Coronaviruses can cause fatal respiratory diseases in humans and are responsible for the most recent worldwide outbreak of the Middle East Respiratory Syndrome (MERS) that claimed more than 400 lives. However, no anti-coronavirus drug is currently available. In this study, resveratrol, a natural compound commonly found in some plants such as grapes, raspberries, and peanuts, was evaluated for any anti-coronavirus activity in an in-vitro cell culture system. In this system, when the cells are infected with a recombinant coronavirus that expresses a green fluorescence protein, virus infection and replication can be monitored in real time by observing the green fluorescence under a microscope. It was found that resveratrol completely blocked virus replication at a concentration of 25 µg/ml or higher. The 50% inhibitory concentration (IC50) was estimated to be 5.5 µg/ml. Importantly, when virus-infected cells were treated with resveratrol starting as late as 6 hours following infection, resveratrol still exhibited significant inhibitory effects on virus replication. These results demonstrate that resveratrol is potentially a potent anti-coronavirus drug that can be further developed for treatment of coronavirus-caused diseases.