

Trends in Nanotechnology Patents Applied to the Health Sector

Adelaide Maria de Souza Antunes^{1,5,*}, Maria Simone de Menezes Alencar^{2,*},
Cicera Henrique da Silva³, Jeziel Nunes⁴ and Flávia Maria Lins Mendes⁵

¹Instituto Nacional de Propriedade Industrial, Praça Mauá, nº 7 sala 1011, Centro, Rio de Janeiro, Brazil; ²Fundação Oswaldo Cruz - Instituto de Comunicação e Informação Científica e Tecnológica em Saúde, Av. Brasil, 4.365 - Pavilhão Haity Moussatché - Manguinhos, Rio de Janeiro, CEP: 21.045-360, Brazil; ³Fundação Oswaldo Cruz - Instituto de Comunicação e Informação Científica e Tecnológica em Saúde, Av. Brasil, 4.365 - Pavilhão Haity Moussatché - Manguinhos, Rio de Janeiro, CEP: 21.045-360, Brazil; ⁴Instituto Nacional de Propriedade Industrial, Praça Mauá nº 7 sala 718, Rio de Janeiro, Brazil; ⁵Universidade Federal do Rio de Janeiro, Escola de Química, Av. Horácio Macedo, 2030, Centro de Tecnologia, Bloco I sala I-222, Cidade universitária, Rio de Janeiro, Brazil

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Abstract: The aim of the article is to present a method for identifying trends in patent applications for nanotechnology applied to the health sector around the world, based on the International Patent Classification. This classification divides the sector into: dental care, drugs, diagnostic kits, and medical apparatus & medical care. The Derwent database was mined for patent documents using nanotechnology terms associated with the IPC subclasses from the health subsectors. The number of patents was found to be rising, led by the United States, particularly universities and R&D centers. In the dental care subsector, nanotechnology was found to be used in composite material for manufacturing dental appliances. In drugs, the focus is on the use of nanoparticulate compositions comprising agents that are useful for a variety of diseases. In diagnostic kits, nanostructures have been patented that are capable of detecting target analytes. Meanwhile, in medical apparatus & medical care, patent applications have been made for nanocapsules and/or nanocomposite materials inserted in devices and guide catheters. A study was also made of patents in Brazil, where the same assignees and the same country (United States) as in the survey of global patents were found to be the leading patent applicants / holders.

Keywords: Health, international patent classification, nanotechnology, patents, patent analysis, technological trends.

1. INTRODUCTION

The use of patent analysis as a method for technological foresight yields strategic intelligence on technologies and can reveal competitive advantages derived from leadership in technological development. It gives an understanding of who the leading patent applicants/holders for a given technology are, enabling comparisons to be made between companies, countries or technological areas, as well as areas where patenting is intensive.

Several authors have investigated the future development of nanotechnology by data mining of patents [1-6]; what makes this study different is that it focuses exclusively on the area of health. Patent documents are the most important sources of technological information, as they contain 71% of all the technology developed around the world, while just 16% of the other sources (journals, congresses, seminars, etc.) will publish the technology divulged in full, and less than 13% of these same sources will publish it in part [7]. Another advantage of patent documents is that they follow a

global standard. The World International Property Organization (WIPO) developed a procedure for standardizing the bibliographical data in patent documents, using a minimum set of data that are followed by every country that is a member of this organization. One of the most important of these is the International Patent Classification (IPC), which classifies patents by the technologies they pertain to. Created in 1971 by the WIPO as a result of the Strasbourg Agreement, the IPC facilitates the systematization and organization of the information contained in patent documents [8]. The classification is reviewed periodically in order to keep pace with technical developments. The IPC's hierarchical structure is split into sections, subsections, classes, subclasses, groups and subgroups that take the level of detail down from the general to the very specific for the purposes of classifying patents.

The application of nanotechnology to the screening, diagnosis, and treatment of disease, known as nano-medicine, is an emerging field that has the potential to revolutionize individual and collective health care in the 21st century. At the beginning of this century, health, science and technology were identified as prerequisites for social and economic development, as set out in the United Nations Millennium Development Goals [9, 10].

In the field of nanotechnology, the United States has its own National Nanotechnology Initiative, a multiagency umbrella program to build, characterize and understand nanoscale

*Address correspondence to this author at the Instituto Nacional de Propriedade Industrial, Praça Mauá, nº 7 sala 1011, Centro, Rio de Janeiro, Brazil; Tel: (+55 21) 3037-3211; Fax: (+55 21) 2562-7426; E-mail: aantunes@inpi.gov.br; and Fundação Oswaldo Cruz - Instituto de Comunicação e Informação Científica e Tecnológica em Saúde, Av. Brasil, 4.365 - Pavilhão Haity Moussatché - Manguinhos, Rio de Janeiro, CEP: 21.045-360, Brazil; Tel: (+55 21) 3865-3260; Fax: (+55 21) 2562-7426; E-mail: salencar@icict.fiocruz.br

devices, and in which medicine is one of the priority areas. The National Institutes of Health, including the National Cancer Institute, are involved in the program [11].

Furthermore, major advances have been seen in medical devices that make use of nanotechnology. These enable less invasive procedures, reduce the risk of post-operative infection and improve recovery times for patients. Nanotechnology researchers from leading institutions around the world are studying a number of issues: biological processes (mimicry), with a view to creating new devices on a nanometric scale that will provide a better understanding of life processes; the application of magnetic nanoparticles to disease diagnostics; “automated diagnosis”, which offers the opportunity to monitor the state of health of an individual permanently (as already happens with astronauts and SWAT teams); nanoparticle systems for the delivery of drugs (e.g. brain tumors, accessing the blood brain barrier). From this point on, it is likely that the developments will be far more radical [12]. These prognoses are starting to gain shape in the many nanotechnology solutions already available on the market, and can also be seen in the huge number of patent applications being made around the world.

Nanotechnology also presents real potential for developing techniques capable of repairing or reproducing tissue, diagnosing diseases at a very early stage (e.g. cancer), delivering medicine on the cell level, and even reversing diseases with the functional replacement of living tissue (either natural or not) or even synthetic tissue. Breakthroughs of this kind have the potential to radically alter the way health care is delivered, since with this technology it is possible to monitor the state of health of each client/patient, taking preventive action and reducing the need for medical check-ups in the presence of a doctor, who will only be needed to step in under certain circumstances. Technology of this kind reduces the time taken to make error-free diagnoses to a minimum, giving many more people access to health care based on these advances. The emerging scientific literature on the use of nanotechnology in dental care points to its use in fillers for dental composite resins. Such innovations have the capacity to improve people’s quality of life, increase their life expectancy and reduce the total cost of health care [13-17].

Nanotechnology is also on the agenda of developing countries like Brazil, where the Brazilian Agency for Industrial Development (Agência Brasileira de Desenvolvimento Industrial) undertook a foresight study in conjunction with the Center for Management and Strategic Studies (Centro de Gestão e Estudos Estratégicos) into the importance of nanotechnology in medicine and health to the country’s development [18].

Nanotechnology is not confined to a single field of endeavor, but exploits the idiosyncratic properties of matter on a nanoscale across many different fields of modern engineering. Consequently, a given nanotechnology patent may have implications for semiconductor design, biotechnology, materials science, etc [19]. Furthermore, there are already nanotechnology patent applications that anticipate the difficulties the intellectual property system will have to face in the short term, from the definition of what “nano” means to the definition of the concepts of invention and patentability, since a nanotechnology could be just a reproduction of an

existing product or structure on an atomic scale, or may actually be novel or even a novel step.

Given this initial overview of nanotechnology and its applications in the health sector, this study was developed with the aim of presenting a method for mining patent data in order to identify global trends in the patenting of nanotechnology with applications in the health sector. This method is also used to investigate similar patenting trends in Brazil, providing a case study that could be applied to any country or region of interest.

Taking into account the issues raised in the specialized literature concerning the application of nanotechnology to the health sector, the findings of our study into patenting trends was scrutinized with a view to verifying the following hypotheses:

- 1) In view of the America’s National Nanotechnology Initiative, is the United States the leading patent holder?
- 2) Given that science and technology are prerequisites for the development of countries, as set out in the Millennium Development Goals, are universities the leading patent applicants / holders in the health sector?
- 3) In the light of current research into disease diagnostics, medicine delivery, medical devices that enable less invasive procedures, and fillers in dental care, do the main patent applications address the concerns of this research?
- 4) Taking Brazil as a case study of a developing country, do the world’s leading patent holders also make patent applications in Brazil? Do Brazilian universities hold any patents in nanohealth?

2. METHOD

The database used for the patent data mining was the Derwent Innovations Index (DII), produced by Thompson Scientific, which contains patent data from as far back as 1966 (starting data varies according to the technological area) from over 40 patent offices around the world. The DII was accessed via the CAPES periodicals portal, a service provided by the Brazilian government to public universities and research centers of excellence in the country.

To select the patents related to nanotechnology in health, these two concepts (nanotechnology and health) were combined in different forms.

In the International Patent Classification (IPC), technology is divided into sections. As nanotechnology involves a variety of different technologies and is relatively recent from the perspective of intellectual property, the IPC does not yet have a full set of classifications to represent it. Only in version 7 did the IPC include class B82, referring to nanotechnology, but it is not completely comprehensive, since it encompasses only subgroup B82B¹, which relates to “nano-structures; manufacture or treatment thereof”. Therefore, in order to identify the nanotechnology-related patents, we not only searched the B82B subclass, but also used keywords

¹ In the IPC 2011.01 version, B82 underwent some changes, including subgroup B82Y (specific uses or applications of nano-structures; measurement or analysis of nano-structures; manufacture or treatment of nano-structures).

from titles and abstracts. The choice of keywords was based on the author's prior experience [1, 20] and expanded by observations of the most frequent terms present in a search made of the Web of Science based on the search strategy presented in an article by Porter *et al.* [21]. The terms used are presented in Table 1.

The second concept needed for our search was health. This sector was delineated by means of an analysis of the IPC classes and subclasses related to the topic made by experts from the Brazilian Industrial Property Agency (Instituto Nacional de Propriedade Industrial) and researchers at Fundação Oswaldo Cruz, a leading R&D center in Brazil that operates under the auspices of the Ministry of Health. This analysis resulted in the segmentation of the health sector into four subsectors based on the Health section in the IPC: (i) dental care, (ii) drugs, (iii) diagnostic kits, (iv) medical apparatus & medical care, the last of which is split into seven subclasses, as shown in Table 2. These four subsectors are covered in section A (Human Necessities), subsection "Health; Life-Saving; Amusement", class A61 (medical or veterinary science; hygiene). For the diagnostic kits subsector, other subclasses (G01 and C12Q) were also used to supplement subclass A61B [22, 23].

Combined searches were then undertaken using both concepts (nanotechnology and health) for each of the health subsectors and respective subclasses. The raw data were retrieved and the patent documents published between 2000 and 2010 were selected. The software used to do this was VantagePoint®, developed and sold by Search Technology, which is a data mining tool that can process large quantities of data by automating tasks like standardization and production of reports and maps to make it easier to visualize for analysis purposes [24].

The data mining was first done on a broad scale for patents in the area of health, then for each of the IPC classes and subclasses. In order to assess trends, the country that had the highest number of patents / patent applications was identified, then the main patent applicants/holders in this country. For each top patent applicant/holder an analysis was undertaken of the titles and abstracts relative to that IPC subclass in order to identify the area for which they had most patents/applications.

As a case study of the application of this method for a given country, an analysis of health care patenting in Brazil was undertaken. In this case, alongside the macro view, the main patent holders/applicants for each of the subsectors and IPC subclasses were identified. The analysis of the focus of patenting of the top patent holders/applicants was undertaken using the same method as described above.

3. ANALYSIS OF GLOBAL TRENDS

The combined search, using both concepts, of patents published between 2000 and 2010 yielded 9719 patent documents. Fig. (1) shows the growth in patent applications for nanotechnology designed for the health sector. It can be seen that every three years or so, the number of patents doubles. For instance, in 2002 around 400 patent applications were filed for nanotechnologies in the health sector around the world, while in 2005 there were 800. A similar trend can be seen between 2000 (200) and mid 2002 (400) and between 2002 (400) and 2005 (800).

It should be explained that 2010 is not contained in the graph because there is a lag in the database consulted due to the standard period during which the contents of patent applications can be kept secret.

In market terms, it can be seen that the USA is the leading patent holder in the Health Sector with around 5500 nano-health-related patents. In second place comes China, but it lags far behind the leader, with just over 1100 patents. Fig. (2) shows the five leading patent holders in the health sector applied to nanotechnology.

Fig. (2) shows clearly that two continents, North America and Asia, are at the forefront of the development of nanotechnology in the health sector. The same trend was noted by Alencar *et al.* in a study of scientific articles on nanotechnology [25].

The general table of results obtained per Health subsector / IPC subclass is shown in Table 3. The subsector with the most patent applications is drugs, followed by medical apparatus & medical care, diagnostic kits and dental care.

In many cases, a single patent may appear in more than one subsector, but for the purposes of analyzing trends, each IPC subclass was initially assessed in isolation.

Table 1. Keywords used in search

Keywords			
Fulleren*	Nanob*	Nanoc*	Nanod*
Nanoelectr*	Nanoemuls*	Nanoengineer*	Nanof*
Nanog*	Nanohybr*	Nanoj*	Nanolithograp*
Nanomateri*	Nanomedic*	Nanometrol*	Nanomesh*
Nanonet*	Nanop*	Nanorod*	Nanos*
Nanot*	Nanowire*	Nems	Quantum-dot*
Quantum-wire*	Quasi-crystal*	Spintronic*	

Source: prepared by the authors

N.B. The asterisk is used as a wildcard, so that any word with this root will be searched for.

Table 2. Subsectors of Health and Respective IPC Subclasses

Subsectors	IPC Subclass	Description
Dental care	A61C	Dentistry; oral or dental hygiene
Drugs	A61K not (A61k-007 or A61k-008)*	Preparations for medical, dental
	A61P	Therapeutic activity of chemical compounds or medicinal preparations
Diagnostic Kits	G01N	Investigating or analysing materials by determining their chemical or physical properties
	C12Q	Measuring or testing processes involving enzymes or micro-organisms; compositions or test papers therefore; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes
	A61B	Diagnosis; surgery; identification
Medical apparatus & medical care	A61F	Filters implantable into blood vessels; prostheses; orthopaedic, nursing or contraceptive devices; fomentation; treatment or protection of eyes or ears; bandages, dressings or absorbent pads; first-aid kits
	A61G	Transport or accommodation for patients; operating tables or chairs; chairs for dentistry; funereal devices
	A61H	Physical therapy apparatus, e.g. Devices for locating or stimulating reflex points in the body; artificial respiration; massage; bathing devices for special therapeutic or hygienic purposes or specific parts of the body
	A61J	Containers specially adapted for medical or pharmaceutical purposes; devices or methods specially adapted for bringing pharmaceutical products into particular physical or administering forms; devices for administering food or medicines orally; baby comforters; devices for receiving spittle
	A61L	Methods or apparatus for sterilising materials or objects in general; disinfection, sterilisation, or deodorisation of air; chemical aspects of bandages, dressings, absorbent pads, or surgical articles; materials for bandages, dressings, absorbent pads, or surgical articles
	A61M	Devices for introducing media into, or onto, the body; devices for transducing body media or for taking media from the body; devices for producing or ending sleep or stupor
	A61N	Electrotherapy; magnetotherapy; radiation therapy; ultrasound therapy

*Subgroups A61K-007 and A61K-008 relate to cosmetics or similar toilet preparations.

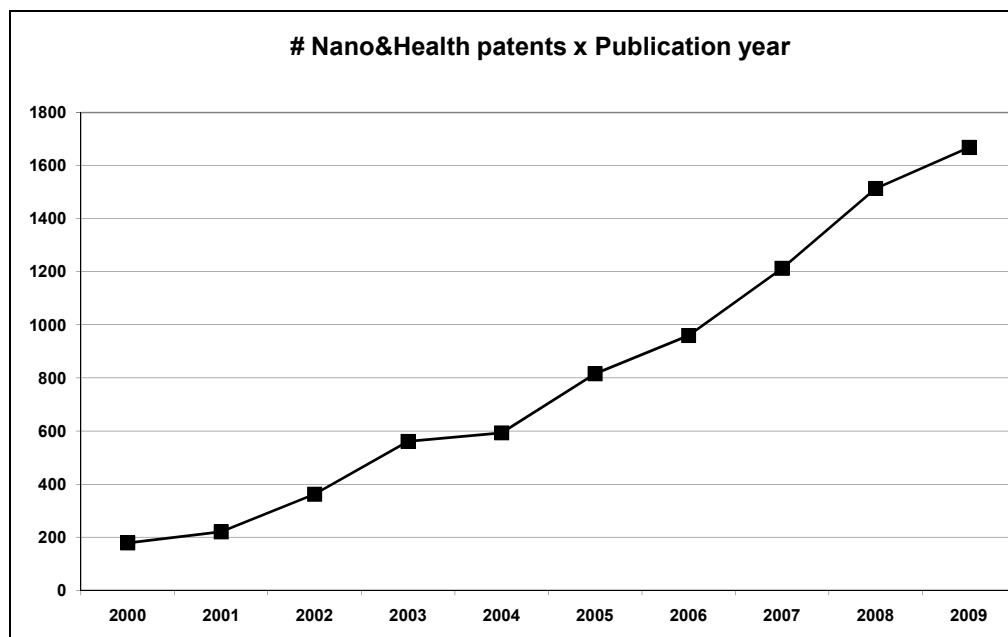


Fig. (1). Number of nano-health-related patents per year.

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

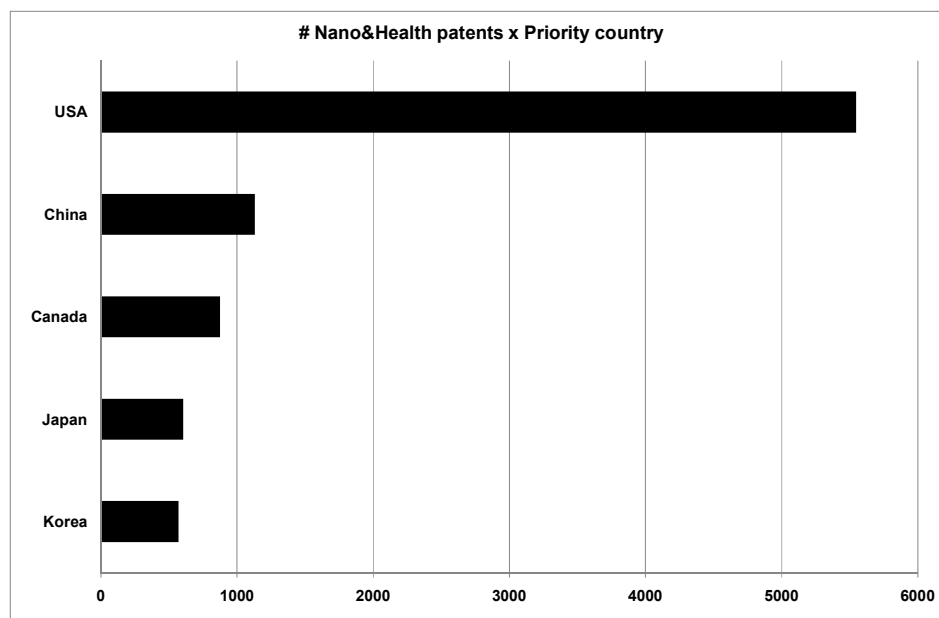


Fig. (2). Number of nano-health-related patents per priority country.

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

The sum of the total number of patents in Table 3 is greater than the total number of patents because a single patent may be classified in more than one health subsector or IPC subclass.

Trends in Health Subsectors

Analyzing all the sectors as a whole, there is a marked presence of education and research institutions amongst the

top patent holders and applicants, especially the University of California and the Massachusetts Institute of Technology, the former being the top firm in nano-health, with 132 patents / patent applications (left-hand column) in the period under study. Table 4 shows the ten leading organizations and the number of patents for each one in the health subsectors analyzed in this study.

Table 3. Number of Patent Documents Relating to Nanotechnology and Health Published between 2000 and 2010

Health subsectors /IPC Subclasses	No. of Patents
Dental care	151
Drugs	6,457
Diagnostic kits	2,216
Medical apparatus & medical care	2,627
<ul style="list-style-type: none"> Filters implantable into blood vessels; prostheses; orthopaedic, nursing or contraceptive devices; fomentation; treatment or protection of eyes or ears; bandages, dressings or absorbent pads; first-aid kits 	973
<ul style="list-style-type: none"> Transport or accommodation for patients; operating tables or chairs; chairs for dentistry; funereal devices 	14
<ul style="list-style-type: none"> Physical therapy apparatus, e.g. devices for locating or stimulating reflex points in the body; artificial respiration; massage; bathing devices for special therapeutic or hygienic purposes or specific parts of the body 	42
<ul style="list-style-type: none"> Containers specially adapted for medical or pharmaceutical purposes; devices or methods specially adapted for bringing pharmaceutical products into particular physical or administering forms; devices for administering food or medicines orally; baby comforters; devices for receiving spittle 	90
<ul style="list-style-type: none"> Methods or apparatus for sterilising materials or objects in general; disinfection, sterilisation, or deodorisation of air; chemical aspects of bandages, dressings, absorbent pads, or surgical articles; materials for bandages, dressings, absorbent pads, or surgical articles 	1409
<ul style="list-style-type: none"> Devices for introducing media into, or onto, the body; devices for transducing body media or for taking media from the body; devices for producing or ending sleep or stupor 	500
<ul style="list-style-type: none"> Electrotherapy; magnetotherapy; radiation therapy; ultrasound therapy 	342

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

Table 4. Leading Global Patent Holders in Nanotechnology and Health and Respective Subsectors of Application

No. of Patents	Patent Holder	Subsector			
		Drugs	Diag. Kits	Medical App. & Medical Care	Dental Care
132	Univ California	86	62	25	4
122	Elan Pharma Int Ltd	122	4	16	0
103	Massachusetts Inst Technology	79	36	26	1
99	Boston Sci Scimed Inc	26	16	97	1
98	Univ Texas System	76	43	16	0
66	Cnrs Cent Nat Rech Sci	47	27	10	0
62	3M Innovative Properties Co	49	3	22	14
62	Northwestern Univ	33	32	12	0
55	Univ Florida Res Found Inc	41	29	8	0
53	Abbott Cardiovascular Systems Inc	34	2	37	0
53	Searete LLC	36	16	12	0

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

As observed above, one patent may be associated to more than one IPC subclass, such as the University of California, which has patents / applications in all four health subsectors with links to nanotechnology. While it is the leader in diagnostic kits with 62 patents (column 4/Table 4), it also has a strong presence in the drugs subsector (86, column 3/Table 4).

Nevertheless, in many cases the same patent document is related to one or more area. In drugs, of the 86 patent applications (column 3/Table 4) made by the University of California, 52 are exclusive to this subsector, 24 relate to both drugs and diagnostic kits, and nine refer to drugs and medical apparatus & medical care, as can be seen in Fig. (3). Below, showing the three subsectors for which this university has made most patent applications.

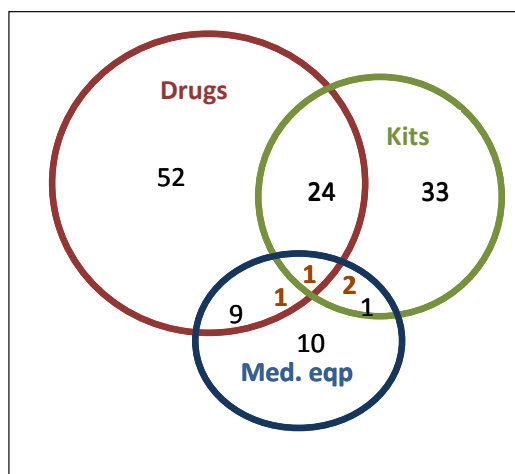


Fig. (3). Distribution of the University of California patents in nanotechnology per health subsector.

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011. Dental care does not appear in this figure.

The analysis of the applications made by the second largest patent holder / applicant, Elan Pharma, with a total of 122 nanotechnology patents in the health sector, can be seen in Fig. (4). All the applications are classified as drugs, of which four are also related to diagnostic kits, and 16 are also related to medical apparatus & medical care. No applications were found by this company for dental care applications.

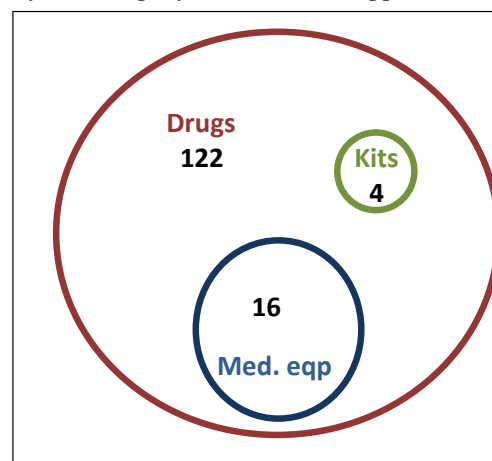


Fig. (4). Distribution of the Elan Pharma patents in nanotechnology per health subsector.

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

The Massachusetts Institute of Technology (MIT) is the third largest patent holder / applicant (103) considering the three most representative subsectors. The majority of its patents are exclusively for drug applications (47), but 16 of these are also related to diagnostic kits, and another 16 involve both drugs and medical apparatus & medical care. Fig. (5) shows the patents for nanotechnology applied for / held by MIT, showing the overlaps of the health areas they can be

applied to. There is one patent document that is not represented in Fig. (5) which relates jointly to dental care, diagnostic kits and medical apparatus & medical care.

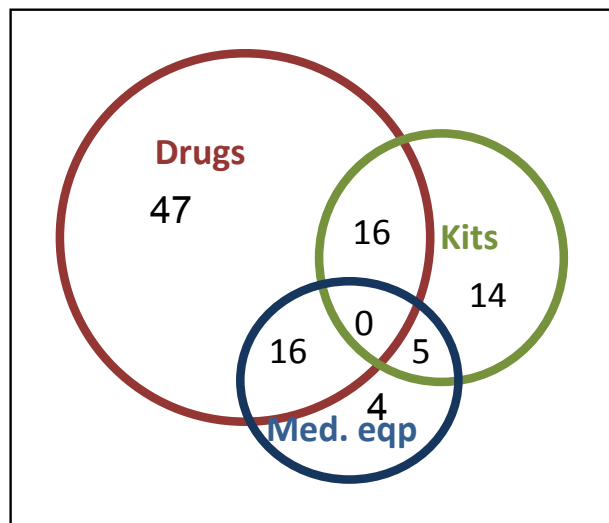


Fig. (5). Distribution of the MIT patents in nanotechnology per health Subsectors.

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

Below, we set out the trends for each subsector using the proposed method: selection of leading country, and top patent holders/applicants in that country. A few examples are given of the technologies being patented by the leading patent holders / applicants.

Subsector Dental Care

In the last ten years 151 patents have been applied for / granted that apply nanotechnology to dentistry, oral or dental hygiene (A61C).

The leading country is the USA, with 52% of the patents/applications. Of all the American patent holders/applicants, 3M Innovative Properties Co. holds the largest share: 18%. Its patents are for dental prostheses (A61C13/00), filling or capping teeth (A61C5/00) including tooth crowns, and securing crowns in the mouth (A61C5/08). Some examples of these patents are:

- Mill blank comprises an uncured self supporting hardenable organic composition. The use is for manufacturing dental appliance such as crown, inlay, onlay, bridge, orthodontic appliance. The organic composition consists of increased composite material which contains polymerizable resin system, an initiator system and a filler system. A portion of the filler system has particulate filler and inorganic material comprise nanoscopic particles [26].
- Hardenable dental composition, useful for forming dental restorative, as orthodontic adhesive and filler and for preparing. The nanoscopic particles comprise fumed silicon [27].

Subsector Drugs

This area covers preparations for medical (A61K) and therapeutic activity of chemical compounds or medical preparation (A61P).

In the ten-year period under study, 6457 patents were applied for / granted for drug-related innovations by 4095 different entities that make some use of nanotechnology. The USA holds the lion's share of these (around 60%). Four organizations from this country hold or have applied for 75 or more patents: Elan Pharma (121), the University of California (86), Massachusetts Institute of Technology (76), and the University of Texas System (75).

- Elan Pharma has patents/applications for medical preparations characterized by special physical form and by carriers, inert additives.
- The University of California acts in medical preparations by special physical form but also in preparations for testing *in vivo* and medical preparations containing peptides for antineoplastic agents.
- The Massachusetts Institute of Technology is active in antineoplastic agents, gene therapy, medicine preparations containing organic active ingredients and medical preparation characterized by special physical form.
- The University of Texas System also acts in medicine preparations containing antigens or antibodies for antineoplastic agents.

Examples of Elan Pharma Institute Ltd.'s latest patents/applications are:

- Nano particulate angiogenesis inhibitor composition e.g. for treating or preventing tumor or cancer growth. The composition is bio adhesive; also used for treating inflammatory condition (rheumatoid arthritis) [28].
- Composition for treating patients suffering moderate or severe migraine, comprises triptan nanoparticulate non steroidal anti inflammatory drug nanoparticulate (naproxen) and surface stabilizer adsorbed on its surface [29].
- Nanoparticulate injectable composition, useful to relieve symptoms of e.g. arthritis, comprises an active agent (meloxicam) [30].
- Pharmaceutical compositions used comprises solid particles of immunosuppressive agent coated with surface modifier(s). The particles have an average effective particle size of less than 50 nm to less than 2 μ m [31].

Subsector Diagnostic Kits

The diagnostic kits area covers the following categories: investigating or analyzing materials by determining their chemical or physical properties (G01N); measuring or testing processes involving enzymes or micro-organisms (C12Q) and diagnosis, identification (analyzing material) (A61B).

In the first decade of this century, 2216 patents for diagnostic kits were applied for / granted, with the second half of the decade seeing an almost twofold rise in patent activity compared to the first half.

The country with the most patents and patent applications is again the USA, with 66% of the total. The main US patent holders are the University of California, with 52 patents, followed by Nanosphere, Intel Corp, University of Texas System, Massachusetts Institute of Technology, Northwestern University, Agilent Technologies Inc and the General Hospital (Gen Hospital Corp), all with over 20 patents.

A detailed analysis of the University of California patents reveals a great number of patents in testing and measuring processes involving enzymes or microorganisms; compositions therefor (C12Q1/68 and C12Qa/02); processes of preparing such compositions involving nucleic acids (C12Q1/68) or involving viable microorganisms (C12Q1/02). Some examples of these patents include:

- Colorimetric bio-barcode method for detecting nucleic acids, in urine; forms complex between nucleic acids, porous microparticle probe and magnetic nanoparticle probe if nucleic acid is present in sample [32].
- Composition for modulating gene expression or gene product production in a cell; comprises nanostructure that absorbs energy at a near infrared wavelength. The composition and method allow for the perturbation of single gene expression and the study of this single effect on an entire system of genes and proteins, thus having far-reaching implications in biotechnology, systems biology, cancer therapy and gene therapy [33].
- A device for the detection of kinase and/or phosphatase surface comprising features that enhance Raman scattering. This feature comprises nanoscale features e.g. nanoscale pyramids, nanoscale dots, nanotubes etc [34].

Nanosphere Inc., with 33 patents/applications, focuses on measuring or testing processes involving enzymes or microorganisms and investigating or analyzing materials. Some examples are:

- Method for detecting the presence of target analytes in a sample by illuminating nanoparticle probes in the confinement conditions. This invention provides high-sensitivity detection of target proteins or nucleic acids based on flow analysis of single particles [35].
- Detection of target analyte, e.g. nucleic acids or proteins, useful for diagnosis of genetic and infectious diseases. Detection of target analyte having at least two portions, comprises a type of nanoparticle having a specific binding complement of a target analyte attached to the nanoparticle, the complement being capable of recognizing at least two different segments of the target analyte; forming a light scattering complex by contacting a sample containing specific binding complement with nanoparticle and with polysaccharide under conditions to allow binding of specific complement to two or more portions of the target analyte; illuminating the light scattering complex under conditions to produce scattered light from the complex; and detecting the scattered light from the complex as a measure of the presence of the target analyte. The method provides much higher sensitivity in nucleic detection. It enables the detection of aggregates in the presence of excess non-aggregate particles which drives hybridization in the presence of low target concentrations [36].

Subsector Medical Apparatus and Medical Care

Medical Apparatus and Medical Care involves seven health IPC subclasses connected to nanotechnology.

1st Subclass

Included in A61F: filters implantable into blood; prostheses, i.e. artificial substitute appliances for connecting them with the body; absorbent pads.

There were a total of 975 patents applied for / granted in the last ten years in this subclass, with 70% going to organizations from the United States. The top patent holders/ applicants from this country were Boston Sci Scimed (around 10% of the US patents), followed by Abbot Cardiovascular Systems Inc. and Kimberly-Clark Worldwide Inc., each with 5% of the US total.

The focus of Boston Sci Scimed's patents is on formation devices, e.g. blood filters, artificial heart valves and delivery devices (A61F2/82 and A61F2/06), examples of which are:

- The medical device is formed by depositing a biocompatible metallic layer. The metallic layer has a grain structure, nanocrystalline. The devices have desired mechanical properties and geometries used for forming stents, blood filters and artificial heart valves [37].
- The medical device e.g. guide catheter comprises at least one nanocomposite material and nanoparticulate filler [38].
- Nanocapsules for localized drug delivery comprise therapeutic agent useful for implantable or insertable medical devices [39].
- Nano-actuated medical device for deploying other medical devices (catheter and stent) comprises housing and nano actuator associated with housing. It is used for processing a tissue sample for biopsy using medical device [40, 41].
- Medical apparatus for medical treatment comprises a medical device sized for insertion into patient, having several nanotubes on one surface that enhance the performance and diagnostic capabilities of the medical device. A therapeutic agent is delivered into the target site, once the nanotube containing the therapeutic agent reaches the delivery site [42].
- Coating article useful in medical appliances e.g. stent; involves treating a solution comprising bioactive agent and carbon nanotube precursor to form several carbon nanotubes and applying the solution to the article [43, 44].
- Guide catheter has at least one component prepared from nanocomposite material; comprises matrix material and nanoparticulate filler particles [38].

At Abbot Cardiovascular Systems, the patents are for:

- Medical device (stent) useful for treating disorders, e.g. atherosclerosis, thrombosis, vascular aneurysm; comprises bioactive agent and nanoparticles [45].

Examples of Kimberly-Clark Worldwide's patents are for:

- Compositions useful for absorbent article, preferably diaper [46], method of reduction of odor involves contacting substrate containing thin coating of colloidal nanoparticles with odorous compound [47, 48].
- Disposable absorbed article has nanofabricated attachment unit with adhesive hairs; comprises hollow materials, microspheres and carbon nanotubes [49].

2nd Subclass

Included in A61G (A61G12/00, A61G7/057, A61G17/00, A61G17/06, A61G9/00). This group involves accommodation and beds for nursing, e.g. hospitals; devices for lifting patients or disabled persons; coffins, wrappings; sanitary devices.

In this group, there were only 14 patent applications submitted by 14 entities, nine being firms and five, inventors, dating from 2006 to 2010. No patents were identified for the first five years of the period under study. Some examples are:

Neubauer claims a coated narrow body substance provided with nano-technologically modified antimicrobial oligodyne silver compound. The coated narrow body substance prevents body odor; releases the active substance for long-term; and is comfortable and useful for wheelchair seats and arm supports [50].

DuPont has a patent for a nanosensor for detecting analytes for use in medical applications for bedridden persons; comprises semi-conductive carbon nanotube and responds to a target analyte by altering the redox potential of redox effectors in solution [51].

Inventors Sung C L. and Jeoung H. K. claim a multifunctional urn wrap used for preserving bones of dead bodies (improved antibacterial property) produced by depositing nanosilver colloidal on fabric and applying a mixture of nanosilver colloid [52].

Digomed claim a mobile roll car for use by doctors in hospitals, for guiding actual information e.g. test reports, of patients; has monitor housing exhibiting a degree of protection for contact. The surface of the monitor housing has an antimicrobial coating e.g. lacquering with a nanoscale silver as active substance [53].

3rd Subclass

This relates to physical therapy apparatus, e.g. percussion or vibration massage, exercisers for eyes; bathing devices for special therapeutic or hygiene purposes (A61H 23/02, A61H33/02).

Between 2002 and 2010, 42 patent applications were made by 28 firms; only two made more than one application: Sharp KK (three) and Candela Corp in partnership with Inolase 2002 Ltd (two).

Below are the Sharp KK patents:

- Therapeutic bathtub apparatus for treating various illness (e.g. diabetes treatment, central nerves) has nanobubble and/or nanosized medical component generating section combining nanobubble or a nanosized medical component with bath water from bathtub and circulates the bath water to the bathtub, so that the nanobubbles

are easily absorbed into the user's skin, thus obtaining a therapeutic effect for various illness and maintaining health [54, 55].

The patents held / applied for by Candela Corp in partnership with Inolase 2002 Ltd. concern the time (nanosecond) for the application of monochrome light.

- The invention controls the depth of light absorption by blood vessels under skin surface [56].
- Control of light absorption by blood vessels under skin surface: the wavelength is 400-1800nm. The pulse duration is 10 nanoseconds to 900nsec [57].

4th Subclass

This group concerns devices or methods specially adapted for bringing pharmaceutical products into particular physical or administering focus (A61J3/06, A61J3/07).

A total of 90 patents were applied for / granted between 2000 and 2010. The country with the most patents was the United States, with 41, distributed amongst a number of different organizations. The only firms to apply for two were Hewlett-Packard Development Co (HP), LP and UMD Inc. An example of the HP patent is:

Preparation of deposited bioactive agent in the form of nanoparticles that exhibit selected morphology. The particles, measuring less than 1 micron, may offer improved bioavailability when administered to a patient [58].

5th Subclass

This group relates to materials for catheters, prostheses or coatings therefor (A61L29/00, A61L27/00), materials for coating surgical articles, characterized by their function or physical properties (A61L31/14, A61L31/08, A61L31/16).

1409 patents were granted / applied for in the last ten years by 942 organizations, with 47% going to the United States.

The top patent holder/applicant is Boston Sci Scimed Inc., with 72 patents, followed by Abbott Cardiovascular Systems Inc. (27) and Kimberly-Clark Worldwide Inc. (21). Examples of the Boston Sci Scimed patents are:

- A process of covering the surface of medical devices useful in the treatment of, e.g. restenosis: Coating medical device to be implanted in the body of a patient involves spraying a carrier polymer at the exterior of medical device, and spraying therapeutic particles at the exterior of the medical device [59].
- Medical device comprises at least one nanocomposite material comprising matrix material and nanoparticulate filler particles; use in medical care as guide catheter. Also useful in urinary application, cardiovascular application, balloon, guide wire, etc. The device can be produced with a desired array of properties and capabilities using a lesser amount of materials and processing techniques, and the device allows for the delivery of therapeutic agent [38].
- A method of embedding nanoparticles into medical devices by spraying a solution containing the nanoparticles from a charged nozzle, evaporating the solution to form

a stream of charged nanoparticles, energizing electrode, having polarity opposite to charged nanoparticles, and placing the medical device in the stream so that the charged nanoparticles are embedded in the medical device upon impact [60].

- Nanocapsule for localized drug delivery comprises therapeutic agent, a polyelectrolyte multilayer shell encapsulating the therapeutic agent and a tissue specific ligand. For use in implantable or insertable medical device e.g. catheter, guide wire, stent, pacemaker, heart valve, used in the delivery of therapeutic agent, e.g. immunosuppressive and/or anti proliferative agents, to the body. By providing magnetic nanoparticles inside a biodegradable coating, upon inflation into patient, the number of particles will diminish, making the device less magnetic over time [61].

6th Subclass

This subclass concerns catheters, balloon catheters, devices for introducing or retaining media, e.g. remedies, in cavities of the body (A61M31/00, A61M25/00, A61M25/10, A61M29/00, A61M29/02, A61M25/01).

Between 2000 and 2010, 500 patents were applied for by/granted to 374 entities. The United States accounted for 66% of these, of which 10% went to Boston Sci Scimed Inc. Examples include:

- Guide catheter has at least one component prepared from nanocomposite material, comprising matrix material and nanoparticulate filler particles. By employing nanocomposite materials, medical devices can be produced with a desired array of properties using a lesser amount of materials and/or processing techniques [38]
- Other example is related to nano actuated medical device for, e.g. procuring tissue sample for biopsy, deploying other medical devices, e.g. catheter and stent, comprises housing and nano actuator associated with housing; the invention provides higher actuator forces and mechanical energy density [40].

7th Subclass

This covers electrotherapy, electrodes for implantation or insertion into the body, e.g. heart electrode (A61N 1/05, A61N 1/00).

In the time period in question, 342 patents or patent applications were identified, 80% for the United States, with two firms accounting for over ten each: Boston Sci Scimed (12) and Medtronic (11).

Boston Sci Scimed's patents / patent applications include:

- Medical device for implantation/insertion into subject for diagnostics, systemic/localized treatment of mammalian tissue or organ, has particle-containing region that comprises electrically aligned, elongated particle with matrix. The elongated particles comprise ceramic elongated particles, conductive elongated particles, carbon nanofilaments, carbon, nanotubes, derivatives carbon nanotubes, polymer-functionalized carbon nanotubes [62].

- Leadless implantable medical device, for e.g. stimulating cardiac tissue of patient, has electrodes comprising nanostructures, where portions of electrode nanostructures are partially encapsulated within living cells such as myocardial cells, so that the nanostructures are compatible with cell membranes, and hence facilitating growth of the cell membranes around the nanostructures while increasing cell life in a easy manner [63].

Analyzing all the patent documents for the seven subclasses of medical apparatus and medical care, a total of 2627 patents were identified, with the leading firms being Boston Sci Scimed (97 patents), Abbott Cardiovascular Systems (37 patents) and Medtronic (30 patents). The patents are often listed in more than one subclass. Subclass A61L, which also includes methods or apparatus for sterilizing materials or objects in general, disinfection and sterilization, is a category that applies to over half (54%) of the patents relating to Medical Apparatus and Medical Care. Another example is Boston Sci Scimed, around 30% of whose 97 patents are classified under A61L and A61F (filters implantable into blood vessels; prostheses, etc.).

4. CASE STUDY: BRAZIL

Patenting in nanotechnology and health in Brazil is spread amongst several foreign firms, headed by Elan Pharma. Only three of the ten biggest patent holders / applicants are Brazilian institutions, and all of these are public universities (Federal University of Minas Gerais, State University of Campinas, Federal University of Rio Grande Do Sul) Table 5. The patent applicants / holders for dental health are not amongst these leading organizations.

Elan Pharma's patents mostly relate to drugs, although two of their patents also relate to diagnostic kits. The Brazilian institutions focus primarily on drugs.

Health Subsectors in Brazil

In Brazil, a total of 352 patent documents were identified that involved nanotechnology applied to health for 2000 to 2010, corresponding to around 5% of the total patents / patent applications in the world. Their distribution in different areas of health is shown in Table 6.

Research in nanotechnology in conjunction with health expressed in terms of patent applications in Brazil from 2000 to 2010 shows that patents for drug applications predominate.

There were just eight patents applied for / granted for dental care, with 3M Innovative Properties Co. and Bayer Material Science AG accounting for two each, both focusing on material for dental prostheses filling capping teeth (A61C13/00, A61C13/08, A61C5/08).

In the period, 299 applications were made for nanotechnology patents with drug applications by 15 organizations, the largest being Elan Pharma, Merck & Co., Pfizer and the University of Illinois, with Elan Pharma accounting for 19 and the others with six apiece. The focus of all the patents is on nanoparticulate composition useful for treating several diseases.

Table 5. Leading Holders / Applicants of Patents in Nanotechnology and Health in Brazil and Respective Sectors of Application

No. of Patents	Patent Applicant / Holder	Drugs	Diag. Kits	Medical App. & Medical Care
19	Elan Pharma Int Ltd	19	2	0
7	Cinvention AG	2	6	1
7	Blue Membranes GMBH	2	6	1
7	Federal University of Minas Gerais	6	2	0
7	Kimberly-Clark Worldwide Inc	5	7	1
6	Pfizer Inc	6	0	0
6	Asgari S	1	6	1
6	Unicamp (State University of Campinas)	6	0	0
6	Univ Illinois Found	6	0	3
5	Novartis AG	4	3	0
5	Federal University of Rio Grande do Sul	5	0	0
5	Johnson & Johnson	5	4	0

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

Table 6. Number of Patent Documents Relating to Nanotechnology and Health Published between 2000 and 2010 in Brazil

Health Subsectors /IPC Subclasses	No. of Patents in Brazil
Dental care	8
Drugs	299
Diagnostic kits	85
Medical apparatus & medical care	119
<ul style="list-style-type: none"> Filters implantable into blood vessels; prostheses; orthopaedic, nursing or contraceptive devices; fomentation; treatment or protection of eyes or ears; bandages, dressings or absorbent pads; first-aid kits 	48
<ul style="list-style-type: none"> Transport or accommodation for patients; operating tables or chairs; chairs for dentistry; funereal devices 	0
<ul style="list-style-type: none"> Physical therapy apparatus, e.g. devices for locating or stimulating reflex points in the body; artificial respiration; massage; bathing devices for special therapeutic or hygienic purposes or specific parts of the body 	1
<ul style="list-style-type: none"> Containers specially adapted for medical or pharmaceutical purposes; devices or methods specially adapted for bringing pharmaceutical products into particular physical or administering forms; devices for administering food or medicines orally; baby comforters; devices for receiving spittle 	12
<ul style="list-style-type: none"> Methods or apparatus for sterilizing materials or objects in general; disinfection, sterilization, or deodorization of air; chemical aspects of bandages, dressings, absorbent pads, or surgical articles; materials for bandages, dressings, absorbent pads, or surgical articles 	74
<ul style="list-style-type: none"> Devices for introducing media into, or onto, the body; devices for transducing body media or for taking media from the body; devices for producing or ending sleep or stupor 	19
<ul style="list-style-type: none"> Electrotherapy; magnetotherapy; radiation therapy; ultrasound therapy 	7

Source: Prepared by the authors using data collected from the Derwent Innovation Index in May 2011.

Elan Pharma applied for patents for medicinal preparations characterized by special physical form (A61K9/10).
Examples:

- Injectable nanoparticulate olanzapine composition, useful to treat e.g. central nervous system disorder and schizophrenia [64].

- Injectable nanoparticulate tacrolimus formulation for treatment or prophylaxis of e.g. organ refection and psoriasis [65].
- Nanoparticulate benzothioephene composition useful for treating osteoporosis and breast cancer [66].
- Nanoparticulate composition used as aerosol or injectable composition for treating e.g. status epilepticus and acute psychosis [67].

When it comes to diagnostic kits, Brazil has 85 patents / patent applications, but only five patent applicants / holders accounting for more than one patent: Bayer Material Science AG, University of Illinois Foundation, Astra-Tech AB, Becton Dickinson & Co and the University of Texas. The first two have three patents/applications each, while the others have two apiece.

- Bayer Material Science acts in medical devices e.g. cannulas and catheters for diagnosis. The device comprises a coating containing nanocrystalline silver particles thickener [68].
- The University of Illinois Foundation focuses on investigating or analyzing materials. New membrane scaffold protein for forming nanoscale particles, useful in biological research in pharmaceutical industry and in biotechnology [69].

In Medical Apparatus and Medical Care, which contains seven subclasses, there is:

- Subclass 1, corresponding to filters implantable into blood; prostheses, i.e. artificial substitutes appliances for connecting them with the body, absorbents pads (A61F), had 48 applications from 2001 to 2010. The main applicant was Kimberly-Clark Worldwide, with a focus on absorbent articles e.g. diaper, adult incontinence garment or feminine napkin. The article contains bodily excaudate modifying agent neutralizer, it can be a nanoemulsion comprising vegetable oil in water emulsion [70].
- Subclass 2, corresponding to transport and accommodation for patients (A61G), was not the target of any patent applications in the ten-year period in question.
- Subclass 3, physical therapy apparatus, percussion or vibration massage exercisers for eyes; bathing devices for special therapeutic or hygiene purposes (A61H), had only one application by VP Holding LLC for bath apparatus for stimulating reflex points in the bath through nanobubbles [71].
- Subclass 4, corresponding to devices or methods specially adapted for bringing pharmaceutical products into particular physical or administering focus (A61J), was the target of 12 patent applications in Brazil, practically two a year. Bayer Material Science AG had two, focusing on feeding tubes for therapeutic purposes A61J15/00, e.g. cannulas and urological catheters comprising a coating comprises nanocrystalline silver particles [68].
- In Brazil, subclass 5 (materials for catheters, for prostheses or for coating them, materials for coating surgical articles, characterized by their function or physical

properties - A61L) is related to deodorization. A total of 74 patents were applied for / granted throughout the ten-year period. Kimberly-Clark Worldwide is the leader, with seven patents / applications, focusing on A61L15-16 (absorbent pads for physiological fluids such as urine or blood, e.g. sanitary towels, tampons). The absorbent article has an agent for controlling, e.g. nanoemulsion (vegetable oil in water emulsion) [72].

- Subclass 6, devices for introducing media into or onto the body (A61M), attracted only 19 applications from 2000 to 2009, and only two firms made more than one application: Bayer Material Science AG and Pharmacia Corp (two each). Bayer Material Science AG focuses on medical devices (cannulas and catheters) for carrying off, for treatment of, or for carrying-over body liquids. The device comprises a coating comprises nanocrystalline silver particles with an average size of 1-100 nm [68].
- Subclass 7, relating to electrotherapy (A61N), was the target of seven patent applications in Brazil between 2000 and 2009, with Bayer Material Science AG (two patents) as the only one with more than one application, for devices e.g. circulatory support the medical device provides improved strength and capable of releasing active antimicrobial substances with satisfactory performance. The device comprises a coating. The coating comprises nanocrystalline silver particles measuring 1-100 nm [73].

CONCLUSION

Generally speaking, there has been a rise in the number of patents in the health sector that make use of nanotechnology. The hypotheses of US leadership in patenting was confirmed in all the subsectors studied, based on the IPC classification: dental care; diagnostic kits; drugs and medical apparatus, and medical care.

As for which organizations are the leading patent applicants / holders, American universities have a marked presence in nanotechnology patents applied to health in the four subsectors studied. In the private sector, the two most active companies are Elan Pharma (in drugs) and Boston Sci Scimed Inc (in medical apparatus and medical care).

When it comes to nanotechnology applications, the three subsectors with the highest number of patents are drugs, medical apparatus and medical care & diagnostic kits. Dental care was the target of fewer patent applications than the other health subsectors in the ten-year period under study. The patents involving nanotechnology for this segment were for composite material for the manufacturing of dental appliances. In the drugs subsector, the focus is on the use of nanoparticulate compositions, which are useful agents for a variety of diseases. Patents for diagnostic kits include the use of a nanostructure capable of detecting a target analyte. Meanwhile, in medical apparatus & medical care the patent applications are primarily for nanocapsules and/or nanocomposite materials inserted in devices and guide catheters.

Looking specifically at patents in Brazil, the same leadership by the United States as seen in the global trend is apparent in Brazil, with the top patent applicant / holder likewise

being Elan Pharma, in the drugs subsector although there are also Brazilian universities active in patenting in the area.

CURRENT AND FUTURE DEVELOPMENT

The use of nanotechnology in the health sector is still incipient, but the number of patents is rising considerably with each year that passes. The vast majority of the patented inventions derive from research carried out primarily at American universities and research institutions. The likelihood is that this will change, with technology-based firms operating in health care and devices making ever more use of nanotechnology, since this permits less invasive procedures to be used and allows medicine to be delivered to a specific site. It is also likely that there will be an increase in patent applications by Asian countries such as China, Japan and South Korea, which already hold significant numbers of patents in the health sector.

CONFLICT OF INTEREST

The authors have no conflicts of interest that are directly relevant to the content of this review.

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