

Lecture

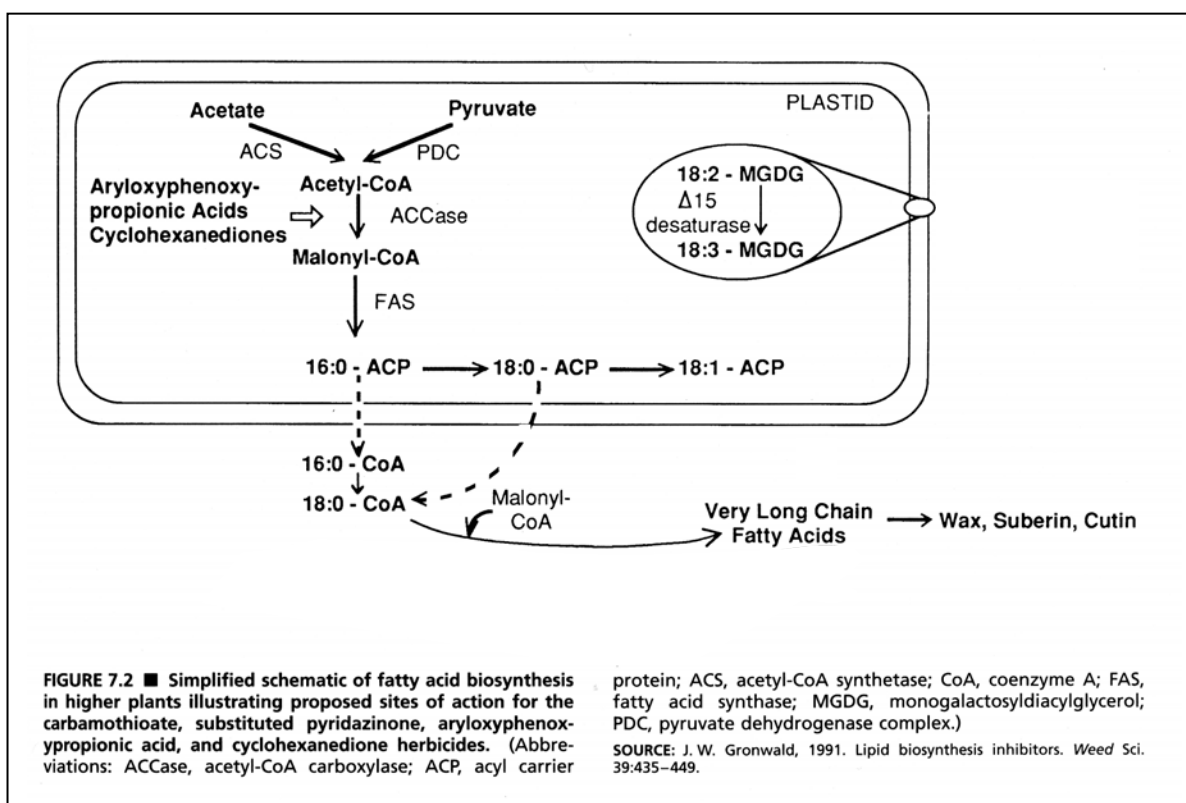
Inhibition of Lipid Synthesis

1. General Information

Lipids serve numerous functions in the plant and are key components of cell membranes, cuticle, and suberin surrounding the endodermal cells of the casparian strip. Lipids also serve as fuel molecules and signal molecules within the cell. In cell division, development of a cell membrane would be critical to cell survival. It would be expected that any herbicide that inhibits the formation of lipids would successfully kill the plant.

Herbicides that have this mode of action consist of two groups: the acetyl CoA carboxylase (ACCase) inhibitors and the acyl CoA elongase inhibitors (non ACCase inhibitors).

2. Mode of Action – Inhibition of Lipid Synthesis (Inhibition of Acetyl CoA Carboxylase /ACCase Inhibitors)



These herbicides block the conversion of acetyl-CoA to malonyl-CoA by inhibiting the activity of the enzyme acetyl-CoA Carboxylase (ACCase). This inhibition of fatty acid

synthesis blocks production of phospholipids used in building new cell membranes required for cell growth.

Broadleaf weeds are naturally resistant to herbicides with this mode of action because of an insensitive ACCase.

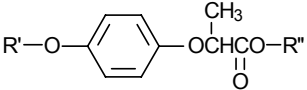
3. Site of Action – Inhibition of Lipid Synthesis (Inhibition of Acetyl CoA Carboxylase /ACCase Inhibitors)

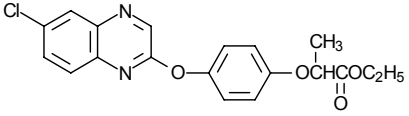
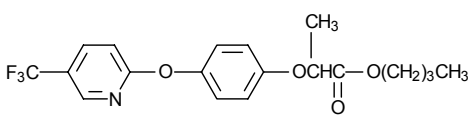
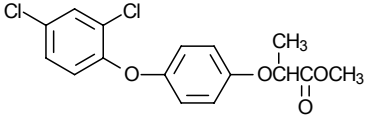
Inhibition occurs at the ACCase enzyme of the fatty acid synthesis pathway occurring in the stroma of plastids.

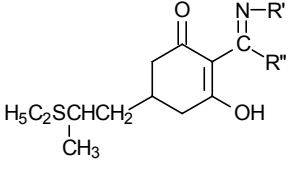
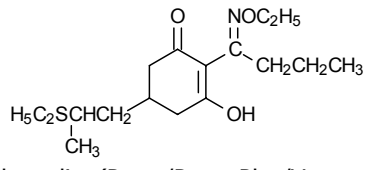
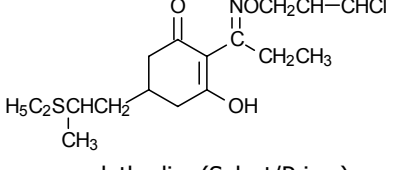
4. Symptoms – Inhibition of Lipid Synthesis (Inhibition of Acetyl CoA Carboxylase /ACCase Inhibitors)

- growth of grasses ceases within a few days following postemergence application
- leaf sheaths become soft and brown at or just above the point of attachment to the node (the new leaf in the whorl is easily removed)
- older leaves of some grasses turn purple, orange, or red before chlorosis occurs
- chlorosis followed by necrosis within 1 to 3 weeks
- Although not applied preemergence, soil application can result in primary root inhibition and leaves fail to emerge from the coleoptile.

5. Herbicide Families – Inhibition of Lipid Synthesis (Inhibition of Acetyl CoA Carboxylase/ACCase Inhibitors)

Aryloxyphenoxypropionates		
Base Structure		<p>R' refers to <u>aryl</u>-derived group bonded to the O; <u>oxy</u> refers to O bonded to the aryl group; <u>phenoxy</u> refers to the benzene ring with O attached (remember phenoxy herbicides); <u>propionates</u> refers to 3 carbon acid group; R'' is the ester group since herbicides are formulated as esters of their acids (note butyl ester of fluazifop-p-butyl); herbicides may be racemic mixtures as denoted by the (±) preceding their chemical name; a racemic mixture contains both dextro (+) and levo (-) enantiomers in equal proportions <u>or</u> herbicides may contain only the herbicidally active dextro enantiomers denoted by either a (+) or <u>R</u> preceding their chemical names; herbicides in this group referred to as graminicides and the “fops”</p>

<p>Examples</p>	<div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;">  <p>Quizalofop-p (Assure II, Matador)</p> <p>(<i>R</i>)-2-[4[(6-chloro-2-quinoxalinyloxy)phenoxy]propionic acid</p> </div> <div style="text-align: center;">  <p>fluazifop-p-butyl (Fusilade 2000/Fusilade DX)</p> <p>(<i>R</i>)-2-[4-[[5-(trifluoromethyl)-2-pyridinyloxy]phenoxy]propionic acid</p> </div> </div> <div style="text-align: center; margin-top: 20px;">  <p>diclofop (Hoelon)</p> <p>(±)-2-[4-(2,4-dichlorophenoxy)phenoxy]propionic acid</p> </div>
<p>Others</p>	<p>fenoxaprop (Whip/Acclaim) - used in soybeans, turf, wheat, and rice (rice has a graminicide-tolerant ACC'ase)</p>
<p>Metabolism</p>	<p><u>plant</u> – herbicides are applied as esters of their acids; esters are rapidly converted to acids by carboxyesterase activity; the acid is readily translocated and is the phytotoxic form <u>soil</u> – rapidly degraded by microbes half-life – quizalofop 60d; fluazifop 15d; diclofop 30d</p>
<p>Absorption & Translocation</p>	<p><u>quizalofop</u> and <u>fluazifop</u> readily absorbed by foliage and translocated in symplast accumulating in meristematic regions of root and shoot; translocation is slow <u>diclofop</u> rapidly absorbed into roots and leaves and translocated in symplast</p>
<p>Selectivity</p>	<p>selective – in general control grasses but <u>not</u> broadleaves; graminicide-tolerant ACC'ase enzyme in broadleaves and absent in grasses; some grasses also have a graminicide-tolerant ACC'ase enzyme for diclofop-methyl, wheat is tolerant due to ability to metabolize the herbicide to inactive form</p>
<p>Herbicide Use</p>	<p>controls annual and perennial grass weeds <u>quizalofop</u> used POST in soybeans and noncrop areas (may provide some control of grasses germinating after POST application, but would be related to rate, soil type, and soil moisture) <u>fluazifop</u> used POST in cotton, soybeans, stone fruits, asparagus, carrots, garlic, coffee, pecans, rhubarb, tabasco peppers <u>diclofop</u> used POST in wheat, barley, Austrian winter peas, lentils, bermudagrass turf; PRE/PPI winter wheat for ryegrass and cheat control; low rates of some of these herbicides can suppress seedhead development in grasses such as red rice; weed resistance is an issue</p>

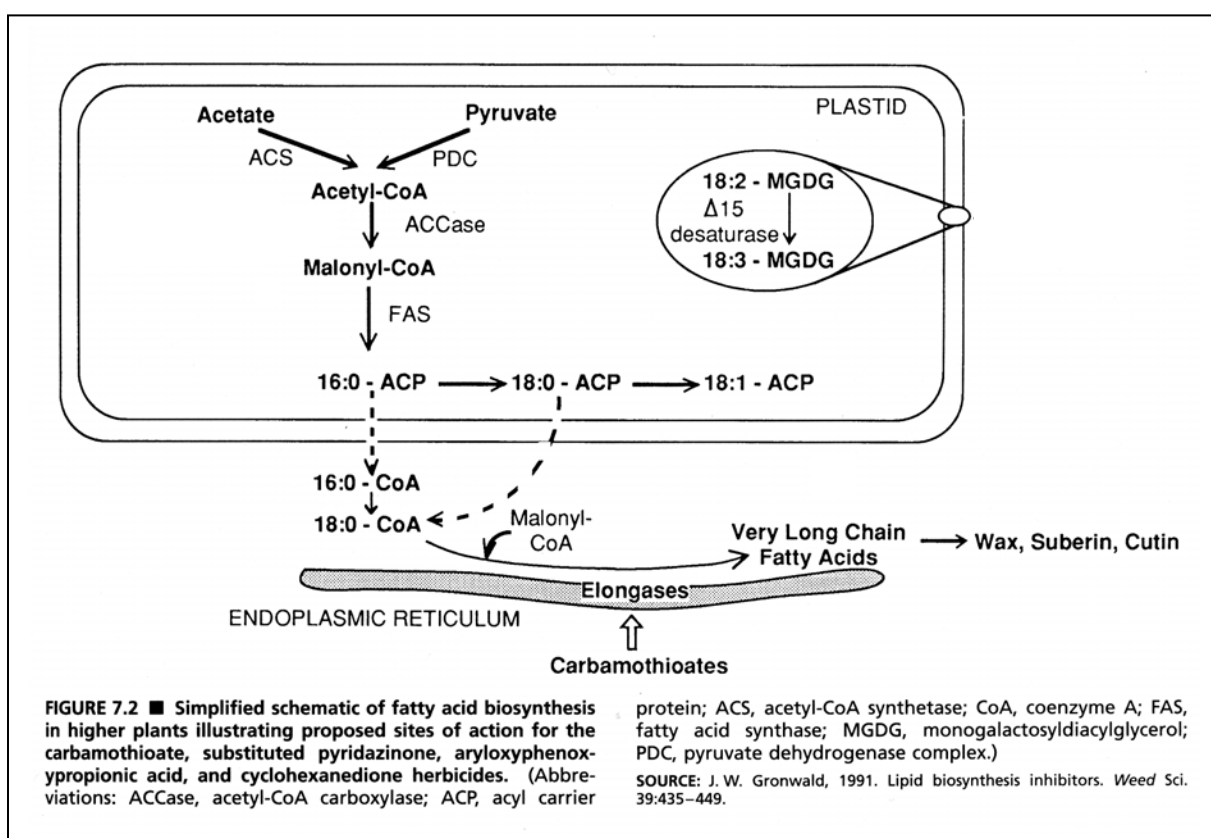
Cyclohexanediones	
Base Structure	 <p>base structure is a cyclohexane with an O double bonded to the ring at 1-position (1-one), a hydroxyl group bonded at the 3-position with other substitutions at the 2- and 5-positions of the hexane ring; herbicides in this group referred to as graminicides and the “dims”</p>
Examples	 <p>sethoxydim (Poast/Poast Plus/Vantage)</p>  <p>clethodim (Select/Prism)</p>
Others	tralkoxydim (Achieve)
Metabolism	<p><u>plant</u> – metabolism to inactive form <u>soil</u> – photolysis (photodegradation), microbial, hydrolysis half-life – sethoxydim 5d; clethodim 3d</p>
Absorption & Translocation	readily absorbed by foliage and roots translocated in both phloem and xylem (primarily in phloem), accumulating in meristematic regions of roots and shoots
Selectivity	selective – controls grasses but <u>not</u> broadleaves; graminicide-tolerant ACC’ase enzyme in broadleaves and absent in grasses; some grasses also have a graminicide-tolerant ACC’ase enzyme (e.g. centipede and fine fescues)
Herbicide Use	<p>controls annual and perennial grass weeds <u>sethoxydim</u> used POST in soybeans, peanuts, alfalfa, sugarbeets, sunflower, cotton, flax, ornamental trees, shrubs, flowers, ground cover; Vantage used in centipede for control of other grasses e.g. bermudagrass; low rates can increase sugar content in sugarcane <u>clethodim</u> used POST in cotton, soybeans, turf (under development for use in centipede); seedhead suppression for red rice in soybeans</p> <p>weed resistance is an issue</p>

6. General Comments – Inhibition of Lipid Synthesis (Inhibition of Acetyl CoA Carboxylase/ACCase Inhibitors)

The “fops” and “dims” are mainly used to control grass weeds in broadleaf crops. Fluazifop, one of the first aryloxyphenoxypropionates, was discovered by Ishihara Sangyo Kaishi, Ltd. and ICI Plant Protection (Zeneca/Syngenta) and was first tested in the U.S. in 1981.

Sethoxydim was discovered by Nippon Soda Co. and was developed by BASF in the U.S. where it was first tested in 1978. Clethodim was not discovered until 1987.

7. Mode of Action – Inhibition of Lipid Synthesis (Inhibition of Elongases / non ACCase Inhibitors)



Elongase inhibiting herbicides (also referred to as non ACCase inhibitors) do not affect the ACCase enzyme and the conversion of acetyl-CoA to malonyl-CoA occurs in a normal fashion. This is important since malonyl-CoA is necessary to produce very long chain fatty acids that comprise the surface lipids: waxes, suberin, and cutin.

Herbicides with this mode of action inhibit acyl-coenzyme A (acyl-CoA) elongases. These enzymes are integral membrane proteins associated with the endoplasmic reticulum and are

necessary to catalyze the condensation of malonyl-CoA with fatty acid acyl-CoA substrates to form surface lipids.

8. Site of Action – Inhibition of Lipid Synthesis (Inhibition of Elongases / non ACCase Inhibitors)

The herbicides in this group are generally thought to act at the endoplasmic reticulum of cells in the developing shoot.

9. Symptoms – Inhibition of Lipid Synthesis (Inhibition of Elongases / non ACCase Inhibitors)

- With preemergence application seedlings fail to emerge. This can be attributed to inability of plants to produce suberin in root and subsequent dehydration.
- Broadleaves that emerge may have cupped, puckered, or crinkled leaves and thickened cuticle.
- Leaves fail to unroll properly because cuticle waxes are not formed in a normal fashion (this is a very distinctive symptom of this mode of action).

10. Herbicide Family – Inhibition of Lipid Synthesis (Inhibition of Elongases / non ACCase Inhibitors)

Thiocarbamates	
Base Structure	$\text{R}^{\text{m}}-\text{CH}_2-\text{S}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}\begin{matrix} \text{R}' \\ \text{R}'' \end{matrix}$ <p>contains a sulfur (thio) in the place of the hydroxyl O of carbamic acid; have alkyl groups at the R positions; no rings in the structure</p>
Examples	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> $\text{CH}_3\text{CH}_2\text{CH}_2-\text{S}-\overset{\text{O}}{\parallel}{\text{C}}-\text{N}\begin{matrix} \text{CH}_2\text{CH}_2\text{CH}_3 \\ \text{CH}_2\text{CH}_2\text{CH}_3 \end{matrix}$ <p>vernolate (Vernam)</p> </div> <div style="text-align: center;"> $\text{CH}_3\text{CH}_2\text{CH}_2-\overset{\text{O}}{\parallel}{\text{N}}-\text{C}-\text{S}-\text{CH}_2\text{CH}_3$ <p>EPTC (Eptam/Eradicane)</p> </div> </div>
Others	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>butylate (Sutan) cycloate (Ro-Neet) molinate (Ordram)</p> </div> <div style="text-align: center;"> <p>thiobencarb (Bolero/Abolish) triallate (Avadex/Fargo) pebulate (Tillam/Edge)</p> </div> </div>
Metabolism	<p><u>plant</u> – oxidation and conjugation <u>soil</u> – microbial half-life – vernolate 12d; EPTC 6d, but provides 4 to 6 weeks of weed control</p>

Absorption & Translocation	absorbed by roots and coleoptiles of emerging grass seedlings (absorption by coleoptilar node probably most important); translocation basipetally and acropetally from POST application; extensive translocation not important if soil applied
Selectivity	selective - differential metabolism
Herbicide Use	controls annual grass and broadleaf weeds and nutsedges <u>vernolate</u> used PPI in soybeans, peanuts, tobacco, sweet potatoes <u>EPTC</u> used PPI in alfalfa, clover, lespedeza, beans, flax, potatoes, safflower, sugarbeets, sunflowers, citrus, cotton, pine seedlings, sweet potatoes, green peas, table beets, walnuts, almonds, tomatoes, and corn (only with safener in formulation – Eradicane Extra) these herbicides are incorporated to prevent volatilization losses; losses greatest when soil surface is moist at application and when EPTC is not incorporated immediately; label states to apply and incorporate in same operation <u>Note:</u> when S atoms replace both the hydroxyl O and carbonyl O of the thiocarbamate the resulting compound is called a dithiocarbamate; Metham, a soil fumigant, is a dithiocarbamate and is under review by EPA and will probably lose registration; alternative are currently being investigated

11. General Comments – Inhibition of Lipid Synthesis (Inhibition of Elongases / non ACCase Inhibitors)

The details of the precise mode of action of the thiocarbamates is not truly known and the symptoms of the family may vary among herbicides.

One of the more well known thiocarbamates is EPTC, a chemical discovered in 1957 by Stauffer Co. Sold under the original trade names of Eradicane and Eptam, the addition of a safener to the formulation (Eradicane Extra) was effective in altering the selectivity of the herbicide.

12. References

Ahrens, W. Herbicide Handbook, seventh edition. 1994. Weed Science Society of America, Champaign, IL.

Anderson, W.P. Weed Science – Principles and Applications, third edition. 1996. West Publishing, NY.

Stryer, L. Biochemistry – fourth edition. 1995. W.H. Freeman, NY.