Fungicides: Past, Present and Future of Fungicides Used for Late Blight Control

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Abstract

The first effective fungicides developed for potato late blight control were cupric, later came bisdithiocarbamates and then others, all currently known as contact fungicides. A new era started with the launching of systemic fungicides. Contemporary pressures to protect the environment and human health opened the way to different kinds of compounds, the resistance activators and fungicides from natural origin or similar ones. At present, a broad spectrum of products exists that can be used in appropriate strategies for the chemical control of late blight — effective, efficient, economic and sensitive to environmental and human health concerns. In this paper some important characteristics, advantages and disadvantages of these fungicides are described.

Introduction

From the appearance of the late blight problem as a rampant epidemic in Europe in 1845, attempts were made to control it using chemicals. The first products, sodium chloride (common salt) and copper sulphate used as seed treatments in Ireland (Moore, 1846), and sulphur applied to foliage in Peru in 1875 (García Merino, 1878), were unsuccessful at controlling the “potato disease” as blight was then known in Peru.

After the chance discovery in Bordeaux, France, that copper sulphate controlled grapevine downy mildew, in 1845 Millardet demonstrated that control could be improved by mixing lime with a solution of copper sulphate (Millardet 1875a; 1875b), which later became known as Bordeaux mixture. In 1888, Prillieux carried out the first trials of the mixture on late blight in France (Prillieux, 1888). From 1905 onwards it was tested in Peru. Plots treated with Bordeaux mixture produced up to twice as much as non-treated plots in a year where it was not unusual to see fields on the coast completely flattened by the “potato disease” (Vanderghen, 1907).

Other copper-based fungicides followed. In 1934 the fungicide properties of the dithiocarbamates and the bidithiocarbamates were discovered, then later others were developed, all of them contact fungicides (i.e.

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not systemics). In 1976, a new era in the chemical control of late blight began with the launching of cymoxanil — systemic fungicides had arrived.

At present, the impetus provided by the current emphasis on the protection of the environment and human health is leading to the development of different types of chemical products — resistance activators, the natural defense mechanisms against other organisms, and to fungicides of natural origin.

**Types of fungicides used in the chemical control of late blight**

Two types of fungicide are used to control blight, contact (or more correctly non-systemics) fungicides also known as residuals, and systemic fungicides (Fernández-Northcote et al., 1999).

In addition, the contact fungicides are commonly referred to as protectant or preventive fungicides, and systemics as curatives. These terms are not applied appropriately and confuse farmers, who apply systemics only when they see blight symptoms (because they think they are ‘curative’) which is usually too late to obtain good disease control. We will only use the terms contact and systemic in the present article.

Contact fungicides affect pathogen structures on the surface of the plant during the phases of germination and penetration. Once the pathogen has entered into the plant it is beyond the reach of these fungicides. Because new shoots and plant parts that develop after an application must be protected and treatment must be repeated if it rains right after an application, good control of late blight is only possible with this type of fungicide with frequent and closely spaced applications. For this reason, between 16 and 20 treatments are made in blight zones in developing countries, and even then control may not be very effective if the conditions are highly favorable for the disease and if rainy conditions do not permit treatment at the right moment.

With contact fungicides it is very important to maintain an adequate film of fungicide on the foliage on both the upper and lower surfaces of the leaves. All aerial parts of the plant must be covered. The product will remain active as long as it stays on the leaf and is not washed off by rain, that is, they have good persistence. In the experience of other researchers, farmers and the author, the relative persistence of contact fungicides available at the moment, in order from least to best, are dithiocarbamates, phthalimides, chloronitriles, cuprics, tin-based, and phenyl-pyrimidines.

In addition to the characteristics of contact fungicides and the conditions for effectiveness mentioned earlier, is the fact that farmers in many developing countries, such as Bolivia, do not apply fungicides correctly. They do not cover the whole plant because they do not realize the importance of doing so or because they are short of time, thus reducing the efficacy of these fungicides. The development of systemic fungicides in the 1970s gave an alternative to resolve these problems and attain better blight control.

The systemic fungicides (Table 1) penetrate into the plant and move across the leaves from the upper to the lower surfaces (or vice versa, i.e. a translaminar movement) and then upwards into the rest of the plant from the point of contact (an acropetal movement). Only one of the systemic fungicides used against late blight, phosetyl-aluminium that strictly speaking is not a fungicide, moves downwards into the plant (basipetal movement) as well. With systemic fungicides it is not as important to obtain a constant and uniform a cover as for contact fungicides because the systemic fungicide penetrates into the plant and moves acropetally, even to parts of the plant that were not treated. Also, the interval between applications can be increased and shortly after application they cannot be washed off by rainfall. These are the significant advantages of systemics over contact fungicides, especially in areas heavily affected by blight in developing countries. The disadvantages of systemics are that they are more expensive and that they select for pathogen resistance when they are used inappropriately.

To tackle the problem of resistance to systemic fungicides, the International Group of National Associations of Agrochemical manufacturers has constituted an action committee on fungicide resistance (FRAC, Fungicide Resistance Action Committee) with has proposed general recommendations designed to prevent or delay the onset of resistance (Wade and Delp, 1985). One of the most important recommendations is that systemics should be sold in mixtures with contact fungicides. Based on information from the FRAC (http://www.gcpf.org/frac) and the author’s experience, the risks of generating resistance goes from low to high as follows a) Very low risk: resistance activators, phosphonates, b) Low risk, requiring resistance management, cyano-acetamide oximes, c) High risk, requiring resistance management, phenylamides.
Contact fungicides

Copper-based

Copper-based fungicides were the first to be commonly used to control late blight. The most used are Bordeaux mixture and, more recently, fungicides based on copper oxychloride and cupric oxide. Among contact fungicides, copper-based chemicals have the advantage of having good persistence. Their disadvantage is that they tend to slow down the vegetative development of the plant and, for this reason the recommendation is not to use them before the onset of flowering. They act by denaturing enzymes of the respiration pathway in the sporangia and zoospores (Schwinn and Margot, 1991).

The present trend to improve the efficacy of copper fungicides has been directed towards reducing particle and crystal sizes to enable their absorption into the leaves, thus transforming them into systemics.

Dithiocarbamates

Dithiocarbamates are organic sulphur compounds derived from bidithiocarbamic acid. Their salts are 1,2-bidithiocarbamates and the common chemical names of these fungicides are based on the chemical groups (methyl, ethyl, etc.) and metals in them. The most commonly used for late blight control are zineb (containing ethylene and zinc), maneb (containing ethylene and manganese), mancozeb (containing ethylene, zinc and manganese), metiram (containing ethylene and zinc) and propineb (containing propylene and zinc).

Compared with the copper fungicides the dithiocarbamates are not phytotoxic and can therefore be used throughout growing period. However, they have the disadvantage of lacking persistence, that is, they are easily washed off in the rain. They affect sporangial and zoospore germination in particular, but also mycelial development, disrupting important biochemical processes involving enzymes of the thiol group (Schwinn and Margot, 1991).

The dithiocarbamates are presently the most widely used fungicides in late blight control. While the low cost of these fungicides encourages their use, control strategies based solely, or principally on them are inadequate in heavy blight zones. In such zones, treatments must be made very often, increasing exposure for the farmer and the environment. In Switzerland the use of maneb and propineb have been suspended for reasons related to human health and/or the environment (Emmerman, 1996). In other countries, such as Denmark, policies have been implemented to replace maneb (Jorgensen, 1996). The EPA in the USA has sufficient evidence from studies on animals of a probable carcinogenic effect on humans of maneb, zineb and mancozeb (The Pesticides Trust, 1994). Crissman et al. (1994) and Cole et al. (1997) reported cases of chronic dermatitis associated with the frequent use of mancozeb in Ecuador.

Phthalimides

Folpet, captan and captan belong to this group of fungicides. The first two have played an important role in the control of late blight. Captan was considered by the WHO (The World Health Organization) as extremely hazardous (The Pesticides Trust, 1994). At present captan is being promoted. The fungicide and fungistatic action against fungal structures is restricted to the leaf surface. Zoospore mobility and germination are affected. These fungicides react with thiol groups bringing about a series of non specific biochemical effects that affect enzyme activity (Schwinn and Margot, 1991).

Chloronitriles (Phthalonitriles)

Chlorothalonil is found in this group. It differs from the dithiocarbamates and phthalamides by having better persistence and dispersion, with strong adherence to the leaf surface permitting greater intervals to be left between treatments than for these two groups. Its mode of action is to capture free glutathione, preventing the activation (reduction) of glyceraldehyde-3-phosphate dehydrogenase and perhaps similar enzymes as well (ISK-Biotech, 1990).
Phenyl-Pyridinamines

Fluazinam is a new fungicide in this group. It is reported to have better persistence on the leaf surface compared to other contact fungicides. Its use at low concentrations enables the quantity of fungicide applied per hectare to be reduced. It inhibits spore germination, appresorium development, penetration and hyphal growth, as well as sporulation. Fluazinam is a powerful uncoupler in oxidative phosphorylation and inhibits proton transfer across the mitochondrial membrane (Guo et al., 1990).

Tin-based fungicides

Triphenyltinacetate and triphenyltin hydroxide are effective against blight and are more persistent than copper fungicides and dithiocarbamates. They act on spores and hyphae by interfering with oxidative phosphorylation (Schwinn and Margot, 1991). However, the phytotoxicity of these fungicides limits their use to the end of the growing period. These fungicides appear on lists drawn up by the European Community of chemical products whose use should be prohibited or reduced to protect the aquatic environment (The Pesticides Trust, 1994).

Systemic fungicides

Systemic fungicides and their type of movement in the potato plant (Table 1).

<table>
<thead>
<tr>
<th>Common name of the chemical product</th>
<th>Translaminar Penetration</th>
<th>Acropetal Movement</th>
<th>Basipetal Movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cymoxanil</td>
<td>++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Propamocarb</td>
<td>++</td>
<td>(+)</td>
<td>-</td>
</tr>
<tr>
<td>Dimetomorf</td>
<td>++</td>
<td>(+)</td>
<td>-</td>
</tr>
<tr>
<td>Iprovalicarb</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Phenylamides</td>
<td>++</td>
<td>++</td>
<td>(+)</td>
</tr>
<tr>
<td>Phosetyl-aluminium</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
</tbody>
</table>

++=strong, rapid; +=weak, slow (+)= minimal; -= absent.

Cyano-acetamide oximes

Cymoxanil belongs to this group of fungicides. It penetrates and moves from one surface of the leaf to the other, but does show acropetal movement within the plant. Its persistence in the plant is limited to a few days, so the treatment intervals required resemble those for contact fungicides. Cymoxanil affects DNA synthesis and to a lesser extent RNA synthesis (Ziogas et al., 1987). A synergistic effect has been reported for mixtures of cymoxanil and mancozeb. This mixture gives better control of late blight than cymoxanil or mancozeb alone (Samoucha and Cohen, 1989; Evenhuis et al., 1996). Cymoxanil is a low-risk compound for the development of resistance in the pathogen.

Carbamates

Propamocarb is in this group. It is basically a translaminar fungicide. It has little effect on sporangial germination. It affects the permeability of the cell membrane of the young mycelium, but is not effective on established mycelium (Papavizas et al., 1978). Propamocarb is not effective on plants that are already infected and cannot control disease development three days after infection (Samoucha y Cohen, 1990). Intervals between treatments must therefore be short (seven days).

Iprovalicarb is a new systemic fungicide that has been launched onto the market recently. It is an amino acid amidocarbamate (Seitz et al., 1999). Its limited penetration across the cuticle is enough to provide systemic protection. The residues that remain on the treated leaf surface inhibit the germination of sporangia and zoospores, while the absorbed fungicide prevents mycelial development. The result is that colonization of epidermal and palisade parenchyma cells is significantly inhibited, greatly impeding deeper penetration of
the spongy parenchyma of the leaves. It shows acropetal movement within the plant. The mode of action is not understood, but it is assumed to be novel and specific (Stubler et al., 1999; Jende et al., 1999).

**Cyclic acid derivatives**

Dimethomorph, on the market since 1990, is one of the newest fungicides. It is fundamentally a translaminar fungicide with reportedly excellent anti-sporulation activity, preventing the production of sporangia and oospores. Dimethomorph interferes with cell wall formation provoking lysis and cell death. It is considered as a low risk fungicide for the development of pathogen resistance (Leroux et al., 1993).

**Phenylamides**

The first fungicide of this group to be released on the market was metalaxyl in 1977. Other phenylamides followed: ofurace, benalaxyl, oxadaxyl, furalaxyl and mefenoxam (metalaxyl-m). These fungicides generated high expectations due to their post-infection action and their outstanding activity under conditions highly favorable for disease. The widespread and intensive use of metalaxyl alone to treat late blight during a cropping season and the fact that it was often used after the appearance of disease symptoms combined to put pressure on the pathogen with the result that variants of *P. infestans* resistant to metalaxyl appeared three years after its introduction (Davidse et al., 1981; Dowley and O'Sullivan, 1981). Its later sale in the form of mixtures with contact fungicides and their use in accordance with the recommendations of the FRAC phenylamides working group (Wade and Delp, 1985; http://www.gcp.org/frac/PhenylamidesWGBody.html) has led to the use of metalaxyl and other phenylamides for the effective, efficient and stable control of late blight despite the initial levels of resistance of 30 to 50% to these fungicides in the field (Nuninger et al., 1995; Dowley et al., 1995). Various studies have shown that while the frequency of variants resistant to phenylamides increases throughout the season at a rate that is proportional to the selection pressure exerted, this frequency is low at the start of each season (Figure 1), suggesting that resistant types are at a selective disadvantage compared with non-resistant types regarding between season survival (Williams and Gisi, 1992).

![Dynamics of *P. infestans* under selection pressure from PA](image)

**Figure 1.** Dynamics of the *P. infestans* population under selection pressure from phenylamides (PA). The level of sensitivity in the population ranges from S (sensitive) to R (resistant). Kindly provided by Dr. J.A. Guerra, Novartis.
Metalaxyl has little effect on the germination of sporangia and zoospores or on zoospore mobility. Penetration into the plant and the formation of haustoria in potato plants are not affected. The fungitoxic effect of metalaxyl is only exercised inside the plant (Staub et al., 1980, cited in Schwinn and Margot, 1991). Phenylamides strongly inhibit sporulation and to a lesser extent mycelial development (Bruck et al., 1980). They disrupt RNA synthesis by inhibiting the enzyme RNA polymerase. Distribution throughout the plant and persistence are best obtained with young actively growing plants.

Of the pesticides evaluated by EPA, oxadixyl figures as a possible carcinogen in humans based on limited information from animal studies (The Pesticides Trust, 1994).

**Phosphonates**

Phosetyl-aluminium (phosetyl-Al) belongs to this group. It has a direct fungicidal effect and, additionally, indirectly activates the plant’s own defense mechanisms. Another advantage of this compound is that its movement within the plant is both acropetal and basipetal (moving upwards and downwards into the plant from the point of penetration), meaning that excellent late blight control in tubers can be achieved with this product.

Phosetyl-Al penetrates rapidly into the plant and persists for a long time (several weeks), allowing treatments to be more widely spaced.

**Resistance activators and natural fungicides**

Plant defense mechanisms have been studied for about a hundred years, but only recently has the emphasis been put on their possible use as a part of integrated pest management. In 1989, scientists at Ciba-Geigy discovered that acibenzolar-S-methyl (CGA 245704), a synthetic compound, was an effective inducer of plant natural self-defense mechanisms, giving rise to the phenomenon known as Systemic Activated Resistance (SAR), by which plants become more resistant to pathogens. CGA 245704 was developed for the protection of several different crops against diseases caused by various pathogens (Ruess et al., 1995). In 1996 it was introduced in Germany under the brand name Bion 50 WG and in Switzerland as Unix Bion 63 WG for controlling oidium (*Erysiphe graminis*) on wheat. Trujillo et al. (1997; 2000) have demonstrated the effectiveness of Bion 50 WG for controlling late blight in mixtures with a systemic or contact fungicide. This enables the number of treatments with the systemic to be reduced, which consequently reduces the risk of fungicide resistance developing.

After application, BION penetrates and is rapidly distributed throughout the plant, moving both acropetally and basipetally. It is assumed that BION combines with a plant molecule and then activates a defense response, similar to that induced by salicylic acid, without prior infection by a pathogen.

Another line of investigation being followed by a few agrochemical companies is to isolate or to synthesize substances similar to those produced by plants that carry out an essential role in the mechanism of plant defense. At the present time, none have been developed for controlling late blight.

**Timing of fungicide applications**

Based on the preceding descriptions of the different types of fungicides used for controlling late blight, Figure 2 presents their action on the different phases of the biological cycle of *P. infestans*. Contact fungicides are only active during the first hours of contact of the sporangium with the wet leaf (or other aerial part of the plant) surface, in sporangial phases, zoospore liberation, zoospore germination, germ tube formation, appressorium formation and initial penetration. Cymoxanil, propamocarb and phosetyl-Al are also active on these phases. Once *P. infestans* has penetrated into the plant, translaminar fungicides are effective in the place where they were applied and systemics are active in all parts of the plant to which they move (acropetally or basipetally) after penetration. The younger, more turgid and vigorous the plant is, the better the mobility and more durable the action of the fungicide will be. For this reason, fungicide use is not recommended in the later stages of crop development. In addition, acropetal systemics that provide very good disease control can bring about a hormonal type of rejuvenating effect that depresses yield. Contact fungicides, cymoxanil and phosetyl-Al are also active on sporangiophores and sporangia growing out of stomata generally of the abaxial leaf surface. Based on these characteristics and others described earlier, the main periods of fungicide application for controlling blight are illustrated in Figure 3.
Figure 2. Action of fungicides used for controlling late blight on the different phases of the life cycle of *P. infestans* on leaflets of a susceptible potato cultivar.

Figure 3. Main periods during which the use of fungicides against late blight is recommended on potato, according to the phenological stage of crop development.
Conclusions

A large range of effective chemicals for controlling late blight is now available that may be used for developing chemical control strategies that are effective, efficient and economical, and that minimize the effects on the environment and human health. These strategies, such as those developed by PROINPA (Fernandez-Northcote et al., 1999), as part of the integrated management of blight, enable fungicide use to be reduced, sustainable production to be increased and the socioeconomic situation of the farmer to be improved.

Literature cited


Moore, D. 1846. Irish farmers' journal 26 August, 650.


