FUNGICIDES IN AGRICULTURE AND HORTICULTURE

FROM time to time estimates are published of the enormous annual loss of crops throughout the world due to pests and diseases. A considerable proportion of these losses, equal to the produce of millions of acres of agricultural land, arises from fungal diseases, and in most cases the use of fungicides provides the most effective remedy. In recent years there has been good progress in the development of new fungicides; crop losses are still great, however, even in Britain, where potato blight, for example, still destroys thousands of tons of potatoes each year. Meetings concerned with research on fungicides do not occur frequently in Britain and considerable importance was therefore attached to the symposium entitled "Fungicides in Agriculture and Horticulture" organized by the Pesticides Group of the Society of Chemical Industry and held in London during March 20–21.

The programme was well balanced to include treatment of fundamental as well as practical aspects of the subject. The three papers delivered on the first morning under the general heading of "Current Usage and Recent Developments" and dealing with fruit, glasshouse crops and agriculture respectively were mainly practical. It is well known that organic fungicides have been used increasingly in crop protection in recent years, but it was interesting to hear from these three speakers that inorganic materials such as elemental sulphur, lime-sulphur and Bordeaux mixture still hold a very important position.

Dr. A. H. M. Kirby dealt briefly with soft and stone fruits and more fully with pome fruits. Scab has been the disease requiring most attention on apple and pear, but of all the chemicals used for its control none is without some defect. For example, captan, which gives excellent control, allows mildew to increase—this, incidentally, is now the most important disease for which a safe, cheap and adequate control is still required. The dangers of phytotoxicity and mammalian toxicity with some of the materials in current use were emphasized, and a particular point made was that the harmonizing of biological and chemical control of pests and diseases is worthy of greater attention in spray programmes.

In glasshouse crops, as W. H. Read pointed out, a system of monoculture is usually practised and the methods and costs of partial soil-sterilization to combat the soil-borne diseases encouraged by this system were given. The disadvantage with chemical soil sterilants is the long period required for the chemical or its breakdown products to disappear from the soil.

Since most glasshouse crops are susceptible to phytotoxicity and mechanical damage, there is usually no definite spray programme in glasshouses, the policy being to wait until disease needs to be controlled. The uses of sprays, aerosols, smokes and vaporization were discussed as methods of dispersing the chemicals employed to control a number of important diseases of glasshouse crops.

Unlike the previous speakers, Dr. F. C. Gayner was not restricted to considering the use of fungicides in Britain. Under the title "Fungicide Usage in World Agriculture" he gave the amount and value of sulphur, copper, mercury and organic fungicides used throughout the world during 1958. Although 12,000 tons of organic fungicides and 300 tons of mercury were used in that year, 275,000 tons of sulphur, used mostly as a dust, and 56,000 tons of copper were sold, the latter mainly as copper sulphate for the manufacture of Bordeaux mixture. Most of this interesting paper was concerned with the use of fungicides to control the eight major diseases on crops of world importance.

The second session of the symposium comprised three fundamental papers on "Theoretical Bases for Fungicides". The first of these, prepared by Dr. A. H. McIntosh, was read by Dr. C. Potter; but in the absence of the author it was inevitable that the discussion suffered some limitations. The results were given for the fungistatic action of nineteen chemicals, some of them well-known fungicides, against *Botrytis fabae* at temperatures between 10° and 25° C. and at intervals of up to 14 days. In general, an increase in temperature was shown to increase the toxicity and speed of action, whereas the apparent toxicity at any one temperature decreased as time passed. It emerged that there is little evidence for the generally held belief that spores are more resistant to fungicides at their optimum temperature for germination and also that the results may be misleading if spore germination tests are assessed before the ED_{50} has been allowed time to reach a steady value. An important point was made here concerning the loss of fungicides by sorption on the glassware used in spore-germination tests. This is particularly true of heavy-metal salts and, in one case cited, using mercuric chloride, some 70 per cent of the original amount was lost from solution in 24 hr.

Physical measurements and biological behaviour also formed an integral part of the succeeding paper by Dr. M. J. Janssen of Utrecht. Work on fungicides in the Netherlands has long been in the forefront of world research, and in recent years a series of papers dealing with the dithiocarbamate fungicides has been published by the team led by Prof. G. J. M. van der Kerk. Dr. Janssen's contribution was concerned with the mode of action of the dithiocarbamates, and he divided the work on this subject into three phases, dealing mainly with the most recent work relating to metal complex formation. He showed that the dithiocarbamates act in much the same way as 8-hydroxyquinoline, for which the importance of metal chelation has been demonstrated by Albert. A quantitative agreement exists between toxicity and concentration of the dithiocarbamate ion itself and its complexes with copper. Thus the different growth pattern in several fungi can be ascribed to their sensitivity not only to the dithiocarbamate ion in the medium but also to the complexes in which one or two dithiocarbamate ions are attached to the bivalent copper ion. Reference was also made in this paper to the current fashion of postulating metal-binding as responsible for the observed phenomena in other biological systems. In the discussion, there was general support for Dr. Janssen's opinion that the theory that chelation is of basic importance in relation to the activity of plant growth-regulating substances is unwarranted.

Dr. E. Somers pointed out that in terms of weight of chemical removed from solution by fungal spores, the fungicides in current use possess low toxicity compared with animal poisons, insecticides or even bactericides. He felt that the common method of determining uptake of fungicide by measuring the amount remaining in solution after fungal spores have been removed from it gives little information on the actual amount which has penetrated the spores. Using captan and a series of ring-substituted derivatives no correlation could be established between lipid solubility on one hand, and uptake or fungitoxicity, in terms of the ED_{50}, on the other. It was shown that thiol-groups within the cell are concerned in the action of captan ; furthermore, the chemical appears to be taken up only by living cells. This is quite different from the results obtained with radioactive copper, the uptake of which was found to be non-specific. Thus, any part of the fungal cell, whether living or dead, will apparently remove copper-64 from solution ; that which accumulates on the outside of the cell therefore probably plays no part in the fungicidal activity of this metal.

The first paper on the second day of the symposium, given by Prof. G. J. M. van der Kerk of Utrecht, was concerned with new developments in organic fungicides. An authority in this field, Prof. van der Kerk first described how fungicide research in Holland is co-ordinated between several institutions. He then went on to forecast that another general group of organic fungicides superior to the dithiocarbamates on grounds of activity, simplicity of molecular structure and cost is unlikely to be found. He considered it more likely that in the future specific materials will be developed to control specific diseases.

In the field of protectant fungicides, the organo-tin compounds have recently been introduced commercially as a result of research which started in 1950. Triphenyltin acetate is already marketed by Germany for use on a wide range of crops, but its phytotoxicity and mammalian toxicity require special attention. The triphenyltin sulphides, on the other hand, are much less toxic towards higher plants and animals but their antifungal spectra also show more specificity.

In the search for systemic fungicides progress has been made along three main lines: by using chemicals which are translocated within the plant and are themselves fungitoxic; by using chemicals which are broken down by the plant or the pathogen to form systemically distributed fungicides; and by using compounds which are neither fungicidal *per se* nor give rise to fungicidal degradation products but interfere with the host's metabolism and render it resistant to attack. Prof. van der Kerk reported on the progress being made in Holland along all three of these lines. Procaine (diethylaminoethylester of *para*-aminobenzoic acid) shows promise as a systemic fungicide *per se*, but none of its derivatives is of interest and it may be significant that procaine has so far been shown to be active only against powdery mildew on cucumber. This disease again showed itself to be useful for the demonstration of systemic fungicidal activity with sodium dimethyldithiocarbamate. This compound, which is an active plant-growth regulator, is degraded within the bean plant and, by means of an elegant bioassay technique involving *Glomerella cingulata*, can be shown chromatographically to form at least three antifungal derivatives. Resistance to *Cladosporium cucumerinum* has been increased by providing cucumber plants with enantiomorphs of naturally occurring amino-acids; likewise, thiourea and phenylthiourea, which are inactive *in vitro*, have been found to confer resistance against certain diseases when provided to plants through their roots.

The activity of fungicides in relation to their chemical structure was considered by several speakers in relation to the particular compounds with which they were interested. Dr. D. Woodcock, in his contribution, dealt specifically with structure-activity correlationships of some nitrogenous antifungal chemicals. The importance of physical properties such as lipophilic character was discussed in relation to mode of action. Chelation was also considered, in particular with regard to its influence on the fungitoxicity of oxine (8-hydroxyquinoline) and related compounds. Other compounds dealt with by Dr. Woodcock included imidazolines, guanidines and triazines.

Prof. R. L. Wain and his colleagues at Wye College have been closely associated with research on systemic fungicides for some years and Prof. Wain gave an account of the progress made in this field. He directed attention to the important fact that most plants possess a wide degree of resistance to fungal attack, and pointed out that in some cases this resistance may depend on the possession by the plant of anti-fungal chemicals within its tissues. The observation that the tissues of *Vicia faba* were fungitoxic provided an opportunity of investigating this system from the point of view of "natural systemic fungicides". The isolation of the anti-fungal compounds present in *Vicia faba* has, in fact, been in progress at Wye for some time. Early in these investigations it had to be shown that the observed effect was due to the presence of fungitoxic chemicals and that the broad bean was the most suitable subject for the investigation. Details of the biological work leading to chemical extraction of the fungal inhibitors and the techniques developed for dealing with large numbers of fractions obtained from the extracts were given by Dr. D. M. Spencer. Dr. C. H. Fawcett then described the successful extraction of the most potent two chemicals : one a keto-yne and the other a sulphur-containing acid with certain properties similar to those of a nucleotide. While somewhat unstable, there is no doubt that these materials are highly fungitoxic and their presence in *Vicia faba* may well prove to be of considerable significance.

The last two contributions dealt with two new fungicides now in use. D. J. Higgons described the research which led to the field trials and ultimate commercial application of 2,6-dichloro-4-nitroaniline, particularly against *Botrytis cinerea* on lettuce, and Dr. W. F. Jepson dealt with the orchard use against scab diseases and the possible mode of action of *n*-dodecylguanidine acetate.

The contributions to this symposium ranged widely within the field of fungicides. The practical aspects of their use were discussed, theories on mode of action were described, research being carried out towards the development of new fungicides was reported and details were given of two new materials now on the market. Perhaps part of its undoubted success can be ascribed to the comparative rarity of meetings such as this and it is to be hoped that others will follow at suitable intervals. The organizers of the symposium are to be congratulated on their choice of subject, and the participants—indeed all those interested in fungicides—look forward to the early publication of the monograph containing the contributions and discussions. D. M. SPENCER