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Safety and feeding value for farm animals and the food chain of insect protected and herbicide tolerant genetically enhanced plants.

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Introduction

In a controversial world with the quick adoption of genetically modified GM crops covering nowadays 59 million hectares, the question for the scientists responsible for health and consumer protection is not to be in favour or against the products issued from new technology. Scientists and users must be objectively informed on the safety of the genetic constructs, of expressed proteins and finally of new feeds/foods. New recombinant genes as rDNA representing 1 X 10^{-4} % of the total nucleus DNA mainly code for functional proteins conferring tolerance to herbicides (soybean) or insect resistance (maize, cotton) or both traits for a few. GM plants are used directly as animal feeds such as maize green forage or silage, soybean, maize kernel, canola and cotton used as raw seeds or oil meals. From the consumer point of view, the safety, concerned by the presence of the rDNA, the new proteins (Table 1) and eventually of other substances not intended and synthesised in the plant. Scientific authorities or agencies such as the FDA, AAC, and the European Commission are responsible for the authorisation of their dissemination on the basis of results on risk assessment derived from appropriate tests, often available in the scientific literature. Examples on the compositional analysis, substantial and nutritional equivalence, long term safety tests are summarised and discussed in the present review (Aumaitre 2004). Results on the quality and the safety of animal products, milk and meat issued for animals fed GM plants have been also interpreted .

1. Typical genes, expressed proteins and substantial equivalence

The most frequent genes inserted by GM techniques confer resistance to Lepidopterae damaging maize or cotton, resistance to Coleopterae damaging corn roots (*Diabrotica sp*) or tolerance to herbicides glyphosate and glufosinate. New proteins such as Bt CryIA(b,c), Pat and Cp4epsps are generally expressed in low amounts (0.1 to 10 µg/g fresh weight in leaves) representing 0.00005 to 0.0005 % of total proteins (agbios.com 2003). These proteins are present at low level in the kernel and in the senescent plant. Acute toxicity tests in mice revealed a high safety factor for expressed proteins which are easily degradable in vitro at low pH in simulated gastric or intestinal fluid: their enzymatic activity disappeared after less than 10 minutes except for the CRY9C protein. Similarly, because of massive destruction into small nucleotides during fermentative processes, functional rDNA (> 2000bp) is low or absent from the silage and from the small intestine of ruminants. The low level of rDNA and expressed protein in plants does not lead to a significant modification of the chemical composition of green chop or silage in the case of insect resistant or herbicide tolerant maize, either when expressed as common nutrients or well identified toxicants and anti-nutritional factors (Table 2 and 3). Similarly, the protein and amino acid content, the carbohydrate or fibrous content, the fat and fatty acid content of soybean and maize kernels are not modified by the new genes. A typical unexpected and unintentional bonus in favour of the insect protected maize leads in its low level in mycotoxins. The resistance of maize to the damage of the corn borer, preventing the plant in the development of mould (*Fusarium sp*) contamination before and after harvesting (Table 4). It has been almost always concluded that new GM plants are substantially equivalent to their near isogenic parents. However, the concept of substantial equivalence identifying known nutrients and toxicants is neither a safety assessment *per se* but that characteristics and composition of the novel food as equivalent to the conventional food with a history of safe consumption.

2. Safety and nutritional equivalence of GM plants and feeds.

The experimental demonstration of the safety and the nutritional equivalence for farm animals has been attempted before the early dissemination of GM plants as soon as 1996. Results of long term experiments corresponding to toxicological studies systematically run on high producing animals such as the dairy cow for forages, the fattening steer, the growing chicken and the growing-fattening pig for maize kernels, oilseeds and oilmeals are available in the referred literature. None of the comparative performance of the dairy cows including average daily dry matter intake, fat corrected milk and milk composition are modified by the use of Bt or herbicide resistant maize silage (Table 5). GM cotton seeds bearing various rDNA and fed as raw seeds at the level of 2.3 kg/ cow/day did not affect either milk production or milk composition. Moreover, nitrogen and rumen metabolism characterised by N balance and the proportion of rumen volatile fatty acids have not been modified in cows fed raw soybean resistant to glyphosate. No physiological and hormonal disturbance have been associated with feeding GM beets to dairy cows. Not only the content of milk in total protein, but also the proportion of casein, non protein nitrogen, α-lactalbumin and β-lactoglobulin are not modified, leading to the absence of effect on the physicochemical characteristics of the curd and the characteristics of the cheese made with milk issued from cows fed GM maize.

Additional digestibility trials in adult rams confirmed the nutritional equivalence of GM maize forage and sugar or fodder beets to their near isogenic parental plants. Similarly, across 8 long term studies lasting from 101 to 234 days and undertaken on fattening steers fed up to 96 % of their dietary dry matter intake with GM maize silage or grain, no deleterious effect on performance, health, frequency of liver abscess have been found in hundreds of experimental animals (Table 6). As a consequence, the nutritional equivalence, carcass performance, dressing percentage, the 12th rib fat thickness and ribeye area have not been modified by the ingestion of insect and glyphosate resistant maize. The chemical composition of the *Longissimus dorsi* muscle in steers as in pigs fed glyphosate tolerant maize or soybean, respectively are also not modified by feeding GM grains.

3. Safety of animal food.

Animal food produced by animals fed GM plants has been suspected to be of lower quality, on the basis of the transient presence of foreign plant DNA fragments (140bp) in organs (liver, spleen, ovary) and tissues (muscle, blood). The first observation in mice species has been confirmed in farm animals without an explanation on their physiological significance.

Opposed to that, all samples of milk, muscle and eggs (yolk and albumen) of animals fed Bt maize silage, Bt cotton or soybean resistant to glyphosate were negative of the presence of transgenic DNA for either traits or fragment thereof and the protein encoded in the GM plants (Table 7).

4. Conclusion and the near future.

Up to now, the GM plants authorised commercially mainly belong to the categories of insect resistant or herbicide tolerant family. No significant modification in the compositional traits have been claimed by the petitioners, leading to little nutritional and physiological consequences. Nowadays, maize (26%), oilseed rape (21%), sugar beets (16%), potatoes and even wheat are concerned by genetic modification. Major modifications in the proportion and in the balance of nutrients could be particularly concerned (18 % of the new requests) as abiotic stress yield (13%) or resistance to pathogens which are still in the laboratory phase. Further experimental tests and experimental approaches concerning the safety and more importantly the nutritional value of the new plants will be required. The safety and the nutritional value for animals must be tested and the results published. The quality and the safety of animal food must also be considered for health and consumer protection. Methods for testing and guidance documents on the information need for the risk assessment of GM plants and derived food and feeds are available.

Résumé

Sécurité et valeur alimentaire des plantes génétiquement modifiées pour les animaux et la chaîne alimentaire. Maïs, soja, colza, coton génétiquement modifiés ont couvert près de 60 millions d'hectares dans le monde en 2003. Ils ont été autorisés dans l'alimentation animale et humaine sur la base d'un dossier d'évaluation des risques. Les données nutritionnelles et toxicologiques disponibles dans la littérature scientifique ont toujours conclu à l'absence de toxicité et à leur équivalence alimentaire avec les plantes parentales.

Table 1. Typical genes and safety factor of expressed proteins in GM plants used as feed in ruminants

Item	Plant, event	Resistance	Acute toxicity, mg/kg b. weight	Safety factor
Cry IA (b), (c)	Maize: (Bt 176; Bt 11; Bt MON810); cotton Bollgard	Lepidopterae	4,000	10^{-4}- 3 10^{-5}
	Soybean, maize, sugar beet	Glyphosate	572	10^{-3}
Cp4epsps	Maize, canola; sugar beet	Glufosinate	2,500	2 x 10^{-7}
Pat nptII	Maize, canola	Marker gene	5,000	10^{-6}

Table 2. Insect and herbicide resistance do not modify the chemical composition of maize silage (% of DM)

Event	Control	Bt 176	Control	Bt MON810	Control	Gly nk603
Moisture	68.0	69.3	59.9	59.0	63.4	57.5
C. protein	7.4	8.2*	8.3	8.3	7.3	7.9
NDF	44.9	44.6	37.5	35.6	39.9	41.6
IV DM (%) Digestibility	72.6	72.6	70.5	73.6	78.8	77.3

Table 3. Antinutritional factors (ANFs) and isoflavones in control and glyphosate (Gly) resistant soybean

ANFs	Lectin	Trypsin in **	Genistein	Daidzein	Coumesterol	αGalactosides
Units	HU/mg DM *	mg TI/g DM	μg/ g DM ***			g/ kg DM
Beans:						
Control	1.2	22.6	833	734	4.6	-
Gly resistant	1.0	23.7	830	721	5.6	-
Meal:						
Control	< 0.01	3.4	938	837	0	6.63
Gly	<0.01	3.3	976	856	0	6.63
* Hemaglutinating units ; ** trypsin inhibitor; ** *Isoflavones						

Table 4. Insect resistant Bt maize kernels are less contaminated by mycotoxins

Country	North America		Europe		Italy	
Event	Control	Bt	Control	Bt	Control	Bt
Aflatoxin B1, ppb	4	<2	0.01	0.02	-	-
DO Nivalenol, ppb	30	<LOD	365	288	873	152
Fumonisin, B1, ppm	1.3-3	3-12	20	2	0.5-10	0-0.1

Table 5. Milk yield in dairy cows and milk composition are not modified by feeding GM maize

Item	DM intake, kg	Fat cor. milk	Fat, %	Protein, %	Urea, mg/dl	SS count 10^3
Control	23.3	33.0	3.64	3.21	23.8	138
Bt maize	23.8	33.7	3.65	3.14	21.6	171
Control	23.6	33.0	3.75	3.17	20.3	99
Gly resistant	22.3	31.4	3.73	3.14	20.3	102

SSC: somatic cells count/ml. Experiments lasting 21 to 91 days

Table 6. Comparative slaughtering characteristics of steers fed glyphosate resistant (Gly)maize grain during fattening

Treatment	Control	Gly GA 21	Control	Gly nk603
Final weight, kg	561	558	564	566
Dressing, %	62.2	62.3	61.2	61.1
Liver abscess, %	0.15	0.17	0.24	0.22
12^{th} Rib fat, cm	0.91	0.92	0.99	1.04
Ribeye area, cm^2	92.3	88.0	82.6	84.5

Table 7. Milk and tissue samples are negative for the presence of trangene DNA in animals fed GM plants

Item	Gene inserted	Plant	Test of samples (Positive / total)	Reference*
Milk;	CryIA(b)	Maize kernel	0/147	Faust, 2000
Muscles; eggs	Cry IA(b)	Maize kernel	(0/20); (0/22)	Faust, 2000
Milk	CryIA(b)	Maize, silage	0/12	Phipps 2001
Milk	CryIA©	Cotton seeds	0 / 10	Jennings, 2003a
Milk	Cp4epsps	Soybean	0 / 10	Phipps, 2002
Muscle (Pig)	Cp4epsps	Soybean meal	0/50	Jennings, 2003b.

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