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Short communication

Scale-up of an emulgel as semisolid dosage form: Case study of successful process transfer

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Introduction

Topical drug delivery systems have attracted considerable attention in pharmaceutical science owing to their ability to deliver active substances directly to the site of action, thereby minimizing systemic side effects and circumventing hepatic first-pass metabolism. The scale-up of emulgel as semisolid dosage forms remains as one of the most technically demanding steps in product development (Evans et al., 2019). This paper presents a case study for scale-up of an emulgel used as nonsteroidal anti-inflammatory agent from a batch size of 300 kg to a batch size of 1500 kg on geometrically non-equivalent equipment.

Materials and methods

Equipment

The emulgel was prepared using two vacuum mixer homogenizers at different manufacturing scales. The batch size of 300 kg was produced using an Olsamix vacuum mixer homogenizer equipped with an anchor agitator, counter-rotating blades and a bottom-mounted rotor–stator homogenizer. The batch of 1500 kg was manufactured on a Fryma Koruma vacuum mixer, featuring an anchor-type agitator and an inline rotor–stator homogenizer operating in a recirculation loop.

Manufacturing process

The emulgel was prepared with the following manufacturing steps: hydration of the gelling agent, melting of the oily phase and emulsification of the oil and aqueous phases under controlled temperature and mixing conditions. The system was then cooled to a certain temperature, followed by addition of solution of active substance and gel formation through polymer neutralization and final cooling and mixing.

Critical process parameters

The critical process parameters identified as having the most significant influence on the critical quality attributes - viscosity, droplet size, content uniformity and emulgel stability are homogenization speed, mixing speed, temperature, and mixing time.

Results and discussion

In phase hydration of the polymer, the temperature remained constant (40–45 °C) and the impeller speed decreased from 70 rpm to 25 rpm. This reduction is consistent with scale-up principles, where agitator speed is lowered to maintain similar power per unit volume and avoid excessive shear that could damage the gel structure. The homogenizer speed was slightly reduced (1200 rpm to 1000 rpm), while mixing time decreased significantly (240–360 minutes to 30–40 minutes), likely due to improved recirculation efficiency in

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large-scale systems, which enhances bulk movement and reduces dead zones (Plegue, 2018). During the emulsification phase, the temperature remained identical (73–77 °C) as it is crucial for the oily and water phase to be properly emulsified. The central impeller speed was reduced (80 rpm to 25 rpm), while homogenizer speed increased significantly (600 rpm to 2000 rpm). In the cooling and homogenization step, temperature remained constant (38–42 °C), but homogenization changed from continuous to intermittent operation (1500 rpm/60 s – 0 rpm/600 s). During addition of the solution of active substance, parameters were largely maintained, with only minor adjustments in homogenizer speed (1800 rpm to 1500 rpm).

The gelling process showed major differences, with homogenizer speed increasing (800 rpm to 1500 rpm) while mixing time dramatically decreased (50–70 minutes to 5 minutes). This reflects the higher efficiency of large-scale homogenizers in generating rapid dispersion and uniform neutralization. Finally, during cooling and final mixing, the introduction of intermittent homogenization at commercial scale ensured consistent microstructure while preventing over-shearing. Mixing time increased slightly (from at least 40 minutes to at least 60 minutes), which is expected due to reduced heat transfer efficiency in larger vessels.

Overall, the parameter adjustments follow fundamental scale-up principles, including reduction of agitator speed to maintain a comparable shear environment, increased reliance on homogenization for effective droplet size control, adjustment of mixing time according to equipment efficiency and batch volume and precise control of temperature and cooling rates to preserve the microstructure of the formulation. All critical quality attributes, including viscosity and content uniformity were comparable to those obtained at smaller scale and remained within the predefined specification limits, confirming the robustness of the scale-up process.

Conclusion

The study demonstrated that the use of large-scale equipment improves process efficiency through enhanced recirculation and homogenization, resulting in reduced processing times. The findings further confirm that scale-up cannot be achieved by direct parameter transfer; instead, process conditions must be adjusted according to hydrodynamic principles, such as maintaining comparable shear conditions and flow behavior, to ensure consistent product quality across scales.

References

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