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Bioethics and Genetically Modified Foods

Bioética y alimentos transgénicos

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Abstract:

Currently, the genetic modification of plants, animals and other organisms has intensified and has allowed the development of increasingly advanced methods. The creation of transgenic foods, their use and distribution have generated various positions, since there is no certainty about their effects on human health or the environment. The objective of bioethics is then to question what is the best environment for the development of new food technologies and balances the ideas of the sectors that support or reject the production and use of genetically modified organisms, and in this way promotes clear and free knowledge of the information contained in these products.

Keywords:

Genetically Modified, foods, production, development

Resumen:

En la actualidad la modificación genética de plantas, animales y otros organismos se ha intensificado, permitiendo desarrollar métodos cada vez más avanzados. La creación de alimentos transgénicos, su uso y su distribución han generado diversas posturas, pues no se tiene certeza sobre sus efectos en la salud humana o el medio ambiente. La bioética viene, entonces, a cuestionar ¿cuál es el mejor ambiente para el desarrollo de nuevas tecnologías en alimentos? y pone en la balanza las ideas de los sectores que apoyan o rechazan la producción y el uso de organismos genéticamente modificados, y de esta forma promueve el conocimiento claro y libre de la información que encierran estos productos.

***Palabras Clave**:*

Transgénico, alimentos, producción, desarrollo

INTRODUCTION

Since a few years ago, common language has introduced terms like, “transgenic” or “transgenic foods”, which convey suspicion by only mentioning them, and frequently they lead to a social debate with controversial opinions[1]. There is no doubt that any scientific advance that takes humankind to produce more food with better quality, always with safety conditions, must be well taken, as we should not forget that today, millions are suffering and starving in very large regions of the world. According to Food and Agriculture Organization (FAO), it is expected that agriculture allows feeding humankind (constantly increasing) increasing approximately 8 million people by 2020. Among these, more than 840 million people are starving and about 1.300 million have no clean water, same number of people earning less than 1 dollar per day[2]. Biotechnology, science that generates genetically modified foods, other organisms, and microorganisms, influence directly and indirectly to counteract these effects[3].

The advance of biology in the last few years has been spectacular. The 20th century has been especially important regarding these accomplishments regarding the knowledge of living beings (animals or microorganisms) in their natural habitats. Above all, it has been clear that all living beings have in common a type of organic macromolecules named nucleic acids (deoxyribonucleic acid-DNA- and ribonucleic acid -RNA-) which are the main element, the molecular unit of biology. Both host the essence of life and its projection from parents to children in a way of inheritance[4]. This great discovery, made in the middle of the 19th century, curiously from experiments made out of bacteria, shown the crucial role of DNA in the transference of information and inheritance. Since then, the availability of biological tools (each time more tools and each time more useful) has allowed advances leading to a new branch of Biological Science called Genetic Engineering or Recombinant DNA Technology with the objective of recombining to originate the so-called “Genetically Modified Organisms”, from which the “Genetically Modified Foods” arise[4].

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DEVELOPMENT

Genetically Modified Foods

These are foods obtained from living beings (plants, animals or microorganisms) that have been genetically manipulated by incorporation, inactivation or suppression of genes (modifying their genome). In the first case, coming from the same or different species[5].

According to the Biosafety Work Group of FAO (1998), GMO includes chromosome manipulations, genes transference, fusion or reordering, gene destruction, inactivation or loss, transplant of cellular organelles, cellular fusion, nuclear transplants or clonation of multicellular organisms through cell cultivations or transferred embryos with new genes[2].

The techniques of genetic modification (production of transgenic) were used for the first time in animals in 1981, and shortly after in plants. The first tests with genetically modified cultivations were carried out almost simultaneously in France and the United States in 1986. A few years later, in 1992, a genetically modified tobacco plant started to be cultivated in China, resistant to a certain virus, commercialized since 1993[6].

Types of Genetically Modified Organisms (GMO)

Normally, there are three groups of GMO, depending on the biological group they are part of: plants, animals or microorganisms[7].

1. Genetically modified plants: these are basically vegetables whose genome (its DNA) has been modified with different objectives:

- The obtention of a new plant from a perspective of its use as a food; that means, that it is expected the obtention of a new plant-based type of food or the modification of the plant in order to be more useful as a food (they are going plant-based genetically modified foods)
- The production of genetically modified foods that are useful as biological fuels (bio-fuels), by fermentation. The reason is that such plants have a high concentration of carbohydrate polymers.
- The production of GM plants where genes with therapeutic proteins have been introduced to (drugs) or vaccine antigens, represents an option of genetic modification with a high practical utility, as it can be useful to the plant itself to get resistances or make a useful product to men (e.g. edible vaccines)[7].

2. Genetically modified animals: they are animals that have been genetically modified to improve their production (more meat production, more milk, etc.) or simply to get new production (a protein, for example), directly used by men (it is the case of some animals that have been modified to produce human lactoferrin, antihemophilic, etc.), or to accelerate their growth by introducing genes of other species allowing to duplicate or triplicate that rate. A special type of genetically modified animals are the ones called knockout animals (KO animals) where the gene that codifies the animal itself for a certain character has been inactivated, transferring to it the gene of a man or another animal species, behaving as "models" to study human diseases, or "experimental models for animal diseases". These animals are also produced to serve as potential organ donors for humans (xenotrasplants), although this is still an experiment and a very polemic social and medical topic[7].

3. Genetically modified microorganisms: normally, they are yeasts and bacteria of industrial interest that through a genetic modification technique are modified to eliminate industrial inconveniences or even just to produce something (for example a drug, a protein o just a vaccine antigen)[7].

Fig. 1. 1.1: Genetically modified vegetables (tomato, carrot, broccoli).

1.2 GM cruciferous plants useful to depollute the soil
1.3 GM plant used as bio-fuel
1.4 GM mouse
1.5 GM pigs
1.6 GM yeasts

Expected characters in GM of plants

Resistance (to infections, insects, chemical compounds, etc.) is one of the chapters with a higher interest in these proceedings, as well as the modifications to certain processes in the biological cycle of the fruit and its seed, or other changes that produce an added value to the crop[8].

Plants resistant to virus: the strategy typically followed has been to transfer a gene (or several genes) to the attacking virus itself that it is expected to be resistant to or even to other related viruses (for example a gene that codifies for a protein of viral capsids) acting like a vaccine. That is how, plants like tobacco, tomato, alfalfa, potato or rice have been transformed making them resistant to certain studied virus[3].

Plants resistant to bacteria: Just like before, the transformation of vegetable cells caused by the transfer of genes from other plants and even from insects or animals, allows the expression of proteins (of defensins type or equivalent substances like cercopine B or sarcotoxin, etc.) that give resistance to some type of bacteria[9].

Plants resistant to insects: Insects attacks represent one of the most important aspects to cultivate vegetables. There are many types of plagues in all types of plants produced by larvae or adult insects. There is a great interest for them from an economic perspective (there are annual losses of millions of dollars including not just a crop loss but also the expenses for its control and prevention, normally of a chemical type). Also, the social effect must not be forgotten as there is a reduction in food supply for citizens, particularly in developing countries[9]. Some of the obtained results through the use of these techniques have been incorporated and traded by big multinational companies. Bacteria genes that express proteins toxic for insects have been used. Plant genes expressing proteins that inhibit digestive enzymes of insects (generally proteases and amylases), have also been used[7]. A good example of this type of resistance to insects is mediated by a protein produced by the Bacillus thuringiensis bacteria, called δ-toxina or toxina Bt, which results toxic, selectively, for many insects. There are different variants and each one has a different action, like the Cry I, which is only toxic for lepidopterous (butterflies), the Cry III for coleopterous (beetles) or the Cry IV for dipterous (flies). Genetically modified plants that incorporate these genes are called Bt Plants. A variety of Bt corn resistant to "drills" is one of the examples known around the world[7].

Plants resistant to herbicides: Unwanted weed represent a negative factor in vegetable production with a great economic impact, as it has been estimated that up to 10% of the world's crops are lost because of their contamination with bad weed. There is also a loss of significant amount of money in combating and controlling the weed (according to some authors, more than ten million dollars per year, only for chemical herbicides), with the added inconvenience that the majority of these products do not distinguish between good crops and bad weed, leading to unavoidable "collateral" damages[9]. Given these facts, for years, the recombinant DNA technology suggested to obtain GM plants resistant to the active substances of some chemical herbicides. So it is expected that, through genetic manipulation, genes are transferred from other sources capable of providing the plant with resistance to herbicides; although other strategies have also been applied[9,1].

Plants resistant to fungus: The same strategy is followed and genes from different sources capable of expressing proteins, are introduced (they are called response proteins, RP) with enzymatic activity (chitinases or glucanases) degrading the fungus wall causing its death. Trials with genes capable of producing proteins with a toxic activity for the fungus, as it is the case of tionines or osmotines, have also been performed[8].

Controlled maturation by GM fruits

The process of maturation of the majority of fleshy fruits depends on the production of hormones (ethylene gas) inducing, therefore, the production of enzymes (like the polygalacturonase), pigments and scents that are characteristic of ripe fruit. Ethylene gas is used for the artificial maturation of fruits collected green because of the time imposed by trading channels and the shelf life of the fruit itself[1]. Through a technique that uses a synthetic antisense RNA (a sequence of RNA in opposite direction-3'-5'- that pairs up with the normal sequence and prevents its translation into ribosomes), it has been possible to suppress the expression of polygalacturonase, delaying the natural softening of tomatoes (the enzyme is the one responsible for the softening and senescence of the ripe fruit). The first commercialized GM tomato, the Flavr-Savr tomato (MacGregor tomato), belongs to this group and its commercialization was the first one authorized by the FDA in the United States, in May of 1994[8]. This same technique has also been used to get soy that contains 80% or even more oleic acid (the normal one contains 20%) by inhibiting the oleate desaturase enzyme[8].

Fig. 2. 2.1: Tomatoes Flavr-Savr
2.2. GM melons of controlled maturation

Also, other variants of GM interventions have been described, acting on the synthesis of the hormone that induces maturation (ethylene), controlling the suppression of 1-aminocyclopane- 1-carboxylate synthase or oxidase (ACC-synthase or ACC-oxidase) enzymes with similar effects. This is how GM tomatoes and melons of controlled maturation have been obtained[9].

Foods with vitamins and hypoallergenic foods

It is well known that there no complete foods, valid statement particularly in the case of vegetables. Therefore, its intake has to be necessarily supplemented to meet the needs of the living being (proteins, lipids, carbohydrates, vitamins, minerals, etc.). The possibility of introducing genes that express some of the lacking elements of specific food can solve traditional problems linked to large geographic areas of the planet. This is what happens, for example, with rice, which is the basic diet (if not the only diet) of millions of people all over the world. Its traditional deficiency is vitamin A causing serious health problems, particularly sight problems (blindness)[4,2]. It has been described the obtention of GM rice with genes that express ß-carotene (provitamin A) solving this problem. Rice gets a brown tone explaining its name of "brown rice". It has also been explained the production of tomatoes with a gene that triplicates its content of ß-carotene[7]. This type of "reinforced" foods are also called "functional foods"[3]. Some people cannot consume some products due to their hypersensibility to some components that make them have allergic reactions. In this sense, in the case of rice, it has been described the obtention of a variant for genetic modification that drastically reduces the expression of albumin (protein) of 16 kDa (kilodaltons), a very allergenic one, which causes hypersensibility in some people. Also, in the case of soy, a protein called P34, known for its allergizing capacity, has been suppressed by inactivating the gene codifying for. For that purpose, a process called "gene silencing" consists of introducing extra copies of the gene that codifies for the P34 protein, having the plant responding with its suppression when interpreting it is an excessive replication originated by a viral infection[3].

Modification of Nutritional Quality

There are several studies that have helped to improve the composition of some traditional foods. They generally refer to one or some immediate principles (carbohydrates, proteins or fats) [2]. For example, when referring to **proteins**, there is the case of the albumin 2S gene of Brazil nut, particularly rich in methionine (one of the main sulfur-containing amino acids) which has been used as a donor to transfer it by genetic modification to soy, rapeseed and kidney beans. Nevertheless, the initial advantages resulted in inconveniences related to their inclination to hypersensibility (generation of allergies), making them exclusive for animal use. Genes that codify for other proteins rich in amino acids such as lysine, tyrosine, and cysteine, also of great nutritional relevance, have also been described[6].

In the case of **lipids**, genes that modify the composition of fatty acids that are part of triacylglycerols and phospholipids, two of the most biologically important fatty acids, have been incorporated. The same happens in the case of some polysaccharides like starch, modified by transgenesis, both its quality and quantity, on behalf of some plants[7].

Modifications to quality affecting clinical situations of the consumers

GM foods can help to prevent or correct critical situations of certain patients, particularly kids under not very favorable environmental and familiar conditions. In this sense, it is important to point out that recently, a team of Brazilian researchers achieved to transform corn plants making them produce human growth hormone (HGH). Today, the price of producing HGH, used to treat children with growth disorders, can reach the $20,000.00 per gram, while by using transgenesis techniques in vegetables, the costs decrease drastically (the first estimations calculate that from a ton of GM corn it can be obtained no less than 250 gr of HGH) [9]. The same team shared the success on the obtention of other GM corn plants that contain a gene that codifies a viral protein capable of eliminating the agent that causes avian coccidiosis (Eimeria spp), which leads to an interesting way of preventing avian coccidiosis by feeding these animals[1].

Methods to detect GM foods

Two general systems can be considered that show the GM condition of suspicious food. On one hand, there are procedures that detect new expressed proteins because of the introduced transgenes, and that is why there are methods that identify the DNA that corresponds to the gene or genes that were introduced[3].

Methods that detect new proteins

In the first place, one of the most common study procedures is the ELISA technique, a type of enzyme immunoassay where a known antibody facing a GM protein under investigation, get stuck to (get adhered to) the microplate where the analysis is been performed[15]. The sample is added to the plates and if there is a GM protein it will be recognized and detected by the specific antibody. By washing the material, any element not specified that has not been recognized by the antibody will be erased[4]. Afterward, a new antibody (secondary) will be added and linked to the first one to which an enzyme is fixed to. The last stage will consist of adding the specific substrate of the enzyme, that linked to the other will develop color and fluorescence, measured with a special spectrophotometer[8].

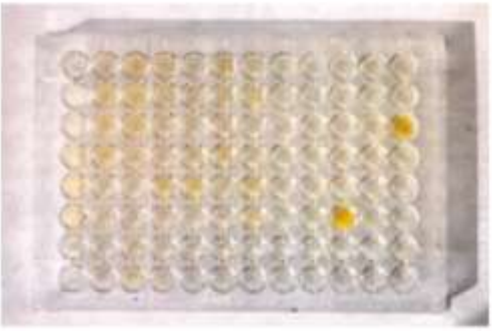

Fig. 3 ELISA plate

The **lateral flow assay method** is a procedure executed on a long rectangular glass plate, where the specific antibody that recognizes the GM protein (capture antibody) is fixed in one of the edges, while the secondary antibody (marked) is placed in the opposite edge [3]. The sample is added in this last edge and is forced to flow in the opposite direction. In a positive case, when the capture antibody coincides with the marked one in the presence of the GM protein, a colored band is formed. A second band of capture antibody that serves as reaction control, is placed, is arranged[6].

A method that detects GM genes

The polymerase chain reaction (PCR) is useful to directly detect the transgene. *Primers* (oligonucleotides) can be used for any of the elements that are part of the sequence. The use of a thermal cycler helps to get the amplification of the fragments, separated in an agarose gel according to their size. Dyeing with a fluorescent compound allows to easily identify the DNA fragment that is searched for [5].

A **Southern Blot** is also a very useful technique to detect weird genes. For that purpose, after extracting all the DNA of the plant where the transgene is searched, it is fragmented with restriction enzymes and separated in a gel because of its molecular size[2]. Afterward, the transference to a nylon membrane (or something similar) is made, and then, the only thing thas hs to be done is to reveal the presence of the gene that is searched, using a complementary sequence specially designed for that purpose, already marked with a radioactive isotope. Finally, the only thing left to do is to detect the radioactive compound that remains in the membrane if the problematic gene is present because otherwise it will be eliminated[1].

Fig. 4 Thermal cycler for PCR and Southern Blot

Current situation of transgenic plants cultivation

As it was mentioned before, since 1992, when the first GM cultivations of tobacco in China were made, it has been a long path. According to available data, which started to be public in 1996, by 2002 the whole amount of GM cultivated surface was almost 58,7 million hectares, certainly an extension larger than our country, increasing 12% more than the previous year and the sixth consecutive year with an increase of two numbers[4].

Today, practically 70% of the cultivated surface with genetically modified plants belongs to the United States, followed by Argentina with more than 23%, placing Canada in third place with 7% of the surface. An additional 1% corresponds to China and the rest is distributed in descending order among South Africa, Australia, Rumania, Mexico, Bulgaria, Spain, Germany, France, and Uruguay. If the set is divided into developed and developing countries, the ratio would be 3:1, approximately (75%:25%)[2].

The most common GM cultivations are soy, corn, cotton, and rapeseed; set that represented more than 20% of the total cultivated surface dedicated to these four products. In a relative form, around 40% of all the cultivated soy ys genetically modified, almost 10% of corn is GM, 16% of cotton is GM and about 11% of rapeseed is GM (cultivations in the year 2000, include 72 million hectares of soy, 140 of corn, 34 of cotton and 25 of rapeseed)[4]. Depending on the type, the percentage of the total surface dedicated to the cultivation of GM products was 58% in the case of soy, 23% in the case of corn, 12% in the case of cotton and 6% in the case of rapeseed[4]. Finally, if it is the character the parameter used, the cultivations resistant (tolerant) to herbicides have the most relative representation, with about 74% del total, followed by the cultivations resistant to insects with a 19% and an additional 7% where characters are overlapped in the same cultivations[7]. The GM products were approved for human consumption for the first time in the United States in 1994. It has been mentioned that 60% of the food offered in American stores has been produced using ingredients that come from GM cultivations. Until now, there are no specific health problems related to the intake of foods derived from these crops[7].

Current situation of GM animals

In the case of animals, the situation admits no comparison with plants, as the approaches and objectives are completely different. In this case, apart from the scientific and technical problems (in mammals, the genes have to be injected directly into the nucleus of the fertilized ovule, entering in the chromosomes, then the zygote implants in receptive females), there are other ethical, social and sanitary problems which are particularly complex[5].

Until now, the list of animals used for successful GM experiments includes the mouse, the rat, the rabbit, cattle, the pig, the sheep, and the goat amount the mammals; while birds include the chicken (the hen) and the quail. Among the successfully harvested fish, there are the salmon, the trout, the tilapia, the carp, the catfish, the medaka and the Sparus aurata [5]. Like in the case of vegetables, among the animals, the genetic modification has as its important objectives: the improvement of productive characters and of the production's quality (particularly their growth), the resistance to diseases (specially mastitis in ruminants) and, of particular interest, the development of animal models to study human diseases or to study the diseases of domestic animals or useful animals of great value, the development of GM animals as organ donors in practices of transplants (xenotrasplants) and, finally, the development of GM animals with the purpose of producing "therapeutic" proteins of high value for humans; in one word, use "pharmaceutical of molecular farms" from animals with modifications that allow them to produce substances that can only be substituted by a very complex and expensive chemical synthesis[9].

Current situation of GM microorganisms

In the fabrication of bread, the traditional strains of yeast Saccharomyces cerevisiae degrade carbohydrates present in flour dough in an order starting from sacarose, after glucose and fructose[1]. Only when those sugars have been used, the degradation of maltose starts, which, on the other hand, represents the main principle. This means, in terms of time, a significant expense. To reduce these costs, different GM yeast strains have been obtained which are capable to start the degradation of carbohydrates in bread dough caused by the maltose, resulting in a substantial increase of the fermentation capacity and of the production of CO2, which represents not only a faster fermentation, but also the obtention of a flufflier and tastier bread[1]. Also, strains of GM S. cerevisae have been obtained through the incorporation of an Aspergillus oryzae gene that is capable of expressing the α-amylase enzyme. This is translated in the obtention of a product with better organoleptic characteristics[4].

In the case of wine, yeasts have been modified by inserting the gene that codifies for L-lactate dehydrogenase (from Lactobacillus casei), capable of producing lactic and alcoholic fermentation allowing to obtain wines with more acidity.

In the case of beer production, genes from Trichoderma reesei or Tr. longibrachiatum have been inserted expressing a β-glucanase enzyme that solves an important problem in brewing like the one represented by colmatation and an accumulation of β-glucans from barley, demanding to clean the tanks and a significant expense for technical aspects[1]. Also, strains of beer yeast have been obtained which have a S. diastaticus gene that expresses a glucoamilase, characterized for degrading dextrins and starch, responsible for the great energetic load of beer (some types of them specifically) obtaining a low-calorie beer.

The genetically modified microorganisms (GMM) have been an important source for vaccine alternatives different from classic products. The genetic modification of the microbial structure that means a reduction of wild, viral strains of the tested microorganism, is a procedure that has been researched for several years with the purpose of obtaining more efficient and safer antigens[9]. The European Union has been, until now, very rigorous and restrictive regarding the authorization of GM, demanding a thorough control until assuring there is no risk for the environment and the possibility of identifying its use through detectable changes in the laboratory, as it happens, for example, in the case of vaccine against the Aujeszky's disease and few more cases[5]. In the case of humankind, clinical experiences have been informed about a vaccine against diarrhea produced by E. coli based on mitigated microorganisms that maintain their intestinal colonization capacity but they do not have a pathogenesis of their own[1].

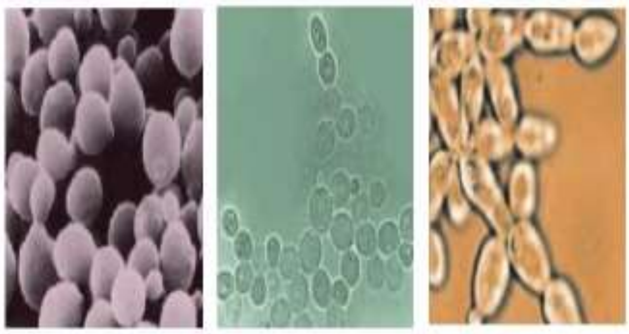

Fig.5 Different images of Sacharomyces cerevisae

CONCLUSION

The introduction of this type of food into the market has been very controversial among environmental organizations which have generated a great number of arguments against them. On the contrary, there are many scientists including molecular biologists, engineers and other technicians, for whom the tools available today guarantee, more than ever, the genetic modification process that leads to new characters in traditional food. On the other hand, its introduction to ordinary levels of cultivation would allow increasing the production capacity up to the necessary levels to supply the globally growing demand, above all, for the people living in less fortunate countries. In the third angle of this hypothetical triangle there are the multinational companies, for whom the main interest (although not the only one) is, naturally, to benefit their stockholders. Probably, all the parties are right; in either case, as it was previously stated, today, the United States control over this field is favored when the research about new GM products or their development in Europe is brought into question. The following lines try to collect the most evident benefits of this technology, as well as the main inconveniences highlighted by (but not only) environmental organizations that were mentioned before. Whatever the case, even when there is a suspicion of one negative effect on any aspect previously mentioned, the question must be solved through rigorous analysis of the product, whatever its result may be. Ideally, the consumer must have the opportunity to know what he/she is consuming, so it is necessary to develop and adapt methods and procedures that allow showing the transgenic character of food for human consumption and that such information is shown in the product's label.

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