It will be seen from the above observations that, although the main principles of tumor formation appear to be common to all stocks, characteristic minor differences are still present between the several stocks. A number of problems present themselves in this connection, and further studies are in progress. A detailed report will be published elsewhere.

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A New Plant Growth Regulator—α-Cyano-β-(2,4-Dichlorophenyl) Acrylic Acid

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In the course of a search for novel plant growth regulators, a new chemical compound, α-cyano-β-(2,4-dichlorophenyl) acrylic acid (Ethyl-214) was synthesized and tested in greenhouse experiments on tomato and marigold plants. When applied at low concentrations, this compound produced the striking effects of inhibiting the growth of tomato and the flowering of marigold.

The discovery of the growth inhibitory action of maleic hydrazide (*1*) has drawn attention to the possibilities of plant growth control without visible injury. Preliminary studies indicate that the inhibitory effect of α-cyano-β-(2,4-dichlorophenyl) acrylic acid on tomato is similar to that of maleic hydrazide. Both materials inhibit the growth of tomato without apparent injury. However, tomato plants treated with α-cyano-β-(2,4-dichlorophenyl) acrylic acid show a decrease in apical dominance, permitting activation of the axillary buds, whereas response to maleic hydrazide is an over-all slowdown of growth. The application of α-cyano-β-(2,4-dichlorophenyl) acrylic acid to budding marigold plants caused a marked delay in flowering. However, maleic hydrazide was ineffective at comparative concentrations in delaying the flowering of marigold. Thus, it appears that the new compound has a mode of action different from that of maleic hydrazide, and a different range of selectivity as a plant growth regulator.

α-Cyano-β-(2,4-dichlorophenyl) acrylic acid was synthesized by the condensation of 2,4-dichlorobenzaldehyde with cyanoacetic acid. After recrystallization from benzene, it is obtained as white leaflets, melting at 197.5°–198.3° C. The diethanolamine salt is obtained in the form of white crystals, melting at 137.9°–138.9° C. Further details of the synthesis of α-cyano-β-(2,4-dichlorophenyl) acrylic acid and its derivatives will be published elsewhere.

Preliminary toxicological data[1] have been obtained, employing a small number of animals. The approximate lethal dose of α-cyano-β-(2,4-dichlorophenyl) acrylic acid for rats, when given by oral administration, lies between 50 and 250 mg/kg body weight, and that of its diethanolamine salt lies between 250 and 500 mg/kg. Both the free acid and the diethanolamine salt have been applied to the abraded skin of rabbits. In each instance the rabbit survived a 24-hr period of contact with 250 mg/kg of body weight.

Four tests were used to evaluate the effects of α-cyano-β-(2,4-dichlorophenyl) acrylic acid on tomato plants: seed germination, lanolin paste, single leaf dip, and total spray. No evidence of unusual growth response was noted in the seed germination or lanolin

[1] Toxicity tests were conducted by J. F. Treon, of the Kettering Laboratory, University of Cincinnati.

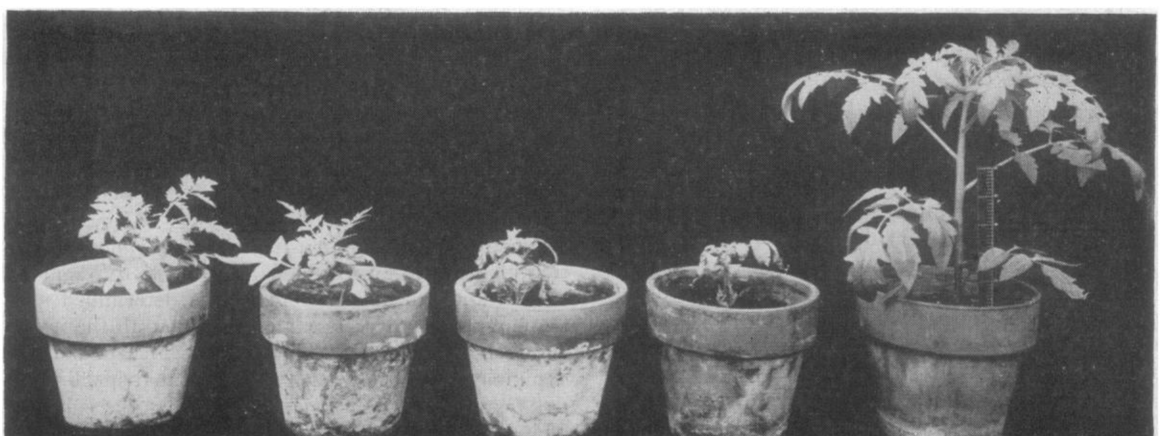

FIG. 1. Effect of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, when applied to tomato plants at four different concentrations, 0.05, 0.1, 0.2, and 0.4% and control, 3 weeks following treatment.

paste tests. In the leaf dip and total spray tests, however, marked inhibition of growth resulted.

When a single leaf of young tomato seedlings was dipped in a 1% aqueous suspension of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, the treated leaf died, but no other immediate effects on the rest of the plant were noted. Ten days later, the treated plants were only one third the height of the control plants. At the end of a month, the height of the treated plants was one half that of the control.

Death of the plants resulted when a 1% suspension of the compound was sprayed on young tomatoes. However, when a 0.1% suspension was used, growth inhibition occurred without visible tissue damage. In the latter experiment 2-in. tomato plants, growing one to a pot, were sprayed with 10 ml of a 0.1% aqueous suspension of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, using 0.1% Tween 20 as the wetting agent. At the end of one week, the treated plants were noticeably smaller than the controls. Average measurements of height taken at the end of three weeks were: treated plants, 5.5 in.; control plants, 14 in. Although there was no tissue damage, and the color was normal, the treated plants exhibited formative effects, being unusually bushy with numerous axillary branches. The growth-inhibiting effect of α-cyano-β-(2,4-dichlorophenyl) acrylic acid, when applied to tomato plants at four different concentrations, is illustrated in Fig. 1.

Preliminary studies have indicated that, on a mole basis, the diethanolamine salt of α-cyano-β-(2,4-dichlorophenyl) acrylic acid is more effective than the free acid in inhibiting growth of tomato. This increased activity is probably due to the greater water-solubility of the salt.

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Crystalline and Amorphous[1] Insulin-Zinc Compounds with Prolonged Action

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The presence of zinc in pancreas and in crystalline insulin has given rise to a series of investigations on the interaction between insulin and zinc. As a result, protamine-zinc-insulin has become extensively used. The clinical results have been rather disappointing, for the weak initial action of this preparation has been very troublesome, especially in cases of severe diabetes.

In an effort to develop more suitable insulin preparations for single injection, we have carried out some combined chemical, biological, and clinical experiments, designed to elucidate the interaction between insulin and zinc.

It was first discovered that phosphate ions, which are used in the protamine-zinc-insulin preparation, are able to influence the physical-chemical relation between insulin and zinc.

In Fig. 1, *A* illustrates the solubility of insulin as a function of pH in phosphate buffer (an acid solution of insulin—40 u/ml—is adjusted to different pH values, and the dissolved insulin is determined spectrophotometrically). It can be seen that all the insulin is dissolved at the pH of blood, 7.3, which presumably explains why isoelectrically precipitated insulin does not possess a sustained effect. *B* shows the solubility of insulin in the same buffer, to which has been added the same amount of zinc as is found in protamine-zinc-insulin—2 mg/1000 u. The conditions for solubility

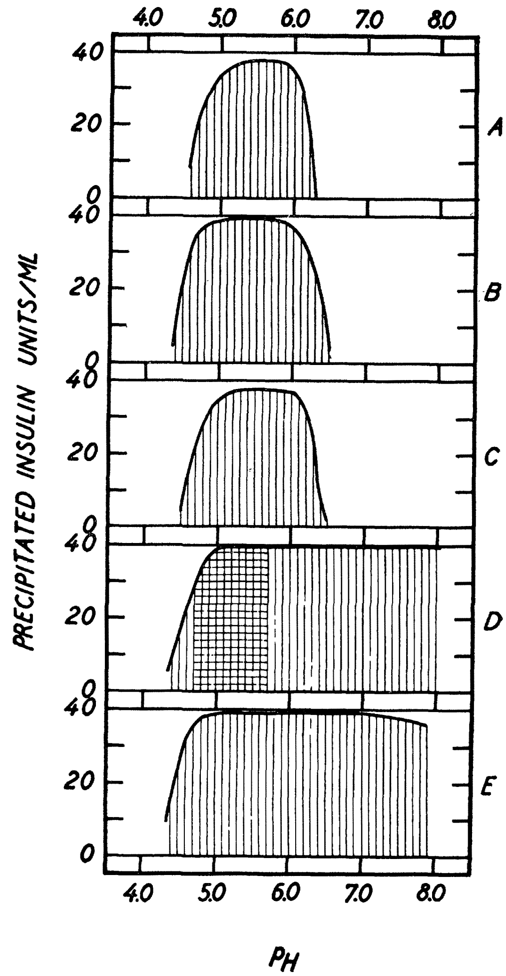

FIG. 1. Precipitation zone of insulin (40 u/ml) in: *A*, 0.01 mol sodium phosphate; *B*, 0.01 mol sodium phosphate with 2 mg zinc (as chloride)/1000 u; *C*, 0.01 mol sodium acetate; *D*, 0.01 mol sodium acetate with 2 mg zinc (as chloride)/1000 u; *E*, 0.01 mol sodium phosphate with 2 mg zinc (as chloride)/1000 u and 8.5 mg protamine/1000 u.

[1] Amorphous insulin, in this paper, refers only to the physical state of the insulin and not to the purity. The amorphous insulin is thus prepared by precipitation of dissolved crystalline insulin.