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Biophysical Investigation of Biodegradable Nanoparticle Interactions with Lung Surfactant Model

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Biological Sciences
from biomolecules to the biosphere

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Introduction

Drug delivery through the lungs is an attractive route of drug administration, due to the ease in treatment, lung specific disease targeting, and bypassing of first-pass metabolism.

Here we investigated the interactions of gelatin and polybutylcyanoacrylate (PBCA) nanoparticles with model lung surfactant systems using biophysical, *in vitro* methods.

Due to the biodegradability and biocompatibility of these materials, they are being considered as building blocks for nanoparticle based pulmonary drug delivery systems.

Goals

1. Synthesize and characterize biodegradable nanoparticles and to select suitable sized nanoparticles for the study

2. Attain relevant data on nanoparticle-lipid interactions to be utilized in understanding their effects on lung surfactant

Methods

Synthesis
Gelatin nanoparticles were formulated through a two-step emulsion diffusion method. Polybutylcyanoacrylate (PBCA) nanoparticles were formulated through polymerization of the butylcyanoacrylate monomer.

Characterization
Dynamic light scattering (DLS) and Zetasizer were used to determine the size distribution of the nanoparticles which was 170.7 ± 2.3nm for gelatin and 165.3 ± 2.7nm for PBCA nanoparticles .

Model Lung Surfactant
Dipalmitoyl-phosphatidylcholine (DPPC) and dipalmitoyl-phosphatidylglycerol (DPPG) are the main phospholipid components of lung surfactant and were selected as the model system.

Surface pressure-Area Isotherms
For the control experiments the phospholipids were spread on top of an aqueous subphase. For the subsequent experiments, nanoparticles were suspended in the aqueous subphase at a concentration of 1mg/ml, and the monolayer was spread on top before compression to record changes in surface pressure.

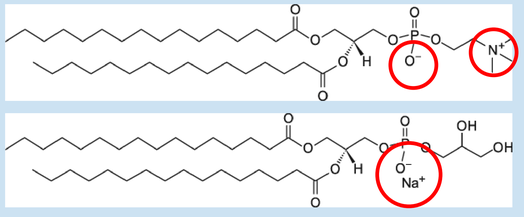

Figure 1. Structural diagram of DPPC

Figure 2. Structural diagram of DPPG

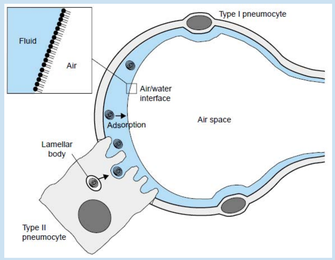

Figure 3. Diagram of alveolae and lung surfactant (Piknova et al., 2002)

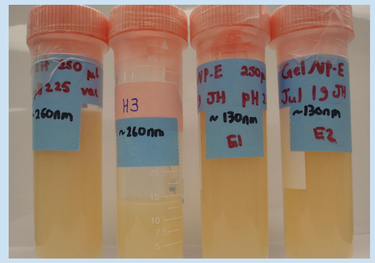

Figure 4. Gelatin nanoparticles of 260nm and 130nm.

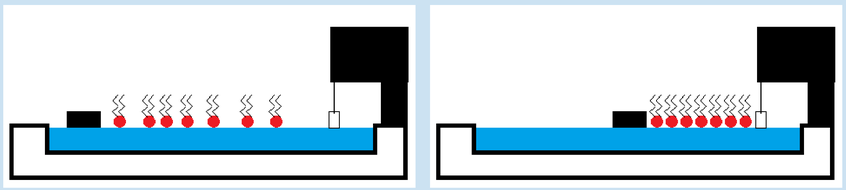

Figure 5. Illustration of lipid monolayer compression and surface pressure-area recording on Langmuir trough.

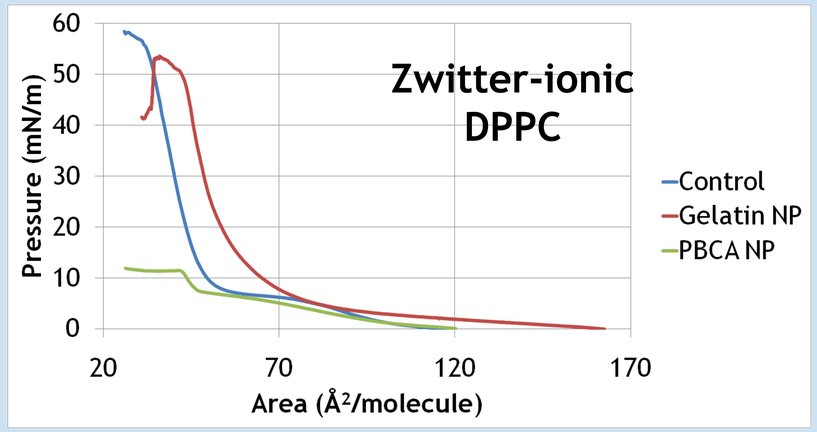

Figure 6. Surface pressure-area isotherms of DPPC monolayers in the absence and presence of both nanoparticle preparations.

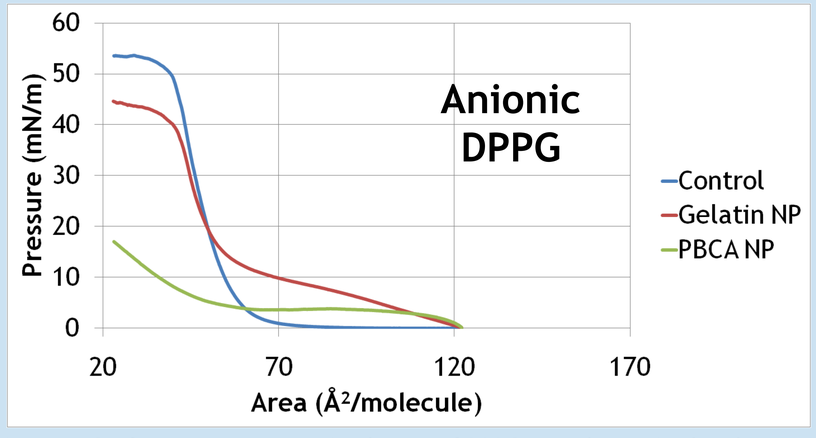

Figure 7. Surface pressure-area isotherms of DPPG monolayers in the absence and presence of both nanoparticle preparations.

Results

	DPPC	DPPG
Control	58 mN/m	53mN/m
Gelatin NP	53mN/m	45mN/m
PBCA NP	12mN/m	17mN/m

Gelatin nanoparticles weakly reduced the maximum surface-pressure of both DPPC and DPPG.

PBCA NPs dramatically reduced model surfactant stability by inducing premature film collapse.

Discussion & Conclusion

A key role of lung surfactant is maintaining the integrity of the lung during inhalation and exhalation by retaining high surface pressures.

Both controls (DPPC, DPPG) reach very high surface pressures This stability needs to be maintained for make pulmonary drug delivery feasible.

Gelatin nanoparticles do not reduce the surface pressure greatly and may be feasible materials for drugs carriers.

PBCA eliminates the stability of model lung surfactant and is thus not a suitable for drug delivery purposes.

The study demonstrates that pulmonary drug delivery via nanoparticle is possible and proper biophysical assessment is an effective tool to screen suitable material.

Acknowledgements

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References

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Piknova B., Schram V. and S.B. Hall. (2002). Pulmonary surfactant: phase behaviour and function. Current Opinion in Structural Biology. 12: 487-494.

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