# POLY(SEBACIC ANHYDRIDE) MICROPARTICLES LOADED WITH CURCUMIN FOR PULMONARY PURPOSES

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## Introduction

Fast biodegrading polymeric microparticles (MP) used as the inhaled drug delivery systems (DDS) are considered a superior treatment method for pulmonary infections, allowing to obtain the therapeutic effect at lower antibiotic doses, reduced side effects, and smaller chances of developing antibiotic resistance [1].

The common problem of using MP as DDS is the need to use a relatively big amount of them due to limited drug loading capacity. This issue may possibly be solved by the use of quorum sensing inhibitors (QSi) e.g. curcumin (CU) – commonly applied in the food industry as a coloring factor. QSi prevent bacteria from creating biofilms, making them more sensitive to antibiotics [2].

Herein, we present the study of CU-loaded MP from poly(sebacic anhydride) (PSA) – a polymer investigated for drug delivery due to its favorable degradation kinetics. The aim was to evaluate the entrapment efficacy of CU in the MP and to assess the influence of encapsulated CU on the cytotoxicity of the system in contact with lung epithelial cells.

## Materials and Methods

PSA was obtained from sebacic acid via polycondensation. MP were manufactured using oil-in-water (O/W) emulsification, where; O: PSA and CU in different ratios dissolved in dichloromethane (DCM); W: water solution of poly(vinyl alcohol) (PVA). CU at different ratios was dispersed in PSA solution using ultrasounds. MP were obtained by adding the oil phase to the water phase, and then the organic solvent was evaporated under constant stirring. MP were washed 3 times in UHQ-water to get rid of surfactant residues, and freeze-dried. MP were observed using optical microscopy.

CU entrapment efficacy was evaluated by the fluorometric study of the residual water phase diluted in dimethyl sulfoxide (DMSO) at excitation wavelength 485-412 nm and emission wavelength 590-510 nm. Cytotoxicity was determined using AlamarBlue assay on human lung epithelial cells (BEAS/2B) after 24 h contact with MP dispersed in Dulbecco modified Eagle's medium (DMEM) at different concentrations from 0.1 µg/ml to 1000 µg/ml (n=3 for each concentration; analyzed by Tukey HSD test).

## Results and Discussion

Obtained MP were round in shape with diameter sizes below 5 µm and yellow coloration from encapsulated CU (FIG. 1). The experiment showed that the addition of CU up to 10% of PSA mass results in entrapment efficacy around 55% of initial values (54.60 ± 1.01% and 54,98 ± 2.58% for 5% and 10% CU, respectively) and decreased at higher concentration (42.76 ± 0.70% for 20% CU). Although the efficacy decreased, the MP loading increased with the concentration up to around 11% of MP mass. Obtained CU loadings are very promising for future combinations with antibiotics and prove the ease of manipulating the amount of entrapped CU within PSA MP.

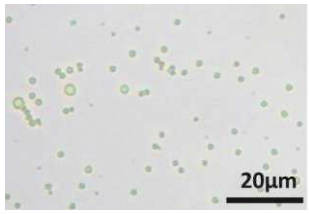


FIG. 1. 20% CU-loaded MP under optical microscope

AlamarBlue assay showed no cytotoxicity of empty or CU-loaded MP at concentrations lower or equal to 10 µg/ml. At 50 µg/ml, significant decrease in cell metabolism appear in both types of MP. In the case of CU-loaded MP the decrease in cell activity seems to be lower (differences at concentration 50 µg/ml are at $p<0.001$ for empty MP and $p<0.01$ for CU loaded MP) (FIG. 2).

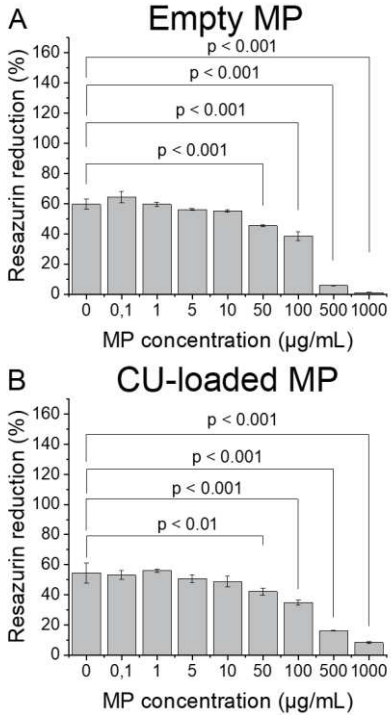


FIG. 2. BEAS/2B cell viability cultured in contact with Empty MP (A) and 20% CU-loaded MP (B); (error bar: SD, n=3).

## Conclusions

This study showed a great potential of CU as a QSi to be administrated via inhalation in polyanhydride MP-based delivery systems. The final drug loading may easily be controlled by changing the initial concentration of CU. CU entrapment does not increase the cytotoxicity of PSA MP. It is even possible for CU to make the MP more less cytotoxic, but this hypothesis has to be proved by further studies.

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## References

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