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ORIGINAL ARTICLE

Farnesol, a sesquiterpene alcohol in essential oils, ameliorates serum allergic antibody titres and lipid profiles in ovalbumin-challenged mice

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KEYWORDS
Allergic asthmatic inflammation;
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Abstract
Background: Farnesol, a natural sesquiterpene alcohol in essential oils, was found to have potential for alleviating massive inflammation, oxidative stress and lung injury. However, effects of farnesol supplementation on allergic asthma remain unclear.
Objectives: To clarify the puzzle, this work investigates the effects of farnesol on allergic asthma using an ovalbumin (OVA)-sensitised and challenged mouse model.
Methods: Farnesol was administered to OVA-sensitised and challenged mice for 5 weeks. Three farnesol doses, namely 5, 25 and 100 mg farnesol/kg BW/day, non-sensitised control, dietary control, and positive control (dexamethasone 3 mg/kg BW by gavage) were included. Sera and bronchoalveolar lavage fluids from the experimental mice were collected to measure farnesol concentrations, serum lipid profiles, antibody titres, differential cell counts or Th1/Th2 cytokines levels.
Results: The results showed that farnesol supplementation increased serum farnesol concentration dose-dependently, significantly increased ($P < 0.05$) OVA-specific IgG2a/IgE antibody titre ratios, but decreased total IgE levels. Farnesol supplementation markedly reversed the aberrated LDL-c/HDL-c and HDL-c/TC ratios in the sera of asthmatic mice, suggesting that farnesol supplementation might ameliorate serum lipid profiles in the OVA-sensitised and challenged mice.
Conclusion: Our results evidenced that farnesol supplementation might improve serum allergic antibody titres and lipid profiles in asthmatic mice.

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Introduction

Allergic asthma is a chronic airway inflammatory disease with increased infiltration of eosinophils into the airway, over-expression of T helper type 2 (Th2) cytokines such as IL-4, IL-5 and IL-13, elevated serum immunoglobulin (Ig)E levels, mucus hyper-secretion by goblet cells, resulting in airway hyper-responsiveness and inflammation.[1,2] Patients of allergic asthma have an imbalance between Th1 and Th2 immune responses; nowadays it is recognised that allergic asthma is a Th2-skewed disease.[3] Several studies have indicated that Th2-skewed diseases can be effectively improved by enhancing Th1-favoured immune responses,[4] or by mediating Th2 subpopulation and eosinophils differentiation, as well as modulating B cell proliferation and IgE isotype switching.[5,6] In Th1-favoured immune responses Th1 cells play the leading role that secrete interferon (IFN)-γ, tumour necrosis factor (TNF)-α/β and interleukin (IL)-2 to inhibit over-expression of Th2 cytokines. Regulation of an imbalance between Th1 and Th2 immune responses in allergic asthmatic patients using bioactive compounds is a good strategy for ameliorating an allergic injury.

Although numerous drugs such as steroids, leukotriene inhibitors, mast cell stabilisers and β_2-adrenergic agonists have been utilised to treat asthma currently,[7] about 50% patients remain difficult to improve and even suffer from adverse side effects, further suggesting that these drugs are not suitable for patients with severe asthma.[8] It is most important to prevent the early manifestations of the disease and thus to suppress its evolution into severe asthma.[9] It is therefore necessary to seek other new therapeutic methods or alternative agents for improving allergic asthma. The morbidity of allergic asthma is increasing and becoming a problem of public health in the world. Natural plant compounds are suggested for use in preventing or treating asthma.[5] Traditional herbal medicines, health foods and their possible active compounds that can be ingested daily shed a light for preventing or treating allergic asthma.

Farnesol is a sesquiterpene alcohol that exists widely in fruits such as peaches, vegetables such as tomatoes and corn, herbs such as lemon grass and chamomile, as well as the essential oils of ambrette seeds, and citronella.[10,11] It can also be produced endogenously in animal cells from farnesyl pyrophosphate, the precursor of squalene in the cholesterol biosynthetic pathway.[10] Farnesol has been widely used in cosmetics, pharmaceuticals, industrial materials and as a material for carotenoid, tocopherol or co-enzyme Q10 syntheses.[12,13] Recently, farnesol was found to have potential for alleviating massive inflammation, oxidative stress and lung injury induced by intratracheal instillation of cigarette smoke extract in rats.[14] Farnesol also ameliorated 1,2-dimethylhydrazine induced oxidative stress, inflammation and apoptosis in the colon of Wistar rats.[11] Most recently, farnesol was found to exhibit a relative Th1-inclination and anti-inflammatory property to immune cells in vitro, suggesting that it may be applied to improve Th2-skewed allergic asthma.[15]

Ovalbumin (OVA) is a known allergen to induce allergic asthma. OVA sensitisation and challenge to experimental mice could induce both systemically and locally allergic inflammation responses including changes in serum OVA-specific antibody titres and cells infiltration into the airways.[16] To investigate the possible effects of farnesol supplementation on allergic asthma, an OVA-sensitised and challenged asthmatic mouse model was established in the present study. Farnesol at different doses was administered to the OVA-sensitised and challenged mice for 5 weeks. Changes in serum farnesol concentrations and antibody tilters, as well as differential cell counts and Th1/Th2 cytokines levels in bronchoalveolar lavage fluid (BALF) of the experimental mice were measured.

Materials and methods

Sample

Farnesol ($C_{15}H_{26}O$) is a natural sesqui-terpenoid in essential oils found in many plants.[11] In this study, farnesol (Sigma, St. Louis, MO, USA) was purchased at the highest available purity (>95%, a mixture of isomers).

Experimental animals and dietary groups

The experimental feed was prepared according to the recommendation of the American Institute of Nutrition AIN-76 that satisfies the nutritional requirement for mouse growth and varied only in farnesol composition.[17] Three farnesol doses, including low dose (0.003%), medium dose (0.017%) and high dose (0.067%), were added into the AIN76 feed.[18] The components of each feed were prepared by thoroughly mixing and storing at $-20\,^{\circ}C$. Approximately, 3 g of AIN76 feed were consumed by each individual mouse with 20 g body weight (BW) per day. The designed farnesol low (FL), medium (FM), and high (FH) doses corresponded to 5, 25 and 100 mg farnesol/kg BW/day, respectively. It could be estimated that farnesol supplementation at the indicated doses might not produce significant energy in vivo. The energy contribution of each experimental diet was 67.5% from carbohydrate, 20.8% from protein and 11.7% from fat. The calorie density of each diet was 3.85 kcal/g. The animal use protocol listed below was reviewed and approved by the Institutional Animal Care and Use Committee (IACUC), National Chung Hsing University, Taiwan, ROC. Generally, both male and female animals were administrated into different animal models. Male and female animals have similar immune responses in many situations; however only female mice were used in this study.[19] Unfortunately, in the present study the experimental mice were not controlled for testing during a particular phase of the oestrous cycle. The female BALB/cByJNarl mice (7 weeks old) were obtained from the National Laboratory Animal Center, National Applied Research Laboratories, National Science Council in Taipei, ROC and maintained in the Department of Food Science and Biotechnology at National Chung Hsing University College of Agriculture and Natural Resources in Taichung, Taiwan, ROC. The animal room was kept on a 12-h light and 12-h dark cycle. Constant temperature ($25 \pm 2\,^{\circ}C$) and ambient humidity (50–75%) were maintained. The mice were housed and kept on a chow diet (laboratory standard diet, Diet MF 18, Oriental Yeast Co., Ltd., Osaka, Japan) to acclimate for 1 week before feeding the experimental diet. After