

## TECHNOLOGY PROSPECTING OF INFANT STOOL AS A SOURCE OF NOVEL PROBIOTIC PRODUCTS

## PROSPECÇÃO TECNOLÓGICA DE FEZES DE LACTENTES COMO FONTE DE NOVOS PRODUTOS PROBIÓTICOS

Hermínio Benítez Rabello Mendes<sup>1,2</sup>, Julio Plaza-Díaz<sup>4</sup>, Maria Rosa Quaresma Bomfim<sup>2</sup>, Angel Gil Hernandez<sup>4</sup>, and Valério Monteiro-Neto<sup>2,3</sup>

<sup>1</sup> Programa de Pós-graduação em Biodiversidade e Biotecnologia da Amazônia Legal-Rede BIONORTE, Universidade Federal do Maranhão-UFMA, São Luís-MA, Brasil

[herminio.mendes@ceuma.br](mailto:herminio.mendes@ceuma.br)

<sup>2</sup> Universidade CEUMA, São Luís-MA, Brasil

[marqbomfim@gmail.com](mailto:marqbomfim@gmail.com)

<sup>3</sup> Universidade Federal do Maranhão-UFMA, São Luís-MA, Brasil

[vmonteironeto@ceuma.br](mailto:vmonteironeto@ceuma.br)

<sup>4</sup> Universidad de Granada, Granada, Andalucía, España

[jplaza@ugr.es](mailto:jplaza@ugr.es); [a.gil@ugr.es](mailto:a.gil@ugr.es)

### Abstract

*Probiotics are live microorganisms that provide health benefits to the host when they are ingested in adequate amounts. The strains most frequently used as probiotics include lactic acid bacteria and bifidobacteria. These microorganisms have significant potential as therapeutic options for a variety of diseases, but the mechanisms responsible for these effects have not yet been fully elucidated. In general, new probiotic strains for human use are sourced from human intestinal flora and breast milk. This study sought to survey the existing research regarding the potential for and development of technologies regarding infant stool-associated probiotics. The study was performed using information from the European Patent Bank, the Bank of the World Intellectual Property Organization and the database of the National Institute of Industrial Property of Brazil. The most abundant international classification prospected was Subsection C12, particularly class A61N. The Republic of Korea has the most patents filed. The results indicate a promising area with significant growth in the number of patents.*

**Keywords:** infant stools; probiotics products; technology prospecting; patents

## 1. Introduction

According to the Food and Agriculture Organization of the United Nations and the World Health Organization (WHO), probiotics are live microorganisms that confer a health benefit to the host when they are administered in adequate amounts (FAO/WHO, 2006). Specially, bacteria belonging to *Bifidobacterium* and *Lactobacillus*, which are the predominant and subdominant groups of the gastrointestinal microbiota, respectively, are the most widely used probiotic bacteria and are included in many functional foods and dietary supplements (GOURBEYRE et al., 2011). Generally, the selection of new probiotic strains for human use is sourced from human intestinal flora and breast milk (MARTIN et al., 2009). With a long history of the safe use of probiotics in fermented dairy products and growing recognition of their beneficial effects on human health, the food industry has become increasingly interested in these types of microorganisms (SHERIDAN et al., 2014). Often, the criteria for the selection of probiotics include tolerance to gastrointestinal conditions (gastric acid and bile), the ability to adhere to the gastrointestinal mucosa and competitive exclusion of pathogens (SANDERS, 2013). The mechanisms underlying the beneficial effects of probiotics are largely unknown but are likely to be multifactorial. Several mechanisms related to the antagonistic effects of probiotics on various microorganisms include the following: secretion of antimicrobial substances, competitive adherence to the mucosa and epithelium, strengthening of the gut epithelial barrier, and modulation of the immune system (NEAL-MCKINNEY et al., 2012; GIORGETTI et al., 2015).

Probiotic bacteria, both native and those introduced by feeding the host organism, can control the initiation and/or development of many pathogenic microorganisms, including *Salmonella typhimurium*, *Shigella* spp., *Clostridium difficile*, *Campylobacter jejuni* and *Escherichia coli*. Probiotics also provide important protection against urogenital pathogens such as *Gardnerella vaginalis*, *Candida albicans*, and *Chlamydia trachomatis* (MENARD, 2011).

Thus, these probiotic strains have been the subject of numerous studies because of an increase in the variability of microbial species that have been discovered and tested with potential probiotic capabilities. This change has meant that the previous target audience, consisting of elderly people, children and adults with poor health, has since expanded to also cover healthy individuals and even animals (KORTERINK et al., 2014)

Therefore, the accelerated development of scientific knowledge regarding the role of probiotics conveyed by dairy products and certain non-dairy products on the health of the host will almost certainly result in an expansion of the range of probiotic product options available to consumers (ROWLAND et al., 2010).

Furthermore, consumers are now more aware of probiotics and are increasingly opting for products that support a balanced lifestyle, provide health benefits and are attractive from a sensory standpoint. Consequently, the market for these products is increasingly competitive.

The objective of this research is to conduct a survey on patent bases of documents related to probiotic products from infants stools, in order to evaluate the panorama of the use of this raw material in the elaboration of these products for human health.

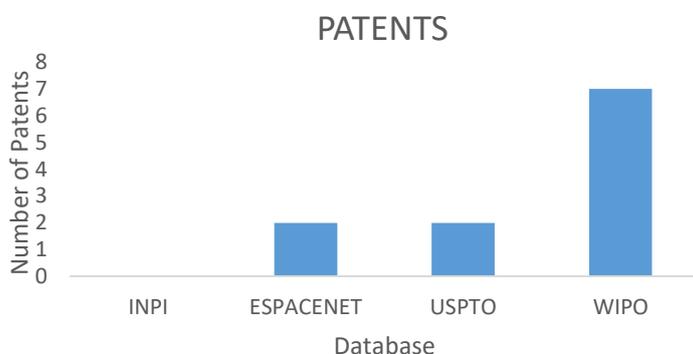
## 2. Methods

We used the following terms in conjunction with probiotics in the database search: infant stools, breast-fed-infant stools, feces of infants, and baby's stool. The databases used for patent research were: INPI - National Institute of Industrial Property; Espacenet - European Patent Office (EPO); USPTO - United States Patents and Trademarks Office; and WIPO - Intellectual Property Digital Library. The databases used for research papers, theses and dissertations were CAPES Periodicals; PubMed; and SCIELO. Initially, the search in the patent databases used the search term "probiotic and infant stool", which resulted in a much lower number of results in the EPO and WIPO databases compared with the USPTO database.

## 3. Results and discussion

The searches of the patent databases (INPI, EPO, USPTO and WIPO) identified a total of 7 relevant patents in the WIPO database, 2 patents in the EPO database and 2 patents in the USPTO database, as shown in the data presented in Figure 1. No patents were found in the INPI database.

Figure 1. Patents filed by database

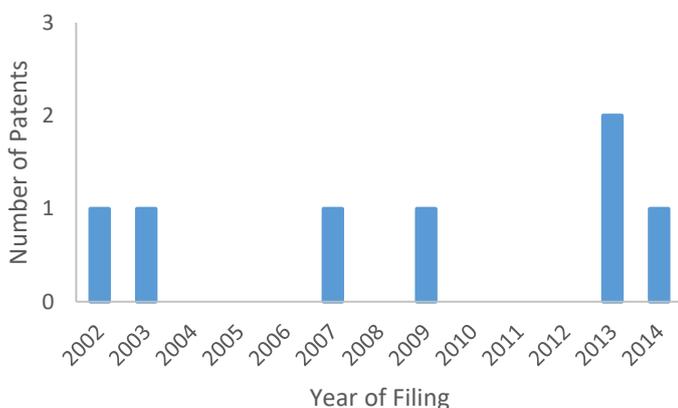


Source: Author's own figure

Recently, the INPI has concentrated on using the system of industrial property for more than its function of protecting intellectual property. The restructuring work, undertaken since 2004, has intended to allow use of the system as a tool of empowerment and competitiveness, which are essential to improving countries' economic and technological development (BARROSO et al., 2009)

The documents identified by our searches provided us with the number of relevant patents deposited each year. Using the WIPO, which is the most specific patent database (because the necessary information to register a patent in the WIPO includes a set of legal references related to the patent's theme of development), we noted that the deposition of patents fluctuated in the past decade but remained constant in recent years, although the last year of record is 2014.

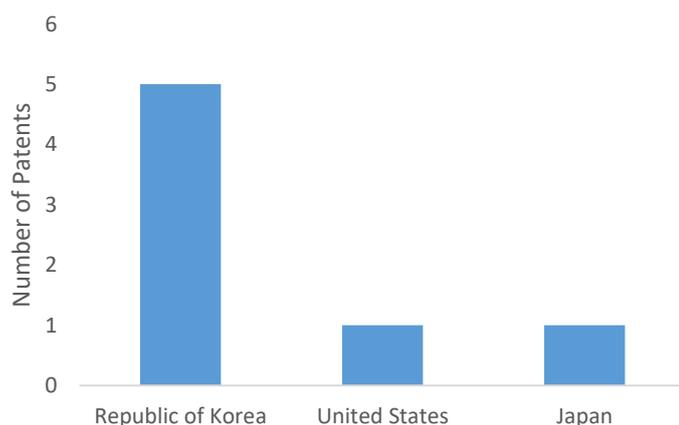
Figure 2. Number of patent filed per year, 2016



Source: Author's own figure

The analysis of the country of origin of each depositor can be observed in Figure 3. The Republic of Korea is the largest patent holder, with 5 deposited patents. The United States and Japan each have only one registered patent.

Figure 3. Patents filed by country of origin, 2016



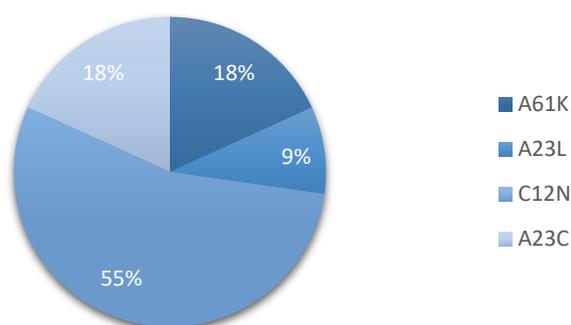
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Brazil does not have any patents in the area of probiotics associated with infant stools. perhaps this fact maybe associated with the provisions of Brazilian Law n° 13.123/15 which provides for access to genetic heritage, protection and access to associated traditional knowledge, and sharing of benefits for the conservation and sustainable use of biodiversity. However it is possible to patent genetically modified microorganisms, except for all plants or animals or parts thereof (MATTOS; CARDOZO, 2013). In Brazil, the ANVISA, National Sanitary Surveillance Agency, which is responsible for certifying the production of food products, decided to exclude the list of approved probiotics and defines that the company should propose a functional or health claim and it will be evaluated case by case, based on the definitions and principles set out in Resolution no. 18/1999.

At the same time, functional properties and/or health claims on a food label are tools that allow the consumer to know the possible benefits the food can offer. However, it is necessary to clearer rules for the industry so that the consumer is not deceived by false cure promises (SILVEIRA et al., 2009)

Among the documents identified in the survey, 55% are related to the field of microorganisms or enzymes and their compositions (C12N); 18% are in the area of food, food products and non-alcoholic beverages and preparations for medical purposes (A61K and A23C, respectively); and 9% are in the area of dairy products (A61K) (Figure 4).

Figure 4. Patents filed by application area, 2016.



Source: Author's own figure

As proposed by Vasconcellos et al. (2001), the subclass C12N was used as most representative of modern biotechnology, as it encompasses the technologies related to "Microorganisms or enzymes; their compositions; propagation, preservation or maintenance of micro-organisms or tissues; genetic engineering or mutation; culture mediums". Significant advances in the area of biotechnology in Brazil came mainly with the approval of Law No. 9279/96, which controls industrial property rights and obligations.

A61K (preparations for medical, dental or hygienic purposes) and A23C which is part of Section A - for human needs, linked to class 23 related to food or food products; not covered by other classes and subclass C dairy products, ex. milk, butter, cheese; substitutes for milk or cheese; important feature associated mainly with products with probiotic purposes.

Among the probiotics, the genera *Bifidobacterium* and *Lactobacillus* stand out (VARAVALLO et al., 2008), in particular, the species *Lactobacillus acidophilus* (THAMER; PENNA, 2005). These genera are present in yogurts, fermented dairy products and dietary supplements (RAIZEL et al., 2011). *Enterococcus faecium* are also employed, but on a smaller scale, in addition to other lactic acid bacteria, non-lactic acid bacteria and yeasts (PROBIOTICS, [2010?]).

The search on patent databases and scientific production identified 17,166 documents in PubMed (US National Library of Medicine), 596 scientific papers in the Scielo (Scientific Electronic Library Online) and 15,672 scientific papers in the CAPES database, as shown in Table 1.

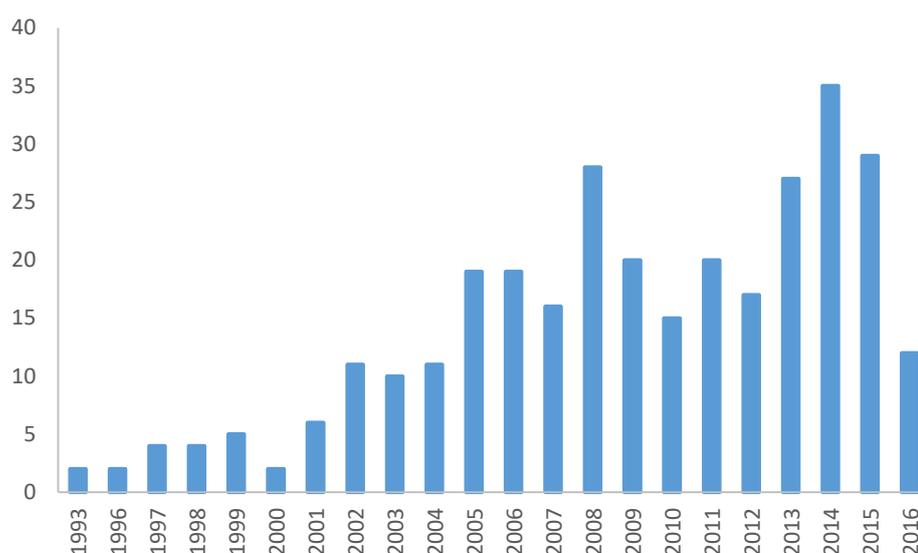
Table 1. Number of research papers, theses and dissertations from keyword searches in different databases

<b>Keyword</b>	<b>CAPES</b>	<b>PubMed</b>	<b>SCIELO</b>
Probiotic*	15,478	16,682	573
Probiotic* and (breast-fed-infant stools OR infant feces OR baby's stool)	130	324	21
Food* and probiotic* and (breast-fed-infant stools OR infant feces OR baby's stool)	37	147	1
Probiotic* and Product* and (breast-fed-infant stools OR infant feces OR baby's stool)	27	13	1
<b>Total</b>	<b>15,672</b>	<b>17,166</b>	<b>596</b>

With the search keywords and associations using Boolean operators outlined in Table 1, the largest volume of documents was found with the PubMed search. This is because PubMed is the search engine for the MEDLINE database of references and abstracts, and MEDLINE is the largest medical and natural sciences database in the world.

According to the analysis of the articles extracted from MEDLINE by year, the annual production of work related to probiotics and associated with the word "infant stool" was scarce until the end of the 1990s and fluctuated greatly in the 2000s, with the highest number of publications in 2014. The number of scientific papers found was much higher than the number of patents in the WIPO database (Figure 5).

Figure 5. Annual number of articles deposited into the PubMed database (1992-2016).



Source: Author's own figure

#### 4. Conclusions

The Republic of Korea has largest number of patent applications in this area, followed by the United States and Japan. Brazilian legislation is not clear as to the use of probiotics, since in the market are found foods considered probiotics, and often used as medicines. Although, several scientific projects specifically in the area of probiotics has grown tremendously in recent years. The public expects future innovations to produce more diverse probiotic products aimed at contributing to the improvement of consumer health.

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