0273-2289/00/87/0219/$13.50

Toxicity Assessment of Tamoxifen by Means of a Bacterial Model

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Received May 1, 1999; Revised September 1, 1999; Accepted October 1, 1999

Abstract

A strain of *Bacillus stearothermophilus* was used as a model to study physical perturbations induced in the membrane by the cytostatic tamoxifen (TAM). This study was carried out using two lines of criteria: (1) bacterial growth, and temperature growth range, with determination of growth parameters as a function of TAM concentration; and (2) biophysical studies by differential scanning calorimetry (DSC) and by means of two fluorescent probes to evaluate perturbations promoted by the drug on the structural order of bacterial lipid membranes. The inhibition of growth induced by TAM, the structural bilayer disordering, and the shift in the phase transition temperature to a lower range were also determined in the presence of Ca^{2+}, i.e., a natural membrane stabilizer, to elucidate further perturbing effects of TAM on membranes with putative implications in cell toxicity. Growth inhibition promoted by TAM is potentiated by an increase in growth temperature above the optimal range, but attenuated or relieved by the addition of 2.5 m*M* Ca^{2+} to the culture medium. Consistently, fluorescence polarization and DSC studies showed that Ca^{2+} ions (2.5 m*M*) effectively compensated for the destabilizing effects promoted by TAM in bacterial lipid membranes.

Index Entries: *Bacillus stearothermophilus*; calcium; tamoxifen; bacterial growth; membrane physical effects.

Introduction

In the past decade, the triphenylethylene compound tamoxifen (TAM) has been the subject of intensive research because of its therapeutic interest

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