

COLIN BLACKWELL, DEANNA SCHMITT, and JOSEPH HORZEMPA, Department of Natural Sciences and Mathematics, West Liberty University, West Liberty, WV 26074. The Utilization of Resazomycins in a Tularemia Infection Model.

*Francisella tularensis* is a highly pathogenic bacterium that causes the disease tularemia. The pneumonic form of this disease is often lethal without treatment. This bacterium has been categorized by the Centers for Disease Control and Prevention as a Category A Select Agent. Therefore, the development of novel therapeutics is essential to prepare society against potential bioterrorism. We previously showed that the compound resazurin exhibits antimicrobial activity against *F. tularensis* in vitro. The purpose of this study was to determine the efficacy of resazurin-based antibiotics (resazomycins) in vivo. Therefore, we infected chicken embryos to model tularemia (this is an established surrogate for mammalian tularemia). Chicken embryos treated with resazurin and the reduced form of this compound, resorufin, did not show enhanced survival compared to the control-treatment groups. This indicated that although effective in vitro, these compounds were being inactivated in vivo. A separate study from our laboratory revealed that serum proteins can bind and inactivate resazurin and resorufin. Modification of this compound to pentoxyresorufin (RPE) resulted in a resazomycin with efficacy in the presence of serum proteins. Therefore, chicken embryos were infected with *F. tularensis* LVS (live vaccine strain) and were treated with various doses of RPE or a vehicle. Results showed that various doses of RPE significantly enhanced the survival of the infected chicken embryos compared to those treated with the vehicle. This study indicates that resazomycins have potential for the treatment of tularemia.