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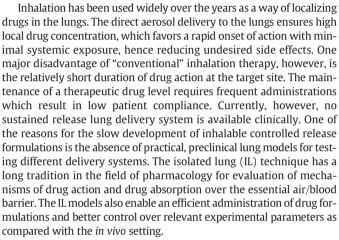
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Cover story Isolated lung model for assessing drug absorption from PLGA microparticles



The study performed by Beck-Broichsitter and his colleagues expands our understanding of the drug release and absorption processes of lung-delivered sustained release formulations [1]. A rabbit IL model was used to assess the performance of poly(lactide-co-glycolide) (PLGA) microparticles loaded with the drug sildenafil which is used for treating pulmonary hypertension. Administration of the free drug via inhalation, however, necessitates frequent daily inhalations, due to its short duration of action (<1-2 h following aerosol delivery). Sildenafil-loaded PLGA microparticles (particle size of ~5 µm) with distinct drug release profiles were prepared by vibrational spray-drying and administered to the airspace of the IL model using a dry powder insufflator. Drug delivery vehicles demonstrated an in vitro sildenafil release with a half-life of 15-200 min. The release kinetics of employed microparticles correlated well with the glass transition temperature and the molecular weight of the utilized polymers/polymer blends. The carriers composed of PLGA of lower molecular weight (and glass transition temperature) resulted in a faster in vitro drug release. The authors then followed the lung-specific absorption profiles, which differentiated the diverse sildenafil-loaded polymeric microparticles according to their in vitro release characteristics (half-life of 5-230 min).

The study by Beck-Broichsitter et al. has provided important information on sustained lung delivery of medications. The IL model enabled a precise analysis and discrimination of drug release from the distinct sildenafil-loaded polymeric microparticles, even though the differences in temporal delivery rate were comparably small (minute scale). The ex vivo sildenafil absorption also correlated well with the observed in vitro drug release kinetics. At the same time, however, the IL model discloses potential limitations of the technique in the analysis of longacting medications. As compared with typical in vivo studies, IL preparations offer comparatively short duration of study time (~6 h) due to deterioration of the isolated organ. Furthermore, the IL model needs to be adapted to the specific properties of the utilized drug (e.g., total recovery). In this respect, addition of albumin to the perfusion medium improves the analysis of absorption and distribution characteristics of hydrophobic drugs, such as sildenafil, simulating the expected plasma protein binding [2]. Most importantly, it still remains open whether the ex vivo findings are directly transferrable to the in vivo behavior of prolonged release formulations in the lungs. The drug release data for diverse PLGA vehicles in intact animals or humans often differ from what was observed during in vitro testing.

The study by the Beck-Broichsitter team presents valuable information for further development of inhalable controlled release formulations. The preclinical IL technique was able to differentiate diverse sildenafil-loaded PLGA microparticles with their own *in vitro* release characteristic. The IL model will continue to improve to expand its applicability to various drugs and delivery systems, which in turn will enhance our knowledge for accelerated development of inhalable sustained release formulations for clinical applications.

References

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