LICENCIATURA EM BIOLOGIA

DISCIPLINA

BIOQUÍMICA

Ano Letivo de 2013/2014

Aula nº 5

26 FEV **Ricardo Boavida Ferreira** **Sala 40**

Aminoácidos, péptidos e proteínas

Aminoácidos proteicos, aminoácidos raros das proteínas e aminoácidos não-proteicos; importância biológica. Aminoácidos proteicos: classificação, características estruturais e propriedades. Breve referência às aminas biogénicas.

Ligação peptídica: ligação eupeptídica e ligação isopeptídica. Oligopéptidos e polipéptidos. Péptidos de importância biológica.

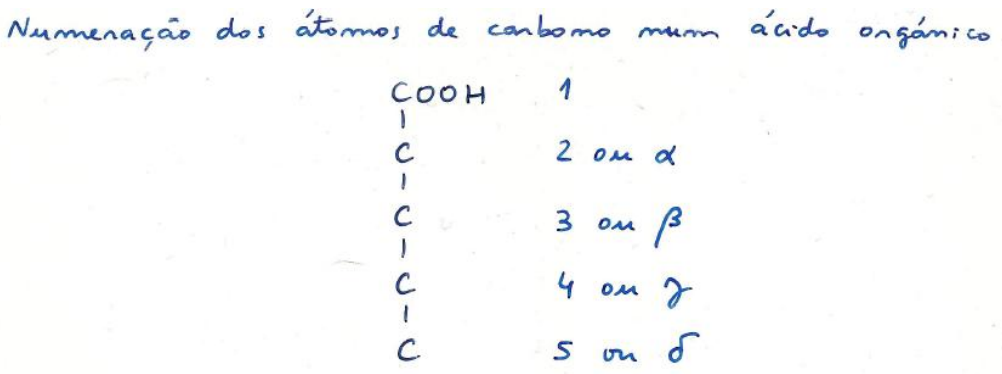
Material de estudo: diapositivos das aulas, bibliografia recomendada e textos de apoio.

AMINOÁCIDOS

Definição

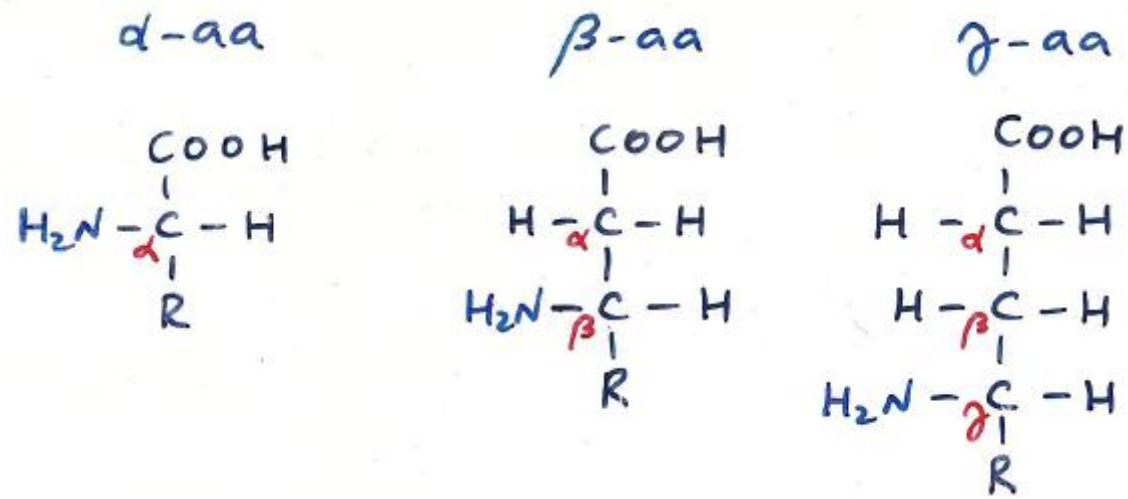
É um composto orgânico contendo na sua molécula, pelo menos, um grupo carboxilo e um grupo amina.

Dois sistemas de nomenclatura dos átomos de carbono num ácido orgânco



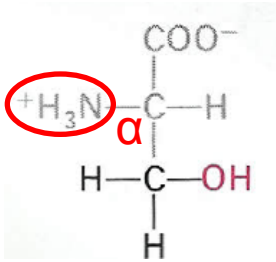
Fórmula geral dos aminoácidos

Dependendo do átomo de carbono de menor nível a que está ligado o grupo amina, assim os aminoácidos são agrupados em **α-aminoácidos**, **β-aminoácidos**, **γ-aminoácidos**, etc.

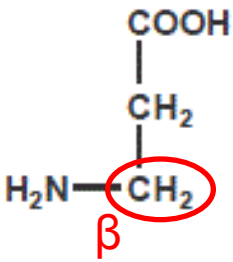


Exemplos:

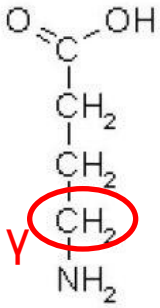
L-α-Serina



β-Alanina



Ácido γ–aminobutírico (GABA)

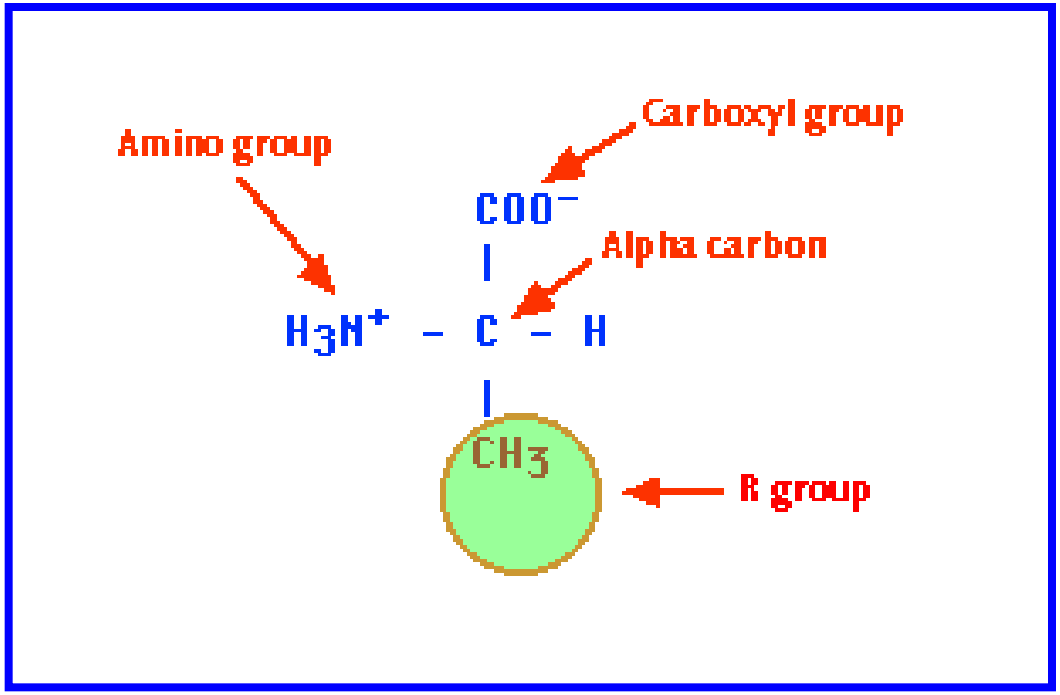


Todos os aminoácidos que participam na constituição das proteínas são L- α-aminoácidos

α-Amino acids

α-Amino acids are the building blocks (monomers) of proteins. Twenty two different amino acids are used to synthesize proteins.

The shape and other properties of each protein is dictated by the precise sequence of amino acids in it.



Each α-amino acid consists of an alpha carbon atom to which is attached

- a hydrogen atom;

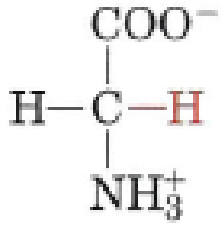
- an amino group (hence "amino" acid);

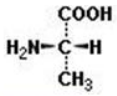
- a carboxyl group (-COOH). This gives up a proton and is thus an acid (hence amino "acid");

- one of 22 different "R" groups. It is the structure of the R group that determines which of the 22 it is and its special properties. The amino acid shown here is **L**-alanine.

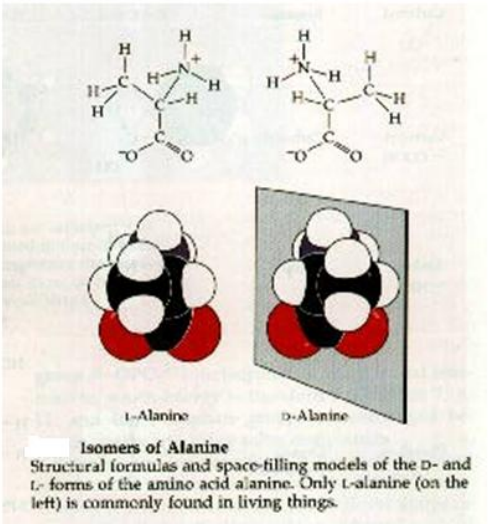
Configuração dos aminoácidos

Glycine
Gly
G

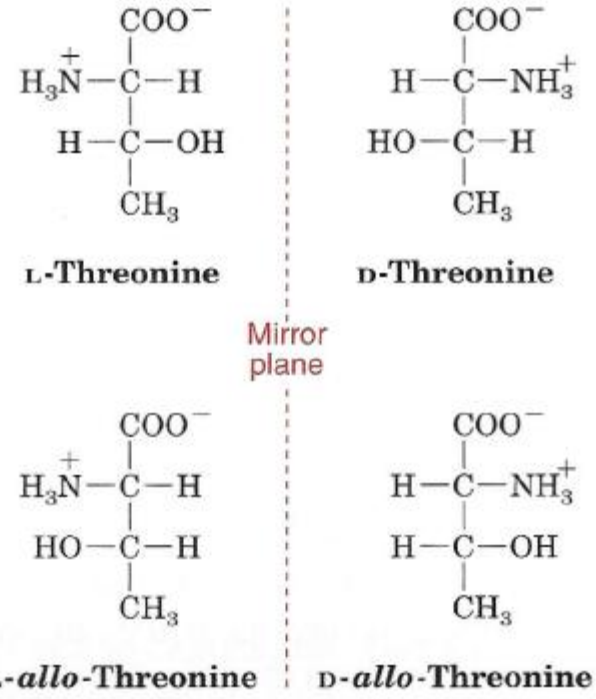




L-Alanina



Isomers of Alanine
Structural formulas and space-filling models of the D- and L- forms of the amino acid alanine. Only L-alanine (on the left) is commonly found in living things.



Fischer projections of threonine's four stereoisomers. The D and L forms are mirror images as are the D-*allo* and L-*allo* forms. D- and L-threonine are each diastereomers of both D-*allo*- and L-*allo*-threonine.

TONY HALLAS/SCIENCE FACTION/CORBIS

Soggy space rocks and left-handed life

WET rocks hurtling around the solar system may have given life on Earth its addiction to left-handed building blocks.

Almost all life on Earth uses left-handed amino acid molecules instead of their right-handed counterparts. In the 1990s, scientists found that meteorites contain up to 15 per cent more of the left-handed versions too. So space rocks bombarding the early Earth may have biased the planet's chemistry. A linked theory has it that polarised starlight can preferentially destroy right-handed amino acids on asteroids, though this alone cannot explain the strength of the bias on meteorites.

Now Daniel Glavin and Jason Dworkin of NASA's Goddard Space Flight Center in Greenbelt, Maryland, have shown that water amplifies the bias. They studied an amino acid called isovaline in six meteorites that showed ancient evidence of 1000 to 10,000 years' exposure to liquid water. The longer water persisted in the rock, the stronger its left-handed isovaline bias, the pair found (*Proceedings of the National Academy of Sciences*, DOI: 10.1073/pnas.0811618106).

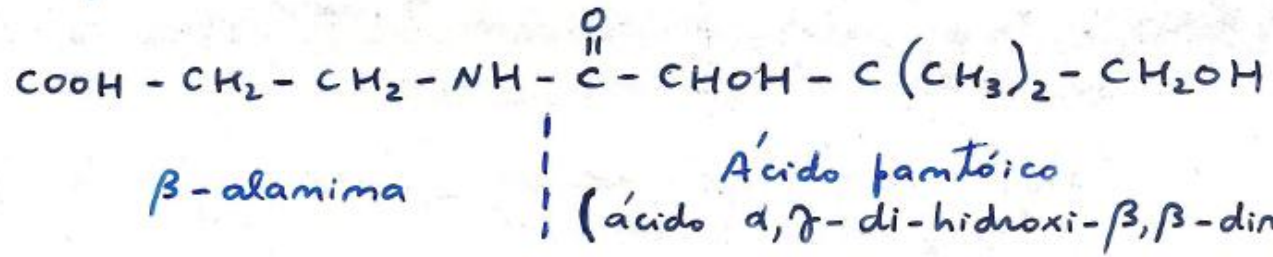
NASA scientists have discovered glycine, a fundamental building block of life, in samples of comet Wild 2 returned by NASA's Stardust spacecraft. "Glycine is an amino acid used by living organisms to make proteins, and this is the first time an amino acid has been found in a comet, (...). A glycine molecule from space will tend to have more of the heavier carbon 13 atoms in it than glycine that's from Earth. That is what the team found. "We discovered that the Stardust-returned glycine has an extraterrestrial carbon isotope signature, indicating that it originated on the comet."

β-aminoácidos, γ-aminoácidos e D-aminoácidos de ocorrência natural

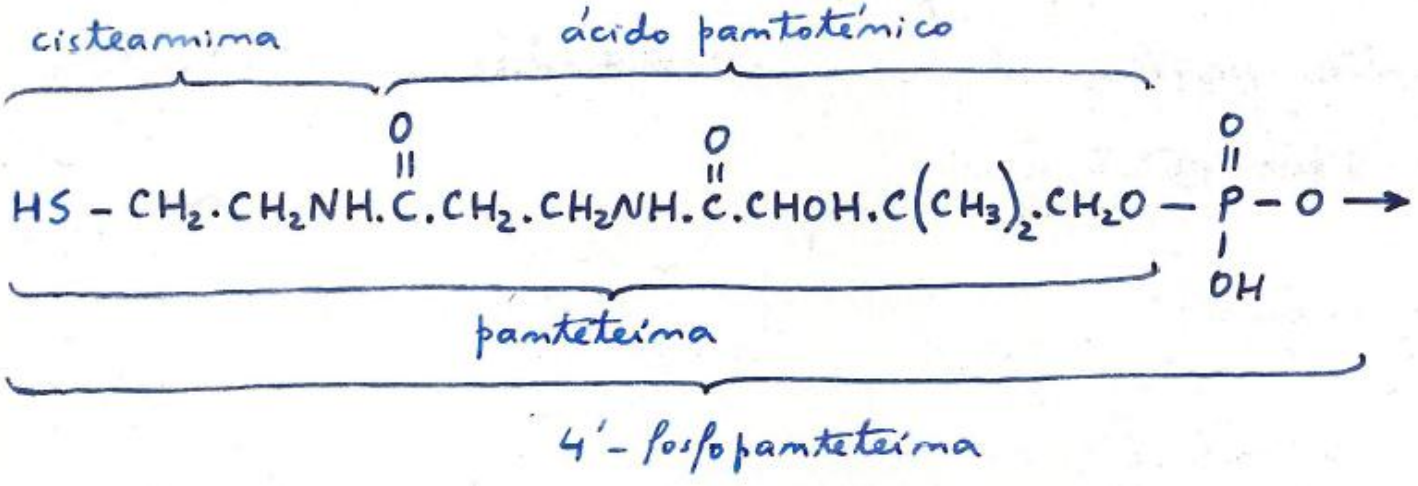
β-Alanina

Vitamina B5

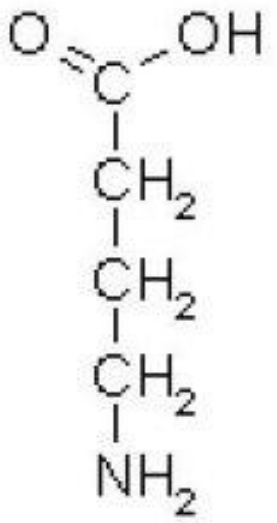
Ácido pantoténico



Coenzima A (CoA)

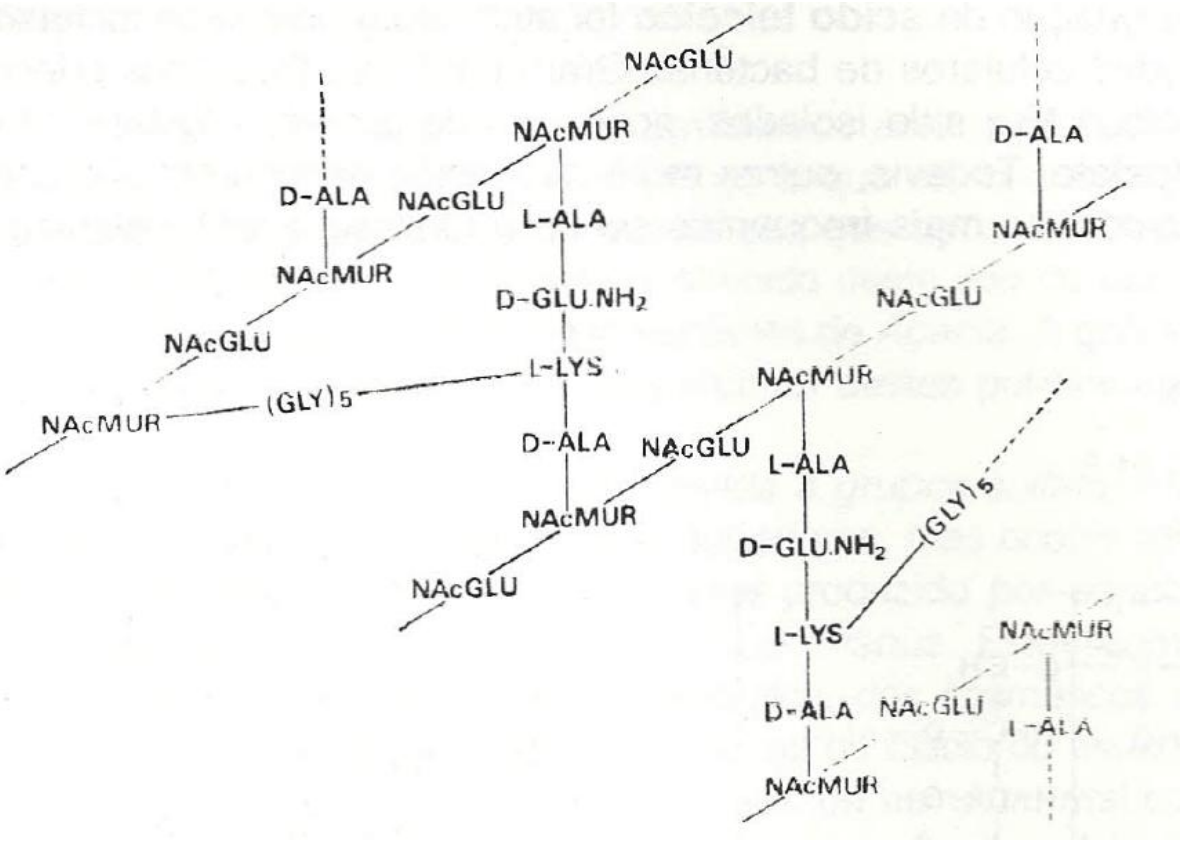


Ácido γ-aminobutírico (GABA)



GABA $C_4H_9NO_2$

D-Alanina e ácido D-glutâmico, componentes das peptidoglicanas ou mureínas das paredes celulares das bactérias



Questão:
Porque é que as bactérias têm aminoácidos da série D na constituição das suas paredes celulares?

Classificação dos aminoácidos

Os aminoácidos de ocorrência natural podem dividir-se em três categorias:

1 – Aminoácidos proteicos, standard, primários ou normais;

2 – Aminoácidos raros das proteínas;

3 – Aminoácidos não-proteicos.

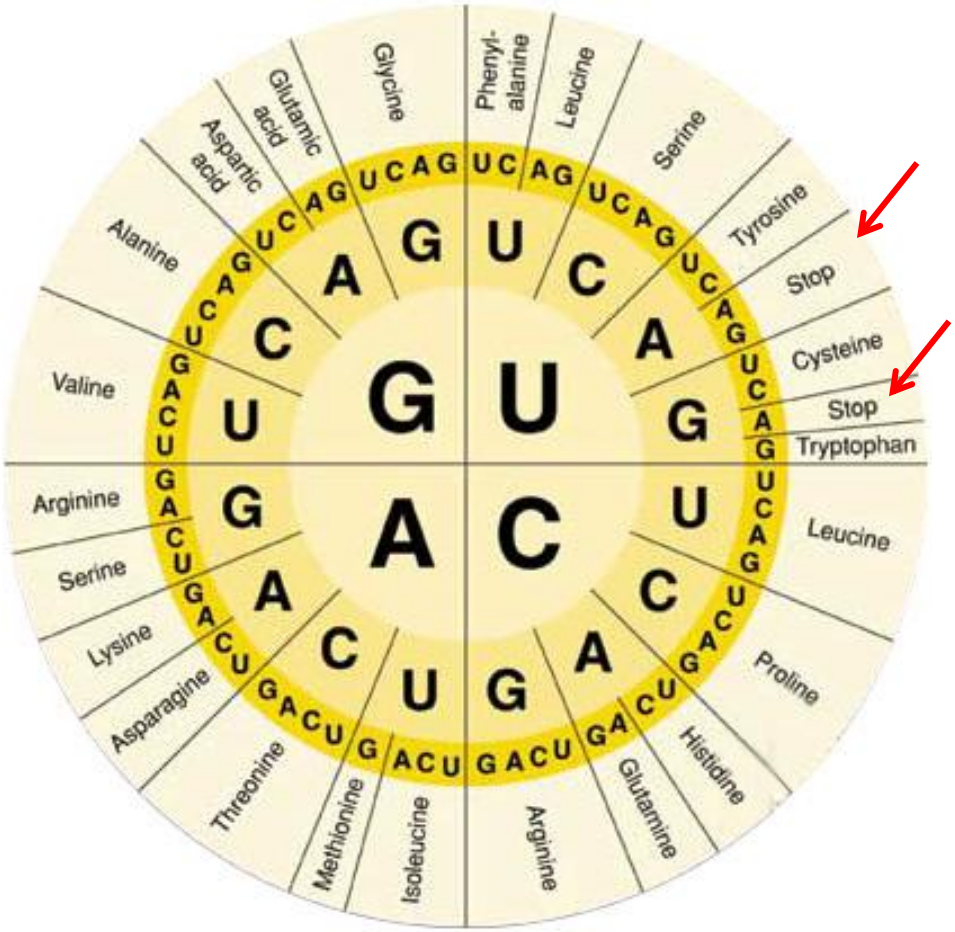
Aminoácidos proteicos

Definição

São aminoácidos que ocorrem naturalmente na constituição das proteínas e que se encontram codificados no código genético.

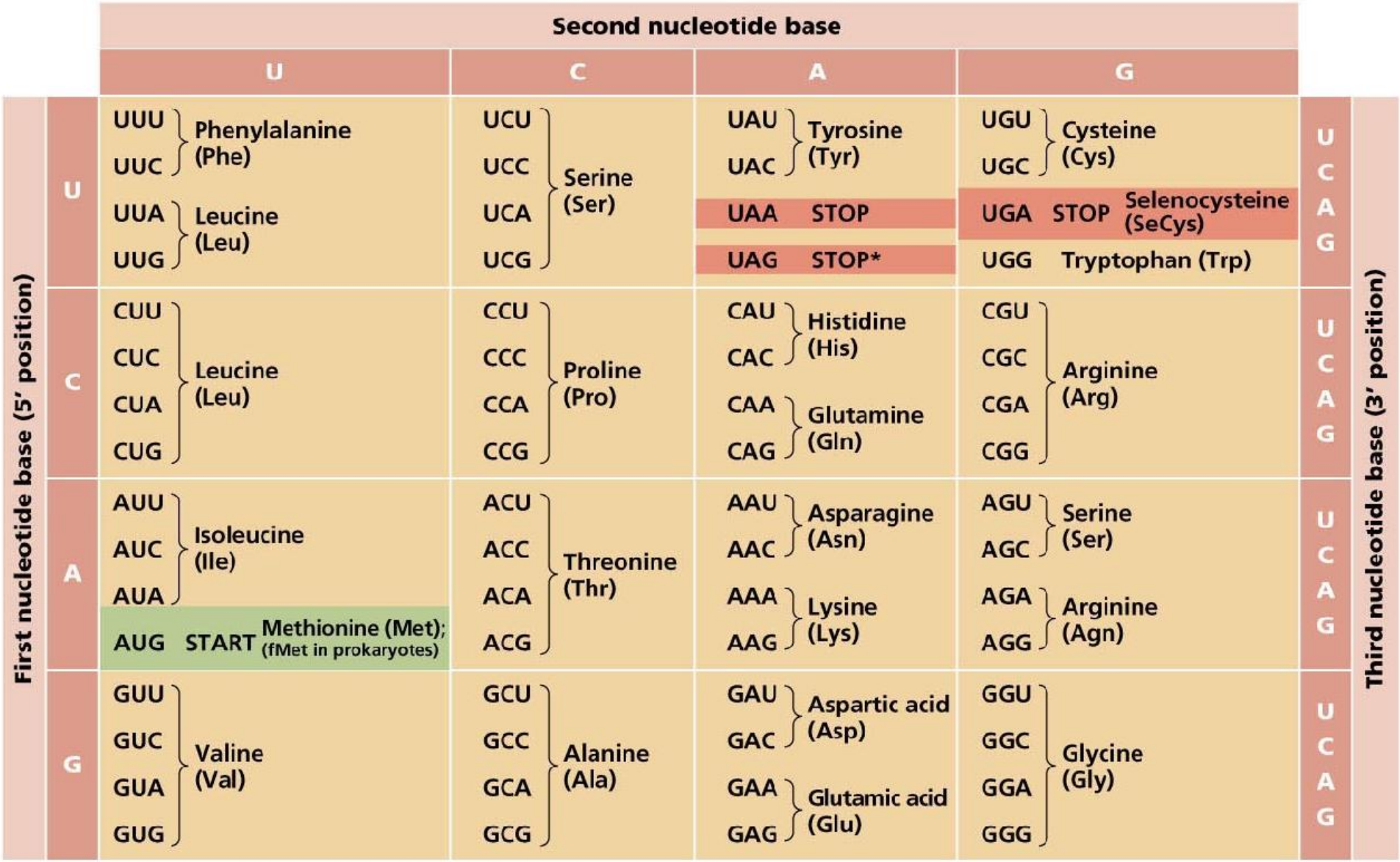
Código genético

First Letter	Second Letter: T	Second Letter: C	Second Letter: A	Second Letter: G	Third Letter
T	TTT Phe TTC Phe TTA Leu TTG Leu	TCT Ser TCC Ser TCA Ser TCG Ser	TAT Tyr TAC Tyr TAA Stop TAG Stop	TGT Cys TGC Cys TGA Stop TGG Trp	T C A G
C	CTT Leu CTC Leu CTA Leu CTG Leu	CCT Pro CCC Pro CCA Pro CCG Pro	CAT His CAC His CAA Gln CAG Gln	CGT Arg CGC Arg CGA Arg CGG Arg	T C A G
A	ATT Ile ATC Ile ATA Ile ATG Met	ACT Thr ACC Thr ACA Thr ACG Thr	AAT Asn AAC Asn AAA Lys AAG Lys	AGT Ser AGC Ser AGA Arg AGG Arg	T C A G
G	GTT Val GTC Val GTA Val GTG Val	GCT Ala GCC Ala GCA Ala GCG Ala	GAT Asp GAC Asp GAA Glu GAG Glu	GGT Gly GGC Gly GGA Gly GGG Gly	T C A G



Questão:
Porque é que se diz que o código genético é degenerado?

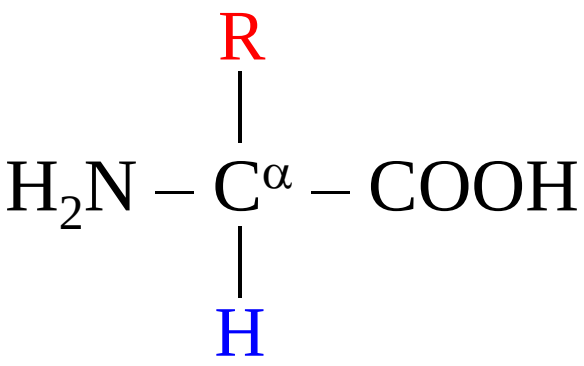
The genetic code



*also codes for a 22nd amino acid, pyrrolysine, in some prokaryotes.

Aminoácidos proteicos, standard, primários ou normais

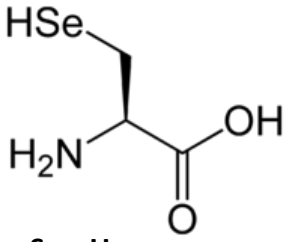
São todos L-α-aminoácidos.



Numa classificação mais simples mas menos rigorosa, os aminoácidos proteicos são classificados com base na polaridade da sua cadeia lateral, a um valor de pH fisiológico, em quatro grupos:

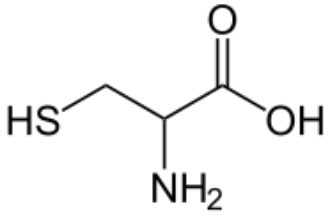
- Aminoácidos com cadeia lateral apolar;
- Aminoácidos com cadeia lateral polar mas não carregado;
- Aminoácidos com cadeia lateral carregado positivamente;
- Aminoácidos com cadeia lateral carregado negativamente.

L-Selenocisteína (Sec, U): o 21º aminoácido padrão



Sec, U

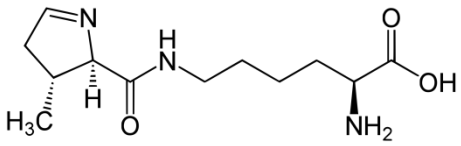
Selenocysteine has a structure similar to cysteine, but with an atom of selenium taking the place of the usual sulfur. Proteins that contain one or more selenocysteine residues are called selenoproteins.



Cys, C

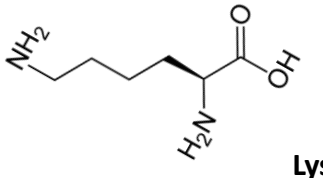
Selenium is sometimes responsible for the antioxidant activity of some plant extracts.
Selenomethionine is readily absorbed in the human intestine. Once inside the body it is readily converted to selenocysteine.
Selenocysteine is an amino acid that is present in several enzymes (for example glutathione peroxidases, tetraiodothyronine 5´deiodinases, thioredoxin reductases, formate dehydrogenases, glycine reductases and some hydrogenases).
Unlike other amino acids present in biological proteins, however, it is not coded for directly in the genetic code. Selenocysteine is encoded in a special way by a UGA codon, which is normally a stop codon. The UGA codon is made to encode selenocysteine by the presence of a SECIS element (SElenoCysteine Insertion Sequence) in the mRNA. The SECIS element is defined by characteristic nucleotide sequences and secondary structure base-pairing patterns. In eubacteria, the SECIS element is located immediately following the UGA codon within the reading frame for the selenoprotein. In archaea and in eukaryotes, the SECIS element is in the 3' untranslated region (3' UTR) of the mRNA, and can direct multiple UGA codons to encode selenocysteine residues. When cells are grown in the absence of selenium, translation of selenoproteins terminates at the UGA codon, resulting in a truncated, nonfunctional enzyme.
Like the other amino acids used by cells, selenocysteine has a specialized tRNA. The primary and secondary structure of selenocysteine tRNA, tRNA(Sec), differ from those of standard tRNAs in several respects, most notably in having an 8-base (bacteria) or 9-base (eukaryotes) pair acceptor stem, a long variable region arm, and substitutions at several well-conserved base positions. The selenocysteine tRNAs are initially charged with serine by seryl-tRNA ligase, but the resulting Ser-tRNA(Sec) is not used for translation because it is not recognised by the normal translation factor (EF-Tu in bacteria, EF1-alpha in eukaryotes). Rather, the tRNA-bound seryl residue is converted to a selenocysteyl-residue by the pyridoxal phosphate-containing enzyme selenocysteine synthase. Finally, the resulting Sec-tRNA(Sec) is specifically bound to an alternative translational elongation factor (SelB or mSelB) which delivers it in a targeted manner to the ribosomes translating mRNAs for selenoproteins.

L-Pyrrolysine (Pyl, O): o 22º aminoácido padrão



Pyl, O

Pyrrolysine has a structure similar to lysine, but with a pyrroline ring attached



Lys, K

Pyrrolysine is a naturally occurring, genetically coded amino acid used by some methanogenic archaea and one known bacterium in enzymes that are part of their methane-producing metabolism. It is similar to lysine, but with an added pyrroline ring linked to the end of the lysine side chain. Produced by a specific tRNA and aminoacyl tRNA synthetase, it forms part of an unusual genetic code in these organisms, and is considered the 22nd proteinogenic amino acid.

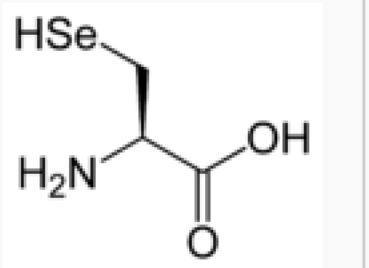
The joint nomenclature committee of the IUPAC/IUBMB has officially recommended the three-letter symbol Pyl and the one-letter symbol O for pyrrolysine.

Unlike posttranslational modifications of lysine such as hydroxylysine, methyllysine, and hypusine, pyrrolysine is incorporated during translation as directed by the genetic code, just like the 20 standard amino acids. It is encoded in mRNA by the UAG codon, which in most organisms is the 'amber' stop codon. This requires only the presence of the *pylT* gene, which encodes an unusual tRNA with a CUA anticodon, and the *pylS* gene, which encodes a class II aminoacyl-tRNA synthetase that charges the pylT-derived tRNA with pyrrolysine.

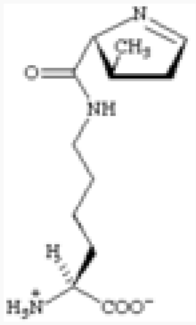
The extra pyrroline ring is incorporated into the active site of several methyltransferases, where it is believed to rotate relatively freely.

There are 22 standard amino acids, but only 21 are found in eukaryotes. Of the twenty-two, twenty are directly encoded by the universal genetic code. The remaining two, selenocysteine and pyrrolysine, are incorporated into proteins by unique synthetic mechanisms.

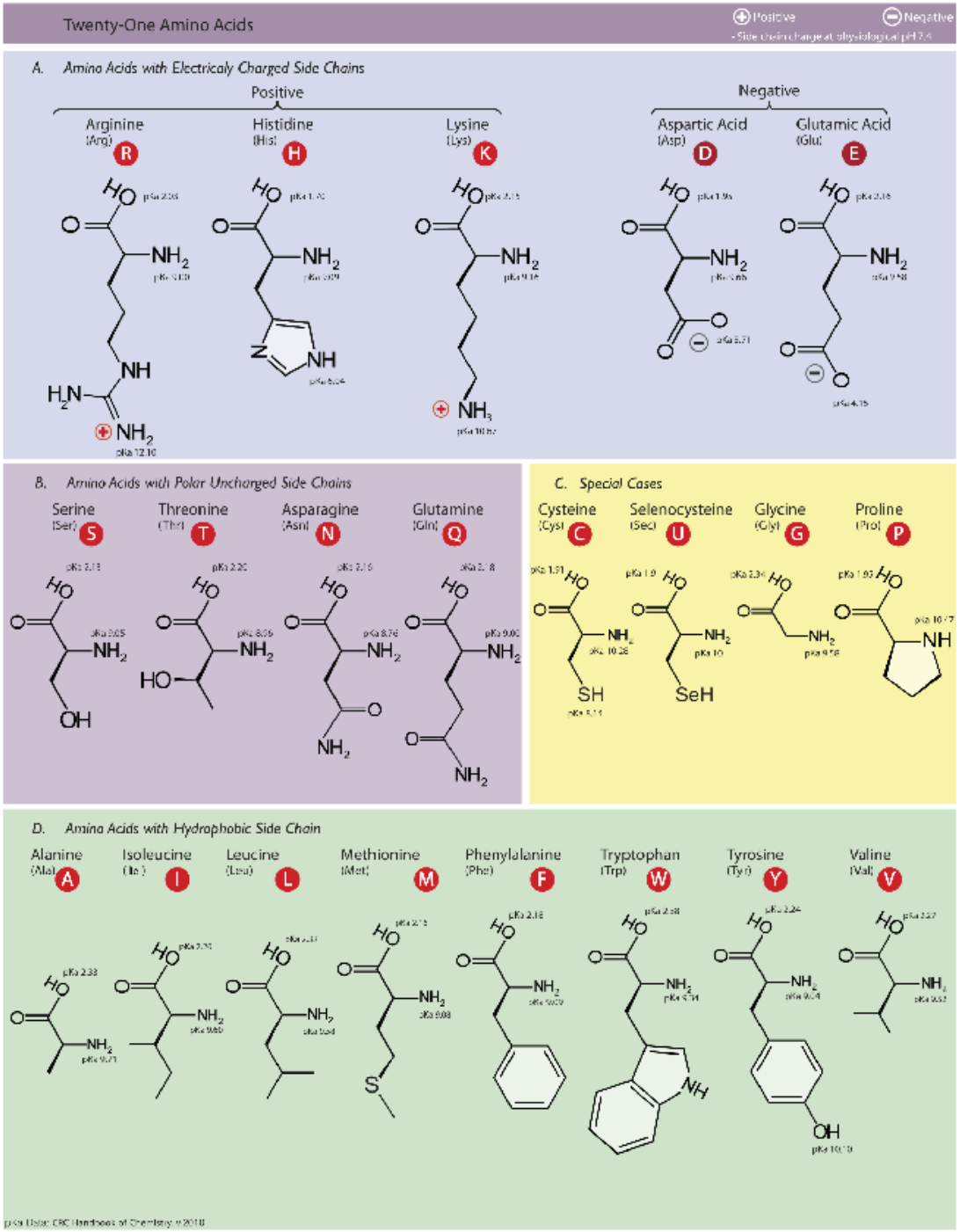
IUPAC/IUBMB now also recommends standard abbreviations for the following two amino acids:



L-Selenocysteine
(Sec / U)



L-Pyrrolysine
(Pyl / O)



Grouped table of 21 amino acids structures, nomenclature, and their side chain pK_a values

General chemical properties

Amino Acid	Short	Abbrev.	Avg. Mass (Da)	pI	pK_1 (α-COOH)	pK_2 (α-$^+NH_3$)
Alanine	A	Ala	89.09404	6.01	2.35	9.87
Cysteine	C	Cys	121.15404	5.05	1.92	10.70
Aspartic acid	D	Asp	133.10384	2.85	1.99	9.90
Glutamic acid	E	Glu	147.13074	3.15	2.10	9.47
Phenylalanine	F	Phe	165.19184	5.49	2.20	9.31
Glycine	G	Gly	75.06714	6.06	2.35	9.78
Histidine	H	His	155.15634	7.60	1.80	9.33
Isoleucine	I	Ile	131.17464	6.05	2.32	9.76
Lysine	K	Lys	146.18934	9.60	2.16	9.06
Leucine	L	Leu	131.17464	6.01	2.33	9.74
Methionine	M	Met	149.20784	5.74	2.13	9.28
Asparagine	N	Asn	132.11904	5.41	2.14	8.72
Pyrrolysine	O	Pyl				
Proline	P	Pro	115.13194	6.30	1.95	10.64
Glutamine	Q	Gln	146.14594	5.65	2.17	9.13
Arginine	R	Arg	174.20274	10.76	1.82	8.99
Serine	S	Ser	105.09344	5.68	2.19	9.21
Threonine	T	Thr	119.12034	5.60	2.09	9.10
Selenocysteine	U	Sec	168.053			
Valine	V	Val	117.14784	6.00	2.39	9.74
Tryptophan	W	Trp	204.22844	5.89	2.46	9.41
Tyrosine	Y	Tyr	181.19124	5.64	2.20	9.21

Side chain properties

Amino Acid	Short	Abbrev.	Side chain	Hydro-phobic	pKa	Polar	pH	Small	Tiny	Aromatic or Aliphatic	van der Waals volume
Alanine	A	Ala	$-CH_3$	X	-	-	-	X	X	-	67
Cysteine	C	Cys	$-CH_2SH$	X	8.18	-	acidic	X	-	-	86
Aspartic acid	D	Asp	$-CH_2COOH$	-	3.90	X	acidic	X	-	-	91
Glutamic acid	E	Glu	$-CH_2CH_2COOH$	-	4.07	X	acidic	-	-	-	109
Phenylalanine	F	Phe	$-CH_2C_6H_5$	X	-	-	-	-	-	Aromatic	135
Glycine	G	Gly	-H	X	-	-	-	X	X	-	48
Histidine	H	His	$-CH_2-C_3H_3N_2$	-	6.04	X	weak basic	-	-	Aromatic	118
Isoleucine	I	Ile	$-CH(CH_3)CH_2CH_3$	X	-	-	-	-	-	Aliphatic	124
Lysine	K	Lys	$-(CH_2)_4NH_2$	-	10.54	X	basic	-	-	-	135
Leucine	L	Leu	$-CH_2CH(CH_3)_2$	X	-	-	-	-	-	Aliphatic	124
Methionine	M	Met	$-CH_2CH_2SCH_3$	X	-	-	-	-	-	-	124
Asparagine	N	Asn	$-CH_2CONH_2$	-	-	X	-	X	-	-	96
Pyrrolysine	O	Pyl									
Proline	P	Pro	$-CH_2CH_2CH_2-$	X	-	-	-	X	-	-	90
Glutamine	Q	Gln	$-CH_2CH_2CONH_2$	-	-	X	-	-	-	-	114
Arginine	R	Arg	$-(CH_2)_3NH-C(NH)NH_2$	-	12.48	X	strongly basic	-	-	-	148
Serine	S	Ser	$-CH_2OH$	-	-	X	-	X	X	-	73
Threonine	T	Thr	$-CH(OH)CH_3$	-	-	X	weak acidic	X	-	-	93
Selenocysteine	U	Sec	$-CH_2SeH$	X	5.73	-	-	X	-	-	
Valine	V	Val	$-CH(CH_3)_2$	X	-	-	-	X	-	Aliphatic	105
Tryptophan	W	Trp	$-CH_2C_8H_6N$	X	-	-	-	-	-	Aromatic	163
Tyrosine	Y	Tyr	$-CH_2-C_6H_4OH$	-	10.46	X	-	-	-	Aromatic	141

Note: The pK_a values of amino acids are typically slightly different when the amino acid is inside a protein. Protein pK_a calculations are sometimes used to calculate the change in the pK_a value of an amino acid in this situation.

Gene expression and biochemistry

Amino Acid	Short	Abbrev.	Codon(s)	Occurrence in human proteins (%)	Essential‡ in humans
Alanine	A	Ala	GCU, GCC, GCA, GCG	7.8	-
Cysteine	C	Cys	UGU, UGC	1.9	Conditionally
Aspartic acid	D	Asp	GAU, GAC	5.3	-
Glutamic acid	E	Glu	GAA, GAG	6.3	Conditionally
Phenylalanine	F	Phe	UUU, UUC	3.9	Yes
Glycine	G	Gly	GGU, GGC, GGA, GGG	7.2	Conditionally
Histidine	H	His	CAU, CAC	2.3	Yes
Isoleucine	I	Ile	AUU, AUC, AUA	5.3	Yes
Lysine	K	Lys	AAA, AAG	5.9	Yes
Leucine	L	Leu	UUA, UUG, CUU, CUC, CUA, CUG	9.1	Yes
Methionine	M	Met	AUG	2.3	Yes
Asparagine	N	Asn	AAU, AAC	4.3	-
Pyrrolysine	O	Pyl	UAG*		-
Proline	P	Pro	CCU, CCC, CCA, CCG	5.2	-
Glutamine	Q	Gln	CAA, CAG	4.2	-
Arginine	R	Arg	CGU, CGC, CGA, CGG, AGA, AGG	5.1	Conditionally
Serine	S	Ser	UCU, UCC, UCA, UCG, AGU, AGC	6.8	-
Threonine	T	Thr	ACU, ACC, ACA, ACG	5.9	Yes
Selenocysteine	U	Sec	UGA**		-
Valine	V	Val	GUU, GUC, GUA, GUG	6.6	Yes
Tryptophan	W	Trp	UGG	1.4	Yes
Tyrosine	Y	Tyr	UAU, UAC	3.2	Conditionally
Stop codon†	-	Term	UAA, UAG, UGA	-	-

* UAG is normally the amber stop codon, but encodes pyrrolysine if a PYLIS element is present.
** UGA is normally the opal (or umber) stop codon, but encodes selenocysteine if a SECIS element is present.
† The stop codon is not an amino acid, but is included for completeness.
‡ An essential amino acid cannot be synthesized in humans and must, therefore, be supplied in the diet. Conditionally essential amino acids are not normally required in the diet, but must be supplied exogenously to specific populations that do not synthesize it in adequate amounts.

Stoichiometry and metabolic cost in cell

Following table lists the abundance of amino acids in *Escherichia coli* cell and the metabolic cost (ATP) for synthesis the amino acids. Negative numbers indicate the metabolic processes are energy favorable and do not cost net ATP of the cell. Note that the abundance of amino acids include amino acids in free-form and in polymerization form (proteins).

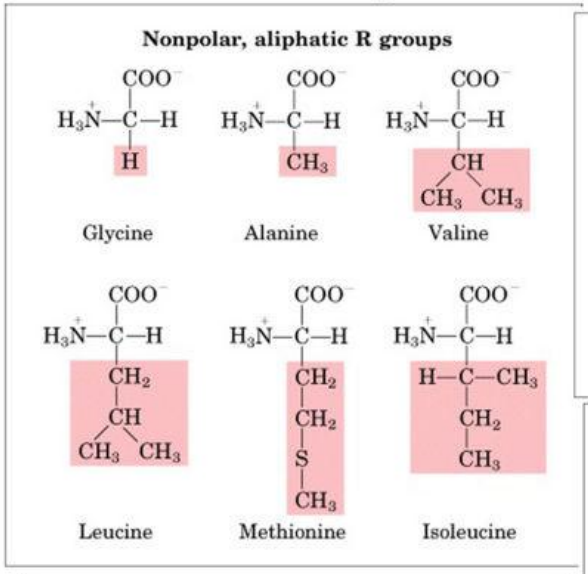
Amino acid	Abundance (# of molecules ($\times 10^8$) per *E. coli* cell)	ATP cost in synthesis under aerobic condition	ATP cost in synthesis under anaerobic condition
Alanine	2.9	-1	1
Cysteine	0.52	11	15
Aspartic acid	1.4	0	2
Glutamic acid	1.5	-7	-1
Phenylalanine	1.1	-6	2
Glycine	3.5	-2	2
Histidine	0.54	1	7
Isoleucine	1.7	7	11
Lysine	2.0	5	9
Leucine	2.6	-9	1
Methionine	0.88	21	23
Asparagine	1.4	3	5
Proline	1.3	-2	4
Glutamine	1.5	-6	0
Arginine	1.7	5	13
Serine	1.2	-2	2
Threonine	1.5	6	8
Tryptophan	0.33	-7	7
Tyrosine	0.79	-8	2
Valine	2.4	-2	2

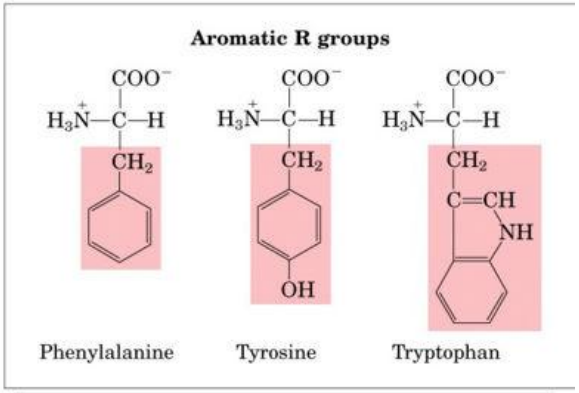
Amino Acid	Abbrev.		Remarks
Alanine	A	Ala	Very abundant, very versatile. More stiff than glycine, but small enough to pose only small steric limits for the protein conformation. It behaves fairly neutrally, and can be located in both hydrophilic regions on the protein outside and the hydrophobic areas inside.
Asparagine or aspartic acid	B	Asx	A placeholder when either amino acid may occupy a position.
Cysteine	C	Cys	The sulfur atom bonds readily to heavy metal ions. Under oxidizing conditions, two cysteines can join together in a disulfide bond to form the amino acid cystine. When cystines are part of a protein, insulin for example, the tertiary structure is stabilized, which makes the protein more resistant to denaturation; therefore, disulfide bonds are common in proteins that have to function in harsh environments including digestive enzymes (e.g., pepsin and chymotrypsin) and structural proteins (e.g., keratin). Disulfides are also found in peptides too small to hold a stable shape on their own (eg. insulin).
Aspartic acid	D	Asp	Behaves similarly to glutamic acid. Carries a hydrophilic acidic group with strong negative charge. Usually is located on the outer surface of the protein, making it water-soluble. Binds to positively-charged molecules and ions, often used in enzymes to fix the metal ion. When located inside of the protein, aspartate and glutamate are usually paired with arginine and lysine.
Glutamic acid	E	Glu	Behaves similar to aspartic acid. Has longer, slightly more flexible side chain.
Phenylalanine	F	Phe	Essential for humans. Phenylalanine, tyrosine, and tryptophan contain large rigid aromatic group on the side-chain. These are the biggest amino acids. Like isoleucine, leucine and valine, these are hydrophobic and tend to orient towards the interior of the folded protein molecule. Phenylalanine can be converted into Tyrosine.
Glycine	G	Gly	Because of the two hydrogen atoms at the α carbon, glycine is not optically active. It is the smallest amino acid, rotates easily, adds flexibility to the protein chain. It is able to fit into the tightest spaces, e.g., the triple helix of collagen. As too much flexibility is usually not desired, as a structural component it is less common than alanine.
Histidine	H	His	In even slightly acidic conditions protonation of the nitrogen occurs, changing the properties of histidine and the polypeptide as a whole. It is used by many proteins as a regulatory mechanism, changing the conformation and behavior of the polypeptide in acidic regions such as the late endosome or lysosome, enforcing conformation change in enzymes. However only a few histidines are needed for this, so it is comparatively scarce.
Isoleucine	I	Ile	Essential for humans. Isoleucine, leucine and valine have large aliphatic hydrophobic side chains. Their molecules are rigid, and their mutual hydrophobic interactions are important for the correct folding of proteins, as these chains tend to be located inside of the protein molecule.
Leucine or isoleucine	J	Xle	A placeholder when either amino acid may occupy a position
Lysine	K	Lys	Essential for humans. Behaves similarly to arginine. Contains a long flexible side-chain with a positively-charged end. The flexibility of the chain makes lysine and arginine suitable for binding to molecules with many negative charges on their surfaces. E.g., DNA-binding proteins have their active regions rich with arginine and lysine. The strong charge makes these two amino acids prone to be located on the outer hydrophilic surfaces of the proteins; when they are found inside, they are usually paired with a corresponding negatively-charged amino acid, e.g., aspartate or glutamate.
Leucine	L	Leu	Essential for humans. Behaves similar to isoleucine and valine. See isoleucine.
Methionine	M	Met	Essential for humans. Always the first amino acid to be incorporated into a protein; sometimes removed after translation. Like cysteine, contains sulfur, but with a methyl group instead of hydrogen. This methyl group can be activated, and is used in many reactions where a new carbon atom is being added to another molecule.
Asparagine	N	Asn	Similar to aspartic acid. Asn contains an amide group where Asp has a carboxyl.
Pyrrolysine	O	Pyl	Similar to lysine, with a pyrroline ring attached.
Proline	P	Pro	Contains an unusual ring to the N-end amine group, which forces the CO-NH amide sequence into a fixed conformation. Can disrupt protein folding structures like α helix or β sheet, forcing the desired kink in the protein chain. Common in collagen, where it often undergoes a posttranslational modification to hydroxyproline.
Glutamine	Q	Gln	Similar to glutamic acid. Gln contains an amide group where Glu has a carboxyl. Used in proteins and as a storage for ammonia. The most abundant Amino Acid in the body.
Arginine	R	Arg	Functionally similar to lysine.
Serine	S	Ser	Serine and threonine have a short group ended with a hydroxyl group. Its hydrogen is easy to remove, so serine and threonine often act as hydrogen donors in enzymes. Both are very hydrophilic, therefore the outer regions of soluble proteins tend to be rich with them.
Threonine	T	Thr	Essential for humans. Behaves similarly to serine.
Selenocysteine	U	Sec	Selenated form of cysteine, which replaces sulfur.
Valine	V	Val	Essential for humans. Behaves similarly to isoleucine and leucine. See isoleucine.
Tryptophan	W	Trp	Essential for humans. Behaves similarly to phenylalanine and tyrosine (see phenylalanine). Precursor of serotonin. Naturally fluorescent.
Unknown	X	Xxx	Placeholder when the amino acid is unknown or unimportant.
Tyrosine	Y	Tyr	Behaves similarly to phenylalanine (precursor to Tyrosine) and tryptophan (see phenylalanine). Precursor of melanin, epinephrine, and thyroid hormones. Naturally fluorescent, although fluorescence is usually quenched by energy transfer to tryptophans.
Glutamic acid or glutamine	Z	Glx	A placeholder when either amino acid may occupy a position.

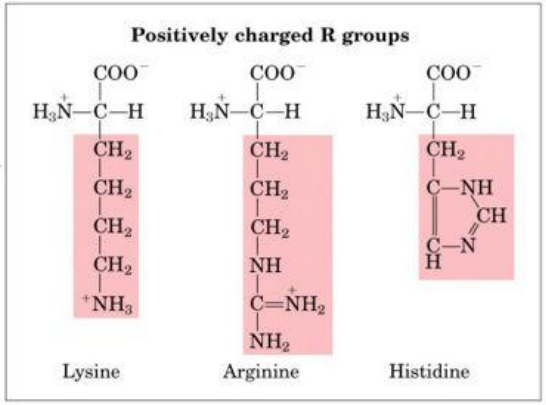
Classification of the 20 basic standard amino acids

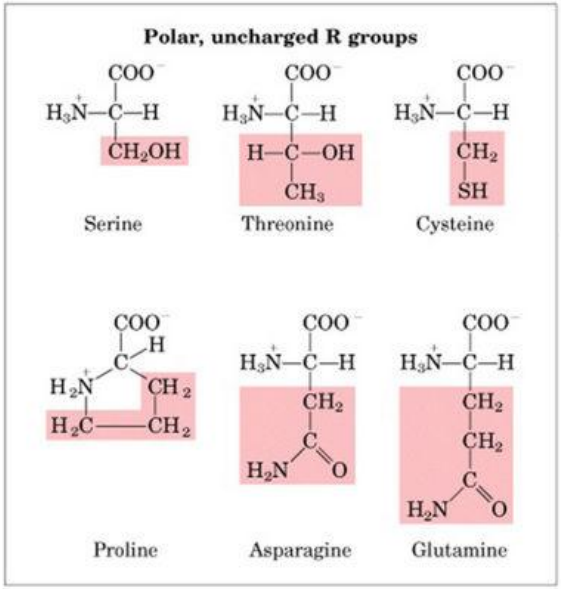
Branched-chain amino acids	Isoleucine (dp) · Leucine (dp) · Valine (dp)
Non Branch-chain	Alanine (dp) · Arginine (dp) · Asparagine (dp) · Aspartic acid (dp) · Cysteine (dp) · Glutamic acid (dp) · Glutamine (dp) · Glycine (dp) · Histidine (dp) · Lysine (dp) · Methionine (dp) · Phenylalanine (dp) · Proline (dp) · Serine (dp) · Threonine (dp) · Tryptophan (dp) · Tyrosine (dp)
Other classifications	Essential amino acids · Ketogenic amino acid · Glucogenic amino acid

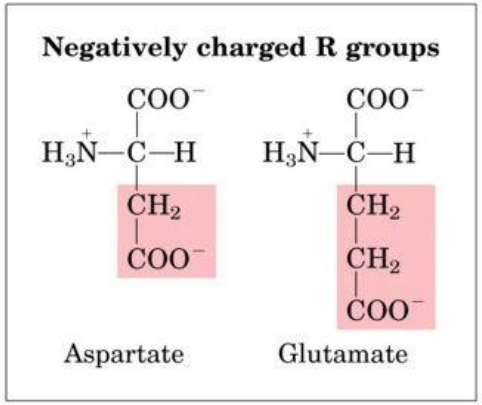
Twenty standard Amino Acids











Abreviaturas dos aminoácidos

The Amino Acids

For each amino acid, both the three-letter and single-letter codes are given.

Alanine	Ala	A	hydrophobic
Arginine	Arg	R	free amino group makes it basic and hydrophilic
Asparagine	Asn	N	carbohydrate can be covalently linked ("N-linked) to its -NH
Aspartic acid	Asp	D	free carboxyl group makes it acidic and hydrophilic
Cysteine	Cys	C	oxidation of their sulfhydryl (-SH) groups link 2 Cys (S-S)
Glutamic acid	Glu	E	free carboxyl group makes it acidic and hydrophilic
Glutamine	Gln	Q	moderately hydrophilic
Glycine	Gly	G	so small it is amphiphilic (can exist in any surroundings)
Histidine	His	H	basic and hydrophilic
Isoleucine	Ile	I	hydrophobic
Leucine	Leu	L	hydrophobic
Lysine	Lys	K	strongly basic and hydrophilic
Methionine	Met	M	hydrophobic
Phenylalanine	Phe	F	very hydrophobic
Proline	Pro	P	causes kinks in the chain
Serine	Ser	S	carbohydrate can be covalently linked ("O-linked") to its -OH
Threonine	Thr	T	carbohydrate can be covalently linked ("O-linked") to its -OH
Tryptophan	Trp	W	scarce in most plant proteins
Tyrosine	Tyr	Y	a phosphate or sulfate group can be covalently attached to its -OH
Valine	Val	V	hydrophobic

Aminoácidos proteicos

Informação detalhada e individual sobre cada um dos 20 aminoácidos proteicos pode ser encontrada, sob a forma de entradas/textos individuais, na Enciclopédia Luso-Brasileira de Cultura:

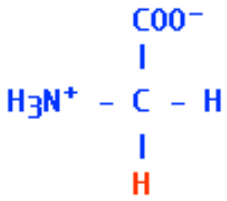
Enciclopédia Luso-Brasileira de Cultura (1993-2004). Edição Século XXI, Editorial Verbo, Lisboa/São Paulo.

Aminoácido	*Abreviaturas*	
Alanina	Ala	A
Arginina	Arg	R
Asparagina	Asn	N
Ácido aspártico	Asp	D
Cisteína	Cys	C
Glutamina	Gln	Q
Ácido glutâmico	Glu	E
Glicina	Gly	G
Histidina	His	H
Isoleucina	Ile	I
Leucina	Leu	L
Lisina	Lys	K
Metionina	Met	M
Fenilalanina	Phe	F
Prolina	Pro	P
Serina	Ser	S
Treonina	Thr	T
Triptofano	Trp	W
Tirosina	Tyr	Y
Valina	Val	V

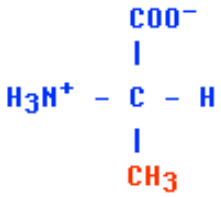
Numa classificação mais complexas mas mais rigorosa, os aminoácidos proteicos são classificados com base na estrutura e composição da sua cadeia lateral, a um valor de pH fisiológico, em dezo grupos:

- aa alifáticos lineares ..... Gly, Ala
- aa ramificados ..... Val, Leu, Ile
- hidroxi aa ..... Ser, Thr
- aa sulfunados ..... Cys, Met
- aa aromáticos ..... Phe, Tyr
- aa heterocíclicos ..... Trp, His
- aa básicos ..... Lys, Arg
- aa acídicos e suas amidas ..... Asp, Glu, Asm, Glm
- iminoácido ..... Pro

1 - Aminoácidos alifáticos lineares

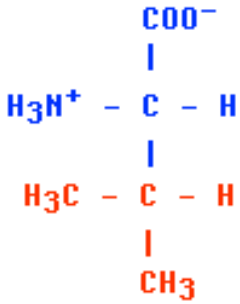


Glycine (Gly)[G]

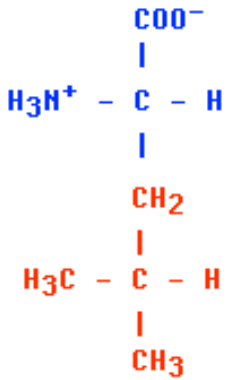


Alanine (Ala)[A]

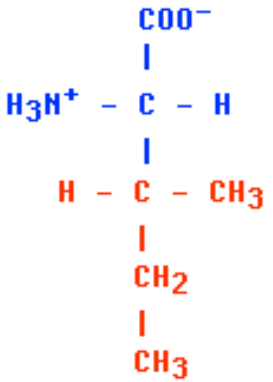
2 - Aminoácidos ramificados



Valine (Val)[V]

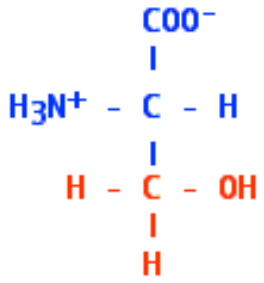


Leucine (Leu)[L]

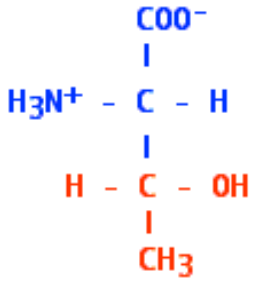


Isoleucine (Ile)[I]

3 - Hidroxiaminoácidos

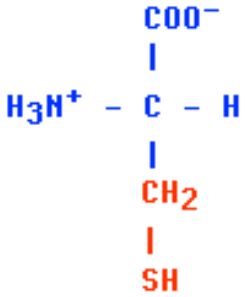


Serine (Ser)[S]

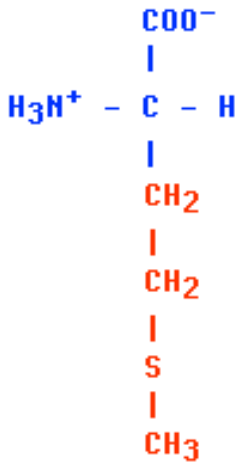


Threonine (Thr)[T]

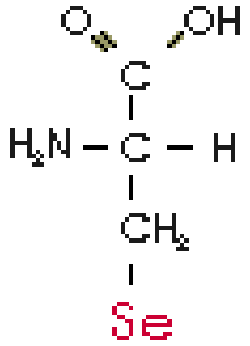
4 - Aminoácidos contendo enxofre or selénio



Cysteine (Cys)[C]

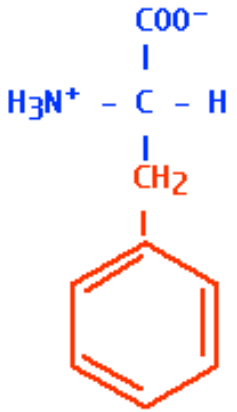


Methionine (Met)[M]

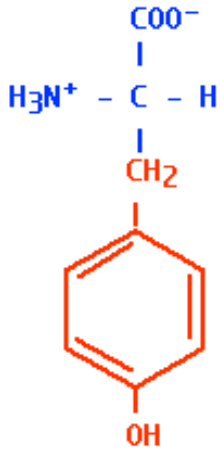


Selenocisteína (Sec) (U)

5 - Aminoácidos aromáticos

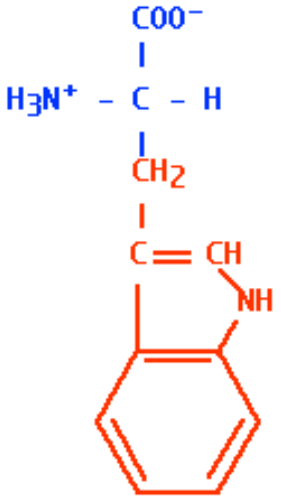


Phenylalanine (Phe)[F]

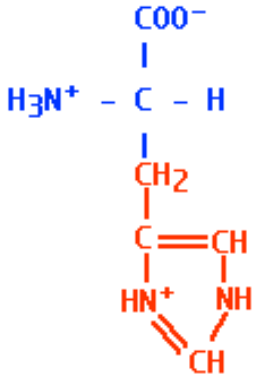


Tyrosine (Tyr)[Y]

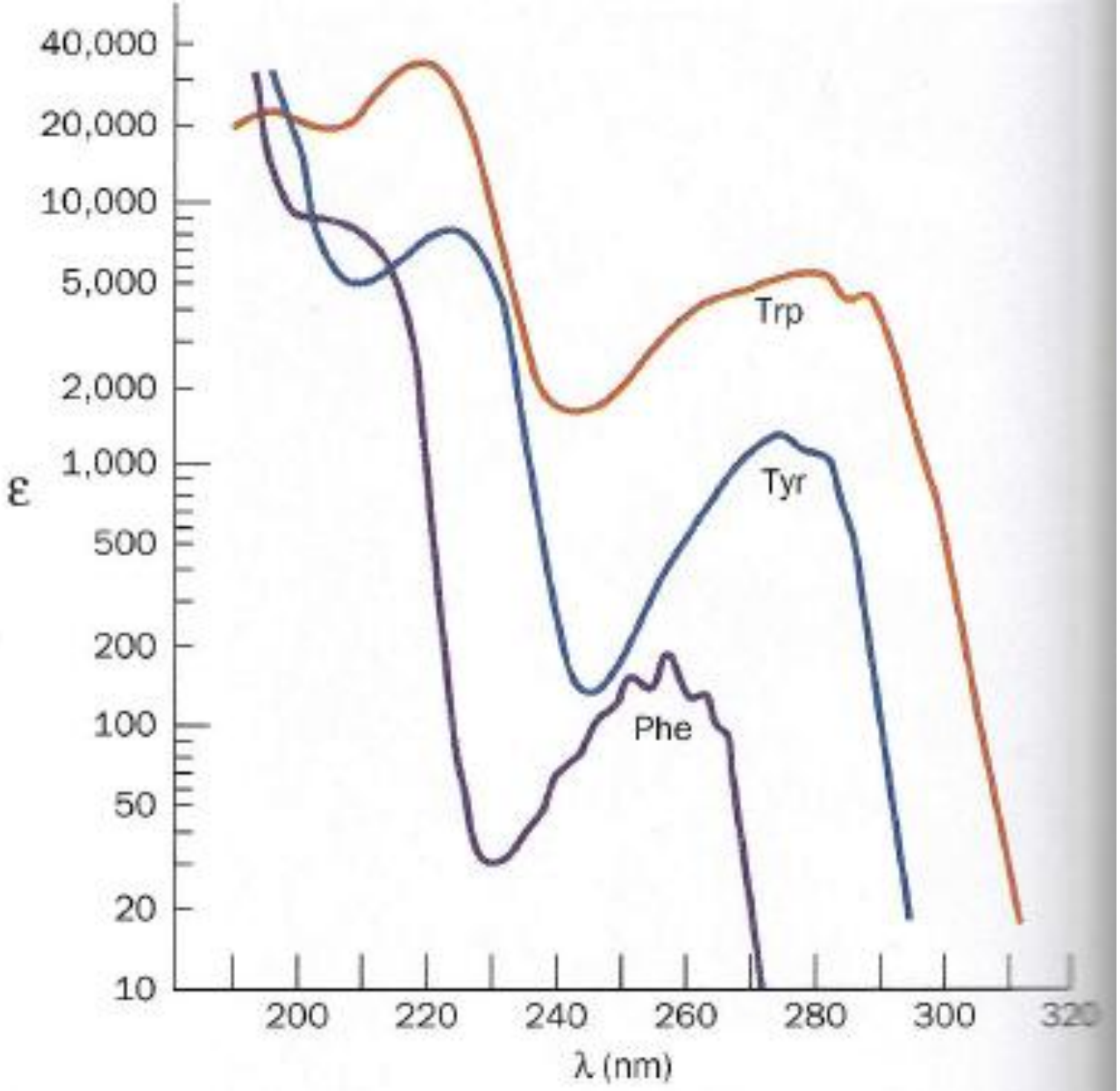
6 - Aminoácidos heterocíclicos



Tryptophan (Trp)[W]



Histidine (His)[H]

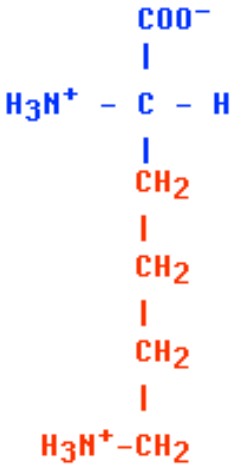


UV absorbance spectra of the three aromatic amino acids, phenylalanine, tryptophan, and tyrosine. Note that the molar absorbance, ε, is displayed on a log scale.

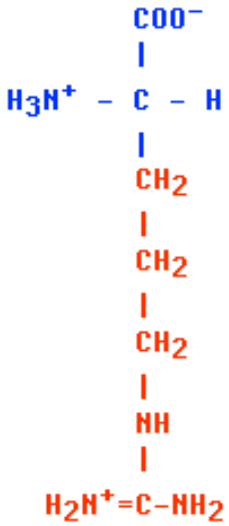
Questão:
Porque é que a parvalbumina não absorve radiação de 280 nm?

Parvalbumin is a calcium-binding albumin protein with low molecular mass (typically 9-11 kDa).
It is localised in fast-contracting muscles, where its levels are highest, and in the brain and some endocrine tissues.

7 - Aminoácidos básicos

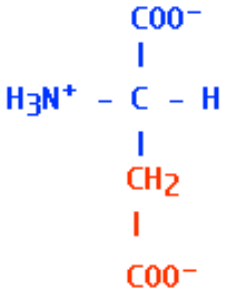


Lysine (Lys)[K]

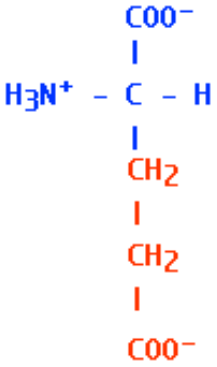


Arginine (Arg)[R]

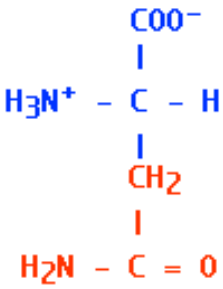
8 - Aminoácidos acídicos e suas amidas



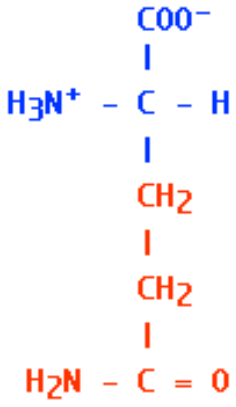
Aspartic acid (Asp)[D]



Glutamic acid (Glu)[E]

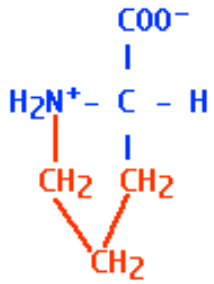


Asparagine (Asn)[N]

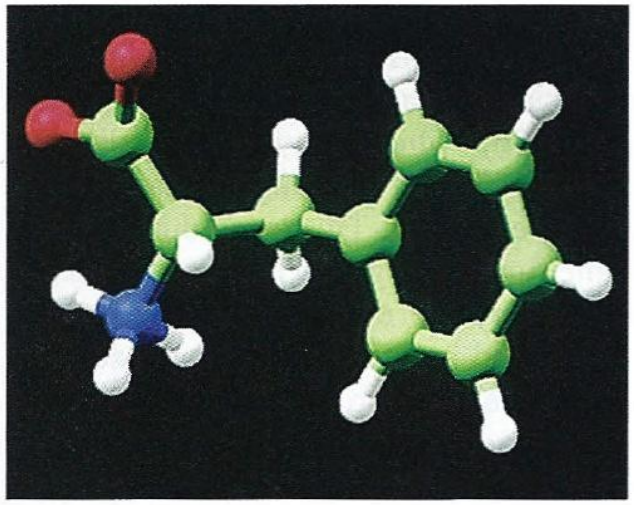


Glutamine (Gln)[Q]

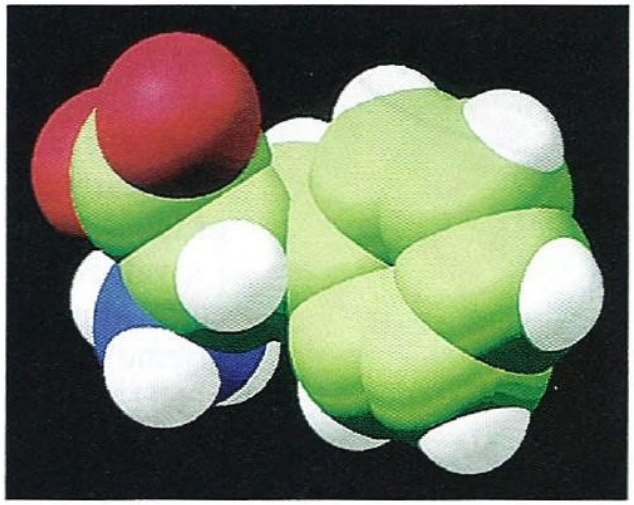
9 - Iminoácido



Proline (Pro)[P]



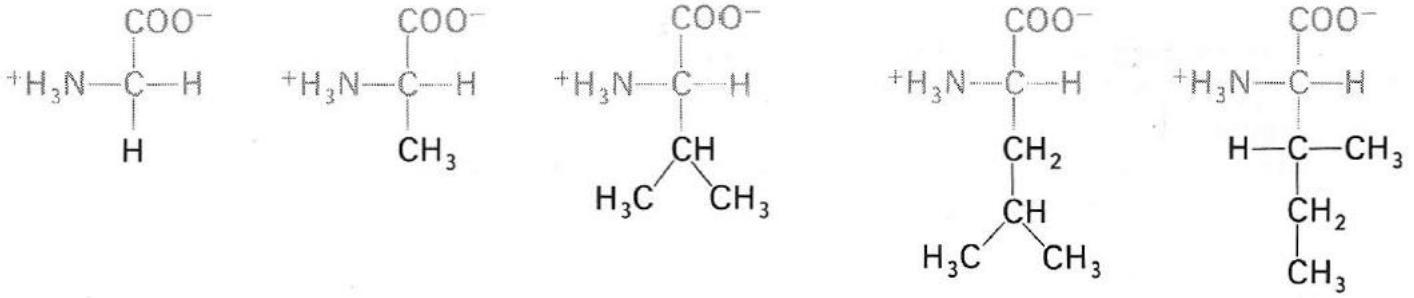
(a) **Ball-and-stick model**



(b) **Space-filling model**

Structure of phenylalanine. Computer graphics drawings showing the α-amino acid phenylalanine represented in (*a*) ball-and-stick form and (*b*) space-filling form. The molecule, which is colored according to atom type (C green, H white, N blue, and O red), has the same conformation and orientation in both drawings.

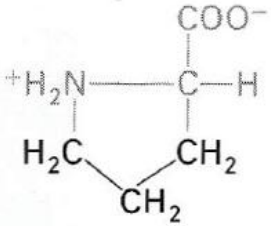
ou



Glycine (Gly) **Alanine (Ala)** **Valine (Val)** **Leucine (Leu)** **Isoleucine (Ile)**

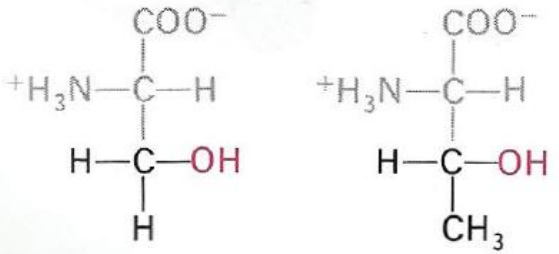
Amino acids having aliphatic (linear or branched) side chains.

Imino acid



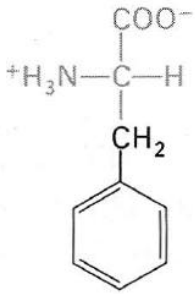
Proline (Pro)

Proline differs from the other common amino acids in that it has a secondary amino group.

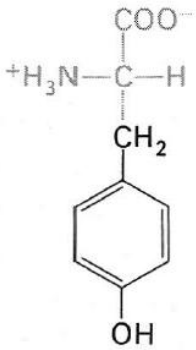


Serine (Ser) **Threonine (Thr)**

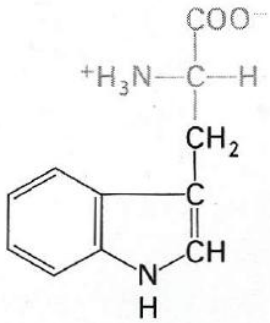
Serine and threonine have aliphatic hydroxyl side chains.



Phenylalanine (Phe)

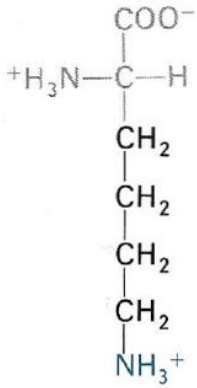


Tyrosine (Tyr)

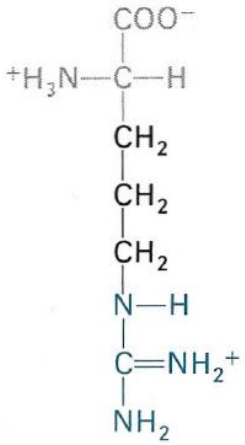


Tryptophan (Trp)

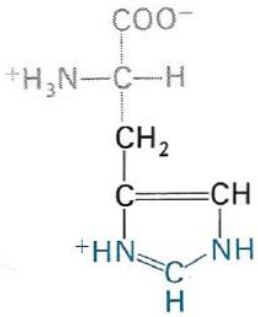
Phenylalanine, tyrosine, and tryptophan have aromatic side chains.



Lysine (Lys)

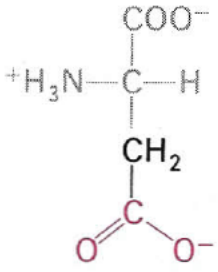


Arginine (Arg)

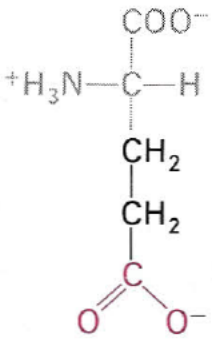


Histidine (His)

Lysine, arginine, and histidine have basic side chains.

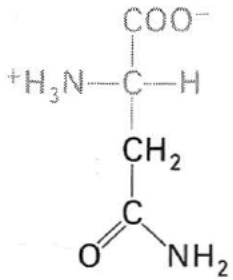


Aspartate (Asp)

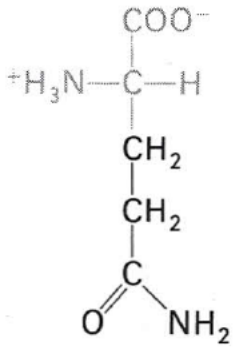


Glutamate (Glu)

Aspartate and glutamate have acidic side chains.

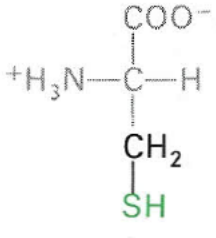


Asparagine (Asn)

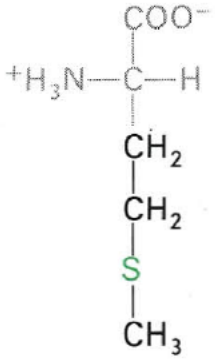


Glutamine (Gln)

Asparagine and glutamine have amide side chains.



Cysteine (Cys)

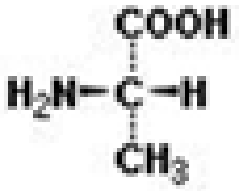


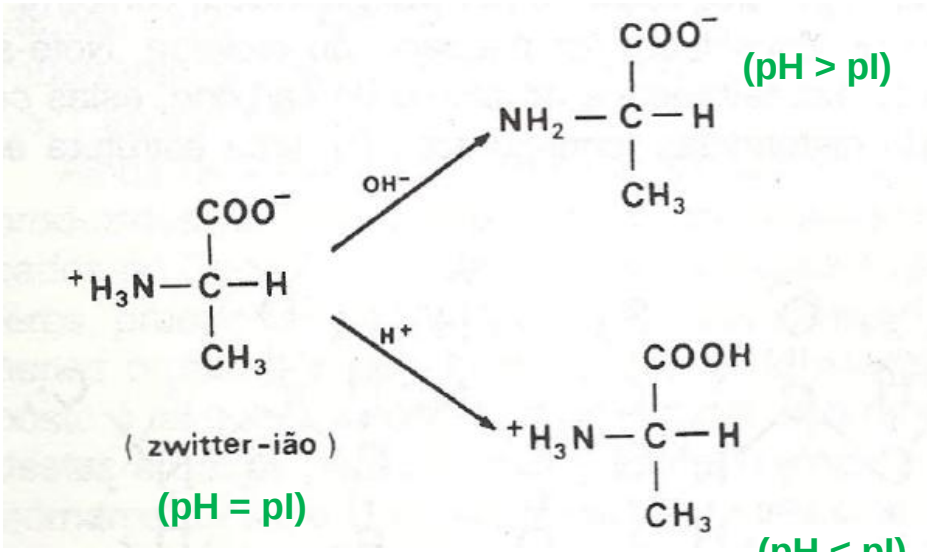
Methionine (Met)

Cysteine and methionine have sulfur-containing side chains.

Amino Acid	3-Letter	1-Letter	Side chain polarity	Side chain charge (pH 7)	Hydropathy index	Absorbance λ_{max} (nm)
Alanine	Ala	A	nonpolar	neutral	1.8	
Arginine	Arg	R	polar	positive	-4.5	
Asparagine	Asn	N	polar	neutral	-3.5	
Aspartic acid	Asp	D	polar	negative	-3.5	
Cysteine	Cys	C	nonpolar	neutral	2.5	250
Glutamic acid	Glu	E	polar	negative	-3.5	
Glutamine	Gln	Q	polar	neutral	-3.5	
Glycine	Gly	G	nonpolar	neutral	-0.4	
Histidine	His	H	polar	neutral	-3.2	211
Isoleucine	Ile	I	nonpolar	neutral	4.5	
Leucine	Leu	L	nonpolar	neutral	3.8	
Lysine	Lys	K	polar	positive	-3.9	
Methionine	Met	M	nonpolar	neutral	1.9	
Phenylalanine	Phe	F	nonpolar	neutral	2.8	257, 206, 188
Proline	Pro	P	nonpolar	neutral	-1.6	
Serine	Ser	S	polar	neutral	-0.8	
Threonine	Thr	T	polar	neutral	-0.7	
Tryptophan	Trp	W	nonpolar	neutral	-0.9	280 219
Tyrosine	Tyr	Y	polar	neutral	-1.3	274, 222, 193
Valine	Val	V	nonpolar	neutral	4.2	

Ionização e propriedades ácido-base dos aminoácidos

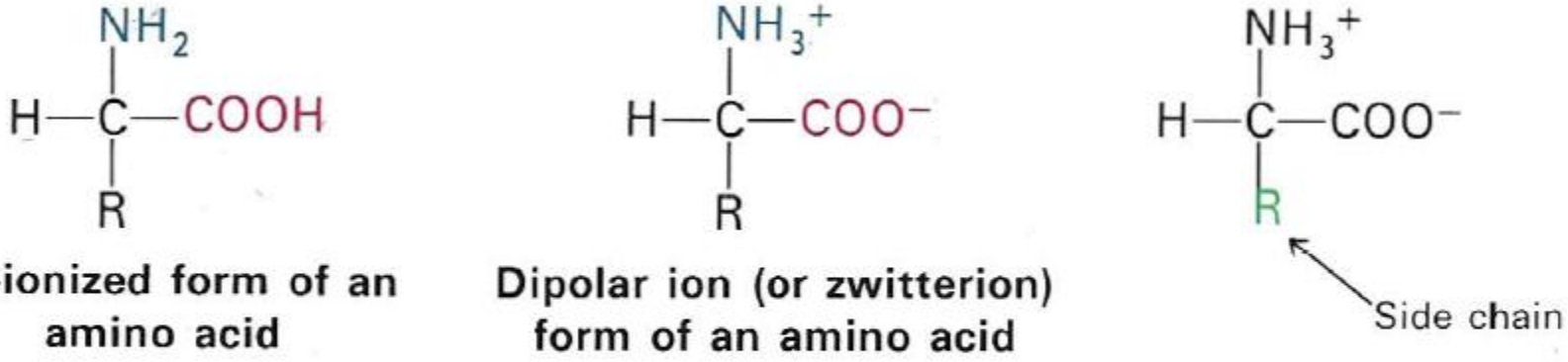




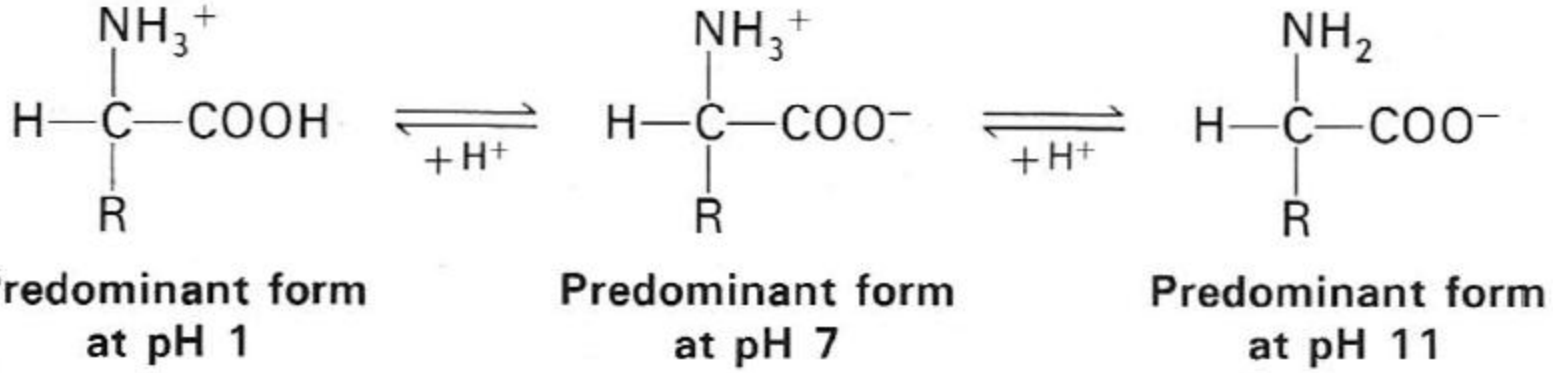
Representação da ionização do aminoácido alanina, em função do pH. Note-se que a um determinado pH (ponto isoeléctrico), o aminoácido apresenta simultaneamente carga positiva e negativa, forma que é designada por zwitter-ião.

L-Alanina

- Forma ionizada em solução
- Zwitter-ião (do Alemão *Zwitter* = hibrido)
- Ponto isoelétrico (pI)
- Aminoácidos são substâncias anfotéricas



Structure of the un-ionized and zwitterion forms of an amino acid.

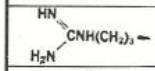
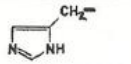
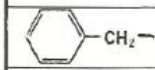
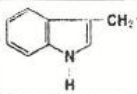
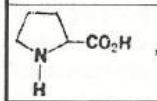
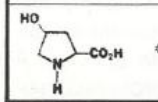


Ionization states of an amino acid as a function of pH.

Tabela com os pontos isoeléctricos dos aminoácidos proteicos

Tabela

Algumas propriedades e radical R dos aminoácidos constituintes das proteínas

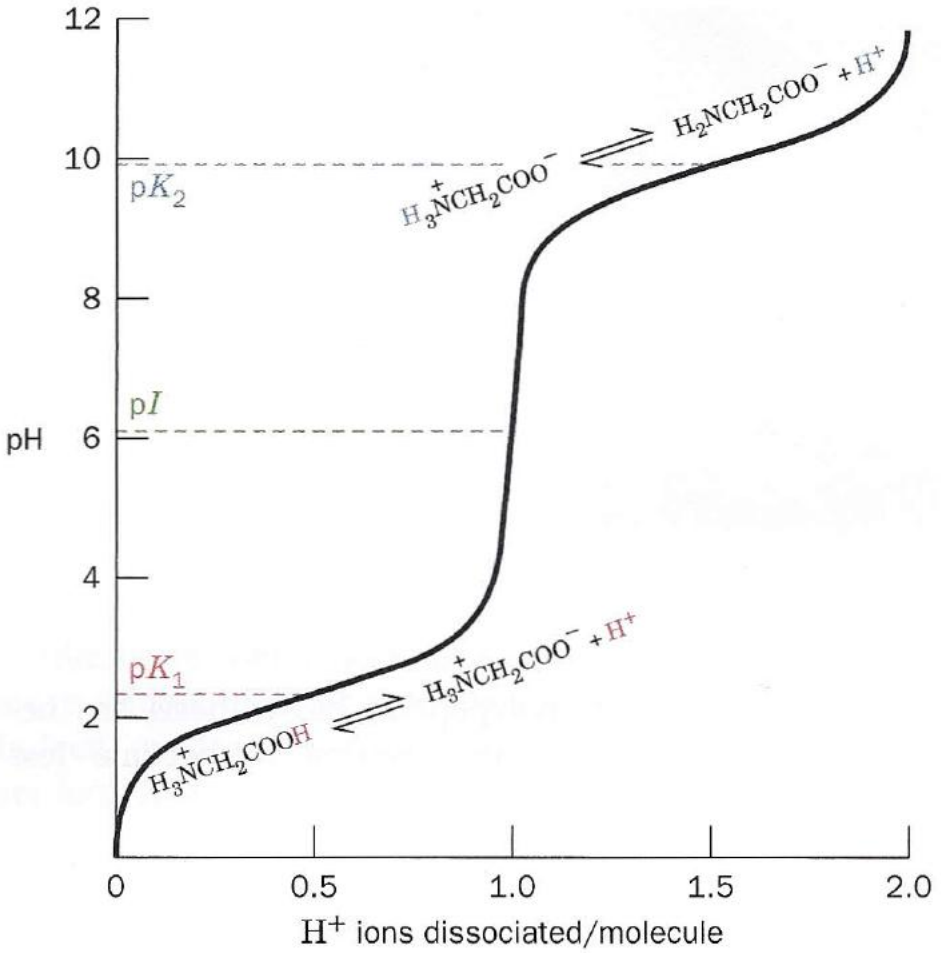
Radical R	Aminoácido e sua abreviatura	*** pI	Características
H-	Glicina (Gly)	5,97	Apolares
H_3C-	Alanina (Ala)	6,00	
$(H_3C)_2CH$-	Valina (Val)* (1,6)	5,96	Hidrofóbicos (com afinidade para as gorduras, solventes orgânicos, detergentes, etc.)
$(H_3C)_2CHCH_2$-	Leucina (Leu)* (2,2)	5,98	
$H_3CCH_2CH(CH_3)$-	Isoleucina (Ile)* (1,4)	6,02	
$HOCH_2$-	Serina (Ser)	5,68	Hidrofílico. Ocorre no centro activo de muitas enzimas
$(H_3C)CHOH$-	Treonina (Thr)* (1,0)	5,60	Hidrofílico
$HOOCCH_2$-	Ac. aspártico (Asp)	2,77	Hidrofílicos; de natureza acídica
$HOOCCH_2CH_2$-	Ac. glutâmico (Glu)	3,22	
H_2NCOCH_2-	Asparagina (Asn)	5,41	De natureza amídica
$H_2NCOCH_2CH_2$-	Glutamina (Gln)	5,65	
$H_2N(CH_2)_3CH_2$-	Lisina (Lys)* (1,6)	9,74	Hidrofílico; de natureza básica
	Arginina (Arg) *	10,76	Hidrofílico; fortemente básico
	Histidina (His) *	7,59	Fracamente básico; importante para a actividade catalítica de muitas enzimas
	Fenilalanina (Phe)* (2,2)	5,48	Hidrofóbico; de natureza aromática
	Tirosina (Tyr)	5,66	Aromáticos, sendo a tirosina de natureza fenólica. Absorvem radiação ultravioleta, com picos máximos entre 275 e 285 nm.
	Triptofano (Trp)* (0,5)	5,89	
$HSCH_2$-	Cisteína (Cys)	5,07	Oxidável; forma ligações covalentes —S—S— com outra cisteína; importante para a actividade catalítica das enzimas
$H_3CSCH_2CH_2$-	Metionina (Met)* (2,2)	5,74	Sulfurado; oxidável
 **	Prolina (Pro)	6,30	Por vezes designados iminoácidos, por o radical R formar um anel com o NH_2, deixando livre apenas um NH; a ligação peptídica que formam é mais rígida do que aquela originada entre os outros aminoácidos
 **	Hidroxiprolina (Hyp)	5,80	

* Aminoácidos não sintetizáveis pelo organismo humano, designados por aminoácidos essenciais; entre parênteses indicam-se as quantidades, em gramas, necessárias por dia.

** Fórmula completa do aminoácido.

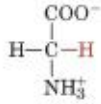
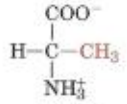
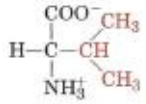
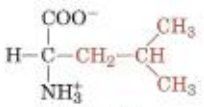
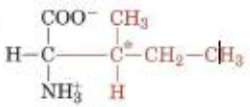
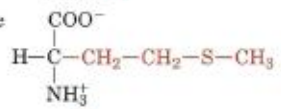
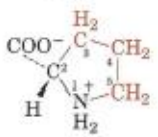
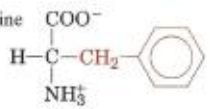
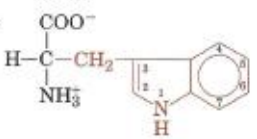
*** pI= ponto isoeléctrico.

Curva de titulação do aminoácido glicina



Titration curve of glycine. Other monoamino, monocarboxylic acids ionize in a similar fashion. [After Meister, A., *Biochemistry of the Amino Acids* (2nd ed.), Vol. 1, *p.* 30, Academic Press (1965).]

Covalent Structures and Abbreviations of the "Standard" Amino Acids of Proteins, Their Occurrence, and the p*K* Values of Their Ionizable Groups

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]
Amino acids with nonpolar side chains						
Glycine Gly G		57.0	6.8	2.35	9.78	
Alanine Ala A		71.1	7.6	2.35	9.87	
Valine Val V		99.1	6.6	2.29	9.74	
Leucine Leu L		113.2	9.5	2.33	9.74	
Isoleucine Ile I		113.2	5.8	2.32	9.76	
Methionine Met M		131.2	2.4	2.13	9.28	
Proline Pro P		97.1	5.0	1.95	10.64	
Phenylalanine Phe F		147.2	4.1	2.20	9.31	
Tryptophan Trp W		186.2	1.2	2.46	9.41	

(*continued*)

[a]The ionic forms shown are those predominating at pH 7.0 (except for that of histidine[e]), although residue mass is given for the neutral compound. The C_α atoms, as well as those atoms marked with an asterisk, are chiral centers with configurations as indicated according to Fischer projection formulas. The standard organic numbering system is provided for heterocycles.

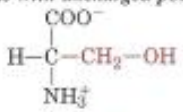
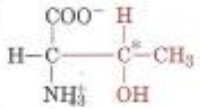
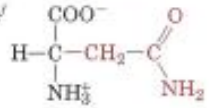
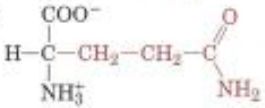
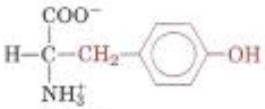
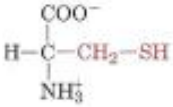
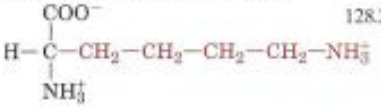
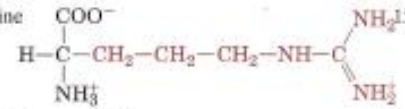
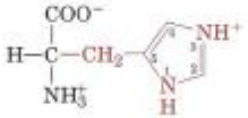
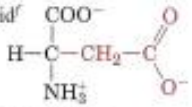
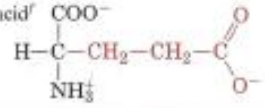
[b]The residue masses are given for the neutral residues. For molecular masses of the parent amino acids, add 18.0 Da, the molecular mass of H_20, to the residue masses. For side chain masses, subtract 56.0 Da, the formula mass of a peptide group, from the residue masses.

[c]The average amino acid composition in the complete SWISS-PROT data base (http://www.expasy.ch/sprot). Release 40.7.

[d]From Dawson, R.M.e., Elliott, D.e., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), *pp.* 1-31, Oxford Science Publications (1986).

[e]Both the neutral and protonated forms of histidine are present at pH 7.0 because its pK_R is dose to 7.0. The imidazole ring of histidine is numbered here according to the biochemistry convention. In the IUPAC convention, N3 of the biochemistry convention is designated N1 and the numbering increases clockwise around the ring.

[f]The three- and one-letter symbols for asparagine *or* aspartic acid are Asx and B, whereas for glutamine *or* glutamic acid they are Glx and Z. The one-letter symbol for an undetermined or "nonstandard" amino acid is X.

Name Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]
Amino acids with uncharged polar side chains						
Serine Ser S		87.1	7.1	2.19	9.21	
Threonine Thr T		101.1	5.6	2.09	9.10	
Asparagine[e] Asn N		114.1	4.3	2.14	8.72	
Glutamine[e] Gln Q		128.1	3.9	2.17	9.13	
Tyrosine Tyr Y		163.2	3.2	2.20	9.21	10.46 (phenol)
Cysteine Cys C		103.1	1.6	1.92	10.70	8.37 (sulfhydryl)
Amino acids with charged polar side chains						
Lysine Lys K		128.2	6.0	2.16	9.06	10.54 (ε-NH_3^+)
Arginine Arg R		156.2	5.2	1.82	8.99	12.48 (guanidino)
Histidine[e] His H		137.1	2.2	1.80	9.33	6.04 (imidazole)
Aspartic acid[e] Asp D		115.1	5.2	1.99	9.90	3.90 (β-COOH)
Glutamic acid[e] Glu E		129.1	6.5	2.10	9.47	4.07 (γ-COOH)

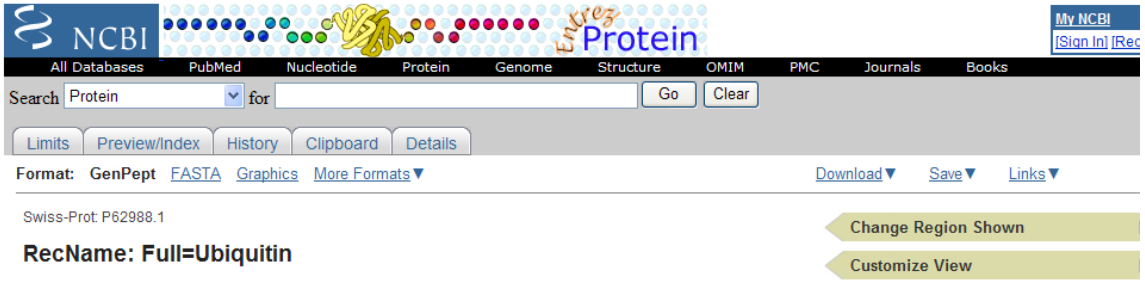
Aminoácidos proteicos

Questões:

1 – Se ingerirmos um aminoácido proteico, ele poderá ser incorporado numa das nossas proteínas?

2 – Qualquer uma?

3 – E se se tratar do aminoácido cisteína (símbolos: Cys e C) e da proteína ubiquitina (ver diapositivo seguinte)?



Human ubiquitin

Amino acid residue sequence:

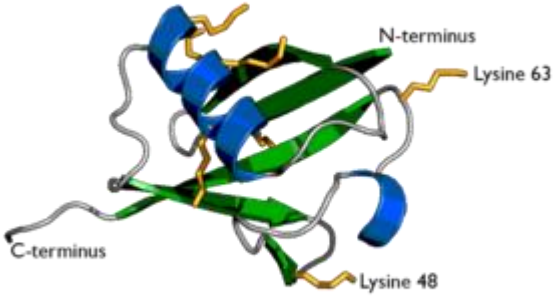
1 MQIFVKTLTG KTITLEVEPS DTIENVKAKI QDKEGIPPDQ *
41 QRLIFAGKQL EDGRTLSDYN IQKESTLHLV LRLRGG

Source:
ORGANISM Homo sapiens Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.

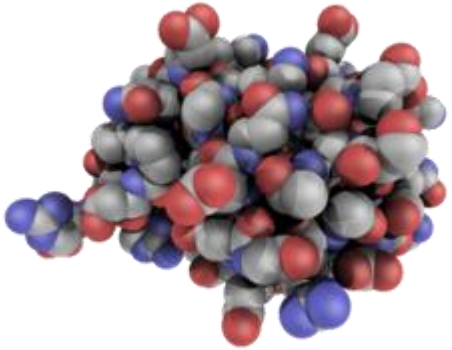
*Ver diapositivo seguinte

Ubiquitin properties (human)

- Number of residues: 76
- Molecular mass: 8564.47 Da*
- Isoelectric point (pI): 6.79



A diagram of ubiquitin. The seven lysine sidechains are shown in orange.



A space-filling model of ubiquitin, shown in the same orientation as the diagram above.

Table
Abbreviations for amino acids

Amino acid	*Three-letter abbreviation*	*One-letter symbol*
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Asparagine or aspartic acid	Asx	B
Cysteine	Cys	C
Glutamine	Gln	Q
Glutamic acid	Glu	E
Glutamine or glutamic acid	Glx	Z
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

Dalton—
A unit of mass very nearly equal to that of a hydrogen atom (precisely equal to 1.0000 on the atomic mass scale).
The terms "dalton" and "molecular weight" are used interchangeably; for example, a 20,000-dalton protein has a molecular weight of 20,000.
Named after John Dalton (1766–1844), who developed the atomic theory of matter.

Kilodalton (kdal)—
A unit of mass equal to 1000 daltons. Most proteins have a mass of between 10 and 100 kdal.

Aminoácidos raros das proteínas

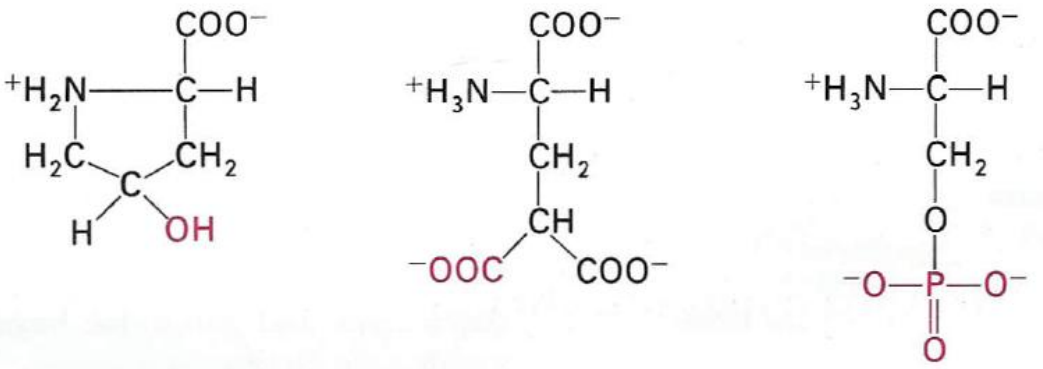
Aminoácidos raros das proteínas

Definição

São aminoácidos que ocorrem ocasionalmente na constituição das proteínas e que não se encontram codificados no código genético.

Questão:
Se não se encontram codificados no código genético, como aparecem os aminoácidos raros das proteínas na constituição destas?

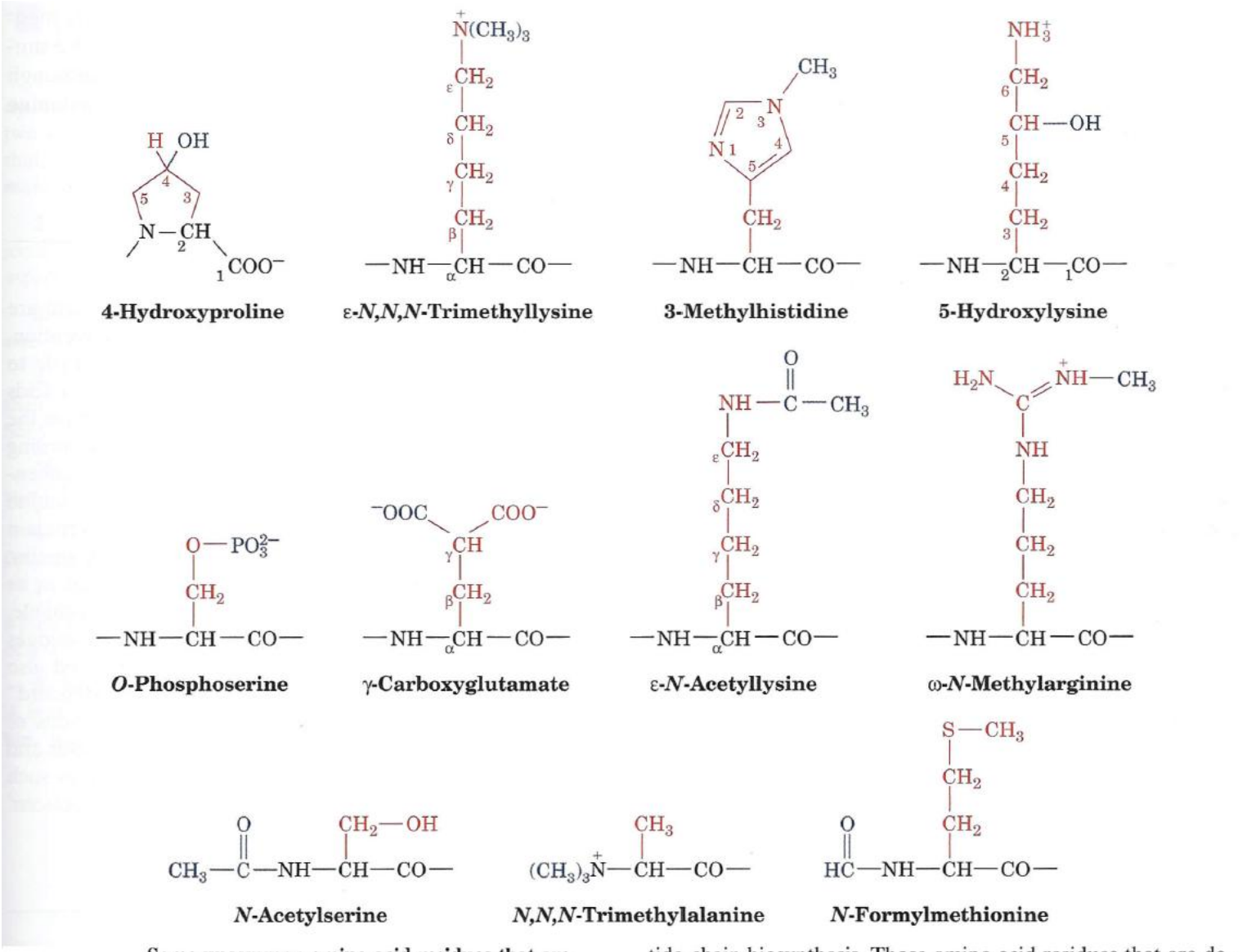
Exemplos de aminoácidos raros das proteínas



Hydroxyproline **γ-Carboxyglutamate** ***O*-Phosphoserine**

Some modified amino acid residues in proteins: hydroxyproline, γ-carboxyglutamate, and phosphoserine. Groups added after the polypeptide chain is synthesized are shown in red.

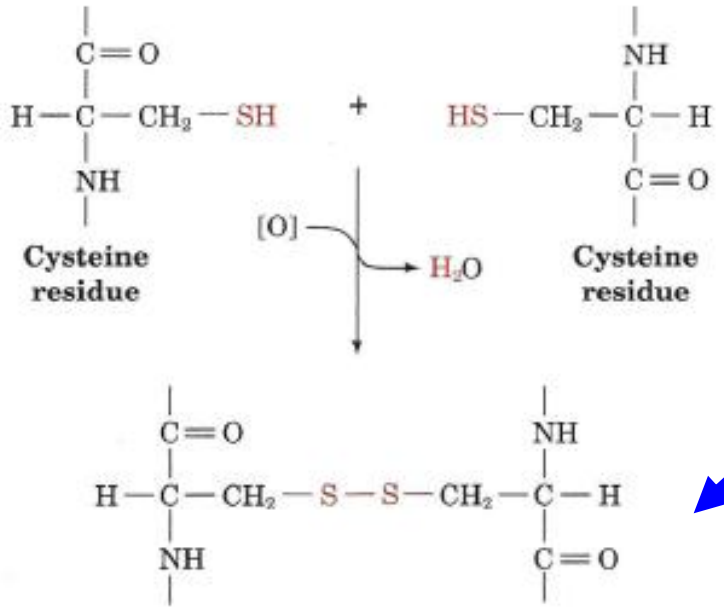
Exemplos de resíduos de aminoácidos raros das proteínas



Some uncommon amino acid residues that are components of certain proteins. All of these residues are modified from one of the 20 "standard" amino acids after polypeptide chain biosynthesis. Those amino acid residues that are derivatized at their N_α position occur at the N-termini of proteins.

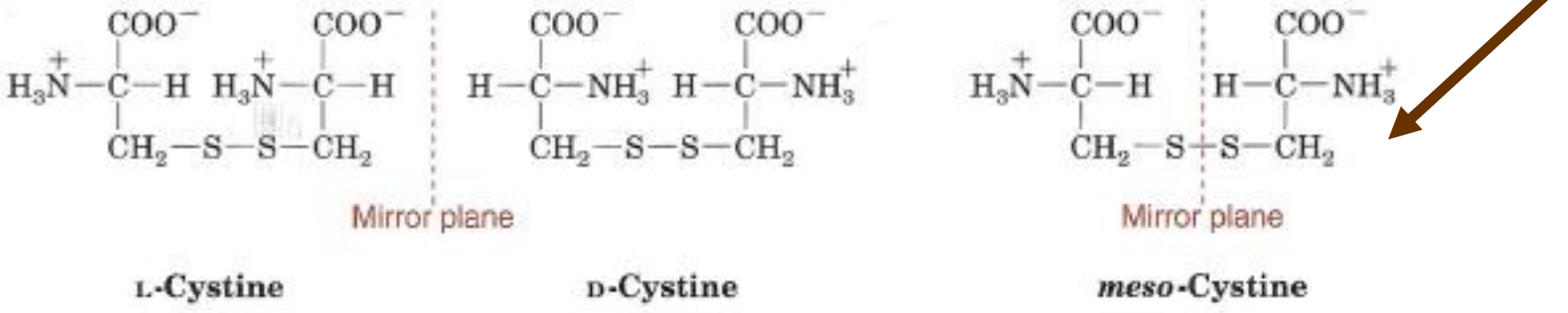
Cistina, um importante aminoácido raro das proteínas

Cysteine is a thiol that is unique among the 22 amino acids in that it often forms a disulfide bond to another cysteine residue through the oxidation of their sulphydryl groups. This dimeric compound is referred to in the older biochemical literature as the amino acid cystine. The disulfide bond has great importance in protein structure: It can join separate polypeptide chains or cross-link two cysteines in the same chain. The confusing similarity between the names cysteine and cystine has led to the former occasionally being referred to as a half-cystine residue. However, the realization that cystine arises through the cross-linking of two cysteine residues after polypeptide biosynthesis has occurred has caused the name cystine to become less commonly used.

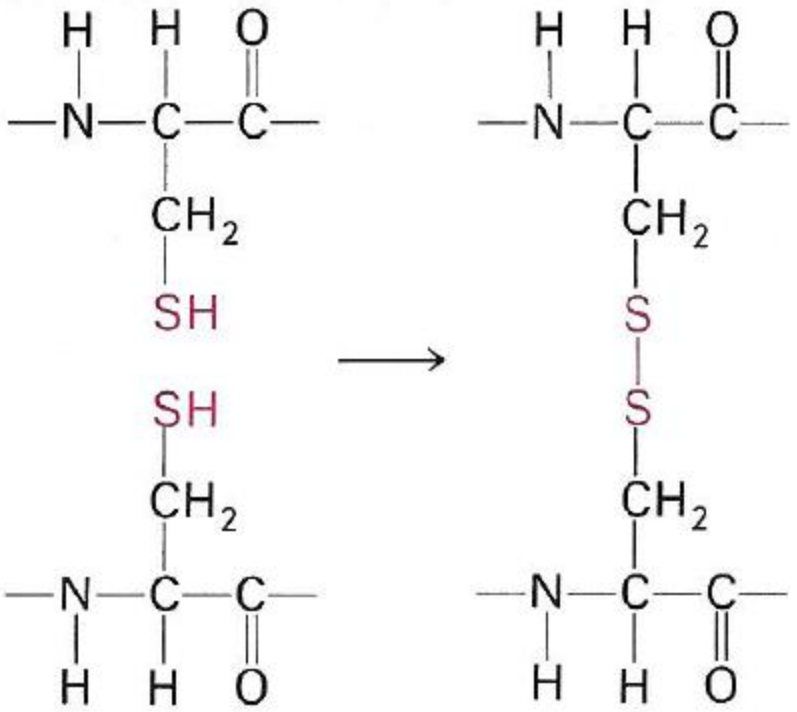


Structure of cystine. The cystine residue consists of two disulfide-linked cysteine residues.

A special case of diastereoisomerism occurs when the two asymmetric centers are chemically identical. This is because ***the two asymmetric centers in this molecule are mirror images of each other. Such a molecule is superimposible on its mirror image and is therefore optically inactive***. This so-called *meso* form is said to be internally compensated. The three optical isomers of cystine are shown, where it can be seen that the D and L isomers are mirror images of each other as before. Only L-cystine occurs in proteins.



The three stereoisomers of cystine. The D and L forms are related by mirror symmetry, whereas the *meso* form has internal mirror symmetry and therefore lacks optical activity.



A disulfide bridge (—S—S—) is formed from the sulfhydryl groups (—SH) of two cysteine residues. The product is a *cystine* residue.

Como se forma a cistina nas proteínas?

- Por oxidação espontânea de dois resíduos de cisteína
- Numa reacção catalisada por uma enzima: a proteína dissulfeto isomerase (PDI).

A hidroxiprolina e a hidroxilisina do colagénio

O **colagénio**, por exemplo, contém, na sua constituição, resíduos de hidroxiprolina e de hidroxilisina.

Papel do ácido L-ascórbico a nível da síntese do colagénio e sua relação com o escorbuto

O colagénio (do Grego kolla = cola) ocorre em todos os organismos multicelulares e é a proteína mais abundante dos animais vertebrados. É responsável pela grande resistência dos tecidos conjuntivos, como ossos, dentes, cartilagens, tendões, ligamentos e matrizes fibrosas da pele e vasos sanguíneos.

Os mamíferos têm 20 tipos diferentes de colagénio que ocorrem no mesmo indivíduo, formados a partir de 33 polipéptidos geneticamente distintos.

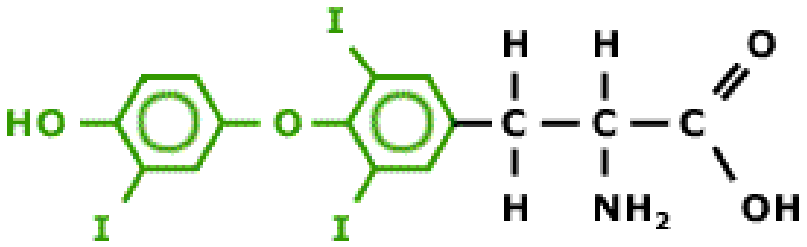
O colagénio tem uma composição em aminoácidos muito particular: cerca de um terço dos seus resíduos são de glicina e 15 a 30% são de prolina e de hidroxiprolina. A prolina é um aminoácido proteico, ao passo que a hidroxiprolina é um aminoácido raro das proteínas. Se fornecermos hidroxiprolina radioactiva a um rato, o colagénio deste não fica radioactivo. Ficará sim se lhe administrarmos prolina radioactiva. Primeiro são introduzidos resíduos de prolina nas cadeias polipéptídicas do colagénio, durante a síntese proteica. Depois, uma enzima, a prolil-hidroxilase, que requer a presença de ácido L-ascórbico (vitamina C) para a sua actividade catalítica, converte resíduos de prolina em resíduos de hidroxiprolina.

O colagénio normal desnatura, pelo calor, a 39 ºC, convertendo-se em gelatina. Sem resíduos de hidroxiprolina, como acontece na ausência de ácido L-ascórbico, o colagénio desnatura a 24 ºC.

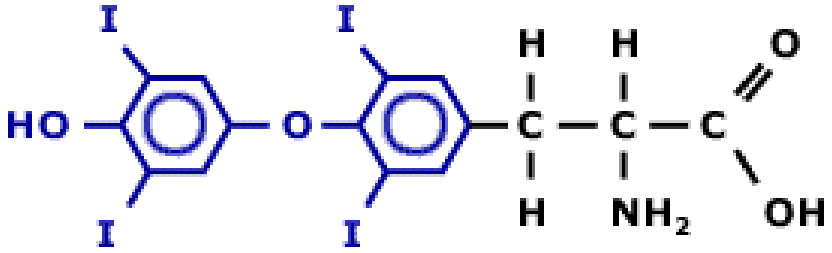
O escorbuto, que resulta de uma deficiência de vitamina C, é provocado por uma estrutura deficiente do colagénio, de que resultam lesões na pele, fragilidade dos vasos sanguíneos e dificuldade na cicatrização de feridas.

O “estranho” mecanismo de síntese das duas hormonas da tiróide, tiroxina e tri-iodotironina

A tiroxina, ou 3,5,3’,5’-tetraiodotironina (T4) e a tri-iodotironina (T3) são hormonas da tiróide e as duas únicas moléculas biológicas conhecidas contendo iodo. São aminoácidos raros das proteínas, com um mecanismo de síntese particular.



3', 3, 5-triiodothyronine
T3



3', 5', 3, 5-tetraiodothyronine
thyroxine, T4

A tiroglobulina (Tg) é uma proteína dimérica de 660 kDa, inteiramente produzida e utilizada na glândula tiróide.

Tg is produced by the thyroid epithelial cells, called thyrocytes, which form spherical follicles. Tg is secreted and stored in the follicular lumen.
Via a reaction with the enzyme thyroperoxidase, iodine is covalently bound to tyrosine residues in thyroglobulin molecules, forming monoiodotyrosine (MIT) and diiodotyrosine (DIT).
Thyroxine is produced by combining two moieites of DIT.
Triiodothyronine is produced by combining one molecule of MIT and one molecule of DIT.
Small globules of the follicular colloid are endocytosed (hormone (TSH)-mediated) and proteases in lysosomes digest iodinated thyroglobulin, releasing T3 and T4. The T3 and T4 are then transported across (TSH-mediated) the basolateral thyrocyte membrane by an unknown mechanism while the lysosome is recycled back to the follicular lumen.

Aminoácidos raros das proteínas

Questões:

O colagénio possui alguns resíduos de aminoácidos raros das proteínas na sua constituição, designadamente a hidroxiprolina (símbolo Hyp) e a hidroxilisina.

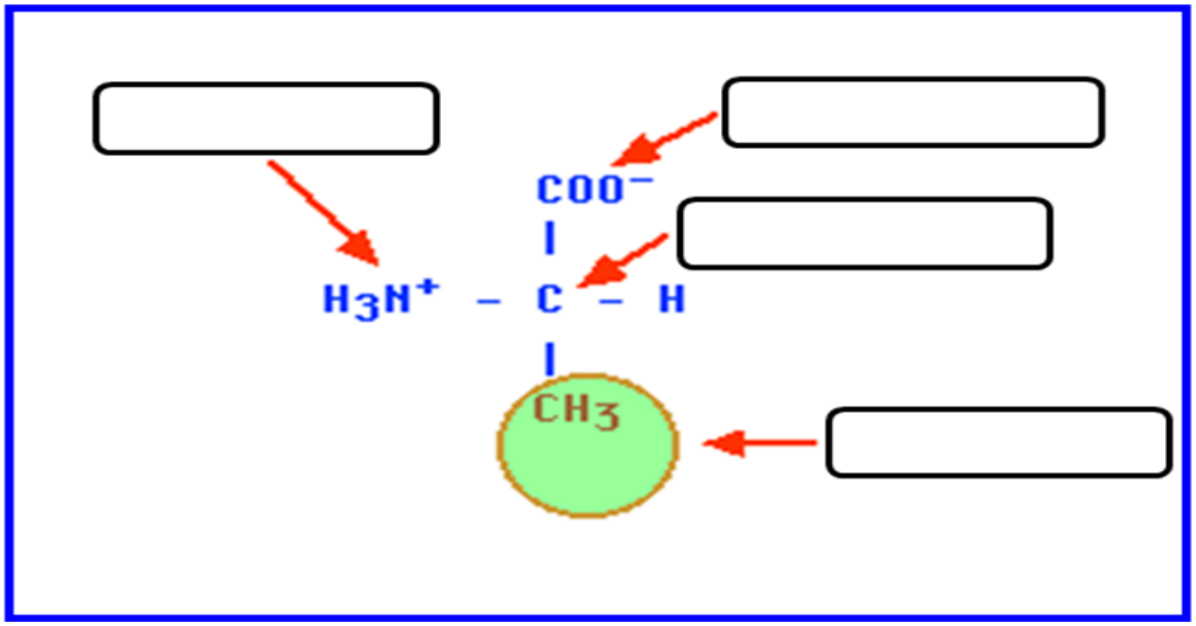
1 – Se ingerirmos hidroxiprolina marcada radioactivamente com ^{14}C (a fim de podermos seguir, teoricamente, o seu percurso no nosso organismo), ela poderá ser incorporada no nosso colagénio?

2 – Porquê?

3 – Em caso negativo, como poderemos obter colagénio com ^{14}C-hidroxiprolina?

4 - Consider o L-α-aminoácido L-alanina:

a) Complete a figura preenchendo os quatro campos em branco:



b) Quais as duas abreviaturas utilizadas comummente para esta aminoácido?

c) Defina ponto isoeléctrico da L-alanina e escreva a sua abreviatura.

d) Sabendo que o ponto isoeléctrico da L-alanina é 6,0, escreva a estrutura da forma predominante em que este aminoácido ocorre a pH 2,0, a pH 6,0 e a pH 9,5.

e) Como classifica a L-alanina em termos de ser essencial, semi-essencial ou não-essencial para o homem? Justifique.

f) Escreva a fórmula da β-alanina.

g) Como classifica a β-alanina em termos de ser um aminoácido proteico, raro ou não-proteico? Justifique.

h) Indique uma função biológica importante para cada um destes aminoácidos.

Aminoácidos não-proteicos (aanp)

Aminoácidos não-proteicos

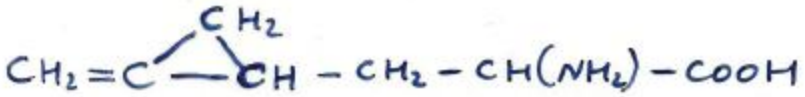
Definição

São aminoácidos que ocorrem naturalmente na forma livre ou combinada, mas não na constituição de proteínas.

Exemplos de aminoácidos não-proteicos (aanp)

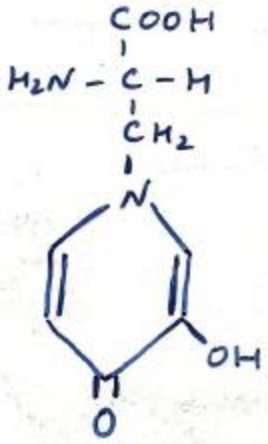
Alguns aanp foram identificados na sequência de estudos onde se procuravam identificar os componentes tóxicos de plantas reconhecidas como venenosas:

- Hipoglicinas A e B, presentes nos frutos não-maduros da *Blighia sapida*



hipoglicina A
3-(metilenociclopropil) alanina

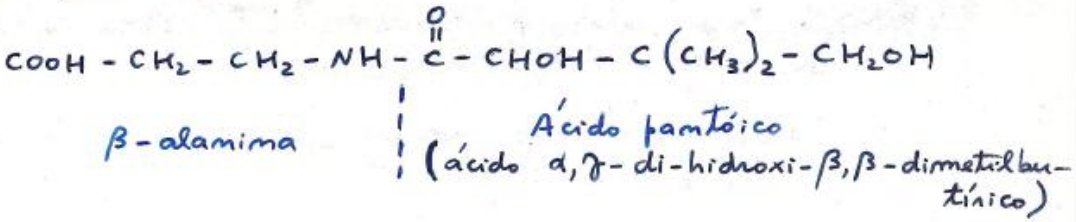
- Mimosina, presente nas folhas e sementes da leguminosa *Leucaena leucocephala*



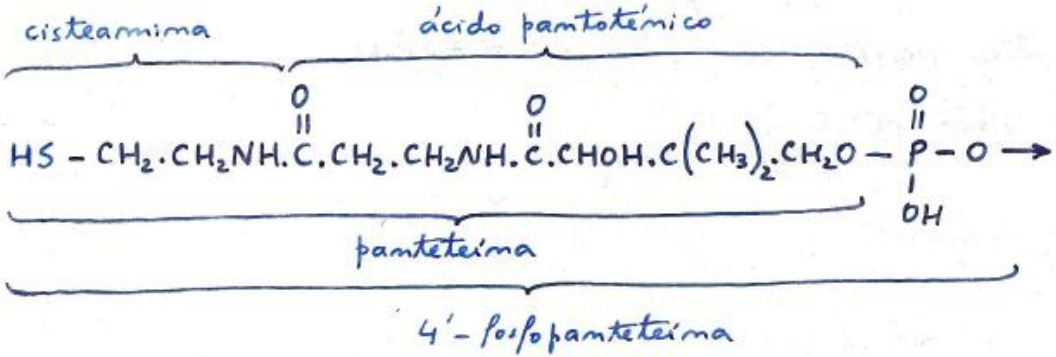
mimosina

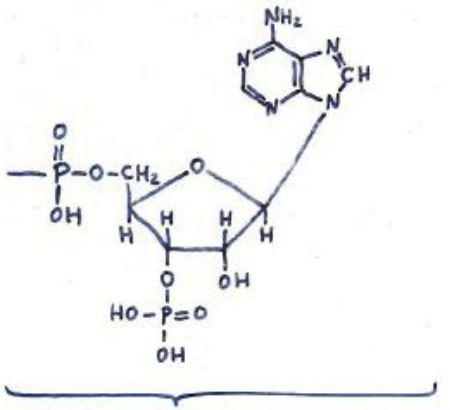
(A)

Ácido pantoténico



Coenzima A (CoA)





(B) Péptidos responsáveis pela toxicidade de certas espécies de cogumelos do género Amanita

- Faloidinas : heptapéptidos cíclicos formados por Cys, Ala, hidroxileucina e allo-hidroxiprolina.
- Amanitinas : octapéptidos cíclicos formados por Leu, Leu, Ile, di-hidroxi Ile, Asn, hidroxiprolina, Trp e Cys.

(C) Outros péptidos contendo aminoácidos não-proteicos

- Ácido oftálmico:
  Glu - ácido α-aminobutírico - Gly
- Carnosina
  β-alanina - His
- Anserina
  metil - carnosina

$H_2N(CH_2)_2COOH$

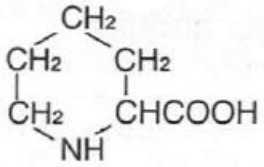
β -alanina

$H_2N(CH_2)_3COOH$

ácido
γ -aminobutírico

$H_2N(CH_2)_3CH(NH_2)COOH$

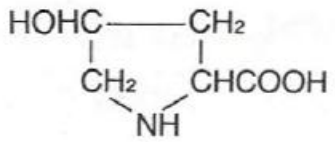
ornitina
(ácido α, δ -diaminovalérico)



ácido pipecólico

$HO_3S(CH_2)_2NH_2$

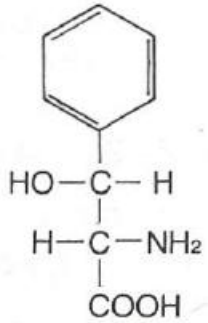
taurina



alo-4 hidroxiprolina

$H_2NCONH(CH_2)_3CH(NH_2)COOH$

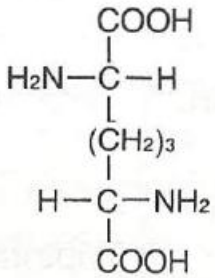
citrulina



fenilsserina

$HS(CH_2)_2CH(NH_2)COOH$

homocisteína



ácido
α, ε -diaminopimélico

$HO(CH_2)_2CH(NH_2)COOH$

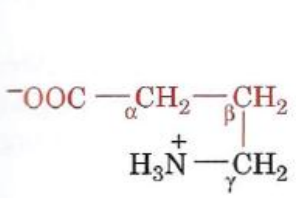
homosserina

Fórmulas de alguns aminoácidos não constituintes de proteínas.

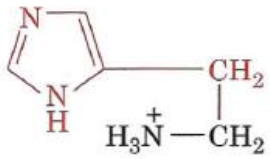
Um isómero da alanina, a **β-alanina**, é o único aminoácido β que ocorre naturalmente nos seres vivos. Além de ocorrer na forma livre, por exemplo no sistema nervoso, a β-alanina é um constituinte da vitamina ácido pantoténico e da coenzima A. O **ácido γ-aminobutírico** (formado por descarboxilação do ácido glutâmico) é um mediador químico da transmissão de impulsos nervosos, mas também se encontra nas plantas. O **ácido α,γ-diaminobutírico** está presente em certo número de sementes em germinação, podendo aí actuar como reserva de azoto amínico. A este respeito convém referir que os aminoácidos constituintes das proteínas, glutamina e asparagina, também ocorrem em concentrações apreciáveis, na forma livre, principalmente nas plantas, onde exercem função de reserva de azoto.

Tanto a **ornitina** (Orn) como a **citrulina** são compostos intermediários na formação da ureia (ciclo da ureia), importante produto de excreção de alguns anírnais. Nas plantas, o ciclo da ureia não parece ser funcional, no entanto qualquer destes dois aminoácidos é frequente em diversas espécies vegetais. A citrulina foi mesmo descoberta pela primeira vez na melância (*Citrullus lanatus*), de onde deriva o seu nome, e tem sido encontrada na seiva de muitas árvores. A ornitina é, por outro lado, um constituinte de antibióticos peptídicos. O **ácido pipecólico** é formado a partir da lisina, tendo grande distribuição nas plantas, particularmente nas leguminosas, onde se encontra em concentrações apreciáveis.

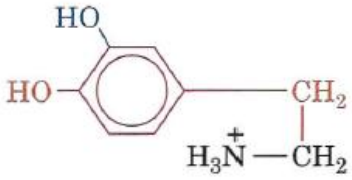
Tanto a **homocisteína** como a **homosserina** são precursores de aminoácidos constituintes de proteínas, respectivamente da metionina e da treonina. A homosserina é produzida em quantidades elevadas pelas raízes de ervilheira. A **taurina**, que possui um grupo sulfato e é desprovida de carboxilo, pois resulta da descarboxilação do ácido cisteínico, é um constituinte da bílis. A ***allo*-4–hidroxiprolina** é o princípio tóxico do cogumelo *Amanita phaloides.* Certas estirpes de *Streptomyces* produzem derivados da serina, com acção antibiótica. Os mais bem conhecidos são a **azasserina** e a **ciclosserina**. Outro antibiótico, o **D**-cloranfenicol, é relacionado com o aminoácido **fenilsserina**, sendo uma substância bastante pouco usual entre os compostos naturais, pelo facto de conter um grupo NO_2 e átomos de cloro. Muitos outros aminoácidos podiam ser citados. As paredes celulares das bactérias são particularmente abundantes em aminoácidos da série **D**, como o **ácido D-glutâmico**, a D-glutamina e a D-alanina. Também frequente nas paredes celulares das bactérias é o **ácido α,ξ-diaminopimélico**.



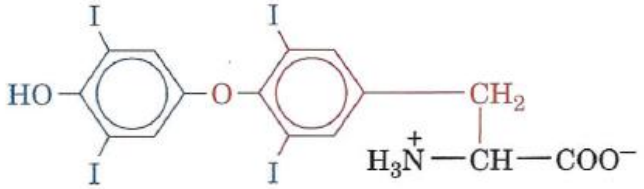
γ-Aminobutyric acid (GABA)



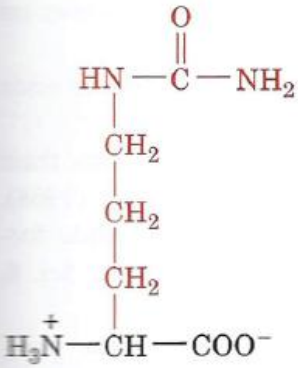
Histamine



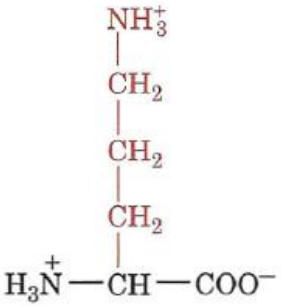
Dopamine



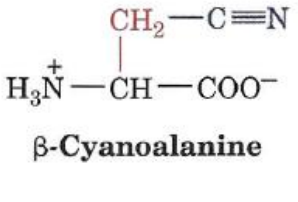
Thyroxine



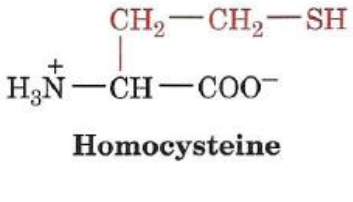
Citrulline



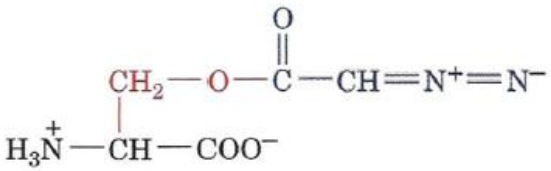
Ornithine



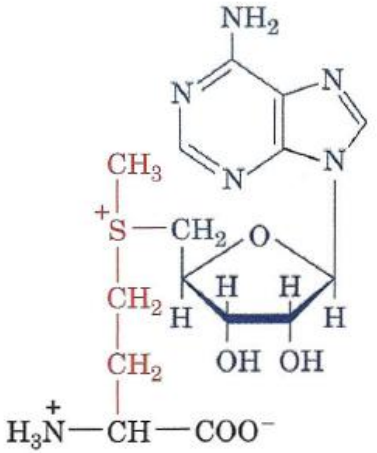
β-Cyanoalanine



Homocysteine



Azaserine



S-Adenosylmethionine

Some biologically produced derivatives of "standard" amino acids and amino acids that are not components of proteins.

Funções biológicas dos aanp:

- São mal conhecidas na maioria dos casos;

- Intermediários da biossíntese de aminoácidos proteicos;
- Intermediários da biossíntese de outros compostos biológicos;
- Reserva;
- Defesa.

Classificação dos aminoácidos não-proteicos

- Com base na sua distribuição em espécies, géneros ou famílias de plantas
  - aminoácidos não-proteicos do género Acacia
  - aminoácidos não-proteicos da família das sapindáceas
  - etc.

- Com base na estrutura da cadeia lateral R
  - aa alifáticos lineares

$CH_3-CH_2-CH(NH_2)-COOH$ ácido α-aminobutírico

$CH_3-(CH_2)_5-CH(NH_2)-COOH$ ácido α-aminooctamóico

  - aa ramificados

$CH_3-CH_2-CH(CH_3)-CH_2-CH(NH_2)-COOH$ homoisoleucina

  - hidroxi aa

$CH_3-CH(OH)-CH(CH_3)-CH(NH_2)-COOH$ γ-hidroxi-isoleucina

$CH_3-CH(OH)-CH_2-CH(NH_2)-COOH$ γ-hidroxinorvalina

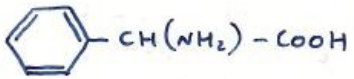
  - aa contendo S ou Se

$COOH-CH(NH_2)-(CH_2)_2-S-CH_2-CH(NH_2)-COOH$ cistationina

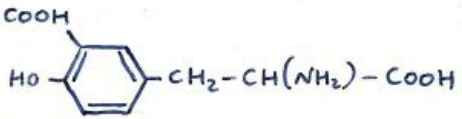
$COOH-CH(NH_2)-CH_2-S-CH_2-S-CH_2-CH(NH_2)-COOH$ ácido djencólico

$CH_3-Se-CH_2-CH(NH_2)-COOH$ Selenometionina

  - aa aromáticos

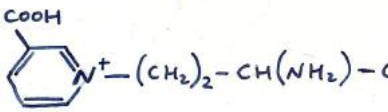


fenilglicina

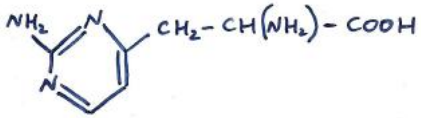


3-carboxitirosina

- aa heterocíclicos



micotiamina



latirina

- aa básicos

$NH_2-C(=NH)-NH-O-(CH_2)_2-CH(NH_2)-COOH$ canavamina

$NH_2-CO-NH-(CH_2)_3-CH(NH_2)-COOH$ citrulina

$NH_2-CO-NH-CH_2-CH(NH_2)-COOH$ albizina

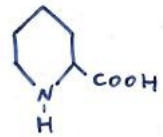
- aa acídicos e amidas

$COOH-(CH_2)_3-CH(NH_2)-COOH$ ácido 2-aminoadípico

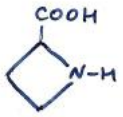
$COOH-(CH_2)_4-CH(NH_2)-COOH$ ácido 2-aminopimélico

$CH_3(NH)-CO-CH_2-CH(NH_2)COOH$ $\underline{N}^4$- metilasparagina

- imino ácidos



ácido pipecólico



ácido azetidina 2-carboxílico

- Outros aa

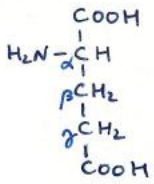
$COOH-CH(NH_2)-(CH_2)_4-NH-CH(COOH)-(CH_2)_2-COOH$ sacaropina

$NH_2-(CH_2)_4-CH(COOH)-NH-CH(CH_3)-COOH$ lisopina

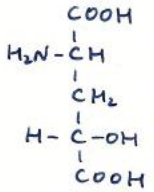
Aminoácidos alifáticos neutros

Ácido γ-aminobutírico $CH_2(NH_2).CH_2.CH_2.COOH$

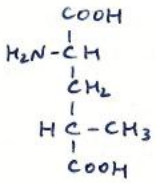
Aminoácidos acídicos e amidas



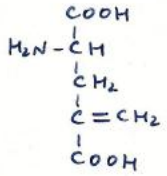
Glu
(ácido L-α-aminoglutárico)



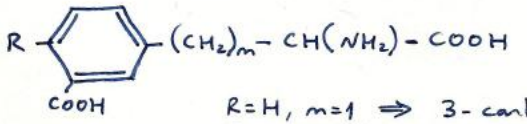
Ácido γ-hidroxiglutâmico
(isolado de Phlox decussata)



Ácido γ-metilglutâmico
(isolado de Phyllitis scolopendrium)



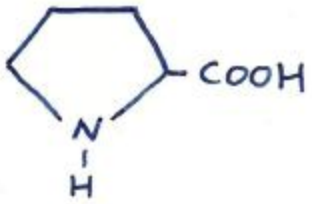
Ácido γ-metilenoglutâmico
(obtido de Anachis hypogea e Tulipa gesneriana; recentemente detectado em fetos e em fungos)



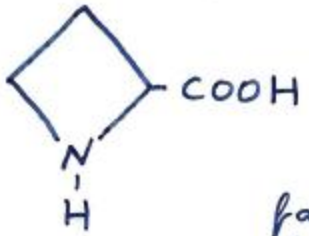
R=H, m=1 ⇒ 3-carboxifenilalamina
R=OH, m=1 ⇒ 3-carboxitirosina
R=H, m=0 ⇒ 3-carboxifenilglicina

Presentes nalgumas espécies das famílias das iridáceas e resedáceas.

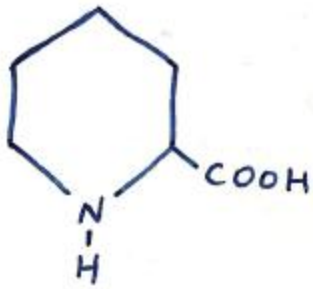
Iminoácidos



Pro
(ácido pirrolidina-2-carboxílico)

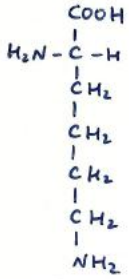


Ácido azetidina-2-carboxílico
(inicialmente isolado de espécies da família das liliáceas; é o composto solúvel de azoto predominante nos tecidos de Convallaria majalis e Polygonatum multiflorum; presente nas sementes e plântulas de algumas leguminosas e na beterraba sacarina).

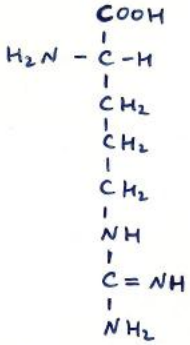


Ácido pipecólico
(presente em muitas plantas)
(ácido pipenidina-2-carboxílico)

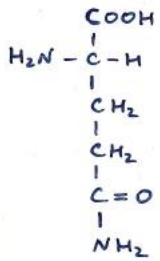
Aminoácidos básicos



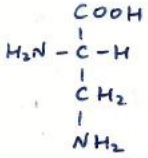
Lys
(ácido 2,6-diaminocapróico)



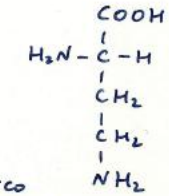
Arg
(ácido 2-amino-5-guanidovalérico)



Glm

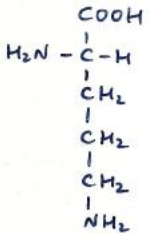


ácido α,β-diaminopropiónico

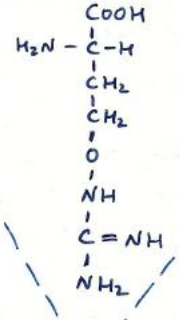


ácido α,γ-diaminobutírico

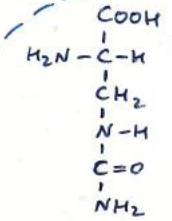
presente em sementes de alguns géneros de leguminosas (e.g., Acacia e Lathyrus).



Ornitina (Orn)
(ácido α,δ-diaminovalérico
ou
ácido 2,5-diaminopentanóico)
distribuição generalizada

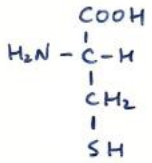


Canavamina
(ácido 2-amino-4-guanidimo-
-hidroxibutírico)
Detectado inicialmente em Canavalia ensiformis, ocorre em várias espécies de leguminosas.

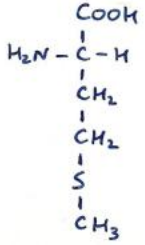


Albizina
(ácido 2-amino-3-
-ureidopropiónico)
Presente em espécies do género Albizzia

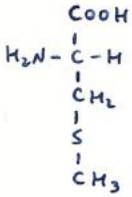
Aminoácidos contendo S ou Se



Cys
(ácido L-2-amino-3-mercaptopropiónico)

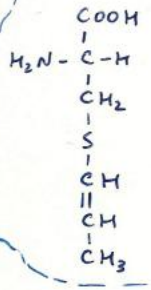


Met
(ácido α-amino-γ-metilmercaptobutírico)



S-metilcisteína

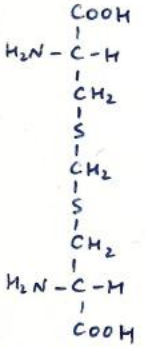
Presente nas sementes de espécies de vários géneros de leguminosas



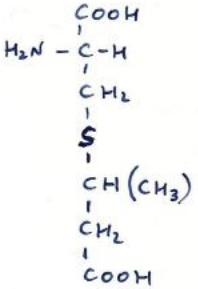
S-(propil-1-enil)-cisteína

Presente em espécies do género Allium

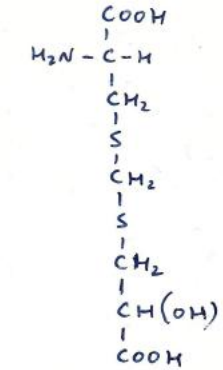
Aa não-proteicos contendo S presentes em espécies do género Acacia



ácido djencólico



S(2-carboxi-isopropil) cisteína

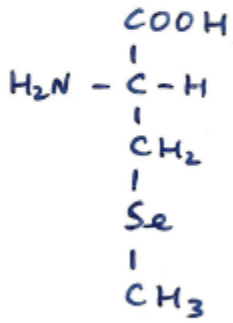


S-(2-hidroxi-2-carboxietatiometil) cisteína

ácido N-acetildjencólico

Aminoácidos contendo S ou Se (cont.)

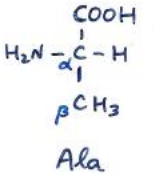
Aa não-proteicos contendo Se sintetizados nas espécies do género Astragalus acumuladoras de Se:



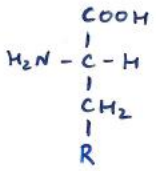
Se-metilselenocisteína

γ-glutamil-Se-metilselenocisteína

Alaminas β-substituídas



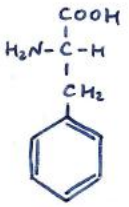
Ala
(ácido aminopropiónico)



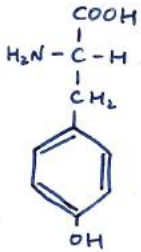
R =  fenil

R =  N ou outro

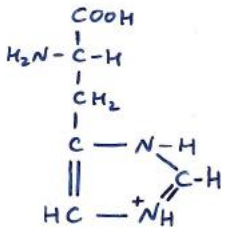
---



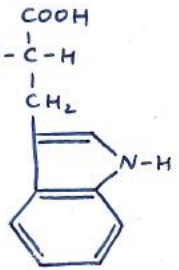
Phe
(ácido α-amino-β-fenilpropiónico)



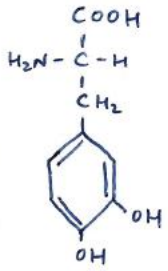
Tyr
(ácido α-amino-β-(p-hidroxi-fenil)-propiónico)



His
(imidazolilalamina)

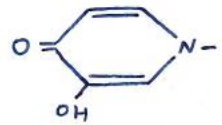


Trp
(ácido α-amino-β-indolepropiónico)

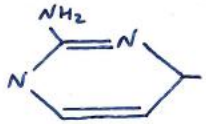


DOPA
(3,4-di-hidroxi-fenilalanina)
Ocorre no feijoeiro e nas sementes de espécies do género Mucuna

Alaminas β-substituídas heterocíclicas

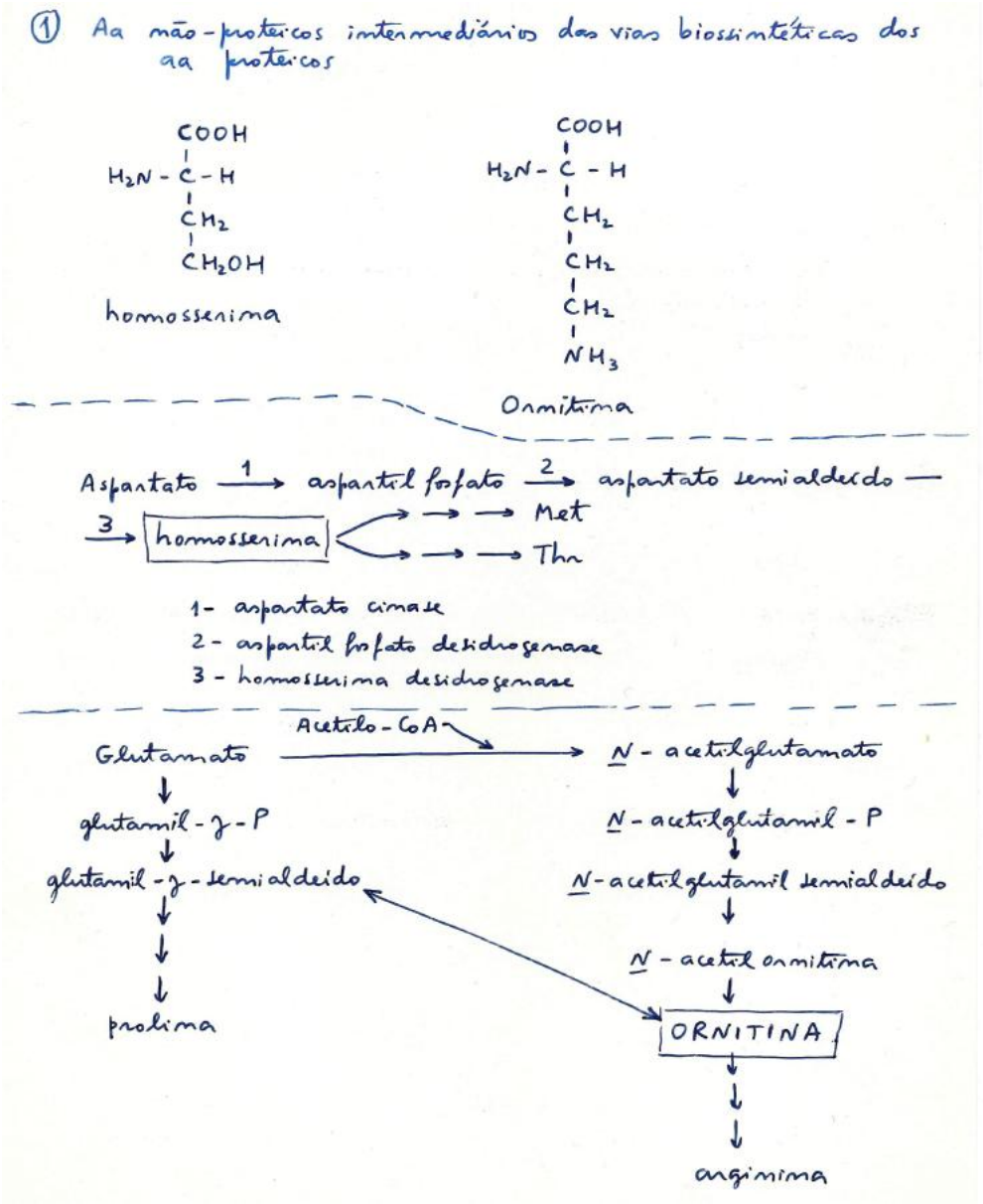
R = 

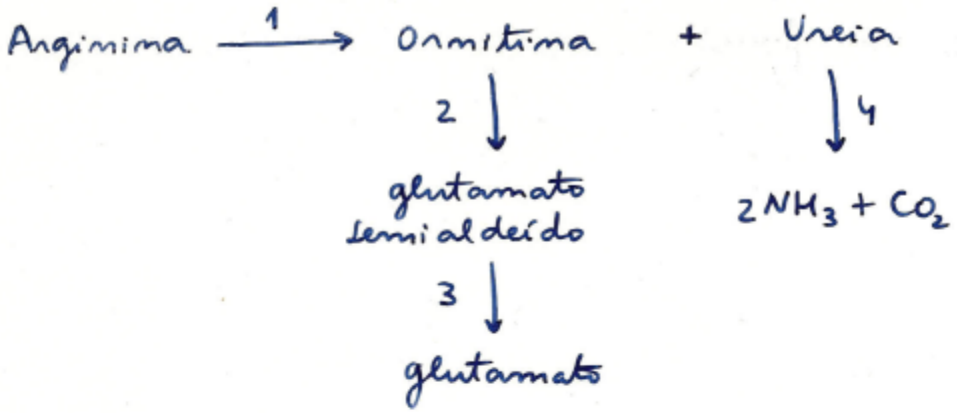
mimosina
presente em espécies dos géneros Mimosa e Leucaena

R = 

latirina
presente em espécies do género Lathyrus

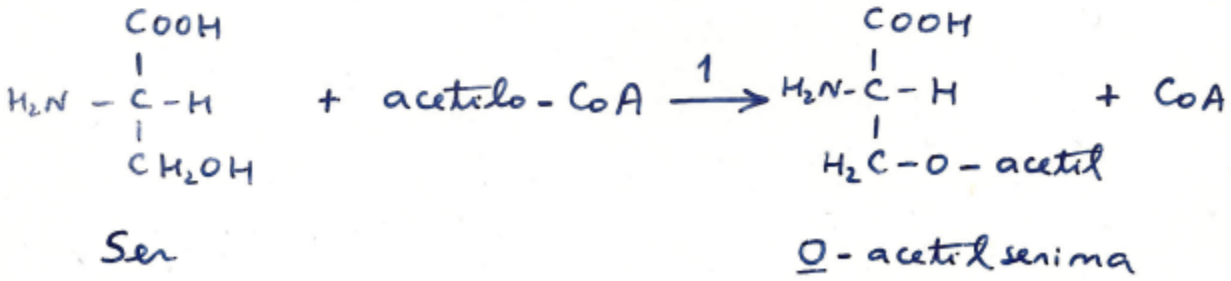
Biossíntese dos aminoácidos não-proteicos





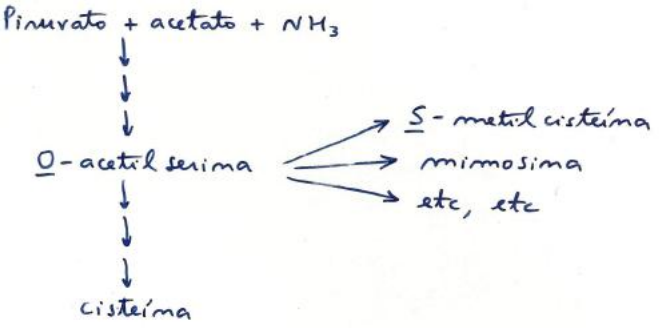
1: arginase
2: 2-oxoglutarato ornitina transaminase
3: desidrogenase
4: urease

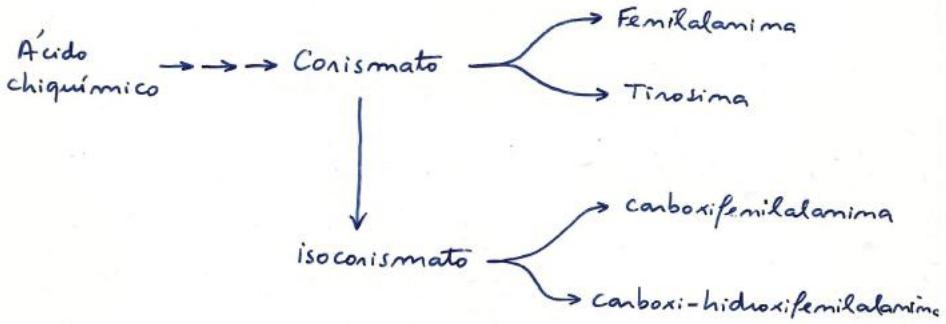
② Modificação de aa proteicos



1: L-serina acetil transferase

③ Modificação de vias biossintéticas de aa proteicos





④ "Novas" vias biossintéticas

Síntese do ácido azetidina-2-carboxílico

Síntese da latirina

Aminoácidos não-proteicos

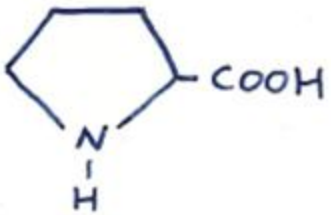
Questões:

1 – Se ingerirmos um aminoácido não-proteico, ele poderá ser incorporado numa das nossas proteínas?

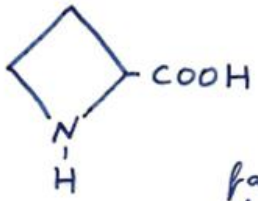
2 – E se se tratar de um análogo, muito parecido com um aminoácido proteico, como o iminoácido ácido azetidina-2-carboxílico, um análogo do iminoácido proteico prolina?

3 – Se for incorporado, qual o resultado para a proteína e para a célula/organismo?

4 – No caso anterior, como concilia essa observação com a própria definição de aminoácido proteico?



Pro
(ácido pirrolidina-2-carboxílico)



Ácido azetidina-2-carboxílico
(inicialmente isolado de espécies da família das liliáceas; é o composto solúvel de azoto predominante nos tecidos de Convallaria majalis e Polygonatum multiflorum; presente nas sementes e plântulas de algumas leguminosas e na beterraba sacarina).

5 - Considere a proteína animal colagénio.

a) Defina aminoácido proteico;

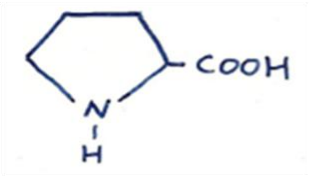
b) Defina aminoácido raro das proteínas;

c) Como é formado um resíduo de hidroxiprolina no colagénio?

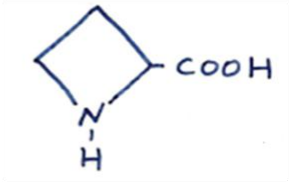
d) Indique que composto radioactivo deve ser fornecido a um rato para obter resíduos radioactivos de hidroxiprolina no seu colagénio;

e) Porque razão os marinheiros portugueses, durante as suas longas viagens no tempo das descobertas, sangravam com facilidade e tinham dificuldade em cicatrizar as suas feridas?

6 –



L-Prolina (ácido pirrolidina-2-carboxílico).



Ácido azetidina-2-carboxílico. É o composto solúvel de azoto predominante nos tecidos de *Canvallaria majalis* e *Polygonatum multiflorum*. Presente das sementes e plântulas de algumas leguminosas e na beterraba sacarina.

a) Defina aminoácido proteico, aminoácido raro das proteínas e aminoácido não-proteico.

b) Dê três exemplos de cada.

c) Porque é que a prolina é considerada um iminoácido?

d) Descreva como é que o iminoácido não-proteico ácido azetidina-2-carboxílico pode ser introduzido em proteínas?

e) Com base na resposta anterior, modifique a definição de aminoácido não-proteico de modo a torná-la mais rigorosa.

f) Os rizomas de *Polygonatum multiflorum* podem conter até cerca de 6% da sua massa em ácido azetidina-2-carboxílico. Qual a função biológica desempenhada por este iminoácido? Explique como e porquê.

g) Como é que as células de *Polygonatum multiflorum* não introduzem o ácido azetidina-2-carboxílico nas suas proteínas?

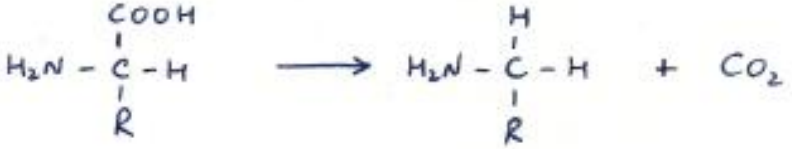
AMINAS

AMINAS - Principais classes

- primárias NH_2R
- secundárias $NHRR'$
- terciárias $NRR'R''$
- quaternárias $N^+RR'R''R'''$

Principais vias de síntese das aminas

- Por descarboxilação de aminoácidos



- Por aminação de aldeídos (reacção de transaminação)

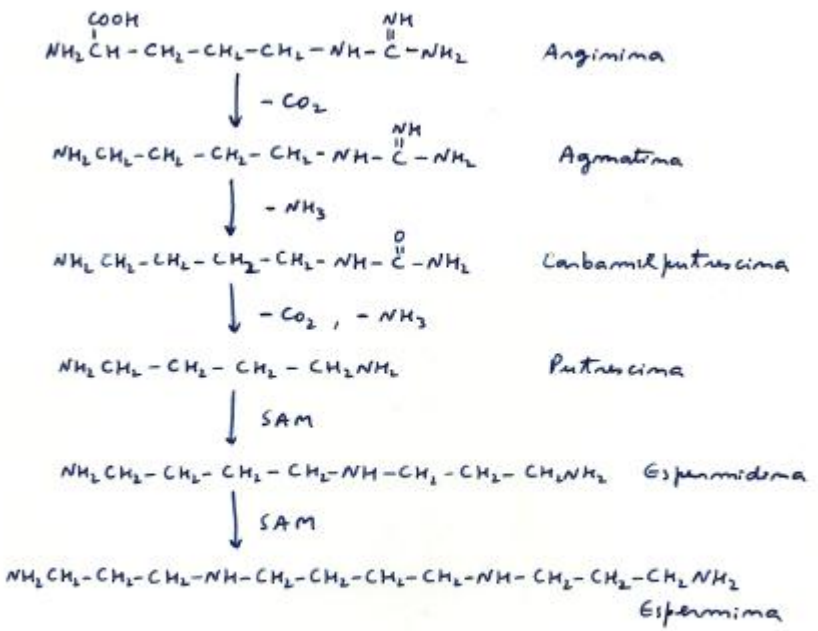
AMINOÁCIDOS COMO PRECURSORES DE AMINAS EM PLANTAS

Aminoácido	Produto da descarboxilação	Ocorrência
Gly	metilamina	Limonium vulgare liquenes
Ala	etilamina	Cucumis sativus Zea mays rodofíceas
ácido 2-aminobutírico norvalina	n-propilamina n-butilamina	Claviceps rodofíceas
Val	iso-butilamina	Arum maculatum Vicia faba
norleucina	n-amilamina	Claviceps rodofíceas
Leu	iso-amilamina	Crataegus monogyna Claviceps purpurea rodofíceas
Ile	2-metilbutilamina	
ácido 1-aminoheptanóico	n-hexilamina	Claviceps purpurea
ácido 1-aminocaprílico	n-heptilamina	Claviceps purpurea
Ser	etanolamina	Cucumis sativus
Ornitina	putrescina	Ecballium elaterium Pisum sativum Nicotiana tabacum
citrulina	N-carbamilputrescina	Saccharum officinarum Sesamum indicum Glycine max Hordeum vulgare Lathyrus sativus Lupinus luteus Pisum sativum
Arg	agmatina	
homoarginina Lys	homoagmatina cadaverina	
Cys	2-tioetilamina	rodofíceas
homocisteína	3-tiopropilamina	"
Met	3-metiltiopropilamina	"
S-adenosilmetionina	S-metiladenosilhomocisteamina	Daucus carota Phaseolus aureus
His	histamina	Spinacea oleracea Gossypium hirsutum Solanum tuberosum Citrullus vulgaris Lycopersicon esculentum rodofíceas
Trp	triptamina	
5-hidroxitriptofano	5-hidroxitriptamina	
Phe	feniletilamina	Lolium multiflorum Hordeum vulgare Cytisus scoparius Trichocereus pachanoi
Tyr	tiramina	
dihidroxifenilalanina	dopamina	

MONOAMINAS ALIFÁTICAS PRESENTES NAS PLANTAS

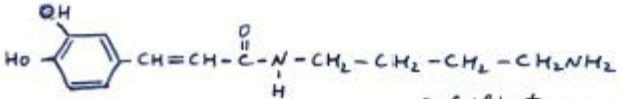
Metilamina	$CH_3 NH_2$
Dimetilamina	$(CH_3)_2 NH$
Trimetilamina	$(CH_3)_3 N$
Etilamina	$CH_3 . CH_2 NH_2$
Etanolamina	$CH_2OH . CH_2 NH_2$
Etilmetilamina	$CH_3 . NH . CH_2 . CH_3$
Dietilamina	$CH_2 . CH_2 . NH . CH_2 . CH_3$
n - Propilamina	$CH_3 . CH_2 . CH_2 NH_2$
n - Butilamina	$CH_3 . (CH_2)_2 . CH_2 NH_2$
Dibutilamina	$CH_3 . (CH_2)_3 . NH . (CH_2)_3 . CH_3$
Amilamina	$CH_3 . (CH_2)_3 . CH_2 NH_2$
n - Hexilamina	$CH_3 . (CH_2)_4 . CH_2 NH_2$
n - Heptilamina	$CH_3 . (CH_2)_5 . CH_2 NH_2$
n - Octilamina	$CH_3 . (CH_2)_6 . CH_2 NH_2$
Iso - Propilamina	$(CH_3)_2 CH NH_2$
Iso - Butilamina	$(CH_3)_2 CH . CH_2 NH_2$
Iso - Amilamina	$(CH_3)_2 CH . CH_2 . CH_2 NH_2$
2 - Metilbutilamina	$CH_3 . CH_2 . CH(CH_3) . CH_2 NH_2$
3 - Metiltiopropilamina	$CH_3 . S . (CH_2)_2 . CH_2 NH_2$
2 - Propanolamina	$CH_3 . CHOH . CH_2 NH_2$

BIOSSÍNTESE DA PUTRESCINA E DAS POLIAMINAS EM PLANTAS SUPERIORES

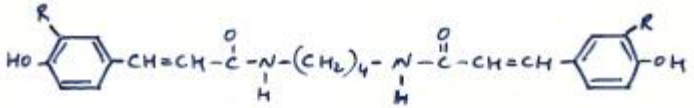


Cadaverina $NH_2CH_2-CH_2-CH_2-CH_2-CH_2NH_2$

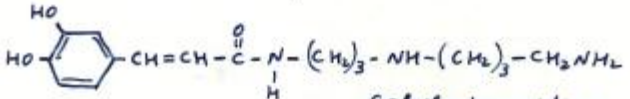
AMIDAS AROMÁTICAS PRESENTES EM VÁRIOS ORGÃOS DE PLANTAS DE TABACO

1. 

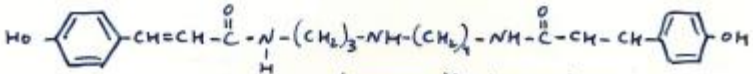
cafeilputrescina

2. 

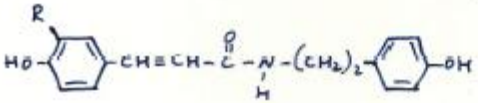
a) R = H dicumarilputrescina
b) R = OCH_3 diferulilputrescina

3. 

cafeilespermidina

4. 

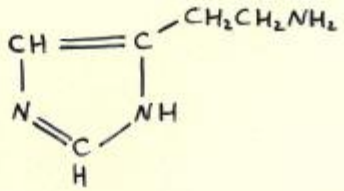
dicumarilespermidina

5. 

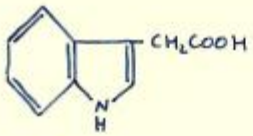
a) R = H cumariltiramina
b) R = OCH_3 feruliltiramina

Anteras de tabaco	:	amidas aromáticas		2a, 4, 5a
ovários de "	:	"	"	1, 3
Sementes de "	:	"	"	2b, 5b

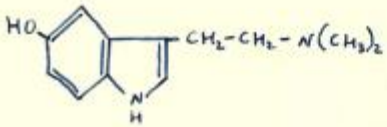
Histamina



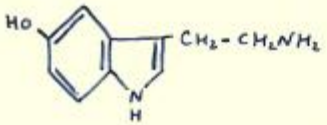
TRIPTAMINAS



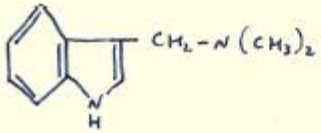
ácido indol-3-acético



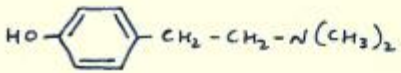
bufotenina



serotonina
(5-hidroxitriptamina)

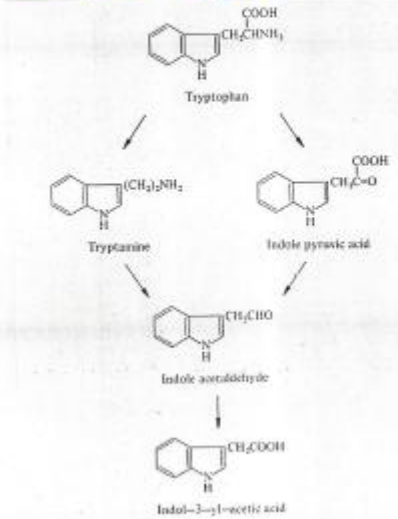


gramina

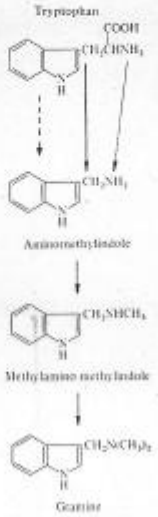


hordenina

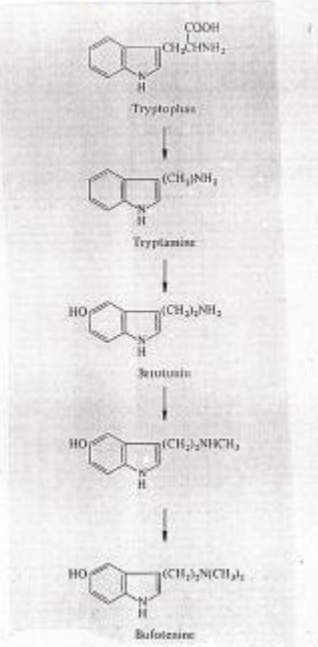
Via de síntese do IAA nas plantas superiores



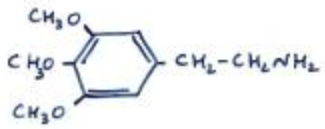
Biossíntese da gramina a partir do triptofano em folhas de cevada



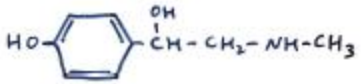
Formação da bufotenina em Piptadenia peregrina



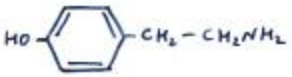
FENETILAMINAS



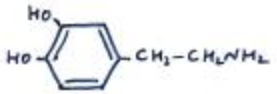
mescalina



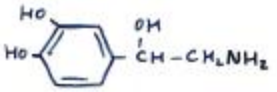
simpatina



tiramina

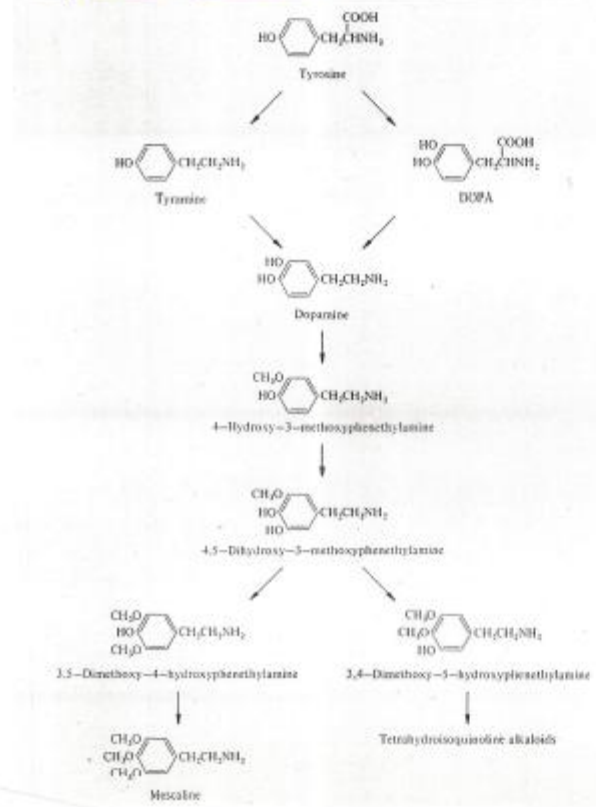


dopamina

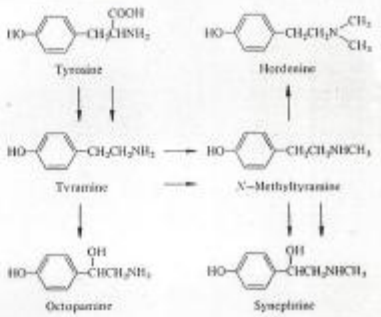


noradrenalina

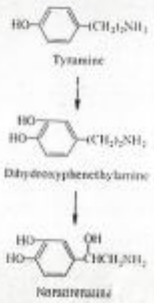
Síntese da mescalina no cacto *Lophophora williamsii*



Formação da sinefrina e de outras aminas fenólicas em plântulas do género *Citrus*



Biossíntese da noradrenalina na banana

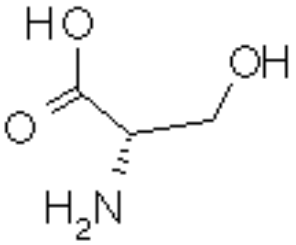
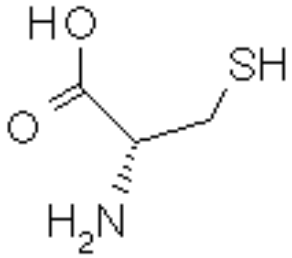
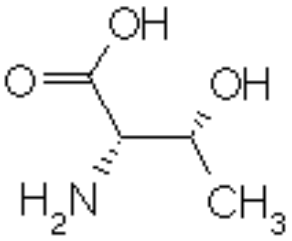
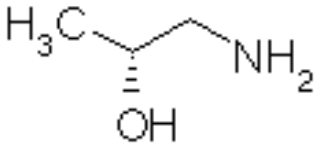


AMINAS BIOGÉNICAS

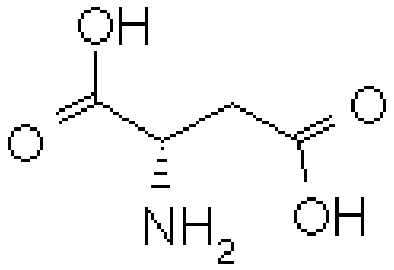
Definition

Any of a group of naturally occurring, biologically active amines, such as norepinephrine, histamine, and serotonin, that act primarily as neurotransmitters and are capable of affecting mental functioning and of regulating blood pressure, body temperature, and other bodily processes.

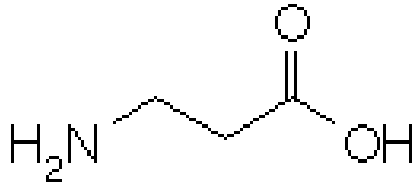
Biogenic amines

Amino acid		Amine
Serine	-->	Ethanolamine
 C00065		 C00189
Cysteine	-->	Cysteamine
 C00097		 C01678
Threonine	-->	Aminopropanol
 C00188		 C03194

Aspartate --> **beta-Alanine**

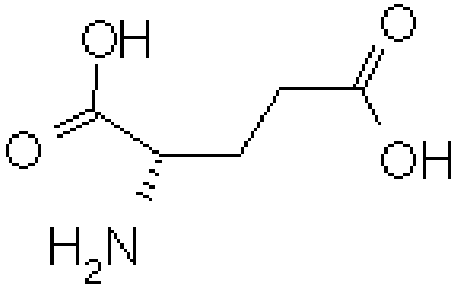


C00049



C00099

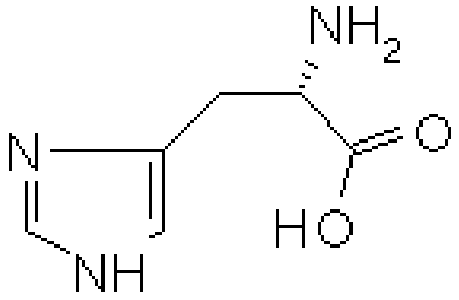
Glutamate --> **gamma-Aminobutylate (GABA)**



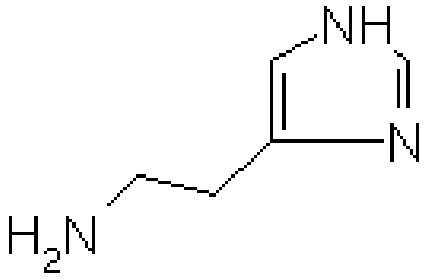
C00025

C00334

Histidine --> **Histamine**

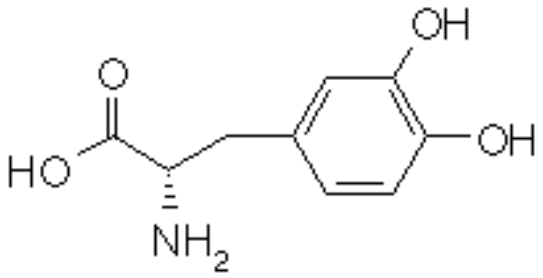


C00135

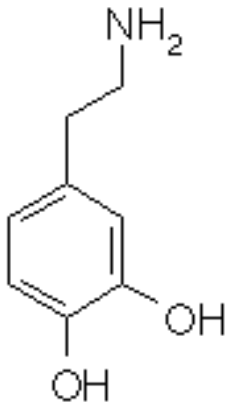


C00388

Dopa --> **Dopamine**

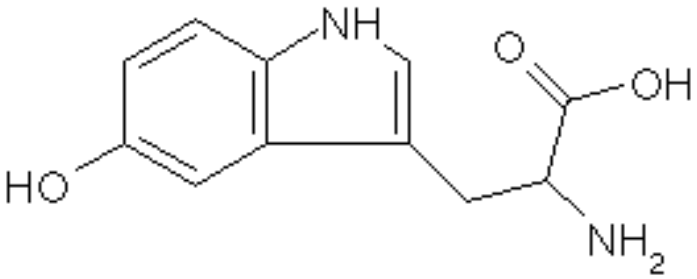


C00355

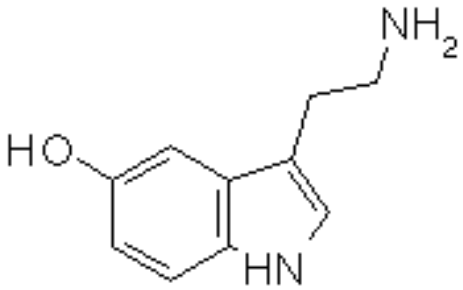


C03758

5-Hydroxytryptophan --> **Serotonin**

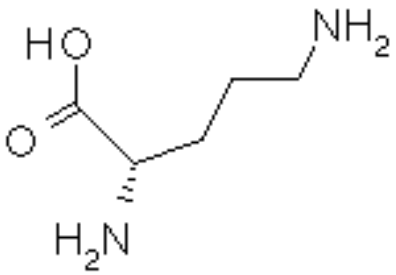


C01017

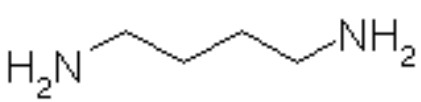


C00780

L-Ornithine --> **Putrescine**

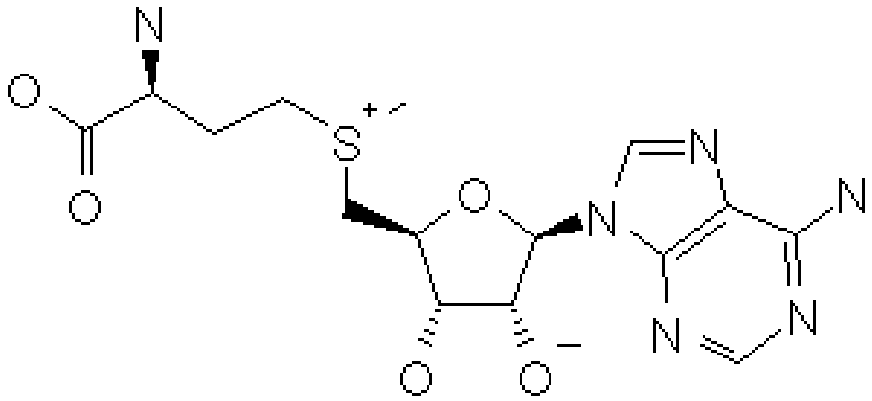


C00077



C00134

S-Adenosylmethionine



C00019

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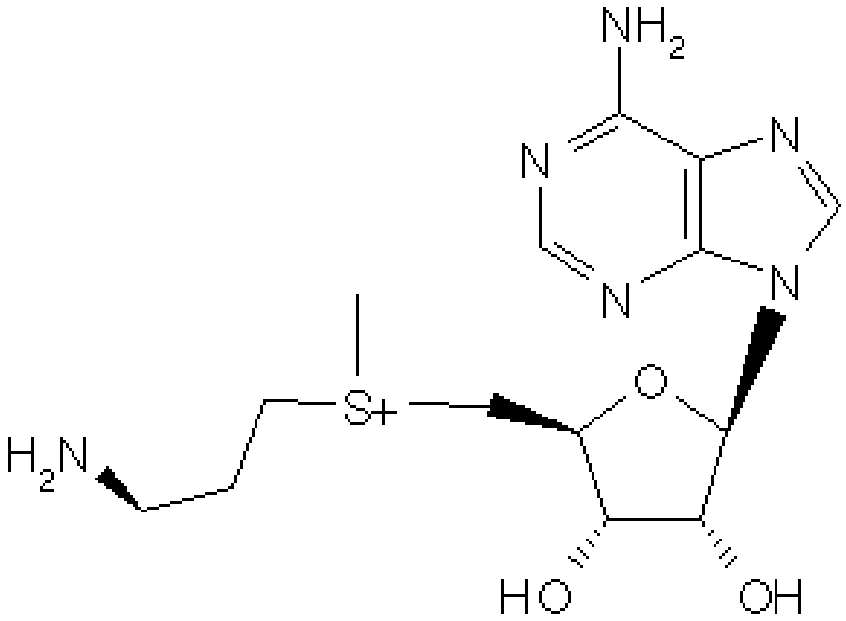
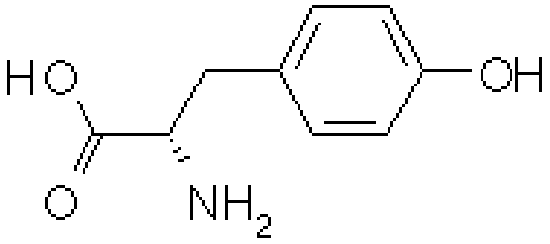
S-Adenosylmethioninamine



C01137

L-Tyrosine



C00082

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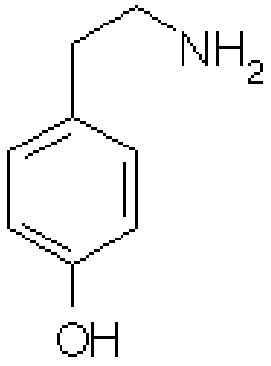
Tyramine



C00483

Some prominent examples of biogenic amines include:

Acetylcholine (ACh) - the first neurotransmitter identified, in 1914; involved with Parasympathetic Nervous System but predominantly acts at the Neuromuscular Junction (NMJ)
Histamine - a substance derived from the amino acid histidine that acts as a neurotransmitter mediating arousal and attention, as well as a pro-inflammatory signal released from mast cells in response to allergic reactions or tissue damage. Histamine is also an important stimulant of HCl secretion by the stomach through histamine H2 receptors.
Tyramine - a substance that is found in many common foods, and is associated with increased blood pressure and headaches.
Serotonin - a central nervous system neurotransmitter involved in regulating mood, sleep, appetite, and sexuality.
The three catecholamine neurotransmitters:

- Norepinephrine (noradrenaline) - a neurotransmitter involved in sleep and wakefulness, attention, and feeding behavior, as well as a stress hormone released by the adrenal glands that regulates the sympathetic nervous system.
- Epinephrine (adrenaline) - an adrenal stress hormone, as well as a neurotransmitter present at lower levels in the brain.
- Dopamine - a neurotransmitter involved in motivation, reward, addiction, behavioral reinforcement, and coordination of bodily movement.

Tryptamine - a monoamine alkaloid found in trace amounts in the brains of mammals, and believed to play a role as a neuromodulator or neurotransmitter.

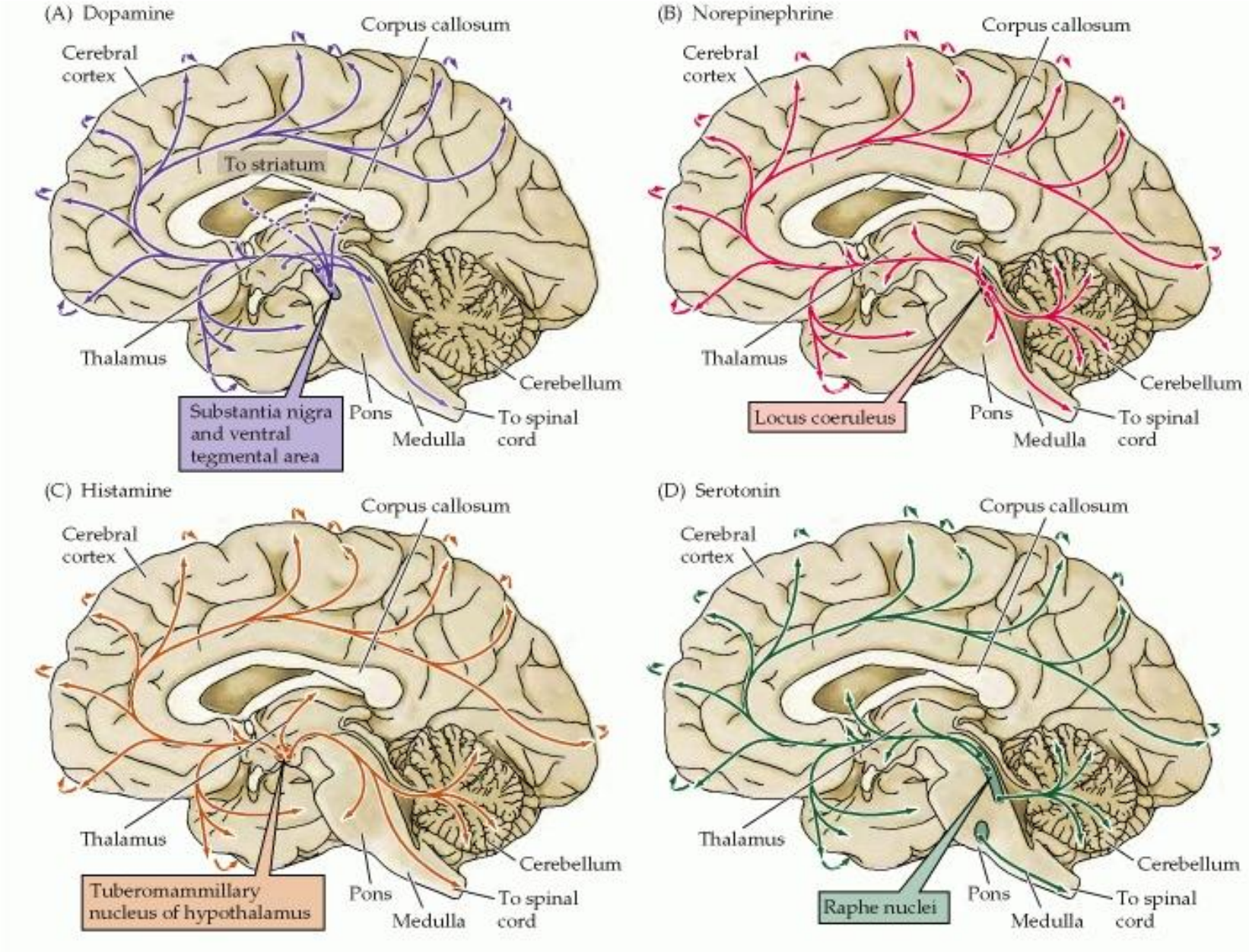
Physiological importance

There is a distinction between endogenous and exogenous biogenic amines. Endogenous amines are produced in many different tissues (for example: adrenaline in adrenal medulla or histamine in mast cells and liver). The amines are transmitted locally or via the blood system. The exogenous amines are directly absorbed from food in the intestine. Alcohol can increase the absorption rate. The monoamineoxidase (MAO) breaks down biogenic amines and prevents excessive resorption.

The Biogenic Amines

There are five established biogenic amine **neurotransmitters**: the three **catecholamines**—**dopamine**, **norepinephrine** (**noradrenaline**), and epinephrine (**adrenaline**)—and **histamine** and **serotonin**. In terms of synthesis, packaging, release, and degradation, the amine **neurotransmitters** fall somewhere between the properties of the other small-molecule **neurotransmitters** and those of the **neuropeptides**.

All the **catecholamines** (so named because they share the catechol moiety) are derived from a common precursor, the amino acid tyrosine. The first step in **catecholamine** synthesis is catalyzed by tyrosine hydroxylase in a reaction requiring oxygen as a co-substrate and tetrahydrobiopterin as a cofactor to synthesize dihydroxyphenylalanine (DOPA). Because tyrosine hydroxylase is rate-limiting for the synthesis of all three **transmitters**, its presence is a valuable criterion for identifying catecholaminergic **neurons**.



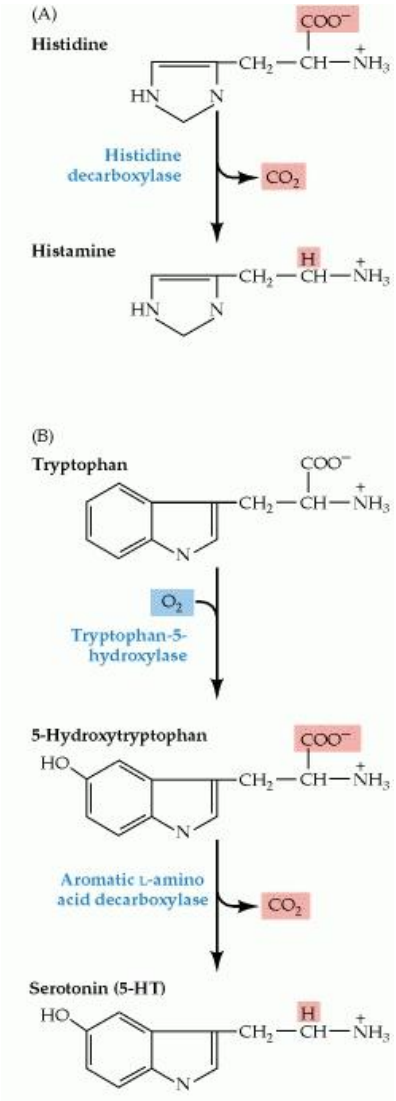
The distribution in the human brain of **neurons** and their projections (arrows) containing biogenic amine **neurotransmitters**. Curved arrows along the perimeter of the **cortex** indicate the **innervation** of lateral cortical regions not shown in this midsagittal plane of section.

Dopamine is produced by the action of DOPA decarboxylase on DOPA. Although present in several brain regions, the major **dopamine**-containing area of the brain is the **corpus striatum**, which receives major **input** from the **substantia nigra** and plays an essential role in the coordination of body movements. In Parkinson's disease, for instance, the dopaminergic **neurons** of the **substantia nigra** degenerate, leading to a characteristic **motor** dysfunction. Although **dopamine** does not readily cross the **blood-brain barrier** (BBB), its precursor, levodopa, does. Levodopa is absorbed in the small bowel but is rapidly catabolized in the GI tract and in peripheral tissues. Hence, the disease can be treated by administering levodopa together with carbidopa, a **dopamine** decarboxylase inhibitor, and selegiline, a monoamine oxidase inhibitor. **Dopamine** is also believed to be involved in motivation, reward, and reinforcement. For example, cocaine and other addictive drugs act by stimulating the release of **dopamine** from specific brain areas. Once released, **dopamine** binds to specific **dopamine receptors**, as well as to some β-**adrenergic receptors**. It not only acts as a **neurotransmitter** in the **central nervous system** but also plays a poorly understood role in some sympathetic ganglia. **Dopamine** is also used clinically to treat shock because it dilates renal arteries by activating **dopamine receptors** and increases cardiac output by activating β-**adrenergic receptors** in the heart.

Norepinephrine (also called noradrenaline) synthesis requires **dopamine** β-hydroxylase, which catalyzes the production of norepinephrine from **dopamine**. **Dopamine** is transported by **vesicles** into **adrenergic terminals**, where it is converted to norepinephrine. The most prominent **class** of **neurons** that synthesize norepinephrine is sympathetic **ganglion cells**, since norepinephrine is the major peripheral **transmitter** in this division of the **visceral motor system**. Norepinephrine is also the **transmitter** used by the **locus coeruleus**, a **brainstem** nucleus that projects diffusely to a variety of **forebrain** targets, where it influences sleep and wakefulness, **attention**, and feeding behavior.

Epinephrine (also called **adrenaline**) is present in the brain at lower levels than the other **catecholamines**. The enzyme that synthesizes epinephrine, phenylethanolamine-*N*-methyltransferase, is present only in epinephrine-secreting **neurons**. Epinephrine-containing **neurons** in the **central nervous system** are found in two groups in the **rostral medulla**, the function of which is not known.

All three **catecholamines** are removed by reuptake into **nerve** **terminals** or surrounding glial cells by a **Na**+-dependent transporter. The two major enzymes involved in the catabolism of **catecholamines** are monoamine oxidase (MAO) and catechol *O*-methyltransferase (COMT). Both **neurons** and glia contain mitochondrial MAO and cytoplasmic COMT. Inhibitors of these enzymes, such as phenelzine and tranylcypromine, are used clinically as antidepressants.

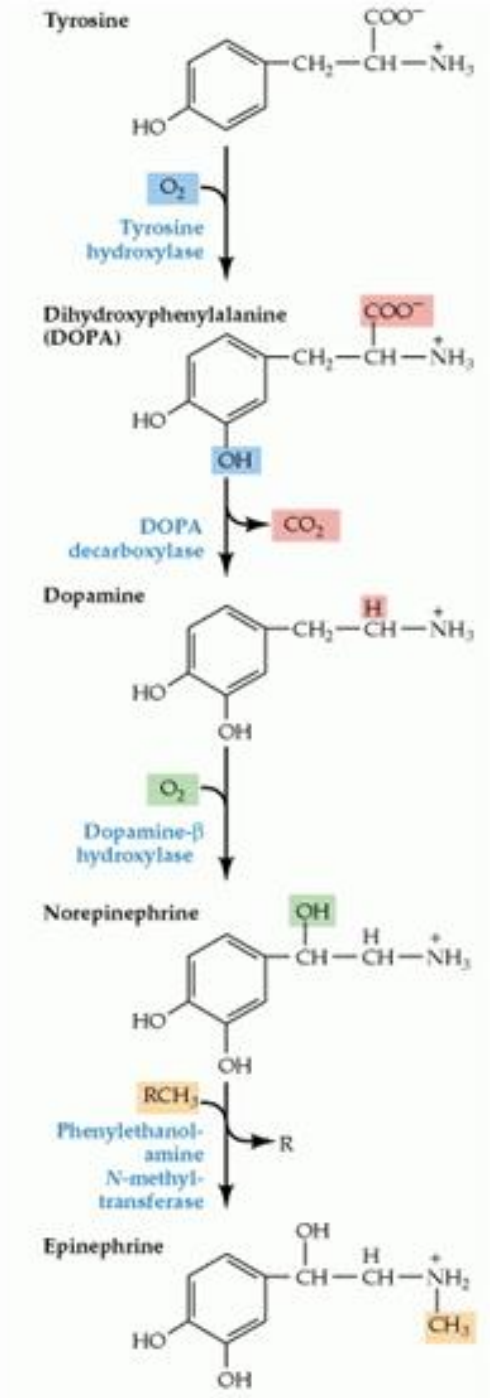


Synthesis of **histamine** and **serotonin**. (A) **Histamine** is synthesized from the amino acid histidine. (B) **Serotonin** is derived from the amino acid tryptophan by a two-step process that requires the enzymes tryptophan-5-hydroxylase and a decarboxylase.

Histamine is produced from the amino acid histidine by a histidine decarboxylase and is metabolized by the combined actions of **histamine** methyltransferase and MAO. High concentrations of **histamine** and **histamine** decarboxylase are found in **neurons** in the **hypothalamus** that send sparse but widespread projections to almost all regions of the brain and **spinal cord**. The central **histamine** projections mediate arousal and **attention**, similar to central ACh and norepinephrine projections. This partly explains why antihistamines that cross the **blood-brain barrier**, such as diphenhydramine (Benadryl®), act as sedatives. **Histamine** also is released from mast cells in response to allergic reactions or tissue damage. The close proximity of mast cells to blood vessels, together with the potent actions of **histamine** on blood vessels, raises the possibility that **histamine** may influence brain blood flow.

Serotonin, or 5-hydroxytryptamine (5-HT), was initially thought to increase vascular tone by virtue of its presence in serum (hence the name **serotonin**). 5-HT is synthesized from the amino acid tryptophan, which is an essential dietary requirement. Tryptophan is taken up into **neurons** by a plasma membrane transporter and hydroxylated in a reaction catalyzed by the enzyme tryptophan-5-hydroxylase, the rate-limiting step for 5-HT synthesis. As in the case of other **biogenic amines**, the synaptic effects of **serotonin** are terminated by transport back into serotonergic **nerve terminals**. The primary catabolic pathway is mediated by MAO. **Serotonin** is located in groups of **neurons** in the raphe region of the **pons** and upper **brainstem**, which have widespread projections to the **forebrain** and have been implicated in the regulation of sleep and wakefulness. A number of antipsychotic drugs used in the treatment of depression and anxiety are thought to act specifically on serotonergic **neurons**.

Because **biogenic amines** are implicated in such a wide range of behaviors (ranging from central homeostatic functions to cognitive phenomena such as **attention**), it is not surprising that drugs affecting the synthesis, **receptor** binding, or catabolism of these **neurotransmitters** are among the most important in the armamentarium of modern pharmacology.

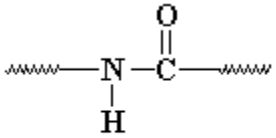


The biosynthetic pathway for the catecholamine neurotransmitters. The amino acid tyrosine is the precursor for all three catecholamines. The first step in this reaction pathway, catalyzed by tyrosine hydroxylase, is rate-limiting.

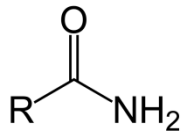
LIGAÇÃO PEPTÍDICA

Formação de uma ligação peptídica

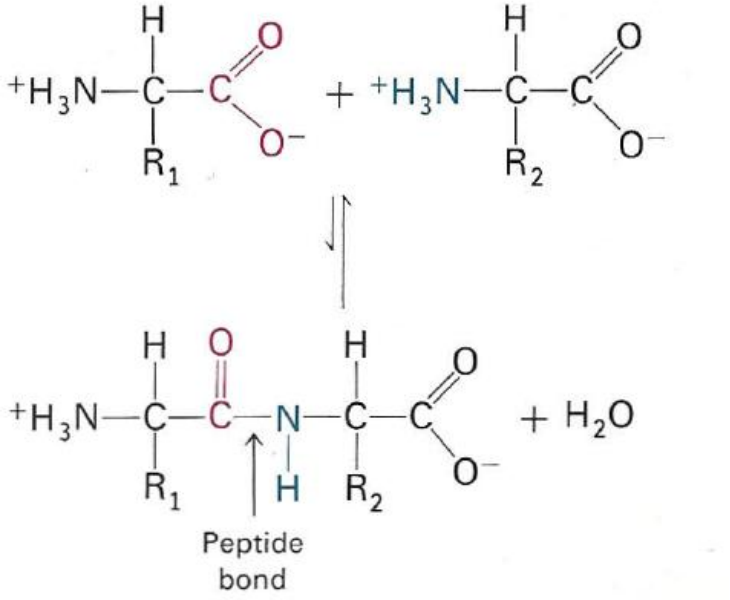
É uma ligação éster, **do tipo amida**, que se estabelece entre o grupo carboxilo de um aminoácido e o grupo amina de outro aminoácido.
A reacção inversa é, por isso, uma reacção de hidrólise, catalisada por enzimas genericamente designadas por proteases.



an amide group



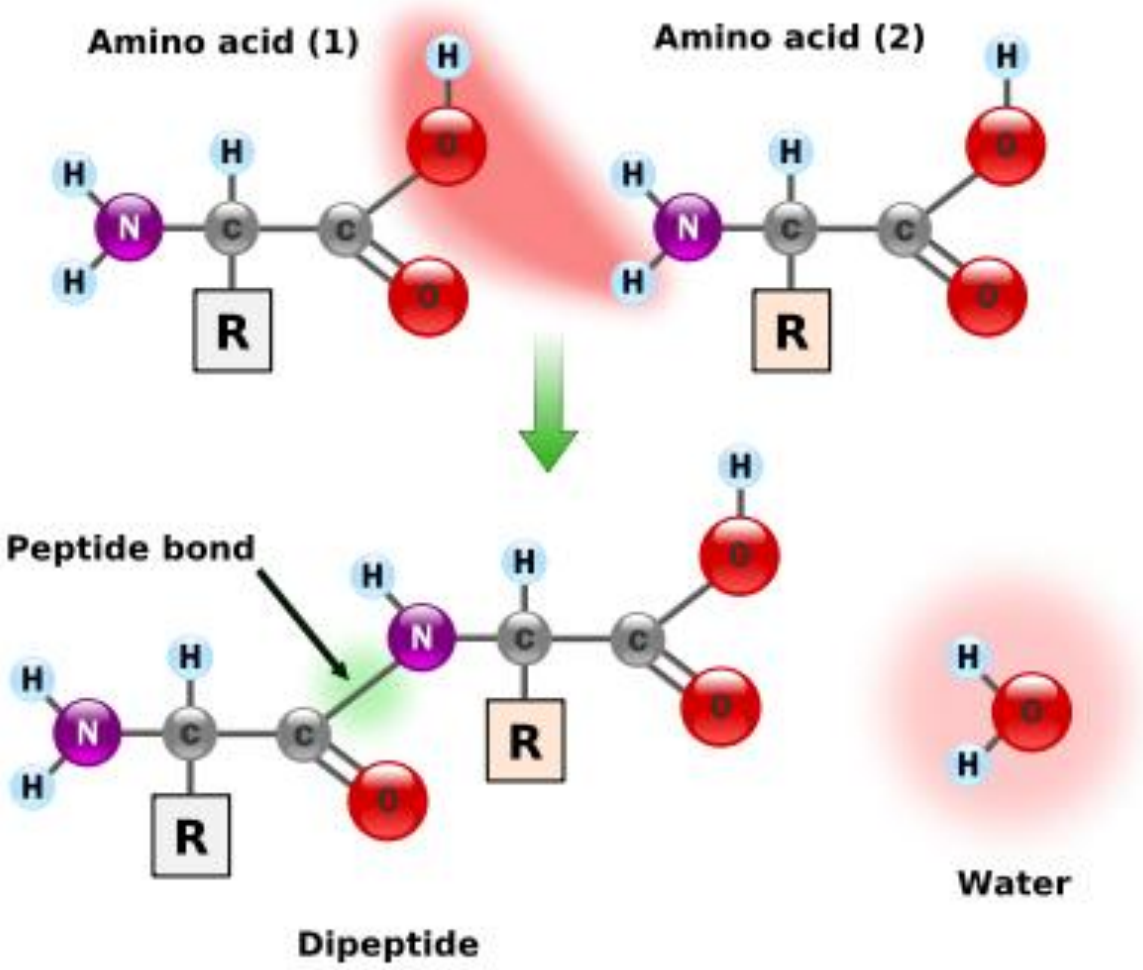
Grupo amida

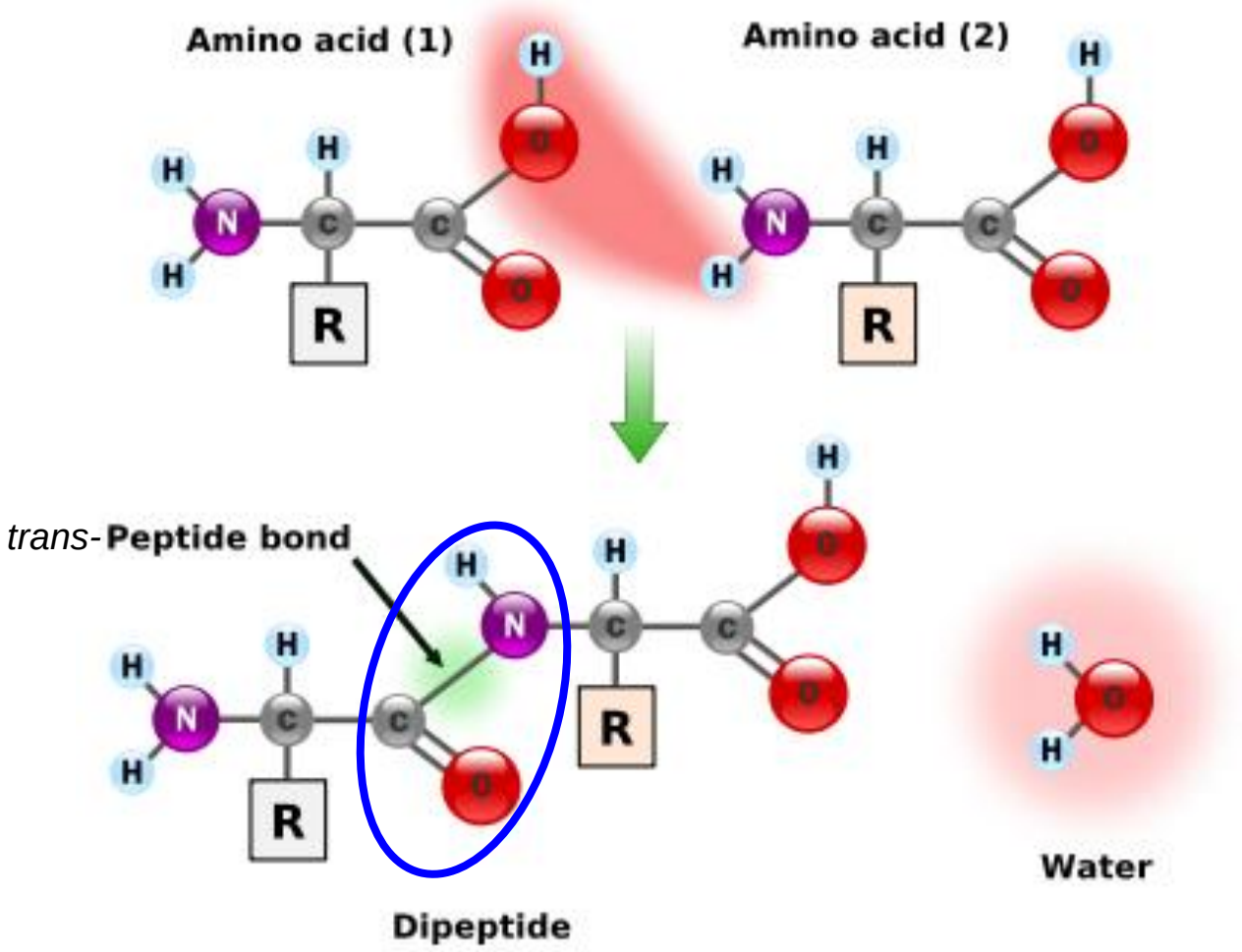


Formation of a peptide bond.

Notar a saída de uma molécula de água por cada ligação peptídica formada.
O que fica de cada aminoácido designa-se, por isso, por **resíduo de aminoácido**, a que corresponde, evidentemente, uma massa molecular inferior à do aminoácido que lhe deu origem – ver a tabela dos diapositivos números 43 e 44 deste ficheiro.
Assim sendo, a síntese de um polipéptido com n resíduos de aminoácidos originou a libertação de n-1 moléculas de água.

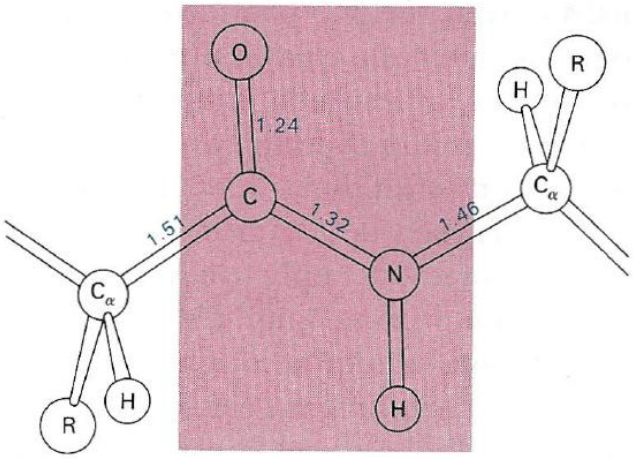
Temos, deste modo, um resíduo glicilo de glicina, alanilo de alanina, tirosilo de tirosina, leucilo de leucina, prolilo de prolina, etc.


Amino acid (1)
Amino acid (2)
Peptide bond
Dipeptide
Water

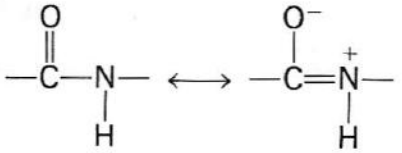

Amino acid (1)
Amino acid (2)
trans-Peptide bond
Dipeptide
Water

Peptide group

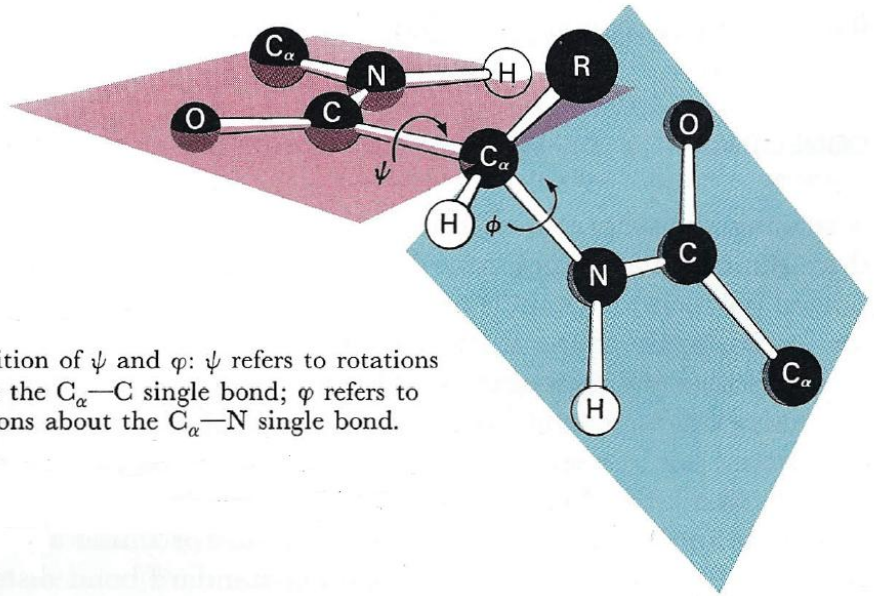
The peptide group is a rigid planar unit. Standard bond distances (in Å) are shown. *



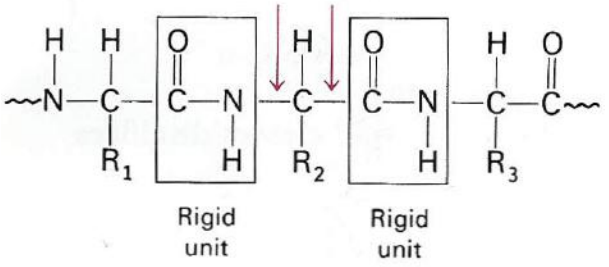
* *Angstrom* (Å)—
A unit of length equal to 10^{-10} meter.
$1\ Å = 10^{-10}\ m = 10^{-8}\ cm$
$= 10^{-4}\ \mu m = 10^{-1}\ nm$
Named after Anders J. Ångström (1814–1874), a spectroscopist.



The peptide group is planar because the carbon–nitrogen bond has partial double-bond character.



Definition of ψ and φ: ψ refers to rotations about the C_α—C single bond; φ refers to rotations about the C_α—N single bond.



There is considerable freedom of rotation about the bonds joining the peptide groups to the α-carbon atoms.

Nomenclatura das ligações peptídicas

Ligação eupeptídica, frequentemente denominada apenas ligação peptídica, é uma ligação covalente do tipo amida, que se estabelece entre o grupo α-carboxilo (i. é, o carbono 1) de um aminoácido (ou resíduo de aminoácido) e o grupo α-amina de outro aminoácido (ou resíduo de aminoácido).

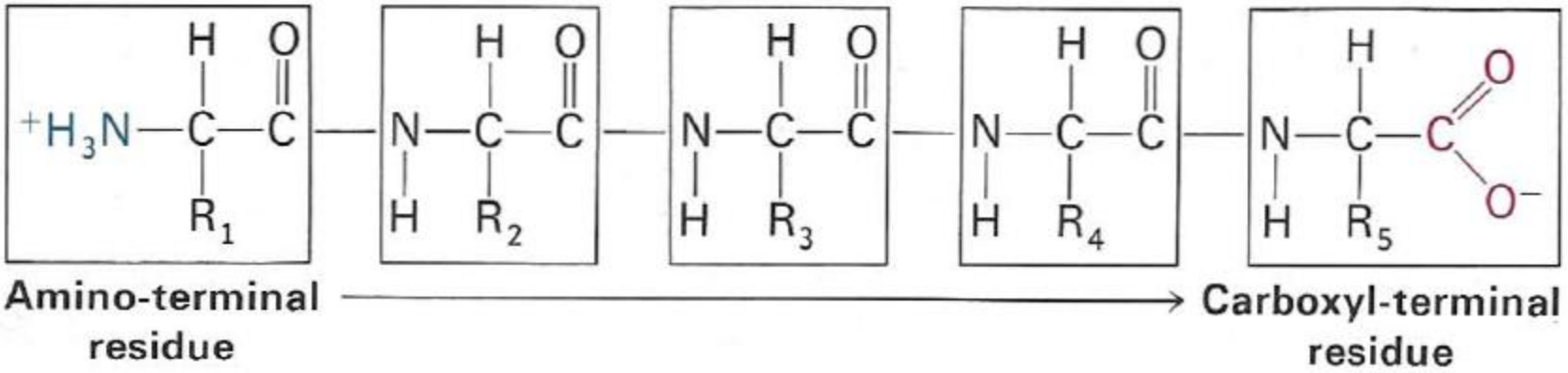
Ligação isopeptídica é qualquer ligação peptídica que não seja uma ligação eupeptídica, i. é, qualquer ligação covalente do tipo amida que se forme entre um grupo carboxilo de um aminoácido (ou resíduo de aminoácido) e um grupo amina de outro aminoácido (ou resíduo de aminoácido), desde que, pelo menos, um dos grupos não se encontre directamente ligado ao átomo de carbono α.
Constituem exemplos as ligações peptídicas em que participem o grupo β-carboxilo do ácido aspártico, o grupo γ-carboxilo do ácido glutâmico, o grupo ε-amina da lisina e tanto o grupo carboxilo como o grupo amina da β-alanina.
A formação da ligação isopeptídica desempenha também um papel fundamental na via proteolítica da ubiquitina/proteassoma. Nesta via, uma molécula de ubiquitina é ligada à proteína-substrato por meio de uma ligação isopeptídica, que se estabelece entre o grupo α-carboxilo do resíduo de glicina do terminal C da ubiquitina (Gly76) e o grupo ε-amina de um resíduo de lisina da proteína aceitadora. A formação de cadeias multiubiquitiladas é subsequentemente conseguida pelo estabelecimento de ligações isopeptídicas adicionais entre o grupo carboxilo do resíduo de glicina do terminal C de moléculas de ubiquitina e o grupo ε-amina dos resíduos de Lys11, Lys29, Lys48 ou Lys63 de outra molécula de ubiquitina.

Ligação peptídica é qualquer ligação covalente do tipo amida que se estabelece entre dois aminoácidos ou resíduos de aminoácidos. Esta designação inclui não só a ligação eupeptídica, formada entre o grupo α-carboxilo de um aminoácido e o grupo α-amina de outro aminoácido, como também a ligação isopeptídica, estabelecida entre um grupo carboxilo de um aminoácido e um grupo amina de outro aminoácido, um dos quais, pelo menos, não se encontra ligado directamente ao carbono α. O termo ligação peptídica é, no entanto, comummente utilizado como sinónimo de ligação eupeptídica.

Nomenclatura de péptidos, polipéptidos e proteínas

Um péptido, oligopéptido ou polipéptido começa-se a enumerar, designar, contar (i.e., o nº dos seus resíduos de aminoácidos) a partir da extremidade que tem um grupo amina livre - o **terminal N** ou **terminal NH_2**. A outra extremidade livre tem um grupo carboxilo - o **terminal C** ou **terminal COOH**.

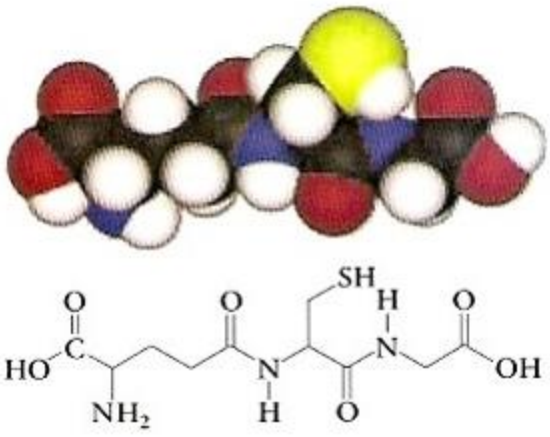
Devido à libertação de uma molécula de água em cada ligação peptídica estebelecida, os resíduos resultantes recebem designações particulares. Temos, deste modo, um resíduo glicilo de glicina, alanilo de alanina, tirosilo de tirosina, leucilo de leucina, prolilo de prolina, etc.

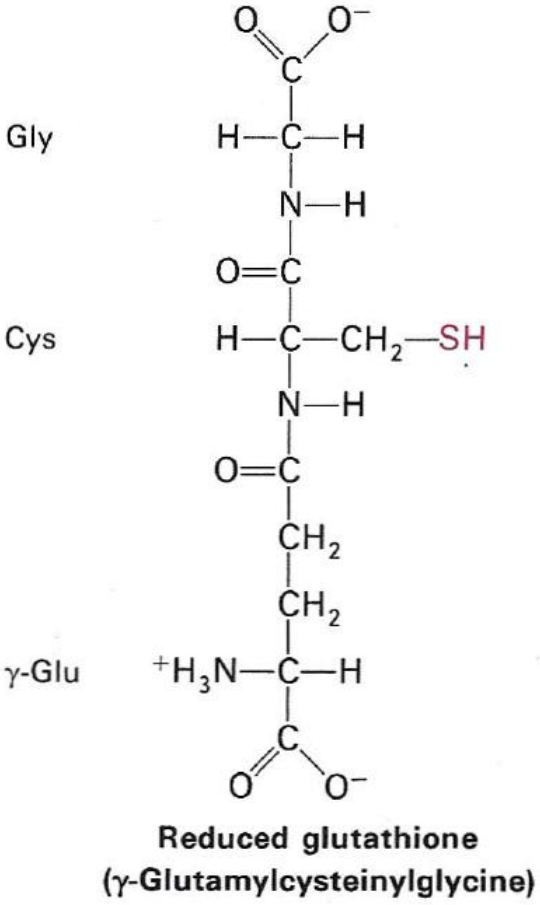


A pentapeptide. The constituent amino acid residues are outlined. The chain starts at the amino end.

No tripéptido **glutationa**, por exemplo, também denominada γ-glutamilcisteinilglicina, a ligação peptídica estabelecida entre os resíduos de ácido glutâmico e de cisteína é uma ligação isopeptídica, por ser o grupo γ -carboxilo (e não o α-carboxilo) do ácido glutâmico que participa na ligação.

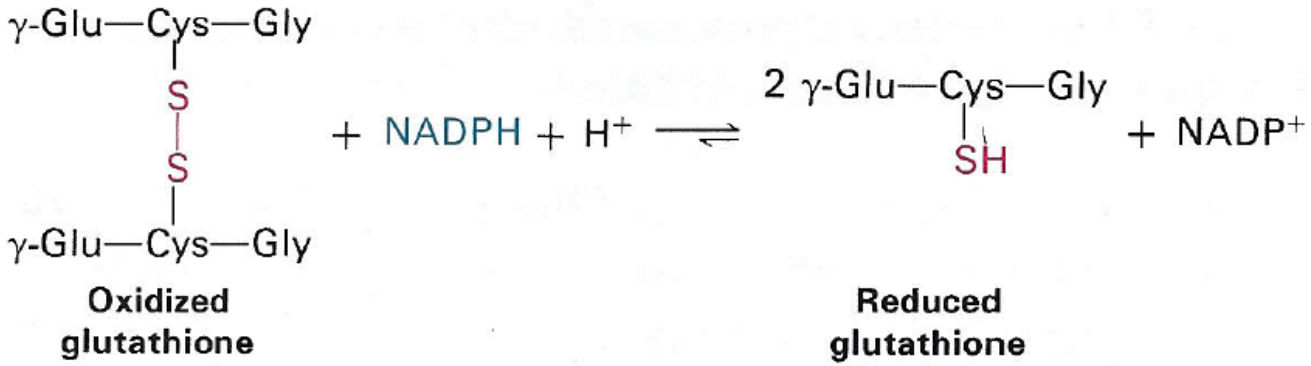
γ-Glutamilcisteinilglicina
(GSH)





Reduced glutathione
(γ-Glutamylcysteinylglycine)

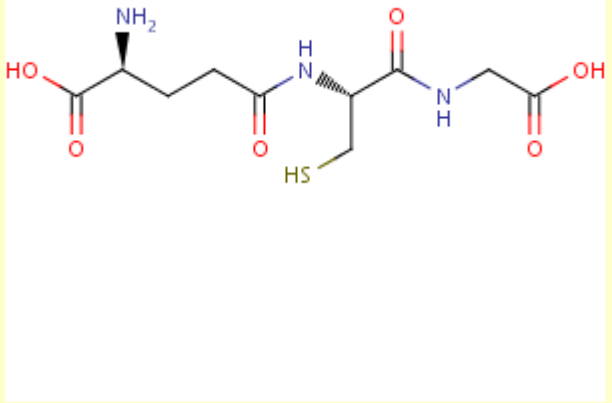
The major role of NADPH in many cells (*e.g.* red blood cells) is to reduce the disulfide form of glutathione to the sulfhydryl form. This reaction is catalyzed by glutathione reductase.



Oxidized glutathione **Reduced glutathione**

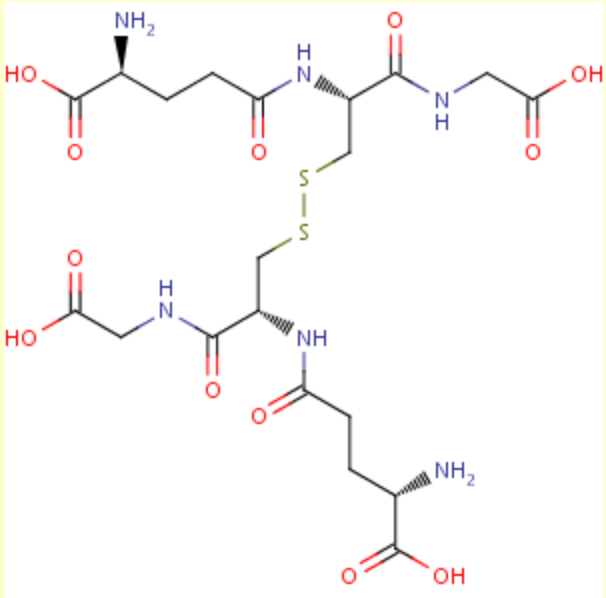
The reduced form of glutathione, a tripeptide with a free sulfhydryl group, serves as a sulfhydryl buffer that maintains the cysteine residues of hemoglobin and other red-cell proteins in the reduced state.
The ratio of the reduced form of glutathione (GSH) to the oxidized form (GSSG) is normally about 500. The reduced form also plays a role in detoxification by reacting with hydrogen peroxide and organic peroxides:

2 GSH + R-O-OH → GSSG + H20 + ROH



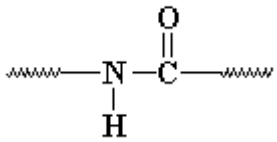
L-Glutathione reduced

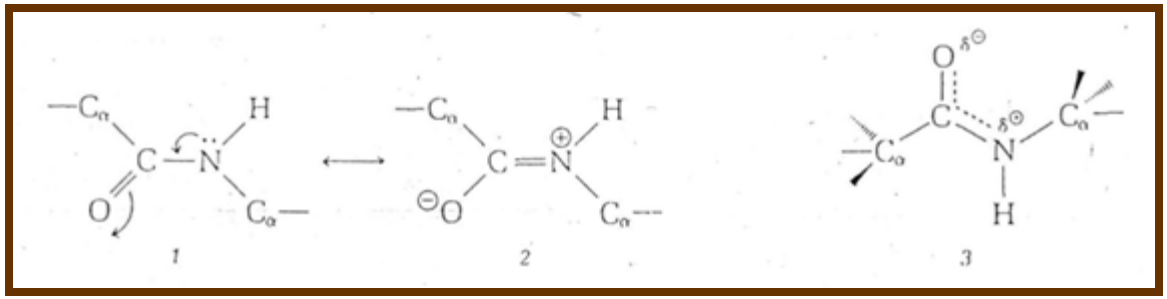
GSH



L(-)-Glutathione, oxidized GSSG

Estrutura da ligação peptídica





As propriedades da ligação peptídica são largamente determinadas pela ressonância entre o par de electrões 2s do azoto amídico e o grupo carbonilo adjacente.

Uma das estruturas contribuintes para a ligação –C-N- é uma ligação covalente simples, em que não há sobreposição entre o par de electrões 2s do azoto e o carbono do grupo carbonilo (estrutura 1).
Na estrutura 1, o C do grupo carbonilo está hibridado em sp^2 e é, por isso, planar, enquanto que o N amídico está hibridado em sp^3 e é tetraédrico.

Na estrutura 2, tanto o C do grupo carbonilo, como o N do grupo amida estão hibridados em sp^2 e, por isso, ambos são planares → todos os seis átomos representados estão no mesmo plano. A ligação –C=N- é dupla.

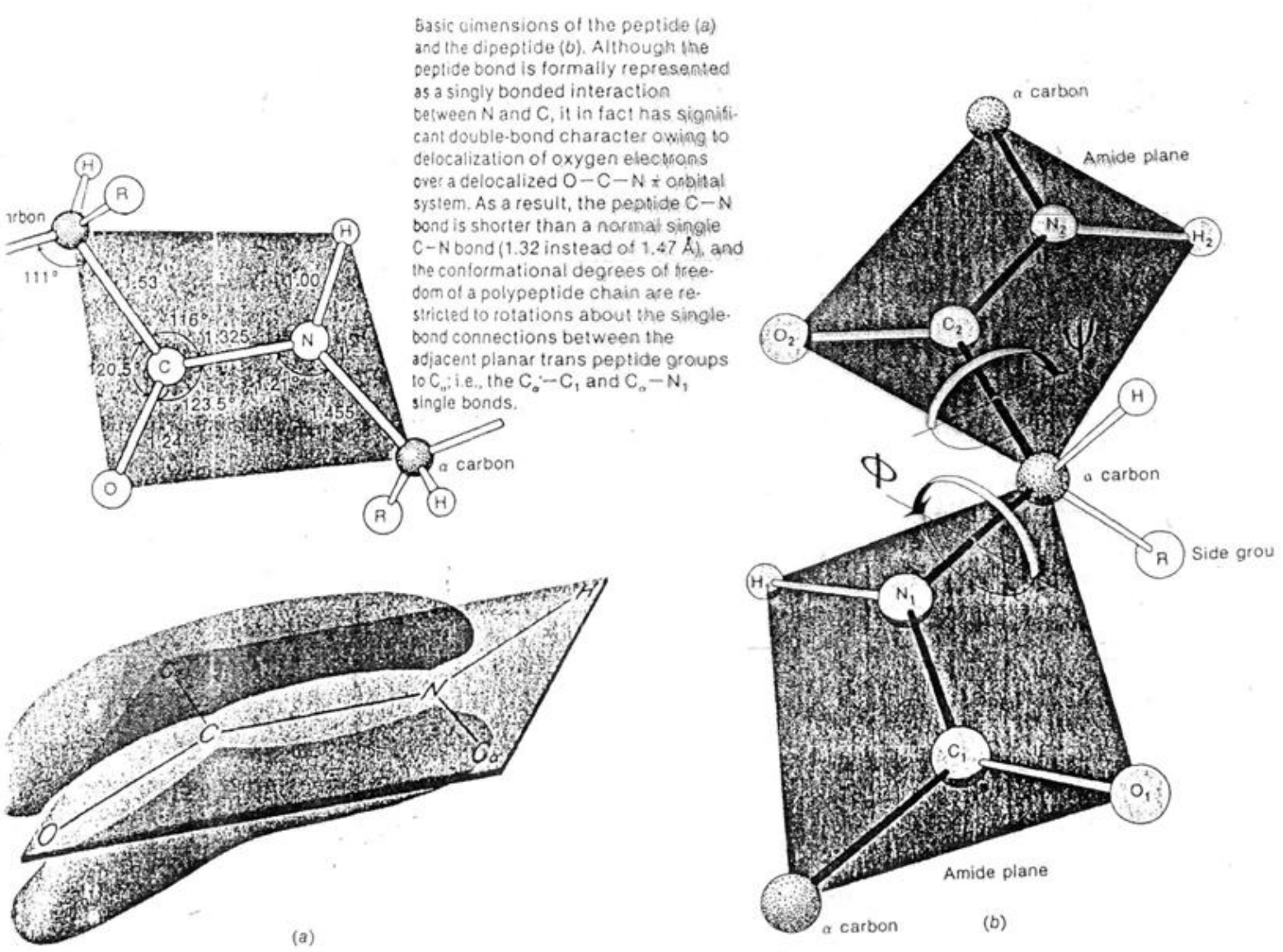
A estrutura da ligação peptídica é um híbrido de ressonância (estrutura 3), formado a partir das estruturas contribuintes 1 e 2.

O comprimento da ligação –C-N- na estrutura contribuinte 1 é de 0,1487 nm, versus 0,1325 nm para a ligação peptídica (estrutura 3) e apenas 0,127 nm para a ligação –C=N- da estrutura contribuinte 2.

O híbrido de ressonância 3 tem cerca de 40% de carácter de dupla ligação.

A ligação peptídica tem, deste modo, um carácter parcial de dupla ligação, devido à formação de uma orbital π envolvendo três átomos:

- Os átomos de C e de O do grupo carbonilo;
- O átomo de N do grupo amídico.



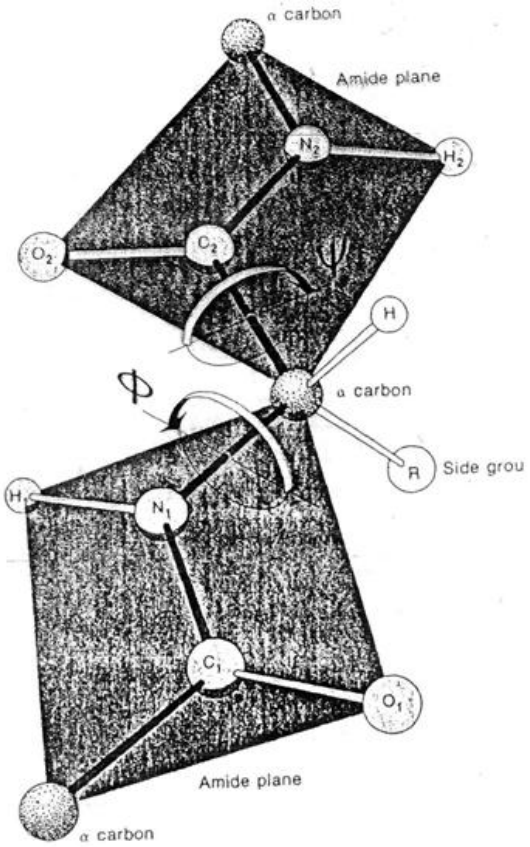
Consequências do carácter parcial de dupla ligação da ligação peptídica

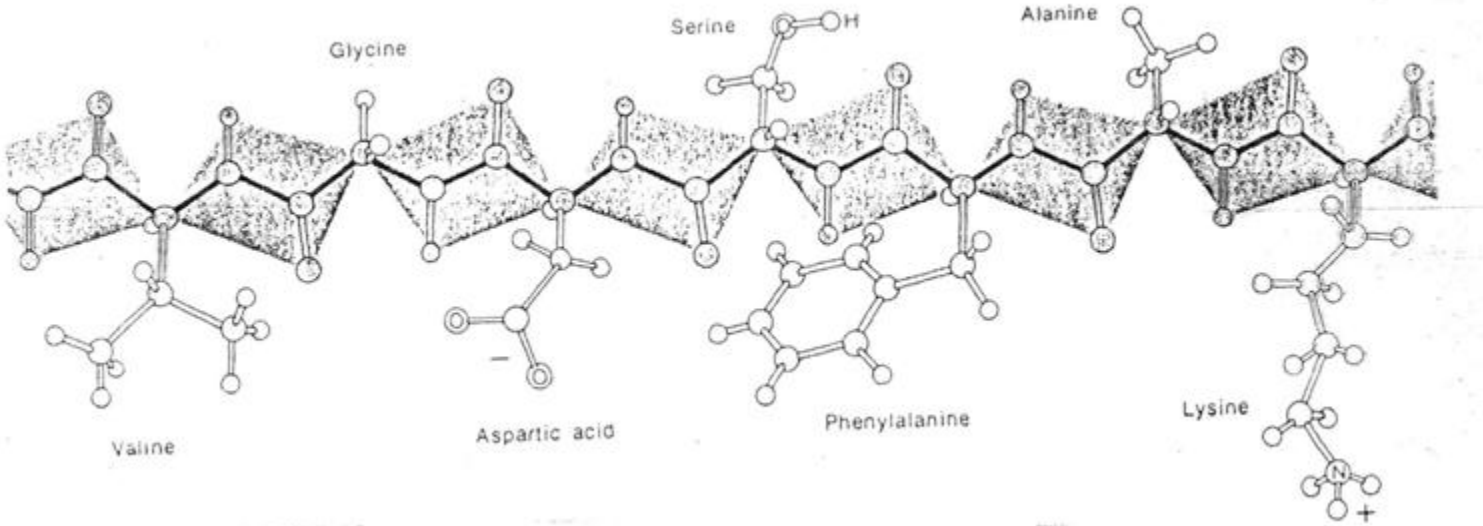
1 – O grupo imina (-NH-) da ligação peptídica não tem tendência significativa para se ionizar ou protonar dentro de uma gama de valores de pH de 0 a 14.

2 – A ligação peptídica é planar, i.e., todos os seis átomos da ligação peptídica (os dois carbonos α dos dois aminoácidos adjacentes, o C e o O do grupo carbonilo e o N e o H do grupo imina) são complanares.

3 – A ligação peptídica é relativamente rígida, i.e., existe uma restrição relativamente elevada à rotação, que é de cerca de 18 kcal/mol.
Para os péptidos, esta barreira é suficientemente elevada para impedir a rotação à temperatura ambiente.
Este aspecto é de extrema importância, no que diz respeito à conformação tridimensiopnal das cadeias polipeptídicas.

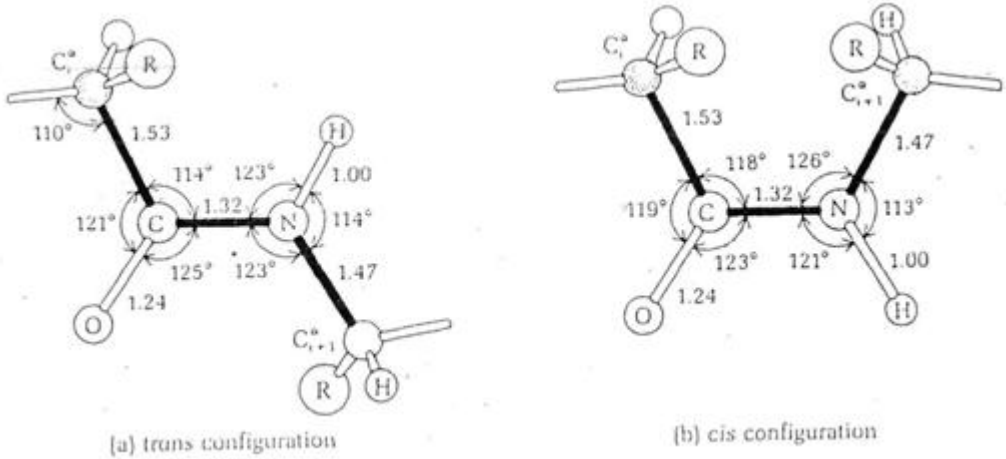
Assim, as rotações permitidas numa cadeia peptídica são as que envolvem rotações em torno das ligações covalentes simples que ligam cada átomo de carbono α aos grupos peptídicos planares adjacentes





Deste modo, o esqueleto de uma cadeia polipeptídica pode ser visualizado como uma série de planos rígidos separados por grupos metileno (-CHR-), contendo o carbono α, que é tetraédrico.

Ligação peptídica: configurações *cis-trans*

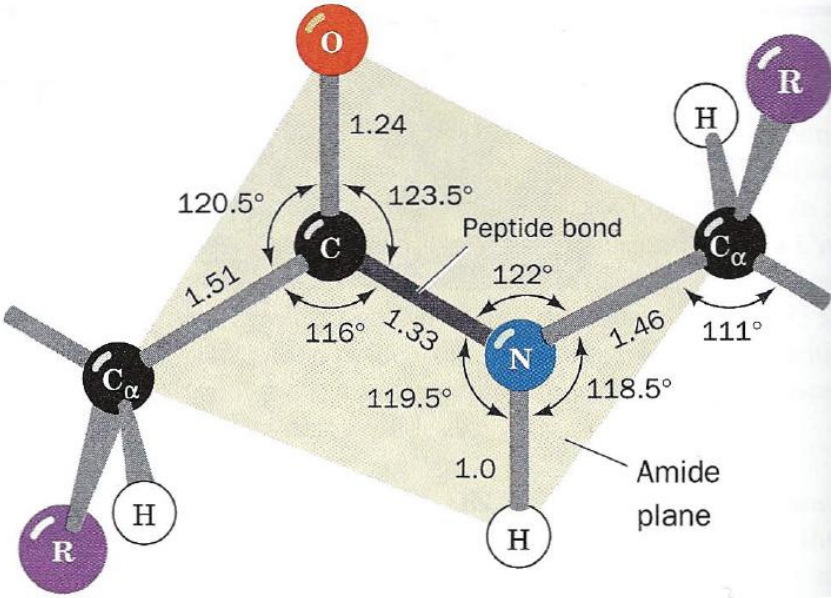


Em cada ligação peptídica, os átomos de carbono α podem ocorrer em duas configurações possíveis: *cis* ou *trans*.
Na configuração *trans*, os dois carbonos α com os seus grupos laterais R estão longe um do outro.
Na configuração *cis* eles estão próximos um do outro, o que leva a restrições de natureza espacial entre as duas cadeias laterais volumosas adjacentes R.

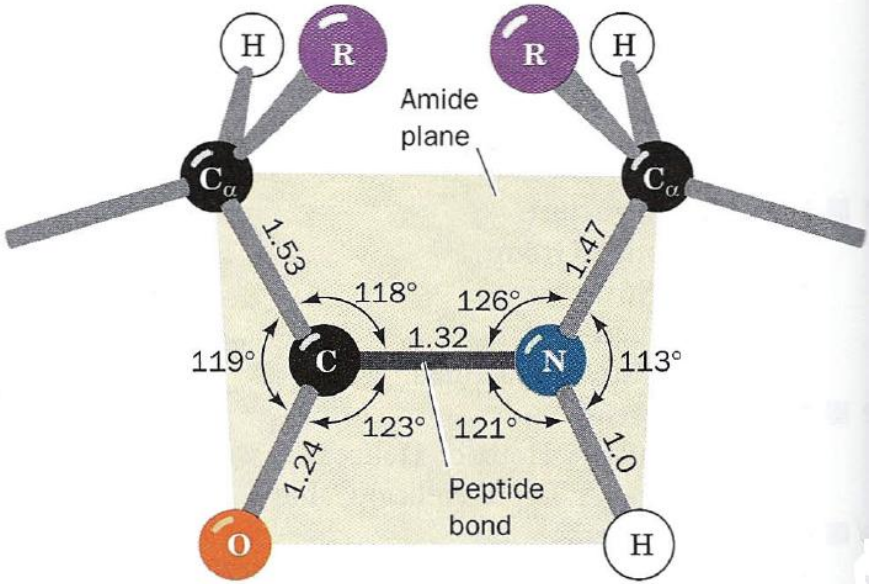
Por este motivo, a configuração *trans* é mais estável, em cerca de 2 kcal/mol, que a configuração *cis*, sendo, por isso, a configuração mais estável e, consequentemente, a configuração que predomina nas cadeias peptídicas.

Há uma excepção importante a esta generalização:
Ligações peptídicas envolvendo a prolina podem igualmente assumir uma configuração *cis* ou *trans*, porque a natureza espacial do anel tetra-hidropirrólico da prolina elimina as vantagens de estabilidade da configuração *trans*.

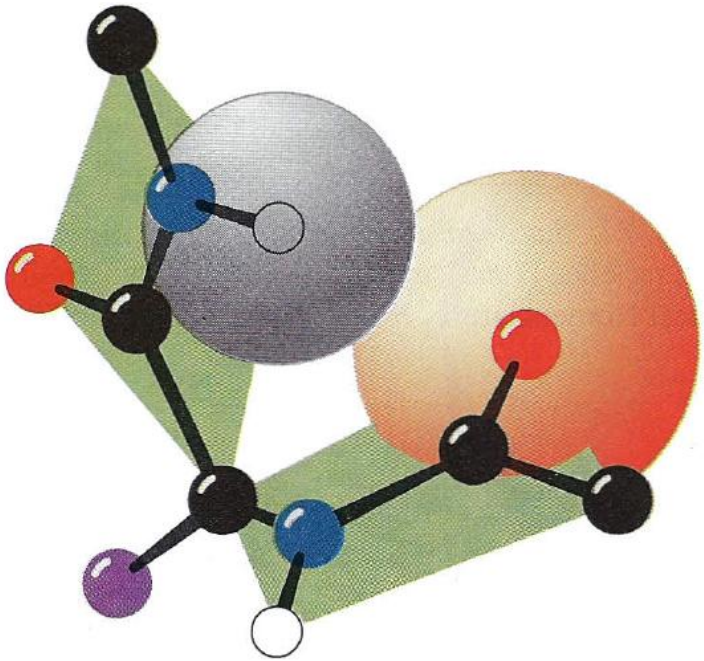
Existe uma enzima, a peptidil-prolil *cis-trans* isomerase, que catalisa a isomerização *cis-trans* de ligações peptídicas aminoácido X - prolina, não só durante a fase de aquisição da estrutura biologicamente activa de proteínas, como em proteínas já na forma nativa.



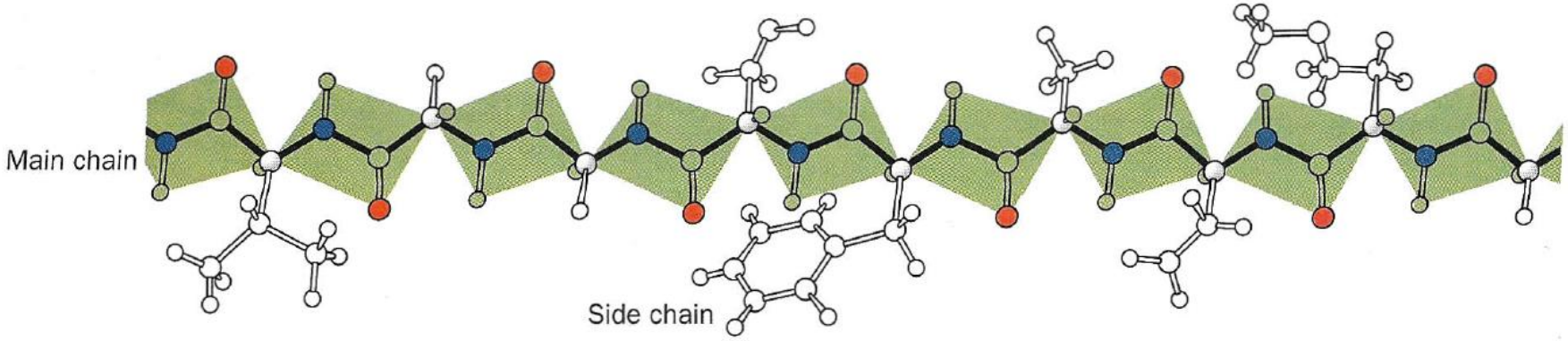
The trans-peptide group. The standard dimensions (in angstroms, Å, and degrees, °) of this planar group were derived by averaging the corresponding quantities in the X-ray crystal structures of amino acids and peptides.



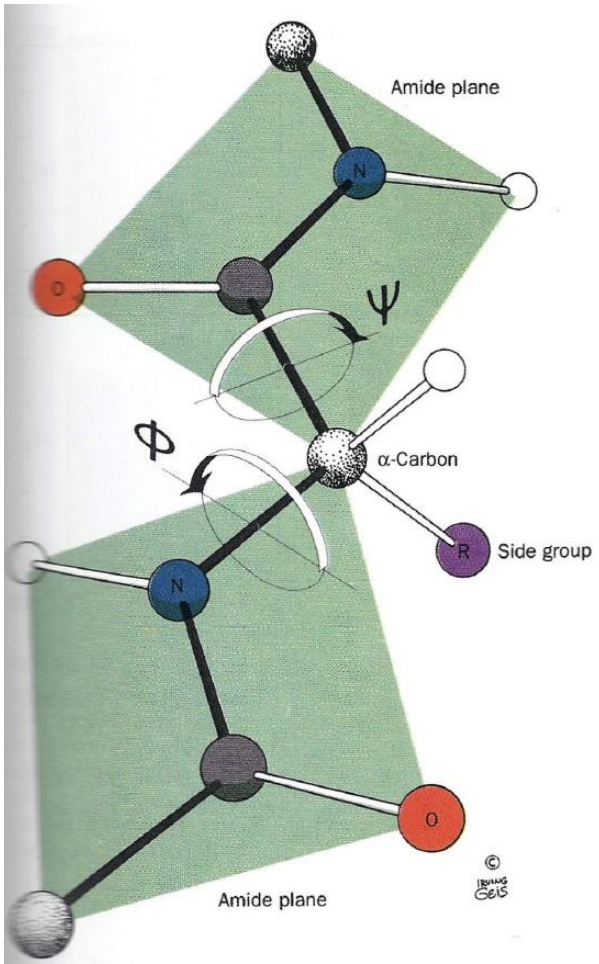
The cis-peptide group.



Steric interference between adjacent residues.

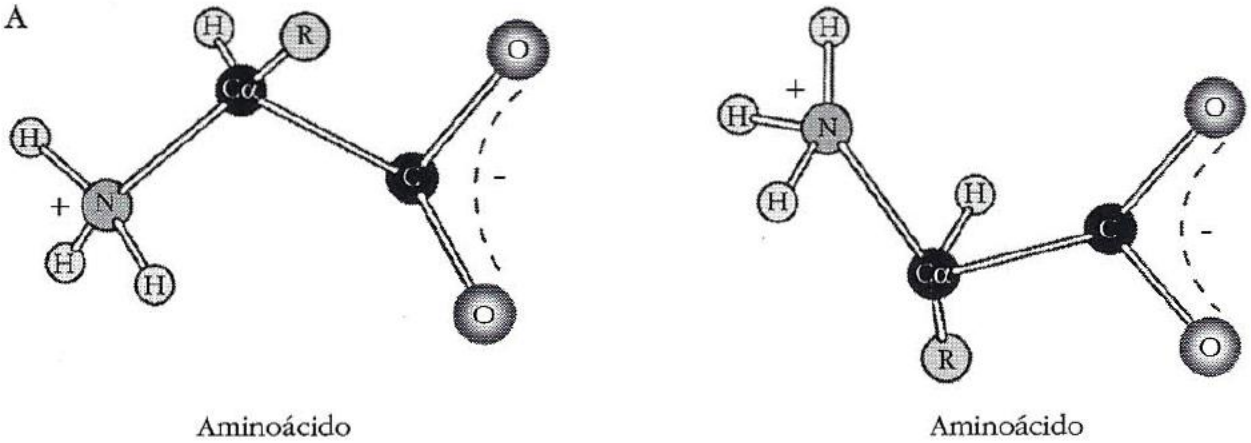


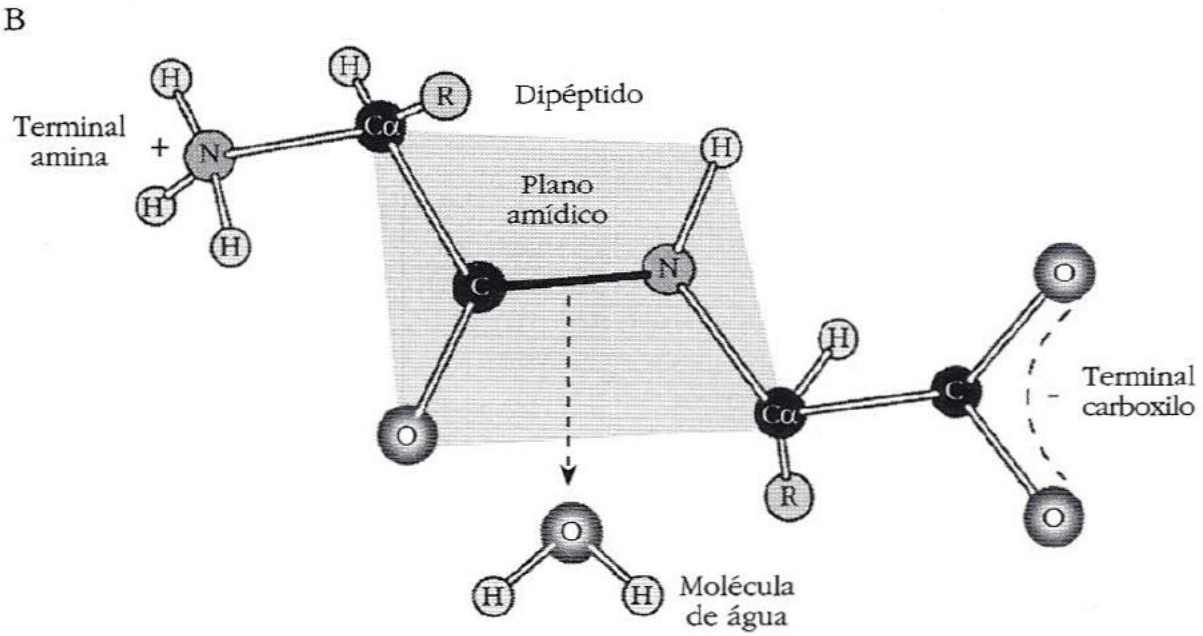
A polypeptide chain in its fully extended conformation showing the planarity of each of its peptide groups.



The torsional degrees of freedom in a peptide unit.

Formação de um dipéptido a partir de dois aminoácidos. A — Dois aminoácidos; B — Dipéptido contendo uma ligação peptídica. R representa a cadeia lateral dos aminoácidos





PÉPTIDOS

Oligopéptidos

Definição

São oligómeros de aminoácidos ligados sequencialmente (isto é, cabeça-com-pés, ou grupo carboxilo → grupo amina) uns aos outros por ligações peptídicas.

Definição

São oligómeros formados por aminoácidos ligados uns aos outros por ligações peptíticas. Podem ser sintetizados:

- quimicamente;

- enzimaticamente a partir de precursores mais simples, i.e., aminoácidos (exemplo: glutationa);

- por hidrólise de proteínas

Classificação

Consoante o número de resíduos de aminoácidos constituintes, assim o oligopéptido é denominado dipéptido, tripéptido, tetrapéptido, pentapéptido, hexapéptido, etc.

O termo oligopéptido é pouco usado e a fronteira entre péptido e polipéptido não está estabelecida com exactidão. Daí estes termos serem por vezes usados com um significado um tanto diverso.

Os oligopéptidos podem ser lineares (a situação mais geral) ou cíclicos.

Exemplos de péptidos de ocorrência natural

Encontram-se nas células vários péptidos simples, formados por um pequeno número de resíduos de aminoácidos, que pode ser de dois, três, quatro, até cerca de uma dezena. Referem-se seguidamente alguns exemplos.

O tripéptido **glutationa** (ver diapositivo atrás) está grandemente difundido entre os seres vivos, encontrando-se desde os microrganismos aos mamíferos e às plantas superiores. Parece ter um importante papel antioxidante na célula, contribuindo para a manutenção do estado reduzido de proteínas e enzimas, participa em reacções de oxidorredução e pode também participar em transaminações.

Um péptido semelhante à glutationa, o **ácido oftálmico** (ácido glutâmico - ácido α-aminobutírico - glicina) foi isolado do cristalino de vitela. Os dipéptidos **carnosina** (β-alanina - histidina) e **anserina** (metilcarnosina) estão presentes no músculo dos mamíferos, mas o seu papel fisiológico é desconhecido. Os músculos de cobra possuem um outro derivado metilado da carnosina, a **ofidina.**

No cérebro existem dois pentapéptidos, as **encefalinas**, com propriedades idênticas às da morfina (inibição de percepção da dor). A, identificação destes péptidos, do cérebro de porco, mostrou possuírem a seguinte composição:

Tyr - Gly - Gly - Phe - Met (Met-encefalina) e
Tyr - Gly - Gly – Phe-Leu (Leu - encefalina),

existindo na proporção de 3:1. Após síntese e ensaios laboratoriais verificou-se terem uma acção três vezes mais potente do que a morfina e 20 vezes mais do que a normorfina.

Octa a decapéptidos do plasma sanguíneo normal dos mamíferos, as **cininas** (como a bradicinina e a calidina) e as **angiotensinas** são importantes reguladores da circulação. A **bradicinina** (Arg- Pro - Pro - Gly - Phe - Ser - Pro - Phe - Arg) é um hipotensor potente, um relaxante muscular e participa nas reacções aos choques e às inflamações.

A **calidina** (Lys - bradicinina) é também um hipotensor**.**

As **angiotensinas** são potentes hipertensores, possivelmente envolvidos no desequilíbrio circulatório conhecido por hipertensão arterial; a angiotensina bovina 11 é o octapéptido: Asp - Arg - Vai - Tyr - lIe - His - Pro - Phe. Outra classe importante de péptidos inclui hormonas de animais superiores e de leveduras.

Ainda de importância são os péptidos com acção antibacteriana (antibióticos) produzidos por várias espécies de microrganismos.

Na tabela abaixo são indicados alguns exemplos de péptidos tóxicos para os mamíferos, produzidos por fungos, como, por exemplo, a **faloidina**, que é um dos venenos produzidos pelo cogumelo *Amanita phalloides*. A toxicidade deste composto é tal que bastam 50 μg para matar uma ratazana. Uma característica geral destes e outros péptidos com acção antibiótica ou tóxica é a de conterem, quer isómeros da série **D** de aminoácidos constituintes das proteínas, quer aminoácidos com características pouco comuns, não constituintes das proteínas.

Muitos outros péptidos podiam ser ainda referidos. Por exemplo, uma classe importante de péptidos é formada só por ácido glutâmico. De importância particular são os que se ligam ao resíduo de ácido pteróico do grupo de vitaminas designadas por ácido fólico. Assim, da levedura tem sido obtido um péptido contendo 10 a 11 unidades de ácido glutâmico. Outros péptidos deste ácido têm sido encontrados. Um tripéptido de glutamina, a **fastigiatina**, foi obtido da alga castanha *Pelvetia fastigiata.*

Tabela

Exemplos de péptidos com propriedades antimetabólicas

Compostos	Características	Organismos produtores
Faloidina	É um dos princípios tóxicos do *A. phalloides;* é um heptapéptido cíclico formado por Cys, Ala, hidroxi-Leu e alo-Hyp.	*Amanita phalloides*
Amanitinas	Péptidos cíclicos mais tóxicos do que a faloidina, mas de acção mais lenta.	*A. phalloides*
Ergotaminas Ergoxinas Ergotoxinas	Alcalóides do tipo péptido, produzidos pelo fungo da cravagem dos cereais; contêm D-Pro, Phe, Leu, Ileu, Val e ácido lisérgico.	*Claviceps purpurea*

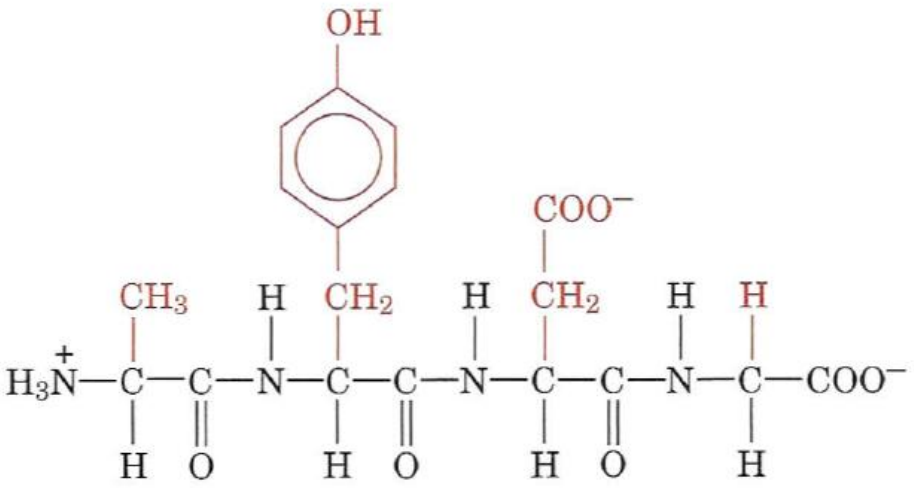
Péptidos bastante mais complexos, os polipéptidos, formados por várias dezenas a milhares de aminoácidos, são as estruturas unitárias que formam as proteínas. A elucidação do mecanismo através do qual a célula sintetiza as cadeias polipeptídicas foi uma das grandes descobertas cientifícas deste século.

Ao contrário do que sucede com os péptidos mais simples, cuja síntese celular ocorre directamente pela acção de enzimas específicas, os péptidos mais complexos e os polipéptidos só podem ser sintetizados ao nível dos ribossomas e graças à informação exacta enviada do núcleo na forma de RNA mensageiro. É necessário um RNA - mensageiro para cada cadeia polipeptídica sintetizada na célula, estabelecendo o RNA - mensageiro o número e a sequência precisa dos vários aminoácidos, ao longo do polipéptido.

Péptidos

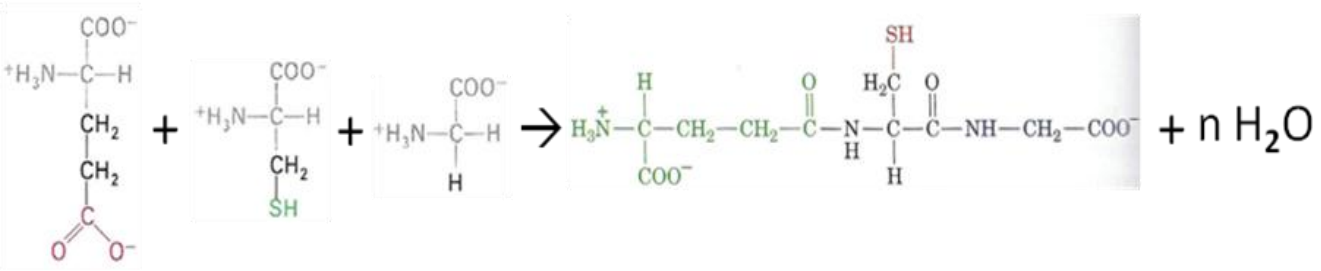
Questões:

1 – Qual o nome sistemático do tetrapéptido representado abaixo?



The tetrapeptide Ala-Tyr-Asp-Gly.

2 - Considere a reacção global de síntese do tripéptido glutationa a partir do L-glutamato, L-cisteína e glicina:



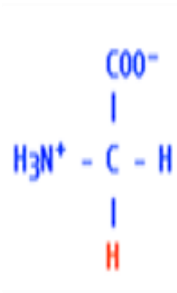
a) Calcule o valor do coeficiente estequiométrico **n**?

b) O nome de cada uma das ligações químicas formadas, sabendo que na primeira participa o grupo γ-carboxilo do L-glutamato?

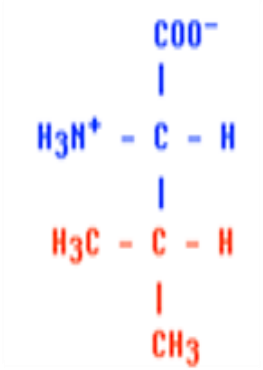
c) O nome sistemático da glutationa?

d) Porque razão não está indicada a configuração no nome do aminoácido glicina?

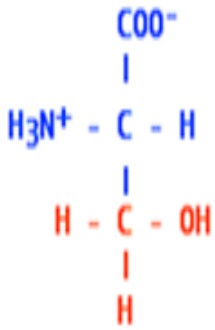
3 - Considere os seguintes nove aminoácidos proteicos:



A



B



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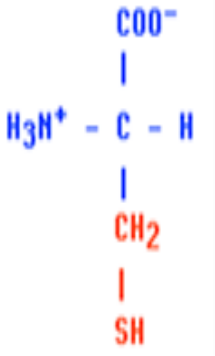

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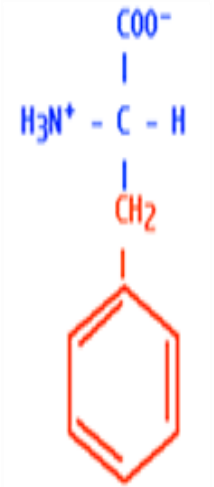
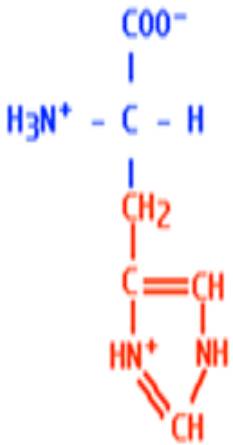
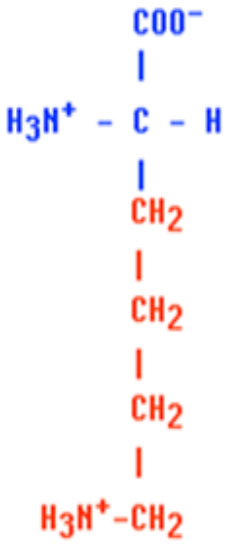


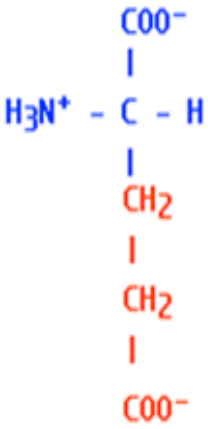
E



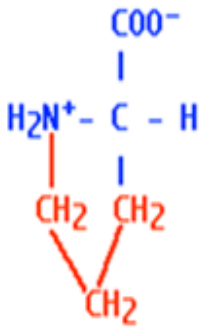
F



G



H



I

a) Indique o nome trivial, bem como as duas abreviaturas de cada um.

A -
B -
C -
D -
E -
F -
G -
H -
I -

b) De acordo com numa das classificações mais frequentes dos aminoácidos proteicos, estes são divididos em quatro grupos em função das características de polaridade/carga eléctrica da sua cadeia lateral. Classifique os aminoácidos **A** a **I**.

A -
B -
C -
D -
E -
F -
G -
H -
I -

c) De acordo com outra das classificações mais frequentes dos aminoácidos proteicos, estes são divididos em nove grupos em função da estrutura da sua cadeia lateral. Classifique os aminoácidos A a I.

A -
B -

C -
D -
E -
F -
G -
H -
I -

d) Defina ponto isoeléctrico (pI) de um aminoácido.

e) O pI da fenilalanina é de 5,48. Escreva a fórmula de estrutura deste aminoácido tal como ele ocorre a valores de pH de 2,1, 5,48 e 10,3. Como se denomina a sua forma a pH = 5,48?

f) Defina ligação eupeptídica e ligação isopeptídica.

g) O tripéptido glutationa tem o seguinte nome sistemático: γ-glutamilcisteínilglicina. Indique:

i) Como classifica este oligopéptido de acordo com o número de monómeros constituintes?

ii) Qual o aminoácido do terminal C da glutationa?

iii) Porque razão aparece a designação de cisteínilo em vez da de cisteína?

iv) A glutationa tem na sua constituição alguma ligação eupeptídica? Em caso afirmativo, indique qual é (ou quais são) e porquê.

v) A glutationa tem na sua constituição alguma ligação isopeptídica? Em caso afirmativo, indique qual é (ou quais são) e porquê.

vi) Qual o grupo químico funcional da glutationa que é responsável pela suas importantes propriedades biológicas? Qual o seu nome?

FIM