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Biological Control of Tomato Phytopathogens as an Alternative to Agricultural Defensives and Antibiotics

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Abstract: The tomato (*Solanum lycopersicum* L.) is one of the most cultivated vegetable in the world. China represents about 25 % of all world production, so there is a dependence and constant use of agricultural defensives in tomato crops. The application of chemical products banned in many parts of the world has as a side effect a major impact on human health and the ecosystem, therefore necessary to adopt other disease prevention strategies. Another method of combating tomato disease is the use of microorganisms as a form of biological control, which is considered an alternative to agricultural defensives and antibiotics offering better sustainability and less toxicity. In this work, the agricultural defensives most used by producers were, Pyraclostrobin, Mancozebe, Copper oxychloride, and derivatives of DDT. For the antibiotics, Streptomycin and Oxytetracycline were the most used, whereas *Bacillus* spp. and Lactic Acid Bacteria (LAB) was the microorganisms most cited as a form of biological control. Lastly the main phytopathogens of tomato were *Xanthomonas* spp., *Clavibacter michiganensis* subsp. *michiganensis* and *Ralstonia solanacearum*. The objectives of this work were to identify the main types of agricultural defensives, antibiotics and genera of microorganisms used to control tomato diseases and to compare their impact on human health and the environment.
Keywords: Tomato disease, Phytopathogens, Lactic acid bacteria, Agricultural defensive, Biological control.

Controle Biológico de Fitopatógenos do Tomate como Alternativa a Defensivos Agrícolas e Antibióticos

Resumo: O tomate (*Solanum lycopersicum* L.) é uma das hortaliças mais cultivadas do mundo. A China representa cerca de 25% de toda a produção mundial, desta forma existe uma dependência e uso constante de defensivos agrícolas na cultura do tomate. A aplicação de produtos químicos proibidos em diversas partes do mundo tem como efeito colateral um grande impacto na saúde humana e no ecossistema, sendo necessário adotar outras estratégias de prevenção de doenças. Outra forma de combate às doenças do tomateiro é a utilização de microrganismos como forma de controle biológico, considerado uma alternativa aos defensivos agrícolas e antibióticos com maior sustentabilidade e menor toxicidade. Neste trabalho, os defensivos agrícolas mais utilizados pelos produtores foram Piraclostrobina, Mancozebe, Oxicloreto de Cobre e derivados do DDT. Para os antibióticos, Estreptomicina e Oxitetraciclina foram os mais utilizados, enquanto *Bacillus* spp. e bactérias do ácido lático (BAL) foram os microrganismos mais citados como forma de controle biológico. Por fim, os principais fitopatógenos do tomateiro foram *Xanthomonas* spp., *Clavibacter michiganensis* subsp. *michiganensis* e *Ralstonia solanacearum*. Os objetivos deste trabalho foram identificar os principais tipos de defensivos agrícolas, antibióticos e gêneros de microrganismos utilizados no controle de doenças do tomateiro e comparar seu impacto na saúde humana e no meio ambiente.
Palavras-chave: Doença do tomateiro, Fitopatógenos, Bactéria ácido láctica, Defensivo agrícola, Controle biológico.

Control Biológico de Fitopatógenos del Tomate como Alternativa a Defensivos Agrícolas y Antibióticos

Resumen: El tomate (*Solanum lycopersicum* L.) es una de las hortalizas más cultivadas del mundo. China representa alrededor del 25% de toda la producción mundial, por lo que existe una dependencia y uso constante de defensivos agrícolas en los cultivos de tomate. La aplicación de productos químicos prohibidos en muchas partes del mundo tiene como efecto secundario un gran impacto en la salud humana y el ecosistema, por lo que es necesario adoptar otras estrategias de prevención de enfermedades. Otro método para combatir las enfermedades del tomate es el uso de microorganismos como forma de control biológico, que se considera una alternativa a los defensivos agrícolas y los antibióticos que ofrece una mayor sostenibilidad y menor toxicidad. En este trabajo, los defensivos agrícolas más utilizados por los productores fueron Pyraclostrobin, Mancozebe, Oxicloruro de cobre y derivados del DDT. Para los antibióticos, la Estreptomicina y la Oxitetraciclina fueron las más utilizadas, mientras que *Bacillus* spp. y las bacterias del ácido láctico (BAL) fueron los microorganismos más citados como forma de control biológico. Por último, los principales fitopatógenos del tomate fueron *Xanthomonas* spp., *Clavibacter michiganensis* subsp. *michiganensis* y *Ralstonia solanacearum*. Los objetivos de este trabajo fueron identificar los principales tipos de defensivos agrícolas, antibióticos y géneros de microorganismos utilizados para controlar las enfermedades del tomate y comparar su impacto en la salud humana y el medio ambiente.
Palabras clave: Enfermedad del tomate, Fitopatógenos, Bacterias del ácido láctico, Defensivo agrícola, Control biológico.

INTRODUCTION

The tomato (*Solanum lycopersicum* L.) is one of the most cultivated vegetable in the world (CASTRO; BRANDÃO; MACEDO, 2008). The main tomato-producing countries in the world in terms of production and exportation are China, India, United States of America (USA), Turkey, Egypt, Italy, Spain, and Brazil. China represents about 48 % of all production when compared to the main producing countries, producing around 61.6 million megagrams in 2018 (Figure 1), (FAOSTAT, 2020).

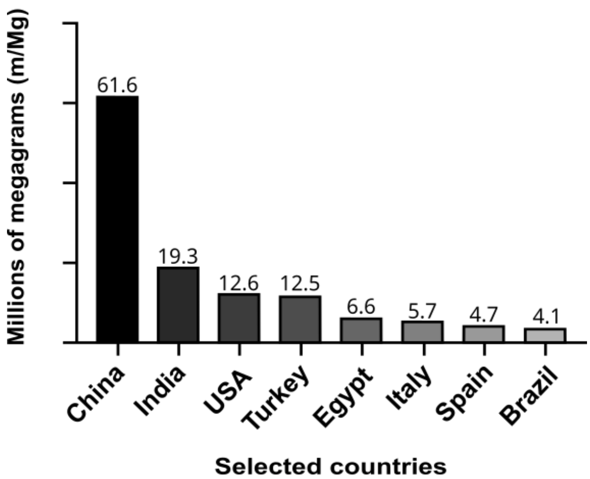

Figure 1 – The Asian continent represented by China and India represents about 80% of the world's tomato production. 1 megagram = 1 ton.
Source: The author himself.

The commercialization of tomato has a strong impact on the economy of several countries, but the susceptibility of some tomato cultivars, the environmental factors and agricultural practices that favor the occurrence of some diseases, making the tomato the target of several types of phytopathogens. On a worldwide scale, it is estimated that around 35 % of production is directly affected, leading to a decrease in fruit quality and losses in the post-harvest process. Due to the low resistance of the tomato, there is a dependence and the constant use of agricultural defensive in tomato crops (ZAVATTI; ABAKERLI, 1999; ENGINDENIZ, 2006).

In the beginning, agricultural defensives or pesticides had low solubility and strongly adhered to the soil, over the years and the improvement of technologies, these synthetics compounds became more and more soluble in water, adhering less and less to the soil and having a more volatile profile in compared to its first formulations, thus this technological innovation allowed the manipulation and creation of chemical compounds that are increasingly toxic and, as a side effect, possessing a high potential to cause damage to human health and the ecosystem (VEIGA *et al.*, 2006; IZZEDDIN; MEDINA, 2011). As the main strategy to combat and prevent pests and diseases, agricultural defensives can also bring complications to the immune system, central and peripheral nervous systems, being associated with the appearance of various types of cancer. Brazil is one of the main countries that use agricultural defensives worldwide, having the approval of substances with different spectrum of fungicidal, acaricidal, herbicidal and bactericidal actions (CALDAS; SOUZA, 2000).

Other products, such as antibiotics, are used to control diseases in tomatoes, however the use of Streptomycin sulfate, copper-based antibiotics or combinations of these, do not always work satisfactorily, because when the disease caused by pathogens such as *Clavibacter michiganensis* subsp. *michiganensis*, which causes bacterial cancer and *Xanthomonas* pathovars, which causes tomato bacterial stain, chemical treatment is not very efficient, in addition to causing the selection of resistant strains (ITAKARO *et al.*, 2015; XU *et al.*, 2015).

Thus, the use of microorganisms as a form of biological control is considered an alternative to agricultural defensives, and antibiotics offering better sustainability and less toxicity (KONDOH; HIRAI; SHODA, 2000). Countries such as Sweden, Indonesia, Norway, Denmark, Holland and Guatemala are examples of countries that had an annual reduction of 35 to 75 % in the use of agricultural defensives without a reduction in production, with emphasis on Indonesia that was successful in decreasing the amount of agricultural defensives and using biological control, obtaining a 12 % increase in production over the years (WILSON; TISDELL, 2001). In this context, several strains are indicated in the fight against several tomato diseases, such as lactic acid bacteria (LAB), growth promoting *Rhizobacteria*, *Trichoderma* spp., *Pseudomonas fluorescens*, *Bacillus* spp., bacteriophages, among others. Therefore, the use of biological control is a viable option for agricultural defensives and antibiotics (SHOKRYAZDAN *et al.*, 2017; GUIMARÃES *et al.*, 2018; MARIN *et al.*, 2019).

Thus, the objectives of this work were to identify the main types of agricultural defensive, antibiotics and genera of microorganisms used to control tomato diseases and to compare their impact on human health and the environment.

MATERIALS AND METHODS

This study is a systematic review of journals and indexed articles. The search was carried out between January 2020 and June 2020, when there was a search in the databases ScienceDirect, Pubmed / Medline and Scielo, without time delimitation.

The database search was performed as follows: in the ScienceDirect and Pubmed database, the keywords used were "Biological control", "Lactobacillus", "Antibiotic", "Tomato biological control", "Chemical control of tomato", "tomato disease", "Pesticides application and Tomato", "Probiotic bacteria", "Antibiotic and tomato", "Plant pathogens", "Phytopathogenic bacteria", "Animal", "Gen". For the Scielo database, the descriptors had to be adapted by the search engine limitation, only the last two descriptors were omitted. The following Boolean operators were used: OR, AND and NOT.

The inclusion criteria were published works and available entirely in scientific database in the online modality, works that address biological control using probiotic microorganisms (bacteria, fungi and viruses), use of pesticides or antibiotics as chemical methods as a way of control against tomato diseases. The exclusion criteria were studies that evaluate the control of tomato diseases using other methods, studies published as posters and articles that present inconclusive evaluations. The works that were considered eligible were read in full and the data available in the text were extracted according to the following criteria: Author, year of publication and control method used.

In addition to the databases mentioned, the database of the *Brazilian Agricultural Research Corporation Ministry of Agriculture, Livestock and Supply* (*EMBRAPA*), *Ministry of Agriculture, Livestock and Supply* (*AGROFIT*) and the *National Health Surveillance Agency* (*ANVISA*), were also consulted, which provide data and regulations on chemical and biological control in Brazil, were used as a research source.

Selection of Articles

The search carried out through the implementation of the protocol returned a total of 943 articles, of which 753 were excluded after the preliminary analysis. Of the remaining 190 articles, 31 did not meet the inclusion criteria. One hundred fifty-nine articles were selected for detailed analysis of the title and abstract and the inclusion and exclusion criteria were applied in parallel. One hundred thirty-one filtered articles were selected, and their texts were read in full. Finally, 40 studies were selected to be part of this review article. Figure 2 presents the summary of the search process for the articles.

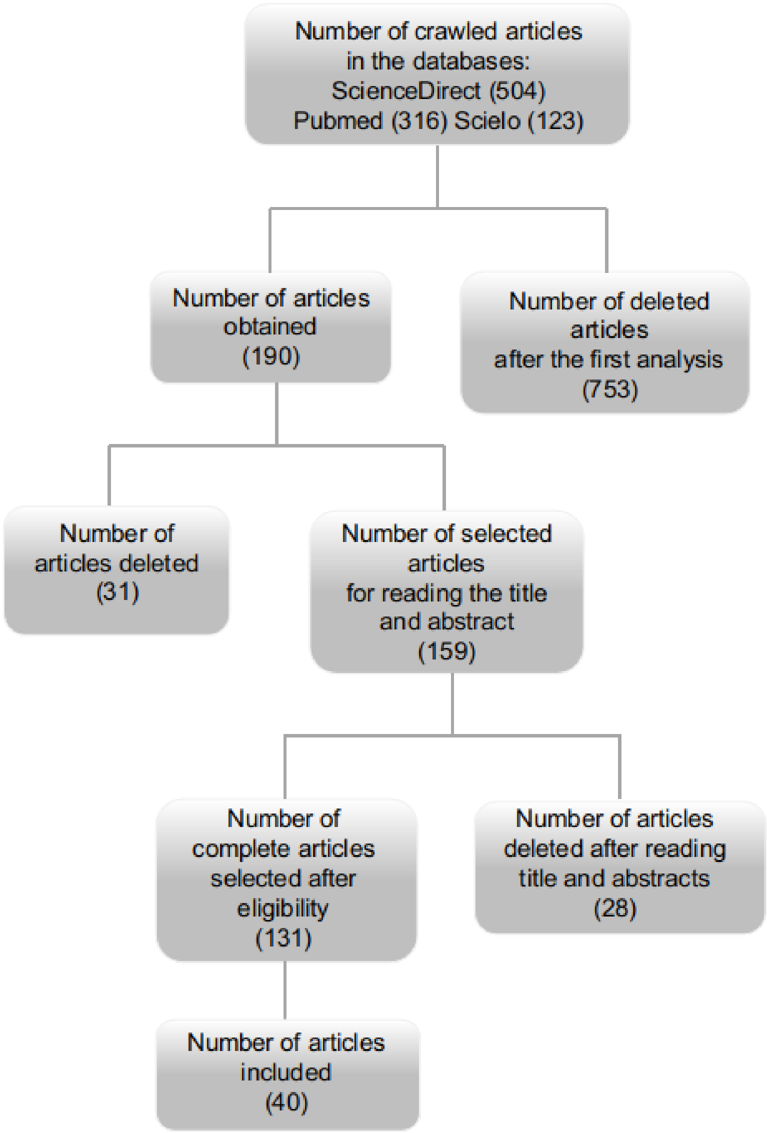

Figure 2 – Summary of the search process for articles.
Source: Adapted from Silva *et al.* (2019).

RESULTS AND DISCUSSION

According to data released by *EMBRAPA*, agricultural defensives are classified by the *ANVISA* according to their degree of toxicity based on their acute effects.

These products are classified based on the lethal dose 50 (LD50), which has as a parameter the dose necessary to kill 50% of the population of animals used in the experiments (often rats and mouse), in a period of approximately 2 weeks (BONVOISIN *et al.*, 2020). For the Ministry of Health (MSB), agricultural defensives are based on the oral LD50 of liquid and solid formulations, while for the World Health Organization (WHO) the toxicological class is also based on the LD50, but in oral and dermal form, per mg/kg of weight of liquid and solid formulations (ANVISA, 2019; BONVOISIN *et al.*, 2020). Although the two entities present certain changes, in both cases agricultural defensives are classified as follows based on the LD50; Class I – extremely toxic (red band); class II – highly toxic (yellow band); class III – moderately toxic (blue band) and; class IV – little toxic (green band), (Table 1).

Table 1 – Acute oral, skin and inhalation toxicological classification (LD_{50})

Class		Class I	Class II	Class III	Class IV
Degree of toxicity		**Extremely Toxic**	**Highly Toxic**	**Moderately Toxic**	**Little Toxic**
Assigned color		Red	Yellow	Blue	Green
Oral exposure route	unity [1](mg/Kg p.c.)	≤ 5	>5 - 50	>50 - 300	>300- 2000
Exposure route cutaneous	[1](mg/Kg p.c.)	≤ 50	>50 - 200	>200 - 1000	>1000- 2000
Inhalation exposure route	Gases [2](ppm/V)	≤ 100	>100 - 500	>500 - 2500	>2500-20000
	Vapors [3](mg/L)	≤ 0,5	> 0,5 - ≤ 2,0	>2,0 - ≤ 10	> 10 ≤ 20

Toxicological classification attributed to different routes of exposure. Legend: 1. milligram of waste per kilogram of body weight, 2. parts per million of volume, 3. milligram per liter.
Source: National Health Surveillance Agency (ANVISA) (Adapted from ANVISA 2019).

It is worth mentioning that, due to the new regulatory framework for the use of agricultural defensives in Brazil, many products are in the process of being reclassified, nevertheless no change in the toxicity of the final product. The new regulatory framework brings, among other changes, an improvement of the information that reaches the rural producer, improving the product label with a more accessible language, aiming to mitigate the negative impacts on health and the environment, thus making Brazil following the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). Therefore, as a result of this transition phase, the classification by bands will be adopted (ANVISA, 2019).

The quantity and use of these agricultural defensives vary according to the demand of each producer and their classification according to the spectrum of action can be as follows; acaricide/fungicide, bactericide, adhesive spreader and fungicide according to the registration certificate (Table 2).

Table 2 – Main groups of agricultural defensives used in tomato plantations in Brazil

Group		**Acaricide/Fungicide**		
Commercial name	**[1]Uni**	**Active principle**	**Toxicological class/Legend**	
Dithane WG NT	[2]Kg	mancozeb	I Extremely Toxic	red
Manzate WG	Kg	mancozeb	I Extremely Toxic	red
Gravun	Kg	cyprodinil	I Extremely Toxic	red
Tradecorp 480 EC	[3]L	chlorpyrifos	I Extremely Toxic	red
Meothrim 300	L	fenpropathrin	I Extremely Toxic	red
Terrazole 350 WP	Kg	etridiazole	I Extremely Toxic	red
Mancozebe CCAB	Kg	mancozeb	II Highly Toxic	yellow
Abamectin Nortox	Kg	abamectin	II Highly Toxic	yellow
Thiodan CE	L	endosulfan	II Highly Toxic	yellow
Evolution	Kg	acefato	III Moderately Toxic	blue
Pirate	L	chlorfenapyr	III Moderately Toxic	blue
Vertimec 18 EC	L	abamectin	III Moderately Toxic	blue
Assist	L	mineral oil	IV Low Toxic	green
Group		**Bactericide**		
Commercial name	**Uni**	**Active principle**	**Toxicological class/Legend**	
Scooter	Kg	mancozeb + copper oxychloride	I Extremely Toxic	red
Kocide Bioactive	Kg	copper oxychloride	III Moderately Toxic	blue
Cobre Atar BR	Kg	cuprous oxide	IV Low Toxic	green
Reconil	L	copper oxychloride	IV Low Toxic	green
Recop	Kg	copper oxychloride	IV Low Toxic	green
Group		**Adhesive spreader**		
Commercial name	**Uni**	**Active principle**	**Toxicological class/Legend**	
Adesil	L	ethoxylated nonylphenol	I Extremely Toxic	red
Group		**Fungicide**		
Commercial name	**Uni**	**Active principle**	**Toxicological class/Legend**	
Cercobin 700 WP	Kg	thiophanate-methyl	I Extremely Toxic	red
Forum Plus	Kg	dimethomorph	I Extremely Toxic	red
Galben-M	Kg	benalaxyl + mancozeb	I Extremely Toxic	red
Orthocide-500	Kg	captan	I Extremely Toxic	red
Thiobel 500	Kg	cartap hydrochloride	I Extremely Toxic	red
Bravonil Ultrex	Kg	chlorothalonil	I Extremely Toxic	red
Daconil WG	Kg	chlorothalonil	I Extremely Toxic	red
Folio Gold 440 SC	Kg	chlorothalonil + metalaxyl-M	I Extremely Toxic	red

Main classes of agricultural defensives and their toxicological classification, where most agricultural defensives used in tomato plantations in Brazil vary between classes I, III and IV. *For a better comparison consider 1Kg = 1L. Legend: 1. Unit, 2. Kilogram, 3. Liter.
Source: Adapted from Brazilian Agricultural Research Corporation Ministry of Agriculture, Livestock and Supply EMBRAPA 2008.

According to the data presented in Table 2, it was possible to measure the most used agricultural defensives in tomato plantations according to classification and their degree of toxicity (Figure 3).

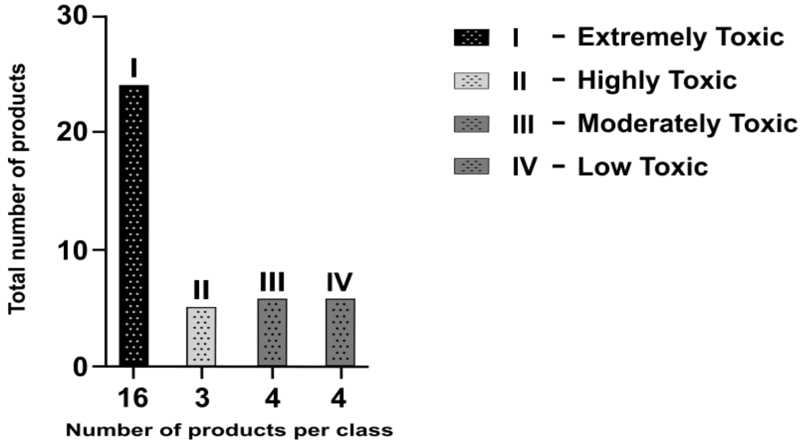

Figure 3 – Classes of agricultural defensives used in the cultivation of tomatoes.
Source: The author himself.

Despite a large number of chemical products intended to combat tomato diseases, there are several alternatives to agricultural defensives, in this sense some of the products used as a form of biological control are shown in (Table 3) (BETTIOL *et al.*, 2012; SOLANKI *et al.*, 2015).

Table 3 – Main biological control agents used in tomato plantations in Brazil and worldwide

Commercial name	Active principle	Registration/marketing
Nemata	*Paecilomyces lilacinus* DSM 15169	Colombia
Agrotrich and Agrotrich Plus	*Trichoderma* spp [1](6x)	Brazil (temporary registration)
ECO-77	*Trichoderma harzianum* cepa B77	South Africa, Kenya and Zambia
Ecotrich ES	*Trichoderma harzianum*	Brazil (temporary registration)
Sentinel – Trichoprotection	*Trichoderma atroviride* LC52	New Zealand
Trichodel	*Trichoderma* spp.	Brazil
Trichonativa	*Trichoderma virens* cepa Sherwood Nativa, *Trichoderma harzianum* cepa Queule Nativa e *Trichoderma parceanamosum* cepa Trailes Nativa	Chile
Trichozam	*Trichoderma* spp.	Honduras
Amylo-X	*Bacillus amyloliquefaciens* subsp. *plantarum* D747	Italy
Botrybell	*Bacillus velezensis*	Epain
Nacillus	*Bacillus* spp. e *Brevibacillus brevis*	Chile
RhizoVital	*Bacillus amyloliquefaciens* FZB42	Germany

Main microorganisms used in biological control specifically for tomato. Botrybell and *Bacillus* products are specifically for phytopathogens. Brazil has three products, two of which have only temporary registration. Legend: 1. six different strains of Trichoderma.
Source: Adapted from *Brazilian Agricultural Research Corporation Ministry of Agriculture, Livestock and Supply – EMBRAPA* (2012).

A survey of 10 selected countries was carried out regarding the registration of products used as a form of biological control in North America, Central America, South America, Europe and Oceania (Figure 4).

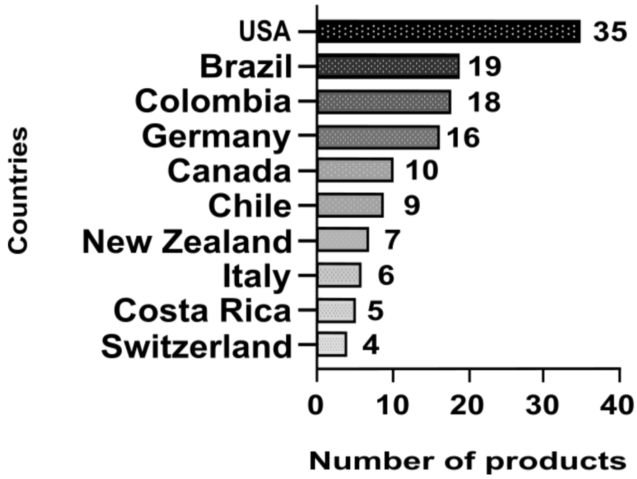

Figure 4 – South America concentrates most of the products used as a form of biological control.
Source: The author himself.

According to the data presented in Table 3 and Figure 4, despite the 19 products for biological control registered in Brazil, only three are intended for use in tomato, two of which received only a temporary registration (Figure 5).

Figure 5 – Products for biological control of tomato diseases in Brazil.
Source: The author himself.

After a careful analysis of the 40 articles selected for the composition of this review article, the main agricultural defensives and the main strains of biological agents used by producers were selected. Finally, the search for keywords in the selected articles resulted in greater frequency for products based on copper, DDT, pyraclostrobin, and mancozeb as the main agricultural defensives used in the chemical control of tomato (Tabela 4).

Table 4 – Main chemical and biological products used to control tomato diseases

Agricultural defensives	References
Copper oxychloride *	ITAKARO *et al.*, 2015; VEIGA *et al.*, 2006; ARNOLD *et al.*, 2004.
Dichloro-diphenyl-trichloroethane (DDT) *	OLISAH *et al.*, 2020; MEFTAUL *et al.*, 2020; WILSON; TISDELL, 2001; VEIGA *et al.*, 2006; BHANDARI *et al.*, 2020.
Pyraclostrobin *	ITAKARO *et al.*, 2015.
Mancozeb *	ENGINDENIZ, 2006; CALDAS *et al.*, 2000.
Diazinon	ENGINDENIZ, 2006; MEFTAUL *et al.*, 2020; CALDAS *et al.*, 2000.
Dieldrin	OLISAH *et al.*, 2020; WILSON; TISDELL, 2001.
Dimethoate	ENGINDENIZ, 2006; CALDAS *et al.*, 2000; ANDRADE *et al.*, 2015.
Heptachlor	OLISAH *et al.*, 2020; OROZCO *et al.*, 2017.
Hexachlorocyclohexane	OLISAH *et al.*, 2020; MEFTAUL *et al.*, 2020.
Biological control agent	**References**
Bacillus spp.	SHODA *et al.*, 2000.
LAB	MARIN *et al.*, 2019.

(*) Represents a frequency of chemical products most adopted by producers. LAB – lactic acid bacteria. Strains of *bacillus* spp. and LAB are identified as the main forms of biological control in diseases such as bacterial spot.
Source: The author himself.

In this research, the main strains of phytopathogens causing disease in tomatoes were *Xanthomonas perforans*, X. *gardneri*, X. *vesicatoria*, X. *euvesicatoria*, responsible for causing the bacterial spot (BLAINSKI et al., 2018), *Ralstonia* spp. causing soft rot and *Clavibacter michiganensis* subsp. *michiganensis* with seed infection (YENDYO; RAMESH; PANDEY, 2017), (Figure 6).

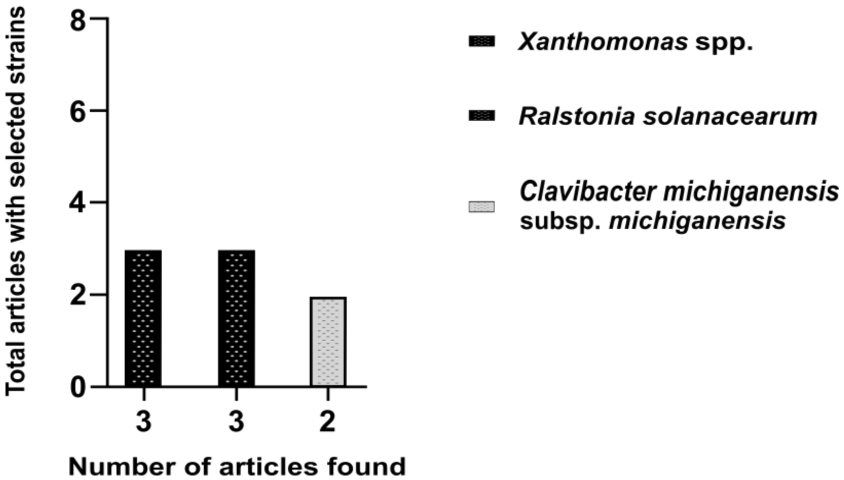

Figure 6 – Main strains of bacteria reported to cause diseases in tomato.
Source: The author himself.

According to published studies, only two articles reported the use of phages as a means of biological control of tomato diseases (ADDY *et al.*, 2012; WANG *et al.*, 2019).

The detrimental effect of exacerbating use of agricultural defensives has been one of the most relevant topics discussed worldwide in recent decades (MEFTAUL *et al*., 2019). These chemical compounds used on a large scale in agriculture can be displaced over long distances from the place firstly sprayed, affecting the environment, domestic animals, the wild, and also to humans, requiring studies on the effects and toxicological interactions between man, environment, and these compounds (OLISAH; OKOH O; OKOH I, 2020).

Thus, these agricultural defensives receive a certain toxicological classification according to the regulatory body of each country, in Brazil *ANVISA* is responsible for the classification related to humans (Table 1) and the Brazilian Institute for the Environment and Renewable Natural Resources (*IBAMA*) is responsible for research on toxicity to the environment (UYEMURA *et al*., *2017;* ANVISA, 2019). Worldwide, WHO classifies these products based on LD50 in rats, oral and dermal, per mg / kg of weight of liquid and solid formulations, according to the data provided by the manufacturer and, if it is not possible to obtain these data from classification is carried out in proportion to the LD50 values (BONVOISIN *et al*., 2020). In an attempt to standardize the use of various forms of controls, protocols were created, according to the following formula according to WHO (2019).

$$\frac{LD^{50} active\ compound \times 100}{percentage\ of\ active\ compound\ in\ the\ formulation} \quad (1)$$

*The LD50 value is a statistical estimate of the number of mg of toxic per kg of body weight required to harvest 50 % of a certain population of test animals.

In the case of formulas containing more than one chemical product (active ingredient, solvents, etc.), if the toxicity of the final product increases, the toxicological classification should represent the total of that combination (WHO, 2019), as is the case with some agricultural defensives shown in Table 2.

The regulation of these products is important because a large part of the agricultural defensives used by rural producers offer a high degree of toxicity as can be seen in Table 2 and Figure 3. In their studies, Engindeniz (2005) reports that in Turkey some tomato farmers make use of disproportionate amount of agricultural defensives for fear of losing the crop. The main agricultural defensives reported in this study were hydrogen oxalate (Evisect), lambda cyhalothrin (Karate), imidacloprid (Confidor), dimethoate (Poligor), basudin 60 EM (Diazinon), propineb (Antracol), metalaxyl mancozeb (Ridomil), trifluralin (Treflan) and abamectin (Agrimec). According to WHO (2019). They represent a high degree of toxicity, and their use, even if controlled or mainly indiscriminate, can put the lives of people, animals and the environment at risk (OLISAH; OKOH; OKOH, 2020). A viable alternative is the use of biological control (KONDOH; HIRAI; SHODA, 2000).

Another relevant factor is the use of products that have already been banned and are still commercialized due to their relatively cheap price, as is the case with carbendazim and dietofencarb (LI *et al.* 2016), dichlorodiphenyltrichloroethane (DDT) and, the hexachlorocyclohexane isomers banned from India and other Asian countries (MEFTAUL *et al.* 2019), and methyl bromide that was expected to be banned by 2005 according to the Montreal protocol for causing depletion in the ozone layer (SANDE *et al.,* 2011).

Similarly, small producers and equipment operators believe that the exacerbated use of low-quality agricultural defensives, generally because they are cheaper, generates better results (Quirós *et al.* 2017), however, these products can cause problems such as burns, skin irritation, vomiting, and headaches, being reported in more than half of the interviewees by the group of (NÁJERA *et al.* 2011), and almost all, when suffering some intoxication in the field, consumed lemon juice or milk as an antidote form.

This data is important because the technical level of the producer and workers can reflect on severe environmental, occupational and comorbidities that go beyond the communities where a product is generated, putting at risk the families that participate in the production process and also to other consumers. In this way, part of the environmental impact and products with a high degree of toxicity can be mitigated by offering training to farmers, using good agricultural practices and eliminating or reducing products from the most toxic classes (ARAÚJO; NOGUEIRA; AUGUSTO, 2000).

Despite the existence of products that less toxic to human health (class IV), agricultural defensive copper-based with a large spectrum action identified in Table 2, possesses a significant impact on the environment, thus according to the studies of Arnold *et al.* (2004), and Meftaul *et al.* (2019), copper is toxic to embryos of certain aquatic animals can impair marine life, cause urothelial carcinoma in dogs, poisoning of birds and non-target insect death due to misuse.

Although most farmers choose to use chemicals such as agricultural defensives and antibiotics, there are other products aimed at the numerous diseases in tomato crops and less aggressive to producers and consumers, the use of live microorganisms as a form of biological control in certain cases are as efficient as chemical control, therefore the use of these compounds is not always justified and, despite the reduced number of biological products compared to agricultural defensives, there are several alternatives aimed only at tomato, as can be seen in Table 3.

The utilization of *Rhizobacteria* and *Bacillus* sp. used as biological control of bacterial wilt caused by *Ralstonia solanacearum* (YAMAMOTO *et al*., 2015; WU *et al*., 2016), and other pathogens had results proportional to the chemical inducer acibenzolar-S-methyl resistance (ASM) reported by Rocha; Moura, (2013), and Itakaro and collaborators (2015), as being efficient in the combat to strains of the genus *Xanthomonas*. Corroborating with these data, Marin *et al*. (2019) report the use of lactic acid bacteria (LAB), Serenade® OPTI-BAYER (a single strain of *Bacillus subtilis* strain QST 713), and AgriPhage ™ (Bacteriophage) as microorganisms successfully used against various *Xanthomonas* pathovars.

Therefore, although solutions based on biological control are smaller than formulations based on agricultural defensives (Table 4), there are several products in other countries (Figure 4) that present good alternatives for important tomato pathogens (Figure 6). In Brazil, there are few registered products aimed only at combating tomato diseases (Figure 5). Although most of the data point to tests carried out "*in vitro*" like those of Rocha; Moura, (2013), biological control is still feasible because, according to Duval *et al*. (2003), and Itako *et al*. (2015) use of certain types of agricultural defensives such as copper derivatives and antibiotics such as streptomycin and oxytetracycline do not always offer satisfactory control of the disease or pathogen such as *Xanthomonas* spp. which can result in the selection of resistant bacterial isolates.

CONCLUSION

The cultivation of tomato represents great economic value for several countries, having a wide range of derived products however, some cultivated species are susceptible to diverse pathogens. Therefore, most of the treatment of diseases is realized through products such as agricultural defensives and antibiotics.

In this work, the agricultural defensives most reported by producers were Copper oxychloride, products derived from DDT, Pyraclostrobin, and Mancozeb, all belonging to the most toxic class. For the antibiotics class, Streptomycin and Oxytetracycline have been reported are mostly used. The biological control agents most cited in this work were lactic acid bacteria and *Bacillus* spp., only two studies reported the use of bacteriophages as a form of biological control.

Regarding the toxicity caused to humans and the environment, some agricultural defensives have been associated with contamination of marine life, the appearance of different types of cancer in humans and domestic animals, and depletion of the ozone layer. Antibiotics have been linked to the emergence of resistant bacterial isolates and water contamination through residues. Some biological control agents have been reported to have similar efficacy to certain chemicals. No data were found related to toxicity in humans and animals by antibiotics or biological control agents. Response speed data to treatment haven't been evaluated in comparison to chemical products.

Finally, more studies "*in vivo*" are needed about biological control agents for better decision-making by producers, in addition to better agricultural practices such as the non-utilization of agricultural defensives banned from the market and better planning, countries like Indonesia, Holland, and Guatemala are examples of the fact that biological control agents can serve as an alternative or decrease in chemical products.

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