

ANALYSIS OF ENDOGENOUS PARTICLES IN EXHALED AIR

Akademisk avhandling

som för avläggande av medicine doktorexamen vid Sahlgrenska akademien vid Göteborgs universitet
kommer att offentligens försvaras fredagen den 15 april 2011 kl. 9.00
Medicinaregatan 16, Göteborg

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Avhandlingen baseras på följande delarbeten:

- I. Almstrand AC, Ljungström E, Lausmaa J, Bake B, Sjövall P, Olin AC. **Airway monitoring by collection and mass spectrometric analysis of exhaled particles.** *Anal Chem*, 2009, 81 (2), 662-668
- II. Almstrand AC, Josefson M, Bredberg A, Lausmaa J, Sjövall P, Larsson P, Olin AC. **Phospholipids in exhaled particles from subjects with asthma and healthy controls.** *Revised version submitted to Eur Respir J*
- III. Almstrand AC, Bake B, Ljungström E, Larsson P, Bredberg A, Mirgorodskaya E, Olin AC. **Effect of airway opening on production of exhaled particles.** *J Appl Physiol*, 2010, 108:584-588
- IV. Almstrand AC, Evert L, Olin AC, Bredberg A, Larsson P, Mirgorodskaya E. **Collection and determination of glutathione in exhaled air.** *Manuscript.*

Göteborg 2011



UNIVERSITY OF GOTHENBURG

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Abstract:

Exhaled air contains non-volatile particulate material from the respiratory tract. The precise location in which exhaled particles are formed is unknown, and details on their chemical content are scarce. The aim of this work was to chemically characterize and to study the mechanisms of formation of endogenous particles in exhaled air.

A new instrument for counting and sampling particles in exhaled air by impaction was developed, as a part of this thesis, at the Department of Public Health and Community Medicine, Occupational and Environmental Medicine in collaboration with the Department of Chemistry, Atmospheric Science at the University of Gothenburg. In the first instance, exhaled particles were analyzed using time-of-flight secondary ion mass spectrometry (TOF-SIMS), which is a very sensitive technique for surface analysis. This method was also used to compare the composition of particles in exhaled air from subjects with asthma to that in healthy controls. Second, a method for the quantitative determination of glutathione was developed and applied in the analysis of exhaled particles and exhaled breath condensate. In parallel to chemical analysis, the hypothesis that particles are formed during the reopening of closed airways was tested by measuring particle number concentrations in the air exhaled by healthy volunteers performing different breathing maneuvers.

This is the first study involving chemical analysis of particles in exhaled air. TOF-SIMS analysis revealed that exhaled particles contain several phospholipids (phosphatidylcholine, phosphatidylglycerol and phosphatidylinositol). These lipids are characteristic of the pulmonary surfactant which is present in the respiratory tract lining fluid (RTLFL) that covers the epithelium in the alveoli and the airways. Using this method, it was found that the TOF-SIMS spectra of the particles exhaled by healthy subjects differed from those of the particles exhaled by subjects with asthma. These differences were attributed to differences in the abundance of phosphatidylcholine and phosphatidylglycerol between the two groups. By using the newly-developed method for glutathione analysis, it was possible to demonstrate the presence of glutathione in exhaled particles for the first time. The method was used to compare glutathione levels in exhaled particles to those in exhaled breath condensate; it was found that analysis of particles was more revealing in terms of the levels of glutathione in exhaled air. Studies of particle formation showed that deep exhalations to residual volume (RV) caused significantly higher concentrations of particles in the subsequent exhalation than did exhalations to functional residual capacity (FRC). This supports the theory that film rupture during airway reopening after airway closure is an important mechanism of particle formation.

The results of these studies show that particles in exhaled air can be sampled by impaction, that surfactant phospholipids and glutathione are part of their chemical composition, and that they are largely formed in the peripheral airways, where airway closure takes place.

Keywords: exhaled particles, time-of-flight secondary ion mass spectrometry, OPLS, airway closure, exhaled breath condensate, glutathione

ISBN: 978-91-628-8250-1