ULTRA SCALE-DOWN MIMICS FOR PERFUSION CULTURE: EXPERIMENTAL STUDY FOR RAPID BIOPHARMACEUTICAL PROCESS DEVELOPMENT

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With the industry driving towards the implementation of whole continuous bioprocess sequences, there becomes a requirement for the development of scale-down tools with the same consistency, reliability and throughput as those already available for traditional batch processes. This work aims to develop a perfusion scale-down system capable of reproducing the specific characteristics of the perfusion culture process, namely cell retention capabilities, the ability to support high cell densities and to operate for extended periods compared to fed-batch cultures. Cell culture in microwell plates in fed-batch mode is well defined and is in widespread use; however to the best of our knowledge this represents the first attempt at the development of quasi-perfusion cell culture at this scale.

Cultivation approaches in the microscale have been developed using a GS-CHO cell line in 24 well microwell plates, with a working volume of 1.2mL. Quasi-perfusion was achieved via sedimentation or centrifugation of the plate and the subsequent removal of supernatant to mimic cell retention, generating separation efficiencies higher than 98%. Media exchanges commenced on day 3 at a rate of 1 vessel volume per day (VVD).
The use of the quasi-perfusion approach generated improvements in cell densities of up to 2.5 fold in comparison to fed-batch studies. Additionally, volumetric productivities increased up to 1000 fold than those generated in fed-batch. Metabolic profiles in microwell plates are consistent with those typically obtained at large scale.
The results demonstrate that many of the characteristics of perfusion culture can be simply mimicked in microwell plate systems. This suggests the ability of microwell plates to be implemented into early phase development of perfusion culture, for cell line and media screening, resulting in substantial time and cost savings. Integration into a liquid handling system and automated platform is under way in an effort to generate robust high-throughput cell line or media screening data in early-phase development.