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Enhanced Condensational Growth in the Upper Airways Induced by Specific Climatic Conditions as a Major Factor for Increased Deposition of Inhaled Aerosols: Short Report †

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Abstract: While significant advances have been made in understanding the aerosol dosimetry in the last decades, many aspects of adverse effects on respiratory health as weather conditions and environmental or occupational air contaminants require further development. It was found that weather patterns can play a significantly more important role in the deposition of ambient submicron aerosols in human airways than previously assumed and unusually high underestimation of deposition efficiency may be typical for most classical studies and approaches.

Keywords: air pollution; airways; respiratory health; hygroscopic growth

1. Enhanced Condensational Growth (ECG) as A Pulmonary Drug Delivery Method

It is well known that only a very limited deposition of aerosol particles in the submicron range (100 nm–1000 nm) occurs in the respiratory tract, due to a lack of sufficient inertia and Brownian motion for efficient deposition [1,2]. It is also commonly accepted that a small size increase due to the hygroscopic growth under normal conditions in human airways does not lead to a significant increase in the deposition of submicron aerosols [3–8].

In fact, the low pulmonary deposition of inhaled nano- and submicron particles is one of the primary limitations of the current generation of inhaled pharmaceuticals. The pharmaceutical delivery of nano- and submicron particles to the respiratory system offers a unique opportunity, because such particles possess a small size with a large surface area, together with altered dissolution properties compared to micrometer-sized particles. However, pulmonary deposition is low, with approximately 70% of the particles exhaled [9–12].

To solve this problem the enhanced condensational growth (ECG) method was proposed and used as a respiratory drug delivery platform [13,14]. This approach consists of creating short-term supersaturated conditions (when relative humidity (RH) of air inside airways exceeds 100 %) in the upper airways during inhalation. Under such conditions, the condensation of water vapor onto droplet surfaces causes the significant condensational growth of inhaled submicron particles up to 3–7μm, which should ensure full lung retention [15,16].

To create the supersaturation in the airways the inhalation of warm saturated air a few degrees above body temperature were used in ECG platform: inhalation of warm-humid air of T = 40 °C, RH = 100%, and hot-humid air of T = 47 °C, RH = 100% [13,14,16].

2. Enhanced Condensational Growth (ECG) as A Problem in An Everyday Life

It is obvious that supersaturated conditions in the airways may be induced by specific environmental conditions in our everyday life, potentially leading to enhanced deposition of ambient submicron aerosols and particulate matters in the respiratory tract. This effect would be similar to the deposition of submicron drug particles in the pulmonary drug delivery platform where ECG is used. Xi et al. [16] concluded that high deposition rates of inhaled aerosols in hot-humid environments, or on a hot and humid day, might indicate higher health risks to individuals than normal environmental conditions or on a regular day. Therefore, they summarized that people under such conditions would have a higher possibility of developing respiratory symptoms and connected such conditions with manufacturing workplaces (such as industries of paper, textile, mining, food, industries), humidified hospital units, and specific tropical geographical locations.

However, the most interesting and important point is the observation on the onset of supersaturation in the nasopharyngeal/oropharyngeal regions and upper airways during cool/cold air inhalation (T < 10–20˚C) which was indicated in the other studies [17–24]. Because such conditions like cold weather and cold seasons could be associated with the possibility of the onset of supersaturation in the human airways. Thus, there is a real risk of a higher possibility of developing respiratory symptoms associated with enhanced deposition of inhaled aerosols due to the effect of ECG in the airways for millions of people in the world.

3. National Ambient Air Quality Standards of Inhaled Particles and ECG

National ambient air quality standards of inhaled particles use well-known standard methods of estimation of inhaled doses of ambient aerosols. For reference, the International Commission on Radiological Protection (ICRP) deposition model [25] and Multiple-Path Particle Dosimetry Model (MPPD) [26] commonly used for this aims.

The problem of the classical view on the deposition of ambient aerosols in the airways exist in the postulate that under any external or environmental conditions, the conditions inside human airways will be 'normal' (RH = 90–99.5 %; T = 30–37˚C) (see the related review in [27]). However, as was shown above the conditions in the airways can be supersaturated (RH > 100%), and it can lead to effects of unlimited ECD and induce enhanced deposition of inhaled aerosols and particulate matter in the airways. Furthermore, Haddrell et al [28] concluded that: "the sensitivity to the ambient RH is typically not considered in lung inhalation models; in the literature review made during the preparation of this manuscript, no articles discussing this point were found." Such a state of affairs has not changed in recent years. Thus, nearly all computational fluid dynamics (CFD) studies do not consider the possibility of air oversaturation/supersaturation in the airways and the nearly all CFD studies do not consider even sensitivity to the change in ambient RH.

4. ECG and Hygroscopic Growth in the Airways: What Is the Difference?

There are many existing studies that use the hygroscopic growth model on computational lung aerosol dynamics, – and this is not a problem for the estimation of health risks connected with hygroscopic growth. Almost all known studies use such models to meet their aims: health risks assessments, pulmonary drug delivery, aerosol deposition, national ambient air quality standards, and etc. For reference, under normal conditions in the airways (RH = 90–99.5%; T = 30–37˚C), hygroscopic and condensational growth of inhaled particles are limited by a growth factor of 1.3-1.7 (with a maximum of 4 in rare cases) [3–8] . While the ECG under supersaturated conditions (RH > 100%) in the airways which could be induced by cold weather can lead to practically unlimited growth of inhaled particles (growth factor of more than 10–20).

That's why the ECG effects allow to significantly increase the deposition of inhaled submicron aerosols of pharmaceuticals in the airways: an exhaled fraction of aerosol decreases from 70% to 0% [13,14,16]. It is obvious that the deposition rate of ambient aerosols and particulate matter in the submicron size range for which ECG is most pronounced can significantly increase as it happens with aerosols in pulmonary drug delivery platforms where ECG used.

4. Conclusion

Air pollution and deposition of ambient aerosols in human airways are associated with many detrimental health effects. National ambient air quality standards of inhaled particles are mainly based on the particulate concentration and sizes. While the impact of the climatic or weather conditions on the possibilities potentially leading to effects of ECG and enhanced deposition of ambient submicron aerosols in the respiratory tract is not taken into account.

Thus, a significant scientific gap can exist within the present knowledge on the estimation of deposition of ambient submicron aerosols in the human airways under different climatic conditions (especially for T < 20 ˚C). The presented work improves our picture on the effect of atmospheric conditions on the humidity driven growth and enhanced deposition of submicron aerosols inside the human airways.

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