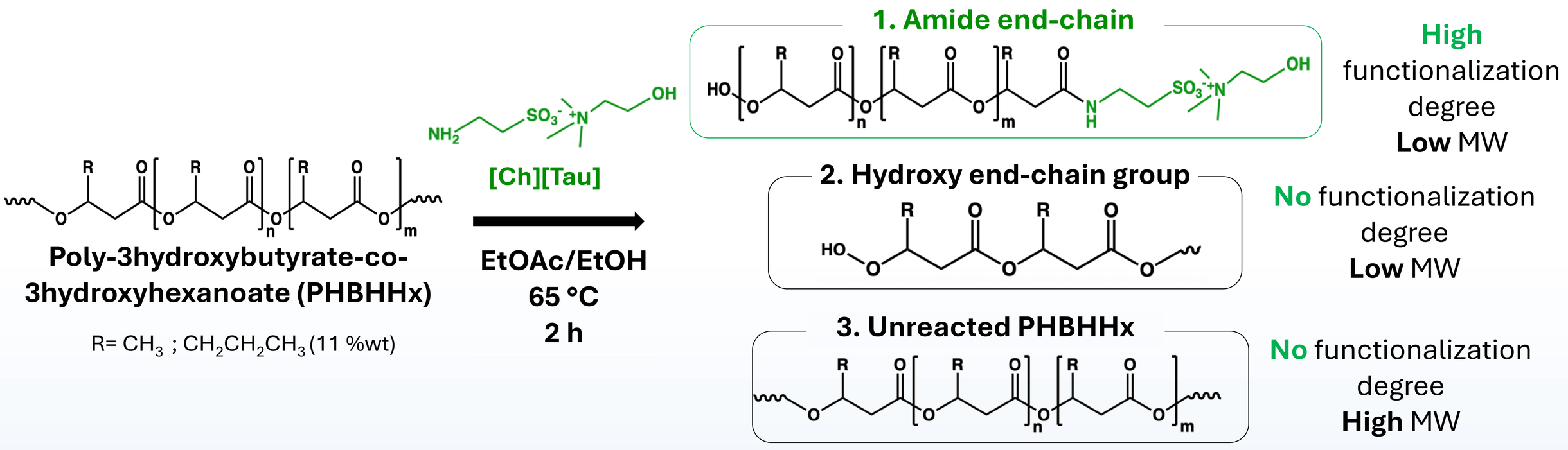
AMPHIPHILIC POLYHYDROXYALKANOATES (PHA): UNLOCKING VERSATILITY

Sara Alfano[1], Lorenzo Ceparano[1], Benedetta Brugnoli[1] , Luca Pellegrino[2], Iolanda Francolini[1], Andrea Martinelli[1]

[1] *Sapienza University of Rome, Department of Chemistry, P.le A. Moro 5, 00185 Rome, Italy*
[2] *Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20072 Pieve Emanuele, Italy*

INTRODUCTION

Polyhydroxyalkanoates (PHAs) are promising for drug delivery due to their ability to encapsulate lipophilic drugs. However, their hydrophobicity limits stability and compatibility. Traditional surfactants improve PHA nanoparticle properties but often require purification posing risks. Self-surfactant systems offer a sustainable alternative.

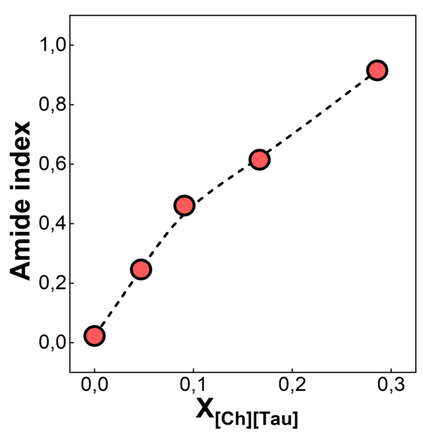


Schematic representation of the aminolysis reaction of PHBHHx using [Ch][Tau] at 65 °C. The reaction product presumably is a mixture of 1. aminolyzed PHBHHx with surfactant activity, 2. Unreacted PHBHHx with high hydrophobicity, and 3. Hydroxy end-chain group.

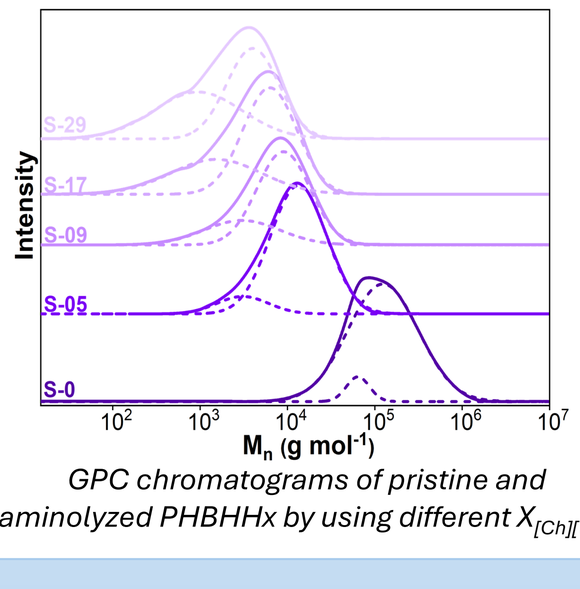
Amidated PHBHHx characterization

PHBHHx modification was assessed through FTIR and GPC analysis, which demonstrated the obtainment of a wide MW distribution and different amidation degree

$$\text{Amide index} = \frac{Abs\ 1759\ cm^{-1}}{Abs\ 1453\ cm^{-1}}$$



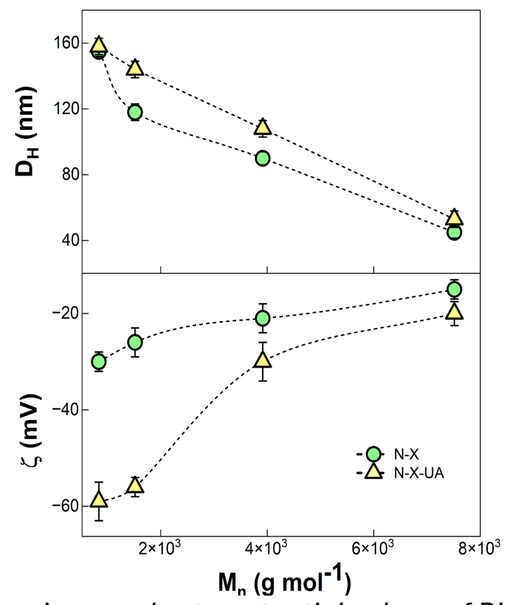
Variation of the amide index as a function of $X_{[Ch][Tau]}$.



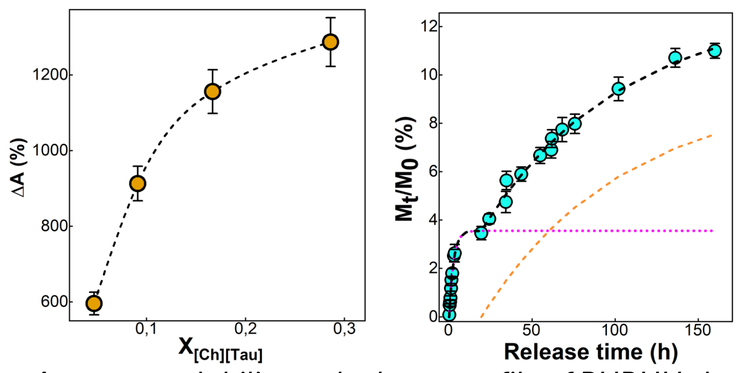
GPC chromatograms of pristine and aminolyzed PHBHHx by using different $X_{[Ch][Tau]}$

Nanoparticles characterization

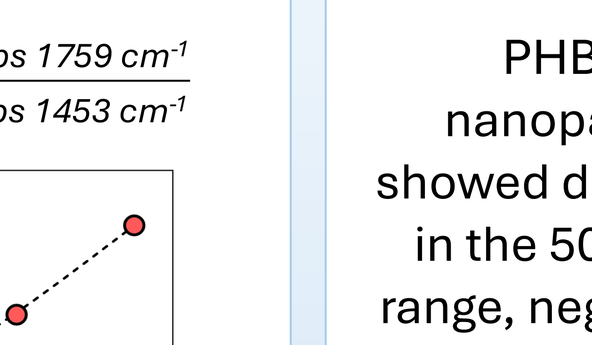
PHBHHx nanoparticles showed dimensions in the 50-150 nm range, negative zeta potential, good encapsulation ability and a double-phase release of usnic acid (UA).



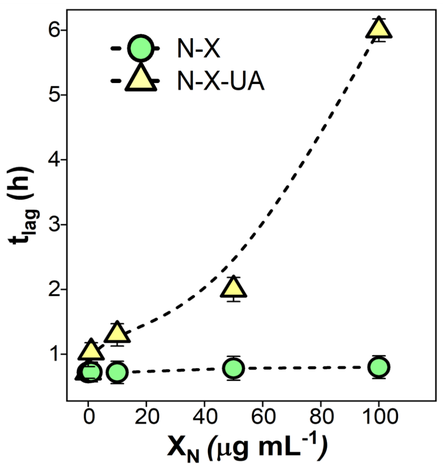
Dimensions and zeta potential values of PHBHHx nanoparticles



Apparent solubility and release profile of PHBHHx based nanoparticles



Antimicrobial activity



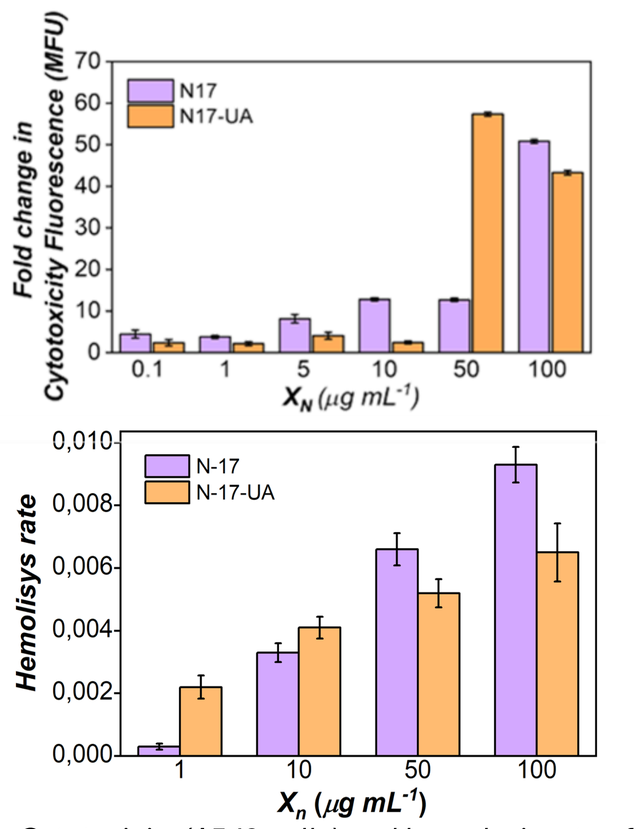
Lag time (t_{lag}) as functions of nanoparticle concentration.

PHBHHx-based nanoformulations were tested against *S.* showing promising antimicrobial potential

Fluorescence optical microscopy images of S. aureus biofilms formed within the microfluidic channel at 12 hours in the presence of unloaded and UA-loaded nanoparticles.

In vitro cytotoxicity

PHBHHx nanoparticles showed no cytotoxicity on A549 cells. PHBHHx nanoparticles biosafety was confirmed by hemolysis assay.



Cytotoxicity (A549 cells) and hemolysis rate of unloaded and UA-loaded nanoparticles

CONCLUSION

The design of the proposed formulations was guided by consideration of key properties of the chemicals focusing on sustainability, safety, ease and efficacy of nanoparticle production. Overall, this approach is suitable for systemic drug-delivery of lipophilic compounds, smart implant coatings and antibacterial topical formulations.

Alfano S.* et al. *Self-surfactant poly-3hydroxybutyrate-co-3hydroxyhexanoate (PHBHHx) for the preparation of usnic acid-loaded antimicrobial nanoparticles using non-toxic chemicals,* ACS Appl. Bio Mat. 2025