

**The Effects of Exogenous Phospholipids on Airway Function
in Asthmatics**

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Abstract

The studies described in this thesis examined whether application of lecithin to the oropharyngeal mucosa in asthmatics protected against bronchoconstriction and cough induced by airway challenge with inhaled mannitol powder. An initial study was conducted with 24 physician diagnosed adult asthmatics to determine the safety, convenience and suitability of mannitol airway challenge. Mannitol airway challenge was found to be a safe and convenient type of airway challenge in asthmatics, but marked interindividual variation in the degree of bronchoconstriction evoked by mannitol airway challenge was evident which confirmed previous reports.

Twelve suitable adult asthmatics (6 men and 6 women) who showed a fall in the forced expiratory volume in one second (FEV_1) of $\geq 10\%$ after mannitol airway challenge successfully completed the second study. This entailed airway challenges with equivalent doses of inhaled mannitol on two separate days after gargling with water or an aqueous suspension of soy lecithin in random order. Soy lecithin was used because of its high phospholipid content (1,680 mg of phosphatidylcholine, 960 mg of phosphatidylinositol). Prechallenge lung function values were reproducible over the two experimental test days. The results suggest that oropharyngeal application of phospholipids can protect asthmatics against mannitol airway challenge in addition to improving baseline lung function, and that these effects may be sustained for at least an hour. The mechanisms for this protective effect have not been elucidated but it is plausible that attenuated reflex bronchoconstriction and cough resulting from the masking and desensitizing of oropharyngeal neural receptors by adhering phospholipids was responsible. Thus, the findings of this study provide new evidence suggesting that oropharyngeal afferent pathways may be involved in the reflex regulation of airway function and cough during asthmatic exacerbations. The findings also suggest that oropharyngeal phospholipids may have therapeutic potential in the clinical management of asthma by providing the airways with sustained protection against factors that commonly provoke worsening asthmatic symptoms such as inhaling cold dry air and exercise, as well as alleviating upper airway irritation and cough in other common disorders such as viral respiratory tract infections. These findings and the implications arising from them warrant further investigation.

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List of Abbreviations

ATS:	American Thoracic society
BTS:	British Thoracic Society
CDR:	Cough-to-dose ratio
COPD:	Chronic Obstructive Pulmonary Disease
C2:	Cough threshold
DPPC:	Dipamitoylphosphatidylcholine
FEV ₁ :	Forced Expired Volume in 1 second
FVC:	Forced Vital Capacity
GINA:	Global Initiative on Asthma
HDR:	Higher Degree Research
ICS:	Inhaled Corticosteroids
MDP:	Mannitol Dry Powder
MMEF:	Mid Maximum Expiratory Flow
PEFR:	Peak Expiratory Flow Rate
PC:	Phosphatidylcholine
PI:	Phosphatidylinositol
PE:	Phosphatidylethanolamine
PS:	Phosphatidylserine
PD5:	Dose of inhaled mannitol required to produce 5% decreases in baseline
PD10:	Dose of inhaled mannitol required to produce 10% decreases in baseline
PD15:	Dose of inhaled mannitol required to produce 15% decreases in baseline
RDR:	Response-to-dose ratio
VC:	Vital Capacity