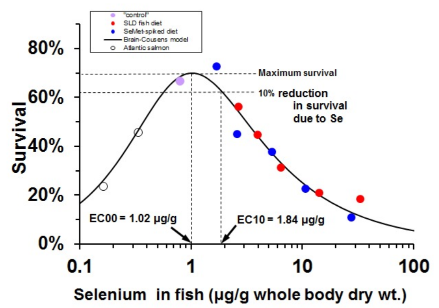
Although selenium is an essential trace element, it is toxic if taken in excess. Exceeding the Tolerable Upper Intake Level of 400 micrograms per day can lead to selenosis.[87] This 400 microgram (μg) Tolerable Upper Intake Level is based primarily on a 1986 study of five Chinese patients who exhibited overt signs of selenosis and a follow up study on the same five people in 1992.[88] The 1992 study actually found the maximum safe dietary Se intake to be approximately 800 micrograms per day (15 micrograms per kilogram body weight), but suggested 400 micrograms per day to not only avoid toxicity, but also to avoid creating an imbalance of nutrients in the diet and to account for data from other countries.[89] In China, people who ingested corn grown in extremely selenium-rich stony coal (carbonaceous shale) have suffered from selenium toxicity. This coal was shown to have selenium content as high as 9.1%, the highest concentration in coal ever recorded in literature.[90]

Symptoms of selenosis include a garlic odor on the breath, gastrointestinal disorders, hair loss, sloughing of nails, fatigue, irritability, and neurological damage. Extreme cases of selenosis can result in cirrhosis of the liver, pulmonary edema, and death.[91] Elemental selenium and most metallic selenides have relatively low toxicities because of their low bioavailability. By contrast, selenates and selenites are very toxic, having an oxidant mode of action similar to that of arsenic trioxide. The chronic toxic dose of selenite for humans is about 2400 to 3000 micrograms of selenium per day for a long time.[92] Hydrogen selenide is an extremely toxic, corrosive gas.[93] Selenium also occurs in organic compounds, such as dimethyl selenide, selenomethionine, selenocysteine and methylselenocysteine, all of which have high bioavailability and are toxic in large doses.

On 19 April 2009, 21 polo ponies died shortly before a match in the United States Polo Open. Three days later, a pharmacy released a statement explaining that the horses had received an incorrect dose of one of the ingredients used in a vitamin/mineral supplement compound that had been incorrectly compounded by a compounding pharmacy. Analysis of blood levels of inorganic compounds in the supplement indicated the selenium concentrations were ten to fifteen times higher than normal in the horses' blood samples, and 15 to 20 times higher than normal in their liver samples. It was later confirmed that selenium was the ingredient in question.[94]

Selenium poisoning of water systems may result whenever new agricultural runoff courses through normally dry, undeveloped lands. This process leaches natural soluble selenium compounds (such as selenates) into the water, which may then be concentrated in new "wetlands" as the water evaporates. High selenium levels produced in this fashion have been found to have caused certain congenital disorders in wetland birds.[95]

In fish and other wildlife, low levels of selenium cause deficiency while high levels cause toxicity. For example, in salmon, the optimal concentration of selenium in the fish tissue (whole body) is about 1 microgram selenium per gram of tissue (dry weight). At levels much below that concentration, young salmon die from selenium deficiency;[97] much above that level they die from toxic excess.[96]



Relationship between survival of juvenile salmon and concentration of selenium in their tissues after 90 days (Chinook salmon[96]) or 45 days (Atlantic salmon[97]) exposure to dietary selenium. The 10% lethality level (LC10=1.84 µg/g) was derived by applying the biphasic model of Brain and Cousens[98] to only the Chinook salmon data. The Chinook salmon data comprise two series of dietary treatments, combined here because the effects on survival are indistinguishable.

Deficiency

Selenium deficiency is rare in healthy, well-nourished individuals. It can occur in patients with severely compromised intestinal function, those undergoing total parenteral nutrition, and[99] in those of advanced age (over 90). Also, people dependent on food grown from selenium-deficient soil are at risk. Although New Zealand has low levels of selenium in its soil, adverse health effects have not been detected.[100]

Selenium deficiency as defined by low (<60% of normal) selenoenzyme activity levels in brain and endocrine tissues only occurs when a low selenium status is linked with an additional stress, such as high exposures to mercury[101] or as a result of increased oxidant stress due to vitamin E deficiency.[102]

There are interactions between selenium and other nutrients, such as iodine and vitamin E. The interaction is observed in the etiology of many deficiency diseases in animals and pure selenium deficiency is rare. The effect of selenium deficiency on health remains uncertain, particularly in relation to Kashin-Beck disease.[103]

Controversial health effects

A number of correlative epidemiological studies have implicated selenium deficiency (as measured by blood levels) in a number of serious or chronic diseases, such as cancer,[104] diabetes,[104] HIV/AIDS,[105] and tuberculosis. In addition, selenium supplementation has been found to a chemopreventive for some types of cancer in some types of rodents. However, in randomized, blinded, controlled prospective trials in humans, selenium supplementation has not succeeded in reducing the incidence of any disease. Nor has a meta analysis of such selenium supplementation studies detected a decrease in overall mortality.[106]

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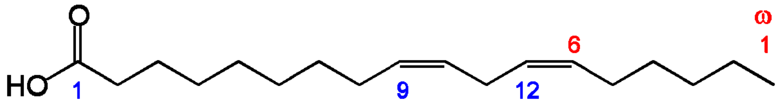
External links

- National Institutes of Health page on Selenium (http://ods.od.nih.gov/factsheets/selenium.asp)
- Assay (http://www.sas-centre.org/assays/trace_metals/selenium.html)
- ATSDR – Toxicological Profile: Selenium (http://www.atsdr.cdc.gov/toxprofiles/tp92.html)
- Peter van der Krogt elements site (http://elements.vanderkrogt.net/element.php?sym=Se)

Omega-6 fatty acid



The chemical structure of linoleic acid, a common *n*−6 fatty acid found in many vegetable oils.

***n*−6 fatty acids** (popularly referred to as **ω−6 fatty acids** or **omega-6 fatty acids**) are a family of unsaturated fatty acids that have in common a final carbon–carbon double bond in the *n*−6 position, that is, the sixth bond, counting from the methyl end.[1]

The biological effects of the *n*−6 fatty acids are largely mediated by their conversion to *n*-6 eicosanoids that bind to diverse receptors found in every tissue of the body. The conversion of tissue arachidonic acid (20:4n-6) to n-6 prostaglandin and n-6 leukotriene hormones provides many targets for pharmaceutical drug development and treatment to diminish excessive n-6 actions in atherosclerosis[2], asthma, arthritis, vascular disease, thrombosis, immune-inflammatory processes, and tumor proliferation. Competitive interactions with the *n*−3 fatty acids affect the relative storage, mobilization, conversion and action of the n-3 and n-6 eicosanoid precursors. (See Essential fatty acid interactions for more information.)

Key *n*−6 fatty acids

Linoleic acid (18:2, *n*−6), the shortest-chained *n*−6 fatty acid, is an essential fatty acid. Arachidonic acid (20:4) is a physiologically significant *n*−6 fatty acid and is the precursor for prostaglandins and other physiologically active molecules.

Negative health effects

Some medical research suggests that excessive levels of certain *n*−6 fatty acids, relative to certain *n*−3 (Omega-3) fatty acids, may increase the probability of a number of diseases.[3][4][5]

Modern Western diets typically have ratios of *n*−6 to *n*−3 in excess of 10 to 1, some as high as 30 to 1. The optimal ratio is thought to be 4 to 1 or lower.[6][7]

Excess *n*−6 fats interfere with the health benefits of *n*−3 fats, in part because they compete for the same rate-limiting enzymes. A high proportion of *n*−6 to *n*−3 fat in the diet shifts the physiological state in the tissues toward the pathogenesis of many diseases: prothrombotic, proinflammatory and proconstrictive.[8]

Chronic excessive production of *n*−6 eicosanoids is associated with arthritis, inflammation, and cancer. Many of the medications used to treat and manage these conditions work by blocking the effects of the potent *n*−6 fat, arachidonic acid.[9] Many steps in formation and action of n-6 hormones from n-6 arachidonic acid proceed more vigorously than the corresponding competitive steps in formation and action of n-3 hormones from n-3 eicosapentaenoic acid.[10] The COX-1 and COX-2 inhibitor medications, used to treat inflammation and pain, work by preventing the COX enzymes from turning arachidonic acid into inflammatory compounds.[11] (See Cyclooxygenase for more information.) The LOX inhibitor medications often used to treat asthma, work by preventing the LOX enzyme from converting arachidonic acid into the leukotrienes.[12][13] Many of the anti-mania medications used to treat bipolar disorder work by targeting the arachidonic acid cascade in the brain.[14]

A high consumption of omega-6 polyunsaturated fatty acids (PUFAs), which are found in most types of vegetable oil, may increase the likelihood that postmenopausal women will develop breast cancer.[15] Similar effect was observed on prostate cancer.[16] Another "analysis suggested an inverse association between total polyunsaturated fatty acids and breast cancer risk, but individual polyunsaturated fatty acids behaved differently [from each other]. [...] a 20:2 derivative of linoleic acid [...] was inversely associated with the risk of breast cancer".[17]

Dietary linoleic acid requirement

Adding more controversy to the *n*−6 fat issue is that the dietary requirement for linoleic acid (the key *n*−6 fatty acid), has been seriously questioned, because of a significant methodology error discovered by University of Toronto scientist Stephen Cunnane.[18] Cunnane discovered that the seminal research used to determine the dietary requirement for linoleic acid was based on feeding animals linoleic acid-deficient diets, which were simultaneously deficient in *n*−3 fats. The *n*−3 deficiency was not taken into account. The *n*−6 oils added back systematically to correct the deficiency also contained trace amounts of *n*−3 fats. Therefore the researchers were inadvertently correcting the *n*−3 deficiency as well. Ultimately, it took more oil to correct both deficiencies. According to Cunnane, this error overestimates linoleic acid requirements by 5 to 15 times.

Dietary sources

Four major food oils (palm, soybean, rapeseed, and sunflower) provide more than 100 million metric tons annually, providing more than 32 million metric tons of n-6 linoleic acid and 4 million metric tons of n-3 alpha-linolenic acid.[19]

The evening primrose flower (*O. biennis*) produces an oil containing a high content of γ-linolenic acid, a type of *n*−6 fatty acid.

Dietary sources of *n*−6 fatty acids include:[20]

- poultry
- eggs
- avocado
- nuts
- cereals
- durum wheat
- whole-grain breads
- most vegetable oils
- evening primrose oil
- borage oil
- blackcurrant seed oil
- flax/linseed oil
- rapeseed or canola oil
- hemp oil
- soybean oil
- cottonseed oil
- sunflower seed oil
- corn oil
- safflower oil
- pumpkin seeds
- acai berry
- cashews
- spirulina

List of *n*−6 fatty acids

Common name	Lipid name	Chemical name
Linoleic acid (LA)	18:2 (*n*−6)	*all-cis*-9,12-octadecadienoic acid
Gamma-linolenic acid (GLA)	18:3 (*n*−6)	*all-cis*-6,9,12-octadecatrienoic acid
Eicosadienoic acid	20:2 (*n*−6)	*all-cis*-11,14-eicosadienoic acid
Dihomo-gamma-linolenic acid (DGLA)	20:3 (*n*−6)	*all-cis*-8,11,14-eicosatrienoic acid
Arachidonic acid (AA)	20:4 (*n*−6)	*all-cis*-5,8,11,14-eicosatetraenoic acid
Docosadienoic acid	22:2 (*n*−6)	*all-cis*-13,16-docosadienoic acid
Adrenic acid	22:4 (*n*−6)	*all-cis*-7,10,13,16-docosatetraenoic acid
Docosapentaenoic acid	22:5 (*n*−6)	*all-cis*-4,7,10,13,16-docosapentaenoic acid
Tetracosatetraenoic acid	24:4 (*n*−6)	*all-cis*-9,12,15,18-tetracosatetraenoic acid
Tetracosapentaenoic acid	24:5 (*n*−6)	*all-cis*-6,9,12,15,18-tetracosapentaenoic acid
Calendic acid	18:3 (*n*−6)	8E,10E,12Z-octadecatrienoic acid

Notes & references

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Borage

Borage	
	
Borage flower	
Scientific classification	
Kingdom:	Plantae
(unranked):	Angiosperms
(unranked):	Eudicots
(unranked):	Asterids
Order:	(unplaced)
Family:	Boraginaceae
Genus:	*Borago*
Species:	***B. officinalis***
Binomial name	
Borago officinalis L.	

Borage, (***Borago officinalis***), also known as a **starflower**, is an annual herb originating in Syria,[1] but naturalized throughout the Mediterranean region, as well as Asia Minor, Europe, North Africa, and South America. This plant was thought to be native of Assyria, but is probably of North African origin, where there are other Borago species. It grows to a height of 60–100 cm (**unknown operator: u'strong'unknown operator: u'strong'unknown operator: u'strong' unknown operator: u'strong'**), and is bristly or hairy all over the stems and leaves; the leaves are alternate, simple, and 5–15 cm (**unknown operator: u'strong'unknown operator: u'strong'unknown operator: u'strong' unknown operator: u'strong'**) long. The flowers are complete, perfect with five narrow, triangular-pointed petals. Flowers are most often blue in color, although pink flowers are sometimes observed. White flowered types are also cultivated. The blue flower is genetically dominant over the white flower. [2] The flowers arise along scorpioid cymes to form large floral displays with multiple flowers blooming simultaneously, suggesting that borage has a high degree of geitonogamy[3]. It has an indeterminate growth habit which may lead to prolific spreading. In milder climates, borage will bloom continuously for most of the year.

Characteristics and uses

A white flower cultivar

Traditionally borage was cultivated for culinary and medicinal uses, although today commercial cultivation is mainly as an oilseed. The seed oil is desired as source of gamma-linolenic acid (GLA, 18:3, cis 6,9,12-octadecatrienoic acid), for which borage is the highest known plant-based source (17-28%).[4] The seed oil content is between 26-38% and in addition to GLA contains the fatty acids palmitic acid (10-11%), stearic acid (3.5-4.5%), oleic acid (16-20%), linoleic acid (35-38%), eicosenoic acid (3.5-5.5%), erucic acid (1.5-3.5%), and nervonic acid (1.5%). The oil is often marketed as "starflower oil" or "borage oil" for uses as a GLA supplement, although healthy adults will typically produce ample GLA through dietary linoleic acid.

Two blossoms, the younger one is pink, the older blue

Borage production does include use as either a fresh vegetable or a dried herb. As a fresh vegetable, borage, with a cucumber like taste, is often used in salads or as a garnish.[5] The flower, which contains the non-toxic pyrrolizidine alkaloid thesinine, has a sweet honey-like taste and as one of the few truly blue-colored edible substances, is often used to decorate dessert.[5] It is notable that the leaves have been found to contain small amounts (10 ppm of dried herb) of the liver-toxic pyrrolizidine alkaloids: intermedine, lycopsamine, amabiline and supinine.[6] The levels are extremely low (2-10 ppm). Leaves contain mainly the non toxic lycopsamine also amabiline and the non-toxic saturated PA thesinine (the only alkaloid found in seed contained thesinine and amabiline in a ratio of 10:1). No alkaloids have been found so far in seed oil.[7][8]

Vegetable use of borage is common in Germany, in the Spanish regions of Aragón and Navarra, in the Greek island of Crete and in the Italian northern region Liguria. Although often used in soups, one of the better known German borage recipes is the Green Sauce (Grüne Soße) made in Frankfurt. In Italian Liguria, borage is commonly used as filling of the traditional pasta ravioli and pansoti. The leaves and flowers were originally used in Pimms before it was replaced by mint or cucumber peel. It is used to flavour pickled gherkins in Poland.

Borage is also traditionally used as a garnish in the Pimms Cup cocktail,[5] but is sometimes replaced by a long sliver of cucumber peel if not available. It is also one of the key "Botanical" flavourings in Gilpin's Westmorland Extra Dry Gin. Borage leaves have a cucumber like flavor.[5]

In Iran people sometimes put it in their tea.

Medicinal uses


Aragonese cuisine. Borage boiled and sautéed with garlic, served with potatoes.

Naturopathic practitioners use borage for regulation of metabolism and the hormonal system, and consider it to be a good remedy for PMS and menopause symptoms, such as the hot flash. Borage is sometimes indicated to alleviate and heal colds, bronchitis, and respiratory infections, and in general for its anti-inflammatory and balsamic properties. The flowers can be prepared in infusion to take advantage of its medicinal properties. The oleic and palmitic acid of borage may also confer a hypocholesterolemic effect. Traditionallly *Borago officinalis* is used in hyperactive gastrointestinal, respiratory and cardiovascular disorders.[9] A methanol extract has shown in vitro amoebicidal activity against Entamoeba histolytica[10]

Theoreticallly, omega-6 fatty acid γ-linoleic acid (GLA),may lower the epileptic seizure threshold[11], and **one** case of status epilepticus has been reported that was assciated with borage Oil ingestion and high blood GLA levels[12]

Companion plant

Borage is used in companion planting.[13] It is said to protect or nurse legumes, spinach, brassicas, and even strawberries.[14] It is also said to be a good companion plant to tomatoes because it confuses the search image of the mother moths of tomato hornworms or manduca looking for a place to lay their eggs.[15] Claims that it improves tomato growth [16] and makes them taste better [17] remain unsubstantiated.

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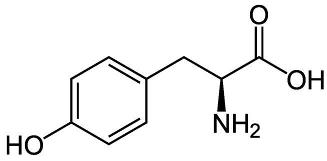
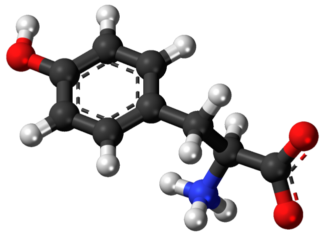
Tyrosine

Tyrosine	
	
	
Identifiers	
CAS number	60-18-4 [1] (L) ✓
PubChem	1153 [2]
ChemSpider	5833 [3] ✓
DrugBank	DB03839 [4]
ChEBI	CHEBI:58315 [5] ✗
ChEMBL	CHEMBL925 [6] ✓
Jmol-3D images	Image 1 [7]
Properties	
Molecular formula	$C_9H_{11}NO_3$
Molar mass	181.19 g mol^{-1}
✗ (verify) [8] (what is: ✓/✗ ?) Except where noted otherwise, data are given for materials in their standard state (at 25 °C, 100 kPa)	
Infobox references	

Tyrosine (abbreviated as **Tyr** or **Y**)[9] or **4-hydroxyphenylalanine**, is one of the 22 amino acids that are used by cells to synthesize proteins. Its codons are UAC and UAU. It is a non-essential amino acid with a polar side group. The word "tyrosine" is from the Greek *tyri*, meaning *cheese*, as it was first discovered in 1846 by German chemist Justus von Liebig in the protein casein from cheese.[10][11] It is called **tyrosyl** when referred to as a functional group or side chain.

Functions

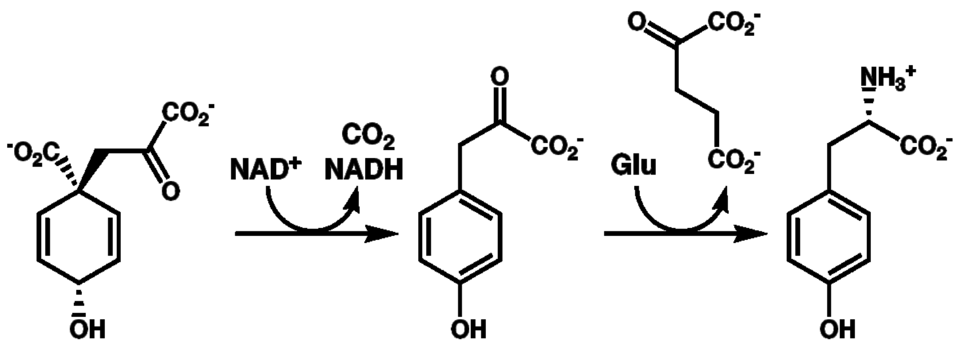
Aside from being a proteinogenic amino acid, tyrosine has a special role by virtue of the phenol functionality. It occurs in proteins that are part of signal transduction processes. It functions as a receiver of phosphate groups that are transferred by way of protein kinases (so-called receptor tyrosine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

Dietary sources

Tyrosine, which can also be synthesized in the body from phenylalanine, is found in many high-protein food products such as chicken, turkey, fish, peanuts, almonds, avocados, milk, cheese, yogurt, cottage cheese, lima beans, pumpkin seeds, sesame seeds, bananas, and soy products.[12] Tyrosine can also be obtained through supplementation.

Biosynthesis

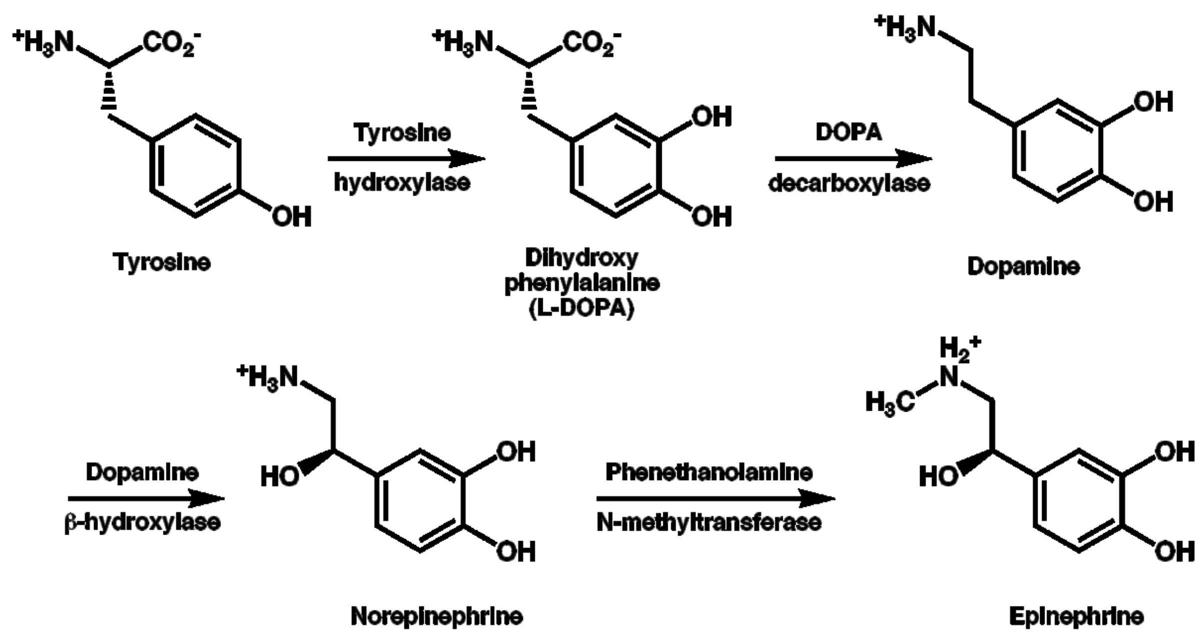


Plant biosynthesis of tyrosine from shikimic acid.

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 a 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.[13] 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 neurotransmitters and hormones

In dopaminergic cells in the brain, tyrosine is converted to levodopa by the enzyme tyrosine hydroxylase (TH). TH is the rate-limiting enzyme involved in the synthesis of the neurotransmitter dopamine. Dopamine can then be converted into the catecholamines norepinephrine (noradrenaline) and epinephrine (adrenaline).

The thyroid hormones triiodothyronine (T_3) and thyroxine (T_4) in the colloid of the thyroid also are derived from tyrosine.

Precursor to alkaloids

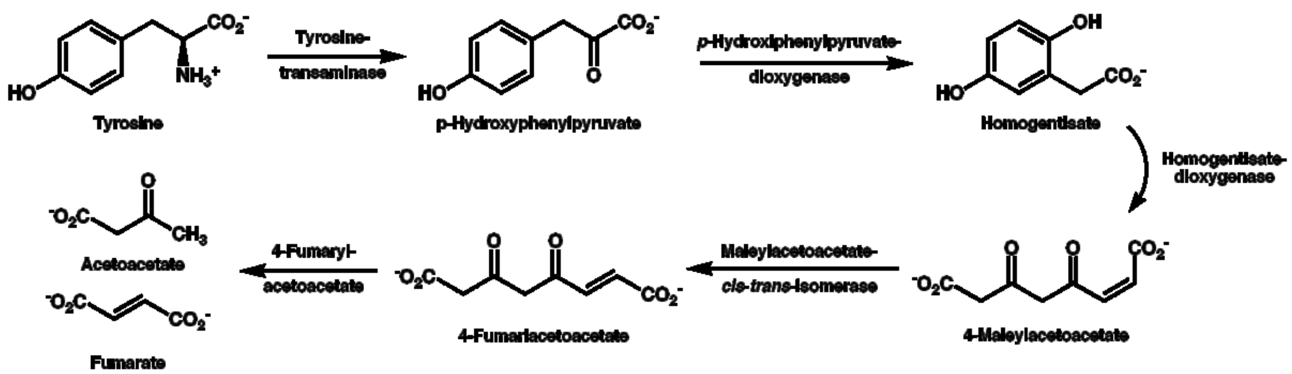
The latex of the *Papaver somniferum*, the opium poppy, has been shown to convert tyrosine into the alkaloid morphine and the bio-synthetic pathway has been established from tyrosine to morphine by using Carbon-14 radio-labelled tyrosine to trace the in-vivo synthetic route .

Also , mescaline producing cactus bio-synthesize tyrosine into mescaline when injected with it .

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.

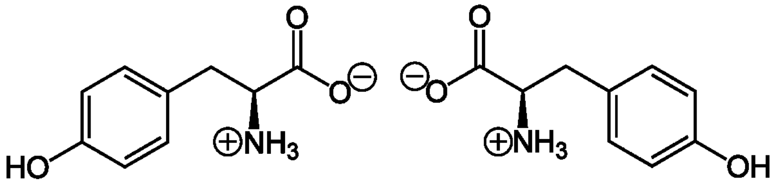
The decomposition of L-tyrosine (syn. *para*-hydroxyphenylalanine) begins with an α-ketoglutarate dependent transamination through the tyrosine transaminase to *para*-hydroxyphenylpyruvate. The positional description *para*, abbreviated *p*, mean that the hydroxyl group and side chain on the phenyl ring are across from each other (see the illustration below).

The next oxidation step catalyzes by *p*-hydroxylphenylpyruvate-dioxygenase and splitting off CO_2 homogentisate (2,5-dihydroxyphenyl-1-acetate). In order to split the aromatic ring of homogentisate, a further dioxygenase, homogentistate-oxygenase is required. Thereby, through the incorporation of a further O_2 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.

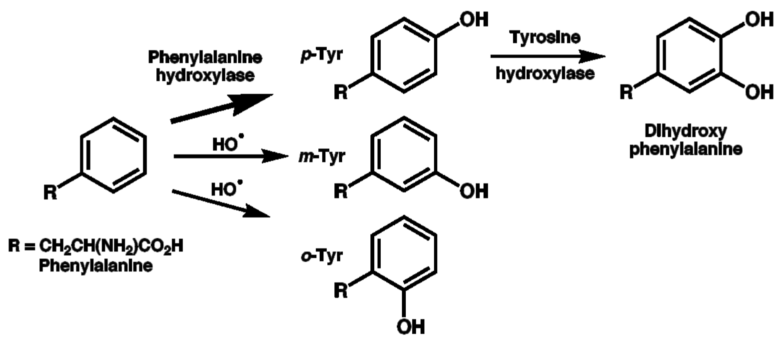
Thereby fumarate (also a metabolite of the citric acid cycle) and acetoacetate (3-ketobutyroate) are liberated. Acetoacetate is a ketone body, which is activated with succinyl-CoA, and thereafter it can be converted into acetyl-CoA, which in turn can be oxidized by the citric acid cycle or be used for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

Betaines



(*S*)-Tyrosine (left) and (*R*)-tyrosine (right) in zwitterionic form at neutral pH

Ortho- and meta-tyrosine



Enzymatic oxidation of tyrosine by phenylalanine hydroxylase (top) and non-enyzmatic 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), that 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.[14][15]

m-Tyrosine and analogues (rare in nature and therefore available synthetically) have shown application in Parkinson's Disease, Alzheimer's disease and arthritis.[16]

Medical use

Tyrosine is a precursor to neurotransmitters and increases plasma neurotransmitter levels (particularly dopamine and norepinephrine)[17] but has little if any effect on mood.[18][19][20] 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,[21] loss of a loved one such as in death or divorce, prolonged work and sleep deprivation,[22][23] with reductions in stress hormone levels,[24] reductions in stress-induced weight loss seen in animal trials,[21] improvements in cognitive and physical performance[19][25][26] seen in human trials; however, because tyrosine hydroxylase is the rate-limiting enzyme, 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.[27][28][29] A daily dosage for a clinical test supported in the literature is about 100 mg/kg for an adult, which amounts to about 6.8 grams at 150 lbs.[30] 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.[27] Tyrosine may decrease the absorption of other amino acids in high or chronic doses. It decreases absorption of l-dopa.

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External links

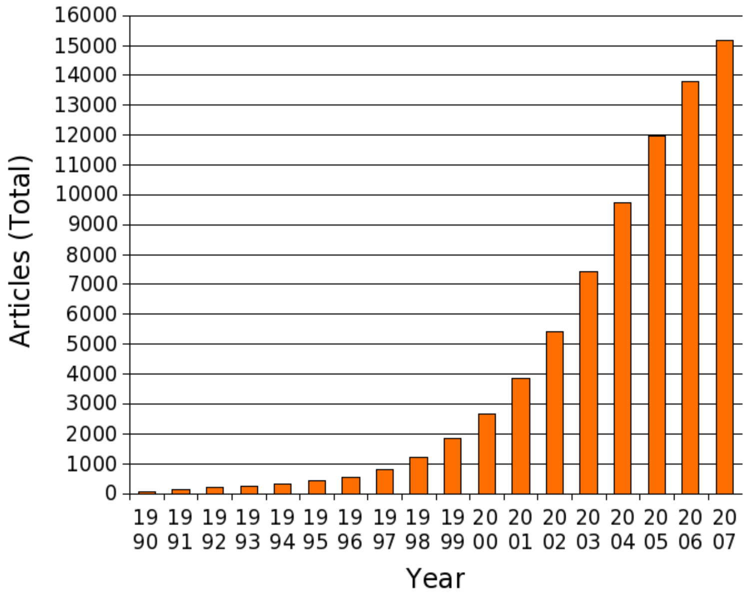
- Tyrosine metabolism (http://www.genome.jp/kegg/pathway/map/map00350.html)
- Phenylalanine and tyrosine biosynthesis (http://www.chem.qmul.ac.uk/iubmb/enzyme/reaction/AminoAcid/PheTyr.html)
- Phenylalanine, Tyrosine, and tryptophan biosynthesis (http://www.genome.jp/kegg/pathway/map/map00400.html)
- *Tyrosine* (http://chem.sis.nlm.nih.gov/chemidplus/direct.jsp?regno=60-18-4) in the ChemIDplus database

Phytotherapy

Phytotherapy is the study of the use of extracts from natural origin as medicines or health-promoting agents.

Traditional phytotherapy is a synonym for herbalism and regarded as alternative medicine by much of Western medicine. Although the medicinal and biological effects of many plant constituents such as alkaloids (morphine, atropine etc.) have been proven through clinical studies there is debate about the efficacy and the place of phytotherapy in medical therapies.

Modern phytotherapy, following the scientific method, can be considered the study on the effects and clinical use of herbal medicines.



Running total of the number of research papers listed on PubMed from 1990-2007 containing the word "phytotherapy."

Points to consider in phytotherapy

Standardization

In herbal medicine, plant material that has been processed in a repeatable operation so that a discrete marker constituent is at a verified concentration is then considered standardized. Active constituent concentrations may be misleading measures of potency if cofactors are not present. A further problem is that the important constituent is often unknown. For instance St John's wort is often standardized to the antiviral constituent hypericin which is now known to be the active ingredient for antidepressant use. Other companies standardize to hyperforin or both, although there may be some 24 known possible constituents. Only a minority of chemicals used as standardization markers are known to be active constituents. Standardization has not been standardized yet: different companies use different markers, or different levels of the same markers, or different methods of testing for marker compounds. Herbalist and manufacturer David Winston points out that whenever different compounds are chosen as 'active ingredients' for different herbs, there is a chance that suppliers will get a substandard batch (low on the chemical markers) and mix it with a batch higher in the desired marker to compensate for the difference.[1]

Quality

The quality of crude drugs or plant medicines depends upon a variety of factors, including the variability in the specie (or species) of plant being used; the plant's growing conditions (i.e. soil, sun, climate); and the timing of harvest, post-harvest processing, and storage conditions. The quality of some plant drugs can judged by Organoleptic factors (i.e. sensory properties such as the taste, color, odor or feel of the drug), or by administering a small dose of the drug and observing the effects.

These conditions have been noted in historical herbals such as Culpepper's Complete Herbal[2] or The Shen Nong or Divine Farmer's Materia Medica.[3] This was standard pharmacognosy curriculum for many years.

Storage after collection is a factor worthy of study; researchers in Nara, Japan have stored samples of ginseng root (Panax ginseng), licorice root (Glycyrrhiza glabra) and rhubarb root (Rheum emodi) that have been shown to retain their active properties for over 1,200 years.[4]

In modern times the foregoing aspects are no less important, but have been neglected with the advent of laboratory testing, although it generally is true that only certain constituents are identified and measured. Processes like HPLC (High performance liquid chromatography), GC (gas chromatography), UV/VIS (Ultraviolet/Visible spectrophotometry) or AA (atomic absorption spectroscopy)are used to identify species, measure bacteriological contamination, assess potency and eventually creating Certificates of Analysis for the material.

Quality should be overseen by either authorities ensuring Good Manufacturing Practices or regulatory agencies by the US FDA. In the United States one frequently sees comments that herbal medicine is unregulated, but this is not correct since the FDA and GMP regulations are in place. In Germany, the Commission E has produced a book of German legal-medical regulations which includes quality standards.[5]

Investigations by the scientific community

Common sense, as advocated above, is essential when working with, and consuming, plant-based medicinal products. Research by the scientific community attempts to explore, validate -- and above all -- understand the physiological aspects of traditional herbal and vegetative treatments.

Safety

A number of herbs are thought to be likely to cause adverse effects.[6] Such herbs, like most herbs for example in Traditional Chinese Medicine, are used in small doses within the herbal formula.

Furthermore, "adulteration, inappropriate formulation, or lack of understanding of plant and drug interactions have led to adverse reactions that are sometimes life threatening or lethal."[7] Proper double-blind clinical trials are needed to determine the safety and efficacy of each plant before they can be recommended for medical use.[8] Although many consumers believe that herbal medicines are safe because they are "natural", herbal medicines may interact with synthetic drugs causing toxicity to the patient, may have contamination that is a safety consideration, and herbal medicines, without proven efficacy, may be used to replace medicines that have a proven efficacy.[9]

The political issues around the safety of crude drugs vary from considering natural remedies "safe" regardless of potential dangers to considering them a dangerous unknown.[10]

Ephedra has been known to have numerous side effects, including severe skin reactions, irritability, nervousness, dizziness, trembling, headache, insomnia, profuse perspiration, dehydration, itchy scalp and skin, vomiting, hyperthermia, irregular heartbeat, seizures, heart attack, stroke, or death.[11] Ephedra has been an object of difficulty;

having legitimate western medicine uses, illegal uses and powerful side effects. Known and used as Mormon Tea or Indian Tea, the plant contains the potent chemical drugs ephedrine and pseudoephedrine. Aside from being chemicals used to create methamphetamine they have direct CNS stimulant effects including high blood pressure and high heart rate. These effects have led to strokes and other CNS or cardiac issues in certain people at certain dosages. In recent years, the safety of ephedra-containing dietary supplements has been questioned by the United States Food and Drug Administration (FDA), the National Center for Complementary and Alternative Medicine, and the medical community as a result of reports of serious side effects and ephedra-related deaths. [12][13][14][15][16] However, when used appropriately by the correct people it is an effective decongestant, a bronchodilator for use in asthma and an adjuvant for the common cold.

There is no evidence to conclude that herbs have more side effects and adverse actions than western (chemically synthesized) medications, which routinely have the same adverse side effects declared on their packages.

Poisonous plants which have limited medicinal effects are often not sold in material doses in the United States or are available only to trained practitioners, these include:

- Aconite
- Arnica
- Belladonna
- Bryonia
- Datura
- Gelsemium
- Henbane
- Male Fern
- Phytolacca
- Podophyllum
- Veratrum

Other plants contain potent alkaloids which may cause physical harm when used incorrectly, but are not treated as possibly dangerous, leaving an uninformed public at risk for side effects or herb to chemical drug interactions. Gingko biloba arguably has positive effects for many people but it is a blood thinner which may increase or cause spontaneous bleeding. White Willow, the source of salicin which through salicylic acid is the base for acetylsalicylic acid or Asprin. Salicylate drugs such as A.S.A. are effective in reducing pain and fever but are also blood thinners. If, for example, one were to take Gingko Biloba and White Willow reduced blood clotting may lead to increased length of wound bleeding or to situations such as hematuria.

Plants such as Comfrey[17][18] and Petasites have specific toxicity due to hepatotoxic pyrrolizidine alkaloid content.[19][20] There are other plant medicines which require caution or can interact with other medications, including St. John's wort and grapefruit.[21]

"Paraherbalism"

Phytochemical researcher Varro Eugene Tyler described paraherbalism as "faulty or inferior herbalism based on pseudoscience", using scientific terminology but lacking scientific evidence for safety and efficacy. Tyler listed ten fallacies that distinguished herbalism from paraherbalism, including claims that there is a conspiracy to suppress safe and effective herbs, herbs can not cause harm, that whole herbs are more effective than molecules isolated from the plants, herbs are superior to drugs, the doctrine of signatures (the belief that the shape of the plant indicates its function) is valid, dilution of substances increases their potency (a doctrine of the pseudoscience of homeopathy), astrological alignments are significant, animal testing is not appropriate to indicate human effects, anecdotal evidence is an effective means of proving a substance works and herbs were created by God to cure disease. None of these beliefs have any basis in fact.[22][23]

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Fucus vesiculosus

Fucus vesiculosus	
	
Scientific classification	
Kingdom:	Chromalveolata
Phylum:	Heterokontophyta
Class:	Phaeophyceae
Order:	Fucales
Family:	Fucaceae
Genus:	*Fucus*
Species:	***F. vesiculosus***
Binomial name	
Fucus vesiculosus L.	

Close-up of bladder wrack's eponymous vesicles

Fucus vesiculosus, known by the common name **bladder wrack** or **bladderwrack**, is a seaweed found on the coasts of the North Sea, the western Baltic Sea, and the Atlantic and Pacific Oceans, also known by the common names **black tang**, **rockweed**, **bladder fucus**, **sea oak**, **black tany**, **cut weed**, **dyers fucus**, **red fucus**, and **rock wrack**. It was the original source of iodine, discovered in 1811, and was used extensively to treat goitre, a swelling of the thyroid gland related to iodine deficiency.

Description

The fronds of *F. vesiculosus* have a prominent midrib and almost spherical air bladders which are usually paired but may be absent in young plants. The margin is smooth and the frond is dichotomously branched. It is sometimes confused with *Fucus spiralis* with which it hybridises.[1]

Distribution

Fucus vesiculosus is one of the most common algae on the shores of the British Isles.[2] It has been recorded from the Atlantic shores of Europe, Northern Russia, the Baltic Sea, Greenland, Azores, Canary Islands, Morocco and Madeira.[3][4] It is also found on the Atlantic coast of North America from Ellesmere Island, Hudson Bay to North Carolina.[5]

Ecology

The species is especially common on sheltered shores from the middle littoral to lower intertidal levels.[5] It is rare on exposed shores where any specimens may be short, stunted and without the air vesicles.[6] *F. vesiculosus* supports few colonial organisms but provides a canopy and shelter for the tube worm *Spirorbis spirorbis*, herbivorous isopods, such as *Idotea* and surface grazing snails such as *Littorina obtusata*.[1] Phlorotannins in *Fucus vesiculosus* act as chemical defences against the marine herbivorous snail *Littorina littorea*.[7]

Biology

Plants of *F. vesiculosus* are dioecious. Gametes are generally released into the seawater under calm conditions and the eggs are fertilised externally to produce a zygote.[1] Eggs are fertilised shortly after being released from the receptacle. A study on the coast of Maine showed that there was 100% fertilisation at both exposed and sheltered sites.[1] Continuously submerged populations in the Baltic Sea are very responsive to turbulent conditions. High fertilisation success is achieved because the gametes are only released when water velocities are low.[8]

Consumption

Primary chemical constituents of this plant include mucilage, algin, mannitol, beta-carotene, zeaxanthin, iodine, bromine, potassium, volatile oils, and many other minerals. The main use of bladder wrack (and other types of seaweed) in herbal medicine is as a source of iodine, an essential nutrient for the thyroid gland. Bladder wrack has been used in the treatment of underactive thyroid glands (hypothyroidism) and goitre.[9]

Bladder wrack has been shown to help women with abnormal menstrual cycling patterns and menstrual-related disease histories.[10] Doses of 700 to 1400 mg/day were found to increase the menstrual cycle lengths, decrease the days of menstruation per cycle, and decrease the serum levels of 17B-estradiol while was later carried out and showed similar effects.[11]

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External links

External identifiers for *Fucus vesiculosus*	
Encyclopedia of Life	893114 (http://www.eol.org/pages/893114)
ITIS	11335 (http://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=11335)
NCBI	49266 (http://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?mode=Info&id=49266)
WoRMS	145548 (http://www.marinespecies.org/aphia.php?p=taxdetails&id=145548)
Also found in: Wikispecies (http://species.wikimedia.org/wiki/Fucus_vesiculosus), MarLIN (http://www.marlin.ac.uk/speciesinformation.php?speciesID=3348), AlgaeBase (http://www.algaebase.org/search/species/detail/?species_id=87)	

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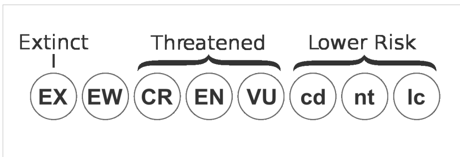
Commiphora wightii

Commiphora wightii	
	
Commiphora wightii resin (guggul)	
Conservation status	
	
Data Deficient (IUCN 2.3)	
Scientific classification	
Kingdom:	Plantae
(unranked):	Angiosperms
(unranked):	Eudicots
(unranked):	Rosids
Order:	Sapindales
Family:	Burseraceae
Genus:	*Commiphora*
Species:	***C. wightii***
Binomial name	
Commiphora wightii (Arn.) Bhandari	
Synonyms	
Commiphora mukul (Stocks) Hook.	

Commiphora wightii (**Guggal**, **Guggul** or **Mukul myrrh tree**) is a flowering plant in the family Burseraceae. The guggul plant may be found from northern Africa to central Asia, but is most common in northern India. It prefers arid and semi-arid climates and is tolerant of poor soil.

It is a shrub or small tree, reaching a maximum height of 4 m, with thin papery bark. The branches are thorny. The leaves are simple or trifoliate, the leaflets ovate, 1–5 cm long, 0.5–2.5 cm broad, irregularly toothed. It is gynodioecious, with some plants bearing bisexual and male flowers, and others with female flowers. The individual flowers are red to pink, with four small petals.

Traditional medicinal use

Guggul has been a key component in ancient Indian Ayurvedic system of medicine. But has become so scarce because of its overuse in its two habitats in India where it is found — Gujarat and Rajasthan that the World Conservation Union (IUCN) has enlisted it in its Red Data List of endangered species.

Guggul produces a resinous sap known as gum guggul. The extract of this gum, called gugulipid, guggulipid or guglipid, has been used in Ayurvedic medicine, a traditional Hindu medicine, for nearly 3,000 years in India.[1] The active ingredient in the extract is the steroid guggulsterone, which acts as an antagonist of the farnesoid X receptor, once believed to result in decreased cholesterol synthesis in the liver. However, several studies have been published that indicate no overall reduction in total cholesterol occurs using various dosages of guggulsterone, and levels of low-density lipoprotein ("bad cholesterol") increased in many people.[2][3]

Cultivation and other uses

Guggul is sought for its gummy resin, which is harvested from the plant's bark through the process of tapping. In India and Pakistan, guggul is cultivated commercially. The resin of the guggul plant, known as *gum guggulu*, has a fragrance similar to that of myrrh and is commonly used in incense and perfumes. It is the same product that was known in Hebrew, ancient Greek and Latin sources as bdellium.

Guggul can be purchased in a loosely packed form called *dhoop*, an incense from India, which is burned over hot coals. This produces a fragrant, dense smoke. The burning coals which let out the smoke are then carried around to different rooms and held in all corners for a few seconds. This is said to drive away evil spirits as well as remove the evil eye from the home and its family members.

Endangerment and rescue

Because of its medicinal properties, guggul has been overharvested in much of its habitat, and has been listed on the IUCN Red List of threatened species.[4] Several efforts are in place to address this situation. India's National Medicinal Plants Board launched a project in Kutch District to cultivate 500 to 800 hectares (**unknown operator: u'strong'** to **unknown operator: u'strong' unknown operator: u'strong'**) of guggal,[5] while a grass-roots conservation movement, led by IUCN associate Vineet Soni, has been started to educate guggal growers and harvesters in safe, sustainable harvesting methods.[6][7]

'Save Guggul Movement' in Rajasthan, India

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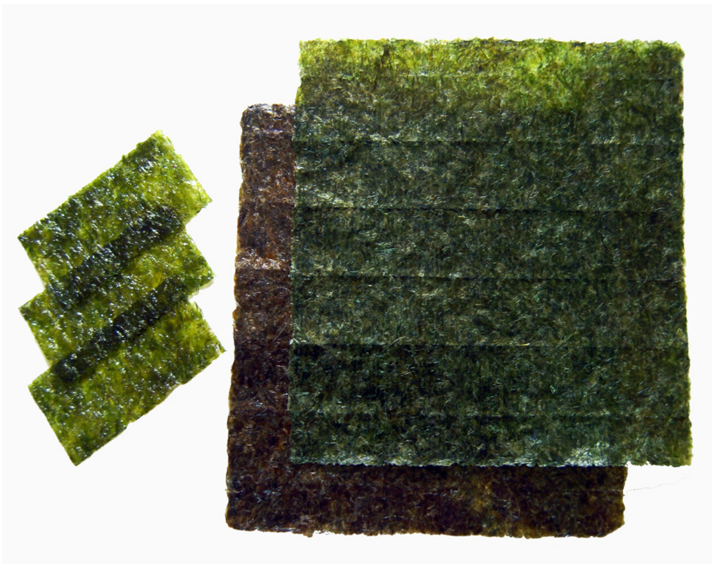
Nori

Nori (海苔) is the Japanese name for edible seaweed species of the red alga genus *Porphyra*, including most notably *P. yezoensis* and *P. tenera*, called **laver** in Wales and other English-speaking countries[1] - though the rampant popularity of sushi in the United States means that the United States is often an exception to this, either referring to the product as "nori" as the Japanese do, or simply "seaweed". Finished products are made by a shredding and rack-drying process that resembles papermaking.



Nori

History

Originally, the term *nori* was generic and referred to seaweeds including *hijiki*.[2] One of the oldest descriptions of nori is dated to around the 8th century. In the Taihō Code enacted in 701, *nori* was already included in the form of taxation.[3][4] There is a description "local peoples was drying nori" in Hitachi Province Fudoki (721–721), and also there is a description "nori was harvested" in Izumo Province Fudoki (713–733). These show nori was used as food from ancient times.[5] In *Utsubo Monogatari*, written around 987, *nori* was recognized as a common food. The original *nori* was formed as a paste, and the sheet form was invented in Asakusa, Edo (contemporary Tokyo), in the Edo period through the method of Japanese paper-making.[6]

In 1867, the word "*nori*" first appeared in an English-language publication — "A Japanese and English Dictionary," by James C. Hepburn.[7]

The word *nori* started to be used widely in the United States, and the product (imported in dry form from Japan) became widely available at natural food stores and Asian-American grocery stores starting in the 1960s, due to the influence of the macrobiotic movement, and in the 1970s with the growing number of sushi bars and Japanese restaurants.

People of Japanese descent have been shown to be able to digest the polysaccharide of the seaweed, after gut microbes developed the enzyme from marine bacteria. Gut microbes from North American subjects lack these enzymes.[8]

Production

Production and processing of *nori* is an advanced form of agriculture. The biology of *Porphyra*, although complicated, is well understood, and this knowledge is used to control the production process. Farming takes place in the sea where the *Porphyra* plants grow attached to nets suspended at the sea surface and where the farmers operate from boats. The plants grow rapidly, requiring about 45 days from "seeding" until the first harvest. Multiple harvests can be taken from a single seeding, typically at about ten-day intervals. Harvesting is accomplished using mechanical harvesters of a variety of configurations. Processing of raw product is mostly accomplished by highly automated machines that accurately duplicate traditional manual processing steps, but with much improved efficiency and consistency. The final product is a paper-thin, black, dried sheet of approximately 18 × 20 cm (**unknown operator: u'strong'** × **unknown operator: u'strong'** in) and 3 grams (**unknown operator: u'strong'** oz) in weight.

Several grades of *nori* are available in the United States. The most common, and least expensive, grades are imported from China, costing about six cents per sheet. At the high end, ranging up to 90 cents per sheet, are "delicate *shin-nori* (*nori* from the first of the year's several harvests) cultivated in Ariake Bay, off the island of Kyushu in Japan".[9]

In Japan, over 600 square kilometres (**unknown operator: u'strong'** sq mi) of Japanese coastal waters are given to producing 350000 tonnes (**unknown operator: u'strong'** long tons) of *nori*, worth over a billion dollars. China produces about a third of this amount.[10]

Use

Nori is commonly used as a wrap for sushi and *onigiri*. It is also a garnish or flavoring in noodle preparations and soups. It is most typically toasted prior to consumption (*yaki-nori* in Japanese). A common secondary product is toasted and flavored *nori* (*ajitsuke-nori* in Japanese), in which a flavoring mixture (variable, but typically soy sauce, spices, and sugar in the Japanese style or sesame oil and salt in the Korean style) is applied in combination with the toasting process. It is also eaten by making it into a soy sauce-flavored paste ,*noritsukudani* (海苔佃煮).

Negitoro gunkanmaki (葱トロ軍艦▯き)

Nori is sometimes used as a form of food decoration.

A related product, prepared from the unrelated green algae *Monostroma* and *Enteromorpha*, is called *aonori* (青海苔 literally blue/green *nori*) and is used like herbs on everyday meals, such as *okonomiyaki* and *yakisoba*.

Since *nori* sheets easily absorb water from the air and degrade, a desiccant is indispensable when storing it.

Nutrition

Nori is about a third protein and a third dietary fiber. It contains high proportions of iodine, carotene, vitamins A, B and C, as well as significant amounts of calcium and iron. While the nutritional value varies, one example of 100 g of dry *yaki-nori* contains:

41.4 g of protein

3.7 g of fat

36.0 g of dietary fiber

280 mg of calcium

300 mg of magnesium

2.4 mg of potassium

6 mg of iodine

3.6 mg of zinc

11.4 mg of iron

That same 100 g of dry *yaki-nori* also contains:

25 mg of vitamin A (β-carotene)

4.6 mg of vitamin E

390 µg of vitamin K

690 µg of vitamin B1

2.33 mg of vitamin B_2

11.7 mg of niacin

590 µg of vitamin B_6

57.6 µg of vitamin B_{12}

1.90 µg of folic acid

1.18 mg of pantothenic acid

210 mg of vitamin C[11]

According to Food Standards Australia New Zealand, one sushi roll contains 92 micrograms of iodine and the recommended daily intake of iodine for adults is 150 micrograms.[12]

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- Suria Link Seaplants Handbook (http://web.archive.org/web/20080616010414/http://www.surialink.com/HANDBOOK/Genera/reds/Porphyra/Porphyra.htm)
- Nori 海苔 :: Sushi Ingredients (http://sushi.pro/ingredients/nori.html)
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- Nori Dishes(w/video) (http://marutokunori.jp/en/nori/)
- About Nori::What's Nori,Nutritional Content,History (http://marutokunori.jp/en/about/)

Desiccated thyroid extract

Desiccated thyroid extract

Combination of	
Levothyroxine	Thyroid hormone
Liothyronine	Thyroid hormone
Clinical data	
Pregnancy cat.	A
Legal status	℞-only (US)
Routes	Oral
Identifiers	
ATC code	H03AA05 [1]
✓ **(what is this?) (verify)** [2]	

Desiccated thyroid or **thyroid extract**, refers to porcine (or mixed beef and pork) thyroid glands, dried and powdered for therapeutic use. Pork (or mixed beef and pork) thyroid preparations were developed in the late 19th century, and are still used today to treat hypothyroidism, the condition of having an underactive thyroid gland. This product is sometimes referred to as "natural thyroid", "natural thyroid hormones", "pork thyroid", thyroid USP, thyroid BP, or by the name of a commercial brand, such as "Armour Thyroid" or "Nature-Throid" & "Westhroid".

Desiccated thyroid has been described in the United States Pharmacopoeia for nearly a century as *the cleaned, dried, and powdered thyroid gland previously deprived of connective tissue and fat... obtained from domesticated animals that are used for food by man* (USP XVI). In the last few decades, pork alone is the usual source. Historically, before modern assays, the potency was specified only by iodine content ("not less than 0.17% and not more than 0.23%"), rather than hormonal content or activity.

Brands include Forest Lab's **Armour**, and **Naturethroid** & **Westhroid** by RLC Labs. Also available is a new generic NP thyroid by Acella Pharmaceuticals. Canada's desiccated thyroid is made by Erfa and is called **Thyroid**. All consist of desiccated porcine thyroid powder, differing only in the binders and fillers.

Nature-Throid and Westhroid are available in the following strengths: 1/4(16.25 mg), 1/2(32.5 mg), 3/4(48.75 mg), 1(65 mg), 1.25(81.25 mg), 1.5(97.5 mg), 1.75(113.75), 2(130 mg), 2.25(146.25 mg), 2.5(162.5 mg), 3(195 mg), 4(260 mg), & 5(325 mg) grain. Each one grain (65 mg) contains 9 mcg of T3, and 38 mcg of T4. www.nature-throid.com, www.westhroid.com.

All brands contain a mixture of thyroid hormones: T4 (thyroxine), T3 (triiodothyronine) in the proportions usually present in pig thyroids (approximately 80% T4 and 20% T3). Armour is made in the following strengths: 1/4, 1/2, 1, 2, and 3 grain as well as 4 and 5 grain tablets. One grain (about 60 mg) of desiccated thyroid contains about 38 mcg of T4 and 9 mcg of T3.[3] Because the preparation is whole thyroid gland, each 60 mg tablet also contains over 59 mg of all of the other constituents of pork thyroid glands.

History

The earliest oral treatment for hypothyroidism consisted of thyroid extract. George Redmayne Murray of the United Kingdom first described treatment of myxedema with thyroid extract in 1891, and published a description of long-term successful treatment (28 years) of a patient with myxedema (severe hypothyroidism) in 1920[4] His treatment was quickly adopted in North America and Europe. The first recorded American use dates to 1891 by a woman who was still taking it 52 years later at 84 years of age [5]

Desiccated thyroid extract is prepared from pig and cow thyroid glands. The glands are dried (desiccated), ground to powder, combined with binder chemicals, and pressed into pills. This was a new use for parts that were previously unwanted slaughterhouse offal, and Armour and Company, the dominant American meatpacker in the 20th century, supplied the best-known brand of thyroid extract.

Replacement by thyroid extract in hypothyroidism was one of the most effective treatments of any disease available to physicians before the middle of the 20th century, and in severe cases afforded dramatic relief of the myriad symptoms. The decision to treat was usually based on the presence of signs and symptoms of hypothyroidism because there were no accurate, readily available laboratory tests of thyroid function. Many less severe cases of hypothyroidism went untreated. Dosage was regulated by improvement of symptoms.

Desiccated Thyroid became a commercial treatment option in 1934 with Westhroid, and has to this day, never been recalled for instability. In the early 1960s, desiccated thyroid hormones (thyroid extract) began to be replaced by levothyroxine (T4), or by combinations of T4 and T3. Replacement occurred faster in the United Kingdom than in North America, but by the 1980s more patients were being prescribed levothyroxine or T4/T3 combinations than desiccated thyroid extract.

Several reasons have been identified as to why prescriptions changed from the previously-effective desiccated thyroid treatment. These factors included a desire for improved effectiveness, medical evidence, scientific theory, cultural fashion, and effective marketing.

- Although thyroid extract was useful and usually effective, some patients continued to complain of fatigue, weight gain, or other symptoms. Dosing until the 1960s was often a matter of prolonged adjustment trials.[6]
- It was known that not all of the iodine content of thyroid extract was in the form of effective T4 and T3 and that actual content of available preparations varied more than the permitted 15%.[7][8][9][10] It was hoped that better dosing precision with levothyroxine alone would increase the proportion of patients effectively treated. In 1980, a widely publicized investigation published in JAMA revealed continued large ranges of hormone content and potency in all of the available thyroid extracts on the American market.[11]
- By the 1960s, it was known that thyroxine was the essential hormone produced by the thyroid gland, and that most T3 was manufactured in other parts of the body by deiodination of thyroxine. It was demonstrated in hypothyroid animals and people that replacement of thyroxine alone corrected the measurable manifestations (laboratory test results) of hypothyroidism.[12] By the 1970s doctors could measure T4, T3, and TSH in human blood with approximate accuracy and confirmed that treatment with thyroxine alone could produce normal blood levels of both T4 and T3,[13] but desiccated thyroid caused supraphysiologic levels of T3.[14] In the majority of patients normalization of these levels eliminated all signs and symptoms of hypothyroidism.[15]
- It was discovered that a healthy person varied the amount of T3 produced from T4 in response to changing needs and conditions and it seemed wiser not to bypass this control system by providing larger amounts of T3 than were naturally produced each day.
- Furthermore, when T3 could be measured, it was discovered that thyroid extract and synthetic combinations of T4 and T3 produced significantly greater fluctuations of T3 throughout the day than occurred in healthy people or hypothyroid people treated with thyroxine alone.[16]
- Endocrinologists found that treatment with thyroxine alone worked as well or better than thyroid extract for the majority of patients, although even thyroxine did not reverse all the symptoms of a minority.[15]

- Cultural fashion and marketing played a role. In the middle of the 20th century, pharmaceutical chemists had been discovering the active molecules in a variety of plant and animal remedies, from aspirin and digitoxin to vitamins, and producing them synthetically with improvements in purity and dosage control. In that cultural context, it was easy to market pure levothyroxine as superior to dried animal glands.
- Synthroid, one of the most successful brand names in pharmaceutical marketing history, became as synonymous with thyroid replacement to generations of American primary care doctors as Kleenex or Xerox became with their respective products.[17]

Thyroid care changed in other ways as well. Accurate T4 and T3 measurements became widely used in the 1970s, and by the late 1980s, TSH measurement had become sensitive enough to detect mild degrees of hyperthyroidism and overtreatment. To no one's surprise, blood levels of thyroid hormones and TSH were found to be the best predictors of objective benefits from thyroid replacement: those with the most severe measurable deficiency enjoyed the most dramatic and sustained benefits. It was also discovered that even mild hyperthyroidism as defined by a suppressed TSH level, whether due to disease or overtreatment, was associated with poorer bone density in women, and with higher rates of atrial fibrillation in elderly patients. Doctors began to trust the TSH measurement more and more as the index of optimal replacement dose.

As more doctors prescribed thyroxine instead of thyroid extract, the use of thyroid extract became associated with those whose medical practices deviated in many ways from standard care. (See complementary and alternative medicine.) This association became a disincentive for using thyroid extract, and those prescribing it were considered to be unscientific and irrational practitioners.

Thyroid extract proponents

Desiccated thyroid is preferred by a growing body of patients and doctors who claim better relief of symptoms such as fatigue and depressed mood. Many proponents of desiccated thyroid feel passionately about the issue. .

A number of specific claims are commonly made about thyroid extract:

- Thyroid extract is better than thyroxine because it contains both T4 and T3, and both are made by a healthy thyroid gland.
- Doses should be increased until symptoms are relieved regardless of laboratory tests.
- Other constituents of the dried thyroid glands besides the T4 and T3 (e.g., unmeasured amounts of diiodothyronine (T2), monoiodothyronine (T1), calcitonin, other protein-bound iodine) may contribute to a perceived greater effectiveness or confer additional benefits.
- A product produced by farm, slaughterhouse, and factory is "natural", and therefore preferable to thyroxine molecules synthesized in a factory alone.

To endocrinologists the preference of some hypothyroid people for thyroid extract raises some important questions which current evidence cannot answer with certainty:

1. Is the reason some people fail to have complete relief of symptoms when tests show normal levels simply because there are other causes of fatigue, depression, and weight gain and these people are mistakenly attributing the problems to the thyroid and simply enjoying a placebo effect if they claim better relief from thyroid extract?
2. Does a combination of T4 and T3 provide more effective symptom relief for some people than T4 alone? Multiple controlled trials have shown inconsistent benefits of various ratios of T4 and T3.[18][19][20] Even if most people with hypothyroidism enjoy complete relief of symptoms with thyroxine alone, are there people who need T3 as well because they cannot generate normal amounts from T4 as most people do?
3. Is the perceived benefit simply a result of overtreatment, such that the same relief could be achieved by pushing a thyroxine dose to higher levels?
4. Is the TSH measurement, and its associated 'normal' range, the best indicator of optimal replacement dose? Most research evidence suggests it is, but some patients feel better at doses which produce abnormally high blood levels of T4 and T3 and suppressed TSH. Is this simply a stimulant effect of high doses, similar to caffeine or

amphetamine? How high is the risk of prolonged overtreatment to the bones, heart, and other parts of the body, and is it worth an improvement in subjective well-being?

Despite claims of proponents that desiccated thyroid pills are superior to thyroxine or combinations of T4 and T3 for most people with hypothyroidism, no controlled clinical trials have been published, and many physicians remain unconvinced that the superiority is anything other than a placebo effect or an overtreatment effect.

Current status of thyroid extract use

At present, a large majority of people (at least in the English-speaking world) of all ages with hypothyroidism are being treated with levothyroxine. When their blood levels of thyroid hormones and TSH are most normal, the majority have no more signs or symptoms of hypothyroidism than similar members of the population. The Royal College of Physicians has recommended the exclusive use of synthetic levothyroxine for the treatment of hypothyroidism.[21]

Books

There are several books promoting thyroid hormone replacement with desiccated thyroid:

- Janie A. Bowthorpe. "Stop the Thyroid Madness: a Patient Revolution Against Decades of Inferior Treatment". Laughing Grape Publishing, 2008. ISBN 978-0-615-14431-3 Revised Edition: 2011. ISBN 978-0-615-47712-1
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- Barry Durrant-Peatfield. *The Great Thyroid Scandal and How To Survive It*. Barons Down Publishing, 2002. ISBN 0-9544203-0-6.
- Steven F. Hotze. *Hormones, Health, and Happiness*. Forrest Publishing, 2005. ISBN 0-9765751-0-8.
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External links

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