

Abstract

THESIS: Synthesis of Novel Lavendamycin Analogues and Related Heterocyclic Containing Quinoline-5,8-Diones

STUDENT: Raheleh Ravanfar

DEGREE: Master of Science

COLLEGE: Sciences and Humanities

DATE: July 2016

PAGES: 60

Lavendamycin is a quinoline-5,8-dione antibiotic and antitumor agent with a pentacyclic structure including the 7-aminoquinoline-5,8-dione and the indolopyridine (β -carboline) moieties. Despite the interest in lavendamycin as an antitumor agent, this agent was precluded from preclinical development due to its poor aqueous solubility and its toxicity toward normal human cells. Lavendamycin has been the focus of several synthetic studies to elucidate the structural features that are required for its cytotoxic activity and to develop improved analogues with potent antitumor properties and lower animal toxicity.

The purpose of the present study is to synthesize new lavendamycin analogues by changing the functionality, at the C2 position of the quinoline-5,8-dione, and investigate the new analogues' reactivity with the NQO1 enzyme. Therefore, 7-N-acylamidoquinoline-5,8-dione-2-carboxaldehyde oximes were synthesized in 7 steps from commercially available 8-hydroxy-2-methyl quinoline. 7-N-(acetamido, propionamido, butyramido and isobutyramido)-5,8-dione

aldehyde, and finally oxime formation. Several 3-(7-N-acylamido-5,8-quinolinedion-2-yl)-5-t-butylisoxazoline and 3-(7-N-acylamido-5,8-quinolinedion-2-yl)-5-methoxymethylisoxazole derivatives were synthesized in good to excellent yields. The new analogues were characterized by $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and IR spectroscopy.