

Efficient, high-titer monoclonal antibody production in a fed-batch process using single-use stirred-tank and rocking bioreactor systems

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Abstract

This work shows monoclonal antibody (MAB) production in parallel fed-batch processes using the single-use Xcellerex™ XDR-200 stirred-tank and ReadyToProcess WAVE™ 25 rocking bioreactor systems. Cell expansion was performed in a 15 L rocking bioreactor culture to seed a 200 L stirred-tank bioreactor culture. To compare the performance of ReadyToProcess WAVE 25 with that of XDR-200, 7 L of the 200 L culture was transferred to a parallel ReadyToProcess WAVE 25 system to a total culture volume of 10 L. This study showed that, although, having different vessel geometry, the ReadyToProcess WAVE 25 and the Xcellerex XDR-200 bioreactor were very comparable in performance and allowed for high performing fed-batch cultures.

Materials and methods

The initial expansion of Chinese hamster ovary (CHO) DG44 cells (licensed from Cellca GmbH, Laupheim, Germany) was performed in shaker flasks before further propagation in ReadyToProcess WAVE 25. The culture was used to seed to the XDR-200 system for MAB production. The volume in the XDR-200 bioreactor after inoculation was 145 L, giving approximately a 10-fold split ratio of the seed culture. Thereafter, 7 L of the XDR-200 culture was removed and transferred into a satellite ReadyToProcess WAVE 25 bioreactor. The resulting XDR-200 culture volume was 138 L. The final volumes at harvest, including feed additions, were calculated to be approximately 200 L for XDR-200 and 10 L for ReadyToProcess WAVE 25. The cell culture media and feeds were from the ActiCHO™ platform. Cell growth, MAB production, metabolite content, and osmolality were monitored during the culture. Cells were harvested after 13 elapsed days and/or when culture viability was < 60%. The experimental layout is shown in Figure 1.

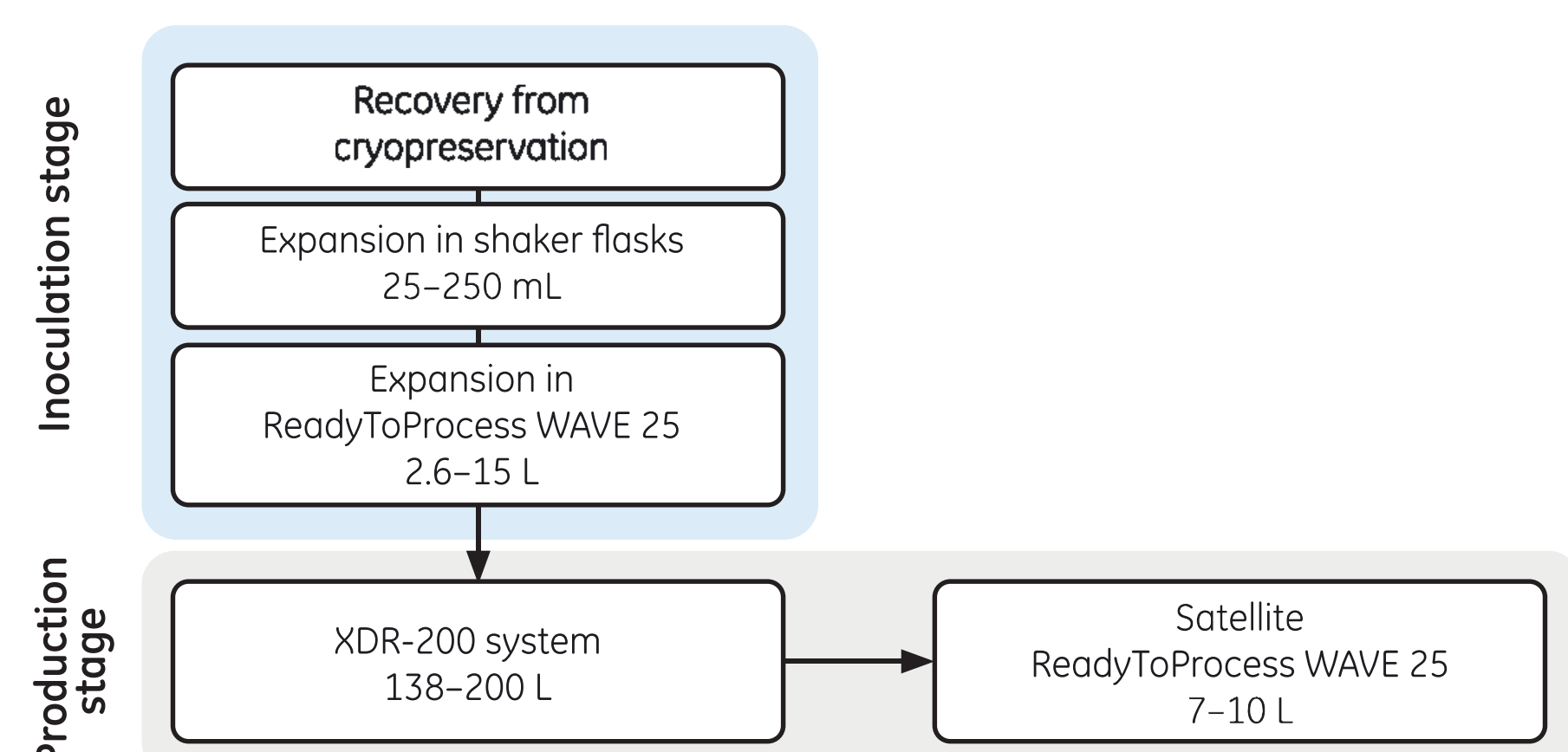


Fig 1. Study outline.

Conclusions

- ReadyToProcess WAVE 25 can be used for both seed culturing and process development purposes.
- The XDR-200 bioreactor system supported high cell growth and protein yields in 200 L production scale.
- Although having a different vessel geometry, ReadyToProcess WAVE 25 gave a representative reflection of the process at larger scale using the XDR-200 system.
- The combination of ReadyToProcess WAVE 25 and Xcellerex bioreactor systems offers an efficient, reliable, and scalable solution for recombinant protein production.

Reference

Application note: Efficient, high-titer monoclonal antibody production in a fed-batch process using single-use stirred-tank and rocking bioreactor systems, GE Healthcare, 29-1193-76, Edition AA (2014).

Results

Cell growth and viability in the ReadyToProcess WAVE 25 seed culture is shown in Figure 2. Results from the MAB production cultures are summarized in Table 1. Cell growth and productivity in the production cultures are shown in Figure 3. Metabolite profiles are shown in Figure 4. Figure 5 shows osmolality, and partial carbon dioxide pressure is displayed in Figure 6.

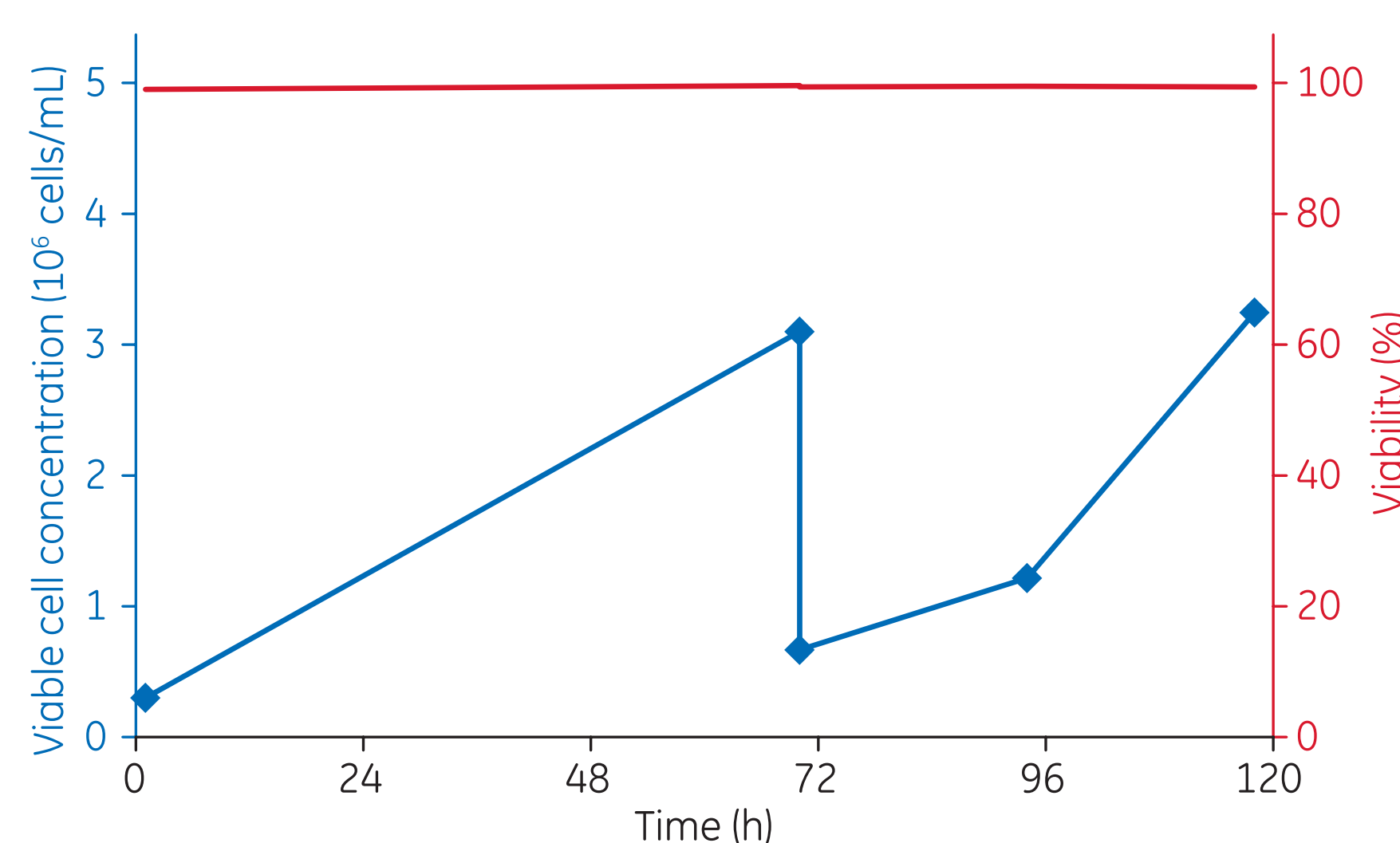


Fig 2. Cell growth and viability in the ReadyToProcess WAVE 25 system used to seed the production bioreactor cultures. The volume was expanded from 2.56 L to 15 L at 72 h.

- XDR-200
- ReadyToProcess WAVE 25 satellite, MAB concentration
- XDR-200
- ReadyToProcess WAVE 25 satellite, viability
- XDR-200, viability
- ReadyToProcess WAVE 25 satellite, viability

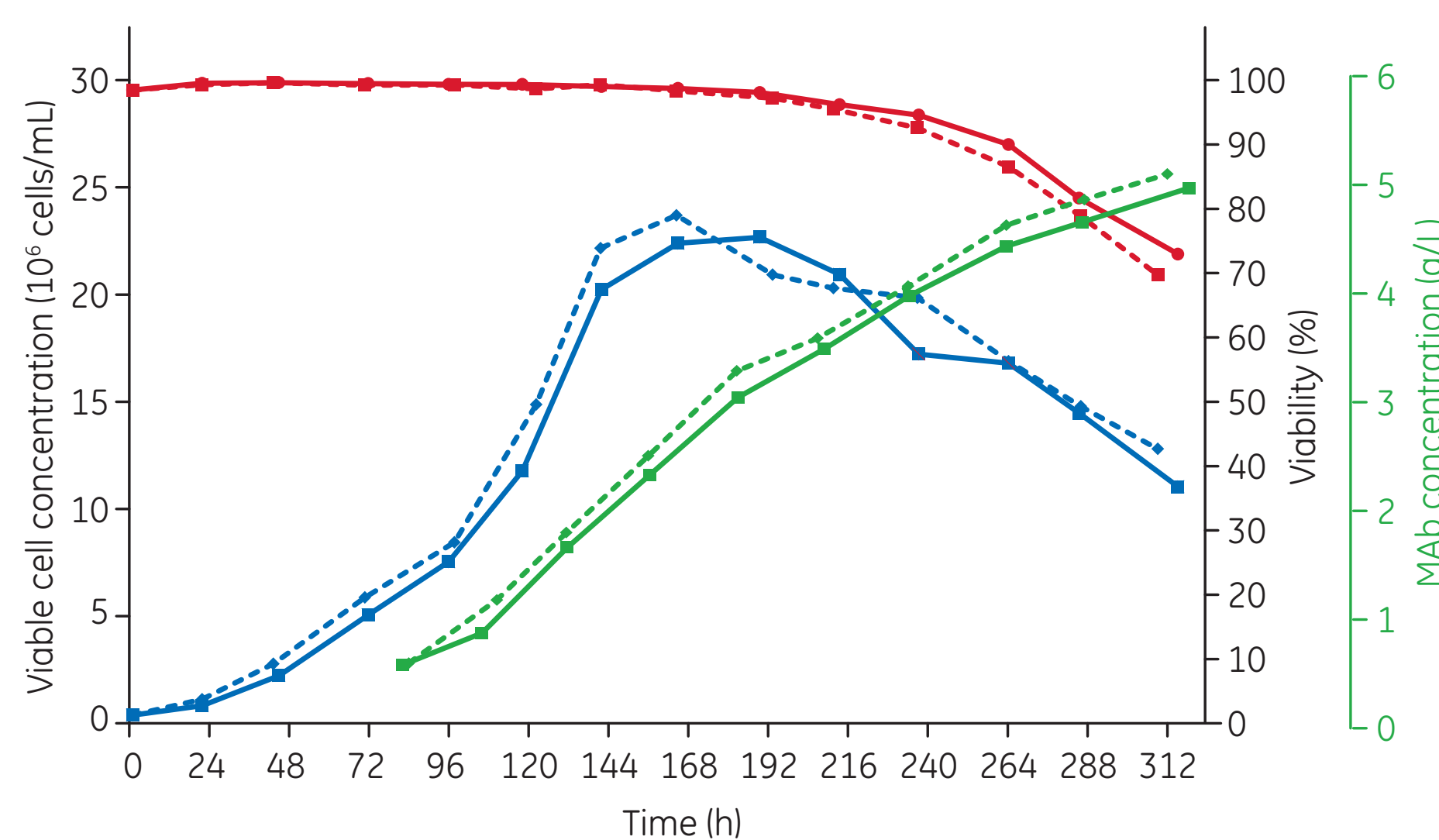


Fig 3. Viable cell concentration, viability, and MAB concentration in the two parallel production cultures. Samples were taken just prior to feeding.

Table 1. Results from the bioreactor MAB production cultures

	XDR-200	ReadyToProcess WAVE 25 satellite
Culture max. viable cell count (10 ⁶ cells/mL)	23.7	22.7
Harvest viability (%)	65.3	73.0
Harvest product concentration (g/L)	5.0	4.9
Cell-specific productivity (pg/cell/d)	27	28

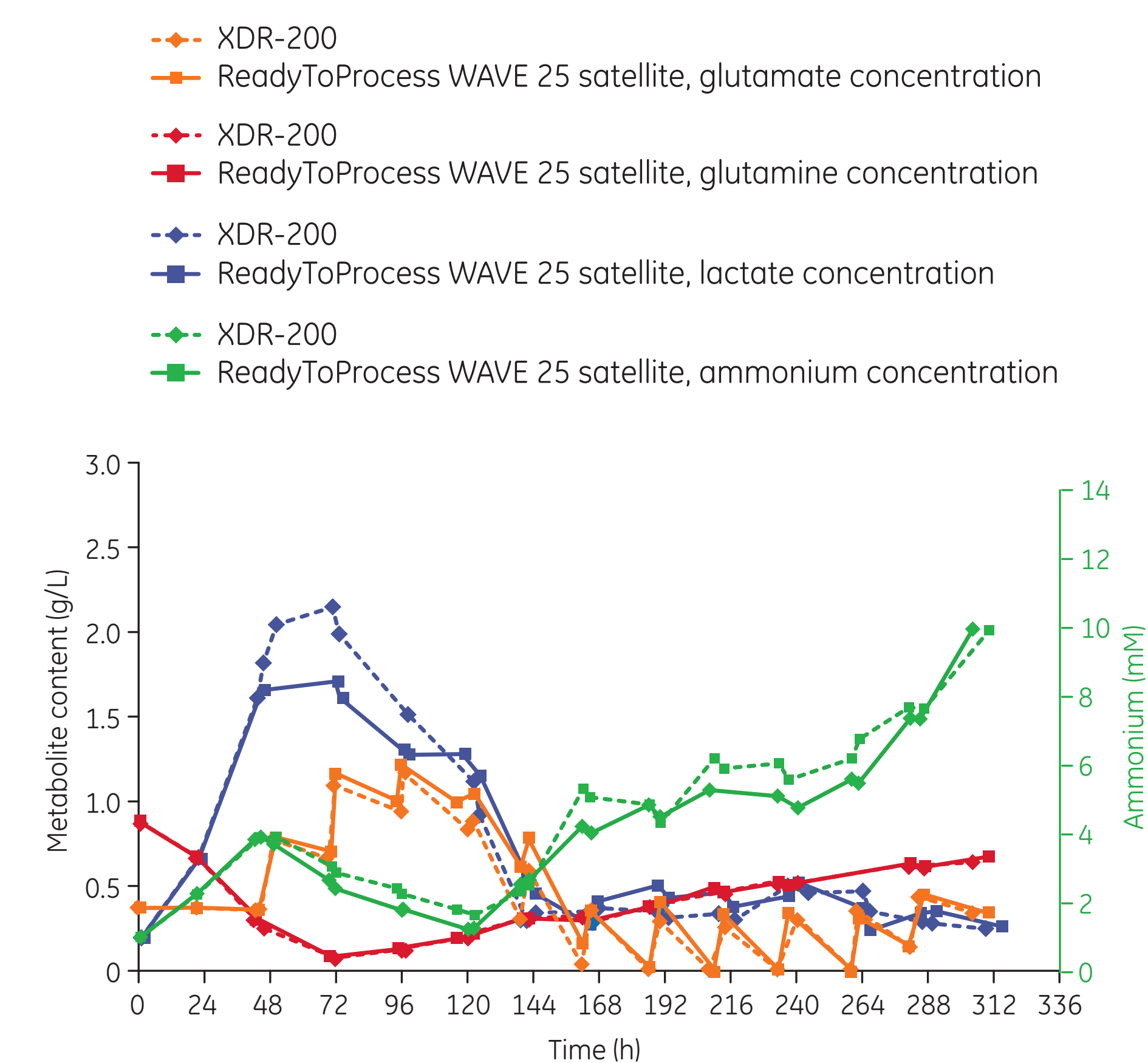


Fig 4. Metabolite concentrations in the two parallel production cultures.

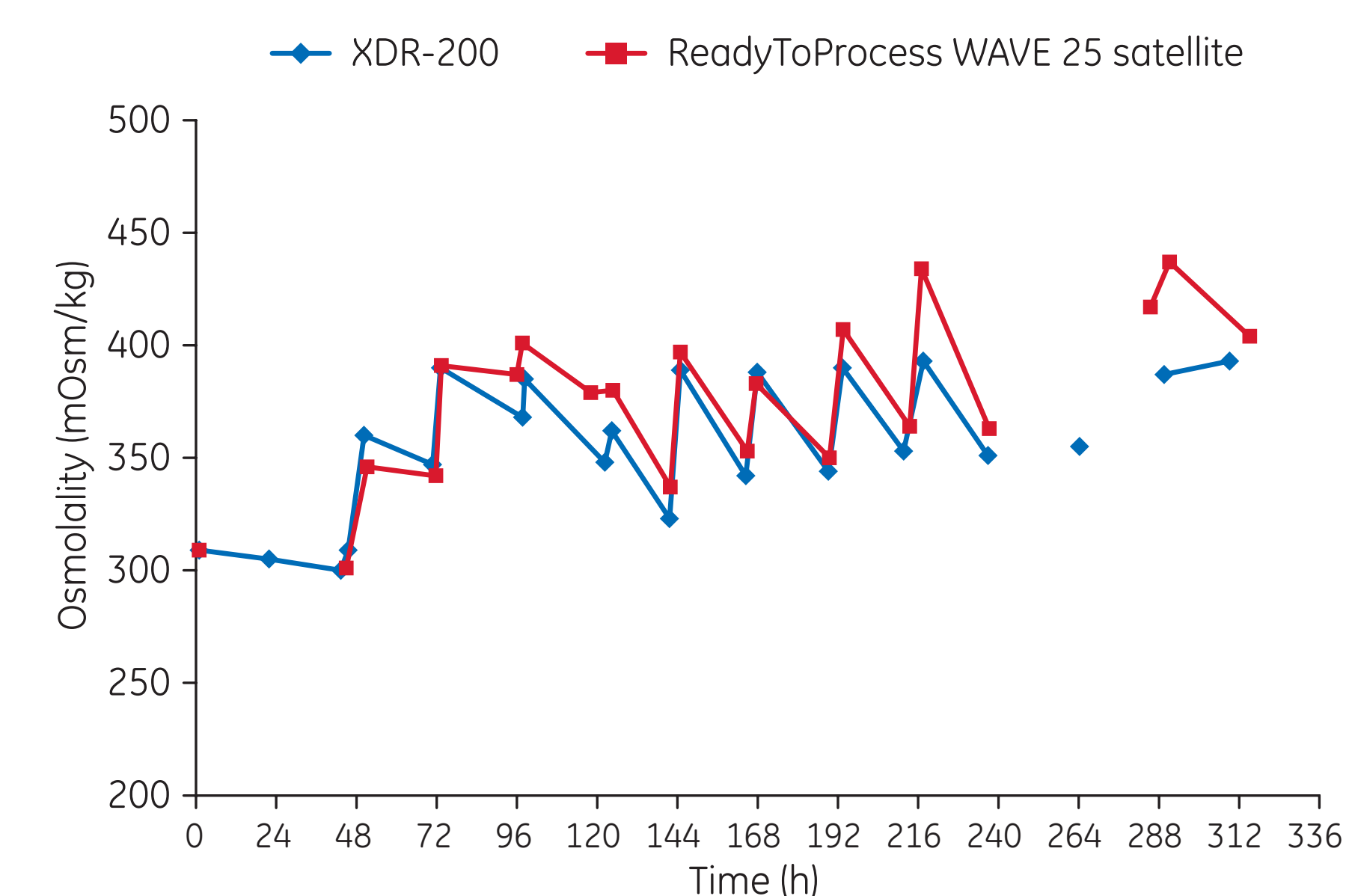


Fig 5. Osmolality in the two parallel production cultures. Samples were taken just prior to and after feeding.

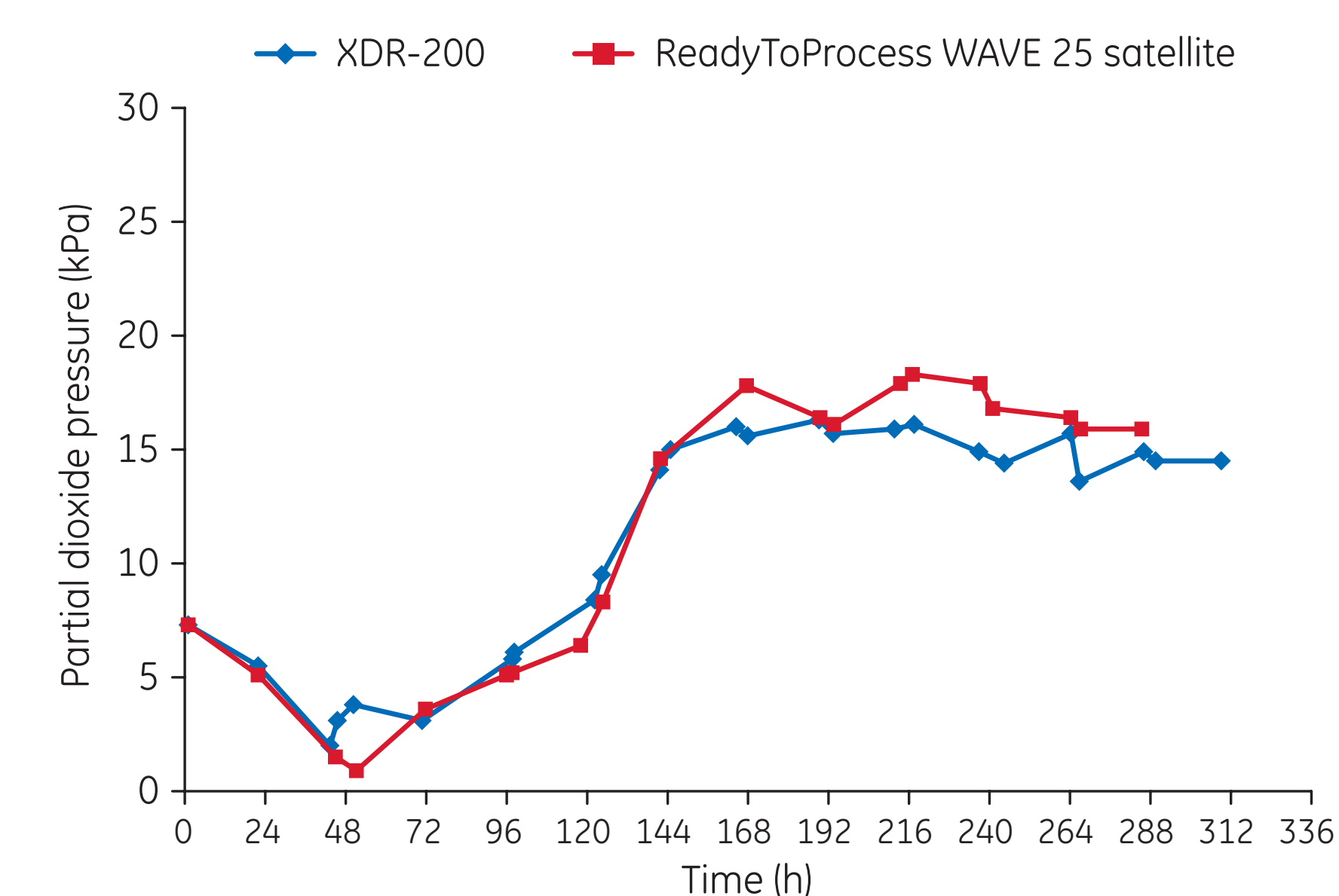


Fig 6. Partial carbon dioxide pressure in the two parallel production cultures.