

Lecture

Inhibition of Protoporphyrinogen Oxidase

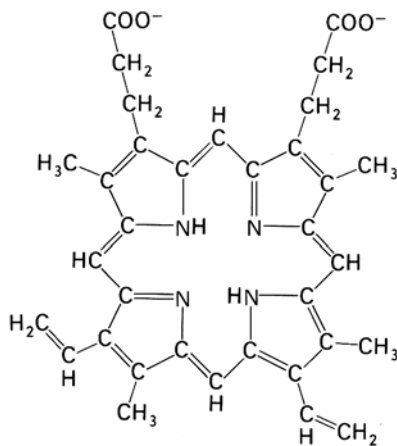
1. General Information

The herbicidal properties of the protoporphyrinogen oxidase (PPOase) inhibitors have been known for years, but the mode and site of action were only recently discovered.

Porphyryns are important biological compounds because they have many double bonds in their tetrapyrrole ring which allow for efficient energy transfer and give them their brilliant colors. It is because of these characteristics that porphyrin compounds are often called “photodynamic dyes”.

Both chlorophyll and cytochrome pigments have porphyrin prosthetic groups and are products of the pathway.

Heme, the oxygen-carrying component in mammalian blood, is another porphyrin containing compound. As with all biological compounds, a metabolic pathway exists for the formation of porphyryns.



Protoporphyrin IX

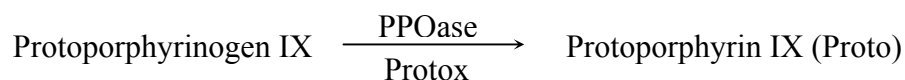
Source: Biochemistry – fourth edition. L. Stryer. 1995.
W.H. Freeman, NY.

Herbicides with this mode of action inhibit a key enzyme, protoporphyrinogen oxidase (PPOase, also referred to as Protox), disrupting the pathway. Light is required for the herbicide to exert its effects, but unlike the photosynthetic inhibitors, photosynthesis is not necessary.

The herbicides sharing this mode of action are very diverse in their mode of entry and translocation in plants. Some chemistries have more postemergence activity than others, while some are used primarily preemergence.

2. Mode of Action

The normal reaction is:



Protoporphyrin IX (Proto) is present at low concentrations as an intermediate in the porphyrin synthesis pathway, but is toxic to the plant at higher concentrations. Toxicity to plants is due to accumulation of Proto / protoporphyrin IX.

☞ How can inhibition of PPOase / Protox lead to accumulation of protoporphyrin IX / Proto?

When PPOase is inhibited, protoporphyrinogen IX accumulates.

Protoporphyrinogen IX moves away from the reaction center in the chloroplast into the cytoplasm.

In the cytoplasm, the conversion to protoporphyrin IX / Proto occurs.

Interactions with O₂ and light results in formation of singlet O₂ radicals (¹O₂), which causes lipid peroxidation (membrane disruption) and plant death.

☞ Why is there not the same negative consequences when protoporphyrin IX is produced within the normal pathway where PPOase / Protox is not inhibited?

When the normal conversion from protoporphyrinogen IX to protoporphyrin IX occurs in the chloroplast the effect is not detrimental – only when the conversion occurs outside the chloroplast in the cytoplasm is the consequence detrimental to the plant.

See Figure 12.1; page 3

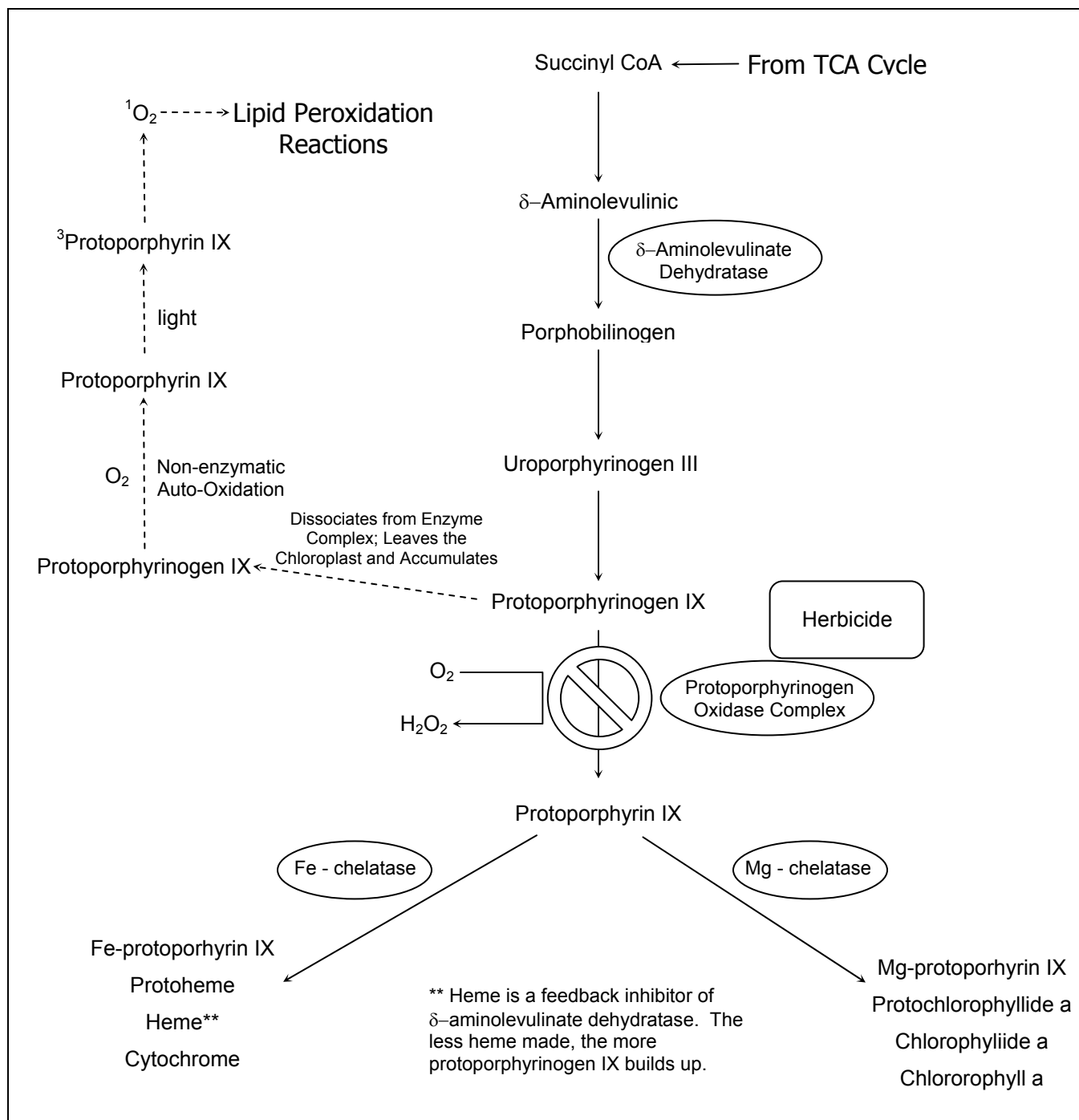


Figure 12.1 Inhibition of protoporphyrinogen oxidase in the porphyrin synthesis pathway

3. Site of Action

The herbicide acts at the protoporphyrinogen oxidase enzyme complex spanning the chloroplast membrane.

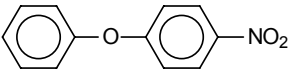
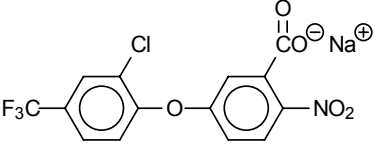
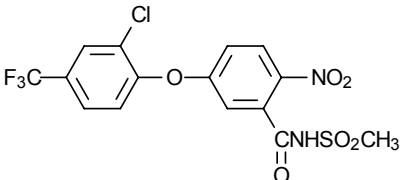
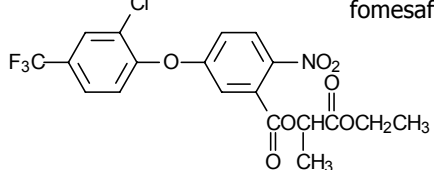
4. Symptoms

foliar absorption – contact type injury; herbicide is not extensively translocated and injury occurs in plant tissues contacted

injury noted as a bronzing of leaves (tolerant plants) and chlorosis followed by necrosis within 1-3 days for susceptible plants

root absorption – reddening of foliage can occur, susceptible plants die very rapidly (chlorosis followed by necrosis)

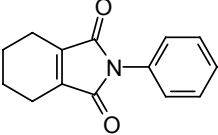
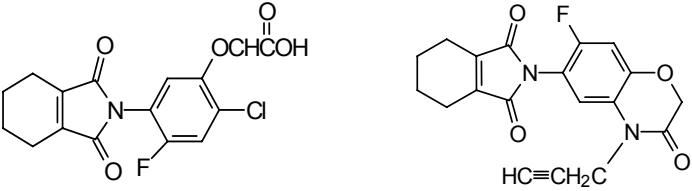
5. Herbicide Families

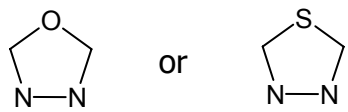
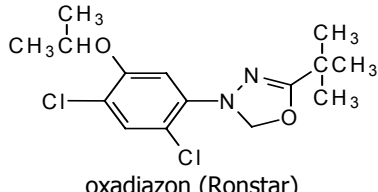
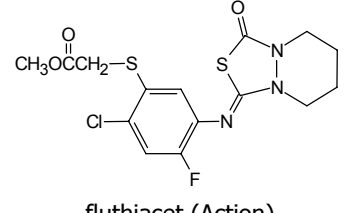
Diphenyl Ethers	
Base Structure	 <p>base structure contains 2 benzene (phenyl) rings linked with an ether bridge and a nitro (NO₂) group bonded to the 4-position (para position); herbicides in this family considered to be contact herbicides</p>
Examples	<div style="display: flex; justify-content: space-around;"> <div style="text-align: center;">  <p>acifluorfen (Blazer)</p> </div> <div style="text-align: center;">  <p>fomesafen (Reflex/Flexstar)</p> </div> </div> <div style="text-align: center; margin-top: 20px;">  <p>lactofen (Cobra)</p> </div>
Metabolism	<p><u>plant</u>: cleavage of ether bond and further metabolism <u>soil</u>: microbial half-life – acifluorfen 14-60 d; fomesafen 100 d; lactofen 3 d</p>
Absorption & Translocation	<p>little to no translocation following root or foliar absorption other than local short distance movement in treated tissue</p>
Selectivity	<p>selective – tolerant plants rapidly metabolize to inactive metabolites whereas susceptible plants are unable to do so</p>

Herbicide Use	<p>these herbicides control broadleaf weeds</p> <p><u>acifluorfen</u> used POST in peanuts, soybean, rice</p> <p><u>fomesafen</u> used POST in soybeans</p> <p><u>lactofen</u> used POST in soybeans, pine seedlings; PD in cotton</p> <p>referred to as contact herbicides; strongly adsorbed to soil colloids with little or no leaching in soils; of the three herbicides, fomesafen has the most soil activity and is being looked at PRE in cotton; soil residue of fomesafen can persist long enough to injure certain susceptible crops (sugarbeets, sunflower, sorghum) one year after application</p>
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Aryl Triazinones	
Base Structure	<div style="display: flex; align-items: center;"> <div style="flex: 1;"> </div> <div style="flex: 2; padding-left: 10px;"> <p>base structure contains a 5 member ring (triazole) of which there are 3 N's (2 of which are adjacent to one another) and 2 C's ; the "one" refers to the double bonded O to the C in the ring; a benzene ring is attached to one of the N's in the ring</p> </div> </div>
Examples	<div style="display: flex; justify-content: space-around; align-items: flex-start;"> <div style="text-align: center;"> <p>sulfentrazone (Authority/Spartan)</p> </div> <div style="text-align: center;"> <p>carfentrazone (Aim)</p> </div> </div> <div style="text-align: center; margin-top: 20px;"> <p>azafeniden (Milestone)</p> </div>
Metabolism	<p><u>plant</u>: oxidative hydroxylation, decarboxylation, ring cleavage</p> <p><u>soil</u>: microbial primary means of degradation</p> <p>half-life – sulfentrazone 110-280 d; carfentrazone 2-4 d; azafeniden 25-40 d</p>
Absorption & Translocation	<p><u>sulfentrazone</u> – absorption by roots and foliage; symplastic phloem movement assumed to be limited because of rapid foliar desiccation</p> <p><u>carfentrazone</u> – absorption by foliage; symplastic movement limited</p> <p><u>azafeniden</u> – absorption by roots and shoots; translocation in xylem and phloem is minimal explaining the limited POST activity on well developed plants</p>

Selectivity	selective – differential metabolism ?
Herbicide Use	<p><u>sulfentrazone</u> controls annual grasses and broadleaf weeds PPI/PRE in soybeans, tobacco, sugarcane; carryover problems with certain crops in particular cotton</p> <p><u>carfentrazone</u> controls broadleaf weeds POST in corn, cereals, rice; this herbicide is a contact herbicides and has no soil residual activity; rainfast in 15 min</p> <p><u>azafeniden</u> controls annual grasses and broadleaf weeds PRE/POST in vineyards, citrus, olive orchards, industrial sites, forest situations, sugarcane (pending); combinations with other herbicides increase overall activity and speed of action</p>

N-phenylphthalimides	
Base Structure	 <p>in the base structure the N of the phthalimide group is attached to a benzene ring (phenyl), hence N-phenylphthalimide; phthalimide group contains a 5 member ring with 1 N and 4 C's - 2 O's are double bonded to C's</p>
Examples	 <p>flumiclorac (Resource)</p> <p>flumioxazin (Valor)</p>
Metabolism	<p><u>plant</u>: not available</p> <p><u>soil</u>: hydrolysis, microbial primary means of degradation</p> <p>half-life – flumiclorac 1-6 d; flumioxazin 12-18 d</p>
Absorption & Translocation	<p><u>flumiclorac</u> - readily absorbed into leaves with little to no basipetal translocation in the phloem to roots</p> <p><u>flumioxazin</u> – absorbed by roots and foliage; symplastic movement limited because of rapid foliar desiccation</p>
Selectivity	selective – rapid metabolism by tolerant crops
Herbicide Use	<p>both herbicides control broadleaf weeds</p> <p><u>flumiclorac</u> used POST in soybeans and corn</p> <p><u>flumioxazin</u> used PRE in soybeans, peanuts (rapid burndown with residual)</p> <p>both herbicides strongly adsorbed to clay and organic matter</p>

Oxadiazoles		
Base Structure		base structure has a 5 member ring (diazole) with 2-N's adjacent to one another and 2- C's; the other ring component can be an O or a S
Examples	 oxadiazon (Ronstar)	 fluthiacet (Action)
Metabolism	<u>plant</u> : not available <u>soil</u> : microbial primary means of degradation half-life – oxadiazon 60 d; fluthiacet 1-2 d	
Absorption & Translocation	<u>oxadiazon</u> - readily absorbed by shoots of emerging seedlings, but less so by roots; if foliar applied readily adsorbed by leaves; in both cases little movement to growing points <u>fluthiacet</u> – readily absorbed by leaves; little movement to growing points	
Selectivity	selective – differential metabolism ?	
Herbicide Use	<u>oxadiazon</u> – controls annual grasses and broadleaf weeds when soil applied to established or newly established bermudagrass, perennial ryegrass, and fescue turf, and in various ornamentals; Regal Star II (active ingredient formulated with N fertilizer) <u>fluthiacet</u> – controls velvetleaf and other broadleaves POST in soybeans; being developed in corn leaching potential of both herbicides is low due to strong adsorption to soils	

6. General Comments

With the exception of the diphenyl ethers and oxadiazon, the herbicides classified as PPOase inhibitors have only recently been discovered. Many of the compounds are used in soybeans to control broadleaf weeds.

Introduced in the late 1970's, the diphenyl ethers are multifunctional herbicides, meaning that their mode of action depends on the substituent groups attached to the base structure. Though most diphenyl ethers are PPOase inhibitors, oxyfluorfen (Goal) is classified as a carotene biosynthesis inhibitor.

Current research is underway by Syngenta (formerly Novartis Crop Protection) to incorporate a gene into crops for resistance to PPOase inhibitors. This could open up new avenues for weed management.

7. References

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