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Citrulline

The organic compound **citrulline** is an α-amino acid.[2] Its name is derived from *citrullus*, the Latin word for watermelon. Although named and described by gastroenterologists since the late 19th century, it was first isolated from watermelon in 1914 by Japanese researchers Yotaro Koga and Ryo Odake[3][note 1] and further codified by Mitsunori Wada of Tokyo Imperial University in 1930.[4] It has the formula $H_2NC(O)NH(CH_2)_3CH(NH_2)CO_2H$. It is a key intermediate in the urea cycle, the pathway by which mammals excrete ammonia by converting it into urea. Citrulline is also produced as a byproduct of the enzymatic production of nitric oxide from the amino acid arginine, catalyzed by nitric oxide synthase.[5]

Contents

Biosynthesis

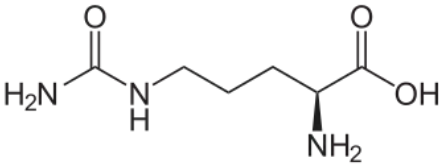
Citrulline can be derived from:

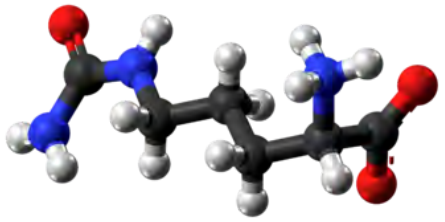
- from arginine via nitric oxide synthase, as a byproduct of the production of nitric oxide for signaling purposes
- from ornithine through the breakdown of proline or glutamine/glutamate
- from asymmetric dimethylarginine via DDAH

Citrulline is made from ornithine and carbamoyl phosphate in one of the central reactions in the urea cycle. It is also produced from arginine as a byproduct of the reaction catalyzed by NOS family (NOS; EC 1.14.13.39).[6] It is made from arginine by the enzyme trichohyalin at the inner root sheath and medulla of hair follicles.[7] Arginine is first oxidized into *N*-hydroxyl-arginine, which is then further oxidized to citrulline concomitant with release of nitric oxide.

Citrulline is also made by enterocytes of the small intestine.[2][8]

Citrulline





Names	
IUPAC name	2-Amino-5-(carbamoylamino)pentanoic acid[1]
Identifiers	
CAS Number	627-77-0 (https://commonchemistry.cas.org/detail?cas_rn=627-77-0) ✓ 13594-51-9 (https://commonchemistry.cas.org/detail?cas_rn=13594-51-9) (*D*) ✓ 372-75-8 (https://commonchemistry.cas.org/detail?cas_rn=372-75-8) (*L*) ✓
3D model (JSmol)	Interactive image (https://chemapps.stolaf.edu/jmol/jmol.php?model=NC%28CCCNC%28N%29%3DO%29C%28O%29%3DO)
3DMet	B01217 (http://www.3dmet.dna.affrc.go.j

Function

Several proteins contain citrulline as a result of a post-translational modification. These citrulline residues are generated by a family of enzymes called peptidylarginine deiminases (PADs), which convert arginine into citrulline in a process called citrullination or deimination with the help of calcium ions. Proteins that normally contain citrulline residues include myelin basic protein (MBP), filaggrin, and several histone proteins, whereas other proteins, such as fibrin and vimentin are susceptible to citrullination during cell death and tissue inflammation.

Circulating citrulline concentration is a biomarker of intestinal functionality.[9][10]

See also

- Citrullinemia

Notes

1. Early references spell Ryo Odake's name as *Ryo Othake*.

References

1. "Citrulline - Compound Summary" (https://pubchem.ncbi.nlm.nih.gov/summary/summary.cgi?cid=833&loc=ec_rcs#x291). *PubChem Compound*. USA: National Center for Biotechnology Information. 16 September 2004. Identification. Retrieved 1 May 2012.
2. Banerjee, Aryamitra (2014-01-01), Gupta, Ramesh C. (ed.), "Chapter 15 - Gastrointestinal toxicity biomarkers" (http://www.sciencedirect.com/science/article/pii/B9780124046306000154), *Biomarkers in Toxicology*, Boston: Academic Press, pp. 269–277, doi:10.1016/b978-0-12-404630-6.00015-4 (https://doi.org/10.1016%2Fb978-0-12-404630-6.00015-4), ISBN 978-0-12-404630-6, S2CID 88798984 (https://api.semanticscholar.org/CorpusID:88798984), retrieved 2020-11-10
3. Fragkos, Konstantinos C.; Forbes, Alastair (September 2011). "Was citrulline first a laxative substance? The truth about modern citrulline and its isolation" (http://discovery.ucl.ac.uk/1317394/1/1317394.pdf) (PDF). *Nihon Ishigaku Zasshi. [Journal of Japanese History of Medicine]*. **57** (3): 275–292. ISSN 0549-3323 (https://www.worldcat.org/issn/0549-3323). PMID 22397107 (https://pubmed.ncbi.nlm.nih.gov/22397107).

	p/cgi/show_data.php?acc=B01217)
Beilstein Reference	1725417, 1725415 *D*, 1725416 *L*
ChEBI	CHEBI:18211 (https://www.ebi.ac.uk/chebi/searchId.do?chebiId=18211) ✗
ChEMBL	ChEMBL444814 (https://www.ebi.ac.uk/chembldb/index.php/compound/inspect/ChEMBL444814) ✓
ChemSpider	810 (https://www.chemspider.com/Chemical-Structure.810.html) ✗ 553200 (https://www.chemspider.com/Chemical-Structure.553200.html) *D* ✗ 9367 (https://www.chemspider.com/Chemical-Structure.9367.html) *L* ✗
DrugBank	DB00155 (https://www.drugbank.ca/drugs/DB00155) ✓
ECHA InfoCard	100.006.145 (https://echa.europa.eu/substance-information/-/substanceinfo/100.006.145)
EC Number	211-012-2
Gmelin Reference	774677 *L*
IUPHAR/BPS	722 (http://www.guidetopharmacology.org/GRAC/LigandDisplayForward?tab=summary&ligandId=722)
KEGG	D07706 (https://ww

4. Fearon, William Robert (1939). "The Carbamido Diacetyl Reaction: A Test For Citrulline" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1264464). *Biochemical Journal*. **33** (6): 902–907. doi:10.1042/bj0330902 (https://doi.org/10.1042%2Fbj0330902). PMC 1264464 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1264464). PMID 16746990 (https://pubmed.ncbi.nlm.nih.gov/16746990).
5. "Nos2 - Nitric Oxide Synthase" (https://www.uniprot.org/uniprot/P29477). *Uniprot.org*. Uniprot Consortium. Retrieved 10 February 2015.
6. Cox M, Lehninger AL, Nelson DR (2000). *Lehninger principles of biochemistry* (https://archive.org/details/lehningerprincip01lehn) (3rd ed.). New York: Worth Publishers. p. 449 (https://archive.org/details/lehningerprincip01lehn/page/449). ISBN 978-1-57259-153-0. Retrieved 13 March 2020.
7. Rogers, G. E.; Rothnagel, J. A. (1983). "A sensitive assay for the enzyme activity in hair follicles and epidermis that catalyses the peptidyl-arginine-citrulline post-translational modification". *Current Problems in Dermatology*. **11**: 171–184. doi:10.1159/000408673 (https://doi.org/10.1159%2F000408673). ISBN 978-3-8055-3752-0. PMID 6653155 (https://pubmed.ncbi.nlm.nih.gov/6653155).
8. DeLegge, Mark H. (2019-01-01), Corrigan, Mandy L.; Roberts, Kristen; Steiger, Ezra (eds.), "Chapter 7 - Enteral Access and Enteral Nutrition in Patients With Short Bowel Syndrome" (http://www.sciencedirect.com/science/article/pii/B978012814330800007X), *Adult Short Bowel Syndrome*, Academic Press, pp. 81–96, doi:10.1016/b978-0-12-814330-8.00007-x (https://doi.org/10.1016%2Fb978-0-12-814330-8.00007-x), ISBN 978-0-12-814330-8, S2CID 81295089 (https://api.semanticscholar.org/CorpusID:81295089), retrieved 2020-11-10
9. Fragkos, Konstantinos C.; Forbes, Alastair (2017-10-12). "Citrulline as a marker of intestinal function and absorption in clinical settings: A systematic review and meta-analysis" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5833233). *United European Gastroenterology Journal*. **6** (2): 181–191. doi:10.1177/2050640617737632 (https://doi.org/10.1177%2F2050640617737632). PMC 5833233 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5833233). PMID 29511548 (https://pubmed.ncbi.nlm.nih.gov/29511548).
10. Crenn, P.; et al. (2000). "Post-absorptive plasma citrulline concentration is a marker of intestinal failure in short bowel syndrome patients". *Gastroenterology*. **119** (6): 1496–505. doi:10.1053/gast.2000.20227 (https://doi.org/10.1053%2Fgast.2000.20227). PMID 11113071 (https://pubmed.ncbi.nlm.nih.gov/11113071).

	w.kegg.jp/entry/D07706) ✓
MeSH	Citrulline (https://www.nlm.nih.gov/cgi/mesh/2014/MB_cgi?mode=&term=Citrulline)
PubChem CID	833 (https://pubchem.ncbi.nlm.nih.gov/compound/833) 637599 (https://pubchem.ncbi.nlm.nih.gov/compound/637599) *D* 9750 (https://pubchem.ncbi.nlm.nih.gov/compound/9750) *L*
UNII	1OYO2NV4NM (https://fdasis.nlm.nih.gov/srs/srsdirect.jsp?regno=1OYO2NV4NM) ✓ KNS2VUH6P2 (https://fdasis.nlm.nih.gov/srs/srsdirect.jsp?regno=KNS2VUH6P2) (*D* ✓ 29VT07BGDA (https://fdasis.nlm.nih.gov/srs/srsdirect.jsp?regno=29VT07BGDA) (*L*) ✓
CompTox Dashboard (EPA)	DTXSID80883373 (https://comptox.epa.gov/dashboard/chemical/details/DTXSID80883373)
InChI	
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SMILES	
NC(CCCNC(N)=O)C(O)=O	

Properties	
Chemical formula	$C_6H_{13}N_3O_3$
Molar mass	175.188 g·mol^{-1}
Appearance	White crystals
Odor	Odourless
log *P*	−1.373
Acidity (pK_a)	2.508
Basicity (pK_b)	11.489
Thermochemistry	
Heat capacity (*C*)	232.80 J K^{-1} mol^{-1}
Std molar entropy ($S^{\ominus}_{298}$)	254.4 J K^{-1} mol^{-1}
Related compounds	
Related alkanoic acids	*N*-Acetylaspartic acid Aceglutamide *N*-Acetylglutamic acid Pivagabine
Related compounds	Bromisoval Carbromal
Except where otherwise noted, data are given for materials in their standard state (at 25 °C [77 °F], 100 kPa). ✗ verify (what is ✓✗ ?) Infobox references	

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