



News Release

FOR RELEASE May 19, 2013, 2:00 p.m. EST

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Session A108: Poster Discussion Session - Poster Presentation

Sunday, May 19, 2013, 2:00 p.m. – 4:30 p.m.

Location: Room 201 C (200 Level) Pennsylvania Convention Center

Ginger Compounds May Be Effective in Treating Asthma Symptoms

ATS 2013, PHILADELPHIA — Gourmands and foodies everywhere have long recognized ginger as a great way to add a little peppery zing to both sweet and savory dishes; now, a study from researchers at Columbia University shows purified components of the spicy root also may have properties that help asthma patients breathe more easily.

The results of the study will be presented at the ATS 2013 International Conference.

Asthma is characterized by bronchoconstriction, a tightening of the bronchial tubes that carry air into and out of the lungs. Bronchodilating medications called beta-agonists (β -agonists) are among the most common types of asthma medications and work by relaxing the airway smooth muscle (ASM) tissues. This study looked at whether specific components of ginger could help enhance the relaxing effects of bronchodilators.

“Asthma has become more prevalent in recent years, but despite an improved understanding of what causes asthma and how it develops, during the past 40 years few new treatment agents have been approved for targeting asthma symptoms,” said lead author Elizabeth Townsend, PhD, post-doctoral research fellow in the Columbia University Department of Anesthesiology. “In our study, we demonstrated that purified components of ginger can work synergistically with β -agonists to relax ASM.”

To conduct their study, the researchers took human ASM tissue samples and caused the samples to contract by exposing them to acetylcholine, a neurotransmitting compound that causes

bronchoconstriction. Next, the researchers mixed the β -agonist isoproterenol with three separate components of ginger: 6-gingerol, 8-gingerol or 6-shogaol. Contracted tissue samples were exposed to each of these three mixtures as well as unadulterated isoproterenol and the relaxation responses were recorded and compared.

At the conclusion of their study, the researchers found that tissues treated with the combination of purified ginger components and isoproterenol exhibited significantly greater relaxation than those treated only with isoproterenol; of the three ginger components, 6-shogaol appeared most effective in increasing the relaxing effects of the β -agonist.

Once they were able to demonstrate that the ginger components enhanced the relaxing effects of the β -agonist, they turned their attention to learning why. First, the researchers wanted to determine if the ginger components might work by affecting an enzyme called phosphodiesterase4D (PDE4D). Previous studies have shown that PDE4D, which is found in the lungs, inhibits processes that otherwise help relax ASM and lessen inflammation. Using a technique called fluorescent polarization, they found that all three components significantly inhibited PDE4D.

Next, the study looked at F-actin filaments, a protein structure which previous studies have shown plays a role in the constriction of ASM, and found that 6-shogaol was effective in speedily dissolving these filaments.

“Taken together, these data show that ginger constituents 6-gingerol, 8-gingerol and 6-shogaol act synergistically with the β -agonist in relaxing ASM, indicating that these compounds may provide additional relief of asthma symptoms when used in combination with β -agonists,” Dr. Townsend noted. “By understanding the mechanisms by which these ginger compounds affect the airway, we can explore the use of these therapeutics in alleviating asthma symptoms.”

Dr. Townsend and her colleague, Dr. Charles Emala, hope future studies will enable them to gain a better understanding of the cellular mechanisms that facilitate ASM relaxation and to determine whether aerosol delivery of these purified constituents of ginger may have therapeutic benefit in asthma and other bronchoconstrictive diseases.

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** Please note that numbers in this release may differ slightly from those in the abstract. Many of these investigations are ongoing; the release represents the most up-to-date data available at press time.*

Abstract 38824

Active Constituents Of Ginger Potentiate β -Agonist-Induced Relaxation Of Airway Smooth Muscle

Type: Scientific Abstract

Category: 03.10 - Smooth Muscle: Airway (RSF)

Authors: E.A. Townsend, Y. Zhang, C. Xu, R. Wakita, C. Emala; Columbia University - New York, NY/US

Abstract Body

Rationale: Asthma prevalence has steadily increased and is characterized by bronchoconstriction. Bronchodilators are the first-line therapy to reverse airway obstruction by relaxing airway smooth muscle (ASM). Asthma therapies include β -agonists that induce bronchodilation by activating adenylyl cyclase, increasing cAMP and activating protein kinase A. Despite improved understanding of the pathogenesis of asthma, few novel therapeutics have been approved for targeting asthma symptoms in the last 40 years. This highlights the need for new therapies that relax contracted airways while also augmenting traditional therapies. We demonstrated that purified components of ginger can relax ASM. By understanding the mechanisms by which these compounds exert their effects on the airway, we can explore the use of these phytotherapeutics in alleviating asthma symptoms. We hypothesized that unique chemical components of ginger have bronchorelaxant properties and work synergistically with β -agonist signaling to relax ASM.

Methods and Results: Epithelial-denuded human ASM tissue (deidentified; exempt from Columbia's IRB) was contracted with acetylcholine in organ baths. ASM tissues were then relaxed dose-dependently with β -agonist, isoproterenol (100 pM – 10 μ M, half-log increments). The tissues were treated concurrently at 300 pM isoproterenol with vehicle, 6-gingerol, 8-gingerol, or 6-shogaol (100 μ M). Significant potentiation of isoproterenol-induced relaxation was observed with each of the ginger constituents. 6-shogaol showed the largest leftward shift in the EC₅₀ for isoproterenol. Purified phosphodiesterase 4D enzyme, the prominent isoform in the lung, was used to assess PDE inhibitory action of the ginger constituents using fluorescent polarization analyses. 6-gingerol, 8-gingerol, and 6-shogaol (100 μ M, 15 min) significantly inhibited PDE4D compared to vehicle control (0.2% DMSO), the PDE4-selective inhibitor, rolipram (10 μ M) and non-selective PDE inhibitor, IBMX (250 μ M) were used as positive controls. β -agonist induced depolymerization of actin via a PKA-HSP20-dependent pathway contributes to ASM relaxation. In primary human ASM cells transiently transfected with RFP-actin, treatment with 6-gingerol, 8-gingerol, or 6-shogaol showed acute (within seconds) dissolution of F-actin filaments. This was not due to PKA phosphorylation of HSP20.

Conclusions: Taken together, these data show synergistic effects of ginger constituents 6-gingerol, 8-gingerol, and 6-shogaol with β -agonist in relaxing ASM. This may be attributed to increased cAMP due to PDE4D inhibitory activity. Additionally, these compounds stimulate actin depolymerization through a novel PKA-independent pathway, providing another pathway for potentiation with β -agonists. These compounds may provide additional relief of asthma symptoms when used in combination with β ₂-agonists and highlight novel use of phytotherapeutics in the treatment of obstructive lung disease.