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Harnessing The Therapeutic Potential of Selenium

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In recent years, selenium has garnered significant interest in biomedical research, particularly through its integration into bioisosteres, and chemical sensors. Despite these promising developments, selenium remains significantly underutilized as a redox-responsive trigger for drug delivery and prodrug activation. In contrast, sulfur—selenium's lighter chalcogen counterpart—has been extensively utilized in these contexts, primarily through disulfide-based motifs that exploit sulfur's well-characterized redox properties and metabolic behavior. Notably, disulfides function exclusively through reductive activation, and no broadly established oxidative triggering mechanism exists using sulfur. While selenium and sulfur share similar oxidation states and fundamental reactivity, selenium exhibits distinct chemical behavior arising primarily from its larger atomic size and higher polarizability. These distinctions give rise to unique reactivity profiles that can be strategically leveraged in the design of next-generation prodrugs, enabling unprecedented levels of reactivity and selectivity not achievable with traditional approaches. Here, we report the development of selenium-based prodrugs that harness this unique reactivity to enable dual responsiveness to both reducing and oxidizing conditions. This work highlights how selenium's divergent chemical behavior can unlock entirely new and more versatile avenues for controlled drug release and targeted delivery—offering a breakthrough strategy to overcome longstanding limitations of traditional sulfur-based systems.