Nippon Paper Chemicals Co. is converting wood pulp into the functional natural compound cellobiose using completely new enzyme technology.

NONDIGESTIBLE FUNCTIONAL SUGAR FROM WOOD IMPROVES DIGESTION

Nippon Paper Chemicals Co. (NPC) has started producing the functional oligosaccharide cellobiose from wood cellulose. It has invested JPY 240 million (USD 2.2 million) in a new production facility at Gotsu in Shimane prefecture in Japan with an initial production capacity of 80 metric tons per year. The new facility began operations in December 2007 and sales of cellobiose started in March 2008.

In the initial phase, the cellobiose will be sold for feed applications in order to increase the weight gain of farm animals such as pigs and poultry. In the future, the market will expand to cover functional food, medical and cosmetic applications, etc.

Made from pulp

Cellobiose is a disaccharide of glucose. NPC uses wood pulp as the raw material to make cellobiose. The company produces pulp and also wants to develop high-value compounds derived from pulp. During their investigations, they found that cellobiose has interesting functional properties.

It was known that a chemical method to make cellobiose produces too many by-products. An enzymatic method using cellulase worked much better to produce large amounts of cellobiose with only a small proportion of cellotriose and glucose.

Koji Hosokawa, Research Manager of the Research & Development Laboratory at NPC, considers the main benefits of using enzymes to be a high cellobiose yield, easier purification of cellobiose, mild reaction conditions and a simple process. This is a clean biological process where chemicals are only used to adjust the pH.

NPC believes it is essential to use pure and wet pulp without any hemicellulose for producing cellobiose. When dried pulp was used, the results were poor. It is the only company in Japan producing pure and wet pulp and therefore it will be very difficult for other Japanese companies to copy their cellobiose method. In addition, patents are pending to protect the new technology and the new product.

The collaboration with Novozymes on the cellobiose project started in 2003 and has been coordinated by Hiromichi Sakaguchi of Novozymes. NPC also had a collaboration with Kyoto University, Japan Chemical Engineering and Machinery Co., and Matsutani Chemical Co. in developing a pilot plant to produce cellobiose from cellulose.

Professor Takashi Watanabe of the Wood Research Institute at Kyoto University came up with the original idea of making cellobiose using cellulase. However, his basic process needed modification for industrial conditions and the right type of enzymes had to be selected. There were a number of issues to be solved and Novozymes in Japan helped with the optimizations of pH, temperature, and the enzyme absorption process. Many lab experiments were carried out by Naoto Uyama, a researcher at Novozymes' research center in Chiba prefecture.

After a number of years, NPC has succeeded in developing a commercial product containing 90% cellobiose called NPC Cello-Oligo. NPC Cello-Oligo is a low-calorie, white, crystalline powder with 30% of the sweetness of sucrose.

Cellobiose stimulates growth

Cellobiose is nondigestible by humans and certain animals. In other words, it arrives at the large intestine without being degraded by the digestive enzymes in the mouth, stomach, or small intestine.

It is hydrolyzed by microorganisms in the large intestine. Bifidobacteria and lactic acid bacteria hydrolyze cellobiose slowly. These groups of bacteria are claimed to have several beneficial effects, especially in terms of improving digestion and the strength of the immune system.

Clostridium butyricum in the large intestine decomposes cellobiose much faster and produces butyric acid. The butyric acid activates the metabolism of the epithelial cells resulting in better regulation of the large intestine.

Nondigestible food ingredients that have a beneficial effect by selectively stimulating the growth of bacteria in the colon are known as prebiotics. Cellobiose is a prebiotic that supports

In December 2007, Nippon Paper Chemicals Co. began to produce cellobiose from wood pulp at the Gotsu plant in Japan.

Feeding trials in Japan have shown that cellobiose increases the daily weight gain of piglets significantly.

ANOTHER UNCOMMON CONNECTION FROM NOVOZYMES

Cellulose is the most abundant plant material on earth. It is also one of the most indigestible – at least for humans and certain animals. The new enzyme technology converts cellulose into a valuable ingredient for animal feed or a functional compound for human consumption. Cellobiose is derived from cellulose with the help of enzymes.

the growth of many different species of intestinal microorganisms, both cellulolytic and noncellulolytic. And the more of these microorganisms, the better the intestines work at digesting food.

Better fiber digestion

It is believed that cellobiose stimulates the growth of microorganisms responsible for the digestion of fibers. This was confirmed in a paper in *Animal Science Journal*[1] in 2006, which concludes: "This is the first report showing increased fiber digestion by cellobiose. The main reason may be due to the increased number of cellulolytic bacteria." The scientific research was based on ruminal fluid collected from a cow. The researchers found that the breakdown of dry matter and fiber was increased by 11.2% and 8.9% respectively when cellobiose was added to the ruminal fluid.

Other researchers[2] in Japan did field trials to test a feed additive from NPC containing 96% cellobiose. They found that the average daily weight gain was significantly higher in piglets fed a diet supplemented with cellobiose than in pigs fed the same diet without cellobiose. Over a four-week period, the average daily gain was 559 grams in the control group and 617 grams in the cellobiose group.

NPC sells cellobiose direct to the feed market, but they also have a technical and marketing collaboration with Miyarisan Pharmaceutical Co., which has extensive expertise in animal medicines and feed additives. Miyarisan will investigate the functionality of cellobiose further and there are plans to develop a number of products for different applications.

Future applications

In the future, cellobiose could be used as a dietary supplement for humans, too. Research[3] results show that almost all orally ingested cellobiose reaches the large intestine of humans with little digestion on the way by enzymes. The cellobiose is readily fermented by intestinal microorganisms and acts as a prebiotic.

Cellobiose may also be used in cosmetics such as skin foundations and antiperspirants. It was confirmed in safety tests for cosmetics that cellobiose has no irritation or sensitization effect.

There are also possibilities in pharmaceuticals for use in drug delivery or as a filler for tablets.

Now available!

NPC Cello-Oligo is a brand new product that has just come onto the Japanese animal feed market. The new enzyme technology to make it was developed thanks to a close cooperation between NPC and the technical staff and researchers at Novozymes in Japan. It is a high-value natural product made from wood pulp using only enzymes. Money really does grow on trees! ■

REFERENCES

1. Zeenat Ara LILA et al.: Increase of ruminal fiber digestion by cellobiose and a twin strain of *Saccharomyces cerevisiae* live cells in vitro. *Animal Science Journal*, 2006; 77:407–413.

2. Makoto Otsuka et al.: Dietary supplementation with cellooligosaccharide improves growth performance in weaning pigs. *Animal Science Journal*, 2004; 75:225–229.

3. Sadako Nakamura et al.: Bioavailability of cellobiose by tolerance test and breath hydrogen excretion in humans. *Nutrition*, 2004; 20:979–983.

Commercializing cellobiose: Yuji Nakahara (left), General Manager Business Development, and Masahiko Tabata, Senior Manager Business Development, both of the Technical Division of Nippon Paper Chemicals Co.

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