Uses of Biotechnology and Technology Transfer to Keep Food Safe

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ABSTRACT

The era of biology is composed of 1) the definition of molecular laws of biology, 2) the exponential expansion of the data base, and 3) the establishment of the first generation molecular and cellular tool kit; this era is driving the development and commercialization of biotechnological products and processes for agriculture and the food system. These products and processes should have a major impact in maintaining and improving food safety. Several meeting and organizational initiatives on biotechnology and food safety are summarized. Possible roles of biotechnology in areas of food safety involve microbial contaminants, nutritional quality, natural antimetabolites, allergens, toxicants, and synthetic chemical residues. Biotechnology will have an impact on all these areas through both improved ability to measure as well as to modify microbes, animals, and plants used as food. Diagnostics for microbial contaminants and biobased alternatives to synthetic chemicals are most advanced. However, all these biotechnological products and processes for food safety are in very early stages of development and commercialization.

(Key words: biotechnology, food safety, technology)

INTRODUCTION

Consumers have major concerns about the safety of food. These concerns almost reached hysteria in 1989. For example, the cover of Time magazine (March 27, 1989) proclaimed: "...two tainted Chilean grapes triggered a panic about what we eat." This first panic was followed by a second one from alar residues in apples (4). These two examples clearly document the priority consumers place on food safety and how misinformed consumers are on relative food risks (9). The largest risk in food is microbial contamination, and the smallest risk is synthetic chemical residues with nutritional quality and natural antimetabolites, allergens, and toxins in the middle (7). This report outlines the possible uses of biotechnological products and processes not only to keep food safe but also to improve food safety. These biotechnological products and processes will result from the new era of biology which is based on molecular and cellular approaches.

DISCUSSION

The Era of Biology

The first three quarters of the 20th century constituted the era of the physical sciences and engineering; the last quarter initiated an era of biology. In this era of biology, the molecular laws of biology are being defined. The laws are as rigorous as those of the physical sciences but easier to understand. They apply to all living organisms: viruses, microbes, plants, animals, and humans. These laws of biology are the following:

Law I. Nucleic acids (DNA/RNA) are the genetic material.

Law II. DNA is self replicating.

Law III. DNA $\leftrightarrow$ RNA $\leftrightarrow$ linear protein interconversion.

Law IV. Linear protein folds predictably to three-dimensional protein.
Law V. Three-dimensional protein has a predictable biological activity.

Laws I to III are established; Law IV is being established; and establishment of Law V is expected in the 21st century, although at this stage of knowledge its establishment appears impossibly difficult.

In addition to these laws, an exponentially expanding data base is occurring in biology. The human genome mapping and sequencing initiative is the most significant, concrete example of the expanding data base. The tools developed for this human initiative will facilitate, in time, the mapping and sequencing of genomes of interest to agriculture and food. Huge data bases will exist for use in the application of the laws of biology.

In addition, the first-generation "tool kit" for molecular and cellular work on nucleic acids is in hand and is being developed for proteins. This tool kit enables the isolation, characterization, synthesis, design, and directed movement of genes. These tools can be applied to microbes, plants, and animals.

Together, the laws of biology, the expanding data base, and the tool kit are enabling a theoretical and predictive biology with unprecedented products and processes. These products and processes fall under the canopy of biotechnology. Biotechnology at the organism level is an old and well-established technology including plant and animal breeding, and bread, wine, and cheese making. Biotechnology at the molecular and cellular level is a new technology with its earliest products and processes just beginning to impact human health care. The first products for agriculture and food are in the testing stage.

Biotechnology and Food Safety

Biotechnology and Food Safety Reports and Meetings. Biotechnology can make many changes in microbes, plants, animals, and the foods produced from them. These products and processes are in the early stages with the major ones projected for the 1990s and beyond. Anticipation of these biotechnological products and processes has led to initiatives to assess and guide food safety.

In early 1989, the Federation of the American Society for Experimental Biology established an Expert Panel on Criteria for Determining the Regulatory Status of Food and Food Ingredients Produced by New Technologies. The panel was to study and provide guidance on new technologies to FDA, but legal action initiated by specific interest groups has terminated this activity. This legal action illustrates the sensitivity of the area.

In 1988 the International Food Biotechnology Council (IFBC) was formed by food and biotechnological companies and the Industrial Biotechnology Association (IBA). The IFBC plans to issue a report in 1990 to guide regulation of food and food products produced by biotechnology. Both industrial and academic scientists are involved in developing the report.

Boyce Thompson Institute (BTI) in 1987 organized a workshop on agricultural and environmental regulatory considerations of genetically engineered plants (6). This workshop composed of environmentalists, plant biologists and breeders, lawyers, academicians, regulators, industrialists, and public interest representatives reached a new level of consensus. Risk is negligible for US field introduction for either testing or commercial use of major US crops genetically engineered with the modifications expected during the next few years. The key to attaining this consensus was to focus on 1) major US crops, 2) field introductions only into the US, and 3) genetic changes expected in the short term.

In May 1989, BTI organized a workshop on food and feed regulatory considerations of genetically engineered plants (7). This workshop focused on four specific genetic modifications of plants: 1) insecticidal plants containing Bacillus thuringensis toxin; 2) viral-resistant plants containing viral coat proteins; 3) herbicide-tolerant plants containing proteins with increased tolerance to selected herbicides such as glyphosate, sulfonyl ureas, and imidazolinones; and 4) plants with modified protein quantity or quality. All products of the above genetic modifications were proteins containing only common amino acids. Safety questions considered by this workshop included those of nutrition and of allergenic and neuropeptidal activities. The consensus of the workshop was that the safety risk to food and feed of the genetic changes described were very low and that many of the modified products should be considered generally recognized as safe (GRAS). For ex-
ample, the viral-resistant plants produced by biotechnology contain less viral protein than do the nonviral-resistant plants where viruses are present. The report of this food and feed meeting will be published in mid-1990 and free copies can be requested from BTI (7).

The National Agricultural Biotechnology council was formed in 1988 to support research and dialogue on the efficacious and safe development of biotechnological products and processes for agriculture. The council presently involves the senior administrators of BTI, the University of California at Davis, Cornell University, Texas A&M University System, and Iowa State University. In May 1989, the first NABC meeting was held at Iowa State University. The meeting focused on biotechnology and sustainable agriculture. Specific topics included animal growth promotants, animal diseases, biopesticides, and herbicide-tolerant crops. At the meeting, representation was sought from all relevant interests: technology to economics, the environment, food safety, sociology, and ethics. The meeting made significant progress on identifying areas of consensus on such provocative topics as bovine growth hormone and herbicide-tolerant crops. Factual cross-discipline communication from farmer to agribusiness input to food processor, to consumer, and to public interest groups is essential to facilitate progress of biotechnological products and processes.

The Second International Symposium on Biotechnology and Food Safety was held at the University of Maryland, October 10 to 12, 1989. Topics included natural control of microorganisms, detection of pathogenic organisms, biological control of pests, and food ingredients and food safety. All of the presentations on detection of pathogenic organisms (Shigella, Escherichia coli, Listeria, Salmonella, and enteric viruses) considered only gene probes. The developing gene-probe methodology, as described below, may provide methods for diagnosis of the major pathogenic microbial contaminants of food. As indicated in this summary of reports and meetings, food safety and biotechnology are in a dynamic stage of advance.

Microbial Contaminants. Microbial contaminants are recognized as the major problem in food safety. In recent months, the popular press (8, 14) as well as technical organizations have publicized this conclusion (unpublished paper by L. M. Crawford, entitled "Food Safety—a Regulatory Viewpoint," presented at Annual Meeting of the Agricultural Research Institute in October 1988). Frank E. Young, the previous US Commissioner of the Food and Drug Administration, has stated: "We are seeing a marked increase in microbial contamination and a constantly diminishing contamination by pesticides in our food supply." The microbial contaminants include Salmonella, Listeria, Shigella, Escherichia coli, Campylobacter, and Yersenia enterocolitica. An accompanying presentation discussed these organisms, especially Listeria, in dairy products (10).

The Food Safety and Inspection Service of the US Department of Agriculture analyzed 34,000 samples for microbes in 1988. That number is nearly double that of previous years. Laboratory capability limits the amount of monitoring; therefore, faster tests are needed. Biotechnology through DNA probes may provide such tests.

The basic technology to enable development of diagnostics for any need is available. These diagnostics are either protein-based (immunoassays) or DNA-based (DNA probe assays). These tests are or will become highly sensitive, user-friendly, and rapid. The technologies of polymerase chain reaction developed by the Cetus Company and ligase chain reaction developed by BioTechnica Diagnostics, Inc. are super sensitive, enabling detection of as little as 1 to 10 molecules. The polymerase and ligase chain reactions are being automated for ease of use. Application of DNA probe technology is more advanced for human health care than for agriculture and food. In agriculture and food, these diagnostics could be used to assess microbial contamination, quality, impurities, and proprietariness. The key to the extent of application to food safety will be the economics of the tests including the value per test and the number of tests per year.

An example of a DNA probe diagnostic (5, 13) for dental health (11) is provided to illustrate the use of such tests. A development-stage biotechnological company, BioTechnica International, in the early 1980s identified the dental market as an opportunity for biotechnological products and processes and approached Forsyth Dental Center, a world leader in dental research. Forsyth, a not-for-profit research insti-
tute, had identified several microbes associated with periodontal disease and had several of these organisms in pure culture.

Based on a business evaluation, BioTechnica concluded that periodontal disease was a major problem and that a diagnostic would be useful. From 4 to 10 million Americans suffer from major periodontal disease and spend $4 billion annually for treatment. Although microbial cultures had been used to diagnose difficult cases, the anaerobic nature of the disease organisms made their culture inadequately effective as well as slow.

BioTechnica developed DNA probes for the major pathogens associated with periodontal disease. These organisms were Actinobacillus actinomycetemcomitans, Bacteroides gingivalis, and Bacteroides intermedius (11). The probes had the necessary specificity to detect these organisms among about 300 other microbes normally present in the mouth. Sensitivity of 100 to 1000 microbes was adequate for detection, and results were reported as uninfected if less than 1000 microbes/sample, infected if 1000 to 100,000 microbes, and highly infected if more than 100,000 microbes. This DNA probe test was established as a reference laboratory and made available mainly to periodontists as the DMDx test in 1987, and a test called Pathotek™ was made available mainly to dentists. The American Dental Association certified the test in 1987, and in 1988 it selected this test as one of the four major events in dentistry in 1988. These tests are becoming useful tools to assist periodontists and dentists in treatment of periodontal disease.

Similar tests are being developed for foodborne pathogens. The key to such developments and their use is economics.

In addition to diagnostics, biotechnological products and processes may be developed to eliminate or inactivate microbial contaminants. A possible example is the recent USDA report on a sugar treatment for Salmonella (15). Addition of lactose or D-mannose to drinking water can reduce Salmonella by 99.9% in broilers. The cost per broiler is 2¢ for lactose and 50¢ for D-mannose. It is hypothesized that D-mannose blocks adhesion of Salmonella in the digestive tract while lactose supports growth of competing bacteria. Undoubtedly, other biotechnological approaches could be developed to reduce or eliminate foodborne pathogens.

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**Nutritional Quality.** After foodborne pathogens, nutritional quality is the next major food concern. Biotechnology can have a positive effect on nutritional quality. Microorganisms have been genetically engineered to convert glucose to phenylalanine, the major component of aspartame. Undoubtedly, similar approaches will provide economical processes for other amino acids such as tryptophan. Porcine somatotropin not only increases feed efficiency and shortens growth time for swine but also increases the ratio of protein to fat, thereby making pork a more nutritious meat. Traditional plant breeding has converted rapeseed to low erucic acid rapeseed to canola. Decreasing the content of erucic acid in oil improved the nutritional quality of the edible oil, and decreasing the content of glucosinolates improved the quality of the meal as an animal feed.

Biotechnology will produce many other nutritional benefits. A corn seed with elevated tryptophan received the first Patent and Trademark Office allowance for a plant patent in 1986.

**Other Natural Food Antimetabolites, Allergens, and Toxicants.** Natural foods contain examples of antimetabolites, allergens, and toxicants. Legumes contain antimetabolites such as trypsin inhibitors. Some individuals have allergies to one or more natural foods such as milk, eggs, shellfish, and certain plants. Biotechnology could provide methods to eliminate either antimetabolite or allergy-producing proteins. Genes producing the causative protein could be deleted or the technology of antisense RNA could be used to inactivate production of the protein in domesticated plants and animals. Alternatively, the protein might be inactivated by bioprocessing. To my knowledge, significant research has not been initiated in this area. Such research could contribute to food safety.

In recent years, the toxins in natural foods have been emphasized, especially by Ames (1, 2, 3). These agents include solanine in potatoes, hydrazines in mushrooms, theobromine in cocoa and tea, aflatoxin in peanuts and milk, ethyl carbamate in yogurt, diacetyl in butter, allyl isothiocyanate in horseradish, mustard, broccoli, and cabbage, and piperine in black pepper, nutmeg, and cinnamon. These compounds produce carcinogenic, mutagenic, and other effects. Although it is probably more difficult to change these nonprotein molecules than to change protein antimetabolites and allergens, biotechnology may be applied to reducing or
eliminating these naturally occurring toxic agents in our foods.

**Synthetic Chemical Residues.** Synthetic chemicals have been used to protect plants against pest insects, disease, and weeds and as agents to facilitate animal production. Most consumers are concerned about the presence of any detectable residues of synthetic chemicals in food (12). Recent polls of consumer attitudes show that 82% think pesticides in food are a serious threat (9). Biotechnology will provide alternatives in many cases to synthetic chemicals. Examples already being field tested are bovine and porcine somatotropin for improved efficacy of milk and pork production and plants genetically modified so as to produce biopesticides. The advantages of these biotechnological alternatives are that they are proteins with high species specificity and are inactive in humans. Furthermore, they are degraded in the digestive tract. The already low risk of synthetic chemical residues in food should become even lower with biotechnological alternatives. The examples mentioned illustrate the major potential role of biotechnology to produce products and processes to keep our food even safer than it now is.

**REFERENCES**