Lactic acid bacteria – a new tool for medicine and pharmacology?

Food as a Shield

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Lactic acid bacteria, utilized by mankind for millennia, are now earning a new place for themselves in the modern world in view of their vast diversity. They are beginning to be valued not only for their probiotic properties, but also intensively studied for potential applications in biotechnology, medicine, and pharmacology

Lactic acid bacteria are a heterogeneous and highly diverse group of microorganisms classified with the status GRAS (*Generally Regarded As Safe*), meaning that they do not cause illness in humans. They play and important economic role – having been used in the basic production of foods and animal feeds for several millennia. Nowadays such bacteria are being harnessed ever more frequently in developing foodstuffs of particularly beneficial impact for humans and animals. Among other favorable properties, lactic acid bacteria have been shown to reduce the allergenic nature of food, to assist in reestablishing the microflora balance in the alimentary tract to protect against certain pathogenic bacteria, and to exert a beneficial influence on immune system. They therefore seem to have a bright future ahead in pharmacy and medicine. Advances in research have led scientists to attempt to utilize lactic acid bacteria in preventing and treating various ailments, using their cells to act like small factories producing substances of medicinal value. This means we can say that lactic acid bacteria can not only feed us, but shield us as well.

Such current and potential future applications of lactic acid bacteria stimulate research into the better

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A food technologist takes samples from a fermenter used to grow a *Lactobacillus* culture. Many important molecules, i.e. bacteriocins, may be isolated from a culture solution after a predetermined amount of time, and then purified

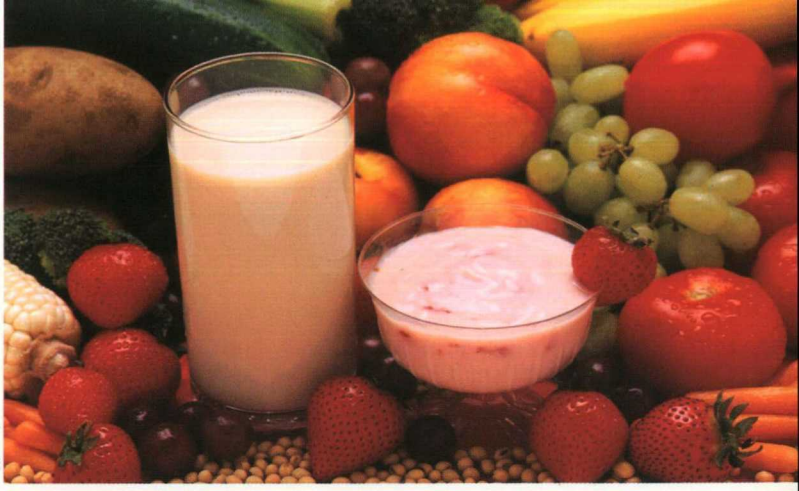
use of such bacteria in biotechnology, the food production industry, and the wider protection of humans and animals. Such research is being pursued at the PAN Institute of Biochemistry and Biophysics. Our broad range of investigations, employing diverse techniques of molecular biology, concerns both the nutritive value and "defensive" properties of lactic acid bacteria. Many projects also involve efforts to preserve the natural abundance of lactic acid bacteria, i.e. gathering collections of "wild" strains and determining the extent of their biological diversity.

Bacteria "cocktail"

Our experiments have shown that the metabolic processes leading to the breakdown of cellobiose (a disaccharide that is a component element of plants) and lactose (a sugar contained in milk) are related to one another. Thus it seems that bacteria initially dwelling in a plant environment are somehow prepared (pre-adapted) to colonize a secondary environment - milk.

We have also discovered another interesting phenomenon: some strains of *Lactococcus*, despite the prevailing opinion, are indeed capable of producing extra-cellular amylases. Amylases are enzymes that break starch down into simple absorbable sugars, facilitating many organisms' production of various useful metabolites: sugars, alcohols, acids, etc. Amylases are therefore very valuable for humans, and the fact that they are secreted outside the cell makes them easier to isolate. When working with lactic acid bacteria the culture solution itself can be directly tapped as a source of amylases, and by raising various strains of bacteria together, secreting different extra-cellular enzymes, we can produce a specific "cocktail" of desired substances.

Another project involves plasmids and their role in adapting bacteria to various environmental conditions. Plasmids are DNA molecules independent of the bacterial chromosome, which bacteria often exchange with one another among cells of the same or different species (called the "horizontal" transfer of genes - as opposed to the transfer of genes in successive generations of descendants). The specific arrangement and organization of genes within such plasmids enables bacteria to adapt to changing environmental conditions - for example, they may encode the resistance to heavy metals, low temperature, the presence of complex sugars, etc. Interestingly, we have found the genes that code for amylases to be located in plasmids, thus enabling them to be classified among the adaptive genes. Moreover, we have identified the nucleotide sequence of 7 plasmids occurring in the cells of a model *Lactococcus lactis* strain and made a range of fascinating observations concerning the conformity and stability of plasmids in the cell, the presence of adaptive genes, and horizontal gene transfer.



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Diversity as defense

One more topic of interest at our laboratory involves viruses that reproduce and cause death of *Lactococcus* cells. Viral infections pose a considerable problem for industry, upsetting technological processes and causing economic losses. Our objective is to identify the degree of biological diversity present in phages, to pinpoint the dominant phage types and their harmfulness to bacteria, and to begin investigating genomic issues. In the future, such research may pave the way for developing a means of combating bacteriophages.

The research topics at our Institute have also recently come to include the defensive function of lactic acid bacteria. Here we are concentrating on seeking and characterizing bacteriocins, i.e. proteinous substances with bactericidal action. We are likewise trying to test lactic acid bacteria's capacity to synthesize substances of potential therapeutic and prophylactic use.

Such research has been and is made possible by funding from the Polish State Committee for Scientific Research and the EU, and it is a topic of our longstanding cooperation with both domestic centers (e.g. Łódź University of Technology and the Agricultural University of Lublin) and foreign ones (INRA and CNRS in France and the University of Groningen in the Netherlands). Also important is our research cooperation with the industrial partners Danisco Biolacta (former Rhodia Food Biolacta) in Olsztyn and Biomet in Lublin. We provide bacterial strain genetic identification services as an expert group in the molecular biology of lactic acid bacteria, acting as an informal reference center for diagnosing such bacteria though molecular biological methods. ■

Further reading:

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