This Week's Citation Classic

Ninnemann H, Zeevaart J A D, Kende H & Lang A. The plant growth retardant CCC as inhibitor of gibberellin biosynthesis in *Fusarium moniliforme*. *Planta* **61**:229-35, 1964.
[Division of Biology, California Institute of Technology, Pasadena, CA]

The plant growth retardant (2-chloroethyl)trimethylammonium chloride (CCC) was shown to inhibit gibberellin production in the fungus *Fusarium moniliforme*. The data support the hypothesis that the dwarfing effect of retardants in higher plants is due to inhibition of gibberellin biosynthesis. [The *SCI*® indicates that this paper has been cited in over 130 publications since 1964.]

Jan Zeevaart
and
Hans Kende
MSU-DOE Plant Research Laboratory
Michigan State University
East Lansing, MI 48824

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"Around 1950, several synthetic compounds were described which reduce stem height in many plants.[1] The best known of these growth retardants or dwarfing agents are Amo-1618, CCC, and Phosfon D. Although these compounds have quite different structures, their effects on plants are similar. The general responses are reduction of stem elongation, dark green leaves, and thick stems and leaves. These responses are opposite to those caused by gibberellin (GA). Furthermore, application of GA to dwarfed plants will restore normal growth. Thus, it would appear that growth retardants could reduce the amount of physiologically active GA in plants by (a) inhibition of GA biosynthesis, (b) interference with GA action, or (c) destruction of GA.

"In the early 1960s, Anton Lang at the California Institute of Technology had an active group working on GA. Helga Ninnemann, then a visiting graduate student and now at the University of Tübingen, and we, then postdoctoral fellows, participated regularly in the weekly plant physiology journal club. During a discussion on the mode of action of growth retardants, the idea arose that these chemicals might inhibit GA biosynthesis. We then proposed that it would be much easier to test this hypothesis with the fungus *Fusarium moniliforme*, which produces copious amounts of GA, rather than with higher plants, since the methodology for measuring GA in green plants was still relatively poor. Unknown at that time, but essential to our hypothesis, was that the GA biosynthetic pathway is the same in the fungus and in higher plants. The results of the initial experiments[2] clearly demonstrated that fungal cultures did not accumulate GA in the presence of Amo-1618 or CCC. In the paper under discussion, proof was provided that, in the case of CCC, this effect was due to a block in GA biosynthesis, and not to destruction of GA. Growth retardants were also shown not to be competitive inhibitors of GA action in higher plants.[3]

"Work in Charlie West's group at the University of California, Los Angeles, subsequently demonstrated that growth retardants block the cyclization of geranylgeranyl pyrophosphate to kaurene, an important step in GA biosynthesis in *Fusarium*[4] as well as in higher plants.[5] It became clear, therefore, that the inhibition of GA biosynthesis could account for most of the physiological effects of growth retardants observed in plants.

"This paper has often been cited because it provides evidence that the growth retardant CCC blocks GA biosynthesis. It was the first instance where the mode of action of a plant growth regulator was explained at the biochemical level. Growth retardants have been useful for the study of GA biosynthesis, a topic reviewed recently.[6] Moreover, these chemicals have become important tools for the study of the physiological roles of GA in plants. Finally, growth retardants have found wide practical applications, such as production of compact ornamental plants and promotion of flowering in fruit trees. In Europe, CCC is used extensively to prevent lodging of wheat by reducing the height of the plants and stiffening the stems."

1. **Cathey H M.** Physiology of growth retarding chemicals. *Annu. Rev. Plant Physiol.* **15**:271-302, 1964.
2. **Kende H, Ninnemann H & Lang A.** Inhibition of gibberellic acid biosynthesis in *Fusarium moniliforme* by Amo-1618 and CCC. *Naturwissenschaften* **50**:599-600, 1963.
3. **Paleg L, Kende H, Ninnemann H & Lang A.** Physiological effects of gibberellic acid. VIII. Growth retardants on barley endosperm. *Plant Physiol.* **40**:165-9, 1965.
4. **Shechter I & West C A.** Biosynthesis of gibberellins. IV. Biosynthesis of cyclic diterpenes from *trans*-geranylgeranyl pyrophosphate. *J. Biol. Chem.* **244**:3200-9, 1969.
5. **Robinson D R & West C A.** Biosynthesis of cyclic diterpenes in extracts from seedlings of *Ricinus communis* L. II. Conversion of geranylgeranyl pyrophosphate into diterpene hydrocarbons and partial purification of the cyclization enzymes. *Biochemistry* **9**:80-9, 1969.
6. **Hedden P, MacMillan J & Phinney B O.** The metabolism of the gibberellins. *Annu. Rev. Plant Physiol.* **29**:149-92, 1978.