

The Summer Undergraduate Research Fellowship (SURF) Symposium  
3 August 2017  
Purdue University, West Lafayette, Indiana, USA

## Synthesis of hydroxybenzylidene-indolinones, Schiff bases and N-substituted analogs and their effects on bacterial physiology.

Catherine E. Cabrera, Neetu Dayal, Moloud Aflaki, Herman O. Sintim  
Department of Chemistry, Universidad de Los Andes  
Purdue Institute for Drug Discovery, Purdue University  
Department of Chemistry, Purdue University

### ABSTRACT

c-di-AMP is a global stress response regulator involved in some processes of biofilm formation and antibiotic resistance. It has become a candidate target for the development of new antibacterial treatments. Previous studies have shown that hydroxybenzylidene-indolinones can act as c-di-AMP synthase inhibitors. They also act as antibacterial and anti-biofilm inhibitors and re-sensitize resistant bacteria to methicillin and vancomycin. In this project, potent analogs of these compounds, including Schiff bases and N-substituted compounds, have been synthesized. The objective of this work is to explore the effect of these modifications on their biological activity. Base-catalyzed condensation and acid-catalyzed reactions were performed in order to obtain the products. Antibacterial, anti-biofilm and c-di-AMP synthase inhibition (in-vitro) assays were performed. Halogenated and di-substituted compounds show the highest biological activity. Compounds with hydrophilic groups as well as the Schiff base do not show biological activity. Two compounds completely inhibited growth of *Staphylococcus aureus* (Gram positive bacteria). One of these compounds also shows biofilm inhibition for the same bacteria. The results suggest that some current synthetic compounds are potentially great antibacterial and anti-biofilm inhibitors. Further study will continue in order to enhance the biological activity of the molecules already synthesized.

### KEYWORDS

Hydroxybenzylidene-indolinones, c-di-AMP, antibacterial activity, anti-biofilm activity, isatin Schiff bases.