

CYSTEINE –MASTER ANTIOXIDANT

Pravina Piste

P.G. Department of Chemistry, Y. C. Institute of Science, Satara, Maharashtra, India.

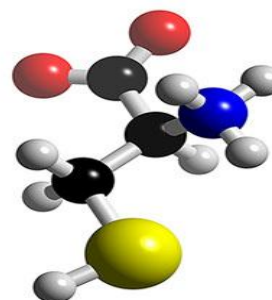
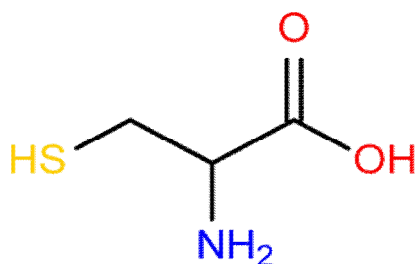
ABSTRACT

Cysteine is one of the most versatile molecules in biology, taking over such different functions as catalysis, structure, regulation and electron transport during evolution. It plays a key role in stabilizing extracellular proteins and defining the structures of many proteins. Disulfide bond in cysteine play an important role in folding and stability of some proteins by stabilizing the folded form. Extracellularly by the cross linking proteins, cysteines increase the molecular stability of a protein in the harsh extracellular environment and also function to confer proteolytic resistance. Scientists in Finland believe that cysteine containing chewing gum could become a new way of preventing upper digestive tract cancers.

Key words: Cysteine, glutathione, cystinosis , Human hair.

INTRODUCTION

Cysteine is a naturally occurring sulphur-containing amino acid that is found in most proteins, although only in small quantities. It is one of the 20 standard amino acids required by human beings and is unique among them in that, it contains a thiol group. A thiol group (sulfhydryl group) is a functional group composed of a sulfur atom and a hydrogen atom (-SH). It is responsible for a number of important functions of cysteine, such as allowing the formation of disulfide bonds that are crucial to defining the structures of many proteins. The other sulphur containing amino acid, methionine cannot form disulfide bonds.



Structure of Cysteine

Cysteine is often involved in electron transfer reactions and helps an enzyme catalyze reaction. It is also vital for the intracellular manufacture of the important antioxidant glutathione found in living animal an levels in major organs and bone marrow, providing the body with especially useful in the reduction and accrual of age spots.

A genetic abnormality can impact the normal complex co-ordination of the human body resulting in a condition known as Cystinuria where this amino acid forms hard cysteine kidney stones. Cysteine is on oxidized form of a disulfide bond. Cysteine is named after cystine, which comes from

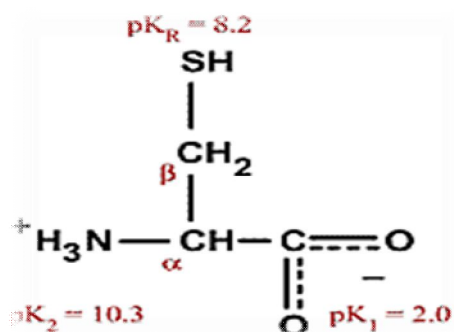
the greek word kustis meaning bladder and it was first isolated from kidney stones.

Wacker Biochem informed us that they produce L-cysteine through a microbial fermentation process developed in 2001 using corn sugar as growth medium. Doug Hacklt of premium ingredients, a major supplier of L-cysteine derived from human hair or duck feathers. L-cysteine is considered a substance that is generally recognized as safe by the food and drugs administration. It is manufactured in Japan, China and Germany only. Human hair is cheapest source for L-cysteine. Some reports suggest that European union countries are thinking to ban the use of L-cysteine from human hair in food products.

Cysteine is an extremely remarkable substance, as an amino acid, cysteine earth but unlike the other 19 amino acids used by living organisms to synthesize proteins cysteine sulfhydryl group. This process entails benefits not only because of its consistently high purity but also because production itself until now the use of human hair or animal hair as base material to made cysteine.

Properties of Cysteine

Like most thiols, cysteine undergoes a variety of redox reactions. Oxidation by removal of hydrogen of cysteine produce the aforementioned disulfide cysteine. More aggressive oxidants produce sulfinic acid or sulfonic acid. The cysteine thiol group is also nucleophilic and thus can undergo addition and substitution reactions.



Thiol groups become much reactive when they are ionized and cysteine residues in proteins have PKa values close to neutrality

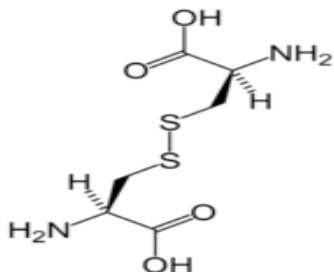
so are often in their reactive thiolate form in the cell.

The thiol group also has a high affinity for heavy metals so that proteins containing cysteine will bind metals such as Mercury, Lead and Cadmium tightly. Cysteine residues in proteins are reactive and readily form disulfide bonds with other cysteine residues. Reduction and s-Carboxymethylation is used to cap cysteine residues and prevent them from reacting and forming disulfide linkage. The RCM reaction is normally used as a prelude to enzymatic digestion of a protein or as a prelude to HPLC or LC/MS analysis of cysteine containing peptides, s-carboxymethylation makes it easier for proteolytic enzymes to more efficiently and completely digest a protein. In addition the RCM reaction is used to simplify reverse phase peptide maps. A peptide map that contains multiple disulfide linked peptide makes the analysis and identification of those peptides difficult. Another complication is that most enzyme digests are performed at elevated pH. At high pH disulfide bonds can scramble further complicating the peptide mapping analysis by the introduction of the artificial disulfide linkages.

Biochemistry

Cysteine is a standard amino acid, being required by people for normal functioning. Amino acids which are the basic structural building blocks of protein are organic molecules with three main components, an R- group or side chain, unique to each amino acid. Although over 100 amino acids exist in nature, human body requires about 20 amino acids called standard amino acids for normal functioning. Most amino acids in occur in two possible optical isomers called D and L. The L-amino acids represents the vast majority of amino acids found in proteins. The naturally occurring form of cysteine is L-cysteine. As noted, cysteine is characterized by presence of thiol group since thiol group can undergo reduction reactions. Oxidation of cysteine can produce a disulfide bridge is a single covalent bond derived from coupling of thiol groups. The overall connectivity is C-S-S-C that is, when cysteine is oxidized it can

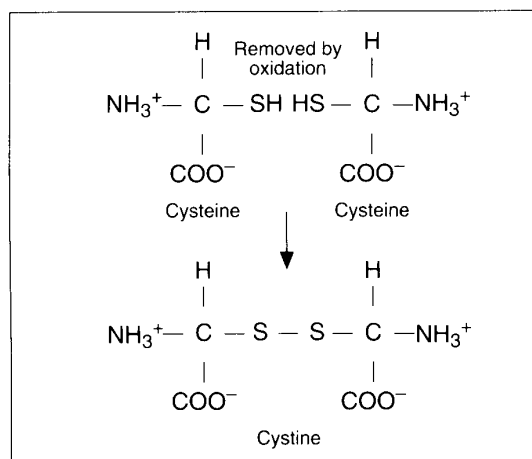
form cystine which is two cysteine residues joined by disulfide bond (cys-S-S-cyn) between the -SH group. This reaction is reversible, as reduction of this disulfide bond regenerates two cysteine molecules.



Cysteine showing disulfide bond

This disulfide bonds of cysteine are crucial to defining the structures of many proteins. Disulfide bond play an important role in folding and stability of some proteins by stabilizing the folded form. Extracellularly by the cross linking proteins, cysteines increase the molecular stability of a protein in the harsh extracellular environment and also function to confer proteolytic resistance. Intracellularly, disulfide bridges between cysteine within a polypeptide support the proteins secondary structure. Insulin is an example of protein with cystine crosslinking where two separate peptide chains are connected by pair of disulfide bonds. Some important cysteine derived nucleophiles include ubiquitin ligases which transfer ubiquitin to its pendant proteins. Ubiquitin is small regulatory protein that is ubiquitous in eukaryotes. Another example are capping enzymes which engage in proteolysis in apoptotic cycle. These roles are typically limited to intracellular milieu where the environment is reducing and cysteine is not. Cysteine also plays a key role in stabilizing extracellular proteins. Cysteine can react with itself to form an oxidized dimer by formation of a disulfide bond. The environment within a cell is too strongly reducing for disulfides to form, but in the extracellular environment, disulfides can form and play a key role in stabilizing many such proteins, such as the digestive enzymes of the small intestine, Protein

disulfide isomerases catalyze the proper formation of disulfide bonds. The cell transfer and dehydroascorbic acid to the endoplasmic reticulum which oxidizes the environment. In this environment, cysteines are generally oxidized to cystine and no longer functions as a nucleophile.

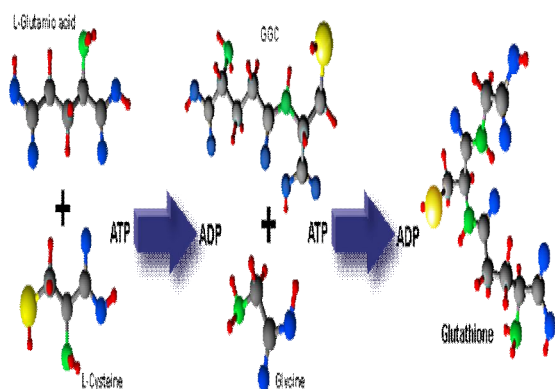


Biological functions

Due to ability to undergo redox reactions, Cysteine has antioxidant properties. Cysteine is an important source of sulphur in human metabolism and although it is classified as a non essential amino acid, it may be essential for infants, the elderly and individuals with certain disease metabolic diseases or who suffer from mal-absorption syndromes.

It is an important precursor in the production of antioxidant glutathione, which protects cells from toxins such as free radicals, in the human body and other organisms. The systematic availability of oral glutathione (G-SH) is negligible, the vast majority of it must be manufactured intracellularly.

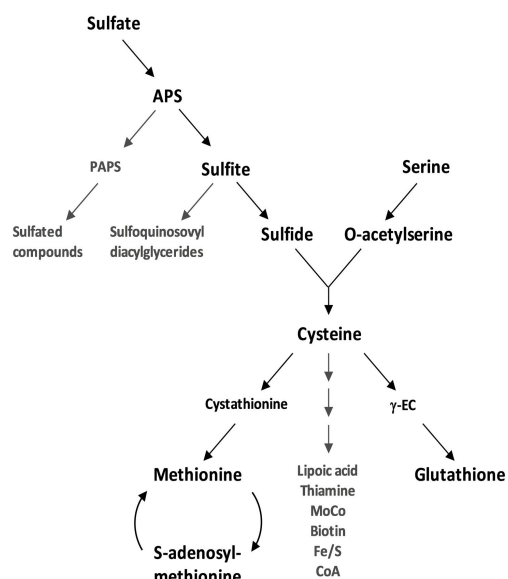
Glutathione is a tripeptide antioxidant made up of three amino acids viz. cysteine, glycine and glutamate. Glutamate and glycine are readily available in most North American diets but the availability of cysteine makes it be the rate limiting substance for the synthesis of glutathione within the cell.



Structure of Glutathione

It is sulphahydryl (Thiol) group of cysteine that serves as proton donor and is responsible for the biological activity of glutathione. Sometimes referred to as the master antioxidant.

Glutathione regulates the actions of lesser antioxidants such as vit.C and vit. E and the levels of glutathione in cells are predictive of how long someone will live. The free amino acid cysteine (supplied supplementary by NAC) does not represent an ideal delivery system to the cell. Cysteine is potentially toxic and spontaneously catabolized in the gastrointestinal tract and blood plasma. Conversely, cysteine absorbed during digestion as cystine in the gastrointestinal tract is more stable than the free amino acid cysteine. It travels safely through the GI tract and blood plasma and is promptly reduced to the two cysteine molecules upon cell entry.



Health benefits

According to a health products retailer, cysteine is one of the body's most effective antioxidants and destroyers of the metabolisms toxic waste products that are said to accelerate ageing. It is also naturally produced in sulphur containing foods such as egg yolks, red peppers, garlic, onions, broccoli and Brussels sprouts. It is hairy by nature. It can help prevent hair loss and stimulate its growth and used extensively in the food industry as a dough conditioning agent and to produce meat flavours, also has applications in other industries including pharmaceuticals and cosmetics. It is precursor in some dietary supplements.

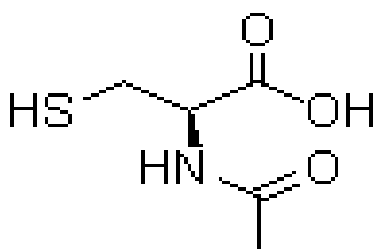
Cysteine properties as a free radical scavenger reducing agent and glutathione precursor may be raw material for the fast growth market of functional food supplements. Also it is in great pharmaceutical field. N-Acetyl cysteine breaks open the disulphide bonds in bronchial phlegm, is prevented from lodging in the bronchial tubes and can be coughed up. Cysteine is thus used for coughs and even mucoriscidosis. There is also a great demand for vegetarian amino acids and pharmaceuticals. Human creativity is also reflected in the commercial production and application of cysteine and its derivatives in adding flavor to food, a baking processing aid and hair care among other practical applications.

One report states that not only it is effective in preventing the side effects of drinking such as a hangover but it prevents liver and brain damage as well it also reduces lung damage such as emphysema, resulting from smoking. It is used in the treatment of skin diseases for low count of white blood cells and in some cases for anemia. To prevent the formation of such stones large amount of fruits and vegetables especially citrus fruits are recommended. They help to produce an alkaline urine which prevents crystal formation in these amino acids. Excessive loss of cysteine in the urine is said to be a hereditary disorder.

Cysteine supplements taken along with Vit.C at the end of a meal, somehow neutralize some of the excess insulin which is responsible for fat production. It protects body from damage by oxidants. A good way

to keep your cysteine level high is to eat foods that contain cysteine or methionine, the essential amino acid your body needs to make cysteine. Good choices are eggs, meat, dairy products and whole grains. Accumulation of free cysteine in the body tissues can lead to a rare disease known as cystinosis. This results in appearance of cystine crystals in the cornea, conjunctiva, bone marrow, lymph nodes, leukocytes and internal organs.

N-acetyl cysteine (NAC) is modified form of cysteine a non essential amino acid wherein an acetyl group is attached to the nitrogen atom that can be manufactured in the liver which helps the body make the antioxidants enzyme glutathione. . This compound is sometimes considered as a dietary supplement. NAC is often used as a cough medicine as it breaks up the disulfide bonds in the mucus and thus liquefies it, easier to cough up. Several studies have found that it is beneficial to people with chronic bronchitis and there is preliminary evidence to suggest that it may help prevent colon cancer. It is believed by some that NAC may help to promote hair growth and prevents hair loss. It is also used as nutrient in baby milk formula and dietary suppliments. Scientists in Finland believe that cysteine containing chewing gum could become a new way of preventing upper digestive tract cancers.



Structure of N-Acetyl Cysteine

The Pharmacological role of cysteine in ameliorating or exacerbating mineral toxicities and contributions to the chemistry of human hair, analyze of cysteine and cysteine oxides in untreated human hair .The role of the thiol N-acetyl cysteine in the prevention of markers and reduces the exacerbation rate in respiration and effect of supplementation with a cysteine donar on muscular performance .

A cysteine rich extracellular protein, LAT 52, intracts with the extracellular domain of the pollen receptor kinase LePRK 2. Acetyl cysteine protects against acute renal damage in patient coronary procedure and the antioxidant acetyl cysteine reduces cardiovascular failure. The prevention of contract angiography can be controlled by acetyl cysteine. Microbial processes for the production of the sulphur compounds such as L-cysteine, glutathione and biotin which are useful cosmetic materials.

The thioglycolic acid and cysteine is used in hair treatment products at ceramic carbon composite electrodes. Epidermal cysteine-rich secretory protein 1 encoding gene is expressed by Peterson in murina hair follicles and down regulated in mice over expressing Hoxc 13. Human hair keratin-Associated proteins are a major component of the hair fiber and play crucial roles in forming a strong hair shaft through a cross linked which are produced from hair keratins. Recently the study of human KAP genes has advanced significantly. So far five clusters of human KAP genes have been characterized by Yutaka.

Hangover Remedy

Cysteine has been linked to aiding in the remedy of certain hangover symptoms. It directly counteracts the poisonous effects of acetaldehyde, a particularly toxic by-product of alcohol in the human body. Cysteine attracts the toxin, breaking it down into the non toxic acetate, a substance similar to vinegar. The actual effectiveness of consuming cysteine as part of hangover remedy is unclear.

CONCLUSION

Cysteine is an important source of sulphur in human metabolism. It is an important precursor in the production of antioxidant glutathione, which protects cells from toxins such as free radicals, in the human body and other organisms. According to a health products retailer, cysteine is one of the body's most effective antioxidants and destroyers of the metabolisms toxic waste products that are said to accelerate ageing. It can help prevent hair loss and stimulate its growth and used extensively in the food industry as a dough conditioning agent and

to produce meat flavours, also has applications in other industries including pharmaceuticals and cosmetics. It is effective in preventing the side effects of drinking such as a hangover but it prevents liver and brain damage as well it also reduces lung damage such as emphysema, resulting from smoking. It is used in the treatment of skin diseases for low count of white blood cells and in some cases for anemia. To prevent the formation of such stones large amount of fruits and vegetables especially citrus fruits are recommended. They help to produce an alkaline urine which prevents crystal formation in these amino acids. Excessive loss of cysteine in the urine is said to be a hereditary disorder. It protects body from damage by oxidants. A good way to keep your cysteine level high is to eat foods that contain cysteine or methionine, the essential amino acid your body needs to make cysteine. Good choices are eggs, meat, dairy products and whole grains. Accumulation of free cysteine in the body tissues can lead to a rare disease known as cystinosis. This results in appearance of cystine crystals in the cornea, conjunctiva, bone marrow, lymph nodes, leukocytes and internal organs.

REFERENCES

1. Tozowa K, Okamoto T, Hayashi Y, Sasaki S, Kawsci N and Kohri K. Estrogen and the selective estrogen receptor modulator Nature Cell Biology. 2011;2-7.
2. Huang Z, Derksen DJ and Vederds JC. A seminaphthofluorescein-based fluorescent chemodosimeter for the highly selective detection of cysteine. Org Lett. 2010;12(10): 2282-2285.
3. Bulaj G, Kortemmne T and Goldenbrg D. Ionization-reactivity relationships for cysteine thiols in polypeptides. Biochemistry. 2007; 37(5):8965-72.
4. Suzanne PM, Kitty B, Cleutjens JM and Daeman JAP. Cathepsin cysteine proteases in cardiovascular disease J of Federation of Am Soc Exptl Biol. 2007,21(12):3029-3041.
5. Morno J, Munia M and Navano J. Rubisco conformation and activity through its cysteine residues. J Exp Bot. 2007;59(7):1605-1614 .
6. Sass JO, Skladal D, Zaiger B, Romani N and Utermann B. Archives of Dermatological Research. 2007; 296(4):188-191.
7. Walker JRL and Reddish CES. J of Mood and Agric. 2006;15:902-904.
8. Doming JE, Simmons CR, Karplus A, Gehring AM and Stipanuk MH. J of Bacteriology. 2006;188(15):5561-5569.
9. Marika B, Lind B, Bjornberg KA, Palm B, Einarsson O and Vahter M. Environmental Health, A Global Access Science Source.2005;4,:20.
10. Wang L. Determination of thioglycolic acid and cysteine in hair-treatment. Electroanalysis. 2005;9:1294-1297.
11. Oidemeyer JB, Biddle WP and Wurdeman RL. N – Acetyl Cysteine. Am Heart J. 2003; 146:E 23.
12. Tepel M, Vander GM and Statz M. J Am Coll Cardiol.2003;107:992-5.
13. Shyu KG, Cheng JJ and Kuan P Acetylcysteine protects against acute renal damage in patients with abnormal renal function undergoing a coronary procedure. J Am Coll Cardiol. 2002;40:1383-8.
14. Tang W, Ezcurra I and Cormick SM. The Plant Cell. 2002; 14:2777-2287.
15. Regnier M, Duval C, Galey JB, Philippe M, Tuloup R and Schmit R. Cell Mol Biol. 1999;45:469-980 .
16. Lands LC, Grey VL and Smountas AA. Glutathion: For Energy and Muscle Growth. J of Appl Physiology. 1999; 4:1381-1385 .
17. .Pela R, Calcagni AM, Subiaco S. N-Acetyl Cysteine Overview infirmation. J Am Coll Cardial. 1999;66:495-500.
18. Morini MT and Aluigi CM. In vivo role of cytochrome P470 2E1 and Glutathione-S Appl Pharmacol. 1999;143:266-71 .
19. Sekharam M, Trotti A and Cunnick JM. Suppression of fibroblast cell cycle progression in G1 phase by N-acetylcysteine. Appl Pharmacol. 1998; 149: 210-6 .

20. Regnier M, Staquet MJ, Schmidt D and Schmidt R. Reactivity of Langerhans cells. *J Invest Dermatol.* 1997;109:510-512 .
21. Schmidt R, Krien P and Regnier M. *Anal Biochem.* 1996;235:113-118.
22. Darmon M and Blumenberg M. *Mol Bio of Skin.*1993;107-150 .
23. Ghio S, servi S and Perotti R. *J Natl Cancer Inst.* 1992; 86:798-800.
24. Schmidt R. Reconstructed human skin. *Skin Pharmacol.* 1990;3:65-148.
25. Sabine HT and Zahn H. Contributions to the chemistry of human hair. Analyses of cystine, cysteine and cystine oxides in untreated human hair. *Int J of Cosmetic Science.* 1987;9:101-110.
26. Kizawa K, Inoqe T and Troxler H. *J of Nutrition.* 1987;117(6):1003-1010.
27. Schmidt R, Reichert U, Michel S, Shroot B and Boucliev M. Modulation of Cellular Cholesterol and Its Effect on Cornified Envelope Formation in Cultured Human Epidermal Keratinocytes. *FEBS Lett.* 1985; 186:201-204 .
28. Zlotkin SH and Andpiison GH. Amino acids, methionine and cysteine. *Am J of Clinical Nutrition.* 1982; 36:862-67.
29. Rollitt RJ and Stanier PD. Reversal of premature hair greying in adult coeliac disease. *Biochem.* 1971; 122(4):433-444.
30. Vickery HB. White Amino acids" prescription for Nutrition.1932; 701.