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Exhaled breath barbotage: A new method of pulmonary surfactant dysfunction assessing

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ABSTRACT

Exhaled air contains submicron droplets of alveolar lining fluid (ALF), which are generated in the small airways of human lungs and are in fact ALF micro-samples. The trapping of these droplets makes it possible to collect a native material from respiratory tract in a non-invasive manner, which holds great promise for lung diagnostics. In this work, we present an aerosol droplet sampling technique based on the exhaled breath barbotage (EBB) procedure. The proposed technique offers a unique opportunity to accumulate pulmonary surfactant (PS), a major constituent of ALF, on a liquid surface. The Wilhelmy plate method was used to measure the variation of the surface pressure over the surface area for the EBB samples collected in a Langmuir trough. A data processing algorithm was derived to evaluate the surface pressure (π) – surface concentration (Γ) isotherm from the raw data. With this algorithm, one can restore the isotherm even in the case when the amount of surfactant adsorbed on the surface is unknown. The ($\pi - \Gamma$) isotherms found for the samples collected in the groups of healthy volunteers and patients with pulmonary tuberculosis were compared with the isotherms obtained for artificial PS. It has been established that the isotherms measured for healthy people and artificial surfactant coincide, and the isotherms obtained in the TB group have lower inclination, which is indicative of a lower surface activity. The EBB method developed in this study can be used as a diagnostic tool for assessment of the functional status of PS in screening tests and subsequent treatment.

1. Introduction

With every single exhalation, the human lung emits an aerosol containing small droplets of alveolar lining fluid (ALF) (Fairchild & Stampfer, 1987; Papineni & Rosenthal, 1997; Fritter et al., 1991; Holmgren, Ljungstrom, Almstrand, Bake, & Olin, 2010; Papineni & Rosenthal, 1997; Schwarz, Biller, Windt, Koch, & Hohlfeld, 2010, 2015). Although the mechanisms responsible for droplet formation are still unclear, the most probable one is associated with the processes of closure and reopening of the airways during normal breathing (Haslbeck, Schwarz, Hohlfeld, Seume, & Koch, 2010; Johnson & Morawska, 2009). At the end of exhalation the fluid layer, lining bronchioles, can collapse due to the Rayleigh instability, which results in plug formation and airway closure. During the subsequent inhalation the rupture of the fluid film is accompanied by droplet formation. The studies of the concentration and size distribution of aerosols (Fairchild & Stampfer, 1987; Papineni & Rosenthal, 1997; Fritter et al., 1991; Holmgren et al., 2010; Papineni & Rosenthal, 1997; Schwarz et al., 2010,2010; Schwarz, Biller, Windt, Koch, & Hohlfeld, 2015) have demonstrated that an

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exhaled air of a healthy human during normal breathing contains, on average, a few submicron droplets per cubic centimeter. Both characteristics show a high inter-subject variability and a strong dependence on breathing maneuvers and physical activity during sampling (Fairchild & Stampfer, 1987; Schwarz et al., Schwarz, Biller, Windt, Koch, & Hohlfeld, 2010, 2015).

Over the last years, the studies of exhaled aerosols have attracted increasing interest, since the emitted droplets represents micro-samples of the ALF. The analysis of the droplet composition has revealed the presence of all ALF components in undiluted concentration (Olin, 2013; Tinglev et al., 2016; Ullah, Sandqvist, & Beck, 2015). From this point of view, the trapping of exhaled droplets provides a new non-invasive method of obtaining the native material from the respiratory tract. The results of separate droplet analysis were presented in a few recent studies of ALF samples collected by various capturing systems. The studies demonstrated detectable differences in droplet composition and size distribution between the groups of subjects with chronic obstructive pulmonary disease (Schwarz et al., 2015; Almstrand et al., 2009), asthma (Schwarz et al., 2015), cystic fibrosis (Almstrand et al., 2009) or pulmonary tuberculosis (Wurie, Lawn, Booth, Sonnenberg, & Hayward, 2016) and healthy people. These findings indicate a high potential of the exhaled aerosol droplet analysis as a tool for identifying and monitoring pathological processes in the ALF.

In this paper, we present a new method, which is based on the exhaled breath barbotage (EBB) procedure, for aerosol droplets capturing, which is accompanied by pulmanory surfactant (PS) accumulation on a liquid surface. Being the main component of the ALF, the PS is a surface-active lipoprotein complex produced in a human lung by type II alveolar cells (Notter, 2000). The most important function of PS is to reduce the alveolar surface tension, which results in increasing pulmonary compliance and allows the lung to inflate much more easily, reducing thereby the work of breathing. Moreover, the unique ability of the compressed PS layer to decrease surface tension to a very low, almost zero, level prevents as well atelectasis (collapse of lung alveoli) at the end of expiration. A variety of pulmonary diseases (such as asthma, pneumonia, adult respiratory distress syndrome, tuberculosis, etc.) are able to cause surfactant deficiency or to change its composition, which results in reduced surface activity, provoking alveolar instability and development of inflammatory processes in the lung (Hohlfeld, 2002; Baritussio, 2004; Wright, Notter, Wang, Harmsen, & Gigliotti, 2001; Willson, Chess, & Notter, 2008; Schwab et al., 2009; Raghavendran, Willson, & Notter, 2011; Chroneos et al., 2009; Chimote & Banerjee, 2005; Hasegawa & Leblanc, 2003; Wang et al., 2008). The study of PS surface-active properties is an effective way to monitor the functional status of a lung surfactant system. In our investigation, we show that the accumulation of the captured aerosol droplets on the saline surface in the Langmuir trough makes it possible to examine the surface-active properties of the collected material immediately after the barbotage procedure. Based on the proposed data processing algorithm, we construct the surface pressure (π) - surface concentration (Γ) isotherm using the raw experimental data. Finally, we analyze the ($\pi - \Gamma$) isotherms obtained for the samples collected in the groups of healthy volunteers and patients with lung tuberculosis and compare them with the isotherm measured for the artificial PS.

2. Materials and methods

2.1. Samples collection method

2.1.1. Exhaled breath barbotage

We use the procedure of barbotage (or bubbling) of exhaled air through liquid to capture ALF droplets. Complex vortex air motion that occurs in the course of bubble formation is accompanied by abrupt variation in the direction and value of flow velocity, especially near the bubble surface, where the flow decelerates sharply. Under such conditions, the small but heavy droplets suspended in a moving air do not follow fluid streamlines and this causes their collision with the bubble surface. The mechanical contacts of the droplets with the bubble surface initiate their spreading, which leads to the adsorption of PS. The latter accumulates at the upper liquid-air interface as the bubbles come to the surface. The adsorbed layer can be further investigated by tensiometric methods.

This idea lies behind the design of the collecting system shown in Fig. 1. This system consists of a Teflon tube connected to a saliva trap, through which a patient breathes out. The other end is immersed in the saline solution within Langmuir trough. The inner diameter of the tube is a compromise between two requirements. It should be large enough to help the patients breathe easier during the procedure. On the other hand, the smaller is the diameter of bubbles, the more frequent are the contacts between the droplets and the bubble surface, and the higher is the efficiency of droplet collection. The inner diameter of the tube is 3 mm.

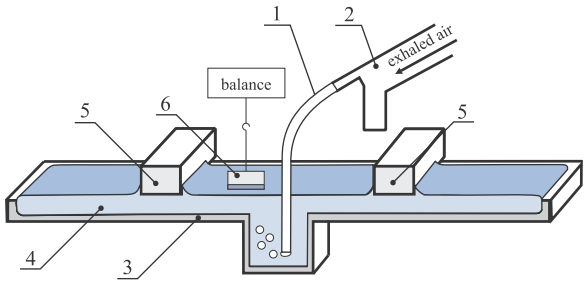

Fig. 1. Experimental set up for exhaled breath barbotage and examination of the dynamic surface-active properties of samples: 1 - Teflon tube, 2 - saliva trap, 3 - Teflon trough, 4 - saline subphase, 5 - Delrin barriers, and 6 - platinum Wilhelmy plate.