



## Review Article

## Biomedical applications of hydrogels: A review of patents and commercial products



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## ABSTRACT

Hydrogels have become very popular due to their unique properties such as high water content, softness, flexibility and biocompatibility. Natural and synthetic hydrophilic polymers can be physically or chemically cross-linked in order to produce hydrogels. Their resemblance to living tissue opens up many opportunities for applications in biomedical areas. Currently, hydrogels are used for manufacturing contact lenses, hygiene products, tissue engineering scaffolds, drug delivery systems and wound dressings. This review provides an analysis of their main characteristics and biomedical applications. From Wichterle's pioneering work to the most recent hydrogel-based inventions and products on the market, it provides the reader with a detailed introduction to the topic and perspective on further potential developments.

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## 1. Introduction

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of absorbing large amounts of water or biological fluids. Due to their high water content,

porosity and soft consistency, they closely simulate natural living tissue, more so than any other class of synthetic biomaterials. Hydrogels may be chemically stable or they may degrade and eventually disintegrate and dissolve [1].

Hydrogels are called 'reversible' or 'physical' gels if molecular entanglements and/or secondary forces such as ionic, H-bonding or hydrophobic forces play the main role in forming the network. Physical gels are often reversible

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and it is possible to dissolve them by changing environmental conditions, such as pH, and the ionic strength of solution or temperature. In ‘permanent’ or ‘chemical’ gels, the network of covalent bonds joining different macromolecular chains can be achieved by cross-linking polymers in the dry state or in solution [2]. These gels may be charged or non-charged depending on the nature of functional groups present in their structure. The charged hydrogels usually exhibit changes in swelling upon variations in pH, and it is known that they can undergo changes in shape when exposed to an electric field [3].

Chemical hydrogels are commonly prepared in two different ways: ‘three-dimensional polymerization’ (Fig. 1), in which a hydrophilic monomer is polymerized in the presence of a polyfunctional cross-linking agent, or by direct cross-linking of water-soluble polymers (Fig. 2). Polymerization is usually initiated by free-radical generating compounds such as benzoyl peroxide, 2,2-azo-isobutyronitrile (AIBN), and ammonium peroxydisulphate or by using UV-, gamma- or electron beam-radiation. However, three-dimensional polymerization often results in materials containing significant levels of residual monomers and therefore purification of these materials has to be performed thoroughly because the unreacted monomers are often toxic and could leach out from the hydrogels continuously. The purification of hydrogels containing residual monomers is typically performed by extraction into excess water, and can take up to several weeks to be completed [4–7].

There are numerous approaches that could be used to improve or avoid the purification process. One possibility is the use of additional processes that lead to the highest

possible degrees of monomer conversion, which could be achieved by conducting three-dimensional polymerization followed by subsequent post-polymerization curing (e.g. by thermal treatment or irradiation of the resulting products) [8,9]. Alternatively, the selection of non-toxic monomers used for the three-dimensional polymerization, such as oligomers or macromonomers (e.g. polyethylene glycol dimethacrylate) could be a solution [10].

It is also possible to avoid the need for purification of hydrogels after their synthesis by cross-linking ready-made water-soluble polymers. Water-soluble polymers such as poly(acrylic acid), poly(vinyl alcohol), poly(vinylpyrrolidone), poly(ethylene glycol), polyacrylamide and some polysaccharides are the most common systems used to form hydrogels. These water-soluble polymers are non-toxic and widely used in various pharmaceutical and biomedical applications and therefore do not require removal from the system, eliminating the need for a purification step. Radiation induced cross-linking, such as of an aqueous solution of hydrophilic polymers with gamma rays, allows simultaneous formation of a hydrogel and its sterilization. Rosiak et al. [11,12] used cross-linking of natural polymers (such as gelatine or agar) and synthetic polymers (such as poly(vinyl pyrrolidone) (PVP) or poly(vinyl alcohol) (PVA) which were cross-linked by gamma radiation for the production of sterile hydrogels used in wound care. Currently their hydrogels are manufactured and marketed as ‘Kikgel’ and ‘Aqua-gel’ wound dressings [11,12].

Recently, Khutoryanskiy et al. [4,13] reported an alternative method to synthesise hydrogels from ready-made water-soluble polymers in aqueous solutions using thermal treatment or microwave irradiation. In this method

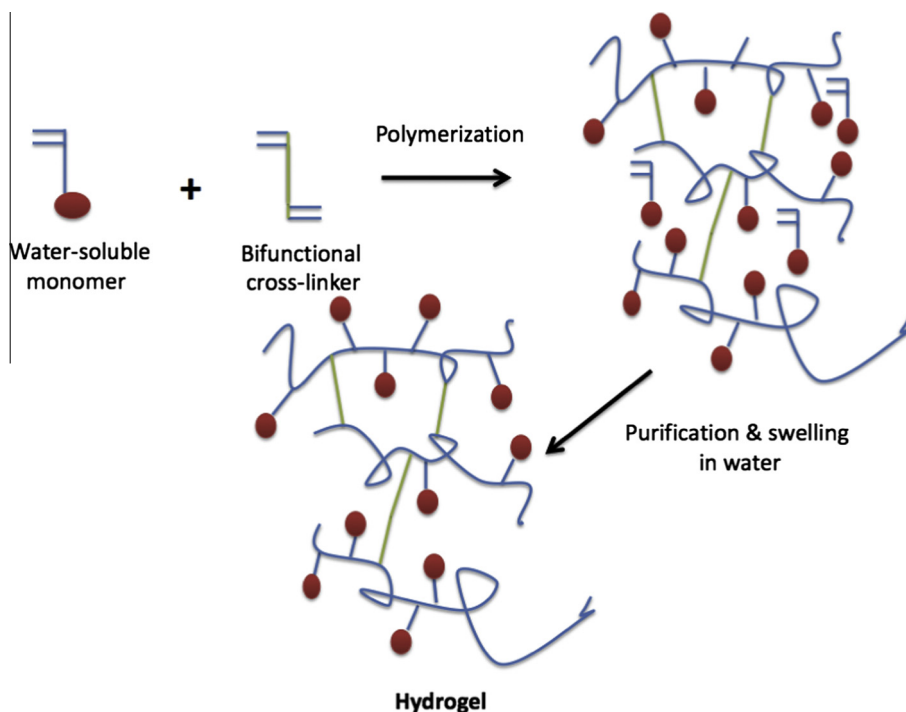


Fig. 1. Synthesis of hydrogels by three-dimensional polymerization.

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