

## Hybrid Fermentation System for Improvement of Ergosterol Biosynthesis

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**Abstract :** Ergosterol (ergosta-5,7,22-trien-3 $\beta$ -ol), also known as provitamin D<sub>2</sub>, is the precursor of vitamin D<sub>2</sub> (ergocalciferol), because it is converted under UV radiation to this vitamin. The natural sources of ergosterol are mainly the yeasts (*Saccharomyces* sp., *Candida* sp.), but it can be also found in fungus (*Claviceps* sp.) or plants (orchids). In the yeasts cells, ergosterol is accumulated in membranes, especially in free form in the plasma membrane, but also as esters with fatty acids in membrane lipids. The chemical synthesis of ergosterol does not represent an efficient method for its production, in these circumstances, the most attractive alternative for producing ergosterol at larger-scale remains the aerobic fermentation using *S. cerevisiae* on glucose or by-products from agriculture of food industry as substrates, in batch or fed-batch operating systems. The aim of this work is to analyze comparatively the influence of aeration efficiency on ergosterol production by *S. cerevisiae* in batch and fed-batch fermentations, by considering different levels of mixing intensity, aeration rate, and n-dodecane concentration. The effects of the studied factors are quantitatively described by means of the mathematical correlations proposed for each of the two fermentation systems, valid both for the absence and presence of oxygen-vector inside the broth. The experiments were carried out in a laboratory stirred bioreactor, provided with computer-controlled and recorded parameters. n-Dodecane was used as oxygen-vector and the ergosterol content inside the yeasts cells has been considered at the fermentation moment related to the maximum concentration of ergosterol, 9 hrs for batch process and 20 hrs for fed-batch one. Ergosterol biosynthesis is strongly dependent on the dissolved oxygen concentration. The hydrocarbon concentration exhibits a significant influence on ergosterol production mainly by accelerating the oxygen transfer rate. Regardless of n-dodecane addition, by maintaining the glucose concentration at a constant level in the fed-batch process, the amount of ergosterol accumulated into the yeasts cells has been almost tripled. In the presence of hydrocarbon, the ergosterol concentration increased by over 50%. The value of oxygen-vector concentration corresponding to the maximum level of ergosterol depends mainly on biomass concentration, due to its negative influences on broth viscosity and interfacial phenomena of air bubbles blockage through the adsorption of hydrocarbon droplets-yeast cells associations. Therefore, for the batch process, the maximum ergosterol amount was reached for 5% vol. n-dodecane, while for the fed-batch process for 10% vol. hydrocarbon.

**Keywords :** bioreactors, ergosterol, fermentation, oxygen-vector

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