Seventy-five years of synthetic herbicide use in agriculture: Will there be 100?

Glyphosate-resistant (GR) soybean and corn in Brazil: past, present, and future

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Abstract: Glyphosate-Resistant Crops (GR crops) have caused considerable changes in weed management worldwide. In Brazil, GR cultivars of soybean and corn were officially introduced in the 2005/06 and 2011/12 crops, respectively. This technology has radically changed the weed management system, having an enormous impact on national agriculture. The objective of this review was to analyze the general aspects that led to the adoption of this technology in Brazil and present its future consequences and challenges. The adoption of GR soybean and corn was swift and comprehensive. Ten years after its introduction, GR soybean and corn are grown in most areas with these crops in Brazil. This

success can be attributed to the reduction of costs, the broad spectrum of control provided by glyphosate, the solution for effective management resistance to ALS and ACCase inhibitors, the excellent managing of weeds that are difficult to control, the reduction of crop injury and carryover problems. However, the exclusive and consecutive use of glyphosate alone resulted in intense selection pressure for resistant weeds to this herbicide, which has become one of the most prominent challenges with these crops. Therefore, the future sustainability of GR soybean and corn will not be possible without the combination with other technologies, within integrated weed management.

Keywords: weed resistance; weed tolerance; volunteer plants; GR cultivars; integrated weed management

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1. Introduction

Soybean and corn are the two crops with the largest production areas in Brazil. In the 2020/2021 cropping season, soybeans were cultivated on 38.5 million ha, with an estimated production of 135.9 million tons, while corn was grown on 19,305,900 ha, with an estimated production of 85.7 million tons (Companhia Nacional de Abastecimento, 2021). In most regions of Brazilian, soybean and corn are grown under a no-till system, which stands out for its conservationist origin. There is little to no soil movement and preservation of plant residues on the surface in this system, resulting in a gradual increase in organic matter, vital for environmental sustainability, especially in tropical regions (Triplett, Dick, 2008).

For a successful implementation of a no-till system, weed management has always been a critical factor. Before sowing soybean and corn, weed control is exclusive with herbicides in a procedure known as burndown (Roman, 2002). The main herbicides used in this operation are the broad-spectrum, non-selective ones, mainly glyphosate, applied alone or in association with other herbicides to improve its spectrum on hard-to-control weeds (Procópio et al., 2006). After burndown, weed control was carried out with selective herbicides applied either in pre or in post-emergence of crops.

Due to the constantly evolving national agriculture, new technologies are systematically incorporated in grains production. For soybean and corn, one of the most critical factors related to their management in Brazil was the introduction of transgenic cultivars with glyphosate resistance, called Glyphosate-Resistant crops (GR crops). The development of genetically modified crops for glyphosate resistance is based on the insertion of a transgene encoding a GR form of 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS), the target of glyphosate. Only two transgenes for GR EPSPS have been used: the CP4 EPSPS from *Agrobacterium tumefaciens* (Padgette et a., 1995) and GA21 from mutagenized corn (Sidhu, 2000). In GR plants, the glyphosate-insensitive enzyme provides a "by-pass" in the shikimate route, allowing normal activity even when the native EPSPS enzyme is inhibited by glyphosate (Dill et al., 2008).

From the mid-2000s onwards, the adoption of soybean and corn cultivars resistant to glyphosate was swift and wide-ranging by Brazilian farmers, radically modifying

the weed management system of these crops and having a significant impact on national agriculture. This review analyzes the general aspects that led to the implementation of this technology in Brazil and, its consequences and future challenges.

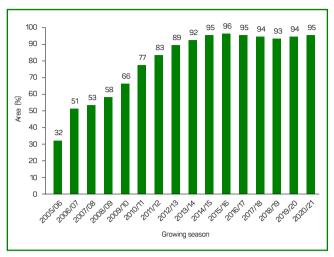
2. History of GR soybean in Brazil

The first commercial cultivation of GR soybean took place in the United States and Argentina in 1996 (Dill, 2005). In Brazil, GR soybean was introduced in the 1996/97 cropping season, in the Southern, through seeds illegally obtained from Argentina, as there was no specific regulation for the use of GMOs. In Brazil, GMO regulations only came into effect when the National Technical Biosafety Committee, CTNBio, was created in 1996. CTNBio's development is intended to support the establishment of technical biosafety standards for the use of GMOs and issue technical opinions on the release of these organisms in the environment and on experimental and commercial scales (Fonseca, Guivant, 2019).

In 1998, CTNBio approved the first genetic transformation case in Brazil, the soybean "GTS-40-3-2", resistant to the herbicide glyphosate (Ministério da Ciência e Tecnologia, 1998). However, this approval was challenged in court by some civil entities and the Ministry of the Environment, resulting in the prohibition of GR soybean cultivation. In 2005, the commercial GR soybean cultivation was legalized due to the enactment of Law n. 11.105/05, which instituted the National Committee on Biosafety and restructured the CTNBio (Ultchak, 2018).

Since 2005, Embrapa Soybean has periodically diagnosed this technology's impact. This database consists of surveys carried out directly with producers and consultations with institutions that work in research, teaching, technical assistance, agronomic consulting, market, production and commercialization of seeds and herbicides. The general result of these diagnoses allowed us to analyze the influence of this innovation, both in the weed management and the soybean production system.

The adoption of GR soybean by Brazilian producers was quick. In the first harvest after the official release of the technology in 2005/06, the GR soybean was planted in 32% of the total cropped area, reaching 51% of the total area in 2006/07. With a significant increase in subsequent crops, GR soybeans production exceeded 90% of the total cultivated area after ten years of technology official release, maintaining a level close to 95% in recent years (Figure 1). This adoption model was similar to the USA's, where the GR soybean cultivation reached 50% of the total area four years after its introduction and 90% after ten years (US Department of Agriculture, 2020). Similarly, nine years after the GR technology introduction in Argentina, it occupied more than 90% of the cultivated area (Burachik, 2012).



Source: Embrapa Soybean.

Figure 1 - Evolution of the GR soybean cultivated area in Brazil from 2005/06 to 2020/21 cropping season

The main factors pointed out by Brazilian farmers for the adoption of GR soybeans were: the lower control cost provided by the use of glyphosate in soybean postemergence; the broad spectrum of weed control, a solution for areas with problems of resistance to ALS and ACCase inhibitors, one of the main problems at the time; an excellent option for managing areas with the infestation of weeds that are difficult to control; the ease of use provided by glyphosate; the reduction of crop injury and carryover problems for crops in succession or rotation. In the USA and Argentina, the adoption of GR soybeans also occurred due to similar factors, especially the greater effectiveness in weed control and the decrease in costs (Pelaez et al., 2004).

When GR soybean was introduced, some significant changes occurred in the Brazilian crop production system. The most significant changes were: the consolidation of the no-till system; the expansion of areas with corn and cotton cultivated in autumn/winter, in succession to soybeans; and the introduction of the Asian soybean rust. As a result, soybean farmers began to look for varieties with characteristics that would adapt to this new production context, especially those that had the potential to be sown early and had better plant architecture, specifically with smaller leaf area, to facilitate the application of fungicides to control Asian soybean rust (Godoy et al., 2009).

These characteristics were relatively common among the varieties produced in Argentina. However, due to the difficulty of weed management in conventional soybean and the need to change the cultivars' characteristics, some producers in the Rio Grande do Sul, a state latitude neighboring Argentina, clandestinely imported GR soybean seeds from that country during the 1996/97 harvest. As the climatic conditions between these regions were similar, some of these varieties were well adapted to Brazilia areas bordering Argentina. These GR varieties were sown in the Rio Grande do Sul and later throught Southern Brazil.

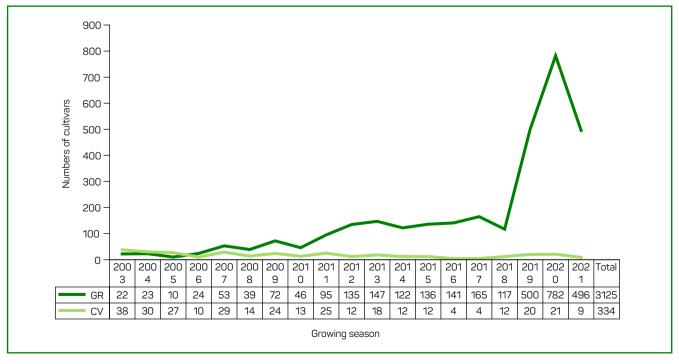
The GR soybean expansion to other Brazilian regions followed at a slower pace, mainly due to the limited initial offering of varieties adapted to lower latitude regions. In Brazil, the regulation of varieties is carried out by the National Cultivar Registry, RNC, which regulates the production, processing, and marketing of seeds and seedlings, subject to prior registration of the variety in RNC (Lima et al., 2018). From the creation of RNC in 1998 to 2002, seven companies registered 308 soybean varieties. Since 2003, the year that the first GR soybean variety was recorded, the total number of varieties have increased year by year, reaching a total of 803 varieties and soybean lines registered in 2020 (Figure 2) by 21 different breeders, which demonstrates how attractive the seed market has become after the approval of GMO crops. RNC numbers help explain the significant expansion of GR soybeans in Brazil. In 2003, the offer of conventional varieties represented 63% of the records; by, 2020, this number was only 1.8%. Therefore, there were fewer options for producers who did not want to opt for GR soybean.

Research also played a determining role in consolidating GR soybean technology in Brazil. Among the main scientific initiatives, were the genetic improvement, which created GR cultivars adapted to the different regions of the country; general studies on the management of glyphosate, aimed at optimizing its use; and evaluations of the agronomic and environmental impacts of this technology.

3. History of GR corn in Brazil

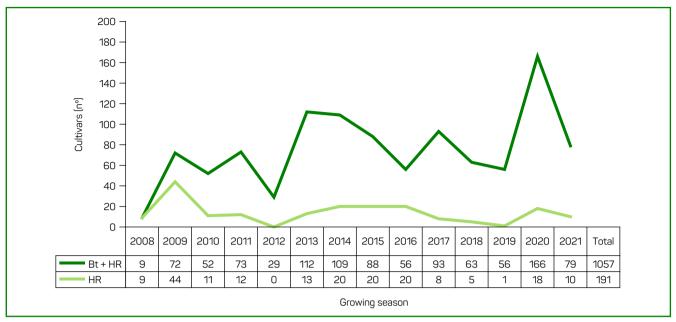
The introduction of GR corn takes place in a different scenario compared to GR soybean. At the time, corn's main pest problem was the management of caterpillars (Farias et al., 2014), so weed control in the crop was seen as a complementary, simple practice without significant challenges. The low incidence of difficult-to-control species and the effectiveness of the registered herbicide molecules made weed management easy. Given this context, the producers wanted transgenic hybrids resistant to caterpillars, especially the fall armyworm (*Spodoptera frugiperda*), so transgenic corn cultivation was the first release hybrids resistant to insects of the order Lepidoptera in 2007 (Ministério da Ciência e Tecnologia, 2021).

The commercial release of herbicide-resistant corn was not a priority for the productive sector. Farmers and technicians were concerned about the intensive use of glyphosate in no-till production systems, mainly due to its use both on burndown and on crop postemergence applications. Thus, people considered the use of this technology unnecessary. However, most transgenic commercial hybrids were launched to the market with joint resistance to lepidopterans and herbicides, glufosinate or glyphosate (Figure 3). The new hybrids were made available only with these two traits with better genetics and higher yield potential. Glyphosate resistance was often considered of little value, a freebie. A widely used argument was that despite the resistance to glyphosate, its use was optional.



Source: SRNC/CGSM/DSV/SDA/MAPA.

Figure 2 - Glyphosate resistant (GR) and conventional (CV) soybean cultivars and lines officially registered for commercialization in Brazil, from 2003 to 2021



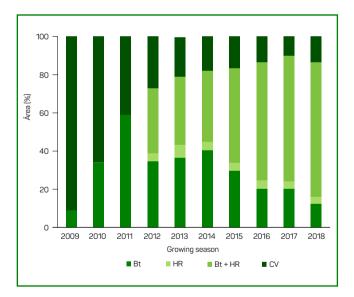
Source: SRNC/CGSM/DSV/SDA/MAPA.



Before the commercial availability of these hybrids, several events with consultants, technicians, and producers were held. The campaigns addressed the advantages of using GR corn and its position in the production system.

The first release for commercial cultivation of herbicideresistant corn in Brazil occurred in 2007 with the approval of glufosinate resistance (Ministério da Ciência e Tecnologia, 2021). However, the use of this herbicide is still not widespread in corn. This fact can be attributed to different factors, such as: its high market value when compared to other available alternatives; its low translocation in plants, being effective in controlling only young plants; and low efficacy in controlling grasses and perennial species (Takano, Dayan, 2020). The first recorded hybrid with resistance to this herbicide occurred in 2011 (Ministério da Agricultura Pecuária e Abastecimento, 2021), which was also resistant to glyphosate. Hybrids registered with resistance only to glufosinate occurred in 2013. In 2008, GR corn cultivation was officially approved, registering nine resistant hybrids. However, it is essential to point out that the commercialization of GR corn started in the 2011/12 harvest, thus in 2021 its cultivation completed ten years.

The stacking of events that promote resistance to insect pests and herbicides is the most common transgenic in corn crops (Figure 3). The number of registered cultivars resistant only to herbicides is approximately 20% of the total with both traits (Ministério da Agricultura Pecuária e Abastecimento, 2021), mainly used as a refuge area in *Bacillus thuringiensis* (Bt) corn. This phenomenon can be observed by analyzing the area and the participation of each trait (Figure 4). Considering the area of winter and summer corn, around 74% of it is cultivated with hybrids



Source: Céleres.



resistant to insects and herbicides (Céleres, 2018). These data demonstrate that despite the initial resistance, the adoption of the technology was widespread. Currently, glyphosate and atrazine are the main molecules used for weed management in corn crops.

In total, six events have proteins that confer resistance to herbicides in corn crops (Ministério da Ciência e Tecnologia, 2021). These can be stacked singly or together, providing resistance, respectively, to a herbicide group or different mechanisms of action. In addition, there are cases in which the proteins are similar, but the events are different because the construction process is also different.

Among the events that confer resistance to herbicides, glyphosate is the primary molecule. Among the 1057 transgenic cultivars registered with a resistance transgene, 1028 are glyphosate.

4. Weed management in GR soybeans

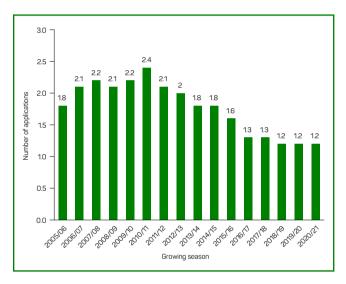
In the 1970s, the advance of soybean cultivation in Brazil took place within the conventional soil preparation system using plowing and harrowing. In this system, weed control was based on residual herbicides applied before soybean sowing, such as trifluralin, *S*-metolachlor, alachlor, and metribuzin, alone or in association to broaden the control spectrum. However, from the mid-1980s, no-tillage has dramatically expanded, and new, post-emergent herbicides selective in soybeans have been launched. Thus, post-emergence herbicides gradually replaced preemergence herbicides.

Post-emergence applications of conventional soybeans require a lot of attention and care, especially concerning weed size, soybean stage, climate issues, besides the mixture of broadleaf and grass herbicides in the spray tank, due to the possibility of antagonism between the products. In the late 1990s, the main problems regarding weed management in soybean crops were: the high infestation with difficultto-control weed species; high control costs (ca. US\$ 50.00/ ha); the fact that it was considered the crop production practice of greatest difficulty; and a significant increase in cases of resistance (Adegas et al., 2012).

The most significant resistance problems were the broadleaf species, mainly Euphorbia heterophylla (Wild poinsettia), in the south and southeast, and Bidens pilosa (Hairy beggarticks), in the Cerrado region, to the herbicides that inhibit the enzyme acetolactate synthase (ALS) (Francischini et al., 2014; Gelmini et al., 2005; López-Ovejero et al., 2006). After identification, the ALS inhibitors were quickly replaced or complemented by herbicides inhibiting the enzyme protoporphyrinogen oxidase (PPO). Subsequently, as no other management strategy was adopted, individuals with multiple resistance to these two mechanisms of action were selected (Trezzi et al., 2005; Francischini et al., 2019). In a smaller proportion and spotted areas, the presence of grasses such as Digitaria horizontalis (Jamaican crabgrass) and Brachiaria plantaginea (Signalgrass) resistant to herbicides that inhibit the enzyme acetyl-CoA carboxylase (ACCase) were identified (Agostinetto et al., 2002).

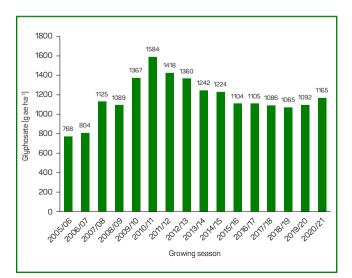
The adoption of GR soybeans offered farmers a new option to control weeds by using a single herbicide, glyphosate, which had, among its main characteristics, a broad spectrum of action, without carryover problems, besides facilitating the no-till system. At the beginning of GR soybean cultivation, in the 2005/06 harvest, the average number of glyphosate applications post-emergence of the crop was 1.8. In the 2010/11 harvest, the highest average number of applications was 2.4, and in 2018/2019, it stabilized at 1.2 (Figure 5). This process is mainly related to the shorter cycle of varieties used in the country's central producing regions and the increased use of other herbicides in the control system. The substantial increase in the glyphosate use can be observed by the doses applied in post-emergence of soybean, since in 2005/06 the average was 768 g ae/ha, and it has gradually increased to 1,584 g ae/ha in 2010/11 cropping season, mainly due to the increase in resistant weed populations. The doses decreased to 1,165 g ae/ha (Figure 6) because other herbicides were introduced in weed management.

The cultivation of GR soybeans in Brazil officially started in 2005, expecting to solve all weed management problems.



Source: Embrapa Soybean.

Figure 5 - Average number of glyphosate applications in postemergence of GR soybean in Brazil



Source: Embrapa Soybean.

Figure 6 - Average dose of glyphosate applied in the postemergence of GR soybean in Brazil However, the same "old" system problems soon arose due to the intense selection pressure from glyphosate. Currently, the management is as complex as in conventional soybeans. The difficulty of managing glyphosate-resistant and/or resistant weed species requires changes in the replacement or inclusion of other herbicides in production systems and changes in behavior, such as the adoption of integrated weed management (IWM).

Even after the adoption of GR soybean, many herbicides were still registered for soybean. Some, such as imazaquin, were withdrawn from the market but later returned through other companies. Others, such as diuron and clomazone, remained available in mixtures with sulfentrazone or carfentrazone-ethyl, respectively, focusing on application in pre-sowing soybean, in addition to glyphosate. Similarly, *S*-metolachlor is used in a mixture with fomesafen or metribuzin, which are commercial mixtures recently launched in Brazil. The herbicide market adapted to the new reality of weed management in the GR soybean crop in Brazil, reflecting the increased infestation of glyphosateresistant weeds.

5. Weed management in GR corn

Weed management after the development of GR hybrids underwent modifications. Before this technology, or even with non-GR hybrids, chemical weed control in corn crops was with atrazine, an electron transport chain inhibitor in the PSII (Cobb, Reade, 2010). Atrazine is effective in both pre and post-emergence of weeds. This herbicide controls several species; however, it has better efficacity on broadleaf weeds (Rodrigues, Almeida, 2018). The use of herbicides complementary to atrazine was directly linked to the composition of the weed community and the grain's value. Historically, the cost-effectiveness of cultural treatments is a determining factor for the choice of management, especially in corn.

For preemergence herbicide use in corn, there are the following registered inhibitors: long-chain fatty acid synthesis inhibitors (acetolachlor, pyroxasulfone, and s-metolachlor), carotenoid biosynthesis inhibitors polymerization (isoxaflutole), tubulin inhibitors (pendimethalin and trifluralin), and PSII inhibitors (e.g., atrazine, simazine, ametryn and terbutylazine) (Ministério da Agricultura, Pecuária e Abastecimento, 2003). Nevertheless, preemergence herbicides in corn cultivation is not a usual practice. This fact is directly linked to the more technical positioning of these products, the good control efficiency obtained by post-emergence, and the control cost related to the economic return.

For post-emergence control, mesotrione and tembotrione, which inhibit 4-hydroxyphenylpyruvato dioxygenase (HPPD), stand out, as well as nicosulfuron, an ALS enzyme inhibitor. These herbicides provide good control of grass and broadleaf species (Timossi, Freitas, 2011). In conventional corn, one of these products is usually used in a tank mixture with atrazine. However, selectivity in corn can vary depending on the hybrids, and the joint application of organophosphate insecticides and nitrogen fertilization can reduce crop selectivity (Silva et al., 2005; Souza et al., 2019). In addition, for the control of species such as *Commelina benghalensis* (benghal dayflower) and *Richardia brasiliensis* (Brazil puzley), the application of carfentrazone, a PPO inhibitor, can also be used (Christoffoleti et al., 2002).

Besides the herbicides already mentioned, there are other active ingredients registered for the corn crop, with 11 different mechanisms of action (Ministério da Agricultura, Pecuária e Abastecimento, 2021). However, even with all the herbicide options, many producers choose GR corn technology for its lower cos and simplicity (Thomas et al., 2004).

Currently, the GR soybean-GR corn succession has changed the composition of the weed community. There was an increase in the number of resistant biotypes to glyphosate in this crop succession. GR clumped sourgrass (Digitaria insularis) is one of the primary management challenges in GR-soybean and GR-corn. These plants are usually defoliated due to being cut by the combines, making the control during corn sowing inefficient. In the postemergence, the available herbicides do not control these plants satisfactorily. This fact reinforces the need to manage this specie in previously cultivated soybeans properly. The increase in resistant biotypes, coupled with the good market value of the grain price, has contributed to a change in the producers' mindset. There is a tendency to increase pre-emergent herbicide use in corn crops to control these species despite limited use.

6. Consequences of GR soybean cultivation

With the adoption of GR soybean, farmers enjoyed the simplicity, flexibility, and broad spectrum of glyphosate control for some years. The advantages of this herbicide are undeniable, but some information was ignored, such as the existence of tolerant species to glyphosate, which are naturally harder to control by this herbicide, and the possibility of selecting resistant biotypes. A broad control spectrum with glyphosate exists, but for some species, the effectiveness is linked to the plant stage at the time of the application (Fadin et al., 2018). This lack of information led to the selection of tolerant species such as *Commelina benghalensis* (Benghal dayflower), *Richardia brasiliensis* (Brazil puzley), *Ipomoea* spp. (Morning glory), *Spermacoce* spp. (Buttonweed), among several others (Correia et al., 2008; Lucio et al., 2019).

Moreover, the selection of GR biotypes made the misuse of GR crop technology evident. The frequent use of the same herbicide over the years without rotating the mechanism of action, associated with the absence of other management strategies, results in the selection of resistant weeds, as happened with glyphosate in Brazil (Heap, Duke, 2018). It was just a matter of time for the first official report of resistance of Italian ryegrass (*Lolium perenne*

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ssp. *multiflorum*) to glyphosate to come out, in 2003. It was reported in Rio Grande do Sul state and identified in orchards and soybean areas (Heap, 2021). Since then, several other cases of resistance have been reported, both for grasses and broadleaves, either single resistance to glyphosate or multiple resistance, associated with other mechanisms of action, mainly ALS inhibitors and ACCase inhibitors (Table 1).

By 2021, 19 official cases of glyphosate-resistant weeds were reported in Brazil. Resistant sourgrass (*Digitaria insularis*) has the most significant impact in the country, as it is present in almost all soybean-producing agricultural

Table 1 - Glyphosate-resistant weed species in Brazil.				
ld.	Specie	Popular name	First year	Site of action
1	Lolium perenne ssp. multiflorum	Ryegrass	2003	EPSPS
2	Conyza bonariensis	Hairy fleabane	2005	EPSPS
3	Conyza canadensis	Horseweed	2005	EPSPS
4	Digitaria insularis	Sourgrass	2008	EPSPS
5	Lolium perenne ssp. multiflorum	Ryegrass	2010	EPSPS+ACCase
6	Conyza sumatrensis	Sumatran fleabane	2010	EPSPS
7	Conyza sumatrensis	Sumatran fleabane	2011	EPSPS+ALS
8	Chloris elata	Windmill grass	2014	EPSPS
9	Amaranthus palmeri	Palmer amaranth	2015	EPSPS
10	Eleusine indica	Goosegrass	2016	EPSPS
11	Amaranthus palmeri	Palmer amaranth	2016	EPSPS+ALS
12	Lolium perenne ssp. multiflorum	Ryegrass	2017	EPSPS+ALS
13	Conyza sumatrensis	Sumatran fleabane	2017	EPSPS+ALS+PSI
14	Eleusine indica	Goosegrass	2017	EPSPS+ACCase
15	Conyza sumatrensis	Sumatran fleabane	2017	EPSPS+PSI+Auxin
16	Amaranthus hybridus	Smooth pigweed	2018	EPSPS+ALS
17	Euphorbia heterophylla	Wild poinsettia	2019	EPSPS
18	Echinochloa crus-galli var. crus-galli	Barnyardgrass	2020	EPSPS
19	Digitaria insularis	Sourgrass	2020	EPSPS+ACCase

Source: Adapted from Heap (2021).

regions in Brazil (Lucio et al., 2019; Takano et al., 2020). Very light seeds with intense hairiness facilitate the natural spread of the species, but grain harvesters also disseminate weed taking the seeds to other areas, inside or outside the property, even over long distances (Ovejero et al., 2017). In 2008, glyphosate-resistant sourgrass was found, and after 12 years, a case of multiple resistance to ACCase inhibitors was also recorded (Heap, 2021). This was expected due to the exclusive use of ACCase inhibitors to control glyphosateresistant populations.

Another serious problem, especially in Southern Brazil, is the control of *Conyza* spp., since biotypes with multiple resistance have already been reported (Albrecht et al., 2020). Three species of the genus *Conyza* have been identified in Brazil: *C. bonariensis*, *C. canadensis*, and *C. sumatrensis*. The seeds of these species are very small, hairy, and easily spread by the wind, and glyphosate-resistant populations are distributed in most grain-producing regions (Lucio et al., 2019). Thus, the most significant difficulty in chemical management is experienced in areas with a mixed infestation of sourgrass and *Conyza* spp., requiring herbicide mixtures in soybeans pre-sowing and post-emergence, which increasing the production cost (Adegas et al., 2018).

GR soybeans have also favored burndown misuse. The glyphosate applications are single, without sequential herbicide applications, and have become increasingly closer to the crop sowing, without the proper formation of mulch on the soil, which is recommended in the no-till system (Fidelis et al., 2003). However, the interval between soybean sowing and post-emergence glyphosate application increased, because it was not necessary to apply the herbicide on such small weeds, as it controls large plants. However, post-emergence applications on small plants are effective and avoid the initial competition of weeds with the crop, preferably between soybean stages V1 and V3 (Green-Tracewicz et al., 2012), which has also been ignored with glyphosate use in soybeans.

The control of GR soybean volunteer plants must be highlighted. Volunteers that used to be easily controlled by glyphosate now require other chemical strategies, making it more complicated and expensive with the adoption of GR corn. Therefore, other herbicides had to be inserted into the system to control GR volunteer plants in soybean-corn second crop successions or soybean-corn first crop rotations. The many applications of ACCase inhibitors on soybeans to control GR volunteer corn have increased production cost and pressure for resistant weeds selection. The chemical management of volunteer corn is not simple, as its emergence in the field is staggered and depends on how the grain is laid out in the area - loose grains or in the cob, and cob with and without straw (López-Ovejero et al., 2016). However, atrazine facilitates the control of GR volunteer soybean in corn because soybean emergence is uniform, not staggered and uneven as it is in volunteer corn.

At the beginning of GR soybean implementation, there was a general belief in the ease and convenience of

chemical control. Nevertheless, production systems are more complex than in the past due to poor control and increased infestation of glyphosate-tolerant or resistant species (Green, 2018). Tank mixtures are increasingly frequent; however, errors remain the same, such as poor burndown, no sequential application when necessary, no use of residual herbicides, and no rotation of the herbicide action mechanism, even in extreme situations (Beckie, 2011; Young, 2006). In addition, few producers adopt good agricultural practices, including IWM strategies, such as the management of the soil seed bank and the adoption of non-chemical methods, including the maintenance of cover crops in the agricultural interseason (Marochi et al., 2018).

There were no proven adverse effects of glyphosate on soybean nodulation and mycorrhizal colonization, not reported to have insecticidal or other activities against arthropods, or problems of persistence in the soil, environment and leach into groundwater (Cerdeira et al., 2007).

Soybean yield has increased by approximately 22% since GR soybean was launched in Brazil (Companhia Nacional de Abastecimento, 2021). However, this increase is more related to the genetic gains of cultivars launched in the period and general crop management than GR technology. The same situation occurred with the corn crop.

7. Consequences of GR corn cultivation

The main criticism about the use of GR technology in corn is that in Brazil, the traditional sequence of soybeans in the first harvest, between September-February/March, followed by corn in the second harvest, February/March-July/August, would end up causing excessive annual glyphosate application in the same crop season, resulting in the selection of glyphosate-resistant weeds. This worry became true because the indiscriminate use of this herbicide has caused the selection and dispersion of resistant weeds in grain production systems, including corn. Currently, out of the 11 glyphosate-resistant weed species (Table 1), only *Echinochloa crus-galli* (barnyardgrass) is not found in corn crops.

Another problem involving the GR soybean-GR corn succession is the occurrence of volunteer plants. After GR corn was approved, it has become the primary weed of GR soybeans, with a high potential for competition, since one corn volunteer plant per m^2 can reduce soybean yield by up to 25%. This is a dire situation for Brazilian agricultural production. Second-crop corn is characterized by being sown immediately after the soybean harvest, often on the same day. According to *Companhia Nacional de Abastecimento* – Conab (2021) data, second-crop corn was planted on approximately 15 million hectares with a 60.6 million ton production in the 2020/2021 cropping season. This value corresponds, respectively, to 75% and 70% of the sown area and total corn production in the country. Furthermore, the second-crop planting area corresponds to approximately 39% of the soybean cultivation area. These values indicate the difficulties of managing volunteer plants in which crops.

The emergence of volunteer corn is directly related to rainfall and the type of grain loss at harvest. Silva et al. (2018) report that when parts of corn cobs from the previous crop losses are incorporated into the soil, volunteer corn infestation in the subsequent soybean crop is increased, and the importance of the infestation level is greater when loose grains from the spike end up staying in the field. In the Cerrado region, the beginning of the wet season starts the emergence of volunteer corn; thus, the control carried out before the rains are not effective. In Southern Brazil, the decrease in cold weather is responsible for the first flushes of volunteer corn infestation in soybean crops.

Volunteer corn control in soybean crops is primarily carried out using herbicides that inhibit ACCase (Chahal et al., 2016). The number of applications of these herbicides is related to emergency flushes directly linked to the types of grain losses (Silva et al., 2018). Besides, the control of volunteer corn that emerges later during the soybean growing season causes less damage to the crop yield. Still, the volunteers can cause other problems during harvest and subsequent crops, such as wear on the combines, lower grain quality, a source for pests and diseases, etc.

8. The future of weed management in GR corn and soybean

Weed tolerance and resistance to glyphosate is expected to be key factor for the future of GR crop technology. Therefore, we must IWM. IWM can be defined as the selection and integration of control methods and the set of criteria for their use, with favorable results from the agronomic, economic, ecological, and social points of view. IWM incorporates various weed prevention methods, such as exclusion, monitoring, and suppression, supported by the biology of agroecosystems (Wilson et al., 2009). The development of IWM was motivated by a desire to provide farmers with systematic methods to reduce dependence on herbicides (Swanton, Weise, 1991), delaying the selection of resistant weed biotypes.

Even before the official launch of the first GR crop, several works had already reported on the importance of integrated management to the technology's success, requiring individual analysis for each type of situation in its adoption (Ateh, Harvey, 1999; Gonzini et al., 1999). In the beginning, the opportunity to control resistant weeds, especially ALS and ACCase inhibitors, was indicated as an advantage of GR soybeans, using an herbicide with a different mechanism of action, in this case, glyphosate (Culpepper, 2000). However, due to the consequences of the continued use of the same herbicide, which was already known in Brazil, integrated management should not be disregarded, even with this new technology (Gazziero et al., 2001). The implementation of integrated management in GR crop systems has shown that this is the path to be pursued for the future, as the studies carried out with USA farmers show (Weirich et al., 2011; Shaw et al., 2011). These studies have compared the weed resistance management system with the farmers' standard production system. The results confirmed that farmers could implement resistance management systems with equivalent net returns, both short and long terms, besides preventing or mitigating the evolution of glyphosate-resistant weeds.

Among the integrated practices to be used in the future management of GR soybeans, the following stand out:

- preventative, such as precautions in seed acquisition, strict cleaning of machines and implements, as well as cleaning of roadsides, trails, and terraces;
- mechanical, such as mowing perennial weeds, hand weeding, and, when feasible, replacing the chemical burndown operation with mechanical control;
- cultural, such as reducing fallow seasons, rotating crops, and implementing cover crops;
- chemical, such as standardizing the control areas, dividing them into homogeneous plots; surveying the distribution of the weed flora; analyzing the various herbicide alternatives, taking into account the aspects of efficiency, effectiveness, applicability, and cost, with rotation of the mechanisms of action; and improving application technology.

Regarding chemical control, the first recommendations from Brazilian research indicated the need for rotating herbicides and mechanisms of action, or even rotating conventional cultivars with GR cultivars, to maximize control and avoid the selection of GR weeds (Embrapa Soja, 2006). At that time, the issue was discussed in several technical meetings. The main general concern was to prevent the possibility of a significant change in the weed community with the increase of GR species. This worry justified the need to preserve the herbicides used in conventional soybeans as it was believed that they would be important to complement glyphosate in the future. Unfortunately, due to most farmers' lack of proactivity, this happened; therefore, the herbicide rotation recommendation should be maintained.

The main objectives of herbicide rotation and diversification in GR crops are to include the residual effect, provide a greater spectrum of control, and prevent the selection and dispersion of GR weeds (Krausz et al., 2001; Gazziero, 2003).

Unfortunately, since the 1990s, no new mechanism of action for soybean or corn herbicides has been launched on the market, so the herbicides that will be used in association or rotation with glyphosate are those currently registered. Nandula (2019) considers the lack of new herbicide options as one of the most significant problems in managing GR crops but indicates the possibility of launching two new herbicide action mechanisms by 2030. In addition to new herbicides, the future in the management of GR soybean and corn might incorporate other traits of herbicide resistance, such as auxinics, including the commercial release in the 2021/2022 harvest of Enlist® soybean, resistant to herbicides 2,4-D, glufosinate, and glyphosate, and Xtend® soybean, resistant to dicamba and glyphosate. Furthermore, resistance to other herbicides such as ALS and HPPD inhibitors are also being addressed in soybean crops, combined with resistance to glyphosate and/or glufosinate (Green, Siehl 2021).

Regarding corn, hybrids resistant to 2,4-D and dicamba will also be available in Brazil. Even though they are broadleaf herbicides, the selectivity for the crop depends on several factors, such as corn stage, dose, and environmental conditions (Cao et al., 2011). Therefore, the use of genetically modified plants resistant to these herbicides will provide greater safety to the crop in their application. Another trait under development is the haloxyfop-*p*methyl-resistant corn, a grass herbicide that inhibits the ACCase (Wright et al., 2010). In practice, the relevance of this event will be the control of grasses, such as sourgrass and ryegrass, in the post-emergence of corn since this is one of the main difficulties in conventional crops.

In the somewhat further future, other herbicideresistant crops might be on the market, including nontransgenic Crispr-based ones. Also, technologies currently under development, such as bioherbicides, RNAi for reversal resistance, and robotic weeding, might be launched, and they may affect the role of GR crops in weed management (Duke, 2015).

The future of GR soybean and corn in Brazil clarifies that, even with existing technologies and those yet to come, none of them should be treated as a single solution in managing these crops, but they should all be considered tools that will help the IWM system.

9. Conclusion

The GR soybean and corn technologies have made a significant positive impact on Brazilian agriculture. Adopted by more than 90% of the farmers, this technology has caused a massive change in weed management by using glyphosate post-emergence in these crops. Furthermore, an essential feature of these crops is that they represent the main cultivation system in Brazil, in the traditional sequence of soybeans in the first crop, between September-February/March, followed by corn in the second crop, February/March-July/ August.

GR technology has meant simplicity, flexibility, a broad spectrum of control, and relatively low cost for many years, presenting undeniable advantages. However, the technology misuse, mainly due to the non-rotation of crops and herbicides, with recurrent and exclusive use of glyphosate, associated with the absence of any other management strategies, resulted in the selection of biotypes resistant to the herbicide. This selection process has become one of the main problems in soybean and corn production in the country.

Weed tolerance and resistance to glyphosate are expected to be the negative factor in the future of GR crop technology. Another critical point is the occurrence of volunteer corn within the soybean crop, and vice versa, which were easily controlled by glyphosate in the past.

Therefore, the management of glyphosate-resistant weeds and volunteer plants requires changes in the replacement or inclusion of new herbicides in production systems and, behavior, such as the adoption of IWM systems. Preventive, mechanical, cultural, and chemical management practices stand out among the integrated management practices. Regarding chemical control, the main recommendations are to rotate and/or combine herbicides with various mechanisms of action, including GM and conventional cultivars.

Authors' contributions

All authors participated in the preparation of this manuscript.

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