The genus *Alternaria* is responsible for different plant diseases such as tobacco brown spot, tomato blight, and citrus seedling chlorosis but can also be present during storage of grain. The objective of the present paper is to summarize the knowledge concerning regulation of secondary metabolism in *Alternaria*, particularly *A. alternata* (*A. tenuis*). The paper mainly deals with regulation of polyketide biosynthesis, one of the major pathways leading to the biosynthesis of mycotoxins in *Alternaria*.

The mostly studied *Alternaria* mycotoxins are dibenzopyrones such as alternariol (AOH) and alternariol monomethyl ether (AME) and altenuene along with the tetramic acid tenuazonic acid.

The biosynthesis of *Alternaria* mycotoxins has been reviewed by Stinson (12). Most information is available for the biosynthesis of the polyketides AOH / AME while a few biosynthetic studies have been accomplished for tenuazonic acid (11).

**Regulation of AOH and AME accumulation**

Several factors such as light, nitrogen, or divalent cations have been demonstrated to influence the synthesis of AOH and AME when the fungus is grown under laboratory conditions.

**Effect of light**

White light was shown to inhibit the accumulation of AOH and AME in *A. alternata* when the fungus was continuously illuminated but also when light was applied during the exponential growth phase only (10). Blue light (420 to 520 nm) was the most efficient in inhibiting polyketide synthesis (4).

The possible inhibitory effect of light on biosynthesis of AOH and AME under field conditions has not been investigated. However, production of AOH and AME was completely inhibited by white light when *A. alternata* was cultivated on a natural medium such as rice (Bottalico, personal communication).
Possible involvement of NADPH in the regulation of AOH and AME synthesis

It has been suggested that the NADPH / NADP ratio in the fungal cell influences the incorporation of acetyl units into either fatty acids, when the ratio is high, or into polyketides (7). It is therefore interesting that A alternata has been shown to produce more lipids under conditions of limited polyketide synthesis (5, 3). When the specific activity of enzymes in the main NADPH generating pathways in A alternata, the pentose phosphate pathway, mannitol cycle and NADP-isocitrate dehydrogenase, were compared between light and dark grown mycelia, no large differences were found. Since incorporation of $^{14}$C-mannitol into lipids was similar in darkness and light, it was suggested that the NADPH generating capacity was not reduced in dark-grown as compared with light-grown mycelia (9).

Influence of nitrogen on the biosynthesis of AOH and AME

Nitrogen regulates the biosynthesis of secondary metabolites in many microorganisms. Nitrogen inhibition of polyketide accumulation is known from a number of fungi (1, 2, 13). Increasing the nitrogen concentration in a semisynthetic medium also inhibited AOH and AME production by A alternata (8). This effect was only seen when the nitrogen source was added before the production phase started.

Turnover of AOH and AME

Pulse-chase experiments using $^3$H acetate showed that AOH and AME produced by A alternata was metabolized by the fungus (6). During early stationary growth phase the radioactivity in AOH and AME decreased rapidly but at late stationary growth phase the rate of turnover was much slower. The results indicate that AOH and AME are not stable end products of metabolism. The studies show that in order to understand the accumulation of polyketides not only biosynthetic mechanisms are important to know but also mechanisms that cause turnover of the products.

Conclusions

It is clear from this review that the biosynthesis of common mycotoxins in Alternaria is easily affected by environmental factors such as light or nitrogen. The mechanisms by which these factors operate are at present unknown. More information about the enzymes involved in the polyketide pathway is necessary before the understanding of these phenomena will be more comprehensive.

References