The reproducibility of silica-based controlled release therapeutics manufacturing

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Introduction

DelSiTech is a pharmaceutical company specializing in formulation of long-acting injectables. Their manufacturing process is based on sol-gel-technique and the product is a gel-depot with an encapsulated active pharmaceutical ingredient (API). The aim of this study is to study this innovative manufacturing process in terms of its reproducibility.

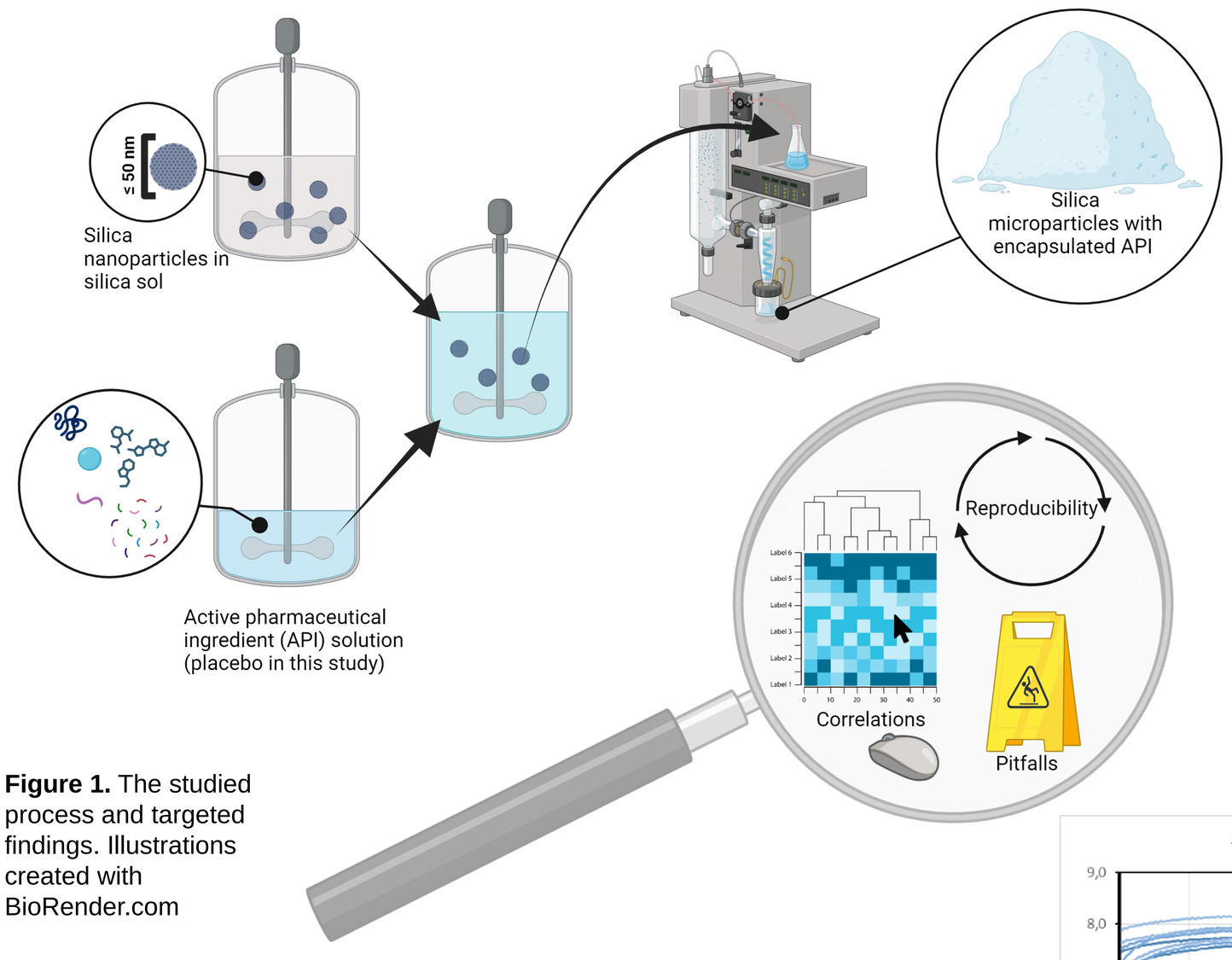

Figure 1. The studied process and targeted findings. Illustrations created with BioRender.com

Materials and methods

With help of literature, knowledge in the company and a software-generated **Design of Experiments** structure, the first part of the manufacturing process, silica sol preparation based on **sol-gel-technique**, was studied. The sols were analyzed by **reaction thermodynamics**, **rheological measurements** and **oxidability**. Guided by results gained, a **spray drying** step was executed to produce an intermediate product of the manufacturing process, silica-microparticles. These microparticles were analyzed based on **particle size distribution** and ***in vitro* dissolution**. For the nature of the study, no active pharmaceutical ingredient was used.

Results

Source	Logworth	PValue
X1	12,486	0,00000
X4	8,208	0,00000
X8	6,146	0,00000
X9	2,352	0,00445
X3	1,113	0,07712
X6	0,444	0,35945
X7	0,330	0,46778
X2	0,322	0,47632
X5	0,314	0,48476

Table 1. Few parameters were found to have a statistically significant effect on the silica sol properties.

- The parameters with the biggest effect on the silica sol properties were determined (*Table 1*)
- No manufacturing parameters were found to cause significant **unintentional** variation to the silica sol's properties

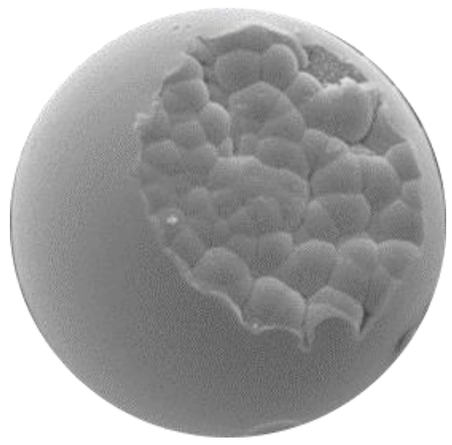

Figure 2. A scanning electron microscope picture of a silica microparticle (diameter of ~2-3 µm). It can be seen that a microparticle consists of nanoparticle agglomerates formed in the silica sol.

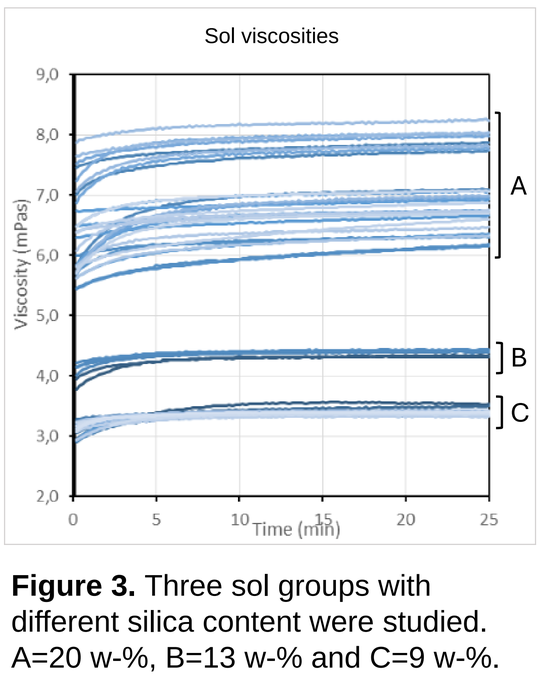

Figure 3. Three sol groups with different silica content were studied. A=20 w-%, B=13 w-% and C=9 w-%. The viscosity varied more in the silica sols with most dry content (i.e. silica).

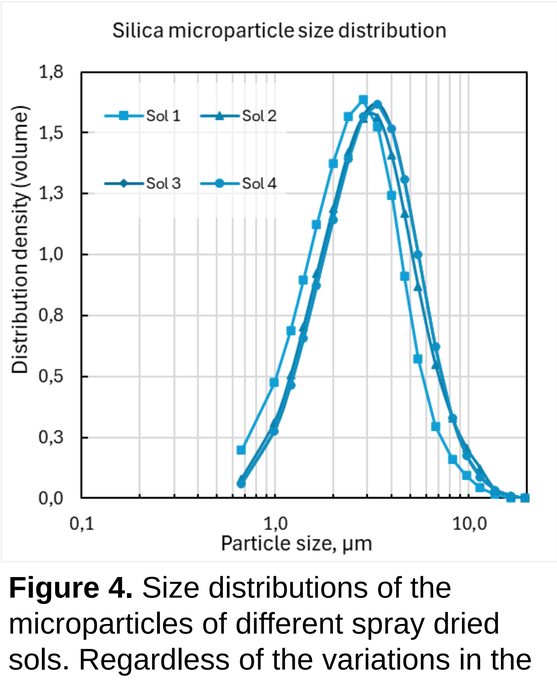

Figure 4. Size distributions of the microparticles of different spray dried sols. Regardless of the variations in the silica sol properties, the microparticle sizes were similar.

Conclusions

Results this far imply that the manufacturing process is rigid and reproducible. The process will be studied further.

References

- Noppari, P., Jokinen, M., Dargelas, F., Mikkola, J. & Leino, L. (2021) CHAPTER 9. Parenteral Delivery of Therapeutic Proteins, Peptides and Small Molecules Using Biodegradable Silica. In V. Srivastava, Drug Development and Pharmaceutical Science (ss. 188–215). Cambridge: Royal Society of Chemistry

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