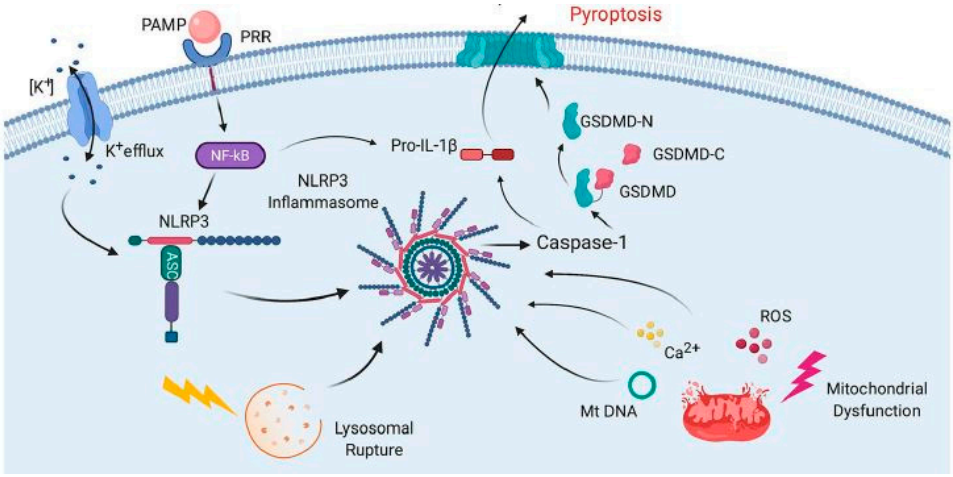

Figure S1. Mechanisms of inflammasome activation. The activation in general relies on two signals. First, a Pathogen-Associated Molecular Patterns **(**PAMP) binds to a pattern recognition receptors (PRR), resulting in synthesis of NLRP3 and pro-IL-1β. Then a second signal causes inflammasome assembly, leading to the activation of Caspase-1, and processing pro-IL-1β into IL-1β and pyroptosis. The second signal may come from a variety of pathways, including K^+ efflux, lysosomal rupture or mitochondrial dysfunction. This results in the release of ROS, Ca^{2+} and mitochondrial DNA (mtDNA), all of which have been shown to activate the inflammasome. Pyroptosis occurs as a result of Caspase-1-mediated cleavage of GSDM-D at the linker region of GSDM-D. Following GSDM-D cleavage, the amino terminus of GSDM-D (GSDM-D-N) forms a non-selective pore at the cell membrane through which IL-1β is then released. (From [6], with permission).

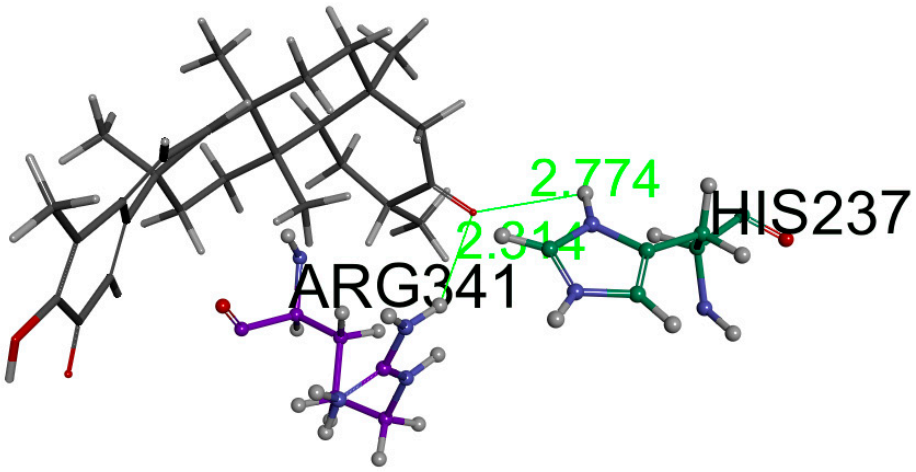

Figure S2. Atomic display of tingenone pose 1 related to Figure 5. The non methide-quinone carbonyl establishes H-bonds to the donor imidazole ring of His237 and the donor guanidino group of Arg341, 2.774 Å and 2.314 Å, respectively.

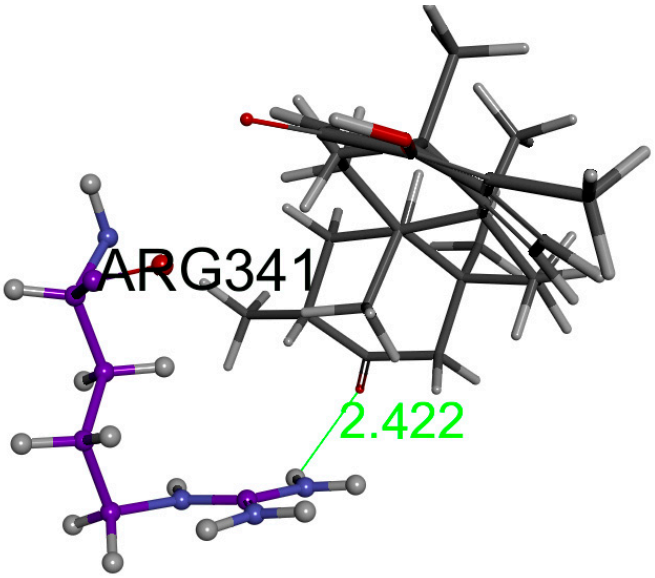

Figure S3. Atomic display of tingenone pose 5 related to Figure 7. The non methide-quinone carbonyl establishes a H-bond with the guanidino group of Arg341, 2.422Å.

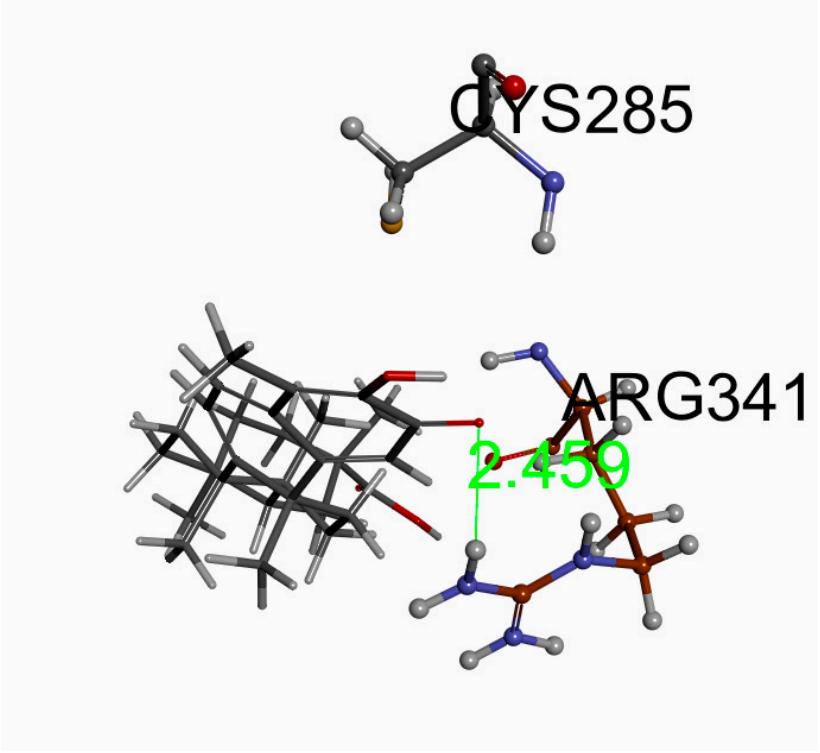

Figure S4. Atomic display of pristimerin docking pose 4 related to Figure 9. The non methide-quinone carbonyl establishes with donor guanidino a H-bond Arg341, 2.459 Å. Although Cys285 is close to pristimerin methide-quinone ring, a π-sulfur interaction is not obvious.