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Title: Synthesis and Antioxidant Studies of Some Pyridine Connected α,β- unsaturated Acrylamides as

Potential FAB Inhibitors

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Abstract:

Antibiotics, once considered as miracle drugs, revolutionized medicine in the 20th century with the isolation of penicillin. The discovery of several types of life-saving antibiotics played vital role in the infectious diseases. However, decades of overuse have led to an enhanced evolution of antibiotic resistance, and bacterial infections have again turned out to be a major health problem worldwide. Since most of the clinically used antibiotics inevitably evoke bacterial resistance, there is an emerging need for novel approaches to combat that can will lead to the discovery of new and broad-spectrum antibiotics, which can ensure the treatment against infectious diseases. Among the modern approaches towards new antibiotics, inhibition of bacterial fatty acid biosynthetic (FAB) pathway is a valid dated yet underexplored strategy. Even though a cascade of process and related enzymes are involved in FAB, our prime interest is on enoyl-acyl carrier protein (ACP) reductase (Fabl). This particular NAD(P)H cofactor dependent enzyme catalyzes the reduction of trans-2-enoyl-ACP to acyl-ACP, which is one of the four essential steps required for every twocarbon elongation pathway in FAB in bacteria. In our work, we have considered a recent drug molecule (AFN-1252, currently in clinical trials) as our lead, and designed few candidates based on the pyridine derivative of acrylic acid/amide. To broaden and enhance the activity spectrum, we have introduced the quartenization on pyridine nitrogen, which we adapted from another current generation cephalosporin based antibiotic, namely ceftaroline fosamil. During the investigations, we have also studied the antioxidant properties for the targeted molecules using two different assay methods, which showed a moderate activity compared to the standard, ascorbic acid. However, the targeted antibiotics activities for the derivatives through MIC (minimum inhibitory concentration) studies have not been completed yet, which is currently underway.

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