AMINO ACID INHIBITION HERBICIDES

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Over the last 20 years, a number of herbicides have been discovered which inhibit amino acid metabolism. This review describes three herbicide classes which act through this mode-of-action; including glufosinate (also called phosphinothricin or Ignite®) which inhibits ammonia assimilation, glyphosate (Roundup®) which blocks aromatic amino acid biosynthesis, and several chemical families of acetolactate synthase inhibitors (sulfonylureas, inidazolinones, triazolopyrimidines and pyrimidinyl thiobenzoates). These families of herbicides share several characteristics including: a plant specific target site (with the exception of glufosinate), low mammalian toxicity, and a single biochemical target site.

Inhibitors of Ammonia Assimilation: Glufosinate:

Mode-of Action:

Glufosinate: is a non-selective ammonia assimilation inhibitor isolated from the bacterial *Streptomyces viridichromogenes.* This inhibitor occurs naturally as one component of a small herbicidal peptide. The commercial product is the isolated herbicidal peptide component, and is produced commercially by chemical synthesis. Glufosinate is an inhibitor of the enzyme glutamate synthetase (GS). This enzyme catalyses the formation of glutamine from glutamate by the addition of ammonia. The herbicidal result of GS inhibition is the rapid accumulation of ammonia in plant chloroplasts. Ammonia is a known uncoupler of photosynthetic electron transport in plant cells. Ammonia accumulation can occur within 1 hour of glufosinate treatment, with photosynthetic inhibition following in as little as 4 hours. This activity is light dependent, as is glufosinate induced visible symptoms of herbicide injury. Plan necrosis can occur in 1 to 5 days.

Activity:

Glufosinate is a non-selective herbicide used at 1 to 1.5 lb./A. This inhibitor has contact non-systemic activity, is not active by root uptake, and has minimal translocation within the whole plant. Glufosinate is rapidly degraded in soil.

Resistant Crops:

Several crops (corn and canola) have been genetically engineered to posses resistance to glufosinate. The glufosinate resistance gene, (called *bar* fro bialaphos resistance) was also isolated from *Streptomyces viridichromogenes*. This gene encodes a metabolizing enzyme that prevents autotoxicity in the bacteria. Plants transformed with the *bar*-gene are highly resistant to glufosinate.

Inhibitors of Aromatic Amino Acid Biosynthesis: Glyphosate:

Mode-of-Action:

Glyphosate was identified in the late 1960's in a discovery program that initially produce the sugar cane ripener glyphosine. This herbicide was introduced in 1971 at the North Central Weed Science Conference. Glyphosate is a biosynthesis inhibitor of the aromatic amino acids, phenylalanine and tyrosine. Specifically, glyphosate inhibits the enzyme 3-phospho-5-

enoylpyruvateshikimate (EPSP) synthase, thus, preventing the conversion of shikimate to chorismic acid. Inhibition of this biosynthetic pathway results in an unregulated accumulation of shikimate. Following glyphosate treatment, as much as 10 to 20% of the plants total soluble carbon can be found to accumulate in shikimate. Plant death is apparently the result of the unregulated accumulation of carbon in that intermediate. As the rate of plant death is dependent on the amount of stored carbon in plant tissues, small plants may die relatively quickly (1 to 4 weeks) whereas larger shrubs or small trees may require a year or more to be fully controlled.

Activity:

Glyphosate is a non-selective broad spectrum herbicide which is highly phloem mobile in plants. Use rates range between 0.25 and 2 lb./A. Glyphosate is not metabolized in treated plants and has no soil activity.

Resistant Crops:

Table 1: Glyphosate Resistant Crops:

CROP	STATUS
Soybeans	Commercial-996
Cotton	Target~1998
Corn	Target~1998
Sugarbeet	Target~1997
Wheat	Target~1998
Rice	Target~2000
Canola	Target~1998

Resistance to Glyphosate has been engineered into a number of crops (table 1). Glyphosate resistance is the result of a mutant EPSP synthase gene isolated from *Salmonella typhimurium*. This mutant gene contains a single amino acid change from proline to serine and possess altered glyphosate binding characteristics.

It is probable that a technology fee will be charged to growers (on a per acre basis) independent of the price paid for glyphosate-resistant seed.

Inhibitors of Branched Chain Amino Acid Biosynthesis: Acetolactate Synthase Inhibitors:

Four new families of herbicides with remarkable activity have been discovered over the last 15 years, including the sulfonylureas, imidazolinones, triazolopyrimidines and pyrimidinyl thiobenzoates. These herbicides inhibit the production of branched chain amino acids by the inhibition of acetolactate synthase (ALS). Commercial examples of these new herbicide families are listed in table 2..

Table 2: Commercial Examples of Acetolactate synthase Inhibitors:

Chemical Class	Trade Name	Target Crop	Common Name
Sulfonylureas	Londax® Classic®\ Oust®	Rice Soybean Non-Crop	Bensulfuron-methyl Chlorimuron-ethyl Sulfometuron-methyl
Imidazolinones	Pursuit® Sceptor®	Soybean Soybean	Imazethapyr Imazaquin
Triazolopyrimidines	Broadstrike®	Soybean	Flumetsulam
Pyrimidinyl thiobenzoates	Staple®	Cotton	Pyritiobac-sodium

Mode-of-Action:

ALS inhibiting herbicides prevent the biosynthesis of branched chain amino acids, including valine, leucine, and isoleucine through the specific inhibition of ALS. Through an as yet

unknown mechanism, the suppression of branch chain amino acid biosynthesis results in a rapid inhibition of cell division at the G1 or G2 phases if interphase; there is no direct affect on mitosis. Plant growth can be inhibited within 2 hours following treatment. While cell division and growth are quickly arrested, ultimate plant death is slow. Since plant growth stops almost immediately, the competitive potential of treated weeds is non-significant and the presence of affected plants in the field is of no agronomic concern. The rate of plant death is likely related to the total pool of branched chain amino acids available. Thus, small plants will succumb much more rapidly than larger species with more reserves. ALS inhibitor symptomology includes the rapid inhibition of root and shoot growth, vein reddening, chlorosis, and meristematic necrosis.

Herbicide Resistant Crops:

Several herbicide resistant crops have been engineered through the mutation of the gene encoding ALS. Crops include STS Soybeans (for sulfonylureas) and IR/IT corn (for imidazolinones). Sulfonylurea resistant cotton is planned.

Herbicide Resistant Weeds:

Unlike most herbicidal enzyme inhibitors, ALS inhibiting herbicides do not bind to the catalytic domain of the target enzyme. Instead, ALS inhibitors appear to bind to an to an evolutionary vestige of pyruvate oxidase contained within ALS. Both pyruvate oxidase and ALS apparently share a common evolutionary origin. Since ALS inhibitors do not bind to the catalytic domain of the enzyme, mutations in the herbicide binding site are rarely lethal and have minimal selective disadvantage. This has allowed for the rapid selection of herbicide resistance by compounds with this mode-of-action.

ALS Inhibitor Resistance Working Group Guidelines For Managing Herbicide Resistance

- Determine which weeds infest the crop or non-crop site.
- Use historical weed densities or weed thresholds, as appropriate, to determine the need for herbicide treatment.
- Use a diverse herbicide treatment program that includes a tank-mix or sequential treatments with herbicides that have different modes-of-action.
- Use non-chemical weed control practices such as tillage or mowing in conjunction with herbicides whenever possible.
- Rotate crops and use herbicides with different modes-of-action.
- Discourage the extended use of ALS-inhibiting herbicides by themselves on the same field for the same weed.
- Use certified crop seed, and clean equipment when moving from one field to another to prevent the spread of resistant weed seed or plant material.