

Letter to the Editor

Therapeutic Effects of Inhaled 1,8-Cineole on Allergic Airway Inflammation

With great interest, we read the recent article by Bastos *et al.*, [1] in which a monoterpen (1,8-cineole) suppresses allergic features in ovalbumin-sensitized guinea pigs. The authors implied in the Introduction that there are no previous studies that have examined the potential therapeutic effects of inhaled administration of 1,8-cineole on airway inflammation including asthma. We have previously shown that intratracheal (i.t.) administration of volatile constituents of a rosemary extract, in which 1,8-cineole is abundantly contained (approximately 43% weight percentage), ameliorates airway inflammation elicited by house dust mite allergen [2]. Although there are some differences between their study and ours regarding experimental design such as animal species (guinea pig *versus* mouse), allergens (ovalbumin *versus* crude extract of house dust mite), sensitization style (i.p. *versus* i.t.), duration (3 *versus* 6 weeks) etc., the results are similar as to overall trend, characterized by reduction in the number of inflammatory leucocyte recruitment in bronchoalveolar lavage recovery with relatively weaker effects on lung cytokine (chemokine) expression. We have demonstrated that volatile constituents of a rosemary extract can significantly attenuate both eosinophilic and neutrophilic airway inflammation, whereas it does not decrease allergy-related cytokine and chemokine levels such as interleukin-5, eotaxin, macrophage inflammatory protein-1 α , and thymus and activation-regulated chemokine in both lung homogenates and bronchoalveolar lavage fluids except for macrophage inflammatory protein-1 α in the bronchoalveolar lavage fluids ($p < 0.05$ *versus* house dust mite control; recent observation) [2 and Inoue K, Takano H, Shiga A & Fujita Y, unpublished data]. Therefore, when combining the studies of Bastos *et al.* with ours, 1,8-cineole and/or volatile constituents of a rosemary extract may influence chemotactic factors for polymorphonuclear leucocytes other than the cytokines and chemokines examined in these studies, for example, adhesion molecules, lipid mediators and/or anaphylatoxins (C3a and C5a) which should be clarified in the future.

Of note, on the other hand, we have confirmed that volatile constituents of a rosemary extract significantly suppress lung IL-13 expression [2]. IL-13 reportedly plays an essential role in the pathogenesis of airway hyper-responsiveness in asthma [3]. Accordingly, the phenomenon found by Bastos *et al.* in their *ex vivo* study that 1,8-cineole calms carbamylcholine-elicited airway responsiveness may be explained, in part, through the repressing effect of 1,8-cineole on lung IL-13 expression.

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Another important bioactivity of terpenes is their anti-oxidative property. A previous headspace analysis has shown that 1,8-cineole is most attributable to the anti-oxidative potential of volatile constituents of a rosemary extract we used among the five compounds contained [4]. In their study, Bastos *et al.* reported that 1,8-cineole treatment significantly reduced enzyme activity of myeloperoxidase, a generator of reactive oxygen species such as hydrogen peroxide, in the bronchoalveolar lavage fluids. Thus, it is attractive to speculate that their study has partly shown anti-oxidative potential of 1,8-cineole as well as a previous study implicating the potential of its anti-allergic efficacy on the allergic guinea pig model.

Taken together, the study by Bastos *et al.* extends previous studies [2] and suggests that inhaled 1,8-cineole can be a candidate in the future for the treatment of allergic airway diseases including bronchial asthma.

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References

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