OPINION

Hydrogels are strengthened by mesoporous materials in biomedicine

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ABSTRACT

Since the 1990s, researchers have been working to enhance the characteristics of mesoporous materials and broaden their applications; one of the current research foci is the coupling with hydrogels, macromolecular biological materials. Combining mesoporous materials is more appropriate for the continuous release of loaded pharmaceuticals than using single hydrogels due to their uniform mesoporous structure, high specific surface area, strong biocompatibility, and biodegradability. Together, they are able to target tumours, stimulate the tumour environment responsively, and utilise a variety of treatment modalities, including photothermal therapy and photodynamic therapy. Mesoporous materials can considerably increase the antibacterial efficacy of hydrogels and provide an unique photocatalytic antibacterial mode due to the photothermal conversion capacity.

Mesoporous materials are utilised in bone healing systems to load and release different bioactivators to induce osteogenesis as well as to enhance the mineralization and mechanical characteristics of hydrogels. Mesoporous materials drastically increase the water absorption rate of hydrogels during hemostasis, improve the blood clot's mechanical strength, and significantly reduce bleeding duration. Mesoporous materials can be promising for improving vascular formation and cell proliferation of hydrogels in terms of wound healing and tissue regeneration. We describe the types and techniques for making mesoporous material-loaded composite hydrogels in this study and emphasise their uses in drug administration, tumour therapy, antimicrobial therapy, osteogenesis, hemostasis, and wound healing.

Key Words: *Herbal medicine; Biopolymers; Nanofibers; Drug delivery*

INTRODUCTION

Porous materials are a form of network structure material made of linked or closed holes. Porous materials often contain several linked pores and a large surface area similar to the natural transmission system of plant leaf veins and the respiratory and circulatory systems of animals, structure can offer a conduit for material transfer and dispersion. The International Union of Pure and Applied Chemistry (IUPAC) states that porous materials may be categorised simply based on their pore size. Microporous materials have pores smaller than 2 nm, such as zeolites and Metal-Organic Frameworks (MOFs), whereas macroporous materials have pores bigger than 50 nm, with aerogels serving as prominent illustrative examples raw materials. The use of synthetic and natural polymer materials is crucial throughout the production process.

An example of a polymer having a three-dimensional network structure is a hydrogel, which can absorb water swelling while maintaining its original structure. It is highly flexible, adaptable in terms of structural design, and has strong biocompatibility .

Moreover, hydrogels have the ability to detect minute changes in external stimuli (such temperature and pH level) and respond to stimuli by expanding and contracting. The majority of scientific researchers are now interested in hydrogels because of their great qualities, which have also led to their widespread usage in a number of industries. Hydrogels can be utilised to cleanse dye wastewater and to adsorb heavy metal ions in the treatment of environmental pollutants.

In the field of biomedicine, bioactive substances can be easily combined with hydrogel precursors and enclosed in porous, expansive three-dimensional networks that have intriguing bionic properties and are frequently used in tissue engineering, drug delivery, tumour therapy, and wound dressings. While hydrogels offer several benefits, their application is typically constrained by their poor mechanical characteristics, inadequate temperature stability, and drug burst release. Researchers have recently made several attempts to address these issues. Examples include combining hydrophilic polymers with bioactive and functional nanomaterials to produce compounds with improved physicochemical and biological properties, releasing drugs more steadily and gradually to prevent sudden release, and giving hydrogels additional biological properties like photothermal effects.

Classification of mesoporous material-loaded composite hydrogels

mesoporous silica-loaded composite hydrogels

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Mesoporous silica is a nonmetallic, inorganic substance with uniform and controllable pore size, a sizable surface area, surface that may be functionally modified, and high biocompatibility. Since 1992, when the silicon-based mesoporous material was created by Mobil Corporation.

Researchers initially produced the material M41S (MCM-41, MCM-48, MCM-50) series. Thereafter, the SBA series, MCF series, and MSU series were developed.

Due to the rapid advancement of nanosynthetic chemistry, a number of hybrid analogues of mesoporous silica nanoparticles have also been created. These include the well-known periodic mesoporous organosilicas and mesoporous organosilica nanoparticles. Such versatile nanomaterials have undergone over two decades of evolution. Focusing on the study and development of mesoporous silica composite hydrogels, researchers have discovered that adding mesoporous materials may significantly enhance certain hydrogel characteristics and broaden their range of applications. For instance, the mesoporous silica MCM-41 greatly improved the thermal stability, liquid absorption ratio, and salt tolerance of poly (aspartic acid) hydrogels. Spruce xylan/2-hydroxyethyl methacrylate hydrogels' mechanical properties were enhanced by the addition of SBA-15. characteristics, as well as avoiding fractures and delaying hydrogel breakdown, by boosting the surface area and optimising the contact between the inorganic particles and the polymer matrix . Combining MCM-41 or SBA-15 as drug carriers into carboxymethyl cellulose hydrogels improved the hydrogels' in vitro mucoadhesion as well as their in vitro swelling, erosion, water vapor/oxygen permeability, and antibacterial activity . In addition, the loaded drugs were completely released after 12 hours.

Mesoporous bioglass-loaded composite hydrogels

A silicate glass called "bioactive glass" has the ingredients SiO_2, Na_2, CaO, and P_2O_5. The only synthetic biological substance that, to date, can link with both soft tissue and bone tissue and repair, replace, and regenerate bodily tissue is bioactive glass. Hence, bone tissue engineering is the major focus of the functional development of bioactive glass. Mesoporous bioactive glasses are more physiologically active than pure silica mesoporous materials due to their highly organised pore structure, greater pore volume, and much higher specific surface area. The incorporation of mesoporous bioactive glasses is thought to be a potential strategy for enhancing the hydrogels' mechanical and physicochemical stability in hard tissue engineering . The efficacy of loaded pharmaceuticals can be increased by combining mesoporous bioactive glass with hydrogels to maximise drug transport and release performance. In addition to promoting MG-63 cell proliferation and osteogenesis-related gene expression, a naringin or calcitonin gene-related peptide coprinted into the mesoporous bioactive glass/sodium alginate/gelatin hydrogels exhibited a steady sustained release behaviour for up to 21 days without an initial burst release.

It is difficult to promote bone regeneration while maintaining the bioactivity of growth factors and accomplishing the two linked processes of osteogenesis and angiogenesis.

Mesoporous non-silicon-loaded composite hydrogels

Scientists began attempting to create non-silicon mesoporous materials, such as mesoporous metal oxides, because the chemical inertness of silica limited the applicability of silicon-based mesoporous materials. Mesoporous titanium dioxide can prevent the loaded medicines from degrading into an inactive state during multi-mode anticancer therapy by acting as an efficient photosensitizer, hydrogel formation initiator, and photosensitizer. Drug transport is another function of mesoporous zinc oxide. The hydrogel's mesoporous zinc oxide addition successfully reduces the loaded drug's undesirable burst release, allowing for a sustained release at a neutral pH over time.

By indubitably boosting the breakdown of H_2O_2 present in inflammatory conditions, mesoporous manganese dioxide has the unique ability to treat localised hypoxia.

Localized oxidative stress and extended oxygen deprivation can be alleviated by a hydrogel encapsulated with mesoporous manganese dioxide.

Due to the fact that manganese dioxide is a redox-active substance that can be degraded under glutathione, H_2O_2, and acid conditions, mesoporous manganese dioxide can also aid composite hydrogels in achieving satisfactory glutathione/pH/thermal-responsive controlled drug release in the tumour microenvironment.

Mesoporous polydopamine is a novel substance with high photothermal characteristics and strong biocompatibility that may efficiently destroy cancer cells *in vivo* and *in vitro* by converting near-infrared light into heat. Drugs can be coupled with the many groups on the surface of polydopamine by chemical bonding, electrostatic adsorption, and stacking to increase drug load rate, extend drug release duration, and lessen burst release behaviour. Moreover, mesoporous polydopamine/cellulose nanofibril hydrogels have potential uses in both chemical and physical treatment because the infrared absorption feature of mesoporous polydopamine may be used to enhance the drug release rate by near-infrared light irradiation.

Crosslinking methods of mesoporous material-loaded composite hydrogels

Physical crosslinking, chemical crosslinking, and radiation crosslinking can all be used to crosslink composite hydrogels.

Physical crosslinking method

The crosslinking between linear molecules known as physical crosslinking is created by hydrogen bonds, electrostatic interactions, coordination bonds, and hydrophobic interactions.

Using a sustainable process of multiple freeze-thaw cycles, pineapple peel carboxymethyl cellulose/polyvinyl alcohol/ mesoporous silica SBA-15 hydrogels were created.

Chemical crosslinking method

The crosslinker method and the chemical reaction method are two categories of the chemical crosslinking technique. In the crosslinker technique, a crosslinker is utilised to create a network structure in the polymer aqueous solution. For poly (HEMA-co-AA) @ZnO compsites

the employment of an initiator (2, 2-Methylpropionitrile) and a crosslinker (Ethylene Glycol Dimethacrylate) prevented copolymer breakdown and increased system stability.

Radiation crosslinking method

Radiation crosslinking primarily employs light (visible light, ultraviolet light, near-infrared light, etc.), rays, and electron beams to create free radicals and start crosslinking reactions that result in the formation of chemical bonds between the linear molecules that make up the main chains of polymers. The radiation crosslinking approach offers several benefits over the methods mentioned above, including high efficiency, ease of use, reaction at room temperature, and non-polluting nature.

Application of mesoporous material-loaded composite hydrogels Hydrogels are now often employed in biomedicine, particularly for controlled medication release and tissue regeneration. Nevertheless, their drawbacks, such as inadequate wet surface adhesion, low heat stability, poor mechanical capabilities, and uncontrolled deterioration, restrict future clinical use.

Drug delivery

With the growth and advancement of medicine, it is now necessary to design and build a new medication delivery system that is highly effective and toxic-free. The rising demands of medication delivery can no longer be met by drug encapsulation in a hydrogel precursor. Hydrogels' shortcomings are made up for by the special benefits of porous mesoporous materials for transporting medicines. Mesoporous materials were initially added to hydrogel drug delivery systems to lessen the explosive impact and boost stability.

Tumor therapy

Platinum-based antitumor medications have a number of limitations that prevent their long-term and high-dose administration, including severe toxicity and developed tumour resistance. To reduce toxicity and boost anticancer efficiency, mesoporous silica nanoparticles impregnated with platinum medicines were created. This opened the door for the active targeting of nanoparticles by different functionalization. With much higher medication concentrations at tumour locations, mesoporous material modification and surface functionalization using hydrogels can enable tumour targeting or microenvironmental stimulation responsiveness.

Antibacterial treatment

One of the most tried-and-true and efficient ways to improve the antibacterial and anti-inflammatory effects of hydrogels is to introduce antibacterial drugs, antimicrobial peptides, or other antibacterial substances into the three-dimensional network structure of hydrogels through mesoporous materials. With more time and lesser dosages, mesoporous materials loaded with antibacterial chemicals exhibit overwhelming anti-inflammatory and antibacterial activity. Among these, hydrogels modified by mesoporous materials containing Ag, Au, Cu, and other transition metal ions, oxides, or photocatalytic antibacterial agents offer enormous therapeutic potential and a wide range of applications.

Osteogenesis

Due to its porous three-dimensional structure and flexible flow pattern, which enable the progressive release of loaded compounds and less invasive administration, hydrogels have emerged as a research hotspot in bone healing systems. Unfortunately, hydrogels' weak mechanical characteristics and low degree of mineralization after implantation make it impossible for them to provide the necessary mechanical support, which significantly limits their use in the repair of weight-bearing bone defects. One of the most successful methods is the combination of inorganic nanoparticles, especially mesoporous materials. As anticipated, mesoporous cerium-doped mesoporous silica-calcia nanoparticles increased the composite hydrogel's mechanical rigidity, caused the surface to mineralize with apatite, and encouraged the growth, adhesion, and differentiation of preosteoblasts.

Hemostasis

Mesoporous materials have a large specific surface area and pore volume, which can quickly absorb a large amount of water in the blood and promote platelet coagulation. When a mesoporous material is used as a carrier of hemostatic drugs, it can also exert a hemostatic effect by hitting the bleeding site effectively and accurately. The introduction of functional groups to the mesoporous materials adjusts the surface properties (hydrophilic/hydrophobic) and pore size and, more importantly, improves the biocompatibility and coagulation function.

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