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Genetically Modified Food: A Review of Biosafety of Genetically Modified Organisms in and as Food

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Abstract—*Genetic Engineering (GE) has emerged as a significant tool, modifying living organisms across the natural barriers. This breakthrough science, based on recombinant DNA technology has been applied to various fields including pharmacy, medicine, forensics, agriculture and attaining food security. Release of any Genetically Modified Organism (GMO) in environment is fraught with lots of perils. Their affect on ecology, environment, health, ethics, economy and society as whole has lead to perplexing debate. Apparently, introduction of GMOs in food line has been met with resistance from various sections of the society. GMOs if once released in environment are bound to enter our food chain one way or the other. Adverse health effects may occur due to the new GM gene product or the GM transformation process or both. Corroborating evidence, repeated patterns of illness and health reactions of GMOs has been reported and have increased consistently in past few years superimposing their known potential risks. Efforts have been made by scientific community world over to study, analyse, and dissect its health implications and improve this technology for welfare of society and achieve food security. Every researcher studies it from their angle of expertise. The current research paper is in direction to assimilate and correlate the existing secondary data on biosafety of GMOs. The aim of this review study is to bring together variegated research at the same table and analyse it through the impartial eye of a scientist to draw an honest and fair conclusion.*

1. INTRODUCTION

Genetically Modified Organisms (GMOs), whose genetic constitution is altered by inserting one or more genes from other organisms, are considered as the most successful application of Genetic Engineering (GE). But it still remains as one of the most ticklish issue world faces today. Even after two decades of its commercial use, high uncertainty governs its efficacy and usefulness. It is a complex science with many intricacies involved. Various direct and indirect potential impacts of these organisms on human health, ecology and environment as whole have not been scientifically scrutinized.

From the first commercial cultivation of Genetically Modified Flavr Savr Tomato in 1993, numbers of Genetically Modified Crops (GMCs) have undergone rigorous research, lab testing, and field testing for one or more transgenics. Today, nearly 189 million hectare of global land is under GMCs, with USA, Brazil and Argentina as the leading top three countries. Soya, maize, cotton and canola are the top four GMCs [1]. Herbicide tolerance (HT) and Insect resistance (IR) are the two most widely transgenically induced traits, expected to decrease the pesticide usage and increase crop yields. But, on closer analysis, 189 million hectarage under GMCs makes for meager 3.43% of global agricultural land [2].

Issue of biosafety of GMOs has been debated world over by scientists. GMOs if once released in environment are bound to enter our food chain one way or the other. Adverse health effects may occur due to the new Genetically Modified (GM) gene product or the GM transformation process or both [3]. In humans it may lead to emergence of new allergens in the food supply, antibiotic resistance, production of new toxins, and concentration of toxic metals. It can also lead to increased cancer risks as was reported by George *et al.* [4] in case of glyphosate resistant crops. It leads to degradation of the nutritional food value, and many other unknown risks that may arise later [5]. Such corroborating evidence, repeated patterns of illness, and health reactions have increased consistently in past few years and superimposed the known potential risks of GM foods [6]. Thus, a detailed and comparative review of research papers on biosafety of GMOs was drawn to highlight lacunae and gaps in current research and draw a comprehensible conclusion.

2. COMPARATIVE REVIEW

One of the earliest study on rats fed with GM potatoes reported excessive growth of the gut lining similar to a pre-cancerous condition [7]. These research findings reporting GM potatoes to be poisonous to mammals caused ripples in the scientific community. Since Dr. Pustzai's findings, many animal feeding trials have been conducted around the globe. A tabulated and comparative review of few biosafety research papers is drawn here (see table 1 &2).

Table 1: Long term Bio-safety studies on GM plants

S. No.	Research paper	GM Plant	Affected Species	Test Duration	Result
1.	Malatesta *et al*., 2003 [8]	Glyphosate-tolerant soybean (CP4 EPSPS)	Mice	240 days	A diet containing significant amounts of GM food influence the pancreatic metabolisms
2.	Vecchio *et al*., 2004 [9]	Glyphosate-tolerant soybean (CP4 EPSPS)	Mice	240 days	Enlarged vesicles of the smooth endoplasmic reticulum, Decrease in the number of nuclear pores.
3.	Sakamoto *et al*., 2007 [10]	Glyphosate-tolerant soybean (event not mentioned)	Rats	26 and 52 weeks	Differences in growth, feed intake, organ weight between groups. Body weight and feed intake similar between GM and non-GM soybean
4.	Malatesta *et al*., 2008 [11]	Glyphosate-tolerant soybean (CP4 EPSPS)	Mice	2years	Indications of reduced metabolic rate in GM-fed mice GM soybean can influence some liver features during ageing
5.	Sissener *et al*., 2009 [12]	Glyphosate tolerant soybean (event not mentioned)	Salmons	7 months	Mid intestine smaller in GM-fed group. Triaclyglcerol increased in GM-fed group.
6.	Domon *et al*., 2009 [13]	Rice- 7Crp#10 (7Crp gene derived from cedar pollen Cryj I and Cryj II allergen protein genes)	Macaques	26 weeks	With few exceptions, no significant differences in hematological or biochemical values between them.
7.	Steinke *et al*., 2010 [14]	Maize Bt-MON810 containing Cry1Ab protein	Dairy Cows	25 months (100 weeks)	Small changes in milk composition and body weight in GM-fed cows but fall within normal ranges
8.	Daleprane *et al*., 2009a [15] .	Soybean Glyphosate-tolerant soybean (event not mentioned)	Rats	455 days	GM group and organic group weight the same, higher than control group. Lower protein intake in control group. Growth, albumin, serum similar in all three groups

Table 2: Multi generational bio-safety studies on GM plants

S. No.	Research paper	GM Plant	Effected Species	Test Duration	Result
1.	Brake *et al*., 2004 [16]	Maize Bt (event not mentioned)	Mice	8, 16, 26, 32, 63, and 87 days after birth	No differences in fetal, postnatal, pubertal, or adult testicular development with the GM maize diet
2.	Rhee *et al*., 2005[17]	Potato Phosphinothricin acetyltransferase (bar gene)	Rats	5 generations; 70-Day intervals before reproduction	No difference in all parameters studied. Safe, no multigenerational effects
3.	Kilic and Akay, 2008 [18]	Maize Bt (event not mentioned)	Wistar albino rats	Duration not précised at least 3.5 months (14 weeks)	No difference in all parameters studied. Safe, no multigenerational effects
4.	Trabalza-Marinucci *et al*., 2008 [19]	Maize Bt176	Sheep	44 months (188)	Changes in cell nuclei of liver and pancreas
5.	Daleprane *et al*., 2009b [20]	Soybean Glyphosate-tolerant soybean (GTS 40-3-2)	Wistar rats	Fed throughout life, exact time unclear	Differences between experimental and control
6.	Haryu *et al*., 2009 [21]	Maize Bt11	Mice	1072 days (153 approx.)	No differences in all parameters studied. Safe, no Multigenerational effects
7.	Tudisco *et al*., 2010 [22]	Glyphosate-tolerant soybean (GTS 40-3-2)	Goats	60–67 days (8–9 approx.)	Presence of transgenic DNA in milk (parents) and blood (parents and offsprings). A Significant difference for the level of Lactate Dehydrogenase and substitutions between the iso-enzymes

8.	Krzyowska *et al*., 2010 [23]	Glufosinate ammoniumtolerant wheat(Basta) (and containing the b-glucuronisdae gene)	Mice x	Mice 120 days then mated/killed (at each generation)	Enlarged inguinal and axillary lymph nodes detected. Decrease in T cells in spleen and lymph nodes and decrease in B cells in lymph nodes and blood

Snell *et al*., claimed GM plants to be nutritionally equivalent to their non-GM counterparts and could be safely used in food and feed on the basis of detailed review examining 12 long-term studies (of more than 90 days, up to 2 years in duration) and 12 multigenerational studies (from 2 to 5 generations). They reported that the results from all the 24 studies do not suggest any health hazards and, in general, there were no statistically significant differences within parameters observed [24]. However, some small differences were observed, though these fell within the normal variation range of the considered parameter and thus had no biological or toxicological significance.

In a perverse, Seralini *et al*., reported that meta analysis of all the *in vivo* studies published, revealed that the kidneys were particularly affected, concentrating 43.5% of all disrupted parameters in males, whereas the liver was more specifically disrupted in females (30.8% of all disrupted parameters). It further indicated that the 90-day-long tests are insufficient to evaluate chronic toxicity, and these signs highlighted in the kidneys and livers could be the onset of chronic diseases [25].

Taking lieu from their review findings, they conducted a long-term chronic toxicity studies for roundup herbicide and roundup tolerant GM Maize in rats. The study showed that females developed large mammary tumors, pituitary was disabled and sex hormonal balance modified when compared to the controls. While in males liver congestions and necrosis were 2.5 to 5.5 times higher. Further biochemistry data confirmed very significant kidney chronic deficiencies, for all treatments and both sexes, as 76% of the altered parameters were kidney related [26].

Presence of GM residues in human body has been contested by many scientists. A pioneer study in this field was done to evaluate the correlation between maternal and fetal exposure, and to determine exposure levels of Glyphosate and its metabolite aminomethylphosphoricacid (AMPA), Glufosinte and its metabolite 3-methylphosphinicopropionicacid (3-MPPA) and Cry1Ab protein (a Bt toxin) in Eastern Townships of Quebec, Canada. It reported presence of Cry1Ab toxin in 93% and 80% of maternal and fetal blood samples, respectively and in 69% of tested blood samples from non pregnant women [27].

Hematotoxicity of four genetically modified Bt-spore crystals was evaluated on swiss albino mice. The short term study reported selective hematotoxicity on eryhtroid lineage and significant reduction in bone marrow cells at all exposure times becoming more evident at 7 days suggesting need for further studies [28].

Recent study based on bio-informatic analysis was performed to assess the safety for human and animal health of putative translation products of gene VI overlapping P35S. No relevant similarity was identified between the putative peptides and known allergens and toxins, using different databases [29].

Another in vitro study of Cry 1Ab and Cry 1Ac alone or with Glyphosate based herbicide was done on human cells. The Cry1Ab caused cell death from 100 ppm concentration while Cry1Ac, showed no effects under same conditions. This study highlighted the fact that modified Bt toxins are not inert on non-target human cells, and that they can lead to combined side effects with other residues of pesticides specific to GM plants [30].

In vitro studies also evaluated the toxicity of four glyphosate (G)-based herbicides in Roundup (R) formulations, from 10^5 times dilutions, on three different human cell types; umbilical, embryonic, and placental cells. It reported that all glyphosate formulations cause total cell death within 24 h, through an inhibition of the mitochondrial succinate dehydrogenase activity, and necrosis, by release of cytosolic adenylate kinase leading to membrane damage. [31].

Many reports have also linked GMCs with increased allerginicity in humans. Goodman (2008) reviewed the existing criteria for allerginicity evaluation of introduced GM protein. He reported lack of practical guidance on serum testing and suggested use of bioinformatics interpretation for an efficient serum IgE tests [32].Contrastingly, another study reported that the likelihood of up-regulating an endogenous allergen due to transgenesis is no greater than from traditional breeding which has a history of safety and is largely un-regulated [33].

A review of biosafety provisions for four African countries of West Africa (Ghana, Senegal, Mali and Burkina Faso) highlighted that whereas high-quality research was proceeding in the countries visited, funding is not sustained and there is little evidence of practical application of biotechnology and benefit to farmers and the wider community [34].

Parrott *et al*., (2010) reviewed the main aspects of the current safety assessment paradigm and also recommended scientifically sound principles for conducting a safety assessment for GMCs [35].

Another review of food and feed safety studies published internationally from 2000 to 2006 showed that the number of references concerning human and animal toxicological/health risks studies on GM foods/plants was very limited. It also reported that an equilibrium existed between the number research groups suggesting, GM products (mainly maize and soybeans) as safe and nutritious as the respective conventional non-GM plant, and those raising still serious concerns [36].

Another research highlighted the fact that, the successful application of profiling techniques to the safety evaluation of GM foods required linked databases. These databases would contain information on variations in profiles associated with differences in developmental stages and environmental conditions [37].

Conclusions and recommendations of Working Group 1 of the ENTRANSFOOD project under European Union (EU) were summarized into a paper. It provided guidance on how to assess the safety of foods derived from GMCs. The paper provided an approach for adapting the test strategy to the characteristics of the modified crop and the introduced trait, and assessing potential unintended effects from the genetic modification [38]. The proposed approach to safety assessment included the comparison of the new GMC with a traditional counterpart that is generally accepted as safe based on a history of human food use (the concept of substantial equivalence) and ensured that foods derived from GMCs that have passed this extensive test-regime and are as safe and nutritious as currently consumed plant-derived foods [39].

In addition to the wide range of published data on GMCs and GMOs, large amount of un-published work and reports on the GMCs have aroused public interest and doubts. Many Non Government Organisations (NGOs) based on their surveys report deleterious effects of these crops on farmers, cattle and the ecosystem. There have been reports of allergies form the farmers working in Bt cotton fields in Punjab. Death of sheep after feeding on Bt Cotton foliage was reported from Andhra Pradesh. These GMCs are claimed to have entered the Indian market and even food chain. Although there is no scientific proof of these claims, yet they hint towards possible damages which could be incurred because of the use of these crops.

3. CONCLUSION

The current review of literature generates massive asymmetrical database with multiple gaps. World Scientific community stands divided on this issue with research studies both in favour and against GMOs. The biosafety research studies on different transgenic traits with different test animals and time scale makes drawing a comparison very difficult. The review also highlights lack of any chronic biosafety research on GMOs which holds substantial importance as these organisms may persist in the system and may affect later in life. The contentions on this issue augment with poor regulatory system at national and international level. Development of GMOs has raised a variety of novel legal questions, which our regulatory system fails to answer. Instead, the current regulations are a burden in terms of time and cost, abandonment of research, as well as exploitation of farmers [40]. Till date, no country in the world has a stringent Biosafety Risk Assessment Mechanism for GMOs [41]. Before releasing any GMO in environment, countries rely on the biosafety assessment done by the developer who has vested interest. The industries and governments around the world made a big mistake by levying the society with this technology without winning its confidence and creating a necessary awareness of it [42]. Thus the review aimed at gauging the sustainability and biosafety of GMOs, necessitates the need to evaluate these organisms on long term ecological and biosafety aspects and then develop an effective regulatory framework.

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