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HYDROGELS IN NEUROSURGERY/NEUROREGENERATION, APPLICATIONS AND PERSPECTIVES

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Abstract

Hydrogels represent a promising class of biomaterials used in neurosurgery and neuroregeneration due to their high biocompatibility, adjustable mechanical properties, and ability to mimic the natural extracellular matrix. This review explores their diverse applications, from neural tissue repair and peripheral nerve regeneration, to cell therapies and controlled drug delivery. Their unique properties, such as in situ gelling and porosity, allow them to provide effective structural support and facilitate neuronal regeneration. Recent developments highlight the use of hydrogels functionalized with growth factors or nanoparticles to improve axonal regeneration and integration with existing tissues. At the same time, biodegradability challenges, incomplete integration with tissues and high costs are significant barriers to their widespread application. The future of research in this field focuses on the development of personalized hydrogels, integration with 3D-printing technologies and the creation of smart materials responsive to stimuli. These advances can revolutionize treatments for central and peripheral nervous system injuries, providing innovative and effective solutions for patients. Therefore, hydrogels have the potential to fundamentally transform therapeutic approaches in neurosurgery and neuroregeneration.

Keywords: hydrogels, neurosurgery, neuroregeneration, biomaterials, controlled delivery, 3D-printing

Introduction

Modern neurosurgery and neuroregeneration are interconnected areas in the treatment of central and peripheral nervous system disorders. Neurological conditions, such as brain trauma, degenerative diseases or peripheral nerve damage, require advanced therapeutic solutions that promote tissue regeneration and restore lost functions. In this context, biomaterials have become an essential component in the development of innovative medical technologies [1-3].

Neural tissue exhibits a limited capacity for regeneration, which has led to the exploration of biomimetic materials that mimic the properties of the natural extracellular matrix. These materials can provide a suitable micro-environment to support cell growth, promote axonal regeneration, and functionally integrate with existing tissues. Among them, hydrogels stood out for their structural flexibility, high biocompatibility and adaptability to various clinical applications [2,3].

Hydrogels, defined as three-dimensional polymer networks capable of absorbing large amounts of water, have attracted attention in neurosurgery due to their ability to mimic the extracellular matrix of neuronal tissues. Their physicochemical properties allow for the

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controlled delivery of drugs, stimulation of cell regeneration and the creation of structural supports for nerve regeneration. Hydrogels can also be adjusted to specifically meet therapeutic needs, being used in various applications, from repairing nerve defects to treating glioblastoma [2-4].

This review explores the current applications and future prospects of hydrogels in neurosurgery and neuroregeneration. We will analyze their unique properties, their use in neural reconstruction, their role in cell and pharmacological therapies, as well as the challenges that this evolving field faces. Thus, the work provides a synthesis of the contribution of hydrogels to the progress of neurological treatments, highlighting their transformative potential.

Properties of hydrogels relevant to neurosurgery

Hydrogels are three-dimensional structures made up of natural or synthetic polymers, capable of retaining significant amounts of water. Natural ones, such as collagen, alginate and hyaluronate, are biocompatible and bioresorbable, providing excellent integration with biological tissues. Synthetic ones, such as poly (ethylene glycol/PEG) and poly (vinyl alcohol/PVA), are easier to adjust according to the requirements of the application, having controllable mechanical and chemical properties. The choice of material depends on the specific application, balancing biocompatibility and stability [3-7].

Hydrogels can be customized according to clinical requirements, providing flexibility in varied applications. For example, for peripheral nerve regeneration, hydrogels can be used as axonal growth guides, while in central neurosurgery, they can support cell therapies or drug delivery. The ability to integrate nanoparticles and biomolecules into their structure further expands the range of uses, making them a promising tool in neurosurgery (Table 1) [4-9].

Table 1. Properties of hydrogels relevant for neurosurgery [4-10].

Category	Property	Description	Relevance in neurosurgery
Composition	Natural	Hydrogels based on collagen, alginate, hyaluronate, fibrin.	High biocompatibility, excellent integration with nervous tissues.
	Synthetic	PEG (polyethylene glycol), PVA (polyvinyl alcohol), PLA (polylactic acid).	Better mechanical control, chemical customization for specific applications.
Physical-chemical properties	Water retention capacity	Absorbs up to 99% water, mimicking natural extracellular matrix.	Allows diffusion of nutrients and oxygen to nerve cells.
	Porosity	3D networks with adjustable pores (micrometric/nanometric).	Supports cell migration, transport of growth factors, and waste elimination.
	In situ gelation	Transition from liquid to gel under temperature, pH, or enzymatic influence.	Facilitates minimally invasive application through injection.
	Elasticity and flexibility	Ability to adapt to delicate neural tissue.	Reduces risk of mechanical damage and improves integration.
Biocompatibility	Reduced immunogenicity	Natural materials are well tolerated by the body.	Minimizes inflammation and rejection risk.
	Controlled biodegradability	Degradation rate can be adjusted through chemical composition.	Ensures complete regeneration before material elimination.
Functionalization	Growth factors	NGF, BDNF, VEGF integrated	Stimulates neuronal

Category	Property	Description	Relevance in neurosurgery
		into the matrix.	regeneration and local angiogenesis.
	Nanoparticles	Incorporation of gold, silver, or magnetic nanoparticles.	Allows controlled drug delivery or stimulation via magnetic fields.
Adaptability	Adjustable mechanical properties	Regulation of stiffness and elasticity based on tissue requirements.	Ideal for diverse applications, from the spinal cord to peripheral nerves.
	3D-printing compatibility	Capability to be used for printing complex structures.	Creates axonal guides and personalized supports for regeneration.

Applications in neurosurgery

Hydrogels provide ideal structural support for neural tissue regeneration, being used to guide and support the growth of damaged axons. For example, in peripheral nerve injuries, hydrogels function as a synthetic extracellular matrix, facilitating cell migration and the synthesis of new neuronal connections. In central neurosurgery, they are used to restore brain defects, promoting brain tissue regeneration and reducing glial scarring [6,8-11].

Hydrogels allow for the controlled and localized delivery of drugs and growth factors, reducing systemic toxicity and increasing therapeutic efficacy. For example, in the treatment of glioblastoma, injectable hydrogels can deliver chemotherapeutic agents directly to the tumor site, increasing the effectiveness of treatment and reducing adverse effects. In the case of traumatic brain injury, they can release neurotrophic factors such as BDNF or NGF to stimulate neuronal regeneration [8-12].

Hydrogels are used as supports for neuronal stem or progenitor cells, providing a suitable environment for their proliferation and differentiation. They can be injected together with therapeutic cells directly into brain or spinal injuries, where they contribute to tissue regeneration through the functional integration of the transplanted cells. The combination of hydrogels and cell therapies promises personalized solutions for neurological diseases such as Parkinson's disease or multiple sclerosis [9-13].

Injectable hydrogels have become a promising approach in the treatment of glioblastoma, an aggressive brain tumor. They can be used for the delivery of drug-laden nanoparticles or for the release of molecules that target the tumor microenvironment, inhibiting the proliferation of malignant cells. The flexibility of these materials allows the personalization of treatments for different types of tumors [8,10-14].

The in situ gelling property makes the hydrogels ideal for minimally invasive techniques. They can be injected in liquid form through a catheter or needle and then solidified at the desired site, reducing the risk of post-operative complications. Such applications are valuable in the treatment of complex brain lesions or for the precise administration of therapeutic agents [10-15].

Hydrogels in neuroregeneration

Hydrogels are successfully used in peripheral nerve regeneration, where bioactive guides made from these materials promote axonal growth and functional reconnection. In contrast, the regeneration of the central nerves (brain and spinal cord) is more difficult due to the inhibitory environment and biological barriers. Hydrogels can enhance this process by creating a favorable micro-environment that supports the growth and differentiation of neuronal cells [11-16].

Porous hydrogels allow axon growth through a structured matrix, providing mechanical support and controlled transport of growth factors. Protein-functionalized hydrogels such as laminin or collagen can stimulate axon regeneration by mimicking the natural environment of the extracellular matrix. In combination with nanoparticles, these materials ensure the slow and controlled release of biofactors essential for regeneration [12-16].

The addition of neurotrophic factors, such as BDNF (brain-derived neurotrophic factor) and NGF (nerve growth factor), to hydrogels significantly amplifies neuronal regeneration. These biofactors are gradually released from the hydrogels, providing sustained stimulation that promotes the survival and regeneration of nerve cells. The integration of these bioactive molecules increases the effectiveness of therapies for brain and spinal injuries [10,13-17].

Conductive hydrogels, impregnated with materials such as carbon nanoparticles or conductive polymers, are used to connect implantable devices (e.g. neural prostheses) to nerve tissue. These hydrogels provide a soft interface, reducing inflammatory reactions and maximizing the efficiency of signal transmission. Such approaches hold promise for the creation of advanced technologies in neuroprosthetics [13-17].

The development of personalized hydrogels, adapted to the needs of each patient, represents a promising direction. This concept, integrated into precision medicine, involves adjusting the composition and properties of hydrogels to match the specifics of the lesion and the characteristics of the patient. Data-driven technologies such as artificial intelligence can help design these personalized materials [14-18].

3D-printing allows the fabrication of customized hydrogel structures with complex architectures, tailored to the specific requirements of neural tissue. This technology can be used to create axonal guides or detailed cell supports, improving the accuracy and effectiveness of regenerative treatments [16-19].

Conductive hydrogels, used at the interface between nerve tissue and implantable devices, represent an area of research with huge potential. The integration of hydrogels with advanced neural prostheses could revolutionize treatments for severe nervous system injuries, offering more effective solutions for functional reconnection. [17-23].

Conclusions

The unique properties of hydrogels – biocompatibility, porosity, in situ gelling capacity and adaptability – position them as innovative solutions in neurosurgery. Their integration with nerve tissues and their ability to support cell regeneration gives them an essential role in addressing the challenges of neuroregeneration.

Hydrogels have demonstrated remarkable versatility in neurosurgery, being used both for neural tissue regeneration and for the administration of pharmacological and cellular therapies. Their ability to adapt to clinical requirements and improve therapeutic outcomes gives them a central role in the treatment of complex neurological conditions.

Hydrogels play a central role in neuroregeneration, facilitating neural tissue reconstruction through structural support, biofactor delivery, and integration with advanced devices. Their versatility, combined with customizable properties, makes them indispensable in modern treatments for neuronal injuries, offering new perspectives for patients with severe neurological conditions.

The limitations of hydrogels, from biodegradability control to integration with nerve tissues and economic challenges, pose significant barriers to their widespread application.

However, continuous research into optimizing their properties and reducing production costs can turn hydrogels into viable and affordable solutions for complex neurological treatments.

Progress in the use of hydrogels requires close collaboration between specialists from various fields – neurosurgery, bioengineering, chemistry and physics. In addition, the support of international institutions can accelerate the deployment of these technologies, reducing the differences in access to innovative treatments between developed and developing regions.

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