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PROBLEM OF GENETICALLY MODIFIED FOODS SAFETY: A TOXICOLOGIST'S VIEW

E. L. LEVITSKY

Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Kiyv

E-mail: Levitsky@biochem.kiev.ua

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This study aimed to analyze the published literature regarding the problem of safety of consuming food products containing genetically modified organisms. Genetically modified food products are given a brief definition, purpose and methods of their production are described, and the pro- and contra-arguments for their consumption are presented. The discussion is mostly focused on results of evaluating possible toxicity of such foods and their safety for macroorganism using traditional methods of toxicological analysis. Test results for long-term toxic effects, namely allergenicity, carcinogenicity, reproductive toxicity, and the possibility of mutagenic effects of these food products on the human body and the intestinal microflora are discussed separately. These data are based on the current understanding of the laws of the penetration and functioning of foreign genetic material outside the body, its entry and the possibility of integration into the genome during intake of foods manufactured by genetic engineering. The basic principles of the toxicological and hygienic regulation of these food products are also considered.

An analysis of published experimental results allowed to draw a general conclusion about the absence of reliable scientific information indicating the presence of the toxic properties of genetically modified foods, and therefore of credible evidence of the dangers of consuming for humans and pets.

Key words: genetically modified foods, toxicity, safety.

In one article it is impossible to fully illuminate the problem associated with the consumption of foods containing components of genetically modified organisms (GMOs). Unfortunately, its solution affects both the interests of manufacturers of traditional food, produced using pesticides and other toxic chemicals and thus toxic to animals and humans, as well as of the producers of modern genetically modified food (GMO foods) [1–9]. Therefore, only the most common questions relating to the scientific evidence of possible toxicity and safety of consuming foods that contain genetically modified ingredients are discussed here.

The present century is rightly called the century of biology. Specifically, the hopes of this science solving the urgent problems in the fields of industry, agriculture, pharmacy, and medicine are pinned on the rapid development of one of the most promising of its practical sectors, namely biotechnology [10–12].

Over the past decades, biotechnology as a synthesis of molecular genetics, microbiology, cell biology, botany, zoology and emerging technologies, including nano-, reached indisputable success. It is connected, first of all, with the achievements of genetic engineering that allow getting new high-yielding, pest-resistant crop varieties, breeds of domestic animals, effective and popular pharmaceuticals, as well as coming close to the introduction of methods of treating the most dangerous diseases through stem cell transplantation and gene therapy. Also on the agenda is the creation of artificial organs to replace the damaged ones via integration of special microchips developed with modern computer technologies [13–15].

One of the most important biotechnological achievements was the creation of GMOs, successfully implemented in agriculture, in biomedicine, and to create high-performance biofuels [16].

There are objective reasons that cause the rapid development of biotechnology. Thoughtless use of toxic substances in food and agriculture is a growing concern of the world community. Environmental pollution by harmful products of industry and agricultural chemistry results in an extremely adverse effect on the health of all living things, global warming, deterioration of soil, food, water quality. And these are only some of the effects of environmental and agricultural crisis. The development of traditional medicine is at a standstill because of ignorance of the basic molecular mechanisms of diseases and the absence of effective methods of treatment [13–16].

Against this background, the most promising for solving the problems is the use of the approaches and achievements of biotechnology.

The use of GMOs — viruses, bacteria, yeasts, fungi, plants and animals — is the reality of the modern biotechnological world, the world of the third millennium, nuclear energy, the Internet, microchips, hardware, space exploration and genetic engineering. Regardless of our opinion on GMOs, their development and creation is one of the factors of human progress. And like any other product of scientific and technological development, GMOs can be an unquestinable boon, but can also be seriously dangerous. The GMOs are constantly and heatedly debated over, sometimes passing from the area of pseudo-scientific discussion and information exchange into the political and emotional fields, complicating the already difficult situation even more.

Recently, the media heavily rumors about the alleged unsafe use of human food and pet food containing GMO genes. The authors of these publications suppose that the danger lies primarily in the possibility of "harmful" mutations due to incorporation of GMO genes in the DNA of either macroorganisms or microorganisms that form intestinal flora.

The problem under consideration is too extensive to be analyzed in one article. Therefore, the emphasis here will be placed solely on the analysis of the evaluation results of possible toxicity and safety of GMO food products for humans and animals. Determination and methods of their production will be examined here very briefly. The range of issues associated with the development and practical use of GMOs is in more detail covered in other scientific publications, for example see [17, 18].

The aim of this review was to analyze, in the terms of available scientific information, whether concerns related to the consumption of GMO foods are consistent with modern ideas about the laws of functioning of foreign genes *in vitro* and their possible penetration (integration) into genomes of humans and pets if their food contained components with genes of organisms obtained by genetic engineering techniques, with possible consequences of toxic effect and occurrence of mutations (up to lethal) in the organism.

Determination of GMO foods and the purpose of their production

In modern world, the development of plant genetics and industrial agriculture lead to completely new varieties of exceedingly high-yield crops, amazing in size and notably adaptive to climatic conditions, and with fruits that bear long-term storage while maintaining the form of smell and taste.

Extended genetic engineering experiments substantiated the idea of replacing some parts of DNA strand in order to increase the productivity of various crops. The genetic material of animals served as the hereditary information introduced into the genotype of cultivated plants. Thus, scientists have been able to raise unique species different from their parents in a number of features [1–12].

GMO food products are produced from GMO plants (as a rule) or animals. If the food is produced using GMO and it includes at least one of the GMO-derived components, the food may also be considered genetically modified depending on the national legislation. GMOs have some new properties due to the transfer of separate genes theoretically from any organism (in case of trans-genesis) or from the genome of closely related species (cis-genesis) into a chosen genome [12]. An organism is referred to as genetically modified if it possesses an intentionally altered genotype, and the changes are purposeful and carried out with the help of genetic engineering methods. Genetic engineering allows to work not only with the normal genetic material of an organism, but also to introduce foreign genes or a synthetic nucleotide sequence (so-called "transgenes"), previously not typical of the recipient.

The aim of such operations is to obtain GMO with predetermined and desirable properties (in the case of edible GMO plants, these properties would be, for example, drought and pest resistance, higher yield compared with conventional plants, etc.).

Methods of production

It should be noted that the production of GMO foods (here the primary subject will be eating GMO plants that are most widely used as a food source) has a long history. Classical selection experiments also were based on the transfer of necessary genes, however, unlike the genetic engineering techniques, entire gene clusters were transferred in them. Selection driven by genetic engineering approaches allows purposefully obtaining products with preset properties by transferring one or more genes of interest.

GMO plants are produced by transformation using one of the following methods: agrobacterial-mediated transfer, ballistic transformation, electroporation or viral transformation [12]. A lot of commercial transgenic plants are generated using agrobacterial transfer or ballistic transformation. Normally, the transfer is carried out with a plasmid containing a gene whose activity imparts the desired properties, the promoter regulating the activation of this gene and the transcription terminator cassette which comprises a selective antibiotic resistance gene for kanamycin antibiotic or herbicides. Creating new plant varieties and breeding animals with new technologies is much faster and less expensive than traditional breeding techniques. Furthermore, desired changes can be achieved in fewer generations. Increased resistance to pests, drought and soil salinity makes it possible to grow a lot of grain crops cultures in places where previously it could not be implemented [16, 17].

Genetic modification can impart to the plant and its alimentary produce a veritable number of essential features. Most cultivated GMOs are resistant to the pathogens (viruses and fungi), insect pests or herbicides. This greatly facilitates the cultivation, and also reduces the costs of pesticide treatments.

Evaluation of the toxicity of GMO food products for humans and animals

Typically, to assess the danger of a compound to the body, its toxicological profile is determined in animal studies according to the following parameters: determination of the target (or targets) of possible toxic effect and the critical effect (s) value; dose-response; NOAEL (level at which there are no side effects — the "threshold" concept); safety factor, an acceptable level of consumption (ADI, mg per kg of body mass), the minimum level of safety [19].

From the viewpoint of toxicology based on classical analysis of toxicity and safety of various objects and substances, the study of acute and subacute toxicity of GMO foods does not make sense, because their toxic concentrations are very high and do not differ from such ones for conventional foods (although such studies have been done and will be discussed). Regarding their possible real danger, only chronic toxicity and long-term toxic effects can be argued.

For an objective answer to these and similar questions related to the safety of the GMO products, it is necessary, first of all, to introduce a common procedure for testing of the presence (or absence) of harmful (toxic and other listed above) properties. As it was already noted, in toxicology acute, subacute, chronic, and specific toxicity (reproductive toxicity, mutagenicity, allergenisity, etc.) are typically determined. All substances or products that pose a potential danger to human health (pesticides, pharmaceuticals, and so on) are subjected to such mandatory testing procedure. Upon detection of such properties the matter will be settled. In their absence, given the possibility of insufficient resolving power of the applied testing methods we should, at least theoretically, consider possible mechanisms of potential toxic and mutagenic properties of GMO foods, associated with the possible penetration and insertion of their genes into the genome of a person or of intestinal microflora, followed by induction of deleterious mutations. This possibility is the very foundation of fears of the general public about the dangers of eating these foods.

Theoretically, this situation may be provoked by either DNA, RNA fragments or foreign proteins originated from the GMO food [20, 21]. Most of recently created transgenic plants are different from the parent varieties by the presence of a protein that determines a new character, and the gene that codes the synthesis of this protein (recombinant DNA). Therefore the safety evaluation is focused on studying these carriers of genetic modification. The presence of the recombinant DNA itself in foods and feeds does not pose a risk to human and animal health, as compared with conventional products, since any DNA consists of nucleotide bases and a genetic modification leaves their chemical structure unchanged and does not increase the overall genetic material.

As for the possibility of penetration into the organism, the food DNA arrives in the gastrointestinal tract and is almost

completely decomposed into nucleotides whose chemical composition is the same for all living organisms. Hence, in this case the risk of inserting foreign genes into the host genome is minimum.

Aspects concerning the safety of GMO foods have been comprehensively analyzed in [22]. They include: the possibility of acquiring fragments of foreign DNA from food products containing transgenic sequences; horizontal gene transfer caused by these sequences; integration of transgenic DNA fragments into the genomes of the host and microbial intestinal microflora. Approaches and guidelines on applying methods of modern molecular genetics to assess the safety of these foods were generalized. Also, based on the results of published experimental researches, the following conclusions indicate a lack of toxicity and existence of the safety of the consumption of GMO foods. Firstly, it is stated that small fragments of bacterial and plant DNA (prior to 100 genes) can be detected after ingestion of food in human gastrointestinal tract (GIT). However, since they degrade very fast, horizontal gene transfer from bacteria and plants to man could not be detected [22]. Moreover, these fragments were not detected in germ-line cells. It was found that the transfer of marker genes for antibiotics resistance from GMO plants into the genome of human intestinal microflora and expression of such genes are extremely rare events. The grounds for this are specific conditions in the gastrointestinal tract that contribute to rapid degradation of the fragments of foreign DNA (acidic environment, presence of DNases, temperature conditions, etc.). In such conditions, degradation of plasmid DNA of GMO food products by DNAase I was demonstrated. In addition, the foreign DNA is degraded by enzymes of intestinal microflora.

No toxic effect of the consumption of vegetable feed containing either normal or recombinant corn possessing recombinant plant DNA, *Bacillus thuringiensis* toxin-maize (Bt-maize), for domestic animals (cattle and chickens) was found in [23]. Only the probability of PCR detection of chloroplast-specific gene fragments of different lengths (from 199 to 532 base pairs) and of Bt-maize-specific fragment has been shown. It was found that short fragments of DNA (less than 200 base pairs) from plant chloroplasts can be detected in blood lymphocytes of cattle (bulls). In all other organs of these animals (muscle, liver, spleen, kidneys), plant DNA was absent, moreover, it also has not been found in any of examined organs of the cows. However, shorter amplified fragment of the gene of chloroplast DNA were revealed in tissues of examined organs of chickens. In the eggs, the foreign DNA was not detected. Bt-gene-specific constructs derived from Bt-corn were not found in any of the examined bird organs.

However, it was found that small fragments of the foreign DNA still remain in the gastrointestinal tract after the food is digested, and can be absorbed from the intestinal mucosa of the host. More information on this subject can be found in the monograph [22]. Also, in [24] there is a list of studies relating to digestion and incorporation of transgenic DNA and proteins into mammalian cells. Kuiper noted [22] that "in the process of transgenic DNA digestion in the gastrointestinal tract out of the corresponding food products, it quickly becomes unavailable for transformation, but theoretically such transformation of bacteria can not be excluded, especially if the presence of homologous sequences is considered. Although the presence of small fragments of transgenic DNA in gastrointestinal tract cells of mammals have been demonstrated, there is no evidence of its presence in the germ-line cells. The transfer of antibiotic resistance genes from GMO plant food into the bacterial cells of the human intestinal microflora and their subsequent expression are very rare events, given the small amounts of undigested plant DNA as a result of the environment in the gastrointestinal tract that promotes its digestion". Further in the same article it is stated that given the existing conditions in the gastrointestinal tract that contribute to the degradation of the foreign DNA, as well as the presence of a "competing" bacterial population, transformation and horizontal gene transfer are very rare events. Acidic environment in the gastrointestinal tract and high temperature promote rapid degradation of foreign DNA. Acidic environment catalyzes its depurination. However, fragments of foreign DNA can be detected in the gastrointestinal tract even at 1 hour after consumption of GMO food products. In the chyme in the small intestine of rats and pigs, the DNA is rapidly degraded to concentrations that can not be detected by PCR. However, despite the rapid degradation of DNA in the small intestine, small transiently existing DNA fragments were detected in the intestines of rats even in case of consumption of free DNA. Apparently, there are mechanisms by which they can avoid nuclease degradation even in the absence of the membrane or cell wall.

The authors of a review published in 2012 [25] studied the possibility of transforming DNA in rats with the DNA of food and DNA of GIT microbiota. They pointed out the length of such DNA sequences, insufficient for both these species to presence of homologous recombination (the result of which could be the transfer of antibiotic resistance genes). The DNA of the GIT bacteria was injected with plasmid DNA constructed with two resistance genes (nptI and aadA), homologous to DNA present in the digestive tract, with the genes 16S rRNA and 23S rRNA. The resulting bacteria were fed to rats. Six rats with normal microflora were fed daily for four days with food containing this constructed DNA. Then the microbiota from different parts of the GIT (stomach, small, large intestine and cecum) was analyzed. Two rats were used as negative control. Screening for recombination of introduced DNA with antibiotic-resistant colonies on selective medium using PCR was performed. No transformants were found among the 441 tested isolates. Based on these studies, the authors concluded that extensive digestion of the DNA (100 μg of plasmid per day) did not increase the proportion of kanamycin-resistent bacteria and transformants detected in aerobic microbiota in six rats. The findings coincide with the results of similar studies and indicate no detectable bacterial transformation in mammalian GIT.

In [26] it is noted that the existing evidence indicates the equivalence of GMO food and normal food on indicators such as composition, nutritional value and digestibility: "In hundreds of scientific studies such equivalence has been established, and the presence of GMO DNA and proteins in the tissues of domestic animals (meat, milk and eggs) that consumed GMO food, was not detected".

Previously (2000), such evidence has been analyzed in the review of Beever and Kemp [27]. The authors came to the conclusion that there is full equivalence of DNA behavior of normal and transgenic food. The same emphasis is in [28]: "Based on available data, we do not believe that there is gene transfer of DNA of GMO foods of plant origin into the tissues of animals that consume this food, and if this process occurs its frequency is not different from that of traditional foods".

However, in some studies, the foreign DNA has been detected in the tissues. In 2013, presence of foreign DNA fragments (up to whole genes) in food was established even in human blood [29]. The authors claim that as the human blood is rigidly separated from the inner (GIT) and the external environment, in accordance with standard paradigm large food macromolecules can not pass directly into the bloodstream. In the process of digestion, food proteins and DNA are degraded to smaller fragments, amino acids and nucleic acids respectively, which are than absorbed in a complex active process, and then the blood circulation system distributes them in various body compartments. Based on analysis of more than 1000 samples of human blood, the authors identified food-originated DNA fragments, large enough to contain entire genes, which may avoid degradation and by unknown mechanism penetrate into the human bloodstream. In one of the studied blood samples, the concentration of plant GMO DNA was even higher a person's DNA. The exact log-normal distribution of plant DNA in the plasma was determined, while outside the plasma (in cord blood) of the control samples, plant DNA was not detected. In [30] the authors found transgenic DNA in milk of cows fed GMO foods.

Convincing experimental evidence, testifying in favor of the safety of GMO food products, is given in [31]. In this study, the fate of orally and intramuscularly injected DNA fragments of bacteriophage M13 and the cloned gene of green fluorescent protein (GFP) in the organs of mice was analysed. Using RT-PCR method, absence of horizontal transfer of foreign genes, as well as of the foreign DNA fragments in the intestine and muscle cells of experimental animals was established. Their removal is likely to occur through the mechanism of "liver-bile-gut". In this case, "as indeed it was expected, the entire DNA was eliminated, and there was no case of its insertion into the genome of mice, either as a result of oral consumption or as a result of injection. Hence, even if the foreign DNA pervades the blood in the form of large fragments, germline transfer is not observed".

Recently the term "resistome" was introduced to indicate the resistance to insertion of foreign DNA into the genome of the macroorganism host [32]. The authors emphasize that in recent decades the topic of antibiotic resistance of bacterial pathogens in connection with the consumption of GMO food has become particularly relevant. The human intestine contains microbial population, the so-called intestinal microbiota, which may theoretically serve as a target for the horizontal transfer of genetic material, including antibiotic resistance genes. Recent

advances in the development of appropriate research methods allowed to study the dynamics of the distribution and stability of the genes of the microbiota (corresponding term: "the gut resistome"). Based on analysis of available data, the authors conclude that the genes responsible for antibiotic resistance are ubiquitous among human intestinal microbiota, and the majority of these genes are masked by strictly anaerobic intestinal commensals. The horizontal transfer of genetic material, including conjugation and transduction, is a fairly frequent event for intestinal microbiota. But in most cases this is determined by nonpathogenic intestinal commensals which dominate into the intestine of a healthy individual. The transfer of these genes from the commensals to opportunistic pathogens is relatively rare, but may contribute in a way to the emergence of multidrug-resistant strains, as illustrated for the vancomycin-resistant determinants, common for aerobic intestinal commensals and nosocomial pathogen *Enterococcus faecium*.

The research on RNAs of GMO food is in a similar situation. In [33] the safety of GMO foods was evaluated based on the analysis of mediated non-coding RNAs (ncRNAs), involved in gene regulation. Aside from the today widely used analysis of small interfering RNA (siRNA), suggestions were made to include other RNA variants in this analysis of GMO plants: artificial miRNA (amiRNA), miRNA mimics and artificial transacting siRNAs (tasiRNAs). This approach was applied in [33], and evaluation of the possible toxicity of GMO plant foods due to the presence of foreign RNA was conducted. It was based on the analysis of low molecular weight RNA in conventional and GMO-containing food products. In that study, the authors compared the genetic suppression mechanisms by determining mediators of RNA interference (RNAi): extended double-stranded RNA (dsRNA), small interfering RNA (siRNA) and micro RNA (miRNA) in conventional and GMO foods. It was found that the systematic consumption of both types of products by higher organisms is accompanied by intense degradation of digested nucleic acids, and that there are biological barriers for such dietary ingredients. A small amount of short RNA can be absorbed in the intestine consuming GMO food products. However it was found that, despite the possibility of activation of RNA-mediated gene regulation, the GMO foods are as safe for consumption as conventional plant food [34].

This pattern was also confirmed in the study of the possible toxicity of the proteins of GMO foods. Toxicological evaluation of proteins introduced into the organism in corn, soybean, rice, canola foods revealed that changes in the amino acid composition of GMO proteins do not cause the development of toxic properties. Various effects faced by these proteins when introduced into the body (mechanical, changing pH, temperature, denaturation) likewise do not occasion such properties, known for other marker proteins toxic to mammals [35, 36].

There is also other evidence of the absence of toxicity introduced with GMO food proteins. For example, Lutz et al. [37] using the method of immunoblotting showed degradation of Cry1Ab-protein of GM maize in the GIT of the bull.

However, some authors still allow for the possibility that toxic effects of GM food proteins occur in the mammal macroorganism. According to the author of [38], there are problems associated with the production of transgenic food and its possible negative impact on the body. In the light of data on molecular mechanisms of formation of the protein structure and of sustenance of interprotein complementarity there is a hypothesis about the complex nature of the functioning of the structure-supporting, depleting and eliminating systems. The author considers it is possible that the use of GMO products leads to development of certain disorders of interprotein coordination mechanisms likely with consequences for the organism. However, given the fact that GMO foods are exposed to the abovementioned heavy impacts in the GIT (pH change, denaturation, thermal treatment, reducing agents, mechanical stress, etc.) that alter the structural profile of GM-proteins, resulting in their denaturation and loss of functional activity, consumption of this food can be considered safe [36].

Without going into detail on the highly publicized researches of Ermakova, Pusztai and Seralini [39–41], in which the authors allegedly discovered the presence of toxic, and in carcinogenic and particular allergenic properties of the GMO foods, we only note that when other researchers tried to revise these experiments, they failed to reproduce the results due to the wrong setting and interpretation of original ones. In 2013 an article was published in "Nature" [42], in which the author analyzes in detail the reasons for withdrawal of Seralini's publication.

Publications of aforementioned authors have caused an outcry in the international scientific community including such prestigious organizations as the EFSA and Germany's Federal Institute for Risk Assessment (Berlin), which also did not support the conclusions of their researches.

Recently, in connection with the ongoing debate over the safety of GMO foods and inconsistent results obtained in some studies [43], there are more and more reports demanding thorough evaluation studies of GMO safety and more open discussion on the scientific problem. For example, Devos et al. [44] call for more open debates, more thorough data analysis, discussion of conflicting results of some researches, as well as the relation between the factors of "benefit-risk" using GMO plants in human and pets' nutrition.

As highlighted in that publication, the inconsistency of data on the safety of GMO products is most often caused by political motives. In particular, in developing countries that are still strongly influenced by pesticides producing companies, and where frightening propaganda regarding the consumption of GMO foods is widely used, people are not ready to perceive them as an alternative to their familiar food. For example, the author of [43] from Turkey and most of the authors cited by him that testify in favor of the alleged evidence of toxicity in GMO foods also come from developing countries. He considers foods produced through genetic modification to be able to cause undesirable mutations and determine the development of their toxic to man properties. In this case, he refers to another research of Turkish authors [45], in non-scientific publication, as evidence. He further claims that this toxic material penetrates into the soil and water, causing ecological pollution. These toxins can possibly enter the food chain formed by other organisms. The author cites an old study of 1998 [46] when the possibility of getting Bt-toxin gene into the human body through the soil in which these genes are supposedly stored for a long time was widely discussed. Based on the more recent works, for example [47], that possibility was discarded later. In this paper, the authors studied the effects of transgenic and normal food on three rat generations. Rat stomach, duodenum, liver and kidneys were investigated histopathologically. The volume and average diameter of the renal tubule, as well as thickness of the adrenal cortex were counted. The biochemical parameters in the blood serum that were analysed included, total protein, albumin and globulin, and activities of aspartate and alanine aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, amylase and creatine kinase and also urea volume, urine nitrogen, creatinine, uric acid. The results revealed strong evidence of absence of significant differences between the experimental and control groups of rats on indicators such as the relative weight of organs, blood creatinine, total protein and globulin. Only minimal histopathological changes were found in the liver and kidneys. In another recent paper regarding this aspect [48], the background of the issue was illuminated with description of results of the relevant experiments, and with appropriate conclusions. The authors note that there is 50-year history of safe use of microbial pesticides based on *Bacillus thuringiensis* (*Bt*) in agriculture. These pesticides include such active insecticidal ingredients as Cry proteins. Their coding genes have been introduced into the corresponding GMO products using modern biotechnological approaches. Often, these genes are modified to prohibit expression in plant cells, and a few Cry proteins were changed to increase biological activity. Also, by combining the respective domains, these proteins have been structurally converted with increased insecticidal activity. This was done by extensive research involving such subjects as invertebrates, mammals and birds. Mammals were used for consumption and evaluation of the safety of the GMO food products. The results of these experiments allowed the authors to confirm their safety for man and studied animal species.

Thus the author of [43] quotes very early, outdated work from the 1960–1980s, with results testifying about the alleged toxic effect of GMO foods on the human body that have been refuted by later studies [49, 50].

The authors of two monographs [51, 52] once again sum up and summarize the results of studies of GMO foods safety, concluding that in recent years the assessment involves the latest methods and high-precision technologies. The general conclusion to be drawn from these works is that there are no signs of the genetic modification, as well as of unforeseen events, even when using traditional methods of crossing and selection of plants. In addition, it is emphasized that "unexpected effect" will not necessarily be harmful for humans and pets.

A recent review [53] presented an analysis of the safety studies of GMO foods. It was stated that at the time of writing,

the production technology of genetically engineered plants has been applied for 30 years, and one of its main achievements was the creation of GMO food products. The food's safety has over the years been the subject of intensive research, the results of which are often ignored by the general public. The authors extensively reviewed the scientific literature on this subject over the last 10 years. They collected and processed surveys, experimental articles, reports and modern opinions on this issue; given its importance (it is sufficient to note that at the time of publication, GMO vegetable products have been widely used all over the world). The main conclusion drawn by the authors is that the results of researches carried out so far indicate the absence of any danger of the use of these products. However, discussions on this issue are continuing. Creating a scientific research base will help all professionals engaged in the industry, as well as a wide circle of non-scientific public to obtain reliable and impartial information regarding the safe use of GMO products. In the end, the authors note that 5% of the cited papers present negative results.

A 90-days trial in rodents, described in [54], aimed to identify possible toxic effects of GMO foods based on corn, soybeans and cotton that differed from the usual plants by increased content of some biologically active substances. Foods containing no GMOs were used as a control. A number of parameters relating to possible sub-acute toxicity were determined: the expression of GM-foreign proteins, the presence of altered metabolites with known toxicity, arising from the protein degradation. It has been found that the margins of safety for GMO foods reach 100-fold and do not differ from those for ordinary food. The same applies to the frequency of possible side effects, which also did not differ for GMO- and traditional foods. Based on the studies the authors report the absence of any toxic effects ~~in~~ of the GMO food compared with conventional food.

The authors of the review [55] conclude that there is sufficient evidence of absence of acquired toxic properties of GMO food, and that it is not expedient to resume coincident experiments on animals. In another survey [56] it is stated that: "The results of testing of GMO foods in rodents suggest the existence of extended safety margins (at least 100-fold) of the food consumption without having observed adverse effects (of recalculated daily consumption of this food by humans). There was no evidence of any biologically significant differences in the studied parameters between control and experimental animals". Further information regarding the safety of GMO foods can be found in [57–61].

Thus, on the basis of the information provided we can draw a general conclusion about the absence of serious researches indicating the presence of toxic properties of the GMO food compared with conventional food.

Test results of long-term effects of GMO food products

Research of the researches on possible long-term toxic effects from GMO foods will be considered on the example of the usually evaluated allergenicity, mutagenicity and reproductive toxicity.

Allergenicity

A lot of people are allergic to certain foods (non-GMO). In particular, the soybean allergen is particularly problematic because soy products are finding increasing use in food production due to the high nutritional value of soy proteins. This means that people allergic to soy are finding it increasingly difficult to obtain non-allergenic foods. In addition, pigs and calves consuming soy food can also have allergic reactions. Food allergens are almost always natural proteins. One highly-allergenic soybean seed protein is Gly-m-Pd-30-K, which is about 1% of total seed protein. This protein causes more than 65% of allergy sufferers to react. Using genetic engineering it is possible to lock the gene of this protein and to develop soybean lines that do not contain the allergen [62].

Cotton yield per kilogram of fiber produces approximately 1.6 kg of seeds, which contain about 20% oil. After soybean, cotton is the second most rich oil source, with limited usage in food due to high amounts of gossypol and other terpenoids. Gossypol is toxic to the heart, liver, reproductive system. Theoretically, 44 megatons of cottonseed each year could satisfy the need for oil to 500 mln people. There are conventional methods to produce gossypol-less cotton, but in this case the plant is left unprotected from insect pests. Genetic engineering techniques enable purposeful interruption of one of the first steps of the biochemical synthesis of gossypol in seeds. Gossypol content in seeds is reduced by 99%, while the remaining organs of plants continue to produce it protecting the plant from insects [63].

Reducing allergencity and detoxification of foods by genetic engineering methods are in process of scientific development. Possible allergenicity of GMO food is also a concern of its opponents. Food allergies are an adverse reaction to food that affects the immune system, it affects about 8–10% of children and 1–2% of adults. In theory, each protein may act as an allergen. The most common allergens are milk, eggs, fish, soy, peanuts, nuts and wheat. As evidence of allergenicity of GMO foods opponents of GM plants usually refer to problems associated with the use of transgenic soybean and corn.

However, there is strong evidence of absence of allergenic properties of the GMO food proteins. For example, based on significant experimental data it was concluded that GM proteins are no more allergenic than similar conventional food proteins [64, 65]. In truth, the genetic modification alters the protein structure of the plant, introducing new proteins, modifies or alters their existing amount, and so plant's allergenicity after modification can also vary. That's the reason why GM plants are carefully and mandatory tested for allergenicity.

Most scientists believe that the risk of inducing allergy is much more from the new rarely checked for allergenicity food, than from comprehensively studied GM products. One or two new proteins are consumed with GMO foods while a new product can carry hundreds of new proteins (the same applies to using traditional selection methods). Par example, the broad sell of kiwis caused the development of allergies to this fruit (similarly to soy). It was later found that fruits of this plant contain several allergenic proteins. If the kiwi first came on the market today, under the current rules it would be considered as a new product, tested for allergenicity, and perhaps it never would be on sale [66].

Here are results of several researches that proved the absence of any allergenic properties of GMO foods. For example, in [67] mice were injected with purified Cry1Ab protein from GMMON810 maize, and its effect on metabolism and immune status of mouse organism was evaluated. The results confirmed the presence of immunogenic potential of this protein in absence of allergic reactions. Immunological and metabolic tests have revealed slight differences in the metabolic profile of the experimental rats compared with controls at introduction of the protein, but no reliable unforeseen effects of genetic modification on the immune response were observed. Reiner et al. [68] evaluated the ability of GMO food induce allergic reactions in mice after feeding them GM maize GM *Bacillus thuringiensis* (Bt)-maize (MON810). No noticeable allergic reactions in mice in the model of allergic asthma were induced. In a similar study, Andreassen et al. [69] investigated the possible activity of plant-originated Cry1Ab expressed in transgenic corn MON810 as adjuvant against allergen ovalbumin via aerosol administration to mice. No systemic adjuvant effect under the experimental conditions was detected.

Thus, on the basis of the available experimental material it can be argued that GMO food products possess no more allergenic activity compared to normal diet.

Reproductive toxicity

Considering the above material evidencing the lack of significant toxic potential of the main components of GMO food products (DNA, RNA and proteins), it is difficult to assume toxic effects on the reproductive system and the presence of mutagenic properties.

Nevertheless, studies have been conducted in the vein of evaluating reproductive toxicity of the consumption of food products containing GMOs. For example, in [54] the effect of GM maize in the pre- and postnatal development of the rat offspring was evaluated. Corn was included in the diet as much as possible without upsetting the balance of main nutrients. Analysis of the data did not reveal any impact of GMO maize on the development and emergence of the rat offspring.

In the 90-days trial on rodents that included histopathological evaluation and measurement of the mass of reproductive organs of adults, no reproductive or developmental toxicity in the use of GMO foods was shown [53, 54]. Another already mentioned research [47] evaluated the effects of GMO maize on some histopathological and biochemical indicators in three generations of rats. Samples of rat stomach, duodenum, liver and kidneys were used in histopathological evaluation. The volume and average diameter of the renal tubule, as well as thickness of the adrenal cortex were counted. The biochemical parameters in and urine that were additionally analyzed included urea volume, urine nitrogen, creatinine, uric acid, total protein, albumin and globulin, and in the blood serum activities of aspartate and alanine aminotransferases, alkaline phosphatase, gamma-glutamyl transferase, amylase and creatine kinase. No statistically significant differences in the

relative mass of the organs within the groups were found. Insignificant changes were detected in levels of creatinine, total protein and globulin.

Tyshko et al. [70] evaluated the effect of GM maize Liberty Link® on pre- and postnatal development of the offspring of three generations of Wistar rats. In the experiment, 630 adult animals and 2837 immature rats were used. The animals were divided into 5 groups that received corn-enriched diets: GM maize was given to the experimental group, the traditional analog of GM maize in such investigations was fed to the control group, and 3 traditional varieties of corn, ROSS 144 MW, ROSS 197 MW and Dokuchaevsk 250 MB were given to 1st, 2nd and 3rd reference groups respectively. Corn was included in the diet as much as possible without upsetting the balance of main nutrients. Analysis of the data did not reveal any impact of GM maize on the development of the rat offspring: the study of reproductive toxicity of GM maize Liberty Link® on three generations of rats found no negative impact of GM maize on the reproductive function in experimental animals. Parallel studies of the reproductive toxicity of traditional maize varieties showed the absence of specific varietal effects on reproductive function, pre- and postnatal development of the offspring, and, at the same time, a fairly wide range of fluctuations of the studied parameters, consistent with the literature. The results of the research can be regarded as direct evidence of absence of any negative effect of GM maize on the reproductive function in experimental animals and on the development of their offspring.

In her doctoral thesis, Utembayeva [8] notes: "... an algorithm was developed for evaluation of the reproductive toxicity of GMO of plant origin, including a study of the generative function, prenatal and postnatal development of the offspring of three generations of rats; defined a set of methods to assess the reproductive toxicity of GMOs, including a study of the generative function by fertility, hormonal status and level of gametogenesis in the gonads of males and females; prenatal development of the offspring by the pre- and post-implantation mortality by zoometric parameters of state of internal organs and skeletal system of the fetus; postnatal development of the offspring by the dynamics of zoometric indicators, parameters of physical development, viability from 0 to 5^{th} and 6^{th} to 25^{th} days of life. The lack of impact of genetically modified corn resistant to glufosinate ammonium on the generative function of rats generations P0–P1 was experimental proved, as well as the lack of influence of GM corn resistant to glufosinate ammonium on the prenatal development of the offspring of rats generations P1–P2. Comparative analysis of indicators characterizing the prenatal development of the offspring revealed no significant difference between the control and experimental groups. Evidence of absence of influence of GM maize on the postnatal development of the offspring of rat generations P1–P2 was thus proved. Comparison of indicators characterizing the postnatal development of the offspring showed no significant differences between the control and experimental groups: physical development of the offspring and the dynamics of zoometric parameters correspond to the values of physiological characteristics of the animals of that species and age".

Thus, on the basis of published data, the absence of GMO food toxic effects on the reproductive system and offspring, i.e. the absence of reproductive toxicity, can be considered proven.

Mutagenicity

Batista et al. [71] compared the effects on gene expression of rice obtained by a conventional method of breeding (mutation breeding, in this case the gamma-irradiation) and transgenic rice. The authors used a method of oligonucleotide microarrays for transcriptome modification assessment. As a result, the researchers found that plants obtained by conventional breeding, as compared with the control, caused a far more significant changes in gene expression of non-specific genes (through ~~by~~ abiotic stress induction) than GM plants (ratio 10: 3).

Previously nucleic acids and proteins were shown to have mutagenic activity [72–75]. However, as already mentioned above, these substances upon consumption are broken down to small organic molecules by the digestive enzymes. The ordered information stored in the product's DNA is entirely destroyed, that is, the food is eaten but it does not change our DNA. GMO food differs from conventional in that it has a few extra genes. At the same time, if GMO product is consumed, these genes are digested in the same way as conventional food.

Similar findings were made in [76]: "The likelihood of unintended mutations is much greater with using for sustenance plants obtained by means of conventional breeding, as compared with GMO foods. In addition, the

latter, in contrast to the traditional food, are subject to rigorous testing in rats and cattle before entering the distribution chain". And further: "It is unlikely that consumption of foods containing transgenic DNA, and approving such food products can have any significant harm to human health".

Apart from the above arguments supporting the safety of GMO food products, it should be noted that there are special mechanisms in the organism that reduce the adverse effect of harmful genetic mutations. As a result of their appearance, the meaning of biological information changes. The consequences of this are twofold. With habitat conditions varying only slightly, new information usually reduces the survival rate. If there is a rapid change in living conditions, in case of settling in a new ecological niche it is useful to have variable information. Thus, the intensity of the mutation process in nature is maintained at a level not causing a dramatic drop in viability of the species. An important role in limiting the adverse effects of mutations belongs to anti-mutation mechanisms arising in the course of evolution.

First of all, these are specifics of the functioning of DNA polymerase alpha that selects the required nucleotides during DNA replication, and ensures self-correction during the formation of a new strand of DNA along with endonuclease. Various repair mechanisms of DNA structure and the role of the degeneracy of the genetic code, etc. are studied in detail [77–81]. Realization of this task can be the triplet genetic code, which allows for a minimum number of substitutions within the triplets, leading to distortion of information.For example, 64% of substitutions in the third nucleotide of a triplet do not change their meaning. However, replacements of the second nucleotide distorts the meaning of the triplet in 100%. Another factor of protection against the adverse effects of gene mutations is the paired chromosomes in diploid karyotypes of eukaryotic somatic cells. Pairing alleles prevents the phenotypic expression of mutations if they are recessive in nature. Some contribution to the reduction of harmful consequences of gene mutations is contributed by phenomenon of extra-replicated genes encoding vital macromolecules, present in the genotype in a few tens and sometimes hundreds of identical copies of such genes. Examples include genes of rRNA, tRNA, histone proteins, without which vital functions of cells are impossible. If there are extra-replicated copies, mutational changes in one or even several identical genes does not lead to catastrophic consequences for the cell. The unchanged copies are sufficient to ensure cell's normal functioning [82, 83]. Of considerable importance is also the functional nonequivalence of amino acid substitutions in the polypeptide. If the new and the replaced amino acids are of similar physical and chemical properties, changes in the tertiary structure and biological properties of the protein are insignificant. The occurrence of mutations and the impermanence of the genome are an essential mechanism of variation and the driving force of evolution [77, 82, 84, 85].

Hence, these mechanisms contribute to the preservation of selected genes during evolution, simultaneously accumulating different alleles in the gene pool of a population, forming a reserve of genetic variation. The latter determines high evolutionary plasticity of the population, i.e. the ability to survive in different conditions. As already mentioned, there are no scientifically sound evidences of the GMO food exhibiting more pronounced mutagenic properties compared to conventional food. Thus, the National Academy of Sciences of the United States of America considers it appropriate to carry out regular testing of possible mutagenic activity of GMO food products instead of having on the market the foods derived through mutation breeding [86]. This is supported by mentioned above frequency of mutations that occur when using genetic engineering methods much rarer than with the methods of plant mutagenesis [71].

The basic principles of toxicological and hygienic regulation of GMO foods

All existing evaluating systems of GMO food products' safety involve as the primary phase the analysis of information about the plant to be modified, about the donor organism of new genes, and on the nature of the genetic modification [84].

In the early 1990, the Organization for Economic Cooperation and Development (OECD) has developed the concept of substantial equivalency, currently shared by the majority of experts in the countries of the world community, including the World Health Organization (WHO). This concept is based on a comparison of the GMO with its traditional analog source, in respect of which there is a long history of safe use as a food or food product, according to their appearance, key substances' (protein and amino acid

composition, fat and fatty acid composition, carbohydrates, vitamins, minerals) content, toxins that are standardized in food and forage, allergens and biologically active substances, typical for this type of product [85, 86].

In the absence of sufficient equivalence of GMO food product to its traditional analog, further safety assessment comprises of the following steps: the study of nutritional value of the product; quotas in the diets of humans and animals; methods of use in nutrition, and during breast-feeding; digestibility, evaluation of intake of individual components (if the expected intake is more than 15% of the daily requirement); impact on the intestinal microflora (if GM product contains live microorganisms). Then, such characteristics of GM product are analyzed: the toxicokinetics of the chemicals present only in the test GM product, and not in traditional products; DNA-damaging activity of GM product or its individual components that distinguish it from the traditional product; allergenicity; if the product contains live microorganisms, including genetically modified, potential gastrointestinal colonization and pathogenicity are evaluated. If test product exhibits DNA-damaging activity, long-term studies for carcinogenicity are carried out [27, 87, 88].

When new biotechnology products come to the market, the consumer must be confident of their quality and safety. Therefore, there must be toxicological approaches for the development of new food products and their components, to assess any potential risks of biotech products. Safety assessment of new foods and food ingredients must meet the needs of producers, regulators and consumers. It is essential that this approach is consistent with accepted scientific theories, the results of the safety assessment could be reproduced and are acceptable to the health authorities, and the result must satisfy and convince the consumer.

Currently, the EU has a regulating (controlling) structure established to protect human health and the environment. Adopted by the Directive, which involves software horizontal control, control unnecessary use and development of GMOs.-Control over the use of GMOs is regulated by the regulation "Genetically modified organisms (Contained Use)", published by Health and Safety Executive (HSE) in the UK. HSE receives the recommendations of the Advisory Committee on Genetic Modification. This regulation implements Directive 90/219/EEC and governs all of the GMO contained uses including the production of nutritional supplements or other purposes. All programs must thoroughly assess the risks with special emphasis on the possible organism changes resulting from the consumption of GMO foods.

It should be noted that none other new technology has been the object of as much attention of scientists around the world as the technology of production of GMO foods. This is due to the fact that the scientists have differing opinions about the safety of genetically modified food sources [34, 89, 90]. There is no scientific evidence against the use of transgenic products. At the same time, some experts believe that there is a risk of release of unstable species of plants, transfer of the specified properties to weeds, the impact on biodiversity of the planet, and, most importantly, the potential threat to biological and human health due to the transfer of the inserted gene in the intestinal microflora, or the formation of the modified proteins due to exposure of normal enzymes, and so-called minor components that can have a negative impact [6, 91].

Most of the presently developed transgenic plants differ from parental varieties by presence of protein that determines a new character, and of gene that encodes the synthesis of this protein (recombinant DNA). Therefore safety evaluation is focused on studying these carriers of genetic modification. As noted above, the presence of recombinant DNA itself in the food and forage does not pose a risk to human and animal health, as compared with conventional products, since any DNA consists of nucleotide bases and a genetic modification leaves unchanged their chemical structure and does not increase the overall content of the genetic material. An individual human daily ingests (with food) DNA and RNA in an amount of from 0.1 to 1.0 g depending on the type of food consumed and the extent of their processing. Furthermore, it was found that the percentage of recombinant DNA into the genome of a genetically modified crop is negligible. For example, in the lines of pest-resistant maize, the percentage of recombinant DNA is 0.00022, in pesticide-resistant soybean lines it is 0.00018, in pest-resistant potato varieties it's 0.00075. Food processing significantly reduces the amount of DNA in the product. Highly refined products such as sugar produced from sugar beet or soybean oil contain trace amounts or no DNA. The experts fear possible transfer of antibiotic

resistance genes used in creating transgenic plants into the genome of the bacteria of the gastrointestinal tract. However, the bulk of food DNA would be destroyed in GIT and, therefore, survival of the entire gene with appropriate regulatory sequences is unlikely. In addition, the transfer of recombinant DNA into bacterial genome is virtually impossible, as it requires a sequence of certain stages. These are: penetration of the DNA through the cell wall and membrane of the microorganism, and withstanding the bacterial mechanism of the destruction of foreign DNA; incorporation and stable integration in a specific area of the host's DNA; expression of the gene in the microorganism. Despite the extremely low probability of introducing marker genes into the genome of microorganisms, methods of removing these genes from the plant genome are currently intensively being developed. In particular, the resistant to glyphosate soybean line 40-3-2, and most others recently created transgenic plants contain no antibiotic resistance genes. The discussion and analysis of the problem of safety of food DNA allowed the world scientific community to conclude that the DNA from genetically modified organisms is as safe as any other DNA in the food product. These findings can also be attributed to forage [49, 50, 92].

The GMO safety assessment system focuses on the study of proteins bearing new characters [18, 35, 36, 93]. Amino acid composition of such protein is compared to known structures of protein toxins and allergens in genetic databases [GenBank, EMBL, PIR and Swiss Prot], and based on the analysis, conclusions of degree of similarity are made. Further evaluation of the protein includes determination of acute toxicity in laboratory animals, destruction speed in gastric and intestinal juices on models *in vitro* and in animals, decay during cooking and potential allergenicity. If it is shown that the protein is slowly broken down during digestion and its amino acid composition has a structure similar to known protein toxins or allergens, then chronic toxicity of the protein in question is studied. In the absence of toxicity of the protein, GMO products are deemed as safe as conventional.

All in all, we can say that today there is no evidence suggesting the presence of toxic properties of GMO foods.

Thus, the establishment of vegetable GMO foods was caused by objective reasons, primarily higher yields due to pest resistance and the lack of need for chemicals (pesticides, herbicides). In addition, biotechnological approach allows to manufacture products with predetermined useful properties. However, this food, obtained with the help of gene technologies poorly understood by ordinary consumers (the history of this misunderstanding goes back to the days of "Lysenkoism"), has at first caused a flurry of rejection and criticism. Imaginary threats that supposedly may result from its use are "horror stories" that intimidated and continue to intimidate the commoners, unfamiliar with possible mechanisms of these unjustified fears. The spread of these delusions is owed mainly to representatives of pesticide manufacturers that bear huge financial losses as a result of the ever-increasing introduction of GMO foods on the market. Risking total bankruptcy, they exaggerate and revive long-forgotten myths and legends, as a result of which our biological sciences altogether and the emergent from them biotechnology in particular fared so poorly.

Of course, one cannot categorically claim that GMO food is potentially completely safe. Some authors consider the data and evidence of safety of currently produced GMO foods to be insufficient [43, 49, 50, 55]. According to the author of the latest review, GMO foods are now widely available in the markets of most countries, and approved for use by the relevant national legislative bodies. According to the estimates given in the legislations, there is no risk associated with the toxicity of these foods. However, according to the author, who used the information published in *Medline database*, there are not enough reviews relating to toxicological studies of GMO food products. This applies to researches, conducted on GM plant food (tomatoes, potatoes, corn, rice, peppers, peas and canola) regarding its potential toxicity to humans and animals. In addition, they were performed mostly in research laboratories of biotech companies that produce these products, the assessment of which could have been biased. Thus, the author is right to question: is there any scientific proofs of the toxicological safety of plant GMO foods?

But no similar categorical statements exist about the safety of traditional foods produced using pesticides. From the point of view of toxicologist, GMO foods even are much better studied than ordinary traditional food (which among other things contains pesticide residues [18, 60]), and are at least no more dangerous than products obtained by conventional techniques. Indeed, short

stretches of transgenic DNA and proteins can penetrate the cells of the gastrointestinal mucosa. However, no specific and well-proved results of their future potential toxic effect were published. A lot of testing of these foods on animals did not identify their direct or indirect toxic effect. Delayed toxic effects (mutagenicity, allergenicity, reproductive toxicity, etc.) have not been found either. According to all these indicators, GMO food was not different from the usual. This is natural, given the existence of the currently known powerful extra- and intracellular biochemical detoxification mechanisms. These include the degradation of the foreign nucleotide and protein sequences, repair of damaged DNA regions, and the existence of multiple copies of duplicate genes, and finally, the inconstancy of the genome [18, 72, 87], which allows to avoid long-term mutagenic effects of relevant factors. Moreover, potentially toxic DNA fragments and proteins completely degrade from exposure to both the environment (mechanical stresses, temperature, denaturation, pH etc.) and enzymes (nucleases and proteases, acting against the "unknown" chemical and biological targets) before their entry into target cells.

Biotechnology does not stand still. The development of new genetic engineering techniques that allow for better targeted control over the fate of inserted genes and their safe disappearance during consumption of GMO food, gives reason to believe that in the near future, this food will no longer be the object of violent attacks of opponents of its introduction in the consumer market, and will gradually replace its traditional toxic, allergenic "pesticidal" analog.

Analysis of the published literature indicates that the production process of GMO foods does not cause any toxic properties other than known for ordinary food. The safety of these products can be reliably tested using conventional methods of analytical chemistry, toxicology and nutraceuticals. Substantial limitations may occur in the future, if the use of transgenic technologies will lead to more significant and complex changes in food. For now, there are no methods for complete evaluation of whole foods (as compared with a singular chemical component) regarding the safety of GMO food products. Progress can also be achieved with the development of conclusive methods for identification and characterization of protein allergens, and now it is the main focus of relevant studies. Another important objective is the improvement of methods of analysis of metabolites of plants and microorganisms, as well as proteins in case of their gene expression. This might be useful in detecting sudden changes in the GMO and in establishing the level of sufficient equivalence of GMO food products.

Security level of modern GMO products is for consumers equivalent to that of traditional foods. There is no scientifically proven information on the adverse health effects of these products. However, this conclusion cannot guarantee that all subsequent genetic modifications will have the same positive and predictable results. Further development of toxicological methods and management strategies is a prerequisite for maintaining the level of safety of GMO foods [85, 86].

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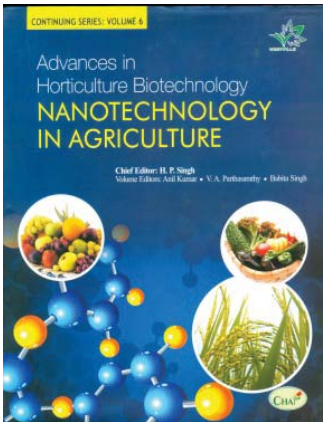

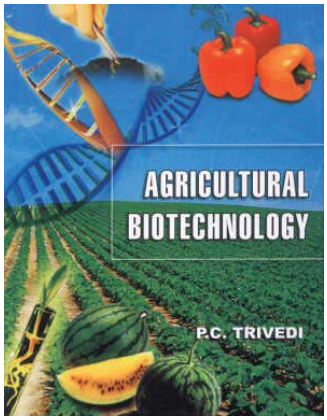

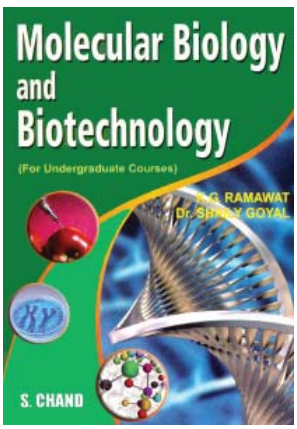

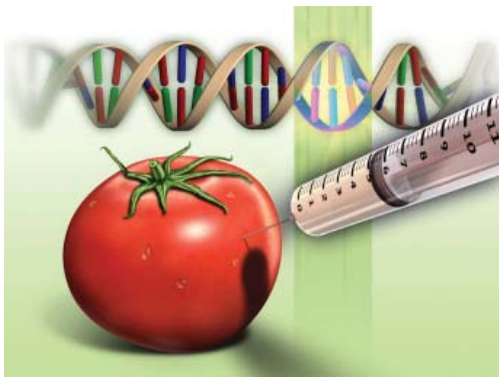

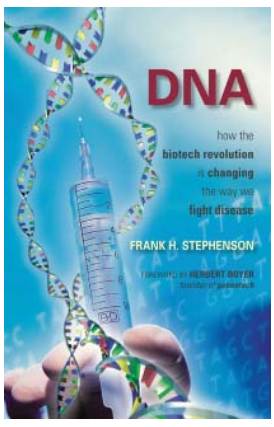

ПРОБЛЕМА БЕЗПЕКИ ГЕНЕТИЧНО МОДИФІКОВАНИХ ПРОДУКТІВ ХАРЧУВАННЯ: ПОГЛЯД ТОКСИКОЛОГА

Є. Л. Левицький

Інститут біохімії ім. О. В. Палладіна
НАН України, Київ

E-mail: Levitsky@biochem.kiev.ua

Метою роботи був аналіз даних літератури стосовно проблеми безпеки вживання продуктів харчування, що містять генетично модифіковані організми. Подано стисле визначення генетично модифікованих продуктів харчування, описано мету і методи отримання, наведено думки «за» і «проти» їх вживання. Основну увагу приділено обговоренню результатів оцінки можливої токсичності і безпеки їх для макроорганізму з використанням традиційних методів токсикологічного аналізу. Окремо обговорюються результати тестування віддалених ефектів цих харчових продуктів, а саме: алергенності, канцерогенності, репродуктивної токсичності, а також можливості мутагенного впливу на організм людини і мікрофлору кишечника. Ця інформація базується на сучасних уявленнях про закономірності проникнення і функціонування чужорідного генетичного матеріалу поза організмом і можливості його потрапляння (вбудовування) в геном у разі споживання продуктів харчування, отриманих методами генної інженерії. Наведено основні принципи токсиколого-гігієнічного регламентування таких продуктів харчування.

Аналіз опублікованих експериментальних результатів дав змогу зробити загальний висновок про відсутність наукової інформації, яка свідчить про наявність токсичних властивостей у генетично модифікованих продуктів харчування, і, отже, вірогідних доказів небезпеки їх вживання людиною і домашніми тваринами.

Ключові слова: генетично модифіковані продукти харчування, токсичність, безпека.

ПРОБЛЕМА БЕЗОПАСНОСТИ ГЕНЕТИЧЕСКИ МОДИФИЦИРОВАННЫХ ПРОДУКТОВ ПИТАНИЯ: ВЗГЛЯД ТОКСИКОЛОГА

Е. Л. Левицкий

Институт биохимии им. А. В. Палладина
НАН Украины, Киев

E-mail: Levitsky@biochem.kiev.ua

Целью работы был анализ данных литературы, касающейся проблемы безопасности употребления продуктов питания, содержащих генетически модифицированные организмы. Дано краткое определение генетически модифицированных продуктов питания, описаны цель и методы получения, приведены мнения «за» и «против» их употребления. Основное внимание уделено обсуждению результатов оценки их возможной токсичности и безопасности для макроорганизма с использованием традиционных методов токсикологического анализа. Отдельно обсуждаются результаты тестирования отдаленных эффектов этих пищевых продуктов, а именно: аллергенности, канцерогенности, репродуктивной токсичности, а также возможности мутагенного влияния на организм человека и микрофлору кишечника. Эта информация базируется на современных представлениях о закономерностях проникновения и функционирования чужеродного генетического материала вне организма и возможности его попадания (встраивания) в геном при потреблении продуктов питания, полученных методами генной инженерии. Приведены основные принципы токсиколого-гигиенического регламентирования таких продуктов питания.

Анализ опубликованных экспериментальных результатов позволил сделать общий вывод об отсутствии научной информации, свидетельствующей о наличии токсических свойств у генетически модифицированных продуктов питания, и, следовательно, достоверных доказательств опасности их употребления человеком и домашними животными.

Ключевые слова: генетически модифицированные продукты питания, токсичность, безопасность.