Electrosprayed Dry Powder Inhaler (DPI) Formulations of Bevacizumab for the Treatment of NSCLC

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INTRODUCTION

- Lung cancer remains the leading cause of cancer-related deaths worldwide, with non-small cell lung cancer (NSCLC) representing around 85% of cases and remaining a key focus of research.[1]
- Pulmonary drug delivery via DPIs offers targeted treatment for NSCLC with faster onset, improved safety, and better patient compliance compared to oral or IV routes.[2]
- Electrospray can be used to produce uniform particles <5 µm for optimal lung deposition.
- Bevacizumab inhibits tumour growth by blocking VEGF-A, preventing angiogenesis and reducing the tumour's blood supply.[3]

AIM

- To optimise an inhalable dry powder formulation of bevacizumab-loaded microparticles via coaxial and triaxial electrospraying, enabling localised lung delivery for targeted inhibition of VEGF-driven angiogenesis in NSCLC (Figure 1).

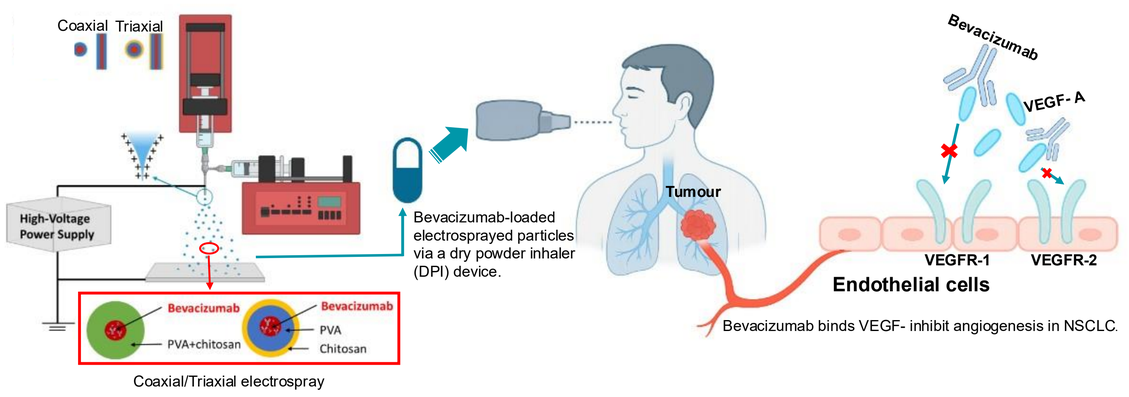

Figure 1. Electrosprayed bevacizumab microparticles for inhalable NSCLC therapy.

METHODS

1. Formulation Optimisation
2. Morphology
3. Characterisation
4. Bevacizumab Quantification
5. Pulmonary Potential
6. *In Vitro* Mucoadhesiveness
7. Cell Viability
8. Cellular Uptake
9. Angiogenesis Inhibition Assay

2. Scanning/Transmission electron microscopy (SEM/TEM) and confocal microscopy.

4. Bicinchoninic Acid (BCA) assay/Enzyme-linked immunosorbent assay (ELISA).

5. SEM: individual particle size; Mastersizer: D_{50}; Next generation impactor (NGI): Mass Median Aerodynamic Diameter, MMAD.

6. Alcian Blue staining method; Type IS mucin.

7. CellTiter-Glo® 3D Cell Viability Assay and LIVE/DEAD™ Viability kit (EVOS/Flow Cytometry); Cell line: A549.

9. Cellular scratch (HUVEC) and Chorioallantoic membrane (CAM) model.

RESULTS & DISCUSSION

- SEM images confirm all eight formulations produce dispersed, spherical microparticles ranging from 0.7 to 1.1 µm. (Figure 2).
- Bevacizumab encapsulation ranges from 52.52 ± 5.04% to 62.49 ± 8.91%, with Tri-PVA+CS+Bev showing highest loading.
- Pulmonary potential: all formulations (except Co-PVA+CS and Co-PVA+CS+Bev) fall within the optimal range of < 5 µm for pulmonary delivery.

RESULTS & DISCUSSION (CONTINUED)

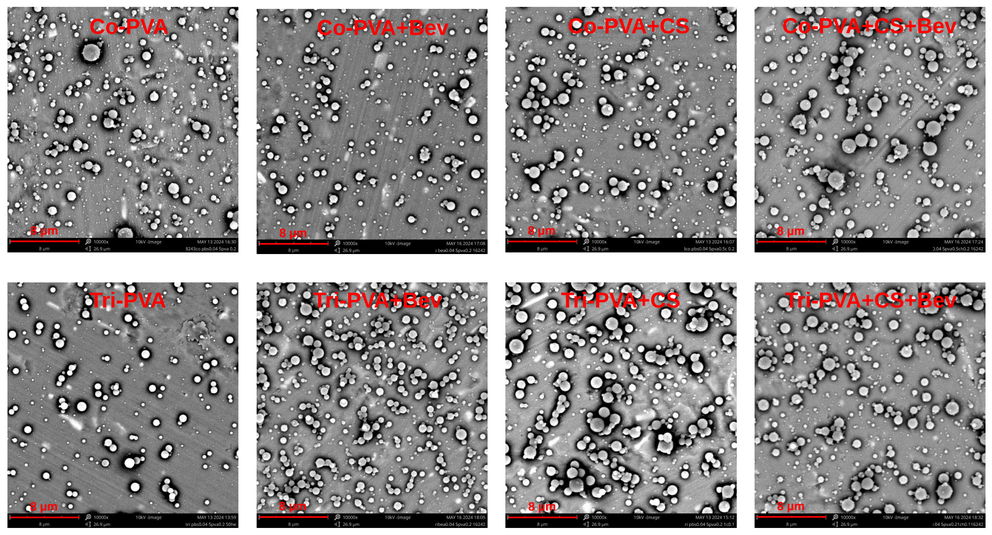

Figure 2. SEM images of eight formulations at 10,000× magnification.

- Cell Viability (Figure 3): Bevacizumab (10–500 µg/mL) shows no significant cytotoxicity in A549 cells over 72 h, while formulations cause slight cytotoxicity at high doses after 48 h.

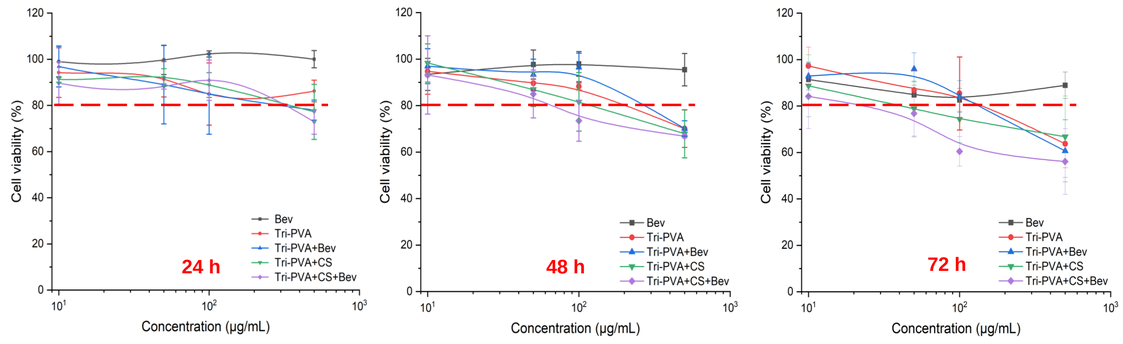

Figure 3. CellTiter-Glo® 3D Cell Viability Assay results for tri-formulations at (A) 24 h, (B) 48 h, and (C) 72 h.

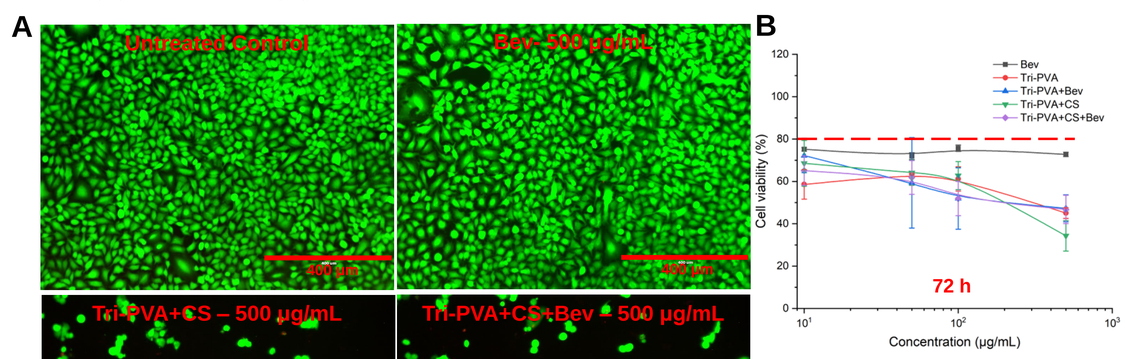

Figure 4. LIVE/DEAD™ Viability Kit results for (A) EVOS fluorescent imaging and (B) cell viability of tri-formulations at 72 h using flow cytometry.

- LIVE/DEAD™ Viability Kit indicates low toxicity for bevacizumab alone, but significant toxicity from the formulation at 72 h (EVOS & flow cytometry, Figure 4).
- Microparticle encapsulation enhances uptake at both 4/24 h, with Tri-PVA+CS+Bev as the most effective one (Figure 5).

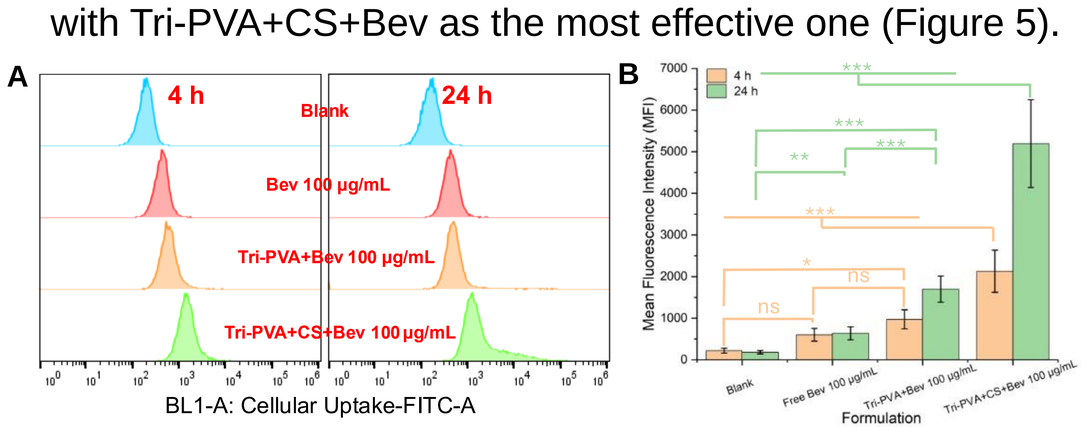

Figure 5. Cellular uptake results of Tri-formulations (A and B) at 4 and 24 h. Single factor ANOVA with post hoc Tukey's test. ** P ≤ 0.01; *** P ≤ 0.001.

CONCLUSION & FUTURE WORK

We present dry powder formulations of bevacizumab-loaded microparticles with pulmonary potential, showing some cytotoxicity at high doses after 48 h. Future work includes anti-angiogenic testing via HUVEC scratch assay and CAM model.

Reference

[1] Burt, J.R. *et al.* BMC Med. 2025.

[2] Wang B. *et al.* Materials Today Bio. 2024.

[3] Kazazi-Hyseni F, Beijnen JH, Schellens JH. Oncologist. 2010

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