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

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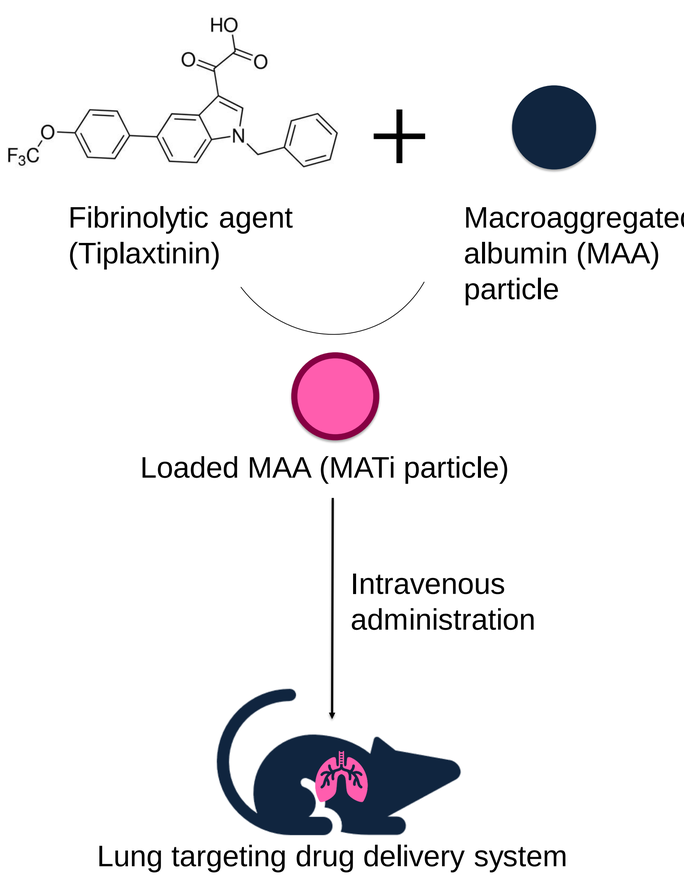
Graphic Summary



Introduction

- Empty radioactive macroaggregated albumin particles (MAA) are clinically use 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[1].

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

- Treatment of pulmonary embolism often involves infusion of thrombolytic agents. Due to the systemic exposure of the patients to the drug, it can cause considerable side effects[2].
- A targeted delivery system would result in less systemic exposure, lower dose, thus decreased side effects.

Methods

Synthesis

- Bulk synthesis in controlled temperature and pH environment using bovine serum albumin (BSA), Tiplaxtinin, and $FeCl_2$

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 (^{111}In-MATi) into healthy mice
- Radioactivity accumulation in the organs of interest measured by gamma counter

Results

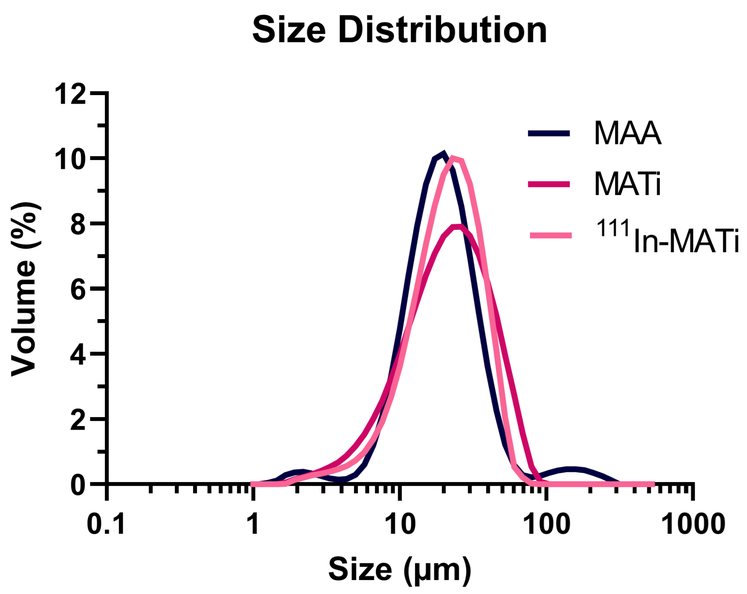


Fig. 1 MAA (control), MATi, and ^{111}In-MATi showed comparable size distribution with an average diameter of 23.6, 23.4, and 21.6 µm, respectively. MATi particles had an average 37% drug loading.

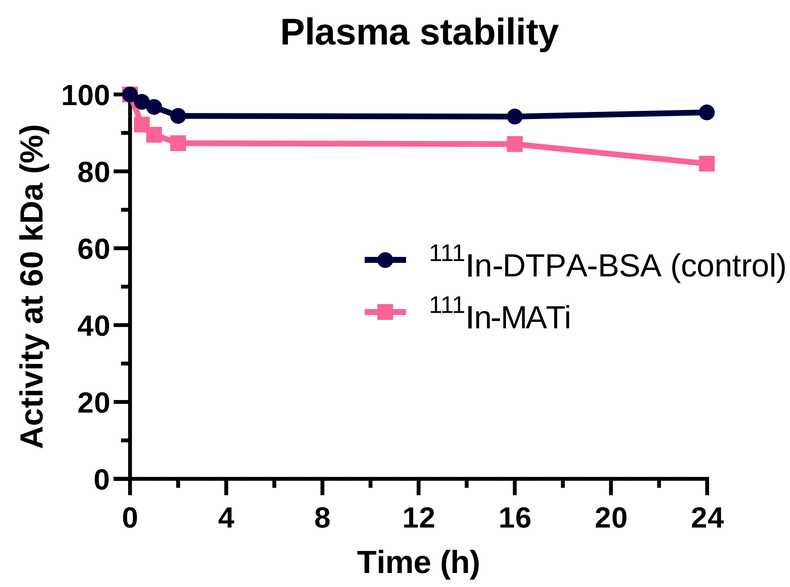


Fig. 2 ^{111}In-MATi showed good stability in human plasma, with 80% albumin still intact after 24 h incubation at 37° C.

Fig. 3 *In vivo* accumulation of ^{111}In-MATi in relevant organs following intravenous administration into healthy mice. Upon injection, ^{111}In-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.

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.

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[1] Bajc M., et al., EJNMM, 2019. *46*(12): p. 2429-2451
[2] Marshall P.S., et al., Journal of Intensive Care, 2011. *26*(5): p. 257-294

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