# Media and buffer mixing using the Xcellerex™ magnetic mixer

Powder-liquid mixing is a common requirement in biopharmaceutical processing for media and buffer preparation. This can pose a challenge to ensure complete mixing is achieved in an acceptable time. This can be at risk if a mixer used provides insufficient power input, resulting in an inability to create a vortex. For this reason, we evaluated the mixing performance of the Xcellerex™ magnetic mixer 3000 L system for preparation of aqueous solutions.

# Introduction

We evaluated the mixing performance of the Xcellerex magnetic mixer 3000 L system for preparation of a typical floating powder (Dulbecco's Modified Eagle Medium [DMEM]) and a typical sinking powder (sodium chloride) (Fig 1). The required time to achieve homogeneity was assessed both visually by the time at which no undissolved solids remained visible, and by using a conductivity sensor. The solution was homogenous at the time when the conductivity sensor had stabilized within ± 1%.

**Fig 1.** Xcellerex magnetic mixer 3000 L system.

# Materials and methods

The materials and equipment used in this experiment are presented in Table 1. The Xcellerex magnetic mixer 3000 L system was prepared according to its instructions for use. The single-use mixing system was installed and inflated, and the pre-calibrated pH and conductivity sensors were installed at the locations as shown in Figure 2. The single-use system then was filled with demineralized water to 90% of the nominal mixer volume. Mixing was started at an impeller speed of 310 rpm, data recording was initiated, and then the required quantity of powder was added. In the case of DMEM, an additional pH adjustment step was required with a sodium bicarbonate addition once the media solution was clear of solid particles, and when conductivity values had stabilized for five minutes (min). The media preparation was finally completed with a demineralized water addition to reach 100% of the nominal volume.

**Table 1.** Materials and equipment.

| Equipment | Supplier | Product code |
|---|---|---|
| Xcellerex magnetic mixer 3000 L | Cytiva | XM3000JHT-B4N |
| Xcellerex magnetic mixer I/O cabinet | Cytiva | XMCABINET-FPID |
| pH sensors | Mettler-Toledo | InPro325i/SG/120 |
| Conductivity sensors | Mettler-Toledo | InPro7100/12/120/4435 |
| M300 2-channel transmitter | Mettler-Toledo | ING30280773 |
| Xcellerex magnetic mixer single-use system 3000 L | Cytiva | 6407-1067Z |
| 3000 L inflation set | Cytiva | 6407-1243S |
| Demineralized water | IMES | IMS3774742 |
| Single and double-concentrated DMEM (13.4 g/L and 26.8 g/L, respectively) | Sigma Aldrich | D5648 |
| 1.5 M sodium chloride (NaCl 98%) | Marsel | 21018 |
| 3.7 g/L and 7.4 g/L, sodium bicarbonate | Sigma Aldrich | S5761-5KG |

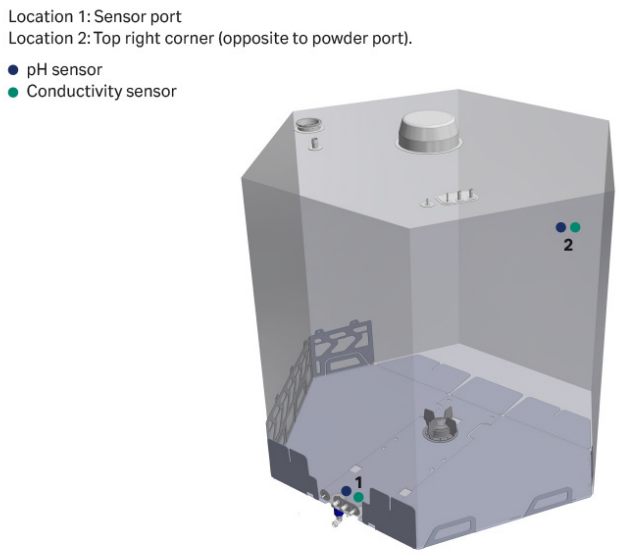


**Fig 2.** Schematic drawing of the Xcellerex single-use 3000 L system with the pH and conductivity sensor locations.

The test conditions are presented in Table 2.

**Table 2.** Test conditions.

| Parameter | Test condition |
|---|---|
| Working volume | 3000 L |
| Temperature | Room (20 ± 2°C) |
| Mixing parameters | pH, conductivity, visual |
| Agitation speed | 310 rpm |
| Mixing time criteria | Visual and conductivity ± 1% |

## Results and discussions

For the 1× DMEM mixing experiment, the Xcellerex magnetic mixer 3000 L system was filled with 2700 L of demineralized water and mixing started at 310 rpm. Once stable, 40.2 kg of DMEM was added via the powder port within 4 min 20 seconds (s). Conductivity was stable after an additional 5 min 45 s and media was clear of undissolved particles after 6 min 40 s of mixing. 11.1 kg of sodium bicarbonate ($NaHCO_3$) was added at 20 min 36 s to adjust the pH of the media to 7.5 ± 0.1. Once final pH was reached, demineralized water was added up to 100% of the nominal volume to complete media preparation.

For the 2× DMEM mixing experiment, the Xcellerex magnetic mixer 3000 L system was filled with 2700 L of demineralized water and mixing started at the speed of 310 rpm. Once stable, 80.4 kg of DMEM was added via the powder port in 8 min 26 s. Conductivity was stable after an additional 10 min 7 s, and media was clear of undissolved particles after 8 min 8 s of mixing. 22.2 kg of sodium bicarbonate was added at 26 min 32 s to adjust the pH to 7.5 ± 0.1. Once the final pH was reached, demineralized water was added up to 100% of the nominal volume to complete media preparation.

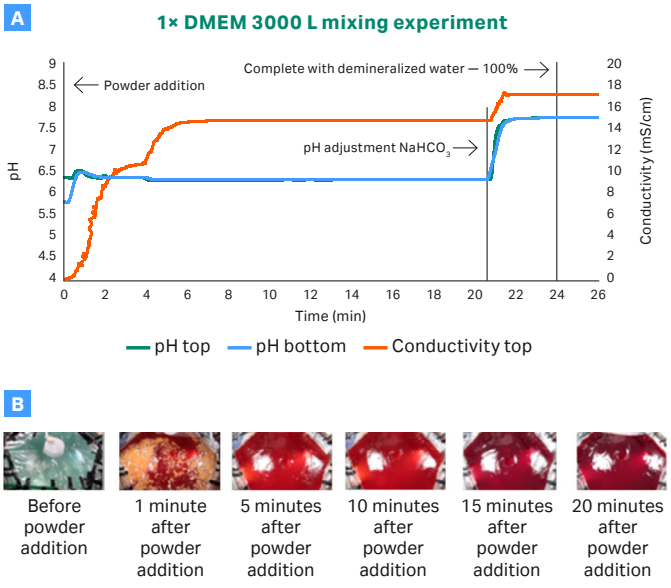


**Fig 3.** Graph of pH and conductivity, and photos of 1× DMEM mixing in Xcellerex magnetic mixer 3000 L.

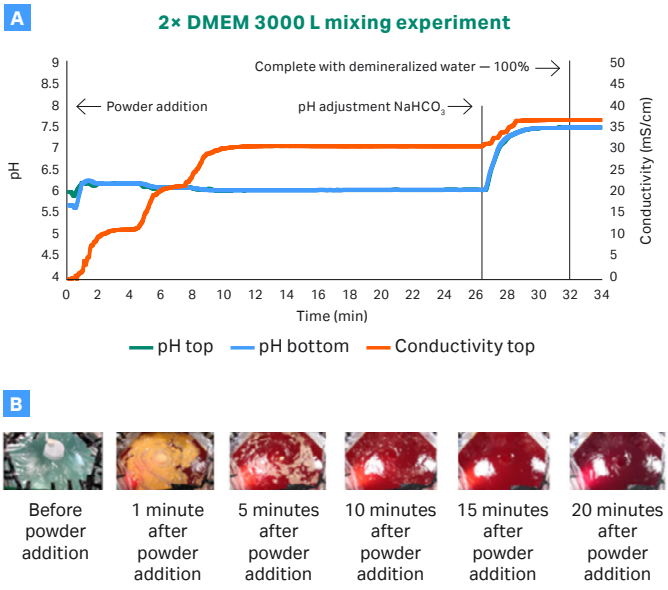


**Fig 4.** Graph of pH and conductivity, and photos of 2× DMEM mixing in Xcellerex magnetic mixer 3000 L.

For the 1.5 M NaCl mixing experiment, the Xcellerex magnetic mixer 3000 L was filled with 2700 L of demineralized water and mixing started at the speed of 310 rpm. Once stable, 262.98 kg of sodium chloride was added via the powder port in 2 min 45 s. Final conductivity was reached after an additional 4 min 49 s of mixing, and the solution was clear of undissolved particles within 5 min. Once final conductivity was reached and remained stable for five minutes, demineralized water was added up to 100% of the nominal volume.

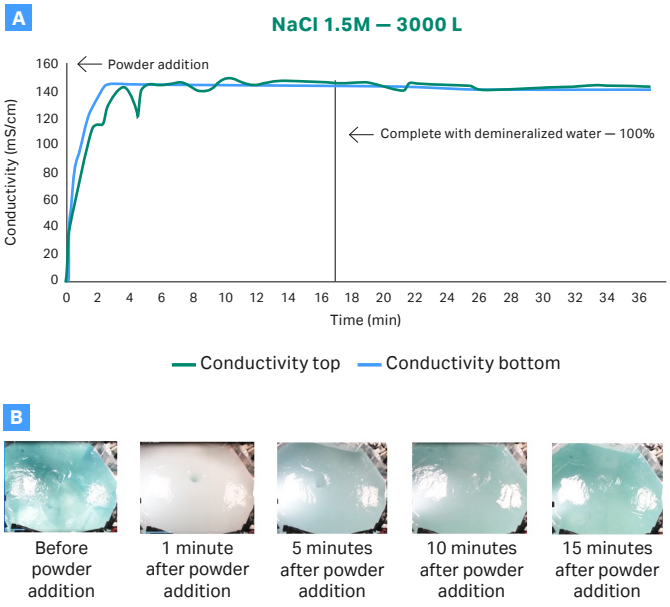


**Fig 5.** NaCl 1.5 M mixing in the Xcellerex magnetic mixer 3000 L.

A summary of the mixing times for the various experiments is presented in Table 3.

**Table 3.** Visual and conductivity based mixing times, presented as mixing time excluding the powder addition time (mixing time including the powder addition time).

| Media and buffer concentrations | Visual (min:s) | Conductivity (min:s) |
|---|---|---|
| 1× DMEM | 6:40 (11:00) | 5:45 (10:05) |
| 2× DMEM | 8:08 (16:34) | 10:07 (18:33) |
| 1.5 M NaCl | 5:00 (7:45) | 4:49 (7:34) |

## Conclusion

The results of this study confirm the ability of the Xcellerex magnetic mixer 3000 L to disperse and dissolve the selected floating powder (DMEM, both single and double concentration) and sinking powder (1.5 M sodium chloride) within a timeframe of 20 min, including powder addition time.

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