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Chapter 3

Strategies of Chemical Protection for Controlling Soybean Rust

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Additional information is available at the end of the chapter

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Abstract

Asian soybean rust (*Phakopsora pachyrhizi*) is an aggressive and destructive disease that undermines the current 34 million hectares of soybean production system in Brazil. The disease is present throughout the entire cultivated area. The disease control has required a combination of several practices in order to avoid losses. In the last 15 harvests, the application of fungicides has been shown as an effective alternative for the producer in the control of this aggressive disease. Since the first fungicides emergency recommended for the 2002/03 season (azoxystrobin, difenoconazole, fluconazole, pyraclostrobin + epoxiconazole, and tebuconazole), a large number of new formulations were added to the arsenal to control rust. There are today recorded in MAPA (Ministry of Agriculture and Supply) about 45 active ingredients (alone or in combination are about 120), trademarks, and formulations for the rational use against rust. Among fungicides, there are differences in efficacy, residual period, metabolic stability, and translocation rate, requiring care from the producer and technical assistance in the choice of the product to be used in each situation. In this review, the chemical control of rust is analyzed in Brazil from 2001/02 to 2013/14; its economic importance, strategic variables for the rational fungicides practice, factors that complicate the chemical control and the risk of resistance to the main chemical groups.

Keywords: Soybean, Asian rust, chemical control, active ingredient, triazole, strobilurin

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1. Introduction

Soybean rust is caused by two species: *Phakopsora meibomiae* genus, which causes American rust, which naturally occurs in several legumes from Puerto Rico, Caribbean, the Southern State of Paraná (Ponta Grossa), and *Phakopsora pachyrhizi*, which causes Asian soybean rust, present in most countries that grow soybeans and from the 2000/01 season, also in Brazil and Paraguay. A distinction between the two species is made by teliospores morphology and DNA analysis [1–3].

Asian soybean rust caused by *P. pachyrhizi* has been a serious disease in Asia for many decades. It appeared in Africa in 1997, and appeared in the Americas fields in 2001. In the USA, it was first found in the continent, in late 2004, probably brought in by a hurricane; it was considered such a threat that it was listed as a possible weapon of bioterrorism. Soybean rust cannot overwinter in areas with freezing temperatures, but it can spread by wind rapidly over such large distances, its development can be so explosive, and it can cause such rapid loss of leaves that it is now one of the most feared diseases in the world's soybean-growing areas.

Asian soybean rust (P. pachyrhizi) is a very destructive disease that undermines the current soybean production system in Brazil. ASR can cause yield losses of up to 90%. The disease was first reported in Brazil in open field areas in 2001. The disease importance can be judged by its rapid expansion, virulence, and amount of losses (**Table 1**). This situation was common in the Cerrado and South regions, where the climate favors the disease, makes its control difficult and the large extensions of crops represent one more challenge in spraying [4–7].

Crop season	Grain loss(1)	Rust cost(2)	Observations
2001/2002	569.2 thousand tons (US$ 125.5 million)(a)	US$ 177 million	First year with the disease occurrence on commercial areas. No fungicides registered for soybean rust. Economic losses were observed in the states of Rio Grande do Sul, Paraná, Mato Grosso do Sul, Mato Grosso, and Goiás.
2002/2003	3.4 million tons (US$ 737.4 million)(b)	US$ 1.16 billion	Rust occurred in 80% of Brazilian cultivated area, receiving three spray applications, on average. Five commercial fungicides were registered as an emergency. Major losses in the state of Bahia. Rust was reported in all producer states.
2003/2004	4.6 million tons (US$ 1.22 billion)(c)	US$ 2.08 billion	Soybean rust occurred in 70% of the cultivated area, receiving 3.5 sprays per hectare on average. Lack of fungicides to spray. Rust reported in all producer states, except in Roraima and Pará, and in Distrito Federal.

Crop season	Grain loss[(1)]	Rust cost[(2)]	Observations
2004/2005	Losses not estimated; only localized occurrences	US$ 1.215 billion Control cost: US$ 1.215 billion (US$ 32.6/spray × 2 sprays – 80% of cultivated area)	Drought in most of the regions; rust did not have significant impact. Mato Grosso was the most affected state. No disease was registered in Distrito Federal or in the states of Bahia, Piauí, Roraima, and Pará.
2005/2006	2.9 million tons (US$ 640 million[(a)] + 10% taxes)	US$ 2.124 billion Control cost: US$ 1.42 billion (US$ 40/spray × 2 sprays – 80% of cultivated area)	Off-season soybean sowing increased rust incidence in the crop season. Rust was reported in all producer states, except in Piauí, Roraima, and Pará, and in Distrito Federal.
2006/2007	2.67 million tons (US$ 615.7 million)[(d)]	US$ 2.19 billion Control cost: US$ 1.58 billion (US$ 33/spray × 2.3 sprays – 99% of cultivated area)	The soybean-free period implemented in the states of Tocantins, Goiás, and Mato Grosso reduced early onset of rust. Rust reported in all producer states, except in Roraima and Pará, and in Distrito Federal.
2007/2008	418.5 thousand tons (US$ 204.5 million)[(e)]	US$ 2.38 billion Control cost: US$ 1.97 billion (US$ 43/spray × 2.2 sprays)	Soybean-free period implemented in the states of Tocantins, Goiás, Mato Grosso, Mato Grosso do Sul, Minas Gerais, São Paulo, and Maranhão. At the end of the growing season, a lower efficiency of DMI fungicides was reported. Rust reported in all producer states, except in Piauí, Pará, and Roraima, and in Distrito Federal.
2008/2009	571.8 thousand tons (US$ 71.7 million)[(f)]	US$ 1.74 billion Control cost: US$ 1.67 billion (US$ 30/spray × 2.4 sprays)	Soybean-free period also implemented in the state of Paraná. Drought in most of the growing regions. Rust reported in all producer states, except in Pará and Roraima, and in Distrito Federal. Epidemics in the state of Bahia.
2009/2010	Losses not estimated; only localized occurrences	US$ 2.09 billion Control cost: US$ 2.09 billion (US$ 33/spray × 2.7 sprays)	The rainy winter was favorable for the survival of the fungus in volunteer soybean plants, and the weather was favorable during the crop season for epidemics. Fungicide sprays avoided losses. Rust reported in all producer states, except in Pará and Roraima.
2010/2011	Losses not estimated; only localized occurrences	US$ 2.10 billion Control cost: US$ 2.10 billion (US$ 35/spray × 2.5 sprays)	Dry winter helped to decrease the fungus population. The Anti-Rust Consortium started recommending only the application of a premix of DMI and QoI fungicides due to the lower efficiency of DMIs in all regions. Fungicide sprays avoided losses. Rust reported in all producer states, except in Piauí, Maranhão, Tocantins, Pará, and Roraima, and in Distrito Federal.

Crop season	Grain loss[1]	Rust cost[2]	Observations
2011/2012	363.5 thousand tons (US$ 191.6 million)[g]	US$ 1.73 billion Control cost: US$ 1.54 billion (US$ 22/spray × 2.8 sprays)	La Niña weather condition: drought in the southern region and in the state of Mato Grosso, with lower incidence and severity of soybean rust. Losses in Mato Grosso. Rust reported in all producer states, except in Piauí, Maranhão, Tocantins, and Roraima.
2012/2013	Losses not estimated; only localized occurrences	Control cost: US$ 1,94 billion (US$ 25/spray × 2.8 sprays)	Volunteer soybean plants with rust overwinter in Mato Grosso. El Niño weather condition: irregular rain occurrence. Low disease severity in the South of the country. Rust reported in all producer states, except in Piauí, Tocantins, Pará, and Roraima.
2013/2014	Losses not estimated; only localized occurrences	Control cost: US$ 2.2 billion (US$ 25/spray × 3 sprays)	Low disease pressure on South and Southeast regions due to below-average rainfall and high temperature. In the Center-West region, late-sowed soybean had high severity (with rains in February). Lower efficiency of QoI and of a premix of QoI + DMI. Rust reported in all producer states, except in Piauí, Pará, and Roraima.

Source: Consórcio Antiferrugem (2015).

[1]Calculated considering soybean price: (a) US$ 220.50 per ton; (b) US$ 220 per ton; (c) US$ 266 per ton; (d) US$ 230.6 per ton; (e) US$ 488.72 per ton; (f) US$ 230.65 per ton; and (g) US$ 527.07 per ton.

[2]Control cost + grain losses. DMIs, demethylation inhibitor; and QoI, quinone outside inhibitor. By Godoy et al, 2016 (19).

Table 1. Estimated grain losses and costs due to Asian soybean rust control in Brazil, since the 2001/2002 crop season [19].

The fact that Asian soybean rust is a disease of recent occurrence (from 2001) and the limited availability of information about the climatic influences of soybean cultivation regions could have an influence on the severity of the disease each year, which makes the generic control recommendation that satisfies all the regions difficult. The continuous periods of leaf wetness, because of 8h of rain or dew, and daily temperatures ranging from 15 to 30° C favor the development of the disease [4, 8–11]. Control strategies for Asian soybean rust require a combination of management practices to avoid or minimize losses [7, 10, 12]. The main measures adopted must be: (1) to increase the rotation area with non ASR host crops (corn, cotton per example), (2) to sow earlier maturity groups cultivars, concentrating sowings in the beginning of the period indicated for each region: earlier sowings usually develop under conditions less favorable to rust, (3) to avoid planting in various times and late cultivars, because soybean planted later (or of long cycle) will be more damaged by the load of spores multiplied in the first crops, (4) to sow soybean with plant density that favors good leaf aeration in order to optimize the penetration and leaf coverage by fungicides, (5) do not sow soybean in the off-season period and eliminate as much of volunteers or guaxa soybean as possible, (6) rational use of fungicides following epidemiological criteria and resistance management strategies, and (7) to sow cultivars with genetic resistance (partial resistance—slow rust) to ASR.

2. Importance of the chemical control for soybean rust

Soybean cultivation methods done by farmers increase the occurrence of biotrophic pathogen such as *P. pachyrhizi*, the chemical control of the soybean rust has been shown feasible and efficient. However, problems with correct disease management, lack of information about the biology, and pathogenesis of the disease under environmental conditions in Brazil and operational limitations of spraying in extensive cultivation areas have hampered the performance of various control programs implemented on a commercial scale [13, 14]. The chemical control of Asian soybean rust is the most widely used method for controlling the disease. Fungicide application has been shown to be an effective alternative for the producer in the management of this aggressive disease. Fungicides from chemical groups of triazoles, strobilurins, carboxamides, and, from the last three seasons, the protectants are the mostly used to control the disease, with difference in the preventive and curative efficiency between the active ingredients within each group [8, 15–18].

Under the technical, epidemic and economic point of view, the application numbers used to control rust are from two to five applications of fungicides. Over the 16 years managing soybean rust in Brazil, the fungicides management changed according to compounds' evolution and also according to soybean rust resistance to fungicides. In 2007/08 season, triazole + strobilurin mixtures dominated the fungicide application market for the control of the Asian soybean rust. In 2013 was launched the first compound with carboxamides (fluxapyroxad, solatenol, or benzovindiflupyr) fungicides in mixture. Also, with fungicides efficacy reduction, the adoption of integrated measures to control the disease will be important for the sustainability of the crop [19]. This review aims to discuss the main features of triazoles, strobilurins, carboxamides, protectants, and their mixtures, groups of systemic and protectants fungicides most important and used to control the rust, as their chemical structure, biological activity, translocation in the plant, and synergism between mixtures. In addition, some biological properties of these fungicides indispensable for the treatment of rust in adverse control situations will be discussed in this work, among them: penetration, translocation, curative effect, and absolute residual period. The control programs adopted in different Brazilian soybean regions will also be discussed, as well as the problem of decreased sensitivity of the fungus to fungicides and the risk of resistance to these products.

3. Main chemical groups of fungicide for soybean rust

3.1. Multisite fungicides

The protective fungicides are intended to ensure the protection of plants before pathogen attack. They must be applied before pathogens infect, forming a protective barrier toxic for fungi and bacteria in plants. When applied to the surface of plant organs, exert a toxic barrier preventing the penetration of fungi by inhibiting the spores germination process Syngenta

[20]. The characteristic of the contact protective fungicides as not to penetrate the plant is essential that they do not become phytotoxic to plants.

3.2. Biological properties of the multisites

Recently, after problems in efficacy with the two most used fungicides group DMI's and QoI's due to sensitivity reduction of Asian rust in soybeans, some multisite groups as copper-based, dithiocarbamates, and chloronitriles products have been tested in combination with more specific systemic products to the disease in order to improve the effectiveness and resistance management.

Fungicides copper base are contact products and are characterized by forming a toxic barrier that prevents the germination of spores on the surface of the sheet, as altered metabolism and inhibits proteinic and enzymatic action over 20 mechanisms impeding the penetration of the fungus in the tissue leaf. A low risk of resistance due to the large number of work sites in the pathogen. It is necessary to caution in the preparation and application of fungicides, because in some situations can cause phytotoxicity or burning the plants. Other care and constant hustle to keep the product in suspension evenly and avoid settling in the application tank bottom is fundamental.

Phthalonitriles (chlorothalonil) are characterized by benzene ring formed only by carbon. In cyclic structures from group lying one nitrogen atom and may also be a sulfur atom depending on the formulation and active ingredient. These fungicides are rapidly metabolized in plants, and become constituent proteins. The mode of action of the heterocyclic nitrogen is of the interference of DNA and RNA synthesis exhibits good protective action depending on the concentration used.

The dithiocarbamates fungicides mark the beginning of the use of organic fungicides. They are derivatives of carbamic acid compounds and generally have a broad action being one of the most used fungicides consumption. Dithiocarbamates were originally used in the rubber production process. The first dithiocarbamate fungicide known was patented in 1934. Since then, new generations of dithiocarbamates base metal salts (ferbam) showed good control levels in diseases in ornamentals. This group is currently performing as a very important tool in resistance management in various pathosystems. The dithiocarbamates act primarily through inhibition of enzymes of the power production cycle of the pathogen cells, and makes them unavailable for the body of metal ions such as copper and iron.

3.3. Fungitoxicity

The protectant fungicides cupric copper base are widely used for the control of downy mildew, rusts, blights, and bacterial spots and other diseases caused by pathogenic fungi and bacteria. In crops such as tomatoes and peppers, use is often seen as the protection profile of these products and illnesses caused by bacteria in these cultures.

Dithiocarbamates fungicides group had good acceptance due to the lower level of phytotoxicity in comparison to copper fungicides and sulfur. In the early 1960s, EBDC (manganese ethylene bisdithiocarbamate) fungicides were considered the most important and versatile group of organic fungicides. The mancozeb, for example, is used in more than 70 cultures, 120 countries, and many pathosystems. Main multisites under development and registered for soybean rust as the protectants research and use in Brazil to control soybean rust is quite new, the number of registered is small (mancozeb, mancozeb + azoxystrobin, chlorothalonil + tebuconazole and copper oxyclhoride). But regarding the field trial tests by antirust consortium diverse mixtures with protectants and systemic compounds are under development as important soybean diseases management tool.

4. Demethylation inhibitors fungicides

According to FRAC (Fungicide Resistance Action Committee) [21] International, the group of sterol biosynthesis inhibitors, based on the mechanism of action of compounds, includes four classes of fungicides, but only three of them, G1, G2, and G3 are used as fungicides in agriculture: DMIs, amines (formerly called morpholine), and hydroxyanilides. The compounds that inhibit the ergosterol biosynthesis are very effective as agents to control plant diseases. They are systemic and have protective, curative, and eradicative properties [22, 23]. The first class shows inhibitors of the demethylation of C14 from the sterol synthesis. DMI fungicides are also known as sterol biosynthesis inhibitors reaction (SBIs). They are commonly known as pyrimidines, pyridines, piperazines, imidazoles, triazoles, and conazoles, and these extremely effective and versatile compounds were responsible for the emergence of the world's largest market of agricultural fungicides, especially for cereal crops. They are found within this group of fungicides with broad and restricted spectrum of action, high systemicity, high fungitoxicity, selectivity, chemically stable, and with long residual effect. The second class of DMIs is composed of amines (current name for morpholine), compounds that inhibit Δ8-Δ7 isomerase and Δ14 reductase in sensitive fungi. The third class consists of hydroxyanilides, compounds that inhibit C3 keto-reductase.

4.1. Triazole fungicides

Triazoles are versatile organic fungicides of broad spectrum, with apoplastic preferential systemicity, eradicative/curative action and long residual effect. Chemically, they are formed by the addition of different radicals to a basic molecule of 1,2,4-triazole. They are classified as (a) triazoles with keto: triadimefon radicals; (b) triazole with ketal: propiconazole radicals and etaconazole; (c) triazoles with hydroxy: triadimenol radicals, bitertanol, and dichlobutrazole; (d) triazoles without other functional groups: fluotrimazol [23].

According to Hewitt [22] and Azevedo [16], the importance and use of fungicides in agriculture has increased rapidly in recent years due to the combination of a series of biological qualities, among them: high fungitoxicity to several pathogens that cause major diseases such as rusts, powdery mildew, and leaf spots, especially in cereals, quick penetration and translocation in plant tissues with uniform distribution; eradicative/curative action on infections already begun, being used based on preestablished control levels, avoiding costs with preventive applications, often unnecessary and with prolonged residual effect, enabling the use of lower doses and/or longer intervals between applications, thereby reducing the number of sprays.

4.2. Biological properties of triazoles

4.2.1. Fungitoxicity

The fungitoxicity of some triazoles such as tebuconazole, frutriafol, and cyproconazole has been one of the main safety reasons of these compounds in the control of the Asian soybean rust. The curative and eradicative action of the products on the structures of this destructive fungus has allowed success in the control and protection of the culture, even in field curative situations.

4.2.2. Systemicity

Soybean rust has caused, among other things, a real movement in the research field, development, and registration of agrochemical companies. Several works have been conducted not only in research and development of new products, but mainly in the pursuit of effectiveness of products in more appropriate dosages, in the timing of application and in the phenological stadiums more favorable to applications [16].

One of the first works to demonstrate the difference in translocation of recommended fungicides to control soybean rust was conducted by Fundação MT, in the person of Dr. Arlindo Harada. The study was conducted with cultivar BR 154, the fungicides applied were in 06/23/03 and the assessment on 07/15/03. The crop was at phonological stadium from R2 to R3. The systemicity of different triazole fungicides and their mixtures was evaluated when applied in different regions of the leaf (center, base, apex, and petiole). The results showed a better systemic effect of flutriafol, followed by tebuconazole and epoxiconazole + pyraclostrobin mixture [24].

The systemicity for specific fungicides (strobilurin and triazole) to control soybean rust has been demonstrated in an experiment conducted under controlled conditions. Analyzing the behavior of strobilurins, it could be observed that azoxystrobin has a mild redistribution throughout the leaf, moving through the xylem, following the transpiration stream, thus proving its systemic effect. Pyraclostrobin is only visible in nervures and at low concentrations; not spreading to the rest of the leaf, showing no significant systemic effect [25]. Cyproconazole presents a fast movement at high concentrations throughout the leaf, shortly in the first days after treatment, moving through the xylem, following the transpiration stream, demonstrating its systemic effect; epoxiconazole has a slower translocation, with initially high concentration in the nervures, which will be diluted to the rest of the leaf over time.

The easiness through which fungicides penetrate and translocate within the plant is due in part to its physicochemical properties. This easiness can be measured based on the ability of the fungicide to distribute between alcohol (octanol) and water when applied to form a mixture of two substances. It is the so-called partition coefficient or log P value. All systemic fungicides with log P value of 3.2 or less move fast in the plant. Systemic fungicides with values greater than 3.2 do not move very fast, although they enter the plant [24]. The

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octanol-water partition coefficient (K ow) or Log P has been used as a parameter to measure the translocation rate or the systemicity of systemic fungicides, when applied to plants [26] (**Table 2**). It has been accepted that compounds with lower Log P values are faster and will control the disease with higher efficiency. In the specific case of soybean rust, with frequent use of triazoles alone or in mixtures with strobilurin, fungicides that have lower Log P values such as flutriafol and cyproconazole (**Table 2** and **Figure 1**) translocate faster in soybean leaves and the advantage is only when these products are curatively applied in the fungus postinfection phase. When applied preventively and according to the phenological stadium more favorable to rust, this advantage disappears. Another factor that influences the systemicity use of systemic fungicides is their solubility in water expressed in ppm [16, 26].

Active ingredient	Log P or Ko/w
Flutriafol	2.3
Cyproconazole	2.9
Tetraconazole	3.1
Triadimenol	3.3
Epoxiconazole	3.4
Tebuconazole	3.7
Propiconazole	3.7
Hexaconazole	3.9
Difenoconazole	4.3

Table 2. Log *P* values or Kow of different triazoles, some of them used for soybean rust.

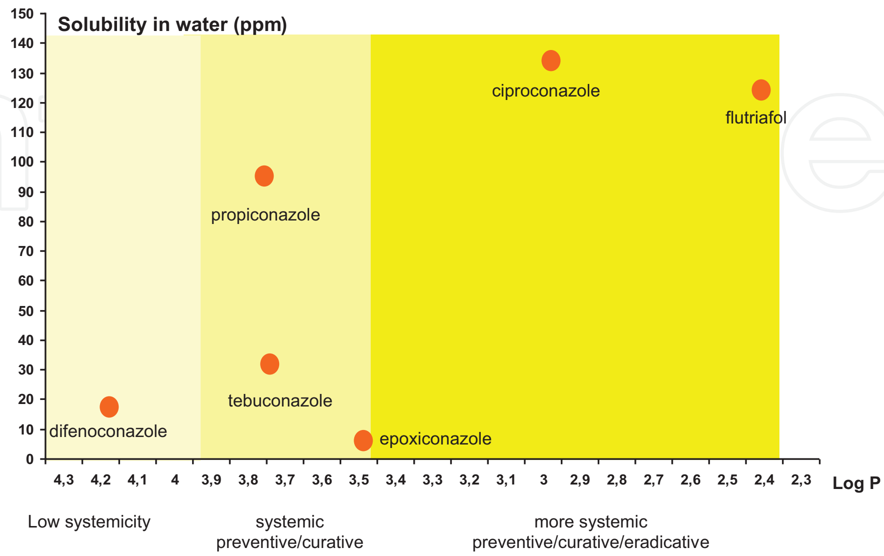

Figure 1. Solubility and Log P values of different triazoles.

4.3. Main triazoles registered for Asian soybean rust

The main triazoles registered in Brazil to control soybean rust are cyproconazole, difenoconazole, epoxiconazole, fluquinconazole, flutriafol, tebuconazole, tetraconazole, metconazole, and prothioconazole. There are some triazoles + triazole mixture registered propiconazole + cyproconazole, cyproconazole + difenoconazole. The main of triazoles and strobilurin mixtures registered for the control of soybean rust are: azoxystrobin + cyproconazole, azoxystrobin + tebuconazole, azoxystrobin+flutriafol, epoxiconazole + pyraclostrobin, trifloxystrobin + cyproconazole, trifloxystrobin + prothioconazole, trifloxystrobin + tebuconazole, picoxystrobin + cyproconazole, and picoxystrobin + tebuconazole. As main triazoles and benzimidazoles mixtures to control soybean rust are: methyl-thiofanate + flutriafol, epoxiconazole + methyl-thiofanate, carbendazim + flutriafol and tebuconazole + carbendazim. In 2016 was launched the first triple ready mix with triazole + carboxamide and strubilurin.

5. Strobilurin fungicides: fungicides inhibitors of fungal mitochondrial respiration (QoI)

Fungicides known as QoIs (quinoline outside inhibitors) are broad-spectrum fungicides and include three families of strobilurin fungicides and two other represented by compounds fenamidone and famoxadone [27]. The mechanism of action of strobilurins occurs through inhibition of the mitochondrial respiration, which blocks the electron transfer between cytochrome b and c_1 at the Qo site, interfering with the ATP production. Strobilurins are referred to as "QoI" or Group II fungicides, which is simply a reference to their unique mode of action [16].

According to Hewitt [22] one of the most significant advances in the discovery of fungicides was the introduction of synthetic analogues of strobilurin A, a compound produced by *Strobilurus tenacellus* basidiomycete. It is a successful and recent example of the use of natural products as a model of discovery and development of new systemic fungicides. In 1969, it was discovered that culture extracts of the *Oudemansiella mucida* basidiomycete fungus that grows on decomposing wood, had antifungal activity, or were capable of killing fungus. In the decade of the 1970s, several compounds of the extract of this fungus were isolated, including the one responsible for the antifungal activity, mucidicin. This discovery led other researchers to investigate the chemical composition of various basidiomycete fungi, and in 1978, a compound with fungicidal properties called strobilurin was isolated from *Strobilorus tenacellus*. The studies showed that the compound initially called mucidicin had the same structure of strobilurin. In view of the good results so far found, around 20 species of basidiomycetes were studied, and this resulted in the synthesis of a large number of new compounds with fungicide activity. These compounds, although different, had some similarity from the chemical point of view, i.e., the presence of the structural unit derived from the B-metoxy acrylic acid [25, 28].

5.1. Fungitoxicity and field uses

The fungitoxicity of strobilurins has been one of the reasons for using these compounds in programs aimed to control diseases in plants. In the specific case of soybean rust, these fungicides have been widely used in mixtures with triazoles. The use of simple formulations for this disease is unusual, although there are registered products [9, 29]. From the Products tested and registered for soybean rust, pure, or in mixtures with triazoles, it could be observed that the dosages of these compounds range from 0.20 to 0.5 L of cyproconazole (**Table 3**).

5.2. Systemicity

In a study by Embrapa [2] the azoxystrobin + cyproconazole and pyraclostrobin + epoxiconazole systemicity was compared in soybean leaves. Fungicides were brushed on the basis of leaf area (at concentrations recommended for use in the field), which were inoculated with rust (*P.pachyrhizi*) in the next day and incubated in greenhouse. After 16 days, the percentage of area above the point of application on which products controlled the disease was assessed. Azoxystrobin + cyproconazole fully controlled the disease throughout the extension of leaves, while the pyraclostrobin + epoxiconazole did not, showing that the faster translocation of azoxystrobin + cyproconazole reflects in better control (inoculation 1 day after the application of fungicides).

The translocation of strobilurins certainly is not one of the most important features of this chemical group of fungicides. The fungitoxicity, the action spectrum and the effective residual period are peculiar characteristics of this group of products, but there are differences in the translocation of these compounds when applied to control soybean rust (**Table 4**) [16].

The main strobilurins registered in Brazil to control soybean rust are: azoxystrobin, pyraclostrobin, trifloxystrobin, and picoxystrobin.

Active ingredient	Commercial product name	Dose L or kg cp*.ha^{-1}
Azoxystrobin	Priori	0.20
Picoxystrobin	Aproach	0.20
Cyproconazole + azoxystrobin	Priori Xtra	0.30
Cyproconazole+trifloxystrobin	SphereMax	0.30
Epoxyconazole+pyraclostrobin	Opera	0.5
Propiconazole+trifloxystrobin	Stratego	0.4
Tebuconazole+ trifloxystrobin	Nativo	0.5
Prothioconazole+ trifloxystrobin	Fox	0.4
Azoxystrobin+benzovindiflupyr	Elatus	0.2
Fluxapyroxad+piraclostrobin	Orkestra	0.35
Piraclostrobin+epoxiconazole+fluxa pyroxad	Ativum	0.8

*Commercial product.

Table 3. Fungicides from the strobilurin group, pure or in mixtures and their respective doses for the control of soybean rust (*P. pachyrhizi*).

Active ingredient	Log P or Ko/w
Azoxystrobin	2.5
Kresoxim-methyl	3.4
Pyraclostrobin	4.0
Trifloxystrobin	4.5

Table 4. Translocation rate of different strobilurins used to control soybean rust.

6. Fungicides inhibitors of succinate dehydrogenase (SDHIs)

Fungicides known as SDHIs include eight different chemical groups of carboxamides represented by phenyl-benzamides, phenyl-oxo-ethyl thiofene amide, pyridinyl-ethyl-benzamide, furan-carboxamides, oxathiin-carboxamides, thiazole-carboxamides, pyrazol-carboxamides, and pyridine-carboxamides. The mechanism of action of carboxamides occurs on the target enzyme succinate dehydrogenase (SDH, so-called complex II in the mitochondrial respiration chain), which is a functional part of the tricarboxylic cycle and linked to the mitochondrial electron transport chain. SDH consists of four subunits (A–D) and the binding site of the SDHIs (the ubiquinone binding site) is formed by the subunits B–D. Carboxamides are broad-spectrum fungicides that inhibit fungal cell respiration, which prevents energy production and leads to rapid cell death. While it may not be critical to know how carboxamides work, it is important to recognize the SDHI designation and be aware that all carboxamides have the same mode of action. The new broad-spectrum fungicides class has been quickly adopted by the market, which may lead to a high selection pressure on various pathogens. All of the 17 marketed SDHI fungicides bind to the same ubiquinone-binding site of the SDH enzyme. Their primary biochemical mode of action is the blockage of the TCA cycle at the level of succinate to fumarate oxidation, leading to an inhibition of respiration.

The Fungicide Resistance Action Committee has developed resistance management recommendations for pathogens of different crops in order to reduce the risk for resistance development to this class of fungicides. These recommendations include preventative usage, mixture with partner fungicides active against the current pathogen population, alternation in the mode of action of products used in a spray program, and limitations in the total number of applications per season or per crop [30].

6.1. Biological properties of SDHI fungicides

SDHI fungicides were discovered more than 40 years ago. Due to the limited disease and application spectrum of the "first generation" carboxamides, resistance under commercial conditions remained limited to a few crop/pathosystems (primarily Basidiomycetes), e.g., *Puccinia horiana*, chrysanthemum rust, and Ustilago nuda, loose smut in barley. In addition to these "first generation" molecules, SDHIs with increased spectrum and potency were launched starting in 2003 and new ones continue to be launched today. This modern generation of SDHIs is rapidly achieving market share in many crops and new SDHIs are currently in development. They are classified by FRAC (Fungicide Resistance Action Committee) activity group code number 7 [21].

The market adaptation to the new technology and its penetration has been to be very fast around the world and it was not different for soybean rust control in Brazil. The reason for the rapid adoption of SDHIs is their high level of activity and the lack of effective alternative control options. Many soybean pathogens have developed resistance to the QoI's, and reduced sensitivity to the demethylation inhibitor (DMI) fungicides, which generates increased challenges for the farmers to efficiently control diseases and maintain or increase crop yield and quality. The class of compounds inhibiting complex II of fungal respiration was originally called carboxamide fungicides, with the earliest compound in this class, carboxin, being first marketed in 1966. This narrow-spectrum fungicide was used mainly as a seed treatment to control basidiomycete pathogens such as smuts. Thereafter, benodanil, fenfuram, mepronil, flutolanil, furametpyr, and thifluzamide followed between 1971 and 1997; however, these compounds gave only slightly broader-spectrum control compared with carboxin. The first carboxamide with truly broad-spectrum foliar activity was boscalid, launched in 2003. FRAC is currently listing 19 SDHI compounds (benodanil, benzovindiflupyr, bixafen, boscalid, carboxin, fenfuram, fluopyram, flutolanil, fluxapyroxad, furametpyr, isofetamida, isopyrazam, mepronil, oxycarboxin, penflufen, penthiopyrad, pydiflumetofen, sedaxane, and thifluzamide), belonging to different chemical types. Currently the "overall" spectrum of SDHI fungicides is extremely broad, being comparable with the QoI spectrum, with the exception of oomycete activity, which is still lacking. Adepidyn™ (pydiflumetofen) is the first member of a new chemical group among the succinate dehydrogenase inhibitor fungicides (SDHI, FRAC Group 7), the N-methoxy-(phenyl-ethyl)-pyrazole-carboxamides. The common name for Adepidyn™ is pydiflumetofen. Adepidyn™ has a wide range of plant pathogen species.

6.1.1. Fungitoxicity

The fungitoxicity of carboxamides has been one of the reasons for using these compounds in programs aimed to control diseases in plants. Generation II SDHIs are intended for use in integrated disease management programs, or as mixing or alternation partners to prevent fungicide resistance. Fungicides from this class are effective against various diseases of cereals, fruits, and vegetables. In the specific case of soybean rust, these fungicides have been firstly used in mixtures with QoIs. Due to the detection of F129L resistance to QoIs in 2013/14 season (officially informed by FRAC), the fungicides research against soybean rust advanced for another mixture partners. In 2016 were launched epoxiconazole, pyraclostrobin, and fluxapyroxade, fungicide triple mixture containing in ready mixture to offer in Brazilian Market.

6.1.2. Systemicity

SDHI fungicides are derived from a diverse range of chemistry and, depending on the host and pathogen, have protectant, translaminar, or systemic activity.

7. Residual period of fungicides for soybean rust

According to Balardin et al. [4] and Azevedo [31], the effective residual period of a fungicide is beyond the intrinsic features that the active ingredient presents under experimental conditions may vary depending on the relationship between its pathogenesis and the general physiological conditions of the plant. The application of fungicides after the infection onset undergoes more drastic reductions in the residual according to the population density of the pathogen at the application time.

The residual period of a fungicide, being systemic, mesostemic, or protective, is a biological property quite peculiar to the various chemical groups. According to Balardin et al. [4], it is the maintenance of the active ingredient within the plant tissues at sufficient concentration to inhibit or delay the infection caused by a pathogen. In this case, the period of time that fungicide can provide protection to the plant is considered as absolute residual, i.e., benzimidazoles have an absolute residual around 15 days, triazoles, between 22 and 25 days, and strobilurins between 27 and 30 days. Considering mixtures of fungicides from different groups, the synergistic effect may cause an absolute residual period longer than that observed for products used alone. When there is no synergism between the components of the mixture, it is expected that the residual of the mixture is the same as the product with higher residual.

Under current field conditions, there are big differences between the effective and absolute residual of some systemic fungicides. According to Balardin et al. [4] and Yorinori [6], the residual period of a particular active ingredient is only one reference, since, for all that is done from the viewpoint of a culture management and population dynamics of the pathogen, the effective residual becomes the residual actually achievable under field conditions. The effective residual period of a fungicide exceeds the intrinsic characteristics that the active ingredient presents under experimental conditions, which may vary depending on the reaction between the pathogenesis and the general physiological conditions of the plant. Overall, the effective residual period is the result of strategy and tactics established in the form of an integrated management planning and may be influenced by factors as diverse as the time of fungicide application in relation to plant development or its pathogenesis, the population density of the pathogen, age, nutrition, and various components of the plant phytotechnical management, or even the expression of minor genes associated with partial resistance.

8. Strategies of chemical control for soybean rust

The strategies of chemical control for soybean rust should be based on five main points: (1) disease monitoring, (2) phenological stages of the culture, (3) choice of the fungicide, (4) application timing, and (5) application technology [16, 29, 32].

The disease monitoring and its identification in the early stages are essential for the efficient use of the chemical control and the frequent inspection of the tillage should be carried out. The protecting of plants must occur before the appearance of the first lesions (preventive) or at the beginning when the inoculum potential is still low. The spraying should reach maximum leaf area, and fungicides with longer residual period and systemicity should be selected [4, 16, 29].

According to Azevedo [16], the spraying programs based on phenological stages can also be used for major crops such as soybeans, corn, bean, and rice. The most illustrative and practical example is the soybean culture. For diseases of the aerial parts, there is what is called the critical period of protection. This period runs from the end of the vegetative period until R6 stadium. It changes between cultivars, and a difference of 15 days between early and intermediate cycles is common. Fungicide applications should be made within this period, especially respecting the critical stage of each disease and the residual period of several products. The protection of the culture against rust will always require the observation of the phenological stadium, and stage from the beginning of flowering until full flowering is currently considered as critical period (R1 | R2) for the first spraying of fungicides [4, 5, 10].

The success of a phytosanitary treatment program for the control of several diseases primarily depends on the use of a fungicide of proven efficiency and of a technology developed for its application. The influence of uncontrollable meteorological, biological, and agronomic factors should also be considered [16, 33]. Fungicides manufactured to control soybean rust are effective. However, success will largely depend on proper application. Proper application starts with selecting the right equipment, specifically nozzles, and spraying the right amount of fungicide uniformly across the field before the disease is detected. Pesticide manufacturers have invested heavily to determine the most effective as well as economical application rate for the fungicides labeled for soybean rust.

Spraying the right amount of fungicide on each acre of soybean is not enough to achieve effective pest control. How uniformly the fungicide is deposited on the spray target is as important as the amount deposited. Each nozzle produces a unique spray pattern. Some nozzles require precise overlapping of patterns from adjacent nozzles. Setting the proper boom height for a given nozzle spacing is extremely important in achieving proper overlapping. A low boom does not allow proper overlap while a boom set too high causes overdosed areas. Other situations that cause improper overlapping and poor uniformity include: clogged nozzles, misaligned nozzles spraying at different directions, and mixing nozzles with different spray angles. All these common errors contribute to nonuniform coverage.

The control of Asian soybean rust is a major concern for soybean producers in Brazil [9, 32, 34]. Considering the plant development stage at the time of applications, often with complete closure and large leaf area, it is generally agreed that the application techniques need to provide droplets with good penetration and coverage of leaves, even for fungicides with systemic action [35]. In the case of systemic fungicides for control of soybean rust, there is a false assumption that the application technology and the spraying programs are not as important as the implementation of protective products, because less coverage and amount of deposits would be needed, since they are products that penetrate and translocate on the leaf surface. However, most systemic fungicides display only partial translocation, usually from the leaf base to apex, with no translocation from lower leaves to the upper ones. This fact alone reinforces the value of application technology, which is able to make these products to penetrate into the body of plants through the use of small and medium-sized droplets [16].

Another important point concerns the timing (timing of application). Since the appearance of rust, the control with preventive applications proved to be more efficient than the curative applications. This recommendation is now considered standard [9, 16, 29] and most technical recommendations for the rust control is based on the following procedure: "giving preference to preventive applications from the flowering stadium (R1), opting for curative applications only if rust appears still in vegetative stages." Despite these recommendations, what has been observed in recent harvests was a significant number of curative applications, especially in regions where inoculum pressure was too high, as in the region of Primavera do Leste/MT, for example. These curative applications occurred due to two basic factors: (1) early beginning of rust in the crop, with the appearance of symptoms in the vegetative stadiums, and (2) inadequate applications, with errors regarding both the technique and the time of application, which compromised the control. These facts led to drastic reduction in the residual period of products, resulting in the need for a greater number of applications for the disease control.

Another reason that supports preventive applications concerns the epidemiology of the disease. Systemic fungicides, even those with curative and eradicative properties should not be curatively recommended, because in practical control situations, it is extremely difficult to determine the disease intensity threshold for which the "eradication" with systemic fungicides is effective. This fact became very evident at the time of the resurgence of the soybeans rust in Brazil, early in the first control recommendations. Triazoles have been and still are used to control this disease, many times in curative applications, out of the "biological timing," in some cases with 10–20% of rust infection, which lead to failure situations, with irreversible damage to the producer [16, 36].

Soybean rust has its greatest development after flowering, with large leaf area, so it is difficult for the fungicide to penetrate in the mass of leaves [34]. Field experiments have shown that the average coverages in the soybean canopy in the application of fungicides for rust control are: 70–90% for the upper canopy, 15–40% for the medium canopy, and 1–15% for the lower canopy [35, 37]. Leaf coverage tests conducted with sensitive paper showed that the deposition of fungicides on the inside of the leaf decreases from top to bottom of plants, whatever is the application technology and volume. This indicates subdose deposition on lower leaves, which may not affect the fungus or have a very short effect, thus allowing the rust resurgence in a few days. According to Yorinori [29], Balardin [4], and Antuniassi [32], this is the main reason for complaints about the reduction of the residual period of a fungicide that should be active for 25–30 days.

Soybean is cultivated in many regions of the country, with quite diverse weather conditions. The diversity of climatic conditions from one year to another, in different regions of Brazil, makes it impossible to formulate a package of chemical protection (cake recipe) that meets the needs of the entire country. Up to the present moment, there is no chemical protection strategy for the management of the Asian rust that meets efficiency, cost, and operability of all producing regions, but rather application programs based on researches carried out by public and private institutions, which are being improved every year, according to the rust occurrences [17, 38, 39].

A good example is the latest recommendations summarized by the Antirust consortium in Brazil, where differences between the spraying programs recommended in different soybean cultivation regions in Brazil could be observed (**Table 5**).

State	Criterion adopted	Chemical group	Average number of applications
Rio Grande do Sul	Flowering | Control Control | Calendar	Strobilurin + Triazole Strobilurin	1.5
Paraná	Flowering | Control Control | Calendar	Strobilurin + Triazole Triazole Strobilurin + Triazole	1.7
Minas Gerais	Flowering (preventive)	Strobilurin + Triazole Strobilurin + Triazole	1.6
Bahia	Flowering (preventive) Control | Calendar	Strobilurin + Triazole Strobilurin + Triazole	2.0

Table 5. Chemical fungicide group, criterion adopted by state and average number of applications summarized by the latest Antirust Consortium Londrina, 2008.

9. Efficacy of fungicides for soybean rust

Since the first fungicides recommended in emergency situations for the 2002/03 harvest (azoxystrobin, difenoconazole, fluquinconazole, epoxiconazole + pyraclostrobin and tebuconazole), a large number of new formulations have been added to the current arsenal to control rust. There are currently registered in MAPA [3, 9, 29] about 45 active ingredients (alone or in combination), trademarks, and formulations for the rational use against rust. Among fungicides, there are differences in efficacy, residual period, metabolic stability, and transportation rate, demanding from producer, researcher, and technical assistance, criteria in choosing the product to be used in each situation. Another every important point: in addition to rust, it is necessary to take into account the occurrence of other diseases such as anthracnose, late season diseases (target leaf spot, leaf blight, and powdery mildew), which may require a combination of different active ingredients.

Fungicides have greatly reduced their effectiveness when applied after the establishment of soybean rust [10, 40]. These facts hinder the implementation of a control system based on levels of disease severity. Data from this research indicate that soybean rust can only be detected by the naked eye from a severity level of 5%, which is very high and risky to start the chemical control. Results obtained by Andrade and Andrade [41], in the chemical control of rust, showed that a delay of seven days in the fungicide application (after detection of the disease), is already enough for an increase in defoliation of 82%, when compared to fungicide treatment performed when the disease appears. When the delay in the beginning of spraying was by 14 days, defoliation increased by 155%.

Juliatti et al. [42] studied the efficacy of fungicides to control Asian soybean rust and found proven efficiency of the strobilurine + triazoles mixture, even after 10% of leaf area infected with rust.

Godoy et al. [12] tested the protective, curative, and eradicative effects of azoxystrobin, carbendazim, tebuconazole, difenoconazole and epoxiconazole + pyraclostrobin fungicides in the control of Asian soybean rust in greenhouses. Except for carbendazim, all fungicides had a protective effect with control over 90%, up to 8 days after treatment. No product showed eradicative effect when applied during the incubation period of the disease; however, all treatments reduced disease severity and the viability of urediniospores. Azevedo [8] tested in greenhouse conditions, different fungicides from chemical groups of triazole and strobilurin, preventively, and curatively applied to control rust. The best results were obtained with flutriafol, azoxystrobin + cyproconazole, tebuconazole and pyraclostrobin + epoxiconazole preventively applied. When curatively applied, the best results were with tebuconazole and flutriafol.

According to Godoy [9] the use of fungicides has been intensified in soybean crops due to the resurgence of rust and lack of resistant varieties, therefore, the information on the efficiency of fungicides for the control of various diseases are increasingly required to guide their proper use in the field. The various tests for the disease control in soybeans emerged during the XXV Soybean Research Meeting of the Central Region of Brazil, held in 2003, in Uberaba-MG (Minas Gerais State from Brazil), whose objective was to provide research results that could be used throughout the country to help the technical assistance in choosing the correct fungicide for the control of different diseases that affect the culture. The tests were not intended to evaluate the timing of application and the residual of different products, but rather to compare the efficacy of products in the same situation. Trials comparing different registered products, and those in registration phase, are performed by public and private research institutions, foundations, universities and cooperatives [39]. In studies to assess the efficacy of products carried out in 2002/03 and 2003/04 harvest by the official tests network, a different behavior of fungicides was observed as for their efficacy to control Asian rust in different regions of soybean cultivation. As for fungicides recommended in XXV and XXVI Soybean Research Meeting of the Central Region of Brazil, held in Uberaba, Minas Gerais, and Ribeirão Preto, SP (São Paulo State from Brazil), respectively, the best results were obtained by the products from the chemical groups triazole and strobilurin [2, 36]. On average, there are currently two sprayings with pure fungicide (triazoles) or mixed (triazoles + strobilurins) to control the disease [9, 12, 43–45].

During the 2006/2007 harvest, experiments were conducted to evaluate the efficiency of products registered and of those under registration phase for the control of soybean rust. In function of the number of products, treatments were divided into two tests, according to the group of fungicides, including a list of triazoles and strobilurins, mixtures of triazoles with strobilurins and mixtures of triazoles with benzimidazoles in another list. The results obtained in different regions of the country have confirmed the efficacy of mixtures of triazoles with strobilurins as the most effective fungicides for the control of soybean rust [9].

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10. The risk of resistance of *Phakopsora pachyrhizi* to fungicides

Resistance is a stable and heritable change in a fungal population in response to the application of a fungicide, resulting in a reduction of sensitivity to the product [46]. With the introduction of systemic fungicides with specific mechanism of action, the problem worsened and since then, several plant pathogens of economically important crops have shown resistance to a variety of groups of fungicides. The inherent risk of resistance depends on several factors that may be associated with the product (persistence in the plant, mechanism of action, monogenic resistance, among others) and with the target (life cycle, genetic variability, mutation potential, existence of cross-resistance, adaptability or fitness, among others). These factors do not necessarily operate alone and do not apply in all cases. The agronomic risks should also be considered, i.e., crops over large areas with short rotation, monoculture, use of transgenic plants with genes expressing pesticide activity, geographic isolation of populations, and high population densities.

The resistance mechanisms may vary, but involve mainly changes in the primary site of action of the fungicide on the plant pathogen. According to FRAC International, the group of sterol biosynthesis inhibitors comprises four classes of fungicides, but only three of them, G1, G2, and G3 are used as fungicides in agriculture: DMI's, amines (formerly called morpholines), and hydroxyanils. They all act in fungi by inhibiting the sterol biosynthesis, but differ with respect to the target site. Fungicides called triazoles belong to the group of products that act by interrupting the functions of the cell membrane of fungi. They act by inhibiting the sterol biosynthesis, more specifically, ergosterol, which is an important substance for maintaining the integrity of the cell membrane of fungi [22]. Sterol biosynthesis inhibitors (SBIs) are divided into two distinct groups: C14-demethylation inhibitors (DMIs), of which main representatives are triazoles, and inhibitors of enzymes A-isomerase and A-reductase represented by morpholine fungicides. In the case of DMIs, the resistance mechanisms are not yet fully understood. Mutations in the CYP51 site have been identified in plant pathogens of cereals and related to loss of sensitivity to triazoles [47]. Regarding the likelihood of resistance emergence, in general, they are classified as with intermediate risk.

Fungicides known as QoIs (Quinone outside inhibitor) include three families of fungicides: strobilurin and two others represented by fenamidone and famoxadone. These fungicides act on the inhibition of mitochondrial respiration. The mechanism of action of strobilurins occurs through inhibition of mitochondrial respiration, which blocks the electron transfer between cytochrome b and c_1 (cytochrome 1), at the Qo (Quinone oxydase) site, interfering with the production of ATP. In most cases, resistance is conferred by a single mutation point in the cyt (cytochrome) gene, leading to a change in position 143 of the amino acid from glycine to alanine (G143A). There are species such as *Pythium aphanidermatum* (Edson) Fitzp and *Pyricularia grisea* Sacc, in which the change is from phenylalanine to leucine at position 129 F129L, also conferring resistance to QoIs, but to a lesser degree than G143A [48, 49]. The resistance of *Blumeria graminis* in wheat and barley to fungicides from the QoIs group (strobilurins, famoxadone and fenamidone) is related to mutation at a specific point, namely the replacement of glycine by alanine at position 143 of cytochrome b [50]. Several mutations in mitochondrial cytochrome b have been reported, however, only two-G143A and F129L have occurred in field populations, and mutation G143 is the main responsibility for failures in disease control. This group, according to Brent and Hollomon [51], presents a high risk of resistance.

Worldwide, there are no reports of resistance of fungi that cause rust to triazoles and strobilurins, but populations or races with different requirements regarding the same fungicide (more or less sensitive) [52].

According to the model proposed by Brent and Hollomon [51], the risk of appearance of resistant of fungi that cause rust in general to the group of strobilurins is low, and is even lower for the group of triazoles. Due to this, the sensitivity monitoring is only recommended in cases where there are suspicions. Based on genetic information, rusts such as *Puccinia spp., Uromyces appendiculatus, P. pachyrhizi, Hemileia vastatrix* cannot acquire resistance to the group of QoIs based on mutation in the cyt b gene-position G143A due to specific genetic structure that does not allow the mutation directly after position 143. These fungi are therefore considered of low risk for the development of resistance [27].

The fungicides most widely used for the chemical management of soybean rust are strobilurins and triazoles, both with specific site inhibitors. In this case, the occurrence of mutation in the target site of the plant pathogen may lead to high levels of resistance (higher gene resistance), with consequent loss of agronomic efficiency of products [53]. The risk of emerging resistant populations of *P. pachyrhizi* to fungicides currently in use exists; however, the results obtained in monitoring the sensitivity of the pathogen populations that have been carried out by two pesticides manufacturers show that there is no resistance in *P.pachyrhizi* populations to tebuconazole, azoxystrobin, and cyproconazole [27, 52].

Since the 2005/2006 harvest, the companies Syngenta Crop Protection and Bayer CropScience have conducted surveys to monitor the sensitivity of *P. pachyrhizi* populations. The method used to quantify the fungus sensitivity and the definition of different population profiles is a bio-assay in detached soybean leaves (detached leaf test), through which the effective fungicide concentration to control 50% of the population (EC50) is determined in values expressed in parts per million (ppm) [54].

According to Singer et al. [52], for tebuconazole in the 2005/2006 harvest, the lowest EC50 value obtained was 0.016 ppm, and the highest was 0.52 ppm. These values are considered extremely low, since the dose practiced in field is 500 ppm. Moreover, the set of results showed that there were no differences in sensitivity of the pathogen among the various producing regions of the country. Therefore, it could be concluded that the predominant populations of the fungus this season proved to be very sensitive to triazole.

In the 2006/2007 harvest, the lowest EC50 value obtained for tebuconazole was 0.08 ppm, and the highest was 1.85 ppm. Only three sites showed higher values, namely 1.3, 1.74, and 1.85 ppm. The set of results showed a marked predominance of populations very sensitive to tebuconazole; however, the few higher values found can already mean the occurrence of populations with different sensitivity to the fungicide.

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In the last harvest (2007/2008), which represents the third year of monitoring, the lowest EC50 value obtained for tebuconazole was 0.04 ppm, i.e., similar to values of the last 2 years. Values between 1.04 and 1.8 ppm were also observed, which represented the highest for the previous crop and now are considered as average values.

According to Singer et al. [52] and based on existing information, in monitoring systems and also considering the baseline values for other fungi such as the pathogen that causes wheat leaf rust (*Puccinia triticina*), it could be concluded that from the results obtained in the last three harvests, the standard values for populations more or less sensitive to *P. pachyrhizi* have already been established. In this context, values between 0.01 and 10 ppm could be acceptable, and values between 0.01 and 1.0 ppm refer to very sensitive populations, values from 1.0 to 2.0 ppm characterize populations of intermediate sensitivity, and from 2.0 to 10 ppm, represent the less sensitive.

According to Buzzerio [27], following the recommendations of the FRAC International and also FRAC Brazil, the company Syngenta Crop Protection monitors *P.pachyrhizi* populations for active ingredients azoxystrobin and cyproconazole using *in vitro* and *in vivo* sensitivity bioassay methods. According to results obtained in the 2005–06 harvest for active ingredient azoxystrobin (*in vitro* method) the estimated lethal concentration (CL) 90 was between 0.0103 and 0.4945 ppm. In the 2006–07 harvest, the estimates were between 0.0861 and 0.5065 ppm for the same product. For active ingredient cyproconazole (*in vivo* method) the estimated CL 90 was between 0.0934 and 0.5007 ppm. According to results obtained and taking into account that the recommended dose of azoxystrobin is 300 ppm and cyproconazole is 120 ppm, when used in combination, it could be concluded that for both active ingredients, there is no change in sensitivity of the fungus that causes rust. The variation between estimates can be considered within the natural range of populations.

Soybean rust arrived in Brazil in 2001, and severe epidemics outbreaks resulted in heavy applications of triazoles alone. This led to warnings by concerned chemical companies and scientists of the risks of soybean rust fungicide resistance developing against the triazoles. Sure enough, in the first quarter of 2008, a lower than expected efficacy of triazoles was observed in Mato Grosso and Mato Grosso do Sul states. However, no sensitivity change was detected in the triazole-strobilurin mixtures which continued to perform very well.

According to Godoy et al. [19], this efficiency reduction of triazoles is mainly due to overexposure of soybean rust to triazole fungicides used by themselves. Tebuconazole is cheap in Brazil and is sold in competition with a number of generic brands. Many farmers in the Mato Grosso used up to four applications of tebuconazole per season, despite the FRAC recommendation of only two applications per season. Although tebuconazole is a recommended fungicide, its single site mode of action makes it vulnerable to resistance. The use of a strobilurin-triazole mixture is a major strategy to manage resistance, promoted by the agrochemical industry, for reducing risk of resistance towards both fungicide groups. These two active ingredients are complimentary in their action because strobilurins inhibit fungal respiration and consequently inhibit spore germination, whereas triazoles inhibit germ tube elongation, fungal penetration, and mycelial growth.

11. Antiresistance strategies for fungicides in soybean

Just like its use in the field, the antiresistance strategies for fungicides should always be applied in a preventive way [16]. The most safe and ideal situation would be the use of an antiresistance strategy before the occurrence of the problem, because once the pathogen population has become resistant, the only control possibility would be the application of another fungicide with a different mechanism of action, or a nonchemical control method. This keeps happening most of the times in the field. It is the fungicide syndrome. This no longer works; let us switch to another. The resistance problem has become so serious that the agrochemical companies have considered the problem from the screening of new molecules, with the information on the risk of the group to which the product belongs as criterion [55]. The way it is launched to market, including registration and usage recommendations, and monitoring of the product are also designed following antiresistance strategies and have greatly contributed to the decrease of the resistance problems in Brazil.

The availability of a large number of commercial products for the control of soybean rust does not necessarily mean the existence of several chemical groups. The main fungicides registered are restricted to only two groups of active ingredients: strobilurins and triazoles. This fact is reason of concern due to the possibility of the fungus to develop mutants resistant to these chemical groups [16, 29, 38, 53]. The chemical control strategies are based almost exclusively on the use of these products. Therefore, the vulnerability exists and the antiresistance strategies should be increasingly implemented.

Management strategies: use of fungicides in mixtures rather than products used alone, restriction on the number of treatments applied per harvest, use of the dose recommended by the manufacturer, use of integrated disease management, avoid eradicative use, and increased chemical diversity through the use of other fungicides in subsequent treatments should be implemented to minimize or even avoid the problems of fungicide resistance.

The development or evolution of resistance can be minimized through antiresistance strategies [21]. The following antiresistance strategies are mentioned: minimize the use of fungicides and particularly repeated applications of fungicides from the same chemical group; restrict the number of fungicide applications per season and chemical group, and apply only whenever needed, implement the use of rotation of fungicides from different chemical groups or the use of ready formulations or tank mixtures always following the manufacturer's recommendations, always use fungicides at doses recommended by the manufacturer, use of integrated disease management such as to eliminate the primary sources of inoculum, use of resistant varieties, crop rotation, sanitation of tools, etc., and baseline studies and sensitivity monitoring. Monitoring methods have been described in various publications [56–58]. In an attempt to standardize the testing internationally, FAO and FRAC [40, 59] show in details the recommended methods for the major groups of fungicides. In Brazil, almost all companies that produce and market fungicides make the monitoring of fungal populations, while introducing some new molecule or existing products.

These strategies are general. However, in the case of soybean rust, treatment programs that address the rotation of active ingredients is a basic foundation for the sustainability

http://dx.doi.org/10.5772/67454

of the system and an official recommendation from the FRAC. Furthermore, it should be complemented by other measures such as preventive control of diseases, use of the correct dosage specified by the manufacturer, to follow the sanitary standards, and adoption of good agricultural practices. Recently in Brazil we are using multisite fungicides to soybean rust control using copper compounds and dithiocarbamates, ex. Mancozeb to control in vegetative stages mixed triazoles and strobilurins because after 2013 the fungi resistance increased in Brazil's fields after the massive use of triazoles and strobilurins and curative uses.

12. Conclusions

Plant diseases reduce production and decrease the quality of agricultural products, requiring more and more practical and effective strategic chemical programs of phytosanitary control and treatment. When these treatments are not applied correctly, the agricultural production may suffer losses and damages ranging from negligible percentages up to a total loss, depending on the virulence potential of the pathogens involved, environment, and crop resistance against them. The influence of humans should also be stressed, which has been great in the technological management of cultures that occupy large areas and require the observation of details in choosing the adequate spraying program of products.

In cases of diseases that occur as epidemics caused by exotic or resurgent pathogens as is the case of *P. pachyrhizi*, the first control alternative always used has been the use of fungicides, especially those with systemic and curative activity. At first glance, chemical control has provided satisfactory results; however, there is need for its integration with other control methods. In the case of epidemics, the alternative is the resistant cultivars adoption or at least those with some level of tolerance. Another important point is the registration of products from different mode of action from those available in the market. This is an urgent need, given that the *P. pachyrhizi* populations are changing the sensitivity to key triazole used in their control. Finally, the importance of developing new technologies for application of fungicides or the refinement of existing techniques for the application of products in large areas of cultivation should also be stressed. Undoubtedly, the need to control soybean rust in curative situations in large areas of cultivation and in adverse climate conditions triggered a series of studies and research studies in the sector, so far unprecedented in the current agricultural environment. Many field results have proven the effectiveness of terrestrial and air applications, techniques such as LOV (low oil volume); however, further advances are still needed in this field of study, with the development of field techniques that allow the placement of the product at the bottom of the soybean crop. The higher risk of developing resistance or loss of sensitivity of the fungus in Brazil to carboxamides group of fungicides associated with strobilurin would be no use of multiple site fungicides in the field's crops. In these conditions the evolution of resistance or sensitivity loss will be fast.

Studies on soybean rust in Brazil are still very recent and insufficient There is still lack of information on fungus biology, epidemiology, variability, and host conditions on weeds that remain between seasons together with soybean, in addition to the offer of some cultivars with high resistance potential, and even the correlation of varieties with different responses regarding the efficacy of fungicides, data sowing, and application times. **Figure 2** shows the main points of action of fungicides in the life cycle of the Asian soybean rust (ASR) (black arrow). The definition of data sowing per state and sanitary rules they are the most important strategy of ASR in Brazil joint combination of systemic and multisite fungicides uses and genotypes with partial resistance. The future shows the combination of this kind of strategy after the carboxamides fungicides (mutation in ASR) resistance discovered by FRACC in 2017.

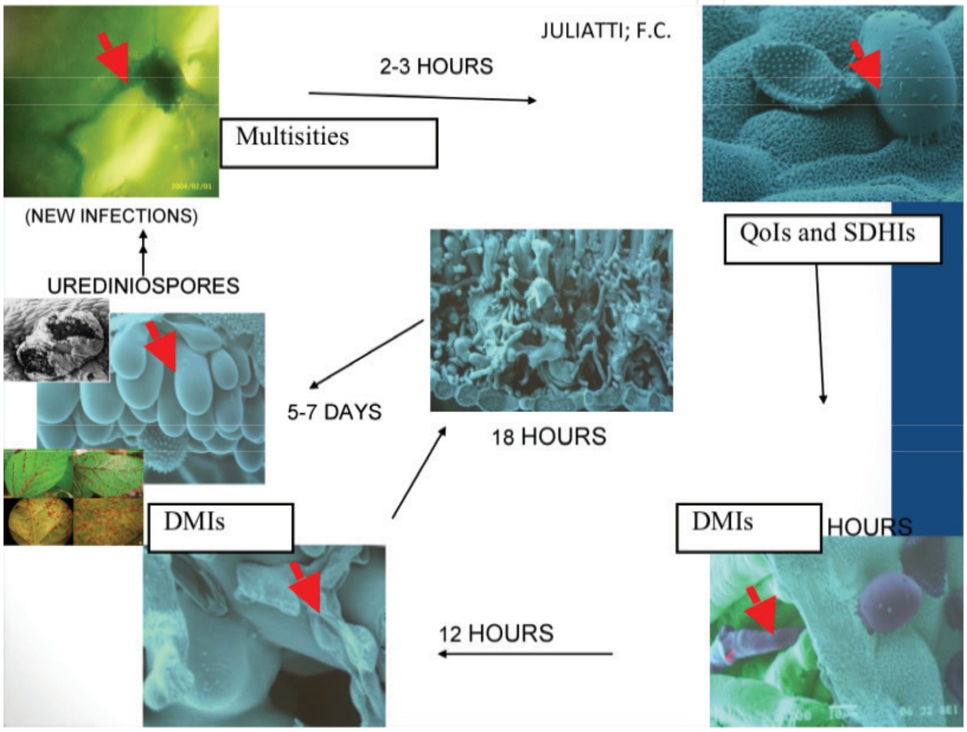

Figure 2. Asian soybean rust (*Phakopsora pachyrhizi*) lifecycle and main fungicide chemical groups used to control rust action.

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