Bioactivation of the Fungal Phytotoxin 2,5-Anhydro-D-glucitol by Glycolytic Enzymes is an Essential Component of its Mechanism of Action

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An isolate of *Fusarium solani*, NRRL 18883, produces the natural phytotoxin 2,5-anhydro-D-glucitol (AhG). This fungal metabolite inhibited the growth of roots (I_{50} of 1.6 mM), but it did not have any *in vitro* inhibitory activity. The mechanism of action of AhG requires enzymatic phosphorylation by plant glycolytic kinases to yield AhG-1,6-bisphosphate (AhG-1,6-bisP), an inhibitor of Fru-1,6-bisP aldolase. AhG-1,6-bisP had an I_{50} value of 570 μM on aldolase activity, and it competed with Fru-1,6-bisP for the catalytic site on the enzyme, with a K_i value of 103 μM. The hydroxyl group on the anomeric carbon of Fru-1,6-bisP is required for the formation of an essential covalent bond to ζ amino functionality of lysine 225. The absence of this hydroxyl group on AhG-1,6-bisP prevents the normal catalytic function of aldolase. Nonetheless, modeling of the binding of AhG-1,6-bisP to the catalytic pocket shows that the inhibitor interacts with the amino acid residues of the binding site in a manner similar to that of Fru-1,6-bisP. The ability of *F. solani* to produce a fructose analog that is bioactivated by enzymes of the host plant in order to inhibit a major metabolic pathway illustrates the intricate biochemical processes involved in plant-pathogen interactions.