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Conference on Fungicides

FUNGICIDES and their Mode of Action was the subject of a conference held November 24 and 25 at the National Research Council. The conference was called by the Prevention of Deterioration Center, a council agency, in response to the growing feeling that work in this field is largely empirical in nature and broad guiding principles are needed.

The conference opened with a discussion of growth and spore germination as a basis for testing (J. G. Horsfall, Connecticut Agricultural Experiment Station), and of factors controlling spore germination in specific instances (P. J. Allen, University of Wisconsin). It was brought out that many growth inhibitors do not affect spore germination, and vice versa. The arrested growth state typical of spores is apparently due to rather specific enzyme blocks, and in one case to a volatile inhibitor. Although further study of spore germination is important, it is clear that the results of evaluation tests will vary with the principle used. Tests based on the weakening of cellulose fibers may well involve both factors, since the fungus is usually inoculated as spores, and the extent of attack will roughly parallel the growth. The test organism must be chosen with full appreciation of the specificity of response sometimes shown. Thus *Botrytis* is 100 times more sensitive to dimethyldithiocarbamate than *Aspergillus niger*, yet both are equally sensitive to trichlorophenol (H. L. Klopping, Du Pont).

Although toxic substances are generally considered to act on specific enzyme systems, little attempt has yet been made to view the action of fungicides in this way. An important step in this direction was taken at the conference by considering enzyme inhibitors. D. E. Green (University of Wisconsin) defined three major categories of enzyme inhibition: (1) by resemblance to the substrate (e.g., malonic and fluorocitric acids and the antivitamins), (2) by modifying an enzymic prosthetic group (e.g., HCN, CO, and azide), (3) by modifying the protein

moiety of an enzyme (e.g., sulfhydryl reagents).

By the end of the conference it developed that most of the known fungicides fall into one or the other category. In discussing the activity of chelating agents, conditions were described in which these agents can activate enzyme systems by altering their colloidal state rather than by combining with metals (W. D. Bonner, Jr., Smithsonian Institution). Other systems were described in which chelating agents cause an inhibition reversible by specific metals (W. J. Nickerson, Rutgers University). These, of course, are clear examples of inhibition by combining with a metal, even when that metal is in relatively stable complex form, for the stability constants of metal-chelates like copper oxine are very high. However, the remarkable fact that the fungitoxicity of oxine is exceeded by that of its copper complex remains unexplained. The behavior of halogen-substituted derivatives of oxine shows that these are less active at neutral pH, but much more so at high acidities, where copper-oxine is appreciably dissociated (S. S. Block and E. G. Kovach, University of Florida).

In the important group of substituted phenols it was pointed out that *ortho*-substitution, especially with normal- or cyclo-alkyl groups, always increases fungicidal activity. Some of the puzzling effects of substitution on activity parallel those on the dissociation of the phenolic hydroxyl (H. Shirk, National Research Council). Similar effects are seen in the bis-phenols, the fungicidal activity and stability of which are on the whole greater (P. B. Marsh, U. S. Department of Agriculture).

Among the acrylates, many compounds have been quantitatively compared (C. Wessel, NRC). A discussion of the basis of their action (L. P. Hammett, Columbia University; R. C. Elderfield, University of Michigan) led to the conclusion that it may depend on combination with thiols.

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