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Systemic Fungicides: A Perspective After 10 Years

Since Delp and Klopping first reported on benomyl in *Plant Disease Reporter* (1), dramatic acceptance of Benlate by farmers and widespread development of other systemic fungicides have evolved. Thiabendazole and one or two antibiotics were reported as systemics as early as 1964, but the real escalation in use of systemic fungicides began with the discovery of carboxin and benomyl in the late 1960s. A compilation of fungicides currently used in the world lists 44 systemic (Table 1) and 85 nonsystemic agents.

What "Systemic" Means

We have investigated many of the new systemic fungicides. Before analyzing the progress and potential of these chemicals, however, we should clarify the word "systemic" as used by plant pathologists. The word implies movement throughout the plant system, but this is misleading because most systemic fungicides are only partially systemic in plants. With the exception of several unregistered experimental fungicides that move "systemically" into fruit, roots, buds, and other plant organs along with the plant photosynthates (sugars), the so-called systemics are carried along with the transpiration stream. Leaves are the primary transpiring organs, and movement within plants is from the soil to the expanded leaves. Very young leaves, flowers, and fruit do not transpire significant quantities of water and therefore receive only minute amounts of fungicides applied to soil or to seed. Actually, this is fortuitous, as the chances of residues in fruit are minimal. Certainly, no more residues would be expected than with the old conventional "protectants" applied to the surface of plants.

Why is a fungicide systemic—or partially systemic? Before the discovery of systemics, fungicides were only protectants, remaining on the surface of plants. The protectants are toxic to many processes common in plants and fungi but do not enter the plant and therefore are not phytotoxic. Examples of protectants are maneb (Dithane M-22), chlorothalonil (Bravo), and captan (Captan). Systemic fungicides, however, penetrate the plant and are selectively toxic to processes unique to fungi. This selectivity is so specific that among the hundreds of different fungi attacking plants, only certain taxonomic groups of fungi are sensitive to each particular systemic fungicide (Table 1).

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Selectivity of Systemics

Fungicides of similar chemical structure are toxic to similar types of fungal organisms (Table 1). Obviously, as any farmer knows, a particular crop is not plagued by only mildew, rust, or any other single disease. Researchers and industry have been busy combining fungicides to control pathogens in a particular crop. For example, Ridomil, a new systemic fungicide, looks very effective against late blight of potato caused by *Phytophthora*. However, a farmer must also use mancozeb or some other fungicide for early blight caused by *Alternaria solani*, because Ridomil is selectively toxic to *Phytophthora*. The particular niche for each new systemic in a combination is being developed for each crop and often each geographical region.

A systemic fungicide appears to be selective because it is toxic to only a single site within the fungus. This can cause problems, since a single change in the fungus can result in resistance to the fungicide. The threat of resistance can be reduced, however, by using different systemic fungicides in combination or alternately in a pest management program.

Use on Seed

Seed treatments have always been the most economical use of fungicides in preventing plant diseases in many crops. Protective fungicides, such as captan and thiram, control surfaceborne pathogens and, to a limited extent, protect germinating seedlings from soilborne pathogens. The advent of systemic fungicides has dramatically improved this picture: 1) Systemics offer control against pathogens within the seed as well as those on the surface; 2) the systemic is taken into the germinating seed and moves in an upward direction, protecting the seedling during development as well as after emergence; and 3) much less fungicide is required with systemics than with protectants.

Loose smut of cereals is an excellent example of an internal seedborne disease controlled by systemic fungicides. Bunt, which is borne by soil and on the seed surface, was effectively controlled by general protectants, such as hexachlorobenzene and organic mercuries. These proved ineffective, however, against the loose

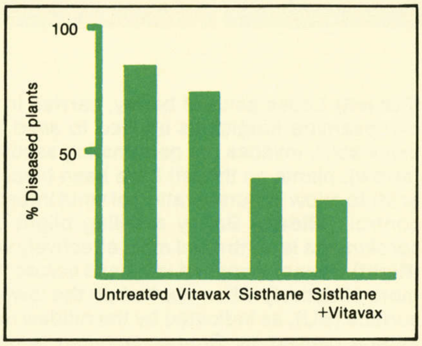


Fig. 1. Control of barley seedling blight caused by *Bipolaris sorokiniana* is more effective with combined Sisthane and Vitavax treatment than when either fungicide is used alone.

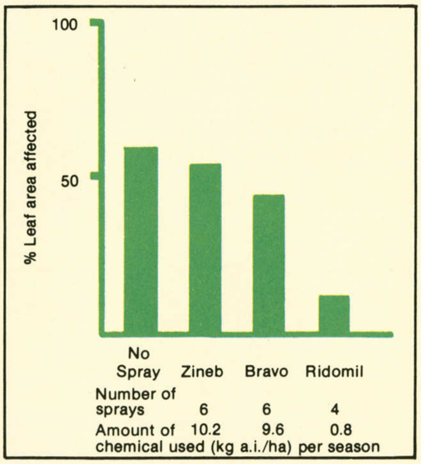
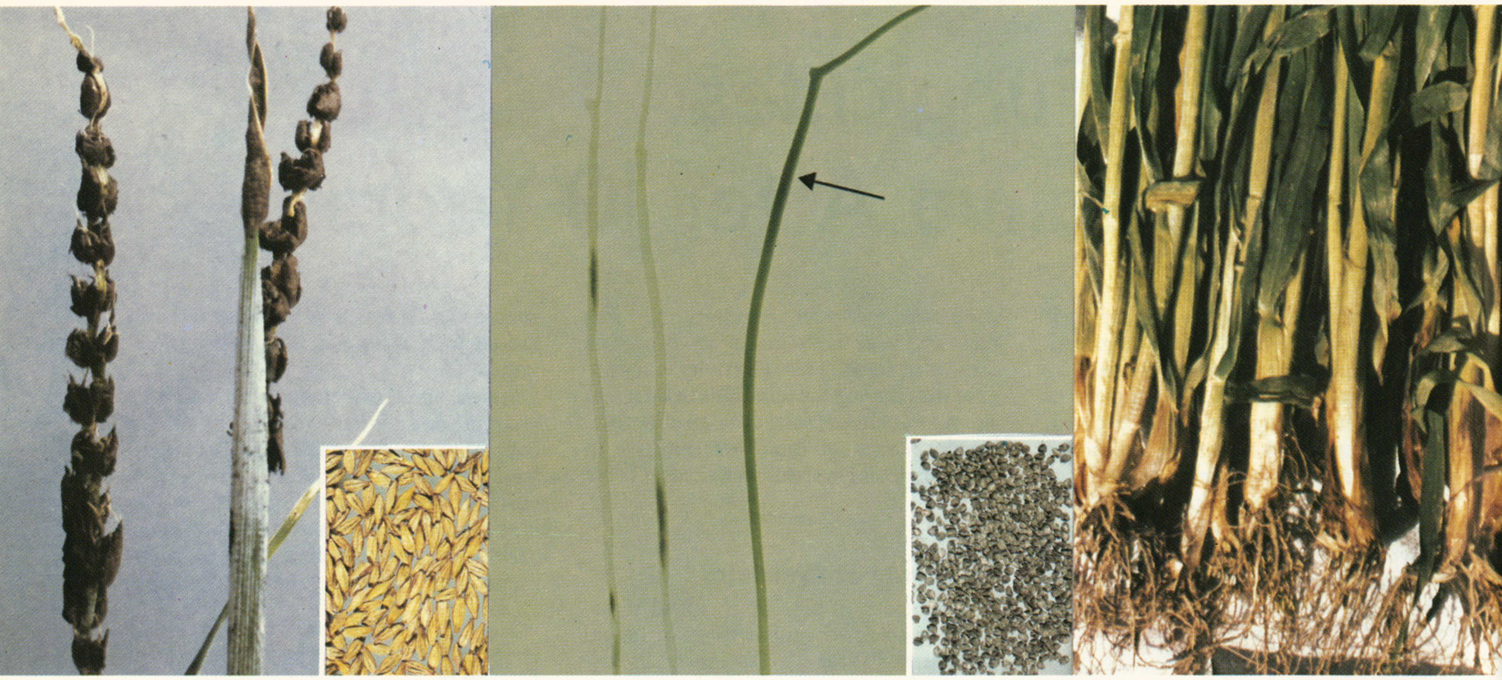


Fig. 2. The incidence of downy mildew of lettuce caused by *Bremia lactucae* is lower after biweekly applications of the systemic Ridomil than after weekly sprayings with the protectants zineb and Bravo. In addition, the amount of Ridomil used is smaller than that of the other two chemicals.



(Far left) Loose smut of barley, carried in the embryo of the seed, may be controlled by carboxamide fungicides applied to seed (inset). **(Left)** Onion smut, indigenous in cool muck soils, invades the germinating seedling but is difficult to observe in the green plant (arrow); plants on the left have been bleached with Carnoy's solution (3:1 ethanol:acetic acid) to allow accurate rating of smut infections. ProGro seed treatment (inset) gives good control. **(Middle)** Barley seedling blight caused by soilborne and seedborne *Bipolaris sorokiniana* is controlled most effectively with combined Sisthane and Vitavax (see Fig. 1). **(Right)** Benomyl applied in a band across the proximal end of cucumber leaves penetrates more effectively when applied on the lower surface (BL) than when applied on the upper surface (BU), as indicated by the mildew moving acropetally. **(Far right)** Downy mildew of lettuce caused by *Bremia lactucae* is controlled better with smaller amounts of the systemic Ridomil than with the protectants zineb and Bravo (see Fig. 2).

smut organisms, which are carried in the embryo of the seed; furthermore, they were environmentally undesirable and were phased out. Von Schmeling and Kulka (7) introduced the systemic carboxin to control loose smut of barley caused by *Ustilago nuda*. Carboxin is now the most widely used seed-treatment fungicide for small grains in Canada.

Benzimidazole systemic fungicides also provide effective seed treatment. In 1978, white beans (*Phaseolus vulgaris*) in Ontario were threatened by a new delta race of the anthracnose fungus *Colletotrichum lindemuthianum*. Maude and Kyle in England (4) had previously reported that seed treatments with benomyl would control seed-borne anthracnose. Research in Ontario during 1977-1978 showed excellent control of seedborne anthracnose with a benomyl or thiophanate-methyl seed treatment in combination with captan (to reduce seed decay) and diazinon (for seed corn maggot control). In 1978, experimental labels were granted in Canada for this combination and seed was treated for over 40,000 hectares. A protectant fungicide would never have succeeded.

The control of onion smut shows how less fungicide may be required by systemics than by protectants. The pathogen *Urocystis cepulae* is common in cool muck soils and invades the first leaf (cotyledon) as it grows upward to the soil surface. In Canada, the protectant fungicide thiram may be applied as a soil granule at 2.2 kg a.i. ha^{-1} plus 0.8 kg a.i. ha^{-1} with seed for a total of 3 kg a.i. ha^{-1}. ProGro (50% thiram and 30% carboxin, a sys-

temic) may also be used to control onion smut and is applied as a seed treatment at 0.12 kg a.i. ha^{-1}. Approximately 96% less fungicide is required with ProGro, which has given consistently good disease control since its registration in 1971.

The postemergence activity of systemic seed treatment against airborne pathogens may have great potential. Rowell (6) first reported excellent postemergence activity with Indar against wheat brown rust (*Puccinia recondita*). In 1978, seed treatment with triadimefon was reported to give up to 100% control of yellow rust of winter wheat at the boot stage in Washington (5); triadimefon is already registered for use in Europe. Ethirimol has shown excellent potential as a seed treatment for the control of powdery mildew of cereals in Europe (3).

Combining two or more fungicides can provide broader, more complete control of plant pathogenic fungi. Combined Sisthane and carboxin is a very effective barley seed treatment (Fig. 1). Sisthane gives excellent control of seedling blight caused by *Bipolaris sorokiniana* and some control of loose smut, while carboxin gives excellent control of loose smut and slight control of seedling blight. Another combination treatment of cereal seed, now being tested in Europe, includes 1) mephfuroxam, a more fungitoxic analog of carboxin, for smut control; 2) thiabendazole for *Fusarium* control; and 3) Ridomil for *Pythium* control. Numerous other combinations of systemics are being tested for control of several different diseases. In some cases, broad-spectrum protectants, such as thiram, are also added.

Application to Soil

The fate of systemic fungicides in soil is not different from that of protective fungicides; both are subject to inactivation by adsorption and degradation. Until now, therefore, application of systemic fungicides to soil has been limited primarily to use in greenhouses, where soil drenches are successfully used with benomyl and thiabendazole to control *Verticillium* and *Fusarium* wilts of tomatoes and black root rot of cucumbers caused by *Phomopsis sclerotioides* (2). Soil drenches with dimethirimol, benomyl, or carbendazim show potential for control of such airborne diseases as powdery mildew of cucumber caused by *Sphaerotheca fuliginea*.

In-furrow sprays and granular formulations are applied at planting to be in the proximity of the developing roots. This form of application is outstanding for recently developed systemic compounds, such as Aliette, Ridomil, and prothiocarb, that are active against *Pythium, Phytophthora*, and fungi causing downy mildew. Ridomil as a 5% granular applied at 0.5 kg a.i. ha^{-1} gives excellent control of *Phytophthora* root rot of soybean (R. Pitblado, *personal communication*).

Soil injection of systemic fungicides can be used against numerous diseases of perennials but is still an uncommon practice. Incorporation into seedbeds and into seed blocks for transplants also looks promising for some Oomycete fungicides against *Pythium* damping-off in vegetables and downy mildew of lettuce caused by *Bremia lactucae*.

Root dips of transplants in solutions of Aliette controls red stele of strawberry caused by *Phytophthora fragariae* (8).

The addition of systemic fungicides to irrigation systems can save time and equipment, especially via trickle irrigation distribution, which allows accurate regulation of time and space. In Japan, the fungicide IBP is applied as granules to irrigation water to control rice blast caused by *Pyricularia oryzae* (9); because the active ingredient is only moderately soluble in water (500 μg/ml), the granules persist for up to 3 wk.

Much has yet to be done to find the right formulations and application methods to avoid phytotoxicity and adsorption to soil and to give long enough action for the desired control while not being overly persistent in the environment. The new Oomycete fungicides are a step in the right direction; they are very soluble in water, readily taken up by the roots, and effective in low concentrations.

Application by Foliar Spray

Uptake of systemic fungicides applied as foliar sprays by the cuticle of plants is seriously limited. The outer surface waxes protect plants from excessive desiccation and, conversely, make it difficult for fungicides dissolved in water to enter leaves. In addition, the high surface tension of aqueous sprays prevents systemics from entering stomata. The cuticle on the underside of leaves is easier to penetrate, but sprays are usually applied to the upper surface. Most systemics are relatively insoluble in water, and if applied as wettable powders (WP), as protectants

Table 1. Systemic fungicides in use in the world[a]

Chemical groups Common or chemical name	Trade name	Sensitive fungi[b]
Acetamides		
N-cyanoethyl chloracetamide	Udonkor	powdery mildew
2-cyan-N-(ethylaminocarbonyl)-2-(methoxyimino)-acetamide	Curzate (DPX-3217)	Oomycetes
Acylalanines		
DL-methyl N-(2,6-dimethylphenyl)-N-(2-methoxyacetyl)alaninate	Ridomil, Acylon	Oomycetes
furalaxyl	Fongarid	Oomycetes
Benzimidazoles		
benomyl	Benlate	*Botrytis, Fusarium, Cercosporella, Penicillium, Septoria, Sclerotinia, Venturia, Verticillium,* powdery mildew
carbendazim	Bavistin	
thiophanate-methyl	Easeout, Topsin M	
thiophante	Cercobin, Topsin	
thiabendazole	Mertect	
fuberidazole		*Fusarium*
Carboxamides		
carboxin	Vitavax	smuts, *Rhizoctonia*
furmetamid	BAS389	
mephfuroxam	Trivax (H719)	
fenfuram	Panoram	
benodanil	Calirus	rust, *Rhizoctonia*
oxycarboxin	Plantvax	rust
pyracarbolid	Sicarol	rust, *Stereum*
Hydroxypyrimidines		
dimethirimol	Milcurb	powdery mildew of cucurbits
ethirimol	Milstem, Milgo E	powdery mildew of cereals
bupirimate	Nimrod	powdery mildew
Morpholines		
dodemorph	Meltatox	powdery mildew of roses
tridemorph	Calixin	yellow rust of wheat, *Mycosphaerella,* powdery mildew
Organic phosphates		
IBP	Kitazin P	*Pyricularia*
edifenphos	Hinosah	
pyrazophos	Afugan, Curamil	powdery mildew
triamiphos	Wepsyn	
Pyrimidines, pyridines, piperidines, imidazole		
S-n-butyl-S′-p-tert-butylbenzyl-N-3-pyridyl-dithiocarbonimidate	Denmert	powdery mildew, rusts, *Venturia, Cochliobolus, Mycosphaerella,* "fruit-rots"
fenarimol	Bloc, Rubigan, Rimidin	
imazalil	Fungaflor	
nuarimol	Trimidal, Trimunol	
parimol	Parnon	
triadimefon	Bayleton	
triadimenol	Baytan	
α-butyl-α-phenyl-1H-imidazole-1-propanenitrile	Sisthane (RH-2161)	
triforine	Saprol	
Triazoles		
n-butyl-1,2,4-triazol	Indar (RH-124)	brown rust of wheat
tricyclazole	Beam 75	*Pyricularia*
fluotrimazol	Persulon	powdery mildew
Others		
aluminum ethyl phosphite	Aliette	Oomycetes
griseofulvin	Griseofulvin	*Botrytis,* powdery mildew, *Cladosporium*
cycloheximide	Actidione	rusts, *Fabraea*
prothiocarb	Previcur	Oomycetes
isoprothiolan	Fuziwan	*Pyricularia*
probenazole	Oryzemate	*Pyricularia*

[a]Adapted from *Fungizide 1978,* a book listing important fungicides by E. H. Pommer of BASF, Limburgerhof, West Germany.

[b]Oomycetes = downy mildews, *Phytophthora, Peronospora, Bremia, Plasmopara, Pseudoperonospora,* and *Pythium.*

are, they remain as a suspension on the leaf surface, unable to traverse the cuticular barrier. The fungicide must dissolve in the spray droplet and diffuse into the cuticle, all before the droplet dries on the leaf surface. Once the droplet has dried, very little further uptake occurs.

To improve cuticular uptake, the pesticide industry has switched to formulations that are either emulsifiable concentrates (ECs) or oil emulsions. In 1967, before systemics, 6.5% of the fungicides reported in the APS *Fungicide-Nematicide Report* were formulated as ECs. In 1977, with many systemics in use, the number of EC formulations reported had increased to 28.7%. Systemics formulated as ECs give better disease control, probably because the fungicides are soluble in the organic phase of the EC and can rapidly partition into the water of a spray droplet and then into the waxy cuticle. Even with this improved uptake, however, only about 5% of a systemic applied to leaves enters the plant, with most remaining on the leaf surface and acting as a protectant.

Addition of 1% spray oil has also been used to enhance uptake. The oil possibly "solubilizes" the cuticle by being miscible with the waxes or cutin. Because uptake is increased, less fungicide is required. In Canada, for example, benomyl as a WP is applied to apples for scab control at 0.28 kg a.i. ha^{-1} with oil and at 0.63 kg a.i. ha^{-1} without oil.

Usually, most of a chemical sprayed on a crop is deposited on the upper surface of the leaves, and pathogenic fungi growing on the lower surface, such as downy mildew, are poorly controlled. Systemic fungicides, however, can move translaminarily, being taken up on one side of the leaf and translocated to the other. Another advantage of systemic over protective fungicides is a curative postinfection action. By entering the plant tissue, a systemic fungicide can eradicate pathogens shortly after infection. Because the need for constantly protecting the foliage is avoided, less fungicide is used, minimizing stress on the environment. Another advantage of systemic fungicides is compensation for poor coverage because of redistribution within the plant.

The incidence of downy mildew of lettuce caused by *B. lactucae* in Ontario, Canada, at harvest time after a spray program with protective and systemic fungicides is shown in Fig. 2. The protectants zineb and chlorothalonil were sprayed weekly and gave poor control. The systemic Ridomil was applied biweekly and gave much better control, with about 92% less fungicide being used. The need for less systemics than protectants can be observed in numerous spray programs. For instance, in Ontario, the recommended spray for apple scab caused by *Venturia inaequalis* is 5.4 kg a.i. ha^{-1} for the protectant maneb and 0.28 kg a.i. ha^{-1} for the systemic benomyl. The systemic fenarimol is even more active, requiring only

0.065 kg a.i. ha^{-1}.

In the near future, we expect some systemic fungicides will become available that are also translocated downward in the plant. The results of Zentmyer (9), who was able to control root rot of avocado caused by *Phytophthora cinnamomi* with foliar applications of Aliette and Ridomil, are a hopeful indication that we are entering a new era in disease control with downward-moving systemic fungicides.

Summary

The number of systemics has increased during the last decade to comprise approximately one-third of the total fungicides in use. The systemics are much more selective than the protectants in the spectrum of diseases controlled. Because of selective toxicity to distinct fungal groups and development of resistant fungal strains, a serious look at fungicide combinations and management programs is required. Both the amount of fungicide needed and the frequency of application are markedly reduced with systemics compared with protectants. Formulations have also changed from WPs to ECs to improve cuticular uptake of systemic fungicides. Current systemics are transported upward in plants. The development of fungicides that move downward from a foliar application to control root pathogens is just beginning and requires further investigation.

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