Loaded Macroaggregated Albumin Particles (MAA) as a Lung Targeting Drug Delivery System for the Treatment of Pulmonary Embolism

Marta Bergamo1, Tullio V. F. Esposito1, Thomas Rønnemoes Bobak1,2, Katayoun Saatchi1, Urs Häfeli11

1 Faculty of Pharmaceutical Sciences, University of British Columbia, Canada, 2 SUND Department of Pharmacy, University of Copenhagen, Denmark

Graphic Summary

- Empty radioactive macroaggregated albumin particles (MAA) are clinically used for the diagnosis of pulmonary embolism.
- MAA are administered intravenously and they can passively target lungs due to their size.
- MAA show uneven lung perfusion if thrombi, *i.e.* clots, are trapped in the pulmonary vasculature, leading to pulmonary embolism.

**AIM:** Preparation of loaded MAA with the fibrinolytic drug Tiplaxtinin as targeted delivery system.

**Methods**

**Synthesis**

- Bulk synthesis in controlled temperature and pH environment using bovine serum albumin (BSA), Tiplaxtinin, and FeCl₂

**In vitro** characterization

- Size distribution by mastersizer
- Drug loading by HPLC-UV
- Plasma stability by native PAGE gel (12%)  

**In vivo** acute toxicity

- Intravenous administration of radioactive MATi particles (111In-MATi) into healthy mice
- Radioactivity accumulation in the organs of interest measured by gamma counter

**Results**

**Size Distribution**

- Fig. 1 MAA (control), MATi, and 111In-MATi showed comparable size distribution with an average diameter of 23.6, 23.4, and 21.6 μm, respectively. MATi particles had an average 37% drug loading.

**Plasma stability**

- Fig. 2 111In-MATi showed good stability in human plasma, with 80% albumin still intact after 24 h incubation at 37° C.

**Conclusions**

This study serves as proof-of-concept for the potential use of MATi particles as a targeted drug delivery system for the treatment of pulmonary embolism. Further studies are undergoing to assess *in vitro* and *in vivo* efficacy of the particles.

**Fig. 3** *In vivo* accumulation of 111In-MATi in relevant organs following intravenous administration into healthy mice. Upon injection, 111In-MATi highly accumulated in the lungs (left). When measure full organ activity, lower amounts of particles were found also in excretion organs (right). Both doses did not show overtly signs of toxicity.

**Fig. 2** 111In-MATi showed good stability in human plasma, with 80% albumin still intact after 24 h incubation at 37° C.

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