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Control of bovine viral diarrhea (BVDV): a study focusing on patent documents
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Available in: http://www.redalyc.org/articulo.oa?id=199547464064
Control of bovine viral diarrhea (BVDV): a study focusing on patent documents

Abstract

The virus of bovine viral diarrhea (BVDV) is considered, worldwide, one of the most important pathogens for cattle herds, and despite wide dissemination in Brazil, observational studies that estimate the prevalence and risk factors associated with BVDV in the country still they are scarce. The control of BVDV infection based on identification and removal of persistently infected herd animals, in addition to vaccination of susceptible animals to prevent clinical form, reproductive losses and production of infected animals. Vaccination is therefore widely applied to control these viruses. Thus, this study aimed to verify the technological patents relating to vaccines that are being develop under the control of BVDV, for study patentmetrics. Verification of the global landscape of patent documents related to technology of vaccines paying attention to requests for deposits arranged in the databases of the National Institute of Intellectual Property in Brazil and based European Patent Office (ESPACENET). It was found that the research related to BVDV is held uninterruptedly for everyone. The dynamism of the disease causes more, more vaccines that are new are developed, and recently, researchers from every continent are conducting research with BVDV.

Keywords: Bovine viral diarrhea control; vaccination; technological prospection; virus; infection; patents.

Resumen
La diarrea viral bovina (VDVB) se considera, en todo el mundo, uno de los patógenos más importantes para los rebaños de ganado, ya pesar generalizado en Brasil, los estudios de observación que estiman la prevalencia y los factores de riesgo asociados con VDVB en el país que son todavía escasos. El control de la infección por VDVB se basa en la identificación y eliminación de animales de rebaño persistentemente infectados, además de la vacunación de los animales sensibles para evitar forma clínica, pérdidas reproductivas y la producción de animales infectados. Por lo tanto, la vacunación se aplica ampliamente para controlar estos virus. Por lo tanto, este estudio tuvo como objetivo verificar las patentes tecnológicas relacionadas con las vacunas que se están desarrollando bajo el control del VDVB, por patentometria estudio. Verificación del paisaje global de documentos de patentes relacionadas con la tecnología de vacunas para prestar atención a los depósitos aplicaciones dispuestas en las bases de datos del Instituto Nacional de la Propiedad Intelectual en Brasil y la Oficina de Patentes Europea basada (ESPACENET). Se encontró que la investigación relacionada con el VDVB se lleva a cabo de forma ininterrumpida para todos. El dinamismo de la enfermedad hace más y más nuevas vacunas se desarrollan y, últimamente, los investigadores de todos los continentes también están realizando investigaciones con VDVB.

Palabras clave: control de la diarrea viral bovina; las vacunas; la prospección tecnológica; virus; infección; patentes.

Introduction

The cattle raising is one of the most important sectors of Brazilian agribusiness, and also of the national economy. According to the Foreign Agricultural Service of the United States (USDA, 2015), Brazil has the largest commercial herd in the world, being the largest exporter of beef, second largest meat producer and sixth largest producer of milk. Dairy farming is one of the more traditional activities of the Brazilian countryside.

In accordance with the last agricultural census there are in Brazil approximately 5.2 million rural establishments of which 25% (approximately 1.35 million) produce milk, involving about five million people (IBGE, 2006). The country has always been a traditional dairy importer experiencing periods of surplus in the trade balance and the dairy farming has economic and social importance.

The present article aims to verify the advances and technological research that are being made on the control of bovine viral diarrhea virus by means of patentmetrics study, considering that the technological prospection by means of patents has been an important tool to assist in decision making due to technological advancement of different sectors with accelerated access to the innovation system.
**Theoretical Review**

Bovine viral diarrhea virus (Bovine viral diarrhea virus English - BVDV) belongs to the genus Pestivirus of the Flaviviridae family is a major cause of economic losses in cattle. BVDV transmission by direct contact is the most common, however indirect transmission has also been observed. Injecting contaminated products, clothes and veterinary instruments or the human being can disseminate BVDV, not only within the herd, but also between herds (De Almeida, Miranda, Hein et al., 2010).

The virus can cause transient or persistent infection in cattle, which influences the dynamics of viral transmission within and between flocks. Persistently infected cattle are important BVDV, inducing excretory high prevalence within each herd and maintenance of active infections in cattle. The presence of infection in a group can be indirectly detected by analysis of serum antibody or milk from animals surrounding the infected and can be used for the diagnosis of effective level (Weber, Silveira, Machado et al., 2014).

In addition to respiratory disease, gastroenteric disease, hemorrhagic illness and disease of the mucous membranes can cause embryonic resorption BVDV, miscarriages, foetal malformations and mummification, the birth of infected calves. Calves infected excrete the virus continuously in large quantities and are the main source of spread of the virus. BVDV virus infection is disseminated worldwide; being, for its economic impact, considered the most important viral disease of cattle after the foot-and-mouth disease (Lima, Vogel, Flores & Weiblen, 2005).

The genus Pestivirus of the Flaviviridae family focuses on four recognized species: bovine viral diarrhea virus (BVDV-1), bovine viral diarrhea virus (BVDV-2), Border disease virus (BDV) and classical swine fever virus (CSFV). In addition, a group of atypical pestiviruses, initially detected in fetal calf serum and called "virus HoBi-like", has been associated with clinical disease in cattle (Weber et al., 2014).

BVDV infection is widespread in Brazil, being the virus of two genotypes BVDV-1 and BVDV-2 present in the herd. However, the only vaccine available in the market contains North American inactivated strains, whose effectiveness has been questioned because of their antigenic differences with Brazilian samples of the virus (Flores, Ridpath, Weiblen, Vogel & Gil, 2002).

The infected cattle can present a variety of clinical manifestations, ranging from unapparent infection to severe acute BVDV and mucosa. The BVDV infection control is based on the identification and removal of infected animals from the herd, in addition to the vaccination of susceptible animals to prevent clinical form, the reproductive losses and production of infected animals. Vaccines with BVDV attenuated or inactivated have been used in the control of infection in North America and Europe. The
great antigenic variability of the virus and the existence of two distinct antigenic groups (BVDV-1 and BVDV-2) harm the effectiveness of vaccines (Lima et al., 2005).

In several European Union countries, the bovine herpes virus type 1 (BHV-1) and bovine viral diarrhea virus (BVDV) are both targets of eradication programs. Vaccination is thus widely applied for controlling these viruses. The target animals and vaccination schemes for BHV-1 and BVD are very similar. In general, polyvalent vaccines for cattle are the preferred choice of farmers and veterinarians, as they simplify the handling of animals and, therefore, reduce animal stress and lower costs. In addition, the multipurpose BVDV vaccine currently used in Europe has proven fetal protection, although it is a fundamental requirement for vaccines used to combat BVDV (Alvarez, Bielsa, Santos & Makoschey, 2007).

Within this context, the virus the BVDV is considered, worldwide, one of the most important pathogens to livestock cattle, and despite being so widespread in Brazil, as in other endemic regions, observational studies that estimate the prevalence and risk factors for BVDV in the country are still scarce (De Almeida et al., 2010). BVDV may compromise the health and production of sheep milk, leading to important economic failure and has been associated with significant losses for the global livestock industry (Flores et al., 2002).

Methodology

In order to achieve the objectives of this study, a technological prospecting was carried out on the basis of requests for deposits willing patents in the databases of the National Institute of Intellectual Property (INPI) of Brazil and based European Patent Office (ESPACENET) worldwide.

To be carried out the search were used the keywords “Bovine and viral and diarrhea” (Diarrea y Viral y Bovina), “Vaccine and bovine and viral and diarrhea” (Vacuna y Bovina y Viral y Diarrea), “Treatment and bovine and viral and diarrhea” (Tratamiento y Bovina y Viral y Diarrea), “Flaviviridae and Bovine and viral and diarrhea” (Flaviviridae y Diarrea y Viral y Bovina) e “Prevention and bovine and viral and diarrhea” (Prevención y Bovina y Viral y Diarrea) found in the "Summary" of the Brazilian industrial property office and in the field “Keyword(s) in title or abstract” the ESPACENET, being data collection conducted in June 2015.

The information was extracted to Microsoft Office Excel, and the data was sorted and selected according to the years of patent application filing countries, types of depositors and, finally, amounts of patents according to the IPC classification, duly discussed and presented.

Results and Discussion
The searches were carried out with the keywords according to table 1, and found a total of 490 documents in ESPACENET and 29 base documents on national basis (INPI). There is a large number of filing patents with the keyword “Bovine and viral and diarrhea”.

Table 1 - Total deposits of patent searched in ESPACENET bases and INPI.

<table>
<thead>
<tr>
<th>Keywords</th>
<th>ESPACENET</th>
<th>INPI</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine and viral and diarrhea</td>
<td>330</td>
<td>15</td>
<td>345</td>
</tr>
<tr>
<td>Vaccine and bovine and viral diarrhea</td>
<td>88</td>
<td>7</td>
<td>95</td>
</tr>
<tr>
<td>Treatment and bovine and viral diarrhea</td>
<td>48</td>
<td>5</td>
<td>53</td>
</tr>
<tr>
<td>Flaviviridae and Bovine and viral diarrhea</td>
<td>16</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Prevention and bovine and viral diarrhea</td>
<td>8</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>490</td>
<td>29</td>
<td>519</td>
</tr>
</tbody>
</table>

Source: prepared from the databases consulted (2015).

The survey of patents was held in ESPACENET because it is a base that offers free access to over 90 million patent documents worldwide and contains information about inventions and technical developments from 1836 to today. The keyword used in this article was “Bovine and viral and diarrhea” (Diarrea y Viral y Bovina).

To renew the search was made a combination of keyword “Bovine and viral and diarrhea”, with different codes of international classification (IPC), as shown in Table 2.

Table 2 - Number of patent documents found in the resulting search ESPACENET with combination of keywords and international classification code.

<table>
<thead>
<tr>
<th>Keywords</th>
<th>A61</th>
<th>A61K39/00</th>
<th>A61K39/12</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine and viral and diarrhea</td>
<td>240</td>
<td>19</td>
<td>109</td>
<td>368</td>
</tr>
</tbody>
</table>

Source: prepared from the databases consulted (2015).

The specifications of the codes are referring to IPC A61 (medical or veterinary sciences), A61K39/00 (medicinal Preparations containing antigens or antibodies) and A61k39/12 (viral antigens). The result analyzed was the combination of the keyword “Bovine and viral and diarrhea” with the IPC code A61 to be selected only the documents related to medical or veterinary sciences, where 240 were found patent documents, of those only 94 were computed in this research due to the period of confidentiality.

Figure 1 presents the annual patent applications related to the control of bovine viral diarrhea, being found deposits of 1973 to 2014. The first patent application identified in 1973, entitled “Vaccine for neonatal calf diarrhea” American ownership it is a vaccine prepared by passage of a coronavirus, as in tissue culture or by inactivation of the viral agent. The vaccine is useful for immunization against bovine calf with diarrhea (Mebus, 1973). We can see that the largest numbers of deposits were made in the years of 2004 and 2007 with 9 deposits about technology.
To verify the origin of patent applications, whereas the priority document, that is, the first deposit of the invention patent application stands out, as shown in Figure 2, the United States (US) with 33 requests.

Despite the efforts made for the control and eradication of BVDV in United States and Europe, the economic impact of infection in flocks and milk is still significant (Lima et al., 2005).

Source: prepared from the data base consulted ESPACENET (2015).
The IPC classification related patents deposited more often was the A6139/12 about “Viral antigens” with 19 patent deposits, as shown in Figure 3.

Figure 3: Frequency of IPC classifications in patent applications for bovine Viral Diarrhea.

Source: prepared from the databases consulted (2015).

According to Flowers, P. Weiblen, Vogel et al., (2005), the biggest concern with the effectiveness of vaccines against BVDV refers to the great antigenic variability of the virus. Studies conducted in the country revealed that, in addition to the antigenic diversity among isolated locations, these isolated feature a low cross-serological reactivity with North American strains used in vaccines. This raised questions about the effectiveness of vaccines in use and about the need to re-evaluate production strategies, licensing and use of vaccines against BVDV in Brazil.

Figure 4 shows the category of inventors in developing technology for bovine Viral Diarrhea. Notes that 48 (51%) are companies, 24 (26%) and 22 University (23%) are independent inventors.

Figure 4: percentage of patent documents by type of depositor.
Final Considerations

The BVDV vaccination has been used to protect animals from disease clinic, reduce virus circulation and prevent fetal infection. Searches related to BVDV are held continuously by everyone. The dynamism of the disease causes more and more new vaccines are developed and, lately, researchers from all continents are also developing research with BVDV, especially those directed to the phylogenetic characterization in their countries.

The search results in the ESPACENET database show that the patents deposited for BVDV control are scarce, necessitating further research in some areas of disease, in order to develop a plan for effective control of the transmission of BVDV in populations of cattle, and we can't dismiss the notions of biosecurity, in addition to the function of vaccination Since a vaccine program by itself does not solve the problem.

Therefore the use of vaccines to prevent disease should be considered as a supplementary Act of the control program. Thus, the development of vaccines must be constant, improving their effectiveness and adapting them to the new strains circulating in herds.

Keeping up with the market demand and guided by polls, the national laboratories are developing vaccines against BVDV. Is the Brazilian legislation surface does not allow the use of modified live vaccines against BVDV, in this way, the use of inactivated vaccines will continue in use. So new studies may broaden the discussions on technology transfer and use of vaccines against BVDV, including discussions on the release of attenuated vaccines in our country.
References


Notas

**Identification file**

**Section to which the article is directed:** Varia – 2016-06-10.

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**Resumen:**

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estudios de observación que estiman la prevalencia y los factores de riesgo asociados con VDVB en el país que son todavía escasos. El control de la infección por VDVB se basa en la identificación y eliminación de animales de rebaño persistentemente infectados, además de la vacunación de los animales sensibles para evitar forma clínica, pérdidas reproductivas y la producción de animales infectados. Por lo tanto, la vacunación se aplica ampliamente para controlar estos virus. Por lo tanto, este estudio tuvo como objetivo verificar las patentes tecnológicas relacionadas con las vacunas que se están desarrollando bajo el control del VDVB, por patentometria estudio. Verificación del paisaje global de documentos de patentes relacionadas con la tecnología de vacunas para prestar atención a los depósitos aplicaciones dispuestas en las bases de datos del Instituto Nacional de la Propiedad Intelectual en Brasil y la Oficina de Patentes Europea basada (ESPACENET). Se encontró que la investigación relacionada con el VDVB se lleva a cabo de forma ininterrumpida para todos. El dinamismo de la enfermedad hace más y más nuevas vacunas se desarrollan y, últimamente, los investigadores de todos los continentes también están realizando investigaciones con VDVB.

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**Palabras clave:** control de la diarrea viral bovina; las vacunas; la prospección tecnológica; virus; infección; patentes.

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Declaración de originalidad

Yo Luana Brito de Oliveira manifiesto mi interés de someter a la evaluación de los dictaminadores que asigne la revista Razón y Palabra, el texto El control de la diarrea viral bovina (VDVB): un estudio centrado en los documentos de patente del cual soy autor.

Afirmo que ese texto, de mi autoría, es inédito.

Someto a dictamen del Comité Editorial de Razón y Palabra el referido texto el día 2016-06-11.

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Nombre y Firma.