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Digital Stock

Influencing production

Gunter Festel, *Jürgen Knöll* and *Hans Götz* examine the impact of biotechnology on the chemicals industry

In Brief

- **The most important biotechnological production processes are the fermentation of micro-organisms and enzyme catalysis**
- **The market for biotech-based products accounts today for only 3% ($30bn) of the total chemical market**
- **By 2010, about 20% of chemical products with a sales volume of approximately $310bn will be produced using biotech**

Biotechnology has demonstrated already that it can accelerate innovation in pharmaceuticals, where its application is most advanced. Over the past ten years, most of the truly innovative drugs — those that address an unmet medical need — have come from the application of biotech. Currently, many more biotech-based products are in the pipeline and are expected on the market soon. But what are the implications of biotech for the chemicals industry and how will they change the industrial landscape?

The most important biotechnological production processes for the coming years are the fermentation of micro-organisms and enzyme catalysis. During fermentation micro-organisms (bacteria, yeasts, fungi and algae) or animal and plant cell cultures produce natural materials as metabolic products, from inexpensive carbon and nitrogen sources.

Fermentation with animal and plant cell cultures is especially suitable for the synthesis of complex biomolecules such as sugar- and lipid-modified molecules, and proteins, which are not accessible by chemical synthesis routes. Although the fermentation process requires a high dilution, it is a single step that leads to the desired product.

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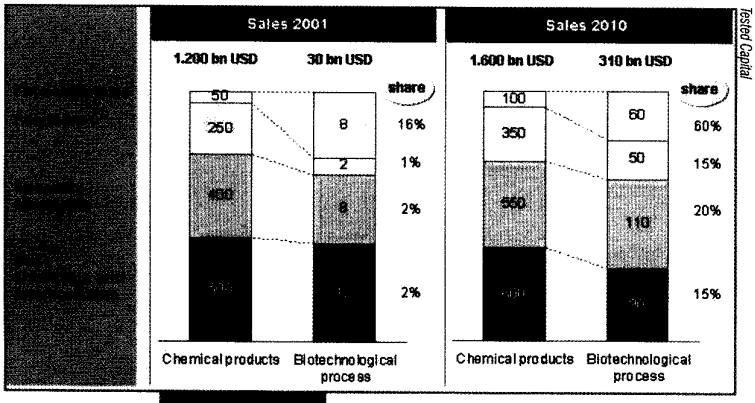

Biotransformations are the conversion of a specific substrate by stereospecific catalysis using isolated enzymes, cells or micro-organisms. Enzyme catalysis can work at concentrations up to 50%, but a single enzymatic step does not necessarily lead to the desired product, so the reaction may need to be performed in multiple steps.

While cell-free biotransformations will widely replace fermentation in the next ten years, transgenic plants and animals are not likely to.

The market for biotech-based products, excluding ethanol and starch derivatives which have been produced by fermentation traditionally, accounts today for only 3% ($30bn) of the total chemical market (see Figure). Some key examples are: biocatalysis and biomolecules in fine chemicals; biopolymers as substitutes for synthetic polymers; enzymes and modified additives in specialities; and, the production of for basic and intermediate organic chemicals using fermentation.

By 2010, about 20% of chemical products with a sales volume of approximately $310bn will be produced using biotech including about 15% of polymer products. A key focus will be regenerating raw materials and development of new product properties. 20% of speciality chemicals, approximately 20% of sales, will be produced by biotech with many opportunities in the food, cosmetics, textile and leather industries. Biotech will deliver 15% of base chemicals and intermediates, due to the production of organic chemicals by fermentation and the increased use of regenerating raw materials. Fine chemicals offer the greatest potential with 60% of sales produced using biotech for the production of enantiomerically pure complex chiral molecules.

More than 50% of the top 100 drugs are based upon enantiomerically pure molecules, and such drugs already today exhibit sales exceeding $100bn. In addition, 60% of the new active pharmaceutical ingredients (APIs) in drug development phases II and III are chiral, and 90% of the new chiral substances are developed enantiomerically pure.

Technical development has progressed rapidly and will further boost the application potential of biotransformations. Increasing knowledge of enzyme reactions in non-aqueous solutions will lead to a broader spectrum of processes and a greater number of potential substrates. Process efficiency will be improved due to new developments in reactor and process design. The versatile application of extremophiles will enable more robust processes, increasing the diversity of process conditions and reducing reaction times. Additionally, the use of directed evolution processes can lead to the development of custom-made and high-performance enzymes. Genetic engineering of micro-organisms will result in the discovery of new enzymes and reactions, as well as lead to a reduction of unwanted side reactions in cell-bound biotransformations.

Cost is a decisive driving force for the transfer to biotechnological processes. Biotech routes often have substantially lower capital and manufacturing costs, and allow greater flexibility due to lower minimum economies of scale. Additionally, biotech is more ecofriendly with less waste produced and less energy consumed. It is more sustainable because it relies more on renewable resources, and its products are often biodegradable.

In some industrial segments, such as the food industry, higher prices can sometimes be achieved for biotech products compared to their chemically produced counterparts. However, factors other than production costs do not usually play a role in the choice of production process.

Restrictions in the use of biotechnological production processes are primarily seen on the economic side, for example, operating and R&D costs, and investments. The synthesis of existing products by chemical procedures is frequently so cheap that the development of a biotechnological production process is generally not cost efficient. The development of a suitable biocatalyst for enzyme catalysis can be very costly and time consuming, and production facilities for chemical syntheses already exist and cannot be converted to biotech production without further investment.

In the product segments where biotech already plays a role it has been able to reach a dominant position within only a few years. For example, it has gained a 80–100% market share in many organic acids, vitamins and amino acids processes, as it can offer a significant cost advantage. For riboflavin, the biotech-based process almost totally replaced the market for products made by chemical synthesis within four years, as production costs were more than 50% lower and investment in new capacity required 40% less capital.

In 1990, lysine was produced only by means of chemical synthesis. But in 1991 Archer Daniels Midland (ADM) built a fermentation plant for the manufacture of lysine and entered the market. The new production process, which was used already by some smaller players in Asia, reduced the investment and the production cost by nearly 50%. In 1998, ADM improved the classical fermentation process by using genetically modified bacteria strains for fermentation and was able to reduce the cost by a further 33%. Now, ADM has a 50% share of the global lysine market. Significantly, this new production process stimulated the market's growth as ADM offered lysine at a price that made farmers switch from soyabean to lysine in their animal feed. As a result, the lysine market grew at some 15% per year between 1990 and 1998.

Biotech is expected to gain further influence on industrial production methods. As biotech research advances, the possibilities of replacing existing chemical processes using biotech routes will increase — especially in textile and fine chemicals, and plastics additives industries. It is unlikely that biotech will impact seriously the chemicals industry in the near-term future, but in the long-term it will bring new growth opportunities.

Other than production costs, the availability of new biotech products, which can not be produced by chemical routes, will drive the sector, especially for fine chemicals, performance biologicals and polymers.

Chemical companies are well placed to move into biotech. They will only have to complement their strong manufacturing skills and distribution networks with specific biotech skills. To understand where and how to move into biotech, companies should analyse their current portfolios and existing capabilities. They should consider the threats and opportunities that biotech can offer regarding impact, timeframe, and the importance of the business from the company's perspective.

This article is based on a series of interviews with chemicals industry executives. Gunter Festel is the founder and managing director of Festel Capital in Huenenberg, Switzerland, and Jürgen Knöll and Hans Götz are associates at Festel.