INTRODUCTION

There is a continuous need to discover and develop new antibiotics to treat infections caused by multidrug-resistant pathogens. In this context, new oxazolidinones such as tedizolid have emerged that show higher intrinsic activity, lower minimum inhibitory concentrations (MICs) than linezolid against Gram-positive pathogens from clinical origins, including methicillin-resistant Staphylococcus aureus, as well as activity against Gram-negative bacteria.3,4 However, tedizolid is poorly distributed in cytosol and not concentrated extracellularly in kidney tissue.3,4

Tedizolid also demonstrates about 10-fold more than linezolid in human FTP4 membranes at pH 7.4 and is approximately 20-fold more than linezolid in human FTP4 membranes at pH 7.4 and is approximately 20-fold more active against E. coli. Although this may confer an advantage in terms of activity against intracellular forms of target bacteria, it also raises concerns with respect to potential toxicity. Indeed, one of the main limits of its use for long-term therapy is hypolipidemia related to its ability to impair mitochondrial DNA dependent protein synthesis.5,6 owing to structural similarities between cholesterol and polyamine/porphyrin.3,4

Consequently, there is a critical need to evaluate the subcellular distribution of tedizolid. Generally, we know that the subcellular localization of antibacterials can account for subcellular distribution of antibacterials. Generally, we know that the subcellular localization of antibacterials can account for antibacterial activity, and it is critical to understand the distribution of antibacterials within the cell to fully exploit their potential as therapeutic agents.7

METHODS

Study of the Cellular Uptake and Subcellular Distribution of the Novel Oxazolidinone Tedizolid in Murine J774 Macrophages: Lack of Association With Mitochondria

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MATERIALS

Murine J774 macrophage cells were infected with a Gram-positive strain of Staphylococcus aureus, and the subcellular distribution of tedizolid was determined by fractionation techniques. This study was funded by Cubist.

17th Making a Difference in Infectious Disease Pharmacotherapy (MAD-ID) Meeting

May 29-31, 2014, Orlando, Florida, USA

ACKNOWLEDGMENTS

This study was funded by Cubist.