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Process performance of parallel bioreactors for batch cultivation of *Streptomyces tendae*

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Abstract:

Batch cultivations of the nikkomycin Z producer *Streptomyces tendae* were performed in three different parallel bioreactor systems (milliliter-scale stirred-tank reactors, shake flasks and shaken microtiter plate) in comparison to a standard liter-scale stirred-tank reactor as reference. Similar dry cell weight concentrations were measured as function of process time in stirred-tank reactors and shake flasks, whereas only poor growth was observed in the shaken microtiter plate. In contrast, the nikkomycin Z production differed significantly between the stirred and shaken bioreactors. The measured product concentration and product formation kinetics were almost the same in the stirred-tank bioreactors of different scale. Much less nikkomycin Z was formed in the shake flasks and MTP cultivations, most probably due to oxygen limitations. To investigate the non-Newtonian shear-thinning behavior of the culture broth in small-scale bioreactors, a new and simple method was applied to estimate the rheological behavior. The apparent viscosities were found to be very similar in the stirred-tank bioreactors, whereas the apparent viscosity was up to two times increased in the shake flask cultivation due to a lower average shear rate of this reactor system. These data illustrate that different engineering characteristics of parallel bioreactors applied for process development can have major implications for scale-up of bioprocesses with non-Newtonian viscous culture broths.

Key-words: milliliter bioreactor, nikkomycin Z, rheology, viscosity, shear rate