American Foulbrood (AFB) is a devastating bacterial brood disease found in many commercial honey bee hives. Traditionally, AFB is treated with continuous general antibiotic applications of oxytetracycline. These antibiotic treatments do not cure the hive, instead they suppress the progression of the disease. The etiological agent of AFB – Paenibacillus larvae – forms infectious spores; in practice, burning infected hives is required to eradicate AFB. Plx2A is a mono-ADP-ribosylating toxin that is a major virulence factor of P. larvae. Plx2A acts by covalently modifying a key signalling protein in honey bee larval cells. This toxin activity ultimately disrupts the actin cytoskeleton in larval cells. Plx2A is an enzyme that cleaves NAD\(^+\) as a substrate molecule and transfers ADP-ribose to a nucleophilic amino acid on the target signalling factor (Asn-41 in RhoA). Experimentally, 8 flavonoids have been shown to inhibit Plx2A enzyme activity. Flavonoids are plant-based compounds that may have utility for the treatment of AFB in hives. These flavonoid inhibitors will be characterized for their ability to bind and inhibit the enzyme activity of Plx2A. We hypothesize that the flavonoids are competitive inhibitors against the enzyme activity of Plx2A. The inhibitor binding affinity (K\text{D}) will be determined for the best inhibitors of Plx2A activity using a tryptophan quenching assay. The impact of the flavonoid inhibitors on the cytoskeletal-disrupting mechanism of Plx2A will be determined with a murine macrophage assay where morphological changes can be quantified. Finally, the crystal structures for Plx2A bound to the best flavonoid inhibitors will be pursued.