ULTRA-INTENSIFIED INTERMITTENT-PERFUSION FED-BATCH (UIIPFB) PROCESS QUADRUPLED PRODUCTIVITY OF A BISPECIFIC ANTIBODY

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Current bioprocess development continues to highlight the need for yield improvement and cost of goods (CoGs) reduction to achieve a more desirable process economy in biologics manufacturing. Cell culture process intensification with options including media optimization and process development has been proven effective to address the need. To further expand the selection of intensification strategies, in this study, we developed a novel cell culture process with improved recombinant protein production, product quality and upstream economics in comparison with the conventional intensified fed-batch or continuous perfusion process. The new culture process was characterized by an upgraded N-1 perfusion coupled with a cell concentration step boosting cell density to up to 350 $x10^6$ cell/mL. The N-1 process allowed for an ultrahigh inoculation density (e.g., 30-80 $x10^6$ cell/mL) in production phase. To sustain healthy cell status and improve productivity in production, an intermittent perfusion (1-2 perfusion cycles) fed-batch process (IPFB) was designed to inherit both the operation simplicity of fed-batch culture and the advantage of superior cell sustainability in a perfusion process. Also incorporated in the process was WuXi Biologics' proprietary cell culture media formulated with a particular purpose for intensified processes. With all the efforts, the resulted UIIPFB process produced a titer of 20 g/L with suitable product quality attributes for a bi-specific antibody in a culture duration of 14 days, which was ~400% higher than the initial traditional fed-batch process. The total harvest protein also increased notably by 7 folds compared to the original process. With the improvement in productivity and the use of in-house proprietary media, both media cost and total process cost per gram DS reduced significantly by over 50%. In summary, this study demonstrated the development of an ultra-intensified cell culture process with our proprietary cell culture platform and media with potentials for wide applications for any cell line and product of interest.