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

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A B S T R A C T

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 peroxodisulphate 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
the aqueous solutions of specific water-soluble polymers such as poly(methyl vinyl ether-alt-maleic anhydride) and poly(vinyl alcohol) are mixed together at room temperature and the cross-linking process is achieved by thermal treatment under high pressure via autoclaving or microwave radiation. Both radiation and thermal cross-linking methods are inexpensive, safe, do not require a purification step and result in sterile hydrogels if a suitable combination of hydrophilic polymers is used.

There are numerous original papers, academic reviews and monographs focused on the synthesis, properties and applications of hydrogels [1,3,14–22]. This review will consider mostly patent literature on ‘chemical’ hydrogels and their potential commercial applications in biomedical areas. As shown by the considerable number of patents and commercial products, the main areas of hydrogel applications are contact lenses, wound dressings, drug delivery systems, tissue engineering, and hygiene products; these will be covered in this review.

2. Contact lenses

In their pioneering 1960 paper, Wichterle and Lim were the first to describe a hydrogel based on poly-2-hydroxyethylmethacrylate (PHEMA) as a synthetic biocompatible material useful for contact lens applications [23]. PHEMA lenses were distributed firstly in western Europe in 1962, but with limited success. In 1965 the National Patent Development Corporation (NPDC) bought the licence to this technology. This was then sold to Bausch & Lomb, which optimised Wichterle’s spin-casting process and finally acquired the approval from the Food and Drug Administration (FDA) for their PHEMA lenses in 1971 [24].

Contact lenses are mainly classified as ‘hard’ or ‘soft’ according to their elasticity. Even though hard lenses are longer lasting, they tend to be poorly accepted by the wearers and can require a lengthier adaptation period. Hard contact lenses are primarily based on hydrophobic materials such as poly(methyl methacrylate) (PMMA) or poly(hexa-fluoroisopropyl methacrylate) (HFIM), whereas soft lenses are based on hydrogels [25].

Soft contact lenses can be produced with different techniques, such as spin-casting, mold-casting and lathe-cutting. In spin- and mold-casting a small amount of liquid monomer mixture is placed into special ‘concave’ optical molds in order to shape the lens. During spin-casting the concave mold rotates to form the lens, causing the liquid monomer to flow out uniformly, coating the whole surface. At the same time, polymerization of the monomer is carried out at elevated temperatures, and the residual monomer is carefully removed at the end of the process. The mold-casting technique employs a convex mold which is inserted into the liquid monomer which already contains a mated concave mold, to make the back surface of the lens. The polymerization takes place in the same way as for the spin-casting. This process produces hard lens interposed between the optical surfaces of the two different molds and once the lens is dry it remains concave [26].

Innovative molds, useful for cast molding silicone hydrogel contact lenses, have been described in the US Patent 6,861,123 B2 assigned to Johnson & Johnson Vision Care Inc. Turner et al. [27] patented their polyolefin inserts for producing the molds and the method in which these are used to make lenses. The preferred method for producing the aforementioned lenses was by direct molding of the silicone hydrogels, placing the reaction mixture in a mold having the shape of the final desired product, and then proceeding with the polymerization.

An alternative method used in the contact lens industry is lathe-cutting (Fig. 3), in which the lenses are formed from solid ‘buttons’ of dehydrated material. The liquid monomer mixtures are usually bulk-polymerized in water tanks for some period of time. This type of polymerization is typically started using free-radical initiators which are then decomposed by an increase in temperature. This process results in the formation of longer polymer chains (with higher molecular weights) and potentially more chain entanglements. Oxygen-mediated degradation could
occur at the surfaces but a button will have a moderately high volume to surface ratio, so it is possible to remove the surfaces during the lathing process. The lenses are finally collected from the centre of a button [24].

A polymeric hydrogel should have some important physical properties to be used as a contact lens material [24]. The ideal characteristics are listed in Table 1:

The equilibrium water content (EWC) of a hydrogel is defined as:

$$\text{EWC} = \frac{m}{m_{\text{tot}}} \times 100\%$$

where $m$ is the weight of water in polymer and $m_{\text{tot}}$ is the total weight of hydrated polymer.

EWC could change with temperature, pH and osmolality. For example, PHEMA contact lenses contain approximately 38–40% of water in the fully hydrated state. They typically show low variability with changes in external factors [24].

In US Patent 3,679,504 [40], Wichterle disclosed a method of forming colored soft contact lenses and ophthalmic prostheses. The colored ingredient was incorporated between two transparent hydrogel layers bound together by polymerizing the hydrophilic monomers mixture. The covering hydrogel layer could also be made from a solution of a hydrophilic macromonomer such as polyethylene glycol mono-methacrylate, which could be manufactured as

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### Table 1

| Characteristics                           | Requirements                                                                 | References |
|-------------------------------------------|------------------------------------------------------------------------------|------------|
| Luminous transmittance                   | The minimum luminous transmittance value for contact lenses is 95%. This value significantly affects the transparency of the lens. A slit lamp microscope is typically used to observe any deposit (proteins, lipids, bacteria, minerals) that may cause a lack of the usual transparency of the lens. | [28,29]    |
| Refractive index                          | The refractive index of the human cornea surface may vary. Ideal hydrogels should have a refractive index value matching the range 1.372–1.381. | [30,31]    |
| Sufficient oxygen-permeability           | The oxygen permeability of the lens is directly proportional to water content and inversely to thickness. In the contact lens industry the oxygen permeability is expressed as $Dk$. In order to prevent anoxia throughout the cornea the oxygen transmissibility of the lens ($Dk/t$, where $t$ is the thickness of the lens) required to be 35 for the open eye and 125 for the closed eye. | [32–34]    |
| Wettability and permeability to water    | The water-permeability of the lens is strictly related to thickness. A constant water diffusion rate is normally reached within the first hour of the experimental analysis. It directly depends on the wettability of the lens, which is evaluated by advancing contact angle ($\theta_{\text{w/a}}$) measurements. The initial value for hydrogel contact lens is usually around 25°. | [35,36]    |
| Stability                                 | The stability of the material used affects the shelf-life and the manufacturing process of the lens. | [37]       |
| Excellent mechanical properties          | The mechanical properties of the lens, such as the elastic modulus ($E$), have a great impact on their adhesion to the corneal epithelium and on the comfort for the wearer. | [38]       |
| Biocompatibility                          | The biocompatibility of the material is essential for the ocular health of wearers who tend to use the lenses for an extended period of time. | [39]       |
described in US Patent 3,575,946 [41]. The use of macromonomers for preparation of hydrogels can potentially eliminate the need for their purification as these materials are often non-toxic [40].

In US Patent 4,472,327 [42] Neefe proposed a method of making cosmetic hydrogel contact lenses which modified the apparent color of the iris by using small light reflecting particles imbedded in a colored transparent matrix. The lenses described in this patent are of a dual purpose: to correct the visual defects and to change the apparent color of the eye. The whole lens area was transparent, providing peripheral vision and allowing the natural iris pattern to be visible through them. Neefe discovered that when a small amount of high refractive index fine particles was placed in a matrix of transparent lens material of a substantially lower refractive index, the reflected light had the color of the lower refractive index media [42]. Selected particulate material had been employed in the polymerization of HEMA with benzoyl peroxide as an initiator. Furthermore, it was possible to add a selected antimicrobial agent, for example 3-(trimethoxysilyl)propyloctadecylmethyl ammonium chloride, to the liquid monomer mixture before polymerization to ensure that the resulting lenses were more resistant to microbial growth [24].

Numerous attempts have been made to develop new contact lenses with better physical and chemical properties. For instance, Jay Kunzer and Friends [43] disclosed that certain hydrophobic monomers, such as those shown in Fig. 4, can act as strengthening agents when copolymerized with hydrophilic monomers such as HEMA, or N-vinyl-2-pyrrolidone (NVP).

The soft contact lenses made from these monomers combined with HEMA or NVP are large enough to cover the whole cornea and present good oxygen permeability, ensuring more comfort for wearers [43].

![4-t-butyl, 2-hydroxy cyclohexyl methacrylate (TBE)](image)

![methacryloylamino-4-t-butyl-2-hydroxy cyclohexane](image)

![4-t-butyl, 2-hydroxy cyclopentyl methacrylate](image)

Fig. 4. Some of the hydrophobic monomers used by Kunzer et al. [43].

Lai and Quinn [44] proposed the use of a new class of optically clear silicone thermoplastic hydrogel materials in the production of contact lenses. The general formula of the polymers, which includes a silicone-containing segment derived from polysiloxane linked with hydroxyl or amino groups, is shown in Fig. 5.

These materials offered good physical strength and excellent oxygen permeability. A drawback of ‘soft’ contact lenses in general is their relatively poor gas permeability resulting in oxygen deprivation of the cornea, which receives oxygen only from the atmosphere. In the contact lens industry oxygen permeability is defined as ‘Dk’, where ‘D’ is the diffusivity of the lens and ‘k’ is the oxygen solubility in the lens material [24]. Dk essentially depends on EWC in conventional hydrogels because oxygen has the capability to diffuse through water rather than through the gel. The relationship between these two parameters is:

\[ Dk = 1.67e^{0.0397EWC} \]

where ‘e’ is the base of the natural logarithm. Oxygen transmissibility of contact lenses may be calculated from the Dk of the material divided by the lens thickness (t). The units of Dk are called Fatt units (named after Professor Irving Fatt) or Barrer [24]:

\[ Dk/barrer = 10^{-11}(cm^2 \times mL_O2)/sec \times mL \times mmHg \] (3)

\[ Dk/t \quad Dk/barrer/cm = 10^{-9}(cm^2 \times mL_O2)/sec \times mL \times mmHg \] (4)

Nowadays, silicone hydrogel (SiHy) lenses have become prevalent on the market (Fig. 6), due to their higher oxygen permeability and comfortable fit [45].

One of the drawbacks associated with the use of SiHy lenses is that they often undergo more protein deposition than conventional lenses which leads to problems with lens spoilage. In European Patent EP 2 365 360 A2, a method for reducing protein deposition on contact lenses has been proposed by adding protein uptake-reducing compounds, such as butylated hydroxytoluene (BHT) or hydroxylamines in the reaction mixture [46]. The reaction mixture may include a ‘silicone-containing monomer’, described in the US Patent 3,808,178 (Fig. 7) [47].

Contact lens surfaces should also have excellent wettability in order to avoid tear-film deposits [47]. The SiHy lenses have been made to compensate the hydrophobicity of silicone and to improve its wettability. The silicone hydrogel lenses were molded and plasma-treated afterwards [49]. The clinical performance of any contact lens material depends on its ability to produce a stable pre- and post-lens tear film, which is dependent on its wettability. This can be described as the formation of a continuous superficial fluid film over a solid surface. The wettability index is usually determined by measuring the contact angle (x) of water on a lens surface. If x = 0° then water is able to fully wet the lens, if x < 90° water wets the lens and if x > 90° the lens is practically not wettable [48].

‘Soft’ lenses with greater adherence to the eye have been developed in order to enhance the fit, but on the other hand, they have poor gas permeability and often do not allow oxygen to reach the cornea at a sufficient rate.
SiHy contact lenses have been designed to overcome this problem, because they are composed of hydrated, cross-linked polymeric material that contains silicon and a certain amount of water within the polymer matrix. More recently, Bauman et al. [50] disclosed a method for making SiHy contact lenses with a nano- textured surface, imitating the surface of human cornea. The nano- textured surface coating technique has been developed through controlled soaking of the lens into a polymeric material, which can comprise monomeric units of one or more carboxyl-containing vinylic monomers. The nano- textures are then fixed by crosslinking a water- soluble hydrophilic poly- meric material onto the prime coating.

One of the more recent products of the UK contact lens industry is ‘Gentle 59’, promoted by Vista Optics Ltd. at the European Federation of the Contact Lens and Iols Industries Congress in Budapest in September 2012. Gentle 59 is made of an acrylic acid-co- acrylamide hydrogel, which seems to have very good tensile properties, moisture retention characteristics and a very comfortable fit [51]. In addition to the applications of soft contact lenses in correction of vision, they can potentially be used for drug delivery to the eye. However, conventional hydrogel- based contact lenses exhibit relatively low drug loading capacity and often show a burst release upon ocular administration [52]. Many methods have been developed to modify the conventional contact lenses to improve their drug loading and release. These include modifying the polymeric materials with a controlled hydrophilic/hydrophobic copolymer ratio, impregnating drug-containing colloidal structures, incorporating ligand- including hydrogels and developing multilayered hydrogels [52]. Venkatesh et al. [53] showed the potential of ‘biomimetic hydrogels’ as carriers to load relevant amounts of H1-antihistamines. They also show potential to release therapeutic dosages of drug in vitro in a controlled manner for a period of 5 days, with a possible extension in the presence of proteins. Xu et al. [54] incorporated β-cyclodextrin (β-CD) into hydrogels for contact lenses, observing an increase in the equilibrium swelling ratio and tensile strength. Puerarin was used as a
model drug to study loading and release from PHEMA/beta-CD hydrogels. It was established that puerarin loading and the in vitro release rate depended on the amount of beta-CD in the hydrogel. In rabbit eyes the PHEMA/beta-CD hydrogel contact lenses demonstrated longer residence time of puerarin in the tear fluid compared to conventional PHEMA contact lenses and 1% puerarin eye drops.

Developing safe and cost-effective contact lenses is the focus of the eye care industry. Contact lens materials with optimal characteristics such as oxygen permeability, comfort, compliance, hygiene and disinfection have still not been achieved, which opens exciting opportunities for further developments in this area.

3. Wound dressings

A wound is a defect or a break in the skin which can result from trauma or medical/physiological conditions. Wounds can be classified, depending on the number of skin layers and on the area of the skin affected, as superficial (if only the epidermis is involved), partial-thickness (if the epidermis and deeper dermal layers are affected) and full-thickness wounds (when subcutaneous fat and deeper tissue has been damaged) [55]. Wounds are usually subdivided into ‘acute’ or ‘chronic’ wounds. Chronic wounds require dedicated nursing care that represents a significant cost for national health systems. Design of effective dressings relies on an understanding of the healing process, as well as the specific conditions of a patient and the effect that each material used could have on the wound [55,56]. Wound healing can be hindered by various factors such as desiccation, infection or abnormal bacterial presence, maceration, necrosis, pressure, trauma and edema [57].

### Table 2

| Advanced wound dressings (reprinted from P.S. Murphy, G.R.D. Evans, Plastic Surgery International 2012, 2012, 1) [60]. |
|-------------------------------|---------------------------------------------------------------|
| **Protective dressings**       | Notes                                                         |
| Gauze                         | Inexpensive; readily available                                 |
| Impregnated gauze             | Nonadherent; preserves moisture                               |
| **Antimicrobial dressings**   |                                                               |
| Antibacterial ointments       | Reapply often to maintain moisture                             |
| Iodine based                  | Absorbent; Not for use with thyroid disorders                 |
| Silver based                  | Many forms; Broad spectrum; low resistance                    |
| **Autolytic debridement**     |                                                               |
| Films                         | Occlusive; allows exchange of gasses                           |
| Hydrocolloids                 | Not for exudative or infected wounds                          |
| Hydrogels                     | Rehydrates to soften dry wounds                               |
| **Chemical debridement**      |                                                               |
| Papain/urea                   | Availability issues in US                                      |
| Collagenase                   | Selective debridement                                         |
| **Absorbent dressings**       |                                                               |
| Foam                          | Absorbs moderate exudate                                      |
| Hydrogels                     | Absorbs minimal exudate                                       |
| Hydrofibers                   | Absorbs heavy exudate                                         |
| Alginates                     | Absorbs heavy exudate                                         |

The ‘ideal’ wound management product should absorb excess exudate and toxins, keep a good moisture between the wound and the dressing, preserve the wound from external sources of infection, prevent excess heat at the wound, have good permeability to gases, be supplied completely sterile and be easy to remove without further trauma to the wound [58].

Recently, the wound dressing industry highlighted the importance of providing comfort and conformability of dressings, the need for infrequent changes, cost effectiveness and a long shelf life [58]. The choice of the right dressing to suit a particular wound is therefore fundamental for optimum healing and the quality of life of the patient [59]. The majority of the currently available products can be classified as low adherent dressings, semipermeable films, hydrocolloids, hydrogels, alginates, foam dressings or antimicrobial dressings [57]. Although plain gauze is still one of the most commonly employed products in hospitals, new wound dressing research and development has produced advanced materials with better physical and chemical properties (Table 2). Gauze is certainly cheap, readily available and suitable for a lot of wounds. In particular the gauzes impregnated with some active ingredients such as iodine, zinc oxide/zinc ions, or petrolatum show enhanced performance. Iodine provides antimicrobial properties, whereas zinc oxide could promote wound cleansing and re-epithelialization [60,61]. However, the use of gauze often results in problems associated with its removal as it may cause trauma by stripping off newly formed epidermis [62].

Advanced dressings are designed to maintain a moist environment at the site of application, allowing the fluids to remain close to the wound but not spread to unaffected, healthy skin areas [62]. The relevance of the moist wound environment as a factor accelerating the healing process was first observed by Winter in 1962, but only recently has received more serious attention [63]. Dressings designed for moist wound healing are represented by hydrogel and hydrocolloid products but only the latter can absorb mild to medium exudate or drainage. Both induce autolytic debridement, which facilitates the elimination of the dead tissue [57]. Hydrocolloids are usually composed of sodium carboxymethylcellulose, gelatin, pectin, elastomers and adhesives. Hydrofiber® (Convatec) dressings allow moisture to be captured because they form a swollen gel structure and conform to the wound site forming a ‘seal’. Hydrofiber® may be in the form of a hydrophilic, non-woven flat sheet dressing that can be converted to a soft gel sheet by absorbing the wound exudate [58].

Hydrogels are widely used as debriding agents, moist dressings, and components of pastes for wound care. However, they do not need further wound fluids to become gels and are suitable for dry wounds [60].

The so-called ‘moisture donor’ effect of hydrogels helps autolytic debridement, increasing collagenase production and the moisture content of necrotic wounds [62]. They can absorb and retain contaminated exudate within the gel mass through expansion of crosslinked polymer chains resulting in isolation of bacteria, detritus and odour molecules in the liquid. Their high water content allows vapor and oxygen transmission to the wounds such as pressure...
sores, leg ulcers, surgical and necrotic wounds, lacerations and burns. They seem to play an important role as emergency burns treatment alone or in combination with other products, thanks to their cooling and hydrating effect [63]. For example, Burnshield hydrogel burn dressing (Levtrade International) present even in first aid kits is a polyurethane foam containing 96% of water and 1.06% Melaleuca alternifolia extract [64].

Hydrogel dressings are also used for granulating cavity wounds [65]. Amorphous gels are generally reapplied every day while sheet hydrogels are usually changed 2–3 times a week [66] (see Table 3).

In 1992 Cartmell and Sturtevant [72] proposed a transparent wound dressing as thin-film, with a non-adhesive central portion containing hydrogel material which included polypropylene glycol or polyethylene glycol, and isophorone diisocyanate. This product is described as being flexible in order to facilitate its removal, and transparent to permit constant observation of the wound healing process. Cartmell describes that the edges of this dressing adhere to the skin due to the adhesive layers that protect the wound site from bacteria and foreign bodies. Two years later in the US Patent 5,423,737 Cartmell et al. [73] disclosed an improved version of this transparent wound dressing. In this case there was a release tab inserted between the transparent layer and the release liner. The invention was intended to respond to a need for a cost-effective product which was simple to manufacture and easy to handle and apply. A similar device has been presented by Holm et al. [74], in which a hydrogel pad is included within an adhesive dressing. This demonstrates that many attempts have been made using new technologies but having the same patient goals.

If local or systemic infection is compromising the wound, or could compromise the healing process, one possible therapeutic approach would be to use dressings containing antimicrobial agents, such as iodine or silver. Silver is useful against a large range of microorganisms, including Pseudomonas aeruginosa and Staphylococcus aureus [75]. These two opportunistic pathogens are frequently present and are often resistant to most antibiotics. Silver has a broad spectrum of activity, being useful against a large range of microorganisms, including Pseudomonas aeruginosa and Staphylococcus aureus [75].

Table 3

| Product               | Main constituents                                      | Main characteristics                                                                 |
|-----------------------|--------------------------------------------------------|---------------------------------------------------------------------------------------|
| Purilon Gel® (Coloplast) | Sodium carboxymethylcellulose and propylene glycol    | Indicated in conjunction with a secondary dressing for necrotic and sloughy wounds and first and second degree burns [69] |
| Aquaflo™ (Covidien)   | Polyethylene glycol and propylene glycol               | It has a disc shape that maximizes wound coverage and helps to fill shallow cavities. Translucent gel that allows wound visualization [70] |
| Woundtab® (First Water) | Sulphonated copolymer, carboxymethylcellulose, glycerol and water | The dressing contains a superabsorbent polymeric gel able to absorb bacteria and retain them in its structure. Described as a wound ‘kick-starter’ patch for chronic wounds, it can also be used as a secondary absorbent [71] |
| Intrasite Gel® (Smith & Nephew) | Modified carboxymethylcellulose (2.3%) and propylene glycol (20%) | Amorphous sterile hydrogel dressing for use in shallow and deep open wounds [68] |
| Granugel® (Convatec)  | Pectin, carboxymethylcellulose and propylene glycol    | A clear, viscous hydrogel for the management of partial and full-thickness wounds, may be used as a filler for dry cavity wounds to provide a moist healing environment [67] |

Future developments in wound care products will depend on continued demands from public and healthcare professionals [79]. The important challenge for the future is to establish the appropriate wound care strategy for every single patient, and this can be achieved only by offering the optimal products. Innovative dressings need to be developed while their production costs must be kept low.

4. Drug delivery

Many patents and academic papers about possible applications of hydrogels in drug delivery have been...
Hydrogels have attracted noticeable interest for their use in drug delivery due to their unique physical properties. The high porosity that characterizes hydrogels can easily be adjusted by controlling the density of cross-links in their matrix and the affinity to water. Their porous structure also allows drugs to be loaded and then released. The advantages offered by hydrogels for drug delivery applications include the possibility for sustained release, which results in maintaining a high local concentration of an active pharmaceutical ingredient over a long period. The drug can be loaded into a hydrogel and then its release may proceed through several mechanisms: diffusion controlled, swelling controlled, chemically controlled and environmentally-responsive release.

The diffusion controlled release systems can be represented by reservoir or matrix devices. Both allow the drug release by diffusion through the hydrogel membrane or the pores filled with water. A reservoir delivery system includes a drug-containing core coated with a hydrogel membrane, commonly available as capsules, cylinders, spheres or slabs. The concentration of the drug is higher in the centre of the system to allow a constant release rate.

In matrix systems the drug is dispersed or dissolved uniformly throughout the three-dimensional structure of the hydrogel. Drug release is achieved through the macromolecular mesh or the pores, and the initial release rate in this case is proportional to the square root of time, rather than being constant and time independent as happens in reservoir systems.

In swelling-controlled release devices the drug is dispersed within a glassy polymer as in a matrix device, and when the polymer is in contact with a bio-fluid it starts swelling. The material then expands beyond its boundary allowing the diffusion of drug with the relaxation of polymer chains. This process is also called Case II transport and it shows constant, time-independent kinetics of release. It is known as ‘anomalous transport’, one that combines swelling-controlled release with diffusion. The gradient existing between the dispersed drug in the hydrogel and the surrounding environment permits the diffusion of the active ingredient loaded from the high concentration through the hydrogel, to the lower one. The molar flux of the drug in this case, $J$ (mol/cm²s), is proportional to the concentration gradient ($\Delta c$) as the driving force for this process:

$$J = -D \cdot \Delta c,$$

where $D$ is the diffusion coefficient in the polymer (cm²/s), and $c$ is the concentration of the drug within the polymer (mol/cm³). The release rate normally depends on the time so the release kinetics is determined from:

$$\frac{\partial c}{\partial t} = -\Delta \cdot J = \Delta \cdot (D \cdot \Delta c)$$

This equation describes the transport of drug out of the hydrogel when the boundary is static (static drug delivery).

The hydrogel-based dosage forms can have different designs and shapes depending on the route of drug administration (Table 4).

The topical application of hydrogels can effectively be used to deliver drugs that can help to alleviate the symptoms of many pathological conditions. For instance, Nho et al. proposed a therapeutic hydrogel made of poly(vinyl alcohol) or poly(vinylpyrrolidone) for the treatment of atopic dermatitis. This product contained an extract from medicinal plants such as Houttuynia cordata, elm, celandine and Canavalia gladiata, which could be used for the treatment of dermatitis. To prepare this hydrogel poly(vinylpyrrolidone) and poly(vinyl alcohol) were dissolved in the medicinal plant extract. Then, the solution was left to set to produce a gel. It is possible to freeze/thaw the cast and introduce physical cross-links into the gel. Finally the physical gel must be treated with gamma, UV- or electron beam-radiation to initiate chemical cross-linking and to sterilize the final product. The hydrogel was supported by a hydrophilic non-woven fabric sheet and an air-permeable polyethylene film.

Furthermore, hydrogels are suitable for transdermal iontophoretic delivery of drugs, as was demonstrated in the European Patent Application EP 0 524 718 A1, where polyurethane hydrogel matrices were used as monolithic drug reservoirs. These hydrogels were synthesized from mixtures prepared by adding a prepolymer solution containing an isocyanate-capped oxalkylene-based prepolymer in anhydrous aprotic organic solvent to water. When the organic solvent has evaporated completely, the

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**Fig. 8.** Scheme of drug release through a hydrogel membrane in a reservoir system.
hydrogel matrix can be loaded with a drug. Transdermal iontophoresis is defined as the transport of ionic drugs through the skin, driven by a very weak electric current. The applied current helps to transfer the ionized drugs through the stratum corneum into the dermis, in which the active ingredient can diffuse into capillaries and then into the systemic circulation. Alternatively, hydrogel compositions can be employed as passive transdermal reservoirs. The hydrogels used in the aforementioned work showed a high swelling ratio, good flexibility, strength and transparency [102].

Hydrogels could be useful as ocular drug delivery carriers, not only in the form of lenses as previously discussed. The US Patent 8,409,606 B2 presented a system that provided the release of specific drugs through punctal plugs. In this work very soft biodegradable covalently cross-linked hydrogels with high-swelling capability were used, in order to be able to remain in situ (in the punctum or lacrimal canal) with greater comfort for the patient. The system could be designed to be ‘temporary’ or ‘permanent’ and the plugs could be accordingly made of collagen or silicone, respectively [103].

Ocular therapeutics™ produces ophtalmic drug delivery systems and medical devices using poly(ethylene glycol) hydrogels. For instance, dexamethasone punctum plug is designed for the controlled release of the corticosteroid in case of post-operative inflammation and pain and it has entered the Phase 3 trials. After a four-week treatment period, during which the plug releases the drug from the canaliculus to the ocular surface, it is naturally removed via the nasolacrimal system [104]. Ideally a drug delivery system should be synchronized with the physiological status of the patient and should provide drug release in response to changes in environment. Moreover, if the drug exhibits some side effects, its release when it is not required can cause additional problems. Hydrogels can show changes in their swelling behavior, structure, permeability or mechanical properties in response to various internal and external stimuli [87]. Bae et al. [105] proposed a delivery device capable of releasing a drug enclosed within a hydrogel, which deswells responding to a chemical or physical stimulation (change in temperature, pH, ionic strength or glucose concentration). It utilises either temperature- or pH-sensitive hydrogels already used in drug delivery as cross-linked homopolymers or copolymers, such as the N-isopropylacrylamide based copolymers or cross-linked weak polyelectrolytes. The system presented by Bae et al. [105] was composed of a 'sponge-like' porous gel confined in a walled structure permeable to the loaded drug. Thus, it was
possible to obtain a self-regulated drug delivery, which could be pulsatile if needed.

Biodegradable and nontoxic multi-block hydrogel copolymers have been used as drug delivery matrices and described in the US Patent 5,514,380. They were synthesized from a hydrophilic soft block and a hydrophobic, biodegradable hard block. Their degradation could be achieved with the hydrolysis of intramolecular ester and amide bond that easily occurred in the human body. Polyethyleneoxide (PEO) and/or copolymers of PEO/polypropyleneoxide (PPO) with molecular weight of 600–30,000 Da met the required qualities of the hydrophilic, non-biodegradable polymers employed in the mentioned patent. The biodegradable block could instead be represented by polylactide (PLA), polyglycolide (PGA) or a PLA/PGA copolymer [106].

US Patent 8,383,153 B2 describes a poly(amidoamine) based hydrogel for application as drug carriers. This temperature- and pH-sensitive hydrogel had a molecular structure developed to avoid the initial burst drug release and was instead capable of providing a sustained release. The material can be produced by a one-step process by coupling between secondary amine groups (—NH) of a diamine compound (such as piperazine) and vinyl groups (CH2=CH—) of an alkylene bisacrylamide compound (e.g. N,N'-methylenebisacrylamide (MDA) or N,N'-ethylenebisacrylamide). This hydrogel can be used as a carrier for different types of physiologically active compounds, using different routes of administration [107].

A drug delivery system comprising a hydrogel and a catheter were also proposed in US Patent 7,066,904 B2. The catheter allows the incorporation and the immobilization of a relevant amount of drug into the hydrogel, and then its release by a triggering agent or different condition in the desired location. In this case the polymers used, such as (hydroxyethyl)methacrylate-co-methacrylic acid, are pH-sensitive in order to produce hydrogels able to undergo a volume phase transition at a specific pH. A salt solution, such as sodium phosphate or sodium bicarbonate can be used to alter the microenvironment within the device and trigger the release of the active ingredient. In fact, the pH of this solution could be in the range of 7.5–8.4 or in the range of 6.4–7.3, and could cause alternatively swelling or contraction of the hydrogel [108].

One of the successful examples of hydrogels for drug delivery is the vaginal insert Cervidil® for cervical ripening, which has been on the market since 1995. This controlled release formulation has been used to induce or bring on labor in patients who are at or near the time of delivery. Each insert contains 10 mg of dinoprostone (prostaglandin E2 or PGE2) in 271 mg of cross-linked polyethylene oxide/urethane polymer and it releases the drug over a period of 12 h at approximately 0.3 mg/h. The drug release is triggered by the hydrogel swelling when placed in a moist vaginal environment [109].

Controlled Therapeutics Scotland Ltd. has developed a misoprostol vaginal insert (MVI) that uses the same delivery system as the Cervidil®, but contains misoprostol, a cytoprotective agent active on the cervix and uterus to induce labor. The same company is currently developing a modified release hydrogel buccal patch (Pilobuc®) containing pilocarpine, for the treatment of symptoms of Sjögren’s syndrome, a systemic autoimmune disease in which exocrine glands that produce tears and saliva are destroyed by the immune cells [110].

A hydrogel subcutaneous insert in the form of reservoir system, called SUPPRELIN LA (Endo Pharmaceuticals Solutions Inc.), for the release of histrelin acetate is available on the market. Histrelin acetate is a gonadotropin-releasing hormone (GnRH) agonist indicated for the treatment of children with central precocious puberty (CPP). It produces a decrease in luteinizing hormone (LH) levels and sex steroids serum concentration within the first month of treatment. The implant is made of a hydrogel prepared from 2-hydroxyethyl methacrylate, 2-hydroxypropyl methacrylate, trimethylolpropane trimethacrylate, benzoin methyl ether, Perkadox-16, Triton X-100 and contains 50 mg of histrelin, which is delivered over 12 months time (approximately 65 mcg per day). After this period the device needs to be removed as it is nonbiodegradable [111].

Park et al. [112–115] had proposed the use of superporous hydrogel compositions as gastric retentive devices for long-term oral drug delivery. These hydrogels were produced starting from (meth)acrylic acid or (meth)acrylamide, a so-called ‘disintegrant’, represented by a natural or synthetic cross-linked hydrophilic polymer such as cross-linked carboxymethylcellulose or poly(vinyl pyrrolidone) and a cross-linking agent such as N,N'-methylenebisacrylamide. They were synthesized using the gas blowing technique where polymerization and foaming (with sodium carbonate or bicarbonate as foaming agent) take place at the same time. More specifically, in this process the polymerization has to start only a few minutes after the beginning of foaming in order to entrap the gas bubbles in the network. The final device was able to remain in the stomach up to more than 24 h allowing the slow release of the drug loaded.

Hydrogel devices were suggested for oral delivery of different active ingredients, e.g. non-steroidal anti-inflammatory drugs (NSAIDs) [116]. They can be used to protect drugs or proteins (e.g. insulin) susceptible to the proteolytic degradation that occurs in the stomach [117,118]. In the US Patent application WO1998043615 A1 [119] a hydrogel matrix made of poly(methacrylic acid-g-ethylene glycol) cross-linked with tetraethylene glycol dimethacrylate is presented. This hydrogel could be loaded with insulin simply by immersing it into its solution at pH 7.4. When administered orally, insulin will be protected from the acidic environment of the stomach by the formation of inter-chain complexes within the hydrogel network. Hydrogen bonding between the carboxyl and the ether groups on the grafted chains stabilized these complexes at acidic pH. These hydrogels exhibited pH-sensitive swelling behavior: once in the upper small intestine (at higher pH), the complexes dissociate increasing the pore size and allowing the insulin to be released from the matrix. Additionally, the ability of these hydrogels to strongly adhere to the intestinal mucosa significantly improves the release and absorption of the protein [117,119].

In the future, hydrogel-based products could represent a significant proportion of drug delivery systems, to successfully administer drugs at the desired rate and site in
the body. Specific release rates and dissolution profiles could be achieved with the development of new hydrogels with different hydrophobicity/hydrophilicity and structural characteristics. These systems could improve the delivery of more sensitive molecules and be employed in the treatment of pathologic conditions such as diabetes or even cancer. Specifically, more developments are expected in the use of hydrogels for delivery of therapeutic proteins and peptides.

5. Tissue engineering

There are millions of patients suffering from the loss or failure of an organ or a tissue caused by an accident or a disease every year. Over 8 million surgeries are conducted to treat these patients in the U.S. each year, and the overall cost of these issues to the U.S. economy is estimated to be around $400 billion per year. Tissue and organ transplantations represent generally accepted therapies, but they are dramatically limited by donor shortages [120].

The term “tissue engineering” was originally defined in 1988 as the “application of the principles and methods of engineering and life sciences toward fundamental understanding of structure–function relationship in normal and pathological mammalian tissues and the development of biological substitutes for the repair or regeneration of tissue or organ function” [121]. In other words, it involves the improvement or replacement of specific tissues or organs using engineered materials and synthetic strategies.

Tissue engineering is a more recent application of hydrogels, in which they can be applied as space filling agents, as delivery vehicles for bioactive substances or as three-dimensional structures that organize cells and present stimuli to ensure the development of a required tissue (Fig. 10). Space filling agents are the most commonly used group of scaffolds and they are employed for bulking, to prevent adhesion, and as a biological ‘glue’. Drugs can be delivered from hydrogel scaffolds in numerous applications including promotion of angiogenesis and encapsulation of secretory cells. Additionally, hydrogel scaffolds have also been applied to transplant cells and to engineer many tissues in the body, including cartilage, bone, and smooth muscle [122].

An indispensable property is the biocompatibility of hydrogels, which could be defined as the ability of a material to be in contact with the body organs without any damages for the surrounding tissues and without triggering any undesirable response [114]. Synthetic materials capable of forming hydrogels suitable for tissue engineering include poly(ethylene oxide), poly(vinyl alcohol), poly(acrylic acid), poly(propylene fumarate-co-ethylene glycol), and polypeptides. Agarose, alginate, chitosan, collagen, fibrin, gelatin, and hyaluronic acid are naturally derived polymers that could also be used for this purpose [124,125].

In European patent EP 1 664 168 B1, an interesting hydrogel-based composition for manufacturing porous scaffolds has been presented. It was composed of a biodegradable unsaturated self-cross-linkable polymer such as poly(propylene fumarate), biodegradable hydrogel microparticles (diameters of 1–1000 μm) entrapping water and a free-radical initiator promoting the cross-linking process. The microparticles were made of cross-linked collagen or gelatin and could contain a biologically active substance. The method disclosed ‘super-absorbent semi-solid’ hydrogel microparticles, able to swell in water but not to flow as a liquid, with a defined shape due to the cross-linking. After the polymerization process, the scaffold formed with the mixture could be used directly for the treatment of skeletal defects without leaching out the hydrogel porogen [125].

Harris et al. [126] described a tissue engineering scaffold with the benefits of microporous and nanoporous scaffolds, comprising a nanofibrous and nanoporous hydrogel formed from self-assembling peptides, which are
non-immunogenic, biodegradable, and capable to interact with cells. They were able to stimulate tissue ingrowth and vascularization, and furthermore, this hydrogel could be used for slow-diffusion drug delivery. The self-assembling peptides used to form hydrogels should have alternating hydrophobic and hydrophilic amino acids (more than 8). For instance, one of them had the following amino acid sequence: Arg–Ala–Asp–Ala–Arg–Ala–Asp–Ala–Arg–Ala–Asp–Ala–Arg–Ala–Asp–Ala–Arg. This peptide is commercialized as ‘PURAMATRIX’ (3-D Matrix, Inc., Cambridge, Mass.) Its self-assembly could easily take place in tissue culture medium (Dulbecco Modified Eagle’s Medium, Gibco BRL, Gaithersburg, Md) containing calf serum. The scaffolds presented might also be applied to open wounds or be surgically implanted. It was established that scaffolds made of only one component or phase may not produce the ideal environment for supporting tissue regeneration. Conversely, the so-called ‘hybrid’ materials were found to give better results, in terms of cell proliferation, differentiation and migration.

Hydrogels scaffolds are used for cell-sheet and tissue production. Kumar [127] has recently disclosed a method to produce biodegradable poly(vinyl alcohol) hydrogels complexed with phenylboronate-containing polymers able to encourage cell and tissue growth. PCCs include a phenylboronate ligand (such as 4-vinylphenylboronic acid), an acrylic monomer (such as N-isopropylacrylamide or acrylic acid) and an alkaline tertiary amine (such as N,N-dimethylaminoethylmethacrylate). The cells which could be represented for example by keratinocytes or fibroblasts, are cultured for 5–20 days on the hydrogel scaffolds. It is then possible to collect the cell layers formed by simply dissolving the hydrogel scaffolds using a saccharide solution (such as fructose or mannitol solution). This saccharide biodegradation is possible due to the presence of phenylboronate ligands that are derivatized forms of phenylboronic acid, which can establish reversible covalent interactions with 1,2 or 1,3-cis-diol-containing compounds such as carbohydrates.

Blanchard et al. [128] has reported the use of pure cross-linked keratin-based hydrogels for tissue engineering cell scaffolds. Keratin is biocompatible, and non-immunogenic biopolymer that promotes epithelialization process and can be extracted from patient hair or nails. After purification and partial oxidization of the keratin, the sulfonic acid residues of the protein, which are hydrophilic, form disulfide cross-links between backbones and bind water. Additional hydrogen bonds are then formed in this hydrogel. The material was shown to be suitable as nutrient support and scaffold for cell growth.

Song et al. [129] has proposed beta-glucan-based hydrogel scaffolds for tissue engineering produced by radiation fusion technology. Beta-glucan (beta-1,6-branching-beta-1,3-glucan) can promote cell regeneration and collagen biosynthesis, and it is recognized to be safe and biocompatible. It could be extracted from different fungi such as Schizophyllum commune or Ganoderma lucidum and dissolved in distilled water. This aqueous solution was then cast in petri dishes and irradiated for the cross-linking step using electron, gamma or UV beam at a dose of 5–50 kGy to form a gel. Stem cells could rapidly adhere, grow and differentiate on the scaffold formed.

One of the most important future challenges in tissue engineering is how polymers could be used to stimulate the blood vessel network formation in the desired tissue, essential to supply its needs. Hydrogels could represent a valid option to effectively control the vascularization process, by local delivery of both angiogenic factor and endothelial cells to the intended area [120]. Additionally, many types of tissue such as bone, muscle or blood vessels are located in areas requiring excellent mechanical properties that the majority of the currently available hydrogels do not show, so new approaches should be investigated in the future to achieve better results.

6. Hygiene products

Superabsorbent polymers (SAPs) have been introduced into the agriculture and diaper industry about thirty years ago, and since then their uses have been extended to several other applications due to their excellent water retention [130]. SAPs have been firstly commercially produced in Japan in 1978 for use in feminine napkins, and this early material was represented by a cross-linked starch-g-polyacrylate [131].

At the end of the 90s, ‘superporous hydrogels’ (SPHs) were introduced and presented as a different type of water-absorbent polymer system. As SAPs, SPHs are formed by covalently cross-linked hydrophilic polymers, but unlike SAPs, they show an exceptional size-independent fast swelling kinetics. The first generation of SPHs was generally made from highly hydrophilic acrylamide, salts of acrylic acid and sulfopropyl acrylate. Later generation of SPHs are represented by ‘hybrid SPHs’ produced by adding a so-called ‘hybrid agent’ (natural or synthetic water-soluble or dispersible polymer capable of chemical or physical cross-linking) to the SPH previously made. With this method it is possible to generate an interpenetrating polymeric network. For example, acrylamide-based SPH is synthesized in the presence of sodium alginate and after that, a cross-linking occurs between alginate chains and calcium ions forming a ‘hybrid SPH’. These more recent SPHs have shown better and more useful qualities, such as high mechanical strength and elasticity even in swollen state [130]. Superabsorbent hydrogels, in particular the acrylate-based materials, are extensively used in hygiene products to absorb fluids. In fact they are able to hold moisture away from the skin, promoting skin health, preventing diaper rash and providing a comfortable use. Parents in all the industrialized countries as well as hospitals around the world employ disposable diapers containing SAPs [132].

A further increase in the use of these materials is observed in training pants and adult incontinence product markets. SAPs can also prevent the colonization of germs, reducing the risk of fecal contaminations and potential spread of gastrointestinal infections. The first use of SAPs in the diaper industry was proposed in 1982 by Unicharm in Japan, with its subsequent use in sanitary napkins. After that, diapers became thinner and also had improved water
retention performance. It was possible to develop diapers with leakage values below 2% and the standard weight of a medium size diaper could be reduced by about 50%, with some obvious advantages in terms of environmental issues and reduced manufacturing costs [132].

Regarding the ecological impact of disposable diapers and similar products, it is relevant to consider current diaper consumption. For instance, a child within the 30th month uses approximately six diapers a day and each of them has a volume of 500 cm³, so only one child produces on average 3000 cm³ of litter a day, i.e. 1092 cubic meters every year [132]. Making recyclable disposable diapers, napkins, hospital bed sheets, sanitary towels and other similar products is therefore one of the vital targets for the modern industry. An innovative solution to this problem has recently been proposed, which involves the use of cellulose-based hydrogels, which are totally biodegradable. Novel types of hydrogels, containing sodium carboxymethylcellulose (NaCMC) and hydroxyethyl cellulose (HEC) cross-linked with divinyl sulfone (DVS), can swell like SAPs, and exhibit high water retention under centrifugal loads. These improvements were achieved by introducing microporous structures into the hydrogel, which increases water retention and swelling kinetics due to capillarity effects [132].

US Patent 32,649 describes one of the first hydrogel-forming polymer compositions suitable for hygiene products manufacturing. It consisted of a water-insoluble, slightly cross-linked polymeric material, which could be prepared from carboxylic acids and acid anhydrides, or olefinically unsaturated sulfuric acids, using a free–radical polymerization in the presence of a cross-linking agent in an aqueous solution. This material could be dried to result in polymer compositions capable to form hydrogels upon contact with water or bodily fluids [133]. Only a few years later, in US Patent 5,009,653, Osborn proposed a product consisting of a thin and flexible sanitary feminine napkin with an absorbent core placed between two air-laid tissue sheets. The core was composed of a hydrogel-forming material, prepared from acidic monomers such as acrylic acid, methacrylic acid or 2-acrylamido-2-methyl propane sulfonic acid. This material was highly absorbent, could withstand medium to high menstrual flows and was very conformable to the body of a user, preventing the risk of leakage and staining [134].

Many attempts have been made to develop new products, which could not only swell, but also retain the fluids absorbed under external pressure or against an applied restraining force. An absorbent material composed of a porous matrix of fibers and superabsorbent hydrogel is described in the US Patent 5,147,343, which has the capability to initially imbibe fluids and swell, while being exposed to a load. The matrix can be formed from wood pulp or cotton linters as well as synthetic fibers (polyethylene, propylene, polyesters etc.) and the hydrogel could be produced from polyacrylamides, polypvlin alcohol, ethylene-maleic anhydride copolymers or polyvinyl ethers. The ‘Absorbency Under Load’ (AUL) is defined as the volume of 0.9 wt% NaCl solution which the superabsorbent composition could absorb per 1 g in one hour, being subjected to a load of 21,000 dynes/cm². Hence, the work (W) performed by the material could be calculated using the following formula [135]:

\[ W = (AUL) \times (Restraining\ force) \]

(7)

Pampers (owned by Procter & Gamble) and Huggies (from Kimberly–Clark) are the two most widely used disposable diaper brands, with about 35% and 22% global market share, respectively. Both are sold in over 50 countries and they have wide range of products. Manufacturers have been focusing their efforts on enhancing the production and engineering of SAPs with better properties, i.e. higher AUL, lower levels of residual monomers (RM) and soluble fractions [136]. Further developments in this area are expected with the formulation of the materials containing enzymes and other additives to prevent infections and unpleasant smells. Additionally, taking the scale of production of these materials into consideration, there is a clear need in environmentally friendly hygiene products that undergo biodegradation.

7. Conclusions

Hydrogels are widely present in everyday products though their potential has not been fully explored yet. These materials already have a well-established role in contact lenses, hygiene products and wound dressing markets but commercial hydrogel products in tissue engineering and drug delivery are still limited. Many hydrogel-based drug delivery devices and scaffolds have been designed, studied and in some cases even patented, however not many have reached the market. More progress is expected in these two areas. Limited commercial products with hydrogels in drug delivery and tissue engineering are related to some extent to their high production costs.

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