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Development and innovation on hydrogels in the world: A scientific overview based on patent applications

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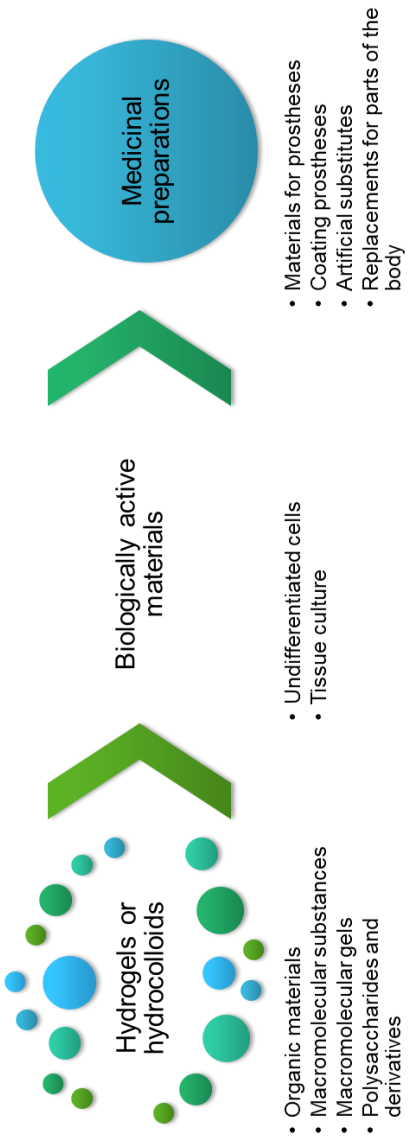
Graphical Abstract



Abstract

This overview concerns the analysis of international patent applications on hydrogels through the global system for filing patent applications which is known as Patent Cooperation Treaty (PCT) and administered by Intellectual Property Organization (WIPO). More specifically, this study presents the state of the art by introducing what has been innovated and patented in relation to hydrogels. As results, a total of 11,757 patent applications related to hydrogels have been filled between 1979 and 2020. The United States leads the patent race in the hydrogel sector. Massachusetts Institute of Technology is one of the top innovators in the hydrogel-based research and development. Based on patent classifications, most patent applications are related to medicinal preparations characterized by special physical form and materials for prostheses or for coating prostheses including structure of prostheses use of preparations for artificial biological organs, as well as materials characterized by their function or physical properties, such as hydrogels or hydrocolloids.

Keywords: *innovation; patent application; patentability; nanomaterials; hydrogels.*

1. Introduction

Nanomaterials together with nanotechnology have fascinated science world to develop and deliver new tools in all areas. As a remarkable class of nanomaterials, hydrogels are used in the field of tissue engineering, in the form of matrix capable of sustaining the life of differentiated and non-differentiated cells in three-dimensional (3D) structure that they can develop there and produce all the compounds for which they are programmed [1]. Hydrogels are crosslinked polymers with high water content. They can be created from a large number of water-soluble polymers including synthetic and natural macromolecules. The three-dimensional structure of hydrogels is due to crosslinking which forms an insoluble macromolecular network in the environment biofluid. The macromolecular network remains in equilibrium in an aqueous medium due to the balance of the elastic forces of the crosslinked polymer and the osmotic forces of the liquid [2]. The chemical composition and the crosslink density determine the swelling rate and the permeability of the structure [3]. In addition, the crosslinking of hydrogels gives them an elastic response to a given stress request. Moreover, the elasticity of these structures and the presence of a large amount of water allow a resemblance to different biological human tissues, which allows them to be used in many biomedical applications [4].

The first hydrogel was synthesized with the aim of designing an ideal and biocompatible substance [5]. This synthesized hydrogel was used for biomedical application as a designed soft contact lens. More specifically, molecular chains of 2-hydroxyethyl methacrylate were linked together by a succession of chemical bonds to form a uniform molecular structure according to Wichterle design criteria [6]:

- Avoid dissolving hydrogel macromolecules in biological fluids;
- Create a stable chemical and biochemical structure;
- Have a high permeability for nutrients and biological waste;
- Reproduce physical characteristics similar to natural biological tissues.

Research on hydrogels is developing rapidly through the innovation and improvement of polymers, chemical synthesis and methods of preparation, formulations and fabrication process, as well as applications. Moreover, research in the field of hydrogels has been actively growing for the past couple of decades. This is evident also from the elevation in the number of patent applications filed each year worldwide in this area [7].

For an invention, in principle, a patent application must be filed in each country for which an inventor is interested in obtaining patent protection. In case the patent protection is sought in a number of countries worldwide, an applicant may consider filing an international application under the Patent Cooperation Treaty (PCT). It's a global system for filing patent applications administered by the World Intellectual Property Organization (WIPO) [8].

This overview concerns the analysis of international patent applications on hydrogels through the PCT global system. More specifically, this study presents the state of the art by introducing what has been innovated and patented in relation to hydrogels, according to preparation methods/process, formulations and applications. A detailed analysis is then given regarding to publication years, patent classifications, inventors and applicants.

2. Methods

The supported field codes used in this study was based on the Patentscope search service of the World WIPO [7,9] and the Lens patent data set [10]. During the search, different keywords and related terms were used and patents were searched according to title, abstract and claims. The search was then

filtered to include only international patent applications through the PCT with the application date until 2020.

Hereinafter, the state of the art will be presented by introducing what has been patented in relation to hydrogels by following these sections: publication years, patent classifications, inventors and applicants.

3. Results

3.1. Publication years

Based on definitions of the terms used generally in the world of patent information, the publication is the step when the patent document (patent application, granted patent, etc.) made available to the public, to which a publication number and a publication date have been assigned by a patent authority. In other words, the publication date is the date on which a patent document is published, thereby making it part of the state of the art. In contrary, the filing date is the date when a patent application is first filed at a patent office [11].

Figure 1 presents the evolution of patent applications as a function of published date of patents related to hydrogels. These patent applications concern only PCT system administered by the WIPO. 11,757 patent applications have been found until 2020. 2020 recorded the publication of 845 patent applications, however, the first year of patentability of hydrogels, 1979, knew publication of one patent application only. In this year Ornstein has invented and patented a method and apparatus based on hydrogel for controlling the relative humidity of the soil environment. In this invention, a crosslinked hydrogel which was water-swellable slightly and permeable, was formulated for controlling and regulating the delivery of water to a soil environment containing growing plants, as a function of the humidity or moisture in the soil. The crosslinked hydrogel was capable of swelling to about 25 times its dry volume when in equilibrium with water at 100% relative humidity [12].

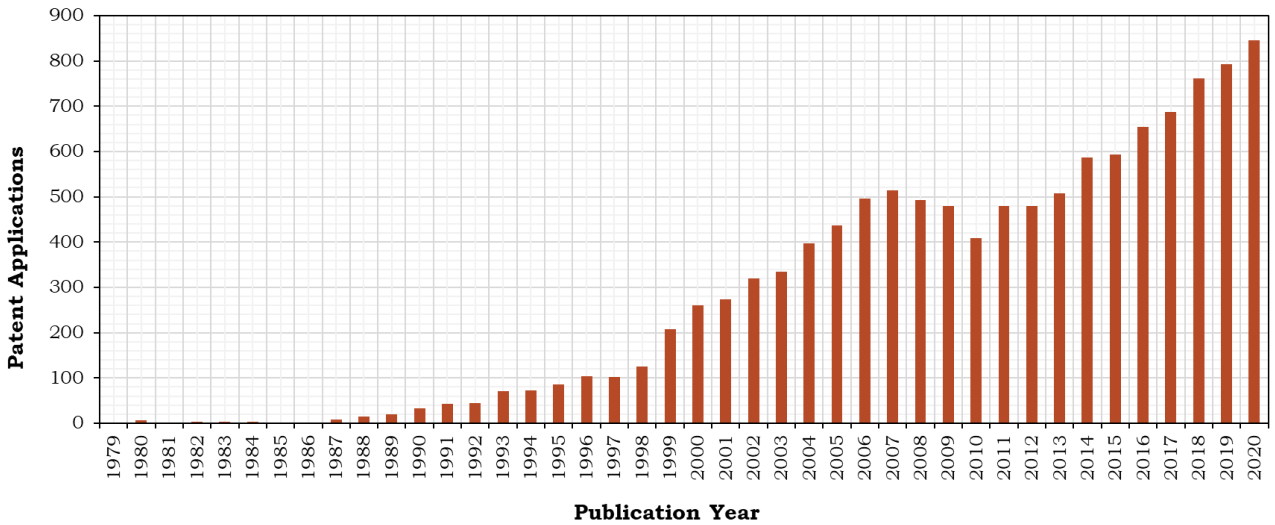


Figure 1. *Evolution of patent applications as a function of published date of hydrogels.*

3.2. Patent classifications

The International Patent Classification (IPC) is a hierarchical system in the form of codes, which divides all technology areas into a range of sections, classes, subclasses, groups and subgroups. It is an

international classification system that provides standard information to categorize inventions and to evaluate their technological uniqueness [13,14].

The top 10 of IPC codes for hydrogels until 2020 are presented in Figure 2. These IPC codes concern only patent applications under PCT system. The most IPC code corresponds to A61K9/00 which is a group of medicinal preparations characterized by special physical form. This group recorded it alone 750 patent applications. The subgroups A61L27/52, reserved to materials for prostheses or for coating prostheses, characterized by their function or physical properties, such as hydrogels or hydrocolloids, recorded 735 patent applications. For mor details concerning the top 10, a description of each IPC code is shown in Table 1.

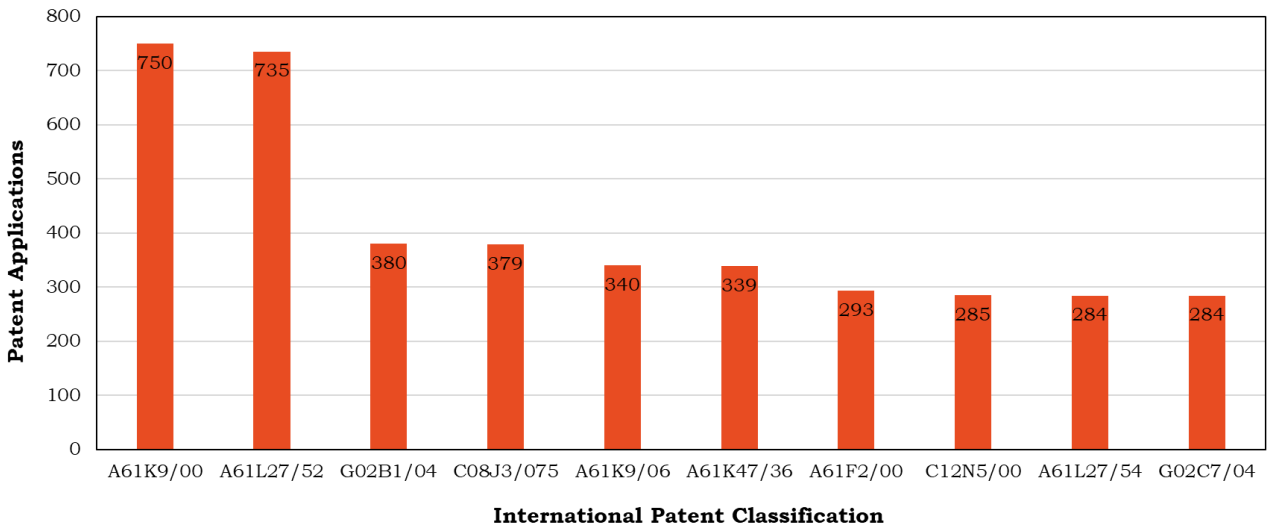


Figure 2. *Top 10 of IPC codes of resulted patents as a function of patent applications of hydrogels.*

Table 1. *Meaning of IPC codes (top 10) concerning the resulted patent applications of hydrogels [13].*

IPC	Description
A61K9/00	Preparations for medical, dental, or toilet purposes. More specifically, medicinal preparations characterized by special physical form.
A61L27/52	Materials for prostheses or for coating prostheses, characterized by their function or physical properties, such as hydrogels or hydrocolloids.
G02B1/04	Optical coatings for optical elements made of organic materials.
C08J3/075	Processes of treating or compounding macromolecular substances. More specifically, making solutions, dispersions, lattices or gels in aqueous media, such as macromolecular gels by other methods than by solution, emulsion or suspension polymerization techniques.
A61K9/06	Preparations for medical, dental, or toilet purposes. More specifically, medicinal preparations characterized by special physical form, such as ointments.
A61K47/36	Medicinal preparations characterized by the non-active ingredients used. More specifically, macromolecular organic or inorganic compounds, such as polysaccharides and derivatives thereof (*e.g.,* gums, starch, alginate, dextrin, hyaluronic acid, chitosan, inulin, agar or pectin).
A61F2/00	Filters implantable into blood vessels and prostheses (*i.e.,* artificial substitutes or replacements for parts of the body), such as stents, artificial nails, dental prostheses, artificial kidneys and artificial hearts.
C12N5/00	Undifferentiated human, animal or plant cells (e.g., cell lines Tissues Cultivation or maintenance thereof Culture media therefor plant reproduction by tissue culture techniques).
A61L27/54	Materials characterized by their function or physical properties, such as biologically active materials (*e.g.,* therapeutic substances).
G02C7/04	Optical parts characterized by the material, such as contact lenses for the eyes.

As resulted keywords from the description of resulted IPC codes, all are based on biomaterials, tissues engineering and biofabrication (Figure 3). All these keywords summarize the strategy of tissue

engineering which aims to regenerate, repair or reconstitute functional tissues or organs similar to those of man by biofabrication using biomaterials.

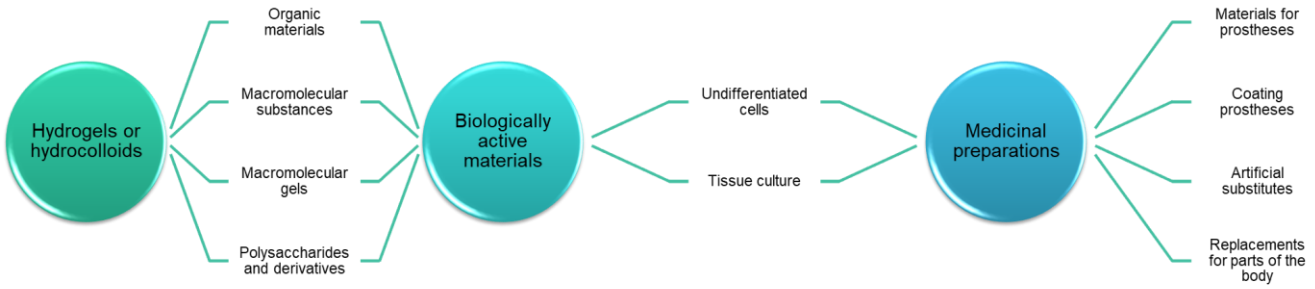


Figure 3. *Schematic illustration of the resulted keywords from the description of IPC codes: biomaterials, tissues engineering and biofabrication.*

3.3. Inventors

Based on definitions of the terms used generally in the world of patent information, the inventor is a natural person designated for a patent application. In several cases, the inventor can also be the applicant, as well as there may be more than one inventor per patent application [11].

The top 10 of inventors concerning patent applications of hydrogels until 2020 are presented in Figure 4. This list of inventors concerns only patent applications under PCT system. Langer Robert from United States is ranked as the first inventor who has recorded 39 patent applications. In the second place, the inventor Chang Frank from United States has recorded 35 patent applications, and thirdly, the inventor Back Arthur from United States has recorded 25 patent applications.

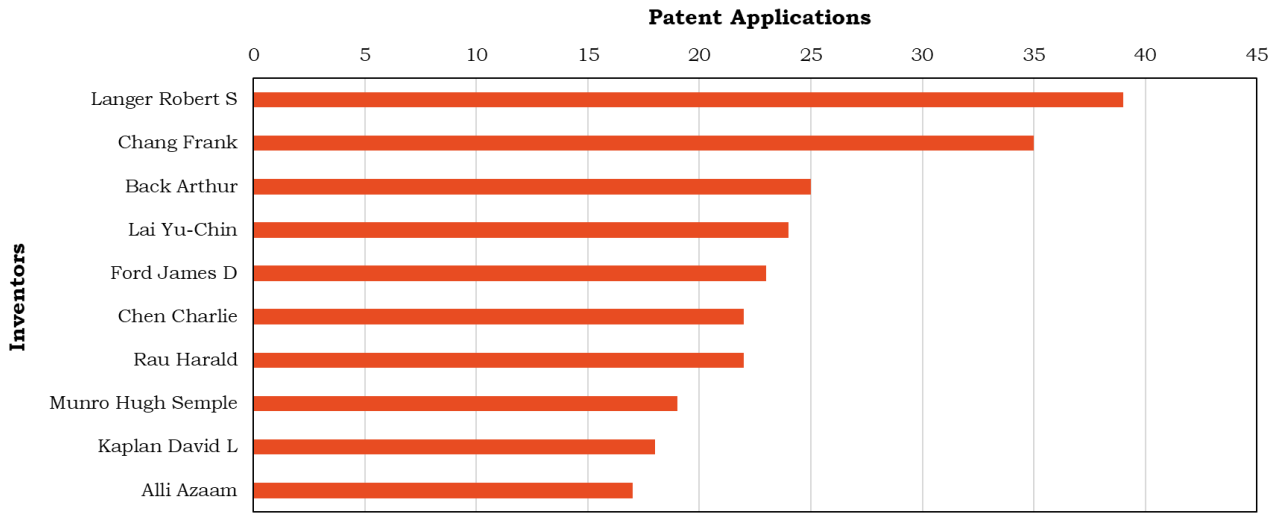


Figure 4. *Top 10 of inventors of resulted patents as a function of patent applications of hydrogels.*

3.4. Applicants

Based on definitions of the terms used generally in the world of patent information, the applicant is a person (i.e., natural person) or an organization (i.e., legal entity) that has filed a patent application. In several cases, the applicant can also be the inventor, as well as there may be more than one applicant per patent application [11].

The top 10 of applicants concerning patent applications of hydrogels until 2020 are presented in Figure 5. This list of applicants concerns only patent applications under PCT system. Massachusetts

Institute of Technology (Cambridge, MA, United States), as a legal entity, is ranked as the first applicant which has recorded 189 patent applications. In the second place, University of California (Los Angeles, CA, United States), as a legal entity, has recorded 188 patent applications. As for the podium of the third place, Novartis AG (Basel, Switzerland), as a legal entity, has recorded 169 patent applications. As presented, all top 10 of applicants are organizations either as universities and companies.

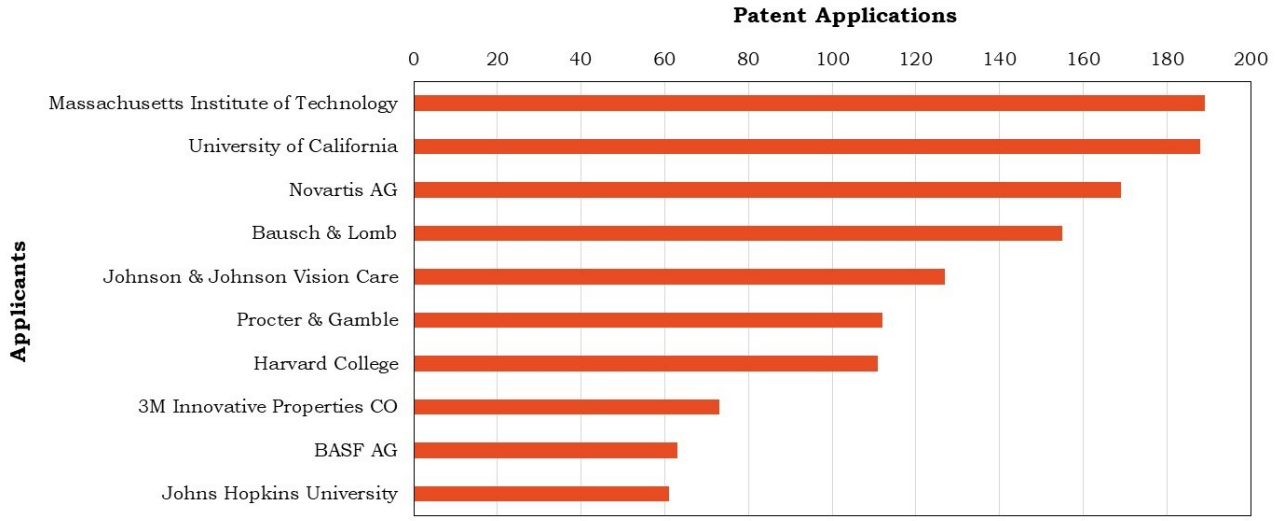


Figure 5. *Top 10 of applicants of resulted patents as a function of patent applications of hydrogels.*

4. Conclusions

This overview presented the analysis of international patent applications on hydrogels through the PCT global system. It concerned only the development and innovation on hydrogels in the world until 2020. A detailed analysis of the patentability of hydrogels has been provided regarding to publication years, patent classifications, inventors and applicants. During the search, 11,757 patent applications have been found. The United States leads the patent race in the hydrogel sector. Massachusetts Institute of Technology is one of the top innovators in the hydrogel-based research and development. The innovation and improvement of hydrogels concerned the raw materials, synthesis and methods of preparation, formulations and fabrication process, as well as applications such as tissue engineering and biofabrication.

Based on the patent classification codes and areas, all filled patents and the most inventions intended for medicinal preparations characterized by special physical form, as well as materials characterized by their function or physical properties, such as hydrogels or hydrocolloids. Knowledge clusters and expert driving factors indicate that the research based on following areas is concentrated in the most patents: (i) Processes of treating or compounding macromolecular substances; (ii) Macromolecular organic or inorganic compounds; (iii) Biologically active materials; (iv) Materials for prostheses or for coating prostheses; (v) Prostheses and artificial substitutes or replacements for parts of the body.

Acknowledgments

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