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Targeting Airway Hyperresponsiveness and Antioxidant Responses in Airway Smooth Muscle by Ginger-inspired Compounds: A Potential Novel Therapeutic Class for Asthma

Abstract

Nearly 10% of the Western population have asthma, and its prevalence is on the rise world-wide. Thus, anesthesiologists and intensivists frequently care for these patients. Perioperative complications, like bronchospasm, are more common in poorly controlled asthmatics and increase patient morbidity and mortality. Despite therapy, 40% of asthma patients have inadequate symptom control, and many turn to alternative therapies, like ginger, which has been used in many cultures for centuries to treat various ailments including those of the respiratory tract. We have previously demonstrated that purified components of ginger, such as 6-shogaol (6S), can relax airway smooth muscle (ASM) by inhibiting an enzyme, phospholipase C (PLC), that is crucial in producing a calcium surge and muscle contraction. However, orally administered ginger components, including 6S, are rapidly metabolized, and, only recently, we showed that those metabolites also retained bioactive properties of the parent compounds, and are able to relax large (human) and small (mouse) airways. Additionally, ginger components such as 6S may also regulate the antioxidant pathway that includes several enzymes, one of which is heme oxygenase 1 (HO-1), whose dysregulated response to oxidative stress is an important contributor to asthma pathology. This proposal will study the effects of 6S metabolites and synthetic derivatives based on those metabolites on airway smooth muscle bronchoconstriction and antioxidant pathways. These studies will expand our knowledge of the mechanism of action of 6S metabolites and synthetic derivatives in these two complementary pathways in airway smooth muscle. Furthermore, our in vivo experiments will demonstrate their potential as much-needed novel asthma therapies.