CHAPTER 11

AGROCHEMICALS

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

INTRODUCTION

- The available agricultural land area per person decreases, e.g., from 0.5 ha per person in 1950 to 0.25 hectare per person today.
- In 2050, only 0.15 hectare of arable land will be available for each person. This illustrates the challenge that agriculture faces.
- To feed the growing world population, the farms must produce more food on less land.

INTRODUCTION

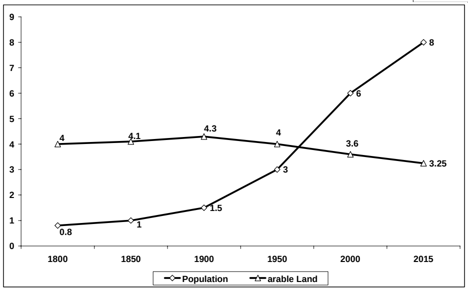


Figure 11-1. Change of the world population and the area of arable land
(population in billion, arable land in relative numbers)

INTRODUCTION

Mineral Fertilizers

- It is estimated that traditional farming without chemical and mechanical support can feed approximately 1.5 billion people. Today Earth has a population of 6 billion.
- That means something has happened in between that led to an enhanced productivity in agriculture.
- The first step to modern field management was the introduction of mineral fertilizers.
- Beginning with the 19th century the world population grew rapidly and a global famine was looming.

INTRODUCTION

Mineral Fertilizers

- Scientists worked hard to find solutions to improving crop yield.
- The first important discovery was that the organic carbon in plants comes from photosynthesis of the carbon dioxide of the air and not from organic matter contained in the soil.

$$n\,CO_2 + n\,H_2O \xrightarrow{light} \left(-\underset{H}{\overset{OH}{C}}-\right)_n + O_2 \qquad \text{Eq. 11.1}$$

INTRODUCTION

Mineral Fertilizers

- The soil supplies the inorganic minerals and water. Justus Liebig, an eminent German chemist and teacher, discovered that four elements are essential for plant growth: nitrogen, phosphorous, calcium and potassium.
- Later additional essential elements ("trace elements") were discovered. The growth rate of plants is limited by the component that is at minimum in the accessible soil layer.
- When one element is in short supply, adding large quantities of the others does not increase the yield. It is like a barrel in which the planks are of uneven height.
- When it is filled with water always the lowest plank determines the capacity, no matter how high the others are.

INTRODUCTION

Crop Protection

- To increase the yield solves only half of the problem. The crop must also be protected from diseases and pests. Without protection, 50 to 90 % of the harvest is destroyed by pests.
- The coffee industry of Sri Lanka collapsed completely due to an infestation by coffee rust (Hemileia vastatrix).
- 50 % of the annual cacao harvest was lost caused by cacao bugs (Miridae).
- The potato blight pest in Ireland caused a disastrous famine that forced millions of Irish to emigrate.

INTRODUCTION

Crop Protection

- The famine in India at the beginning of the 20th century was caused by a rice fungus that destroyed the rice harvest.
- Sulfur is the first documented material used in the war against infection.
- Arsenic was introduced as an insecticide and nicotine and strychnine in extracts from tobacco leaves and Strychnos seeds, respectively, were used as rodenticides.
- Today about 1000 chemical substances are produced as active ingredients that are used in some 10000 different products.

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Chemical Pest Control

- The basis of all plant growth is the photochemical conversion of carbon dioxide and water to carbohydrates with the assistance of chlorophyll as the photocatalyst.
- Therefore, H2O and CO2 are the most important agrochemicals.
- Agrochemicals in the common sense are fertilizers, pesticides and other chemicals that help to protect the quality of agricultural commodities.
- Even feed additives, such as vitamins, or veterinary medicines, such as antibiotics, are usually not considered agrochemicals.

Chemical Pest Control

- Pesticides are applied to control pests and plant diseases. Pesticides used in agriculture to protect living plants and freshly harvested crops are called “plant protection chemicals”.
- When pesticides are used to protect stored food, processed goods, public hygiene and dead objects, they are called “biocides”.
- Pesticides are subdivided in subgroups named after the pest they fight.

Chemical Pest Control

- Examples are insecticides, herbicides, fungicides and miscellaneous agrochemicals such as rodenticides, plant growth regulators, harvest aids and post harvest preservatives.
- Another method to classify pesticides is related to their main chemical structural elements or their mode of action.
- Examples are organochlorines, organophosphates, carbamates, pyrethroids etc.

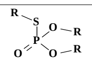
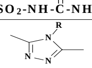
Chemical Pest Control

Table 11-1. Classification of pesticides according to target pest or function:

Class	*Target Pest*	*Remarks*
Insecticide	Insects	Kills insects or larvae
Fungicide	Fungi, mold	Controls plant diseases
Herbicide	Weeds, plants	Total herbicide kills all plants Selective herbicide controls weeds
Rodenticide	Rats, mice	Controls rodents
Plant growth regulator	None	Controls the size of plants, e.g. keep stems of cereals short
Acaricide	Mites	Controls mites, aphids etc.
Pheromone	Insects	Attracts insects into traps, control mating
Repellent	Insects	Repels insects without killing them
Nematicide	Nematodes, worms	Kills worms and similar parasites

Chemical Pest Control

Table 11-2. Classification of pesticides according to chemical structure

Name	*Structural element*
Carbamate	R-NH-C(=O)-O-R'
Dithiocarbamate	R-NH-C(=S)-S-R'
Organophosphate	
Organochlorine	DDT
Pyrethroids	pyrethrum
Sulfonylurea	R-SO_2-NH-C(=O)-NH-R'
Triazole	

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Chemical Pest Control Herbicides

- Herbicides are the most important pesticide class in terms of production volume and market value.
- In agriculture they are used to control weeds. Weeds are unwanted plants, such as grasses, sedges, and broadleaf plants.
- Herbicides have also non-agricultural uses to erase vegetation on streets, railroad tracks, sport fields and other public areas.
- Herbicides can be active through the leaves (foliage active) or by uptake from the soil (soil active) through the roots. They can be applied pre- or post-emergence of the target crop.

Chemical Pest Control Herbicides

- Non-selective or total herbicides kill all plants that are present during application. They are used on fields before emergence of the target crop to remove competing weeds.
- Other applications of total herbicides are selective spraying of the ground under the trees in fruit orchards and plantations (cacao, banana, etc.).
- Selective herbicides are active against certain species only, e.g. broadleaf weeds or perennial grasses. They can be applied also post-emergence of the crop plant.
- For example, some sulfonylurea (e.g. nicosulfuron) can be applied to maize fields during full growth to remove competing weeds without doing any harm to the target crop.

Chemical Pest Control Herbicides

- Modern herbicides are very potent and need only very low application rates (e.g. 50 g/ha) to be effective.
- Broadleaf selective herbicides are applied to turf or grass land to control leafy weeds and bushes. Quizalafop-P is an example of an herbicide that controls annual and perennial weeds in potatoes, sugar beet, oilseed rape, vegetables, etc.
- In industrialized countries many crops are harvested with automatic machines. Their use is impaired by leaves, weeds or broken plants.
- An example is the use of herbicides as defoliants in cotton. The leaves are removed by foliar application of paraquat or triazophos prior to mechanical picking of the cotton balls.

Chemical Pest Control Herbicides

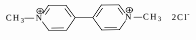
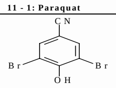
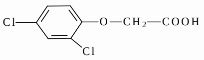
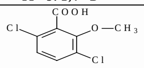
- Another example is the application of a growth inhibitor (e.g. paraquat) to keep the plants short. This prevents breaking of the stems during hail storms or heavy rain.
- A third example is the harvest of olives or nuts, during which the trees are shaken mechanically until the fruits fall off. They are then collected by hand or dedicated machines. Any weeds or bushes under the trees would interfere with this process and are removed by herbicides.
- The most important herbicide on the market is glyphosate. It was originally developed as a total herbicide with many uses in crop and non-crop areas.

Chemical Pest Control Herbicides

- It has many advantages: It is very effective; treated plants die nearly immediately.
- On the other hand, it has no long term effect.
- In addition, glyphosate has a very low toxicity for mammals and is rather benign to the environment.
- It is very popular in many countries and sold under different names, such as *RODEO, ROUNDUP,* or *TOUCHDOWN*. The only disadvantage is the high application rate of 2-5 kg/ha.

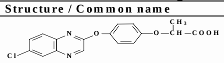
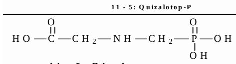
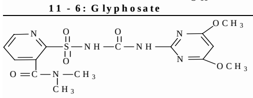
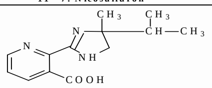
Chemical Pest Control Herbicides

Table 11-3. Foliage active herbicides (examples)

Structure / Common name	Mode of action	Typical uses
 11 - 1: Paraquat	Interrupts photosynthesis, non selective	Orchards, plant-ations, defoliant for cotton, aquatic weeds
 11 - 2: Bromoxynil	Inhibits photosynthetic electron transport, selective for certain annual broad leave weeds	Cereals, maize, sorghum, turf
 11 - 3: 2,4 - D	Effect cell membrane and RNA synthesis, selective for broad leave weeds; esters active through leaves	Cereals, maize, sorghum, rice
 11 - 4: Dicamba	Effect cell membrane and RNA synthesis, absorbed through leaves and soil; broad leaves, brushes	Cereals, pastures, range land

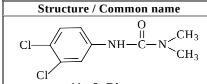
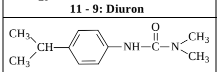
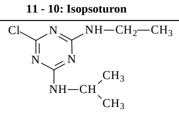
Chemical Pest Control Herbicides

Table 11-3. Foliage active herbicides (examples)

Structure / Common name	Mode of action	Typical uses
 11 - 5: Quizalotop-P	Inhibition of fatty acid synthesis; selective for grass weeds	Potatoes, soy beans, cotton, flax
 11 - 6: Glyphosate	Inhibits amino acid synthesis; non-selective, fast acting herbicides	Used as general weed control and weed control in transgenic maize
 11 - 7: Nicosulfuron	Absorbed through leaves and roots; selective control of some annual grass weeds and broad leaves	Selective control of broadleaf weeds in maize
 11 - 8: Imazapyr	Amino acid synthesis inhibitor; Non-selective	Non-crop areas, railroad tracks, plantations

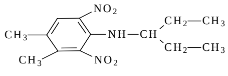
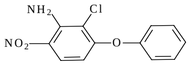
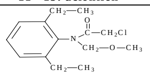
Chemical Pest Control Herbicides

Table 11-4. Soil active herbicides (examples)

Structure / Common name	Mode of action	Typical uses
 11 - 9: Diuron	Inhibits photosynthesis, absorbed mainly by the roots	Total control of weeds and mosses on non-crop land and under fruit trees
 11 - 10: Isopsoturon	Inhibits photosynthesis	Control of annual weeds in winter wheat and barley, rye
 11 - 11: Atrazine	Inhibits photosynthesis	Control of annual weeds in maize, sugar cane, pineapples, nuts and non-crop areas

Chemical Pest Control Herbicides

Table 11-4. Soil active herbicides (examples)

Structure / Common name	Mode of action	Typical uses
 11 - 12: Pendimethalin	Inhibits root growth, must be applied before emergence	Control of annual weeds In cereals, onions, soy beans, potatoes, cotton
 11 - 13: aclonifen	Inhibits carotenoid biosynthesis	Pre-emergence control of weeds in winter wheat, potatoes, etc.
 11 - 14: Alachlor	Inhibits protein synthesis and root elongation	Pre-emergence-control of annual weeds in cotton, brassicas, peanuts, soy beans, etc.

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Chemical Pest Control Insecticides

- Insecticides are the pesticides most commonly known by the public.
- In agriculture, insecticides are used widely to control insects in fruits, vegetables, rice, and other cereals.
- Other application areas are on farm animals and animal housing and to control insects that are vectors of diseases. Mosquitoes (for malaria) and tsetse flies (for the sleeping sickness) are just two examples.
- Control of these insects is a never ending task, especially in hot and humid countries.

Chemical Pest Control Insecticides

- Insects have been a problem in all times. The first insecticides were plant extracts. Tobacco and garlic extracts were and still are particularly popular.
- Indeed, nicotine has some insecticidal properties and is still produced today for this purpose.
- Insecticides may act on direct contact with immediate effect or via the stomach of the insect with delayed efficacy.
- They can be deposited on surfaces or can be incorporated into the plant (systemic effect), killing the insects only when they feed on the plant material.

Chemical Pest Control Insecticides

- The first synthetic insecticides with demonstrated efficacy were polychlorinated compounds, with DDT as the best known example.
- DDT had many advantages such as low price, high efficacy, long term effects, relative low toxicity to mammals and man.
- Unfortunately, as most organochlorines it is persistent in the environment. This has led to soil / water contamination.
- In addition, it accumulates in fat *via* the food chain. Therefore DDT and most other polychlorinated organic compounds were replaced by non-accumulating molecules for agricultural use.

Chemical Pest Control Insecticides

- Today DDT is still used in malaria areas as part of the WHO malaria eradication program.
- DDT has been phased out in most areas as it is considered highly toxic to human as well as wildlife population especially those animals existing higher up in the food chain.
- Another important class of insecticides is the organophosphates, with chlorpyriphos and parathion as typical examples.
- Organophosphates were also discovered in the 1940s. They are less persistent in the environment and food chain, but they are often toxic to humans and to non-target species.

Chemical Pest Control
Insecticides

- They were widely used especially for large area spraying, but also as public area or household insecticides.
- Carbamate insecticides were developed in the 1960s. They are efficacious and non-persistent. Carbofuran, for example, is degraded in soil microbiologically mainly to carbon dioxide.
- However, most carbamates, and especially carbofuran, are toxic to fish, birds, honey bees and other non-target species.
- Today there is a strong tendency to replace organophosphates and carbamates with less toxic alternatives.

Chemical Pest Control
Insecticides

- Pyrethrins (also called Pyrethrum) are very active natural insecticides that have been used since ancient times. Pyrethrins are extracted from chrysantemum flowers using methanol or supercritical carbon dioxide as the solvent.
- Pyrethrin I is a mixture of three esters of chrysanthemic acid, pyrethrin II of the corresponding pyrethrin acids. Pyrethrins bind to the sodium channels of the organisms prolonging their opening and thereby causing death.
- They paralyze the insects on contact nearly immediately ("knock down effect"). Death occurs later.

Chemical Pest Control
Insecticides

- They are used to control a wide range of insects and mites in public health, stored products, fruit production, and on farm and domestic animals.
- Commercial products contain usually synergists, e.g. piperonyl butoxide. Their purpose is to inhibit detoxification thereby increasing the overall effect.
- Pyrethrins are not very toxic to non-target species except aquatic species and bees. The main disadvantage is their sensitivity to sun light, alkali, clay and heat.
- From the chemical point of view, pyrethrins are interesting molecules, because they contain a cyclopropane ring and other structural features that can lead to isomers or enantiomers. Therefore, it is difficult to synthesize the molecules in the laboratory.

Chemical Pest Control
Insecticides

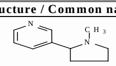
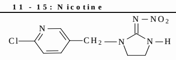
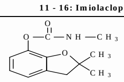
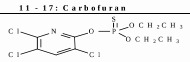
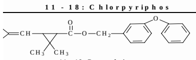
- Synthetic compounds with pyrethrin like properties are called pyrethroids. A well-known example is permethrin.
- It still contains the cyclopropylcarboxylic ester group, but has otherwise a simpler structure and is easier to synthesize than the natural substance.
- Fenvalerate still contains the ester group, but no longer a cyclopropyl moiety. In etofenprox even the ester group is missing, but it still has a similar mode of action.
- It is a non-ester pyrethroid with contact and stomach action and rather low toxicity for mammals, which makes it particularly useful for agricultural application.

Chemical Pest Control
Insecticides

- Neonicotinoids is another class of modern insecticides with high efficacy against insects and low toxicity for humans.
- Imidacloprid and dineotefuran are two examples. They affect selectively the central nervous system of insects.
- They show contact and systemic activity and are readily absorbed by plants, which are then protected against insect attack.

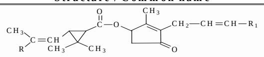
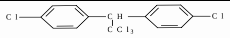
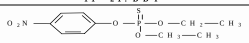
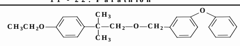
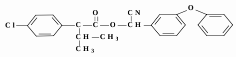
Chemical Pest Control
Insecticides

Table 11-5. Insecticides (examples)

Structure / Common name	Mode of action	Typical uses
 11 - 15: Nicotine	Predominantly respiratory action	Tobacco extracts against sucking insects
 11 - 16: Imiolacloprid	Systemic uptake by plant and further distributed through the leaves, acts through central nervous system of insects	Control of sucking insects, termites, biting insects
 11 - 17: Carbofuran	Cholinesterase inhibitor, systemic action	Control of soil-dwelling and foliar feeding insects and nematodes in vegetables, nuts, cotton
 11 - 18: Chlorpyriphos	Cholinesterase inhibitor, non-systemic contact, stomach and respiratory action	Control of soil-dwelling and foliar feeding insecticides in fruits and vegetables, also non-crop uses
 11 - 19: Permethrin	Contact and stomach action	Control of a broad range of insects in agriculture, public areas and storage facilities

Chemical Pest Control Insecticides

Table 11-5. Insecticides (examples)

Structure / Common name	Mode of action	Typical uses
 R = $CH_3ORCOOCH_3$ R_1 = - $CH=CH_2OR$ CH_3 **11 - 20: Pyrethrum**	Opening of sodium channels, leading to paralysis and later death, non-systemic, contact only action	Control of insects and spider mites
 **11 - 21: DDT**	Nerve poison, affecting sodium balance of nerve membranes, non-systemic contact and stomach action	Mosquito control for malaria eradication; for crop use replaced by less persistent products
 **11 - 22: Parathion**	Cholinesterase inhibitor, non-systemic contact, stomach and respiratory action	Control of sucking and chewing insects and mites in field crops, fruits and vegetables
 **11 - 23: Etofenprox**	Contact and stomach action	Control of insects in rice fields, vegetables, fruit, oilseed rape, public health pests and on animals
 **11 - 24: Fenvalerale**	Non-systemic insecticide and acaricide with contact and stomach action	Control of biting and boring insects in crops and flying and crawling insects in public areas

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Chemical Pest Control Fungicides

- Fungi and similar microorganisms cause severe damage to fruits, cereals, vegetables, and other crops both before and after harvest.
- The effects are seen as mildew, decay, rotting, scorch, blight, rust, and many other plant diseases that reduce the value of agricultural products.
- Therefore, fungicides are probably the pesticides with the highest economic value to the farmers. This is particularly true in humid climatic zones.
- The first fungicides that were used in agriculture were inorganic compounds of copper, mercury and sulfur.

Chemical Pest Control Fungicides

- Copper is applied as oxychloride, sulfate, hydroxide or octanoic acid salt. Cu^{++} ions kill the spore cells. They are sprayed or dusted onto leaves, where they have a protective action when applied before the fungal spores begin to germinate.
- Sulfur reacts with thiol groups in the organisms and interrupts respiration of the organism.
- Copper and sulfur are non-selective and are used on many crops, like fruits, vines, vegetables, flowers.

Chemical Pest Control Fungicides

- Their specific activity is low, however, and frequent applications and high rates of up to 6 kg/ha are required to achieve the desired protection.
- Copper compounds and sulfur are still used today on a large scale. They are allowed in “organic” farming with the justification that copper is an essential element that occurs naturally in the environment.
- Unfortunately, this assumption overlooks that the high rate and frequent applications lead to much higher copper concentrations in the soil than are present naturally.
- Since the element copper cannot degrade, this “organic” farming practice will lead to poisoning of the agricultural soil.

Chemical Pest Control Fungicides

- Dithiocarbamates were the next step of fungicide development. They are organic compounds containing several sulfur atoms and have a similar mode of action as sulfur.
- They also often contain other inorganic atoms, such as Mn, Zn, Cu. Examples are mancozeb, maneb, thiram or ziram. Folpet is a phthalimide containing sulfur.
- It is often applied in combination with other fungicides. Organic sulfur compounds also need high application rates in the kg/ha range.
- Although they are not very toxic themselves, there is some concern about the potential for formation of the possible metabolite ethylene thiourea (ETU), which is a suspected human carcinogen.

Chemical Pest Control Fungicides

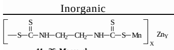
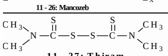
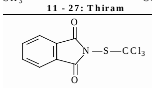
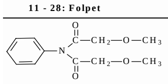
- Later other compounds were discovered that have higher efficacy or selectivity against microorganisms.
- Imazalil inhibits the biosynthesis of ergosterol with systemic and protective action. It is used on vegetables, flowers and fruits and to protect seeds and crops during storage.
- Quinoxyfen is an example of a newly developed fungicide.
- It inhibits the cell growth and offers long-term protection against powdery mildew in cereals, sugar beets, vegetables etc. with application rates of 50 to 150 g/ha.

Chemical Pest Control Fungicides

- This shows that it is nearly 50 to 100 times more active than the traditional sulfur and copper products.
- Strobilurins are derived from natural origin. They have become important modern fungicides. Azoxystrobin is an economically successful example.
- It inhibits mitochondrial respiration by blocking electron transfer between cytochromes. It inhibits spore germination and mycelical growth and is active against many pathogenic microorganisms, even those resistant to other fungicides.
- The toxicity for humans is low and no adverse effects on the environment have been observed.

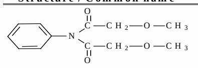
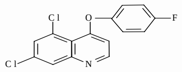
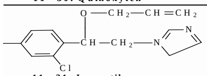
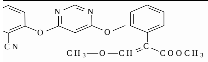
Chemical Pest Control Fungicides

Table 11-6. Fungicides (examples)

Structure / Common name	Mode of action	Typical uses
Copper salts Inorganic	Prevents spore germination; non-systemic	control of powdery mildew, blights and rust
Sulfur Inorganic	Inhibits respiration; non-systemic	Control of mildew, shot-hole, mites
 11 - 26: Mancozeb	Inhibits respiration, non-specific with protective action	Control of many fungal diseases in field crops, fruit, flowers
 11 - 27: Thiram	Contact fungicide with protective action	Control of mildew, rust, scab etc. on fruits and seeds
 11 - 28: Folpet	Inhibits respiration, foliar application with protective action	Control of mildew, leaf spot, scab, rot etc. in fruit, olives potatoes etc.
 11 - 29: Metalaxyl	Inhibits protein synthesis in fungi, systemic with protective action	Control of air- and soil-borne diseases on crops

Chemical Pest Control
Fungicides

Table 11-6. Fungicides (examples)

Structure / Common name	Mode of action	Typical uses
 11 - 29: Metalaxyl	Inhibits protein synthesis in fungi, systemic with protective action	Control of air- and soil-borne diseases on crops
 11 - 30: Quinoxyfen	Growth signal inhibitor, protectant, not an eradicant	Control of powdery mildew in many crops
 11 - 31: Imazotil	Inhibits ergosterol biosynthesis, systemic with protective action	Control of wide range of fungal diseases
 11 - 32: Azoxyshobin	Inhibits mitochondrial respiration by blocking electron transfer between cytochromes, systemic with protective action	Control of wide range of pathogens on cereals, vines, potato, rice, fruits, nuts etc.

CHAPTER 11
OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Chemical Pest Control
Miscellaneous Compounds

- Rodenticides are used to control rats and mice in fields, in storage areas and in household environments. Rodents not only destroy harvested products, they are also vectors for contagious diseases.
- Most rodenticides belong to the coumarin group and act as anticoagulants.
- Bromadiolone is an example of a relative selective rodenticide that is highly toxic to rodents, but less toxic to domestic animals such as dogs and cats.
- Nematodes (“worms”) attack fruits, vegetable or plant roots thereby causing losses to the crop during growth and in storage areas.

Chemical Pest Control Miscellaneous Compounds

- Fumigants like 1,3-dichloropropene or methyl bromide control nematodes in soil or pests in mills, warehouses, grain elevators, ships and in stored products in general.
- Because of their high toxicity and environmental risk these two fumigants cannot be used in the field or on animals.
- Repellents are sometimes added to pesticide formulations to keep non-target species away from sprayed areas without killing them. Anthrachinone, for instance, repels birds.
- It is added to seeds to protect the seeds from being eaten and the birds themselves from being poisoned by toxic treated seeds.

Chemical Pest Control Miscellaneous Compounds

- Some pyrethroids have a repelling effect on honey bees, which is very useful.
- Insect repellents are also used by humans. The most famous active substance used in insect repellents is DEET.
- Recently a new substance came on the market with the trade name BAYREPEL™ that is claimed to be superior to DEET.
- Another topic is the protection of perishable fruits, vegetables, potted plants, and cut flowers.

Chemical Pest Control Miscellaneous Compounds

- Many tropical fruits and vegetables are chill sensitive and can not be transported or stored under low-temperature conditions. Other means for delaying deterioration are therefore needed.
- Traditionally, ethylene induced ripening was the post harvest fruit management tool. Ethylene occurs naturally in plants.
- It starts and coordinates ripening processes (e.g. softening, color change, conversion of starch to sugars, loss of acidity, etc.) in fruits and vegetables.
- This has been utilized commercially to keep fruits edible after transportation and storage. The fruits are harvested well before ripening and are transported “green“ to the far away destination and stored.

Chemical Pest Control Miscellaneous Compounds

- A few days before marketing they are exposed to an ethylene atmosphere. The ethylene facilitates a rapid ripening process, leading to products of high optical quality.
- The quality of taste, however, is compromised, since not all sugar, vitamin and aroma components were developed by the time of harvest and are not improved by the ethylene exposure process.
- Very recently, the opposite of the ethylene techniques has been developed to keep fruits fresh during transportation.
- Fruits are harvested after natural ripening and are protected from deterioration by compounds that suppress the natural ethylene response of the crop.

Chemical Pest Control Miscellaneous Compounds

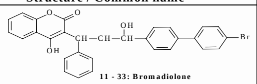
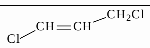
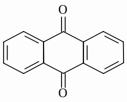
- Such a compound is 1-methylcyclopropene (1-MCP). It extends the post harvest shelf life and quality of numerous fruits and vegetables, in particular, apple, tomato, and avocado fruits.
- In apples, 1-MCP maintains critical taste components including firmness (crunchiness), sugar content (sweetness), and acidity (tartness).
- It is also used to extend the lifetime of cut flowers and potted ornamental plants. 1-MCP acts by attaching to a site (receptor) in fruit tissues that normally binds to ethylene.
- Chemically 1-MCP is very interesting, since it is a highly unstable cyclopropene compound.

Chemical Pest Control Miscellaneous Compounds

- A few years ago scientists thought about cyclopropenes as scientific curiosities without practical value.
- The 1-MCP proves that they were wrong. Being unstable and a gas as a neat substance, it is supplied commercially adsorbed to solid materials in powder form to make handling easier.
- When the powder is mixed with a specified amount of water, the 1-MCP gas is released to the gas phase where it interacts with the plants before it decomposes.

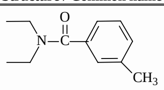
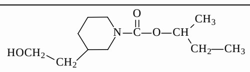
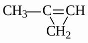
Chemical Pest Control
Miscellaneous Compounds

Table 11.7. Other pesticides and repellents (examples)

Structure / Common name	Mode of action	Typical uses
 11 - 33: Bromadiolone	Anticoagulant, rodenticide	Control of rats and mice in storage areas, households, industrial areas
 11 - 34: (E) - 1.3 dichloropropene	Soil fumigant	Controls nematodes in fruits, nuts, berries
CH_3Br 11 - 35: Methyl bromide	Multi purpose fumigant	Controls a wide variety of pests in glass houses and storage areas
 11 - 36: Anthrachinone	Induces retching in birds	Used as seed treatment for cereals

Chemical Pest Control
Miscellaneous Compounds

Table 11.7. Other pesticides and repellents (examples)

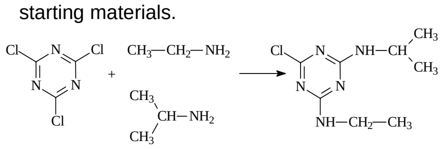
Structure / Common name	Mode of action	Typical uses
 11 - 37: DEET		Insect repellent for human use
 11 - 38: Bayrepel		Insect repellent for human use
$CH_2{=}CH_2$ 11 - 39: Ethylene	Induction of ripening	Induction of ripening of fruits and vegetables
 11 - 40: 1-MCP	Blocks ethylene receptor sites	Delay of ripening, conservation of fruits, flowers etc.

CHAPTER 11
OBJECTIVES

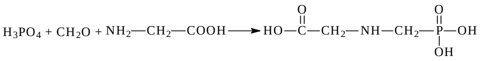
- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Chemical Pest Control
Chemical Synthesis of Pesticides

- The synthesis routes of pesticides are very divers due to the complex nature of the organic molecules.
- For example, atrazine (eq. 11.2) and glyphosate (eq. 11.3) that are produced from readily available, inexpensive starting materials.



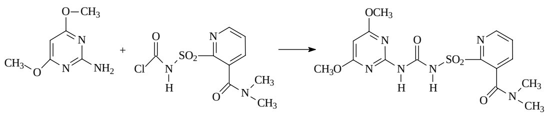
Eq. 11.2



Eq. 11.3

Chemical Pest Control
Chemical Synthesis of Pesticides

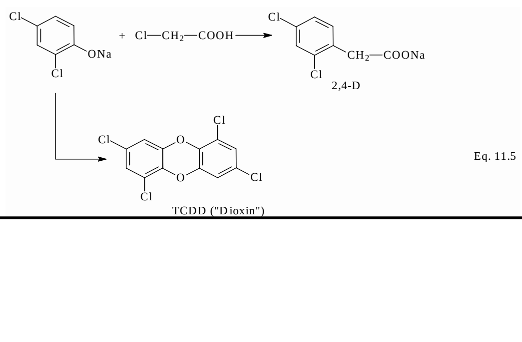
- Modern pesticides are applied in much smaller amounts and the manufacturing cost is no longer the main factor.
- The sulfonylureas or pyrethroids, for instance, are manufactured from rather complex starting materials that themselves need several steps in the synthesis. This is illustrated by the example of nicosulfuron (eq. 11.4)



Eq. 11.4

Chemical Pest Control
Chemical Synthesis of Pesticides

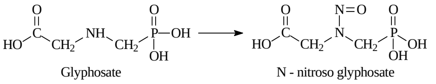
- The best known example is the formation of dioxins during the production of 2,4-D (eq.11.5) and other similar compounds that use dichlorophenol or trichlorophenol as the starting materials.
- Many different compounds belong to the dioxin group, depending on the number and on the substitution pattern of the chlorine atoms (e.g. TCDD=tetrachlorodibenzo-1,4-dioxins;HCDD=Hexachlorodibenzo-1,4-dioxins).



Eq. 11.5

Chemical Pest Control
Chemical Synthesis of Pesticides

- Nitrosamines are another class of highly toxic carcinogenic compounds that are of concern in pesticide chemistry.
- They are formed in nature, for instance in rotten food or even during barbecuing of nitrite containing meat, by nitrosylation of amino acids.
- Pesticides of the amino acid class, like glyphosate, are at risk in containuining nitrosamines as impurities (eq. 11.6).
- This potential is recognized and the main manufacturers have optimized their synthesis to avoid side reactions that may lead to nitrosamines.



Eq. 11.6

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Formulated Products

- The active substances are not used as neat chemicals. They are sold as formulated products.
- Products for small scale use in house or garden are often ready-to-use formulas. That means they come in diluted form, often in spray cans, and can be used as they are.
- For large scale use this is not economical, since a large part of the spray mix is simply water, needed to dilute the active substance.
- Formulated pesticide products contain active and inert ingredients.

Formulated Products

- Active ingredients kill or control the pest(s), while inert ingredients are designed to preserve the active ingredients, make them easier to apply, or improve their activity.
- Surfactants act as wetting agents. They help to disperse the droplets of the applied product on the hydrophobic surface of the leaves of plants and enhance the uptake through the membranes of the cells.
- Solvents are used to dissolve the active ingredient and the other components. The most common solvents are water or oil, depending on the solubility characteristics of the substances.

Formulated Products

- Oils (e.g. diesel oil) often enhance the product properties, since they facilitate the uptake through leaves or bark.
- Drift retardants are polymers, such as polyacrylamides, that reduce the apparent vapor pressure of volatile mixtures by adsorption and help to aggregate very fine droplets formed during the spraying process.
- Foaming or anti-foaming agents are added to facilitate or prevent foam formation during mixing of the product in the sprayers, depending on the properties of the products.
- The risk of accidental ingestion of toxic products can be minimized by addition of emetic (vomiting causing) agents.

Formulated Products

- Pesticide products for large scale use are usually concentrates that must be diluted with water.
- The water properties, like hardness, salt content, pH or temperature can vary widely from region to region and formulations must be designed to cope with such differences.
- Incomplete mixing or precipitation during mixing in the spray tanks would render the uniform application impossible and pose a risk to the applicator and the treated crop.

Formulated Products

- There are many different formulations on the market. The following are the most common types:
  - SC = soluble concentrates are powders or liquids containing components that are completely soluble in water.
  - EC = emulsifiable concentrates are organic solutions (usually petroleum oil fractions) of the active ingredient.
  - WP = wettable powders containing compounds that are insoluble in water and organic solvents. The solid material is finely ground and coated with wetting and dispersing agents. They form suspensions when mixed with water.
  - DG = dispersible granules, which are small beads that disperse in water upon mixing. They are often used when highly water soluble mobile substance should be retained in the soil for an extended time.

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Biological Pest Control

- There were various attempts in history to control pests biologically. Often species (predators) were introduced that feed on the organism that needed control.
- A very simple and extremely successful example is the use of sheep to control grass and weeds.
- Modern biological pest control uses more refined techniques.
- Pheromones are sexual attractants that affect species very selectively. They are used to lure insects into traps, where they can be killed, either with a contact insecticide or mechanically, for instance, with glue.

Biological Pest Control

- Codlemone may serve as an example of how pheromones work. Chemically codlemone is a dodecanedienol, a substance with a low, but measurable vapour pressure.
- It is the sex pheromone of the codling moth and was isolated from virgin females. Since it has a rather simple structure, it can be produced easily by chemical synthesis.
- An example of a “living pesticide” is Bacillus Thuringiensis (Bt). It is a naturally occuring bacteria species with insecticidal properties.

Biological Pest Control

- It lives in insect rich environments, for instance in soil or food storage areas. The strains with the highest potency against a pest are selected from these natural populations.
- They are then used to produce large quantities of Bt in controlled fermentation. The insecticidal endotoxins and spores are harvested as water dispersible concentrates.
- The endotoxins are protein like toxins that are produced inside the bacteria cells and are released after the cell walls are disrupted.
- After being ingested by the insects or larvae the endotoxins are hydrolyzed to smaller fragments. The fragments bind very specifically to selected receptor sites.

Biological Pest Control

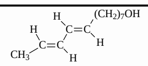
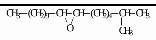
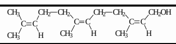
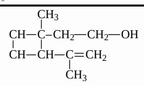
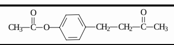
- Bt is active against moths, butterflies, potato beetles and other related species. Bacillus thuringiensis is not infectious or toxic to humans and can be applied on food crops until the last day before harvest.
- Its practical use, however, is limited by its short persistence in the field which makes frequent applications necessary.
- Another disadvantage is that it is efficacious only after the crop is infested and has already been damaged to a certain extent.
- Where this is acceptable, for instance, in forests, Bt is an interesting alternative to chemical pesticides. Other biological systems, such as nematodes, predatory mites, baculovirus, can be used to control pests.

Biological Pest Control

- A famous example is the gene that is responsible for the production of endoxines in Bacillus thuringiensis.
- When the Bt genes are transferred into crop plants, the plants themselves exhibit insecticidal properties and become resistant against insects.
- Bt genes have been introduced into potatoes, cotton, maize and other plants. The action mechanism is similar as described for Bt itself.

Biological Pest Control

Table 11- 10. Pheromones used for insect control (examples)

No.	Common name	Chemical name	Target pest
1	Codlemone		Codling moth, hickory shuck worm
2	Disparlure		Gypsy moth
3	Farnesol		Spider mite
4	Grandlure		Boll weevil
5	Melon fly attractant		Melon fly

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides

Testing Requirements for New Pesticides
General Information and Physical Chemical Properties

- Before a pesticide can be sold, the supplier must ask the competent authorities of the respective countries for a permit, the "Marketing Authorization".
- The applicant must submit a dossier containing all information about the new substance that is needed to make a thorough risk/benefit analysis.
- The studies are conducted under stringent quality control following the OECD guideline of GLP (Good Laboratory Practice).
- GLP is an internationally accepted quality standard. It assures that the personnel are qualified, that the methods are validated and that the instruments are properly calibrated.

Testing Requirements for New Pesticides
General Information and Physical Chemical Properties

- The first part of a dossier contains basic information about the active substance and the applicant. Here are some examples: Name, structure and route of synthesis of the substance must be described.
- Appearance, melting and boiling points, density, spectra and solubility data serve to establish unambiguously the identity of the substance. The vapour pressure value is an indication of the volatility of the substance.
- If a substance is volatile it may evaporate and be transported through the air and inhaled by people, thereby increasing the risk to bystanders or non-target plants.
- Flammability and explosivity are also safety parameters that show whether a substance may be dangerous when shipped or stored.

Testing Requirements for New Pesticides
General Information and Physical Chemical Properties

Table 11.11. Examples of physical and chemical tests required for the registration of new pesticides

No.	Description of test	Purpose of test / remarks
1	Appearance (physical state, color, odor)	Identification
2	Melting point, boiling point, density	Identification, information
3	Vapor pressure	Risk for evaporation
4	Flammability, explosivity, corrosivity, oxidative properties	Hazard during transport and storage
5	Surface tension	Risk to surface water
6	Solubility in water (at 3 pH values) and organic solvents	General information, risk for leaching
7	Spectra (UV/VIS, IR, NMR, Mass)	Identification
8	Partition coefficient n-octanol / water	Risk for bioaccumulation

Testing Requirements for New Pesticides

General Information and Physical Chemical Properties

Table 11.11. Examples of physical and chemical tests required for the registration of new pesticides

No.	***Description of test***	***Purpose of test / remarks***
9	Hydrolysis and photolysis in water	Risk for persistence
10	Stability and photochemical degradation in air	Risk for air pollution, persistence and ozone depletion
11	Stability upon storage / shelf life	Quality of product
12	Analytical methods for purity and impurities in active substance and products	Quality and risk of toxic impurities
13	Analysis of 5 production batches	Reproducibility of process
14	Analytical methods for residues in food	Consumer safety
15	Analytical methods for residues in soil, water, air	Environmental monitoring

Testing Requirements for New Pesticides

General Information and Physical Chemical Properties

- The partition coefficient is a very important property to assess possible accumulation of a substance in the food chain. It is defined as the ratio of the solubilities of a substance in n-octanol and water.

Log (Kow) = Log [(concentration in octanol) / concentration in water)]

- A high Log (Kow) means that the substance dissolves better in octanol than in water (e.g. if Log Kow = 6, a million times).
- In practical terms this means that there is a risk that the substance accumulates in fat.

Testing Requirements for New Pesticides

General Information and Physical Chemical Properties

- On the other hand, a Log (Kow) < -2 shows that the substance is a hundred times better soluble in water than in octanol. This usually is a warning sign that the substance has a tendency to leach into ground water.
- Hydrolysis and photolysis experiments allow conclusions on how stable a substance is and whether it may have a tendency to persist in the environment.
- Here the rate constants and the half live of a substance in water are measured at different pH values and under irradiation with simulated sunlight.

Testing Requirements for New Pesticides

General Information and Physical Chemical Properties

- The hydrolysis is tested at four different pH values: pH 4, pH 7, and pH 9 simulate the natural situation in soil and water, while a pH 1.2 is used to simulate the acidity in the stomach and gives some indication about hydrolysis after accidental oral ingestion.
- Organochlorines are often stable against hydrolysis. Other compounds undergo complicated reactions leading to a variety of products that are difficult to analyze.
- Methyl bromide is a compound that undergoes hydrolysis resulting in the formation of methanol and hydrogen bromide. (eq. 11.7)

$$CH_3Br + H_2O \xrightarrow{\text{pH 4}} CH_3OH + HBr \qquad \text{Eq. 11.7}$$

Testing Requirements for New Pesticides Toxicity

- The toxicity of pesticides (and all other new chemical products) must be tested in/on animal models before a product can be sold on the market. Toxicity tests have different levels of complexity and different objectives.
- Acute toxicity studies are usually carried out on rats and last up to seven days. Their purpose is to determine how toxic a substance is after accidental exposure.
- Tests are conducted with oral uptake and inhalation, but also with exposure to the skin and eye.
- The final result (end point) of the acute oral tests used to be the LD-50 value, the dose after which 50 % of the animals die.

Testing Requirements for New Pesticides Toxicity

- It is now being replaced by the acute reference dose (ARfD). This is the highest dose that is still safe for a human after a single exposure to the pesticide.
- It is calculated from the highest dose that caused no harm in the acute animal studies (NOAEL = no observed adverse effect level) and a safety factor (F).
- The safety factor is usually 100 and it accounts for the uncertainty that is associated with the comparison of the toxic responses in animal and humans.

ARfD = NOAEL (in acute studies) x safety factor (F)

Testing Requirements for New Pesticides Toxicity

- Short term toxicity studies simulate the exposure of workers or farmers to the products they use on a regular basis. They are performed with rats and dogs and last 1 to 6 months.
- Chronic and carcinogenicity studies last up to 2 years and simulate the long term exposure of consumers to small concentrations of pesticides in food. Rats, mice and dogs are used as animal models.
- The final result is the acceptable daily intake (ADI), the highest exposure level that is still safe for humans.

ADI = NOAEL (in chronic studies) * safety factor (F')

Testing Requirements for New Pesticides Toxicity

Table 11-12. Examples of toxicological tests required for the registration of a new pesticide

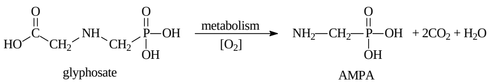
No.	Description of test	Animal Model	Purpose/remarks
1	Acute oral and inhalation toxicity	Rat	Accidental ingestion or inhalation
2	Acute dermal toxicity	Rat	Accidental exposure or skin
3	Skin and eye irritation, sensitization	Rat, rabbit In-vitro	Damage of eye or skin after accidental exposure
4	Short term toxicity up to 6 months	Rat, dog	Risk after multiple exposure (workers)
5	Long term toxicity and carcinogenicity up to 2 years	Rat, dog, mouse	Risk upon lifetime exposure (consumer via food)
6	Reproductive toxicity	Rat, rabbit	Risk for fertility and exposure during pregnancy
7	Neuro-toxicity, endocrine disruption	Rat, hen	Risk to nerve and hormone systems
8	ADME (Adsorption, distribution, metabolism and excretion studies)	Rat, goat, hen	Assessment of fate in the body and risk of transfer to milk or egg

Testing Requirements for New Pesticides Residues in Food

- Food safety is a key issue in modern society, since we are exposed to food from birth to death. Plant protection products are often used on food crops, biocides in food factories or animal housing.
- Therefore tests are required to determine the risk of pesticide residues in the raw agricultural commodity (RAC) and the processed food products.
- The first step is to identify the critical crops and the compounds for which residue studies must be conducted.
- The breakdown and reaction products and metabolites in treated plants and products are often identified after treatment with a C-14 labeled test substance in "plant metabolism" studies.

Testing Requirements for New Pesticides
Residues in Food

- The objective is to determine the fate of the parent substance and its metabolites in the crop plants and their processing products.
- From the results of the studies, the relevant residues are defined ("Residue Definition").
- For example, in plants glyphosate is converted to its main metabolite AMPA (= aminomethylphospohonic acid), which was also studied as part of the residue assessment.



Eq. 11.8

Testing Requirements for New Pesticides
Residues in Food

- After the significant residues are identified, field studies are designed to determine experimentally the level of residues in crops.
- Field trials are required in typical growth areas and in different climate zones. The program must be repeated in a second year to account for climatic fluctuations.
- Samples of the crop and the processed food are collected at various intervals after application of the pesticide and at the normal harvest day.
- They are deep-frozen to < -20 °C to avoid degradation of the residues and sent to the analytical laboratory, where they are analyzed for residues of all compounds included in the residue definition.

Testing Requirements for New Pesticides
Human Safety Risk Assessment

- Risk, in its scientific, meaning, has two components, namely hazard and exposure.
- To swim in an ocean is hazardous, but people living inland are never exposed to the swimming in the ocean. This means that their personal risk of being harmed by the ocean is very small.

Risk = hazard x exposure

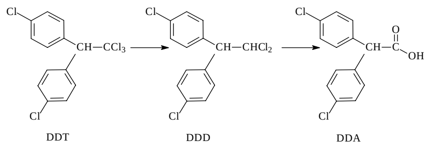
- The hazard of pesticides comes from their toxicity, exposure from their use or from residues in food.

Testing Requirements for New Pesticides
Environmental Fate and Environmental Toxicology

- All pesticides that can come into contact with the environment are subject to a risk assessment.
- The basis for this risk assessment is provided by data from environmental fate and environmental toxicity studies, which are carried out in the laboratory or under field conditions.
- The fate (adsorption, degradation and mobility) of the active substance must be studied in soil, air, water and sediments.
- It is important to know how a substance degrades in the environment, because sometimes the degradation products are more persistent than the parent substance.

Testing Requirements for New Pesticides
Environmental Fate and Environmental Toxicology

- DDT, for instance, is converted to metabolites by stepwise dechlorination (eq. 11.9). The metabolites (e.g. DDD or DDA) can be found in soil for many years after the DDT itself is degraded.



Eq. 11.9

CHAPTER 11 OBJECTIVES

- Introduction
- Chemical Pest Control
  - Herbicides
  - Insecticides
  - Fungicides
  - Miscellaneous Compounds
  - Chemical Synthesis of Pesticides
- Formulated Products
- Biological Pest Control
- Testing Requirements for New Pesticides