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Studies on Mikamycin B Lactonase. V. Metabolic Control in Mikamycin B Fermentation

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Mikamycins A and B (abbreviated MK-A and -B) are the products of *Streptomyces mitakaensis*, which show typical synergistic activity against Gram-positive bacteria. However, the fermentation course was complicated by the participation of another factor, MK-B lactonase, whose action was estimated to be the hydrolysis at the lactonic linkage of MK-B into the antimicrobially inactive MK-B acid : This enzyme reaction caused the depression of MK-B accumulation.

From the view point of antibiotic production, this type of interaction between two metabolites, *i.e.* production of a desired metabolite and its destruction by an enzyme produced by the same organism, is novel, but highly undesirable, hence the metabolic control or the selective elimination of this enzyme activity should be expected to enhance antibiotic production.

The lactonase, purified from the mycelial cells, has a molecular weight of 29,000, and catalyzes the hydrolytic degradation of MK-B and its analogues. The enzyme activity was maximal at pH 7.0～8.0 and 27°C for an incubation of 60 minutes; it was stimulated by the presence of Mg^{2+} ion, but inhibited by heavy metal ions such as Cu^{2+} and Ni^{2+} ions.

S. mitakaensis in normal conditions (control) yielded 90 μg/ml of MK-A and 2 μg/ml of MK-B after 72 hours of cultivation. Adjustment of pH to 7 starting 20 hours and addition of an enzyme inhibitor, especially Ni^{2+} ion (0.01%), increased the yields to 200 μg/ml of MK-A and 12 μg/ml of MK-B at 72 hours of cultivation, a 2- and a 6-fold increase over the control. The properties of the MK-B lactonase have been thus exploited successfully to improve MK-B production and to prevent its degradation.

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