

CELLTECH, NOVO INDUSTRI

TWO EUROPEAN COMPANIES MARKET LIPASES

LONDON—Lipases, the somewhat unglamorous fat-degrading enzymes, have turned into potential products for both Celltech (Slough, UK) and Novo Industri A/S (Bagsvaerd, Denmark). Each company is producing a lipase by recombinant DNA technology but for very different purposes.

Celltech's human stomach lipase has therapeutic potential. It is intended to be given orally to compensate for an insufficiency of the lipase that the pancreas normally secretes into the duodenum. Pig pancreatic lipase, which has already been used in replacement therapy, is not acid stable; it is largely destroyed in the stomach unless protected by some kind of coating.

Celltech's search for an acid-stable lipase that will survive the human stomach ended in what, in retrospect, is the obvious place—the human stomach. The company plans to test the yeast-produced enzyme's therapeutic potential in collaboration with an unnamed West German pharmaceutical company. Celltech already markets products for treating pancre-

atic insufficiency; the human gastric lipase may prove effective in treating cystic fibrosis as well as pancreatitis. In both conditions, lack of the natural enzyme causes unpleasant side effects and, in some cases, malnutrition.

Novo's lipase is destined for use in detergents, alongside the proteolytic enzymes and amylases that are already widely used to assist low-temperature washing processes. After extensive screening of candidate lipases, Novo has identified a fungal enzyme with appropriate properties, and a process for large-scale production. The enzyme, tradenamed Lipolase, is produced from a fungal gene in an *Aspergillus oryzae* expression system. It is purified from the fermentation broth and then granulated—a process of coating the protein dust particles with an inert material to avoid health hazards.

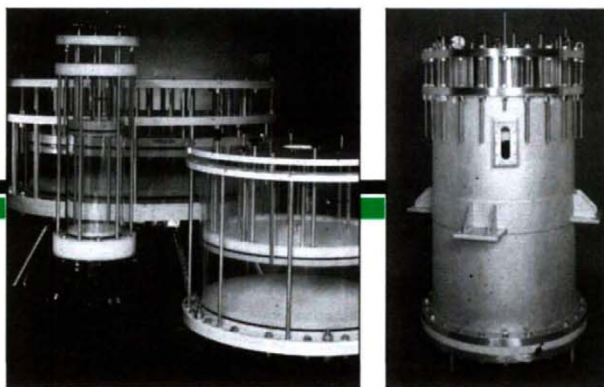
The detergent industry has had access to lipases for some time, says Knud Aunstrup, Novo's vice-president of industrial biotechnology, but the low activity and high cost of those enzymes prevented their wide-spread

use. Lipolase's activity, conversely, is fairly high: the enzyme is relatively resistant both to the detergent itself and to the proteolytic enzymes that are likely to be present. And the *Aspergillus* system will ensure that the granulated enzyme is available in thousands of tons a year—the kind of quantity that may be demanded by detergent manufacturers.

Initial production of Lipolase will be at Novo's plant in Hokkaido, Japan, where the company received manufacturing approval in five weeks. Novo hopes also to produce the enzyme in Denmark but has not yet received approval. Application was made in mid-December, says Aunstrup, and "we are confident that it will be approved sometime this year."

Lipolase is the first enzyme to be produced for the world market by genetic engineering, he says; it is likely that the company's proteolytic enzymes will be produced by a similar process in due course—because of the benefits in yield and purity.

—Peter Newmark



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