



SERUM-FREE MEDIUM FOR CHO CELL CULTURE IN STIRRED TANK BIOREACTOR

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Introduction. Cell culture medium is a key factor in bioprocesses performance (1, 2). For this reason, it is essential to test any modification in this raw material. On the other hand, continuous culture is a powerful tool to establish stationary states for process change studies.

The introduction of a homemade medium instead of a commercial one, from lab to pilot scale, is evaluated in this work.

Methods. CHO cells producing rhEPO were used. The evaluation at lab scale was performed in roller bottles cultured in batch mode, for triplicate. After that, two runs in continuous mode operation were carried out for each medium. A 20L stirred tank bioreactor was used. The evaluated media were: SFM4CHO as control (CM) and the homemade medium (HM). Cell culture behaviour was evaluated in both systems using growth and production yield.

Results. Evaluation in batch mode at lab scale showed better results for the HM in comparison to CM, as Table 1 presents.

Table 1. Cell culture behaviour is presented as ratio between HM and CM. VCD: viable cell density, IVCD: integral of VCD, SGR: specific growth rate, MPC: maximum product concentration, SPR: specific production rate.

Media ratio	VCD (cel/ml)	IVCD (cel/ml h)	SGR (h^{-1})	MPC ($\mu g/ml$)	SPR ($\mu g/cel h$)
HM/CM	1,8	1,5	1,2	1,6	1,2

Same results were found in the continuous cultures, where the same dilution rate was applied for all runs ($D = 0,45 d^{-1}$). The stationary state in HM was reached at higher viable cell density (VCD), (Fig. 1). This was consequence of a higher specific growth rate promotion observed from batch stage. Likewise, the upper specific production rate was achieved in HM medium (Fig. 2).

The results suggest that HM is a good candidate for CHO cell culture in stirred tank bioreactor.

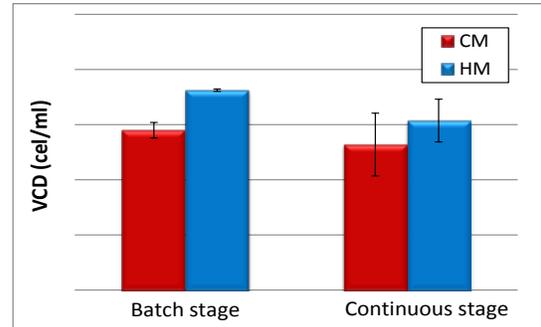


Fig.1 Viable cell density in stirred tank bioreactor operated in continuous cultures. Both culture stages are compared for the studied media.

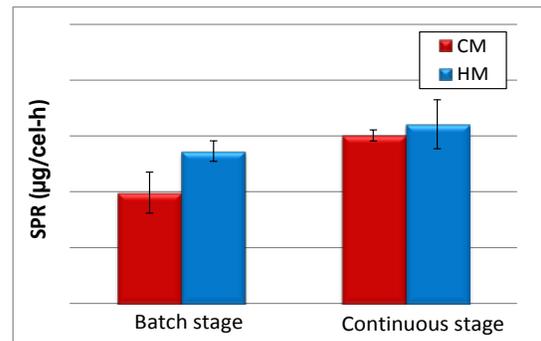


Fig.2 Specific production rate in stirred tank bioreactor operated in continuous cultures. Both culture stages are compared for the studied media.

Additionally, it was proved that the quality of rhEPO obtained from both media was equivalent, a very important issue from regulatory point of view (3, 4).

Conclusions. The HM medium is able to improve the productivity based on CHO cells culture in comparison to the commercial medium evaluated, maintaining quality product.

References.

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