Peptonics: a new family of cell-protecting surfactants for the recombinant expression of therapeutic proteins in mammalian cell cultures

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Abstract

Polymer surfactants are key components of cell culture media as they prevent mechanical damage during fermentation in stirred bioreactors. Among cell-protecting surfactants, Pluronics are widely utilized in biomanufacturing to ensure high cell viability and productivity. Mono-dispersity of monomer sequence and length is critical for the effectiveness of Pluronics - since minor deviations can damage the cells - but is challenging to achieve due to the stochastic nature of polymerization. Responding to this challenge, this study introduces Peptonics, a novel family of peptide and peptoid surfactants whose monomer composition and sequence are de-signed to achieve high cell viability and productivity at a fraction of chain length and cost of Pluronics. A designed ensemble of Peptonics was initially characterized via light scattering and tensiometry to select sequences whose phase behavior and tensioactivity align with those of Pluronics. Selected sequences were evaluated as cell-protecting surfactants using Chinese hamster ovary (CHO) cells expressing therapeutic monoclonal antibodies (mAb). Peptonics IH-T1010, ih-T1010, and ih-T1020 afforded high cell density (up to 3·107 cells·mL-1) and viability (up to 95% within 10 days of culture), while reducing the accumulation of ammonia (a toxic metabolite) by ˜10% compared to Pluronic F-68. Improved cell viability afforded high mAb titer (up to 5.5 mg·mL-1) and extended the production window beyond 14 days; notably, Peptonic IH-T1020 decreased mAb fragmentation and aggregation ˜5%, and lowered the titer of host cell proteins by 16% compared to Pluronic F-68. These features can improve significantly purification of mAbs, thus increasing their availability at lower cost to patients.

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