Saponins have been used as adjuvant agents for decades in vaccines and therapies, but none are as well studied or heavily used as QS-21. This achievement is notwithstanding the fact that QS-21 usage is limited by its stability, toxicity, and scarcity. These shortcomings have only pushed researchers to develop and experiment with artificial recreations of the saponin to harness its unique benefits. A considerable number of research hours have been poured into this topic, but like QS-21 there is a shortcoming here as well. The number of articles that look at QS-21 interactions with the bilayer or the conditions under which QS-21 will interact appeared as scarcely as QS-21 itself. In this work, we used molecular dynamic simulations to study how QS-21 interacts with the plasma membrane also known as the cell bilayer. To gain a proper understanding of the interactions, we created multiple systems designed to address a certain set of questions. Most of these systems are large lipid-cholesterol systems made from dipalmitoyl-phosphatidylcholine (DPPC), dioleoyl-phosphatidylcholine (DOPC), or distearoyl-phosphatidylcholine (DSPC) mixed with cholesterol with differing numbers of QS-21 molecules to investigate how the saponin interacts with the bilayer. Others were reference systems of QS-21 and counterions to understand QS-21 self-interactions. Lastly, some were designed for free energy difference calculations to quantify which bilayer composition was most favourable. We aim to provide an atomic-level understanding of which QS-21 and bilayer interactions that can be used by experimentalists and theoreticians to develop better ways of studying QS-21 themselves by combining these results together.