Dissolvable microcarriers for adherent cell culturing

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INTRODUCTION

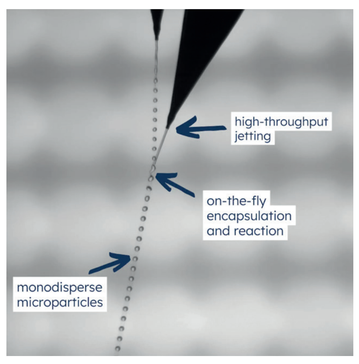
Microcarriers provide an efficient platform for culturing adherent cells by offering a significantly larger surface area for cellular attachment, compared to traditional 2D methods. Adherent cell culturing faces however several challenges. The main challenges are:

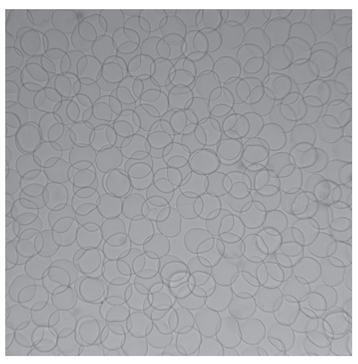
- **Scalability:** Traditional methods are labor-intensive and challenging to scale.
- **Low cell yield:** Conventional, non-dissolvable microcarriers require aggressive detachment methods, leading to substantial cell loss. Typically, approximately 50% of cells perish during harvesting, while surviving cells often exhibit compromised viability.
- **Batch-to-batch consistency:** Variability in culture conditions, contamination risks and manual handling can reduce reproducibility.

Although non-dissolvable microcarriers have improved cell culturing efficiency, their inherent limitations necessitate advancements. The detachment process, involving chelating agents, proteases and mechanical forces, often damages cells. In contrast, dissolvable microcarriers address these challenges by simplifying cell recovery and enhancing overall yield.

MATERIALS AND METHODS

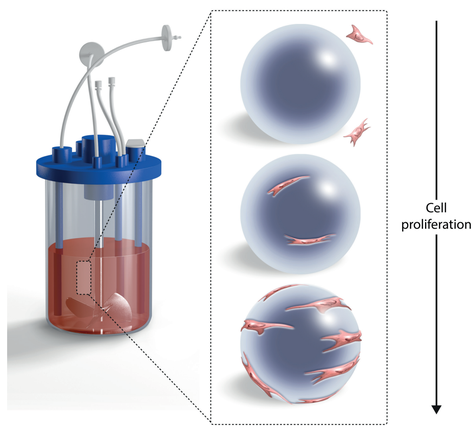
Microcarrier particle preparation.
In air microfluidics is used to
Produce DMC alginate particles coated with gelatin.





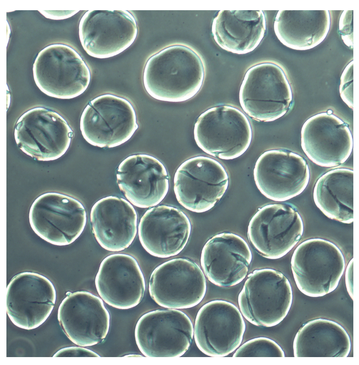
Culturing conditions

Cell Type:	Bone-marrow derived human mesenchymal stem cells
Microcarrier:	1. DMC (IamFluidics/Rousselot) 2. Comparison: Industry standard, dextran microcarrier
Medium:	BM-MSC medium
Condition:	T25 spinner flasks
Read-outs:	- Attachment efficiency - Proliferation rate - Viability - Bead-to-bead transfer (scale-up)

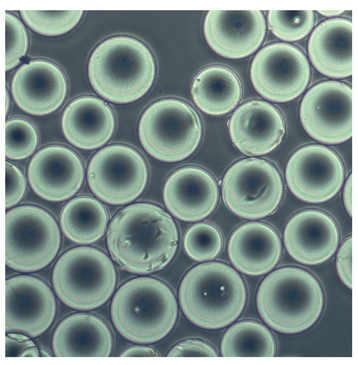


RESULTS

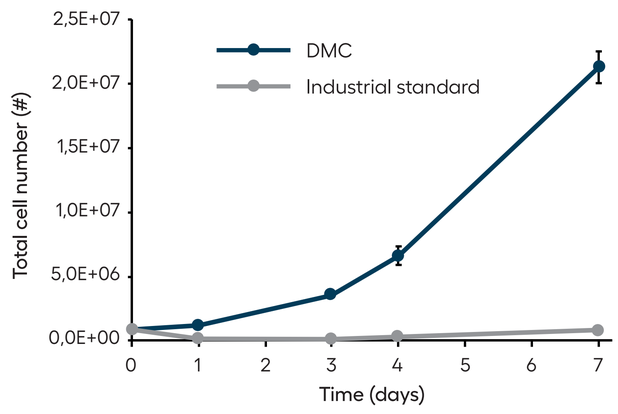
1. Cell attachment and proliferation



DMC

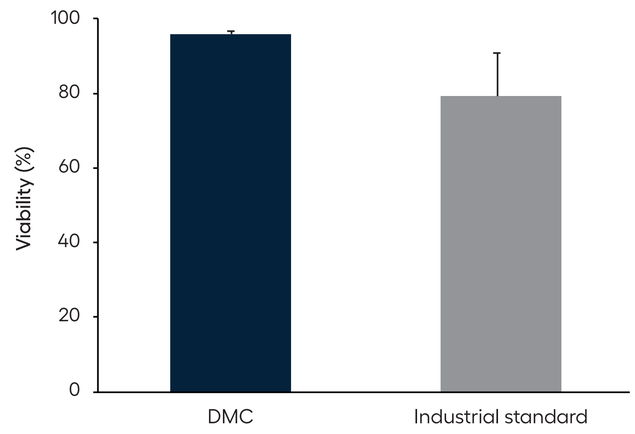


Industrial standard



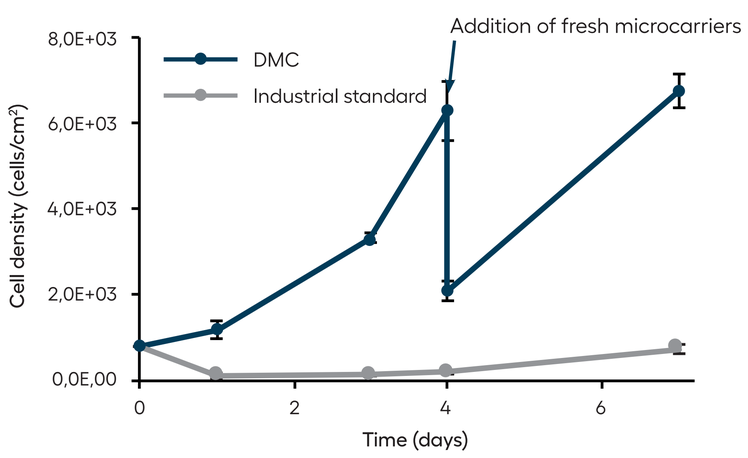
Superior cell culturing and attachment on monodispersed DMC microcarriers.
The denatured collagen coatings promote rapid cellular adhesion, achieving over 95% attachment within 24 hours, which results in fast cell proliferation over 7 days.

2. Viability post harvesting after 7 days



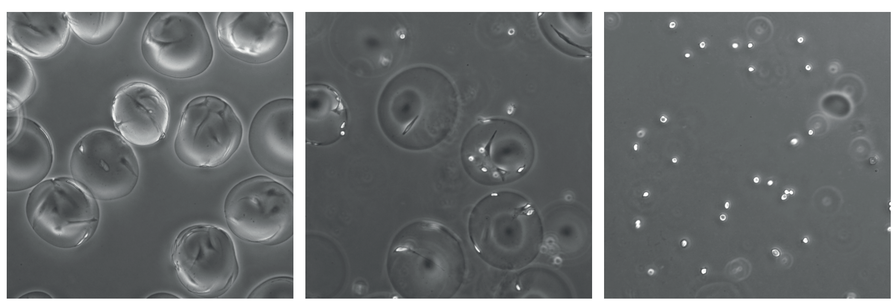
High cell viability is achieved with DMC's during 7 days of culturing. There is more viability variation with the industrial standard

3. Rapid microcarrier cell transfer and cell proliferation

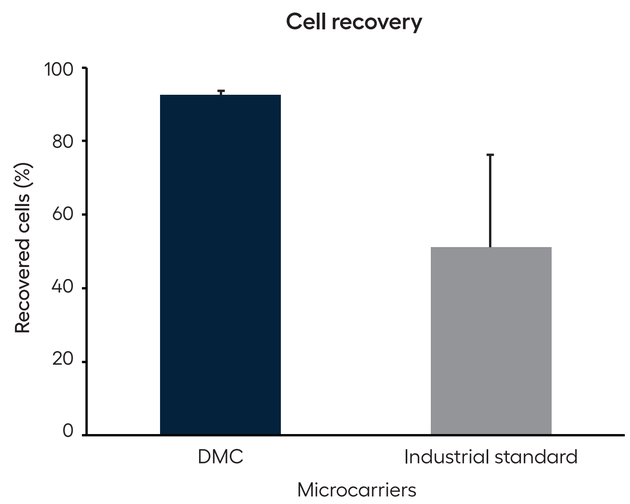


The DMC's facilitate efficient bead-to-bead transfer, streamlining upscaling processes in bioreactor systems.

4. Cell harvesting efficiency after cell proliferation



t=0min t=3min t=15min



DMC can dissolve rapidly within 15 minutes which makes cell recovery highly efficient compared to non-dissolvable current industrial standard microcarriers. This allows easier, faster upscaling and higher cell yields

SUMMARY

Adherent cells readily attach to dissolvable DMC microcarriers coated with denatured collagen, promoting rapid attachment, robust proliferation and seamless bead-to-bead transfer. The introduction of the dissolvable DMC microcarriers can increase post-harvest cell viability to over 90%, a significant improvement over conventional, non-dissolvable microcarriers, which often result in cell yields below 50% due to an inefficient microcarrier separation step.

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