Antibacterial and antiparasitic activity of novel brominated vinylic fatty acids

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Annually 700,000 to 1 million new cases of neglected tropical diseases such as leishmaniasis occur with a mortality rate of 20,000-70,000 around the world. Additionally, nosocomial infections caused by pathogenic bacteria held in hospitals affect annually more than 1.7 million patients generating over 99,000 deaths per year in the United States. However, the latest development in drugs that target such infections have been and are currently in progress. The transition from isolating natural products to the synthesis of novel analogs continues to be the way to seek new potentially active drugs that can treat a variety of diseases, such as the ones mentioned before. Previous work in our laboratory demonstrated that 2-alkynoic acids (e.g., 2-octadecynoic acid) exhibit inhibition of the *Leishmania donovani* DNA topoisomerase IB enzymes (*Ld*TopIB) with an EC_{50} of 5.3 μM. Due to the nature of this fatty acid and its carbon chain length, we decided to synthesize novel acids not found in nature, but promising to synthesize due the nature of their structure. Brominated vinylic acids were our inspiration due to the presence of the halogen moiety and its possible halogen bond with its targets as a potential drug mechanism. Aside of the halogen moiety, we proposed that the length of the aliphatic chain in the acids determines the optimal activity they may possess for each infection. A series of halogenated acids were synthesized with allyl bromide, and different alkynoic acids depending on the carbon chain length desired, by using Kotora's procedure. Among the series, the 3-allyl-2-bromo-2-nonadecenoic was synthesized and inhibited *Ld*TopIB with an EC_{50} of 7.4 μM. Comparatively, the 3-allyl-2-bromo-2-dodecenoic acid was also synthesized and displayed an IC_{50} of 28.3 μM against methicillin resistant *Staphylococcus aureus* (MRSA). These results suggest that short aliphatic chains are more adequate to treat bacteria while acids with longer carbon chains are more suitable to treat parasitic infections such as leishmaniasis. Future work will examine the bioactivity towards leishmania and *S. aureus* of other brominated fatty acids with different chain lengths.