Mycology Answers

What is the mode of action of fungicides and how do fungi develop resistance?

Many factors operate in influencing the establishment of fungal infections in plants. As a result the occurrence of fungal diseases is often unpredictable and may be highly variable. Crop losses due to fungal activity are high both before and after harvesting and means of combating fungal pathogens attracts much attention. The treatment of plants to prevent such diseases and to eradicate the causative agent is often by means of fungicidal chemicals, although the use of biological control systems is now becoming more widely established. However, there is a great deal of controversy about the use of chemicals owing to concern about effects on the environment and other organisms, particularly in areas where there is intensive agricultural practice and large amounts of chemical may be involved. In addition, important fungal pathogens (e.g. *Phytophthora infestans* - potato blight: *Botrytis cinerea* - grey mould) have developed resistance to some chemical treatments.

Some of the older, well established, chemical treatments act by protecting the plant (e.g. sulphur, copper, mercury). These chemicals are applied to the surfaces of plants and act as a barrier preventing spore germination and/or invasion. As a result, the effectiveness of the treatment depends on the timing of the application to a crop in relation to the occurrence and spread of the fungus and to conducive environmental conditions. Such treatments are not very effective against root invading fungi. Inorganic fungicides, such as copper and sulphur, constitute some of the oldest remedies but still provide extremely successful control and are highly effective. Bordeaux mixture, a combination of copper sulphate and calcium hydroxide (lime), was used in the 1880's to protect vineyards in France against powdery mildew disease. Copper-based treatments are still important as fungicides (timber treatments) but are also highly toxic to plants and must be used with care. These treatments prevent spore germination by denaturing proteins and disrupting enzyme synthesis in the fungus. Elemental sulphur is also a very effective chemical treatment, particularly against powdery mildews and rusts, since it interferes with electron transport but it must be used with care because it is also toxic to plants, causing loss of chlorophyll and disrupting photosynthesis. Other protectant treatments include the dithiocarbamates (Thiram, Zineb, Maneb) which disrupt amino acids preventing protein and enzyme production in fungi and leading to their demise. The dithiocarbamates are often used as seed treatments against rust and vascular wilt fungi, but are also toxic to mammals. In general, these compounds are multisite inhibitors, affecting a range of enzymes involved in key pathways which makes them so effective. However, in addition to problems with toxicity, another major drawback to the use of these treatments is that any new growth (shoots, new leaves) of a plant will not be protected as it is formed and also, over a period of time, the chemicals will gradually be washed off the plant. As a result re-application, at intervals, may be required for continued protection.

Some fungicides can be taken up into the plant, transported throughout the plant tissues and interfere with fungal growth from within. These are known as *systemic fungicides*. In theory this is a good way to ensure the treatment of the whole plant. Repeated applications are not needed to protect new growth because the compounds are mobile in the plant. Systemic chemicals are now widely used as seed treatments and can protect young seedlings during the most vulnerable part of their development. However, there is still a problem with root pathogens, in most cases, because these fungicides tend to accumulate in shoots, except for the phosphonates that are more mobile in the plant and provide protection from *Phytophthora* root rot. Most systemic treatments have a site-specific mode of action, in general affecting a particular biochemical process

or a single step in enzyme synthesis. The first systemic fungicides were antibiotics such as streptomycin but many are now available commercially. Of the benzamidazole fungicides, benomyl is effectively used to combat the activities of *Fusarium* spp and powdery mildew fungi. The action is to interfere with nuclear division that eventually prohibits further outgrowth. Some of the systemic compounds e.g. azoles and morpholines affect particular, but different, steps in the biosynthesis of sterols which are important components of fungal membranes, The more modern strobilurin fungicides block electron transport in mitochondria.

Site-specific compounds are useful because of this mode of action and are not as likely to be toxic to the plant. However, because of the site specificity, even a small biochemical change in the fungus may lead to the development of resistance. Resistant strains arise by the selection of resistant individuals or as the result of single mutations. A resistant strain may be able to bypass a block in metabolism and circumvent the action of the fungicide or may produce unusually large amounts of a specific enzyme to compensate. Fungal pathogens often reproduce quickly giving rise to large numbers of spores in a short time and, as a result, resistance may develop and spread surprisingly fast, particularly in instances where the use of the chemical has been repeated. Such intensive use of a particular fungicide favours the development of resistance by placing a high selection pressure on the pathogen. Important plant pathogenic fungi, that are difficult to control, have developed resistance to systemic fungicides (e.g. *Botrytis cinerea* - grapes, *Erysiphe graminis* - cereals, *Bremia lactucae* - lettuce, *Phytophtora infestans* - potato). There is therefore, a good case for only applying fungicides when and where they are necessary.

Resistance to multisite fungicides is less likely to develop because a number of changes in the fungus would be required at one time for it to survive the treatments.

Fungicides will continue to be important as means of disease control but it is clear that a degree of caution in their application is advisable. The use of combinations of fungicides, or alternations of treatments with different modes of action including multisite fungicides, are useful strategies for minimising the development of resistance. Planting disease resistant cultivars and good crop husbandry also have a very important role in general crop management.

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