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DISEASE MANAGEMENT: CHEMICALS

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24.1 Introduction

Some chemicals are toxic to most forms of life and are used as sterilants, disinfectants or fumigants to eradicate pathogenic organisms prior to planting. These chemicals were discussed in Chapter 23. Other, less toxic, chemicals can be used to control diseases that would otherwise cause serious losses in agricultural or horticultural crops. Depending on the target organisms, these substances can be classified as fungicides, bactericides (often called antibiotics) or nematicides. Many substances have been tested for their activity against viruses causing diseases in plants. Most inhibit virus activity to some extent but none have achieved commercial importance so they will not be discussed further.

An 'ideal' chemical control agent must be effective at concentrations which do not injure the plant structures (or growth stages) to which it is applied. It should offer minimal hazard to humans and animals and should not induce allergic reactions. It should have minimal harmful, long-term effects on the normal microflora of plants and soils. It should be chemically stable and persistent relative to the harvesting requirements of the crop product but not so persistent as to cause residue management difficulties. There should be little chance of the pathogen(s) rapidly developing resistance towards the chemical. It should have properties which permit accurate and effective application to the crop or plant material. It should be physically and/or chemically compatible with other biocidal formulations. It should be able to be stored for long periods under normal climatic conditions without any loss in potency (i.e. have a long shelf life). The initial price and application costs must be low enough to warrant its use under a range of cropping conditions and market returns. These specifications are inherently difficult to incorporate into any single chemical. Moreover, the toxic ingredient must be present at a site of actual or potential infection at a vulnerable stage of the pathogen's life cycle in sufficient amounts to be lethal to the pathogen.

Over the years, a wide range of chemicals have been used to control pathogens in plants. Many of these have been replaced as more effective, cheaper or less hazardous chemicals became available. Only the main groups of chemicals currently utilised in crop protection will be described here. Information on superseded crop protection chemicals can be obtained from the references at the end of the chapter. Before describing the chemicals used to control plant diseases, some comments that apply generally to using pesticides are presented.

24.2 Registration, labelling and Material Safety Data Sheets

All chemicals for use in Australian agriculture, whether on plants or animals, must be registered and given clearance for sale under the National Registration Scheme administered by the National Registration Authority (NRA) for Agricultural and Veterinary Chemicals. The NRA assesses new products to ensure that they meet high standards of safety and effectiveness. It also reviews products that have been on the market for some time to ensure that they meet current standards. If they do not, the products or some of their uses may be deregistered. Even after registration, products are subject to ongoing scrutiny to ensure that they meet registration requirements up to the point of sale. It is illegal for consumers to use chemicals in ways that are not approved, unless a permit has been obtained. A permit allows a person, under certain circumstances, to possess and use an unapproved active ingredient or unregistered product, or to use a registered product in a way not specified on the label. Permits are only issued after careful evaluation of each individual situation.

Labels on containers of pesticides must, by law, contain information vital to users. At the head of the main label panel containing the trade name is a red on white signal warning that indicates how toxic the contents are and what level of risk they pose if mishandled. Agricultural chemicals are classified into schedules common to all Australian states and the most toxic have a warning which reads 'Dangerous Poison S7'. This category usually has sales restrictions of some kind such as no public access in display areas of stores and all purchases being recorded. There are five categories of Agricultural and Veterinary chemicals classified in this way. Just to complicate matters, some chemicals are also classified as 'Dangerous Goods' under the Australian Code for the transport of dangerous goods by road and rail (the ADG Code). Under this system, they may be classed as Flammable Liquids, Flammable Solids or 'Poisons'. The symbols indicating the class will appear on the label and can have implications for safe storage and transport. Other information on the label includes the trade name of the product and its active ingredient (a.i.), directions for use, storage and disposal as well as safety and first aid instructions.

More detailed information about products is contained in Material Safety Data Sheets (MSDS) which manufacturers of pesticides are obliged by law to supply to any user who requests that information. The manufacturer's or importer's name, Australian address and telephone number and all hazardous chemicals in the product must be identified fully on the MSDS. The main features used to identify an agricultural chemical are the manufacturers code number, its chemical name, its common name (the name of the active ingredient) and its trade names (depending on the manufacturing company). For example, the chemical name for the fungicide chlorothalonil is 2,4,5,6-tetrachlorisophthalonitrile. Its common name is chlorothalonil and its trade names in Australia include Bravo®, Chloronil®, Chlorothalonil®, Daconil®, Ornatek®, Ornathal® and Rover®. In addition, each product has a U.N. Number, an internationally recognised substance identification code that gives information about the chemical classification of the product. A physical description of the product and its properties on the MSDS assists identification.

MSDS also contain information relating to precautions for safe use, storage and transport of the product such as protective clothing needed, the type of packaging required, any warning signs that must be on the product, the flammability of the product and precautions to be taken in event of a spill or fire. The Poisons Schedule rating for the product is given together with health hazard information which includes possible adverse effects of exposure to the product, specific information on first aid measures and advice to doctors treating patients exposed to the product.

All agricultural chemicals used to control pathogens are designed to kill a target organism or group of organisms. This ability to kill is called the toxicity of the product. Toxicity is traditionally defined by the LD_{50} (lethal dose fifty percent), the amount of product, in mg/kg body weight, required to kill half a test population of animals (usually rats). LD_{50} values are best used to compare the relative toxicities of different products rather than as an absolute assessment of toxicity to humans, since the response of a rat to the product may be different from that of a human. A product with a numerically high LD_{50} value is relatively non-toxic compared with a product with a numerically low LD_{50}. LD_{50} values are given in MSDS. Fungicides mostly have LD_{50} values of about 5,000 mg/kg or more (e.g. the dithiocarbamate fungicide mancozeb has an LD_{50} of 8,000 mg/kg) and pose less of an acute health risk than many other pesticides.

24.3 Formulation of plant protection chemicals

Formulation is a series of processes that converts a chemical with anti-pathogenic properties into a useful product. It aims to produce the active ingredient in a stable, safe and convenient form capable of being transported, stored and economically applied to a crop. Pure chemicals are rarely used to control pathogens. They are usually combined with other materials that improve the physical and chemical properties of the product.

The active ingredient is frequently mixed with an inert **carrier** or filler which dilutes the active ingredient so the very small amounts needed can be spread evenly over the crop. Carriers may also improve the transport and storage properties of the product. Clays such as kaolinite and bentonite and silicate minerals such as diatomaceous earth are commonly used as carriers. The waxy cuticles covering some leaves make it difficult for the spray water carrying the chemical to spread evenly and it accumulates in large drops which sometimes roll off onto the ground. This can be overcome by the addition of a **wetting agent** (surfactant, spreader) either to the formulated product or to the made-up spray solution.

A **dispersant** or suspending agent which reduces the rate of sedimentation of suspensions of chemicals may also be added during formulation. Reducing the rate of sedimentation ensures that the concentration of active ingredient in the spray remains constant throughout the spraying process with very little agitation. The methyl celluloses and sodium carboxy-methyl celluloses are effective dispersants. **Emulsifiers** modify the properties of the interface between the two phases in an emulsion and enable certain formulations such as liquid concentrates and wettable powders to be readily and evenly dispersed in water. They also assist in the adhesion of the chemical to the crop. Many wetting agents also act as emulsifiers.

Stickers which improve the retention (tenacity) of particles on plant surfaces may also be added during formulation. Substances used include methyl cellulose, gelatine and various oils and gums. Stickers are particularly important in the tropics where torrential rains can wash spray from plant surfaces.

Sometimes antifoaming agents or corrosion inhibitors are included in the formulation.

The term formulation is also used to describe the form in which the anti-pathogenic chemical is supplied. If the product is soluble in water, it may be sold as a **concentrated solution** (CS) that is simply diluted with water before application. Concentrated solutions usually contain a wetting agent and spread well on foliage, giving a very even coverage. Substances that do not dissolve well in water may be ground finely and mixed in water to form a suspension. Such a formulation is known as a **wettable powder** (WP). Wettable powder formulations usually include inert material, a wetting agent and possibly a dispersant. Alternatively, insoluble chemicals may be diluted with an inert filler and ground to a very fine dust. **Dusts** are often used as seed dressings, in which case, the active ingredient is more concentrated than for foliar application. A sticker is added to ensure the chemical attaches to the seed.

Chemicals formulated as **emulsions** need surfactants or emulsifiers to prevent the phases of the emulsion from separating. Insoluble compounds may be dissolved in various organic solvents to form an **emulsifiable concentrate** (EC). Emulsifiable concentrates are diluted with water before they are applied to plants. Once on the plant, the water evaporates, leaving the active ingredient to exert its effect. In hot climates, oil may be used as the carrier because water evaporates too rapidly, even before the spray reaches its target.

Currently, there is a trend away from liquid formulations towards gels, crystals and solids, especially water-dispersible granules. This move is to try to reduce the disposal problems associated with plastic containers by using lined cardboard outers which can be composted or burned. **Granules**, small particles 2–5 mm in diameter, can also be placed close to the seed or plant so that they provide maximum protection for the plant with minimum risk of causing large-scale soil pollution. The body of the granule is made of various inert materials. Fine granules, less than 2 mm in diameter, are called **prill** and are used for special application techniques to soil.

In addition to the formulations described above, there are special purpose formulations such as liquid seed dressings and fungicidal paints used to protect pruning wounds.

24.4 Application of plant protection chemicals

Plant protection chemicals must be delivered to sites where they can come into contact with the propagules of pathogens, or where they can be absorbed by the plant and subsequently translocated to other tissues in a concentration which is toxic to pathogens, at a time when they are most beneficial in controlling pathogens. At the same time wastage of chemicals must be minimised. Crop protection chemicals are generally applied to the growing medium (soil, potting medium, hydroponic solution), to seed or to the foliage of growing plants.

Treating soil or potting media usually involves applying chemical agents capable of killing spores or mycelia of pathogenic fungi or nematodes and their eggs, prior to planting. However, the development of systemic chemicals which can be applied to leaves and translocated to roots offers some control of root infections. Soil treatments are expensive and present many practical difficulties in the field and so are largely confined to seed beds and glasshouse soils (see Chapter 23).

Seeds may be treated with liquid chemicals or dusts to prevent the germination of fungal spores or the hatching of nematode eggs, either on the seed or in the soil around the seed. Seeds are not as easily damaged by chemicals as foliage so chemicals which are phytotoxic to leaves or higher concentrations of chemicals may sometimes be used as seed dressings. Sometimes pest control chemicals are coated, together with fertilisers, onto seeds in a process called pelleting. The coat gradually dissolves in the soil moisture releasing the chemicals into the rooting zone of the seedling. When seeds are treated with chemicals, a marker dye (often red) is added to notify users that the seeds have been treated and should be handled with caution.

The foliage of growing plants is usually treated with liquid sprays applied from the ground or from the air. Dusts are used to a limited extent and may be particularly useful where water is in short supply. Sprays consist of atomised fluids which are propelled through turbulent air so that they penetrate the crop canopy. Many types of pumps and atomisers have been developed. Their efficiency in application is largely determined by droplet size and turbulence.

Pesticide sprays contain a large number of droplets (very small spheres of liquid) of various sizes depending on the way in which they are generated. Spray droplets are classified on the basis of their size (Table 24.1). Droplet size should be adjusted to suit the target being sprayed and to minimise chemical drift. Small droplets (50–150 μm) give maximum coverage of surfaces but larger droplets give better penetration of the canopy and deposition. Aerosol sprays are used for drift spraying against flying insects. Coarse aerosols and mists are applied to foliage at very low volume (VLV) or ultra low volume (ULV) (see below for more details) rates of application. Medium and coarse sprays are used when drift must be minimised. A fine spray is used when a compromise between reduced drift and good coverage is needed. There is a trend to reduce the volume of spray applied to crops for environmental and economic reasons. This can be achieved by reducing droplet size and, therefore, the volume of spray needed.

Table 24.1. Classification of sprays according to droplet size. (From Matthews, 1979.)

Median droplet diameter (μm)	Droplet size classification
less than 50	Aerosol
51–100	Mist
101–200	Fine spray
201–400	Medium spray
greater than 400	Coarse spray

Spray droplets are deposited onto plant surfaces by sedimentation or impaction. The relationships between droplet size, momentum and target size are the same as those discussed for airborne inoculum in Chapter 13. In general, droplets over about 150–200 μm sediment onto plant surfaces. The efficiency of sedimentation is largely determined by the terminal velocity of the droplet which, in turn, is influenced by droplet size. Terminal velocity increases with droplet size (Table 24.2). Impaction and turbulent diffusion are important in the deposition of droplets of less than about 100 μm. Even small droplets will impact if they are travelling at a sufficient velocity to resist change in direction of the airstream.

The choice of spray delivery system will depend on the stage of growth of the crop to be sprayed, weather conditions and water availability. High volume spraying delivering between 600 and 1,200 litres per hectare through a hydraulic sprayer such as a boom spray may be needed for adequate coverage on a maturing crop. When lower volumes can provide adequate coverage of the target plants, mist blowers or air blast machines can deliver 100–200 litres of spray per hectare. Mist blowers can take advantage of cross winds to assist in droplet distribution both in terms of wind carry and in getting better cover due to turbulence round individual leaves. In the absence of wind, their blasting effect displaces air and fills the space with air full of fungicidal droplets—a good way to cover leaves in an orchard situation. In Australia, the development of ultra low volume (ULV) formulations (where the active fungicide is dissolved in oil and applied directly without further dilution in water) has enabled aerial spraying to reduce volumes to 10–20 litres per hectare. This technique has not been very effective with fungicides so far, although success has been achieved in controlling Sigatoka disease of bananas.

Table 24.2. Terminal velocity and fall time of spheres with a specific gravity of 1 in still air. (From Matthews, 1979.)

Droplet diameter (μm)	Terminal velocity (m/s)	Time to fall 3 m
1	0.00003	28.1 h
10	0.003	16.9 min
20	0.012	4.2 min
50	0.075	40.5 s
100	0.279	10.9 s
200	0.721	4.2 s
500	2.139	1.7 s

Chemicals are also applied to growing plants in other ways if specialised treatments are required. Pruning cuts, stumps and wounds can be protected against pathogens by painting appropriate chemicals on the exposed surfaces. Pruning implements should also be treated between uses with chemicals that prevent the spread of disease propagules from one plant to another. Plant structures such as cuttings, tubers, rhizomes, corms and bulbs utilised in vegetative propagation, are often dipped in a chemical bath before planting out. Internal fungal infections in trees may be treated by injecting a fungicide into the woody tissues or by pouring the material into a hole bored into the tissues.

Finally, if combining chemicals in one spray application, it is important to check their **compatibility**. In other words, to determine their ability to mix without physical or chemical interactions that would lead to reduction in biological efficiency or increase in phytotoxicity. Information about compatibility may be given on a product's label. Otherwise, it should be available from the product's supplier or manufacturer.

24.5 Fungicides

Fungicides are chemicals used to control fungal diseases of plants. A wide range of chemicals have been used as fungicides so it is not surprising that they affect many different metabolic processes in fungal cells. The biological action of a fungicide is intimately related to its metabolism in the target organism and, in the case of chemicals that are translocated within the plant (systemic compounds), it may also be affected by metabolism in the host plant. Most fungicides are of low acute toxicity to mammals.

Fungicides are frequently classified as either protectant or systemic. **Protectant fungicides** protect plants or plant structures against infection at the sites where the chemical is applied. They usually inhibit or prevent development at several stages of the infection process and are generally described as broad spectrum fungicides because they are effective against a range of fungi. They have little or no capacity to penetrate host tissue and must be applied to the plant surface before infection occurs. They are also removed more easily during weathering because they are only on the surface of the plant. As the plant grows, new tissue is unprotected. Protectant fungicides, therefore, need to be applied repeatedly during the growing season to ensure protection from disease. Protectant fungicides are mainly inorganic compounds, although some organic compounds are also used.

The discovery of non-phytotoxic compounds which can be absorbed through plant surfaces and then translocated to other tissues where they are toxic to fungi constituted a major advance in chemical protection. These compounds, known as **systemic fungicides**, can control and eradicate established infections. They are less subject to the effects of weather than protectant fungicides because they penetrate host tissue. They are usually more specific than protectant fungicides in the fungi they control. Although systemic fungicides have many attributes of the 'ideal' fungicide, they frequently kill fungi by affecting only one step in a biosynthetic pathway. This characteristic, combined with intensive and inappropriate use, has encouraged some fungi to develop **resistance** (insensitivity or tolerance) to these fungicides relatively quickly. This effect has not been observed with the protectant fungicides although, in some cases, they have been in use for over 100 years.

Soon after systemic fungicides were released commercially in the late 1960s, it became obvious that some fungi that had previously been well controlled by the fungicides, were no longer controlled. The fungus was said to have developed resistance to the fungicide. Resistance to a fungicide in a pathogen population is the result of selection from the population, of individuals able to tolerate the effect of the fungicide. If the same fungicide or fungicides with similar effects on fungi are used repeatedly and exclusively, susceptible individuals are removed from the population while resistant individuals survive and multiply until they predominate in the population.

A number of strategies can be used to prevent or delay the development of resistance to fungicides. The key points of any management program are to prevent the build-up of resistant individuals in the population and to minimise selection pressure by not overusing fungicides with similar modes of action. The fungal population can also be reduced by non-chemical practices such as crop hygiene. Self-sown plants should be destroyed and disease-free seed or transplants used. Carry-over of the pathogen population from one planting to the next can be reduced or prevented by allowing as much distance or time as possible between successive plantings.

To minimise selection pressure by chemical overuse, the Avcare (formerly the Agricultural and Veterinary Chemicals Association) Fungicide Resistance Action Committee has classified all registered fungicides into ten groups based on the similarity of their chemical activity. These groups are designated by letters of the alphabet which appear on the product label.

Group A contains the **benzimidazole compounds** which are typically broad-spectrum systemic fungicides although they are ineffective against Oomycetes and Zygomycetes. Fungicides in this group interfere with nuclear division and other activities, such as the orientation of hyphal growth, that depend on processes involving microtubules. Benomyl has both protectant and eradicant properties against many pathogenic fungi coupled with good residual activity. It is not effective when applied to soil as it absorbs tightly to organic matter and soil colloids. Within plant tissues, benomyl is hydrolysed to carbendazim, the active fungitoxin at infection sites. A related compound, thiabendazole, which is also widely used in animals as an antihelminthic drug, is another broad-spectrum systemic fungicide. The thiourea-based compounds, thiophanate and thiophanate-methyl, which can be used on a wide range of crops, are also metabolised in treated plants to carbendazim.

Group B, the **dicarboximide fungicides** (iprodione, procymidone, vinclozolin), are primarily used to control some species of *Botrytis, Sclerotinia* and *Monilinia* in agricultural crops. Although translocation of the fungicide within plants can be demonstrated in the laboratory, these fungicides are generally considered to act as protectants in the field. Their mode of action is not clear. They inhibit germination of conidia and mycelial growth and, at some concentrations, cause hyphal cells to burst, extruding their contents. They are also known to disrupt mitosis and destroy cell membranes, as well as having other nonspecific toxic effects.

Currently, the largest and most important category of systemic fungicides are the **sterol biosynthesis inhibitors (SBIs)**. Their primary mechanism of action is the inhibition of the synthesis of sterols essential for proper membrane structure and function. This results in a strong inhibition of growth and cell death. Two categories of SBIs, distinguished on the basis of their primary site of action in the sterol biosynthesis pathway, contain compounds of agricultural or horticultural interest. The **sterol dimethylase inhibitors (DMIs), Group C** in the Avcare classification, include pyrimidines (fenarimol), imidazoles (imazalil, prochloraz), piperazines (triforine), triazoles (triadimefon, triadimenol, propiconazole, bitertanol, flutriafol, flusilazole, myclobutanil and penconazole) and pyridines (pyrifenox). These fungicides control a wide spectrum of pathogens in all the major groups except the Oomycetes. Fungicides in this group may affect the growth of higher plants by inhibiting the action of an enzyme involved in the synthesis of the plant growth regulator gibberellin. In fact, paclobutrazol which is marketed as a growth regulator is a triazole closely related structurally to some DMI fungicides. The second category of SBIs of agricultural and horticultural interest is the **morpholines** (tridemorph). They are particularly effective against powdery mildew diseases and comprise **Group E** of the Avcare classification. Another morpholine fungicide, dimethomorph, has recently been registered for downy mildew control in onions and cucurbits.

Two categories of **Group D** or **phenylamide fungicides**, the acylamines or acylalanines (metalaxyl, furalaxyl and benalaxyl) and the oxazolidinones (oxadixyl), are currently registered for use in Australia. These compounds act as systemic as well as protectant fungicides and are primarily active against fungi in the order Peronosporales (*Pythium, Phytophthora,* downy mildews and *Albugo*). Relative to other fungicides, they are very water soluble and are readily taken up by roots, green stems and leaves. However, they only move upwards in plants so foliar treatments will not control root infections by *Pythium* and *Phytophthora*. Group D fungicides selectively inhibit the synthesis of ribosomal RNA so they disrupt mycelial growth rather than spore germination.

Group F contains pyrazophos, an **organophosphorous compound** which has excellent fungicidal activity against various powdery mildew diseases of crops. It is taken up by roots and both prevents new infections and eradicates existing infections. It is oxidised by fungi to a fungitoxic phosphate analogue.

The selective fungitoxicity toward various pathogenic Basidiomycetes exhibited by **Group G** or **oxathiin compounds** (also known as carboxamides) has stimulated considerable interest. These compounds penetrate plant tissues well and can be used as seed, soil or foliage treatments. Oxycarboxin has achieved notable success in controlling rust diseases of vegetable crops and ornamental plants. Efficient systemic translocation of the active ingredient upwards towards the growing shoot system has promoted the use of carboxin in the control of seed-borne smut and bunt diseases of temperate cereals. Carboxin selectively inhibits the activity of the enzyme succinic dehydrogenase in the mitochondrial electron transport chain, although why this action should affect Basidiomycetes more than other fungi is not clearly understood.

Group H contains the **hydroxypyrimidine fungicides** such as the pyrimidinols which have primarily been developed for use against powdery mildews, dimethirimol on cereals and cucurbits and bupirimate on woody and ornamental plants. Hydroxypyrimidines may be exuded onto the surface of plants where they inhibit the formation of fungal appressoria and prevent infection of the plant.

Group Y consists of fungicides with a range of modes of action, including inorganic, carbamate, phosphonate, dithiocarbamate, phthalimide, chlorophenyl, quinone and hydroxyquinoline fungicides. Many of the **inorganic fungicides** are relatively insoluble so their effectiveness depends on the fungus dissolving sufficient toxicant from the compound to be killed. At the same time, there must not be enough soluble toxicant present to appreciably damage the host plant. The inorganic fungicides currently in use are mostly compounds of sulphur or copper, although in the past fungicides based on the metals mercury, zinc and cadmium have been used. Many mercury compounds are very efficient fungicides but their high mammalian toxicity severely limits their use. Mercury compounds pose an additional hazard because they accumulate in food chains. This is one of the reasons why the only remaining registered use for mercury fungicides in Australia is for treating sugar cane setts before planting.

Elemental sulphur has been one of the most effective substances in the control of powdery mildews and some seed-borne smut diseases although it is ineffective against soil-borne pathogens. It is relatively cheap, easy to apply, harmless to animals and has been used as numerous formulations such as ground, sublimed, precipitated and wettable sulphurs as well as lime sulphur (calcium polysulphide). Currently, wettable sulphur (finely ground sulphur with a wetting agent to ensure it mixes readily with water for spraying) is the only registered sulphur-based fungicide. Sulphur fungicides are thought to act by diverting electrons from the cytochrome electron transport system to reducing sulphur so that sites of ATP generation are by-passed. Toxicity is attributed to the lack of ATP and the depletion of energy-yielding substrates.

Bordeaux mixture (a variable suspension of copper sulphate, hydrated lime and water) has probably been the most widely used fungicide since its chance discovery in 1882. It is very effective against foliar pathogens, except powdery mildews and has a good reputation for staying on leaves. However, it can produce phytotoxic effects (scorching and russetting) on plants, especially during hot weather. More recently, copper oxychloride, cuprous oxide and copper hydroxide have been more widely used. These compounds have low phytotoxicity and cause little corrosion to spraying equipment. **Copper fungicides** have the added advantage of being effective against bacteria as well as fungi. The fungitoxic component of copper fungicides is cupric ions which accumulate in fungal cells where they are believed to damage cell membranes allowing leakage of metabolites from cells. They may also act at sites within cells, resulting in nonspecific denaturation of proteins and enzymes. There is some danger of copper fungicides reaching toxic levels in soils following frequent application over a period of time, as citrus growers in Florida have found to their detriment.