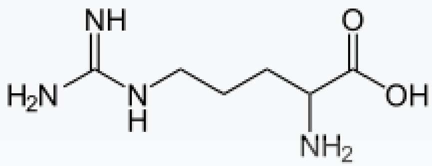
Arginine

Arginine	
	
	
Names	
Other names 2-Amino-5-guanidinopentanoic acid	
Identifiers	
CAS Number	7200-25-1 ✗ 157-06-2 *R* ✗ 74-79-3 *S* ✗
3D model (JSmol)	Interactive image Interactive image
3DMet	B01331
Beilstein Reference	1725411, 1725412 *R*, 1725413 *S*
ChEBI	CHEBI:29016 ✓
ChEMBL	ChEMBL212301 ✗ ChEMBL1485 ✗
ChemSpider	227 ✓

	64224 *R* ✗ 6082 *S* ✗
DrugBank	DB00125 ✗
ECHA InfoCard	100.000.738
EC Number	230-571-3
Gmelin Reference	364938 *R*
IUPHAR/BPS	721
KEGG	C02385 ✗
MeSH	Arginine
PubChem CID	232 71070 *R* 6322 *S*
RTECS number	CF1934200 *S*
UNII	94ZLA3W45F ✓
InChI[show]	
SMILES[show]	
Properties	
Chemical formula	$C_6H_{14}N_4O_2$
Molar mass	174.20 $g{\cdot}mol^{-1}$
Appearance	White crystals
Odor	Odourless
Melting point	260 °C; 500 °F; 533 K
Boiling point	368 °C (694 °F; 641 K)
Solubility in water	14.87 g/100 mL (20 °C)
Solubility	slightly soluble in ethanol insoluble in ethyl ether
log *P*	−1.652
Acidity (pK_a)	12.488

Basicity (pK_b)	1.509
Thermochemistry	
Specific heat capacity (C)	232.8 J K^{-1} mol^{-1} (at 23.7 °C)
Std molar entropy (S°_{298})	250.6 J K^{-1} mol^{-1}
Std enthalpy of formation ($\Delta_f H^{\circ}_{298}$)	−624.9–−622.3 kJ mol^{-1}
Std enthalpy of combustion($\Delta_c H^{\circ}_{298}$)	−3.7396–−3.7370 MJ mol^{-1}
Pharmacology	
ATC code	B05XB01 (WHO) *S*
Hazards	
Safety data sheet	*See: data page* sigma-aldrich
GHS pictograms	
GHS signal word	**WARNING**
GHS hazard statements	H319
GHS precautionary statements	P305+351+338
Lethal dose or concentration (*LD*, *LC*):	
LD$_{50}$ (median dose)	5110 mg/kg (rat, oral)
Related compounds	
Related alkanoic acids	*N*-Methyl-D-aspartic acid *beta*-Methylamino-L-alanine Guanidinopropionic acid Theanine Pantothenic acid
Related compounds	Panthenol
Supplementary data page	
Structure and	Refractive index (n),

properties	Dielectric constant (ε_r), etc.
Thermodynamic data	Phase behaviour solid–liquid–gas
Spectral data	UV, IR, NMR, MS
Except where otherwise noted, data are given for materials in their standard state (at 25 °C [77 °F], 100 kPa).	
✗ verify (what is ✓✗ ?)	
Infobox references	

Arginine (symbol **Arg** or **R**[1]) is an α-amino acid that is used in the biosynthesis of proteins. It is encoded by the codons **CGU**, **CGC**, **CGA**, **CGG**, **AGA**, and **AGG**.[2] It contains an α-amino group, an α-carboxylic acid group, and a side chain consisting of a 3-carbon aliphatic straight chain ending in a guanidino group. At physiological pH, the carboxylic acid is deprotonated ($-COO^-$), the amino group is protonated ($-NH_3^+$), and the guanidino group is also protonated to give the guanidinium form ($-C-(NH_2)_2^+$), making arginine a charged, aliphatic amino acid.[3] It is the precursor for the biosynthesis of nitric oxide.

In humans, arginine is classified as a semiessential or conditionally essential amino acid, depending on the developmental stage and health status of the individual.[4] Preterm infants are unable to synthesize or create arginine internally, making the amino acid nutritionally essential for them.[5] Most healthy people do not need to supplement with arginine because it is a component of all protein-containing foods[6] and can be synthesized in the body from glutamine via citrulline.[7]

History

Arginine was first isolated from lupin and pumpkin seedlings by the German chemist Ernst Schulze and his assistant[8] Ernst Steiger. They confirmed and published the structure in 1886.[9]

Sources

Dietary sources

Arginine is a conditionally essential amino acid in humans and rodents,[10] as it may be required depending on the health status or lifecycle of the individual. For example, while healthy adults can supply their own requirement for arginine, immature and rapidly growing individuals require arginine in their diet,[11] and it is also essential under physiological stress, for example during recovery from burns, injury, and sepsis,[11] or when the small intestine and kidneys, which are the major sites of arginine biosynthesis, have been damaged.[10] It is, however, an essential amino acid for birds, as they do not have a urea cycle.[12] For some carnivores, for example cats, dogs[13] and ferrets, arginine is essential,[10] because after a meal, their highly efficient protein catabolism produces large quantities of ammonia which need to be processed through the urea cycle, and if not enough arginine is present, the resulting ammonia toxicity can be lethal.[14] This is not a problem in practice, because meat contains sufficient arginine to avoid this situation.[14]

Animal sources of arginine include meat, dairy products, and eggs,[15][16] and plant sources include seeds of all types, for example grains, beans, and nuts.[16]

Biosynthesis

Arginine is synthesized from citrulline in arginine and proline metabolism by the sequential action of the cytosolic enzymes argininosuccinate synthetase and argininosuccinate lyase. This is an energetically costly process, because for each molecule of argininosuccinate that is synthesized, one molecule of adenosine triphosphate (ATP) is hydrolyzed to adenosine monophosphate (AMP), consuming two ATP equivalents.

Citrulline can be derived from multiple sources:

- from arginine itself via nitric oxide synthase, as a byproduct of the production of nitric oxide for signaling purposes
- from ornithine through the breakdown of proline or glutamine/glutamate
- from asymmetric dimethylarginine via DDAH

The pathways linking arginine, glutamine, and proline are bidirectional. Thus, the net use or production of these amino acids is highly dependent on cell type and developmental stage.

On a whole-body basis, synthesis of arginine occurs principally via the intestinal–renal axis: the epithelial cells of the small intestine produce citrulline, primarily from glutamine and glutamate, which is carried in the bloodstream to the proximal tubule cells of the kidney, which extract citrulline from the circulation and convert it to arginine, which is returned to the circulation. This means that impaired small bowel or renal function can reduce arginine synthesis, increasing the dietary requirement.

Synthesis of arginine from citrulline also occurs at a low level in many other cells, and cellular capacity for arginine synthesis can be markedly increased under circumstances that increase the production of inducible NOS. This allows citrulline, a byproduct of the NOS-catalyzed production of nitric oxide, to be recycled to arginine in a pathway known as the citrulline-NO or arginine-citrulline pathway. This is demonstrated by the fact that, in many cell types, NO synthesis can be supported to some extent by citrulline, and not just by arginine. This recycling is not quantitative, however, because citrulline accumulates in NO-producing cells along with nitrate and nitrite, the stable end-products of NO breakdown.[17]

Function

Arginine plays an important role in cell division, wound healing, removing ammonia from the body, immune function,[18] and the release of hormones.[4][19][20] It is a precursor for the synthesis of nitric oxide (NO),[21] making it important in the regulation of blood pressure.[22][23][24]

Proteins

Arginine's side chain is amphipathic, because at physiological pH it contains a positively charged guanidinium group, which is highly polar, at the end of a hydrophobic aliphatic hydrocarbon chain. Because globular proteins have hydrophobic interiors and hydrophilic surfaces,[25] arginine is typically found on the outside of the protein, where the hydrophilic head group can interact with the polar environment, for example taking part in hydrogen bonding and salt bridges.[26] For this reason, it is frequently found at the interface between two proteins.[27] The aliphatic part of the side chain sometimes remains below the surface of the protein.[26]

Arginine residues in proteins can be deiminated by PAD enzymes to form citrulline, in a post-translational modification process called citrullination.This is important in fetal development, is part of the normal immune process, as well as the control of gene expression, but is also significant in autoimmune diseases.[28]:275 Another post-translational modification of arginine involves methylation by protein methyltransferases.[28]:176

Precursor

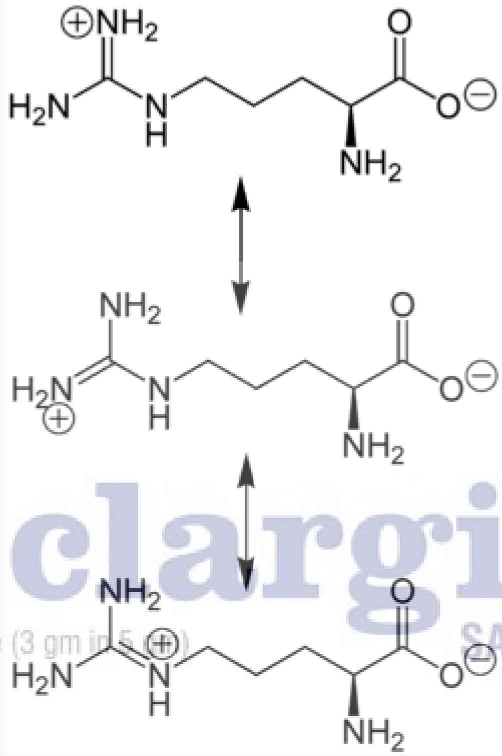
Arginine is the immediate precursor of NO, an important signaling molecule which can act as a second messenger, as well as an intercellular messenger which regulates vasodilation, and also has functions in the immune system's reaction to infection.

Arginine is also a precursor for urea, ornithine, and agmatine; is necessary for the synthesis of creatine; and can also be used for the synthesis of polyamines (mainly through ornithine and to a lesser degree through agmatine, citrulline, and glutamate. The presence of asymmetric dimethylarginine (ADMA), a close relative, inhibits the nitric oxide reaction; therefore, ADMA is considered a marker for vascular disease, just as L-arginine is considered a sign of a healthy endothelium.

Safety

L-arginine is generally recognized as safe (GRAS-status) at intakes of up to 20 grams per day.[29]

Structure



Delocalization of charge in guanidinium group of L-Arginine

The amino acid side-chain of arginine consists of a 3-carbon aliphatic straight chain, the distal end of which is capped by a guanidinium group, which has a pK_a of 12.48, and is therefore always protonated and positively charged at physiological pH. Because of the conjugation between the double bond and the nitrogen lone pairs, the positive charge is delocalized, enabling the formation of multiple hydrogen bonds.

Research

Growth hormone

Intravenously-administered arginine is used in growth hormone stimulation tests[30] because it stimulates the secretion of growth hormone.[31] A review of clinical trials concluded that oral arginine increases growth hormone.[32] However, a more recent trial reported that although oral arginine increased plasma levels of L-arginine it did not cause an increase in growth hormone.[33]

High blood pressure

A meta-analysis showed that L-arginine reduces blood pressure with pooled estimates of 5.4 mmHg for systolic blood pressure and 2.7 mmHg for diastolic blood pressure.[24]

Supplementation with L-arginine reduces diastolic blood pressure and lengthens pregnancy for women with gestational hypertension, including women with high blood pressure as part of pre-eclampsia. It did not lower systolic blood pressure or improve weight at birth.[34]