Locust bean gum microparticles as carriers for lung delivery of bacterial lysates

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Key message

Aerodynamically suitable microparticles containing bacterial lysates aimed at preventing respiratory infections can be obtained by spray-drying

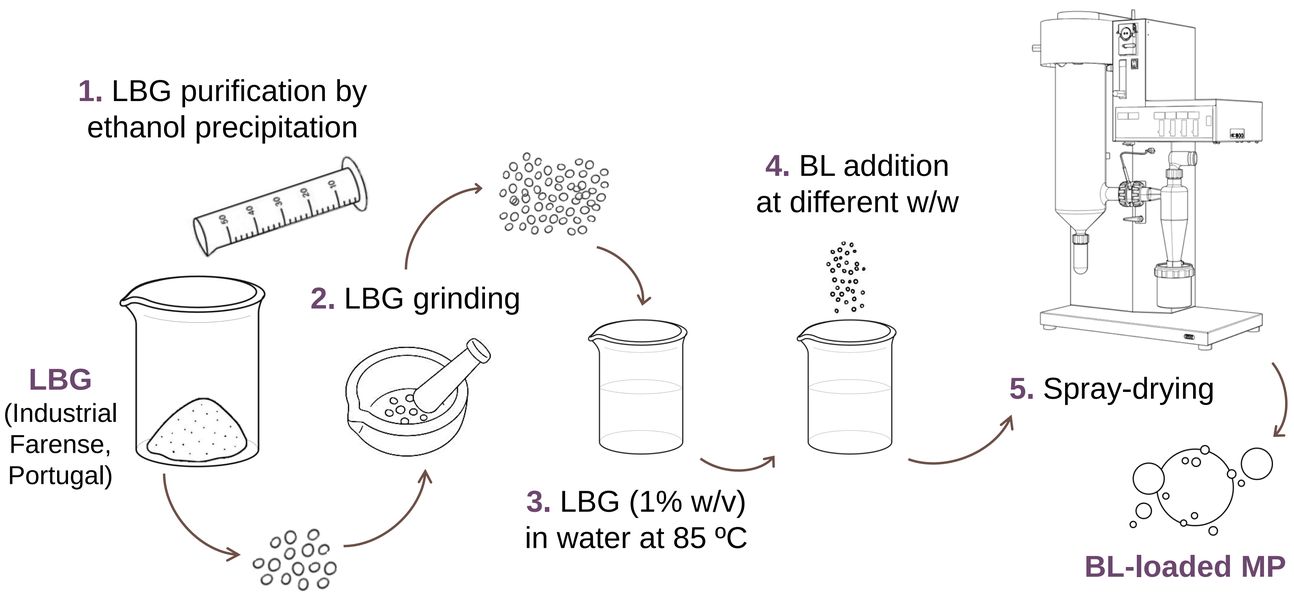
Background

- The prevention of respiratory infections is an important goal in public health
- Bacterial lysates (BL) are often prescribed as parenteral immunomodulators[1]
- Poor mucosal immunity has challenged their use and called for better efficacy[1]
- The inhalation of BL can potentially provide improved immunization

Strategy

- Inhalable spray-dried locust bean gum (LBG) microparticles (MP) are the proposed antigen carriers for delivering BL to the lungs
- LBG is a galactomannan with high affinity for macrophages[2], possibly owning to its mannose content
- Potential interaction with mannose surface receptors of antigen presenting cells populating the bronchus-associated lymphoid tissue is expected[3]
- The induction of an immune response in the local infection site coupled with a systemic effect is anticipated

Material and Methods



Spray Drying Yield

$$\text{Spray Drying Yield (\%)} = \frac{\text{Product microparticles weight}}{\text{Total solids weight in feed}} \times 100$$

Association Efficiency (AE) and Loading Capacity (LC)*

*AE and LC calculated based on protein quantification using the Bradford protein assay

$$\text{AE (\%)} = \frac{\text{loaded BL mass}}{\text{theoretical BL protein mass}} \times 100$$

$$\text{LC (\%)} = \frac{\text{loaded BL protein mass}}{\text{total MP mass}} \times 100$$

Morphology: scanning electron microscopy (SEM)

Aerodynamics: Andersen cascade impactor (ACI) at 60 L/min with a high resistance RS01® inhaler

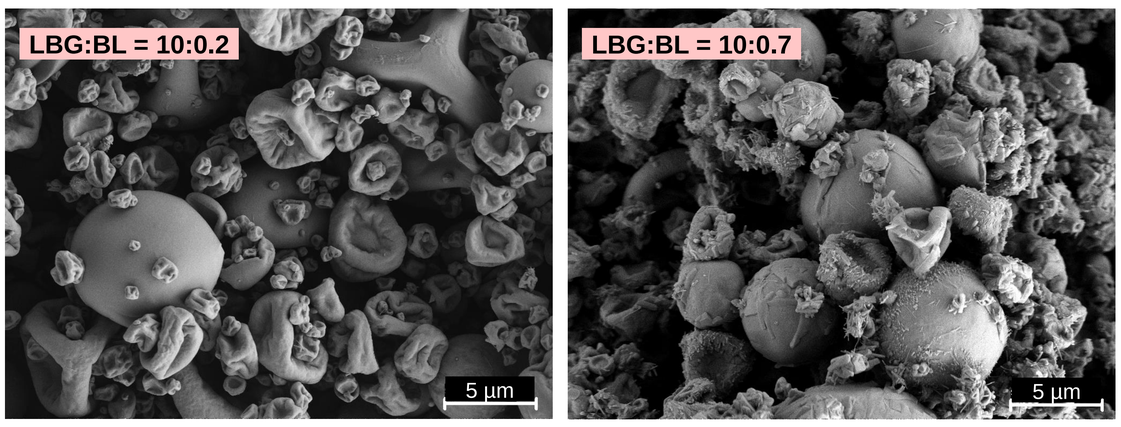
Cytotoxicity: MTT assay in A549 cells 24h exposure

Results and Discussion

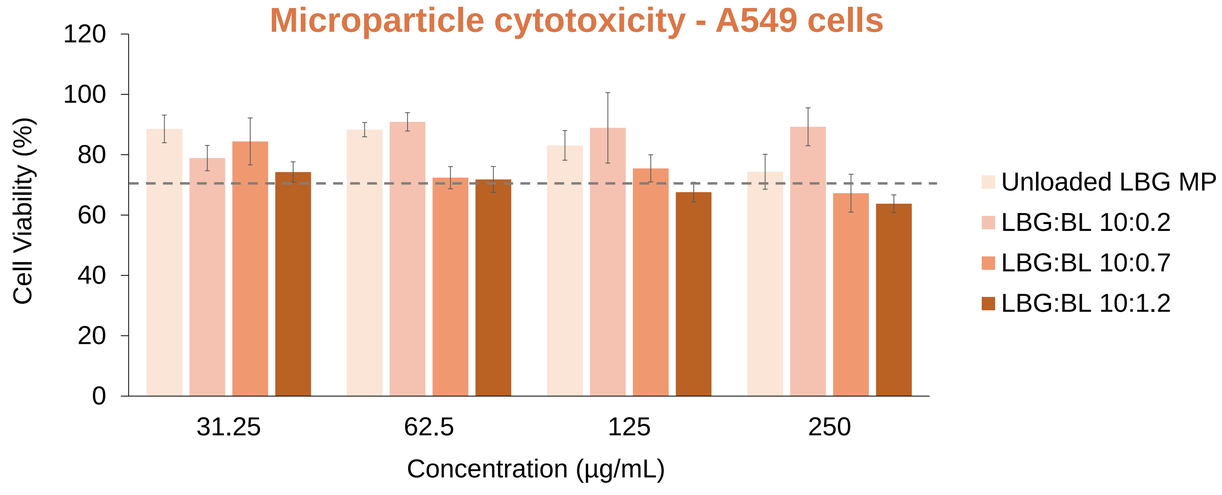
Microparticle characterization (mean ± SD)

Microparticles LBG:BL (w/w)	Spray Drying Yield (%)	Association Efficiency (%)	Loading Capacity (%)	Feret Diameter (µm)
10:0.2	60 ± 4	81 ± 7	1.9 ± 0.2	3.62 ± 4.93
10:0.7	60 ± 6	72 ± 3	2.8 ± 0.1	7.17 ± 5.27
10:1.2	56 ± 2	56 ± 2	2.7 ± 0.1	7.09 ± 5.35

Morphological evaluation



Microparticle cytotoxicity - A549 cells



Aerodynamic parameters

Microparticles LBG:BL (w/w)	MMAD (µm)	FPF (%)	GSD (µm)
10:0.2	4.6 ± 0.4	29.0 ± 3.8	1.89 ± 0.05
10:0.7	7.4 ± 0.3	13.6 ± 0.5	1.78 ± 0.23
10:1.2	8.1 ± 4.0	11.9 ± 2.7	1.52 ± 0.07

FPF: fine particle fraction; GSD: geometric standard deviation; MMAD: mass median aerodynamic diameter

Conclusions

Bacterial lysates were successfully microencapsulated by spray-drying, with adequate association efficiency. The produced microparticles are not aggregated and exhibit a convoluted shape. Microparticles LBG:BL = 10:0.2 (w/w) present appropriate aerodynamic characteristics for inhalation while also displaying an adequate toxicological profile.

References

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