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

Franck E. Dayana*, Agnes M. Rimandoa, Mario R. Telleza, Brian E. Schefflera, Thibaut Royb, Hamed K. Abasc and Stephen O. Dukera

a USDA-ARS Natural Products Utilization Research Unit, P.O. Box 8048, University, MS 38677, USA. Fax 662-915-1035. E-mail: fdayan@ars.usda.gov

b Laboratoire de Biologie Moléculaire et Cellulaire, Université de Bourgogne, 21000 Dijon, France

c USDA-ARS Crop Genetics & Production Research Unit, P.O. Box 350, Stoneville, MS 38776, USA

* Author for correspondence and reprint requests

Z. Naturforsch. 57c, 645–653 (2002); received February 27/March 27, 2002

Bioactivation of Phytotoxin, Plant/Pathogen Interaction, Inhibition of Aldolase

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 (I50 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 I50 value of 570 µM on aldolase activity, and it competed with Fru-1,6-bisP for the catalytic site on the enzyme, with a Ki 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 ε 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 site 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.