In vitro efficiency measurements of the deposition of pMDI generated aerosols in a realistic central airway geometry

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The deposition efficiency of the different inhaled pharmaceutical products in the targeted region of the human respiratory tract is often presented as the results of an in vivo measurement (Newmana, 2006). The drawback is that these results have generally poor resolution and the factors affecting the deposition are not adequately controlled. Consequently, we could get an integrated view of the particle deposition but the in vivo methods are inappropriate for performing deeper analysis of the effects of every individual parameter which is involved in the total deposition process.

If we intend to investigate all the parameters which can influence the deposition process – like the MMAD (mass median aerodynamical diameter) of the inhaler generated aerosol cloud or the initial velocity of the drog particles, the geometry of the actual human airway tract, the breathing waveform of the investigated person, but we could mention the enviromental temperature also etc. – then the implementation of an in vitro experiment would be a good choice for reaching our goals. The amount of the particles that were sucked through the hollow airway model and deposited on the inner surface can be measured by different methods. The ratio of the deposited particles in the targeted area and the particles that were introduced into the human respiratory tract model can be measured in several ways. One way is the preparation of radioactive seeding particles. The intensity of the radiation emitted from the target area is proportional to the concentration of the deposited seeding particles on the investigated surface (Heenan, 2004). Another method is to rinse the deposited particles and measure the concentration of the solution we prepared. These methods are quite cumbersome if we would like to perform a large number of deposition experiments in the same research infrastructure.

In case of in vitro deposition experiments in human airways the Raman or fluorescence spectroscopy has been used relatively infrequently although these methods are suitable for direct detection of the active substance of the inhaled drogs. The reason for this contradiction is the pure scattered Raman intensity from the sample in these types of measurements. The detectation volume, which is determinated by the diameter of the excitation beam and the parameters of the sensing optics, can be increased limitedly. The particle concentration on the investigated surface area is usually not enough for Raman spectroscopy measurements. An other problem is the scaling of the detected signal by one or two order of magnitude, because usually there is not enough scattered Raman intensity.

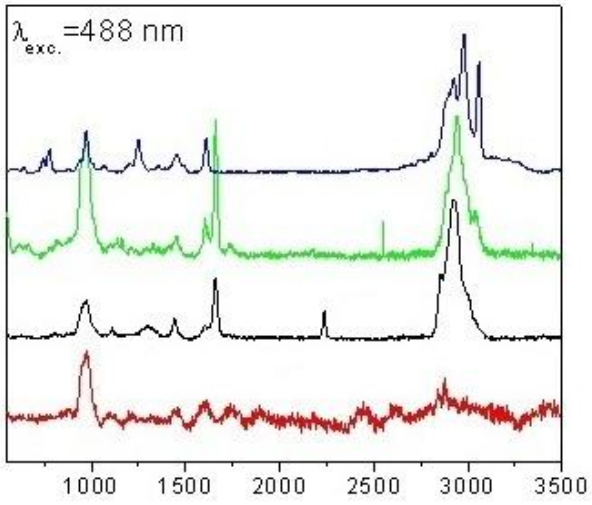

Figure 1. Raman spectra of four different metered dose inhaler. The peaks of the active ingredients are well-defined.

We designed and developed an experimental layout for measuring the efficiency of the inhaled drug deposition by Raman spectroscopy in a human respiratory airway model made by rapid prototyping based on CT image series. The complete system contains a pulmonary waveform generator which is able to increase the correlation between the in vivo and the in vitro measurements. The digital version of the respiratory model is suitable for the comparision of the results by CFD (computational fluid dynamics) simulation technics.

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