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Analysis of patents related to technology to combat bioterrorism and biological warfare

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ABSTRACT

The use of biological weapons in terrorist acts is not a recent phenomenon. Since ancient times, several countries have experienced the devastation caused by the use of biological material harmful to human and animal health and the environment. In recent years, however, the imminent risk of bioterrorist attacks worldwide has reignited the debate on public policies to address this problem. In this sense, this study aimed to map and analyze patents related to combating bioterrorism and biological warfare, focusing on the virus as a biological agent due to its high intercontinental transmissibility. The method used for this consisted of structured searches in the Espacenet® database, resulting in 352 patent deposits between 1996 and 2021. The results showed that 41.8% of the deposits had companies as holders. It was also noted that the United States dominates the market for technologies to combat bioterrorism and biological warfare, with 61.4% of patent deposits made. The technological field ranges from the early detection and disinfection of pathogens to pharmaceutical compositions for treating people or affected areas. Thus, it became evident that efforts are being made to develop different technological solutions to prevent or neutralize the harmful effects of biological weapons used for terrorist purposes.

KEYWORDS: Biological weapons. Antiterrorism. Viral agents. Patents.

INTRODUCTION

Bioterrorism is a form of terrorism in which harmful microorganisms are intentionally released, such as viruses or bacteria. Such actions also apply to biological warfare, with the difference that in biological warfare, these microorganisms are used on enemy troops, while in bioterrorism, the agents are released into the civilian population, crops or animals. With the intent to harm or even annihilate people in a target country, these agents are released into the air or through water contamination to spread the spread of infectious agents. Bioterrorism is intended to generate panic in the population and pressure the government to meet the demands that that group wants to achieve, which may be motivated by political, religious, and ethnic factors, among others (SANTOS, 2018).

At the beginning of the 19th century, military interest in using biological agents as a weapon of war increased significantly due to technological development and the advancement of microbiology. However, the use of biological agents for bioterrorism and biological warfare accompanies humanity. Historical records report that Neanderthals put animal faeces on arrows to increase the destructive power of their weapon. Another account of a biological attack dating to the 15th century BC was the release of strains of anthrax in Egypt, victimizing the Pharaoh himself.

During World Wars I and II, particularly in the United Kingdom, anthrax research continued, but in Japan, advances in this field were used against China during the Sino-Japanese War. It is estimated that approximately 260,000 Chinese died testing these biological agents between 1937 and 1945 (ZILINSKAS, 2017). In the United States, in 2001, letters containing anthrax spores were sent to US senators and journalists, contaminating 22 people and leading to the death of five of them (JERNIGAN et al., 2002).

After World War II, several international legal documents regulated by the modern human rights movement began to recognize health as a fundamental right of every human being. With the end of the Cold War, strategic studies with a view to international security expanded the security agenda beyond the military issue, seeking to restructure the security discourse based on the notion of “threats” that come from other areas and not only from aggression military of one state against another (CARVALHO, 2012; PADULA, 2016).

Aiming to eradicate any means of research, production and use of biological agents for war purposes, in 1972, was the Convention on the Prohibition of Biological Weapons. Open for signature in London, Moscow, and Washington; other countries, such as Brazil, also signed the document. Due to growing concern about recent attacks that focused on the centers of US economic and military power, the issue became of global interest as it posed a threat to the security and stability of all countries. Still, despite the risk of handling material with these agents without proper knowledge, practically all materials needed to obtain biological agents can be legally acquired (BARBOZA, 2018; BERNARDES; COLLI, 2020; BRASIL, 2014).

The member countries of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) consider non-patentable inventions whose

exploitation in their territory is necessary to protect public order or morality, including to protect human, animal or plant life or health or to prevent severe damage to the environment. In this sense, several countries have created legislation to contain the production, development and use of agents such as biological weapons. However, in general, the chemical and pharmaceutical industries, aiming to protect these harmful products indirectly, end up using existing exceptions, such as the Portuguese legislation, which allows the patentability of obtaining these biological agents (POMIN, 2015; SANTOS, 2018).

Large multinational companies currently patent genes and cloning to produce food and medicines. These processes are protected by international institutions above the power of States and the needs of populations, with industrialized nations being the largest holders of these patents. A fact like this shows that it would be possible to manipulate, on an industrial scale, a toxin considered a biochemical weapon or even a virus considered a biological weapon under the allegation that its manipulation and storage are for a peaceful purpose (DALL'AGNO; SILVA, 2020; GRISOLIA, 2013).

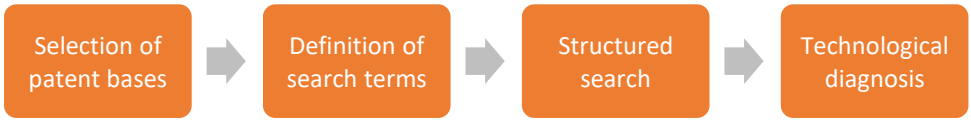
Recently, the COVID-19 pandemic has reignited the debate on public policies to address the imminent risk of bioterrorist attacks worldwide. According to Knight (2021), although a natural zoonotic transfer to humans was determined as the probable cause, speculation around a viral biological weapon was widely disseminated. The similarities between the contamination mechanisms reinforced this conspiracy theory (LYON, 2021). The devastation caused by the COVID-19 pandemic has also raised questions about the possibility of terrorist groups deliberately storing, manipulating and propagating coronavirus strains in future attacks (DASS, 2021; JAGROOP, 2022; MICHALSKI et al., 2022).

From this perspective, this study aimed to map and analyze patents related to combating bioterrorism and biological warfare, focusing on the virus as a biological agent due to its high intercontinental transmissibility and high incidence of morbidity and mortality of infected people. The technological information contained in patent documents can provide evidence of efforts undertaken to develop technologies to combat the harmful effects of biological weapons used for terrorist purposes and guide future proactive biodefense strategies.

RESEARCH METHOD

A descriptive research, cross-sectional and quantitative approach was carried out. The technical procedures were based on documentary research carried out in the patent database of the European Patent Office (EPO), Espacenet®. The universe of this research comprised patent documents that disclosed products and processes to combat bioterrorism and biological warfare. For the sample composition, patent documents were selected that disclosed technologies that act on viral agents. The main steps used in this study can be seen in Figure 1.

Figure 1 – Research methodological procedures



Source: Prepared by the authors (2022)

The search terms were defined after a preliminary reading of scientific articles related to the investigated technology, taking into account documents before the orthographic reform of the English language. The terms selected were: bioterrorism, terrorism, anti-terrorism, antiterrorism, biological, anti-biological, antibiological, warfare, weapon and virus. The searches were performed in March 2022 in the advanced search module of the patent database, using the "nftxt" feature that retrieved files that contained the terms anywhere in the patent document. The Boolean operators "AND" and "OR" and the truncation strategy "*" were also used to expand the possibility of retrieving documents related to the technology of interest (SANTOS; MONTEIRO, 2018). Equation (1) refers to the resulting search expression.

((nftxt = "bioterrorism" **OR** nftxt = "terrorism" **OR** nftxt = "anti-terrorism" **OR** nftxt = "antiterrorism") **AND** (nftxt = "warfare" **OR** nftxt = "weapon*") **AND** (nftxt = "biological" **OR** nftxt = "anti-biological" **OR** nftxt = "antibiological") **AND** (nftxt = "virus")) (1)

The searches returned 1,005 patent documents which, after screening to exclude duplicates and adapting to the scope of the study, were reduced to 352 documents. Data from eligible documents were exported to spreadsheets in Microsoft Office Excel 2016 for Windows®, in which statistical analyzes were performed. The technological diagnosis was carried out based on the following variables: the legal status of the patent, type of protection, annual evolution of deposits, country of origin, the territorial scope of protection, technological field, the profile of the applicant, main holders and inventors.

The thematic structure of the content of patent documents was determined through descending hierarchical classification (DHC) in the Iramuteq® program. This method considered the textual corpus containing the abstracts of the selected patents to obtain categories based on text segments with words that are similar to each other and, at the same time, different from the text segments of the other types. Thus, the fields of application of the technologies reported in the patent documents were grouped into clusters that retained the words with high statistical significance to facilitate the inferences. The inclusion criterion of a word within each cluster was defined by the chi-square (χ^2) value equal to or greater than 3.84 and $p < 0.05$ (IRAMUTEQ, 2021).

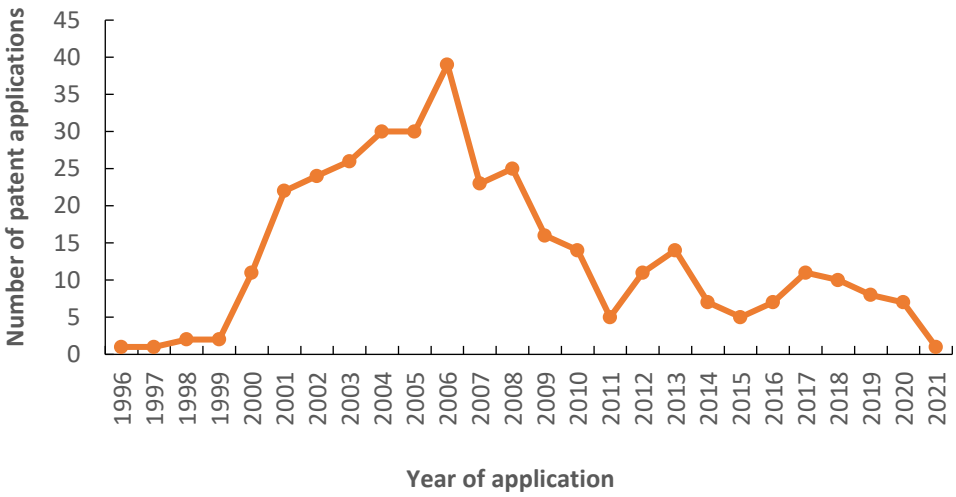
RESULTS AND DISCUSSION

Based on the established methods, 352 patent documents were selected, of which 350 consisted of invention patents and 2 utility models. In addition, 327 applications are still in the filing phase, while 25 have already been granted. The first application was deposited in 1996, with a peak of deposits in 2006, with 39

documents, as shown in Figure 2. However, the number of annual deposits dropped dramatically from that year onwards.

This increase in the number of patent applications related to combating bioterrorism and biological warfare in the early 2000s coincides with the results found by Cardoso and Cardoso (2011). They reported exponential growth in scientific publications, especially after spreading anthrax spores through the US mail in 2001. This attack highlighted how the US health and safety system was ill-equipped to deal with high-lethal emergencies adequately. This has led to a substantial increase in Research, Development and Innovation (RD&I) funding and international cooperation programs to develop emergency plans to deal with future bioterrorist attacks in the country (GOSTIN; NUZZO, 2021).

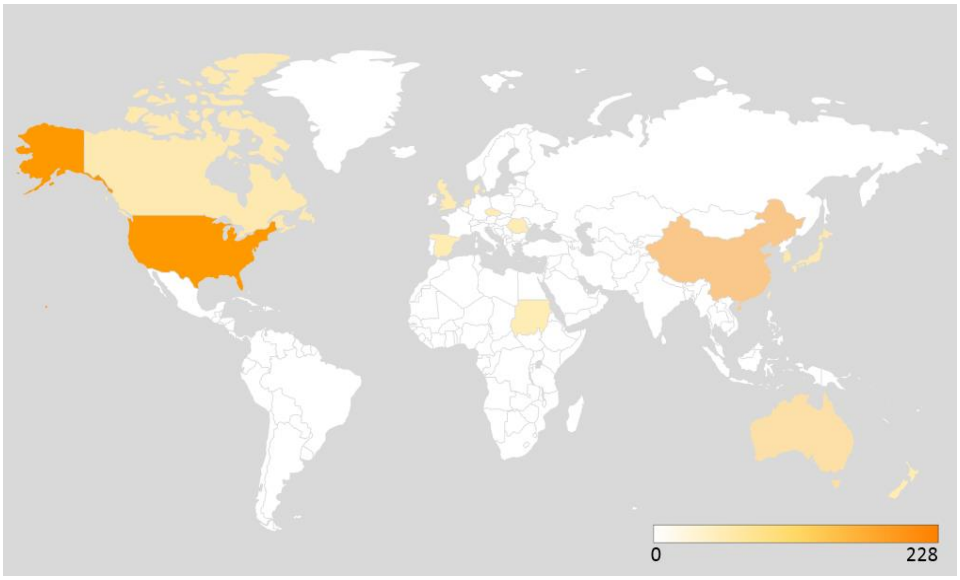
Figure 2 – Patent applications by year (1996-2021)



Source: Prepared by the authors from data from Espacenet (2022)

It is not by chance that the United States has a consolidated market because, as of the 352 patent applications identified, it was responsible for 64.8% of them (Figure 3). Then come China with 18.5% and Australia with 6.5% of deposits. It is essential to highlight that 23.9% of patent applications were made via the Patent Cooperation Treaty (PCT), demonstrating a particular interest in obtaining a competitive advantage in international markets.

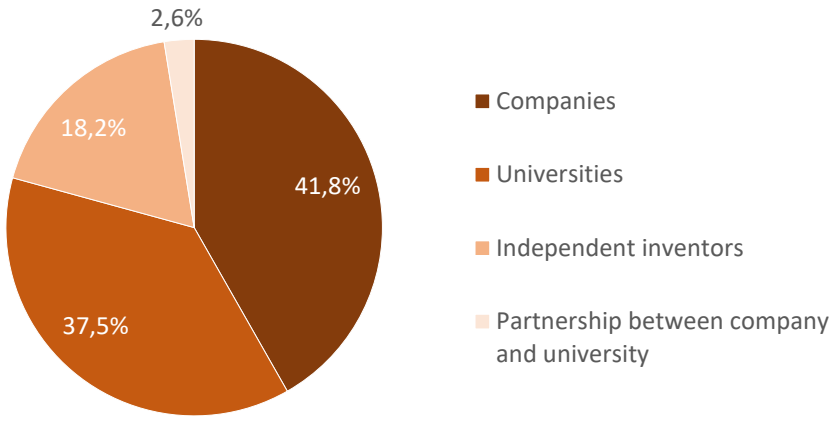
Figure 3 – Patent applications filed by unionist priority country (N = 352)



Source: Prepared by the authors from data from Espacenet (2022)

Concerning the profile of depositors, companies prevailed, with 147 patent deposits related to the investigated technology (41.76%), followed by universities, with 132 deposits (37.50%), and independent inventors, with 64 requests (18.18%). The strategy of technological cooperation between organizations is still incipient in this area, as only 2.56% of deposits were made due to partnerships between universities and companies (Figure 4). According to Menezes et al. (2020), technological cooperation is indispensable for technological innovation. In this process, combining resources, skills, and competencies can increase the countries' economic growth and ensure competitive advantages.

Figure 4 - Percentage of deposits by applicant type (N = 352)



Source: Prepared by the authors from data from Espacenet (2022)

The inventor with the most request for patents, a specific total of 10 (2.84%), is a PhD in Electrical Engineering from Duke University, Michael G. Pollack, whose research interests include droplet-based microfluidic systems (IEEE, 2022). He is followed by Vamsee K. Pamula, with 9 deposits, CEO of the company Baebies Inc. and whose last 5 publications are entitled “Emerging Approaches to Neonatal

Screening Based on Fluorescence of Mucopolysaccharidoses", "Digital Microfluidic Platform to Maximize Diagnostic Tests with Low Sample Volumes of Newborns and Pediatric Patients", "Fluorimetric Assay with a New Substrate for quantification of galactocerebrosidase activity in dried blood samples", "Digital microfluidics comes of age: high-throughput screening for bedside diagnostic testing for genetic disorders in newborns" and "Demonstration of a digital microfluidics platform for the high-throughput analysis of 12 discrete fluorimetric enzyme assays using a single neonate dried blood puncture" (RESEARCHGATE, 2022).

The three depositors with the most applications are located in the United States. Founded in 1869, the University of California featured 13 deposits of patents. It currently has 10 campuses in cities such as Los Angeles, Berkeley and San Francisco (UNIVERSITY OF CALIFORNIA, 2022). Advanced Liquid Logic Inc. is a privately held company founded in 2004 by Michael G. Pollack and Vamsee K. Pamula and has placed 11 orders. Located in the state of North Carolina, it provides, through a multidisciplinary team, solutions to challenges faced by laboratories and clinics (CRUNCHBASE, 2022). These depositors are followed by Harvard College, with 10 documents.

Regarding the International Patent Classification (IPC), 740 different codes were identified in the documents analyzed. The IPC system consists of a hierarchy of symbols that, when grouped, organize patents and utility models into classes referring to the technological areas they cover (INPI, 2022). Table 1 contains the meanings of the 10 IPCs with the highest occurrence in patent documents related to the technology of interest.

Table 1 - Description of IPCs and number of occurrences (N = 352)

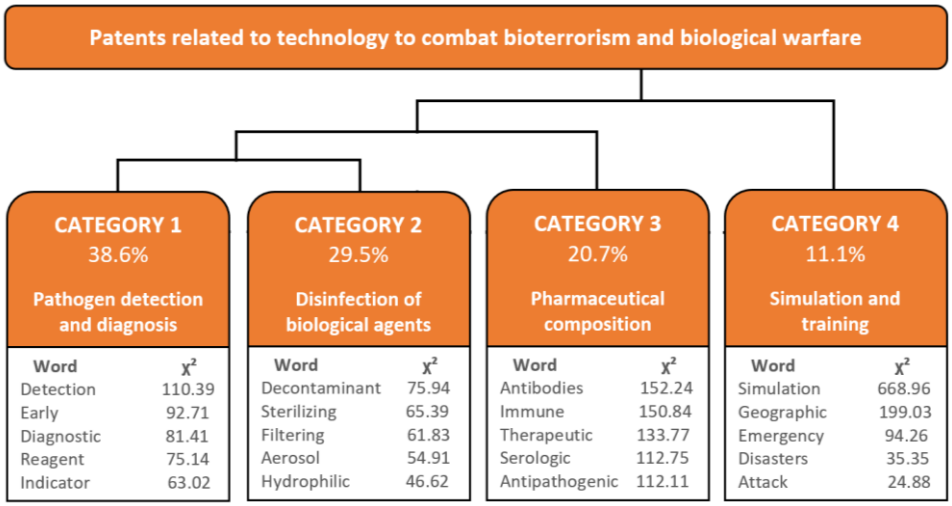
IPC	No	Description
C12Q1/68	63	Measurement or testing processes involving nucleic acids
G01N33/569	32	Investigate or analyze materials by specific methods for microorganisms (protozoa, bacteria, viruses)
G01N33/53	31	Investigate or analyze materials by specific methods per immunoassay or biospecific binding assay
A61K39/00	30	Medicinal preparations containing antigens or antibodies
G01N33/543	27	Investigate or analyze materials with an insoluble carrier to immobilize immunochemically
C12Q1/70	24	Control processes responsive to conditions (devices for tissue, human, animal or plant cells or virus culture devices)
C12M1/34	23	Measure or test with measurement or condition detection means (colony counters)
A61P31/04	21	Antibacterial agents
A61P31/12	19	Antivirals
A61K39/395	18	Antibodies, immunoglobulins, immune serum

Source: Prepared by the authors from data from Espacenet (2022)

The DHC retained 841 text segments from the textual corpus, using 81.21% of them. Based on the analysis of the textual domains, technologies to combat bioterrorism and biological warfare were grouped into four categories: (1) pathogen detection and diagnosis (38.6% of text segments); (2) disinfection of biological agents (29.5%); (3) pharmaceutical composition for prevention or treatment of people or affected areas (20.7%); and (4) simulation and training for

bioterrorist attacks (11.1%). These categories and the five words with significant statistical association ($p < 0.0001$) can be seen in the dendrogram of Figure 5.

Figure 5 - Fields of application of the technologies identified (N = 352)



Source: Prepared by the authors from data from Espacenet (2022)

Regarding the patent documents related to pathogen detection (category 1), one can cite the patent developed by Ha et al. (2012), which discloses integrated equipment for the early detection of biological weapons in real-time. This device allows biological particles suspended in the atmosphere to be collected to analyze the substance and its concentration and implement countermeasures quickly. Dwarakanath, Bruno and Rao (2005) also proposed a method to detect pathogens on surfaces or in humans and animals. The procedure consists of obtaining a fluorescent nanoparticle conjugated to substances capable of binding specifically to an antigen, triggering an immune response to the pathogen.

Ecker et al. (2002) provide methods of rapid identification of bioterrorists based on forensic evidence. This technology makes it possible to track the geographic location of bioterrorists through the genotyping of bioagents harvested at the site of biological warfare. The invention of Beiswenger, Ranck and Taualofai (2002) is aimed at the early warning of health authorities about bioterrorism events. The device has a system that monitors the basal metabolic temperature (BMR) data of individuals, and when the values exceed the established limits, there is an indication of infectious disease at the site.

To minimize physical contact between individuals and pathogens, some inventions have used disinfectant technologies to combat bioterrorism and biological weapons (category 2). Mize and Mize (2002) developed a method and device to be installed in residential mailboxes or sorting centers. The technology allows for the timed application of decontaminant (uniform generation and irradiation of electromagnetic waves) to destroy active biological agents or pathogens in contaminated mail, ensuring protection for postal workers and recipients. The invention proposed by Jeon and Jun (2001) follows the same principle and can be used to eradicate harmful microorganisms and viruses during airport inspections. The drone disclosed in Lacaze, Murphy and Narayanan (2019) allows attacked areas to be decontaminated remotely, without human presence.

There is a technological field of pharmaceutical methods and compositions to prevent infection during or after bioterrorist attacks (category 3). Steiner et al. (2002) provide a composition containing biologically active molecules encapsulated in diketopiperazine microspheres, which can be placed in an inhalation device for self-administration and guarantee immunity to individuals against a broad spectrum of infectious threats. Hammerbeck and Guy (2006) proposed inhalable immunoreactive modulators to reduce infection by pathogens in bioterrorist events. Chandran et al. (2015) provide bispecific antibodies and therapeutic methods to treat or prevent filovirus infections, while Chandran et al. (2014) by hantavirus.

Various technologies have been developed for simulation and training for biological warfare (category 4). Jiang et al. (2018) developed an intelligent visual decision support platform for sudden bioterrorism events worldwide. This tool provides primary data for conducting biological warfare simulations and risk assessments to formulate effective control measures. Wuchun et al. (2010) also offer an emergency platform for bioterrorist attacks. The platform simulates the number of people within a given geographic area that could be infected or killed by unexpected biological warfare. Olson (2005) developed a real-time education program to improve health professionals' individual and collective capacity during acts of bioterrorism.

CLOSING REMARKS

The use of biological weapons is not a recent issue in the world context, as is countries' concern about it. However, the spread of anthrax spores through the postal system in 2001 increased the focus on ways to protect and prevent bioterrorism. The current COVID-19 pandemic has significantly burdened healthcare systems worldwide and has shown how biological agents have highly destructive power. In this context, the present study proposed mapping and analyzing patents related to combat bioterrorism and biological warfare, focusing on the virus as a biological agent. In searches carried out in the Espacenet® database, 352 patent documents related to the technology of interest were identified.

From the data analysis, a prevalence of deposits from the United States and China was observed and significant growth of patent applications from 2001, with its peak in 2006. In addition, the applicants with the most occurrences were companies, with 41.76% of documents of patents, and the technological field with the highest incidence revolved around the detection of harmful agents, with 38.7% of documents. Indeed, rapid and accurate identification of pathogens is a fundamental part of the action plan of the governments to reduce their spread, preserving thus human health and amplify biodefense prospects of the countries.

In general, this study demonstrated how the analysis of patent documents could be an efficient tool for technological monitoring. Based on the results achieved, it is clear that different technological solutions to prevent or neutralize the harmful effects of biological weapons have been developed over the years. However, many countries still have low participation in patenting technologies related to the fight against bioterrorism and biological warfare. In addition, the granting of the letter patent has been slow, as only 7.1% of applications have been

granted and are available for commercial exploitation. This fact points to a shortage of products/processes, which suggests the need for new players to enter this market to foster and expand the technological capacity of countries, aiming at productive self-sufficiency in cases of public health emergencies.

As a continuation of this study, it is suggested that further research be carried out to understand better the predominance of companies as depositors and the high representation of the United States and China in this market. In addition, other biological agents and patent bases can be explored.

Análise de patentes relacionadas à tecnologia de combate ao bioterrorismo e à guerra biológica

RESUMO

O uso de armas biológicas em atos terroristas não é um fenômeno recente. Desde a antiguidade, diversos países já vivenciaram a devastação causada pelo uso de material biológico prejudicial à saúde humana e animal e ao meio ambiente. Nos últimos anos, contudo, o risco iminente de ataques bioterroristas em todo o mundo reacendeu o debate sobre políticas públicas para o enfrentamento desse problema. Nesse sentido, este estudo teve como objetivo mapear e analisar patentes relacionadas ao combate ao bioterrorismo e à guerra biológica, com foco no vírus como agente biológico devido a sua alta transmissibilidade intercontinental. O método utilizado para isso consistiu em buscas estruturadas na base de dados Espacenet, resultando em 352 depósitos de patentes entre 1996 e 2021. Os resultados mostraram que 41,8% dos depósitos tinham empresas como titulares. Constatou-se, ainda, o domínio dos Estados Unidos no mercado de tecnologias voltadas para o combate ao bioterrorismo e à guerra biológica, com 61,4% dos depósitos de patentes realizados. O campo tecnológico abrange desde a detecção precoce e desinfecção de patógenos até composições farmacêuticas para tratamento de pessoas ou áreas afetadas. Assim, ficou evidente que estão sendo empreendidos esforços para desenvolver diferentes tipos de soluções tecnológicas para prevenir ou neutralizar os efeitos nocivos das armas biológicas utilizadas para fins terroristas.

PALAVRAS-CHAVE: Armas biológicas. Antiterrorismo. Agentes virais. Patentes.

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