The Se–S Bond at the Frontline: Exploring the Biological Activity of Organoselenium Compounds Against SARS-CoV-2 and Beyond

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Abstract

The chemistry of selenium–sulfur (Se–S) bonds is crucial for redox control and enzyme functionality, though their overall biological role remains insufficiently understood. Compounds containing selenium, especially those with Se–S linkages, show notable reactivity with thiols, affecting protein behavior and cellular responses to oxidative stress. This research utilizes such properties to examine the antiviral activity of selenium-based molecules against SARS-CoV-2. Due to the virus's ability to form immune-resistant variants, alternative treatments targeting conserved viral proteins like the main protease (Mpro) are urgently needed. A collection of benzisoselenazolones and diselenides was tested for Mpro inhibition, followed by in vitro assays to determine antiviral activity. Mechanistic understanding was achieved using density functional theory (DFT), molecular docking, and molecular dynamics simulations, identifying important interactions between proteins and ligands. Additionally, a bio-organic model was constructed to explore how these selenium compounds react with biologically relevant thiols, offering valuable data on their metabolic behavior. New findings from various biophysical techniques will be reported, providing enhanced understanding of the interaction between organoselenium molecules and Mpro, helping to elucidate their mode of action and antiviral promise.

Besides their immediate therapeutic value, the results also underscore the evolutionary significance of Se–S interactions in biology, emphasizing their role in maintaining redox balance and mediating host-pathogen dynamics. By linking basic chemical principles with applied virology, this work contributes to the informed development of innovative selenium-centered drugs.