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Hollow-fiber Bioreactors: Present and Future in the Biotechnology Industry

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The hollow-fiber membrane systems have been used as bioreactors years ago due to the advantages that present, such as, including two operations, reaction and separation, in the same system; these bioreactors can be used in batch, semi continuous or continuous processes, in biphasic or multi-enzyme reactions, showing high surface area in a small volume. The behavior of these membrane reactors (kinetic, fluid dynamics, modeling) has been studied in the past 30 years. They have been widely used in water purification, as dialyzers for removing low molecular weight species.

In the biotechnology and pharmaceutical industries this membrane configuration has been used with different enzymatic reactions (using lipases, proteases, hydrolases and cellulases), and cells cultures to obtain different products or to produce secreted proteins and antibodies from mammalian cells. The enzymes or cells are located on the membrane, or are confined in the lumen or in the extracapillary space. A suitable selection of the membrane material, flow and molecular weight cut-off allows that the enzymatic reactions or cells cultures evolve correctly, and that the exchange of substrate or products through the membrane was optimal.

In recent years, the use of these membrane bioreactors is growing, since they enable the separation of extracellular products from the cells, and it is possible perform a simple scaling using several units in parallel form, obtaining high productivities. Hollow-fiber cell cultures present advantages versus classic suspension cultures because cells are bound to a porous matrix much, as they are *in vivo,* and they are cultured in a per fused environment without shearing. Also, high-density cell cultures can be achieved, allowing significant reductions in cell culture media and other additives

Some of the present and future uses of the hollow-fiber bioreactor are cultures of endothelial cell and hepatocyte, recombinant protein production or monoclonal antibodies, lymphocyte culture, culture of placental derived cells, or production of viruses in vaccine manufacturing. Hollow-fiber bioreactors offer a compact, highly efficient, scalable and economical method for virus production. The concept of "scaling out" by using multiple small reactors, with each reactor designated to provide a patient-specific treatment, instead of "scaling up" to a single large bioreactor system is gaining popularity.

Another application is its use for "*In vitro* Toxicology" to model pharmacologic bio-availability for different antimicrobial drugs, and also to simulate dosage profiles that generate resistant organisms. Anti-cancer agents, anti-fungals, antibiotics, anti-virals (including anti-HIV) and anti-parasitic drugs have been tested in hollow fiber bioreactors.

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