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An Elegant Micronization Method Enabling The Formulation Of Biopharmaceuticals

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Sustained release drug delivery systems (DDS) offer effective therapies in the treatment of serious chronic diseases, with numerous advantages over traditional therapies. Furthermore, reduced waste streams and less visits to practitioners offer advantages related to sustainability. These treatments also make a tremendous difference for patients by limiting systemic side-effects and addressing the challenge of compliancy with regards to taking medications. When developing a DDS, patient comfort should be considered in the product's design to minimize the size of the needle needed for injection. One DDS design approach that can overcome this challenge is by leveraging therapeutic-loaded microspheres.

Microspheres may be produced by a variety of methods, including Water-in-Oil-in-Water (WOW) and Solid-in-Oil-in-Water (SOW) emulsification. In the SOW process, the Active Pharmaceutical Ingredient (API) is added as a solid to the polymer-containing oil phase, while in the WOW process, a primary emulsion is prepared by mixing a water-based API solution with the polymer-containing oil phase. In both cases the oil phase is further emulsified with a water-based solution that also allows hardening of the created droplets via solvent transfer. In the specific case of biopharmaceuticals, the SOW process offers a significant advantage such as avoiding degradation of the API at the water/organic solvent interface.

Achieving good encapsulation efficiencies and suitable release profiles can be challenging when the SOW process is used with an API raw material that is not suitable in terms of particle size range (typically too large particles). This can be the case for lyophilized powders.

In such case, an extra step of micronization of the API raw material typically increases the loading efficiency and lowers the burst of the obtained microspheres[1],[2].

Perhaps not as obvious, micronization methods such as spray-drying can also be of added value when the API is available as a solution (e. g. use of a commercial API solution to perform an early technical feasibility for the preparation of microspheres). This is typically employed when the API solution is incompatible with the other solutions used to create the microspheres (SOW method) or if there is a desire to concentrate the API prior to forming the microsphere (WOW method).

A summary of these different strategies is given in Figure 1.

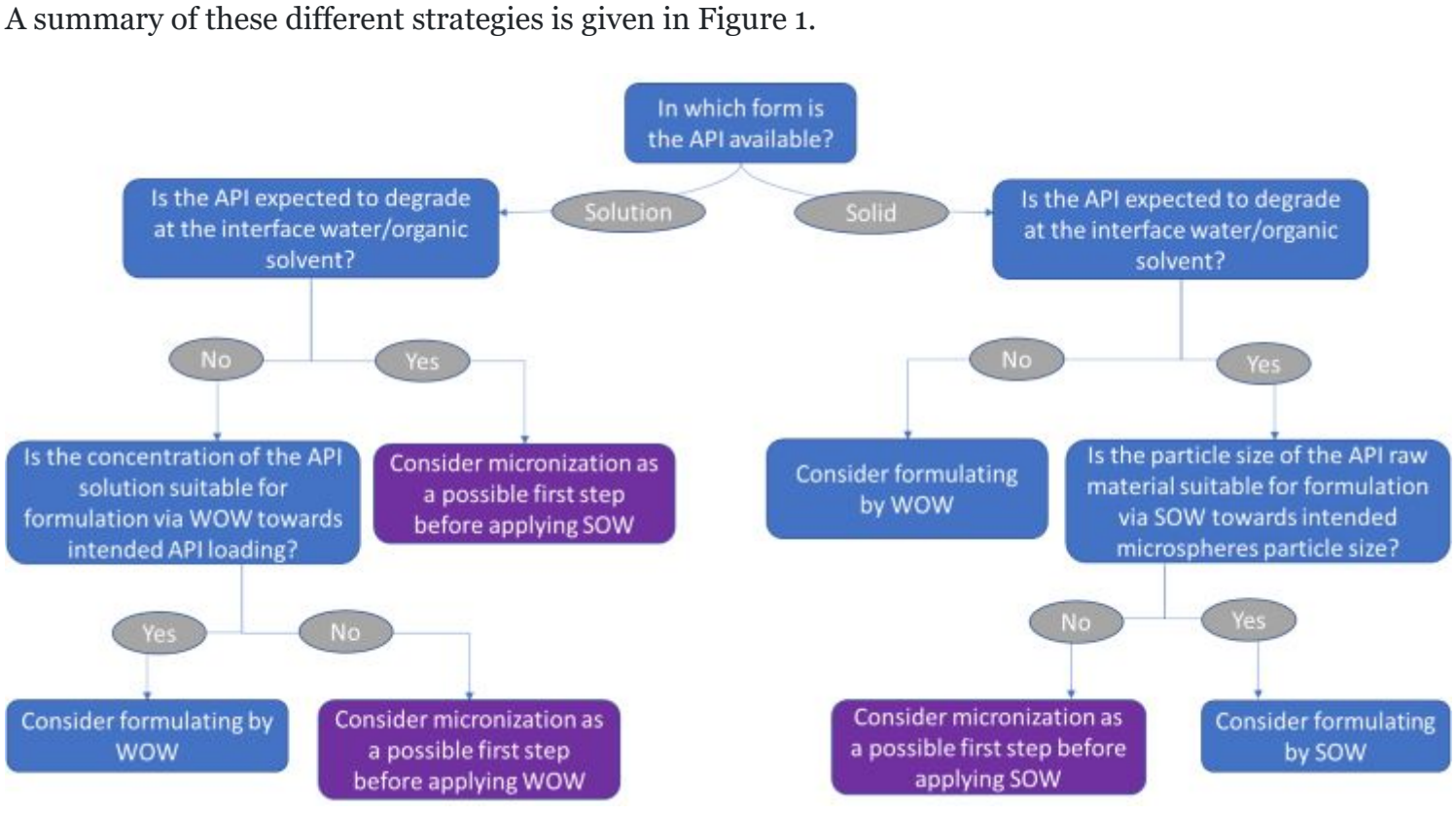

Figure 1. Summary of different strategies applicable for the formulation of biopharmaceuticals via emulsification routes. (Click to enlarge.)

Different methods can be used to micronize APIs, such as spray drying or milling[3],[4], however these methods can be incompatible with the limited API amounts available in early stages of drug development.

As a preparation step for powders of water-soluble APIs before encapsulation into our TheraPEA™ platform of polyester amide-based microspheres via SOW, DSM Biomedical has successfully applied a different, lyophilization-based micronization methodology applicable on a small scale[5]. The method has been proven to result in very narrow particle size distributions for several proteins and peptides, and parameters have been identified that allow tuning of the particle size (Figure 2). Its applicability has been tested for API amounts as low as fifty milligrams, making it a suitable technique for expensive APIs or early feasibility assessments where API has limited availability.

Figure 2. SEM image of micronized bovine serum albumin[6].

Using this methodology, in combination with a broad knowledge of R&D scale emulsification processes, DSM Biomedical can support challenging formulation development projects from early technical feasibility to the preparation of samples for pre-clinical studies. DSM Biomedical also works with a network of CMOs who specialize in microspheres production throughout the DDS development phase to ensure the production processes are scalable.

DSM Biomedical's TheraPEA™ platform offers polymers of choice for the development of microsphere-based therapies, relying on biodegradability, ability to maintain a physiological pH during degradation, and tunable swelling properties to achieve the desired release profile. In future articles, DSM will address the capabilities required for the preparation of API-loaded microspheres via emulsification. Want to learn more on this topic and on which process may work best for your microsphere developments? Connect with us at DrugDelivery.Biomedical@dsm.com to start the discussion!

About DSM Biomedical

DSM Biomedical is the world's unrivaled biomaterials expert and committed partner driving sustainable innovation in healthcare. For 30+ years, their solutions have been recognized for their unmatched quality, consistency, and performance, ultimately supporting their company-wide vision of solving the world's healthcare needs through sustainable science.

To learn more, visit DSMBiomedical.com.

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