Opinion

Pharmaceutical BIOPROCESSING

Review on Fixed-Bed Bioreactors and Rotating Bed Bioreactors

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Fixed-Bed Bioreactors

Fixed- bed bioreactors are a common chief of the food and wastewater assiduity due to their setup - a vessel filled with a macro porous material or large globules to which cells and/or enzymes may be attached, and through which the liquid phase is passed through continuously. In fact, numerous studies have formerly described the use of fixed- bed bioreactors for operations similar as the product of biodiesel and bio hydrogen, and colorful aspects of wastewater treatment. Beyond the possibility for these operations, fixed- bed bioreactors also have some characteristics which have led to their use for culture of harborage-dependant mammalian cells. The figure and setup of these bioreactors confer a large face-to- volume rate, allowing for a lower footmark, compared to stirred-tank bioreactors, and enabling a much advanced volumetric productivity. Depending on their medium, fixed- bed bioreactors may also be naturally compatible with a perfusion feeding governance, and, due to the lack of agitation, the shear stress conveyed to the cells is low. The lack of an impeller is, contemporaneously, a disadvantage, due to allowing for the conformation of attention slants (of nutrients, metabolites, growth factors, oxygen, etc.) inside the bioreactor. Also, cell harvesting until the end of the culture is insolvable, rendering cell growth monitoring specially delicate. Nonetheless, fixed- bed bioreactors have seen used for operations similar as viral product in mammalian cells and indeed hHSPC expansion.

Single- use fixed- bed bioreactors bear both a single- use vessel and cell adhesion matrix. Weber et al. have developed a small-scale disposable fixed- bed bioreactor system using a 3 mL plastic hype, connected to two 250 mL steins for medium feeding and for waste, and equipped with a small oxygen detector in the exodus. This bioreactor system was used for the culture of alginate- reprised hMSC -TERTs. These cells are hMSCs transfected with telomerase, which compensates the telomere shortening which occurs during mitosis, therefore enabling further population doublings in comparison to unaltered hMSCs. These cells weren't proliferative but could be maintained in culture for at least 500 hours with adding viability. The same group also described larger-scale fixed- bed bioreactor systems-using 60 mL glass hypes, and glass tubes between two pristine- sword plates (serving as lid and bottom) for a volume of 300 mL. These bioreactors were filled with 2 mm peripherynon-porous borosilicate glass spheres which served as a face for cell adhesion and made use of non-invasive oxygen detectors both at the bay and the exodus. At the 300 mL scale, the authors were suitable to produce6.2 × 108 hMSC – TERTs after167.3 hours of culture, still, only 50 to 60 of the invested cells attached to the borosilicate spheres.

Rotating Bed Bioreactors

Rotating bed bioreactors apply gyration to the preliminarily described fixed- bed system - the cells cleave to plates, which rotate inside the vessel. These bioreactors can be operated at full volume, or also to comber bottles, by not filling the vessel completely and allowing for the cells to intermittently communicate the medium and the headspace. Rotating bed bioreactors partake most advantages and disadvantages of fixed- bed bioreactors

- both give a large face-to- volume rate, are compatible with perfusion, and convey low shear stress to the cells, while cell harvesting and monitoring cannot be performed during the culture. Rotating bed bioreactors, still, can give some further unity to the contents of the vessel by means of gyration employed. Operations of these systems also include biocatalysis and wastewater treatment, and it has formerly seen use in mammalian cell culture.

Neumann et al. characterised the Z ® RP 2000 H bioreactor and applied it for UCM – hMSC expansion. The authors vindicated homogenisation of the culture under normal operating conditions for both a half-full (70 mL) and full (120 mL) vessel, and the Bodenstein number was characteristic of a stirred-tank reactor- type mixing indeed for the smallest mixing speed and full volume. After 5 days of culture, an aggregate of (2.46 ±0.24) × 107 hMSCs could be attained at a 125 mL scale, maintaining hMSC immunophenotype and trilineage isolation eventuality. Reichardt et al. applied rotating bed bioreactors with a 6000 cm2 face area and a 340 mL working volume for mortal umbilical cord roadway cells (HUCACs), harvesting (3.48 ± 0.55) × 108 cells in 9 days, albeit with full reduction of glucose at some time points (despite the perfusion feeding governance). The authors compared bioreactor culture to conservation in static T-25 steins and estimated 311 of these steins would be needed to achieve the same cell figures, encompassing an over tripartite increase in the medium volume necessary.