CASE STUDY

IamFluidics

Our solution for controlled microparticle production

Key words: microparticles, high-throughput, injectables, porosity, bioresorbable, poly(lactic acid), poly(caprolactone), poly(glycolic acid)

MARKET NEED

Controlled production of uniform, tunable, and bioresorbable microparticles.

BACKGROUND

A key goal in the field of injectable drug delivery systems is to achieve precise control over microparticle composition, size, porosity, and drug encapsulation efficiency. Maintaining uniformity in these particle design parameters is crucial for ensuring well-defined and consistent drug release kinetics and therapeutic efficacy of long-acting formulations.

Long-acting injectable formulations are typically based on bioresorbable polymers such as poly(lactic acid), poly(glycolic acid), poly(caprolactone), and blends or co-polymers thereof (e.g., PLGA). Injectable microparticles are commonly produced by generating sub-100 µm droplets containing a solution of the active pharmaceutical ingredient (API) and a bioresorbable (co-)polymer of interest, followed by a solidification process.

THE CHALLENGE

Microparticle solidification typically starts with skin or shell formation at the droplet's surface, which already happens within milliseconds and has a predominant effect on the subsequent hardening process, as well as the resulting microparticle porosity and API release profile. [1] Therefore, controlling the liquid-liquid reactions during microparticle formation at the spatiotemporal microscale is of key importance, but also challenging and requires precise microfluidic handling. Microparticle generation processes that offer the most control (e.g., microfluidics) are typically not scalable, whereas industrial processes (e.g., batch emulsification) offer poor control over droplet formation and solidification parameters resulting in non-uniform and poorly controlled microparticles.

OUR SOLUTION

Our patented IN-AIR MICROFLUIDICS™ technology enables high-throughput generation of uniform polymeric micromaterials with accurately controlled size, shape, composition, and porosity, which outperforms typical batch emulsification.

COLLABORATION

In collaboration with Corbion, our preferred supplier for bioresorbable polymers.

Corbion

[1] Sharifi F., Otte A., and Park K. Initial Formation of the Skin Layer of PLGA Microparticles. Adv. Healthc. Mater. 2022; 11(7): e2101427.

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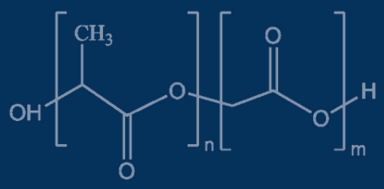
THE METHOD

Our IN-AIR MICROFLUIDICS™ (IAMF) setup was used to combine liquid jets containing (i) 20 wt% poly(lactic-co-glycolic acid) (PLGA; Purasorb® PDLG5002, Corbion) in ethyl acetate or dichloromethane, (ii) an optional aqueous co-flow, and (iii) water with optionally a surfactant. Formed dispersions were collected, vacuum-dried, and analyzed using brightfield and scanning electron microscopy (SEM). A similar method was used to produce micromaterials comprising poly(lactic acid) (PLA; Purasorb® PDL05) and poly(caprolactone) (PCL; Purasorb® PC02).

Featured material:



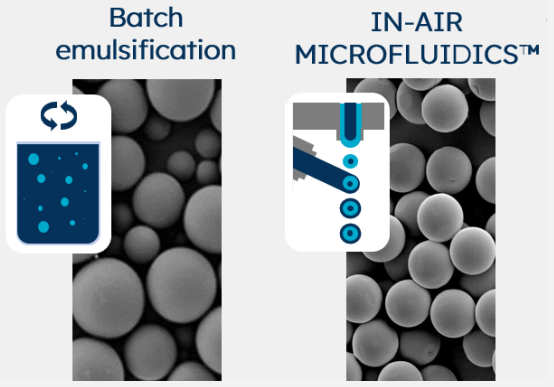
Corbion Purasorb® PDLG 5002
poly(lactic-co-glycolic acid)

THE RESULTS

Size & uniformity

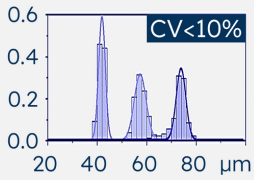
PLGA micromaterials were successfully produced at a rate of ~5 g/h (particles) to 150 g/h (fibers) using non-parallelized IAMF. SEM analysis revealed that IAMF-generated particles were highly uniform as compared to particles produced by conventional batch emulsification.

Tuning the aqueous co-flow readily enabled the production of three distinct monodispersed (i.e., CV<10%) PLGA microparticle batches with designated sub-100 µm size.



SEM photos of microparticles produced using conventional batch emulsification vs IAMF.

D_1 (µm)	41.6 ± 1.2
D_2 (µm)	57.6 ± 3.4
D_3 (µm)	73.0 ± 4.9

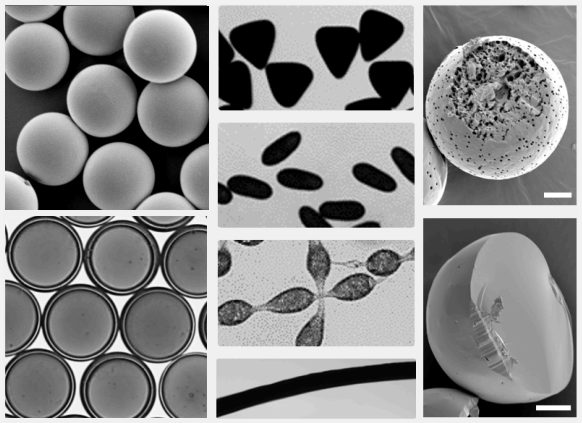


Size analysis of IAMF-generated microparticle batches.

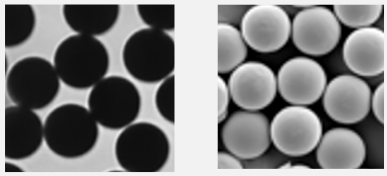
Shape, porosity & composition

Tuning jet impact parameters enabled different microparticle shapes, including spherical solid beads, hollow capsules, triangles, rods, and (beaded) fibers. Furthermore, material porosity could be tuned from porous to solid by changing the solvent from ethyl acetate to dichloromethane.

Various bioresorbable polymers and combinations are compatible with the IAMF process, including PLGA, PLA, and PCL.



PLGA



PLA PCL

Microphotographs of various IAMF-generated micro-materials made of PLGA, PCL, and PLA. Scalebars: 20 µm

IN CONCLUSION

We successfully demonstrated the application of IAMF for rapid, accurate, reproducible, and tunable production of sub-100 µm bioresorbable micromaterials.

Learn more at: **www.IamFluidics.com**

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