What are Hydrogels?

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Introduction

Pittsburgh Plastics Mfg. (PPM) is a contract manufacturer of products for medical, foot care, safety and other industrial markets with focus on polymeric cushioning solutions. Products for these markets employ gel and/or foam to provide cushioning, impact/vibration control and support. For example, PPM contract manufactures gel filled pouches that are designed to cushion preemies during the critical days after birth. Needless to say, the cushioning performance properties of the gel are essential to the comfort and well-being of the preemie.

PPM has expertise with a wide range of gel polymers, including many types of polyurethane, silicone, rubber and thermoplastic elastomer. Several of the specialized gel formulations were developed in-house and are exclusive to PPM. Another important type of gel is hydrogel, and PPM is working to expand the use of lower-cost hydrogels in cushioning applications. The purpose of this technical paper is to introduce our customers to this remarkable material.

Discussion

Definition

The three classical phases of matter on Earth are solid, liquid or gas. Phase transitions occur with sufficient change in pressure and/or temperature. For example, water (liquid) transitions to ice (solid) with a drop in temperature. Gelatin powder, such as Kraft Foods' Jell-O, is a solid. Empty a packet of Jell-O into a mixing bowl and add boiling water. Stir until dissolved and then chill. Now the material in the bowl is neither solid nor liquid nor gas; it's a hydrogel.

Like a solid, hydrogels do not flow. Like a liquid, small molecules diffuse through a hydrogel. So what is a hydrogel? In 1926, Dorothy Jordan Lloyd stated that "the colloidal condition, the gel, is one which is easier to recognize than to define". Hydrogels are currently viewed as water insoluble, crosslinked, three-dimensional networks of polymer chains plus water that fills the voids between polymer chains. Crosslinking facilitates insolubility in water and provides required mechanical strength and physical integrity. Hydrogel is mostly water (the mass fraction of water is much greater than that of polymer). The ability of a hydrogel to hold significant amount of water implies that the polymer chains must have at least moderate hydrophilic character.

Returning to our discussion of Jell-O, what happened at a molecular scale that resulted in the formation of hydrogel? Collagen protein is extracted from skin, crushed bones, connective tissue and other animal parts, and then is partially hydrolyzed to make gelatin, a mixture of peptides and proteins. When gelatin is dissolved in hot water, the long protein polymer chains move freely in solution. As the solution cools, the motion of the polymer chains slows down. Polymer chains encounter each other and become entangled. As the degree of entanglement increases, water is trapped and immobilized. As a result, the material behaves in some ways like a liquid and other ways like a solid.

Types of hydrogels

The polymer chains of a hydrogel are crosslinked (interconnected). The nature of the connections is different for two general classes, physical and chemical. For the former, the connections are weaker and more reversible; for example, heat may break the chain-chain link. Polymers chains of physical hydrogels are held together by electrostatic forces, hydrogen bonds, hydrophobic interactions or chain entanglements. Jell-O is a physical hydrogel. The polymer chains of chemical hydrogels are connected by permanent covalent bonds. A covalent bond is characterized by the sharing of pairs of electrons between atoms.

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A second way to categorize hydrogels is by the starting point for synthesis (production). First, a polymer network may be prepared from monomers (small molecules that may be linked in a repeating fashion to form high-molecular weight polymers). A network is made by copolymerizing hydrophilic monomers with crosslinkers (polyfunctonal monomers). Networks made with PEG and PPO monomers are good carriers for drug delivery. Second, a polymer network may be prepared starting with prepolymers (oligomers [low-molecular weight polymers] that are capable of further polymerization). Polyurethane networks may be prepared using prepolymers. A non-medical application of a polyurethane hydrogel is entrapment (immobilization) of microbial cells for wastewater treatment. Third, polymer networks may be prepared starting with polymers; a network structure is made by crosslinking hydrophilic polymer chains. An example is chitosan (a linear polysaccharide polymer) crosslinked with glutaraldehyde. Two applications are scaffolding for soft tissue engineering and adhesive for peripheral nerve repair.

Another way to classify hydrogels is on the basis of polymer origin, either natural or synthetic. Examples of polymers from natural origin are proteins like collagen and polysaccharides like chitosan, dextran and alginate. Hydrogels from natural origin support cellular activities and are biocompatible and biodegradable. On the other hand, they may contain biological pathogens or evoke an immune response. Two other disadvantages are low mechanical strength and batch variation.

Synthetic polymers are made from monomers such as vinyl acetate, acrylamide, ethylene glycol and lactic acid. Not all monomers for synthetic polymers are derived from petroleum; for example, lactic acid is made from plants such as corn and sugarcane. Synthesis of polymers can be precisely controlled and tailored to give a wide range of properties. Also, they have a low risk of biological pathogens and evoking an immune response. Disadvantages are low biodegradability and inherent bioactive properties are absent. Also, toxic substances may be present.

Classification may be based on physical structure of the polymer chain: amorphous (random, non-crystalline), semi-crystalline (regions of partially ordered structure) or hydrogen-bonded (network held together by hydrogen bonds). Another way to classify hydrogels is by the method of preparation: homopolymer (made from one type of monomer), copolymer (made from more than one type of monomer), multipolymer (more than one type of polymer) or interpenetrating polymer (a second polymer network is polymerized around and within a first polymer network, and there are no covalent linkages between the two networks). Hyrogels may also be categorized based on ionic charges as follows: neutral (no charge) such as dextran; anionic (negative charge) such as carrageenan; cationic (positive charge) such as chitosan; and ampholytic (capable of behaving either positively or negatively) such as collagen

Smart materials

A “smart” or “stimulus responsive” material changes some property, such as shape, in response to a change in environment. Smart materials respond with sharp, large property changes in response to small change in physical or chemical conditions. Types of stimuli include pH, temperature, ionic strength, solvent composition, pressure, electrical potential, radiation and chemical and biological agents. Common stimuli for smart hydrogels in biological applications are pH, temperature and ionic strength.

As mentioned above, polymer chains for hydrogels need hydrophilic character. For some polymers, this character is provided by carboxylic acid groups (RCOOH). The acids are side groups off the polymer backbone. When a carboxylic acid group is added to water, the hydrogen of the acid group may dissociate. The result is a carboxylate ion ($RCOO^-$) with a negative charge. If the environment favors dissociation of the hydrogen, then the polymer chain has lots of negative charges along its backbone. The negative charges along the polymer chain repel each other and force the polymer to uncoil (open up). The negative charge also increases the attraction of the polymer to water. The uncoiling of the polymer and its increased attraction to water causes swelling of the hydrogel.

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The reaction of RCOOH to $RCOO^-$ is reversible, and the chemical environment influences whether the charge of the side groups is negative or neutral. More acid (lower pH) favors a neutral charge, and more alkali (higher pH) favors a negative charge. Therefore, a pH change results in a change in the shape of the polymer network. Salt concentration also can influence its shape. When sodium chloride (table salt) is added to water, it dissociates to positive sodium ions (Na^+) and negative chloride ions (Cl^-). The positive sodium ions associate with negatively charged carboxylate ions. One result of this association is that some water molecules are displaced. Another is that the negative charges along the polymer chain repel each other less. A consequence of these two factors is that the polymer chains become more coiled (less open). A small change in salt concentration can markedly influence the degree of swelling.

The response of the polymer to pH or salt level makes the hydrogel "smart". An application of this property is drug delivery. The hydrogel is called a carrier when loaded with medicine. As the swelling of the hydrogel increases, the chains of the network move further apart. As the chains move away from each other, the drug can diffuse more quickly through the hydrogel to the skin or other target area.

Researchers, such as Yun jung Heo, are working to develop a glucose responsive hydrogel for continuous glucose monitoring. The glucose sensor uses fluorescent hydrogel fibers. The sensor is implanted and the signal is accessed by wireless transmission.

Benefits and limitations of hydrogels

General benefits:

- Biocompatible
- Can be injected in vivo (in a whole, living organism) as a liquid that then gels at body temperature
- Protect cells
- Good transport properties (such as nutrients to cells or cell products from cells)
- Timed release of medicines or nutrients
- Easy to modify
- Can be biodegradable or bioabsorbable

General limitations:

- High cost
- Low mechanical strength
- Can be hard to handle
- Difficult to load with drugs/nutrients
- May be difficult to sterilize
- Non-adherent

Applications

Hydrogels are utilized naturally by the human body; examples are cartilage, blood clots, mucin (lining the stomach, bronchial tubes and intestines), and vitreous humor of the eye.

The following are examples of biomedical applications:

- Soft contact lenses
- Disposable diapers
- Drug delivery (stimulus responsive and un-responsive)
- Wound dressings
- Provide absorption, desloughing and debriding of necrotic and fibrotic tissue
- Component of EEG and ECG medical electrodes
- Hemo-compatible (blood compatible) surface for medical devices
- Scaffolds in tissue engineering

Hydrogels can absorb up to one thousand times their dry weight in water. The ability to absorb and retain water (even under pressure) makes hydrogels useful for the lining of disposable diapers. Plant

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water crystals also take advantage of this property. Crystals of hydrogel are placed in a plant's container; the crystals absorb water and swell. Then the hydrogel slowly releases water as the soil dries, extending the time between waterings.

Water conducts heat better than plastics. Since hydrogel is mostly water, the material helps conduct heat away from the body in skin contact applications. Current research on pressure sores (ulcers) shows that higher skin temperature makes the skin stiffer and more prone to damage by pressure. So hydrogel-based cushions feel cooler and promote healthier skin. For these reasons, PPM is working to expand the use of lower-cost hydrogels in cushioning applications.

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