Amino Acids

Crops

Identification

Chemical Names
The model used to illustrate amino acids used in crop production is glycine, or aminoacetic acid.

CAS Numbers:
Glycine: 56-40-6

Other Names:
See attached list for the amino acids most often found in protein. The model amino acids for crop production is glycine.

Other Codes:
none

Recommendation

Synthetic / Non-Synthetic:	**National List:**	**Suggested Annotation:**
Synthetic (Consensus)	*Not added to the National List. (Consensus)*	*Amino acids produced by chemical synthesis, such as the Strecker process or the Bucherer-Berg process; semifermentation or enzymatic processes on synthetic precursors; or using enzymes produced by a genetically modified organism (GMO) as defined by the NOSB; extracted from GMOs; produced by fermentation on an entirely synthetic (including GMO source) media; or extracted from naturally occurring organisms by use of synthetic strong acids, strong bases, or solvents; or produced by any process not explicitly described as below as "non-synthetic" are considered synthetic. (consensus)*
Not synthetic (Consensus)	*Not added to the National List (Consensus)*	*Amino acids produced from organisms that are not genetically engineered as defined by the NOSB and extracted by extracellular, mechanical, physical, biological, and / or enzymatic processes are considered non-synthetic. (Consensus)*
No consensus	*Not added to the National List*	*Amino acids produced from naturally occurring organisms cultured on a media that contains some but not all synthetic (including GMO) ingredients; and those extracted by the use of hydrolysis or ion exchange may or may not be synthetic depending on the specific circumstances, and should be reviewed on a case-by-case basis. (Not consensus)*

Characterization

Composition:
Amino acids have an amino group or amine (NH_2) adjacent to a carboxyl (COOH) group on a carbon. Glycine is generally considered the simplest amino acid. Glycine's chemical formula is H_2NCH_2COOH.

Properties:
A total of twenty different amino acids are present in protein hydrolysates, and other less common amino acids exist naturally and have biological functions. A growing number of non-protein amino acids that do not occur in nature have been synthesized. Except for glycine, all amino acids resulting from protein hydrolysis possess rotary optical activity. Amino acids that occur in plant or animal tissues are almost always in the L- enantiomer. This stereoisomerism is due to the presence of an asymmetric carbon atom. Therefore we can conclude that only the L-enantiomer amino acids may be considered non-synthetic. The D- isomers of amino acids may be present in the cell walls of microorganisms and in polypeptides endowed with antibiotic action (actinomycin D), gramicidin and tryocidin. Chemical synthesis of amino acids usually results in the creation of a DL-enantiomer or racemic mixture. Glycine is a white, odorless, crystalline powder having a sweetish taste. Solutions are acid to litmus tests. Decomposes at 233°C. Glycine is unique among the protein amino acids in that it is symmetrical and not optically active.

How Made:
Prior to 1950, most amino acids were produced by the denaturing and hydrolysis of various protein sources (Araki and Ozeki, 1991). May be isolated from protein from various sources. These may be plant, animal, or

microorganism derived and may or may not be from organisms that are genetically engineered as defined by the NOSB.

A number of amino acids are produced by fermentation. The fermentation may take place on a culture media composed of grains, sugar, molasses, yeast, or other biological material. The culture media may also be composed of petrochemicals, such as paraffin, and synthetic nutrients such as ammonium chloride, ammonium nitrate, and potassium phosphate. Extractants used may involve the use of physical and mechanical means, such as heat or maceration, as well as chemical methods such ase petroleum solvents, ammonia, strong acids, strong bases, and / or ion exchange. In a number of cases, a synthetically produced amino acid can be biologically transformed into another amino acid by a semi-fermentation or an enzymatic process. The semifermentation process involves the metabolic interaction of a fermentation organism with a synthetic precursor. An increasing number of organisms are genetically engineered. Amino acids may also be formed by reactions catalyzed by enzymes. The substrates may be naturally occurring, but they may also be synthetic, and are often both. They may also be produced by a wide number of non-biological processes that are considered to be synthetic by the TAP (Areki and Ozeki, 1991).

Glycine is the simplest amino acid, and is used in crop production as a chelating agent for micronutrients and has been used as a nitrogen fertilizer, at least on an experimental basis. As such, it is representative of amino acids used in crop production. Practically all commercial glycine is produced by synthetic processes such as the Strecker Synthesis (Areki and Ozeki, 1991). The Strecker Synthesis involves the reaction of formaldehyde, ammonia, and hydrogen cyanide, and hydrolysis of the resulting aminonitrile. It is also produced by other synthetic processes (Areki and Ozeki, 1991).

Specific Uses:
Chelating / complexing agents for cation nutrients, plant growth regulators, substrate for microbiological products, fertilizer source of nitrogen.

Action:
Plant uptake of metal nutrients are a function of the absolute levels, relative levels to each other, soil pH, oxidative state, and solution. The amino acids found in soil organic matter help protect metal cations from harmful reactions with plants and help to regulate plant uptake (Brady, 1974). A number of synthetic compounds have been developed to mimic this natural phenomenon. When a single ligand binds to a cation, that cation is considered 'complexed.' If a metal cation is joined with an organic compound at two or more exchange sites to form a ring structure, then that structure is considered a metal chelate (Meister, 1999). Two amino acids will bind to a metal to form a chelate (Ashmead et al, 1986). Chelation makes otherwise unavailable compounds plant available under normal pH conditions (AAPFCO, 1998). Chelated nutrients are more plant available than complexed nutrients, and complexed nutrients are more plant available than uncomplexed nutrients. Other amino acids used to complex or chelate cation micronutrients include lysine, glutamic acid (Miller, 1998), cysteine, and histidine (Baker and Ammerman, 1995).

AminoethoxyVinylGlycine (AVG) is used as a plant growth regulator to slow the maturation process of pome fruit by temporarily suppressing ethylene production. Other amino acids used as plant growth regulators include L-glutamic acid and gamma amino butyric acid (GABA). These act by stimulating nutrient uptake.

All amino acids have the potential to decompose into amines that can go into solution as plant-available nitrogen. Glycine appears to be the most used as a fertilizer source.

Combinations:
The metal cations most often chelated are calcium, copper, iron, magnesium, manganese, potassium, and zinc. These are usually in sulfate or occasionally in oxide form. Many formulations will be combined with synthetic fertilizers. For example, the combination of amino acid chelated nutrients with urea enhanced nutrient uptake (Ashmead, 1986).

When used as plant growth regulators, amino acids are combined with various inert ingredients used as surfactants, dispersants, carriers, fillers, spreader-stickers, and wetting agents. Many of these are synthetic. In turn, glycine and other amino acids may be included as inert ingredients in biorational pesticide formulations as part of a culture media used to grow certain microbial products.

Various complex protein sources may be decomposed into amino acids that are then turned into available nitrogen sources. Certain commercial formulations of soil amendments and foliar feeds claim 'amino acids' on the label when they are in fact using denatured protein sources such as blood meal, fish meal, whey, soy isolate or other plant or animal by-product.

Different amino acids may serve as the base for certain pesticides. For example, glycine combined with methyl phosphonate forms the herbicide glyphosate (Meister, 1999).

Status

OFPA

May be considered non-synthetic from certain sources. Not clear if synthetic amino acids fit into any exempted category for use in plant crop production, except perhaps as chelating agents for micronutrients and inert ingredients, such as nutrients in fermentation substrates for naturally occurring microorganisms.

Regulatory

Chelating agents for micronutrients regulated by state plant food control officials (AAPFCO, 1998). Plant growth regulator use is EPA regulated under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA--7 USC 136 et seq.). GABA and L-glutamic acid are considered to be reduced risk pesticides by EPA (EPA, 1998).

Status among Certifiers

Amino acids are not restricted separately from the other generic categories in which they appear. For example, those used as chelating agents for micronutrients are regulated as micronutrients. Plant growth regulators from non-synthetic sources are often restricted.

Historic Use

The greatest and longest-standing use of amino acids in organic production has been as chelating or complexing agents for micronutrients used for documented deficiencies. Several certifiers have accepted the use of amino acids as chelating agents and plant growth regulators under the assumption that they are non-synthetic.

International

The Codex Guidelines for organic production do not mention amino acids specifically in any aspect of plant crop production. However, the Guidelines do mention trace elements and natural acids with the condition for use in both cases being "Need recognized by certification body or authority" (Joint FAO/WHO Standards Programme. 1999). IFOAM restricts trace minerals, with the restrictions the responsibility of the certifier (IFOAM, 1998). Amino acids are clearly prohibited by IFOAM if they are derived from a genetically engineered source. IFOAM standards prohibit the use of synthetic growth regulators, discourage the use of non-synthetic PGRs, and states a general principle that "[g]rowth and development should take place in a natural manner" (IFOAM, 1998).

OFPA 2119(m) Criteria

(1) The potential of such substances for detrimental chemical interactions with other materials used in organic farming systems.

As chelating agents, amino acids increase the biological availability of different metals. Chelating agents in general can enhance nutrient uptake, but may also increase the uptake of toxic metals if those are also present. If cation impurities are present in micronutrient sources (e.g. cadmium), chelation of those metals would make those contaminants more readily assimilated by plants than in less available forms.

(2) The toxicity and mode of action of the substance and of its breakdown products or any contaminants, and their persistence and areas of concentration in the environment.

Glycine is one of the least stable amino acids, rapidly degrading into ammonia, amides, and aliphatic amines (Cheshire et al., 1990). Acute oral toxicity is 3,000 mg/kg (cat) (NIEHS, 1999). Salmonella tests for mutagenicity are negative (Haworth et al., 1983). Carcinogenicity and teratogenicity studies are not available (NIEHS, 1999).

(3) The probability of environmental contamination during manufacture, use, misuse or disposal of such substance.

Formaldehyde, ammonia, and hydrogen cyanide are used in the Strecker synthetic process to produce glycine. Formaldehyde is listed as a probable carcinogen by the National Institute for Environmental Health and Safety and the International Agency for Research on Cancer (NIEHS, 1999; IARC, 1982, IARC, 1987). It is highly flammable and is released in the air and in water in manufacturing (EPA, 1999). Acute exposure at higher concentrations may cause bronchitis, pneumonia or laryngitis (Bretherick, 1986). Exposure may also cause headache, dizziness, difficult breathing and pulmonary edema. Ammonia is generally produced by reacting atmospheric nitrogen with methane at high temperatures, a process that requires much energy.

Hydrogen cyanide is produced by further processing of methane and ammonia. Hydrogen cyanide is a gas that is highly toxic. Hydrogen cyanide has a toxicity rating of 6 and is one of the fastest acting poisons known to man (Gosselin, 1984). Exposure causes paralysis, unconsciousness, convulsions, and respiratory arrest. Death usually results from exposure at 300 ppm concentrations for a few minutes (Clayton and Clayton, 1982). Manufacture of hydrogen cyanide is a significant source of atmospheric release of cyanide (Midwest Research Institute, 1993). Ammonia is a corrosive agent. Methane is a central nervous system depressant (Gosselin, 1984).

(4) The effect of the substance on human health.

While glycine and other amino acids are nutrients for humans, they may be toxic in excess and can cause allergic reactions at low thresholds in sensitive people. Exposure to free amino acids in pure available form have been long been linked to a number of genetic disorders and food allergies. The most widely studied are those related to glutamates (Coyle and Puttfarcken, 1993). Glycine inhibits neurotransmissions (Budaveri, 1996). Elevated levels of glycine have been observed in migraine patients (D'Andrea, et al., 1991; Alam, et al., 1998). It is safer to avoid exposure to free amino acids under normal circumstances. Research is incomplete on the role free amino acids play in the human system. NIEHS recommends wearing a respirator when handling glycine (NIEHS, 1999).

(5) The effects of the substance on biological and chemical interactions in the agroecosystem, including the physiological effects of the substance on soil organisms (including the salt index and solubility of the soil), crops and livestock.

References to agroecosystem effects in the literature are scant and speculative. Most are based on laboratory toxicological research. Glycine has a low mammalian toxicity, and appears to stimulate rather than suppress soil microbiological activity. Chelating agents may serve to reduce the amount of synthetic micronutrients needed to effectively correct deficiencies. Long-term effects of amino acids used as plant growth regulators have not been studied because the use of those products is relatively new. Most of the research and data is from sources with proprietary interests and mainly address efficacy questions.

(6) The alternatives to using the substance in terms of practices or other available materials.

There are several alternatives that are either non-synthetic or that the NOSB has already reviewed and recommended to be added to the National List. An increase in soil organic matter and subsequent biological activity can increase the availability of soil micronutrients (Alexander, 1977). Carefully selected mined mineral sources can serve to balance cations for soils where those nutrients are not in appropriate ratios.

For chelating / complexing agents used in foliar applications: citric acid from non-GMO sources are considered non-synthetic; lignosulfonic acid and humic acid derivatives have already been recommended for addition to the National List. Other chelating agents have not been considered in the context of the NOSB's recommendations on synthetic micronutrients. For example, the NOSB may want to address the use of EDTA and glucoheptanate, either by referring them to the TAP or by demurring with explicit recognition that these substances are synthetic and prohibited. It should be noted here that EDTA synthesis shares many of the same environmental pollution problems with amino acid synthesis (Midwest Research Institute, 1993).

Alternatives to use as plant growth regulators are either labor-intensive (e.g. hand thinning and multiple picking) or require different timing of planting and harvest.

As a nitrogen fertilizer: compost, nitrogen fixing legumes, more complex protein sources such as fish.

(7) Its compatibility with a system of sustainable agriculture.

As essential biological products, amino acids are necessary to sustain agricultural production and are an inevitable part of organic farming systems. However, certain sources and applications of these materials appear to be more compatible than others; certain sources may be considered entirely incompatible. Glycine is 18.66% nitrogen in a relatively plant available form when compared with more complex protein sources. When produced from ammonia, formaldehyde, and hydrogen cyanide, it is difficult to see how it is different from other synthetic sources of soluble nitrogen, such as ammonia or urea.

Discussion

Condensed Reviewer Comments

None of the reviewers have a commercial or financial interest in glycine or any other amino acid.

Reviewer 1

Review
Since proteins are composed of amino acids, it is possible (as I have done in laboratory conditions) to hydrolyze proteins to their constituent amino acids from a combination of proteolytic enzymes (as in digestion). Glycine or any other amino acid can be separated and crystallized. This would be a natural method of amino acid production but is not cost effective as chemical synthesis.

Most all commercially available amino acids, such as glycine are synthetic. Additionally all AVG (aminoethoxyvinyl glycine) is produced synthetically and therefore should be classified synthetic.

I also feel the NOSB materials database is accurate for glycine. Generally, organic soil practices should preclude having to add chelating agents even though there is documented enhancement of nutrient uptake. For those soils where a chelating agent is required I would recommend citric acid from a non-GMO source in combination with humic acid derivatives. I see no technical reason to use synthetic glycine for any crop application. Therefore I recommend that glycine and all other synthetic amino acids used for soil/crop applications not be added to the National List of Allowed Non-organic Ingredients.

Reviewer 2
1) It appears, dependent on source and manufacturing process employed, that glycine may be derived from natural, synthetic or transgenic sources. If the material is produced via the Strecker Synthesis (which according to the information provided is the most common method for production of glycine) the material is synthetic. If it is produced via transgenic methods it should be prohibited. If it is produced from non transgenic microbial digestion or hydrolysis from plant or animal proteins it is non synthetic.

2) The information regarding properties, uses and sources appears accurate and complete.

3) The manufacture and disposal consequences indicate the production of the synthetic form of this material is too dangerous to be in compliance with the OFPA. The effect on human health appears to be minimal under normal application technologies and rates of use. The other information in the OFPA criteria appears to be accurate, although the lack of available information on agrosystem biology is troubling.

4) Non synthetic foliar feeding alternatives currently available include in vessel fermentation of micro and macronutrients utilizing humic acids, compost fermentation, and/or biological chelation through aerobic digestion of basic minerals. Additionally ligno sulfonate chelates are commonly available and effective. All of these materials work very well, although they are often not as concentrated as the amino acid chelates, thus requiring higher application rates. Sulfate forms of trace minerals are inexpensive, usually synthetic, usually very effective and as concentrated as the amino acid products.

There are no good non synthetic alternatives for use as plant growth regulators. This may be the best use for amino acids. There are numerous non synthetic sources of nitrogen including: animal and plant proteins, fish extracts, leguminous crops, nitrogen fixing organisms, manures and composts. All of these appear to have less negative environmental impacts than the synthetic production of glycine. Synthetic glycine is not compatible with the OFPA with regards to its use as a nitrogen fertilizer; it is little different from the production of urea, ammonium nitrate and other prohibited synthetic sources of nitrogen.

5) The compatibility should be addressed via consideration of the product's manufacturing process and intended use. Transgenic, Strecker and other synthetic processed forms should be prohibited. Plant, animal or non transgenic microbial extraction appear to be in compliance with the OFPA. The proposed annotation

appears appropriate and should be utilized. Amino acids should be reviewed on a case by case basis. Their use as plant growth regulators should be allowed provided the manufacturing process is in compliance. Their use as nitrogen fertilizer sources should be allowed if the manufacturing process is in compliance with the OFPA. Their use as chelating agents should be allowed if the manufacturing process is in compliance with the OFPA standards.

Reviewer 3
I believe that the NOSB should review amino acids for crop production on a case-by-case basis. There is much concern recently about the use of glutamic acid as a plant growth regulator as there are some groups that believe its use will trigger allergenic response in individuals, similar to a reaction to MSG. This is a very different issue than those covered for glycine.

Since there are other approved chelating agents recommended for inclusion on the National List, it should be a requirement that each individual amino acids' usage be approved only after demonstrating that the alternatives do not work for the same essential purpose.

I agree that a distinction needs to be made as to the process by which amino acids are produced. Only amino acids produced from naturally occurring strains of microorganisms or those derived naturally from plant or animal protein should be used on organic crops.

Conclusion

The TAP finds no basis to add any or all synthetic amino acids to the National List. The NOSB may want to review synthetic amino acids on a case-by-case basis, rather than as a class. However, based on the current use of amino acids in organic production, the addition of a single amino acid would not make much sense. While glycine may serve as a useful model, it is seldom used by itself, and instead is used with other complexing amino acids to chelate micronutrients, with other denatured protein sources as a soil amendment, or as a moiety in a larger, usually synthetic, molecule used as an herbicide or a plant growth regulator.

If the NOSB and the USDA do not add amino acids to the National List, then organic producers and certifiers will need to distinguish those amino acids that are manufactured from fossil fuels feedstocks and those that are produced by the fermentation of genetic engineered microorganisms from ones that are produced from naturally occurring strains of microorganisms, and those that are derived from plant or animal protein.

Given the concerns of those with food allergies and other sensitivities, the NOSB may want to consider adding non-synthetic amino acids to the National List of prohibited non-synthetics, either as a class or individually. While there was insufficient information for the TAP to make that recommendation, it has been raised as a concern and may merit further study if not immediate action.

The recommendation of the TAP is to take no action to add amino acids to the National List as either an allowed synthetic or as a prohibited non-synthetic, but instead to provide a clear line for the Secretary, accredited certifiers, and the organic community to be able to distinguish non-synthetic sources of amino acids that would be allowed in organic production from synthetic ones that would be prohibited.

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